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Analog Computer Analysis of Dilution Curves Recorded by Scintillation Camera : Measurements of Cardiac Chamber and Pulmonary Volumes and Left to Right Shunts

by

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The recent development of the Anger scintillation camera[1,2] and the introduction of short-lived radionuclides, such as ^{99m}Tc-pertechnetate[3~5], have made it possible to visualize dynamic process of blood flow through the heart and great vessels. This technique has been successfully used for the evaluation of various cardiac and/or vascular disorders[6~19]. Although this radioisotopic angiocardiography does not provide details as precisely as standard contrast angiocardiography, it is considered to be useful as a screening procedure prior to cardiac catheterization and as a guide to the evaluation of medical and surgical therapy because of its complete safety and easiness of performance.

The most of previous studies of cardiovascular dynamics with the scintillation camera were directed toward obtaining visual findings of the scintiphoto sequence, such as a shape of chamber, abnormal shunt with reappearance of activity, delayed washout from a chamber or vessel and etc. However, with the technologic advances in data acquisition and analytic system in these days, many attempts of quantitative analysis of radioisotopic angiocardiography have been reported[20~35]. These include the analysis of dilution curves generated from the selected areas of cardiopulmonary regions, and the direct volume measurement from the selected images with or without electrocardiographical triggering.

In this report, an analog simulation technique which is a new method of analyzing the dilution curves obtained from the cardiac chambers and lung field is described and clinical experiences with this technique are shown. This method permits repeated measurements of the important parameters of circulation, such as mean transit time,

mean cardiac chamber and pulmonary volumes, intracardiac shunt rate and cardiac output, without the hazard of cardiac catheterization.

Method

A scintillation camera (Pho/Gamma III, Nuclear Chicago) with 4000 hole collimator, 1600 word memory system (Model 24-3, Nuclear Chicago), a computer compatible magnetic tape recorder(TM-7, TOAMCO), data-store/playback accessory(Nuclear Chicago) and a FACOM 230-60 computer were used in this study (Fig. 1).

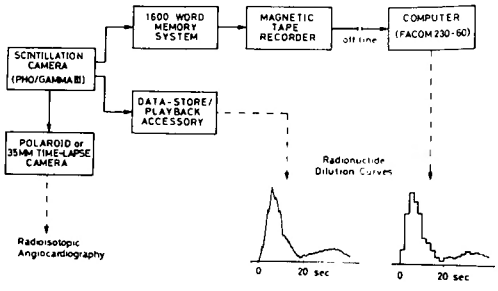


Fig. 1. Diagram of the scintillation camera and recording system. Lower right curves show the dilution curves read out after a region of interest is selected.

The patient was placed in the supine or sitting position. The collimator of a scintillation camera faced at a slight left anterior oblique plane and scintiphotos were routinely taken with a Polaroid or 35mm time-lapse camera at various intervals after a rapid intravenous injection of 5mCi of ^{99m}Tc-pertechnetate or ^{99m}Tc-albumin in a volume of less than 1 ml. At the same time, the positioned pulses from the scintillation camera were accumulated by 1600 word memory as a digitized 40 X 40 matrix during 0.6 second and then transferred to a computer compatible magnetic tape recorder. As the data were collected during first 0.6 second and the subsequent 0.3 second was required for transfer of the data from the 1600 word memory to the magnetic tape, the data points were obtained at 0.9 second intervals. By digital computer processing, the data stored on magnetic tape were printed out in terms of 40 X 40 matrix for each frame sequentially. The areas representing the superior vena cava (SVC), right atrium (RA), right ventricle (RV), lung, left atrium (LA) and left ventricle (LV) were selected as the regions of interest on these printout (Fig. 2). Following the identification of the regions of interest, the dilution curve of each area was read out in the form of an incremental histogram with each increment of 0.9 second duration. Instead of 1600 word memory system, data-store/playback accessory was used in recent study. With this instrument, the entire dynamic sequence was recorded simultaneously on video tape in terms of 256 X 256 elements. During video tape playback,

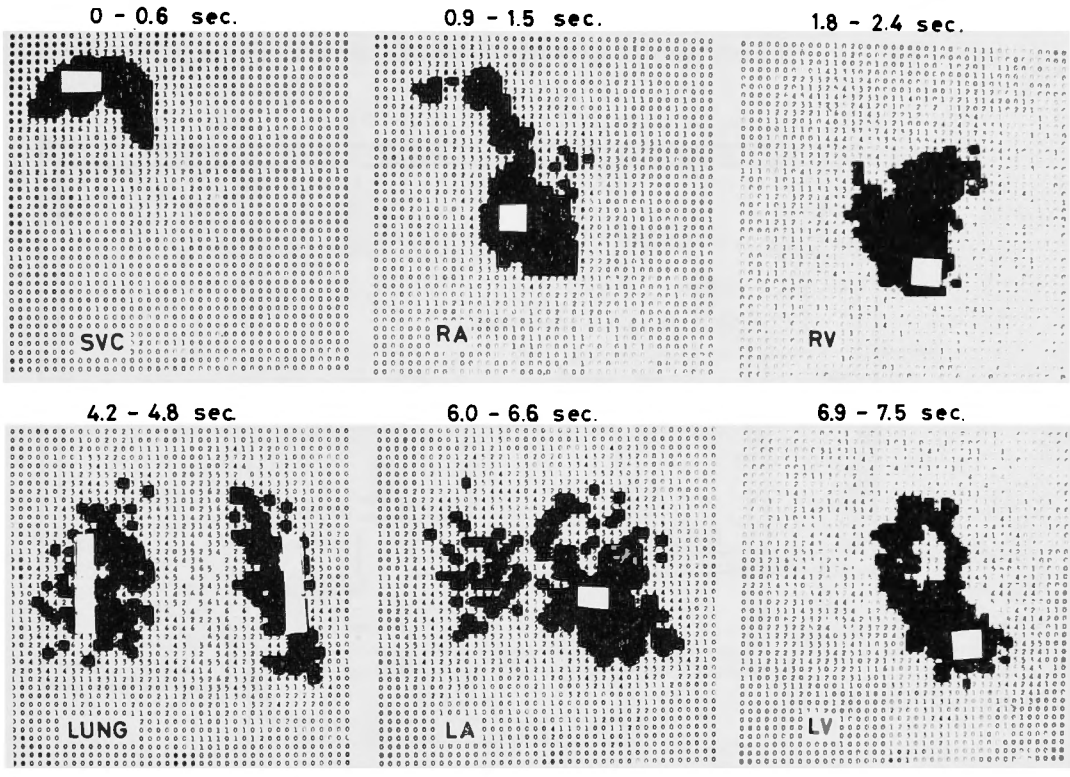


Fig. 2. Computer print-out with black areas representing regions of increased counting rate, and white areas showing regions of interest to derive dilution curves from specific compartments. It is important not to select regions of interest that contain significant activity from adjacent or superimposed chambers. Especially, the pulmonary dilution curve which is used for the determination of shunt rate and of parameters of body compartment must be carefully obtained from the strip areas at the periphery of right or left lung including both upper and lower portions of it, not to contain the heart or the great vessels of pulmonary artery or vein.

analog tracings of radioisotope flow through any selected areas of interest could be obtained on a strip chart more rapidly and simply than with the former system. Thus, the dilution curves obtained from the areas representing SVC, RA, RV, lung, LA and LV are analyzed by means of the analog simulation technique mentioned later.

Mathematical Model and Analog Simulation Circult of The Circulatory System

The whole circulatory system can be simply defined as a closed circuit containing six compartments, that is, RA, RV, lung, LA, LV and body. In addition, left to

right shunts are represented by conduits connecting the left and right cardiac chambers (Fig. 3) . If each cardiac chamber is treated as a single mixing chamber,

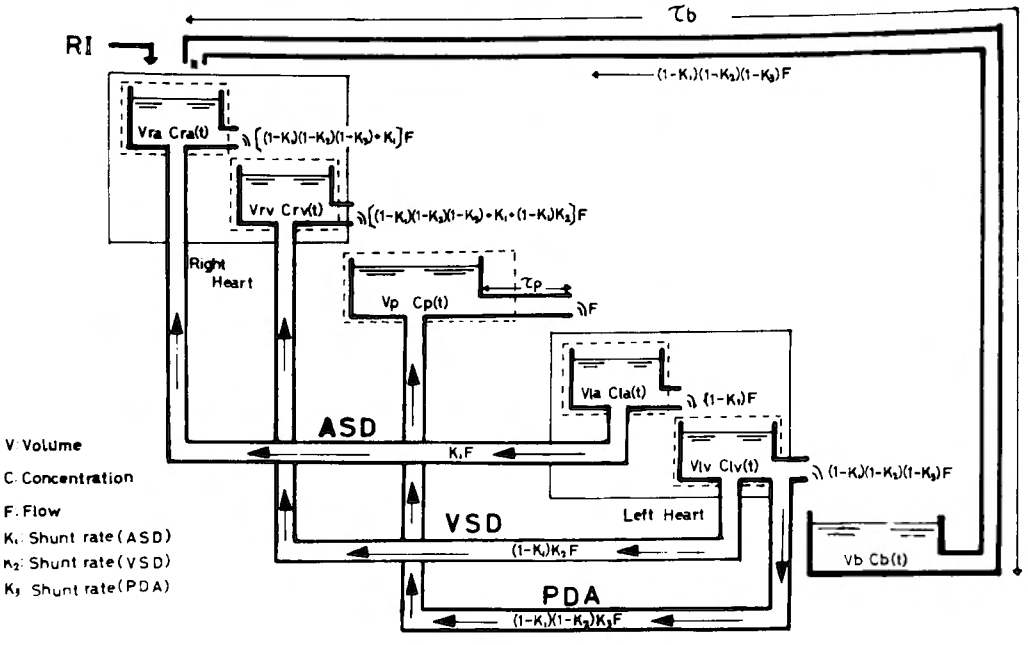


Fig. 3. Simplified model of the circulatory system. Six tanks represent right atrium, right ventricle, lung, left atrium, left ventricle and body. Intracardiac shunts are shown as conduits connecting left and right cardiac chambers. Injection compartment are not shown in this figure.

and lung and body as a single mixing chamber with a transport time delay, this circulatory system can be approximated by a series of first order lag systems with or without time delays.

