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Analysis of Factors Used in Calculations Based Upon Radiocardiograms on Dogs[1,2]

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The radiocardiogram[4] provides information on the circulation of radioactive material through the heart and lungs. Because the radiocardiograph records cardiac output with little trauma to the patient and because it offers minimal interference with circulation, it is a potentially valuable method of studying circulation. This method, however, has not provided the desired accuracy in quantitative measurements, probably because of errors related to the geometry of the detector system. This study suggests identification of the background radioactivity as one method to minimize the effect of geometry.

Prinzmetal *et al* (1) proposed the use of an externally placed detector to determine the characteristics of circulation. Shipley (2) and Huff (3) with their associates provided the basis for the present use of the radiocardiogram in making quantitative estimates of cardiac output. Huff based his calculations on equations derived from the dye-dilution principle, then compared the results with simultaneous estimations obtained by the application of the Fick Principle. Powers and Sevelius (4) have presented a different mathematical model based on mean transit time for the tagged particles. Both theories lead to similar equations for the calculation of cardiac output. In models of circulation, Glick (5) and others (6,7) have tested and supported the use of the radiocardiogram as the basis for estimating cardiac output.

The geometry of the detector system relates the field of the detector and distribution of radioactive particles in the field. During radiocardiograph recording, two sets of conditions lead to different geometries of recording in a single record.

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[4]The recording of gamma emissions from ^{131}I tagged serum albumin from an externally placed detector collimated over the heart. The first passage of the tagged bolus under the detector is identified as the cardiac portion of the radiocardiogram. Equilibrium distribution of the tagged material is recorded in the final portion of the radiocardiogram.

First, distribution of radioactivity in the field of the detector constantly changes during the cardiac phase of the record, but remains uniform during the equilibrium phase of the record. Second, geometry of recording differs in the cardiac and equilibrium phases of radiocardiography because radioactivity from ^{131}I appears in the peripheral circulation after equilibrium distribution has been reached. Other investigators, recognizing these factors, have either considered the influences negligible or by various techniques have minimized variations during the recording. By recording from the arch of the aorta instead of from the heart, Huff (3) minimized effects due to distribution. Others (8,9) have limited the field of the detector by shielding, thus reducing variations attributed to radiation detected from peripheral circulation.

The purpose of this study has been to estimate quantitatively the magnitude of variations which are caused by distribution fluctuations and/or radiation recorded from the peripheral circulation. Such information will enable technical improvement in the recording of radiocardiograms and will indicate to what extent variability in cardiac output estimated by this method can be attributed to factors of geometry. In order to accomplish this, distribution and peripheral circulation factors have been investigated separately.

METHOD

Studies in our laboratory indicated that radioactivity recorded from a chamber of the heart or from the arch of the aorta was influenced by the constantly changing position of the radioactive tagged bolus. As the bolus approached the heart, passed through the chambers of the heart and pulmonary circulation and reappeared in the aorta and peripheral circulation, the contribution of radioactivity from each of these areas was identified. Further studies indicated that small changes in the location of the probe over the heart led to marked differences in equilibrium measurements. These differences were created by inclusion of various percentages of the pulmonary circulation in the detector field.

In all of the experiments reported herein, mongrel dogs weighing 5-20 kilograms were anesthetized with Nembutal[R], 30 mg/kg I.V. Additional dosages were administered during the experiment whenever necessary to maintain the anesthetic level, indicated by EEG readings or reflex testing. Labeled serum albumin injections measured by micrometer syringe were flushed manually or mechanically into the circulation with five milliters of 0.9% saline. Tests of these micrometer syringes showed that repeated volumes varied less than one per cent. The detector was recessed in a lead shield one inch thick to give a flat field less than four inches across at the level of the recording from the heart, with the field centered over the notch in the median border of the central lobe of the left lung. Signals from the detector, a one-inch sodium thalliated iodide crystal, were amplified by a photomultiplier tube and ratemeter and were recorded on a Brown Recorder with a ¼ second transit time or on a Model 5P Grass Polygraph. The time constant used during the actual recording of the radiocardiogram was 0.5 second, and during the equilibrium phase of the record, ten seconds. An Ensco RU 4 respirator provided ventilation with air or with one hundred per cent oxygen throughout both closed and open-chest experiments. Throughout all of the

experiments, EEGs and ECGs were taken and systemic arterial blood pressure readings were recorded. Data reported in this study do not include recordings of experiments in which arrhythmias or fluctuations in blood pressure occurred.

