

Model Reference Adaptive Control of Brain Temperature for Cerebral Hypothermia Treatment

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Abstract – An automatic thermal control system is proposed for the treatment of cerebral injury and/or inflammation. The system is based on the model reference adaptive control method. It works indifferently from the difference of individuals, chronic change of patients' physiological state and environmental change. Using the human thermal system represented by 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 by simulation experiments provide better understanding of the clinical brain cooling treatments, which simultaneously give good evidences for the validity of the concerning model. Then, the brain temperature is shown adaptively controlled in accordance with the appropriate physiological state suggested by various clinical experiences. That is, this kind of the adaptive control system is useful for the practical use of the automatic-hypothermia control in seriously injured and/or inflamed brain.

Keyword cerebral hypothermia treatment, automatic-hypothermia control system, brain temperature

1. INTRODUCTION

It is required to maintain hypothermia in a definite period for the treatment of the seriously damaging brain injured by internal and/or external causes. It is inevitable in such cases to realize the desired range of the brain temperature set by pertinent doctors, although its accurate control is difficult and laborious. It is thus clinically necessary to control the brain temperature of the patients simply, quickly and safely by the theoretically guaranteed methods. Hereby, the model proposed by Stolwijk and Hardy is introduced as a whole body thermal dynamical model [1]. The appropriate control system using the model is proposed for the regulation of brain temperature so that it becomes independent on the various internal and

external conditions of the brain injured patients.

This is a basic study of clinical system for the new therapy including the development of necessary hardware apparatus. It will offer high quality of bio-functional control method, which can indifferently work from the difference of individuals, their chronic change and nonlinearity.

2. BASIC CONCEPT OF CONTROLLING BRAIN TEMPERATURE

2.1 Effectiveness of hypothermic brain

The clinical effect of hypothermia was first proved useful for the treatment of head injury [2]. Since that experience, the hypothermia has been applied to the severely brain damaged patients such as external head injury and/or cerebral hemorrhage. Its effectiveness has been much proved by various kinds of clinical studies and animal experiments [3, 4, and so on]. The well known experiments using dogs meanwhile discovered the decrement 6.7% of brain circulatory blood flow for every 1 centigrade (hereafter, [C]) decrement in their body temperature [5]. It has been regarded as the first and basic study of mechanism of protective reaction of brain nerve by hypothermia. Meanwhile, that mechanism has been clarified according to the progress of molecular cytology. Among various hypotheses, selective neuron death based on glutamate acid-potassium theory has been expected to be its main causality [3,6].

On the other hand, from the macro-view of hypothermia treatment as shown in Fig. 1, various brain cooling methods inclusive of selective cooling of head have been tried in clinics [7,8]. Then, both positive and negative aspects of whole body cooling have been clinically recognized. Meanwhile, an intensive care was established [8], in which control of whole body temperature was applied to the control of brain temperature, and step-by-step brain cooling method was adopted. The treatment scoring has gradually increased in achievement of neural protection avoiding its side effects by hypothermia of body, taking its advantage of protective neurons as much as possible [3,8].

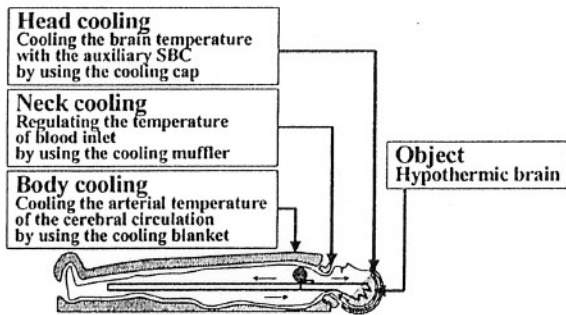


Fig.1. Management of temperature of head, body and extremities in the cerebral hypothermia treatment. (The body cooling by circulating cold water through blanket, muffer and cap)

As for neonatal cases, hypothermia had been tried [9, 10]. It has been in those cases effectively proved both for short and/or long-term [6, 11, 12].

It should however be remarked that hypothermia has some problems of its applicability [13] which yield some bad or no special effects, unless the protective and invasive effects have been well understood in individual patients beforehand [[6, 14].

2.2 Control of body and brain temperature in hypothermia therapy

The critical life of patients with brain injury and inflammation can be effectively protected by hypothermia treatment, which however has harmful side effects on the patients caused by the decrease in immune activity in a lower body temperature.

In order to avoid such negative effects, it has been clinically proposed to control stepwise change in patients' temperature for a long period [3].

