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„Regulation of Cerebral Perfusion Pressure by automatic control of Noradrenaline Infusion“

C.-n. Nguyen, O. Simanski, A. Schubert, B. Lampe
Department of Electrical Engineering, Institute of Automatic Control, University of Rostock, Germany
E-Mail: nguyen-chi.ngon@uni-rostock.de

M. Janda, J. Bajorat, R. Hofmockel
Clinic of Anesthesiology and Intensive Care, University of Rostock, Germany

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Regulation of Cerebral Perfusion Pressure by automatic control of Noradrenaline Infusion

C.-N. NGUYEN[1], O. SIMANSKI[1], A. SCHUBERT[1], M. JANDA[2], J. BAJORAT[2], R. HOFMOCKEL[2], AND B. LAMPE[1]

[1]*Department of Electrical Engineering, Institute of Automatic Control*
[2]*Clinic of Anesthesiology and Intensive Care*
University of Rostock

E-Mail: nguyen-chi.ngon@uni-rostock.de

INTRODUCTION

The cerebral perfusion pressure (CPP) is defined as the mean arterial pressure (MAP) minus the intracranial pressure (ICP), which presents the pressure gradient driving cerebral blood flow (CBF) and hence oxygen and metabolite delivery [Trauma2000]. An intractable increase in ICP leading to a progressive decrease in CPP and CBF is the dominant cause of death in patients with severe brain trauma [Nordström2003]. Therefore maintenance of an adequate CPP is vital to prevent secondary brain damage when anaesthetising patients who may have raised ICP that is a common problem in neurosurgical and neurological practice [Dunn2002]. The paper presents a method of regulating CPP around 70 mmHg by raising the MAP through automatic control of noradrenaline (NA) infusion. Clinical experiments on pigs (n=10) indicated the safety and stability of the CPP control system with the settling time is estimated in 5±1.3 min.

MATERIALS AND METHODS

A. Dynamic model of blood pressure response to NA

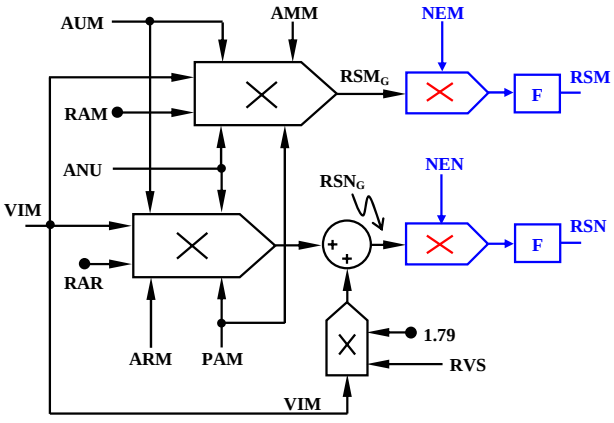

Fig. 1: Modelling the effects of NA on vascular resistances.

In order to develop a model of blood pressure (BP) response to NA, the AS3 monitor system was used to measure the MAP of two pigs in 8 experiments of raising BP by different constant infusion rates of NA. Under administered NA, by stimulating alpha receptors, it causes the muscle to contract, resulting in narrowing of the blood vessels [Netdoctor2004]. It means under dosing NA, the vascular resistances of the circulation are increased. This is the idea used to modify Guyton's model of cardiovascular dynamics for presenting the effects of NA on BP. Fig.1 models the effects of NA on vascular resistances in muscle tissues (RSM) and in non-muscle, non-renal tissues (RSN) through 2 coefficients of NEM and NEN. Where NEM and NEN denote the effects of NA on RSM and RSN, respectively, which can be expressed in (1). All other physiological notations in Fig.1 can be found in [Guyton1972].

$$\frac{x(t)}{NA} = G\left(\frac{e^{-T_1 s}}{\tau_1 s + 1} + \frac{\lambda e^{-T_2 s}}{\tau_2 s + 1}\right)$$
$$z(t) = \begin{cases} x(t), & x(t) \geq 0 \\ 0, & x(t) < 0 \end{cases} \qquad (1)$$
$$NEM = 1 + z(t)$$
$$NEN = 1 + \varepsilon z(t)$$

where NA presents the noradrenaline infusion rate. G and λ express the patient sensitivity and the reaction of the body, respectively. T_1 and T_2 present the transport delays. τ_1 and τ_2 are the response time constants. And ε denotes the different effect of NA on muscle tissues and non-muscle, non-renal tissues.

All parameters in (1) are given in Tab.1, which were estimated from 8 experimental data sets on 2 pigs. A simulation result of model output is illustrated in Fig.2.

