Quantitative Assessment of Cardiac Function by First Pass Radionuclide Angiocardiography: Current Progress and Limitation

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INTRODUCTION

Recently radionuclide methods have been widely applied in the field of cardiology, and are now playing major roles in the non-invasive evaluation of cardiac function. These rapid developments in nuclear cardiology depend upon the successful use of a computer to acquire and process the data, which permits quantitative assessment of cardiac performance. Since the first introduction of the radioactive tracer in human more than half a century ago[1], temporal information of the tracer transit in the circulatory system has been analyzed by many investigators. These include the analysis of time-activity curves in the heart, so-called radiocardiogram, and the analysis of right and left ventricular performance by ECG gated method. This paper describes the general review of the first-pass radionuclide methods in order to clarify the limitations and future trends in clinical cardiology.

ANALYSIS OF TIME-ACTIVITY CURVE

The first transit of the tracer through the heart and lungs was observed initially with a single probe[2], and later with a gamma camera[3]. Radiocardiogram, which is analysis of time-activity curves on the heart obtained following the intravenous bolus injection of the tracer, includes various essential information concerning the flow/volume relations in the central circulatory system[3]. Fig. 1 shows the original radiocardiogram and its frequency spectrum. Two major components are observed in high and low frequency regions, respectively. The high frequency component corresponds to the cardiac beating, and the low frequency component, which reveals the tracer transit in the heart and lungs, is a subject to be analyzed to evaluate the flow/volume relations in the cardiac chambers.

We proposed a constant flow model of the central circulation to analyze the radiocardiogram, as shown in Fig. 2[4]. It consists of four compartments; the right heart, lungs, left heart and body, with two transport delays; one for the pulmonary and the other for the systemic circulation. The radiocardiogram includes the radioactivity both in the right and left cardiac chambers.

The curve fitting between the mathematically simulated curve and the radiocardiogram was performed using the iterative method only in the low frequency region, which is the essential part in this model assuming constant flow through the compartments.[4] Fig. 3 shows the curve fitting results of the radiocardiogram, transformed into the time domain. This simulation study provides cardiac output, which is the flow rate through the compartments, and mean transit times in each compartment, that is the ratio of the volume and the flow of the compartment. From these parameters, the volumes of the right heart, lungs, left heart and body are calculated.

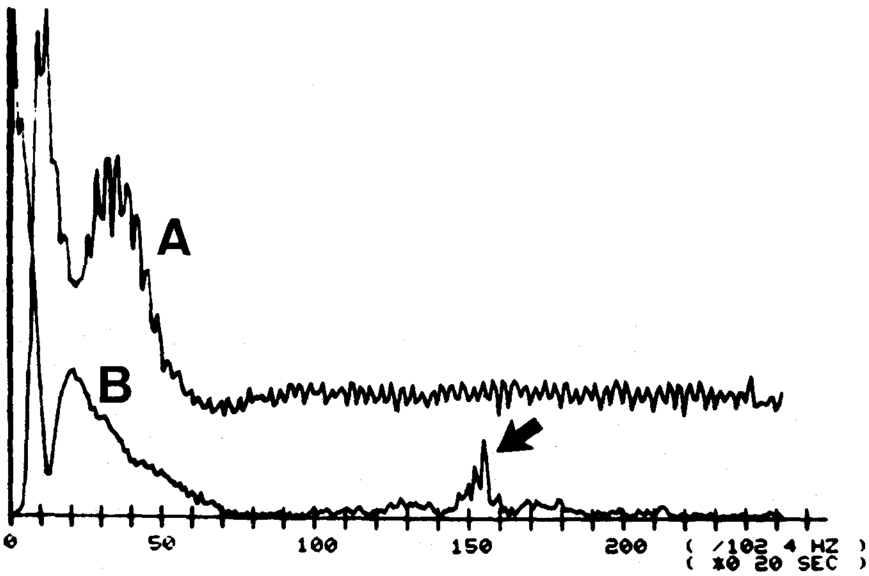


Fig. 1. Radiocardiogram and its frequency spectrum.

