A NEW TECHNIQUE FOR THE CALCULATION OF LEFT VENTRICULAR EJECTION FRACTION

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Zaret and his colleagues (*1*) have described a noninvasive method of measuring cardiac ejection fraction using a gamma camera in which they used the electrocardiograph to control the time intervals for the collection of end-diastolic and end-systolic images. The ejection fraction was then calculated from the change in area of the two images as determined by planimetry.

Their encouraging results prompted us to develop a technique for the measurement of left ventricular ejection fraction using a small, on-line, dedicated digital computer interfaced to an Anger gamma camera. ^{99m}Tc-labeled human serum albumin is used as a blood pool indicator. End-diastolic and end-systolic digital cardiac images are gated from the electrocardiogram. The number of counts obtained is directly proportional to blood volume; therefore, using an area of interest corresponding to the left ventricle, the left ventricular ejection fraction can be calculated from the following equation:

$$\text{ejection fraction} = \frac{\text{diastole counts} - \text{systole counts}}{\text{diastole counts}}.$$

Background (all activity not originating in the left ventricular blood pool) cancels in the numerator but not in the denominator:

$$\text{ejection fraction} = \frac{\text{diastole counts} - \text{systole counts}}{\text{diastole counts} - \text{background}}.$$

The two major contributions to background are (A) nonleft ventricular large blood pools, e.g., left atrial blood pools, and (B) tissue blood pool. With an appropriate gamma-camera projection, the large nonleft ventricular blood pools can be separated from the left ventricle and excluded from the area of interest. An algorithm has been developed with which the computer is able to calculate the tissue blood pool background, standardizing this calculation.

EQUIPMENT

An Anger gamma camera with a high resolution, 15,000 parallel-hole collimator is interfaced to a Digital Equipment Corporation PDP-12A digital computer with 8K 12-bit words of memory, two LINC tape drives, and a standard oscilloscope (*2*). The interface deadtime in the fixed deadtime mode is 15 μsec, introducing only a small additional data loss over the gamma camera, even at high counting rates. Using the special single-cycle stealing direct memory access function of the PDP-12 leaves at least 90% of the central processing unit time free for other computer tasks, e.g., electrocardiogram (ECG) monitoring or initial data processing (*3*). The buffered tape system allows continuous data collection while previous input is stored on tape.

A standard Grass ECG difference amplifier is connected to the patient using ECG leads V_1 and V_6. A ground lead is placed over the lower abdomen. The amplifier output, representing the difference between V_1 and V_6 is connected to one of the PDP-12A analog-to-digital inputs. The ECG is monitored under program control while data is being collected and is used to control data collection.

TECHNIQUE

The data collection is divided into two parts: (A) Following a bolus injection of ^{99m}Tc-labeled albumin into a peripheral vein, a radioisotope angiocardiogram is collected and stored on computer tape. The angiogram is subsequently used to locate and define cardiac structures and to see if separation of the left ventricle from the right ventricle and from the left atrium has been achieved. (B) Electrocardiographically gated end-diastolic and end-systolic digital cardiac images are then collected and stored.

The radioisotope bolus is rapidly injected through a 19-gage scalp vein needle followed by a saline flush. At the time of injection a special data collection program is started which collects a digitized

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image of the gamma-camera output consisting of a matrix of 1024 cells, i.e., a 32 × 32 cell matrix. One hundred frames or images are collected at a rate of 2/sec. A separate program then allows the user to view these data frame by frame. The left ventricle is identified at this time, and an area of interest corresponding to the left ventricle is selected and saved for future use.

The second portion of the study is conducted after the radiopharmaceutical has come to equilibrium within the vascular space. The patient's electrocardiogram is continuously monitored by the computer. An appropriate lead is selected such that there is a large R wave in the cardiogram. It has been found satisfactory to define the R wave by voltage alone. The computer presents a portion of the electrocardiogram to the user via the oscilloscope. The user is asked to select a voltage level attained only by the R wave. He is also asked to locate a cursor at the end of the T wave. The user thus interacts with the computer to make the complex decisions involved in signal recognition. The computer calculates the time from the R wave to the cursor and saves this as a constant.

When the data collection is started, the computer continuously saves images in a circular buffer of three 15-msec frames. With the occurrence of an R wave, the current 15-msec frame is completed and then all three frames are added to an end-diastolic buffer. Thus, data are gated into the end-diastolic buffer during 45 msec which ends at the R wave with a 15-msec jitter. Data are gated into a second buffer, the end-systolic buffer, for 45 msec preceding the time interval denoted by the cursor at the end of the T wave. End-diastolic and end-systolic images are collected for 300 or more cardiac cycles in order to improve statistical accuracy.

After the data have been collected, the end-systolic and end-diastolic images are corrected for nonuniformity. All Anger cameras produce an inhomogeneous picture when viewing a uniform source (*4*). Inhomogeneity due to difference in sensitivity over the crystal will affect the calculation of the ejection fraction, although inhomogeneity due to position misrepresentation or differences in cell size will not. An image of a uniform disk source containing ^{99m}Tc is collected either before or after the study and used to correct the end-diastolic and end-systolic images for nonuniformity. In phantom experiments this correction has been found to improve the accuracy of the ejection fraction calculation.

