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Comparison of Brain Temperature Distribution in Mathematical and Solid Models of Head Thermal Characteristics

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SUMMARY

Accurate temperature control of brain tissue during hypothermia treatment is necessary in order to prevent secondary brain damage and to avoid various side effects. Thus, the visualization of the intracerebral temperature distribution in hypothermia treatment was studied at the fundamental level. For this purpose a virtual reality technology was used to create a mathematical model that reflects metabolic heat production and Fourier heat conduction in a brain with the necessary parameters based on various clinical models. In the present study, an experimental system was developed to examine a mathematical simulation of the blood flow in a human head by using a solid brain model constructed using silicon rubber in the shape of a brain based on MRI data, taking into account the metabolic heat given off by three film heaters and including six sensors for the measurement of regional brain temperature. The mathematical simulation describes the internal temperature distribution in a brain with a similar structure to the brain solid model. The results of mathematical simulations and experiments using the brain solid model were quite consistent in the steady state, including control of regional temperature. This allows for the performance of heat conduction experiments under conditions similar to those of a living body, in which the internal temperature is clinically difficult to observe. Thus, the mathematical simulation is confirmed to be useful together with experiments using the solid model for the study of future brain hypothermia treatment. © 2015 Wiley Periodicals, Inc. Electr Eng Jpn, 193(2): 58–68, 2015; Published online in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/eej.22642

Key words: heat conduction simulation; human head model; brain hypothermia; artificial reality; mathematical model.

1. Introduction

The brain plays a central role in neural activity, including emotions, thoughts, and maintenance of life. In serious brain illness, the brain temperature and intracranial pressure rise due to cerebral edema or swelling, and life-threatening situations may occur. Brain hypothermia is an effective method of minimizing such symptoms and restoring brain function [1]. In this method, cooling of the brain requires temperature management to protect tissues. Inappropriate cooling of the injured area may lead to secondary brain damage and may worsen the patient's symptoms. Furthermore, the time constant of the response of the body temperature to temperature changes passing from the exterior to the entire body in brain hypothermia is large, of the order of two to three hours, and precise temperature management to control the constantly varying brain temperature is difficult.

At present, the temperature in regions such as the bladder or rectum, where measurements can be made noninvasively and quickly, or the temperature in the tympanic membrane or the bulb of the internal jugular vein, assumed to be approximately the same as the brain temperature, are used as brain temperature surrogates for the management of clinical brain hypothermia [2, 3]. However, it has been reported that a temperature difference of approximately 2 °C may occur between trunk of the body and the brain [2]. In the brain hypothermia equipment used in many hospitals, the blanket temperature is determines on the basis of the experience of medical staff, with reference primarily to the bladder temperature, and the temperature is set manually [4]. This does not constitute precise brain temperature control, and in addition, the temperature distribution in the brain due to differences in regional activity and metabolism in the presence of injury are not taken into consideration.

However, brain hypothermia involves the administration of anesthesia or a muscle relaxant, and thus there is no need to take into account the function of body temperature adjustment by shivering, which generates heat through muscle vibration. For this reason, theoretical analysis of the temperature distribution with consideration only of hormonal metabolic adjustment is possible. Various mathematical models have been proposed, and investigations of the cooling ability and control capability of brain hypothermia equipment have been performed.

Zhu et al. [5] created a mathematical model in which the head is represented as a hemisphere with three layers, namely, brain tissue, consisting of gray matter and white matter, the bones of the skull, and the scalp, with the temperature distribution between tissues with uniform thermal characteristics taken into consideration, and used it in hypothermia simulations. Xu et al. [6] geometrically represented the bone layer, the soft tissue layer including fat, muscle, and skin, and the brain layer in hemispheric form and evaluated the temperature distribution due to radiative cooling in which heat was exchanged radially between subdivided regions. Gerard et al. [7] created a model of the brain based on MRI images of newborns, in which the effects of brain hypothermia with the brain enclosed in a cooling cap were represented as temperature distribution contours from the brain surface toward the center. Wakamatsu et al. [8] created a head similar to that of Zhu et al. with three components, and devised a thermal model of brain hypothermia combined with an approximation of the entire body by 18 coaxial cylinders. Lu et al. [9, 10] performed an adaptive control simulation of the brain temperature in brain hypothermia with an 18-compartment model. Based on the results of the above investigations, Wakamatsu et al. [11] performed clinical experiments on brain hypothermia using fuzzy control and adaptive control of brain temperature in stroke patients. The mathematical models used in the above research are all adequate for practical use, but they were investigated as lumped-constant systems, so that the temperature distribution in the brain was not given adequate consideration, and brain hypothermia with consideration of the temperature at particular locations has not been performed [12].

