Assessment of Cardiac Performance with Quantitative Radionuclide Angiography

Sequential Left Ventricular Ejection Fraction, Normalized Left Ventricular Ejection Rate, and Regional Wall Motion

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SUMMARY Sequential quantitative first pass radionuclide angiograms (RA) were used to measure left ventricular ejection fraction (LVEF) and left ventricular ejection rate (LVER), and to assess regional wall motion (RWM) in the anterior (ANT) and left anterior oblique (LAO) positions. Studies were obtained with a computerized multicrystal scintillation camera suitable for acquiring high count-rate data. Background was determined in a new fashion by selecting frames temporally from the left ventricular region of interest time-activity curve. A "representative" cardiac cycle was formed by summing together counts over three to six cardiac cycles. From this background corrected, high count-rate "representative" cardiac cycle, LVEF, LVER, and RWM were determined. In 22 patients with normal sinus rhythm in the absence of significant valvular regurgitation, RA LVEF correlated well with that measured by contrast angiography \( r = 0.95 \). LVER correlated well with LVEF measured at contrast angiography \( r = 0.90 \) and allowed complete separation of those with normal \( LVER = 3.4 \pm 0.17 \, \text{sec}^{-1} \) and abnormal \( LVER = 1.22 \pm 0.11 \, \text{sec}^{-1} \) \( P < .001 \) left ventricular performance. This separation was independent of background. Isoproterenol infusion in five normal subjects caused LVER to increase by \( 81 \pm 17 \% \) while LVEF increased by \( 10 \pm 2.1 \% \). RWM was correctly defined in 21/22 patients and 89% of left ventricular segments with abnormal wall motion.

FIRST-PASS RADIONUCLIDE ANGIOCARDIOGRAMS provide a relatively noninvasive method of evaluating left ventricular performance. This method involves calculation of functional parameters directly from the high frequency components of the left ventricular time-activity curve obtained during the first pass of the radionuclide through the central circulation.\(^1\)\(^-\)\(^3\) Complete mixing of the bolus with blood is assumed to have occurred by the time the radionuclide enters the left ventricle such that changes in radioactivity during the ejection phase accurately reflect proportional changes in chamber volume. The first pass method for determining left ventricular ejection fraction (LVEF) is free of the geometric assumptions inherent in volume calculations based upon measurement of ventricular axes and planimetered areas. However, the efficacy of the first pass method is dependent upon obtaining sufficiently high count rates to assure statistical accuracy and upon accurately assessing background counts within the left ventricular time-activity curve. Ejection phase indices of left ventricular performance other than ejection fraction have not routinely been obtained with this approach. Also, evaluation of regional wall motion has generally been considered impractical due to the inability to obtain sufficient count-rates necessary to form high resolution left ventricular cavity images.

This report describes our initial experience with quantitative first pass radionuclide angiography for evaluating left ventricular performance in man. A multicrystal mosaic detector scintillation camera with high count rate capabilities is used. A new method of objectively estimating background counts within the left ventricular time-activity curve is proposed. The goals of this study are fivefold: first, to define and validate our approach for determining LVEF; second, to define, validate, and standardize our approach for determining left ventricular ejection rate (LVER); third, to study the feasibility of determining regional wall motion from first pass studies; fourth, to evaluate the possibility of performing sequential first pass studies in two positions; fifth, to study potential sources of error associated with this method.

Materials and Methods

Patient Selection

Thirty-seven quantitative first pass radionuclide angiograms were performed in 22 patients within 24 hours prior to elective cardiac catheterization. The only criteria for admission to this study were 1) patient willingness, 2) technically adequate contrast angiograms (in those patients undergoing cardiac catheterization) and radionuclide studies in at least one position, 3) the presence of normal sinus rhythm at the time of study. Of the 22 patients undergoing cardiac catheterization, 15 patients had adequate radionuclide angiograms in two positions (anterior and 45° left anterior oblique), while seven patients had an adequate radionuclide angiogram in one position. The reasons for inadequate two-position studies were: 1) patient reluctance to undergo a second study (one patient); 2) technical errors in data recording (3 patients); 3) inadequate radionuclide bolus due to poor injection technique (3 patients). Inadequacy of the bolus was assessed by both visual detection of persistent activity in the subclavian venous system, and time-activity

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analysis over the region of venous inflow. Three patients had adequate two view radionuclide angiograms but inadequate contrast angiograms and are not included in this study. Heart rates were compared at the time of radionuclide and contrast angiography and no patient had greater than 20% change. Additional clinical data concerning the cardiac catheterization study are summarized in table 1.

