# Assessing cardiovascular dynamics during ventricular assistance. Use of fuzzy clustering techniques



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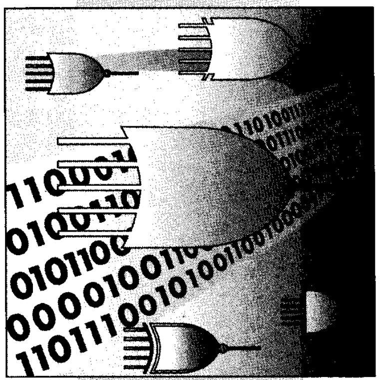
| journal or publication title | IEEE Engineering in Medicine and Biology Magazine |
| volume | 13 |
| number | 5 |
| page range | 687-692 |
| year | 1994 |
| URL | http://hdl.handle.net/10097/48063 |

doi: 10.1109/51.334630



# Assessing Cardiovascular Dynamics During Ventricular Assistance

## *Use of fuzzy clustering techniques*

In the developmental research for the artificial heart, the main field to which fuzzy logic is applied is in producing software algorithms for control and monitoring. This is because fuzzy logic is suitable for linguistic and concrete description of control tasks, malfunction detection, and reasoning processes that have been already carried out by the human operator in the practical clinical use of the artificial heart[1, 2].

In general, realization of high-performance automatic control and effective monitoring requires an appropriate model of the system. For example, a typical traditional method based on a linear dynamic system such as the time series model has been often used. However, the cardiovascular system combined with the artificial heart is considered to be a large-scale, complex, stochastic, non-linear system that included many multi-level feedback loops and time varying unknown parameters. Hence, it is quite difficult to establish a well-approximated and unified global model of the cardiovascular system using traditional mathematical methods.

On the other hand, inside the brain of the medical specialist there must exist a knowledge-base that contains empirical knowledge of control and monitoring or logical rules for decision making accumulated in long-term practical operations of the artificial heart. However, the human knowledge-base is not well organized and may include inconsistent information. Fuzzy logic is good at ex-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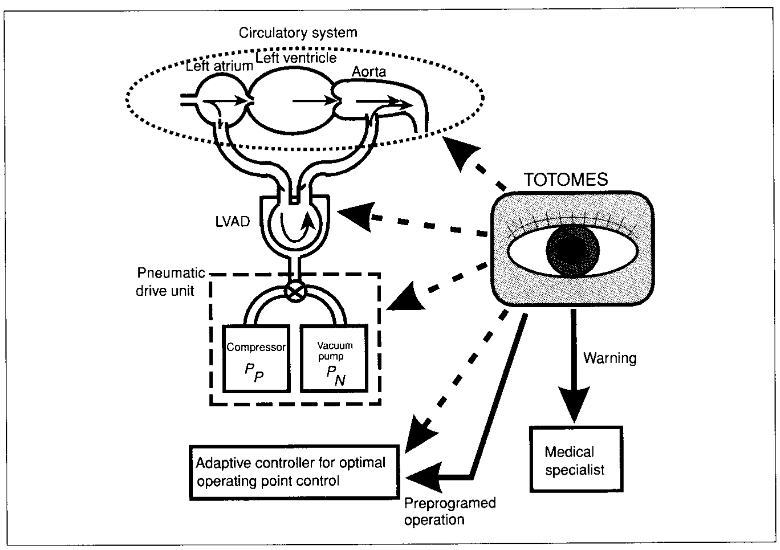


**1. Schematic illustration of the TOTOMES.**



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pressing such uncertain linguistic knowledge in a computer language [3, 4].

As shown in Fig. 1, our group [5] has recently developed an expert system realized by means of fuzzy logic algorithms for monitoring and malfunction diagnosis of the left ventricular assist device (LVAD), one of the many types of artificial hearts developed today. The system is named TOTOMES (Tohoku University and Toyohashi University of Technology, monitoring and estimation system). TOTOMES is suitable for clinical application because it operates in an online and real-time fashion on a widely used personal computer in Japan.

