
Alternative Method for Calculating Right Ventricular Ejection Fraction from First-Pass Time-Activity Curves

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Single-beat right ventricular ejection fraction (RVEF) determined using the first-pass method changes with rapid variations in the concentration of radionuclide tracer in the ventricle. Underestimation of single-beat RVEF occurs when radionuclide tracer rapidly enters the ventricle, and overestimation results when the tracer quickly flows out of the ventricle. In order to attenuate this effect, a data processing technique employing the relative "time-volume" curve was proposed. In the present paper, it was assumed that this time-volume curve could be approximated by dividing the original time-activity curve by a gamma variate function representing the time-concentration curve. Each single-beat ejection fraction calculated from the time-volume curve agreed well with the known phantom ejection fraction although the concentration of tracer varied rapidly. This new method was applied to several clinical cases.

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The first-pass method provides the simplest and most reproducible means for evaluating right ventricular ejection fraction (RVEF), since it permits temporal and anatomic separation of radioactivity in the right heart, lung, and left heart (1,2). However, determination of RVEF by this method is subject to errors attributable to the effect of rapid inflow or outflow of radionuclide tracer, i.e., rapid variation in tracer concentration in the right ventricle (3,4).

Correction for such variation in concentration with time was attempted by constructing a relative "time-volume" curve from the original first-pass time-activity curve. By definition, the time-volume curve can be obtained by dividing the time-activity curve by the time-concentration curve representing variation in the concentration of radioactivity within the ventricle. However, this latter curve is difficult to accurately determine. In this study, it was assumed that the time-concentration curve could be approximately expressed by a gamma variate function fitted to end-systolic points (GA method). Furthermore, justification for performing these procedures also was discussed. The GA

method was compared with the conventional beat-to-beat first-pass method (B-B method) in terms of beat-to-beat variability for the measurement of ejection fraction (EF) in phantom studies, and in clinical studies.

MATERIALS AND METHODS

Phantom Study

Various pulsatile flows were obtained in a ventricular dynamic phantom (Fig. 1). The rubber bellows of the phantom represented the right ventricle, and repeated "relaxations" and "contractions" were sustained by a driving device, the desired EF being obtained by changing the end-systolic volume of the "ventricle" while maintaining a fixed end-diastolic volume (115 ml). Flow direction was controlled by two valves attached at either end of the bellows. Experiments were performed with several heart rates from 55 beats/min to 90 beats/min and several EFs varying between 20% and 70%; stroke volume ranged from 23 ml to 81 ml, cardiac output from 3 l/min to 9 l/min, and bolus transit time through the ventricle from 4 sec to 12 sec. To represent the known phantom standard, EF was calculated from the end-diastolic volume while stroke volume of the ventricle was measured directly with a mess-cylinder. Bolus injection of technetium-99m- (^{99m}Tc) pertechnetate (4-5 mCi/1.5 ml) was performed at various times at a point 0.5 m from the artificial ventricle.

Radionuclide angiograms were obtained using a high resolution parallel-hole collimator and a computerized gamma camera (LFOV) (Shimadzu, Inc.). The photopeak of the cam-

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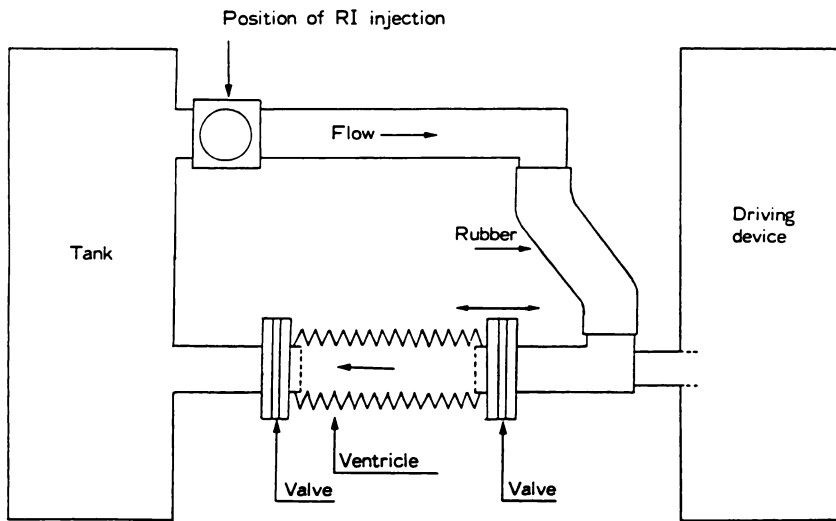


