Newly Developed Automatic Control System for Brain Hypothermia Treatment

Biophysical System Engineering
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Development of Automatic Control System of Hypothermia

• Accurate Management of Brain Temperature
  Adaptive and Fuzzy Control Processes
• Release from Heavy Loads
  Physical, Psychological & Economic Burdens
• Improvement of Medical Condition & Treatment

Based on “System Engineering”

Simulation  ⇔  Experiment
Additional Talk

Concerning Hypothermia Treatment

- Control of Mechanical Respiration
- Optimal Control of Intracranial Pressure
- Monitoring and Determination of Physiological State
What’s matter with him?
It’s awful. It’s terrible.
Hurry up! Bring him to hospital.
Set Quick Cooling Brain Temperature
By Using Cooling Cap and Muffler

Circulation of Cooling Water to Cap & Muffler
Brain Injury and/or Inflammation

Increase of Intracranial Pressure

Prevention of Secondary Damage of Brain Tissue

Bruise on the brain
traffic accident
Ischemic stroke
cerebral infarction
brain hemorrhage (aneurism)
Ischemic heart failure
coronary infarction
Brain tumor
Cause of Intracranial Hypertension

- **Glia + Neurones**: 74%
- **Blood**: 4%
- **CSF**: 9%
- **ECF**: 13%

**intracranial cavity**

- **ICP**: $\geq 10$ mmHg

- **space-occupying lesions** (hematoma)
- **brain volume** (brain edema)
- **blood volume** (brain swelling)
- **CSF volume** (hydrocephalus)

$> 15$ mmHg
• Whole Body Cooling is Effective
• Head Cooling as Assistance
Simple Connecting Operation
Begins Quick Cooling of Brain

To Cooling Blanket

Connecting Socket
Automatic Control of Brain Temperature

Blanket or Suits (Air box)

Patient & cooling apparatus

Physiological state

Medical staffs

Brain temperature

Characteristic system & Desired brain temperature

Manual regulation

Actuator

Signal for regulation

Temperature of water-blanket (Circulating Material)
Manual Regulation of Brain Temperature in clinics

- Water-cooling blanket
- Controller of water temperature
- Diagnosis & measurement
- Manual setting of water temperature
- Information about biomechanism:
  - Brain & body temperature, respiratory & circulatory dynamics, condition of immunity
- Given brain reference temperature
- Physiological state of actual brain temperature
- Decision of appropriate water temperature
Hypothermia under 32 °C Biological Reaction

**Primary reaction**
- Bradycardia
- Arrhythmia
- Peripheral vascular constriction
- Blood viscosity rise
- Hypotension
- Thrombocytopenia
- Electrolyte abnormality
- Easy infectious, loss of hepatic function, deterioration of renal function

**Secondary reaction**
- Impaired consciousness
- Increased total body oxygen consumption
- Atelectasis
- Ichorrhemi

**Bad effect on circulation, respiration, immunity & nervous function**
- Cardiac arrest
- Tissue necrosis
- Stagnation of microcirculation
- Decreased cardiac output
- Hypocoagulability of the blood
- Hypercalciumion
- Acute renal failure
Protection of Brain Cells by Brain Hypothermia

- **Suppression of Damage caused by Energy insufficiency**
  - Improvement of Ca\(^{2+}\) homeostasis
  - Suppression of oxidation by free radicals
  - Activation of antiapoptosis substance
  - Suppression of dopamine A10 neural groups

- **Suppression of Hyperfunction of Endocrine System**
  - Suppression of cathecholamines hypersecretion
Necessity of precise and accurate control of brain temperature!

