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An Attempt of Quantitative Assessment of the Intracardiac Shunts using Radiocardiogram

MICHIO YOKOTA

The 2nd Surgical Department, Kyoto University, School of Medicine
(Director : Prof. Dr. YORINORI HIKASA)

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There is not yet an appropriate non-invasive mothod to detect the existence of and to estimate the magnitude of the intra-or extracardiac shunts. The cardiac catheterization requires insertion of the catheter into the heart chambers and is not without risk in ill patients. The analog computer analysis[15,19,20,21,25~28] of the radioisotope dilution curves can provide those informations such as volume determination of the central circulatory chambers and the shunt quantification. However, it requires special facilities which would not be easy to obtain in the usual hospitals. Various parameters which were used for the analysis of the dye-dilution curves have been used for the analysis of the radioisotope dilution curves for the detection of the intracardiac shunts[10~12,14,16~18,20,24]. The purpose of this paper is to introduce new parameters for the shunt quantification in the manual analysis of the radioisotope dilution curves of the heart and the lungs. This method of manual analysis would be quite useful in the centers where the computer facilities are not available or the cardiac catheterization is difficult to perform.

Material and method

A) *Equipment.*

The scintillation counter consists of the 3×2-in. thallium-activated sodium-iodide crystals, photomultipier and preamplifier*. The collimator with the external aperture of 5 cm in the diameter was used mainly for the adults and that of 3 cm for the children. The output of the scintillation counter is put into the rate meter via the pulse height analyser which is recorded by the 2-pen recorder, and also is stored in the magnetic tape for the late analysis. The time constant of the rate meter was usually set at 0.4 sec.

B) *Materials.*

The author has been applying the radioisotope dilution technic to the various patients for the following purposes ; 1) to screen the patients with the undetermined heart murmur which likely suggests the existence of the shunts, mainly on the outpatient basis, irrespective of their necessity for the corrective surgery, 2) to detect the residual shunts on the post-operative patients with the residual heart murmur after the surgical closure of the defects,

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* Product of Metro Co. Ltd., Japan

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Present address : The 2nd Surgical Department Kyoto University, School of Medicine. Sakyo-ku, Kyoto, Japan 〒606

and also to follow-up these patients in the outpatient clinic, and 3) to detect the existence of the shunt and estimate its magnitude in the poor-risk patients for whom the cardiac catheterization is not recommended due to the patients' serious conditions.

Total patients for the present investigation comprise ; 1) sixty seven patients with the left-to-right shunts (31 with ventricular septal defects, 28 with atrial septal defects, and 8 with patent ductus arteriosus), 49 without shunts, and 45 postoperative patients without residual shunts, and 2) 21 preoperative patients with tetralogy of Fallot and 7 postoperative patients.

The patients with the left-to-right shunts ranged in age from 6 months to 20 years with the avarage of 8.3 years, and those with the right-to-left shunts from 2 years to 16 years with the average of 4.8 years.

C) *Method.*

The study was performed with the patients at the resting condition. Small children were anesthetized by the intramuscular injection of Ravonal* at the dose of 10-15 mg/kg. A couple of scintillation counters were placed precordially over the heart as well as over the peripheral pulmonary vascular beds. Furthermore, another counter was placed over the head in order to obtain a peripheral arterial dilution curve, when the existence of the right-to-left shunt was suspected. The position of the precordial probe was selected carefully in the individual patients consulting the electrocardiogram and the plain chest X-ray films[20]. Usually appropriate curves were obtained at the left sternal border in the 4th intercostal space slightly lateral to the mid-clavicular line. The peripheral arterial dilution curves were obtained at the frontal region. Ten to 20 μCi of RHISA was injected into the left antecubital or the femoral vein as a bolus followed by a rapid saline flush. Total blood volume and cardiac output were simultaneously obtained according to the standard method[1].

D) *Designation of the components of the dilution curves.*

As shown in Fig. 1, various components of the curves were selected to derive pertinent clue for the quantification of the magnitude of the shunt both in the precordial curves and pulmonary curves. Abreviated nomenclature of these components were as follows ;

"AT" (appearance time) represents the period between the time of injection and that of the appearance of the curve

"BT" (build-up time) represents the time interval between the time of appearance of the curve and the time of the peak activity. For the precordial dilution curve (radiocardiogram) the second peak representing the left heart dilution curve was selected.

"DT" (disappearance time) represents the time interval between the second peak of the precordial curve or the peak of the pulmonary dilution curve and the end of the extrapolated descending limb of the curve.

"Rp" (peak radioactivity) represents the radioactivity at the time of the second peak of the precordial curve or the peak of the pulmonary and peripheral arterial dilu-

* Thiopental, product of Tanabe Pharmaceutical Co., Japan

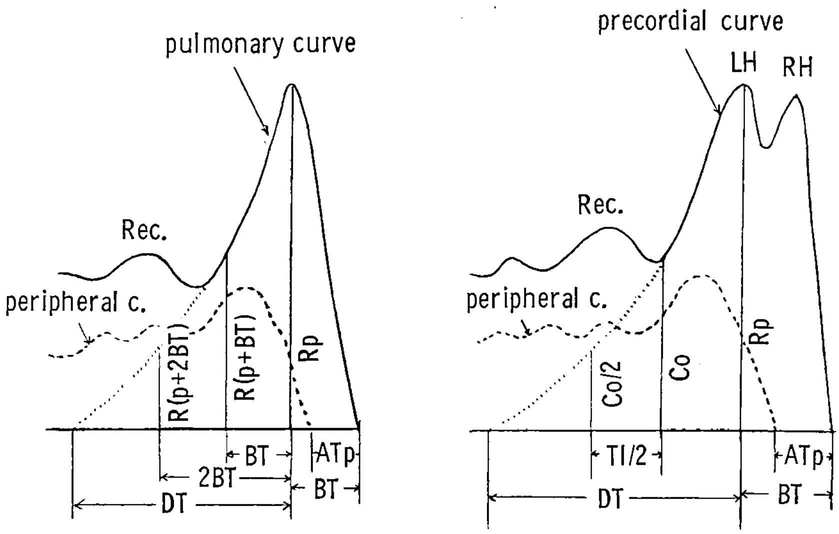

Fig. 1. Components used for the analysis of the radiosotope dilution curves. ATp : appearance time of the peripheral arterial dilution curve from the start of the precordial or the pulmonary dilution curves, BT Build-up time, DT : disappearance time, Rp : peak radioactivity, $T\frac{1}{2}$: half time, R(p+BT): radioactivity at instant once the build-up time after the peak, R(p+2BT) : radioactivity at instant twice the build-up time after the peak.

tion curves derived from the frontal region of the head.

"$T\frac{1}{2}$" (half-time) represents the time to the half decrease of the downslope of the curve assuming the exponential decrease with time.