FIGURE 1
Schematic presentation of ventricular dynamic phantom.

era was always set at 140 keV with a 20% window and the ventricular region of interest (ROI) was manually selected. Counts were recorded with the apparatus in list mode for 30 sec during the first-pass of the radionuclide through the ventricle, with all data subsequently converted to frame mode at 25 frame/sec (Fig. 2). After generation of a time-activity curve, temporal three-point smoothing was performed in order to reduce statistical fluctuation.

Clinical Study

Data from subjects undergoing routine radionuclide angiography was included here only when the full width at half maximum (FWHM) of the first-pass time-activity curve was <4 sec. The detector was placed in a 30° right anterior oblique (RAO) position with the patient supine, and then a bolus of [^{99m}Tc]RBC (15–20 mCi) was injected into the antecubital

vein with a rapid 2-ml saline flush. The right ventricular ROI was manually established and was delineated at end-diastole by the tricuspid valve plane, the right ventricular free wall, and the superior region of the pulmonary outflow tract (Fig. 3). After the count rates were corrected for deadtime losses, a time-activity curve for the fixed ROI was generated in the same way as in the phantom study. The ascending and descending phases of the time-activity curve before appearance of background from the lungs were fitted to a gamma variate function.

GA Method

Temporal variation of radioactivity observed when the first-pass method is applied is not only related to heart beat, but also to bolus ejection of the tracer. If $C(t)$ is the spatially averaged concentration (count rate/unit volume) of radio-

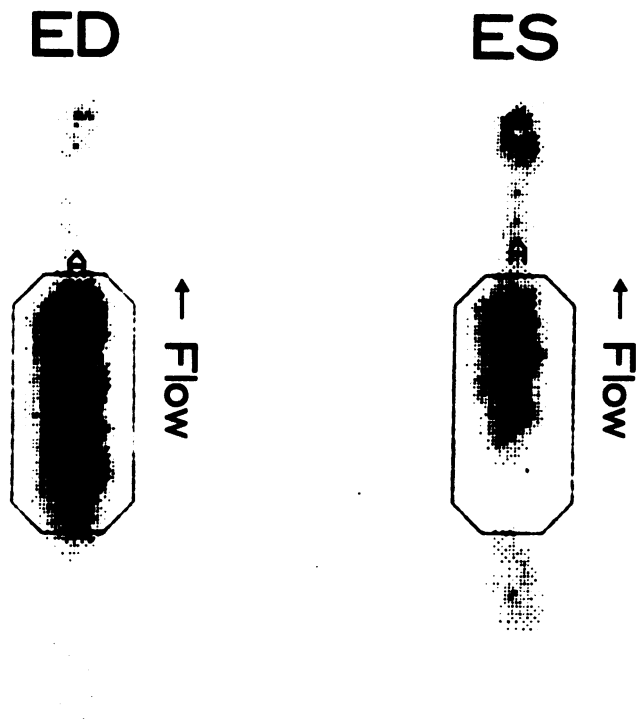


FIGURE 2
Images obtained from a phantom experiment. Ventricular ROIs are marked. ED = end-diastole; ES = end-systole.