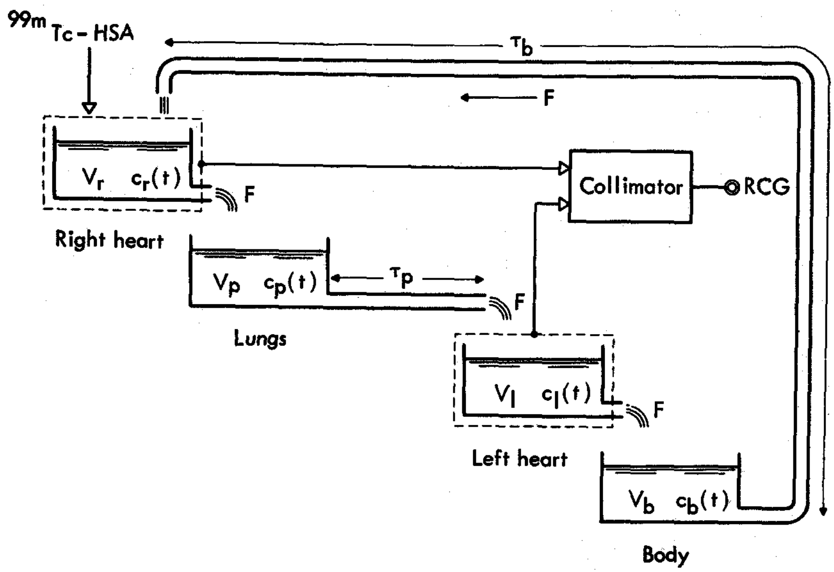


Fig. 2. Compartmental model for the analysis of radiocardiogram.

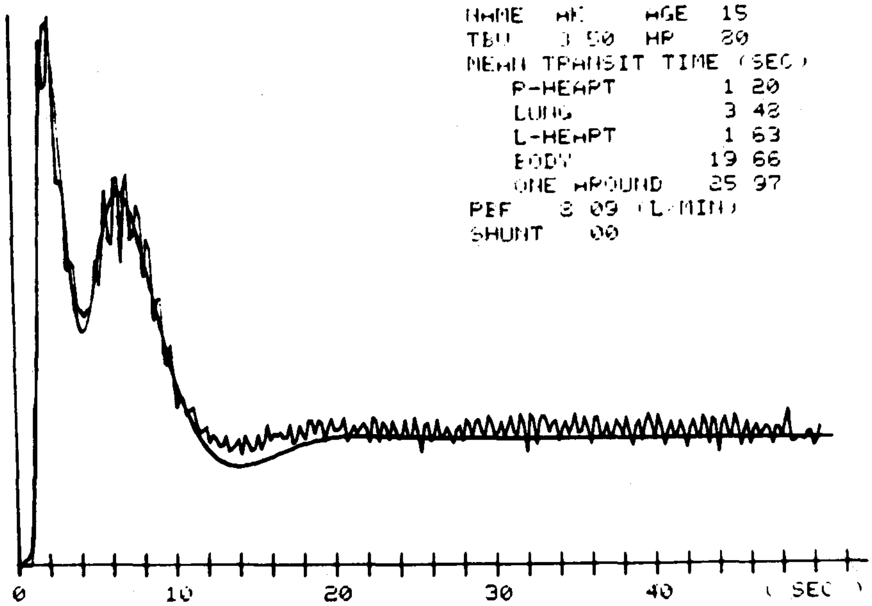


Fig. 3. Result of simulation study for the analysis of radiocardiogram in a normal case.