An additional 14 studies were performed in seven subjects not undergoing cardiac catheterization but undergoing intervention studies. In five of them, measurements were made in the control state and during isoproterenol infusion. These five subjects were clinically normal as assessed by a normal resting ECG, chest X-ray, physical examination, and negative cardiac history. They ranged in age from 31 to 42 years (average 36 years).

In the two other subjects radionuclide angiograms were performed before and during atrial pacing to heart rates comparable to those obtained in the isoproterenol group. These patients were 42 and 31 years of age and were undergoing electrophysiological evaluation for possible cardiac causes of syncope. In one patient (age 42), cardiac catheterization demonstrated no significant coronary artery disease, normal left ventricular contraction, and normal hemodynamics. The second patient (age 31) had no clinical evidence of major anatomic heart disease and demonstrated a normal resting ECG (except for intermittent first degree heart block), normal chest X-ray, and negative physical exam.

**Radionuclide Technique**

Two studies were done sequentially in the anterior and left anterior oblique (LAO) positions, alternating the position of the first and second studies in successive patients. All quantitative radionuclide angiograms were obtained following placement of a \#18 gauge Jelco polyethylene catheter in a large antecubital vein. Ten mCi of \(^{99m}\)Tc sulfur colloid suspended in less than 1.5 ml of saline were used for the first study, and 15 mCi of \(^{99m}\)Tc sodium pertechnetate dissolved in less than one ml of normal saline were used for the second study. Fifteen ml of saline were used to flush the radionuclide bolus into the central circulation. Ten to fifteen minutes were allowed to elapse between the first and second studies so that adequate blood clearance of the \(^{99m}\)Tc sulfur colloid by the liver and spleen was achieved. Although the two radiopharmaceuticals behave in a different manner with regard to remaining within the intravascular space, it can be estimated that during the first pass through the central circulation greater than 95% of both tracers remain intravascular.*

All radionuclide studies were performed within a dedicated nuclear laboratory located in the coronary care unit using a commercially available multicrystal scintillation camera equipped with a 1.5 inch parallel hole collimator (Baird-Atomic System-77). This instrument possesses a detector composed of a mosaic of 294 individual crystals and is interfaced to a small dedicated computer (16K memory). Data were accumulated in frame mode at 0.05 sec intervals for 25 sec, stored on magnetic disc, and then transferred from disc to magnetic tape for permanent storage.

**Data Processing**

All data were corrected for the dead-time of the system using a factory installed computer program. Variations in intercrystal efficiency of \(^{99m}\)Tc radiation detection were corrected for by using a uniform cobalt-57 pool. The study was then replayed on the oscilloscope in serial fashion with each image representing 20 summed 0.05 sec frames; and images representing the left ventricle were identified. Using a magnetic pen and grid array representing each of the detector’s 294 crystals, the left ventricular region of interest was selected. The margins of the left ventricle were determined using the display of the color television console in which the maximum counts of each image are represented by white and each 12.5% gradation in count intensity is represented by a different color. By arbitrarily zoning to the same color coded outer margin (52% of the maximum counts) in every patient, a reproducible and standardized left ventricular region of interest was selected.

A preliminary high frequency (0.05 sec/frame) time activity curve (TAC) was then generated from this region of interest. End-diastolic frames, identified as high count peaks in the left ventricular TAC (fig. 1), were then used as starting points to sum counts at corresponding 0.05 sec intervals over 3-6 (average 4) cardiac cycles. Only cardiac cycles in which the end-diastolic frame had 80% of the maximum end-diastolic counts were used. This limited the cardiac cycles involved in the calculations to the peak of the left ventricular TAC. A series of sequential 0.05 sec background frames then were chosen directly from the left ventricular region of interest TAC just prior to the first discernible left ventricular beat at the beginning of the left ventricular phase (fig. 1). This background, for the most part, represents overlying

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Mean = 55.1 ± 4.3% ± 3.5% ± .26 sec

*Average is either the average of two measurements from a two position study or single value when only one was performed.