ED

ES

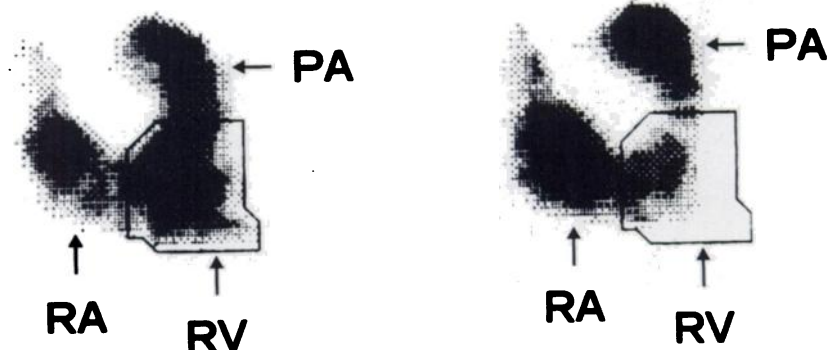
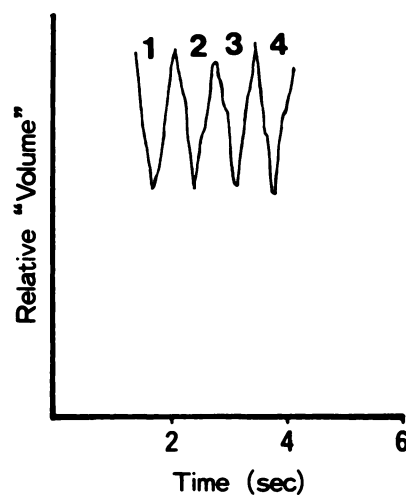
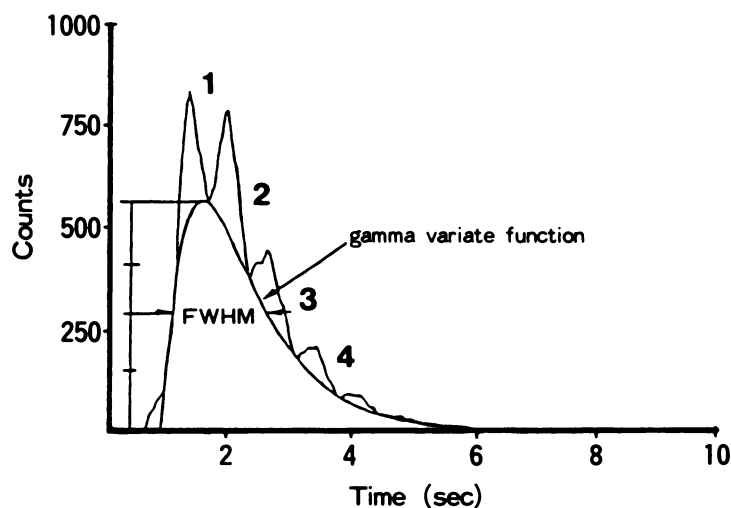


FIGURE 3
Images obtained at end-diastole (ED; left) and end-systole (ES; right) during a clinical study. The right ventricular ROI is marked. PA = pulmonary artery; RA = right atrium; RV = right ventricle.

nuclide tracer in the ventricle at time t , the relative ventricular volume at time t , $V(t)$, is given by the following formula:

$$V(t) = \frac{A(t)}{C(t)}, \quad (1)$$

where $A(t)$ is the count rate in the ventricle at time t . That is to say, the time-volume curve $V(t)$ is obtained by dividing the original time-activity curve $A(t)$ by the time-concentration curve $C(t)$ of the tracer in the right ventricle. When ed and es are the end-diastolic and end-systolic times within the same

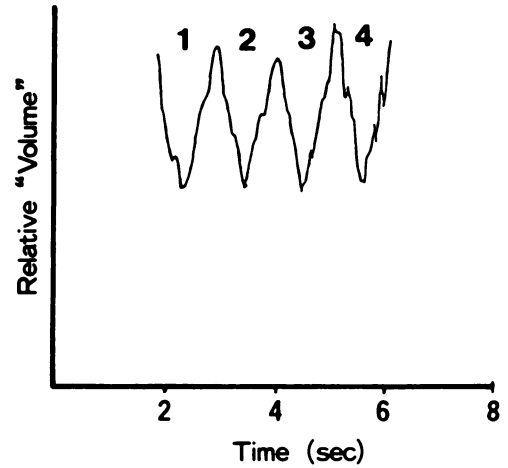
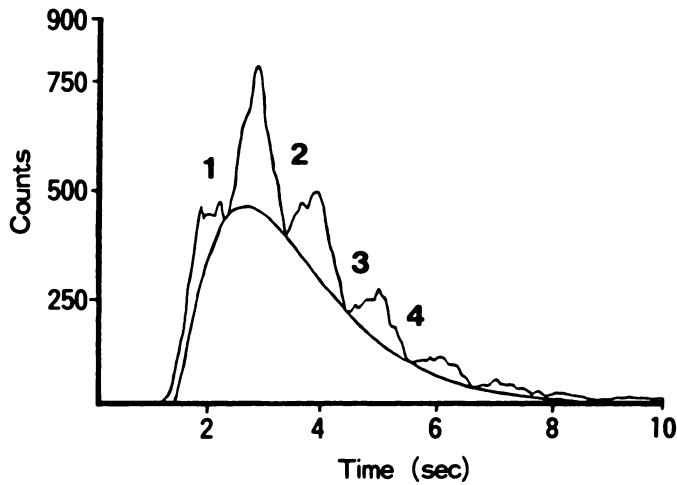


