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Publication Date
1971-10-01

Submitted to Circulation

LBL-387
Preprint

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DONNER LABORATORY

October 1971

AEC Contract No. W-7405-eng-48

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CARDIAC EVALUATION FROM RADIOISOTOPE DYNAMICS

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SUMMARY (ABSTRACT)

A method for radioisotope angiocardiography using the scintillation camera and a quantitative television data system for rapid data recording and readout is described. This essentially non-invasive, risk-free, out-patient procedure, which can be repeated at frequent intervals, shows promise of being a significant supplement to conventional x-ray angiocardiography.

By precise area-of-interest masking and the use of fast response recording, a stroke-by-stroke reading of the left ventricular ejection fraction is obtained. Cardiac output is determined from the same record. In the absence of valvular insufficiency, end-diastolic volume is computed from these numbers. Comparison of this value with end-diastolic volume determined from area measurements of the pictures provides an estimate of the degree of regurgitation when present. Direct comparison of this technique with standard contrast angiocardiography has been made in 17 patients, with confirmatory results which are presented. Clinical application has demonstrated already the ability of isotope cardiography to provide a large amount of information not obtainable by other simple techniques. It is likely that this method will also prove useful in situations requiring serial study, such as the management of intensive care cardiac patients.

KEY WORDS: End-diastolic volume, ejection fraction, radioisotope angiocardiography, ^{99m}Tc human serum albumin, scintillation camera, sequential 80-lens camera, cardiac catheterization, ventricular dV/dt.

After the first few studies it was apparent that ejection fraction, read from recording of the left ventricular area of interest without modification of baseline, was approximately 1/2 the true value, Table 1. Dynamic studies of a single chamber model demonstrated that this was not a fault of the recording system, and must therefore be due to activity in adjacent structures. As an accurate measure of ejection fraction was a prime object, success of the method depended on establishing the baseline from which the ejection fraction was to be measured. The true baseline must be one which results in a constant ejection fraction throughout the left ventricular phase. This requirement is met by any one of a family of curves, Fig. 4. By comparison with the results of contrast angiography, it was apparent that the correct member was one which intercepted the left ventricular curve at its low point after passage of the bolus and before recirculation. All members above a certain value meet this requirement, indicating that the true value must be established from each patient's record. One must look in front of, behind, and around the ventricle to measure the "cross-talk" and background interference. This can be approximated best by recording a 3 mm wide window around the left ventricle, Fig. 5. By recording the activity immediately surrounding the ventricular area of interest, one sees fluctuations due to "cross-talk" when the ventricle is full. By taking only the bottom of that curve (when the ventricle itself is contracted and out of sight) and recording at a sensitivity which brings the low point to the same value as the low point of the left ventricular curve, a satisfactory baseline is established, Fig. 6 and Table 1. As can be seen from the table, the isotope method allows

averaging the results of several beats in all cases whereas contrast angiography must frequently rely on a single beat. Although discrepancies appear in the comparison (r value = 0.77), this method of establishing the baseline appears to be satisfactory.

When the left ventricular area recording is spread out by using a faster paper speed, such as an electrocardiograph or Electronics for Medicine(R) recorder, details of the pattern of left ventricular volume changes (dV/dt) can be seen, upper portion of Fig. 7. The changes in left ventricular volume (dV/dt) are determined by direct recording of the electrically-determined derivative, lower portion of Fig. 7. From such a record the maximum rate of change in volume with time and duration of systolic, diastolic, and isovolumic phases can be measured. A clear, noise-free record of rate of change of volume during left ventricular ejection such as in Fig. 7 is obtained only in a small proportion of cases when a dose of 8 mCi is used. Such data could be obtained consistently by increasing the dose of isotope administered.

RESULTS

The normal pattern, dynamic and static, is sufficiently characteristic that marked abnormalities are immediately recognized on seeing the sequential pictures, viewing the television monitor during the study and on repeated playback and on seeing the curves generated from the areas of interest. Before quantitation the experienced observer is aware of major abnormalities in the central circulation by pattern recognition alone (14). This includes abnormal anatomy, chamber size, transit times, shunt, and whether the ejection fraction is large or small.

A typical record from areas of interest including right atrium, right ventricle, pulmonary artery, lung, left ventricle, and aorta of a normal subject is shown in Fig. 2.

Figure 3 compares records from the left ventricle of a normal subject, a 5-year-old child with a heart rate of 175 beats/minute, and a patient with severe heart failure. The sharp first peak represents the passage of the bolus through the right ventricle, a part of which is also seen in the left ventricular area of interest. The second saw-toothed peak represents passage of the bolus through the left ventricle. The fluctuations represent ventricular contractions, the high point representing the filled ventricle (end-diastole) and the low points representing the end of emptying (end-systole).

To critically evaluate the quantitative technique the system was placed in a standard fluoroscopic angiocardiographic catheterization laboratory (USPHS Hospital, San Francisco) so that the isotope and fluoroscopic techniques could be compared in the same patient at virtually the same time. The scintillation camera was placed adjacent to the fluoroscope over the mobile procedure table. Seventeen patients were studied by quantitative radiocardiography during selective x-ray angiocardiography.

In 17 patients studied nearly simultaneously, cardiac output by the isotope method showed good agreement with output by the Fick method.