Abbreviations: CA = contrast angiogram; RA = radionuclide angiogram; EF = ejection fraction; ER = ejection rate; CM = cardiomyopathy; CAD = coronary artery disease; NAD = no anatomic disease; RHD = rheumatic heart disease; MS = mitral stenosis; MVP = mitral valve prolapse.
and scattered radiation from the left atrium and lungs at the
time when all the radionuclide is in those structures. The
same number of background frames were added together as
cardiac cycles used. This fixed summed background was
subtracted from the summed cardiac cycle forming a high
count-rate, background corrected, "representative" cardiac
cycle. Using the end-diastolic image generated from the
background corrected representative cardiac cycle, the in-
itial zone of the left ventricular region of interest was
rechecked. If the original zone was not entirely accurate, a
new region of interest was selected, another TAC generated,
and the entire process repeated. The resulting final
background-corrected representative cardiac cycle was used
to directly calculate LVEF from the formula (fig. 1):

\[
\text{LVEF} = \frac{\text{Counts in end-diastole} \ - \ \text{Counts in end-systole}}{\text{Counts in end-diastole}} \times 100
\]

Counts in the end-diastolic frame of the background-corr-
corrected representative cardiac cycle averaged (± SE) 1,600 ±
405 and 3,100 ± 650 for the first and second studies, respec-
tively. Beat-to-beat calculation of LVEF was not performed,
because of the statistical unreliability of the low count rates
present in a single cardiac cycle.\(^a\)

Normalized left ventricular ejection rate (LVER) also was
determined from the representative cardiac cycle obtained
from the high frequency components of the first pass ra-
dionuclide angiocardiogram. Using a weighted least
squares analysis\(^b\) and a Hewlett-Packard Model #9830A
desk top computer (8K memory), a straight line was fitted to
the ejection phase data obtained at 0.05 sec intervals (4–8
data points per ejection phase). The slope of this line
(representing the change in counts with time), dC/dT, was
determined and normalized to the average counts (\(C_{ave}\)) over
the ejection phase. \(C_{ave}\) was used because of the greater
statistical reliability of the summed value prior to averaging

as compared to a single value (such as, end-diastolic counts).
The values of LVER (dC/dT/\(C_{ave}\)) were compared to
LVEF, left ventricular end-diastolic pressure (LVEDP), car-
diac index (CI), and stroke volume index (SVI) determined
at cardiac catheterization.

Regional wall motion also was evaluated from data
selected from the representative cardiac cycle. The end-
diastolic and end-systolic images were computer smoothed
by expanding the 294 matrix points by linear extrapolation
to 4,704 points. The margins of the smoothed end-diastolic
image of the left ventricle were visually identified, and a ring
formed around this image by the computer. This ring was
then superimposed by computer on the smoothed end-
systolic image, forming a composite image from which
regional wall motion could be evaluated (fig. 2). For com-
parison with contrast angiograms, the left ventricle was
divided into five segments: inferior, anterolateral, apical,
septal, and posterolateral. Studies done in the anterior posi-
tion were used to evaluate wall motion in the inferior,
anterolateral, and apical regions. Studies done in the LAO
position were used to evaluate posterolateral, septal, and in-
ferior wall motion. Each segment was judged visually to be
either normal or abnormal (akinetic or hypokinetic). The
radionuclide studies were evaluated independently by two of
the investigators and the results then compared to the in-
dependently evaluated contrast studies.