"R(p+BT)" represents the activities at the time with duration same as the build-up time from the second peak of the precordial curve or the peak of the pulmonary as well as the peripheral arterial dilution curves.

"R(p+2BT)" represents the activities at the time with the duration twice the build-up time from the peak of the pulmonary as well as the peripheral arterial dilution curves.

"ATp" represents the time interval between the appearence of the precordial or pulmonary dilution curves and the appearance of the peripheral arterial dilution curves. The appearence of the precordial or the pulmonary dilution curves was chosen instead of the time of injection because of the inaccurate determination of the latter.

Results

1) *Normal pattern of radioisotope dilution curves.*

The precordial dilution curve (radiocardiogram, RCG) was characterized by the diphasic curve with two humps representing the dilution process of the tracer through the right and left heart chambers respectively followed by the recirculation curves. The pulmonary dilution curve was monophasic curve with a hump which represents dilution process of the tracer through the peripheral pulmonary vascular beds which was also followed by the recirculation curves.

B) *Characteristic patterns in the patients with the shunts.*

The curves were distorted according to the magnitude and direction of the shunts[19,20]. In case of the left-to-right shunts the precordial dilution curve showed shortened pulmonary transit time (shortened distance detween the two peaks), elongation of the downslope of the second peak, and obscure recirculation curves. The pulmonary dilution curve showed the elongation of the downslope and obscure recirculation curves. In case of the right-to-left shunts, the peripheral arterial dilution curve showed the characteristic shortening of the appearance time because the indicator reached the peripheral arteries faster than normal through the right-to-left shunts.

C) *Left-to-right shunts.*

1) analysis using $T\frac{1}{2}$ (half-time)

In the precordial dilution curves, $T\frac{1}{2}$ in the shunt group was much longer than that in the control group with the average of 10.3 sec. compared with 3.34 sec. in the latter. Differences in $T\frac{1}{2}$ between the 2 groups were significant ($p<0.001$). Relationship between the shunt ratio calculated by the Fick method at the time of the cardiac catheterization and $T\frac{1}{2}$ of the precordial dilution curves showed a tendency to the positive correlation, which was, however, not good enough to esitimate the magnitude of the left-to-right shunt ($r=0.5456$). $T\frac{1}{2}$ of the pulmonary dilution curves was distinctly longer with the shunt group than in the control group with the average of 6.97 sec. in the former and 2.44 sec. in the latter, statistically significantly ($p<0.001$). However, the relationship between the shunt ratio and the $T\frac{1}{2}$ of the pulmonary dilution curves again did not show a good correlation, although it was much better than that in the precordial curves ($r=0.8240$).

2) analysis using $T\frac{1}{2}$/BT

As was described briefly before, radioisotope dilution curves distort markedly according to the condition of the input injection of the isotopes[19,20]. In order to minimize the influence of the non-uniform injection or arbitrary input, $T\frac{1}{2}$ was divided by BT (build-up time), because BT was regarded as representing a measure to estimate the transit time of the input injection in which the indicator reaches the right heart chamber or the pulmonary vascular beds.

In the precordial dilution curves, $T\frac{1}{2}$/BT was much higher in the shunt group, ranging from 0.50 to 2.86 with an average of 1.61 than in the no-shunt group, ranging from 0.22 to 0.77 with an average of 0.49, showing the statistically significant differences between the 2 groups ($p<0.001$). In the pulmonary dilution curves, there was a good positive correlation between the shunt ratio and the $T\frac{1}{2}$/BT, the correlation coefficient being 0.92. The regression equation was :

$$Y=2.725\times X+0.246$$

or

$$X=28.78\times Y+2.358$$

where X was the shunt ratio by the Fick method and Y was $T\frac{1}{2}$/BT (Fig. 2, 3).

3) analysis using DT/BT

In the analysis of the precordial dilution curves, the left-to-right shunts more than 50 per cent of the pulmonary blood flow were differentiated from the no-shunt group ($p<0.001$),

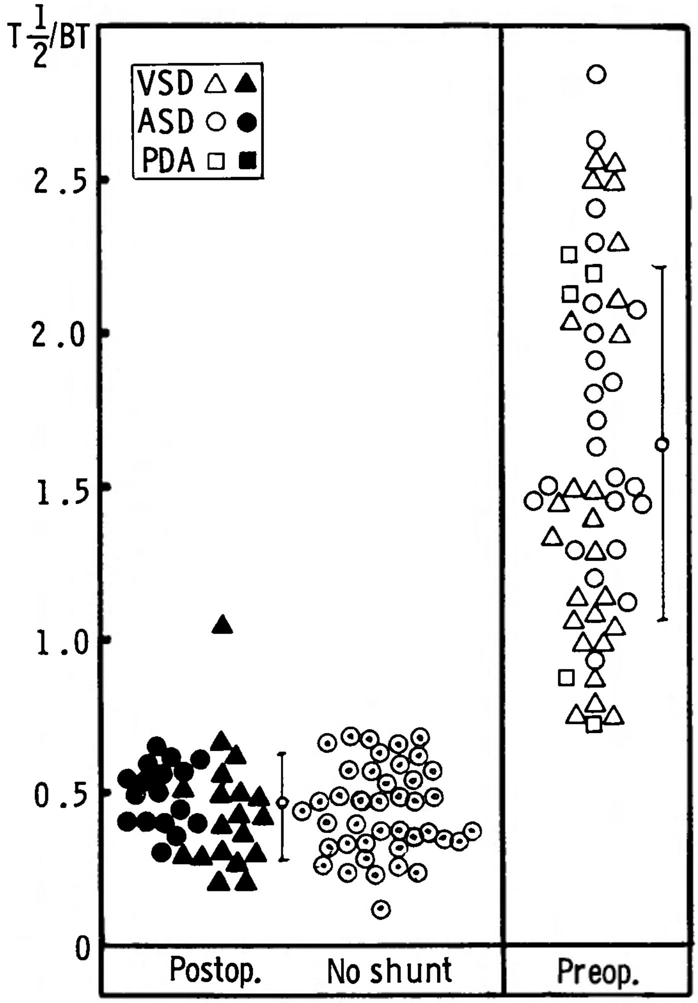

Fig. 2. By analysis using T½/BT of the pulmonary dilution curves, the left-to-right shunt group was clearly separated from the control group. Statistical data are given in the table 1 and 2.

and there was a fairly good positive correlation between the shunt ratio and the precordial DT/BT ($r=0.812$). In the analysis of the pulmonary dilution curves, on the other hand, the correlation was better than that in the precordial dilution curves ($r=0.897$), and the left-to-right shunt more than 40 per cent of the pulmonary blood flow was identified ($p<0.001$).

b) right-to-left shunt

1) analysis using ATp of the peripheral arterial dilution curve.

