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ORIGINAL ARTICLE

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Adaptive control of brain temperature for brain hypothermia treatment using Stolwijk-Hardy model

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Abstract An automatic thermal control system is proposed for the treatment of cerebral injury and inflammation. The system is based on the reference model adaptive control method. It works adaptively according to the difference between individuals, and chronic change of the patient's physiological state, and changes in the environmental conditions. Using the human thermal system of the Stolwijk-Hardy model, the brain temperature is dynamically related to the ambient temperature of the head, trunk, and extremities and their metabolic heat production. The dynamic characteristics of brain temperature under various physical conditions, as examined by simulation experiments, provide improved understanding of clinical brain cooling treatment, which simultaneously give good evidence for the validity of the model. The brain temperature is adaptively controlled in accordance with the appropriate physiological state suggested by various clinical experiences. This kind of adaptive control system is useful for the practical implementation of automatic hypothermia control in seriously injured or inflamed brain.

Key words Brain cooling · Biothermal simulation · Reference model · Automatic control

1. Introduction

It is necessary to maintain hypothermia for a definite period in the treatment of serious brain injuries caused by internal or external causes. It is inevitable that the desired range of brain temperature, as prescribed by pertinent doctors, will be reached, although its accurate control is difficult and laborious. It is thus clinically necessary to control the brain temperature of patients in a simple, fast, and safe manner by theoretically sound methods.

On the other hand, various human biothermal models have been proposed and have been widely applied to medical and/or engineering domains, because they represent human internal thermal dynamics with its relation to environment.[1–5] Stolwijk and Hardy divided the human thermal system into head, trunk, and extremities. Furthermore, the head was divided into shell and core, the trunk into surface (skin and subcutis), muscle, and core, and extremities into surface and core, with an additional blood compartment in the center of the trunk. The lumped model is composed of three segments with eight compartments. Consequently, the Stolwijk–Hardy (SH) model has been regarded as a standard human thermal model, which can be readily applied to many fields for the study of human thermal characteristics.

The model proposed by Stolwijk and Hardy[1] is introduced as a whole-body dynamic thermal model. An appropriate control system for using the model is proposed to allow regulation of brain temperature so that the procedure is independent of the various internal and external conditions of brain-injured patients.

This study concerns the clinical system for this new therapy, including the development of the necessary hardware. It will offer a high-quality biofunctional control method, which can operate according to the difference of individuals patients, their nonlinearity, and changes in the state of environmental conditions.

2. Basic concept of controlling brain temperature

2.1 Effectiveness of hypothermic brain

The clinical effect of hypothermia was first proven useful for the treatment of head injury.[6] Hypothermia has been applied to severely brain-damaged patients with injuries such as external head injury and cerebral hemorrhage. Its effectiveness has been proved by various clinical studies and

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animal experiments.[7,8] Well-known experiments using dogs discovered a decrement of 6.7% in brain circulatory blood flow for every 1°C decrement in body temperature.[7] The experiments are regarded as forming the first study of the mechanism of the protective reaction of brain nerves brought about by hypothermia. Meanwhile, the mechanism concerned has been clarified according to the progress of molecular cytology. Among various hypotheses, selective neuron death based on glutamate-potassium theory has been expected to be its main causality.[7,9,10]

On the other hand, from a macroscopic view of hypothermia treatment, various brain cooling methods including selective cooling of the head, as shown in Fig. 1, have been tried in clinics.[11,12] In time, both positive and negative aspects of whole-body cooling have been clinically recognized. Meanwhile, an intensive-care procedure was established,[12] in which control of the whole-body temperature was applied in order to control of brain temperature, adopting the so-called step-by-step brain-cooling method. The rate of successful treatment has gradually increased in achievement of neural protection avoiding its side effects by hypothermia of body, and taking advantage of its protective effect for neurons as much as possible.[7,12]

Hypothermia has been tried in neonatal cases.[13,14] It has been proven effective in both the short and/or long term.[10,15,16] It should, however, be noted that hypothermia has some problems in its application which yield some bad or no special effects,[17] unless the protective and invasive effects have been well understood in individual patients beforehand.[10,18]