**Intervention Studies**

Sequential intervention studies were all performed in the
anterior position. In each instance, a control first pass radio-
nuclide angiocardiogram was obtained 15 minutes prior to
the intervention. Isoproterenol infusion (1–4 \(\mu\)g/min) then
was initiated under constant heart rate and blood pressure
monitoring, and was continued until a heart rate response of
at least 50% greater than control was obtained. At the time
of appropriate heart rate response, the second radionuclide

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Time activity curve (TAC) and represen-
tative cycle used to calculate ejection fraction (EF) in
a normal patient. The actual TAC is shown in the up-
per panel, the summed representative cycle and EF
calculation in the lower panel. The arrow in the TAC
indicates the region of background selection. Each
high frequency oscillation in the TAC corresponds to
a single cardiac cycle. The counts for each summed
0.05 second frame of the representative cycle (the
equivalent of a volume curve) are shown along with
the EF calculation. On this study end-diastolic counts
were 3900, end-systolic counts 1413, and calculated
EF 64%.
angiogram was obtained. No untoward effects were encountered during or following infusion.

The independent effect of heart rate alone on LVEF and LVER was evaluated in the two patients undergoing diagnostic atrial pacing studies. At the termination of the clinical electrophysiologic study, the patients were moved to the adjacent nuclear imaging laboratory and a control radionuclide study was obtained. Atrial pacing then was performed with a triaxial USCI pacing catheter positioned high in the right atrium. Paced heart rate increases of 69% and 78% of control were obtained in the two patients (comparable paced heart rates had been achieved during the immediately preceding clinical electrophysiologic studies). Pacing at the desired heart rate was maintained for 5 minutes. During the final minute, a repeat radionuclide angiogram was performed. Neither patient experienced chest pain or developed ECG changes.

Sources of Error

Potential sources of error in measuring LVEF were evaluated in 16 studies in eight patients (four with normal and 4 with abnormal left ventricular function). Errors associated with background estimation were evaluated by varying the point of selection of the background frames from the left ventricular TAC. Background frames were chosen earlier in the left ventricular TAC at a time when the bolus was only in the lungs and amount of background subtracted was presumably underestimated. Studies then were repeated selecting as background frames points at a later time in the TAC when the bolus was in the lungs, left atrium and left ventricle and the amount of background subtracted was presumably overestimated. LVEF obtained with each background was compared to that obtained with "optimal" background.

Errors associated with inadequately zoning the left ventricle were studied by over and under zoning the left ventricular region of interest. Standardization of the over and under estimated regions of interest was achieved by using the color television console and arbitrarily zoning to 64% (underestimated) and 40% (overestimated) of the maximum counts in each image. The overestimated left ventricular region of interest did not include left atrium or aorta. The underestimated left ventricular region of interest was placed in the center of the left ventricular cavity. The corresponding representative cardiac cycle of the over and underestimated regions of interest was obtained and the ejection fraction determined from these representative cycles was compared to the ejection fraction obtained from the representative cycles corresponding to the optimal zone.

Intra-observer variation in LVEF calculation (analysis separated by a two-month interval) was studied in eight patients in both anterior and LAO studies (16 studies). Inter-observer variation was studied by two observers in four patients in both positions (eight studies).

Contrast Angiography

Contrast angiograms were evaluated by a single observer independent of the results of the nuclide studies. Single plane left ventricular cineangiography following injection of 45–60 cc of contrast was carried out in the 30° right anterior oblique projection in all patients. Angiographic LVEF was determined for each patient using a modification of the arealength method of Dodge et al.11, 12 A 45° LAO left ventriculogram was performed 10–15 minutes following the first ventriculogram, allowing "biplane" evaluation of regional wall motion. Regional wall motion was evaluated qualitatively, in terms of the presence of akinesis or moderate to severe hypokinesis, from superimposed outlines of cavitory silhouettes drawn at end-diastole and end-systole, ascertaining that diaphragmatic or chest wall movement had not occurred between systole and diastole.18 Specific segments were determined as with the radionuclide studies. Only those ventriculograms free of ectopy were considered technically satisfactory.

Data were expressed as the mean ± standard error (SE). Linear regression equations and correlation coefficients were obtained in a standard manner. Group comparisons were made by Student’s t-test, while comparisons of two studies in individual patients were made by a paired t-test.