ATp was variable and there was no relationship among the preoperative, no shunt and postoperative patients with the mean values of ATp of 6.20, 3.55 and 7.53 sec. respectively.

2) analysis using ATp/BT.

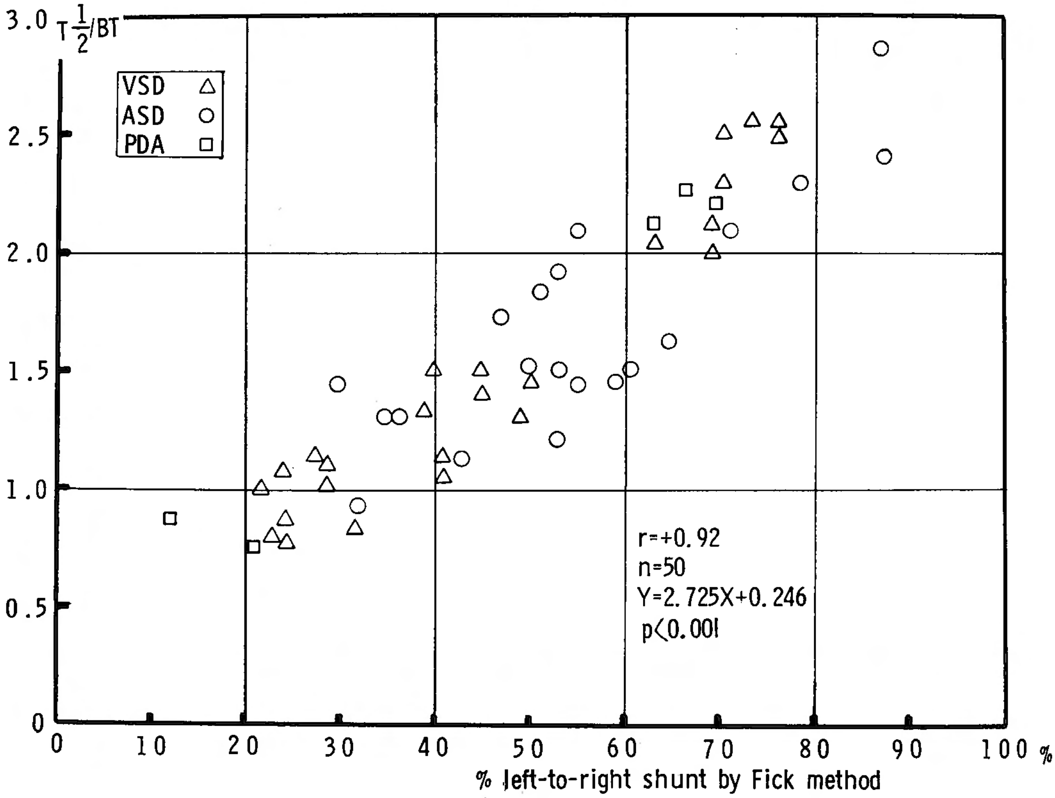

Fig. 3. Relationship between $T\frac{1}{2}$/BT of the pulmonary dilution curves and the left-to-right shunt ratio to the pulmonary blood flow calculated at the cardiac catheterization by the Fick method. There was a good correlation between them.

It is obvious that the appearance time varies considerably with the status of injection of the isotopes. In order to eliminate this factor, ATp was divided by BT (build-up time), because BT was regarded as representing the input status up to the right ventricle. By using ATp BT of the precordial curve the right-to-left shunt group was differentiated from the control group with the mean values of 0.312 in the former and 0.913 in the latter (Fig. 6, $p<0.001$). By using ATp/BT of the pulmonary dilution curve both groups were more clearly separated from each other, the mean values of the right-to-left shunt group and the control group being 0.359 and 1.09 respectively (Fig. 6, $p<0.001$).

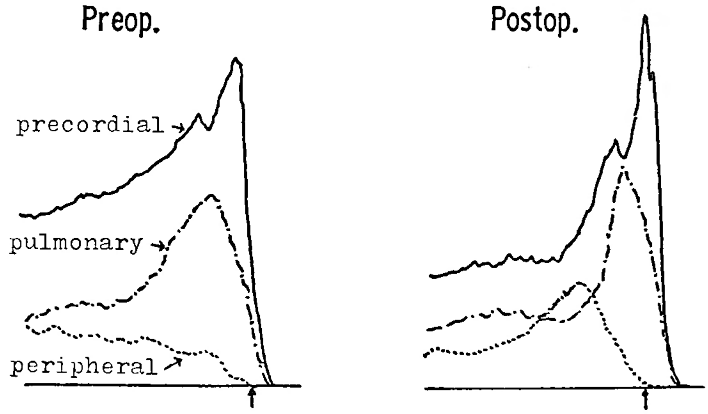

Fig. 4. Preoperative and postoperative radioisotope dilution studies in a 2-year-old girl with a ventricular septal defect. The left-to-right shunt was 76 per cent of the pulmonary blood flow.

$T\frac{1}{2}$/BT : 2.5	$T\frac{1}{2}$/BT : 1.0
R(p+BT)/Rp : 0.86	R(p+BT)/Rp : 0.50
R(p+2BT)/Rp : 0.60	R(p+2BT)/Rp : 0.25

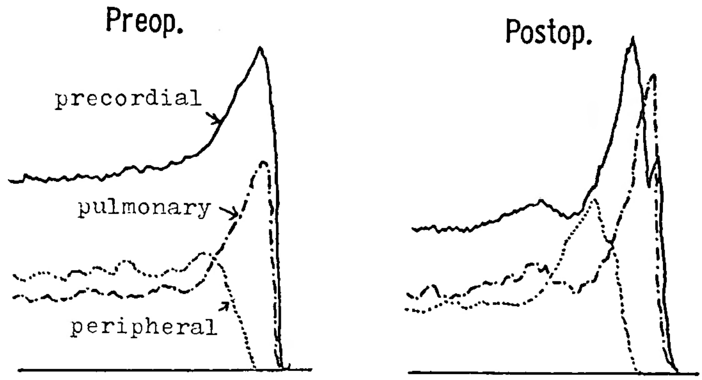

Fig. 5. Preoperative and postoperative studies in a 19-year-old girl with tetralogy of Fallot. Right-to-left shunt was 66 per cent of the systemic blood flow.