The input-output relationship between two adjoining compartments in a series, such as the Xth compartment and the preceding X-1th compartment, is generally expressed as following;

$$V_x C_x(t) = F\int_0^t C_{x-1}(t)dt - F\int_0^t C_x(t)dt \qquad \cdots\cdots(1)$$

(Input) (Output)

where V_x : volume of the Xth compartment

$C_x(t)$ and $C_{x-1}(t)$: concentration of radioisotope in the Xth and the X-1th compartment at time t, respectively

F : blood flow through the system

In the case of the compartment with a transport lag, τ_x, Eq. (1) can be rewritten as ;

$$V_x C_x(t) = F\int_0^t C_{x-1}(t-\tau_x)dt - F\int_0^t C_x(t)dt \qquad \cdots\cdots(2)$$

These equations mean that the total amount of radioisotope in a certain compartment at the time t is the difference between the input and output of the compartment during the time t (Fig. 4).

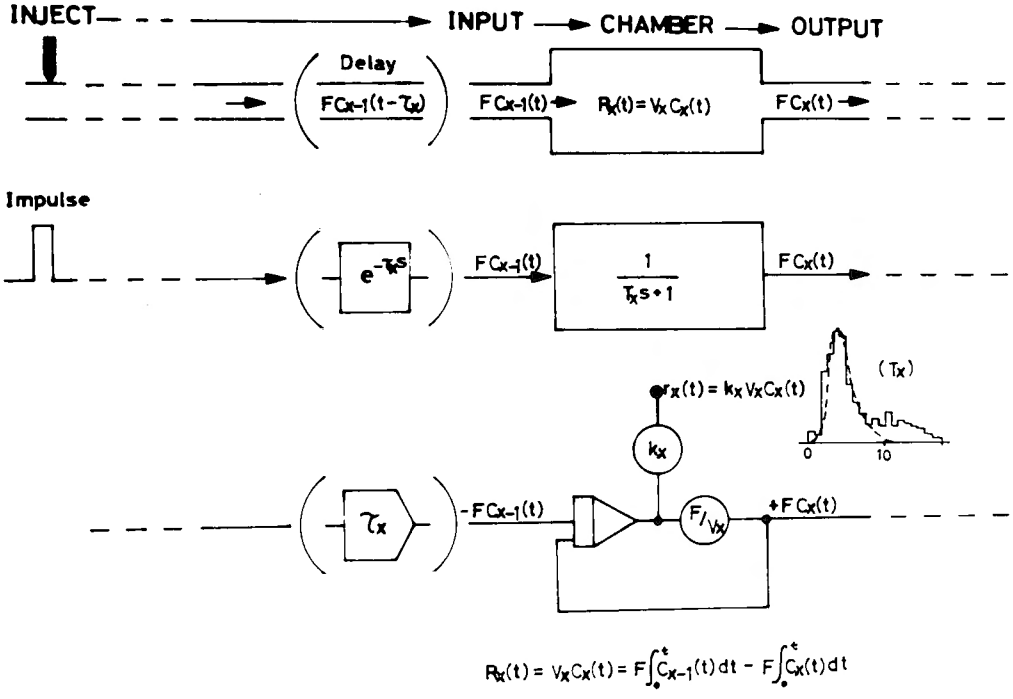


Fig. 4. Input-output relationship of the Xth compartment. Total amount of the radio-isotope in a specific compartment at the time t is the difference between the input and output of that compartment. This relationship is expressed in terms of the Laplace transform and transfer function (middle panel) and the analog simulation circuit of this is shown (lower panel). With the curve fitting, two potentiometers controlling the reciprocal of the mean transit time (F/V_x) and measuring effeciency (k_x) are determined.

Thus, the whole circulatory system is represented by a series of compartments defined by Eq. (1) or (2). Taking left to right shunts into consideration, the transportation processed of the injected radioisotope through six compartments are shown by following equations.

$$RA: V_{ra}C_{ra}(t) = F_i\int_0^t C_i(t)dt+(1-K_1)(1-K_2)(1-K_3)F\int_0^t C_b(t-\tau_b)dt+K_1 F\int_0^t C_{1a}(t)dt-\left[(1-K_1)(1-K_2)(1-K_3)+K_1\right]F\int_0^t C_{ra}(t)dt \quad \cdots\cdots(3)$$

$$RV: V_{rv}C_{rv}(t)=\left[(1-K_1)(1-K_2)(1-K_3)+K_1\right]F\int_0^t C_{ra}(t)dt+(1-K_1)K_2F\int_0^t C_{1v}(t)dt-\left[(1-K_1)(1-K_2)(1-K_3)+K_1+(1-K_1)K_2\right]F\int_0^t C_{rv}(t)dt \quad \cdots\cdots(4)$$

$$\text{lung}: V_pC_p(t)=\left[(1-K_1)(1-K_2)(1-K_3)+K_1+(1-K_1)K_2\right]F\int_0^t C_{rv}(t)dt+$$
$$(1-K_1)(1-K_2)K_3F\int_0^t C_{1v}(t)dt-F\int_0^t C_p(t)dt \qquad \cdots\cdots(5)$$

$$\text{LA}: V_{1a}C_{1a}(t)=F\int_0^t C_p(t-\tau_p)dt-K_1F\int_0^t C_{1a}(t)dt-(1-K_1)F\int_0^t C_{1a}(t)dt \qquad \cdots\cdots(6)$$

$$\text{LV}: V_{1v}C_{1v}(t)=(1-K_1)F\int_0^t C_{1a}(t)dt-(1-K_1)K_2F\int_0^t C_{1v}(t)dt-(1-K_1)(1-K_2)K_3$$
$$F\int_0^t C_{1v}(t)dt-(1-K_1)(1-K_2)(1-K_3)F\int_0^t C_{1v}(t)dt \qquad \cdots\cdots(7)$$

$$\text{body}: V_bC_b(t)=(1-K_1)(1-K_2)(1-K_3)F\int_0^t C_{1v}(t)dt-(1-K_1)(1-K_2)(1-K_3)$$
$$F\int_0^t C_b(t)dt \qquad \cdots\cdots(8)$$

In these equations, subscripts ra, rv, p, la, lv and b denote RA, RV, lung, LA, LV and body, respectively. V is an equivalent mean volume of each compartment, C (t) is concentration of radioisotope in each compartment at the time t. Transport time lag in lung and body are represented by τ_p and τ_b, respectively. The rate of left to right shunt flow to the mean blood flow F are represented by K_1 for interatrial shunt (atrial septal defect, ASD), K_2 for interventricular shunt (ventricular septal defect, VSD) and K_3 for aortopulmonary shunt (patent ductus arteriosus, PDA), respectively.

As the administration of radioisotope into the system is done by peripheral venous injection, further assumption is necessary for the process of the injection and the transportation of the tracer to right atrium. Therefore, the injection compartment defined as a small mixing chamber is added into the system.

$$V_iC_i(t)=\int_0^t i(t)dt-F_i\int_0^t C_i(t)dt \qquad \cdots\cdots(9)$$
$$i(t)=\begin{cases} I/\tau, & 0\leq t\leq\tau \\ 0, & t>\tau \end{cases}$$
$$\int_0^\infty i(t)dt=I$$

where subscript i denotes injection compartment. i (t), I and τ represent injection speed, total amount of injected tracer and injection time, respectively.

The transportation process of the injected radioisotope shown in Eqs. (3) to (9) are simply expressed in terms of the Laplace transform and transfer function as Fig. 5. Time constant, T, in this block diagram can be represented as follows.

$$T_i=V_i/F_i,\ T_{ra}=V_{ra}/\left[(1-K_1)(1-K_2)(1-K_3)+K_1\right]F,\ T_{rv}=V_{rv}/\left[(1-K_1)(1-K_2)\right.$$
$$\left.(1-K_3)+K_1+(1-K_1)K_2\right]F,\ T_p=V_p/F,\ T_{1a}=V_{1a}/F,\ T_{1v}=V_{1v}/(1-K_1)F,$$
$$T_b=V_b/(1-K_1)(1-K_2)(1-K_3)F, \qquad \cdots\cdots(10)$$

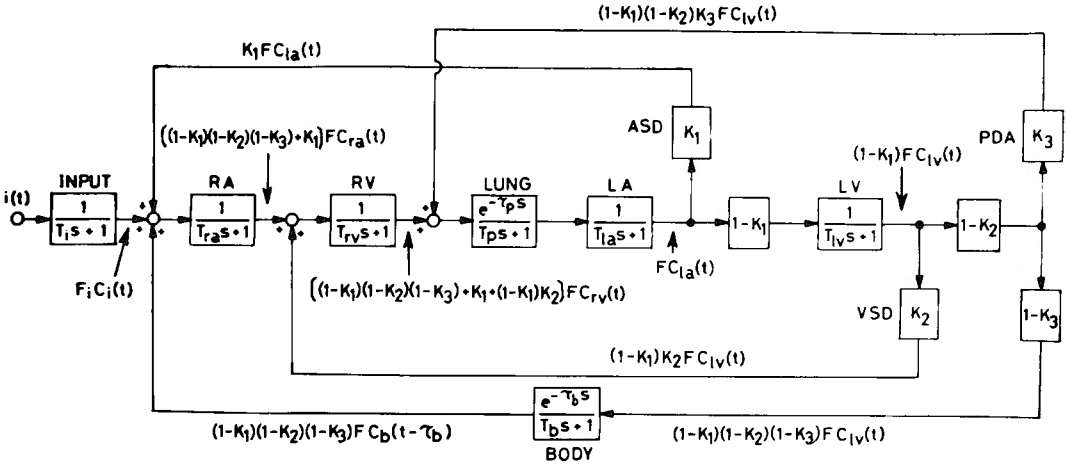


Fig. 5. Block diagram representation of transportation processes of injected radioisotope taking intracardiac shunt flow into consideration.