Left ventricular ejection fraction from the isotope studies is compared to that obtained with contrast media in Table 1. From the table it can be seen that there was reasonable agreement in the majority of the 17 patients studied with serious discrepancy in 3 (r value of 0.77).

Left ventricular end-diastolic volume by area measurements of scintiphotos and contrast radiograms are compared in Table 2. Only the 9 patients in whom both studies were done in the right oblique (30°) projection are compared. There was good agreement in all but 1, with an r value of 0.875.

DISCUSSION

A rapid, high resolution recording of the passage of a bolus of isotope through the central circulation is a reflection of many parameters of dynamic cardiac function. It was the object of this research to determine the information that could be extracted. To accomplish this, one must have a reliable standard for comparison. Whatever its limitations, contrast cineangiography is clearly the "gold standard" by which this technique must be judged. Because of the lability of dynamic cardiac function, comparisons done days or weeks apart would not provide the rigid comparison desired. Because of the nature of the imaging equipment simultaneous studies are not possible, but with the fluoroscope and camera side by side, and by using comparable views, the comparisons were made a few minutes apart. Reasonable values for cardiac output and left ventricular end-diastolic volume were expected on the basis of previous studies (15-17).

This paper emphasizes direct measurement of left ventricular ejection fraction from the tracer curves, and estimation of left ventricular end-diastolic volume from area measurements on the scintigrams. This provides a workable system that is in accord with the results from contrast angiography. Considerable effort is also being expended in attempting to develop a more complete analysis of the tracer curves that may eventually be useful. At the

present writing it is beset with difficulties that prevent its contributing significantly to the workup of the patient. Although the curves obtained by this method are better than any previously available, study of those for the left ventricle and for the "background" from the 3 mm band around it establishes that there still exists a very sizeable mutual interference between counts from the various heart chambers, lung, chest wall, etc. Ideally, one would correct the record from each chamber or region for the effect of radioactivity in each of the others. This involves serious difficulties in determination of the relative counting efficiencies. An apparent way to arrive at such a standardization would require an injection in each region, which would mean having access to all heart chambers for injection, and could no longer be considered non-invasive.

If one can establish curves that are truly proportional to isotope content in some anatomical regions of the central circulation, compartment system analysis or other methods may be used to characterize the behavior of that segment in handling the isotope bolus. Particular effort has been made to treat the left heart as a compartment, with the lung curve as its input function. This was done with analog circuitry and with a variety of digital computer programs, including a fitting program to find best values for the exponential functions used. To date, however, it has not contributed to a useful estimate of left ventricular end-diastolic volume. The present study has shown that the downslope of the left ventricular curve cannot be used to estimate EDV, whether directly or corrected for the slow input from lung.

A purely empirical relationship between such slopes and known EDV has also been investigated, but has so far also been unsatisfactory.

In addition, an effort is being made to obtain information from the various isotope curves by deconvolution methods. We have had to reject Fourier transform and numerical deconvolution methods because of serious instabilities in the solution--such that they seem very unlikely to provide a routine method. Instead, emphasis is being put on simulation and fitting programs that deconvolute by repeated trial convolutions, using simple 3- or 4-parameter curves. This amy eventually simplify methods of obtaining mean values for transit times through individual segments of the central circulation, and in addition show transit-time distributions characteristic of certain disorders. The likelihood of these methods' providing true numerical values for individual heart chamber volumes seems small. At present, however, the real test of such ideas must await curves that are uncomplicated by significant mutual interference (18).

Shunting, if large, may be apparent from viewing the playback monitor or the sequential pictures obtained with the 80-lens camera or other sequential imaging methods (11). Quantitation of the magnitude of a shunt, or recognition of lesser degrees of shunt, is made from characteristic changes in the isotope dilution curves for the various regions in a way similar to that used for analysis of abnormal dye indicator dilution curves (19) or radioisotope dilution curves (20).

Superimposition of the images of the right and left heart can give valuable information regarding anatomical relationships (4, 7). This can be done by photographing the replay monitor, opening the camera shutter only at the appropriate phases of the study.

Quantitative analysis presently includes the following:

1. Blood volume (from plasma volume and central hematocrit).
2. Cardiac output. [BV x height of equilibrium/area of first pass]
3. Net stroke volume. [C.O./heart rate]
4. Right ventricular end-diastolic volume by slope analysis (15) [C.O. x mean time]
5. Right ventricular ejection fraction. [S.V. (#3)/Rt. Vent. EDV (#4)] or [1/(mean time x heart rate)]
6. Analysis of lung curve for evidence of shunt, qualitatively (19) or quantitatively (20).
7. Estimation of pulmonary blood volume from transit time (21).
8. Left ventricular ejection fraction from strip chart record with baseline corrected for "cross-talk", Figs. 4 and 6.
9. Left ventricular end-diastolic volume by area measurement (6, 13)
10. Left ventricular end-diastolic volume (assuming to regurgitation). [Net stroke volume (#3)/ejection fraction (#7)]
11. Comparison of #8 and #9 to calculate percent regurgitation. [EDV (from 8) - EDV (from 9)/EDV from 8.] The accuracy of the two values for EDV is such that differences of 30% or less cannot be relied upon as evidence of regurgitation.