ATp : 4.0 sec.	ATp : 7.0 sec.
ATp/BTprecordial : 0.26	ATp/BTprecordial 0.57
ATp/BTpulmonary : 0.32	ATp/BTpulmonary : 0.63

Discussion

In the hemodynamic investigation of the patients with congenital heart diseases with the shunts, the cardiac catheterization is still the most frequently used method. However, cardiac catheterization requires a skilled team of pediatric cardiologists, radiologists, technical personnel and excellent equipment. Although the cardiac catheterization has become very safe in the recent years, it still has some risk particularly in severely ill babies with

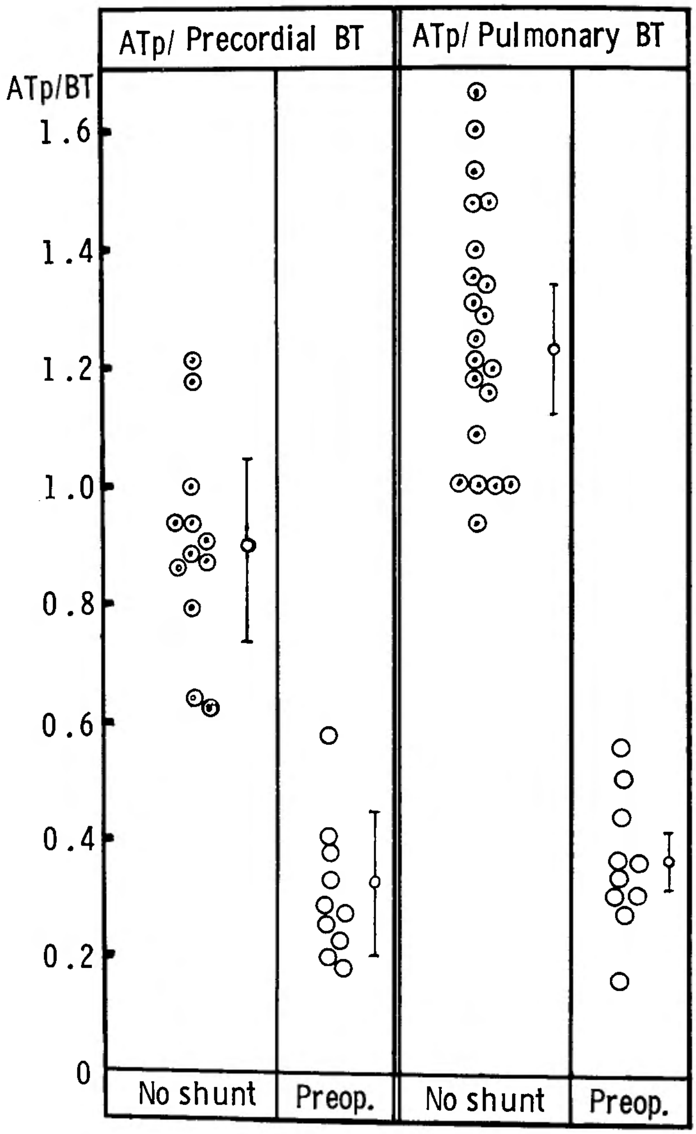

Fig. 6. By the analysis using ATp/BT (appearance time of the peripheral arterial dilution curve divided by the build-up time of the precordial or the pulmonary dilution curves) the separation of the right-to-left shunt group (tetralogy of Fallot) from the control group was distinct. Statistical data are given in the table 1.

complex congenital heart diseases. The cardiac catheterization is not very practical in screening the patients suspected of having the cardiac murmur caused by the shunt in large screening centers, since the cardiac catheterization itself is a time-consumig study and can not handle many patients for the purpose of screening.

Since Prinzmetal first recorded precordially recorded radioisotope dilution curves (RC

G) in 1949, many attempts have appeared to detect and quantitate the intracardiac shunts using radioisotope dilution curves. In addition to the precordial dilution curves, pulmonary dilution curves have also been recorded (FOLSE and BRAUNWALD 1962, FLAHERTY et al. 1967, YOKOTA et al. 1968). In the recent years scintillation camera pulmonary dilution curves also served for analysis (ALAZRAKI et al. 1972). Radioisotopes were given by catheter (GREENSPAN et al. 1957) as well as by peripheral venous injections. Various radioisotopes were used by different investigators ; 24-Na, I-131 albumin, I-131 radium iodohippurate, I-131 diiodofluorescein, Krypton, radioiodide gases such as methyl iodide and 133-Xe, and technetium. In spite of the various attempts to quantitate the shunts, no reliable method has appeared without the assistance of sophisticated means such as computer.

In 1967 analog computer simulation technic for the analysis of the radiocardiogram was developed by KUWAHARA et al[19]. at the Univrsity of Kyoto, Japan and soon clinical application of this technic has been made by several people (YOKOTA, KANAZAKI, ISHII, TORIZUKA, KUWAHARA et al. 1968[20], SAITO, HIRAKAWA et al. 1973[24] and MOTOHARA, KUWAHARA et al. 1974[25], KONISHI 1975[27]). It can be said that comprehensive analysis of RCG was first possible by using this computer method which showed that RCG contained a variety of information to be drawn[14,19,20,22,24~28]. Namely, the estimation of the volumes of the compartments of the central circulation, such as the pulmonary blood volume, right heart and left heart volumes were made with a reasonable accuracy as well as the quantitation of the shunts. RCG study is now an established technic and is routinely used at Kyoto University Hospital for the investigation of cardiopulmonary circulation. However, at the present time, there is practically few places where the facilities of analog computer for RCG analysis is available in japan. Therefore, it is regrettable that RCG and other radioisotope dilution studies can not be fully appreciated without the assistance of analog computer, since the study itself is simple and safe. The purpose of this paper was to introduce a new technic of manual analysis for the quantitative evaluation of the shunt which would be quite useful in the center where the computer analysis is not available or the cardiac catheterization is difficult to perform.

In 1949 PRINZMETAL et al[2]. recorded a radioisotope dilution curve by placing a Geiger Mueller counter over the precordium following the peripheral injection of 24-Na in a patient with patent ductus arteriosus, and described the alteration of the contour of the curve. He gave the curve the name of "radiocardiogram" In 1954 GOLDRING et al.[4] studied 100 children with congenital heart diseases using RCG and demonstrated abnormal contours in the presence of additional lesions ; tetralogy of FALLOT, EISENMENGER complex and tricuspid atresia, but no mathematical analysis was attempted. Following these works, however, no other attempts to extend these observations were reported until 1957, when GREENSPAN et al[8] showed by injecting I-131 methylglucamine diatrizoate (renografin) into the arm or through the cardiac catheterization, that left-to-right shunt could be recognized by an excessively prolonged descending limb of the curve, and also the right-to -left shunts were detected by the rapid appearance of the curve over the femoral artery and the abdominal aorta. Localization of the right-to-left shunt was also determined by making multiple injections into the various chambers.