Honma et al. have combined a physical model, representing deformation and damage by reproducing the organ shapes on the basis of MRI image data, with dynamic visualization in order to investigate the effects of an external force on the human head [13, 14]. They proposed a method of three-dimensional representation in addition to representation in sagittal or transverse section, creating a human head model that combined the shape data of the physical model with a heat conduction model, showing the temperature distribution by color gradations [15]. They used this model to perform a mathematical simulation oriented to selective brain hypothermia [16] and showed that temperature control in an arbitrary part of the brain is possible. However, in practice, control results consistent with theory are not necessarily obtained due to time delays and unexpected external disturbances, and thus there is a need for investigations using experimental apparatus based on the actual system as well as theoretical control results. Calculation errors due to differences in shape must also be taken into account. But in vivo experiments should be minimized for reasons of safety and ethics, and advantage should be taken of simulation apparatus. Thus, in this investigation we created a human head model with the same shape as a mathematical model of the human head and simulated metabolic heat production and heat exchange via blood vessels in order to minimize errors due to differences in shape. We used this model to perform mathematical simulations and similar measurement experiments oriented to selective brain hypothermia. Comparative study of these results is used to discuss the effectiveness of the mathematical model of heat conduction in the human head.

2. Overview of Selective Brain Hypothermia

In clinical brain hypothermia involving whole-body cooling [1], the body temperature is adjusted by passing water at a specified temperature through a cooling blanket that covers the trunk and limbs of the patient, with temperature control by adjusting the temperature of the blood circulating through the brain. In this method, areas outside the brain where temperature control is needed are also cooled, and consequently, complications such as pneumonia more easily occur due to reduced immune function. The problem of a larger time constant in this form of control has also been pointed out.

In selective brain hypothermia [16], which has been proposed as a method of correcting this situation, temperature control of the brain is performed rapidly by using a surgical procedure to access one of the four arteries that lead to the brain, and directly adding temperature-adjusted Ringer's solution. The blood flowing from the remaining three blood vessels and the Ringer's solution are mixed in the basilar artery circle, where the internal carotid arteries and the vertebral arteries join at the base of the brain, and the reduced-temperature blood removes heat from the brain tissue. Before it returns to body circulation from the jugular vein, water equivalent to the amount of introduced Ringer's solution is removed, and the remaining blood is warmed and returned to body circulation, so that the temperature outside the head is maintained within a set range. Consequently, immune function is more readily maintained and the risk of complications can be reduced.

In this investigation, we created an experimental model as shown in Fig. 1, assuming the use of selective brain hypothermia. The following human head model was used. Water (blood substitute) at a temperature equal to the

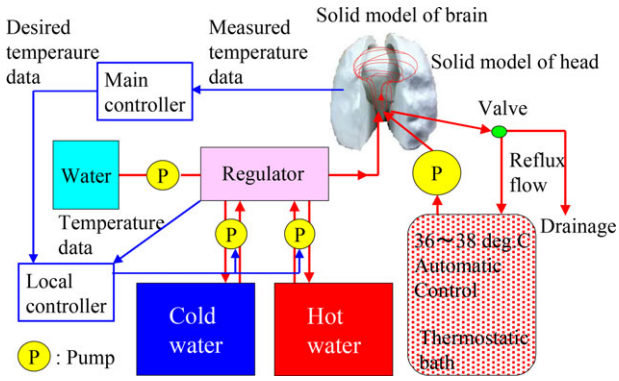


Fig. 1. Outline of the automatic temperature control system for the brain solid model. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

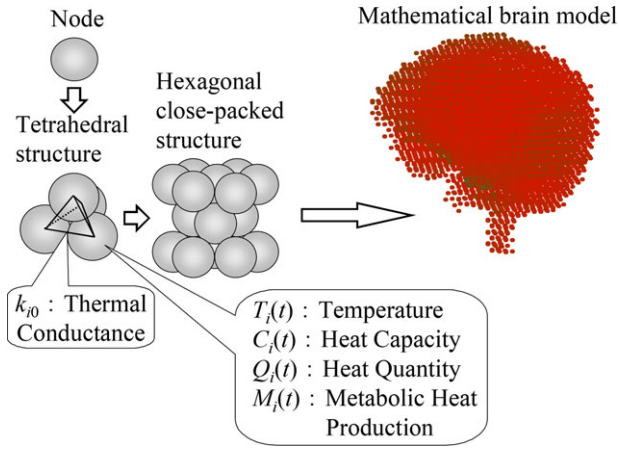


Fig. 2. Outline of the heat conduction model. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

body temperature was circulated from a thermostatic bath that substitutes for the body in the head model. A control experiment to cool the temperature of the brain model to a set value and maintain it there was performed by introducing water (substitute Ringer's solution) with its temperature adjusted by the temperature regulator into some of the blood vessels that enter the brain model. The temperature of the thermostatic bath was chosen in accordance with control theory, and the water temperature in the regulated bath was controlled by mixing cold water and hot water prepared in advance.