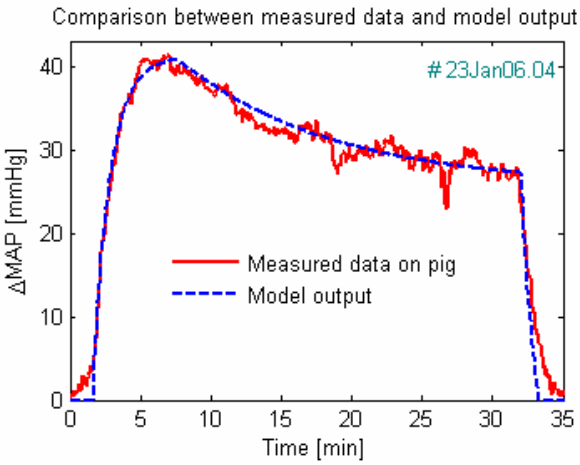

Fig. 2: Model output and measured data on pig.

Tab. 1: Parameters of the model.

Para.	Ave.	Min.	Max.	Unit
G	0.1	0.02	0.4	$(ml/hr)^{-1}$
λ	-0.4	-0.1	-1.0	-
τ_1	40	30	75	sec
T_1	55	20	120	sec
τ_2	7	4	12	min
T_2	4	3	7	min
ε	1.2	1.0	2.6	-

B. Controller design

An overview of the CPP control system can be described in Fig.3. The output of the system is CPP, which is calculated from MAP and ICP measured by AS/3 and Codman® ICP monitoring system:

$$CPP = MAP - ICP \tag{2}$$

The aim of the controller is to drive the NA infusion rate for increasing MAP due to the raised ICP to maintain the CPP at a setpoint. At starting time, an "early estimation method" – detailed in [Nguyen2005] is used to calculate the delay L and the early slope R of the output response curve. These values are used for tuning a PID controller as given in (3). The coefficient ζ in (3) is estimated based on L, which is presented in Tab.2.

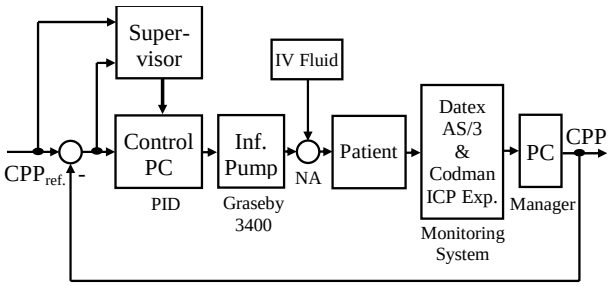

Fig. 3: Structure of CPP control system.

$$K_p = 1.2/RL$$
$$T_d = \zeta L \tag{3}$$
$$T_i = 4T_d$$

Tab. 2: Calculating ζ due to the delay L

L(sec)	[min - 30]	(30 - 60]	(60 - 90]	(90 - max]
ζ	0.6	0.4	0.2	0.1

During control activities, a supervising algorithm is used for online tuning the PID controller to make it acts stronger or weaker against the behavior of patients. This algorithm can be found in [Nguyen 2005].

RESULTS

This CPP control system was tested on animal laboratory with 10 pigs. A selected result is demonstrated in Fig.4. The CPP was maintained at 70±5 mmHg. During each experiment, the raised ICP was also increased by hand to study the responses of the control system that its specifications are given in Tab.3.

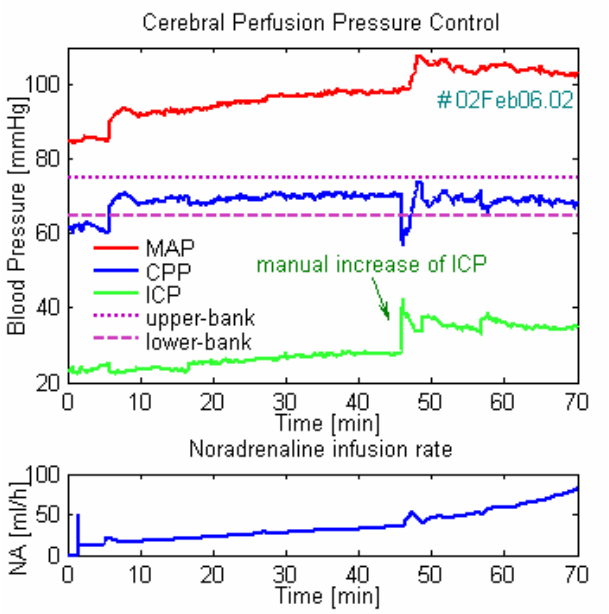

Fig. 4: A result of CPP control on a pig

Tab. 3: Characteristics of the CPP controller

Specifications	Value	Unit
Settling time†	5 ± 1.30	min
Rising time	2 ± 1.06	min
Overshoot	4 ± 1.72	mmHg
Steady-state error	3 ± 2.14	mmHg

†: included the identifying period of estimating R and L.

DISCUSSION and CONCLUSION

The animal experiment with ICP-measurement probe and intraventricular balloon catheter to perform controlled ICP increase seems to be useful. Experimental results indicated that raising MAP by controlling NA infusion rate may be a suitable method to maintain the CPP at an adequate level for raised ICP patients.

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