12. Rate of change of volume (dV/dt) during left ventricular ejection from recording of left ventricle at fast paper speed, Fig. 7.
13. Transit time analysis (15).
14. Assessment of left ventricular wall contraction by superimposition of end-systolic and end-diastolic tracer images (6).

Unlike the injections of larger volumes of hypotonic medium used in angiography, the small volume of isotonic solution injected does not disturb blood viscosity, and this technique is entirely non-irritating to the myocardium. This feature is particularly important when normal physiological states are being studied, or subtle interventions planned, or for repeated evaluation of very sick patients with myocardial infarction or following heart surgery.

In addition, the absorbed radiation dose is in the order of 2% of that received from a comparable angiographic study. Changes in count rate during ventricular contraction are directly related to volume changes, rather than area changes which must be converted to volume, as with the use of contrast media and fluoroscopy. In the fibrillating heart, the isotope method allows one to obtain an average ejection fraction from more beats than are usually obtained in angiographic method.

Disadvantages of the non-invasive isotope technique as compared to the invasive contrast technique are failure to obtain measurements of blood gases or cardiac chamber pressures. Resolution of scintillation camera pictures is much less than that obtained by fluoroscopy, and much anatomic detail cannot be seen.

The numerical data storage and readout system used in these studies is considered to be an interim system. Considerable point by point hand correction is required. This system has provided knowledge of the requirements of the ultimate system which would minimize the need for corrections. An ideal system should have time response to 30 cycles per second without appreciable loss and should have a linear response over the entire count rate range used in clinical practice. Furthermore, the reading obtained from a constant reference source should not change as other activity is introduced or removed from the field.

Although the authors have limited experience with this technique in small children, substitution of this technique for the standard fluoroscopic method should be considered wherever possible because of the reduction in radiation dose alone (22).

Information obtained by the technique described must be extensively evaluated in the clincial setting to determine its practical value. Clinical application of the technique has already demonstrated its ability to definitively confirm the clinician's impression in some cases, thereby eliminating the need for further study. In other cases certain possibilities in the differential diagnosis are clearly ruled out, thereby defining the nature of further studies and justifying the need for invasive procedures. In all cases the technique provides a large amount of added information, easily obtainable and not obtainable by other simple techniques. It is likely that application of this method will find great use in situations requiring serial study.

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DESCRIPTION OF FIGURES

Fig. 1. Print from an 80-lens camera negative showing two simultaneous sequential recordings of passage of the ^{99m}Tc bolus through the central circulation. In the upper series of 40 pictures the starting time interval was 0.5 sec. and exposure time 0.5 sec. per picture. Lower series of 40 pictures, starting time interval 0.5 sec. and exposure times 2 sec. per picture to allow collection of a large number of dots per picture.

Fig. 2. Strip chart recordings of passage of the isotope through 6 areas of interest in the central circulation. The television playback monitor screen was masked around each area of interest in turn as the tape was replayed. 80-lens camera pictures from the time of maximum activity in each area of interest have been inserted for purposes of illustration. Arrows indicate the anatomic structure unmasked for each recording.

Fig. 3. Comparison of recordings of passage of the isotope through the left ventricle of a normal adult, a 5-year-old child, and a patient in severe heart failure. In each case the first peak represents passage of the bolus through the right ventricle, the method relying primarily on temporal separation. In the patient in failure the fluctuations represent "noise", the ejection fraction being too small to be recorded.

Fig. 4. Recording from the left ventricle showing some of the "family" of curves which result in a constant ejection fraction through the left ventricular phase. The solid curve (63%) represents the correct baseline obtained by recording a 3 mm wide window around the left ventricle and confirmed by simultaneous quantitative angiocardiography (first patient in Table I).

DESCRIPTION OF FIGURES - 2

Fig. 5. Illustration of method of masking the left ventricle to record "cross-talk" and background interference. A 3 mm wide window is opened (cut out of black paper) surrounding the left ventricular outline (top). The bottom picture shows the light collecting funnel with light sensitive condution cell in place over the window. Two additional windows in the mask are positioned over sources fixed to the camera face to assure proper magnification and orientation of the mask.

Fig. 6. Examples of the baseline as determined by recording a 3 mm window around the left ventricular borders in 4 patients. Determination of the baseline is essential for calculating ejection fraction.

Fig. 7. Details of the pattern of left ventricular volume changes (dV/dt) seen by spreading out recording using a fast paper speed (top). The electrically determined derivative (bottom) provides a graphic presentation of the rate of change in volume as a function of time . A line was drawn through the isovolumic phase of the graph (rate of filling below, emptying above).