3. Creation of the Mathematical Model

3.1 Overview of the heat conduction model

Most of the metabolic heat produced in the brain is removed by blood coming from the trunk, so that the temperature is maintained within a set range. A method of representing heat transfer between the inflowing blood and the brain tissue by a mathematical heat conduction model, as shown in Fig. 2, in order to reproduce the temperature distribution has been proposed [15]. In this model, nodes are placed at the vertices of continuously connected regular tetrahedra, and heat conduction is assumed to occur between adjacent nodes. Each node is connected to 12 adjacent nodes. In vivo heat transfer occurs by heat conduction, convection, and advection in blood, but previous investigations [8, 17] presented results obtained by representing the above factors by heat conduction. Honma et al. [15] also created a mathematical model that takes these mechanisms into consideration. Heat conduction between nodes proceeds in accordance with Fourier's law, and the effects of convection are not taken into account. Because the objective is to simulate a living body, metabolic heat production occurs at some of the nodes. Thus we have the following equations:

$$Q_0(t) = C_0(t)T_0(t), \tag{1}$$

$$\Delta T_{i0}(t) = T_i(t) - T_0(t), \tag{2}$$

$$T_0(t+1) = T_0(t) + \left\{ \sum_{i=1}^{12} k_{i0}\Delta T_{i0}(t) + M_0(t) \right\} \Big/ C_0(t), \tag{3}$$

where $Q_0(t)$, $C_0(t)$, and $T_0(t)$ represent the quantity of heat, the heat capacity, and the temperature in node 0 at time t. $\Delta T_{i0}(t)$ in Eq. (2) is the temperature difference between node 0 and adjacent node i ($i = 1$ to 12). The temperature $T_0(t+1)$ at node 0 at time $t+1$ can be calculated by means of Eq. (3) from the metabolic heat production $M_0(t)$ at node 0 and the heat transfer coefficient k_{i0} between node 0 and nodes i [15]. The heat transfer coefficient k expresses the rate of heat transfer of the nodes calculated from the thermal conductivity λ. Node 0 represents an arbitrary node in the three-dimensional lattice, and consequently, the nodes i corresponding to each node are uniquely determined.

3.2 Overview of mathematical model of head tissue

In order to estimate the temperature distribution in the head, we set parameter values for the tissues by formulating the heat conduction model described above in accordance with the tissues of the head. Below we define as the tissue model a model created for various tissues, including the brain, skull, blood vessels, eyeballs, and skin. In a mathematical model of the brain, for example, this

means a set of nodes providing the shapes and parameters of brain tissue. Based on continuously captured MRI image data for the human head, we created tissue models of the brain, skull, and eyeballs [15]. However, the brain is a single continuous system consisting of the cerebrum, cerebellum, and medulla oblongata; other tissues such as the facial muscles and the parotid glands are included in the skull; and the cerebrospinal fluid (CSF) is assumed to fill the space between the mathematical model of the brain and that of the head. The microscopic nodes described above are arranged uniformly in these tissues, resulting in a head tissue mathematical model from which the heat distribution of a human head can be calculated.

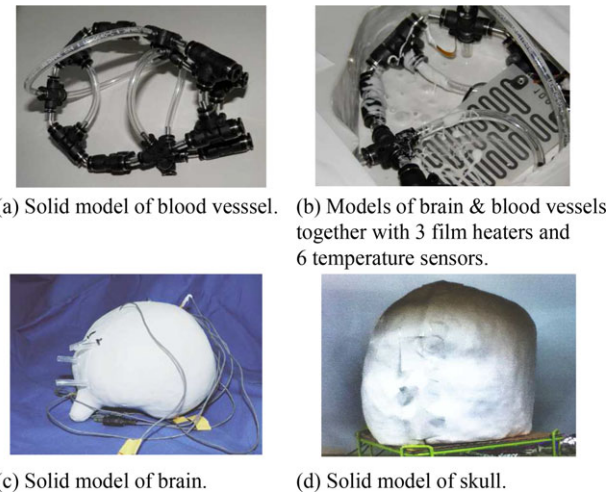
The extracellular fluid mixes with plasma components that pass through the vascular walls, and the water molecules that compose this fluid exchange heat with the intracellular fluid through the cellular membrane by means of ion channels and aquaporins. Thus convection or blood advection similar to that in the capillaries may be regarded as occurring between brain cells. Thus, by modeling only of major blood vessels using averaged parameters, we obtain a blood vessel model in which heat is exchanged between the nodes composing the tissues.