This article introduces the structure and function of the TOTOMES and explains its techniques, such as multi-interrupt tasks and dynamic system identification; as well as fuzzy reasoning used for realizing state estimation, detection, and diagnosis of malfunctions; and monitoring for cardiovascular dynamics under ventricular assistance and the LVAD drive system.

## Methods

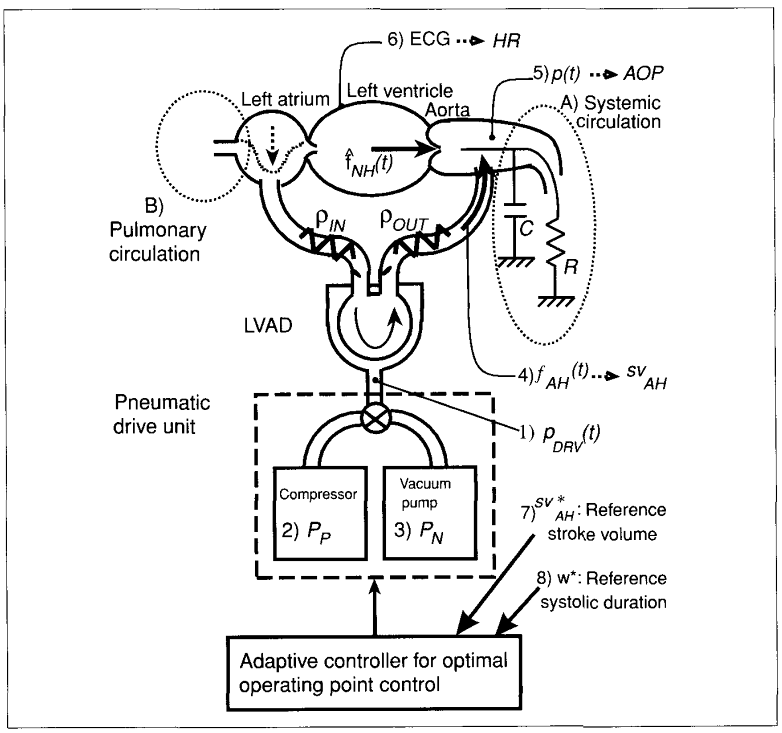
### Aims of LVAD and TOTOMES

The left ventricular assist device (LVAD) is temporarily used in the patient in the state of low cardiac output caused by postcardiotomy or myocardial infarction in order to assist the damaged heart. The LVAD is installed between the left atrium and the aorta and driven by a pneumatic driver, as shown in Fig. 1. The pneumatic drive unit is synchronized with the natural heart beat using a pulse signal triggered by the ECG R-wave.

Any malfunction of the LVAD, if uncorrected, can lead to fatal results. Abnormalities of the pathological state of the patient as well as software and hardware malfunction of the LVAD drive system must be immediately detected.

For clinical application, therefore, it is indispensable to implement 24 hour monitoring of the LVAD operation. At present, the human operator (medical specialist) carries out this monitoring task, and also most of the manipulations for adjusting the control parameters of the LVAD, without relief.

The TOTOMES has been developed as an automatic monitoring system to assist the human monitoring task. In the future, this system will reduce the excessive load of medical specialists and promote clinical use of the LVAD.




**2. Direct measurements and estimated variables of the TOTOMES.**

**TOTOMES operates on-line and in real-time**

### Estimation Procedures

Most of the data directly measured from the cardiovascular system and the LVAD drive system are instantaneous signals. Such intact data are not suitable for fuzzy reasoning algorithms. Hence, the TOTOMES has two processing stages for input information. In the primary stage, the time varying internal state of the cardiovascular system is estimated in a beat by beat and real-time fashion on the basis of instantaneous measurements. In the secondary stage, the fuzzy reasoning engine is applied to the data obtained from the primary stage.