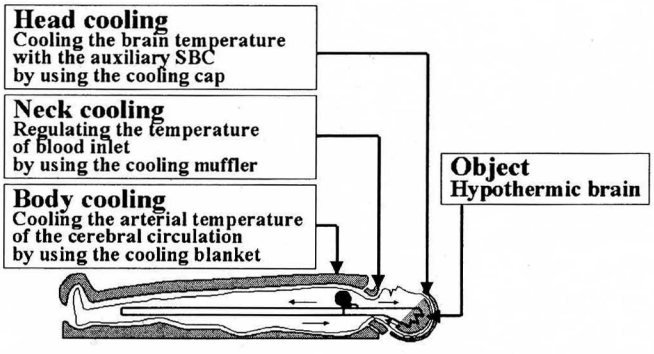

Fig. 1. Management of temperature of head, body, and extremities in brain hypothermia treatment. Body cooling is achieved by circulating cold water through blanket, muffler, and cap. *SBC*, selective brain cooling

2.2 Control of body and brain temperature in hypothermia therapy

The critical condition of patients with brain injury and inflammation can be effectively stabilized by hypothermia treatment. However, a harmful side effect on the patients caused by this treatment is the decrease in immune activity at lower body temperature.

In order to avoid such negative effects, it has been proposed to clinically control stepwise change in patient temperature over a long period.[3] That is, the brain temperature is controlled in accordance with clinical experiences of the step-by-step temperature course as indicated in Fig. 2. It is noted that the body temperatures of about 32°C and 35°C are clinically essential, and should be attained with care, because temperature around 35°C is regarded as the "adaptive zone" and around 32°C is the "critically dangerous zone" for maintenance of the patient's life.

The desirable characteristics are realized by cooling of the head, trunk, and extremities by using a cooling blanket and some other materials with the help of cooling water. The water flow is regarded as constant in all considerations of hypothermia in this study, because of the theoretical nature of the discussion; however, flow control in the cooling blanket has often been applied according to clinical signs.

In the case of seriously brain-injured patients, the maintenance of long-term constant brain temperature is necessary. As the direct clinical experiment is restricted in such a clinical study, simulation experiments are useful in order to develop new concepts, methods, and necessary apparatus for the exact comprehension of the treatment in their clinical application.

3. Representation of human thermal dynamics

3.1 Mathematical human thermal model

Figure 3 shows the Stolwijk and Hardy human thermal model (SH model), which is introduced in the present study.

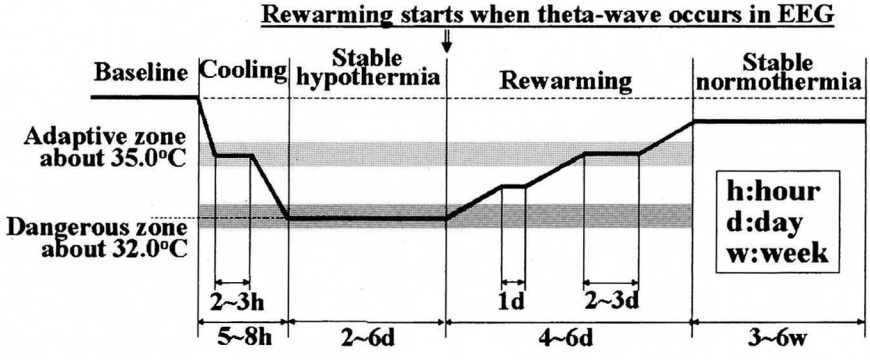

Fig. 2. Step-by-step management of body temperature in brain hypothermia treatment.[7] The temperature curve is based on clinical experience, according to which the patient's brain temperature is controlled by doctors. *EEG*, electroencephalogram

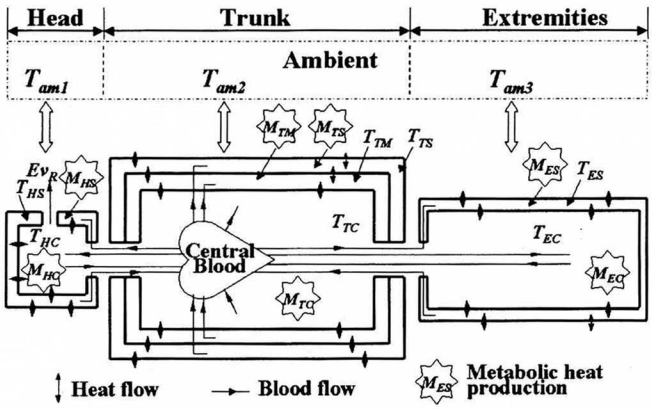

Fig. 3. Revised Stolwijk and Hardy model.[1] T, temperature; M, basal metabolism; Ev_R, heat loss assigned to the respiratory heat dispersion; T_{am}, the water temperature