Large blood pool background can be largely eliminated by using the proper gamma-camera projection. Left and right cardiac blood pools can be separated by using left anterior oblique (LAO) projection. The left atrial blood pool lies superior and posterior to the left ventricular blood pool and can be separated by a projection on a plane which is at approximately 45 deg to the coronal plane on its short axis. These two planes define a projection: LAO 45 deg superior to the coronal plane on its short axis. In this projection the other nonleft ventricular blood pools—aorta, pulmonary vessels, etc.—are largely out of the area of interest. Further, small modifications in this projection for individual anatomic variations can be performed after the radioisotopic angiogram and before the end-diastolic and end-systolic images are collected.

TABLE 1. SYRINGE PHANTOM DATA

Measured "ejection fraction"	Calculated "ejection fraction": % "diastole" at 5 levels of background activity* Bkg.† 110 cps	Bkg. 1,100 cps	Bkg. 2,800 cps	Bkg. 4,100 cps	Bkg. 8,200 cps
20	28	26	23	21	20
40	44	43	42	41	40
60	62	61	60	60	61
80	86	82	81	82	81
90	94	93	92	90	91
Mean difference from measured "ejection fraction"	+4.8	+3.0	+1.6	+0.8	+0.6

* All images collected for 1 min. Specific activity: 650 counts/50 cc/sec.
† Bkg. = Background activity.

The tissue blood pool background tends to be somewhat inhomogeneous. Since an exact calculation of the tissue blood pool overlying the left ventricle is not possible, we have established a correction for this background which is approximately equal to it but which more importantly is standardized. Adopting strict criteria for this calculation should reduce observer bias in its calculation and this has been done by developing an algorithm which the computer can apply. It was thought that the area where the blood pool is during diastole, but is not during systole, would be a good area in which to determine tissue blood pool background. The computer forms an image of diastole minus systole. Within the area which the user has outlined as the "left ventricle", the computer finds that cell with maximum activity in this subtraction image. Then any cell within the area of interest which has half this activity or greater is selected for a new area of interest. In this new subarea of interest the activity recorded in the systolic image is taken to be the tissue blood pool background.

The ejection fraction calculation program allows the user to view the diastolic, systolic, or diastolic minus systolic image on the computer oscilloscope screen. A grey scale picture of the images may be photographed. The diastolic and systolic images also can be viewed sequentially at various rates giving a visual impression of cardiac function. Additionally, the area of interest selected while viewing the angiograms may be read from the tape, modified, and written back on the tape. When satisfied with the area of interest the user directs the computer to calculate the ejection fraction.

RESULTS

Preliminary tests of the system have been performed. Correlation of the results of this new technique with other measures of cardiac ejection fraction are in progress. The data reduction algorithm has been tested with a simple model consisting of two 50-cc syringes connected with a three-way stopcock and a piece of plastic tubing. One syringe was securely taped to the collimator face; the other was placed out of view of the gamma camera. The volume of technetium-labeled fluid in the syringe on the collimator face could be adjusted using the second syringe. A uniform fluid-filled disk with varying amounts of technetium was used to vary the background. Images of the syringe with various known volumes were obtained with different levels of background activity. These images were corrected for nonuniformity, and then the "ejection fraction" of the syringe calculated. A good correlation ($r > 0.99$) between known "ejection fractions" and experimentally calculated "ejection fractions" was obtained, and the differences between the known and calculated values became smaller with higher levels of background activity (see Table 1). In two dogs, changes in the ejection fraction occurred in the expected direction following the administration of isuprel and propranolol. The dogs were lightly anesthetized and lay supine beneath the gamma camera. Control images for the ejection fraction were collected several times and then each drug was given in turn intravenously and further images for the ejection fraction obtained. The changes in ejection fraction are shown in Table 2. The validity of this method of calculating ejection fraction in patients remains to be determined, but initial trials have resulted in calculated ejection fractions in the expected range.

TABLE 2. CHANGES IN LEFT VENTRICULAR EJECTION FRACTION IN DOGS GIVEN ISUPREL AND PROPANOLOL

	Left ventricular ejection fraction %		
	Control	Isuprel (0.5 μg/min)	Propranolol (10 mg)
Dog 1	67	77	59
Dog 2	83	89	57

SUMMARY

A sophisticated technique requiring an Anger gamma camera interfaced to a digital computer has been developed for the determination of left ventricular ejection fraction. By using a modified LAO projection, right ventricular and left atrial activity are separated from left ventricular activity. The remaining tissue background activity is estimated by a special algorithm and the ejection fraction automatically calculated after the region of the left ventricle has been outlined. Preliminary tests of the system have been completed and correlation with other techniques are in progress.

The expensive, nonmobile equipment required to perform this test may be justified by the importance of left ventricular ejection fraction in evaluating cardiac function. The user is required only to outline the area of the left ventricle and then the computer performs the necessary calculations. The technique is noninvasive and readily repeatable. These factors offer advantages for this technique over other methods of calculating left ventricular ejection fraction.

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REFERENCES

1. ZARET BL, STRAUSS HW, HURLEY PJ, et al: Left ventricular ejection fraction and regional myocardial performance in man without cardiac catheterisation. *Circulation* 42 (Suppl 3): 120, 1970

2. LARSON KB, COX JR, et al: Computer processing of dynamic images from an anger scintillation camera. Proceedings of a workshop held at Washington University, St Louis, Mo, January, 1971

3. *PDP-12 System Reference Manual.* Maynard, Mass, Digital Equipment Corp, 1971

4. MORRISON LM, BRUNO FP, MAUDERLI W: Sources of gamma camera image inequalities. *J Nucl Med* 12: 785–791, 1971