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Paper

Temperature Management Methods for Selective Brain Hypothermia in Variable Metabolism

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Brain hypothermia is widely operated to prevent peripheral healthy brain tissue from secondary damage, caused by increased brain temperature due to hypermetabolism around the damaged areas. Selective brain hypothermia is a new clinical technique of brain hypothermia for a brain disorder. Appropriate solution in a controlled temperature is directly infused into the artery to cool down a brain tissue through some catheters. While the brain temperature is controlled quickly, the body temperature has to be kept within a prescribed range by re-warmed cerebrovascular blood return to the systemic circulation. As metabolic changes in the brain is variable due to the complex behavior of the disease state with the treatment effect. . In the present study two adaptive control methods as adaptive-gain control and Fuzzy-adaptive control are provided to carry out for precise temperature control for selective brain hypothermia. Several kinds of mathematical brain models with cerebrovascular damage are specially used to evaluate our temperature control methods. The effectiveness of the management of the brain temperature is demonstrated for four kinds control laws and five mathematical clinical brain models. © 2021 Institute of Electrical Engineers of Japan. Published by Wiley Periodicals LLC.

Keywords: selective brain hypothermia; brain temperature management; mathematical simulation; adaptive-gain control; Fuzzy-adaptive control

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1. Introduction

Brain hypothermia [1–4] is applied to prevent a brain tissue from further degeneration including secondary damage. In good condition of blood flow, the temperature of the brain tissues is adjusted by blood which circulates and washes out the metabolic fever in the brain. However, metabolic heat production in the damaged brain cannot be equilibrated, the temperature of the brain increases by hypermetabolism around the damaged area. The secondary damage proceeds under the increasing temperature. The standard brain hypothermia ever introduced to cool the damaged area of brain, is easily to apply. The blood temperature has been controlled by cooling patients' trunk and limbs of the body by surface cooling methods. However this therapeutic method requires to be continued from 3 to 14 days under the strict temperature control. In addition, lowered body temperature involves the low immunity of a patient with some possible complications. Moreover the response of the brain temperature to the change of water blanket temperature basically takes long time delay. In order to clear these problems, selective brain hypothermia [5–8], which cools only the head selectively introducing temperature-controlled Ringer's solution into the arteries to the brain through some catheters.

Honma *et al.* [9,10] have tried a mathematical simulator to calculate the cooling effect in selective brain hypothermia, by which was visualized the temperature distribution in the brain. Takagi *et al.* [11] have performed to control the temperature of solid brain models which have same structure of their mathematical models. They have confirmed their good agreement experimental results by using solid brain models and by using mathematical simulations. Honma *et al.* [12] further confirmed in some mathematical simulations that brain temperature was controlled precisely in selective brain hypothermia by switching simple to automatic control methods. The simulations were performed under the conditions of constant metabolism with proper thermal properties of the brain. Thereby, they proposed the new-type Fuzzy controller [12] on the basis of the medical experience of the temperature management under various patient's condition. Then, it has been shown to be able to control the brain temperature at desired value within clinically acceptable range under prescribed condition.

Meanwhile, the patients' condition is often variable due to the treatment effects of various medical procedures, the sudden change in the physiological condition of the patient, the influence of disturbance such as drug administration, and other factors. In such cases, the brain metabolism is variable and the ideal temperature management would not be realized by the temperature control methods as described above. Thus, Honma *et al.* tried so called 'Adaptive-gain + integral control' that adaptively regulates the control gain [13,14] in response to patient metabolic change and 'Fuzzy-adaptive control' [15,16] that adaptively regulates the Fuzzy gain introduced into Fuzzy control [12].

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Sepsis can occur during selective brain hypothermia using catheters, even by sterilized instruments in ICU with hygienically controlled environment, but various kinds of damages to the brain and body tissue caused by imprecise temperature control during brain hypothermia may occur rather frequently. However, it is very difficult to control the brain temperature precisely, since the time constant in the temperature dynamics of the brain is large in individual differences. Therefore, the methods of temperature control are mainly focused in the present study. We propose a several kinds of mathematical brain model with cerebrovascular damage, assuming that blood flow is interrupted by ligation of the blood vessel or edema of the surrounding injury site of the brain tissue. And the practicable brain temperature managements are confirmed by the mathematical simulations considering all combinations of the four control methods and the five disease models, under the conditions where there is no predictive data on patients' properties and their variable metabolism, beforehand.