The nodes in the air surrounding the head are treated as air. Reproducing the shape of the skin from MRIs is difficult because the skin is thin; because it participates in heat loss from the head, it is treated conceptually as a model that covers the surface of the skull model. We define a head model combining the various models of the brain, skull, blood vessels, eyeballs, skin, cerebrospinal fluid (CSF), and air, that can be used to calculate the temperature distribution in the brain.

4. Overview of the Human Head Model

4.1 The human head model

For comparison with the results of simulations based on the mathematical model, we built a human head using the shape data of the mathematical model of the head tissues described above [18]. The brain model corresponding to the mathematical model was formed of silicon rubber and was equipped with the blood vessel model shown in Fig. 3(a). The actual thickness of the blood vessels varies with the location, but in this model, which uses nodes, it is uniform. Consequently, the blood vessels were modeled by a combination of No 4 nylon tubes and branch connections. Three film heaters (Shinwa Measurements, model FH-10) used to simulate metabolic heat production and six temperature sensors (Ishizuka Electronics, model 103JT-050) used to measure the temperature distribution were installed as shown in Fig. 3(b). The heat production could be controlled and the temperature could be measured from the outside.



(a) Solid model of blood vesssel. (b) Models of brain & blood vessels together with 3 film heaters and 6 temperature sensors.

(c) Solid model of brain. (d) Solid model of skull.

Fig. 3. Main parts of human head models. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The brain temperature sensors were placed in six locations: in the center, equivalent to the brain stem; at the left and right sides, equivalent to the eardrums, and at the top, front, and rear. Specifically, film heaters were placed on the surfaces obtained by dividing the brain into four sections at the medial sagittal plane and parallel planes, with the center of each film heater on the medial coronal plane. The sensors at the front, top, and rear were set at a depth of 5 mm from the front, top, and rear of the brain on the medial sagittal plane, respectively. The sensors on the left and right sides of the head were set at a depth of about 5 mm from the sides on the medial coronal plane. The central sensor was offset by 5 mm to the right of the medial sagittal plane so as not to come into contact with the heater. The blood vessel model, film heaters, and temperature sensors adhered to by the silicone rubber which was injected to create the brain model, allowing direct heat transfer.

The sensor signals were measured with signal lines passing through the brain model, as shown in Fig. 3(c). A voltage of 5 V was applied to the film heaters from outside, and metabolic heat production of 25 W per sheet, for a total of 75 W, could be produced. This provision made it possible to simulate the occurrence of metabolism is occurring due to the activity of the brain matter or to inflammation, not just the resting basal metabolism. The skull model, including tissues such as the eyeballs, facial muscles, and parotid glands, was formed in plaster and was divided into two parts, in order to create an integrated human head model as shown in Fig. 3(b) by enclosing the brain model described above from the left and right, allowing the performance of experiments equivalent to the simulations based on the mathematical model.

For the purpose of experiments taking individual differences into account, we created three brain models and

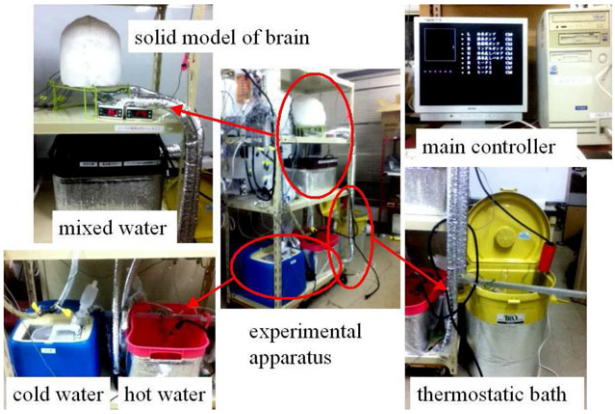


Fig. 4. View of the experimental apparatus for the brain solid model. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

two skull models from the same molds, allowing for flexure of the films due to the inflow of rubber during molding. The calorific value was the same in each brain model, but the distances to the heat-emitting locations and blood vessels varied for each sensor, and the skull models had different locations and areas of contact with the brain models. Consequently, the routes by which heat was released to the surroundings by heat conduction differed, and the individual differences of the six combinations could be investigated. The brain models weighed approximately 2.9 kg, and the skull model weighed approximately 4.8 kg.

4.2 Overview of the brain cooling experimental apparatus

Using the above head models, we performed experiments by the procedure shown in Fig. 1, based on the concept of selective brain hypothermia described above. In order to adjust the temperature means of substitute Ringer's solution and a thermostatic bath, cold water and hot water were mixed at various rates. After passage through the heat exchanger in the temperature-adjusted bath, the substitute Ringer's solution reached the set temperature and was mixed with the blood. Thus, as can be seen in Fig. 4, the equipment simulating the circulation of blood to the brain and the controller regulating the temperature of the substitute Ringer's solution were combined and driven synchronously by a PC.