Results

Ejection Fraction

Of the 22 catheterization patients comprising this study, 15 had radionuclide angiograms in two views, four in the LAO position only, and three in the anterior position only.
LVEF determined by the radionuclide technique ranged from 23–80% (mean 53.8 ± 3.5%). Individual results are detailed in table 1. Radionuclide LVEF in either the anterior or LAO position correlated well with LVEF determined in-

dependently from contrast ventriculography (r = 0.92 and r = 0.97, respectively). In the 22 patients, LVEF determined from the average value for the 15 patients with two studies and the individual value for the seven patients with single studies also correlated well with contrast angiographic ejection fraction (r = 0.95) (fig. 3). A greater than 10% disagreement between radionuclide and contrast LVEF was noted in only three studies (E.D.: anterior radionuclide – 73%, contrast – 63%; A.C.: anterior radionuclide – 23%, contrast – 42%; and A.K.: anterior radionuclide – 74%, contrast – 64%). Despite disagreement in these three patients, radionuclide LVEF still accurately categorized the patients as being either normal or abnormal.

Effect of Position and Temporal Sequence of Studies

LVEF obtained in anterior and LAO positions correlated well (r = 0.97). However, the mean LVEF in the anterior position (55.1 ± 5.1%) was slightly higher than in the LAO position (52.2 ± 4.2%, P < 0.05). This difference probably is related to the different efficiencies in detecting scattered overlying radiation in the lungs and left atrium in the two positions. Although statistically significant, the actual difference between LVEF in either position is quite small, and data obtained in either position proved reliable when correlated with contrast angiographic LVEF. When the sequential studies were compared in terms of the relationship of the first and second studies, irrespective of position, an excellent correlation was obtained again (r = 0.95). The mean LVEF of the first and second studies were not significantly different (54.6 ± 5.0% and 52.0 ± 4.4%, respectively).

![Figure 3](image-url)  
**FIGURE 3.** Correlation between LVEF from either the average of two EF determinations from a two position radionuclide study (or single value, when only one study was performed) and LVEF determined by contrast angiography.

![Figure 4](image-url)  
**FIGURE 4.** Result of varying the site of background determination in patients with both normal and abnormal LVEF, in both anterior (ANT) and left anterior oblique (LAO) positions. Oversubtracting background was produced by choosing background frames later in the LV TAC, undersubtracting background was achieved by selecting background frames earlier in the LV TAC. Statistically significant results were noted in each of the four situations depicted.

![Figure 5](image-url)  
**FIGURE 5.** The effect of varying the LV region of interest upon measured LVEF in normal and abnormal subjects in both the anterior and LAO positions. The method of varying the region of interest is discussed in the text. No overall significant changes were noted.
Potential Sources of Error

As can be seen from figure 4, varying the point of background selection either earlier or later in the TAC introduced a significant error in calculated LVEF in the anterior and the LAO positions. On the other hand, over and underestimating the left ventricular region of interest introduced no consistent error (fig. 5).

Intra-observer and Inter-observer Variation

Sixteen studies in eight patients were analyzed for intra-observer variation. There was no significant difference between the original and the second analysis (mean first study 50.3 ± 5.8%; mean second study 49.6 ± 6.1%). The difference between original and second analysis ranged from 2-7%. Inter-observer variation, studied in eight studies from four patients, showed no significant difference between analyses (mean first study 58.6 ± 6.8%; mean second analysis 57.8 ± 6.7%). The difference between analyses by the two observers ranged from 2-9%.

Normalized Left Ventricular Ejection Rate

LVER was satisfactorily measured in all patients in whom radionuclide angiographic data were technically adequate for measurement of LVEF. In the basal state, LVER averaged 2.41 ± 0.26 sec⁻¹ and ranged from 0.62 to 4.44 sec⁻¹. Measurements obtained in the anterior position correlated well with those obtained in the LAO position (r = 0.96). As with LVEF, there was a small but statistically significant difference between anterior and LAO studies (anterior LVER 2.48 ± 0.34 sec⁻¹; LAO LVER 2.20 ± 0.26 sec⁻¹, P < 0.05). Comparison of measurements obtained from the first and second studies, irrespective of position, also correlated well (r = 0.93). In this instance, there was no significant difference between mean values (LVER first study 2.44 ± 0.34 sec⁻¹; LVER second study 2.24 ± 0.24 sec⁻¹).