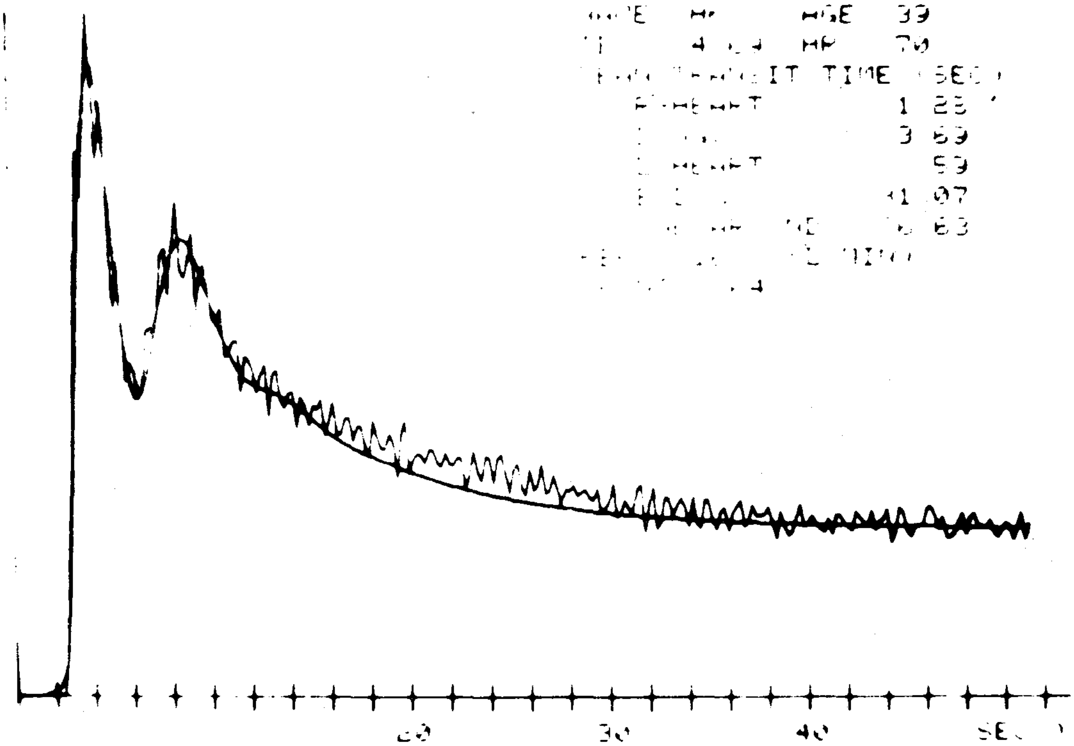


Fig. 4. Results of simulation study for the analysis of radiocardiogram in a case with atrial septal defect.

Intracardiac shunt flow can also be added to this model. Fig. 4 shows the radiocardiogram in a case with left-to-right shunt due to atrial septal defect. The shunt ratio calculated by this method was well matched with the result obtained by cardiac catheterization.

The valvular regurgitation was also detected by this type of analysis. We have developed a method to quantitate the regurgitation through the tricuspid valve[5]. Instead of using the intravascular tracer, Tc-99m labeled macroaggregated albumin was injected to eliminate the activity in the left heart as well as the effect of recirculation. Serial dynamic scans of every 100 msec were performed for 20 seconds following the bolus injection. The time-activity curve was obtained in the right atrium and in the right ventricle, as well as in the superior vena cava for measuring the input function.

The transport process in the right heart was assumed as a linear system, same as the case of the radiocardiogram. We developed a simple compartmental model, as shown in the Fig. 5. The compartments are connected in series, and a positive feed-back from the right ventricle to the right atrium represents the regurgitant flow through the tricuspid valve.

By computer simulation, the mean transit time of each compartment and the regurgitant fraction were calculated. The results obtained in a case with tricuspid valve regurgitation are shown in Fig. 6. These simulated curves indicate the increased mean transit times in the right atrium and in the right ventricle with 70% regurgitation.