In the experimental apparatus, the thermostatic bath and pump (Iwaki RD-05H), with a capacity equivalent to the total amount of blood in the human body were treated as representing the body and heart, and the substitute blood was circulated through the brain model. The amount of substitute Ringer's solution mixed with the substitute blood was treated as a surplus and was removed via a valve, resulting in a system in which the circulating water level was maintained constant. Temperature control of the thermostatic bath was performed by an IC controller (Sunart SCH-900SC). Temperature control of the substitute Ringer's solution was performed by the heat exchanger installed in the thermostatic bath in which cold water and hot water were mixed. The mixed water from the bath was returned to the cold water tank or the hot water tank depending on the amount of water in the hot water bath, and the set temperature was kept within a constant range by the cooler or heater. A small refrigerator (Lotte mini-refrigerator) was used as the cooler, and an electric immersion heater (Fujimak H-500S) was used as the heater.

5. Experimental Methods

5.1 Measurement of heat conduction response characteristics of human head model

We measured the heat transfer response characteristics of the head model with the experimental apparatus described above. We measured the step response at the locations representing the center of the brain and the tympanic membrane during circulation of the substitute blood at 37 $\pm$ 0.1 °C through the blood vessel model, with the pump representing the heart. The flow rate was set to a total of 50 mL/min, taking account of the blood volume in the human brain, the volume of the blood vessel model, and the sojourn time of blood in the brain required for heat conduction. The temperature on the side of the brain was treated as the tympanic temperature, since the tympanic membrane is located anatomically at the side of the brain.

5.2 PI control experiment using the human head model

Total brain hypothermia as now performed clinically involves manual adjustment of the brain temperature. However, clinical examples [11] of the results of automatic temperature regulation by adaptive control or fuzzy control have been reported, indicating that precise temperature control can be performed with total automation, thus reducing the burden on medical staff.

In this investigation we studied the possibility of temperature control at lesion sites in the brain in accordance with the above ideas. We first performed an experiment on temperature maintenance at the location of an arbitrary sensor by PI control. The transfer function of the control law is given by Eq. (4), where K_p is a proportionality constant and T_l is the cumulative time:

$$G(s) = K_p + 1/T_l \cdot 1/s. \quad (4)$$

In clinical brain hypothermia, continuous measurement of the temperature at the center of the brain is not possible due to the need to guard against bacterial infection. Thus, in

Table 1. Parameters of each tissue type in the head solid model

Property/Organ	Brain	Skull	Eye ball	Blood vessel	CSF	Skin	Air
Number of nodes	13,093	24,206	172	497	1805	3310	20,917
Temp. [deg C]	Room Temp.	Room Temp.	Room Temp.	Room Temp.	Room Temp.	Room Temp.	Room Temp.
Metabolic heat production [W/m^3]	0	0	0	0	0	0	0
Thermal conductivity [W/(m·K)]	9.34×10^{-1}	4.30×10^{-1}	4.30×10^{-1}	3.99×10^{-1}	9.34×10^{-1}	4.30×10^{-1}	9.25×10^{-3}
Specific heat [J/(kg·K)]	2.01×10^{3}	8.35×10^{2}	8.35×10^{2}	1.01×10^{3}	2.01×10^{3}	8.35×10^{2}	1.01×10^{3}

brain temperature estimation [8–12] based on the tympanic temperature or bladder temperature, as performed in the past, a lumped constant system is considered, and the estimated temperature is treated as the temperature at the center of the brain. Consequently, in this investigation we used the temperature at the center of the brain as the controlled variable and the temperature in the thermostatic bath as the manipulated variable.

In this experiment, the substitute blood flowed through three blood vessels, and the substitute Ringer's solution was introduced into the remaining blood vessel.

First, current was fed to all of the film heaters until the temperature at the center of the brain reached 40 °C with circulation of the substitute blood at 37 ± 0.1 °C. After that temperature was reached, the film heaters were switched on and off in alternation, with settings intended to maintain a temperature of 40 °C in the uncontrolled state. Thus an average of approximately 35 W of heat was provided to the brain model. PI control was performed by setting the target temperature so that the temperature at the center of the brain reached 38 °C in the simulated heat generation state, and the dynamics of the model was measured. However, in order to reduce fluctuations near the target temperature, a dead zone of ±0.3 °C was set. Assuming the avoidance of excessively invasive operations in a clinical setting, we set the limiters on the temperatures of the cold water and hot water tanks based on experiments and simulations with the mathematical brain model, so that cooling or heating beyond the set values would not occur. Thus the water temperature in the mixing tank, the controlled variable, was kept within 5 °C of 42 °C.

