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# Cooling and Rewarming for Brain Ischemia or Injury: Theoretical Analysis

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**Abstract—**A three-dimensional model is developed in this study to examine the transient and steady state temperature distribution in the brain during selective brain cooling (SBC) and subsequent rewarming. Selective brain cooling is induced through either wearing a cooling helmet or packing the head with ice. The ischemic region of the brain is simulated through reducing the blood perfusion rate to 20% of its normal value. The geometric and thermal properties and physiological characteristics for each layer, as well as the arterial blood temperature, are used as the input to the Pennes bioheat equation. Our data suggest that rapid cooling of the brain gray matter can be achieved by SBC on the head surface (26 min for adults versus 15 min for infants). Suboptimal thermal contact between the head surface and the coolant in most commercially available cooling helmets is suspected to be the main reason for delayed cooling in SBC as compared to the ice packing. The study has also demonstrated that the simulated 3 °C/h passive rewarming rate by exposing the head to room temperature after removing the source of cooling may be too rapid. © *2003 Biomedical Engineering Society.* [DOI: 10.1114/1.1554924]

**Keywords—**Bioheat transfer, Brain ischemia, Head injury, SBC, Hypothermia, Multiple sclerosis.

## INTRODUCTION

Brain injuries are often devastating. Despite enormous amount of research in this field, effective treatments to protect the brain and reduce the extent of neurologic injury are still elusive. Stroke, for example, the third leading cause of death in the United States, produces crippling neurological disability and costs the society an estimated 40 billion dollars annually. Unfortunately, with the exception of intravenous tissue plasminogen activator, there are currently no therapies of proven benefit in stroke patients. Therefore, effective treatments to reduce the extent of neurologic injury are desperately needed.

Overwhelming laboratory and clinical evidence has demonstrated the importance of closely monitoring both brain and core temperature, especially during mild to moderate hypothermia. In animal models of both ischemic and traumatic brain injuries[5] it has been well established that even a small reduction (1–2 °C) in brain temperature can improve neurological outcome. Temperature gradient can develop not only between brain and core temperature but also within regions of the brain.[2,24,29] These data, however, are often difficult to obtain clinically due to the concern of inducing additional tissue damage by the introduction of temperature probes. Current noninvasive temperature measurements such as magnetic resonance imaging lack the desired resolution to monitor small (±2 °C) temperature variations. Therefore, understanding the transient and spatial temperature distribution in the brain tissue during hypothermia therapy is clinically valuable.

Postischemic hypothermia as a potential treatment in brain injured patients remains controversial. The inconsistency in patient outcome in various clinical studies,[3,6,8,14] head trauma in particular, might be due to the delay of hypothermia initiation and other variables. Ischemic and traumatic brain injury (TBI) animal studies have suggested a 1–2 h treatment window within which postischemic hypothermia must be instituted to confer any significant neuroprotection.[13,16] It is difficult to know how to correlate rodent data to humans and other key variables such as the extent of hypothermia and the duration of hypothermia would theoretically also influence the treatment window. Based on the present data, it may be concluded that the treatment window is probably very brief for postischemic hypothermia to be effective in humans. Thus, it would be ideal to initiate hypothermia treatment in the prehospital settings.

Most clinical studies have examined only whole body hypothermia that has numerous methodological drawbacks. Whole body hypothermia has pronounced physiological side effects such as decreased cardiac output, increased vascular resistance, ventricular fibrillation, increase of myocardial ischemia, impaired coagulation, and impaired immune function. The increased risk of systemic complications when using whole body hypother-

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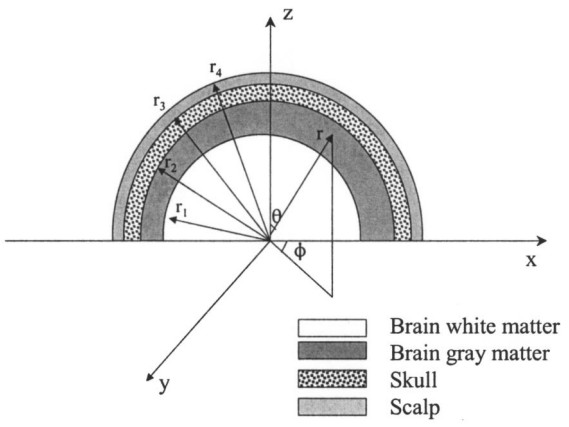


**FIGURE 1. Model representation of the anatomic structure of the head and the spherical coordinate system.**

mia may outweigh the neuroprotective benefits of such therapy. Whole body hypothermia may easily miss the treatment window because it requires intensive monitoring and is not practical in the prehospital settings, where hypothermic protection of the brain can be maximized. Therefore, prehospital induction of selective cooling of the brain may be a more successful way of treating patients with brain injuries and needs to be studied.