	B-B method			
Beat No.	1	2	3	4
Single-beat EF (%)	32	53	60	63
Final EF (1 ~ 2)	40.7%			
(1 ~ 3)	44.8%			
Range (1 ~ 3)	28.0%			

	GA method			
	1	2	3	4
	37	37	34	41
	37.0%			
	36.0%			
	3.0%			

FWHM=2.6sec, H.R.=90beats/min, Directed EF=32%

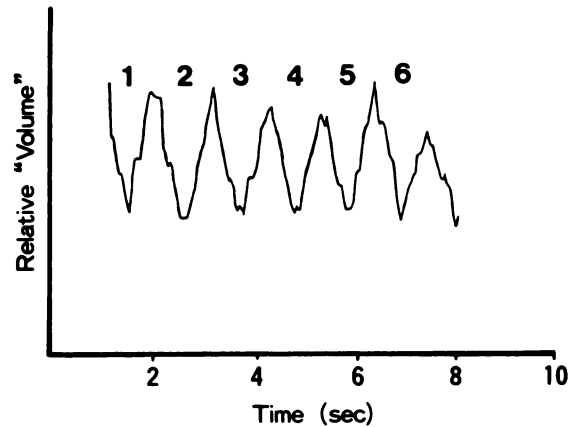
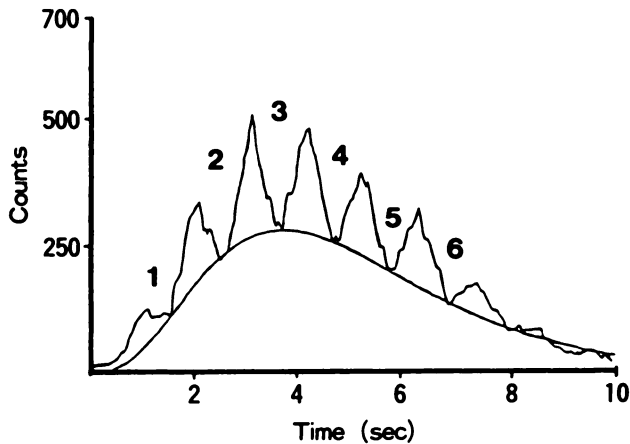
FIGURE 4
Results of a phantom experiment. Top: Gamma variate fit of the original time-activity curve (left), and relative "time-volume" curve constructed with the gamma variate function (right). Bottom: Comparison of EF values determined by the B-B and GA methods.



	B-B method			
Beat No.	1	2	3	4
Single-beat EF (%)	5	51	57	65
Final EF (2~3)	51.9%			
(2~4)	54.1%			
Range (2~4)	14.0%			

	GA method			
Beat No.	1	2	3	4
Single-beat EF (%)	41	42	40	44
Final EF (2~3)	41.0%			
(2~4)	42.0%			
Range (2~4)	4.0%			

A FWHM=2.6sec, H.R.=55beats/min, Directed EF=43%



	B-B method					
Beat No.	1	2	3	4	5	6
Single-beat EF (%)	12	32	46	47	48	60
Final EF (3~4)	46.5%					
(2~5)	45.1%					
Range (2~5)	16.0%					

	GA method					
Beat No.	1	2	3	4	5	6
Single-beat EF (%)	52	47	49	42	39	51
Final EF (3~4)	45.5%					
(2~5)	44.3%					
Range (2~5)	10.0%					

B FWHM=5.2sec, H.R.=55beats/min, Directed EF=43%

FIGURE 5

(A) Results of another phantom experiment with a small FWHM. (B) Results of a third phantom experiment with a large FWHM and with the same hydrodynamic conditions as in Figure 5A.

