MEASUREMENT OF LEFT VENTRICULAR EJECTION FRACTION

R. H. Secker-Walker, L. Resnick, H. Kunz, J. A. Parker, R. L. Hill, and E. J. Potchen

The Edward Mallinckrodt Institute of Radiology and the Biomedical Computer Laboratory, Washington University School of Medicine, St. Louis, Missouri

Left ventricular ejection fraction has been determined in 16 patients using ^{99m}Tc-human serum albumin and a gamma scintillation camera and an electrocardiogram interfaced to a small digital computer. In ten patients, the results were compared with left ventricular angiography. There was a significant correlation between the results of the two methods, r = 0.87, but the radionuclide method tended to produce rather higher figures compared with the angiographic method. Mean inter- and intra-observer differences amounted to 4.2 and 5.2%, respectively. Identification of the plane of the mitral and aortic valves, while outlining the left ventricle, was the least satisfactory part of the procedure.

One indication of the efficiency with which the heart is functioning is the left ventricular ejection fraction. Until recently, measurement of this parameter of cardiac function required catheterization of the left ventricle. In the last few years a number of methods for examining cardiac function using radionuclides have been described (*1–5*). The encouraging results obtained by Strauss and his colleagues (*5,6*) in measuring left ventricular ejection fraction prompted us to devise a method using a scintillation camera and the patient's electrocardiograph interfaced to a small digital computer (*7*). This report describes our results and some of the problems encountered in a small series of patients and correlates the radionuclide method with results obtained from left ventricular angiography.

METHODS

The subjects examined by this technique were 3 healthy physicians and 13 patients. Ten of the patients had left ventricular angiography during the investigation of coronary artery disease or rheumatic heart disease. The method of data collection and analysis have been described previously (*7*). A Pho/Gamma III scintillation camera (Nuclear-Chicago Corp.) fitted with a 4,000 parallel-hole collimator is interfaced to a PDP-12 digital computer (*8*). The gamma camera is placed so that it views the heart from the left anterior oblique position but is tilted caudally as well in an attempt to separate the image of the left atrium from that of the left ventricle (*4*).

A standard Grass electrocardiogram difference amplifier is connected to the patient and its output fed into one of the PDP-12 analog-to-digital inputs (Fig. 1).

The passage of a bolus injection of 5–8 mCi of ^{99m}Tc-human serum albumin (^{99m}Tc-HSA), prepared by the electrolytic method of Benjamin, et al (*9*) is recorded at 0.4-sec intervals as it passes through the heart and is stored on magnetic tape (Fig. 2).

The subject's electrocardiogram (EKG) is then displayed continuously on the computer's oscillo-

Received Jan. 29, 1973; original accepted June 6, 1973.

For reprints contact: Roger H. Secker-Walker, Div. of Nuclear Medicine, Firmin Desloge Hospital, 1325 S. Grand Ave., St. Louis, Mo. 63104.

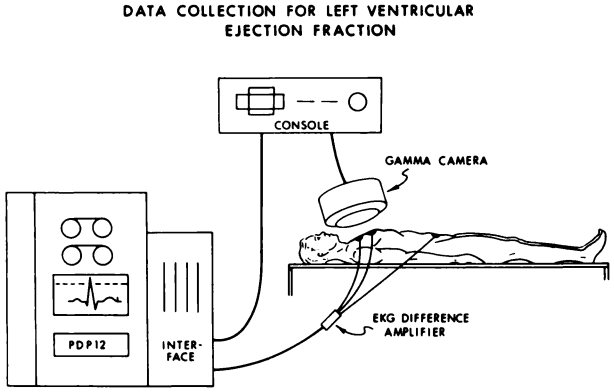

FIG. 1. Arrangement of apparatus used to collect data for left ventricular ejection fraction studies.

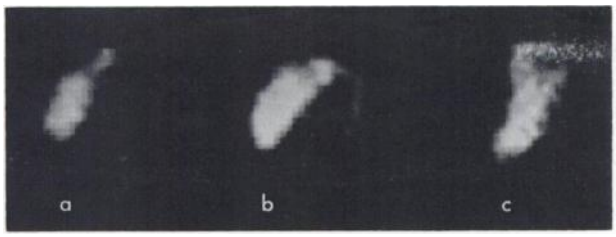

FIG. 2. Three frames from radionuclide angiocardiogram in modified LAO projection showing, from left to right, (A) superior vena cava and right atrium, (B) right atrium, right ventricle, pulmonary artery and some filling of left lung, (C) left ventricle and arch of aorta. Interventricular septum, cardiac apex and left border of heart are readily visualized.