5.3 Simulation using the mathematical model

To compare the step response described above with the experimental results under PI control, we performed a simulation using the mathematical model. The number of nodes in the six tissues composing the head model and the surrounding air was set as shown in Table 1 based on the volume of each tissue type [15]. Published values [17] were used for the heat transfer coefficients and heat capacities of the rubber and plaster composing each tissue type. However, because the values in the reference cited are stated per unit weight or unit length, in the actual calculations we determined the heat capacity per node from the measured weights of the brain model and skull model and the number of nodes in the corresponding heat conduction model. The heat transfer coefficient for each node was calculated with allowance for the fact that the set distance between nodes [15] in the heat conduction model was 6 mm, and the computation time period was set to 1 second [15]. As the initial temperature of each tissue type at the start of the calculation and the air temperature during the simulation, we used measured values obtained in experiments on the human head model. Because in the head model the eyeballs and scalp were included in the skull, the parameter values for the nodes other than those in the eyeballs and skin were the skull values, and the metabolic heat production in each tissue type was set to zero.

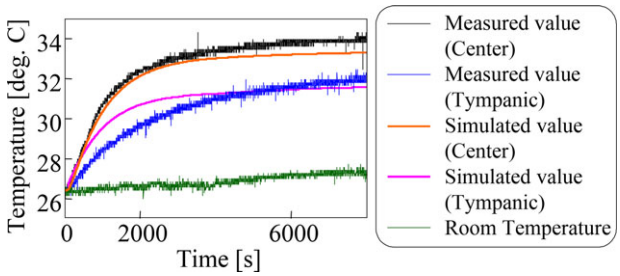


Fig. 5. Various measured temperatures in the solid models for step inputs of the water temperature. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

6. Experimental Results

6.1 Step response of brain temperature in the human head model and mathematical model

We used one combination of head and skull models at a room temperature of approximately 26.5 °C. Figure 5 shows a comparison of the temperatures at the center of

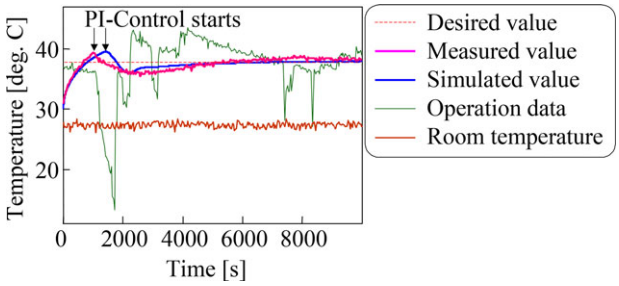


Fig. 6. Measured values for the solid models and the results of the simulation using PI control. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the brain and at the tympanic membrane with step water-temperature inputs with the substitute blood at 37 ± 0.1 °C circulating through the brain, and the results of a mathematical simulation performed with the same conditions. In the mathematical simulation, the room temperature data from the physical experiment were used in reproducing the circulation.

The temperature at the center of the brain rises in almost the same way in the human head model and the mathematical simulation, as shown in the figure. The tympanic temperature rises with a slight delay between the former and the latter, as can be seen in the figure. In this case, the time constants of the human head model and in the mathematical simulation are approximately 1300 seconds and 1250 seconds at the center of the brain, and approximately 2600 seconds and 1450 seconds at the tympanic membrane. Similar results were obtained in experiments with different combinations of skull and brain models.

6.2 Behavior of brain temperature in the human head model and the mathematical model under PI control

Figure 6 shows the results of a PI control experiment and a mathematical simulation using the human head model in accordance with the method described above. "Operation data" in the figure represents the measured temperature in the temperature-regulated bath in the physical model experiment. Therefore, the temperature of the substitute Ringer's solution passing through the heat exchanger in the temperature-regulated bath coincides with this value. The measured values at room temperature are also shown. The parameter values for PI control were set to $K_p = 20.0$ and $T_l = 100.0$. In the measurements on the head model, the temperature at the center of the brain reached 40 °C approximately 1000 seconds after the start of heating of the brain with the film heaters, with the substitute blood circulating through it at 37 ± 0.1 °C; PI control was started at that time.

The manipulated variable was set to cool the brain when control started, and the temperature at the center of the brain declined accordingly. When the temperature at the center of the brain fell below the target value, the manipulated variable was set so to warm it, and the temperature at the center of the brain rose. The temperature at the center of the brain settled to a value close to the target value after approximately 10,000 seconds.