TABLE 1
Beat-to-Beat Variation (Range) in Single-Beat EF and
Relative Error of Final EF Obtained from Phantom
Experiments (n = 8)

Method	Range (%)		Relative error (%)	
	FWHM (sec)		FWHM (sec)	
	<4	4 ≤	<4	4 ≤
B-B	13.6 ± 5.8	6.9 ± 2.8	12.5 ± 6.2	8.8 ± 5.5
GA	4.3 ± 2.2	4.8 ± 3.0	7.6 ± 4.4	8.3 ± 4.8

cardiac cycle, the ratio of end-systolic volume (ESV) to end-diastolic volume (EDV) is $V(es)/V(ed)$, and the concentration-corrected single-beat EF can be obtained by

$$\begin{aligned}
 \text{Corrected single-beat EF} &= 1 - \frac{\text{ESV}}{\text{EDV}} \\
 &= 1 - \frac{V(es)}{V(ed)} \\
 &= 1 - \frac{C(ed)A(es)}{C(es)A(ed)} \quad (2)
 \end{aligned}$$

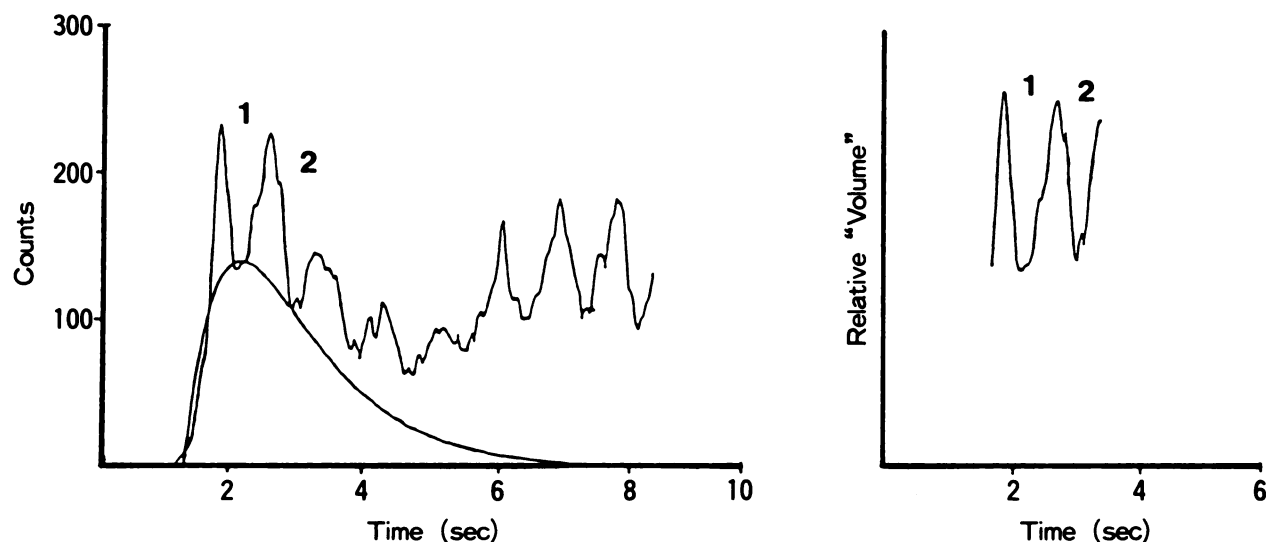
The above expression is the definition of EF, so the correction for time-varying concentration is necessary for increased ac-

curacy. Unfortunately, it is difficult to accurately determine the time-concentration curve $C(t)$. In this study, the shape of $C(t)$ was assumed to be approximately expressed by gamma variate function, and end-systolic volume was selected as unit volume. Consequently, the relative time-concentration curve is a gamma variate function fitted to the end-systolic points. Curve fitting was done by the least squares method after data was converted to logarithmic form. Here, $A(es)/C(es)$ is not always equal to 1, since end-systolic point $A(es)$ often does not exist on the fitted curve $C(t)$. The average of the corrected single-beat EFs derived from two or three beats was available for the final EF.