For clinical application, the use of invasive sensors should be avoided as far as possible because they lead to troublesome problems such as infection, drift, and poor durability. In the TOTOMES, hence, the number of invasive measurements used for detecting circulatory abnormalities and malfunctions of the LVAD control system is only one (the aortic pressure sensor). As shown in Fig. 2, directly measured data are listed below.

1. Instantaneous drive pressure, $p_{DRV}(t)$ in mmHg
2. Ejecting drive pressure saturation level, $P_P$ in mmHg
3. Filling drive pressure saturation level, $P_N$ in mmHg
4. Outflow rate from the LVAD, $f_{AH}(t)$ in l/min
5. Aortic pressure, $p(t)$ in mmHg
6. R-R interval obtained from ECG signal in ms

7. Reference stroke volume of the LVAD, $sv^*$ in ml

8. Reference systolic duration of the LVAD, $w^*$ in ms

Each instantaneous datum is stored every 10 ms into a personal computer system (NEC PC-9801RA), where the TOTOMES is implemented. The direct measurements are processed and transformed beat-by-beat into secondary variables such as mean aortic pressure (*AOP*), stroke volume of the LVAD ($sv_{AH}$) and heart rate (*HR*).

The TOTOMES adopts an electrical circuit model of the systemic circulation for the cardiovascular dynamics corresponding to A) seen in Fig. 2. The model is simple enough so that the variables of cardiovascular dynamics, such as peripheral vessel resistance (*R* in mmHg·s/ml) and arterial compliance (*C* in ml/mmHg), can be identified in a real-time fashion via a time series on the basis of the information of $f_{AH}(t)$ and $p(t)$, described in detail in [6].

The cardiac output of the natural heart partly supported by the LVAD is an important index for management of the LVAD. The instantaneous value ($f_{NH}(t)$ in l/min) is estimated by means of the noted variables without any invasive instrument such as a flow meter [6].

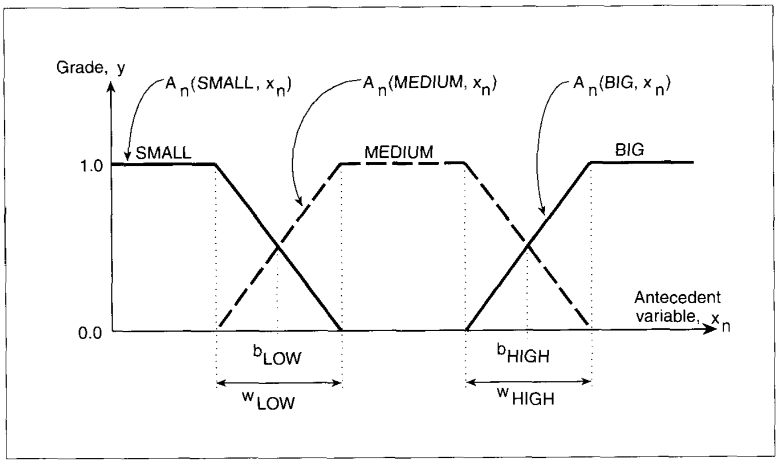
The values of fluid resistance of the inlet and outlet cannulae ($\rho_{IN}$ and $\rho_{OUT}$) seen in Fig. 2 are also useful for judging whether the LVAD is operating normally. Hardware failures such as constriction, leakage, or disconnect of the cannulae; as well as blockage or breakage of the artificial valves will change the fluid resistance of the cannulae. Specifically, the fluid resistance of the inlet cannula, $\rho_{IN}$, will be affected by any abnormality of the pulmonary circulation B) seen in Fig. 2, such as atrial collapse caused by excessive filling drive pressure or decrease in the pulmonary venous return.

Fluid resistance is calculated as the ratio of the pressure difference between two points to the mean flow rate. In steady-state, the inflow volume of a stroke into the sac of the LVAD is the same as the outflow volume of a stroke from the sac. Hence, the mean flow rate of inflow or outflow can be obtained from $sv_{AH}$ (integral of $f_{AH}(t)$) if the inflow time ($w_{IN}$) or outflow time $w_{OUT}$) is known, where the times are defined as period during which there is flow.

