Quantitative Radiocardiography

I. Theoretical Considerations

By L. DONATO, M.D., C. GIUNTI, M.D., M. L. LEWIS, M.D., J. DURAND, M.D., D. F. ROCHESTER, M.D., R. M. HARVEY, M.D., AND A. COURNAND, M.D.

Following the first attempts of Blumgart and Weiss,1 Prinzmetal et al.,2 and Waser and Hunzinger3 injected radioactive sodium into arm veins and recorded the passage of the tracer through the heart cavities, by use of Geiger-Mueller counters directed over the precordium. The curves thus obtained were utilized to measure circulation times and were named radiocardiograms.2

In a later development, substitution of non-diffusible tracers and application of the dye-dilution principle to radiocardiograms made it possible to measure the cardiac output.4 Values of cardiac output within accepted physiologic range were obtained by several investigators who used radio-iodinated (I131) human serum albumin (RIHSA).5-14 Although the method was considered as analogous to dye-dilution techniques4, 15, 16 its theoretical bases and technical limits have not been established, notwithstanding several attempts to validate it by comparison with other methods.5, 11, 14

Injection of RIHSA into the venous circulation and concomitant recording of its passage through the heart cavities by means of an external collimated counter results in a double-peaked curve; the two peaks are due to the passage of the tracer through the right and left sides of the heart respectively. It has been suggested that under appropriate conditions, the downslope of the right heart curve could be used for the measurement of the volume of the right heart.16 Subsequently, it was pointed out that the downslope of the right heart curve was dependent upon the ventricular rate of emptying from which the volumes of blood in the right ventricle might be derived.17 However, the validation of this approach is still lacking; particularly the problems of mixing of the indicator with blood in the right ventricle, and that of the smearing of the indicator between the injection site and the right ventricle have not been assessed.

Radiocardiograms have also been used for the measurement of pulmonary blood volume.7-18 For this purpose Lammerant17 has assumed that the difference between the mean circulation times of the two curves which form a RIHSA radiocardiogram is a measure of the mean pulmonary circulation time, but objections to this assumption have been raised.19 In fact, the actual relationships between pulmonary transit times and the shape of RIHSA radiocardiograms have not yet been established.

The purpose of this paper is to analyze the theoretical background and the limits of radiocardiography for the measurement of cardiac output, and of right ventricular and pulmonary blood volumes. Two subsequent papers deal with the description of a method based on these considerations and the presentation of results secured in order to validate some of the assumptions upon which the method is based.

Measurement of Cardiac Output

Injection of a known amount of radio-iodinated (I131) human serum albumin (RIHSA) into the right atrium, and concomitant recording of a double-peaked time activity curve by means of a shielded scintillation detector placed over the precordium, provides a technic for measurement of cardiac output.
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The contribution of each section of the heart to the counting rate, $r$, of the detector is

$$r = K \int_0^V \epsilon(v) \eta(v) dV$$  \hspace{1cm} (1)

where $K$ is a constant depending on the characteristics of the radiisotope and of the detector used to measure $\epsilon$; $V$ is the actual volume of the section; $\epsilon(v)$ is the concentration at any point in $V$; $\eta(v)$ is the fraction of radiations emitted from any point in $V$ which reaches the crystal. This variable $\eta(v)$ is determined by the geometric efficiency and the over-all transmission coefficient. The latter takes into account the absorption of radiations, primarily aimed at the crystal, and the scattering toward the crystal of radiations primarily directed elsewhere.\textsuperscript{20}

As shown in figure 1, $\eta(v)$ decreases as the longitudinal distance between the source and the counter increases. Lateral displacement of the source from the axis of the counter also decreases $\eta(v)$. Indicating by $\bar{\eta}$ the average counting efficiency for activity uniformly mixed in a section of volume, $V$, equation (1) becomes:

$$r = K \bar{\eta} \int_0^V \epsilon(v) \ dV$$ \hspace{1cm} (2)

In the case of uniform mixing $\epsilon(v) = \bar{\epsilon}$, and therefore,

$$r = \bar{\epsilon} W$$ \hspace{1cm} (3)

where $W = K \bar{\eta} V$ and is termed the effective volume of the section.