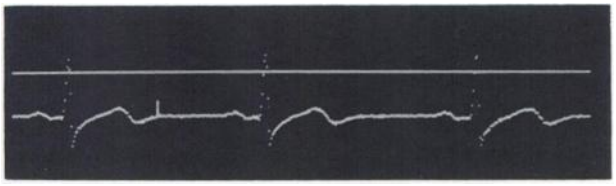

FIG. 3. Electrocardiograph as it appears on computer's oscilloscope, together with horizontal cursor defining R-wave, and vertical cursor at end of first T-wave.

scope and the R-wave and end of the T-wave defined by placing cursors in the appropriate positions (Fig. 3). The R-wave is defined by voltage alone and the time between the R-wave and the end of the T-wave is stored as a constant.

Images of end-diastole and end-systole gated from the EKG are collected for 45 msec during each cardiac cycle and are integrated over more than 300 contractions.

Cine radiographic technique. Left ventricular cineangiocardiography was performed in the appropriate degree of right anterior obliquity so that the long axis of the left ventricle was perpendicular to the central x-ray beam. Injections were performed with a previously described technique (*10*) using three consecutive diastolic EKG-triggered injection impulses for a total volume of 25–35 cc of Hypaque-M 75%. This was done in an effort to avoid the adverse effects of left ventricular injections on left ventricular function (*11,12*). Following the procedure, a 3-mm^2 cross-hatch grid was filmed in the previously determined position of the left ventricle with the same target to image tube distance as used during the injection. Cineangiocardiograms were exposed at 60 frames/sec with a frame marker and simultaneous recording of the injection impulse signal, time marker, and electrocardiogram.

DATA ANALYSIS

The integrated images of end-diastole and end-systole are corrected for the nonuniform response of the scintillation camera using an image of a disk source of ^{99m}Tc collected with the same collimator.

Selection of the region of the left ventricle is made from the radionuclide angiogram, the images of end-diastole and end-systole and the image of end-diastole–end-systole (Fig. 4).

The left ventricular ejection fraction (LVEF) is calculated from the equation

$$\text{LVEF} = \frac{\text{Counts in end-diastole} - \text{Counts in end-systole}}{\text{Counts in end-diastole} - \text{Background counts}}.$$

The background counts represent the activity in the tissues within the outlined end-diastolic image. This tissue-background activity is determined from the region within the end-diastolic image that contains no cardiac blood pool during end-systole. This region is identified in the end-diastolic–end-systolic image by finding those cells that have 50% or more of the maximum counts in the subtracted image (Fig. 5). The tissue background is then determined from the average counts per cell in these cells in the end-systolic image. This background is assumed to remain constant in any one cardiac cycle and so cancels out in the numerator of the equation presented earlier.

Left ventricular ejection fraction was calculated from the cineangiograms by measuring the area of a

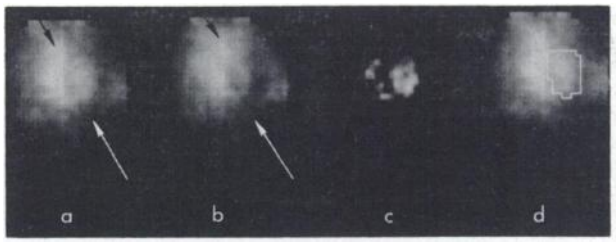

FIG. 4. Computer-generated images of: (A) end-diastole, (B) end-systole, (C) end-diastole–end-systole, (D) outlined region of left ventricular blood pool. Base of heart is indicated by black arrows and apex by white arrows. Change of left ventricular blood pool is quite easily seen between A and B and regions where blood is during diastole, but not systole, in C.