Trade off in Hypothermia

Protection of Brain Tissue

Merit in Hypothermia

Biological Reaction

Demerit in Hypothermia
Hypothermia Treatment in ICU

Hypothermal Control

- Control of Anesthesia
- Control of Respiration
- Prevention of Infection
- Control of Circulation
- Control of Nutrition
- Rehabilitation

- Anesthesiologist
- Nurse
- Dietitian
- Medical Engineer
- Pediatrician
- Clinical Pharmacist
- Clinical Technologist
- Psychotherapist

Critical care medicine
Automatic Control Apparatus of Brain Temperature

- Reference Brain Temperature Course
- Water-Cooling Blanket
- Physiological Data (Temperature)
- Flow Monitoring
- Temperature Monitoring
- Warning
- Touch Panel Display of Manipulation
- Manual/Auto Switching
- Full Automatic Control Apparatus

Calculation & Regulation of Water Temperature
Measurement of Temperature in Hypothermia

Brain Tissue Temperature

Alternative Temperature

Tympanic, Nasopharyngeal, Esophageal, Rectal etc.
Control of Brain Temperature by Water-Cooling System
Schematic Desired Brain Temperature

Step-by-step Management of Body Temperature

EEG θ-wave θ-wave

Recovery of Consciousness

Adaptive zone (about 35°C)

Dangerous zone (about 32°C)

Cooling

Stable hypothermia

Warming

Post hypothermia

37.5°C

35°C

32.5°C
Automatic Controller of Brain Temperature

Patient & Water-cooling Blanket

Reservoir

Apparatus for Making Cold Water

Valve

Computer Algorithm

Adaptive Control Fuzzy Control

Warming

Heating Regulation

Basic Characteristic Estimation

Brain Temp.

Water Temp.

Reference
Concept of Adaptive Control Engineering

- Different regulation
- Various kinds of medical treatment
- Change in external environment

- Change in internal environment
  - Circulatory change
  - Metabolic change etc.
- Unknown thermal characteristic

Patient under the brain hypothermia treatment

Adaptive control

Realization of desired brain temperature
Brain Hypothermia Treatment Using Thermal Mannequin

Mannequin controlled by water circulation (blood flow) and heater (metabolic heat)
Overview of Experimental Equipment

- Computer and monitor
- Temperature sensor
- Mannequin and blanket
- Signal translator
- Relay control box
- 12 l cold water tank
- Heater regulator
- Pump
- Basic metabolism
- Heart
Automatic control apparatus

Monitor

Control box of circulation and metabolism

Mannequin in place of patient with cooling blanket
Body temperature

Tracking of brain temperature for desired brain temperature schedule

Room temperature

Water temperature of blanket

Experimental time 32:00:00
Heater SW ON

Peek of brain temperature

Desired brain temperature schedule

Decrease in water temperature of blanket

Heater SW ON

Experimental time 14:25:03
Opening the door

Brain temperature

Decrease in room temperature

Body temperature

Water temperature of blanket

Experimental time 15:38:50
Fuzzy Control of Brain Temperature by Water-Cooling System
Membership functions and Fuzzy rule

For fuzzy controller-1

The antecedent

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<th>e(k)</th>
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<tbody>
<tr>
<td>PB</td>
<td>ZO</td>
</tr>
<tr>
<td>PB</td>
<td>PB</td>
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<tr>
<td>ZO</td>
<td>PS</td>
</tr>
<tr>
<td>NB</td>
<td>ZO</td>
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</table>

The consequent

Δe(k) vs e(k)

Δu(k) vs e(k)
Membership functions and Fuzzy rule

For fuzzy controller-2

<table>
<thead>
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<th>$\Delta \nu(k)$</th>
<th>$\Delta \varepsilon(k)$</th>
<th>$\varepsilon(k)$</th>
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<tbody>
<tr>
<td>PB</td>
<td>PB</td>
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<tr>
<td>PM</td>
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<td>NB</td>
</tr>
<tr>
<td>NB</td>
<td>PVB</td>
<td>NB</td>
</tr>
</tbody>
</table>

The antecedent

- $\Delta \nu(k)$
- $\Delta \varepsilon(k)$
- $\varepsilon(k)$

The consequent

- $\Delta \nu(k)$
- $\Delta \varepsilon(k)$
- $\varepsilon(k)$
Block Diagram of Fuzzy Control System