2. Method

2.1. Outline of mathematical simulation

We have studied temperature management methods by mathematical simulations and experiments of selective brain hypothermia. In this study, we focus only on temperature control assuming that medical procedures are clinically performed with no adverse events. Figure 1 shows a basic block diagram of feedback control that keeps the temperature of brain center, calculated with the human head mathematical model, at a desired value. Some disturbances are given into basic control diagram for the mathematical simulations by Honma *et al.* [9,12] in this study, to approximate the clinical conditions in selective brain hypothermia [2]. Figure 2 shows the outline of selective brain hypothermia. The Ringer's solution is injected into the blood to the brain and washes out the heat in the brain. The temperature of the Ringer's solution is adjusted in the regulator by heat exchange. The temperature of the regulator, which is determined based on the measured brain temperature, is set by mixing cold and hot water. Some kinds of medicines such as intravenous anesthetics, muscle relaxant agents, anti-inflammatory agents, etc. are mixed into a Ringer's solution, but in this study, the mixed infusion solution is regarded as the Ringer's solution. Blood flow in the blood vessels by the injection of Ringer's solution is blocked by a balloon-tipped catheter and/or other methods. For reflux from the head to the trunk, excess water is drained via a separator to regulate blood flow volume, and remaining blood is rewarmed for the returning to the trunk. The human head model is composed of seven elements such as

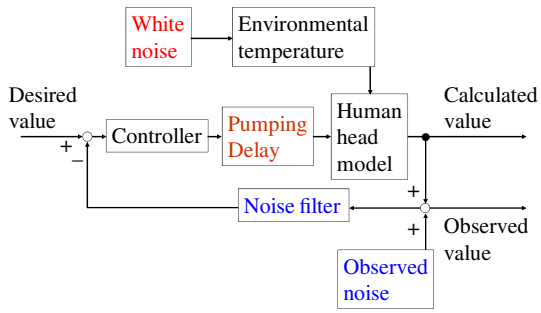


Fig. 1. Block diagram of the mathematical simulations considering various kinds of disturbance

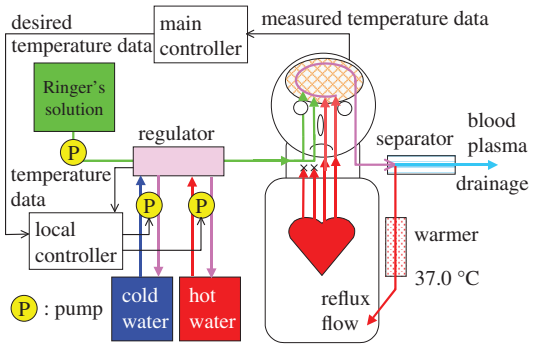


Fig. 2. Outline of selective brain hypothermia

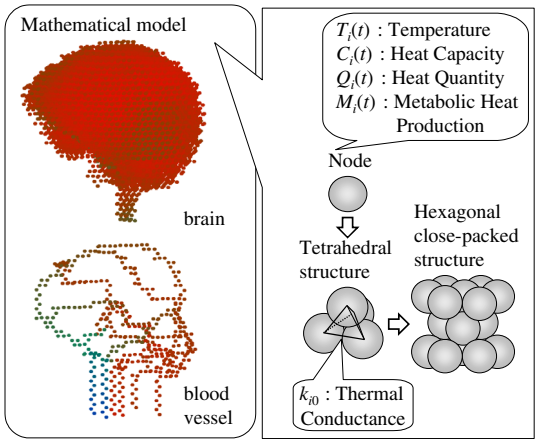


Fig. 3. Outline of heat transfer model

brain, skull, skin, etc. [9,10]. They are constructed with nodes, which is the minimum calculation unit with a diameter of 6 mm, to be arranged evenly in the shape of the human head as shown in Figs. 3 and 4. Each node reflects the thermal characteristics, such as the heat capacity, heat transfer coefficient, and metabolic heat, of 'actual' human brain. In order to reflect the characteristics of experimental devices, delay time and disturbance in the mathematical simulation are given as follows. The delay time is given as 1 s for the Ringer's solution to reach the object by pumping. Room temperature is given as a sinusoidal-like wave whose amplitude is 1.0 °C around the temperature in the room at 1.5 h cycle based on the measured value to be within a definite range by an air conditioner. In addition, white noise within the range of 0.2 °C caused by behavior of medical staffs and actuations of devices are given to the room temperature. Temperature noises within 1.0 °C, raised from the sensor and A/D converter in the experimental devices, are considered to the simulated brain temperature. The observed values, which are defined as brain temperatures, are feed back to the controller through the noise filter.

2.2. Calculation of heat transfer on the regular tetrahedral lattice coordinate system

The human head mathematical model is constructed as collections of nodes arranged at grid points in the regular tetrahedral lattice coordinate system [9,10]. Although the physiological functions of the human body are complicated, this model focuses on only the heat balance and expresses the temperature distribution in the brain. The temperature distribution in a brain is determined by the equilibrium

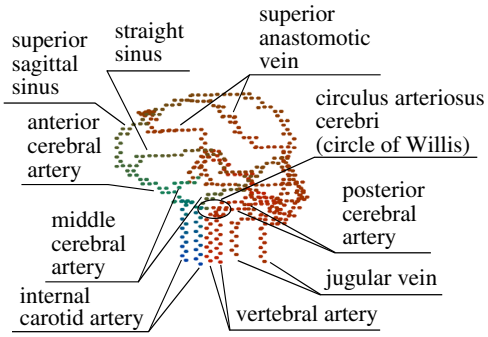


Fig. 4. Outline of mathematical blood vessel model

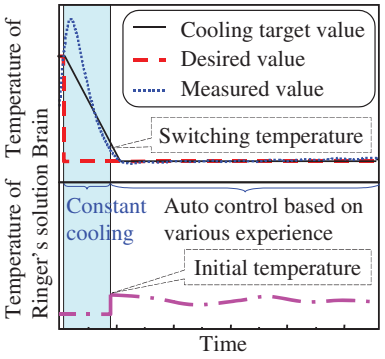


Fig. 5. Cooling patterns switching selective brain hypothermia.

between metabolic heat production and wash-out heat by blood. The shape of each organ in the human head was based on MRI data.

