DETERMINATION OF CARDIAC OUTPUT BY RADIOISOTOPE ANGIOGRAPHY AND THE IMAGE-INTENSIFIER SCINTILLATION CAMERA

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In previous reports from our laboratory (*1,2*) and those of others (*3–6*), it has been suggested that dynamic studies of cardiac blood flow with ^{99m}Tc and the scintillation camera might be of clinical utility. The recent development of the image-intensifier scintillation camera, also capable of recording wide-field radioisotope images from the precordium and incorporating a system for video storage and analysis (*7,8*), has permitted us to extend the scope of these studies to quantitative assessment of cardiac output in animals and man. The present communication reports our initial findings.

MATERIALS AND METHODS

The technique used throughout this study was the single-injection indicator-dilution method with indirect sampling (*9*). Seven patients and six dogs were studied.

Technetium-99m-human serum albumin (specific activity 3–5 mCi/ml), prepared by the method of Kazem and Maier-Borst (*10*), was selected as the

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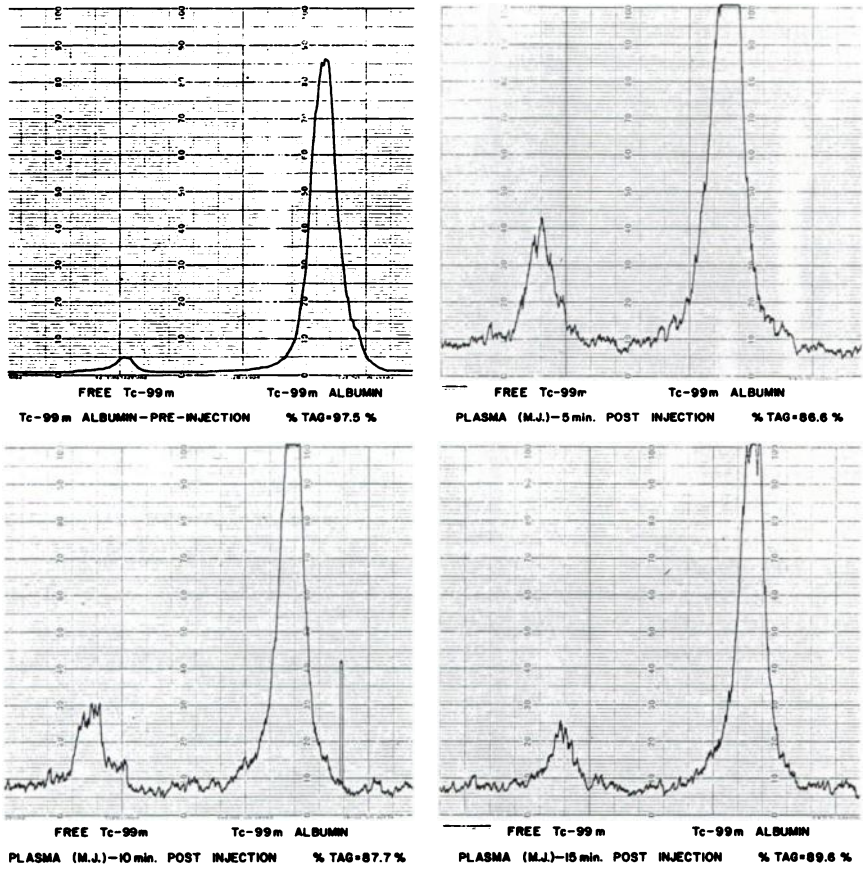

FIG. 1. Radiochromatogram of ^{99m}Tc-albumin before and after intravenous injection.

optimum high specific-activity preparation available to fulfill the necessary criteria for an indicator (*9*); i.e., that it remain entirely in blood between the points of injection and sampling and that it disperse uniformly in blood. The important time periods of the indicator dilution display are: (A) the initial 10–15 sec which include the first passage of indicator through the heart (*1,2*), and (B) the time at which isotopic equilibrium is assumed to be achieved, 10 min postinjection of the bolus (*11*).

Stability of the injected ^{99m}Tc-albumin was tested by ascending thin-layer chromatography (Eastman chromagram sheet 6065) of serially obtained plasma samples in 85% methanol.

The image-intensifier scintillation camera used in these studies has been described in detail elsewhere (*7,8*). The quantifying device, a television "cursor" system (*3*) drives a strip-chart recorder; the strip-chart readout permits digital display of the intensity of radiation detected in the discrete field of view encompassed by the cursors. A 35-mm stop-motion camera mounted on the oscilloscope permits photography of events on the oscilloscope face in any one of eleven different time intervals, ranging from 1/60 sec to 5 min. This permits replay and integration of the entire sequence as often as is necessary to quantitate radioactivity in any area of interest.

RESULTS

The radiochromatogram shown in Fig. 1 indicates an initial rapid breakdown of ^{99m}Tc-albumin in vivo. However, it would appear that following this initial breakdown (5 min postinjection, Fig. 1), no further breakdown occurs during the next 10 min during which time an equilibrium plasma sample has already been obtained and the study completed.

In calculating cardiac output (vide infra), we have assumed that no significant breakdown of labeled albumin occurs during the first passage of the radioactive bolus through the heart (from which events the radiation intensity curves are obtained), and the height of the curve at equilibrium has been corrected for a 10% loss of tag (based on radiochromatograms on three batches of ^{99m}Tc-albumin encompassing eight studies in normal subjects—Table 1).