Current clinical selective brain cooling (SBC) protocols include easily implemented approaches such as using a cooling helmet or packing the head with ice, and invasive approaches such as nasophyaryngeal cooling and intracarotid flushing. Most physicians are reluctant to use cooling helmets or ice for SBC because of the concern of slow rate of cooling. During cardiac arrest it has been shown that significant brain cooling was achieved only after 1 h of ice application to the scalp (personal communication with Dr. P. Safar). However, it should theoretically take a much shorter time to cool the brain tissue when the brain is highly perfused. Another factor that may attribute to the slow cooling may be the thermal contact resistance between the coolant and the scalp. Experimental measurements have shown a significant temperature difference between the scalp and coolant when a cooling helmet was used for multiply sclerosis patients.[11] Therefore, it is important to analyze quantitatively the temperature distribution in the brain tissue during SBC with different cooling protocols.

In this study, a three-dimensional theoretical model is developed to examine the transient and steady state temperature distribution in the brain during selective brain cooling and rewarming. Two cooling approaches are proposed, one is packing the head with ice, and the other is wearing a cooling helmet. The effect of regionally varying blood perfusion rate in the brain tissue during ischemia is examined for both adult and infant brains. Simulation is conducted to evaluate the cooling penetration and the characteristic cooling time of both approaches. The rewarming process, which is proposed as removing the cooling apparatus and exposing the head to the environmental temperature, is also examined.

## MATHEMATICAL FORMULATION

Unlike a purely conductive medium, heat transport in perfused tissue is difficult to model because the vasculature is complicated and the convective effects of the blood flow are not readily assessed. In most of the bioheat transfer analysis, a continuum model, which averages the heat and mass transport equations over a representative control volume, is still widely used. One of the continuum models was proposed by Pennes[19] and is given by

$$\rho c \frac{\partial T_t}{\partial t} = \nabla \cdot (k_t \nabla T_t) + \rho c \omega (T_a - T_t) + q, \qquad (1)$$

where $\rho$ is density of tissue, $c$ is specific heat of tissue, $k_t$ is tissue thermal conductivity, $\omega$ is local blood perfusion rate, and $q$ is local metabolic heat generation rate. $T_t$ is tissue temperature, and $T_a$ is arterial blood temperature of 37 °C. Originally applied to predict temperature fields in the human forearm, this equation is a relatively simple modification of the ordinary heat conduction equation by adding two source terms on its right-hand side. In the first, the moving blood contribution is treated as an isotropic heat source/sink, while the second accounts for the metabolic heat production. The isotropic heat source/sink term is assumed to be proportional to the local blood perfusion rate and the difference between the arterial blood and local tissue temperature.

The Pennes model has been applied frequently and successfully in living tissue heat transfer analyses. With an adjustable blood perfusion rate, the Pennes equation has been used to predict the temperature distribution in kidney cortexes[9] and in canine prostates.[32] Good agreements with experimental results have been obtained for those tissues. Using both the Pennes model and a discrete vessel model, Van Leeuwen *et al.*[26] have showed that the predicted temperature contours in the brain tissue are very similar, except that the temperature contours are refiner for the discrete vessel model due to the presence of the discrete vessels. In this study the Pennes model is also employed to simulate the temperature distribution in the human brain.

As illustrated in Fig. 1, the brain is modeled as a hemisphere of cerebral tissue with overlaying layers of skull and scalp. The first layer represents the scalp, and the second layer represents the skull. The brain tissue consisting of gray and white matter is represented by the inside hemisphere. Brain gray and white matter may

have different blood perfusion rates[18,21,31] even though they have similar thermal properties. They are represented by different layers as shown in Fig. 1.