TABLE 1

EFFECT OF BACKGROUND ERASE ON EJECTION FRACTION (%)

Patient	Isotope		Contrast
	Uncorrected	Minus background	
Johnson, A.	25	63 (9)*	62 (3)*
Odom, V.	34	50 (6)	80 (3)
Briggs, H.	50	87 (14)	94 (1)
Beckner, L.	25	52 (9)	46 (3)
Shishido, M.	23	51 (13)	34 (1)**
Marques, A.	26	47 (7)	48 (1)
Sivridis, E.	26	47 (5)	54 (2)
Matheny, W.	21	43 (8)	63 (1)
Metcalfe, L.	40	54 (6)	60 (3)
Sorensen, V.	66	74 (6)	92 (3)
Takahashi, H.	28	58 (5)	59 (1)
Ogawa, R.	41	72 (7)	88 (3)
Whitney, J.	37	79 (11)	79 (3)
Jones, M.	17	42 (13)	21 (3)
Smith, L.	27	60 (4)	79 (1)
Bouscal, H.		86 (7)	86
Piovarcsik, N.	34	74 (6)	80
AVERAGE***		61	66

* No. of beats in parenthesis

** Fibrillating

*** Comparison of column 2 and 3 gave an r value of 0.77

TABLE 2

COMPARISON OF LEFT VENTRICULAR END-DIASTOLIC VOLUME OBTAINED BY ANGIOCARDIOGRAPHY OR BY ISOTOPE DYNAMICS

Patient	Angio.	Isotope*	# of Frames
TA	134	141 ccs.	1
WH	224	216 ccs.	3
OG	132	129 ccs.	3
BE	138	182 ccs.	3
SO	165	163 ccs.	2
SH	234	238 ccs.*	1
PI	186	131 ccs.*	1
JO	203	187 ccs.	6
SM	116	104 ccs.	4

* Where indicated by asterisk, drawn from enlarged Polaroids. All others measured from enlarged 80-lens camera negative.