Time constant of all compartments except for the lung and body represents the mean transit time of the respective compartments. On the other hand, the mean transit time of the lung and body can be expressed as $T_p + \tau_p$ and $T_b + \tau_b$, respectively.

An analog simulation circuit of the circulatory system represented by Eqs. (3) to (9) is constructed by an analog computer which consists of 9 integrators, 16 adders, 10 operational amplifiers, 4 time delay units, 24 potentiometers, a comparator and an x-y recorder. In order to maintain a stable operation of the simulation circuit, the following equation should be added to the circuit (Fig. 6).

$$F_i\int_0^t C_i(t) = V_{ra}\,C_{ra}(t) + V_{rv}\,C_{rv}(t) + V_pC_p(t) + F\int_0^t C_p(t)d(t) - F\int_0^t C_p(t-\tau_p)dt + V_{1a}\,C_{1a}(t) + V_{1v}\,C_{1v}(t) + V_b\,C_b(t) + (1-K_1)(1-K_2(1-K_3)\,F\int_0^t C_b(t)dt - (1-K_1)(1-K_2)(1-K_3)\,F\int_0^t C_b(t)(t-\tau_b)dt \quad \cdots\cdots(11)$$

This means that the total amount of the injected radioisotope during the time t equals the sum of the doses existing in the system.

The dilution curves, r(t), obtained from the areas representing RA, RV, lung, LA and LV can be expressed as follows.

$$r_{ra}(t) = k_{ra}\,V_{ra}\,C_{ra}(t),\ r_{rv}(t) = k_{rv}V_{rv}C_{rv}(t),\ r_p(t) = k_pV_pC_p(t),$$
$$r_{1a}(t) = k_{1a}V_{1a}C_{1a}(t),\ r_{1v}(t) = k_{1v}V_{1v}C_{1v}(t) \quad \cdots\cdots(12)$$

where k is a constant or gain-factor which depends on the counting efficiency of the camera and on the monitored volume for each compartment.

These dilution curves are fitted by the model curves of the computer according to the respective dilution process in the order of the transportation processes of the

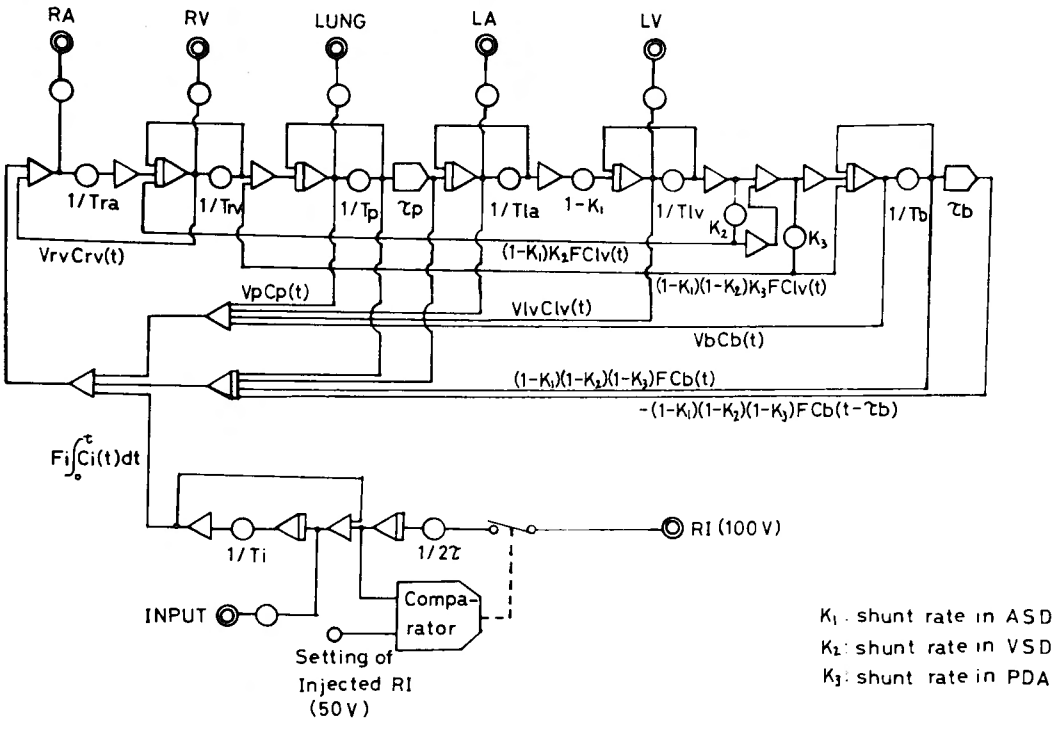


Fig. 6. Analog computer simulation circuit for analysis of the dilution curves derived from cardiac chambers and lung.

injected tracer by selecting the optimal parameter iteratively on the computer. The optimal parameters for each compartment represent time constants (T=V/F) for mixing chambers, time delays for lung and body and shunt rates in cases with intracardiac shunts. Each parameter corresponds to potentiometer on the computer control.

Total circulating blood volume, VOL, is given by

$$VOL = V_{ra} + V_{rv} + V_p + F\tau_p + V_{la} + V_{lv} + V_b + (1-K_1)(1-K_2)(1-K_3)F\tau_b \quad \cdots\cdots(13)$$

On the other hand, mean radioisotope concentration in equilibrium state, $C(\infty)$, can be represented by

$$C(\infty) = I/VOL \quad \cdots\cdots(14)$$

The substitution of Eqs. (10) and (13) into (14) yields the following expression ;

$$F \cdot C(\infty) = I/\{[1-K_1)(1-K_2)(1-K_3)+K_1]T_{ra} + [(1-K_1)(1-K_2)(1-K_3)+K_1+ (1-K_1)K_2]T_{rv} + T_p + \tau_p + T_{la} + (1-K_1)T_{lv} + (1-K_1)(1-K_2)(1-K_3)(T_b+\tau_b)\} \quad \cdots\cdots(15)$$

$C(\infty)$ can be measured by using a well-type scintillation counter and all the parameters in the right side of Eq. (15) can be determined from the analog simulation

of the dilution curves derived from the respective compartments. Subsequently, blood flow, F, is obtained. Therefore, mean blood volume of each compartment is obtained as follows.

$$V_{ra}=T_{ra} \times F,\ V_{rv}=T_{rv} \times F, V_p=(T_p+\tau_p) \times F,\ V_{1a}=T_{1a} \times F,\ V_{1v}=T_{1v} \times F,$$
$$V_b=(T_b+\tau_b) \times F \qquad \cdots\cdots(16)$$

Determinations of The Parameters by The Curve Fitting Analysis

The potentiometers of the analog computer are adjusted sequentially in the following order.

(1) At first the input or SVC curve is fitted by adjusting the potentiometers for injection time, τ, and time constant, T_i. The combination of these parameters determine the shape of input curve as shown in Fig. 7.

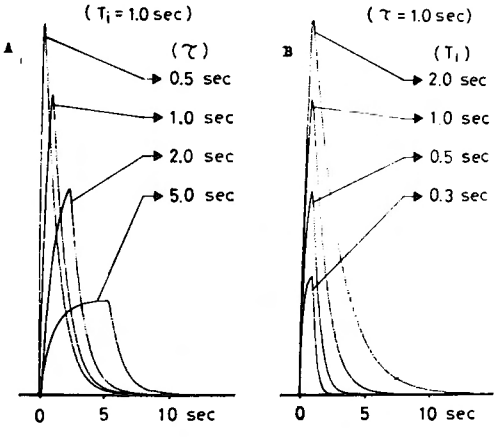


Fig. 7. A&B Changes of input curve with the variations of the parameters, injection time τ(A) and time constant T_i(B).

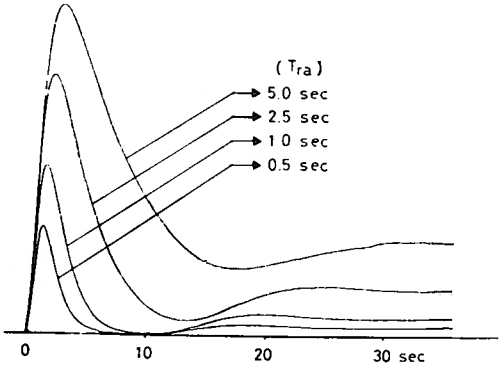


Fig. 8. Changes of RA curve with the variations of time constant T_{ra}.

(2) The dilution curves of RA to LV are analyzed in the order of the transportation processes of the tracer. For each curve, two parameters controlling the mean transit time, T, and counting efficiency (gain factor), k, are adjusted iteratively. Time delay of the lung, τ_p, is determined by the delay of the appearance of LA curve. When LA curve is obscured by activity of adjacent structures, LA compartment is simply treated as a time lag which is added to the time delay part of

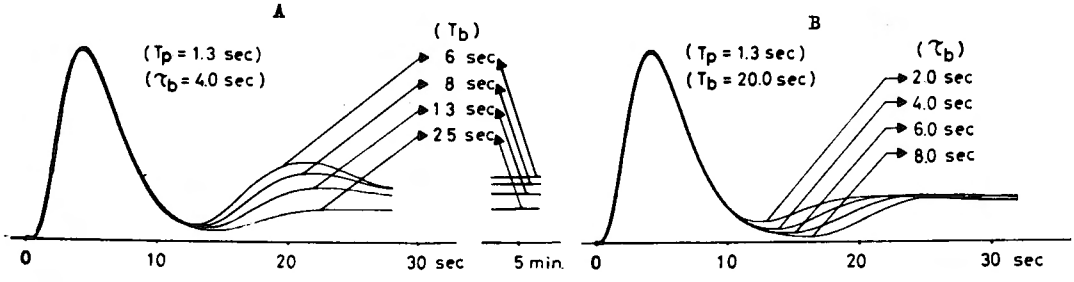


Fig. 9. A&B Changes of pulmonary dilution curve with the variations of T_b (A) and τ_b (B).