Subsystem-1

Fuzzy controller-1

\[ e(k) \]

\[ R(k) \]

\[ z^{-1} \]

\[ \Delta e(k) \]

\[ \Delta u(k) \]

\[ T_{\text{water}}^c(k) \]

\[ T_{\text{brain}}^c(k) \]

Subsystem-2

Patient

Fuzzy controller-2

\[ \nu(k) \]

\[ \Delta \nu(k) \]

\[ T_{\text{water}}(k) \]

\[ T_{\text{brain}}(k) \]

\[ \epsilon(k) \]

\[ \Delta \epsilon(k) \]

\[ z^{-1} \]
Experimental Result during Cooling and Stable Period

- **Desired Brain Temperature**
- **Water Temp. to Characteristic Model**
- **Brain Temp. of Characteristic Model**
- **Objective Water Temp. to Mannequin**
- **Brain Temp. of Mannequin**
- **Actual Water Temp.**

**Timeline:**
- **Suspension of blood (water) flow in 2 Minutes**
- **Warm up the head by heating in 30 Seconds**
Whole Experimental Result

- Body temperature
- Brain temperature
- Decrease in room temperature
- Environmental change
- Water temperature of blanket

Experimental time 31:57:36
Blood Flow Change

Pump for circulation stops in 2 minutes

Experimental time 13:39:06
脳温、体温[℃]  ＜全経過表示モード＞

目標脳温 = 35.00
実際脳温 = 35.05
体温 = 36.95

室温、水温[℃]

目標水温 = 20.48
実際水温 = 20.26

終了 ESC リセット R Experimental time 32:00:00 サンプル数 28827
Control of Brain Temperature by Air-Cooling System
Air-cooling Incubating System

- Transparent air-cooling box
- Fan
- Mannequin
- Radiator
- Peltier module
- Radiator
- Electric power supply
- A/D
- Control mechanism
- D/A
- Air temperature
- Brain temperature
- Air speed
Automatic Air-Cooling Incubating System for Brain Hypothermia Treatment
Simulation Result

Comparison of water and air cooling methods

Temperature [°C]

Time [hr]

$R$, $T_{brain}$, $T_{air}$, $T_{water}$

Adaptive air temperature

Optimal water temperature
Control using Solution by Optimal Calculation

![Graph showing temperature over time with different cooling methods and temperature references.]

- **Brain temperature of model**
- **Reference brain temperature**
- **Cooling apparatus**
- **Blanket**
- **Cap**
- **Muffler**

**Temperature** vs. **Time [hr]**

*Water-cooling*
Automatic Control of Respiration to Deal with Difference of Individual Characteristics
Respiratory Regulation System

Ventilation & Gas-exchange System
Intake of O\textsubscript{2}, Discharge of CO\textsubscript{2}
- Controller: Respiratory Center
- Sensor: Peripheral Chemoreceptor
  Central Chemoreceptor

Interaction

Circulatory System
Transportation of O\textsubscript{2} & CO\textsubscript{2}
Heart
- Controller: Cardiac Center
- Sensor: Baroreceptor
  Vasomotion
- Chemical Regulation
  Vasomotor Regulation

Interaction

Blood Buffer System
Maintenance of [H\textsuperscript{+}] in body fluid

Interaction

Metabolic Rate Change
Points of Design of the Control System

Respiratory Regulation System
- Non-linearity
- Chronic Change
- Individuality
- Change of Environment

In order to control

- Understanding by Detection of Its Characteristics
- Design of Control System based on Detected Characteristics

Deviations of the Parameters of the Mathematical Model

Introduction of an “Adaptive System”
Interior view of the all-built-in-one type respirator

Developed all-built-in-one type respirator
**Controlled Respiration**

- **Sampling Interval**: 30 [sec]
- **Respiration Rate**: 16 [times/min]
- **Period of Experiment**: 30 [min]