In the mathematical model, IP control was begun when the temperature in the brain reached 40 °C, after approximately 1500 seconds, and the temperature declined until approximately 2000 seconds. The subsequent response curve agrees closely with the measured values, and settling to the target value was complete after approximately 10,000 seconds, as in the case of the brain model experiment.

7. Discussion

7.1 Discussion of measured results and mathematical simulation results for the head model with step response

Comparing the results of the experiment with step response using the head model and the simulation results obtained with the mathematical model, we see that the measured values and the calculated values agreed closely when the temperature was rising, but that a small temperature difference appeared in the settling values. On the other hand, although the measured temperature rose more slowly than that calculated in the mathematical simulation during the temperature rise in the tympanic membrane, the settling values agreed well.

Because nodes corresponding to the cerebrospinal fluid were present in the mathematical model, a certain range of heat propagates from the brain to the skull through them. But the head model combining the brain model and the skull model did not have complete adhesion, and consequently, direct heat exchange with the air appears to have occurred in the gaps. Thus, in the region equivalent to the tympanic membrane located next to the brain, the cooling effect of air was greater than in the mathematical model at the start of the experiment, and differences in the temperature rise appear to have occurred. However, this effect is small at the center of the brain, and consequently the temperatures agree closely during heating.

Because the air in the gaps did not have direct circulation with the atmosphere, it appears that the temperature rose due to the heat emitted from the brain model, so that the temperature was approximately the same as that in the region around the brain in the experiment, so that the cooling effect was reduced. Consequently, heat transfer declined starting approximately 4000 seconds after the beginning of the experiment, and thereafter a temperature rise smaller

than that in the mathematical model occurred at the center of the brain.

Thus, when the temperature of the air in the gaps is lower than the brain temperature, a cooling effect appears to occur, and conversely a heat-retention effect appears to occur at temperatures close to the brain temperature. Determining the threshold values of these phenomena from our experimental results alone is difficult. Experiments in which the effects of air is eliminated by placing grease between the brain model and the skull model will be needed.

In the results of the experiment, the tympanic membrane settled to a temperature about 2 °C lower than that at the center of the brain. The tympanic membrane is affected not only by the blood flow in the external carotid artery, but also by the temperatures of the outside air and the facial skin, and consequently it was 0.3 to 0.5 °C lower than the external temperature of the dura mater [2]. The center of the brain is almost completely unaffected by the external air, and this appears to be why it had a higher temperature. Magnetic resonance spectroscopy (MRS) [19] has indicated that the temperature difference in the interior of the brain in the waking state is 2 °C to 3 °C, which is not inconsistent with the results obtained in the present investigation of the temperature distribution in the brain.

7.2 Discussion of responses of the physical model and mathematical model under PI control

In this investigation, assuming patients in whom the temperature at the center of the brain rose to 40 °C due to metabolic activity after brain injury, we applied PI control to maintain the set temperature after cooling to 38 °C, the target temperature for this situation. This represented system control under the assumed brain hypothermia; the objective was to investigate the effectiveness of using a mathematical simulation to estimate the temperature distribution due to heat conduction in the brain, based on a comparison of the two sets of results that we obtained.

First, in the process of raising the temperature at the center of the brain to 40 °C by operating all of the film heaters without control, the measured values in the head model, in which the temperature at the center of the brain reached approximately 38 °C, agreed well with the simulation results obtained with the mathematical model. Subsequently, as in the case of the step response, the measured values reached 40 °C, the temperature of the initiation of control, slightly faster than in the mathematical simulation. The reason for this result appears to be that the heat stored in the brain is more readily transferred to the skull in the mathematical simulation, so that the temperature rise is slightly delayed.

After 40 °C was reached, PI control was performed, and the temperature fell faster in the mathematical simulation than in the physical measurements. But there was a continuing discrepancy of ± 1 °C between the measured values and mathematical simulation results, while settling to the target value took approximately the same amount of time. Thereafter, the set value was maintained in the mathematical simulation, but small oscillations appeared in the physical measurements, apparently because of a time delay in the temperature change in the experimental apparatus, while in the mathematical simulation the mixing of the hot and cold water is approximately instantaneous. Furthermore, in the mathematical simulation, assuming the use of clinical data, measurements are performed to two decimal places, while in the experiments with the physical model, the measurement precision was most one decimal place in view of the performance of the sensors and thermistors. In addition, the temperature of the substitute blood was confirmed only by a thermistor thermometer, which is not reflected in the mathematical simulations, so that there are likely to have been small effects on temperature measurement error.

Although the measurement results include small errors, their agreement with the results of the mathematical simulations suggest that the method of computing the brain temperature distribution by the mathematical model is generally effective. There is a need to create a mathematical simulation model that reflects the speed of water transport and mixing in the experimental apparatus, which appears to be the major cause of error, in addition to improving the experimental apparatus.