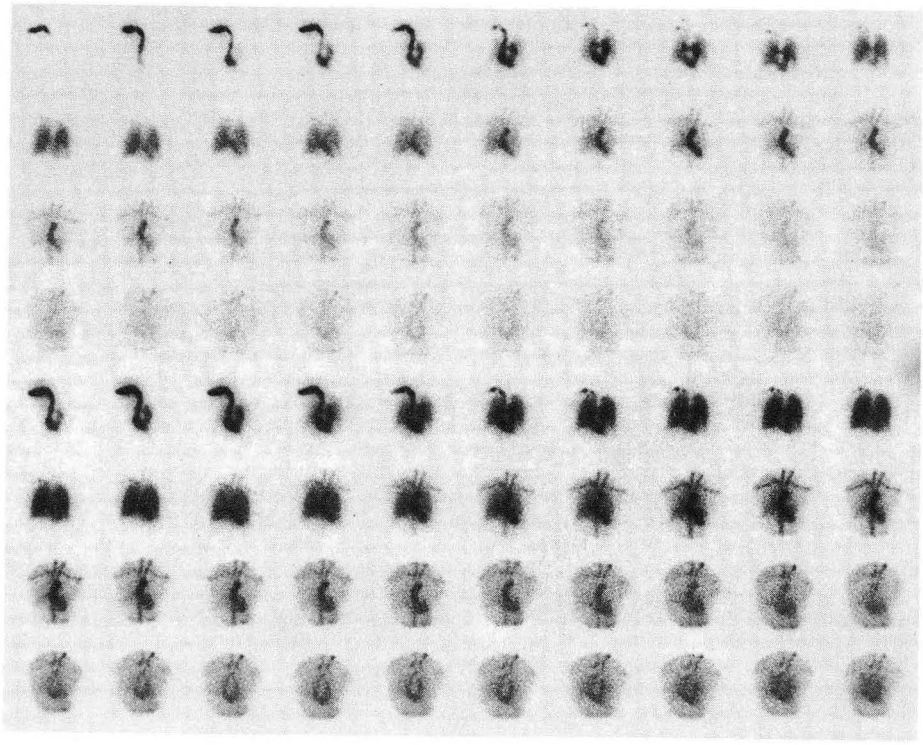

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Fig. 1

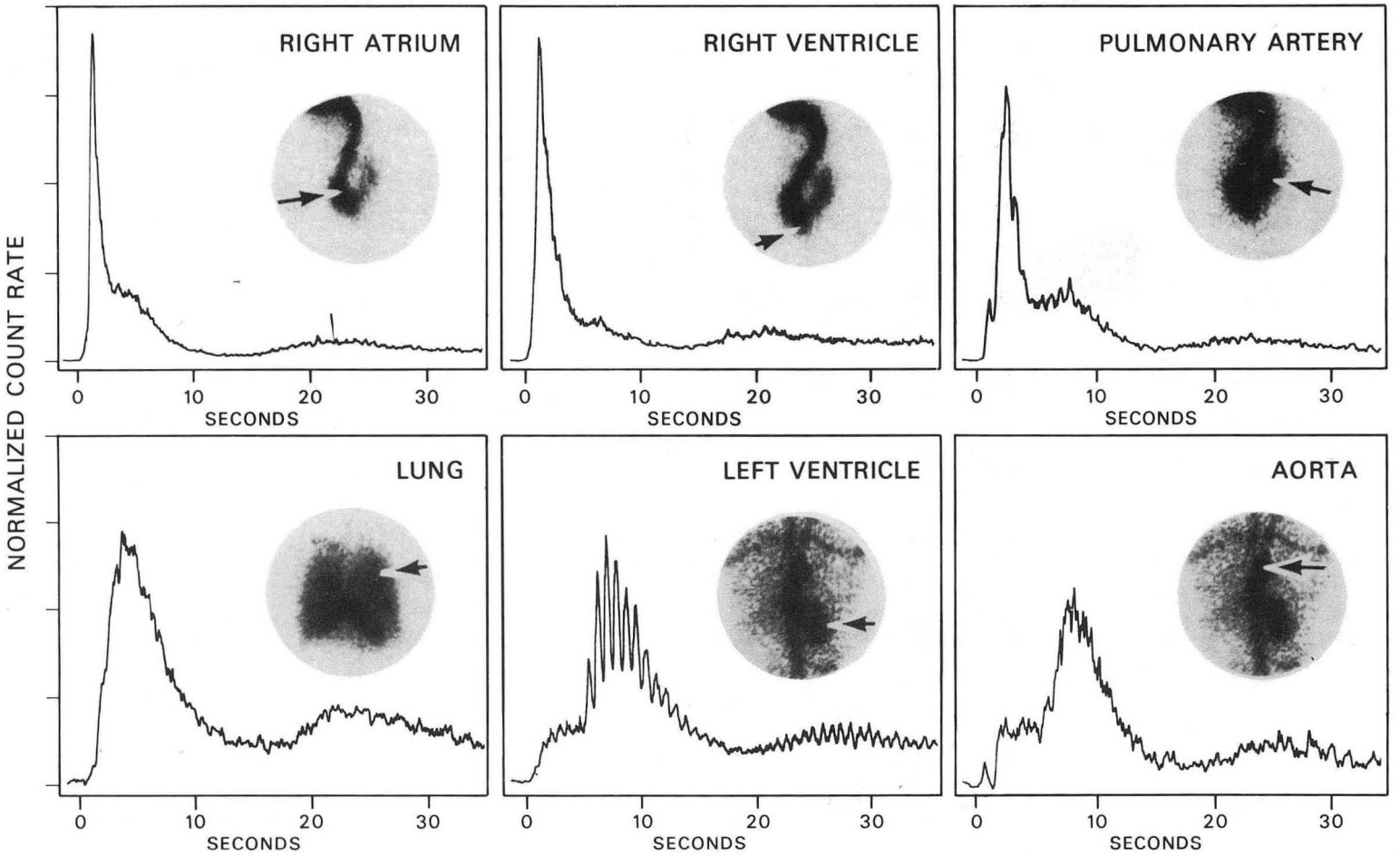

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Fig. 2