**Assisted Respiration**

- **Variable Sampling Interval**: Every 7 Ventilatory Periods (23.3–30.0 [sec])
- **Respiration Rate**: Changed at Random from 14 to 18 [times/min]
Fuzzy respiratory control system with respect to difference of individuals

Data of physical constitution \( r \)

Decision mechanism of individual coefficient \( p \)

Disturbance (Metabolic rate \( m \))

Controlled deviation \( e \)

Desired value

Fuzzy controller

Ventilation \( u + uu \)

Controlled system (Respiratory system)

Alveolar CO\(_2\) concentration \( y \)
Fuzzy control of the same subject with different constitutional coefficients

(a) p=0.5

(b) p=1.0

(c) p=1.25

(d) p=1.5

Ventilation [ml/str] CO₂-Concentration [Vol%]

Ventilation [ml/str] CO₂-Concentration [Vol%]

Ventilation [ml/str] CO₂-Concentration [Vol%]

Ventilation [ml/str] CO₂-Concentration [Vol%]
Control of Intracranial Pressure by Administration of Mannitol based on Mathematical Model
Background and Aim

(Traumatic brain injuries, brain tumors, etc.)

Intracranial hypertension caused by brain edema

Iterative administration based on experience of doctors

Theoretical Analysis

• Determination of most effective administration process
• Dynamical prediction of intracranial pressure
Mannitol Pharmacokinetics + Brain Hydrodynamics

Method

Mathematical Model

Input

Mannitol Pharmacokinetics

Response

Output

Administration of Mannitol

PID Control Optimal Control

Intracranial Pressure
Schematic Representation of Model

- **mannitol excretion**
- capillary extracellular fluid of body (except brain)
- Pcsf (output)
- Pgm
- Pwm
- Cgm-cap
- Cgm
- Fgm-cap
- Cgm-cap
- Fgm
- Cgm
- Cwm-cap
- Cwm
- Fwm-cap
- Fwm
- Cwm
- Fwm-cap
- manitol administration (input)
- manitol excretion
- venous sinus
- blood flow to brain
- blood flow out of brain
- gray matter
- white matter
- CSF
- **extracellular fluid of body (except brain)**
- Cecf
Dynamics of Mannitol Concentration in a Bolus Administration

Administration of Mannitol 0.1g/kg/min in the first 15min

Mannitol concentration of extracellular fluid, gray matter capillary and white matter capillary. They decreases exponentially after their peak on the last moment of infusion.
Comparison of Different Methods by Simulation

Decrease of ICP by Less Amount of Mannitol in an Optimal Control Process
On-line Monitoring of parallel Physiological Data
Monitoring System of Parallel Physiological Data
Conventional Monitoring of Physiological State

- Artificial Respiration
- Respiratory Sound
- Expired gas analysis
- EEG
- Intracranial Pressure
- Decision of Warming Time
- Control of Anesthesia
- Control of Metabolism
- Infusion, Fluid Replacement
- Intravenous Anesthesia
- Urine
- Body Temperature (Brain T., Tympanic Membrane T., Internal Juglar vein blood T., Peripheral cutaneous T.)
- Blood Pressure
- Blood gas analysis
- Control of Circulation
- Control of Circulation
Comprehensive Monitoring of Physiological State

Final Decision and Treatment

Infusion, Blood transfusion, Medicament, Intravenous anesthesia

Urinary analysis

Body, Rectal Temperature

Oxygen saturation

Blood Pressure
ECG, Blood Gas

Summarize Data

Physiological State

Inference, Decision & Description

Indication by Simple Expression

Alarm

Artificial Respiration

Expiratory gas Analysis

Inspiratory anesthesia

Blood Pressure

Anesthesiologist
Various Physiological Data Monitored from Patients

Fuzzy Logic

Estimation of Physiological State

Display & Alarm, if necessary

Evaluation and Alarming System