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3D-Visualised Model of Temperature Distribution in the Brain for Investigation of Brain Cooling Effect

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SUMMARY

Brain hypothermia requires control of its temperature within an appropriate range, considering the change of body temperature over a long period. Various mathematical models have been used for the study of control and cooling capability of brain temperature in hypothermia. In previous models, a lumped-parameter hemisphere of uniform temperature has been assumed as a simplified brain model without considering the temperature distribution. In the present study, however, a new model is proposed to visualize the temperature distribution in the brain. The model has the approximate shape of the organs in the head based on MRI data, and may well reflect properties such as heat transfer coefficients, metabolic heat production, and heat capacity of human organs. The model has a pseudo-blood-flow component in which any temperature can be set as the initial value at the starting place of blood flow. Simulations using this model were performed with the temperature controlled by the introduction of Ringer's solution into any of the four arteries leading to the brain. The simulation results suggest that the various cooling effects are manifested in every region of brain, and that the temperature distribution can be known for applications to controlling brain temperature in a part of interest. © 2014 Wiley Periodicals, Inc. Electron Comm Jpn, 97(11): 56–64, 2014; Published online in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/ecj.11613

Key words: hypothermia; temperature distribution; virtual reality; mathematical model.

1. Introduction

When metabolism in brain tissues increases due to cerebral contusion or blood vessel rupture, or inflammation thus produced, while the brain temperature rises due to blood stagnation caused by swelling of brain tissues and other factors, life maintenance may be threatened. Hypothermia, a treatment that cools the brain under strict temperature control to protect the tissues, is known to be an effective method for recovery from such pathological conditions. In hypothermia, the brain temperature must be maintained within a certain range, with regard to temperature variation with a long time constant in living organisms, so as to cool brain inflammation while avoiding abrupt changes of physiological state and also maintaining immunity.

The brain is an important organ that performs fundamental physiological functions such as memory and emotions, and manipulations on the brain require preparation using simulations and mathematical models. In the case of hypothermia, the thermoregulatory function implemented through patient's muscle vibrations, that is, shivering, is restricted by anesthetics and muscle relaxants, and thus mathematical models have been developed by theoretical analysis considering only the metabolic control functions of hormones, and so on, in order to investigate the cooling capacity and control performance of brain cooling systems.

Zhu and colleagues [1] defined the head region as a hemisphere made of three layers, the brain, skull, and scalp, and assumed a uniform temperature in each layer in order to develop a temperature distribution model and to simulate hypothermia. Xu and colleagues [2] split the cross-section of the brain defined as a hemisphere into multiple sectors and considered the temperature distribution of radiative cooling in each sector. Wakamatsu and colleagues proposed a model of the whole body divided into 18 compartments for simulation of brain hypothermia. Each compartment was represented by a lumped-parameter model, and the head was modeled by the three compartments proposed by Zhu and colleagues [1]. Lu and colleagues [3, 4] used the 18 compartments as a nominal model for simulation of automatic adaptive control in hypothermia treatment. Based on the results, Wakamatsu and colleagues [5] conducted clinical tests and applied adaptive control and fuzzy control to the brain temperature of actual patients.

The mathematical models used in the mentioned studies were quite practicable but did not take account of the temperature distribution inside the brain. In addition, most monitoring systems used with patients under hypothermia treatment provide only numerical indications but not distributions or other visualizations [6]. Thus, only numerical temperature data are available, and there is no information usable for intuitive understanding of the temperature distribution inside the brain. It is therefore difficult to implement selective hypothermia methods with regard to the temperature distribution produced by brain damage or inflammation, and the corresponding changes in metabolism. As a result, the same cooling is applied to healthy sites of the brain.

We have used MRI image data to develop models reflecting the shape and dynamics of every tissue of the human head in virtual space [7, 8]. These models express deformation and breakdown caused by an external force; specifically, every tissue is divided into nodes of a certain size, and dynamic states are calculated differentially in every small period of time to obtain 3D images providing intuitive confirmation of changes in real time.

We use this technique in the present study to express every tissue of the human head by the nodes of a heat transfer model, thus developing a new model that makes it possible to calculate the temperature distribution. In addition, we develop a simulation system that expresses the temperature distribution in terms of color and presents 2D sagittal sections in parallel with 3D images of every tissue.

We also use the model as an experimental model for new hypothermia techniques under development [9], and describe simulations to examine temperature control performance at arbitrary sites, and the respective cooling effects.