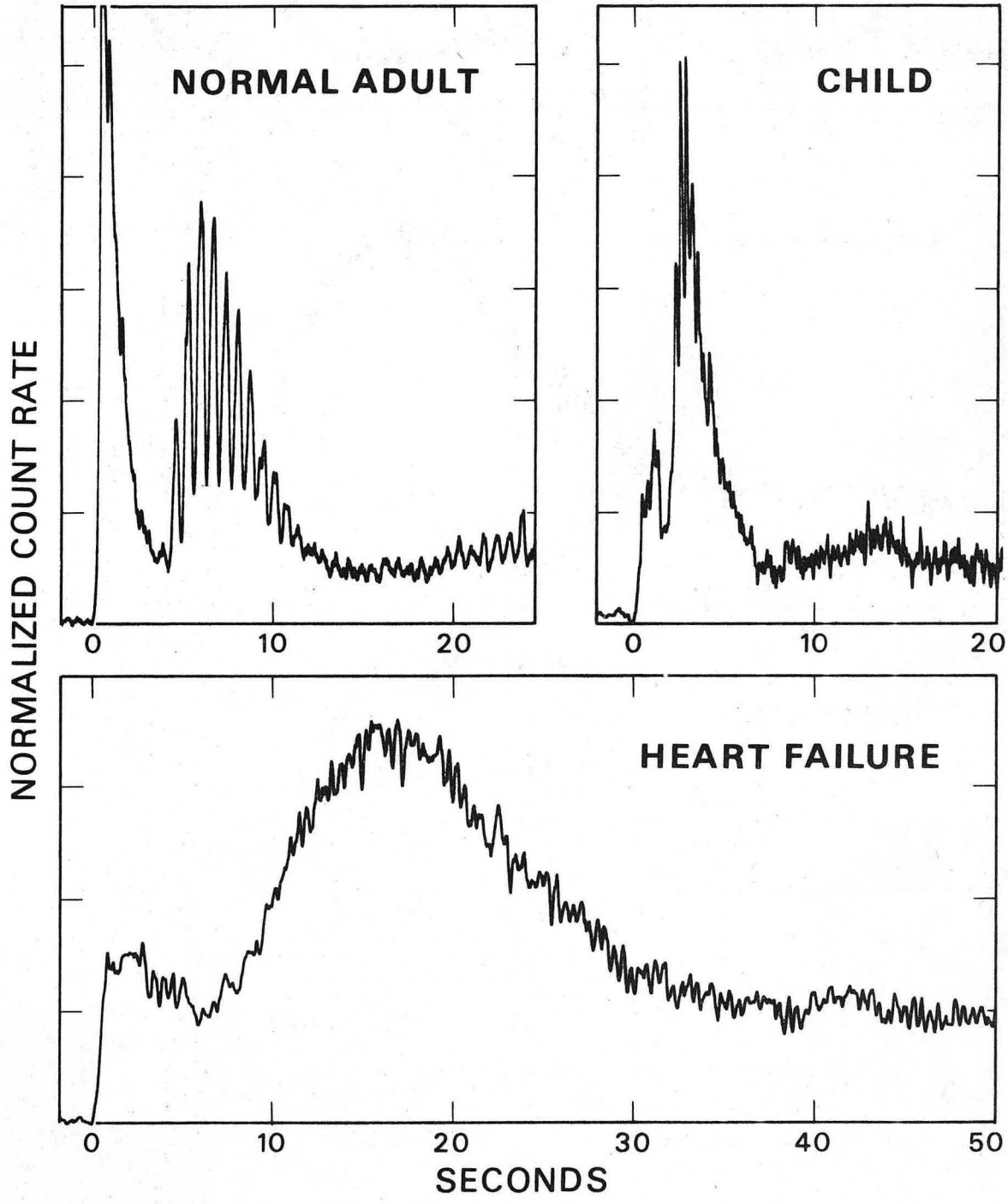

Fig. 3

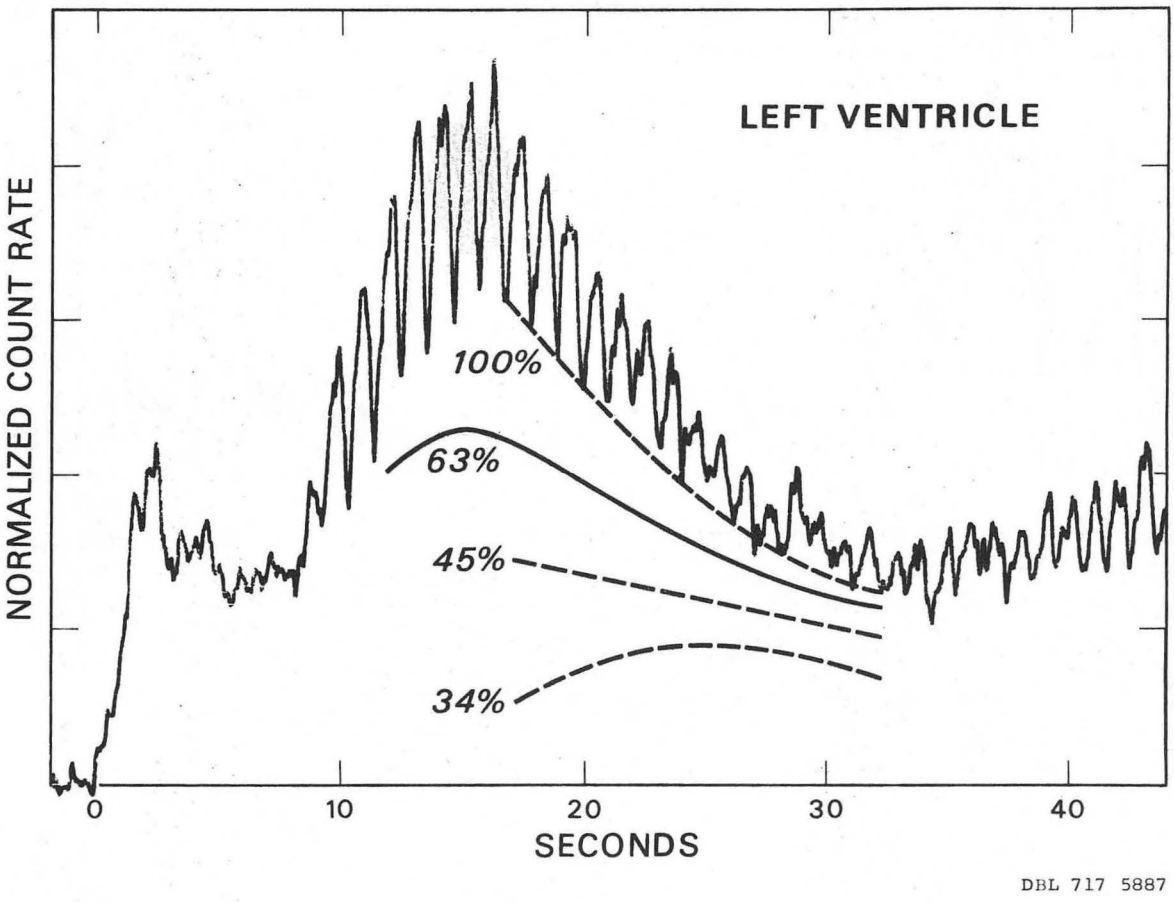
LEFT VENTRICLE
NORMALIZED COUNT RATE
100%
63%
45%
34%
0
10
20
30
40
SECONDS
DBL 717 5887