RESULTS

In the first set of experiments, an open-chest preparation with the heart stabilized in a pericardial cradle was used. The sites and methods of injection are illustrated in Figure 1. Injections in sites selected by a manifold system were made through catheters of uniform size. The radioactive material was flushed into the circulation with five milliliters of physiologic saline. Separate injections were made into the external jugular vein, the pulmonary vein, the pulmonary artery and the root of the aorta.

The records obtained following the injection of a radioactive-labeled bolus into each of the various sites are illustrated in Figure 2. Figure 2A traces the injection which was made into the external jugular vein. The tracing with the injection entering the pulmonary artery appears in Figure 2B. Similarly, Figures 2C and 2D show respectively the radiocardiograms following injections into the pulmonary vein at the entrance to the left atria and into the root of the aorta.

An analysis of the records illustrated in Figure 2 appears in Figure 3. In Figure 3A the hatched area represents radioactivity recorded during the passage of the tagged bolus through the right heart. This figure includes a correction at the base of the hatched area, to account for estimated radioactivity emanating from the large veins entering the heart and from the pulmonary arteries. The estimation is obtained from the slight rise above initial background radioactivity appearing at the beginning of the trace in Figure 2A. Attributed to ^{131}I in the vena cava, the rise has been considered a continuing contribution for one transit time. The contribution of the pulmonary arteries, estimated from the initial rise appearing in the trace in Figure 2B, is of similar magnitude. The descending limb

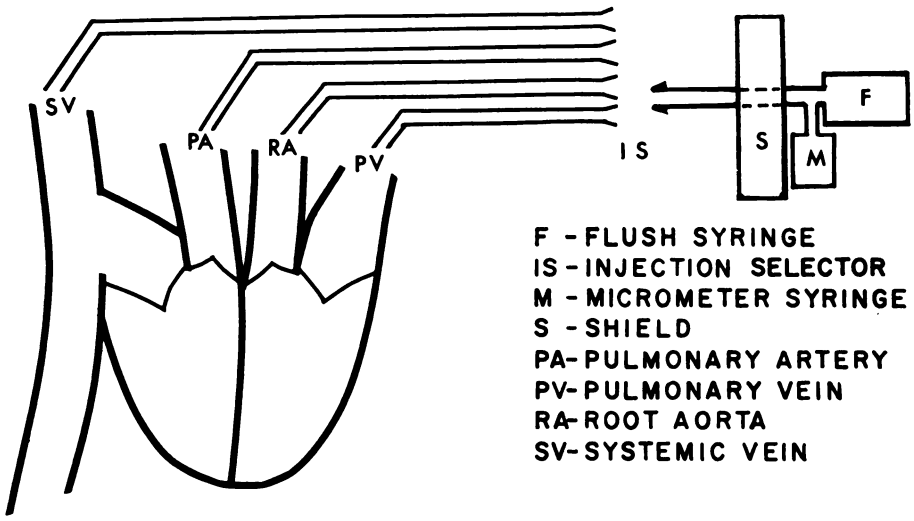

Fig. 1. Method and Site of Injection.

of the trace recorded in 2B was subtracted from the trace recorded in 2A. The intersection of the baseline with the ascending and descending limbs of the hatched area, represented in the figure by T_A and T_D, is used as the criterion for the measurement of transit time. The average radioactivity recorded from the right heart, the hatched area and the transit time are used in the calculation of cardiac output.