7.3 Performance evaluation of the brain model and mathematical simulation with respect to general brain hypothermia

In the human brain, brain cells may undergo necrosis after a rise in temperature from 38 °C to 44 °C in the presence of injury [1]. Therefore, in experiments simulating the use of hypothermia to cool and protect the brain, an ability to reproduce the changes in brain temperature due to pathology or treatment is needed. Each film heater in our brain model had a heat output of about 25 W, equivalent to the resting basal metabolic level in the brain. Simultaneous use of the three internal heaters simulates a situation in which the metabolism is tripled, confirming that the temperature at the center of the brain can rise to approximately 50 °C [20]. This is a temperature slightly higher than that obtained in the mathematical simulations, and although it may vary due to the temperature of the substitute blood circulating through the body and to the production of heat outside the heaters due to current flow, the state of heating occurring in serious encephalopathy can also be simulated.

While in this investigation we used film heaters to simulate heat production in the brain, in the real brain, heating due to metabolic activity occurs for reasons such

as inflammation in other locations than those represented by the film heaters. Consequently the brain model does not adequately reproduce heating due to brain injury. But simulation by a mathematical model in which the heating locations are consistent with the locations where the film heaters are placed in the physical model did closely reproduce the results of the model experiments, indicating that realistic results can be obtained when the heating locations are arbitrarily varied. Since internal states and parameter identification can be clinically estimated by using temperatures at observable locations or by with X-ray CT information, temperature estimates can be made with the mathematical model. Furthermore, if the precision of internal state estimation can be improved, the model can be controlled without directly measuring the temperature distribution in the brain. Repeated model experiments will be necessary for the creation of such a method.

In brain hypothermia by whole-body cooling, brain cooling for the transition to the management period requires 5 to 8 hours, and the brain is cooled to approximately 32 °C after an acclimation period at approximately 35 °C [1, 9]. In the PI control experiment, cooling by 4 °C in a period of approximately 1000 seconds after the start of control was reproduced in the brain model, indicating that it is possible to simulate clinical temperature control with a smaller rate of change in brain hypothermia.

But in whole-body brain hypothermia, a slow temperature change is set in order to reduce the overall burden on the body. In selective brain hypothermia, only the head is cooled, and consequently cooling can be performed more rapidly. In clinical cooling methods, the physician makes decisions by taking a variety of factors into consideration. A cooling method for a specific location in the brain that combines cooling from outside using a cooling cap or a cooling muffler with direct injection of coolant into a specific location with a catheter can also be used for selective brain hypothermia, and this may provide new clinical information.

Furthermore, in addition to being designed with a shape consistent with MRI data, the blood vessel model simulates the major blood vessels in the brain. The size ratios in the brain model size agree well with the physiologic values in humans, so that that blood vessel model has a configuration that approximates the major blood vessels in the real brain. Thus the human head model that implements efficient heat exchange with the blood in several major blood vessels at the center of the brain appears to approximate a set range of heat transfer, especially with the surroundings. The experimental results obtained with the human head model and the calculated results obtained with the mathematical model are in good agreement, and consequently the mathematical model appears able to reproduce the heat distribution in real human head tissue.

In this investigation we performed mathematical simulations using the parameter values of the plaster, rubber, and the like used in the head model, and consequently the present results will not necessarily agree with clinical observations. However, from the viewpoint described above, a mathematical simulation [15] using parameters measured in a living organism provides evidence that the heat distribution in the human head can be measured clinically. But since the head model does not reproduce all of the biochemical activity in the real brain, the mathematical model must be confirmed by comparison with continuous clinical brain temperature measurements [19, 21].

8. Conclusions

We created a human head tissue model based on MRI data in order to evaluate the effectiveness of a mathematical model that can estimate the temperature distribution in the brain from known bioparameter values. We then compared a the results of experiments performed with this model with the results of a mathematical simulation. In experiments oriented to selective brain hypothermia, the human head model was confirmed to exhibit heat distribution tendencies close to those indicated by clinical data. Good agreement with the mathematical model was also found in step response and PI control experiments. These results indicate that the human head mathematical model of the human head was able to represent the brain temperature distribution that would occur in selective brain hypothermia.

A visualized brain temperature distribution allowing a more intuitive presentation to medical staff will allow more effective cooling of injured regions of the brain by selective brain hypothermia, and will help to improve therapeutic results.

The results of this investigation have illustrated the possibility of using mathematical simulation by the model presented in this paper to investigate the effects of treatment with allowance for differences in the injury locations and metabolic levels.

A summary of this research was presented at the 2012 IEEJ Electronics, Information, and Systems Society conference [20].

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