That is, the brain temperature control is performed in accordance with clinical experiences reported by doctors such as its step-by-step desired value given by Fig.2. It is remarked that the body temperature at about 32[C] and 35[C] are clinically essential, which should be carefully treated, because temperature around 35[C] corresponds to *adaptive zone* and 32[C] is *critically dangerous zone* as for the maintenance of patients' life.

The desirable characteristics is realized by the cooling of head, trunk and extremities using cold water with the help of cooling blanket and some other materials in the clinical experiences. The water flow amount is regarded constant in all consideration of hypothermia in this study because of theoretically essential discussion, although its flow control in the cooling blanket has been often applied clinically.

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

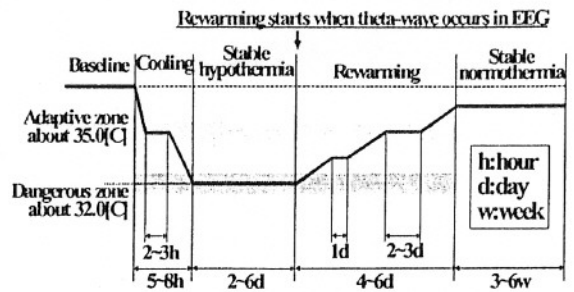


Fig.2. Step-by-step management of body temperature in the cerebral hypothermia treatment [3]. (The temperature curve is based on the clinical experience, according to which the patient's brain temperature is controlled by doctors)

3. REPRESENTATION OF HUMAN THERMAL DYNAMICS

3.1 Human mathematical thermal model

Figure 3 is the human thermal model given by Stolwijk & Hardy (hereafter, named S&H-model), which is introduced in the present study. In the S&H-model, the body is for convenience sake separated into three parts of head, trunk and extremities, to which a blood compartment is added in its center. Each part has the core and skin separated by cocentric circles. Thus, 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 S&H-model, the whole system is represented by the following state equation:

$$\frac{d}{dt} T(t) = AT(t) + BU(t) + Q \quad (1)$$

where its state vector is

$$\mathbf{T}(t) = [T_{hc}(t) \ T_{sk}(t) \ T_{rc}(t) \ T_{rk}(t) \ T_{rc}(t) \ T_{bc}(t) \ T_{es}(t) \ T_{cd}(t)]^T$$

The input vector is

$$U(t) = [T_{am1}(t) \ T_{am2}(t) \ T_{am3}(t)]^T$$

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

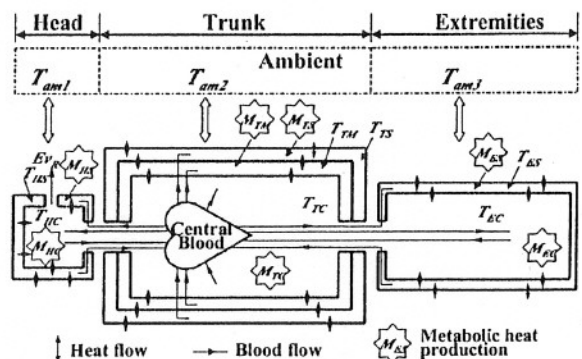


Fig.3. Revised Stolwijk & Hardy model [1]. (T represents the temperature, M the basal metabolism, Ev_R the heat loss assigned to the respiratory heat dispersion and T_{am} the water temperature)

The constant vector is

$$Q = \begin{bmatrix} \frac{M_{hc}-E_{hc}}{C_{hc}} & \frac{M_{hs}}{C_{hs}} & \frac{M_{rc}-E_{hc}}{C_{rc}} & \frac{M_{tm}}{C_{tm}} & \frac{M_{rs}}{C_{rs}} & \frac{M_{bc}}{C_{bc}} & \frac{M_{sx}}{C_{sx}} & 0 \end{bmatrix}^T$$

The system matrices are as given by

$$A = \begin{bmatrix} H & & & BC_H \\ & T & & BC_T \\ & & E & BC_E \\ BL_H & BL_T & BL_E & CC \end{bmatrix}$$

$$B = \begin{bmatrix} 0 & 0 & 0 \\ b_H & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & b_T & 0 \\ 0 & 0 & 0 \\ 0 & 0 & b_E \\ 0 & 0 & 0 \end{bmatrix}$$

Hereby the above elemental submatrices are given in Appendix A2.