When a nondiffusible gamma-emitting tracer (RIHSA), which is uniformly mixed in the blood, flows through a complex of vascular segments in the field of a collimated counter, the integral of the time-counting rate, $R$, derived from a fundamental equation given by Veall et al.\textsuperscript{4} is:

$$\int_0^\infty R(t) dt = W_1 \int_0^\infty c_1(t) dt + W_2 \int_0^\infty c_2(t) dt + \ldots + W_n \int_0^\infty c_n(t) dt$$ \hspace{1cm} (4)

where $c_1, c_2, \ldots, c_n$ are the concentrations at any time in the various sections, and $W_1, W_2, \ldots, W_n$ are the effective volumes of each section, which for the purposes of this derivation, are assumed to be constant. If $I$ is the amount of tracer injected and mixed with the blood flowing at a rate, $Q$, through all the sections, each integral of the second member of equation (4) is equal to $I/\ .$. Substituting, and solving for $Q$:

$$Q_{\text{RIHSA}} = \frac{I}{W_T} \int_0^\infty R(t) dt$$  \hspace{1cm} (5)

where $W_T = W_1 + W_2 + \ldots + W_n$ and is the total effective volume.

In time the tracer reaches a uniform concentration, $c_{eq}$, in the circulation. In this state the external counting rate, $R_{eq}$ is

$$R_{eq} = c_{eq} W_T$$ \hspace{1cm} (6)

from which $W_T$ can be obtained and substituted in (5) to obtain $Q_{\text{RIHSA}}$.

This theory assumes the following: (1) that mixing is complete in each section; (2) that the total effective volume, $W_T$, measured after achieving equilibrium of distribution, is equal to the sum of the effective volumes of all the sections contributing to the primary curve; (3) that the right and left ventricular outputs are equal and constant during the passage of the indicator, and that all the indicator flows through both chambers. The extent to which these criteria are met are now discussed.

Adequacy of Mixing

The determination of cardiac output by the indicator-dilution method is based on the assumption that mixing of tracer with blood takes place between the injection and sampling sites. Since, with the technic to be described, tracer is injected directly into the right atrium where complete mixing cannot be assumed, a discrepancy in the distribution of tracer and flow in this chamber may occur. As a consequence, the time integral of the counting rate as the tracer passes through the

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right atrium is not necessarily proportional to the flow through it. However, the error induced by such a discrepancy can affect only the contribution of the right atrium to the total precordial counting rate, which model experiments* have revealed to be less than 20 per cent, hence its effect on the estimation of total blood flow will be small.

Since there is evidence to indicate that adequate mixing takes place in the right ventricle,21 it may be assumed that blood entering the left atrium is already mixed with tracer. As a consequence, when tracer is injected into the right atrium, the distribution of tracer in the left atrium depends on the distribution of flow. If \( \eta \) were uniform throughout this chamber the contribution of every unit of volume to the time integral of the counting rate would be the same. However, as shown in figure 1, \( \eta \) varies appreciably, within the left atrium, i.e., between 15 and 35 per cent; therefore the contribution of each unit of volume is proportional to its respective \( \eta \) value. Nevertheless, since the situation is analogous to a model with single input, and multiple outputs,22 the time integral of concentration for all individual units of left atrial volume is identical and therefore, for a given distribution of \( \eta \), the time integral of the over-all precordial counting rate will not be affected by the distribution of flow in the left atrium.

Significance of the Total Effective Volume

It is obvious that the size of any heart cavity and its distance from the chest wall vary during a heart cycle. However, in a steady state these changes are cyclically repeated, and it can be assumed that at the same phase of the heart cycle, in a given state, the position and size of the cavity are the same. Therefore, the effective volume of any chamber is constant, provided that the heart cycle does not vary.

The value of \( W_r \) to be introduced in equation (5) must equal the sum of the effective volumes of the four cavities and no other volumes should contribute to this value.

The estimate of \( W_r \), based on the precordial counting rate obtained after uniform distribution of tracer in the whole circulation, may differ from \( W_r \), which prevailed at the time of inscription of the radiocardiogram. This discrepancy stems from two facts: the first is that mixing may have been incomplete in the right atrium at the time of the inscription. Variations in distribution of the tracer will affect not only the time integral of the concentration but also \( W \) according to equations (1), (2), and (3). Since the calculation of \( \eta \) is cumbersome and dependent on factors, such as the scattering of radiations, difficult to assess numerically, the phantom of the heart previously referred to has been used to estimate the possible error. For example, if all the activity in the right atrium is assumed

* A hard rubber model of the normal heart was suspended in a water-filled plastic jar to simulate the chest. Each chamber of the phantom was then successively filled with the same amount of activity and a counting rate obtained.
to be uniformly distributed in either the anterior or posterior one half of the chamber, the deviation of the total precordial counting rate from the ideal situation of complete mixing in the right atrium has been found to be less than ± 4 per cent.

