Analysis of Left Ventricular Function from Multiple Gated Acquisition Cardiac Blood Pool Imaging

Comparison to Contrast Angiography

ROBERT D. BUROW, B.S., H. WILLIAM STRAUSS, M.D., ROSS SINGLETON, PH.D.,
MALCOLM POND, M.D., TERRY REHN, M.D., IAN K. BAILEY, M.D., L. C. GRIFFITH, M.D.,
EDWARD NICKOLOFF, PH.D., AND BERTRAM PITT, M.D.

SUMMARY Global ventricular function was evaluated by both multiple gated cardiac blood pool scans (MUGA) and contrast ventriculograms in a group of 17 patients with suspected coronary artery disease. The contrast ventriculograms were analyzed frame by frame to generate a volume versus time curve for each patient, while the tracer data were analyzed by two methods: 1) the standard method, in which the left ventricle is identified on the end-diastolic frame and the background corrected activity under the region of interest obtained from the entire cardiac cycle, and displayed as a time versus activity curve; and 2) by a semi-automatic method in which the computer applies a threshold detection program to define the ventricular borders, and activity in the chamber at each point in the cardiac cycle is defined after background correction. The tracer data in each patient were analyzed independently by four observers. The tracer data correlated with the contrast data on a point by point basis \( r = 0.87 \) for the standard method, and 0.93 for the semi-automatic technique. An F test of variance revealed the semi-automatic method superior to the standard approach \( (P < 0.05) \).

GATED BLOOD POOL SCANS have been used to evaluate left ventricular function\(^1\,\,^2\) in patients with myocardial infarction,\(^3\) suspected left ventricular aneurysm\(^4\) and recurrent arrhythmias.\(^5\) The evaluation of regional wall motion and ejection fraction was performed from an analysis of the end-systolic and end-diastolic images using the area length formulae and comparing outlines of the left ventricle traced from the images. Recent advances in computer techniques allow up to 56 images to be recorded in each cardiac cycle,\(^6\,\,^7\) and after several minutes of data collection, the information is shown as an endless-loop movie similar to a contrast biventricular cineangiogram.

The purpose of the present report is to present a new semi-automated technique for noninvasively determining left ventricular ejection fraction and ejection rate from the multiple gated cardiac blood pool images and to correlate them with ventricular volume curves obtained from standard contrast left ventricular angiography.

Methods

Seventeen consecutive patients, 12 male and five female with a mean age of 48 years, in whom both left ventricular contrast cineangiography and multiple gated acquisition (MUGA) radioisotope angiography were performed, were evaluated. All 17 patients were evaluated for suspected coronary artery disease, 11 had angina pectoris, and 10 a previous myocardial infarction. Patient selection was based solely on the availability of both contrast left ventricular angiography and multiple gated acquisition blood pool imaging in both the left anterior oblique and right anterior oblique or anterior projections. All patients were in normal sinus rhythm at the time of study.

Multiple Gated Cardiac Blood Pool Imaging

Following intravenous administration of 20 mCi of Technetium-99m labeled human serum albumin, multiple gated acquisition studies were performed for a total collection time of 12–16 minutes per view (200,000 counts/frame over the heart) using a high resolution, 37 per minute tube scintillation camera equipped with high resolution parallel hole collimator. The pulse height analyzer was centered at 140 keV with a 20% window. For these studies, the cardiac cycle was divided into 28 equal segments. During the acquisition period, an average of 500,000 events were collected in the entire field of view in each 1/28th of the cardiac cycle (14 million counts during the total collection interval). A commercially available nuclear medicine minicomputer system was programmed to place data sequentially into each of the 28 data matrices. At the start of acquisition, the patient's heart rate was divided by 28 and all images were obtained with a pre-set framing time appropriate for that heart rate. For example, in a patient with a heart rate of 72 beats/min, each point in the cardiac cycle represented 30 msec. To conserve space in the core of the computer and maintain spatial resolution, only the central portion of the scintillation camera field (an area 15 × 15 cm) was digitized with a picture element resolution of better than 4 mm × 4 mm. At the start of the examination, data were recorded in the first frame for the pre-set time; data then were entered into the second frame for the same interval; thereafter, into the third frame, etc. until a full complement of 28 frames was recorded or another R wave occurred (fig. 1). At the next R wave, the computer was reset to frame 1 and the process repeated. Data from all subsequent cardiac cycles were added to those from the first. Acquisition was complete when at least 200,000 counts were collected over the region of the heart in each of the acquisition frames. After acquisition, the data were presented as a high resolution endless-loop movie for viewing and analysis.

Data were recorded from each patient in both the anterior and left anterior oblique positions.