Fig. 4

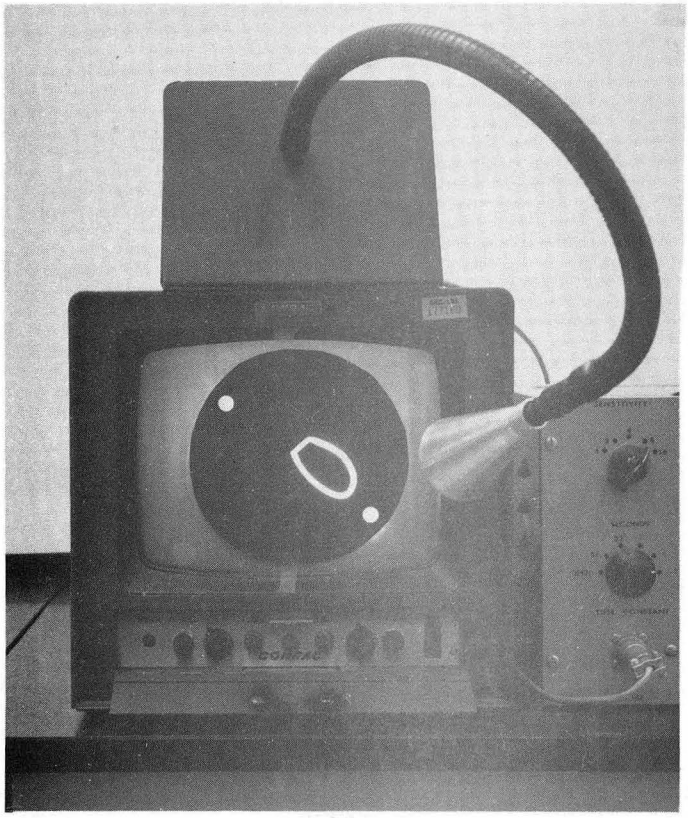

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Fig. 5a

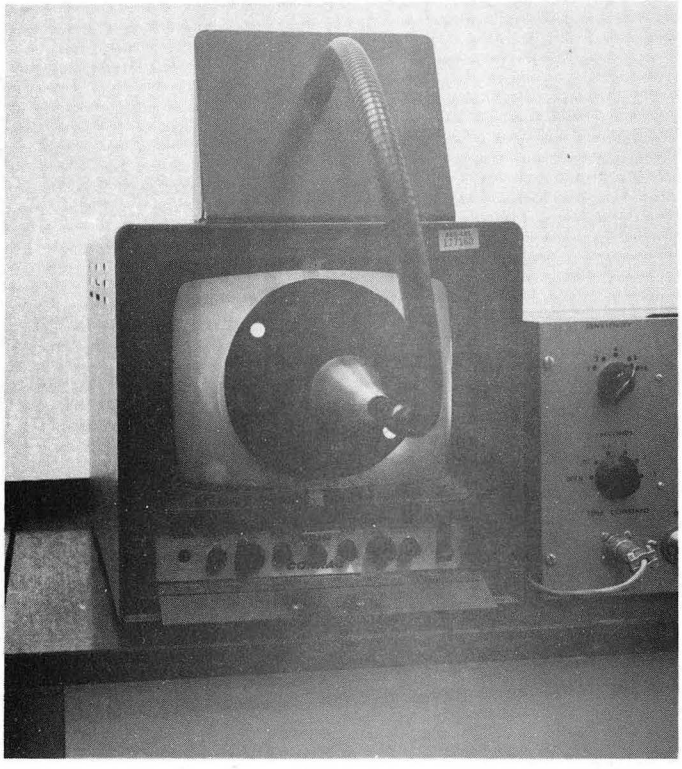

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Fig. 5b

