Radionuclide cinecardiography using minicomputer generated sequential gated images¹

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Noninvasive radionuclide cinecardiography using a minicomputer has been applied to study left ventricular segmental wall motion and to determine ejection fractions. Twenty-five patients who had had left ventriculograms at cardiac catheterisation were studied within two weeks by radionuclide cinecardiography. The radionuclide technique provides images of the heart blood pool during sequential periods of the cardiac cycle. These high information-content images are made by sorting data recorded over several minutes into an on-line minicomputer according to when the data occurred with respect to the recorded QRS spike. The ventricular chambers are anatomically separable in the left anterior oblique position, and allow construction of a background-corrected left ventricular relative volume curve from the counts in the left ventricle without any measurement of dimensions. Sequential display of the consecutive radionuclide images yields a cine image which provides information concerning wall motion during the entire cardiac cycle. Radionuclide wall-motion analysis was identical to the contrast ventriculographic interpretation in 23 of the 25 patients. Left ventricular ejection fractions calculated from the left ventricular counts obtained from the radionuclide images correlate very well with the left ventricular ejection fractions determined from dimensional analysis of the right anterior oblique view of the contrast angiogram (correlation coefficient=0.94). Though absolute volume is not measured, the ability to measure left ventricular ejection fractions independent of the geometry of the ventricle should prove valuable in patients with severe derangement of left ventricular function in whom the prolate spheroid left ventricular model is invalid.

Experience with the addition of motion to a variety of x-ray diagnostic imaging procedures has shown that this feature adds to the ease of diagnosis. This is particularly true for the evaluation of a dynamic process such as ventricular contraction. Unfortunately, with the dose-limited quantities of radionuclide that can be injected, the photon yield is too small to permit formation of high quality diagnostic images over the short period of a single passage of activity through the heart, though excellent quantitative data may be obtained (Kurtz *et al.*, 1976). One solution to this problem has been to inject a tracer which remains in the blood for a prolonged period, permitting, by the use of a physiological trigger, such as the electrocardiogram, repeated imaging only during the brief 40 millisecond periods associated with end systole or the 60 millisecond periods associated with end diastole

over many cardiac cycles (Zaret *et al.*, 1971). The result is an average image of the cardiac blood pool obtained at a defined time from each of several hundred cardiac cycles. Evaluation of such gated images compares quite favourably with contrast angiocardiology in the ability to diagnose abnormalities of left ventricular contraction (Strauss *et al.*, 1971). Pitfalls can occur, however, when electrical and mechanical events become disordered so that placement of the gate becomes uncertain or varies from beat to beat. Furthermore, determination of end diastolic and end systolic volumes requires subjective delineation of the ventricular outline from a very small radionuclide image with indistinct borders. Small errors in measurement are cubed using a prolate spheroid left ventricular model and can produce large errors in calculated volumes. Like contrast angiographic analysis, this method loses validity when ventricular volume and contraction become grossly abnormal.

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An extension of the gated end-systolic and end-diastolic image method is the formation of a series of gated images throughout the cardiac cycle rather than only at end systole and end diastole (Green *et al.*, 1975). Repetitive, sequential display of these images generates a cine image of an average cardiac cycle (Reese and Mishkin, 1975). Analysis of an average cycle produced from several hundred heart beats is advantageous in that the analysis does not depend on only a few beats which may differ considerably from the usual heart beat, as for example, do extrasystolic beats induced by contrast injection. Use of a computer allows selection of the left ventricle as a region of interest so that counts in the left ventricle can be determined. A plot of these counts, corrected for background, against time provides a relative left ventricular volume curve from which relative change in the left ventricular size during the cardiac cycle can be calculated. If desired, absolute dimensions of the left ventricular chamber could be measured using a calibrated image (Strauss *et al.*, 1971), but these measurements would be subject to the same errors encountered in measuring gated images and the same pitfalls inherent in assessing volume change of a non-geometric, three-dimensional cavity by applying two-dimensional measurements. It was

our aim to develop and evaluate a procedure which could be carried out and the results assessed in a short interval while the patient was in the nuclear medicine section.

Patient selection

Twenty-five patients scheduled for left ventriculography were referred as outpatients to the nuclear medicine division within 1 to 2 weeks of the planned catheterisation study. Informed consent was obtained after detailed explanation of the radionuclide study. Most patients were being studied with respect to possible coronary artery disease (Table).