The method for obtaining the areas representing calculation for the left heart utilizes the radiocardiograms pictured in Figures 2C and 2D. The left heart curve is represented by vertical lines in Figure 3B. The base of the area excludes activity recorded from ^{131}I present in the pulmonary veins and activity originating from the root of the aorta. The descending limb of the vertically-lined area is obtained when the curve in Figure 2D is subtracted from the curve in Figure 2C, which includes the extrapolated correction for recirculation (not shown). The transit time for the left heart is taken from the intersection of the base with the ascending and descending limbs of the vertically lined area, represented by T_A and T_D in the figure. Transit times for the right and left heart are nearly identical when determined by this method. The radioactivity represented by the vertically-lined area and the transit time are used to calculate cardiac output. Outputs calculated for the right heart and for the left heart are nearly identical in the records presented.

It is unusual to obtain a trace as clearly related to the circulation of tagged albumin through the various regions of the circulation as the tracing used to illustrate the principle involved in the calculations in this study. The calculations used to support the hypothesis appear in Table I. The First Column represents the total area of a trace such as is given in Figure 2A. The Second Column is the estimated area for contribution for ^{131}I located in the systemic vein. The actual

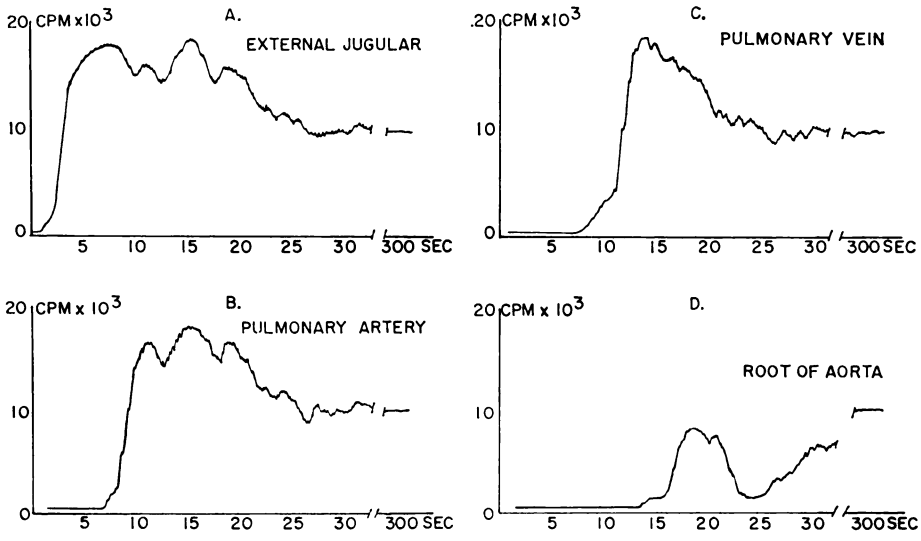

Fig. 2. Radiocardiograms recorded after injection of radioactive labeled serum albumin into the indicated site.