2. Development of Simulation Model

2.1 Heat transfer equation taking account of metabolic heat production

In order to investigate the detailed distribution of brain temperature, we consider the human head as a set of small nodes. All nodes are assumed to be of the same size and are distributed uniformly within a certain shape in each tissue. All nodes are placed at the vertices of regular tetrahedra connected continuously as shown in Fig. 1, and heat transfer between adjacent nodes (that is, nodes connected by tetrahedron edges) is considered. Therefore, every node exchanges heat with 12 surrounding nodes. We assume that heat transfer follows Fourier's law, while ignoring convection and the like. Actually, heat transfer in a living organism involves heat conduction, convection, advection by blood, and so on, but it was shown in previous

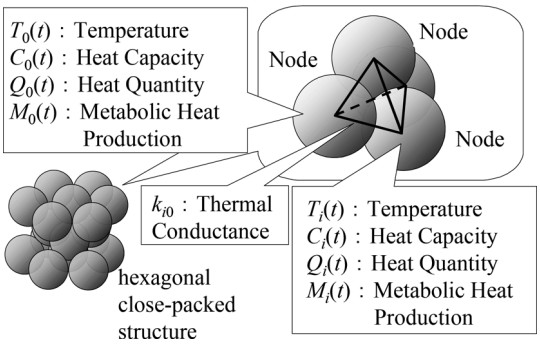

Fig. 1. Outline of heat transfer model.

research [10, 11] that these processes are represented by measured heat conduction data. The same approach is used in this study. In addition, we assume that metabolic heat is produced at some nodes. The following Eqs. (1)–(3) hold true, where $Q_0(t)$, $C_0(t)$, and $T_0(t)$ denote, respectively, the heat quantity, heat capacity, and temperature of node 0 at instant t. $\Delta T_{i0}(t)$ in Eq. (2) is the temperature difference between node 0 and adjacent node i ($i = 1 - 12$). The temperature $T_0(t+1)$ of node 0 at instant $t+1$ is expressed in Eq. (3) in terms of the heat transfer coefficient k_{i0} between nodes 0 and i, and metabolic heat production $M_0(t)$ at node 0. Here, the heat transfer coefficient (thermal conductance) k expresses the proportion of heat transfer at every node calculated from the thermal conductivity λ:

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

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

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

2.2 Development of head tissue model

A head tissue model is built using continuously acquired MRI image data. Specifically, 40 equally spaced images are selected, and the nodes are set by applying a 40×40 grid to each image. Thus, the temperature distributions produced by heat transfer with regard to the parameters of 64,000 ($= 40^3$) nodes are visualized as 2D and 3D images.

All nodes are assigned to the tissues constituting the human head based on MRI data. We assume that the brain, skull, and eyeballs are representative tissues, and that the space between them is filled with cerebrospinal fluid (CSF). From the standpoint of resolution, we assume that the facial muscles, parotid gland, and other tissues are included in the skull. In addition, we consider a pseudo-blood-vessel model simulating the main blood vessels to represent blood flow, which plays an important role in heat transfer in the

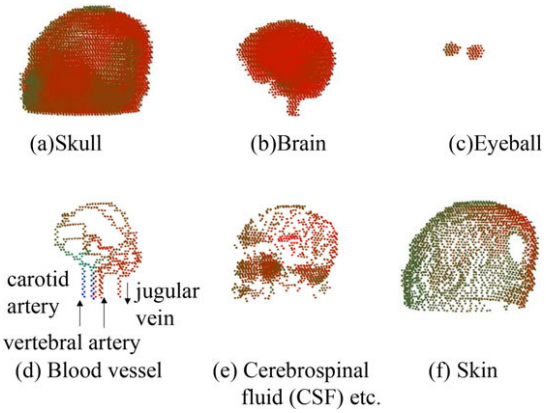

Fig. 2. Classification of brain tissue model. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

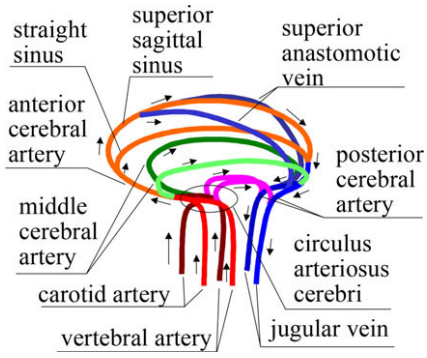

Fig. 3. Outline of blood vessel model in brain. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

head region. We also assume that the head is surrounded by ambient air.