In the SH model, for the sake of convenience, the body is separated into the three parts of the head, trunk, and extremities, to which a blood compartment is added at its center. Each part has the core and skin separated by cocentric cylinder. Thus, the bioheat transfer process is systematically represented by eight differential equations.[1] If the environmental temperatures around head, trunk, and extremities are respectively assigned to the SH model, the whole system is represented by the following state equation:

$$\frac{d\boldsymbol{T}(t)}{dt} = \boldsymbol{A}\boldsymbol{T}(t) + \boldsymbol{B}\boldsymbol{U}(t) + \boldsymbol{Q} \tag{1}$$

where its state vector is

$$\boldsymbol{T}(t) = \left[T_{\mathrm{HC}}(t) \quad T_{\mathrm{HS}}(t) \quad T_{\mathrm{TC}}(t) \quad T_{\mathrm{TM}}(t) \quad T_{\mathrm{TS}}(t) \quad T_{\mathrm{EC}}(t) \quad T_{\mathrm{ES}}(t) \quad T_{\mathrm{CB}}(t)\right]^T.$$

The input vector is

$$\boldsymbol{U}(t) = \left[T_{\mathrm{am1}}(t) \quad T_{\mathrm{am2}}(t) \quad T_{\mathrm{am3}}(t)\right]^T$$

which consists of the neutral temperatures given by $\boldsymbol{T}_{\mathrm{am1}} = \boldsymbol{T}_{\mathrm{am2}} = \boldsymbol{T}_{\mathrm{am3}} = 30°\mathrm{C}$ so that the heat transfer coefficients may remain the same value as suggested by Stolwijk and Hardy.[1]

The constant vector is

$$\boldsymbol{Q} = \left[\frac{M_{\mathrm{HC}} - Ev_{\mathrm{R}}}{C_{\mathrm{HC}}} \quad \frac{M_{\mathrm{HS}}}{C_{\mathrm{HS}}} \quad \frac{M_{\mathrm{TC}} - Ev_{\mathrm{R}}}{C_{\mathrm{TC}}} \quad \frac{M_{\mathrm{TM}}}{C_{\mathrm{TM}}} \quad \frac{M_{\mathrm{TS}}}{C_{\mathrm{TS}}} \quad \frac{M_{\mathrm{EC}}}{C_{\mathrm{EC}}} \quad \frac{M_{\mathrm{ES}}}{C_{\mathrm{ES}}} \quad 0\right]^T$$

The system matrices are as given by

$$\boldsymbol{A} = \begin{bmatrix} \boldsymbol{HE} & & & \boldsymbol{BC}_{\mathrm{H}} \\ & \boldsymbol{TR} & & \boldsymbol{BC}_{\mathrm{T}} \\ & & \boldsymbol{EX} & \boldsymbol{BC}_{\mathrm{E}} \\ \boldsymbol{BL}_{\mathrm{H}} & \boldsymbol{BL}_{\mathrm{T}} & \boldsymbol{BL}_{\mathrm{E}} & \boldsymbol{CC} \end{bmatrix}$$

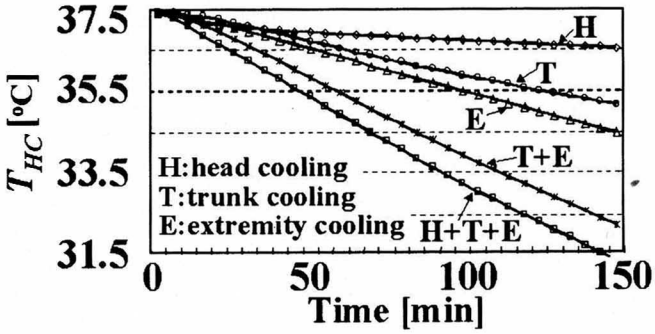

Fig. 4. Comparison of the effects by various methods. *H*, head cooling; *T*, trunk cooling; *E*, extremity cooling

$$\boldsymbol{B} = \begin{bmatrix} 0 & 0 & 0 \\ \boldsymbol{b}_{\mathrm{H}} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & \boldsymbol{b}_{\mathrm{T}} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & \boldsymbol{b}_{\mathrm{E}} \\ 0 & 0 & 0 \end{bmatrix}$$

Hereby, the above elemental submatrices are given in Appendix A2.

3.2 Cooling effects by various methods

The brain temperature is usually controlled by the regulation of environmental temperature using a cooling blanket and a cooling cap with cold water.[11] From investigation of the temperature response to the cooling, it is possible to cool the brain to 35°C with the cooling cap and ice water ($\boldsymbol{T}_{\mathrm{am1}} = 0.0°\mathrm{C}$). The skin temperature of the head becomes very low but its difference from that of the core temperature is large. There is no practical difference between body and brain temperatures where they go down together according to cooling by ice water. This kind of brain temperature control is regarded as being clinically useful only for cooling of the head while the patient is carried to hospital in emergency, because it is possible to attain 35°C for the initial rescue control of brain temperature in ambulance vehicles. It is, however, important and necessary to maintain brain temperature between 32° and 35°C clinically. In order to compare with the effects from cooling various parts of body, the ambient temperature of all parts concerned is altered in a step change from 30°C to 10°C, as the water temperature of the cooling blanket is set about 10°C.[12] Figure 4 shows the temperature response of the head to the step change.