Data Analysis

Data are represented as mean values ± s.d. of the mean unless otherwise stated. The best two to three beats at the peak of the original time-activity curve were selected for this study.

In the phantom trials, beat-to-beat variability of single-beat EF and relative error of the final EF relative to the known phantom standard were analyzed using the various FWHMs of the bolus curve. The range (difference between maximum and minimum single-beat EF) was used as an index of beat-to-beat variability of single-beat EF (Fig. 4). As per the conventional B-B method, the final EF was calculated after first summing the end-diastolic counts and summing the end-systolic counts. The data were divided into two groups accord-



Beat No.	B-B method		GA method	
	1	2	1	2
Single-beat RVEF (%)	41	53	45	44
Final RVEF (1 ~ 2)	47.6 %		44 %	
Range (1 ~ 2)	12 %		1 %	

FIGURE 6
 A clinical study. Gamma variate fit of the original time-activity curve without background input from the lungs (left). Relative "time-volume" curve made with the gamma variate function (right). Bottom: Comparison of RVEFs determined by the B-B and GA methods. FWHM is 2.1 sec.

ing to whether the FWHM of the bolus curve was <4 or ≥ 4 sec, and the range of single-beat EF and relative error of final EF of the two methods were compared.

For each RVEF obtained by the B-B and GA methods in clinical study, two single-beat RVEFs of consecutive beats were compared. Statistical analysis was performed by Student's t-test for paired data.

RESULTS

Single-beat EF determined by the B-B method in the phantom increased with beat number (Fig. 4). It was found that the smaller the FWHM of the bolus curve was, the larger the range of single-beat EF was, whereas when the GA method was applied, the range of single-beat EF was independent of the FWHM, and smaller than that derived by the B-B method (Fig. 5A and 5B). The relative error of the final EF obtained by the B-B method was large in the case of a small FWHM of the bolus curve, while that produced by the GA method was small regardless of the FWHM magnitude (Table 1).

In the clinical study, the first single-beat RVEF (42.0 ± 8.5) obtained by the B-B method was significantly ($p < 0.005$) smaller than the second (51.2 ± 4.5), however, no significant difference between these (51.1 ± 6.8 , 50.8 ± 3.9) was observed when the GA method was employed (Figs. 6 and 7).

DISCUSSION

Assessment of right ventricular function can provide clinically useful information in patients with cardiac as well as noncardiac diseases (1,2,5,6,7). RVEF, as one of the important indices for achieving this, may be calculated by either the first-pass or the gated equilibrium blood-pool method. In such radionuclide studies, changes in radioactive count rate correspond to changes in ventricular volume, so that RVEF can be estimated without the necessity of making assumptions about the complex geometry of the right ventricle. An RAO projection was used here to optimize separation of the right atrium from the right ventricle (7). The ability of the first-pass method to isolate the right ventricle, avoiding overlap by parts of the cardiac chamber, is its primary advantage over analysis of right ventricular function via the gated equilibrium blood-pool method. Therefore, since background activity in the former is very low (7), and as the data used in the present study were obtained before the appearance of background radiation from the lungs, no background subtraction was performed. Obviously, rapid bolus injection in the first-pass method is essential to maximize and isolate counts within the right heart before the spread of radioactivity to the lung and left heart.