When a grid is applied as explained above, it is difficult to classify the head skin because its resolution is the same as that of the facial muscles and other tissues. In skin tissues, blood at near-body temperature flows through the external carotid artery, which cannot be ignored in terms of heat exchange. Thus, we consider a skin model and assume that the heat quantity is maintained by metabolic heat production and blood flow at near-body temperature.

Thus, in this investigation we implement high-accuracy simulations of the temperature distribution by combining a total of seven models, namely, four MRI-based tissue models having realistic shapes and known physiological parameters, conceptually reconstructed blood vessel and skin models (which are hard to derive from MRI data but cannot be ignored in terms of heat transfer), and an ambient air model.

2.3 Outline of blood vessel model

The main blood vessels of the brain, in the order of blood flow, are the left and right carotid arteries and vertebral arteries that cross at the base of the brain, form the cerebral arterial circle, and then connect to the anterior cerebral artery. The middle cerebral artery branches in front of the carotid artery junction. Blood capillaries provide blood circulation between these arteries and the outside of the brain, so that the large and small blood vessels form a network. Blood flow is concentrates in the venous system via blood capillaries. In particular, blood flow passes to the superior sagittal sinus and straight sinus and branches to the superior anastomotic vein from the superior sagittal sinus. The superior anastomotic vein connects to the middle cerebral artery at the rear of the brain, then branches into the left and right jugular veins. In addition, near this branching point, the posterior cerebral arteries connect after branching from the cerebral arterial circle. Modeling of all these blood vessels is impractical considering the number of nodes, and therefore we model only the average patterns of the main vessels. Thus, in this model, the vessels of the arterial system connect directly to those of the venous system, and capillary branching is ignored. This concept is illustrated in Fig. 3.

Data are moved between the nodes of this blood vessel model so as to represent blood flow in a certain direction. That is, the temperature data of the blood vessel nodes are transferred to other nodes in predetermined directions to represent a pseudo-blood flow with regard only to temperature. The blood flow rate can be set in incremental steps by repeating transfer processes within a certain time period.

In order to represent a reduction in blood flow and other pathologies in specific areas caused by angiospasms due to stroke, trauma, and so on, we set, and change as necessary, the parameters expressing capillary branching and confluence. For example, when blood flow is interrupted in an upstream blood vessel, the blood flow in its branches is also interrupted.

2.4 Parameter setting for each tissue in head model

Table 1 gives the number of nodes in the six tissues of the head model and the ambient air. as well as previously measured data [10, 11] on the initial temperature, thermal conductivity, and specific heat of each tissue. Assuming that the average volume and weight of brain tissues are 0.0015 m^3 and 1.5 kg [11], the volume and weight per node were calculated, and the tissue parameters were converted assuming that the densities of the brain, muscle, and bone were 1050, 1050, and 1500 kg/m^3, respectively. The distance between nodes was set as 6 mm, and the calculation cycle was set to 1 s.

Table 1. Number of nodes and parameters of each organ in head

Property/Organ	Brain	Skull	Eye ball	Blood vessel	CSF	Skin	Air
Number of nodes	13093	24206	172	497	1805	3310	20917
Temp. (deg C)	37.10	35.47	36.57	36.41	35.21	36.57	25.00
Metabolic heat production (W/m^3)	1.34×10^4	0	2.50×10^2	0	0	250×10^2	0
Thermal conductivity (W/(m·K))	5.28×10^{-1}	1.16	8.05×10^{-1}	5.49×10^{-1}	5.99×10^{-1}	9.60×10^{-1}	9.25×10^{-3}
Specific heat (J/(kg·K))	3.68×10^3	1.59×10^3	3.75×10^3	3.47×10^3	3.95×10^3	3.77×10^3	1.01×10^3

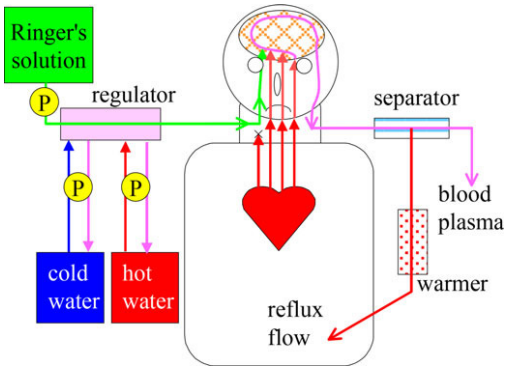

Fig. 4. Scheme of system for control of brain temperature by direct infusion of cooling liquid. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