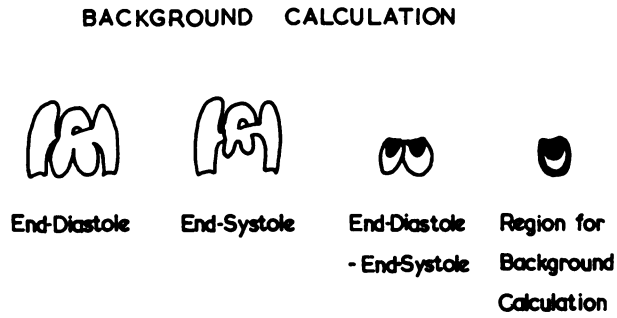

FIG. 5. Schematic diagram showing how small region within outlined left ventricular blood pool is identified within subtracted image, end-diastole–end-systole. Tissue-background activity is determined from average counts per cell in small crescent-shaped area.

tracing of the left ventricular blood pool with a planimeter and its long diameter in those images that correspond to end-diastole and end-systole in normal contractions. The volume of each (V) was calculated from these two measurements assuming that the blood pool could be described as an ellipse of revolution using the equation $V = 8A^2/3\pi L$ where A is the area of the ellipse and L its long diameter.

The vertical structure of the Mallinckrodt Institute of Radiology precluded performance of the angiographic and radionuclide studies in close temporal sequence. We therefore elected to do the studies within 24 hr of each other. The calculations from the radionuclide studies were made by two observers (LR and RHSW) independently and again 6 months later by RHSW so that we could have an indication of observer variation.

RESULTS AND DISCUSSION

The left ventricular ejection fraction of the three healthy subjects ranged from 68 to 81%, while in the patients the range was 32–87%. The individual results are shown in Table 1 together with the angiographic measurements. The correlation between the two methods is shown in Fig. 6, $r = 0.87$, $p < 0.001$. The radionuclide method tended to overestimate left ventricular ejection fraction, the mean absolute difference between the results being 6.7% ± 1.7 (s.e.m.).

The calculated tissue-background activity accounted for a large proportion of the counts in the outlined region and averaged 71.9% ± 1.66 (s.e.m.) of the counts in end-diastole.

At first, considerable difficulty was experienced in determining the plane of the aortic and mitral valves. The present configuration of our PDP-12 with 8K 12-bit words of memory and two LINC tape drives can store 32 × 32 matrices on tape at the rate of one image every 0.4 sec. This means that the radionuclide angiograms have unsatisfactory temporal resolution. In addition, the 32 × 32 matrix provides spatial resolution that is inferior to that of the scintillation camera. These two factors make delineation of the base of the left ventricle from the radionuclide angiogram quite unsatisfactory.

In the modified left anterior oblique projection that we have used, the interventricular septum, apex, and left border of the heart are readily visualized and can be outlined quite consistently. The base of the left ventricle has been defined by studying the images of end-diastole, end-systole, alternating images of these, simulating cardiac contraction, and the subtraction image end-diastole–end-systole.

The correlation between the two observers' estimates of left ventricular ejection fraction from the radionuclide studies was significant at the 2% level, $r = 0.72$. The mean absolute difference between them was 4.2% ± 1.3 (s.e.m.). The correlation between the calculations made 6 months apart by RHSW was a little better, $r = 0.87$, $p < 0.001$.

TABLE 1. COMPARISON OF RADIONUCLIDE AND ANGIOGRAPHIC METHODS OF MEASURING LEFT VENTRICULAR EJECTION FRACTION

				Left ventricular ejection fraction (%)		
				Radionuclide method*		
Subject	Age	Sex	Diagnosis	June 1972	December 1972	Angiographic method†
EP	39	M	Normal	79	81	—
RW	36	M	Normal	59	68	—
AP	25	M	Normal	83	80	—
AL	49	F	Angina familial xanthomatosis	65	74	82
AH	62	M	Angina	66	60	81
GD	60	M	Severe angina	82	87	84
RB	41	M	Angina	63	76	63
HS	50	M	Angina	69	71	72
JH	41	M	Myocardial infarction double bypass	75	76	70
SL	47	F	Mitral stenosis	63	61	56
VP	37	M	Progressive angina	59	61	60
NC	50	F	Coronary artery occlusive disease	58	71	66
AB	41	M	Angina	67	61	60
FT	56	M	Myocardial infarction	69	72	—
NS	46	M	Myocardial infarction chronic congestive heart failure	36	32	—
AK	61	M	Angina	61	64	—

* Performed in the modified left anterior oblique projection. Calculations made 6 months apart in June and December 1972.
† Performed in the right anterior oblique projection.