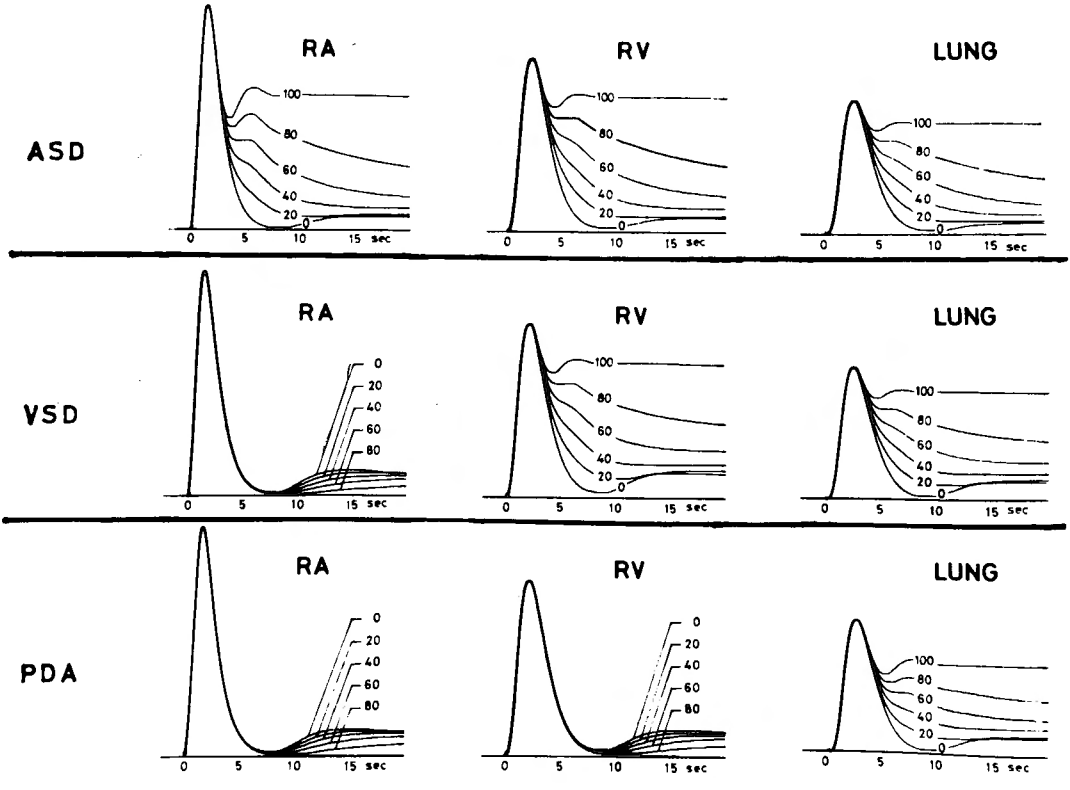


Fig. 10. Effects of left to right shunt rates on the dilution curves derived from RA, RV and lung. ASD, VSD and PDA are differentiated by the configuration of these curves.

the lung. Time delay in this situation is estimated by time delay to the onset of LV curve. Fig. 8 shows the effects of the changes of time constant, T, on the curve of a cardiac chamber.

(3) The parameters for body compartment are determined from the recirculation curve, namely, the height of the equilibrated state of the pulmonary or LV curve that seems to be least contaminated by the radioactivity of surrounding regions. The effect of the two parameters of body compartment, T_b and τ_b, on the pulmonary curve are shown in Fig. 9.

(4) The left to right shunt rate $K_{(1-3)}$ is determined from the down slope of the pulmonary dilution curve and the site of shunt is judged by the configuration of RA, RV and lung curves (Fig. 10).

Model Experiment

A mechanical heart model was constructed to test the practical feasibility of the analog computer analysis of the dilution curves obtained from the scintillation camera. The model consisted of four plastic spheres, two reservoirs, a flow-meter and a pump. These were connected in series by flexible silicone tubing. Cardiac chambers were represented by plastic spheres with the volume of 113 ml, and the lung and body were represented by two reservoirs. Four cardiac chambers were separately arranged so that they did not overlap each other (Fig. 11). The mean water flow of the circuit were measured by a flow-meter.

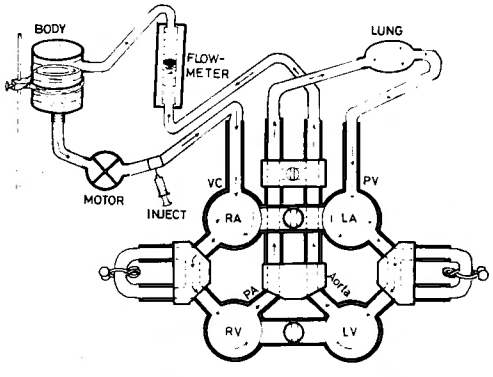


Fig. 11. Schematic presentation of a mechanical heart model. Although the model was constructed in consideration of intracardiac shunts or valvular regurgitation, only the normal condition as shown by arrows was used in the present study.

After the administration of 5 mCi of ^{99m}Tc-pertechnetate, the dilution curve for each compartment was obtained and analyzed using the above-mentioned equipment. However, it was impossible to record the pulmonary dilution curve because

the lung reservoir was out of the field of the scintillation camera. So the parameters for this compartment were determined by actual measurements.

In various flow rates ranging 2.5 L/min to 7.0 L/min, computed volumes of cardiac chambers were compared with actual volumes. An example of the analog simulation analysis of the curves are shown in Fig. 12. Good correlation was obtained between the computed volumes by the analog simulation method and the actual volumes of the model (Fig. 13). From the results of the model experiments, it was concluded that an analog simulation method would be valid and suggested to be reliable for the clinical evaluation of heart chamber volume and so on.

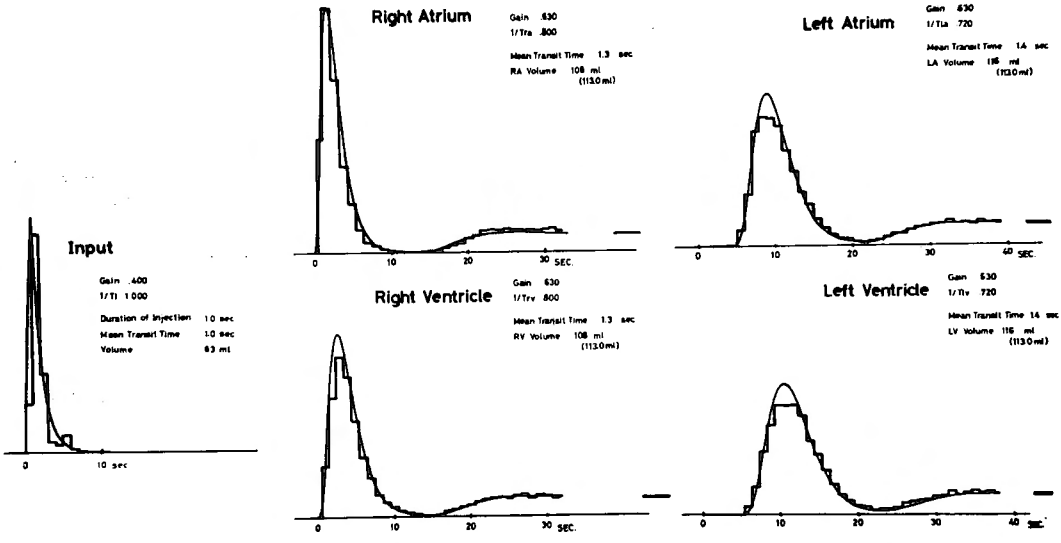
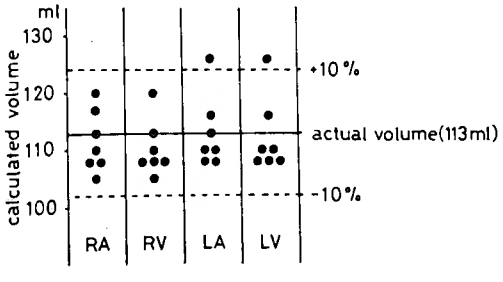


Fig. 12. Dilution curves and simulation results of the model experiment. Total Water Volume : 4,000 ml, Systemic Flow : 82.5 ml/sec (83 ml/sec by Flow-Meter), Mean Volumes (Transit Times) of Cardiac Chambers :RA=108ml (1.3sec), RV=108ml (1.3sec), LA=116ml (1.4sec), LV=116ml (1.4sec).



mean difference (±S.D.)

RA : -1.3 % ± 4.8 RV : -2.4 % ± 4.4

LA : 0 % ± 5.4 LV : -0.6 % ± 5.9

Fig. 13. Correlation of computed volumes and actual volumes in the model experiments.

Clinical Application and Result

The typical dilution curves and their analog simulation data of a normal subject and the patients with intracardiac shunt and valvular lesions are shown in Fig. 14 to Fig. 16. In these cases, either ^{99m}Tc-pertechnetate or ^{99m}Tc-albumin was used as a tracer. It was generally recognized that pertechnetate was not suitable for the measurements of blood volume and cardiac output because of the rapid loss of this agent from the vascular space. Nevertheless, it was assumed to be negligible of the loss during the first passage through heart.

In the initial part of the investigation, ^{99m}Tc-pertechnetate was used in 12 normal subjects and 54 patients with various heart diseases. Only mean transit times of the cardiac chambers and lung were determined by the analog simulation of the dilution curves, and subsequent calculations of blood flows or volumes were not possible. Thus, in 40 subjects who had subsequently undergone cardiac catheterization, volume of each compartment was given by multiplying mean transit time by blood flow measured by the standard Fick method (hereinafter to as simulation-Fick method). As cardiac catheterization were not performed in the normal subjects, the normal cardiac index of 3.6 L/min/m^2 was assumed for comparison. In Table 1 are listed the averages of mean transit times and volumes for the ten groups of patients.