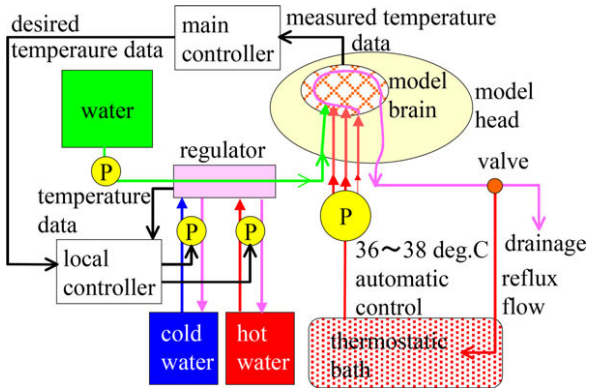

Fig. 5. Outline of experimental system using brain model for temperature control by direct infusion of cooling liquid. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

2.5 Outline of experimental model

In this investigation, we assume a brain temperature control method [9] in which Ringer's solution at an appropriate temperature is infused directly into the internal carotid arteries. In this method, four vessels supplying blood to the brain are taken into account, namely, the left and right internal carotid arteries and vertebral arteries. That is, considering the supply of oxygen and nutrients to the brain, Ringer's solution at an appropriate temperature is infused into one or two internal carotid arteries. Body-temperature blood flowing via the other arteries mixes with the Ringer's solution in the cerebral arterial circle, so that the blood temperature is changed. The blood circulates in the brain while exchanging heat with brain tissues, then flows back to the body via the left and right jugular veins. Blood serum corresponding to the quantity of added Ringer's solution is separated by a separator; upon reaching the appropriate concentration, the blood is warmed with a warmer, and is then returned to the circulation. This method allows temperature control solely of brain tissues. The concept is illustrated in Fig. 4.

In this investigation, assuming model experiments [12, 13] based on the method described, we conducted a simulation using the proposed model. The concept of the model experiments is illustrated in Fig. 5. The temperature in the whole human organism, except for the head, was assumed to fluctuate physiologically within a certain range, and therefore, in the experimental model, the body was simulated by a thermostatic bath, with water circulating instead of blood. Ringer's solution was also replaced with water, and only the excess of the blood substitute flowing out from the brain was discharged through a valve. In addition, the Ringer's solution is adjusted to the target temperature using a heat exchanger. Thus, we consider a regulating tank to mix cold and hot water. The temperature of the cold and hot water tanks is affected by the mixed water returning from the regulating tank, but we assumed that the respective set temperatures were maintained using an intermittently operated cooler or warmer.

Assuming the above experimental model, we consider a control model to change the temperature of the mixed water in the regulating tank so as to obtain the target brain temperature. For this purpose, we performed simulations with the parameters set with regard to tanks' capacities, the temperature regulation performance of the cooler and the warner, the throughput of the pumps, and other conditions.

2.6 Setting of temperature measurement sites

In the clinical measurement of brain temperature, sensors are sometimes applied to brain sites in case of

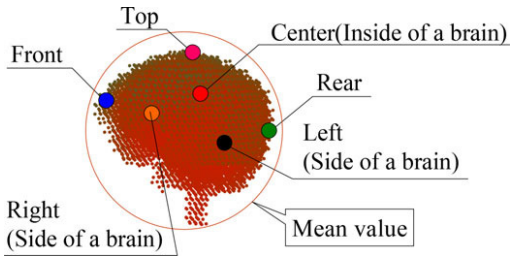

Fig. 6. Places of temperature measurement in brain model. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

craniotomy, but generally the eardrum temperature is taken as the brain temperature so as to avoid infection and injury to the brain. Thus, temperature differences between brain sites are not considered in clinical practice. On the other hand, the temperature data of all nodes can be used in the proposed model, and the mean temperature is calculated for the nodes at six sites, center, top, front, rear, right, and left, as shown in Fig. 6. For the right and left side sites, the nodes closest to the eardrums are selected considering clinical measurement.