Because our LVAD drive system follows the principle of optimal operating point control developed by [7], the following relationship holds:

$$w_{IN} = T_C - w_{OUT} \qquad (1)$$

where $T_C$ is the R-R interval. Hence, the values of fluid resistance are calculated beat-by-beat without measuring the inflow rate directly. However, the left atrial pressure (*LAP*) must be measured to obtain the pressure difference across the inlet cannula. In our system, *LAP* is regarded as an appropriate constant value (10 mmHg) in order to avoid using invasive measurement.




**3. Membership function $A_n(L_n, x_n)$ for label $L_n$ and an antecedent variable $x_n$ (or a consequent variable $z_c$).**

**Table 1**
**Boundary Parameters of Membership Function**

| Antecedent variable | | $b_{LOW}$ | $\omega_{LOW}$ | $b_{HIGH}$ | $\omega_{HIGH}$ |
|---|---|---|---|---|---|
| 0) Consequent variable | | 0.3 | 0.2 | 0.7 | 0.2 |
| 1) Inlet cannula resist. | $\rho_{IN}$[mmHg•s/1] | 0.01 | 0.0025 | 1.5 | 1.9 |
| 2) Outlet cannula resist. | $\rho_{OUT}$[mmHg•s$^2$/1] | 0.0525 | 0.005 | 0.38 | 0.1 |
| 3) Periph. vascular resist. | *R*[mmHg•s/ml] | 15 | 1 | 5 | 2 |
| 4) Arterial compliance | *C* [ml/mmHg] | 0.3 | 0.2 | 1.5 | 0.2 |
| 5) Mean aortic press. | *AOP*[MMHg] | 30 | 20 | 165 | 30 |
| 6) LVAD stroke volume | $s\upsilon_{AH}$ [ml] | 15 | 10 | 35 | 10 |
| 7) NH stroke volume | $s\upsilon_{NH}$ [ml] | 8 | 10 | 35 | 10 |
| 8) Heart rate | *HR* [/min] | 45 | 10 | 165 | 30 |
| 9) S.D. of Heart Rate | $\sigma_{HR}$[/min] | 20 | 10 | 40 | 10 |
| 10) Normalized Heart Rate | *NHR* [/min] | 1.5 | 1 | 3.5 | 1 |
| 11) Ejecting drive press. | $P_p$ [mmHg] | 125 | 50 | 325 | 50 |
| 12) Filling drive press. | $P_N$ [mmHg] | -55 | 10 | 15 | 10 |
| 13) Stroke volume error | $e_{s\upsilon}$ [ml] | 0 | 0 | 20 | 10 |
| 14) Systolic duration error | $e_{\omega}$ [ml] | 0 | 0 | 50 | 20 |

**Heart-rate, cardiac-output, and cardiovascular abnormalities may be detected**

### Detection Procedures

The various abnormalities that may be detected by the TOTOMES are shown below.

1. Hardware failures:
   (a) Air tube of the pneumatic driver
   (b) Cannulae connected to the patient
   (c) Aortic pressure sensor
2. Software failures:
   (a) Malfunction of the software program for the pneumatic controller
   (b) Divergence of the adaptive control algorithm
3. Cardiovascular system:
   (a) Heart rate
   (b) Cardiovascular parameters
   (c) Cardiac output

Each of the above categories includes more detailed items of abnormalitiy, malfunction, or accident.

Abnormality detection is realized by applying fuzzy logic to the beat-by-beat secondary data obtained from the primary processing stage. The algorithm that expresses a set of empirical linguistic rules, i.e., the knowledge-base given by the medical specialist, for abnormality detection is shown below.