In 1959 AMPLATZ et al[9]. pointed out the lack of sensitivity and accuracy of the conventional oxygen determination for the detection of the shunts and developed a new method of inhalating radioactive methyl iodide. They showed accurate detection and localization of the left-to-right shunts by sampling blood through the catheters placed in the right heart chambers, however, no attempt for quantitative analysis was made. In 1959 and 1960 SHAPIRO and SHARPE[10] showed that left-to-right shunt could be detected by using DT/BT of the precordial curve. They did 34 studies in 22 patients without shunts and obtained the mean DT/BT ratio of 3.7 ± 1.8. Twenty-two curves from 13 patients with shunts demonstrated the distorted downstrokes with the mean DT/BT of 7.5 ± 2.3, and differences in DT/BT between the 2 groups were significant ($p < 0.001$). As for the analysis using DT/BT, BROADBENT et al. (1954)[5] already had described dye-dilution technic in 36 patients that DT/BT ratio was useful in detecting the left-to-right shunt greater than 35 per cent of the pulmonary arterial blood flow, and also showed that these abnormalities of the curve could be correlated with the magnitude of the left-to-right shunt. In 1961 CORNELL et al[12]. showed by injecting I-131 labeled Diodrast in 75 patients that the product of build-up time (BT) and of disappearance rate (DR) was useful in differentiating them from normal, and stated that only a rough estimate of the magnitude of the shunt was provided by the precordial dilution curve. In 1962 BRAUNWALD et al[13]. described the krypton-85 inhalation test for the detection and localization of the left-to-right shunt. By calculating the ratio of radioactivity in the samples from the right heart and systemic artery in 410 patients, the shunt group patients (ratio: 13-113%) was separated from no-shunt group (ratio: 0-12%). Localization of the shunt was also possible. However, no quantitative analysis of the shunts was attempted. This method had the drawback of necessity of inserting the catheters into the right heart (MORROW et al. 1948, SANDERS et al. 1959, LONG et al. 1960, BRAUWALD et al. 1960 and 1962). The attempt for quantitative analysis of the left-to-right shunt was first tried by TURNER et al. in 1960[11]. They described the possibility of differentiating the left-to-right shunts over 30 per cent of the pulmonary blood flow in 23 patients.

In 1966 CLARKE et al[16]. pointed out that the use of I-131 for shunt diagnosis is somewhat inadequate since it can not be given in a large dose enough for precise information. They advocated the use of technetium-99m for the recording of pulmonary dilution curves and in 60 patients they could separate the shunt group from no-shunt group statistically significantly (shunt group $C_2/C_1 = 0.68 \pm 0.12$, no-shunt group $C_2/C_1 = 0.38 \pm 0.07$, $p < 0.001$). KAWATA et al. (1967)[17] analysed 90 patients with cardiac shunts by using externally recorded radioisotope dilution curves and by using C_2/C_1 they could separate the shunt groups and also showed a good correlation between the shunt ratio by the cardiac catheterization and the calculated C_2/C_1 ($r = 0.91$). YOKOTA, KANZAKI et al. (1968)[20] showed a good result in the detection and quantification of the left-to-right shunts by using $T\frac{1}{2}/BT$ of the pulmonary curves. KINOSHITA et al. (1969)[21] did the similar analysis using $K \cdot BT(K = 0.693/T\frac{1}{2})$ and

Table 3. Collected results of the manual analysis of the radioisotope dilution curves using various parameters.

			shunt group		no shunt group		
			n	m ± S.D. (range)	n	m ± S.D. (range)	
DT/BT							
Broadbent et al.	(1954)	dye	36				detectable > 35% of Qpa
Shapiro, Sharpe	(1959, 1960)	precordial RI	19	7.5 ±2.3		3.7±1.8 (1.5-7.9)	
This series	(1976)	RI, precordial	35	8.12±3.4	50	3.49±1.26	
		RI, pulmonary	28	7.54±3.2	40	2.79±0.83	
C_2/C_1							
Folse, Braunwald	(1962)	I-131 Diodrast	17	66% (46-94)	16	31% (21-41)	
Clarke et al.	(1966)	Tc-99m	40	68±12%	20	38±7%	detectable > 23% of Qpa Diff. Signif. p < 0.001
Kawata et al.	(1969)	RIHSA	90	68%* (50-90)	92	34% (28-47)	ASD (n=29) > 76%(60-90), small VSD 50%.
Kinoshita et al.	(1969)	RIHSA	29	58.3%* (18.2-48.9)	17	35.7% (31-88)	
Alazraki et al.	(1972)	Scinti. ** camera	50	56% (35-94)	43	23% (15-32)	Diff. signif. p < 0.001= r=0.81
This series	(1976)	RIHSA	56	62±13.2%	76	31±12.4%	Diff. signif. p < 0.001
T½/BT							
Yokota, Kanzaki	(1968)	RIHSA precord.	33				r 0.79
		RIHSA pulmon.	31				r 0.91
This series	(1976)	RIHSA precord.	64	1.60±0.684	91	0.51±0.192	Diff. signif. p < 0.001, r=0.76
		RIHSA pulmon.	53	1.62±0.575	82	0.47±0.168	Diff. signif. p < 0.001, r=0.92
K·BT							
Kinoshita et al.	(1969)	RIHSA	50	4.4 (0.9-11.4)	17	11.8 (6.8-24.5)	

n=number, m=mean, S.D.=one standard deviation, r=correlation coefficient between the shunt ratio and the calculated values of parameters.
* characteristic contours of the dilution curves were noted in ASD.
** scintillation camera pulmonary dilmonary dilution curves.

obtained a good result. In case of patent ductus arteriosus there would be a problem to analyse the pulmonary dilution curve of only one side of the lungs, due to the unequal distribution of the blood through the shunts on each side. Recently MATSUMURA et al. (1975)[28] advocated a new mathematical model for the analog computer simulation of RCG in case of patent ductus arterious.

Reviewing those reports (table 3), the author also performed the analysis of the radiosotope dilution curves to detect the shunts by using the various time-radioactivity components such as T½ of the precordial and pulmonary dilution curves, T½/BT of the both curves, R(p+BT)/Rp and R(p+2BT)/Rp of the pulmonary curve, and DT/BT of the

Table 1. Differences in each parameter were statistically significant between the no-shunt group and the shunt group.

	No-shunt group			Shunt group			Diff.
	n	m	S.D.	n	m	S.D.	
$T\frac{1}{2}$, precordial curve	94	3.62	1.552	67	10.276	4.382	significant $p<0.001$
$T\frac{1}{2}$, pulmonary curve	80	2.61	1.054	53	6.97	2.678	〃
$T\frac{1}{2}$/BT, precordial curve	91	0.51	0.192	64	1.60	0.684	〃
$T\frac{1}{2}$/BT, pulmonary curve	82	0.47	0.168	53	1.62	0.575	〃
R(p+BT)/Rp, pulmonary curve	76	0.31	0.124	56	0.62	0.132	〃
R(p+2BT)/Rp, pulmonary curve	71	0.097	0.062	56	0.41	0.142	〃
DT/BT, precordial curve	50	3.49	1.257	35	8.12	3.429	〃
DT/BT, pulmonary curve	40	2.79	0.826	28	7.54	3.176	〃
ATp/BT	32	1.10	0.277	20	0.34	0.117	〃

n=number, m=mean, S.D.=one standard deviation

Table 2. Correlation between the shunt ratio by the Fick method and the parameters. In most cases better correlation was obtained in the group of VSD than in ASD.

