Physiologically triggered multiple cardiac images are an advance in nuclear medicine. Herein described are methods of analyzing such studies, which perform as available as digitized data, to determine regional distances of myocardial contraction, rates of cardiac wall motion, work of myocardial contraction as well as regional ejection fractions. When applied in a clinical setting these methods have significantly added to the interpretation of cardiac studies.

The desire to study myocardial perfusion and function with radionuclides is probably as old as nuclear medicine. It is, however, only within the last few years that the technology has permitted application of sophisticated and clinically useful studies.

Among the major technologic breakthroughs that permitted these applications were the physiologic trigger and its offspring, the physiologically synchronized multiple acquisition of cardiac data. In the first, a signal, generally the R wave of the electrocardiogram, is used to initiate acquisition, and an image is generated by summing the information obtained over several heart beats. In the latter, the physiologic trigger initiates a series of timed events allowing the information from the corresponding temporal portions of many cardiac cycles to be summed, and displayed in a "real time" representation of cardiac function. The resultant "heart movies" are closely comparable to the radiographic studies obtained by cardiac catheterization.

The intrinsic resolution characteristics of nuclear medicine systems make it unreasonable to hope that the nuclear images would approach the radiographic images in detail and resolution, but the noninvasive nature of the nuclear medicine procedure, which can be performed as an outpatient study, compared to the left heart catheterization procedure which generally requires hospitalization and has an associated morbidity and mortality, gives the isotope study a compensatory advantage.

Manipulations of the nuclear data are relatively simple insofar as it is digitized. The display options include the subtraction of background, enhancement of contrast, alterations in time per frame, display in linear logarithmic or exponential mode, all of which are easily handled within software and can be accomplished without altering the raw data. Determination of edges by one of numerous algorithms, and determination of background are also relatively simply accomplished and once background is subtracted, determination of the ejection fraction is straightforward. Description of wall motion is also accomplished in the same manner as from the radiographically obtained images.

When nuclear and radiographic images are compared, an additional drawback of the nuclear image is apparent. The nuclear image is obtained during equilibrium, and the right ventricle is superimposed on the left ventricle in the projections to the right of anterior. Further, as the right ventricle enlarges, this superimposition becomes more prominent. This leads to difficulties when attempting to interpret the motion of the posterior and inferior walls in that these walls are behind the right ventricle in those projections. Further, since structures are often superimposed upon each other, it is difficult to separate their individual motion. When a series of patients, who had been studied by both radiographic and radionuclide techniques was analyzed in our clinic, it was demonstrated that there was almost perfect correlation on the anterior walls and apex, while on the inferior and posterior wall less than 80% correlation was obtained. When post-myocardial revascularization patients were studied, improvement in ejection fraction was noted, even in cases when there was no perceivable difference in wall motion. When attempts were made at other institutions to evaluate ejection fraction in patients with known coronary artery insufficiency, it was found that patients with multiple vessel disease might have normal ejection fractions. In rest-stress studies, patients with normal coronary
arteries ordinarily increased their ejection fraction but patients with single and multiple vessel disease on occasion also increased their ejection fraction.

In attempts to overcome these difficulties, we have attempted to develop methods for quantitatively describing the motion of different areas of myocardium, as well as their ejection efficiency. Two of the techniques used for this, namely myocardial kymography and regional determination of ejection fraction will be discussed.

**MYOCARDIAL KYMOGRAPHY**

The kymogram is a display of the motion of an area of myocardium in a single dimension as a function of time. In generating a kymogram, the edge image or radionuclide ventriculogram is displayed. For convenience, a grid, in cartesian coordinates, can be superimposed over the image; lines crossing myocardial structures are chosen. Each line is specified by choosing the X and Y coordinates of its initial points and the increment between points along the line.

The activity along each point for each of the serial images representing a cardiac cycle, is displayed in matrix in which the X coordinate represents the image number (and therefore time) within the cycle, the Y coordinate the sequentially numbered point on the line; each point is given a brightness value relative to its activity. The resultant matrix is, therefore, a representation in time of activity along the selected line.

The program as written is initiated with dialogue identifying the location of the study, the number of frames in the study and the number of lines to be examined, and the location of each line. The matrix is then created and kymograms developed and displayed. An image with the lines along which the kymograms were taken superimposed upon the images is also developed.

First and second derivative images of the kymograms in one or two dimensions are easily derived from the original kymograms. The major difficulty in kymogram interpretation is the determination of edge position. However, for ease of interpretation, the edge as determined by any of the commonly used algorithms may be superimposed upon the image.

Once the kymogram is developed, it provides several advantages over the optical interpretation of the studies. These include: (1) The wall motion may be described quantitatively. Included in this is the ability to describe the magnitude of wall motion in millimeters, and the rate of wall motion in centimeters per second. If an intraventricular pressure curve is simultaneously available, the regional work of myocardial contraction can be calculated by multiplying the force distance integral. (2) Examination of the first derivative curve can give information that is of value when two structures are seen superimposed. When the first derivative is observed, a widening of the area in which the first derivative is large is noted. When applied to our series of cases in which the radioisotope and radiographic studies disagreed, this was found to be responsible for the difference in interpretations in roughly one-third of cases.