The second and more important fact is that vascular sections which are in the field of the counter contain radioactivity at the time of equilibrium, which was not present when the curve was recorded. Since the counting efficiency for activity present in tissues in front of the heart is particularly high, an attempt has been made with model experiments to estimate this contribution to the total precordial counting rate, and it has been found to lie between 10 and 20 per cent. An approximate estimate of such a contribution to the precordial counting rate can be obtained independently by measuring the counting rate over the thigh of each patient.

If \( R_{eq} \) and \( R_T \) are the net counting rates over the precordium and thigh respectively, after distribution of the tracer is reached, the fraction of the precordial counting rate, \( H \), due to activity within the heart is obtained as:

\[
H = 1 - \frac{R_T}{R_{eq}}
\]

and the total effective volume is:

\[
W_T = \frac{R_{eq}H}{c_{eq}}
\]

Equality and Constancy of Right and Left Ventricular Outputs

\( Q_{RIHSA} \) reflects \( Q_R \) when \( Q_R \) equals or exceeds \( Q_L \). However, if the left output exceeds the right, \( Q_{RIHSA} \) is a complex resultant of \( Q_R \) and \( Q_L \), and has no physiologic counterpart.

If one indicates by \( I_R \) and \( Q_R \) the amount of tracer and the volume of blood flowing through the right heart cavities, and by \( I_L \) and \( Q_L \) those flowing through the left cavities, equation (4) may be rewritten:

\[
\int_0^\infty R(t)dt = W_R \frac{I_R}{Q_R} + W_L \frac{I_L}{Q_L}
\]

where \( W_R \) and \( W_L \) are the sums of atrial and ventricular effective volumes on the right and left sides respectively.

When the same flow, \( Q \), and the same amount of indicator go through both sides of the heart,

\[
Q_{RIHSA} = Q = Q_R = Q_L
\]

If \( Q_R \) is greater than \( Q_L \), but the ratio \( \frac{I}{Q} \) is the same in both sides of the heart, which might result from diversion of the same proportion of indicator and flow in the transfer between right and left, as in patent ductus arteriosus with reversed shunt, then

\[
Q_{RIHSA} = Q_R
\]

If \( I_R = I \), i.e., if all of the injected tracer flows through the right heart, but \( Q_L \) is greater than \( Q_R \) as occurs in uncomplicated patent ductus arteriosus, \( Q_{RIHSA} \), as calculated by (5) is:

\[
Q_{RIHSA} = \frac{Q_R Q_L (W_R + W_L)}{Q_R W_L + Q_L W_R}
\]

A change in output from one equilibrium level to another may be measured by \( Q_{RIHSA} \), within certain limits, namely that \( Q_R \) equals or exceeds \( Q_L \). Changes in blood flow will be proportionately reflected in changes of \( Q_{RIHSA} \) if the change affects the right and left ventricular outputs in the same proportion, and if \( W_R \) and \( W_L \) remain constant, or are determined again at the new level of flow. However, if at the new level of equilibrium the relation between \( Q_R \) and \( Q_L \) has changed from that at the time of the control measurement, or if the \( \frac{I}{Q} \) ratios have varied in different proportions in the two sides of the heart (i.e., opening or closing of shunts), the significance of \( Q_{RIHSA} \) will be different from the control measurement. Under such circumstances, the variations of \( Q_{RIHSA} \) will not reflect the variations of \( Q_R \) and \( Q_L \).

Measurement of Right Ventricular Volumes

If a bolus containing radioactivity is injected into the right ventricle during a single diastole, and is completely mixed with all the diastolic blood volume, the disappearance of
activity from the ventricle will take place at a rate

\[ R = \frac{\text{activity ejected per beat}}{\text{total activity before ejection}} \]

\[ = \frac{\text{stroke volume}}{\text{ventricular end-diastolic volume}} \]  

(13)

Let \( Y_n \) be the activity injected: the activity \( Y_n \) in the ventricle after the \( n^{th} \) ejection will be:

\[ Y_n = Y_o (1 - R)^n \]  

(14)

The successive values of \( Y_n \) will follow an exponential law of decay, from which the rate of emptying, \( R \), can be calculated as:

\[ R = 1 - e^{-\frac{\ln(Y_n/Y_o)}{n}} \]  

(15)

If the stroke volume, \( SV \), is known, the ventricular end-diastolic volume, \( VDV \), and the ventricular residual volume after ejection, \( VRV \), can be obtained as:

\[ VDV = \frac{SV}{R} \]  

(16)

and

\[ VRV = VDV - SV \]  

(17)

This treatment can be applied when activity is injected upstream to the ventricle, provided that the transfer of the tracer into the ventricle is completed within a finite time, after which a condition of pure washout is established, which can be described by equation (14).