	VSD		ASD		Total group		
	r	n	r	n	r	n	S.D.
$T\frac{1}{2}$, precordial curve	0.6168	30	0.2490	28	0.5456	67	4.382
$T\frac{1}{2}$, pulmonary curve	0.8568	25	0.7177	23	0.8240	53	2.678
$T\frac{1}{2}$/BT, precordial curve	0.8159	30	0.5494	28	0.7565	64	0.684
$T\frac{1}{2}$/BT, pulmonary curve	0.9616	25	0.8297	20	0.9182	50	0.575
R(p+BT)/Rp, pulmonary curve	0.7011	30			0.4770	56	0.132
R(p+2BT)/Rp, pulmonary curve	0.8170	29	0.1401	23	0.6343	56	0.142
DT/BT, precordial curve	0.9206	19	0.8865	20	0.8118	35	3.429
DT/BT, pulmonary curve	0.8801	16	0.9332	8	0.8797	28	3.176

n=numer, r=correlation coefficient, S.D.=one standard deviation

pulmonary dilution curves.

In the analysis using DT/BT in the author's series, the result was similar to that of Shapiro and Sharpe[10], that is, the mean values of DT/BT of the precordial and pulmonary dilution curves without shunts were 3.8 and 2.8 respectively, and in the precordial dilution curves, the left-to-right shunts more than 50 per cent of the pulmonary blood flow were detected and in the pulmonary dilution curves that more than 40 per cent was detected.

Statistical analysis of all parameters is given in the table 1 and 2. Among all the parameters used, $T\frac{1}{2}$/BT of the pulmonary dilution curves gave the best correlation with the shunt ratio obtained by the Fick method at the cardiac catheterization. Thus, the shunt ratio was estimated from the equation :

$$T\tfrac{1}{2}/BT = 2.725 \times \text{Shunt Ratio} + 0.246$$

or

$$\text{Shunt Ratio} = 28.78 \times T\tfrac{1}{2}/BT + 2.358$$

Using this T½/BT of the pulmonary dilution curve, the left-to-right shunt as small as 15 per cent of the pulmonary blood flow could be detected, which is accurate enough for the clinical investigation of the shunt, especially for the screening of the shunt. This is also useful to determine the patency of the Blalock-Taussing shunt (subclavian artery-to-pulmonary artery shunt) and also to detect the residual shunts after the surgical closure of the defect in the early postoperative period when the cardiac catheterization is not practically recommended yet. Feasibility of its frequent determination of the radioisotope dilution curves without much trouble made it possible to follow up the preoperative patients closely until the surgery is schedued ; for example, a patient with a large ventricular septal defect with a large shunt flow and low pulmonary vascular resistance was dicided to go ahead for surgery or recatherization without delay when the shunt flow began to fall indicating the possible increase in the pulmonary vascular resistance. The children with small ventricular septal defects were followed up, however, it was usually impossible to testify the spontaneous closure of the defect on the basis of RCG findings. In one patient of the series the intracardiac shunt was ruled out by the cardiac catheterization, however, the radioisotope dilution curve showed the suspicious evidence of the shunt. Operation was performed and a small ventricular septal defect was found. As for the localization of the shunt it was impossible to differentiate atrial septal defects from ventricular septal defects in this series. However, KINOSHITA et al[21]. showed the possibility of differentiating both of them from the contours of the curves, and KAWATA et al. also noted the similar patterns in ASD. Availability of the scintillation camera together with data processing system has now offered possibilities to determine the location of the shunt as well as quantification of the shunt ratio as we are doing at present[22,27]. Furthermore, accurate localization of the region of interest avoding neighbouring region is possible by using this device. The discussion on radionuclide imaging is out of the scope of this paper.

Precordial dilution curve vs. pulmonary dilution curve

The pulmonary dilution curve was first recorded by GOLDRING et al[4]. in 1954 and by GREENSPAN et al[8]. in 1957, but first analysed by FOLSE and BRAUNWADD in 1962[14] who claimed that it was better than the precordial dilution curves in analysing them for the shunt detection. By analysing C_2/C_1 of the pulmonary dilution curves in 33 patients, they could differentiate the shunt group from normal. Small left-to-right shunts with pulmonary to systemic flow ratios ranging from 1.1/1.0 to 1.2/1.0 could be detected by this method. However, no attempt for quantitative analysis was made in that series. FLAHERTY et al. (1967)[18] described a different method of detecting the left-to-right shunts by injecting a radioactive bolus into the proximal right pulmonary artery at the time of cardiac catheterization. They recorded right lung dilution curves in 110 patients and calulated the areas of the two portions under the curve (area E and area R); area R represented the area of the curve between the extrapolated exponential disappearance slope and area R represented that portion of the curve above this extrapolated slope bounded by the original curve and the vertical line at the time of the second peak. They showed that the ratio of area R to area E correlated well with the magnitude of the left-to-right shunt by the Fick method (linear regression $r=0.89$ $p<0.001$, quadratic regression $r=0.94$ $p<0.001$).

In the author's series also, the pulmonary dilution curves were better than the precordial dilution curves in analysing the left-to-right shunt. The precordial dilution curve is a composite curve of the left heart and right heart dilution. The downslope of the second peak (left heart) is influenced by the status of dilution of the right heart as well as the pulmonary vascular beds. Pulmonary dilution curve, on the other hand, distorts its contour by the dilution of the right heart alone[7,14,15,19,20]. Therefore, theoretically the pulmonary dilution curve is a better curve for the analysis of the shunt.

Right-to-left shunt

In 1954 GOLDRING et al[4]. first noted an abnormal contour of the precordially recorded radioisotope dilution curves in the right-to-left shunts, but it was GREENSPAN et al[8]. who first recorded the peripheral arterial dilution curves over the femoral artery and noticed the rapid appearance time in the right-to-left shunts. In 1959 and 1960 SHAPIRO and SHARPE noticed variable appearance time in the 4 cases of Tetralogy of FALLOT.

In the author's series, the appearance time itself did not differentiate the right-to-left shunt group from normal, contrary to expectation. The appearance time is theoretically influenced by the cardiac output, circulation time, and status of injection. This might be the reason of the variety of AT regardless the existence of the right-to-left shunt. In order to minimize the influence of the injection, ATp was divided by BT (build-up time) since BT was regarded as representing the status in which the tracer input reaches the right ventricle or the pulmonary circulation. By using ATp BT of the peripheral arterial dilution curve the right-to-left shunt was clearly differentiated from normal. Better result was obtained when BT of the pulmonary dilution curves was used than when that of the precordial dilution curves was used.