The heat transfer between two nodes can be calculated by Equation (1). In the regular tetrahedral lattice coordinate system [10], one node is connected to 12 neighbor nodes. So, central node as node 0 exchanges heat with neighboring nodes i ($i = 1$–12). The temperature $T_0(t+1)$ of each node at time $t+1$ is calculated using the temperature $T_0(t)$ at time t and the temperatures $T_i(t)$ of the neighboring nodes. Here, k is thermal conductivity, M is metabolic heat production, and C is heat capacity. And, $\Delta T_{i0}(t)$, which is calculated by Equation (2), represents the temperature difference between node i and node 0. Table I shows the parameters for each node belonging to each organ [9]. These parameters were published in some papers [9,10] as the average measured values, which reflect the affects of blood flow, walls of vessels, flow change around the capillary vessels, and blood–brain barrier. In addition, the blood flow is simulated by a sequential shift of temperature to downstream nodes in the blood vessel model.

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

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

In this research, this human head model is the control target. The control input is the temperature of the first node in the blood vessel to the brain, and the temperature of the node located in the center of the brain is observed as output. The disturbance for the environmental temperature is added to the temperature of the node belonging to Air.

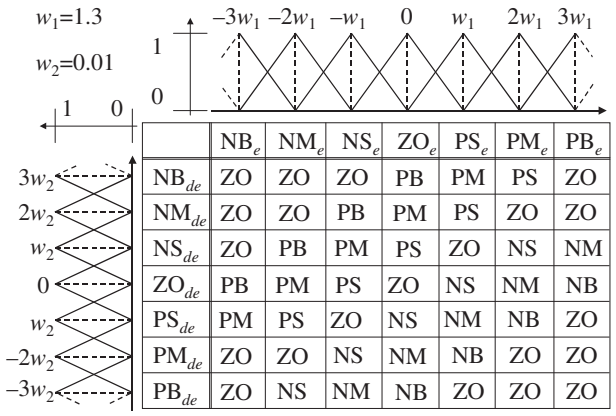
2.3. Outline of switching brain temperature management method Honma *et al.* [12] have proposed a switching cooling method for selective brain hypothermia, that operates by the temperature management based on the control laws after simple- cooling at the beginning. This method brings the brain temperature down rapidly by the infusion of Ringer's solution at a temperature of cold water in case of the rise due to hypermetabolism involving the injury of brain tissue and/or medical surgery. Switching to automatic control of the brain temperature as shown in Fig. 5 reduces the integral amount of deviations including the overshoot amount. Therefore in the case of a patient whose physical condition remains under anesthesia, it is suggested that precise temperature can be within 0.1 °C error, as clinically desired range. The brain temperature to switch the control methods is defined as the switching brain temperature. Even PI controller can manage the brain temperature close to the clinically desired range, when the switching brain temperature and the initial temperature of the Ringer's solution are appropriately set at the time of the concerning switching control method. Fuzzy controller with possible physical properties of the human head and the medical procedure, etc. expected to be more precise control temperature with lower patient's burden.

2.4. Conventional control method Homma *et al.* have studied the method of brain temperature management by PI control and/or Fuzzy control in the mathematical simulation [9,12]. In PI control are given proportional constant $K_p = 20.0$ and integration coefficient $T_I = 100.0$ [9]. These values were determined by trial and error method.

Homma *et al.* also have proposed a special Fuzzy control law considering the time constant of human brain being about 3 h and the metabolic heat production in a human head [12]. Figure 6

Table I. Basic parameters of each organ in a head

Variable Property organ	$T(0)$ Initial temp (°C)	$M(t)$ Metabolic heat production (W/m^2)	k Thermal conductivity (W/m/K)	$C(t)$ Heat capacity (J/kg/K)
Brain	37.10	1.34×10^4	5.28×10^{-1}	3.68×10^3
Skull	35.47	0	1.16	1.59×10^3
Eye ball	36.57	2.50×10^2	8.05×10^{-1}	3.75×10^3
Blood vessel	36.41	0	5.49×10^{-1}	3.47×10^3
CSF	35.21	0	5.99×10^{-1}	3.95×10^3
Skin	36.57	2.50×10^2	9.60×10^{-1}	3.77×10^3
Air	25.00	0	9.25×10^{-3}	1.01×10^3



	NB_e	NM_e	NS_e	ZO_e	PS_e	PM_e	PB_e
NB_{de}	ZO	ZO	ZO	PB	PM	PS	ZO
NM_{de}	ZO	ZO	PB	PM	PS	ZO	ZO
NS_{de}	ZO	PB	PM	PS	ZO	NS	NM
ZO_{de}	PB	PM	PS	ZO	NS	NM	NB
PS_{de}	PM	PS	ZO	NS	NM	NB	ZO
PM_{de}	ZO	ZO	NS	NM	NB	ZO	ZO
PB_{de}	ZO	NS	NM	NB	ZO	ZO	ZO