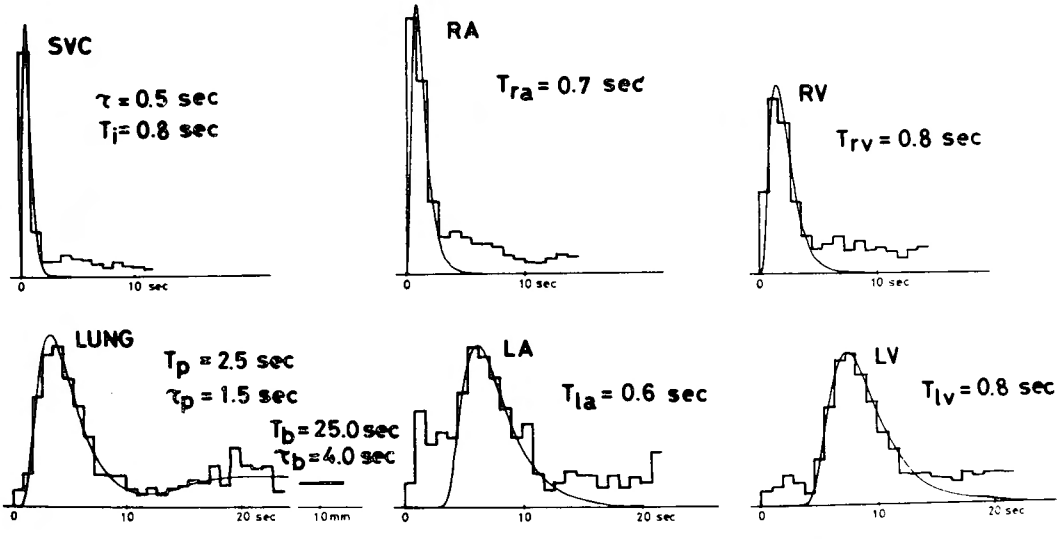


Fig. 14. Simulation results of a normal subject (32y. male). Total Blood Volume : 5.7L, Cardiac Index : 5.27L/min/m^2, Mean Volumes (Transit Times) of Cardiac Chambers, Lung and Body : RA=62 ml/m^2 (0.7 sec), RV=70 ml/m^2 (0.8 sec), Lung=350 ml/m^2 (4.0 sec), LA=53ml/m^2 (0.6 sec), LV=70ml/m^2 (0.8 sec), Body=2.250ml/m^2 (29.0 sec).

With the use of ^{99m}Tc-albumin, the second part of the study was carried out in 17 subjects including 7 normals and 10 cardiac patients. The analog simulation and the subsequent calculations were completely performed in this study according to the above mentioned technique. Mean transit times, cardiac chamber and pulmonary volumes, total blood volumes and cardiac outputs for all patients are tabulated in Table 2.

The mean left ventricular volumes by the simulation method were compared with the left ventricular end-diastolic volumes (EDV) by the angiocardiographic method (Fig. 17 A & B). In the group without valvular regurgitations, the correlation coefficient was 0.83 ($p<0.001$) and the ratios of the mean volumes to EDV were 85%±16 (SD). On the other hand, the correlation coefficient and the ratios in the group with valvular regurgitation were 0.85 ($p<0.001$) and 138% ± 49 (SD), respectively.

Throughout this studies, the left to right shunts were determined from the pulmonary dilution curves and the differential diagnosis of atrial septal defect (ASD), ventricular septal defect (VSD) and patent ductus arteriosus (PDA) was

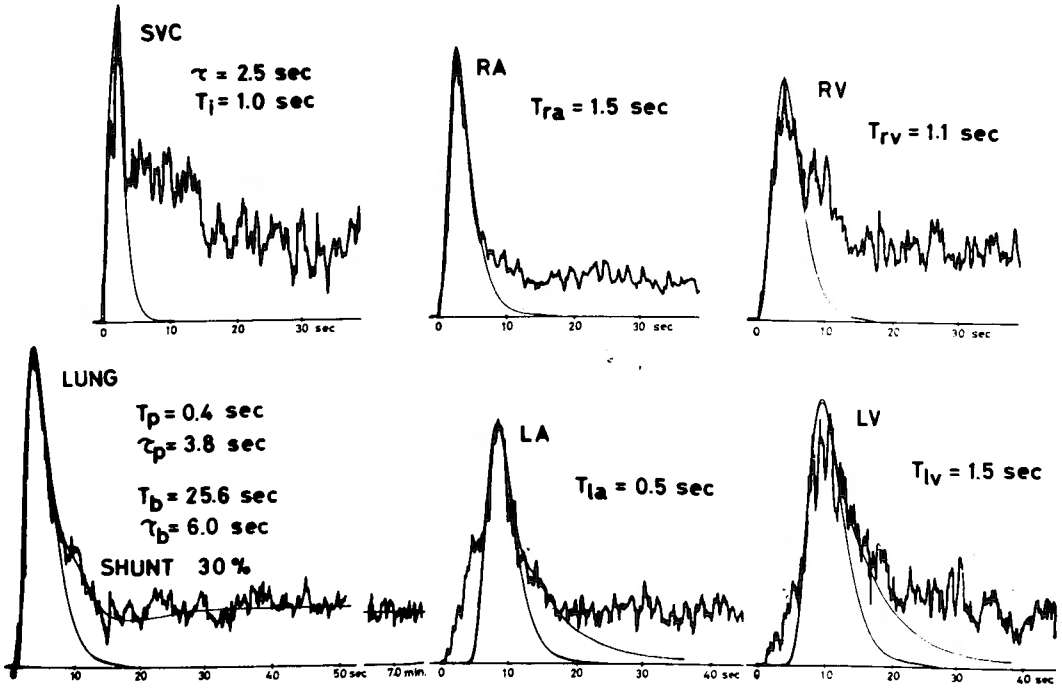


Fig. 15. Simulation results of a patient with ventricular septal defect (30y. male). Total Blood Volume : 4.7 L, Systemic Blood Flow : 4.21 L/min/m², Pulmonary Blood Flow : 6.01 L/min/m², Shunt Rate : 30%, Mean Volumes (Transit Times) of Cardiac Chambers, Lung and Body : RA=107 ml/m² (1.5 sec), RV=111 ml/m² (1.1 sec), Lung=424 ml/m² (4.2 sec), LA=51 ml/m² 0.5 sec, LV=152 ml/m² (1.5 sec), Body=2.240 ml/m² (31.6 sec).

Table. 1. ^{99m}Tc-pertechnetate was used as a tracer in a total of 66 subjects who were divided into 10 groups. In 40 patients who had subsequently undergone cardiac catheterization, the volume of each compartment was calculated as the product of mean transit time of the compartment by the simulation method and its blood flow by Fick method. As cardiac catheterization was not performed in the normal subjects, the normal cardiac index of 3.6 L/min/m² was assumed for comparison.

	Simulation Method							Fick Method						
	Pt. No.	Age (range)	MEAN TRANSIT TIME (sec) RA	RV	Lung	LA	LV	Pt. No.	CI (L/min/m²)	CALCULATED VOLUME (ml/m²) : MTT×CI (or PBF) RA	RV	Lung	LA	LV
NORMAL	12	28.4 (9–67)	1.07±0.22	1.14±0.22	4.07±0.92	1.05±0.36	1.12±0.17		**3.60**	**64±13**	**68±13**	**244±58**	**63±22**	**67±10**
OTAP	2	24.0 (22–26)	1.0±0.4	*0.8±0	3.8±0.6	0.9±0.1	*0.8±0	2	**4.37±0.43	75±18	58±6	275±73	62±11	58±6
MS	8	38.4 (21–48)	**1.6±0.5	**2.0±0.5	**8.4±2.6	**3.4±1.8	*1.7±0.8	7	**2.56±0.76	67±20	80±24	**332±40	**139±53	72±19
AS	2	37.0 (29–45)	1.0±0.5	1.4±0.1	4.1±0	0.8±0	*1.5±0.3	2	3.52±0.12	56±31	82±11	234±0	46±0	*88±20
ASD	13	24.4 (6–47)	1.1±0.4	0.9±0.5	**2.9±0.6	**0.7±0.2	*1.5±0.5	11	3.42±1.02	**176±70	*146±120	**493±290	**130±67	70±15
VSD	12	21.2 (7–54)	1.2±0.5	*0.9±0.3	3.5±1.3	**0.6±0.3	1.1±0.5	6	3.82±1.20	84±33	**99±28	297±66	76±36	**114±31
PDA	2	18.5 (16–19)	0.9±0.3	*0.8±0.1	**2.3±0.3		0.9±0.6	2	4.17±1.15	64±5	55±19	**576±195		**182±64
MI	5	44.8 (24–63)	**2.0±0.9	**1.5±0.2	**6.6±1.9	**3.4±0.6	**2.5±0.6	2	**2.95±0.42	77±21	67±13	278±145	**153±22	*95±28
AI	6	35.7 (23–60)	1.4±0.6	*1.6±0.6	**6.0±0.7	**3.4±2,0	**3.6±1.0	4	3.25±1.14	89±77	98±70	**369±88	**245±230	**211±53
MI·AI	4	37.0 (26–53)	*3.2±2.6	*2.0±1.2	**11.2±5.0	**5.2±2.2	**8.8±3.0	4	**2.69±0.73	*121±75	81±21	**432±76	**194±18	**417±240

All data are presented as mean±1 SD. Mean values which differ significantly from the normal at $P<0.01$ are preceded by the symbol "**" and those which differ at $P<0.05$ by the symbol "*".

Two cases in "AI" group were combined with MS and two in "MI+AI" group with TI.

OTAP : occlusive thromboaortopathy, MS : mitral stenosis, AS : aortic stenosis, ASD (VSD) : atrial (ventricular) septal detect, PDA : patent ductus arteriosus, MI : mitral insufficiency, AI : aortic insufficiency.

made by the shapes of RA, RV and lung curves. In a total of 19 patients including 11 patients with ASD, 6 patients with VSD and 2 patients with PDA, the comparison of the simulation method and the Fick method in determining the shunt rates was shown in Fig. 18. The correlation coefficiency was 0.90 ($p<0.001$).

Table. 2. Results of 17 subjects including 7 normal subjects and 10 patients with various heart diseases who received injections of ^{99m}Tc-albumin.