Assuming homogeneous thermal properties with each layer, the Pennes bioheat transfer equation in spherical coordinates is written as

$$\begin{cases} \text{for scalp:} \\ (\rho c)_{\text{sc}}\dfrac{\partial T_{\text{sc}}}{\partial t}=\dfrac{k_{\text{sc}}}{r^2}\left[\dfrac{\partial}{\partial r}\left(r^2\dfrac{\partial T_{\text{sc}}}{\partial r}\right)+\dfrac{1}{\sin\theta}\dfrac{\partial}{\partial\theta}\left(\sin\theta\dfrac{\partial T_{\text{sc}}}{\partial\theta}\right)+\dfrac{1}{\sin^2\theta}\dfrac{\partial^2 T_{\text{sc}}}{\partial\phi^2}\right]+(\rho c)_{\text{blood}}\omega_{\text{sc}}(T_a-T_{\text{sc}})+q_{\text{sc}} \\ \text{for bone:} \\ (\rho c)_{\text{bone}}\dfrac{\partial T_{\text{bone}}}{\partial t}=\dfrac{k_{\text{bone}}}{r^2}\left[\dfrac{\partial}{\partial r}\left(r^2\dfrac{\partial T_{\text{bone}}}{\partial r}\right)+\dfrac{1}{\sin\theta}\dfrac{\partial}{\partial\theta}\left(\sin\theta\dfrac{\partial T_{\text{bone}}}{\partial\theta}\right)+\dfrac{1}{\sin^2\theta}\dfrac{\partial^2 T_{\text{bone}}}{\partial\phi^2}\right]+(\rho c)_{\text{blood}}\omega_{\text{bone}}(T_a-T_{\text{bone}})+q_{\text{bone}} \\ \text{for brain gray matter:} \\ (\rho c)_{\text{bt},g}\dfrac{\partial T_{\text{bt},g}}{\partial t}=\dfrac{k_{\text{bt},g}}{r^2}\left[\dfrac{\partial}{\partial r}\left(r^2\dfrac{\partial T_{\text{bt},g}}{\partial r}\right)+\dfrac{1}{\sin\theta}\dfrac{\partial}{\partial\theta}\left(\sin\theta\dfrac{\partial T_{\text{bt},g}}{\partial\theta}\right)+\dfrac{1}{\sin^2\theta}\dfrac{\partial^2 T_{\text{bt},g}}{\partial\phi^2}\right]+(\rho c)_{\text{blood}}\omega_{\text{bt},g}(T_a-T_{\text{bt},g})+q_{\text{bt},g} \\ \text{for brain white matter:} \\ (\rho c)_{\text{bt},w}\dfrac{\partial T_{\text{bt},w}}{\partial t}=\dfrac{k_{\text{bt},w}}{r^2}\left[\dfrac{\partial}{\partial r}\left(r^2\dfrac{\partial T_{\text{bt},w}}{\partial r}\right)+\dfrac{1}{\sin\theta}\dfrac{\partial}{\partial\theta}\left(\sin\theta\dfrac{\partial T_{\text{bt},w}}{\partial\theta}\right)+\dfrac{1}{\sin^2\theta}\dfrac{\partial^2 T_{\text{bt},w}}{\partial\phi^2}\right]+(\rho c)_{\text{blood}}\omega_{\text{bt},w}(T_a-T_{\text{bt},w})+q_{\text{bt},w} \end{cases}, \tag{2}$$

where subscript sc, bone, bt,$g$, and bt,$w$ represent scalp, bone, brain tissue gray matter, and brain tissue white matter, respectively.

Since the brain tissue suffering ischemia may be quite different due to different locations and situations, in this study the brain tissue hemisphere is divided into four quadrants. During ischemia, blood perfusion in one quadrant is reduced to 20% of its normal value and it is given by

$$\omega_{\text{bt}}=20\%\,\omega_{\text{bt},0}, \tag{3}$$

where $\omega_{\text{bt},0}$ is the blood perfusion rate under normal conditions (37 °C). For the normal quadrants, the blood perfusion rate is proposed as temperature-dependent. In Xu *et al.*,[30] an analytic expression for the metabolic heat generation as a function of brain temperature is given as

$$q=q_0 3^{(T-37)/10}, \tag{4}$$

where $q_0$ is the metabolic heat generation under normal conditions. If one assumes that the local blood perfusion rate is coupled with the local metabolic heat generation, the temperature-dependent $\omega_{\text{bt}}$ in the normal region could be proposed as