However, the mean absolute difference between his results was 5.2% ± 1.05 (s.e.m.) with the second estimation giving the higher figures.

For the data collection we have assumed a constant R-T interval so that the R-wave could trigger both the end-diastolic and end-systolic images of the same cardiac cycle.

The calculation of the left ventricular ejection fraction by this method makes use of the change in counts in the outlined region between end-diastole and end-systole, and hence, after tissue-background subtraction, determines a change proportional to the change in blood volume. As the end-diastolic and end-systolic images are collected after the tracer has come to equilibrium in the vascular compartment, the tissue background can be regarded as constant in any cardiac cycle. Labeled albumin leaves the vascular compartment quite slowly after intravenous injection, at the rate of 6%/hr (*13*). If the ^{99m}Tc-HSA were poorly labeled so that free ^{99m}Tc-pertechnetate were present and spreading rapidly into the extravascular spaces, the determination of the tissue background should still be valid, for the integrated end-diastolic and end-systolic images are formed from the 45-msec images collected in each cardiac contraction during which time little change would take place in the tissue-background activity. It is also assumed that the tissue background is uniform within the outlined region, for the algorithm that determines tissue background does so within a small part of this region and then scales it appropriately.

Some aspects of this technique may be compared with other radionuclide methods of measuring left ventricular ejection fraction.

The method of data collection and the calculations differ from those of Strauss, et al (*1*) and have several theoretical advantages:

1. The images of end-diastole and end-systole are collected from the same cardiac cycle and then integrated over many cycles. Strauss and his colleagues collected their end-diastolic images first and then their end-systolic images.
2. By continuously storing a small part of the past in the circular buffer, the R-wave of the electrocardiogram initiates collection of the corresponding end-diastole rather than the subsequent end-diastole that Strauss, et al used.
3. Left ventricular ejection fraction is determined from the counts in the two images and hence is directly proportional to blood volume. A modified left anterior oblique projection is the most convenient one for separating the left ventricle from both the right ventricle and the left atrium. Strauss, et al (*1*) used the right anterior oblique projection and measured the change in area of the end-diastolic and end-systolic images by planimetry. By superimposing both ventricles, the right anterior oblique projection is quite unsatisfactory if left ventricular ejection fraction is to be calculated from the counts in the two images as opposed to the areas. The use of the change in counts also avoids the assumption that the volumes of the left ventricle can be derived from an ellipse of revolution of the single plane images of end-diastole and end-systole.

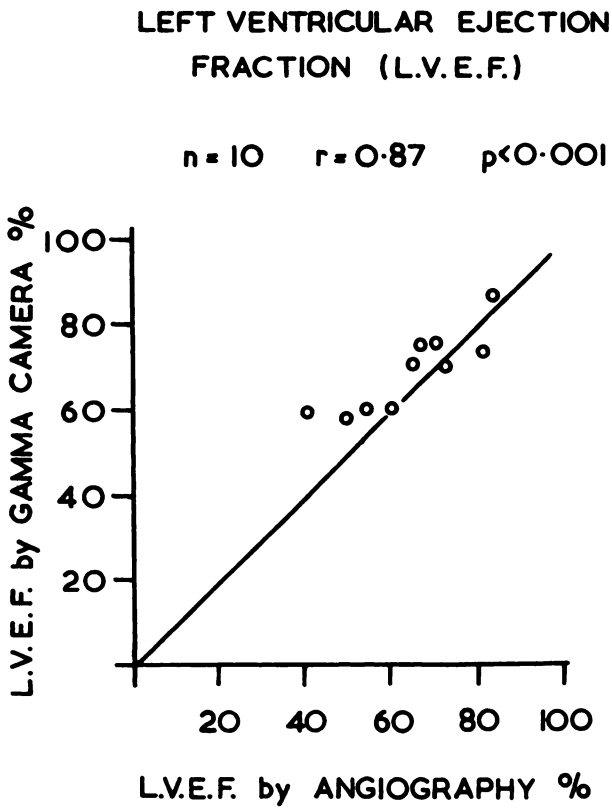

FIG. 6. Correlation between left ventricular ejection fraction determined from angiograms (in right anterior oblique projection), and radionuclide studies (in modified left anterior oblique projection.) Line is line of identity and not regression line.