Let $x_n$; $n = 1, 2,\ldots, N$ denote the $n$-th antecedent real variable (the secondary data) and let $\{L_n$: *SMALL, MEDIUM, LARGE*$\}$ represent a set of labels for $x_n$. Strictly speaking, $L_n$ is an element of the set of different integers corresponding to these labels, as follows:

$$L_n = \begin{cases} 1 \text{ (label is } SMALL) \\ 2 \text{ (label is } MEDIUM) \\ 3 \text{ (label is } LARGE) \end{cases} \quad (2)$$

Let $A_n$ denote the membership function that maps $L_n$ and $x_n$ to the grade $y \in [0,1]$ given by:

$$y = A_n(L_n, x_n) \quad (3)$$

The number of labels is now three, for simplicity and comprehensibility, but it can be larger. The shape of the function is trapezoidal as depicted in Fig. 3. Table 1 shows the boundary parameters ($b_{LOW}$, $\omega_{LOW}$, $\beta_{HIGH}$, $\omega_{HIGH}$) defining the functions that were temporarily decided in our experiments. The left side items (1) to (14) in this table correspond to the secondary data appearing in antecedent variables, $x_n$. Let the consequent variable denote $z_c$; $c = 1,2,\ldots, C$ with the label $L_0$ corresponding to the left side item (0) in Table 1.

The reasoning algorithm consists of IF-THEN rules. Let the number of the rules be $R$. The $r$-th rule is described by:

**If**
antecedent variable $x_1$ is label $L_1$, and
antecedent variable $x_2$ is label $L_2$, and
⋮
antecedent variable $x_N$ is label $L_N$.
**then**
consequent variable $z_c$ is label $L_0$.

Figure 4 shows an example of the fuzzy rules used in the TOTOMES. This rule is concerned with the cannula resistances, $\rho_{IN}$ and $\rho_{OUT}$.

The set of the rules defined above can be represented by the rule function $f$ that maps integers $c$, $r$, $n$ to an integer $L_n$ as follows:

$$L_n = f(c,r,n);$$
$$c = 1,\ldots,C, \ r = 1,\ldots,R, \ n = 0,\ldots,N. \quad (4)$$

The function $f(c, r, n)$ can be simply expressed by a three dimensional integer

a) IF ($\rho_{OUT}$ is *large*) and ($\rho_{IN}$ is *medium*) and (*AOP* is *medium*)
THEN the outlet cannula is constricted.

b) IF ($\rho_{IN}$ is *large*) and ($\rho_{OUT}$ is *medium*) and (*AOP* is *medium*)
THEN the inlet cannula is constricted.

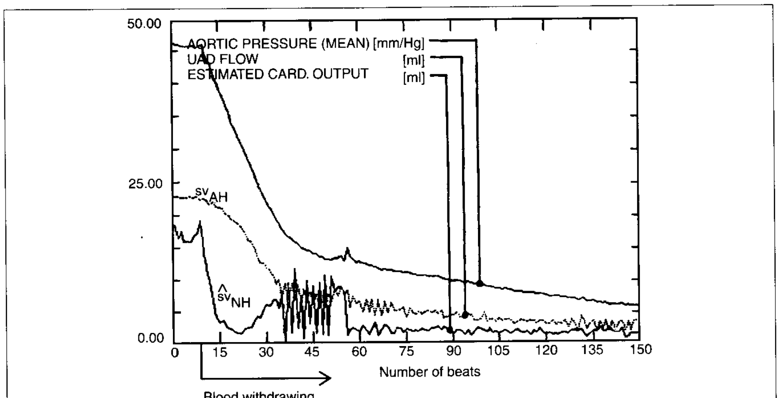
c) IF ($\rho_{OUT}$ is *large*) and ($\rho_{IN}$) is *large*) and (*AOP* is *medium*)
THEN the air tube is constricted or has leakage.

d) IF ($\rho_{in}$ is *large*) and (*AOP* is *small*)
THEN the left atrium is collapsed or the pulmonary venous return decreases.

e) IF ($\rho_{OUT}$ is *small*) THEN the outlet cannula has leakage.

f) IF ($\rho_{IN}$ is *small*) THEN the inlet cannula has leakage.