The method of determining distance is straightforward when parallel hole collimation is used. Parallel hole collimation produces images that are not spatially distorted, and therefore, measurements of distance and lengths of deep structures are possible. By coincidence the field of view of a gamma camera with ten inch crystal is 254 mm. If this field of view fills a 64 x 64 matrix, each matrix point represents almost exactly 4 mm. If the acquisition is in 128 x 128 matrix, each matrix point represents 2 mm. It should be recognized that points on diagonals will represent longer distances. For more precise fixing of edges, interpolative algorithms are available.

In our hands, the kymogram has provided several advantages in interpretation of gated studies. It has enabled us to detect small differences in function in patients after myocardial revascularization procedures as well as patients receiving adriamycin. In another case was the difference visually apparent. It has enabled us to more accurately describe the motion of superimposed cardiac segments, and has allowed us to describe the action of the septum, an area that has been refractory to visual analysis.

**THE REGIONAL DETERMINATION OF EJECTION FRACTIONS**

The left anterior oblique projection in a physiologically triggered gated acquisition study is uniquely suited for determination of the global ejection fraction. The left ventricle is clearly separated from the right ventricle, and the photon energy of technetium is such that the posterior nonventricular structures contribute little in the way of total activity to the cardiac image.

Normal cardiac ejection fraction has been defined as above .5 or .55 in different laboratories. Ejection fractions can normally run as high as .75 or .8. Many studies have shown that most normal patients will increase their ejection fraction when exercised, and that most patients with coronary artery disease will not. There are, however, significant numbers of false positive and false negative stress tests.

In our clinic we have noted patients with known myocardial infarcts whose global ejection fractions have remained in the normal range. This is easily understood if one considers a heart with a scarred akinetic area, but in which the remainder of the myocardium is functioning normally. If the myocardium before infarct were functioning at, let us say, an 80% ejection fraction, and the patient suffered a myocardial infarct of one-quarter of his heart, the remainder of the heart would be expected to continue functioning efficiently, and an ejection fraction of .6 could be expected. This is, of course, an
over-simplification, but the principle that a large area of normally functioning myocardium can mask the decrease in ejection fraction is valid.

The simplest method of determining regional ejection fraction is simply to divide the end systolic image point by point by the end diastolic image, and subtract the result from unity. The equivalent can be done without necessitating use floating point programming by multiplying the end systolic image by 100 before the point by point division. This technique has been successfully applied to images obtained with a Bender Blau imaging system. However, in such an imaging system each matrix point represents an area roughly 1 cm. square, and 1.4 cm. on diagonal. It is unlikely, therefore, that the cardiac wall will move the total distance of one matrix point. When, however, the systems that have matrix points representing .2 cm. are used, many points representing the periphery of the heart will fall within the background of the systolic image.

Consider the example of a perfect sphere which contracts 20% in each of its axes. Its global "ejection fraction" would be 49%. However, the center point would have an apparent ejection fraction of 36% while the peripheral points would have an apparent ejection fraction of 100%. Further, consider the example of a heart where the apex is totally akinetic. The apex will have obligatory motion as the proximal ventricle moves. It will, therefore, show an ejection fraction where in fact no motion or ejection occurred.

Our initial attempt to overcome this difficulty was to find the center point of the cardiac blood pools where center was defined as either the area of maximum activity or the mean point of activity in the diastolic image to divide the heart in quadrants about this point and determine ejection fractions for each quadrant. In the balloon analogy cited above, this method works well. However, in cardiology, the left ventricle does not normally contract about its center point. Our experience has been that the septum moves the least. When the theoretical balloon model was applied to this and the nine o'clock position of the balloon, the ejection fraction for the left quadrant of the balloon will be falsely low, that for the right quadrant elevated, that for the lower and upper quadrants about normal. The algorithm which we developed that best overcomes this difficulty involved the determination of point of maximum activity for each frame of the study, and divides the image about that point. Lines running at 45 degree angles were the easiest to program, and also closely approximate the division of vascular supply within the ventricular wall. Using this algorithm, we have been able to successfully identify the quadrant of an infarct, even in a patient with normal global ejection fractions. We have been able to separate patients with low ejection fractions into patterns of diffuse myocardial disease versus focal disease (Infarct and Ischemia) and when we applied this study to patients who were seen to have poor wall motion on radioisotope study and good wall motion on radiographic study, we found that in five of seven of these patients, the ejection fraction for the quadrant felt to be radioisotopically abnormal in fact had a poorer ejection fraction than the remainder of the heart. This suggests that the cases that the study considered false positives for the radioisotopic procedure were in fact false negatives for the contrast procedure.

In our hands the ability to determine regional ejection fraction has significantly aided in the interpretation of physiologically gated multiple cardiac acquisition studies.