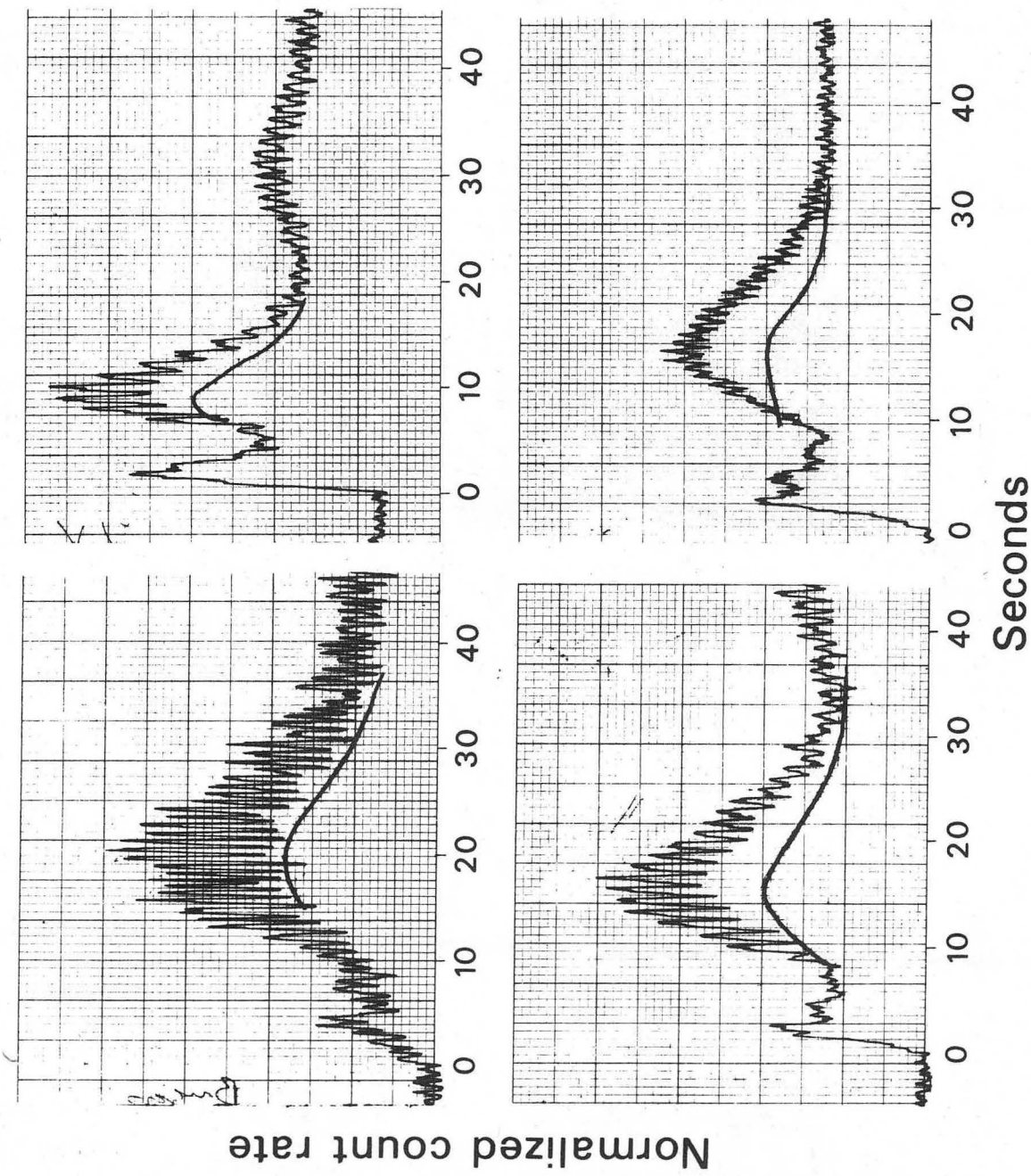

Fig. 6

XBL 715-974

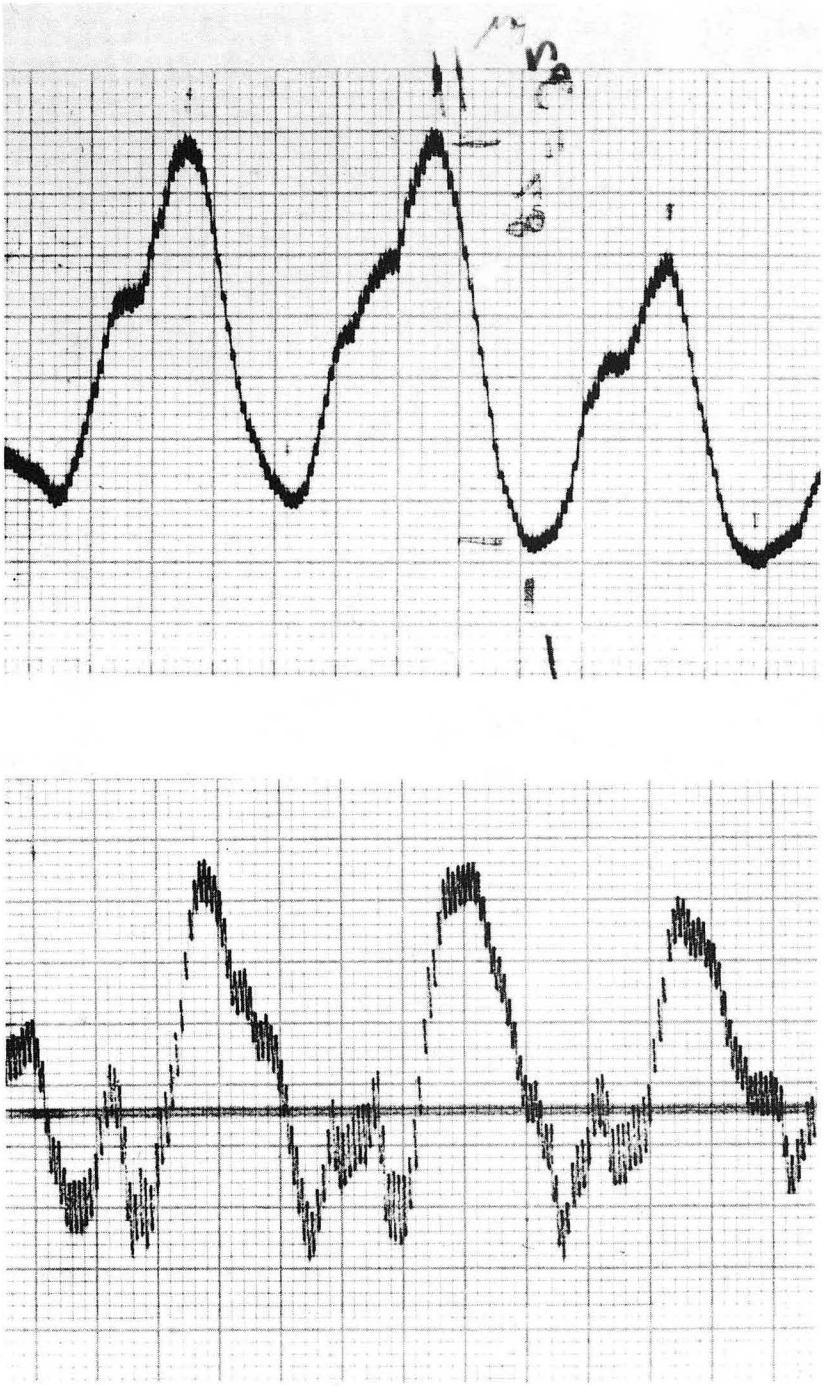

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Fig. 7

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