The application of this theory to the analysis of a curve recorded by a counter collimated over the ventricle from the outside of the body demands the fulfillment of several theoretical and technical requirements.

**Mixing in the Right Ventricle**

Although the degree of mixing of indicator with blood in the right ventricle has been long debated, it appears sufficient to permit measurement of blood flow by use of indicator-dilution principles. Measurement of the emptying rate of the right ventricle also requires mixing. The best evidence for adequate mixing is that the fractional decrease in the total amount of an indicator in this chamber remains constant for several beats. Since, with the type of collimation used most of the right ventricle is seen, a constant fractional decrease in counting rate, observed for at least three heart cycles, can be taken to represent the actual rate of emptying of the ventricle, within the error of the technic.

Equation (13) will be assumed to describe correctly the washout of the tracer from the right ventricle. The validity of this assumption will be discussed subsequently on the basis of the results obtained during this study.

**Selectivity of Recording**

In order that the above theory be applicable it is necessary that the ejection of a given fraction of the ventricular activity results in a proportional decrease of the number of pulses from the detector. This requires that the efficiency of counting for activity in the pulmonary circulation be negligible. It is also necessary that the time interval between the onset of the pure washout state in the right ventricle and the appearance of activity in the left side of the heart is long enough to permit the observation of the pure washout state. Both these conditions should be met by a type of collimator designed to encompass both sides of the heart but a minimum of the lungs, and by a central (right atrial) site of injection. Under these conditions the counting efficiency for the fraction of lung in the direct counting field is much smaller than that for the right ventricle, and the transit curve of...

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**Figure 2**

*Relationship between mean pulmonary circulation time, \( PCT \), time of appearance of the tracer in the left heart, \( t_a \), and peak time of the left curve, \( t_p \). The shaded columns represent the amount of activity ejected by the right ventricle at each systole. A. Time distribution of the activity inflowing into the left heart after a single ejection by the right ventricle (arbitrary distribution of pulmonary circulation times). B. Time distribution of the activity inflowing into the left heart after a series of ejections by the right ventricle; the dotted line is the total inflowing activity, and is obtained by summing up the continuous curves. C. Relationship between inflowing concentration (dotted line), and left ventricular concentration, \( y(t) \), after a series of right ventricular ejections as in B.*

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RIHSA through the right side of the heart is well defined before any activity reaches the left side. Hence, right and left transit curves can be separated in a double-peaked RIHSA radioangiogram.

Another approach to the problem of selectivity for the right heart is the use of a radioactive gas, such as krypton (Kr85), dissolved in saline and injected into the right atrium.\footnote{29} This tracer has recently been shown to be 95 per cent cleared during its first passage through the lungs,\footnote{30} and therefore was deemed suitable for the obtaining of right selective radioangiograms.

**Constant Geometry**

It is necessary to maintain constant geometry in order to have the same efficiency throughout the recording of the curve. In a resting state, this is achieved without difficulty. During exercise, a shoulder brace and padding between collimator and chest is helpful.

**Fidelity of Recording**

The recorded variations of counting rate must be proportional at any time to variations of activity in front of the counter at that time. If a ratemeter is used to record the pulses arising from the detector, the damping induced by the RC circuit of the ratemeter has to be taken into consideration if the actual rate of change of the activity is to be measured.\footnote{31} The recorded counting rate \( R_t \) is related to the actual counting rate \( Y_t \), as:

\[
Y_t = R_t + \tau \frac{dR_t}{dt} \tag{18}
\]

where \( \tau \) is the time constant of the ratemeter. A correction for damping can be obtained by calculating the \( Y_t \) values from the corresponding \( R_t \) on the basis of equation (18).

**Measurement of Pulmonary Blood Volume**

The mean circulation time, MCT, of a curve representative of the passage of a tracer through the left ventricle equals the sum of the mean circulation times through all the vascular sections from the point of injection to the aortic valve, including the left ventricle. Therefore, the volumes obtained by multiplying the cardiac output by the difference of the mean circulation times of the right and left curves of RIHSA radioangiograms\footnote{7} necessarily exceed the pulmonary blood volume. A different approach for the determination of the mean pulmonary circulation time needs to be considered.