All patients were in sinus rhythm at the time of study. The MUGA program has no provision for filtering arrhythmic beats, but the physiological synchronizer will filter out all beats that are not within a 20% average of the three preceding beats. Thus, premature ventricular contractions were not recorded. However, changes in R-R interval caused by sinus
arrhythmias were not excluded, and do cause some artifacts at the end of the recording.

Contrast Angiography

Within two weeks of the tracer studies, each patient underwent cardiac catheterization, left ventriculography and selected coronary arteriography by the Judkins technique. Right and left anterior oblique contrast ventriculograms were recorded sequentially at 60 frames/sec on 35 mm cine film.

Balloon Model

In addition to the patient studies, both multiple gated acquisition recordings and contrast angiography were performed on a balloon model. The balloon was attached to a graduated cylinder via a tube. The graduated cylinder was, in turn, connected to a pump respirator. The graduated cylinder and balloon contained technetium-99m activity and simulated the appearance of the left ventricle. The pump respirator had a cam microswitch, which produced a pulse resembling an R wave to trigger the computer in synchrony with the pump cycle. The balloon was immersed in a water bath containing activity sufficient to produce about one-third the counts per unit area of that in the balloon. The water bath then served as both a scattering medium and a background. Multiple gated acquisition studies were performed with the balloon for 200,000 counts in each image as was performed for the patient studies. Contrast angiography was performed by the addition of contrast material to the graduated cylinder and mixing it thoroughly with the contents of the balloon over several minutes. The beating balloon was then radiographed at 60 frames/sec for a period of 30 sec.

Data Analysis

MUGA

The left anterior oblique projection was chosen for analysis of left ventricular ejection fraction because: 1) the right and left ventricles are best separated in this projection (fig. 2); and 2) the activity in the left ventricle should be linearly related to ventricular volume. The frame recorded following the R wave of the electrocardiogram was defined as the end-diastolic frame and time activity curves were obtained using two approaches to identify the left ventricle and two approaches to define background.

A. Standard Technique.6,7 A region of interest was identified over the left ventricle using the light pen system of the computer. Counts within this area were determined for each of the 28 frames and expressed as average counts per cell. Background activity was determined by identifying the end-systolic frame (that with minimum counts in the ventricle) and drawing a region of interest around the inferior and lateral borders of the ventricle with the light pen system. The average activity in background was then subtracted from each of the 28 points of the time activity curve and the resultant curve plotted against time. Left ventricular ejection fraction (LVEF) was determined by the formula:

![Diagram of how frames are assigned during the cardiac cycle. The R wave acts as a triggering signal and initiates the recording of data in the first frame in the computer memory for a preset time. Data then are recorded in the second frame for the same preset time, etc., until the next R wave occurs and data from that cycle are added to those from the initial cycle. The process is repeated until a sufficient number of counts are recorded.](image1)

![Selected frames from a MUGA study performed in the LAO position: left) in a patient with diminished left ventricular function; right) in a patient with normal left ventricular function.](image2)
LVEF = \frac{\text{maximum counts} - \text{minimum counts}}{\text{maximum counts}}

Four observers evaluated the data independently in each of the 17 patients to define interobserver variation.

B. Semi-automatic Method. Before identifying the left ventricular area of interest, the data were processed to eliminate background activity. A rectangular area posterior to the left ventricle and separate from the great vessels and hepatic area was identified. The counts within this rectangular area were then determined in each of the 28 frames and the resultant activity vs time curve displayed on the computer oscilloscope. If the curve was flat over the 28 frames, this area was accepted as background. If the activity curve had more than a 5% variation, another area was chosen since this suggested that great vessel activity was included within the background region. The average number of counts per image cell within the background area was then calculated and subtracted from each matrix element in every image cell of the 28 frames to obtain the background subtracted image.

The computer program to automatically identify the edge of the left ventricle searched within a predefined region of the image. This region was defined in the background subtracted image by placing a rectangle outside the borders of the left ventricle on the end-diastolic frame. The peak activity within the rectangle was determined. Each horizontal and vertical row of image elements within this region was then examined sequentially beginning at the zone of peak activity and extending to the periphery until the percent of peak activity selected to define the edge was reached. Usually, a starting value of 70% for search in the medial direction and 50% for search in the posterior direction were selected.* The computer then displayed the edge as a series of brightened dots around the perimeter of the ventricle. If this border was unsatisfactory, the operator could then adjust the percentage selected and repeat the process until the intensified picture elements were aligned with the edge of the ventricle. Once this value was accepted, it was then applied automatically to each of the subsequent frames. The edge defined in this manner was superimposed on the left ventricular silhouette in each of the 28 frames and viewed in a movie format to verify the correctness of the threshold values. The viewer then observed the real time display of the outlined beating heart on the screen to determine if the computer selected borders corresponded to the edges of the ventricle selected visually. The number of counts in the left ventricular area defined by the edge program was then determined in each of the 28 frames and a time activity curve plotted. Left ventricular ejection fraction was determined by the same formula as the standard technique. These images were also analyzed by four observers independently to determine the reproducibility of the technique.