LVER (defined as either the single value obtained from an individual study or the average value obtained from two sequential studies) correlated well with LVEF measured from contrast angiography (r = 0.90) (fig. 6). LVER also allowed complete separation of normal (LVEF ≥ 55%) and abnormal patients (normal LVER 3.4 ± 0.17 sec⁻¹; abnormal LVER 1.20 ± 0.11 sec⁻¹, P < 0.001) (fig. 7). LVER did not correlate with LVEDP (r = 0.37), CI (r = 0.04), or SVI (r = 0.03).

LVER also was calculated from representative cardiac cycles in which background was not subtracted to assess the feasibility of functionally categorizing patients utilizing a background independent parameter of left ventricular function. In noncorrected measurements, LVER averaged 1.16 ± 0.12 sec⁻¹ and ranged from 0.30 to 2.33 sec⁻¹. Noncorrected LVER correlated well with background corrected LVER (r = 0.90) and with contrast angiographic LVEF (r = 0.88). Of equal importance, the nonbackground-corrected measurement allowed complete separation of patients with normal and abnormal left ventricular function (fig. 8).

In the five clinically normal volunteers, isoproterenol infu-
Regional Wall Motion

Eleven patients were identified as having normal regional wall motion by both the contrast and radionuclide techniques. Ten of the 11 patients with abnormal regional wall motion by contrast angiograms were identified as abnormal by the radionuclide study. The one patient (R.L.) incorrectly identified by the radionuclide technique had a cardiomyopathy and LVEF of 46 and 52% by contrast and radionuclide angiograms, respectively. Thus, radionuclide regional wall motion analysis in this series yielded no false-positive and one false-negative study. The ability of the radionuclide technique to localize the site of regional wall motion abnormality accurately was evaluated in the 10 patients identified as having abnormal regional wall motion. Of these 10 patients, eight had radionuclide angiograms in two views and two had radionuclide studies in the anterior view only, allowing comparative assessment of 46 left ventricular segments by both contrast and radionuclide techniques. Of the 46 segments, 35 were identified as having abnormal wall motion by contrast angiography. Radionuclide angiography correctly identified 31 of these 35 abnormal segments (89%) (table 2).

Discussion

The results of this study indicate left ventricular ejection fraction, normalized ejection rate and regional wall motion can be readily determined from first pass quantitative radionuclide angiograms in patients with sinus rhythm. The radionuclide data correlate well with those obtained by contrast angiography. In addition, the feasibility of doing two sequential studies and the utility of obtaining data in either the anterior or LAO position have been established. These studies carry virtually no risk and take little time to perform and process.

Regional Wall Motion

This report represents an initial attempt of evaluating regional wall motion from the first pass radionuclide angiogram. Regional wall motion has also been assessed with first pass techniques by Kirch et al. in a preliminary
report utilizing a computerized image-intensifier radionuclide imaging system. The ability to evaluate regional wall motion depends upon the formation of high count-rate end-diastolic and end-systolic images such that counting statistics are sufficient to ensure the resolution necessary to define left ventricular margins clearly. Several aspects of this study require comment. First, all studies were performed using a multicrystal scintillation camera, which provides a higher count-rate capacity than that currently available with conventional single crystal cameras. Second, regional wall motion was evaluated from the end-diastolic and end-systolic images obtained from the representative cardiac cycle, formed by summing together counts over several cardiac cycles, rather than utilizing data from only a single heart beat. Third, a computer smoothing linear extrapolation process was used allowing faster interpretation of the first pass data.

Ejection Fraction

The technique of evaluating LVEF in this study differs somewhat from those described in previous reports. First, a scintillation camera with a multicrystal mosaic detector was used instead of a conventional single crystal camera. This imaging instrument has a shorter dead time (minimum interval between recorded scintillations) than that obtainable with current commercially available Anger scintillation cameras. This short dead time allows accumulation of higher count rates, thereby decreasing the statistical uncertainty of the calculated LVEF. In the previous study of Schelbert et al., the problem of relatively low count rate acquisition necessitated the application of a root mean square analysis, following approximation of the raw data to a sinusoidal function. With this statistical approach, first pass radionuclide ejection fraction correlated well with that measured by contrast ventriculography.