2.7 Development of PI control model

Precise control of the brain temperature is required for hypothermia treatment, but manual temperature regulation is used in current clinical practice. There have been investigations aiming at full automation of temperature control so as to lighten the burden of medical workers and to implement stricter temperature control. These studies do not consider temperature distribution in the brain, but there are reports of successful clinical results obtained by taking the eardrum temperature as the brain temperature and applying adaptive control or fuzzy control [5].

In the present investigation, we examined the possibilities of temperature control at specific sites (e.g., inflammation sites) with regard to the temperature distribution, and showed that the temperature at arbitrary sites could be maintained at a target level by PI control, expressed by transfer function (4), where K_p is the proportional gain and T_I is the integration time. The core temperature of the brain is treated as the controlled variable, and the set temperature of the regulating tank (which determines the temperature of the Ringer's solution) is treated as the manipulated variable. Thus, we estimate controllability of the experimental model.

$$G(s) = K_p + \frac{1}{T_I} \cdot \frac{1}{s}. \tag{4}$$

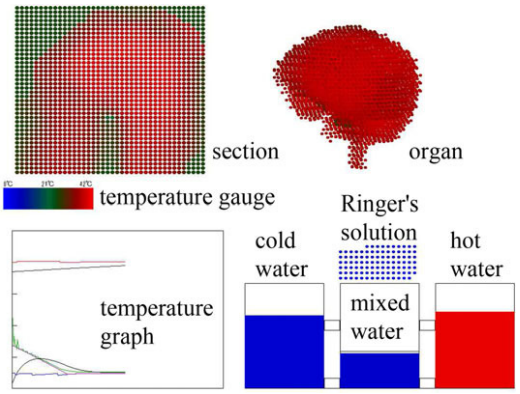

Fig. 7. Visualization during brain temperature control experiment using image indication on screen. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

3. Results of Simulations

3.1 Representation of temperature distribution in brain via simulation

Simulation and visualization using the proposed model are illustrated in Fig. 7. The rectangle (*section*) in the upper left of the diagram is a head section at arbitrary coordinates. The position of the cross-section can be chosen arbitrarily using a PC keyboard. In addition the sagittal plane shown in the diagram can be changed to the transverse plane or coronal plane. In addition, the 3D image (*organ*) at the upper right can be switched among six head tissues. In this example, the brain is shown. This 3D image can be rotated in any direction in the simulations, and the temperature can be observed at any site.

The display color at each node is set as a function of the temperature. The temperature gauge expressing the relationship between temperature and color is shown below the section in the diagram. In this study, the range of the temperature gauge was 0 °C to 42 °C.

The range was set assuming that the hot water used in temperature control was maintained at about 40 °C to prevent low temperature burns, and the cold water was maintained at about 5 °C to prevent frostbite.

The plot of temperature change with time (every 300 s) at every brain site is shown at the lower left. At the lower right of the diagram, the temperatures of the cold water, hot water, and mixed water are shown using the same color representation. The water levels in every tank are shown schematically, taking account of fluctuations in the mixed water tank caused by temperature regulation. The Ringer's solution is initially maintained at room temperature, and its temperature them becomes equal to that of the ambient water as it passes through the heat exchanger. The nodes in the upper part of the mixed water tank represent

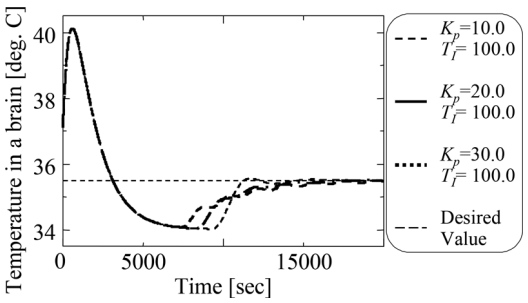

Fig. 8. Temperature dynamics at center of brain model in control with various parameters.

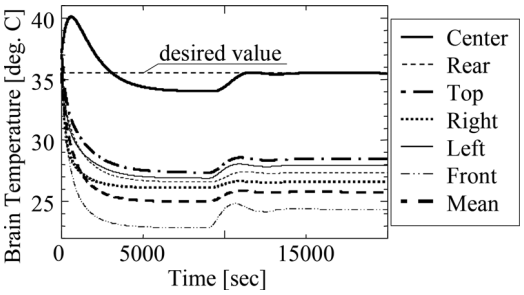

Fig. 9. Dynamics of temperature distribution at center of brain model.

the heat exchanger, and the change from room temperature to the set temperature is expressed by the change of color.