Left Ventricular Contrast Angiography

A representative beat was selected from the left anterior oblique and right anterior oblique cineangiograms. Beats preceded or followed by premature ventricular contractions were avoided. Starting from the frame with the largest left ventricular area, the area of the left ventricle in both the left anterior oblique and right anterior oblique projections was outlined in every other frame. Each of the frames was then traced individually on a Hewlett-Packard digitizer and the left ventricular volume curve determined using the area/length formula for single and biplane images. Left ventricular ejection fraction was calculated first from the single plane left anterior oblique images alone and from the sequential biplane images by the formula:

\[
\text{LVEF} = \frac{\text{end-diastolic volume} - \text{end-systolic volume}}{\text{end-diastolic volume}}
\]

Comparison of Left Ventricular Time Activity Curves and Left Ventricular Volume Curves from Contrast Angiography

Left ventricular time activity curves obtained from the semi-automatic method and the volume curves from both biplane and LAO contrast angiograms were normalized such that maximum counts in the frame immediately following the R wave and maximum volume were set equal to 100%. All other points on the time activity curves and angiographic volume curves were expressed as a percentage of the end-diastolic frame. A point by point correlation was then made between the left ventricular time activity curve and the left ventricular volume curves. The points selected for comparison on the left ventricular time activity curve were time adjusted to the left ventricular volume curve by a linear interpolation technique so that the points on the time activity curve were calculated at the same time as those on the left ventricular volume curve in relationship to the cardiac cycle. A point by point comparison of each patient's time activity curve and left ventricular volume curve as determined by the semi-automatic method was compared to left ventricular volume curve from end-diastole to five frames after end-systole. The terminal points on the left ventricular time activity curve were not correlated with left ventricular contrast angiographic volume curves because sinus arrhythmia

| Table 1. Comparison of Tracer and Contrast Angiographic Values of Ejection Fraction in 17 Patients |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Tracer                          | Standard method*                | Semi-auto*                      | Biplane                         | LAO cine                        |
| 1                               | 67                              | 72                              | 81                              | 72                              |
| 2                               | 54                              | 42                              | 54                              | 45                              |
| 3                               | 74                              | 61                              | 71                              | 61                              |
| 4                               | 37                              | 44                              | 48                              | 48                              |
| 5                               | 51                              | 50                              | 54                              | 54                              |
| 6                               | 76                              | 74                              | 81                              | 80                              |
| 7                               | 23                              | 34                              | 36                              | 40                              |
| 8                               | 72                              | 50                              | 52                              | 58                              |
| 9                               | 54                              | 53                              | 55                              | 50                              |
| 10                              | 63                              | 62                              | 59                              | 61                              |
| 11                              | 41                              | 40                              | 54                              | 45                              |
| 12                              | 60                              | 65                              | 65                              | 64                              |
| 13                              | 46                              | 55                              | 59                              | 48                              |
| 14                              | 71                              | 68                              | 75                              | 60                              |
| 15                              | 29                              | 35                              | 44                              | 32                              |
| 16                              | 62                              | 50                              | 42                              | 53                              |
| 17                              | 68                              | 66                              | 72                              | 78                              |

\*The values of 50% and 70% were selected because they commonly corresponded to the borders of the left ventricle determined visually. In those patients who had a high lung background, the posterior border value had to be increased.

\*Mean of four observers.
leads to fluctuation in cycle to cycle length during the 12-20 minute acquisition period and, therefore, distortion of its terminal portion.

**Results**

The mean left ventricular ejection fraction determined by the single left anterior oblique was 55.8 ± 13.0 (SD) while that for biplane cineangiography was 60 ± 13.9, and the values with the scintiphotographic methods were 55.7 ± 16 with the standard method and 55.2 ± 13 with the semi-automatic technique. These values were not significantly different from each other. The values on each patient are summarized in table 1.

To test the reproducibility of the calculation of ejection fraction with the tracer technique, four experienced observers defined the ventricle using both the standard technique and semi-automatic methods (on two separate occasions) to determine both ejection fraction and ejection rate. The individual values obtained for ejection fraction for each patient by each observer are listed in table 2. An F test of variance was performed to evaluate the reproducibility of the semi-automatic method and that of the standard method compared to biplane contrast angiography on the 15 patients who had both studies. The semi-automatic method was more reproducible than the standard method (P < 0.05). When a similar comparison was made for the 15 patients to the LAO ventriculogram only, the F test results were unchanged.