After the valve replacement in this case, the time-activity curves in both chambers revealed

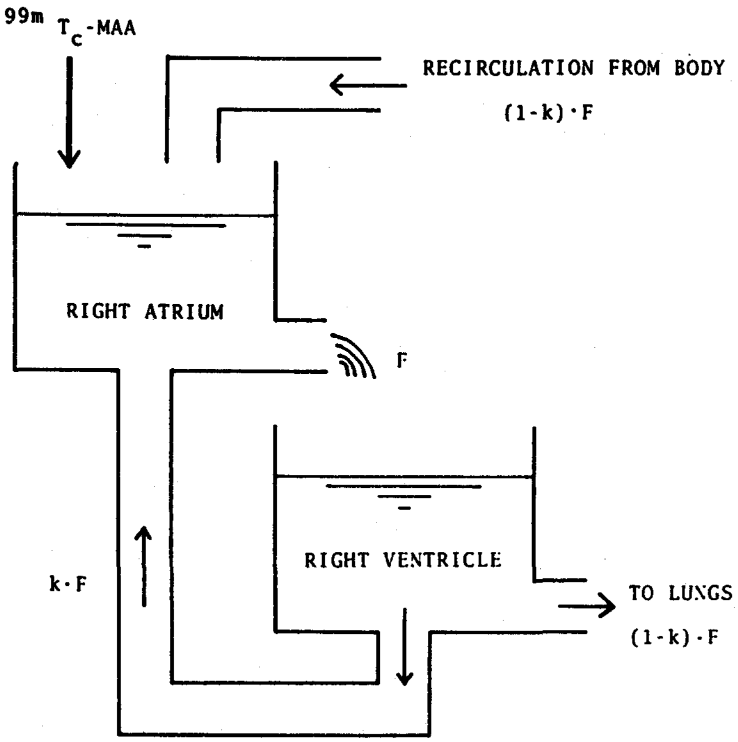


Fig. 5. Compartmental model for the analysis of tricuspid regrugitation.

the apparent improvement; the decreased mean transit times with no regurgitation.

Since the accurate quantification of the regurgitation through the tricuspid valve has not been possible yet by any means, this method seems to be a valuable diagnostic tool in clinical cardiology. However, these models are based on the two assumptions, constant flow and instantaneous complete mixing of the tracer in cardiac chambers. They could be major sources of error when we analyze the rapid transit of the tracer in the right heart with good bolus injection, although the clinical usefulness of this method cannot be interfered by these limitations.

ANALYSIS OF LEFT VENTRICULAR PERFORMANCE

The high frequency component of the time-activity curve, which was neglected as noise in the analysis of the radiocardiogram based on the assumption of the constant flow in the compartmental model, is derived from the rapid changes of the ventricular volume by cardiac beating. Although the ECG gated equilibrium study can extract precise information concerning regional and temporal changes of the left ventriculular volume, the first-pass method also permits evaluation of ventricular performance.

A multi-crystal gamma camera has an advantage of high sensitivity for the analysis of left ventricular performance by first-pass method. Global and regional ejection fraction can be