A second major difference in this study is the use of a new method of estimating left ventricular background. Previous reports have used, with minor modifications, the method first proposed by Van Dyke et al. involving an anatomically selected background zone surrounding the left ventricular region of interest. In our study, background was determined directly from the left ventricular TAC generated from the left ventricular region of interest (fig. 1). In using this background subtraction, two assumptions are made. The first is that overall background stays relatively constant (compared to the change in left ventricular counts between systole and diastole) during the peak of the left ventricular phase used for calculation of LVEF. The background curves obtained using the method of Van Dyke et al. and curves obtained by probe studies do, in fact, appear to remain relatively constant during this time.

The second assumption is that there is a fixed and reproducible relationship between the amount of background prior to the left ventricular phase of the left ventricular TAC and the amount of background at the peak of the left ventricular phase. Although this assumption is difficult to prove firmly, the following argument may be invoked. At any point in time, the amount of background in the left ventricular TAC depends upon the amount of activity in the surrounding and overlying structures (lungs, left atrium, aorta) and the geometric relationship of the structures to the left ventricle and scintillation detector. The geometric relationship of lungs, left atrium, and aorta re-

![Figure 10. Comparison of results in the five patients receiving isoproterenol (I) (stippled columns), and two patients undergoing atrial pacing studies (P) (cross-hatched columns). The control data for each group (C) are shown in adjacent clear columns. Heart rate (HR) is shown in the left column, ejection fraction (EF) in the middle column, and ejection rate (ER) in the right column. Note the major difference in ER measured during isoproterenol and pacing.](http://circ.ahajournals.org/)

Table 2. Analysis of Wall Motion in Contrast and Radionuclide Techniques in 10 Patients with Abnormal Performance Detected by Both Methods

<table>
<thead>
<tr>
<th>Patient</th>
<th>Ant-Lat</th>
<th>Septal</th>
<th>Post-Lat</th>
<th>Inferior</th>
<th>Apical</th>
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<tr>
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<td>N</td>
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<tr>
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</tr>
</tbody>
</table>

Abbreviations: Ant-Lat = anterolateral; Post-Lat = posterolateral; RA = radionuclide angiocardiogram; CA = contrast angiogram; A = abnormal; N = normal.
main fixed for all studies done in the same position.

In order for a fixed and reproducible relationship to exist between the amount of activity present in the lungs, left atrium, and aorta prior to and at the peak of the left ventricular phase of the left ventricular TAC, the shape of the TAC of each of these surrounding structures must have a fixed and reproducible relationship to the shape of the left ventricular TAC. Assuming the central circulation to be a sequential series of mixing chambers, the shape of the TAC for each chamber depends upon the flow-volume characteristics of that chamber. If flow is constant throughout, the relative shape of each chamber's TAC will be determined by its relative volume. Therefore, in normals or in patients in whom all chambers are proportionally enlarged, or in patients in whom an isolated chamber is enlarged prior to the left ventricle, a relatively fixed and reproducible relationship will exist between the TACs of the left ventricle and the surrounding structures. However, theoretically, in those patients in whom there is an isolated enlargement of the left ventricle (or aorta), this same fixed relationship should no longer be present, but rather be replaced by a different fixed relationship based upon the TAC of the individually abnormal left ventricle.

Our results appear to support the assumptions inherent in our method of background subtraction. First, an excellent correlation was noted with LVEF determined from contrast angiograms in patients with both normal and abnormal ventricular performance. Therefore, the theoretic objection stated above would appear to have minimal practical implication in evaluating patients with abnormal left ventricular performance. Second, varying the point of selection of background frames to before or after the beginning of the left ventricular phase consistently led to under or overestimation of background, respectively.