If 32.5°C is the desired temperature of the brain, the previously mentioned skin cooling of the head is not effective when compared with cooling of other parts. It requires a temperature lower than −15°C to maintain the appropriate brain temperature, which is practically impos-

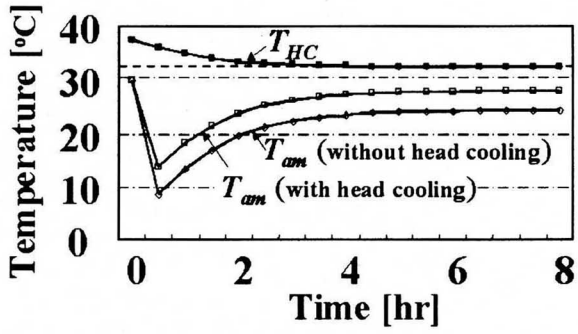

Fig. 5. Body cooling including or excluding head cooling. *Broken line*, the desired temperature of 32.5°C. T_{HC}, controlled brain temperature; T_{am}, temperature of cold water

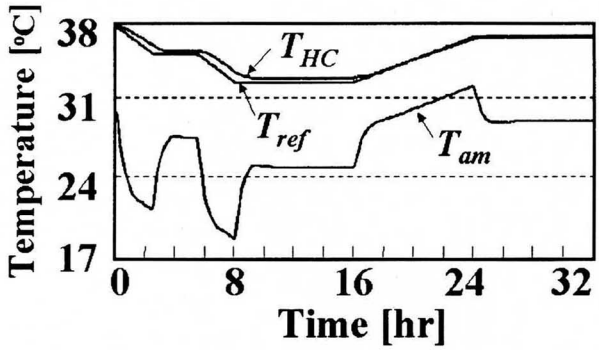

Fig. 6. Control of brain temperature achieved by cooling body. T_{ref}, reference brain temperature prescribed by doctors; T_{HC}, brain temperature controlled by P-control action by the water temperature T_{am} in the cooling blanket

sible to realize because of possible chilblains and the difficulty in maintaining such cold media. For this purpose, all possible parts of body should be cooled clinically, including cooling of the circulatory system of the extremities. This kind of cooling is shown to be effective when compared with cooling through the circulatory system of the trunk, because the SH model gives the relative proportions of the surface area of the head, trunk, and extremities as 9:37:54, respectively. Thus, the simultaneous cooling of the trunk and extremities is expected to provide hypothermia of the brain core much more effectively than by skin cooling of the head.

3.3 Control of brain temperature by body and head cooling

First, cooling of the whole body excluding the head is discussed. The desired temperature of 32.5°C is realized even if the cooling water is colder than 24°C. This phenomenon is consistent with the clinical experience. That is, brain temperature of 32°–33°C can be obtained by controlling the cooling water temperature to 24°–26°C and the bladder temperature to 31°–32°C.[12]

Next, whole-body cooling is considered, including the use of head cooling with ice water. In this case body cooling temperature as high as 28°C can provide the desired brain temperature. Head cooling is thought to be useful as a secondary means to help cool the brain effectively.

Figure 5 shows the results from the regulation of temperatures by body cooling with and without head cooling.

3.4 Follow-up control of the standard temperature change given by doctors

The optimal combination of the temperatures of cooling waters used in blankets should be made clear for each of the cooling parts. It is essential to evaluate the side effects of the proposed cooling methods and it is also important to clarify the response of transient characteristics in the brain-cooling process. Figure 6 shows the result from the control of temperature of the head and other parts.

It is obviously difficult to cool the brain to 32.5°C using only head cooling, in spite of its usefulness in the recovery process. On the other hand, whole-body cooling even excluding the head can easily attain the lower brain temperature. Thus, the combination of various kinds of cooling methods is expected to be useful. Nevertheless, head cooling is applicable to rehabilitation at home, and this application shall require the development of a new cooling apparatus for its specialized use.