Methods

Imaging was performed from the 30° right anterior oblique and the 55° left anterior oblique aspects using an Anger scintillation camera equipped with a special high resolution collimator with parallel holes. The collimator holes form an angle of 20° from the perpendicular to the face of the crystal, thereby allowing the oblique images to be accomplished by only modest tilting of the camera head. The camera head thus remains closer to the chest wall and yields a higher count rate than would

Table Correlation of x-ray and radionuclide cine

Case No.	Final cardiovascular diagnosis	Ejection fraction %		Contraction plot*	
		x-ray cine	Radionuclide cine	x-ray cine	Radionuclide cine
1	Mitral stenosis	50	46	I	I
2	Hypertensive cardiovascular disease; arteriosclerotic coronary artery disease; postcoronary bypass	69	57	I	I
3	Arteriosclerotic coronary artery disease	47	43	III	V
4	Arteriosclerotic coronary artery disease	25	22	III	III
5	Arteriosclerotic coronary artery disease	73	66	II	II
6	Normal	47	51	I	I
7	Arteriosclerotic coronary artery disease	70	69	I	I
8	Normal	52	48	I	I
9	Arteriosclerotic coronary artery disease	38	30	III	III or IV
10	Arteriosclerotic coronary artery disease	46	41	III	III
11	Arteriosclerotic coronary artery disease	77	74	I	I
12	Arteriosclerotic coronary artery disease	40	34	V	V
13	Hypertensive cardiovascular disease	65	62	I	I
14	Arteriosclerotic coronary artery disease	27	26	IV	IV
15	Hypertensive cardiovascular disease	50	43	V	V
16	Normal	56	63	I	III
17	Normal	76	82	I	I
18	Hypertensive cardiovascular disease	53	52	V	V
19	Arteriosclerotic coronary artery disease	38	46	I	I
20	Mitral regurgitation	79	83	I	I
21	Hypertensive cardiovascular disease	71	66	I	I
22	Arteriosclerotic coronary artery disease	42	48	V	V
23	Hypertensive cardiovascular disease	74	70	I	I
24	Hypertensive cardiovascular disease; arteriosclerotic coronary artery disease	33	38	V	V
25	Hypertensive cardiovascular disease	50	62	I	I

*I, normal contraction; II, borderline abnormal contraction; III, localised hypokinesia or akinesia; IV, localised dyskinesia; V, generalised hypokinesia or akinesia.

otherwise be possible. ^{99m}Tc albumin (15 mCi) was injected intravenously and, after allowing 10 minutes for equilibration, data were taken into an on-line minicomputer in list mode.

Standard electrocardiographic limb leads from the patient were connected to a device which generated a 4-volt pulse at the QRS spike. Gating systems were used, but are not necessary. This cardiac cycle marker was used to label data taken into the minicomputer. Data were acquired until the disc capacity of 1.2 million words (counts) was exceeded, which requires approximately 4 minutes. The average heart rate counted during data acquisition is used to divide the cardiac cycle into 9 equal periods. This period is used as the length of each individual frame. For example, with an average rate of 95 beats per minute (mean cycle length 632 ms), a period of 0.07 s is selected. All events

associated with the 0.07 s coincident with the electrocardiographic marker throughout the 4-minute study are placed into the first frame and yield a relatively high data density image of approximately 150 000 counts. The computer then recycles back to the beginning of the study, finds the marker, skips the first 0.07 s, and places the next 0.07 s period for the entire study of several hundred heart beats in the second frame. When the third frame is generated, 0.14 s are skipped before selecting the 0.07 s period and so on repetitively until 9 frames are generated (Fig. 1).