If an amount, \( X_o \), of radioactivity is ejected by the right ventricle into the pulmonary artery and is uniformly mixed with blood, it will enter the left atrium according to a distribution in time which can be expressed as:

\[
Z_t = X_o P_t
\]

where \( P_t \) equals \( q(t)/Q \) and is the fraction of tracer ejected at 0 time which appears in the left heart at time \( t \); \( q(t) \) is the flow going through the pulmonary "channel" with transit time \( t \); and \( Q \) the total pulmonary blood flow. Whatever the distribution of \( P_t \), a minimum and a mean circulation time may be defined, and they are indicated in figure 2a.

If a series of ejections is spaced in time by intervals equal to the duration of a heart cycle, and the distribution of flow through the various pulmonary channels remains constant, the inflow curve in the left heart will be

\[
Z_t = \sum_{t=0}^{t=t} X_i P_{t-i}
\]

where \( i \) indicates the time of ejection and \( P_0 = 0 \). This situation is represented in figure 2b.

If one assumes that the left side of the heart functions as a single mixing chamber, the time-concentration curve of the inflow into the left heart is related to the left heart concentration curve as shown in figure 2c.

If one indicates by \( t_a \) the time at which activity appears in the left side of the heart, it is evident that, if the time of the first ejection, \( t_o \), is taken as the origin of pulmonary circulation times, the mean pulmonary circulation time, \( PCT \), through the pulmonary vascular bed must be at least as long as the time \( t_a - t_o \). On the other hand it is shorter than the interval between the time of the first ejection, \( t_o \), and the time of the peak of the left curve, \( t_p \). Thus,

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Similarly, for the mean pulmonary blood volume, $\overline{PBV}$:

$$Q(t_a - t_o) < \overline{PBV} < Q(t_p - t_o) \quad (19)$$

The location of $PCT$ in the range from $t_a$ to $t_p$ could be established only if the distribution of the pulmonary transit times were known; since it is not known, the pulmonary blood volume is calculated on the basis of the mid point of the range of $PCT$:

$$\overline{PBV} = \frac{SV (t_a - t_o) + (t_p - t_o)}{2} \quad (21)$$

Equation (21) represents an empirical approximation, which would yield the true pulmonary blood volume if $t_p - t_o$ corresponds to the transit time of the longest pulmonary channel, and the distribution of pulmonary transit times is symmetrical.

In applying these considerations to RIHSA radiocardiograms for the measurement of $PBV$, certain questions must be answered, since human radiocardiograms may deviate from the ideal model in several respects:

1. If RIHSA is injected into the right atrium, the peak of the right curve may be reached in one or two beats. In the latter instance, pure washout is not established at the time when the first activity leaves the right ventricle, the peak of the left curve will be delayed and the range in which $PCT$ lies becomes wider.

2. Since the left atrium is interposed between the pulmonary circulation and the left ventricle, and is within the field of the counter, it will affect both the transit time between the right and left ventricles, and the precordial counting rate. Whether the left atrium acts simply as a transit section or as a mixing chamber, its effect will result in a delay of the peak of the left ventricular curve.

3. The counter records left atrial and ventricular concentrations, each multiplied by a factor which depends on the geometric relationships between counter and cavity. Depending on the relative contributions from atrium and ventricle, $t_o$ will be variably displaced between the peak time of the left atrial and that of the left ventricular concentration curves.

None of the above considerations affect the validity of equations (19) and (20) but do affect the range of possible estimates of mean pulmonary circulation time.

**Summary and Conclusions**

The theoretical and technical limits within which the cardiac output can be measured from a curve recorded by a precordial counter after injection of a gamma-emitting tracer have been assessed. The geometric arrangements that best approach ideal conditions have been described. It has been shown that the physiologic significance of the value for output as measured from the radiocardiograms varies with the indicator-flow ratio in the two sides of the heart.

The necessary conditions for measurement of right ventricular volumes from the radiocardiograms have been presented, and the theoretical limits of the technic are evaluated.

The problem of the measurement of pulmonary blood volume from RIHSA radiocardiograms has been discussed. While it is not possible to make a direct measurement of mean pulmonary blood volume from RIHSA radiocardiograms, the limits within which this volume lies have been indicated.

**References**


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