4. Model reference adaptive control

4.1 Necessity of adaptive technique for the control of temperature

The physiological controller of body temperature consists of the hypothalamus with feedback information from the circulation. This thermal control function is forcibly changed by the control law, which is generated from the controller under the environmental conditions, although it would work according to the characterized physiological control law. This physiological control dynamics are strongly dependent on parameters that cannot be exactly known. In addition, there exist numerous unknown factors affecting the dynamics. Thus, the exact physiological function including parameter change cannot be absolutely known in any case. That is, the necessary information for the synthesis of control systems cannot be usually obtained in an exact form beforehand. Therefore, there can always exist in a conventional method some theoretical difficulty with facilities because of imperfect recognition. Such a problem, however, does not have to be considered, so long as an adaptive control system is concerned, which is a significant method in such a situation without explicit parameter estimation. Thus, a desirable brain temperature can be realized by the adaptive control system according to clinical demands. Regardless of chronic change, individual differences of the system concerned, and environmental change, the control system is designed on the assumption of its physiological representation by an appropriate mathematical model. There is no practical knowledge about the

thermal system based on input–output relation, which is naturally different according to individuals and is difficult to estimate exactly. However, exact knowledge of a thermal system is not required for the design of an adaptive control system as mentioned previously.

In the control of the system, the output as a physiologically inner-causal state change of a patient is here regarded as the one resulting from parameter change in the controlled object and environmental change.

4.2 Adaptive control theory for the thermal system with a linear mathematical model

In order to control the brain core temperature, the model reference adaptive control system is adopted. The SH model is used as a practical thermal system represented by its discrete model. For the discussion, the single-input/single-output system is taken into account, which uses the same temperature of cooling water in the head, trunk, and extremities.

The discrete SH model is represented by

$$\boldsymbol{A}_m\left(z^{-1}\right)T_{\mathrm{HC}m}(k) = z^{-1}\boldsymbol{B}_m\left(z^{-1}\right)T_{\mathrm{am}}(k) \tag{2}$$

where

$$\boldsymbol{A}_m\left(z^{-1}\right) = 1 + a_{1m}z^{-1} + \ldots + a_{8m}z^{-8}$$
$$\boldsymbol{B}_m\left(z^{-1}\right) = b_{0m} + b_{1m}z^{-1} + \ldots + b_{7m}z^{-7}$$

and the parameters $a_{1m}, \ldots, a_{8m}, b_{0m}, b_{1m}, \ldots, b_{7m}$ are known according to Eq. a5 (Appendix A1), denoting m, model; HC, head core; am, ambient.

Here, the following linear mathematical model with finite memories is assumed for the thermal system to be identified considering the discrete SH model.

$$\boldsymbol{A}\left(z^{-1}\right)T_{\mathrm{HC}}(k) = z^{-1}\boldsymbol{B}\left(z^{-1}\right)T_{\mathrm{am}}(k) \tag{3}$$

where

$$\boldsymbol{A}\left(z^{-1}\right) = 1 + a_1z^{-1} + \ldots + a_8z^{-8}$$
$$\boldsymbol{B}\left(z^{-1}\right) = b_0 + b_1z^{-1} + \ldots + b_7z^{-7}$$

and the parameters $a_1, \ldots, a_8, b_0, b_1, \ldots, b_7$ are estimated in the adaptation process at the sampling time k.

The adaptive controlling input $T_{\mathrm{am}}(k)$ to the thermal system represented by Eq. 3 is determined using parameters estimated at previous sampling times so that the adaptation error $e^* = 0$ is satisfied.[19]

That is, the adaptation algorithm is given by

$$T_{\mathrm{am}}(k) = \frac{\boldsymbol{A}_m\left(z^{-1}\right)T_{\mathrm{HC}m}(k+1) - \boldsymbol{P}_0^T(k)\Phi_0(k)}{b_0(k)} \tag{4}$$

where the state variables and estimated parameter vectors are defined as follows:

$$\Phi^T(k) = \left[T_{\mathrm{am}}(k), \Phi_0^T(k)\right] = \left[T_{\mathrm{am}}(k), T_{\mathrm{am}}(k-1), \ldots, T_{\mathrm{am}}(k-7), T_{\mathrm{HC}}(k), \ldots, T_{\mathrm{HC}}(k-7)\right]$$