Since the interval from the electrocardiographic marker (QRS spike) to the end of the cardiac cycle varies, especially with atrial fibrillation, the last frame or two contains fewer counts than the initial frames. We drop the last frame when viewing the cine, but if several of the later frames are low in

Fig. 1 Generation of sequential 'gated' images to form cine. The first right anterior oblique blood-pool image, generated from the imaging information of the 0.07 s interval coincident with QRS spike during several hundred heart beats, forms a late diastolic image (left lower frame, a). Data acquired during the next 0.07 s interval provide image of blood pool at end diastole (b). Subsequent serial images arranged counterclockwise around edge of figure represent cardiac blood pool outlines during sequential 0.07 s intervals (c-h). Rapid sequential projection produces a cine effect, which makes the recognition of anteroinferior apical akinesis obvious.

counts, they may be readily corrected in several seconds by simply multiplying the frame by the appropriate correction factor necessary to normalise the frame to the average total counts present in the initial frames. For example, if there are 150 thousand counts in the first 7 frames and 120 thousand in the eighth frame, the eighth frame can be multiplied by 15/12. This correction is made only for viewing purposes to obtain a uniform density of the sequential frames. None of the corrected data is used for calculation purposes. It requires approximately 15 to 20 minutes for our minicomputer to frame the data. With better programming, for the provision of which we do not currently have the necessary expertise available, the frames could be generated simultaneously and the time required for framing reduced to 4 to 5 minutes. The data are viewed by sequentially displaying the consecutive frames on the oscilloscope face for 100 ms giving the illusion of motion. Contrast may be changed, background suppressed, and images smoothed to give a clearer motion picture without destroying the original data.

For the left anterior oblique view, the detector is angled to approximately 55° until the septum can be well seen on end and appears of uniform thickness on the monitoring oscilloscope. The left anterior oblique images are used to generate counts from the left ventricle before normalisation for viewing analysis. The operator displays the image of the left ventricle on the oscilloscope, and labels the region of the left ventricle when it appears largest by using a light pen to flag the cells which contain left ventricular information. The number of points in the left ventricular area is determined by a stroke of the computer keyboard. An exactly similar number of points surrounding the left ventricle in a concentric ring is then labelled as background. This includes activity from the right ventricle, aorta, lungs, and atria as background and thus has no anatomical validity, but is readily reproducible and provides data adequate for clinical purposes.

The frames may be flipped through in sequence with the background ring maintained on the display oscilloscope so that the operator can ascertain that cardiac motion does not displace the left ventricle out of the outlined left ventricular region and into the background ring. Since most of the cardiac displacement takes place along the longitudinal axis, the ventricular outline appears to have very little displacement when viewed perpendicular to this axis from the 55° left anterior oblique position. In practice, it is a simple matter to ensure that the flagged left ventricular area does contain the entire left ventricle throughout the cardiac cycle. Activity versus frame (time in the cardiac cycle) is computed

and plotted for both the left ventricle and the left ventricular background for the first eight frames (Fig. 2). A single fixed background value is used. This is taken as the lowest count in the background ring in a single frame as determined from a print-out of the background counts. The lowest value, which usually occurs during systole, is then subtracted from the left ventricular count in each frame to yield a corrected relative left ventricular volume curve. The ejection fraction is calculated as the relative difference between the numerically highest and lowest counts on this relative left ventricular volume curve.

EF =

$$\frac{\text{Net end-diastolic counts} - \text{net end-systolic counts}}{\text{Net end diastolic counts}}$$

Net end diastolic counts

Ejection fractions were measured, from the contrast cine x-ray films obtained in the right anterior oblique projection from the same 25 patients, by tracing the outline of the left ventricle during systole and diastole for 3 consecutive normal-appearing heartbeats when they were available for analysis. Occasionally only 1 or 2 beats appeared valid. Length and mid-length perpendicular diameter

Fig. 2 Generation of left ventricular relative volume curve. The points plotted are the total counts in the left ventricular area ascertained from left anterior oblique view. The points must be corrected for constant left ventricular background in order to calculate the ejection fraction.

were measured and volume calculated according to the assumption of a prolate spheroid model for the left ventricle (Greene *et al.*, 1967). Left ventricular motion was assessed by an independent observer from tracings of the contrast left ventriculogram in systole and diastole obtained usually only in the right anterior oblique view. Occasionally left anterior oblique views were available in addition to the standard right anterior oblique view. Left ventricular motion analysis was performed from the radionuclide study by observing the cine study on the oscilloscope face. The x-ray cine tracings were analysed for contraction pattern abnormalities (Hamilton *et al.*, 1972). They were classified as normal contraction (I), borderline abnormal (II), localised hypokinesia or akinesia (III), localised dyskinesia (IV), and generalised hypokinesia or akinesia (V). Localised abnormalities were classified according to the left ventricular segment involved as either anterior, posterior, inferior, apical, or septal.