Fig. 6. Membership function and Fuzzy rule

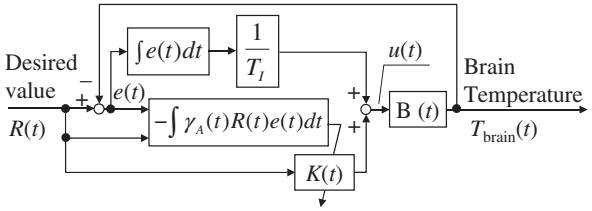


Fig. 7. Block diagram of integral control system with adaptive-gain regulation

shows the membership function of the law. Although membership functions are well given in the Fuzzy control beforehand, brain temperature might be out from the predefined range due to sudden change in patient's metabolism during selective brain hypothermia process. However, the brain temperature would not be controlled even if the patient's life could be threatened. In such a case, the Fuzzy labels remain for those regions as PB or NB, when they exceed the range predefined in the membership function.

2.5. Construction of adaptive-gain and integral control method It may be difficult to manage the brain temperature that the control method designed beforehand under metabolic rate variations caused by individual difference or physical condition of patients and/or difference of the medical treatments. The surface cooling type brain hypothermia with an adaptive controller [14,16] has been expected to realize a good temperature management by the regulation of control parameters relied on patient's condition. The response based on time constant of the control object in selective brain hypothermia which cools only patient's head is quicker than that in the surface cooling brain hypothermia by the whole body cooling. Furthermore the vibration to settle to the desired brain temperature with the simple Adaptive-gain controller [16] is not healthy, so it may not be desirable in consideration of the physical burden on patients. Therefore, 'Adaptive-gain + integral control' [14,16] (below referred to as Adaptive-gain control), in which the coefficients of Adaptive-gain algorithm were set small. Figure 7 shows the block diagram of the controller.

The temperature $u(t)$ of the Ringer's solution infusing into the brain model $\mathbf{B}(t)$ is calculated using the desired brain temperature $R(t)$ at time t and the Adaptive-gain $K(t)$ by the Equation (3). Here, $e(t)$ is a deviation between $R(t)$ and the observed value $T_{\text{brain}}(t)$ as shown in the Equation (4), and the integration coefficient $T_1 = 100$ [9]. Also the Adaptive-gain $K(t)$ is successively regulated according to Equations (5) and (6).

$$u(t) = K(t)R(t) + \frac{1}{T_I}\int e(t)dt \tag{3}$$

$$e(t) = R(t) - T_{\text{brain}}(t) \tag{4}$$

$$\Delta K(t) = -\gamma_A(t)R(t)e(t) \tag{5}$$

$$K(t+1) = K(t) + \Delta K(t) \tag{6}$$

Here, $\gamma_A(t) = 1.53 \times 10^{-6}$. This value has been determined by trial and error method.

2.6. Construction of Fuzzy-adaptive control method The Adaptive-gain control in Section 2.5 is similar to the PI control of introducing the adaptive algorithm. Therefore, it is expected to consume energy for temperature adjustment, even after converging at the desired value. However, the available electrical power for temperature management is limited in clinical practice. Therefore, another temperature control algorithm for the brain temperature management with less energy consumption is required to be suitable to the patient's physical condition. Then we proposed Fuzzy-adaptive controller [15,16], which can response to the change in metabolic rate caused by individual or physical condition of patients, on the basis of Fuzzy controller which consume less energy. Figure 8 shows the block diagram of the control system.

For this purpose, Fuzzy gain $f_g(t)$ at time t is introduced into Fuzzy control law. We constructed Fuzzy-adaptive control system [14,16] which regulates $f_g(t)$ adaptively using the desired brain temperature $R(t)$ and the heat capacity $C_i(t)$ and heat transfer coefficient $k_{i0}(t)$ of the nodes constituting the mathematical brain model. $f_g(t)$ is adjusted according to the transition of metabolic rate.

The temperature of Ringer's solution $u(t)$ is calculated by the Equation (7) by multiplying $\Delta u(t)$ calculated by the membership function of Fuzzy control by the Fuzzy gain $f_g(t)$. The initial value of Fuzzy gain $f_g(t)$ is 1 and it is successively adjusted according to Equation (8). If $f_g(t) = 1$ is fixed with the previous regulation, it agrees with the conventional Fuzzy control [6].