$$\omega_{\text{bt}}=\omega_{\text{bt},0}3^{(T_{\text{bt}}-T_a)/10}. \tag{5}$$

At the interfaces between different layers, the temperature and heat flux continuities are required. On the bottom of the hemisphere, an adiabatic condition is prescribed as previously justified.[33] Cooling of the brain tissue is induced by either a head cooling helmet or ice packed outside the scalp. Hence, the boundary condition at the scalp surface is either a prescribed temperature (ice, $T_{\text{skin}}=0$ °C) or subject to surface (helmet) convection of $h=30\ \text{W m}^{-2}\,\text{K}^{-1}$ and $T_\infty=0$ °C (derived from Ku *et al.*[11]). The head temperature is initially the steady state temperature of the brain without surface cooling.

The boundary and initial conditions are given by

$$\begin{cases} r=0:\dfrac{\partial T_{\text{bt},w}}{\partial r}=0 \\ r=r_1: T_{\text{bt},g}=T_{\text{bt},w},\ k_{\text{bt},g}\dfrac{\partial T_{\text{bt},g}}{\partial r}=k_{\text{bt},w}\dfrac{\partial T_{\text{bt},w}}{\partial r} \\ r=r_2: T_{\text{bone}}=T_{\text{bt},g},\ k_{\text{bone}}\dfrac{\partial T_{\text{bone}}}{\partial r}=k_{\text{bt},g}\dfrac{\partial T_{\text{bt},g}}{\partial r} \\ r=r_3: T_{\text{sc}}=T_{\text{bone}},\ k_{\text{sc}}\dfrac{\partial T_{\text{sc}}}{\partial r}=k_{\text{bone}}\dfrac{\partial T_{\text{bone}}}{\partial r} \\ r=r_4: T_{\text{sc}}=T_{\text{skin}},\ \text{or}\ -k_{\text{sc}}\dfrac{\partial T_{\text{sc}}}{\partial r}=h(T_{\text{sc}}-T_\infty) \\ \theta=\dfrac{\pi}{2},0:\dfrac{\partial T_{\text{sc,bone,bt},g,\text{bt},w}}{\partial\theta}=0 \\ T_{\text{sc,bone,bt},g,\text{bt},w}(r,\theta,0)=T_{\text{sc,bone,bt},g,\text{bt},w}(r,\theta,2\pi) \\ t=0: T_{\text{sc,bone,bt},g,\text{bt},w}=T_0(r,\theta,\phi) \end{cases}. \tag{6}$$

**TABLE 1. Physical and physiological properties under normal conditions.**

| | Specific heat $C$ (W/kg K) | Mass density $\rho$ (kg/m$^3$) | Thermal conductivity $k$ (W/mK) | Perfusion rate $\omega_0$ [ml/(min 100 g)] | Metabolic rate $q_0$ (W/m$^3$) | Radius (adult) $r$ (mm) | Radius (infant) $r$ (mm) |
|---|---|---|---|---|---|---|---|
| Blood | 3800 | 1050 | 0.5 | … | … | … | … |
| Scalp | 4000 | 1000 | 0.34 | 2.0 | 363.4 | 93 | 57 |
| Bone | 2300 | 1500 | 1.16 | 1.8 | 368.3 | 89 | 55 |
| Gray matter | 3700 | 1050 | 0.5 | 80 | 16700 | 85 | 53 |
| White matter | 3700 | 1050 | 0.5 | 20 | 4175 | 67 | 42 |

During rewarming the brain temperature is usually elevated passively by removing the helmet or ice bag and exposing the head to room temperature ($T_{\text{air}} = 25\,^{\circ}\text{C}$). Thus, the initial condition for the rewarming processes is the established steady state temperature field $[T_c(r,\theta,\phi)]$ after SBC. All the boundary conditions and matching conditions are the same as in Eq. (6), except the boundary condition at the head surface. The different boundary conditions at the head surface and the initial condition during rewarming are given by

$$\begin{cases} r = r_4 : -k_{\text{sc}} \dfrac{\partial T_{\text{sc}}}{\partial r} = h_{\text{air}}(T_{\text{sc}} - T_{\text{air}}) \\ t = 0 : T_{\text{sc,bone,bt},g,\text{bt},w} = T_c(r,\theta,\phi) \end{cases}, \tag{7}$$

where the heat transfer coefficient ($h_{\text{air}} = 8\ \text{W m}^{-2}\,\text{K}^{-1}$) of free convection of the air has been determined from a heat transfer textbook.