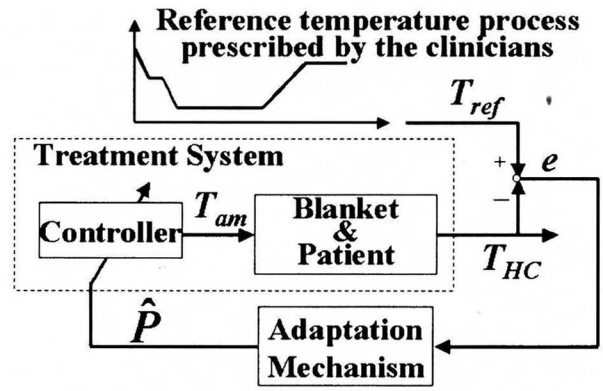

Fig. 7. Diagram of the adaptive hypothermia treatment system. T_{ref}, reference brain temperature given by doctors according to Fig. 2; T_{HC}, controlled brain temperature; e, error of T_{HC} from T_{ref}; $\hat{\boldsymbol{P}}$, estimated parameter vector

$$\boldsymbol{P}^T(k) = \left[b_0(k), \boldsymbol{P}_0^T(k)\right] = \left\{b_0(k), b_1(k), \ldots, b_7(k), \left[a_{1m} - a_1(k)\right], \ldots, \left[a_{8m} - a_8(k)\right]\right\},$$

The adaptation error e^* described by

$$e^*(k) = \frac{\boldsymbol{A}_m\left(z^{-1}\right)T_{\mathrm{HC}}(k) - \boldsymbol{P}^T(k-1)\Phi(k-1)}{1 + \Phi^T(k-1)\boldsymbol{F}(k-1)\Phi(k-1)} \tag{5}$$

is guaranteed to converge to zero, which leads to the realization of characteristics of the reference SH model represented by Eq. 2, if parameters are adaptively estimated by

$$\boldsymbol{P}(k) = \boldsymbol{P}(k-1) + \boldsymbol{F}(k-1)\Phi(k-1)e^*(k) \tag{6}$$

$$\boldsymbol{F}(k) = \frac{1}{\lambda_1(k)}\left[\boldsymbol{F}(k-1) - \frac{\lambda_2(k)\boldsymbol{F}(k-1)\Phi(k-1)\Phi^T(k-1)\boldsymbol{F}(k-1)}{\lambda_1(k) + \lambda_2(k)\Phi^T(k-1)\boldsymbol{F}(k-1)\Phi(k-1)}\right] \tag{7}$$

where $0 < \lambda_1(k) \leq 1$, $0 \leq \lambda_2(k) < 2$, $F(0) > 0$.

Figure 7 shows the block diagram for controlling the thermal system according to the above-mentioned method.

4.3 Adaptive control experiment using SH model

In the present simulation experiment, the reference model output is given directly by the appropriate curve as shown in Fig. 2. The revised SH model is considered to take the place of the actual thermal system. This means that the actual system is introduced as a known system representing the abnormal state of the patient by using different parameters of the previous SH model. It implies that dynamic characteristics have been considered in hypothermia treatment to

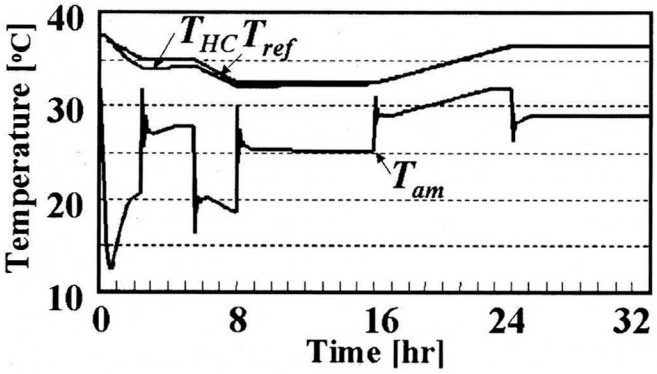

Fig. 8. Simulation result obtained from adaptive control of the brain temperature

simulate more realistic phenomena in order to control the brain temperature, which yields the good result as shown in Fig. 8.

5. Discussion

In the present study, significant results were obtained that are consistent with the physiological and clinical experiences by setting appropriate model parameters. This means that the simulation explained many physiological phenomena. As for the control of brain temperature, step-by-step control is relatively easily realized by the proposed present method by using a combination of head and body cooling according to the state of the patients. However, some problematic phenomena of the high-frequency input wave change were observed, which will be limited and removed in a practical clinical situation. It was also difficult to make the brain cool with the body slightly warmed, which is the clinically expected and more desirable control method. If the face is used as one of the operating parts for the brain cooling, the present method can be expected to cool it more efficiently.

The simulation results using the revised SH model were in accordance with general knowledge of clinical experiences, which justifies it as a proper and useful model. However, the SH model still needs structural improvement, because the blood from lower extremities flows through the body trunk to the brain, whereas the head is represented only by its two-layer concentric and cylindrical parts. Thus, a better head model divided into upper and lower parts, such as our three-layer semispherical model,[20] is necessary for the construction of an appropriate thermal system model, in which the body and extremities remain as given by the SH model. It is hereby remarked that the surface area of the extremities is larger than that of the body trunk. Thus, the cooling effect of the extremities should be utilized more in clinical settings.