Data in the Normal Subjects

PATIENT			TBV	CI	MEAN TRANSIT TIME (sec)						VOLUME(ml/m²)					
No.	Age	Sex	(ml/kg)	(L/min/m²)	RA	RV	Lung	LA	LV	Body	RA	RV	L UN	LA	LV	B OD
1	32	M	87.5	5.27	0.7	0.8	4.0	0.6	0.8	29.0	62	70	350	53	70	2250
2	33	M	84.0	4.02	1.4	1.1	4.3	0.8	1.0	37.4	93	74	288	54	67	2500
3	36	M	92.5	5.10	1.0	1.0	4.0	0.9	1.1	29.5	85	85	340	76	93	2500
4	15	M	80.5	4.50	0.9	1.3	4.6	0.9	1.3	27.0	67	97	344	67	97	2020
5	56	F	93.5	4.06	1.0	1.3	4.3	1.3	1.2	35.3	68	88	291	88	81	2400
6	51	F	86.3	4.30	0.8	1.2	4.4	1.1	1.3	34.8	57	86	315	79	93	2500
7	50	M	92.0	4.62	0.9	1.2	4.7	1.0	1.1	34.4	69	92	362	77	85	2470
Mean			88.0	4.55	0.96	1.13	4.33	0.94	1.11	32.50	72	85	327	71	84	2420
S. D.			4.9	0.48	0.22	0.18	0.27	0.22	0.18	3.92	13	10	29	13	12	182

Data in the Subjects with Heart Diseases

PATIENT			Diagnosis	TBV	CI	VOLUME(ml/m²)					
No.	Age	Sex		(ml/kg)	(L/min/m²)	RA	RV	Lung	LA	LV	Body
1	40	M	PMD	86	3.25	92	135	476	92	194	2010
2	56	M	PMD	90	3.13	47	130	338	73	260	2040
3	28	M	ASD postop.	99	8.60	157	215	717	172	172	2000
4	45	M	AS	75	3.99	87	100	257		113	2120
5	48	F	MS	63	3.14	89	120	345	89	63	1440
6	55	F	AF	126	3.85	109	109	513	135	237	3370
7	56	M	IHD	88	2.40	56	100	284	40	168	2160
8	24	F	MSI, AI, TI	140	3.14	197	120	400	262	293	3120
9	15	F	ASD	110	3.84	156	134	715	112	77	1850
10	30	M	VSD	100	4.21	107	111	424	51	152	2240

PMD : primary myocardial disease, ASD : atrial septal defect, VSD : ventricular septal defect AS : aortic stenosis, MS : mitral stenosis, AF : atrial fibrillation, IHD : ischemic heart disease MSI : mitral stenoinsufficiency, AI : aortic insufficiency, TI : tricuspid insufficiency

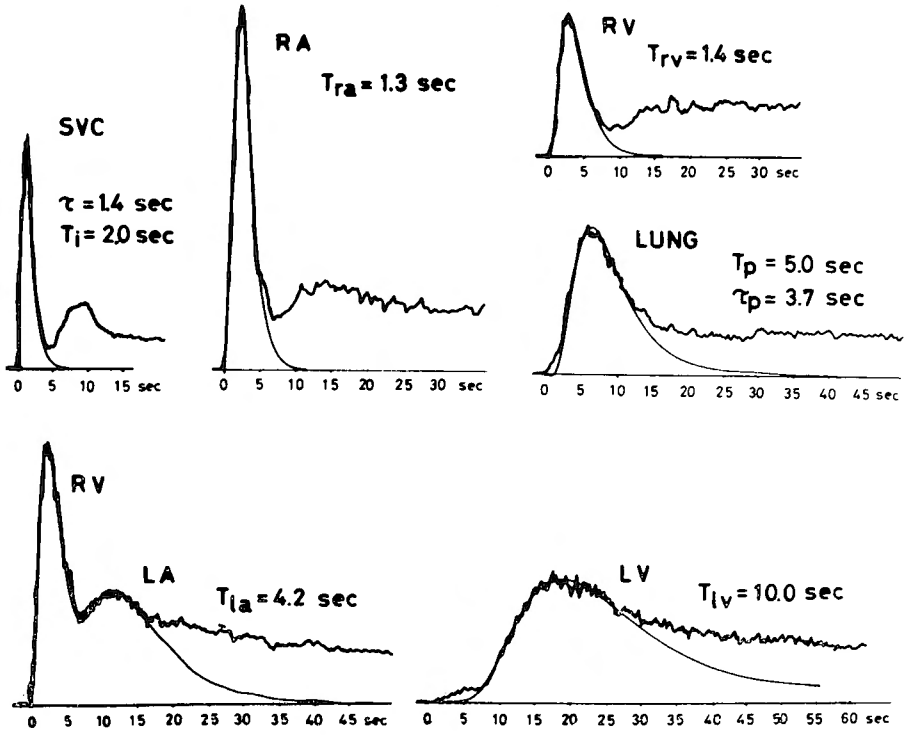


Fig. 16. Simulation results of a patient with mitral and aortic valvular insufficiency (26y. female). In this case ^{99m}Tc-pertechnetate was used. Therefore, only mean transit times were determined. Mean Transit Times : RA=1.3 sec, RV=1.4 sec, Lung=8.7 sec, LA=4.2 sec, LV=10.0 sec.

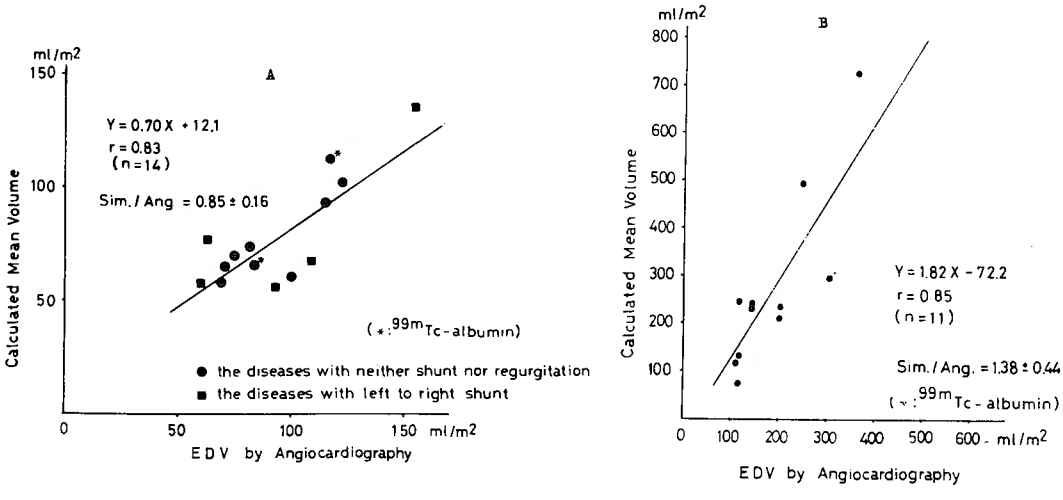


Fig. 17. A&B Mean LV volume by simulation method or simulation-Fick method and LV-EDV by angiocardiographic method were compared in the group without regurgitation (A) and with regurgitation (B).

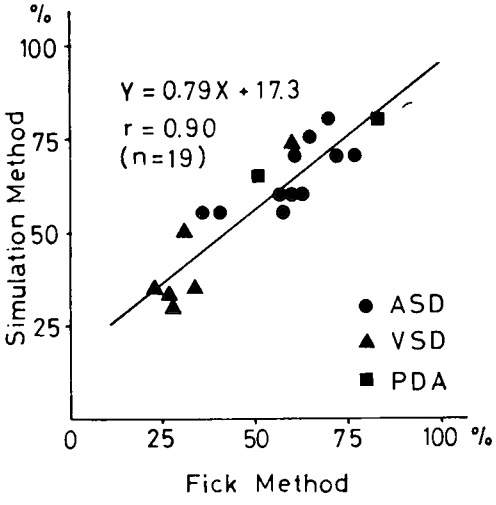


Fig. 18. Comparison of shunt rates determined by simulation method and Fick method.

Discussion

Mathematical Model of Circulation……It is extremely difficult to simulate the actual human circulatory system by a simple mathematical model because of the complexity of the circulation. Many authors have reported the theoretical models of circulatory system in order to facilitate a good understanding of the cardiovascular dynamics. Especially, much efforts have been attempted to construct the more suitable models for pulmonary circulation[36~44]. Whereas, extreme complexities of the model make the clinical applications difficult in spite of its close approximation for the actual circulatory dynamics. Therefore, the simplification become mandatory. In this regard, the circulatory model used in this study was simply approximated by a series of first order lag systems with or without transport time delay. The contractile action of heart was neglected. Each cardiac chamber was treated as a single mixing chamber and lung and body were represented by an individual mixing chamber with a transport time delay. This simplified circulatory model was originally introduced by KUWAHARA et al[45,46]. for the analysis of the standard radiocardiograms. According to their model, the circulatory system was divided into four compartments, that is, right heart, lung, left heart and body. The conventional radiocardiograms were obtained with the detector placed "blindly" over cardiac region. On the other hand, with a scintillation camera it is possible to derive curves separately not only from the right and the left heart but also from the atrium and the ventricle. Thus, the heart can be treated as four compartments containing two atriums and two ventricles.

ADAM et al[22]. have tried to analyze the dilution curves from four cardiac

chambers using an analog computer simulation method and reported the results of the mechanical heart models. ISHII et al[24]. have also carried out the analog simulation analysis of the dilution curves, assuming that the circulatory system was approximated by a series of first order lag systems with or without time delay. Since their model was a open circuit without body compartment and ^{99m}Tc-pertechnetate was used as a tracer, cardiac output was separately determined by a standard method using RISA by external single probe monitoring[47].

In the present study, the whole circulatory system was defined as a closed circuit of six compartments consisting of RA, RV, lung, LA, LV and body. Furthermore, the intracardiac shunts were taken into consideration in order to evaluate various shunt diseases such as ASD, VSD and PDA.

^{99m}Tc-Albumin ……Although both ^{99m}Tc-pertechnetate and ^{99m}Tc-albumin were used in the clinical study and the latter is certainly a more suitable agent for this investigation, the instability of this tracer in vivo has been reported[48,49]. The labeling of human serum albumin with ^{99m}Tc in this study was usually performed using ferrous ion[50] and sometimes using stannous ion[51] as the reducing and complexing metals.