The explicit implementation of the finite difference method is chosen as the numerical method for the solution of the partial differential equation in this formulation. The time and spatial derivatives are approximated by forward and central differences, respectively. Based on the algorithm, a FORTRAN code has been written and run on a personal computer. The program has been tested to ensure that the variations in the grid size or time step would yield less than 0.1% change in the final results.

## RESULTS

All the physical and physiological properties under normal conditions used in the brain model can be found in previous papers[26,33] and are listed in Table 1. It has been shown in most of the literature that blood perfusion rate of the gray matter varies from 75 to 85 ml/(min 100 g),[21,31] except one reference which gives a blood perfusion rate of 50 ml/(min 100 g).[27] Blood perfusion rate in the white matter varies from 15 to 27 ml/(min 100 g).[21,27,31] In this study, the blood perfusion rates in the gray and white matters are selected as 80 and 20 ml/(min 100 g), respectively, as shown in Table 1. The volumes of both the gray matter and white matter are selected so that the volumetric-average blood perfusion rate of the brain tissue is approximately 50 ml/(min 100 g).

Figure 2 shows the radial temperature distribution along lines OA and OB in an adult's brain during steady state. Note that surface cooling is only effective in reducing the temperature in the gray matter. Cooling can certainly penetrate deeper in the ischemic region than in the normal region. The heavy solid line in Fig. 2, which represents the steady state temperature profile when the adult is wearing a cooling helmet, is quite different from that (the solid line) when the head is packed with ice. The overall $h = 30\ \text{W m}^{-2}\,\text{K}^{-1}$ is a lumped value to estimate the thermal resistance between the coolant in the helmet and the scalp. Thus, $h$ should reflect the combined thermal resistance including the convective resistance between the coolant and the inner helmet surface, the conductive resistance of the helmet, and possible contact resistance between the outer surface of the helmet and the scalp. Although the cooling penetration is similar for both approaches, wearing cooling helmet results in a smaller temperature reduction in the gray matter. Thus, this overall thermal resistance significantly decreases the effectiveness of the cooling helmet.

Figures 3 and 4 examine the effect of the uncertainty of the blood perfusion rate on the transient behavior. The

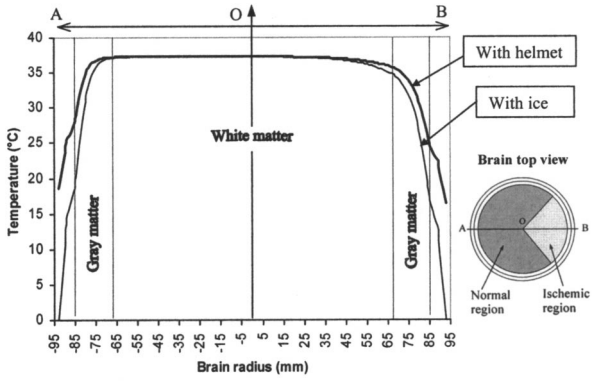


**FIGURE 2. Radial temperature distribution along lines OA and OB in an adult's brain.**

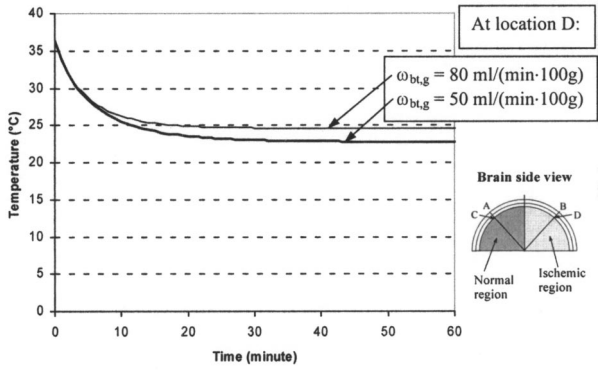


**FIGURE 3. Effect of various blood perfusion rates of the gray matter on the transient temperature profiles in an adult's brain.**