3.2 Cooling effect 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 [7]. From the investigation of the temperature response to the cooling, it is possible to cool the brain until 35[C] by ice water ($T_{am}=0.0[C]$) covering the head. The skin temperature of the head becomes very low but its difference from the core temperature is large. There is no practical difference between body and brain temperatures where they go down together according to the ice water. This kind of brain temperature control is supposed clinically useful only for the cooling of the head while carrying the patient in emergency to hospital, because 35[C] is possible to be realized for the initial rescue control of brain temperature in ambulance cars. It is however important and necessary to maintain 32 or 35[C] of brain temperature clinically. In order to compare with the effects by cooling the various possible parts of body, the ambient temperature of all concerning parts is changed step-like from 30[C] to 10[C], as the water temperature of cooling blanket is clinically set about 10[C] [8].

If 32.5[C] is the desired temperature of brain, the previously mentioned head skin cooling is not effective comparing with the ones by other parts cooling. It

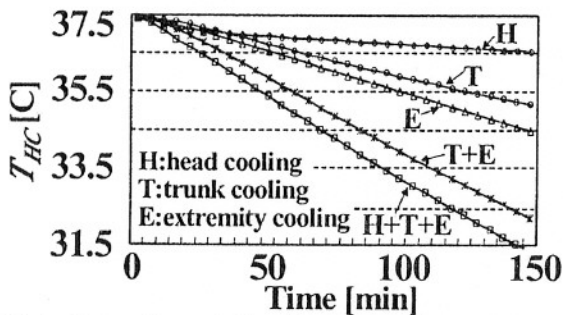


Fig.4. Comparison of the effects by various methods. (H designates head cooling, T means trunk cooling and E extremities cooling)

requires the lower temperature than -15[C] to maintain the appropriate brain temperature, which is practically impossible to be realized as there might be possible chilblain and the difficulty in keeping cold media. For this purpose all the possible parts of body should be cooled clinically, including the cooling by circulatory system of extremities. This kind of cooling is effective comparing with the cooling through the circulatory system of the trunk, because the S&H-model provides the ratio of the surface area of head, trunk and extremities as 9%:37%:54%. Thus, the simultaneous cooling of trunks and extremities is well expected to get hypothermia of the core brain with more effect by the extra head skin cooling.

3.3 Control of brain temperature by body and head cooling

First, the whole body cooling is discussed in the case of excluding head cooling. The desired temperature 32.5[C] is realized, even if their cooling water is less than 24[C]. This phenomenon is coincident with the clinical experience. That is, the brain temperature 32-33[C] can be obtained by controlling water 24-26[C] and bladder temperature 31-32[C] [8].

Next, the whole body cooling is taken into account including head cooling with ice-water. Then, the body cooling temperature with even 28[C] realizes the desired brain temperature. The head cooling is thought useful as a secondary mean to make the brain cool effectively.

Figure 5 indicates the result from the regulation of temperatures by the 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 water in blankets should be made clear for the concerning cooling parts. It is essential to evaluate the human friendliness of the proposed cooling methods and also important to clarify the response inclusive of transient characteristics in the brain cooling process. Figure 6 indicates the result from the control of temperature of the head and other concerning parts.

The control has been performed indicating well following-up characteristics. It is obviously difficult to cool the brain until 32.5[C] only by the method of head

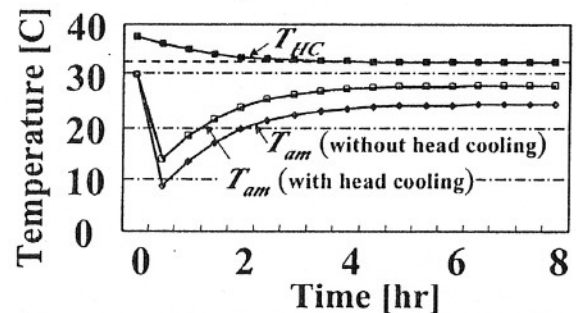


Fig.5. Body cooling including or excluding head cooling (The broken line means the desired temperature 32.5[C] T_{HC} represents the controlled brain temperature and T_{am} the temperature of cold water)

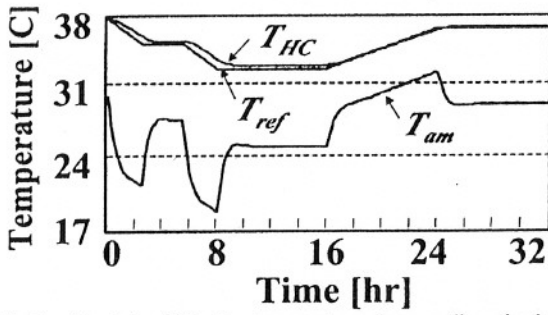


Fig.6. Control of brain temperature by cooling body. (T_{ref} denotes the reference brain temperature prescribed by doctors. T_{HC} represents brain temperature controlled by P-control action by the water temperature T_{am} in the cooling blanket)

skin cooling, in spite of its usefulness in the recovery process. On the other hand, the whole body cooling even excluding head easily realizes the lower brain temperature. Thus, the combination of various kinds of cooling methods is expected useful. Nevertheless, the head cooling is also applicable to the rehabilitation at home which shall require the development of new cooling apparatus for its limited use.