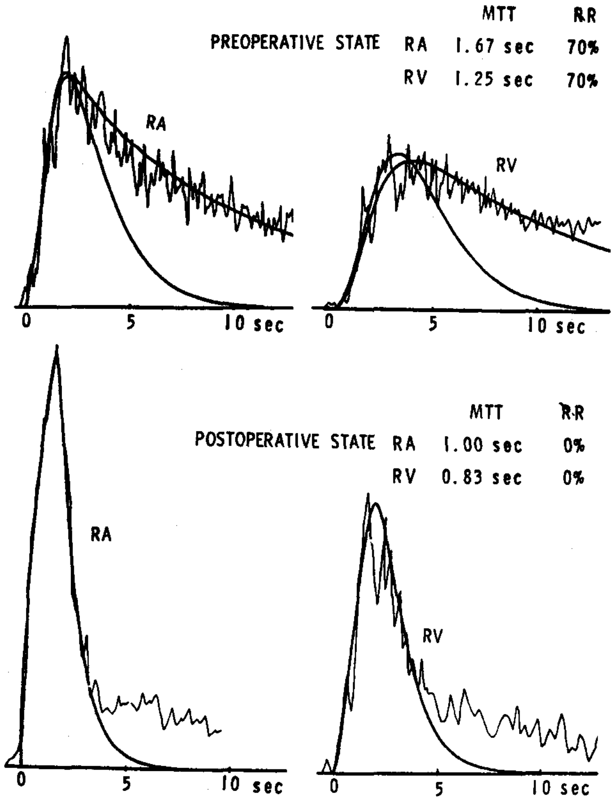
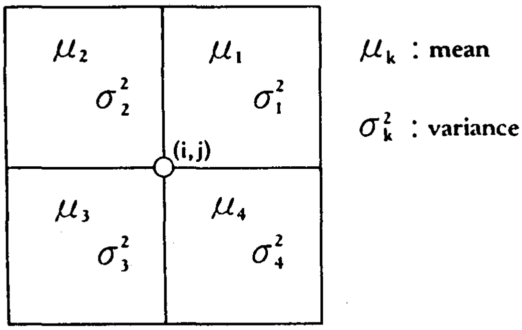


Fig. 6. Results of simulation study in a case with tricuspid regurgitation. Upper; pre-operative study. Lower; post-operative study.



$$F(i,j) = \sum_{k=1}^{4} \mu_k W_k \Big/ \sum_{k=1}^{4} W_k$$

$$\text{where } W_k = \begin{cases} 1\ ;\ \sigma_k^2 \leq \sigma_m^2 \text{ for all } m \neq k \\ 0\ ;\ \text{otherwise} \end{cases}$$

Fig. 7. Method of variance filter.

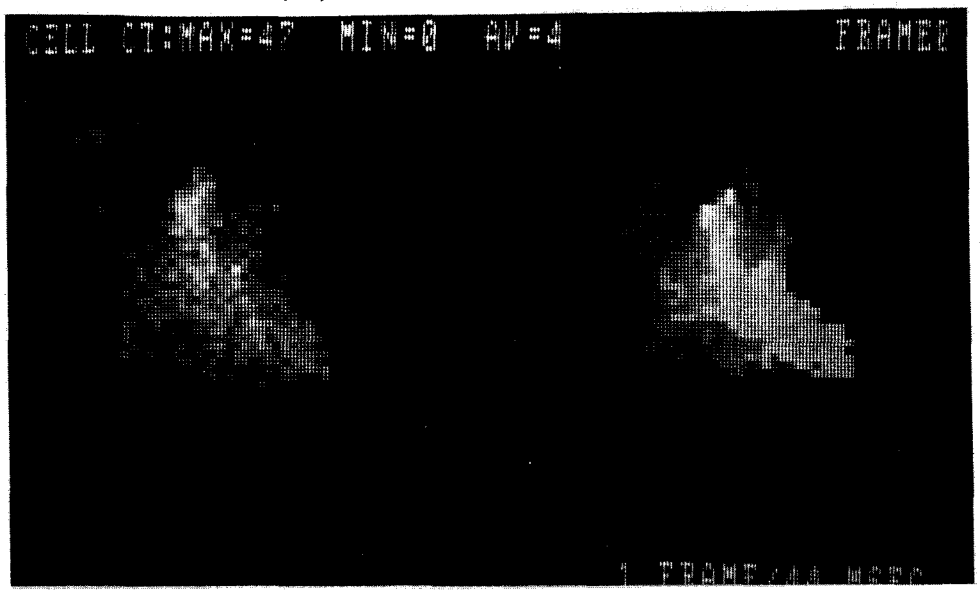


Fig. 8. Original left ventrigular image (left) and post-processed image using V-filter (right).

Table 1. Comparison of first-pass method and contrast ventriculography in detection of left ventricular abnormal wall motion.

Constrast Ventriculography	First-Pass Radionuclide Method		
	Normal	Hypokinesis	Akinesis
Normal	99	9	3
Hypokinesis	13	8	2
Akinesis	3	10	21

Table 2. Ultra-short lived radionuclides possibly used for first-pass studies.