$$u(t) = u(t-1) + \Delta u(t) \times f_g(t) \tag{7}$$

$$f_g(t) = f_g(t-1) - \gamma_F(t)\xi(t)\Delta e(t) \tag{8}$$

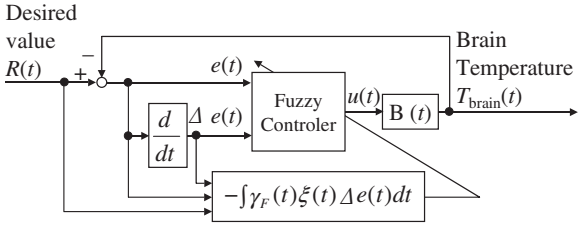


Fig. 8. Block diagram of Fuzzy-adaptive control system

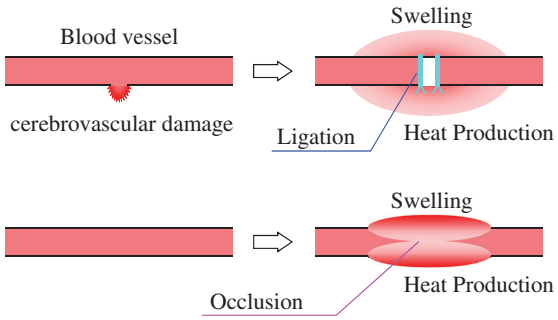


Fig. 9. Concept of metabolic heat production due to interruption of blood flow

Here, $\Delta e(t)$, $\xi(t)$, $\gamma_F(t)$ are given by Equations (9)–(11).

$$\Delta e(t) = e(t) - e(t-1) \tag{9}$$

$$\xi(t) = e(t)/C_i(t)/k_{i0}(t) \tag{10}$$

$$\gamma_F(t) = \gamma_A(t) \times \{0.75 - (R(t) - 35.0) \times 0.25\} \tag{11}$$

2.7. Concept of disease brain model The brain model developed in the previous studies [9,11] has been focused only on metabolic heat production, not considering the decrease in blood flow. However, cerebrovascular damage, ligation of blood flow by surgical treatment or occlusion of blood vessels due to edema of tissues around the injured site, etc. causes uneven blood flow. And the ability of the blood flow to wash out heat decreases particularly in the site where the metabolic heat production increases. From this viewpoint, we constructed some mathematical brain models with description of the disease in terms of heat production and blood flow simultaneously as shown in Fig. 9 [15].

In the present case, metabolism in the brain is increased, and blood flow in one or other specific blood vessels is blocked, and metabolic heat production of surrounding tissues is set to 1.2 times in our disease brain model simultaneously. Specifically, in the human head mathematical model, an appropriate parameter is given to each cerebrovascular model composed of 20 major intracerebral blood vessels referred to the 'actual' human brain vessel. And the interruption in each arbitrary blood vessel and the metabolic heat production can be switched setting to the suitable parameters. Blood flow is interrupted in damaged blood vessels and other blood vessels connected to the downstream, but some remains healthy vessels with normal metabolic heat production.

2.8. Conditions for temperature management simulation The effectiveness of the temperature management systems with Adaptive-gain control or Fuzzy-adaptive control is evaluated by temperature control in mathematical simulation of selective brain hypothermia. Brain temperature management system starts to control the temperature to the desired value (35.0 °C) by the switching cooling pattern in Fig. 5 when the brain metabolism is accelerated and the cerebral temperature rises from the initial temperature of 36.3 °C and reaches 39.0 °C. The brain temperature management simulations calculate about 20 000 s (about 5.5 h) of introduction. The flow rate of blood circulating in the brain and Ringer's solution were set to 50 and 25 ml/min, respectively [11]. This means that the part of the blood flow from the trunk to the brain is blocked to 25 ml/min, adding 25 ml/min of Ringer's solution to keep the total blood flow at 50 ml/min that originally circulates in the brain.

Temperature managements are simulated under the combination of (a) control method, using four control algorithms of PI control [11], Fuzzy control [12], Adaptive-gain control and Fuzzy-adaptive control (b) blood vessel interruption and (c) variation of cerebral metabolism.

We used five kinds of the brain model to confirm the effectiveness of the control algorithms in the simulations. One is the conventional (Normal) model with no interruption of the blood flow. The other four are the disease brain models with interruption of the blood flow. The brain models are deficit models of some components, such as right-middle cerebral artery, left-middle cerebral artery, right-posterior cerebral artery, and left-posterior cerebral artery, respectively. We also considered the cases of metabolic production in the brain both constant and variable. Here, we defined the ratio of heat production to basal metabolism of brain tissue as Ratio to basal metabolism (RBM), and initial value of RBM as initial ratio to basal metabolism (IRBM). Meanwhile, variable metabolism is given as the cases where the metabolic rate gently declines from the initial value to about 1.3 times of the basal metabolism according to a sinusoidal-like curve in this study. In addition, small white noise as disturbance within 0.1 times of basal metabolism is given to variable metabolism. No predictive data on patients is given at the beginning of treatment in all present cases. In the case of switching methods from simple cooling to automatic control with the initial temperature of the Ringer's solution are preset in this study. The preset values have been determined based on data obtained from the temperature management simulations in Fuzzy controller under the condition of constant metabolism.

In this study, we defined the temperature not at the damaged part but from the center of the brain as 'brain temperature', for a comparison of all diseased brain and conventional brain [9,12].

The procedures of brain hypothermia started after the brain temperature rose. Therefore, the differences between the brain temperature and the desired value are large at the start of the treatment. In this study, the control laws were evaluated from the viewpoint of exact temperature control. Thus, the control result of automatic control, shown in the yellow part in the graphs, which switched from simple-cooling procedure, was discussed.