TABLE I

ANALYSIS OF RADIOCARDIOGRAMS FOR RADIOACTIVE BACKGROUND PRESENT

		Right Heart				Left Heart							
(1) J.V. C	(2) COR. C	(3) P.A. C	(4) R.H. C	(5) T.t. Sec.	C.O.* L/Min	(6) P.V. C	(7) R.A. C	(8) L.H. C	(9) T.t. Sec.	C.O.[1] L/Min	B.V. L	Equil. CPM	(10) Diff. %
1730	25	960	745	7.7	0.68	725	90	635	6.2	0.72	0.60	5100	− 6
2410	55	1330	1025	6.7	1.13	875	130	745	5.5	0.97	0.90	7500	−14
2900	40	1605	1255	7.1	1.79	1255	130	1125	6.2	1.84	1.15	6800	+ 3
2610	50	1410	1150	6.7	1.29	1090	120	970	5.6	1.30	1.00	8000	+ 1
3330	45	1890	1395	7.2	2.09	1475	140	1335	6.3	2.37	1.30	7200	+13
3070	45	1725	1300	7.4	1.92	1325	150	1175	6.6	1.94	1.20	6600	+ 1
4170	50	2290	1830	8.4	2.60	1760	150	1610	7.2	2.66	1.55	7800	+ 2
3030	40	1715	1275	7.0	2.11	1315	140	1175	6.2	2.22	1.25	6400	+ 5
3185	55	1805	1325	6.1	2.12	1415	170	1245	5.6	2.16	1.30	8000	+ 2
2885	40	1595	1250	6.1	1.80	1265	110	1155	5.6	1.82	1.10	7500	+ 1
2780	40	1500	1240	6.7	1.87	1150	110	1040	6.0	1.76	1.15	6800	− 6
1985	30	1105	850	6.3	1.26	885	100	785	5.5	1.33	0.98	6300	+ 6
4305	50	2355	1900	7.8	2.73	1805	120	1685	6.8	2.78	1.50	8000	+ 2
3240	25	1785	1430	7.8	2.71	1350	90	1240	6.8	2.68	1.35	5500	− 1
2765	25	1465	1275	6.6	2.74	1155	90	1065	5.5	2.75	1.42	6000	0
2650	55	1445	1150	8.5	1.06	1135	180	955	6.8	1.11	1.05	8000	+ 5
3080	30	1690	1360	7.1	3.44	1380	110	1270	6.2	3.67	1.65	5500	+ 1
3145	35	1720	1390	7.5	3.45	1340	110	1230	6.8	3.37	1.80	5800	− 2
2720	35	1535	1150	7.1	2.08	1135	110	1025	6.2	2.12	1.50	7000	+ 2
3500	35	1890	1575	7.9	2.72	1480	130	1350	6.8	2.70	1.50	6600	− 1
3210	40	1775	1395	7.6	1.68	1365	130	1235	6.6	1.71	1.10	7200	+ 2
3110	40	1670	1400	9.3	1.22	1290	100	1190	7.2	1.34	1.00	7400	+10

Abbreviations—J.V., jugular vein; COR., correction for radiation from large vessels in region of right ventricle; P.A., pulmonary artery; R.H., right heart; C.O., cardiac output; P.V., pulmonary vein; R.A., root of aorta; L.H., left heart; T.t., transit time for bolus; B.V., blood volume; EQUIL., equilibrium; DIFF., difference in cardiac outputs calculated for left heart and right heart in per cent of right heart cardiac output.

[1]Cardiac outputs were calculated by the formula cited in the text. Counts for the right heart or left heart were converted to counting rates using transit times.

area obtained from a tracing following injection into the pulmonary artery is noted in Column Three. In Column Four the area related to tagged albumin passage through the right heart is obtained when the values in Columns Two and Three are subtracted from the value in Column One. Column Five lists the transit time for the right heart. Column Six is the actual area of the curve recorded from injection of the ^{131}I into the pulmonary vein. The Seventh Column is the actual area obtained from the radiocardiogram after the bolus has been injected into the root of the aorta. The Eighth Column which is the difference between Columns Six and Seven, represents radioactivity recorded during passage of ^{131}I through the left heart. The cardiac output for the right and left heart obtained with a single position of the probe and calculated from multiple serial injections are in agreement, Column Ten. The areas for the right and left heart following a single injection and calculated, when possible, by the method indicated in Figure 4 are in better agreement, since the use of fewer injections reduces the initial backgrounds for the trace and prevents some of the complications of an initially high pre-injection background radioactivity.

In a second set of experiments, the influence of the geometry on recording during equilibrium was investigated. In an open-chest preparation, the heart was stabilized in a pericardial cradle. Several radiocardiograms were taken successively with a sufficient interval between each to allow for equilibrium distribution of tagged albumin. After equilibrium distribution was reached, the hilus of each lung was simultaneously clamped at the peak of inflation of the lungs with

TABLE II

RADIOACTIVE BACKGROUND RECORDED FROM THE LUNGS AFTER EQUILIBRIUM DISTRIBUTION OF ^{131}I LABELED SERUM ALBUMIN

A_{eq} *CPM*	A^1 *CPM*	A_{eq}-A^1 *CPM*	*Change* %
Probe collimated over arch of aorta			
72,000	64,000	8,000	11
70,000[2]			
Probe collimated over the heart			
68,000	61,000	7,000	10
81,000	73,400	7,600	9
54,000	49,100	4,900	9
47,000	44,100	2,900	6
Probe collimated over notch in median border left lung			
44,000	42,400	1,600	4
37,000	36,000	1,000	3
59,000	57,900	1,100	2