A point by point comparison of the left ventricular ejection phase of the cardiac cycle was performed using the average result of the four observers with both the standard method and the semi-automatic method compared to that obtained from biplane contrast angiography. The correlation coefficient was 0.87 with the standard method while it was 0.93 with the semi-automatic technique. A point by point comparison of the left ventricular volume curve and the tracer time activity curve in one patient is shown in figure 3. The balloon model had a true ejection fraction of 48% (measured from the changes in fluid volume in the graduated cylinder), while that measured from the MUGA automatic edge method was 47% and that measured from single plane angiography was 44%. The point by point correlation of the volume curve from the balloon determined by the contrast and tracer methods was 0.96.

**Discussion**

Left ventricular ejection fraction and time activity curves determined from the region of the left ventricle by the multiple gated acquisition (MUGA) technique described in this study correlate with standard left ventricular contrast angiography. The technique is rapid, reproducible and free of assumptions as to ventricular shape. To measure ejection fraction precisely with these techniques requires both careful selection of background and identification of the left ventricle.

The method of background selection and correction previously proposed to obtain left ventricular ejection fraction and time activity curves depended upon the operator drawing a horseshoe or crescent around the end-systolic left ventricular cavity in the left anterior oblique projection. With the horseshoe technique, a small change in the distance of the background area from the ventricular cavity may result in a relatively large change in calculated background activity and hence left ventricular ejection fraction. The exact position of the horseshoe is subject to variation from one observer to another. In the semi-automatic technique, a remote area of lung was chosen as background with care being taken to avoid the region of the great vessels. This background area was determined by several observers with minimal training and its accuracy checked by the finding of

![Figure 3](http://circ.ahajournals.org/Downloaded from)

**Figure 3.** Activity vs time curve and volume vs time curve plotted on the same axes.
a linear time activity curve from this area. Background activity is then subtracted from each matrix point prior to determination of the left ventricular time activity curve. The activity adjacent to the left ventricular myocardium in this technique after background subtraction was approximately 1-2 counts/image cell. Because background is subtracted prior to definition of the left ventricular area of interest, any small errors in overestimating the area of the left ventricle will have a minimal effect upon the calculated left ventricular time activity curve and left ventricular ejection fraction.

In previous techniques, the area of interest in the left ventricle in the left anterior oblique projection was outlined with a light pen using the end-diastolic frame. The change in activity throughout the cardiac cycle was then recorded from this area. The use of fixed end-diastolic area to determine the time activity curve may in some patients, especially those with a relatively high left ventricular ejection fraction, result in an underestimation of left ventricular ejection fraction and distortion of the time activity curve, since the left atrium and on occasion the right ventricle may move into this region as the ventricle contracts. The left atrium fills out of phase with the left ventricle so that at end-systole the left atrium is maximally filled and could contribute counts to the calculated end-systolic volume thereby tending to overestimate end-systolic volume and underestimate left ventricular ejection fraction. While special positioning of the detector may minimize this possibility, it cannot be completely avoided in every patient, depending upon heart position. The semi-automatic technique defines activity in the left ventricle separately from each frame of the cardiac cycle. At end-systole counts are obtained only from the end-systolic area, thus minimizing contribution from the left atrium and right ventricle. The advantage of the semi-automatic technique over techniques in which only the end-diastolic area was outlined by light pen can be seen in the better correlation of left ventricular ejection fraction and reproducibility obtained from the preset technique (table 1 and 2). Even with the preset technique, however, some degree of left atrial contribution may be unavoidable in certain patients. The semi-automatic programs described in the present study tend to minimize observer bias and can be performed easily by technicians with minimal computer experience or knowledge of ventricular anatomy. They also should be applicable to the community hospital setting.

The techniques used in this study can be modified further according to clinical needs. In the present study, 200,000 counts were collected from the region of the heart using a high resolution collimator in order to obtain better definition of left ventricular borders. In situations where the time of imaging may be more important than high resolution, such as during exercise, lower count density images can be obtained and a high sensitivity rather than a high resolution collimator used.

With further experience and improvement in technique, it is not unreasonable to expect that the noninvasive radioactive tracer techniques for measuring ventricular function may in many instances supplant contrast left ventricular angiography and serve as a primary means of evaluating patients with suspected ventricular dysfunction.

References

Analysis of left ventricular function from multiple gated acquisition cardiac blood pool imaging. Comparison to contrast angiography.

R D Burow, H W Strauss, R Singleton, M Pond, T Rehn, I K Bailey, L C Griffith, E Nickoloff and B Pitt

_Circulation_. 1977;56:1024-1028
doi: 10.1161/01.CIR.56.6.1024
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/56/6/1024

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/