These results show that in the proposed system, the temperature distribution can be visualized consistently not only in human head tissues but also in the water circulating in the experimental system.

3.2 PI control simulation using human head model

As regards the method of temperature control in clinical hypothermia treatment, we conducted simulations with the PI control described above in order to demonstrate the practicability of the model proposed in this study. We set the overall metabolic rate of the brain tissues 2.8 times as high as normal, assuming that metabolism increases due to brain inflammation. Thus, we simulated an abnormal rise in brain temperature. Specifically, when control was not used in the simulations, temperature in the central part of brain settled at about 45 °C. This temperature is physiologically impossible due to protein denaturation; however, we set severe control conditions considering that the simulations were free of disturbances, and that control is easier than in a clinic. Thus, control is performed to cool the central part of brain to the target temperature. The target temperature was first set to 35.5 °C, and the control response was simulated for various proportionality factors K_p and integration periods T_I. The response obtained at $T_I = 100.0$ and varied K_p is shown in Fig. 8. Considering patient safety, limiters were set in the simulations to maintain the temperature of the hot and cold water as mentioned above. Thus, the temperature of the mixed water (manipulated variable) was controlled in the range from 5 °C to 40 °C. Here, we assumed that Ringer's solution was infused into the left and right carotid arteries. In addition, in order to suppress fluctuations around the set brain temperature, a dead zone of ±0.5 °C was provided.

An example of the temporal change of temperature at every part of the brain when the temperature of the central part is controlled is given in Fig. 9. Here, $K_p = 10.0$, $T_I = 100.0$. The graph shows the temperatures measured at the six points set in Section 2.6 and the mean temperature of all nodes. Immediately after the beginning of the simulation, the temperature at the center of brain rises because of heat produced by high metabolism. Aiming at cooling in PI control, cold Ringer's solution is infused, and the temperature in the parts of brain other than the center decreases according to the distance from the blood vessels in which cooled blood flows. When the temperature at the brain center drops below the set value due to the cooling effect, warm Ringer's solution is infused. As a result, the temperature in other parts of the brain rises faster than at the center.

Thus, parts of the brain located closer in the blood vessel model show a greater response than those in the central part. At about 12,000 s, when the temperature in the central part has nearly converged to its set value, the other brain parts also a settling of temperature, and a positional temperature distribution occurs in the brain.

4. Discussion

4.1 Visualization of temperature distribution in brain

Clinical hypothermia treatment takes at least 3 days and may last for about 2 weeks. Considering hypertension caused by brain swelling, microbial infection, and other hazards, continued measurement of brain temperature using sensors is avoided in many cases. Thus, the brain temperature is estimated based on the doctor's experience by measuring the eardrum temperature or bladder temperature [6]. In addition, monitoring data including the bladder temperature are managed centrally. However, numerous values are displayed, and only quite experienced medical workers can promptly perceive the meaning of the displayed information. Thus most medical workers involved in hypothermia treatment cannot afford to examine the temperature distribution in the brain, and the specifics of the affected sites are seldom taken into account.

Visualization of the temperature distribution by means of an intuitive color representation lightens the burden on the clinical staff, promotes shared understanding of information, and facilitates concentration on medical treatment. The proposed system makes possible the visualization of the temperature distribution in the brain, thus providing more useful clinical information than previous models.

4.2 Usefulness of mathematical model of heat transfer

The human head model developed in this study is based on shape construction of virtual objects using dynamic models [7, 8]. In this method, regular tetrahedra are arranged continuously in a coordinate system, and all nodes are assumed to be located at the vertices of the tetrahedra, that is, at coordinate grid points. All nodes are equivalent from the standpoint of calculation, and the algorithms can be unified. Thus, the simulation results reflect only the parameters set at every node and element. In this study, based on this concept, we developed six tissue models using MRI data. In particular, 40 nodes were set in each of the x, y, and z directions. This arrangement was dictated primarily by computing power. A finer grid with a larger number of nodes makes possible more accurate calculations.

In our simulations, the temperature distribution converged after about 10,800 s, that is, about 3 h. In the one-compartment model developed by Wakamatsu and colleagues, the time constant for step input was 3 h [10]; therefore, the simulations of this study seem realistic.