6. Conclusions

Hypothermia has been recognized as a new medical treatment that gives rise to new knowledge of the border between life and death in patients serious brain injury and inflammation.

From the viewpoint of control engineering, hypothermia control is one example of the few biophysical controls. At present, it is the best possible treatment for the rescue of patients with severely brain damage caused by injury and inflammation.

It is, thus, extraordinarily significant to clarify the clinical applicability of hypothermia treatment through precise investigation and to make further progress in this area in cooperation with numerous studies on biomedical measurements. The adaptive control system allows us to realize a high quality of control and it may be a generally applicable biophysical control, especially to the clinics, by taking into account the difference of individuality, chronic change of state, nonlinearity, and environmental condition of the patients. It presents clinical medicine one of the influential means, which may not only open the door to sophisticated, high-level automatic therapy but also provide significant aid to interdisciplinary research of medicine, physics, and technology.

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Appendices

A1. Discrete SH model and its pulse transfer function

The SISO continuous-time SH model is given by

$$\frac{d\boldsymbol{T}(t)}{dt} = \boldsymbol{A}_C\boldsymbol{T}(t) + \boldsymbol{B}_C\boldsymbol{T}_{am}(t) + \boldsymbol{Q} \tag{a1}$$

$$T_{HC}(t) = \boldsymbol{C}_C\boldsymbol{T}(t) \tag{a2}$$

where

$$\boldsymbol{A}_C = \begin{bmatrix} \boldsymbol{HE} & & & \boldsymbol{BC}_H \\ & \boldsymbol{TR} & & \boldsymbol{BC}_T \\ & & \boldsymbol{EX} & \boldsymbol{BC}_E \\ \boldsymbol{BL}_H & \boldsymbol{BL}_T & \boldsymbol{BL}_E & \boldsymbol{CC} \end{bmatrix},$$

$$\boldsymbol{B}_C^T = (0 \quad b_H \quad 0 \quad 0 \quad b_T \quad 0 \quad b_E \quad 0),$$

$$\boldsymbol{C}_C = (1 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \quad 0).$$

The submatrices or elements are included in A2.

The initial temperature conditions determine the neutral state of the patients characterized by the following constant values:

$$\boldsymbol{T}(0) = \begin{bmatrix} 37.52 & 36.07 & 37.62 & 36.68 & 35.89 & 36.76 & 35.56 & 37.44 \end{bmatrix}^T$$

Its discrete-time representation in sampling period σ with zero-holder gives

$$\boldsymbol{T}(k+1) = \boldsymbol{A}_D\boldsymbol{T}(k) + \boldsymbol{B}_D\boldsymbol{T}_{am}(k) \tag{a3}$$

$$T_{HC}(k) = \boldsymbol{C}_D\boldsymbol{T}(k) \tag{a4}$$

where

$$\boldsymbol{T}(k) = \boldsymbol{T}(k\sigma) + \boldsymbol{A}_C^{-1}\boldsymbol{Q}$$

$$\boldsymbol{A}_D = e^{\boldsymbol{A}_C\sigma}, \quad \boldsymbol{B}_D = \int_0^\sigma e^{\boldsymbol{A}_C(\sigma-\tau)}d\tau\,\boldsymbol{B}_C, \quad \boldsymbol{C}_D = \boldsymbol{C}_C.$$

Then, the pulse transfer function is

$$G(z) = \frac{Z[T_{HC}(k)]}{Z[T_{am}(k)]} = \boldsymbol{C}_D(z\boldsymbol{I} - \boldsymbol{A}_D)^{-1}\boldsymbol{B}_D = \frac{z^{-1}(b_{0m} + b_{1m}z^{-1} + \ldots + b_{7m}z^{-7})}{1 + a_{1m}z^{-1} + \ldots + a_{8m}z^{-8}} \tag{a5}$$

where $a_{1m}, \ldots, a_{8m}$, b_{0m}, $b_{1m}, \ldots, b_{7m}$ are obtained by Fadeeva's algorithm using the parameters given in Table A1.