4. MODEL REFERENCE ADAPTIVE CONTROL

4.1 Necessity of adaptive technique for the control of temperature

The physiological controller of a temperature consists of hypothalamus with feedback information from the circulation. This thermal control function is forcedly changed by the control law, which is generated from the controller under environmental condition, although it would work according to the physiological control law characterized essentially. This physiological control dynamics is much dependent on the parameters which cannot be known exactly. In addition, there exist numerous unknown factors affecting its 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 theoretical difficulty of their facilities resulting from their imperfect recognition. Such problem, however, does not have to be cared, so long as an adaptive control system is concerned, which is a significant method in present 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 and individual difference of the concerning system, 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 different according to individuals and 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. Thus, the mathematical system is assumed so that its dynamics are characterized by only ambient temperature as an input and brain temperature as an output.

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 core brain temperature, the model reference adaptive control system is adopted. The S&H-model is used as a practical thermal system represented by its discrete model. For the essential discussion, the single-input-single-output system is taken into account, which deals with same temperature of cooling water in the parts of head, trunk and extremities.

The discrete S&H-model is

$$A_m(z^{-1})T_{HCm}(k) = z^{-1}B_m(z^{-1})T_{am}(k) \quad (2)$$

where

$$A_m(z^{-1}) = 1 + a_{1m}z^{-1} + \dots + a_{8m}z^{-8}$$

$$B_m(z^{-1}) = b_{0m} + b_{1m}z^{-1} + \dots + b_{7m}z^{-7}$$

and parameters $a_{1m}, \dots, a_{8m}, b_{0m}, b_{1m}, \dots, b_{7m}$ are known according to Eq.(a5).

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

$$A(z^{-1})T_{HC}(k) = z^{-1}B(z^{-1})T_{am}(k) \quad (3)$$

where

$$A(z^{-1}) = 1 + a_1z^{-1} + \dots + a_8z^{-8}$$

$$B(z^{-1}) = b_0 + b_1z^{-1} + \dots + b_7z^{-7}$$

and parameters $a_1, \dots, a_8, b_0, b_1, \dots, b_7$ are estimated in the adaptation process.

The adaptive controlling input $T_{am}(k)$ to the thermal system represented by Eq. (3) is determined using estimated parameters at previous sampling time so that the adaptation error $e^* = 0$ is satisfied [15].

That is, the adaptation algorithm is given by

$$T_{am}(k) = \frac{A_m(z^{-1})T_{HCm}(k+1) - \hat{P}_0^T(k)\Phi_0(k)}{\hat{b}_0(k)} \quad (4)$$

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

$$\begin{aligned} \Phi(k) &= [T_{am}(k), \Phi_0^T(k)] \\ &= [T_{am}(k), T_{am}(k-1), \dots, T_{am}(k-7), T_{HC}(k), \dots, T_{HC}(k-7)] \\ \hat{P}^T(k) &= [\hat{b}_0(k), \hat{P}_0^T(k)] \\ &= [\hat{b}_0(k), \hat{b}_1(k), \dots, \hat{b}_7(k), (a_{1m} - \hat{a}_1(k)), \dots, (a_{8m} - \hat{a}_8(k))] \end{aligned}$$

The adaptation error e^* described by

$$e^*(k) = \frac{A_m(z^{-1})T_{HC}(k) - \hat{P}^T(k-1)\Phi(k-1)}{1 + \Phi^T(k-1)F(k-1)\Phi(k-1)} \quad (5)$$

is guaranteed to converge to zero, which leads to the realization of characteristics of the reference S&H-model represented by Eq. (2), if parameters are adaptively estimated by

$$P(k) = P(k-1) + F(k-1)\Phi(k-1)e^*(k) \quad (6)$$

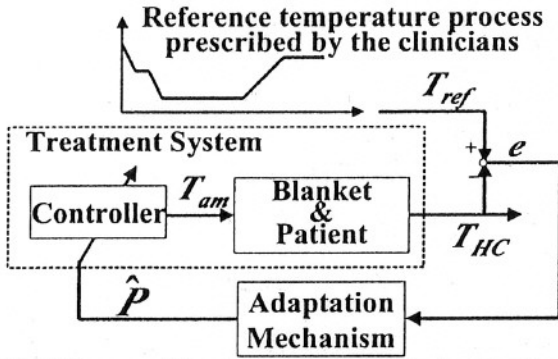


Fig. 7. Diagram of the adaptive hypothermia treatment system. (T_{ref} designates the reference brain temperature given by doctors according to Fig.2. T_{HC} represents the controlled brain temperature, e is the error of T_{HC} from T_{ref} . \hat{P} is the estimated parameter vector and T_{am} is the water temperature of adaptive controlling input into the cooling blanket)