If air temperature, eardrum temperature, and other data that can be actually measured even during hypothermia could be incorporated into the proposed model, and simulation results for the estimation of internal states could be presented in clinical practice, it would provide doctors with criteria to choose a therapeutic strategy. For this purpose, real-time operation is desirable, and the number of nodes must be determined depending on the specific computer's speed and the required calculation accuracy, which is a topic for further research.

On the other hand, there are individual differences in brain shape, and brain temperature distributions adjusted to the patient-specific head tissue shape and pathology could be obtained if there were a method of improving the resolution of the model and extracting shape data from MRI data acquired prior to the beginning of hypothermia treatment. However, faithful reproduction of blood vessels is almost impossible, and the model developed in this study allows the representation of individual differences within a certain parameter range. Thus, one can assume that brain shape matching for every patient is not necessary; this remains a topic for further research.

There is a technology called MRI spectroscopy [14] that makes possible non-invasive measurement of brain temperature using MRI. In hypothermia treatment, MRI images are diagnosed once a day, and the brain temperature might be measured using these data. Such data might be used in combination with the method proposed in this study for data correction, or for parameter identification by internal state estimation.

In the simulations, we assumed an experimental system using direct infusion, and the basic properties of the system components were treated as parameters. This approach makes possible not only simulations of brain temperature control but also estimation of the required performance of the experimental system components at the design stage. It was shown that in the development of a real system, simulation results obtained with the selected component parameters agreed well with the experimental results [13], thus confirming the effectiveness of the proposed model.

4.3 Simulated results

The simulation results show that by using the human head model proposed in this study, control can be based on the temperatures of specific nodes. In this study, we considered stepwise input of the target values but in clinical practice, follow-up control is applied so as to avoid the burden on the patient's body caused by abrupt changes of temperature. For example, the target value is varied gradually so as to change the temperature within 1 °C in 24 h. That is, the actual temperature change is small compared to our simulations, and one can expect a faster response. In addition PI control was used in this study, but it has been shown that adaptive control or fuzzy control is more effective in clinical practice [5]. Thus, simulations with such control methods are a topic for further research.

In addition, one can consider comparison with clinical data obtained with these control methods using compartment models. However, direct comparison is not possible because these methods were applied to whole-body cooling, in contrast to the direct infusion assumed in this study. Therefore, comparison with clinical data would be possible if a similar model were developed for the whole body and simulations were conducted using the same control method as with a cooling blanket.

The temperature at measurement points other than the central area (that is, the temperature of the brain surface) dropped immediately after the beginning of the simulations, which can be explained as follows. In addition to the above-mentioned cooling effects, heat exchange with the skull and spinal fluid, which are not involved in metabolic heat production, resulted in more efficient cooling than in the normal physiological state. In addition there is a natural temperature gradient in the physiological state, but the simulations were started with a uniform temperature in every

tissue, and the transition to temperature equilibrium may have produced some effect. On the other hand, nonskull tissues (simulated muscles, parotid gland, and so on) actually exist in the area defined as the skull model, and there are blood vessels that branch from the external parotid artery in which blood at a near-body temperature flows. These calorific values too cannot be ignored. Thus, the additional skin model should be improved with regard to blood flow, which is a topic for further research.

In contrast to the blood vessel model developed in this study, actual cerebral blood flow covers the whole brain via capillaries, resulting in a strong heat-washout effect. This can be reflected to some extent by the heat transfer coefficients of the brain tissues; however, the blood vessels do not include heat exchange with surrounding nodes, but represent fast flow of heat in a predetermined direction. Therefore, a more detailed blood vessel model including capillary blood flow should be developed for more accurate simulations; this too is a topic for further research.

5. Conclusions

We developed a mathematical model to visualize brain the temperature distribution, representing metabolic heat production and the heat capacity of human body tissues as well as heat transfer coefficients and other characteristics. This model simulates blood flow in blood vessels, and allows arbitrary setting of the inflowing blood temperature. Using this model, we performed simulations of brain cooling in which Ringer's solution adjusted to an arbitrary temperature was introduced into the brain via any of four arteries. We showed that the cooling effect depends on the brain site, and that brain temperature control in brain hypothermia treatment must be performed with consideration of the temperature distribution in the brain.

A summary of this study was reported at the 2011 IEEJ Annual Meeting [15], the 50th JSMBE Meeting [16], and 16th Annual Conference of VRSJ [17].

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