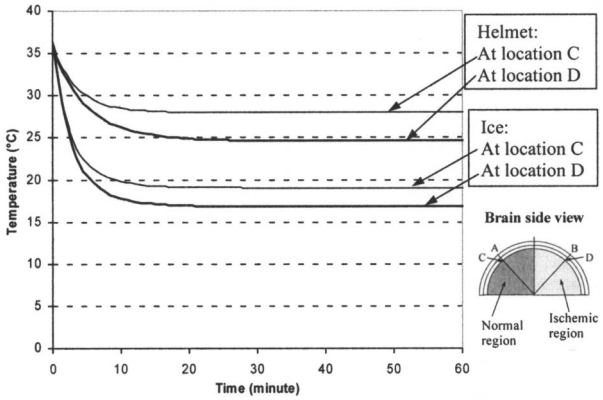


**FIGURE 5. Transient temperature profiles at two spatial locations (C in the normal region and D in the ischemic region) in an adult's brain by either cooling approach.**

characteristic time $t_c$ of the transient process is defined as

$$\frac{T(r,\theta,\phi,t_c)-T(r,\theta,\phi,0)}{T_c(r,\theta,\phi)-T(r,\theta,\phi,0)}=99\%. \tag{8}$$

The two transient temperature profiles shown in Fig. 3 illustrate the variation of the transient temperature at location D in the ischemic region when different blood perfusion rates are used in the gray matter. A smaller $\omega_{\mathrm{bt},g}$ results in a deeper cooling penetration and a longer characteristic time of (32 min vs 26 min when $\omega_{\mathrm{bt},g}$ $=80\ \mathrm{ml/(min\,100\ g)}$. Figure 4 examines the effect of $\omega_{\mathrm{bt},w}$ on the transient temperature profile at location D when $\omega_{\mathrm{bt},w}=15$, 20, and 27 ml/(min 100 g), respectively. Based on the Pennes equation, blood perfusion in tissue affects the temperature field by modifying the perfusion source term. Considering the tissue temperature in the white matter is very close to the arterial blood temperature of 37 °C, it is not surprise to see the minor role played by $\omega_{\mathrm{bt},w}$, to the transient temperature distribution.

Figure 5 gives the transient temperature profile at two locations at the outer surface of the gray matter, one is in the ischemic region and the other is in the unaffected region. Although deeper cooling penetration is observed in the ischemic region, a smaller blood perfusion rate seems to have a minor effect on the transient behavior if one compares the temperature profiles for locations C and D. The large thermal resistance between the coolant in the helmet and the scalp in the second approach is an important factor that results in a longer time for the temperature to reach the steady state. Figure 5 shows that the characteristic time is 26 min in the ischemic region when the cooling helmet is used, while the characteristic time is 18 min when the head is packed with ice. The effect of the head size on the cooling rate of the brain tissue is examined in Fig. 6 in which temperature transients are given for both an adult and an infant. Because of the smaller size in an infant's head, cooling is more

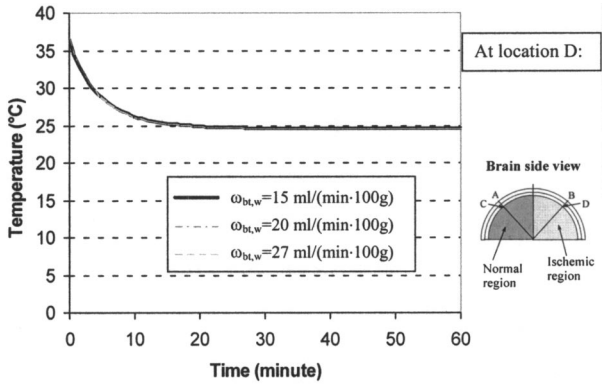


**FIGURE 4. Effect of various blood perfusion rates of the white matter on the transient temperature profiles in an adult's brain.**

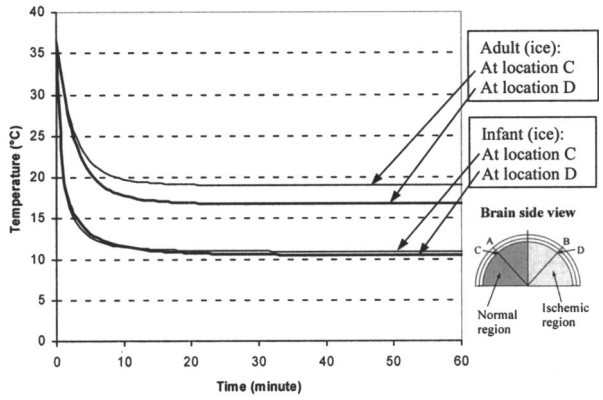


**FIGURE 6. Effect of the brain size on the transient temperature profiles at two spatial locations (C in the normal region and D in the ischemic region) when the head is packed with ice.**