[1]Activity after lungs removed

[2]Activity after lungs returned to approximate original position

angiotribe forceps. The equilibrium activity recorded was measured as a bucking voltage required to center the recording pen at the center of the graph. A second set of clamps was placed between the first set and the heart and the tissue between the two clamps was severed. The lungs were removed from the vicinity and the bucking voltage was redetermined. The radioactivity removed with the lungs was calculated as the ratio of the difference in bucking voltage to the initial bucking voltage[1].

In Table II the results of these experiments are indicated. The presence of radioactivity in the lungs contributed from two to eleven per cent of the radioactivity recorded in the equilibrium portion of the radiocardiogram prior to removal of the lungs. Variations over such a wide range represented variations in the amount of lung tissue included in the field of the detector. The second set of experiments indicated that radioactivity from regions of the circulation not related to the cardiac portion of the radiocardiogram contributed to radioactivity recorded in the equilibrium portion of the ^{131}I radiocardiogram.

DISCUSSION

The status of estimates of circulation obtained by external or indirect measurements of radioactivity concentrations utilizing a radiocardiograph has been given by Conn (10). His summary indicates the unfavorable experience with systematic errors of fifty per cent or greater, and the more favorable experience will less than twenty-five per cent and occasionally less than ten per cent systematic error. His major objections to the method are the variations caused by the geometry of the detector system and the differences for the mean transit time of radioactive tagged material in the different regions of circulation scanned by the detector.

Powers and Sevelius (4) have presented rigorous mathematical proofs based on the dye-dilution theory. Zierler (11) and Gonzalez-Fernandez (12) have written articles on the application of the mean-transit-time theory to calculations from time concentration records. The mathematical considerations are summarized in the following equation:

$$C.O. = B.V. \times aA_{eq}/a'A_{avg}$$

C.O. - cardiac output, B.V. - blood volume, a - geometry factor, A - activity in CPM, eq - equilibrium, avg - average.

The dye-dilution principle restricts calculations to data in which the tagged material is mixed throughout the monitored volume, with no change in mass of tagged material or monitored volume at the time that A_{eq} and A_{avg} are recorded. Mean-transit-time theory restricts calculations to conditions under which the tagged material follows the same paths as the monitored volumes; and the mean transit time, velocities, and paths for movement of radioactive tagged material are similar to those of blood.

Experimental data in this study aid critical evaluation of many of the factors cited above. A_{eq}/A_{avg} is a ratio, a fractional blood volume, according to Shipley

[1]A potentiometer linear to within one per cent was used to regulate bucking voltage.

(2). Or it is a measured value multiplied by a calibration factor, B.V. x A_{eq}/A_{avg}, according to Conn (10). Regardless of the point of view used to develop the mathematical basis, the radioactivities are being determined at two different times. Therefore, the geometry factors (a) and (a′) should be included in the equations to emphasize this consideration even though a/a′ is assigned the