A2. Submatrices and their elements concerning Eq. 1 and A1

$$\boldsymbol{HE} = \begin{pmatrix} -\dfrac{\rho c w_{HC} + K_{HCHS}}{C_{HC}} & \dfrac{K_{HCHS}}{C_{HC}} \\ \dfrac{K_{HCHS}}{C_{HS}} & -\dfrac{\rho c w_{HS} + K_{HCHS}}{C_{HS}} \end{pmatrix}$$

Table A1. Parameters for Stolwijk and Hardy model[1]

Segment	Compartment (symbol)	C (kcal/°C)	M (kcal/h)	w (l/h)	A (m²)	K (kcal/h °C⁻¹)
Head	Core (HC)	3.94	12.42	51.3		$K_{HCHS} = 2.63$
	Skin (HS)	0.27	0.12	1.66	0.165	
Trunk	Core (TC)	20.1	44.7	210.0		$K_{TCTM} = 4.85$
	Muscle (TM)	9.7	4.3	13.3		$K_{TMTS} = 23.0$
	Skin (TS)	1.12	0.48	3.43	0.677	
Extremity	Core (EC)	21.1	8.5	20.3		$K_{ECES} = 17.7$
	Skin (ES)	1.64	0.69	6.42	0.989	
Central blood	(CB)	1.12				

Respiratory heat loss assigned to core of head is $Ev_R = 4.5$ kcal/h. Product of density and specific heat of blood is 0.92 kcal/°C. Environmental heat transfer coefficient is $h = 6.0$ kcal/m²h⁻¹ °C⁻¹

C, Thermal capacitance; M, basal metabolic heat production; w, blood flow; A, area of skin; K, thermal conductance

$$\boldsymbol{TR} = \begin{pmatrix} -\dfrac{\rho cw_{TC} + K_{TCTM}}{C_{TC}} & \dfrac{K_{TCTM}}{C_{TC}} & 0 \\ \dfrac{K_{TCTM}}{C_{TM}} & -\dfrac{K_{TCTM} + \rho cw_{TM} + K_{TMTS}}{C_{TM}} & \dfrac{K_{TMTS}}{C_{TM}} \\ 0 & \dfrac{K_{TMTS}}{C_{TS}} & -\dfrac{\rho cw_{TS} + K_{TMTS}}{C_{TS}} \end{pmatrix}$$

$$\boldsymbol{EX} = \begin{pmatrix} -\dfrac{\rho cw_{EC} + K_{ECES}}{C_{EC}} & \dfrac{K_{ECES}}{C_{EC}} \\ \dfrac{K_{ECES}}{C_{ES}} & -\dfrac{\rho cw_{ES} + K_{ECES}}{C_{ES}} \end{pmatrix}$$

$$\boldsymbol{BC}_{H}^{T} = \begin{pmatrix} \dfrac{\rho cw_{HC}}{C_{HC}} & \dfrac{\rho cw_{HS}}{C_{HS}} \end{pmatrix}$$

$$\boldsymbol{BC}_{T}^{T} = \begin{pmatrix} \dfrac{\rho cw_{TC}}{C_{TC}} & \dfrac{\rho cw_{TM}}{C_{TM}} & \dfrac{\rho cw_{TS}}{C_{TS}} \end{pmatrix}$$

$$\boldsymbol{BC}_{E}^{T} = \begin{pmatrix} \dfrac{\rho cw_{EC}}{C_{EC}} & \dfrac{\rho cw_{ES}}{C_{ES}} \end{pmatrix}$$

$$\boldsymbol{BL}_{H} = \begin{pmatrix} \dfrac{\rho cw_{HC}}{C_{CB}} & \dfrac{\rho cw_{HS}}{C_{CB}} \end{pmatrix}$$

$$\boldsymbol{BL}_{T} = \begin{pmatrix} \dfrac{\rho cw_{TC}}{C_{CB}} & \dfrac{\rho cw_{TM}}{C_{CB}} & \dfrac{\rho cw_{TS}}{C_{CB}} \end{pmatrix}$$

$$\boldsymbol{BL}_{E} = \begin{pmatrix} \dfrac{\rho cw_{EC}}{C_{CB}} & \dfrac{\rho cw_{ES}}{C_{CB}} \end{pmatrix}$$

$$\boldsymbol{CC} = \begin{pmatrix} \dfrac{\rho cw_{HC} + \rho cw_{HS} + \rho cw_{TC} + \rho cw_{TM} + \rho cw_{TS} + \rho cw_{EC} + \rho cw_{ES}}{C_{CB}} \end{pmatrix}$$

$$b_{H} = \frac{A_{HS} h_{H}}{C_{HS}}, \quad b_{T} = \frac{A_{TS} h_{T}}{C_{TS}}, \quad b_{E} = \frac{A_{ES} h_{E}}{C_{ES}}$$

where the necessary physiological parameters are given in Table A1.