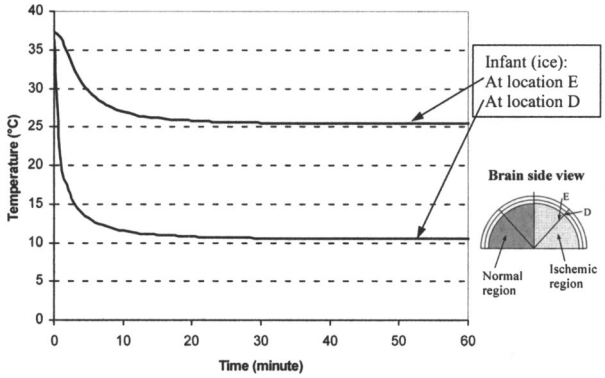


**FIGURE 7. Transient temperature profiles at two radial locations (D and E) in an infant's brain when the head is packed with ice.**

effective in the gray matter of the infant's brain and a shorter characteristic time (less than 15 min) is needed to reach its steady state. Figure 7 examines the transient temperature profiles on two radial locations in the ischemic region, one is on the outer surface of the gray matter, and the other is located in the middle of the gray matter. Obviously, it takes a longer time for the cooling to penetrate into the deeper brain tissue.

The transient temperature profiles at two locations in the gray matter during rewarming are shown in Fig. 8. The rewarming process is simulated by removing the helmet and exposing the head to a room temperature of 25 °C. Note that the initial temperature field is the established steady state after the surface cooling with the helmet. The average rewarming rate is approximately $3\,^{\circ}\mathrm{C\,h^{-1}}$.

## DISCUSSIONS AND CONCLUSIONS

This model is limited by the simplification of the head geometry and the application of the Pennes bioheat equation. The omission of the dura mater and the cerebrospinal fluid (CSF) in the model is based on the following reasons. First, this layer is very thin. Second, the thermal properties of the CSF should be very similar to that of the brain tissue provided that the convective effect of the CSF can be neglected. Thus, the dura mater can be treated as a very thin tissue layer incorporated into the brain gray matter without causing significant error in the calculation. Like most continuum models in which the heat and mass transport are averaged over a representative control volume, the Pennes equation is not capable of predicting point-to-point temperature variation in the vicinity of large discrete blood vessels. However, as compared by Van Leeuwen *et al.*,[26] the predicted temperature contours based on detailed vasculature in the brain agree very well with that predicted by the Pennes model. We believe that the current model based on a simplified geometry can still provide a reasonable prediction of brain temperature field. In fact, our steady state temperature distribution is similar to the previous results in which a direct measurement of the brain tissue temperature has shown that the brain tissue temperature is essentially the same at 20 mm beneath the cortical surface (gray matter).[24] In addition, the characteristic time predicted by this study concurs with the results obtained by Van Leeuwen *et al.*[27] who, using the Pennes equation, calculated the change in brain temperatures due to exposure to a mobile phone.

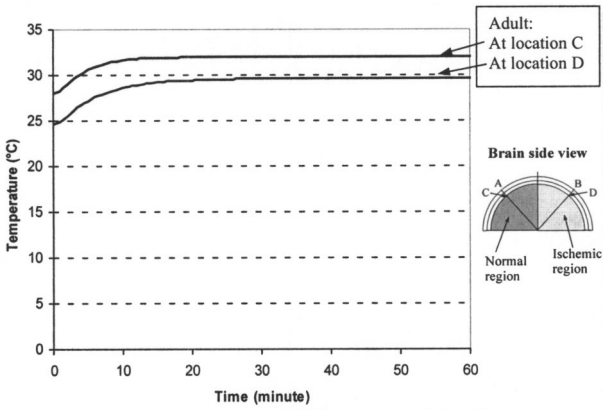


**FIGURE 8. Temperature rises at two spatial locations in the gray matter during the rewarming.**

Blood perfusion rate in the brain tissue plays dual roles in the tissue temperature during SBC. Since the Pennes equation is used in this study, it affects the simulated result via changing the strength of the perfusion source term. Possible variation in the blood perfusion rate of the gray matter can affect the simulated results in two ways. A smaller blood perfusion rate results in deeper cooling penetration into the brain tissue. However, a longer characteristic time is needed for the tissue to reach its steady state. Although most of the literatures have suggested a relatively small range of $\omega_{\mathrm{bt},g}$ , blood perfusion rate of the gray matter may be lower depending on the metabolic activity in the gray matter. For the lower limit of $\omega_{\mathrm{bt},g}$ [50 ml/(min 100 g)] the characteristic time is 23% longer than that using parameters in Table 1.