With both ^{99m}Tc-albumin and ^{131}I-albumin, total blood volume measurements were done in 11 patients (Fig. 19). The blood volumes determined by ^{99m}Tc-albumin were slightly larger than those by ^{131}I-albumin. In addition, the average of total blood volumes in 7 normal subjects receiving ^{99m}Tc-albumin showed somewhat higher value of 88 ml/kg of body weight[52]. These results reveal to indicate the breakdown of ^{99m}Tc-albumin in vivo and the subsequent loss of this tracer from the vascular space. In this respect, WEBER et al[29]. have reported that the instability of this tracer might be improved by a new labeling technique introduced by

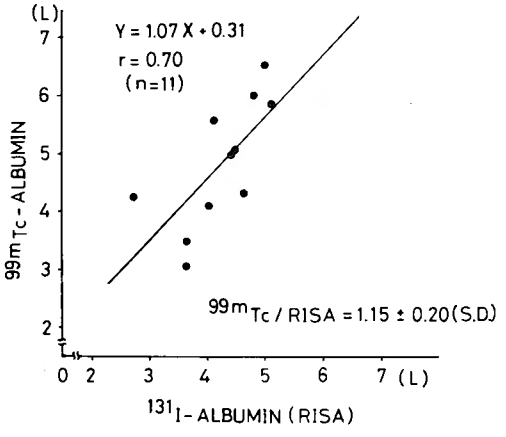


Fig. 19. Comparison of total blood volumes determined by ^{99m}Tc-albumin and ^{131}I-albumin.

BENJAMIN et al.[53].

As for the mean transit time determination, averages of the mean transit times of 12 normal subjects receiving ^{99m}Tc-pertechnetate and those of 7 normals who received injections of ^{99m}Tc-albumin were 1.07 sec and 0.96 sec for RA, 1.14 sec and 1.13 sec for RV, 4.07 sec and 4.33 sec for lung, 1.05 sec and 0.94 sec for LA and 1.12 sec and 1.11 sec for LV, respectively. These numerical differences were not significant judging from their p-values ($p>0.3$ for RA, $p>0.8$ for RV, $p>0.4$ for lung, $p>0.4$ for LA and $p>0.9$ for LV). It was considered, therefore, that either of the tracers might be used for the measurements of transit times.

Data in Normal Subjects……The normal cardiac index of 4.55 L/min/m^2 obtained in the present investigation seemed unreasonably high[54,55]. The major cause certainly considered to be the overestimations of total blood volumes as mentioned above. The proper probe placement which was critical to the methods using collimated scintillation detectors[56] was not so important in those with the scintillation camera. While, it was uncertain how the height of the curves at equilibrium was affected by the liberation of the technetium from the albumin.

The normal mean transit times and mean volumes of cardiac chambers and lung have been determined by many authors (Table 3 A & B[15,23,24,26,39,40,43,57~70]). These values varied within relatively wide range by the methods employed.

The pulmonary mean transit time of 4.33 sec reported here is relatively short as compared with values by the previous methods ranging from 4.0 to 7.6 sec. The larger values by previous methods may be due to the inclusion of parts of the heart because the mean transit times are often approximated by the time between peak pulmonary arterial and peak left atrial counts or by the difference of the mean transit times between the two regions. On the other hand, the right heart to left heart transit time reported by others correlated well to the sum of the mean transit times of RA, RV, lung, LA and LV in this study.

The mean volume for each compartment except for left atrium appeared to be reasonable when compared to the values by other investigators. If the volumes calculated as the product of cardiac output and mean transit time are corrected for the overestimation of cardiac output, the resultant volumes become about 15% smaller and then approximate the data assumed by the simulation-Fick method. These corrected values still correlated well to the wide range of data obtained by other techniques. PERÄSALO et al[69], and TAKAYASU et al[70]. who employed analog simulation analysis have reported the normal mean heart volumes in terms of mixing chambers. The right heart volume was 127 ml/m^2 by PERÄSALO and 137 ml/m^2 by TAKAYASU, and the left heart volume was 133 ml/m^2 and 146 ml/m^2, respectively. The volumes of 157 ml/m^2 for the right heart and 155 ml/m^2 for the left heart in this study were somewhat larger. Therefore, the corrected volumes for the overestimations of cardiac output were considered to be more closely approx-

Table. 3. Normal values of mean transit times (A) and volumes (B) reported by other investigators

A

Author	No. of Patient	Method (tracer)	MEAN TRANSIT TIME (sec)			
			RH→LUNG	LUNG	LUNG→LH	RH→LH
Dock (1960)	4	dye dilution		5.3		
Eich (1962)	10	dual counters (RISA)		7.6		
Donato (1962)	18	single counter (RISA)		5.97		
Segre (1965)	14	single counter (RISA)		4.0		
Burke (1969)	25	scinticamera (^{99m}Tc-per)	1.2		2.4	3.4
Bender (1969)		autofluoroscope (^{99m}Tc-per)	3.33		4.51	7.84
Jones (1972)	10	autofluoroscope (^{99m}Tc-per)	4.28	6.6	4.91	9.19
Konishi (1973)	7	scinticamera (^{99m}Tc-alb)		4.33		8.47

B

Author	No. of Patient	Method	VOLUME (ml/m²)				
			RA	RV EDV/ESV	LUNG	LA MAX/MIN	LV EDV/ESV
Gray (1948)			30				
Freis (1960)	6	dye dilution		79/38			
Lewis (1962)	18	radioisotope		126/73	313		
Rapaport (1965)	15	thermodilution		103/55			
Dock (1960)	4	dye dilution			246		
Eich (1961)	10	radioisotope			436		
Giuntini (1963)	17	radioisotope			293		
Segre (1965)	14	radioisotope			263		
Roy (1965)	15	dye dilution			211		
Preger (1965)	9	angiocardiography				55/3 (1ml)	
Murray (1968)	22	angiocardiography				35/17	
Gorlin (1964)	12	thermodilution					96/54
Bristow (1964)	7	thermodilution					99/62
Kennedy (1966)		angiocardiography					70/25
Levinson (1967)	11	dye dilution					82/37
Peräsalo (1971)	15	radioisotope		127	204	133	
Takayasu (1971)	27	radioisotope		137	293	146	
Ishii (1971)	9	radioisotope	95	88	304	88	81
Konishi (1973)	7	radioisotope	72	85	327	71	84

imated to the true values.

Concerning left atrial volume, there is considerably great difference between the volume by the simulation method and by the angiocardiographic estimation. The reason for this discrepancy may be that left atrial volume in terms of a mixing chamber probably includes the volumes of inflowing pulmonary veins. Besides, the

incompleteness of mixing within the atrium should be considered. If so, the measured volume for this compartment is different from anatomical capacity. Therefore, it may be safe to treat the dilution curves of the atrium only as an input function curve to the ventricle. The similar problems appear to be present in the determination of right atrial volume.

Data in Patiens with Various Heart Diseases ……The mean transit times and volumes of the compartments, which were obtained by the simulation-Fick method with ^{99m}Tc-pertechnetate study, were compared among the ten groups of the patients as shown in Table 1. Because some groups consisted of too small number of patients and the other included the wide range of severity of the disease, and because the radioisotopic angiocardiography and cardiac catheterization were not performed simultaneously, the data must be examined taking considerations of these facts.

The patients with left to right shunt were characterized by the short pulmonary mean transit times and the increased pulmonary blood volumes except patients with VSD in which values remained within normal limits. These observations appeared to be closely related to the average shunt rates of the groups because VSD showed relatively small shunt rate of 36% compared to those of 60 % in ASD and 67 % in PDA. In this connection, JONES et al[26]. demonstrated that patients with larger shunt revealed the more rapid pulmonary transit times. SAITO et al[71]. described that the pulmonary blood volume had tendency to increase in proportion to the pulmonary blood flow.

In patients with mitral stenosis, the mean transit times were prolonged in all compartments and the mean volumes of the lung and left atrium were markedly increased, but the left ventricular volume did not differ from normal. JONES et al[26]. reported that the prolongation of the mean transit times resulted primarily from the decreased cardiac output and that pulmonary blood volume remained almost normal. On the contrary, the increase of pulmonary blood volume in the patients with mitral stenosis was found by DOCK et al[57]. and ROY et al.[62].

The patients with mitral and/or aortic valvular regurgitation demonstrated the delayed transit of tracer in almost all compartments. Especially the marked prolongation of the mean transit times and greatly increased blood volume in the lung and the left heart were observed. It is difficult, however, to provide the detailed discussion about each group because of too small number of patients and the wide divergency of the severity. Furthermore, the high values of the mean transit time and volume of left atrium in the AI group were caused by the two cases combined with mitral stenosis. In the MI + AI group, the increased right atrial volume appeared to result from the inclusion of the two patients with tricuspid insufficiency.

As shown in Fig. 17, the comparison between the left ventricular volumes by

the angiocardiographic method[73] and those by the simulation method for the simulation-Fick method was performed in the group with and without valvular regurgitation. In spite of the good correlation coefficient between two methods in both groups, the ratios of the mean volume by the simulation to the EDV by the angiocardiography were different greatly each other. The ratios were 1.38 and 0.85 for the groups with and without regurgitation, respectively. The mean volume by the present method represents the volume in which the tracer is mixed, and is considered to approximate EDV by other methods, but not really identical to it. Though the actual value for the ratio of the mean volume to EDV is unknown, the value of 1.38 in the group with valvular regurgitation appeared to be considerably high. In addition, the patients with larger regurgitation had the tendency to demonstrate the more prolonged transit times of the involved cardiac chambers. These were probably caused by the fact that the enlargement of left ventricle and the regurgitation in mitral and/or aortic valve had almost the same influence on the shape of the dilution curve of left ventricle. Therefore, if the calculated volume happened to be too large, valvular insufficiency was probable.