In 1953 SWAN, WOOD et al[3]. showed by using dye-dilution technic that the magnitude of the right-to-left shunts could be estimated from calculating the "build-up triangle" and a fair correlation between the magnitude of the shunt and calculated value ($r=0.89$). There has been no reliable method to quantitate the right-to-left shunt from the radioisotope dilution curves except for the computer analog simulation method. In this series no attempt to quantitate the shunt was made due to the fact that in the usual cases of tetralogy of FALLOT there are the shunts of both directions at the same time, and it is difficult and would be inaccurate to quantitate both shunts[17]. KINSOHITA et al. (1969)[21] detected the presence of the right-to-left shunt easily and more sensitively than the analysis of the arterial saturation by recording the head curve following the peripheral injection of I-131 MAA.

Radioisotope dilution study vs. cardiac catheterization

Both procedures have merits and demerits. Cardiac catheterization is still a big procedure requiring a skilled team and excellent equipment whereas the radioisotope dilution study requires only a venipuncture and adequate recording apparatus. Cardiac catheterization is not without risk which requires the insertion of the catheter into the heart and injection of the contrast material into it. The risk of the radioisotope study is almost negligible. Therefore, as a screening test and follow-up test of the patients who require the frequent study, the radioisotope study would be better than the cardiac catheterization. Best indications of the radioisotope dilution study are the one who required definitive study for the verification of the innocent murmur, and the one who needs investigative study for the residual shunt soon after the surgical closure of the defect.

The cardiac catheterization is not without errors of measurement ; which would be caused by several factors ; 1) oxygen as the tracer which is dependent on the metabolism of the patients, which might be changing during the sampling period, 2) inaccurate representation of the blood samples due to inappropriate sampling technic and/or inappropriate sampling site, 3) measurement with Van-Slyke method per se, etc. On the other hand, as long as the placement of the scintillation counter is appropriate ther are no errors caused by the "sampling" technic (namely, the contour of the curve). The critical problem of this placement of the counters has now been solved by the utilization of scintillation camera as described before. Besides the radioisotope is independent on the metabolism.

At present, no other test including the radioisotope dilution study is complete enough to replace cardiac catheterization from the viewpoint of the preoperative investigation. Namely, the cardiac catheterization alone can give us the information on the pressure in the chambers in addition to the angiographic morphology.

Summary

1) In attempting the quantitative analysis of the left-to-right shunts, the radioisotope dilution curves such as the precordial and pulmonary dilution curves were obtained.

2) Various manual analysis using different parameters such as $T\frac{1}{2}$, $T\frac{1}{2}/BT$, $R(p+BT)/Rp$, $R(p+2BT)/Rp$, and DT/BT was made. The new index advocated by the author, $T\frac{1}{2}/BT$ of the pulmonary dilution curve, showed the best result ; namely it could differentiate the left-to-right shunt group from normal, and also there was a good correlation between the index and the left-to-right shunt ratio obtained by the Fick method. The left-to-right shunt as small as 20 per cent of the pulmonary blood flow could be estimated from the regression equation :

$T\frac{1}{2}/BT$ of the pulmonary dilution curve $= 2.725 \times$ Shunt ratio by the Fick method $+ 0.246$

or Shunt ratio by the Fick method $= 28.78 \times T\frac{1}{2}/BT$ of the pulmonary dilution curve $+ 2.358$

3) Peripheral arterial dilution curves were also obtained for the analysis of the right-to-left shunt. Right-to-left shunt was clearly detected by using ATp/BT of the peripheral arterial dilution curve, but no quantitative analysis was made.

4) Since radioisotope dilution study is a simple and safe method requiring only a venipuncture and apprepriate recording apparatus, it should be more widely used for the clinical hemodynamic investigation. The best indications are the screening of the patients with

the heart murmur suspicious of the shunts and the detection of the residual shunts after the surgical closure of the defects. This new manual index analysis would be helpful where the analog computer facilities are not available.

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References

1) MacIntyre, W. J., Pritchard, W. H., Eckstein, R. W., and Friedell, H. L. : The determination of cardiac output by continuous recording system utilizing iodinated (I-131) human serum albumin studies, Circ. **4** : 552, 1915.
2) Prinzmetal, M., Corday, E., Spitzler, R. J., Bergman, H. E. C., Schwartz, L., and Spitzler, R. J. : Radiocardiography . A new method for studying blood flow through the chambers of heart in human beings. Science. **108** : 340, 1948.
3) Swan, H. J. C., Zapata-Diaz, J., and Wood, E. H. : Dye dilution curves in cyanotic congenital heart disease. Circ. **8** : 70, 1953.
4) Goldring, D., Rogers, H. M. Jr., Ter-Pogossian, M., Seaman, W., and Behrer, R. : Radiocardiography in congenital heart disease. J. Pediatrics **44** : 392, 1954.
5) Broadbent, J. C., and Wood, E. H. : Indicator-dilution curves in acyanotic congenital heart disease. Circ. **9** : 870, 1954.
6) Hetzel, P. S., Swan, H. J. C., Ramirez de Arellano, A. A., and Wood, E. H. Estimation of cardiac output from first part of arterial dye-dilution curves. J. Appl. Physiol. **13** : 92, 1958.
7) Parrish, D., Haydon, D. T., Garrett, W., and Huff, R. L. : Analog computer analysis of flow charcteristics and volume of the pulmonary vascular beds. Circ. Res. **7**: 746, 1959.
8) Greenspan, R. G., Marvin, J. F., and Amplatz, K. : Some clinical aspects of isotope circulation studies. Radiology **73** : 345, 1959.
9) Amplatz, K., and Marvin, J. K. : Simple and accurate test for the left-to-right shunt. Radiology **72** : 585, 1959.
10) Shapiro, W., and Sharpe, A. R. Jr. . Precordial isotope dilution curves in congenital heart disease : A simple method for the detection of intracardiac shunts. Am. Heart J. **60** 607, 1960.
11) Turner, R., Salazu, E., and Gorlin, R. : Detection and quantification of intracardiac shunts by the external surface counting technic. Am. J. Cardiol. **6** : 1004, 1960.
12) Cornell, W. P., Braunwald, E., and Morrow, A. G. : Applications in the detection of left-to right circulatory shunts. Circ. **23** : 21, 1961.
13) Braunwald, E., Goldblatt, A., and Morrow, A. G. : The krypton-85 inhalation test for detection of left-to-right cardiac shunts, Brit. Heart J. **24** : 47, 1962.
14) Folse, R., and Braunwald, E. : Pulmonary vascular dilution curves recorded by external detection in the diagnosis of left-to-right shunts. Brit. Heart J. **24** : 166, 1962.
15) Donato, L., Guintini, C., and Lewis, M. L. : Quantitative radiocardiography (1), (2), and (3), Circ. 26 : 183, 1962.
16) Clarke, J. M., Deegan, T., Mockendrick, C. S., Herbert, R. J. T., and Kulke, W. : 99m-Tc in the diagnosis of left-to right shunts. Thorax **21** : 79, 1966.
17) Kawata, S., Yamamoto, H., Nishikawa, K., Koide, S., and Inoue, T., : Pre-and postoperative changes of radioisotope dilution curve in congenital heart diseases with shunts. Jap. J. Thoracic Surg. **20** : 700, 1967 (in Japanese)
18) Flaherty, J. T., Canet, R. V. Jr., Boineau, J. P., Anderson, P. A. W., Levin, A. R., and Spach, M. S. : Use of externally recorded radiosisotope-dilution curves for quantification of left-to-right shunts. Am. J. Cardiol. **20** · 341, 1967.
19) Kuwahara, M., and Hirakawa, A. : Clinical application of analog computer. Quantitative anal-