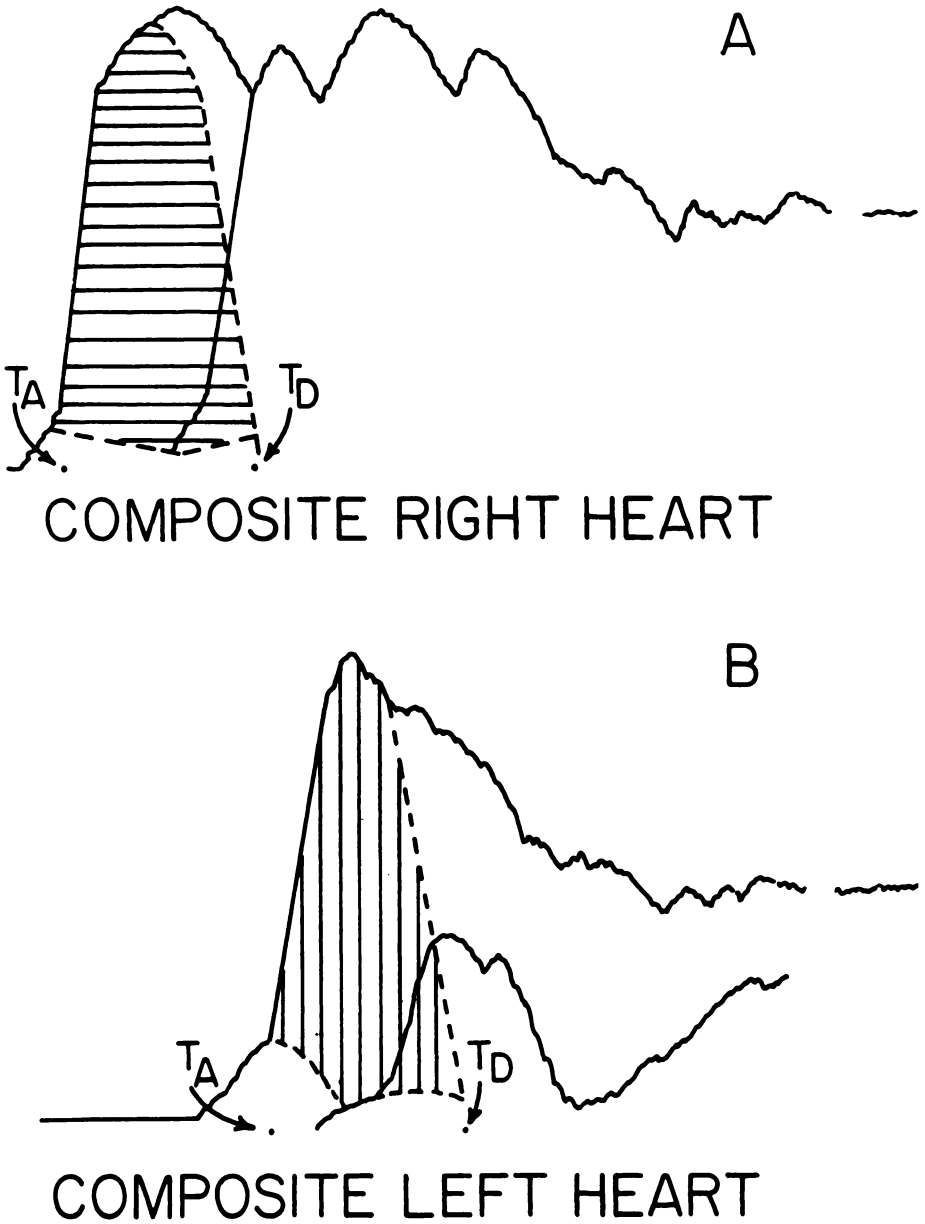

Fig. 3. Analysis of radiocardiograms to identify recorded background radiation in the record and to establish the activity recorded during a single passage through the heart.

arbitrary value of one. It is doubtful that it will be possible to show for external counting that a/a′ equals one, *i.e.*, that regions of circulation, the detector field, and the tagged material distribution are identical at both times of recording. The value will approach unity for a/a′ if the record of radioactivity used in calculation represents passage through a single vessel or chamber within the detector field.