In order to determine the regurgitant flow quantitatively, the model must be modified to be applicable to the cases of valvular regurgitation. In this respect, KUWAHARA et al.[72] have reported a new method to quantify the aortic regurgitant flow. As each side of the heart is assumed to consist of two chambers in the present model, the introduction of their theory to the present model will make it possible to quantify not only aortic regurgitation but also mitral or tricuspid regurgitation. However, the preliminary experiences on the determination of valvular regurgitant flow demonstrated that the practical curve fitting procedure became more difficult as the number of parameters increased.

Left to Right Shunt Rate……The left to right shunt rates determined by the analog simulation of pulmonary dilution curve showed an good correlation with those by the Fick method. Theoretically the shunt rates can also be determined by the simulation of RA or RV dilution curves. However, the values obtained from RA or RV curves differed from those from the pulmonary curves with the range of about 20%. This is probably caused by the facts that the dilution curves of RA and RV are often contaminated by the radioactivity of the surrounding regions and that the shunted blood from the left heart is not adequately mixed with the blood in the right heart. These facts make it impossible to determine the individual shunt rates of the combined diseases, such as ASD+VSD. In cases of high septal VSD the dilution curves may mimic the characteristics of PDA because the shunted blood is expelled into the lung without mixing in the right ventricle.

A simple technique to detect the left to right shunt which was originally described by BRAUNWALD et al[74]. has been applied to pulmonary dilution curves derived from a scintillation camera[19~21]. In this method two points on the curve, C_1 and C_2,

were defined and the ratio C_2/C_1 was measured, that is, C_1 was the peak count rate and C_2 was the count rate at the time of twice the bild-up time. The values of C_2/C_1 in the patients without shunt were 0.23 by ALAZRAKI et al[20]. and 0.31 by BRAUNWALD et al.[74]. The high values of it represent shunts. In the present study, C_2/C_1 ratios were compared to the shunt rates by the Fick method (Fig 20). Although no good linear correlation was observed, this method was useful to detect the left to right shunt of more than 30%. In contrast to the normal value of 0.28, the average C_2/C_1 ratios in ASD and VSD were 0.62 and 0.52, respectively.

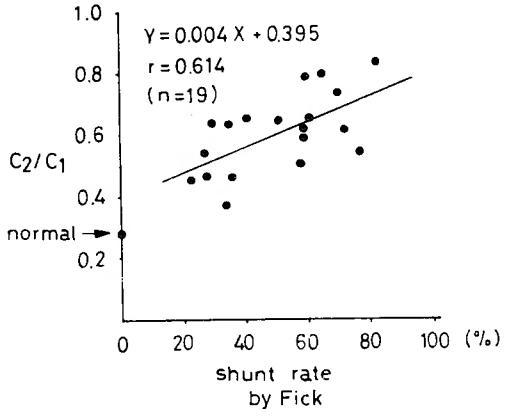


Fig. 20. Comparison of C_2/C_1 ratios and shunt rates by Fick method. The average C_2/C_1 ratios in normal, ASD and VSD were 0.28, 0.62 and 0.52, respectively.

Some Other Problems in This Method……The reproducibility of the method was considered satisfactory. The result of the mechanical heart model experiments demonstrated the adequacy of the technics because the mean differences of seven determinations for each cardiac chamber volume were less than 10%. In clinical applications, the radioisotopic angiocardiography was done twice in five patients with the interval of about 10 minutes. After obtaining the dilution curves in two performances, they were analyzed independently. The mean transit times in the analysis of the two successive dilution curves did not differ more than 5% each other.

The mode of tracer injection is an important part of the procedure for the accurate measurements. It is desirable to administer the tracer in a bolus as rapidly as possible. Two ways of injection were tried in this study, one was a cuff release technique by OLDENDORF et al[75]. and the other was a rapid injection followed by saline flushing. Although the latter was better for the injected volume of more than 2 ml, either of techniques were satisfactory as far as the injected volume was less than 2 ml when performed with a experienced hand.

When one determines regions of interest, much attentions must be paid not to select regions that contain significant activity from adjacent or superimposed chambers. Especially, the pulmonary dilution curve which is used for the determination of shunt rate and of parameters of body compartment must be carefully obtained from the periphery region of the lung because these areas would not contain the heart or great vessels.

As to the position of the patient under the scintillation camera, the left anterior oblique view is usually preferable because of the clear separation of left and right cardiac chambers, but it is difficult to separate right ventricle from right atrium. In this study, 30 degree left anterior oblique view was used. The supine position rather than sitting was employed in children and very ill patients. Consequently, the positioning of the patients may vary with the patient's condition and the purposes of the study.

Summary

(1) After a rapid injection of Technetium-99m (albumin or pertechnetate) into antecubital vein, the dilution curves of the central circulatory system, that is, superior vena cava, right atrium, right ventricle, lung, left atrium and left ventricle, were obtained using a scintillation camera with 1600 word memory system and a computer compatible magnetic tape recorder or with data-store/playback accessory. Assuming that the whole circulatory system was defined as a closed circuit of six compartments in which each of four cardiac chambers was represented by a single mixing chamber and lung and body were represented by a mixing chamber with a transport time lag, respectively, these dilution curves were analyzed by means of an analog computer which allowed the estimation of time constants (volume/flow = mean transit time) for each compartment. The mean blood flow through the system was obtained by dividing total blood volume by total mean transit time. The determination of mean transit time and blood flow permitted the estimation of the volume of each compartment.

(2) The practical feasibility of this method was established by the mechanical heart model experiments.

(3) Clinical study was performed in a total of 83 subjects including 19 normals and 64 cardiac patients using either ^{99m}Tc-albumin or ^{99m}Tc-pertechnetate. With the use of ^{99m}Tc-albumin, the averages of the mean transit times and the mean volumes for 7 normal subjects were 0.96 sec and 72 ml/m^2 for RA, 1.13 sec and 85 ml/m^2 for RV, 4.33 sec and 327 ml/m^2 for lung, 0.94 sec and 71 ml/m^2 for LA and 1.11 sec and 84 ml/m^2 for LV, respectively. In general, these values seemed to be reasonable as compared to the values obtained by other methods.

(4) The patients with relatively large left to right shunt demonstrated short

pulmonary mean transit times and increased pulmonary blood volumes. On the other hand, the prolongation of the pulmonary mean transit time was observed in the patients with mitral stenosis and in those with aortic and/or mitral valvular regurgitation. Moreover, these patients also demonstrated the delayed transit of tracer in almost all cardiac chambers. The valvular insufficiency was characterized by the unreasonably high values of the mean transit times and mean volumes for the involved cardiac chambers.

(5) The left to right shunt rates obtained by the analog simulation method were in good agreement with those obtained by the Fick method and the correlation coefficient was 0.90 ($p<0.001$).

(6) With the safety and simplicity of the technique, the new method used in this study is considered to be advantageous in quantitative evaluation of various heart diseases.

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和文抄録

シンチカメラにより記録された稀釈曲線のアナログコンピューター解析：心肺容量および左—右短絡量の定量について

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近年，シンチカメラおよびその附属機器の発達，更に短半減期の放射性同位元素（以下 RI と略す）の開発などにより，RI を利用しての循環機能検査の進歩はめざましいものがある．すなわちシンチカメラを前胸部にあてがい ^{99m}Tc などの短半減期RIを大量静注し，それらの RI が心肺系を通過する過程を連続的に写真撮影して，いわゆる radioisotopic angiocardiography を行なうことが可能となった．

著者は従来主として視覚的判断にゆだねられていた radioisotopic angiocardiography を定量的に解析することを目的として，シンチカメラ，1600 word memory，磁気テープ装置，更には data/store playback 装置などを使用して，心臓の各 chamber および肺より稀釈曲線をえて，これをアナログ解析法によって各部の容量，更には左→右の短絡量の決定などを試みた．

方法：^{99m}Tc-pertechnetateあるいは^{99m}Tc-albumin 約 5mCi を患者の右肘静脈への急速静注を行ない，シンチカメラおよび前記の附属機器を用いて循環動態を記録し，心肺各部の稀釈曲線をえて，下記のモデルにもとづいて作成したアナログコンピューターを用いて解析を行なった．

循環系の数字モデル：循環系を右房，右室，肺，左房，左室および体の6 compartmentに分かち，それぞれを単一混合室とみなし更に肺および体にはこれに輸送時間遅れを加えて一次系の従続結合で近似せしめた．すなわち，連続した二個のchamber（容量V_{x-1}，V_x，RI 濃度 $C_{x-1}(t)$，$C_x(t)$，流量Fとする）の間には次の関係が存在する．

$$V_xC_x(t)=F\int^{t}C_{x-1}(t)dt-F\int_0^tC_x(t)dt$$

$\left(\begin{matrix}\text{X番目のchamber}\\ \text{のRI総量}\end{matrix}\right)$　(入力)　　(出力)

循環系はこのような chamber が直列に並んだ系と考えられ，左右短絡はこれらを短絡する導管とみなし，シミュレーション回路をアナログコンピューターを用いて作成した．

結果：臨床応用に先立って，既知の値をもつプラスティック製心臓モデルを用いて実験を行なって，この方法が実用可能なることを確認した．

臨床においては83人の被検者に施行して以下の結果を得た．

(1) ^{99m}Tc-albumin を使用した7人の正常人の各compartmentの平均容量（平均通過時間）はそれぞれ右房72ml/m²(0.96sec)，右室85ml/m²(1.13sec)，肺327ml/m²(4.33sec)，左房71ml/m²(0.94sec)，左室84ml/m²(1.11sec)であった．

(2) 左右短絡量は従来の Fick 法に比べて相関係数0.90でよく一致した．

(3) 左右短絡疾患群は正常に比し，肺循環時間の短縮と肺容量の増加が特色的であった．僧帽弁狭窄症および大動脈弁又は僧帽閉塞不全症は肺循環時間の延長がみられた他に，殆んど全部の compartment の循環時間の遅延を認めた．逆流疾患群は特に関連する chamber の循環時間および容量の異常な高値が特色的であった．

以上の結果より，この新しい検査法はカテーテル挿入の必要がなく，患者に与える負荷も少ないことから，重症患者，高令者や小児の患者のスクリーニングテストとして，更には術後のfollow upなどにも簡単に応用出来る利点を有するものと考えられる．