If EDC and ESC are the end-diastolic and end-

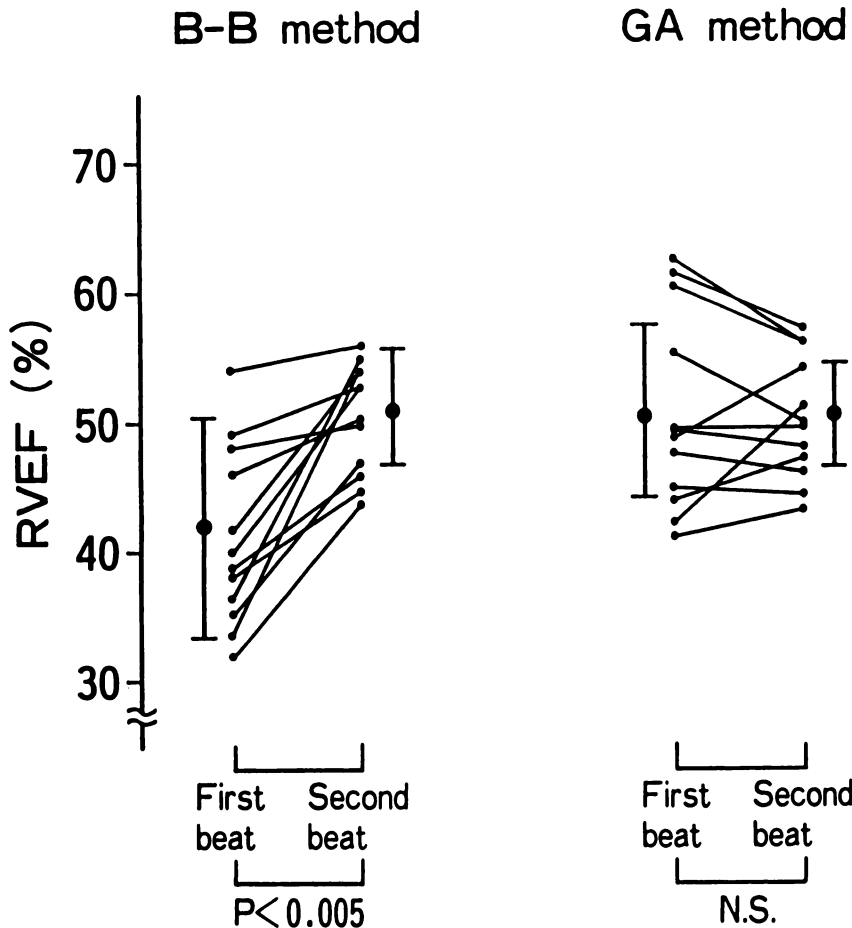


FIGURE 7
Comparisons of the first beat RVEF and the second beat RVEF.

systolic counts respectively in a single beat, the conventional single-beat RVEF by the B-B method has been calculated using the following expression:

$$\begin{aligned} \text{conventional single-beat RVEF} &= 1 - \frac{\text{ESC}}{\text{EDC}} \\ &= 1 - \frac{A(\text{es})}{A(\text{ed})} \end{aligned}$$

When there is a remarkable difference between the concentration of tracer in the ventricle at end-systole and at end-diastole within the same cardiac cycle, the conventional single-beat RVEF does not reflect the true single-beat RVEF. Specifically, the single-beat RVEF determined using the conventional first-pass method is underestimated if there is a rapid increase in the concentration of tracer and is overestimated with a rapid decrease in the concentration of tracer. Therefore, the final RVEF is influenced by the number of utilized beats. Sampling error also occurs due to rapid variations in concentration at the peak of the bolus curve.