It is possible to obtain data which represents passage of radioactive material through a single chamber of the heart. Taplin and his associates (13) have reported a method which yields a radiocardiogram of the right heart. Data from our experiments and analysis indicate that under some conditions, when separate peaks related to circulation of ^{131}I in specific regions of circulation are present, it is possible to correct the radiocardiogram to discount radioactivity from other regions. This method, illustrated in Figure 4, is a graphic method in which the radioactivity recorded from the right heart or from the left heart is approximated by extrapolation. The right heart area is found when a line parallel to the abcissa is extended from the end of the initial small rise in the appearance curve to establish the base. This procedure corrects for background activity caused by ^{131}I in the large veins and the large pulmonary arteries. The curves representing the disappearance of the tagged bolus from the right heart and its appearance in the lungs are extrapolated from the peaks appearing in the radiocardiograms. The appearance curve for the lungs is subtracted from the disappearance curve for the right heart to establish the right boundary of the curve, representing passage through the right heart. The area included between the original curve and the graphed line is an approximation to radioactivity recorded during circulation through the right heart. The area for the left heart is probably less reliably established by extrapolation. The base for the left heart area is presumed to be identical with the base used for the right heart area. The left border of the area is established from the peak of circulation through the left heart and an extrapolated line representing the disappearance of ^{131}I in the left heart. The right border of the curve is obtained by extrapolation of the descending limb of the curve for circulation through the left heart. Transit time for either of the curves is obtained from the intersection of the ascending and descending limbs, representing circulation through the heart, with the base line. An error may be introduced in calculation if the left heart circulation is used for calculation with this method, because radiocardiograms usually do not contain information sufficient to establish an accurate transit time for the left heart.

Data from this study and the earlier data of Huff (3) indicate that the accuracy of cardiac output estimations is improved when the radiocardiogram represents recording from a single portion of the circulation. Both dye-dilution principle and mean-transit-time theory imply recording from a single chamber. Presence of radioactive material at different times in the large veins, chambers of the heart, pulmonary circulation and aorta within the detector field recorded as a single passage of the tagged bolus would seem to invalidate the use of calculations based on the dye-dilution principle. Similarly, mean-transit-time theory requires that the tagged material follow the same path as the normal blood flow and that transit time for tagged particles be reasonably uniform for a valid

calculation. Passage through a single chamber, rather than through variable paths at different rates of flow improve the validity of calculation. Thus, a small amount of material in circulation with long transit time will not contribute to records obtained from material in an area of the circulation associated with rapid flow.

CONCLUSION

In conclusion, data reported herein and theoretical considerations indicate that estimates of cardiac output obtained through the use of radiocardiography can be improved. Background radiation must be reduced during the recording and must be discounted during the analysis of the radiocardiogram. The detector probe is collimated to minimize the inclusion of radiation from the lungs. In addition, the contributions from the large vessels, lungs and other side of the heart identified in the record, establish the boundaries of an area in the radiocardiogram which represents passage of the tagged bolus through a single side of the heart. Calculations limited to the portion of the record representing passage of the radioactive material through a single side of the heart are compatible with the restrictions implicit in the equations.

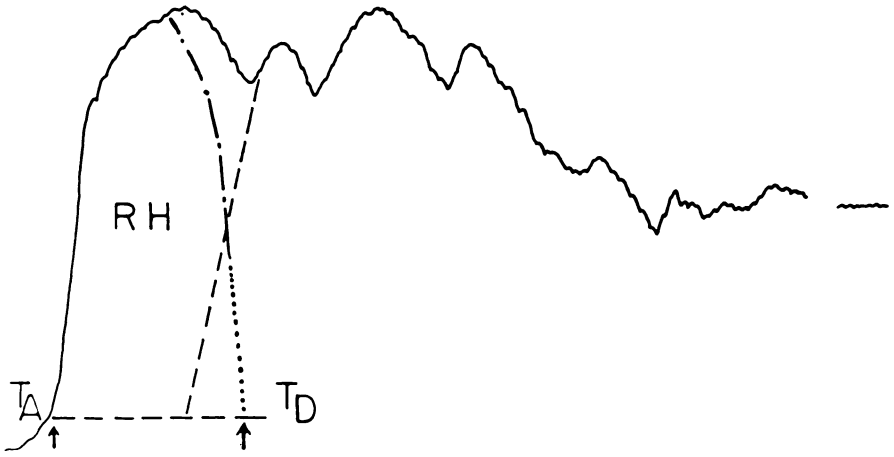

Fig. 4. A method proposed for graphic analysis of conventional radiocardiograms to identify contribution of radioactive background. The analysis provides an approximation of the activity recorded during passage of the radioactive material through one side of the heart.

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