Results

The Table shows that there was excellent agreement in the diagnostic impressions concerning left ventricular wall motion. In no case was a significant area of abnormal wall motion missed by the radionuclide method. One case interpreted on the contrast study as having hypokinesia localised to the inferior wall was determined to have generalised hypokinesia on the radionuclide study (case 3). In another case a patient who had a normal x-ray cine study in the right anterior oblique view only, appeared to have septal wall hypokinesia on the radionuclide cine study in the left anterior oblique view (case 16); the coronary arteriograms appeared to be normal and no other evidence of cardiac disease was found. In general the similarity of appearance of the two motion images, x-ray contrast and radionuclide, was striking. Correlation between the ejection fraction as calculated from the radionuclide left ventricular count curve and from the contrast cines (Fig. 3) was very good with a correlation coefficient of 0.94.

Comment

Our results, obtained in an unselected group of patients undergoing cardiac catheterisation, show that radionuclide cinecardiographic determination of left ventricular wall motion is comparable to that obtained using left ventricular contrast injection. In addition to the obvious advantages of being easily and rapidly performed on outpatients without hazard, the technique possesses the property

inherent in radioactive tracer techniques of being readily quantified, avoiding subjective tracing and tedious measurements. Measurement of relative left ventricular count rate and hence relative left ventricular volume is unaffected by abnormal contraction patterns which affect calculations based on dimension measurements made from contrast ventriculograms. No geometric model has to be assumed for the radionuclide technique. Once the left ventricular region has been outlined by the light pen no subjective measurement is made, and errors in measurement are not multiplied as they are when dimensional analysis is used. Hence, in patients with severe abnormalities of contraction, the radionuclide technique could supply data more readily quantifiable than that given by the x-ray study, though the anatomical detail would be less than that provided by the x-ray cine.

There is no necessity to choose exactly the right time period for end systole and end diastole as is the case when gated imaging is performed. The generation of sequential frames allows visual choice of end systole and end diastole from the left ventricular volume curve. Though the time intervals are relatively long, particularly with slow heart rates, the information from the curve appears valid and

Fig. 3 Plot of averaged x-ray cine ejection fraction obtained by length-diameter measurements in right anterior oblique position versus radionuclide cine ejection fraction calculated from background corrected counts in left ventricle in left anterior oblique position. Correlation coefficient 0.94. Line of identity represented by 45° line. LAO, left anterior oblique; RAO, right anterior oblique.

eight consecutive images suffice to produce excellent motion images. The cine presentation has the obvious advantage of speedy analysis in a format readily understood by those familiar with angiocardiology. The addition of motion itself adds to the ease of diagnosis, the eye and mind substituting motion for resolution. This is apparent in coronary cineangiocardiology in which the cine analysis mode apparently provides more information than viewing of a single frame of the cine. Thus, addition of motion is desirable when the image is formed by a relatively small number of photons.

Other advantages of the technique include the ability to analyse the effect of a variety of physiological or pharmacological interventions, the ability to analyse right and left ventricular contractions side by side, and the ability to repeat the study at regular intervals to follow the course of a disease or therapeutic effects with no risk to the patient other than the radiation burden. For example, since the data are accumulated over only a 4-minute period, the patient could be exercised, paced, or nitroglycerin could be given during repeated data acquisition. Such an approach has proved valuable with gated imaging techniques (Salel *et al.*, 1976). We have done this in only four patients to date, and only one of these has had the manoeuvre repeated and confirmed by contrast angiocardiology. In one patient with severe hypertension studied only by the radionuclide method, reduction of blood pressure with nitroglycerin produced pronounced generalised improvement in ventricular contraction as compared with the baseline study obtained a few minutes beforehand.

Absolute ventricular volumes could be obtained using this method, but must be done by chamber measurement and would require a calibrated single pass image of the filled left ventricle alone to determine aortic and mitral valve planes. Chamber outlining is a time-consuming, subjective procedure and is subject to various errors already enumerated but can yield excellent results (Strauss *et al.*, 1971).

The technique described here has the advantages of convenience to the patient, repeatability, provision of multiple views, with rapidly available, easily analysed results comparable to contrast cine, and calculation of ejection fraction without dependence on model assumptions or dimensional analysis. Against this must be weighed the cost of the highly specialised, expensive equipment and the radiation burden.

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