3. Results of Brain Temperature Management Simulation

3.1. Results of brain temperature management simulation using modified control methods We simulated some temperature managements in selective brain hypothermia with four control algorithms of PI, Fuzzy, Adaptive-gain control, Fuzzy-adaptive control, in constant metabolism and in variable metabolism, respectively. IRBM was set according to 2.4, assuming that the blood flow was not interrupted by brain damage in these simulations as normal model.

Figure 10(a) shows the control results of the brain temperature management simulation in constant metabolism. After brain temperature decreased during simple cooling, and switching to automatic control, the temperatures were kept by Fuzzy control and Fuzzy-adaptive control within 0.1 °C deviation from the desired value. On the other hand, by PI control or Adaptive-gain control, brain temperatures were kept within about 0.3 °C from the desired

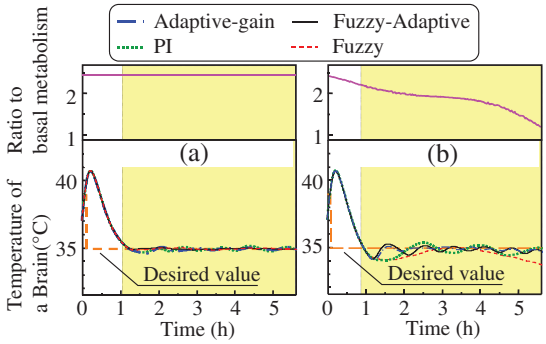


Fig. 10. Results of brain temperature control due to four different control methods: (a) In constant metabolism (b) In variable metabolism

value. After that, the temperatures return to the desired value, and settle with the continuous vibration within 0.15 °C from the desired value.

Figure 10(b) shows the results of the brain temperature management simulation in variable metabolism. Brain temperature decreased about 1.0 °C from the desired value after switching to automatic control in all the control methods. After that, the temperature approached the desired value in vibration. The temperature by Fuzzy control law was realized the less deviation from the desired value in about 4 h in the case of constant metabolism. After that, the temperature decreased according to the variable metabolism and the maximum undershoot of the controlled temperature was more than 1.0 °C. In contrast, the temperatures by Fuzzy-adaptive control or Adaptive-gain control was approaching the desired value while damping oscillation. The temperature response by the PI control was slower than the above ones' results by two control methods, approaching oscillatory within 0.5 °C from the desired value.

3.2. Results of brain temperature management simulation considering interruption blood flow in the brain

The results in Section 3.1 show that the brain temperature can be converged by Adaptive-gain control and Fuzzy-adaptive control even in variable metabolism. So the brain temperature managements were simulated in five brain models, which were four models with and one without blood flow interruption in variable metabolism, whose IRBM was 2.4 times of healthy model.

Figure 11(a) shows the results by Adaptive-gain controller, and Fig. 11(b) shows the results by Fuzzy-adaptive controller. No significant deviation in both control methods was found among the disease brain models with blood flow interruption in the left and right-posterior cerebral arteries and without blood flow interruption model. On the other hand, when the blood flow in the left and right-middle cerebral arteries was interrupted, the delay of the temperature response did not decrease and the difference in responses between the left and right were confirmed.

Brain temperature was settled within 0.1 °C around the desired value in about 2 h by Adaptive-gain control. In contrast, the brain temperature controlled by Fuzzy-adaptive control approached the desired value while damping oscillation. It kept deviations within 0.5 °C around the desired value although it has not been settled within the time of simulation.

Next, for each of Adaptive-gain control and Fuzzy-adaptive control, temperature managements were simulated for cases where

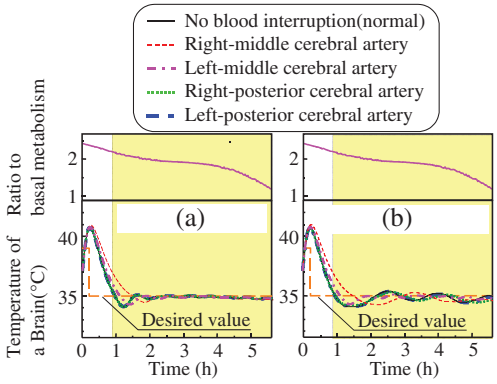


Fig. 11. Comparison of the brain temperature management by adaptive-gain and Fuzzy-adaptive control methods in variable metabolism with five different brain models: (a) Adaptive-gain control (b) Fuzzy-adaptive control.

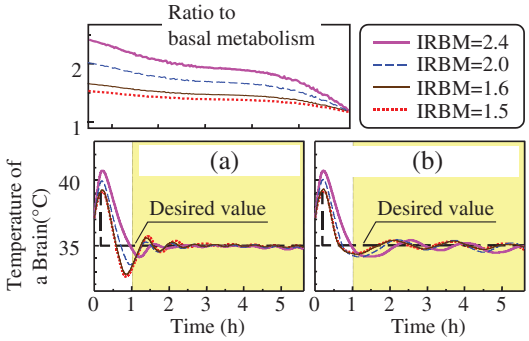


Fig. 12. Comparison of the brain temperature management in right-middle cerebral artery model by adaptive-gain and Fuzzy-adaptive control methods in variable metabolism from four different IRBM: (a) Adaptive-gain control (b) Fuzzy-adaptive control.

the IRBM in variable metabolism were 2.4 times, 2.0 times, 1.6 times, 1.5 times of the value in healthy brain, respectively. The interrupting blood flow of the right-middle cerebral artery was applied for the disease brain model in the simulations. Figure 12(a) shows the results in Adaptive-gain control, and Fig. 12(b) shows the results in Fuzzy-adaptive control.