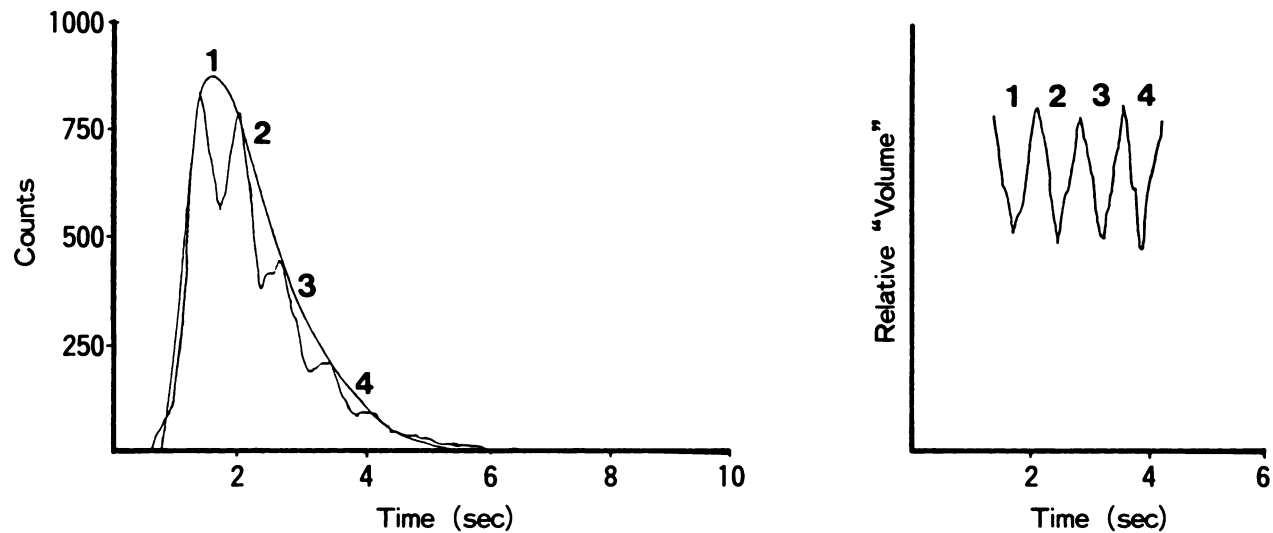
It already has been reported in previous experimental and theoretical investigations that many time-concen-

tration curves can be represented by gamma variate function written as

$$C(t) = \text{const} \cdot t^a \cdot e^{-t/b},$$

where, a and b are constants dependent on the velocity of blood and the mixing of radionuclide tracer (8,9,10). However, since time-concentration curves cannot always be expressed as gamma variate functions, then care must be taken over curve fitting.

When the gamma variate function fitted to the end-systolic points is rewritten as S(t), and point A(es) is exactly on this curve, that is to say A(es) is equal to S(es), Eq. 2 simplifies to: EF = 1 - S(ed)/A(ed). Naturally, such a gamma variate function fitted to the end-diastolic points also may represent the time-concentration curve. An example is shown in Figure 8. Denoting the gamma variate function fitted to the end-diastolic points, A(ed), as D(t), and assuming that A(ed) is equal to D(ed), Eq. 2 becomes EF = 1 - A(es)/D(es). Furthermore, when S(t) is proportional to D(t), the corrected single-beat EF calculated using S(t) is completely equal to that determined by means of D(t). Then, the corrected EF will be expressed by the formula: EF = 1



	B-B method				GA method			
Beat No.	1	2	3	4	1	2	3	4
Single-beat EF (%)	32	53	60	63	36	39	35	41
Final EF (1 ~ 2)	40.7%				37.5%			
(1 ~ 3)	44.8%				36.7%			
Range (1 ~ 3)	28.0%				4.0%			

FWHM = 1.5sec, H.R. = 90beats/min, Directed EF = 32%

FIGURE 8

Top: Gamma variate function fitted to the end-diastolic points on the same time-activity curve as in Figure 4 (left). Relative "time-volume" curve made with the gamma variate function (right). Bottom: Comparison of EFs determined by the B-B and GA methods.

– $S(t)/D(t)$. This expression already has been reported in a previous paper for another aim (11).

In the present study, the effects of deadtime were minimized by using fast shaping amplifiers and electronics for fast pulse-height analysis. Our camera-collimator system had a deadtime of 5.7 μ sec, which was evaluated using a nonparalyzable model. In clinical study, the peak full-field count rate ranged from about 20,000 cps to \sim 30,000 cps; saturation did not occur in any of the subjects.

Phantoms are very useful for evaluating the GA method because:

1. EF can be directly measured, and the error can be estimated.
2. A variety of bolus injections can be repeatedly carried out without changes in hydrodynamic conditions.
3. Single-beat EF is almost constant regardless of beat number.
4. The contribution of background can be ignored, so that it is easy to analyze the effect of variations of concentration with time.

Furthermore, laboratory study using a dynamical phantom is important, since there is no gold standard for the determination of RVEF.

In conclusion, beat-to-beat variability of RVEF due to rapid changes in tracer concentration in the ventricle can be decreased by the use of a curve obtained by dividing the time-activity curve by a gamma variate function.

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