ysis of renogram and radiocardiogram using computer analog simulation. Clin. Science **3** : 1554, 1967 (in Japanese)

20) Yokota, M., Kanzaki, Y., Shirotani, H., Hikasa, Y., Ishii, Y., Hirakawa, A., Torizuka, K., and Kuwahara, M. : Evaluation of radiocardiogram in various cardiac diseases. Lung and Heart **15** : 35, 1968 (in Japanese)

21) Kinoshita, M., Nakao, K., Nohara, Y., Torizuka, K., and Takayasu, M. : Detection of Circulatory Shunts by Means of External Counting Method. Differentiation between ASD and VS D, Semiquatitative Estimation of Left-to-Right Shunt, and the Detection of Right-to-Left Shunt. Jap. Circ. J. **33** : 815, 1969.

22) Ishii, Y., and MacIntyre, W. J. : Measurement of heart chamber volumes by analysis of dilution curves simultaneously recorded scintillation camera. Circ. **44** : 37, 1971.

23) Wesselhoeft, H., Hurley, P. J., Wagner, H. N. Jr., and Rowe, R. D. : Nuclear Angiocardiography in the Diagnosis of Congenital Heart Disease in Infants. Circ. **45** : 77, 1972.

24) Alazraki, N. P., Ashburn, W. L., Hagan, A., and Friedman, W. F. : Detection of left-to-right cardiac shunts with the Scintillation camera pulmonary dilution curve. J. Nucl. Med. **13** : 42, 1972.

25) Saito, M., Motohara, S., Hirakawa, A., Ogino, K., Takayasu, M., and Kuwahara, M. : Determination of intracardiac shunts in patients with congenital heart disease by means of analog simulation of radiocardiogram. Jap. Circ. J. **37** : 1, 1973.

26) Motohara, S., Saito, M., Hirakawa, A., Ogino, K., Takayasu, M., and Kuwahara, M. : Quantitative estimation of aortic regurgitation by analog computer analysis of radiocardiogram. Jap. Circ. J. **38** 169, 1974.

27) Konishi, Y. : Analog computer analysis of dilution curves recorded by scintillation camera : Measurement of cardiac chamber and pulmonary volumes and left-to-right shunts. Arch. Jap. Chir. **43** : 3, 1974.

28) Matsumura, T., Hirakawa, A., Motohara, S., Kawai, C., and Kuwahara, M. : Analysis of PDA by analog computer simulation RCG method. read at Kansai district meeting for Medical Engineering. Sept. 1975.

和文抄録

Radiocardiogram による心内短絡の定量的解析の試み，とくに，その用手的分析について

京都大学医学部外科学教室第2講座（指導：日笠頼則教授）

横　田　通　夫

末梢静脈から急速静注された放射性同位元素の希釈状態を心前（precordial dilution curve, Radiocardiogram, RCG）肺血管床上（pulmonary dilution curve）及び末梢動脈（前頭部）（peripheral arterial dilution curve）にあてたシンチレーション・カウンターでとらえた曲線を分析するいわゆるRI dilution method は，その体外計測という簡便さに加えて，本学工学部桑原らにより開発されたアナログ・シミュレーション方式（1967）により従来の分析方法では得られなかった新らしい情報（例えば右心，左心，肺容量など）が得られるということで，本学では，有力でしかもルーティンの循環機能検査となっている．著者は，1968年このコンピュータ・シミュレーション方式の臨床応用経験を発表したが，本論文では，これらの RI dilution curve の用手的分析をあらためて検討し，コンピュータなしでも短絡の評価が可能なことを示した．

対象：右左短絡群67例（VSD31例，ASD28例，PDA 8例），短絡のない群49例，短絡閉鎖術施行後症例45例，及び右左短絡群（ファロー氏四徴症）術前21例，術後7例．

方法：RIHSA 15～20マイクロ・キューリを末梢静脈より急速注入し，前記各カーヴを得た．$T\frac{1}{2}$, Rp(p+BT)/Rp(= C_2/C_1), Rp(p+2BT)/Rp, DT/BT 更に著者らの考案したパラメータ $T\frac{1}{2}$/BT を用いて分析した．

結果：pulmonary dilution curve の $T\frac{1}{2}$/BT から最も良い結果が得られた．即ち，$T\frac{1}{2}$/BT を用いることにより，左右短絡群は，コントロール群から明瞭に識別され，又，心カテーテル検査時に Fick 法により求めた短絡量と，$T\frac{1}{2}$/BT の間に良い相関が得られた（相関係数 0.92）．

又，回帰直線

短絡量＝28.78×$T\frac{1}{2}$/BT＋2.358

より肺血流量の20%以上の短絡量を推定しうることがわかった．ASD よりも VSD の方が良い相関を示したが，ASD と VSD の鑑別は不可能であった．又，一般的に，precordial dilution curve よりも pulmonary dilution curve の方が分析に適していることがわかった．

右左短絡群では，peripheral arterial dilution curve の appearace time（ATp）は一定の傾向を示さなかったが，precordial 又は pulmonary dilution curue の BT で除した ATp/BT により，右左短絡群をコントロール群より明瞭に識別しえた．

結語：アナログ・コンピュータ・シミュレーション方式を用いることにより RCG から新らしい情報が得られる様になり RCG 検査法の有用性が向上したが，従来の用手的分析法でも短絡の評価が可能なことを示し，コンピュータ設備のない施設においても，RCG 法の簡便性を生かすことが可能なことを示した．non-invasive method であるこの RCG 法は，外来において心雑音を有する患者のスクリーニング，術直後の遺残短絡の発見，及び心カテーテル検査を施行しえない様な poor risk の患者の評価に最も適した方法である．