**4. An example of fuzzy logic with respect to outlet and inlet cannula resistance, $\rho_{IN}$ and $\rho_{OUT}$.**




**5. Variation of mean aortic pressure, *AOP*, stroke volume of the LVAD, $sv_{AH}$, and estimated stroke volume of the natural heart, $\hat{sv}_{NH}$ with heart beat during withdrawal of blood in an adult goat.**

array in the computer program. In the TOTOMES, the conformity rate denoted by $\omega_c(r)$ for the $r$-th rule and the $c$-th consequent variable $z_c$, is defined by:

$$\omega_c(r) = \prod_{n=1}^{N} A_n(f(c, r, n), x_n) \tag{5}$$

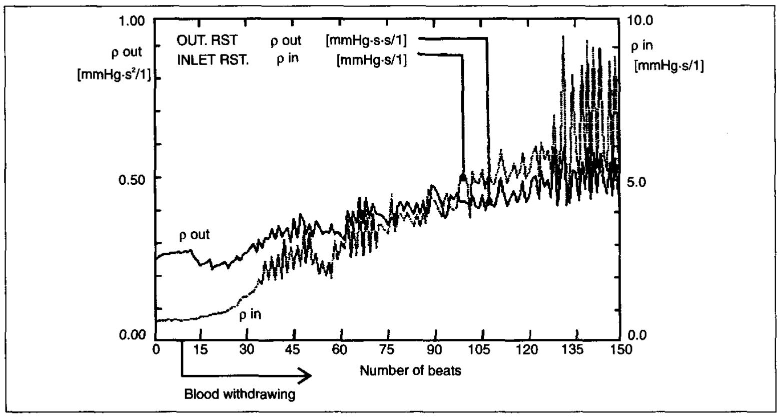
Let $B_c(z_c)$ denote the membership function of the consequent variable, $z_c$. $B_c(z_c)$ is represented by:

$$B_c(z_c) = \bigvee_{r=1}^{R} \omega_c(r) \cdot A_0(f(c, r, 0), z_c) \tag{6}$$

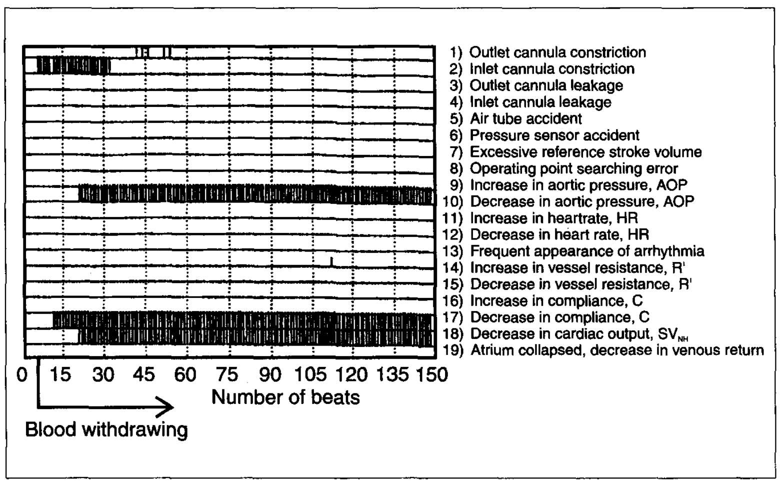
The result of reasoning is displayed by a bar on the monitoring screen, whose length corresponds to the center of gravity of $B_c(z_c)$. All the above operations can be calculated very quickly, as all the membership functions are trapezoidal and can be expressed by integers. However, the parts of the program corresponding not only to these operations, but also to system identification must be written in assembler language as interrupt routines to be implemented on the personal computer. Even with fairly high PC processing speed, real time operations are required to display the reasoning and identification results as well as instantaneous waveform of the measured variables. The other parts of the program were written in QuickBASIC.