Brain temperatures were settled respectively within 0.1 °C from the desired value in a maximum of about 2.5 h in the Adaptive-gain control although the time differs for each IRBM. However, the smaller IRBM, the greater undershoot from the desired value immediately after switching to automatic control, and there was a case that the decrease reached by about 2.5 °C. In Fuzzy-adaptive control, even if IRBM decreased, undershoots from the desired value immediately after switching to automatic control were within 1.0 °C. Although it took a long time to be settled, the deviations from the desired value were kept within 0.5 °C. The concerning result suggested that practical temperature management would be possible by Fuzzy-adaptive control.

3.3. Comparison of control methods focusing on energy consumption

The energy consumptions of the brain temperature management systems in Adaptive-gain control and Fuzzy-adaptive control methods, respectively, were analyzed

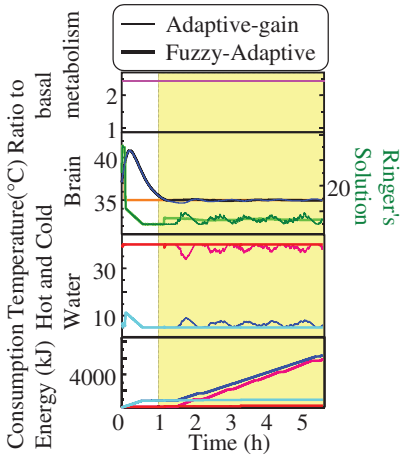


Fig. 13. Relation between control methods and energy consumption in the selective brain hypothermia in constant metabolism

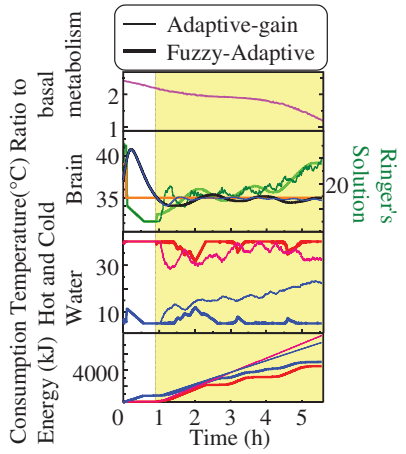


Fig. 14. Relation between control methods and energy consumption in the selective brain hypothermia in variable metabolism

using the disease brain model with no blood flow interruption. Figures 13 and 14 show brain temperature (solid line), Ringer's solution temperature (dotted line), hot water temperature (broken line), cold water temperature (dot-and-dash line) and the energy consumption trends. In these figures, the thin lines indicate the results by Adaptive-gain control, and the bold lines indicate the results by Fuzzy-adaptive control.

Figure 13 shows the results on the constant metabolism. Since Adaptive-gain control used hot water and cold water to regulate the temperature of Ringer's solution frequently, a heater and a cooler keep the water temperature with consuming the energy of about 6000 kJ in about 6 h. In contrast, the temperature of Ringer's solution did not change so much after switching to automatic control by Fuzzy-adaptive control method. It shows that little energy was consumed except for using cooler at simple-cooling of about 1000 kJ.

Figure 14 shows the results in the cases of the variable metabolisms. The temperature of Ringer's solution is frequently regulated by Adaptive-gain control and Fuzzy-adaptive control, respectively. The temperature change of Ringer's solution by Fuzzy-adaptive control was more gently than that by Adaptive-gain control. It means that Fuzzy-adaptive control used hot water and cold water less frequently than Adaptive-gain control, and the waters returned to set temperature quickly by heater and cooler, and energy consumption was decreased. The energy consumption by the heater was about 8000 kJ and the cooling energy consumption was about 7000 kJ by the Adaptive-gain control, whereas both the heating and cooler energy consumption were about 4000 kJ by Fuzzy-adaptive control. The energy consumption by Fuzzy-adaptive control has shown to be smaller than by Adaptive-gain control in the case of constant metabolism.

4. Discussion

In the present study, some disease models are proposed as the targets of temperature control. These models have some blood flow interruption and hypermetabolism. It is reported that brain temperature has been precisely controlled in brain hypothermia with cooling blankets, even when the brain tissues were swollen and blood flow was almost interrupted [4]. Therefore, our disease model is considered to correspond to one of the clinical cases.

Adaptive-gain control and Fuzzy-adaptive control were newly proposed for the temperature management of selective brain hypothermia on variable medical condition. We compared their capabilities of the temperature management in the mathematical simulations by PI control and Fuzzy control methods ever proposed. Thereby, we proposed a several kinds of disease brain model to simulate the patient's physiological condition obtained from some combinations of variable metabolisms and interruption of blood flow in some brain blood vessels. Basically, the metabolism of the patient's brain does not change rapidly due to improvement of the disease condition under brain hypothermia although medicinal substances administered by infusion of solution for the patient's treatment temporarily could induce the patient's rapid metabolism change. The brain temperature should be controlled well even in such clinical situation. So the cases of declining metabolic rate during several hours were also discussed in the simulations.