Doughter Nuclide	Parent Nuclide
$81m_{Kr}$ (13 sec)	81_{Rb} (4.7 hr)
$191m_{Ir}$ (4.9 sec)	191_{Os} (15 d)
$195m_{An}$ (30.6 sec)	$195m_{Hg}$ (41.6 hr)

Physical half-life is shown in the parenthesis.

obtained with this technique in addition to the detection of abnormal wall motion.

Table 1 summarizes the results comparing the detectability of abnormal wall motion by the first-pass radionuclide technique with that obtained by contrast ventriculography. These two methods matched well in general, but the radionuclide technique tends to underestimate the abnormal wall motion. It may be due to the fact that the left ventricular edge in radionuclide technique is not only determined by the anatomical edge but greatly affected by the radioactivity in surrounding region, especially with the equipment of low spatial resolution such as the multi-crystal gamma camera.

One of the major issues in the assessment of ventricular performance with the radionuclide method is the detection of the left ventricular border. Several edge detection algorithm have been proposed. We have developed a non-linear filter for the edge detection of the radionuclide image[6]. This filter, so-called variance filter or V-filter, was developed in order to perform two opposite types of processing simultaneously; sharpening the edge and smoothing the activities inside the edge.

As shown in Fig. 7, four square neighbours around each pixel have been selected to calculate the mean and variance in each neighbour. The mean value of the neighbour, whose variance is smaller than others, is given as the output of this pixel. It is based on the assumption that the pixel in the center belongs to the region of the neighbour square which has minimum variance, where the boundary of the region should not be included. We picked out, for every pixel, one neighbour by the criteria of minimum variance, and took the average counts within this neighbour as an output value at this pixel. Fig. 8 shows the original and the filterd image of the left ventricle. Remarkable noise reduction in the left ventricular region was demonstrated, whereas the left ventricular edge remained to be sharp.

ANALYSIS OF RIGHT VENTRICULAR PERFORMANCE

The needs to measure right ventricular function are increasing. The first-pass technique can evaluate regional wall motion and ejection fraction of the right ventricle, just as in the case of the left ventricle. The first-pass method is superior to the equilibrium gated method because the cardiac chamber can be imaged from the right anterior oblique view in order to separate the right ventricle and the right atrium. However, there are two major problems, less counts and the non-linear relation between the activity and the volume changes due to the incomplete mixing of the tracer, especially in a case of normal or hyper-kinetic heart with good bolus injection.

Continuous infusion of Kr-81m can solve these problems. The ultra-short half-life of this tracer (13 seconds) and the clearance of the tracer from the lungs into the airway can eliminate the background activity in the left heart and recirculation of the tracer, which permits imaging the right heart from the right anterior oblique view with continuous infusion of the tracer. The background activities from the lungs are minimum even with the right anterior oblique projection, so that relatively long time acquisition is possible to obtain good quality of the image. Beat-to-beat assessment of the right ventricular contraction has also been possible using a non-imaging probe.

Another advantage of using the ultra-short half-life tracer is the possibility of repeat studies with various pohysiological interventions, as has been performed routinely in the gated equilibrium method. Some of these tracers, possibly used for the first-pass studies are shown in Table 2. These radionuclides can be obtained by the generator system, which allows the routine clinical use. As the first-pass method provides the image of the cardiac chambers from any direction with less background activity, they will be used more widely for the assessment of right and left ventricular function with less radiation dose.

CONCLUSION

The analysis the tracer transit through the circulatory system can be divided into two components in the frequency spectrum. The analysis of low frequency component provides overall assessment of the circulatory system, including the parameters relating the flow and the volume of the cardiac chambers, the shunt ratio, and the regurgitant fraction. The analysis of high frequency component provides the global and regional measurement of ventricular performance, and the ultra-short lived tracers will play more important roles for the assessment of ventricular function in the near future.

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