$$F(k) = \frac{1}{\lambda_1(k)} \left[F(k-1) - \frac{\lambda_2(k)F(k-1)\mathcal{Q}(k-1)\mathcal{D}^J(k-1)F(k-1)}{\lambda_1(k) + \lambda_2(k)\mathcal{D}^J(k-1)F(k-1)\mathcal{Q}(k-1)} \right]$$

$$0 < \lambda_1(k) \leq 1, 0 \leq \lambda_2(k) < 2, F(0) > 0 \quad (7)$$

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

4.3 Adaptive control experiment by using S&H-model

In the present simulation experiment, the reference model output is directly given by the appropriate curve as shown in Fig. 2. The revised S&H-model is considered to take the place of the actual thermal system. That is, the actual system is introduced as a known system representing abnormal state of the patients by using different parameters of the previous S&H-model. It implies that dynamic characteristics have been considered in hypothermia treatment to simulate more realistic phenomena in order to control the brain temperature, which yields the good simulation result as shown in Fig 8.

5. DISCUSSION

In the present study, significant results have been obtained which coincide with the physiological and clinical experiences by setting appropriate model and its parameters. That is, the simulation has explained lots of physiological phenomena. As for the control of brain temperature, its step-by-step control is relatively easily realized by the proposed present method using combination of head and body cooling according to the state of the patients. However, some problematic phenomena of the high frequency input wave change have been observed, which will be limited and removed in practical clinical situation. It is also remarked that it is pretty difficult to make the brain cool with the body slightly warmed up, simultaneously, which is expected clinically 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.

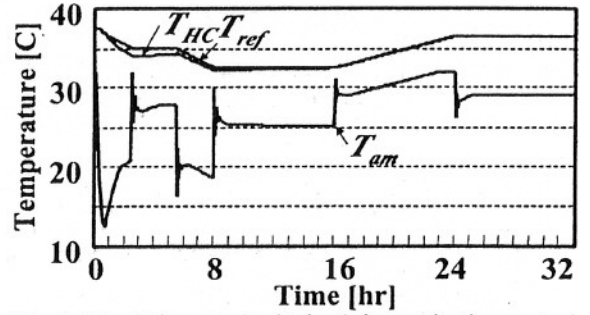


Fig. 8. Simulation result obtained from adaptive control of the brain temperature. (T_{ref} designates the reference brain temperature. T_{HC} represents the adaptively controlled brain temperature by the water of temperature T_{am} as a controlling input)

The simulation results using the revised S&H-model have been in accordance with the general knowledge about clinical experiences, which justify it as a proper and useful model. However, the S&H-model still needs its structural improvement, because the blood from lower extremities flows through the body trunk to the brain, whereas the head is represented only by two-layer concentric and cylindrical parts in the S&H-model. Thus, the better head model divided into the upper and lower parts, such our three-layer semi-spherical model [16], is necessary for the construction of an appropriate thermal system model, in which even the body and extremities remain same as given by the S&H-model. It is hereby remarked that the surface area of extremities is larger than the one of body trunk. Thus, its cooling effect by extremities should be more utilized in clinics.

6. CONCLUSION

It is clinically remarked that hypothermia is expected as a new medical treatment that gives rise to new knowledge about the frontier of life and death of the patients in the case of their serious brain injury and inflammation.

From the viewpoint of control engineering, this hypothermia control is one example of the few biophysical controls. It is the possible best way in the present medical situation for the treatment and rescue of the patients with severely damaging brain by injury and inflammation.

It is, thus, extraordinarily significant to clarify its clinical applicability through its precise investigation in order to make further progress in this area in cooperation with numerous studies on biological measurements. The adaptive control system provides us to realize high quality of control as it may be a general applicable to biophysical control, especially to the clinics, indifferently from the difference of individuality, chronic change of state, nonlinearity and environmental condition of the patients. It presents the clinical medicine one of the influential means, which may not only open the door to new sophisticated high level automatic therapy but also provide the higher significance to the interdisciplinary research among the medicine, theory and technology.