The region used to determine the tissue-background activity differs from that described when left ventricular ejection fraction is calculated from a radionuclide angiogram. We have used a small region within the end-diastolic image where there is no left ventricular blood pool at end-systole. The methods that determine left ventricular ejection fraction during the first passage of the radionuclide through the heart derive the background activity from the region immediately surrounding the outlined left ventricle (*3*). In addition, this background changes from beat

to beat (*3–5*) whereas with our method the background remains fairly constant during the study—providing the ^{99m}Tc is firmly bound to the human serum albumin.

These results suggest that this method can provide reasonably reliable figures for left ventricular ejection fraction. Outlining the left ventricular blood pool requires more subjective judgment than we had anticipated, but, with practice, quite consistent results can be obtained.

Although the technique requires a gamma camera interfaced to a small digital computer, the data can be processed and results obtained within 4–5 min of completing the study.

By using ^{99m}Tc-HSA, serial changes over the course of a few hours could be made from a single injection. We suspect that the magnitude of any change would probably be more reliably determined than the actual value of the ejection fraction. We anticipate that, with a larger memory in the PDP-12 providing greater spatial and temporal resolution, we could calculate ejection fraction from the first passage of the radionuclide as well as use our current gated image system for subsequent determinations. In addition, if several images were collected during each cardiac cycle, a more detailed examination of ventricular wall motion would be possible than can be obtained from the difference between the end-diastolic and end-systolic images alone.

ACKNOWLEDGMENT

This project was supported in part by NIH Training Grant No. LT01 GM01747-01 and USAEC Grant No. AT (11-1)-1653 under which this paper becomes AEC No. Co-1653-136. This material was presented in part at the 19th Annual Meeting of The Society of Nuclear Medicine in Boston, July 1972.

REFERENCES

1. MASON DT, ASHBURN WL, HARBERT JC, et al: Rapid sequential visualization of the heart and great vessels in man using the wide field Anger scintillation camera. Radioisotope-angiography following the injection of technetium 99m. *Circulation* 39: 19–28, 1969

2. SULLIVAN RW, BERGERON DA, VETTER WR, et al: Peripheral venous scintillation angiocardiography in determination of left ventricular volume in man. *Am J Cardiol* 28: 563–567, 1971

3. VAN DYKE D, ANGER HO, SULLIVAN RW, et al: Cardiac evaluation from radioisotope dynamics. *J Nucl Med* 13: 589–596, 1972

4. WEBER PM, DOS REMEDIOS LV, JASKO IA: Quantitative radioisotope angiocardiography. *J Nucl Med* 13: 815–822, 1972

5. STRAUSS HW, ZARET BL, HURLEY PJ, et al: A scintiphotographic method for measuring left ventricular ejection fraction in man without cardiac catheterization. *Am J Cardiol* 28: 575–580, 1971

6. ZARET BL, STRAUSS HW, HURLEY PJ, et al: A noninvasive scintiphotographic method for detecting regional ventricular dysfunction in men. *N Engl J Med* 284: 1165–1170, 1971

7. PARKER JA, SECKER-WALKER RH, HILL R, et al: A new technique for the calculation of left ventricular ejection fraction. *J Nucl Med* 13: 649–651, 1972

8. LARSON KB, COX JR: *Computer Processing of Dynamic Images for an Anger Scintillation Camera.* New York, Society of Nuclear Medicine, 1973

9. BENJAMIN PP, REJALI A, FRIEDELL H: Electrolytic complexation of ^{99m}Tc at constant current: Its application in nuclear medicine. *J Nucl Med* 11: 147–154, 1970

10. SCHAD N, STUCKY J, BRUNNER H, et al: The intermittent phased injection of contrast material into the heart. *Am J Roentgenol* 104: 464–475, 1968

11. CARLETON RA: Change in left ventricular volume during angiocardiography. *Am J Cardiol* 27: 460–463, 1971

12. BROWN R, RAHIMTOOLA SH, DAVIS GD, et al: The effects of angiocardiographic contrast medium on circulatory dynamics in mean-cardiac output during angiocardiography. *Circulation* 31: 234–240, 1965

13. STERLING K: The turnover rate of serum albumin in man as measured by I^{131}-tagged albumin. *J Clin Invest* 30: 1228–1237, 1951