No consistent error in LVEF calculations was introduced by either under or overestimating the region of interest. However, in individual patients, variations of up to 10% were obtained. These results differ from those reported by Schelbert et al. Their results suggested that over and underestimating the left ventricular region of interest produced consistent errors in the calculated LVEF. Part of the reason for this disagreement might be that different anatomic criteria were used for over and underestimation of the region of interest.

### Normalized Left Ventricular Ejection Rate

LVEF remains a clinically valuable index of pump performance. However, its dependence on afterload and preload, as well as its relative insensitivity to subtle changes in inotropic state, are known. For these reasons, additional systolic ejection indices of left ventricular function, derived either from echocardiography or contrast angiography, have been proposed.

This report demonstrates the feasibility of measuring LVER, an ejection phase index, using radionuclide techniques and indicates that this measurement may be a clinically useful index of left ventricular function. Our correlation data on radionuclide LVER are in substantial agreement with a previous report in which peak systolic ejection rate (dV/dt/V) was determined from contrast left ventriculography.

In the present study the sensitivity of radionuclide LVER to changes in inotropy induced by isoproterenol infusion was demonstrated. This change occurred in the presence of a slight increase in blood pressure, indicating detection of a significant inotropic effect overriding any independent effects of afterload. These results illustrate the potential utility of evaluating ventricular reserve by studying ventricular performance in more than one physiologic state.

Absolute values for LVER (dC/dt/Cave) are dependent upon background. However, in comparing values between patients, if the degree of background contribution from patient to patient varied much less than the rate of ejection, then this parameter would be relatively background independent. The results of this study indicate that LVER is relatively independent of background, in that nonbackground-corrected and background-corrected values for LVER provided the same clear separation between patients with normal and abnormal left ventricular function.

We recognize that our current method of quantitatively evaluating the representative cycle to derive LVER represents an initial approximation. Clearly, fitting the ejection phase to a straight line based on a series of 4-8 data points does not recover all the potential information available. Since ejection is more rapid in early systole than in end systole, meaningful data almost certainly are lost within this averaging process. A more detailed analysis requires data collection capabilities at intervals faster than our current rate of 20 per second (0.05 second intervals). Framing rates providing 0.01 to 0.025 second intervals are needed. A higher count rate capability will be necessary if we are to frame more rapidly and not sacrifice statistical reliability. Such instrumental advances can be realistically expected in the near future.

The use of radionuclide techniques for evaluation of ejection phase performance indices has recently been attempted by others. Steele et al. measured velocity of circumferential fiber shortening and systolic ejection rate from first pass radionuclide angiograms obtained following injection of the radionuclide bolus through a wedge balloon-tip pulmonary artery catheter. These investigators found that values for these indices determined from the radionuclide angiograms correlated well with those obtained from left ventricular cineangiography. In addition, both ejection phase indices correlated well with radionuclide LVEF. Another approach to the determination of ejection phase indices from gated cardiac blood pool has been reported in preliminary form by Green et al.

Because of current count-rate limitations and the resulting statistical uncertainties of making measurements from a single cardiac cycle, data from 3–6 cardiac cycles are summed together. This clearly is many cycles fewer than needed for assessing performance from cardiac blood pool imaging. However, this summing process alters the utility of measurements in patients with frequent ectopic beats, atrial fibrillation, or any other irregular cardiac rhythm.

To conclude, this study demonstrates that the first pass radionuclide angiogram provides information, not only concerning LVEF, but also LVER and regional wall motion. These measurements are simple to obtain, reproducible, and can be repeated. These studies carry virtually no risk and take a brief time to perform and process.
From a logistic standpoint, this may allow optimal evaluation of regional and global left ventricular performance in the acutely ill patient. They may furnish insight not only into the basal status of the left ventricular myocardium, but also into the extent of ventricular reserve evaluated under conditions of stress or stimulation.

Acknowledgment

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References

11. Yang SS, Bentivoglio LG, Maranho V: Cardiac Catheterization Data to Hemodynamic Parameters. Philadelphia, Davis, 1972, p 64
Assessment of cardiac performance with quantitative radionuclide angiocardiography: sequential left ventricular ejection fraction, normalized left ventricular ejection rate, and regional wall motion.