In practice, of course, these rules and boundary parameters have to be modified by the medical specialist according to the condition of the patient or the opoeration of the hardware. Modification can be easily carried out during actual patient monitoring because multi-level interrupt routines are used in the key program. The multi-level interrupt routines can realize the pseudo-parallel processing, which consists of three parts: 1) instantaneous data acquisition and displaying on a monitor screen every 10 ms, 2) parameter estimation of the cardiovascular system for producing antecedent variables every time when the R-wave of ECG is detected, and 3) a fuzzy reasoning process which carries out preprogrammed operations such as the artificial vocal warning (ASCII Voice Maker AV-10) and switching the drive mode from automatic control to fixed control.

The combination of several measurements and estimates included in the antecedent of the rules enables us to distinguish the origins of the malfunctions.




**6. Variation of inlet and outlet cannula resistance, $\rho_{IN}$ and $\rho_{OUT}$ with heart beat corresponding to Fig. 5.**




**7. Display screen of monitoring function in the case of Figs. 5 or 6. Each bar represents the beat at which the right hand side item was detected.**

## Results

*In vivo* experiments using an adult goat were carried out. Anesthesia was induced with intramuscular ketamine hydrochloride (0.8mg/kg), followed by 4% halothane, trachael intubation and ventilation with a volume respirator. Inlet and outlet cannulae connected to the LVAD were inserted into the left atrium and the descending aorta, respectively.

Figure 5 shows the change in aortic pressure, *AOP*, stroke volume of the LVAD, $sv_{AH}$, and the estimated stroke volume of the natural heart, $\hat{sv}_{NH}$, during withdrawal of blood. Figure 6 shows the change in the inlet and outlet cannulae resistances, $\rho_{IN}$ and $\rho_{OUT}$ in the same case as Fig. 5. It can be seen that after blood withdrawal, *AOP*, $sv_{AH}$, and $\hat{sv}_{NH}$ began to decrease, while $\rho_{IN}$ and $\rho_{OUT}$ began to increase. Note, the rate of increase of $\rho_{IN}$ is larger than that of $\rho_{OUT}$.

Figure 7 shows the displayed result of the monitoring operation corresponding to Figs. 5 and 6. Each vertical bar represents the beat at which the corresponding right hand side item was detected.

## Discussion and Conclusion

The incorrect judgement of the 2nd item (inlet cannula constriction) was detected from the 6th beat to the 32nd beat. This resulted from the rule b) in Fig. 4, because both *AOP* and $\rho_{OUT}$ can be regarded as normal during this interval. After the 18th beat, however, the correct judgement of the 19th (atrium collapsed, decrease in venous return) item was also detected. This is because the withdrawal of blood caused a decrease in pulmonary venous return, a decrease in aortic pressure, and an apparent increase in the inlet cannula resistance. This resulted from the rule d) in Fig. 4. From the 18th beat to the 32nd, the inconsistent result that both the 2nd and the 19th items were simultaneously shown is due to the fuzzy characteristic of this kind of reasoning.

It has already been confirmed that the TOTOMES worked successfully in the case of hardware malfunction. However, the transient responses of the estimated variables of the cardiovascular dynamics were too complicated to distinguish clearly the origin of physiological abnormalities.

The proposed fuzzy rules have subjective thresholds specified by the medical specialists. These values are not adaptive, and the set of rules may have internal inconsistencies. The present system cannot identify any inconsistency. A more refined algorithm is needed, in which the thresholds are automatically set if the patient or the clinical conditions change. Moreover, the time-series-pattern of the instantaneous data may be considerably in rich information. If this information can be incorporated into the antecedent variable, we will be able to make the medical specialist's knowledge-base reflect the fuzzy reasoning engine in a more dynamic and inclusive manner.

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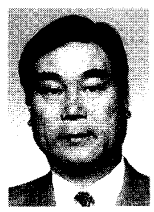

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