The results of the simulations with prescribed value of the switching temperature shown in Fig. 10 suggested that any of four controllers can keep the brain temperature of almost desired value as in the base of the metabolism was constant. Although the prescribed switching temperature is not appropriate for all combinations of four control methods and four disease brain models. It is tentatively considered at least effective as there assumed to given no precise physical data of a patient at the introduction of the relevant treatment. When the blood flow was not interrupted, the results in Fig. 10 suggest that our controller can manage the brain temperature, even if the heat production rate became over twice than in normal state. Thus, present two Fuzzy and Fuzzy-adaptive control methods can control the brain temperature precisely within clinically acceptable range. However, only Fuzzy control method cannot control the brain temperature precisely if brain metabolism is not constant or some of blood flow in a brain is interrupted. Adaptive-gain control method and Fuzzy-adaptive control method which regulate the control parameters according to the patient's condition are confirmed that they can control the brain temperature around desired temperature in the same conditions. PI control method tends to take time to settle than the two 'adaptive' controls, although it decreases the oscillatory change of brain temperature to the acceptable range.

Next, the results on five kinds of disease brain model shown in Fig. 11(a) suggest that Adaptive-gain control method can control the brain temperature precisely even some of the blood flow in the brain are interrupted. However, the results shown in Fig. 10(a) suggest that the temperature may drop from the desired value in the decreasing process of brain metabolism. The results shown in Figs. 11(b) and 12(b) suggest us that the settling time to the desired value by Adaptive-gain control method may be shorter than that by Fuzzy-adaptive control method. Our blood vessel models are asymmetric because they imitate the actual human vessels which have lateralities in shape even in a pair of right-and-left blood vessels. These differences would produce the almost similar results in some clinical cases.

But the deviations of the temperature by Fuzzy-adaptive control remain within about 1.0 °C, even in any kinds of the disease brain or any value of IRBM. Furthermore, the results shown in Figs. 13 and 14 suggest the energy consumption by Fuzzy-adaptive control is smaller than that by Adaptive-gain control.

The results given in Figs. 10–14 show that the temperature could be controlled within a certain range of error even if the metabolic heat production or the disease condition were variable. And the proposed control laws were also confirmed by their performances from the viewpoint of stability.

These simulations being given the characteristic value of the experimental apparatus calculate the brain temperature realistically. So it would be theoretically possible to control the brain temperature by Adaptive-gain control method, within the electric power supplied at bedside. However the energy consumption efficiency might be reduced in some actual systems as the followings.

On the shortage of electric power by unexpected more energy consumption, the system may likely to be out of control. In these cases, adaptive-gain control method had better not be selected at introduction term of the selective brain hypothermia because the brain metabolism would be variable. In contrast, Fuzzy-adaptive control method has lower energy consumption. The energy is stored in hot and cold water, and the control method cut down consuming hot and cold water. So it is desirable at introduction term.

Considering these results, it may be effective to switch the control methods from Adaptive-gain to Fuzzy-adaptive when the deviation between the brain temperature and desired value decrease within 0.5 °C. This procedure will enable both to reduce energy consumption and to control the brain temperature precisely. It is desirable to automate switching of the temperature management in the future study. Thus, the various results of this study are significantly important for the design of temperature management system for clinical use of our future works on selective brain hypothermia.

The tympanic temperature can be clinically regarded as an average brain temperature for our control, while a temperature of the brain center was used in the present study as a target temperature. It is because the tympanic temperature is regarded as the brain temperature in a variety of brain hypothermia clinically, although it does not match up the brain temperature precisely. It is difficult to wash out heat from this area where remains the relatively higher temperature, even if the brain has normal metabolism. Our main purpose was hereby to realize two basic control laws for an appropriate brain temperature in the process of selective brain hypothermia. Thus, we have a further plan to develop some useful algorithms which calculate the temperature distribution in the brain using tympanic and some blood flow temperatures. This algorithm will enable us to identify each parameter during brain hypothermia for the calculation of internal brain state.

5. Conclusion

In the study, we proposed Adaptive-gain control and Fuzzy-adaptive control methods supposing the cases of patient's variable metabolism. Both the methods adaptively regulate the control system according to the patient's condition. Adaptive-gain control was suggested to be able to control the brain temperature desired value precisely. Fuzzy-adaptive control was suggested to be able to regulate well the brain temperature with less energy. And we proposed the disease brain mathematical model with some of blood vessels interrupted blood flow and partly increased metabolism around the tissue to examine the effectiveness of the control algorithms. These models were confirmed to express a variety of the heat properties. In the cases of emergency medical treatment where precise patients' condition was unknown, temperature management on each control method with preset data was suggested to be useful by our mathematical simulations.

New medical technologies should be confirmed for the safety of patients and medical staffs. Thus, mathematical investigations are necessary for the first important steps of the research before some biological and clinical applications are introduced. Our study is now being on the way to the future clinical applications by developing a new temperature control system for more effective selective brain hypothermia.

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