The current clinical literature has increasingly emphasized the importance of brain temperature in the management and prognosis of patients with brain injuries,[23] particularly during hypothermia treatment. Mild hypothermia for brain injury is usually defined as a brain temperature ranging from 32 to 35 °C. In this study, we simulated the temperature field during selective brain cooling. The results have shown that mild reduction in brain temperature can only be achieved in the gray matter. About 80% of strokes are ischemic in nature, via either thrombosis/occlusion of cerebral vessels or carotid/cardiac embolism. Ischemia can occur in any region of

the brain, although some studies suggest that gray matter is more susceptible to ischemia.[28] In this study brain ischemia is simulated as occurring in one quadrant of the brain tissue. Decrease in blood flow in the ischemic region may result in spontaneous temperature reduction. This is consistent with clinical observation of spontaneous cooling in the ischemic region.[4,17] We also observed that selectively cooling the scalp surface would further decrease the temperature in the ischemic region. Therefore, depending on the actual location of the brain ischemia SBC may be an effective approach for inducing local hypothermia.

The extent, duration, and therapeutic window of hypothermia treatment are not well established. Ischemic and TBI animal studies have suggested a 1–2 h treatment window within which postischemic hypothermia must be instituted to confer any significant neuroprotection. Body surface cooling with thermoblankets is used in most clinical application during systemic hypothermia. Because of the large volume of human body, it usually takes more than 3 h to achieve the goal core temperature.[3,10,20] Although intracarotid infusion of cold fluid or blood achieves rapid brain cooling,[12] the methodology is simply too invasive and impractical in prehospital settings. SBC via head surface cooling, however, can be potentially implemented early by EMT personnel in the field to maximize neuroprotection of hypothermia treatment. Experimental study on infant piglets using cooling cap[7] has shown a rapid temperature reduction in both superficial and deep brain tissue and our simulation has generated similar results. Our simulated characteristic time agrees well with the animal study on infant piglets[7] and a previous study in which ice surface cooling of head and neck lowered deep brain temperature to 34 °C only after 30 min.[15] Our data also suggested that cooling helmet is less effective than direct surface application of ice pack mainly because of the thermal contact resistance between the coolant and the scalp. Experimental measurement has shown a scalp temperature of 20 °C when a cooling helmet of coolant temperature of 0 °C was used in sclerosis patients.[11] Improving the thermal contact would theoretically shorten the time required to achieve selective cerebral hypothermia.

Rapid rewarming may dangerously result in rebound intracranial pressure elevation and cerebral perfusion pressure reduction and the importance of gradual rewarming has been emphasized in multiple clinical studies.[1,22] Our study simulated passive rewarming process by exposing the head to room temperature and the average calculated rate is about $3\,^{\circ}\mathrm{C\,h^{-1}}$. As suggested in Thoresen *et al.*,[25] the rewarming process should be conducted slowly at a rate of less than 0.5 °C/h. Thus, passive rewarming by exposing the head to the room temperature after removing the source of cooling may result in deleterious rebound effects. Further study on optimal rate of rewarming and trials of different rewarming protocols are warranted.

In conclusion, using the Pennes bioheat transfer equation, a three-dimensional theoretical model was developed to study the transient and steady state temperature distribution in human brain during selective head cooling and rewarming. The temporal and spatial temperature distributions in the brain are strongly dependent on the cooling protocol, the blood perfusion rate of the gray matter, the brain size, and the location. Our simulations have suggested that selective brain cooling may be an effective way to rapidly achieve regional hypothermia in the gray matter. The cooling helmet can be optimized by further reducing the thermal contact resistance between the head and the helmet surface. Passive rewarming may be unsafe and protocols to tightly regulate the rate of rewarming need to be studied. Further experimental study on blood flow response to cooling is warranted to shed light on the understanding of temperature-sensitive pathological processes.

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