Mongrel dogs were studied immediately after cardiac output had been determined using the cardiogreen direct-sampling indicator-dilution technique (*9*). Immediately before the ^{99m}Tc-albumin cardiac output study, a blood volume was obtained using radioiodinated albumin (*12,13*). The animal was then positioned under the detector, and 3 mCi

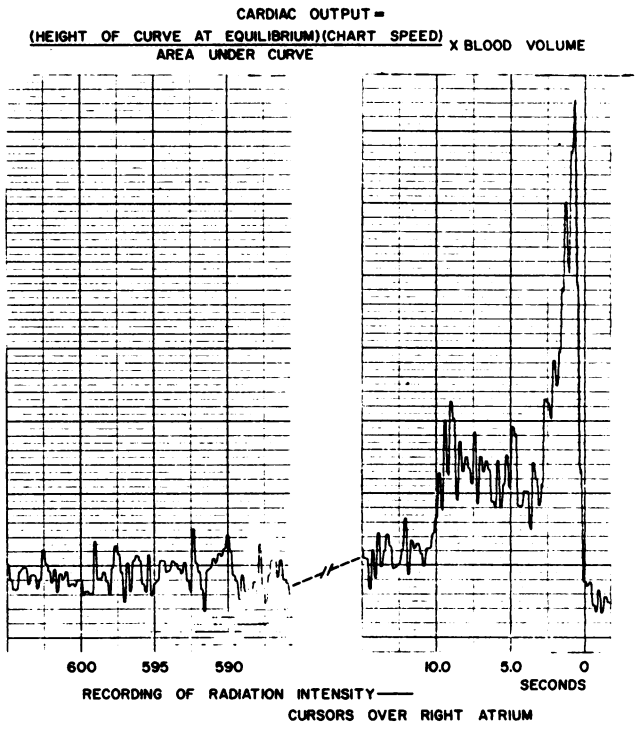

FIG. 2. Intensity curve, cursors over right atrium, obtained from ^{99m}Tc-albumin study performed in mongrel dog.

TABLE 1. LOSS OF ^{99m}Tc-ALBUMIN TAG OVER TIME

$$\%\ \text{tag} = \frac{^{99m}\text{Tc tagged albumin}}{^{99m}\text{Tc tagged albumin} + \text{free } ^{99m}\text{Tc}} \times 100$$

^{99m}Tc-albumin batch No.	Patient No.	time (min) 0	5	10	15	% loss of tag time (min) 0–5	0–10	0–15
1	1	97.5	86.6	87.7	89.6	11.2	10.0	8.1
	2	97.5	87.2	88.5	87.6	10.5	9.2	10.1
2	3	95.3	85.1	84.8	84.6	10.7	11.0	11.2
	4	95.3	84.4	85.2	86.1	11.4	10.6	9.7
3	5	95.6	85.6	85.3	84.7	10.4	10.8	11.4
	6	95.6	84.8	85.6	86.1	11.3	10.4	9.9
	7	95.6	85.1	84.8	85.5	10.9	11.3	10.6
	8	95.6	85.2	84.5	85.8	10.9	11.6	10.3
					mean % loss of tag	10.9	10.6	10.2

^{99m}Tc-albumin were injected through an indwelling catheter placed in the jugular vein. The passage of the bolus through the heart was recorded on videotape. Thereafter, the tape was replayed, areas of interest localized, and intensity recordings in these areas obtained. Figure 2 shows a representative intensity curve obtained from an area of interest in the right heart. The descending limb of the curve was then extrapolated on semilog paper and replotted. The area under the curve was determined by planimetry. Cardiac output was calculated using the formula (*11*):

$$\text{Cardiac output (liters/min)} = \frac{[\text{Height of curve at equilibrium}]\ [\text{Chart speed (in./min)}]}{\text{Area under curve [in.}^2\text{]}} \times \text{Blood volume [liters].}$$

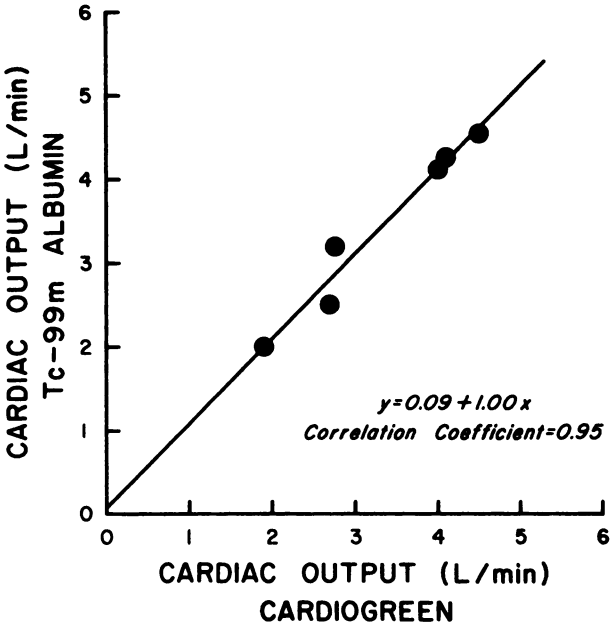

FIG. 3. Correlation between sequential cardiac outputs as determined by cardiogreen technique and isotopic method in six mongrel dogs.

Figure 3 shows the correlation between sequential cardiac outputs as determined with the cardiogreen technique and the isotopic method in six dogs. As can be seen from the correlation coefficient of 0.95, $p < 0.02$, the agreement between the two techniques is excellent. The statistical identity of these measurements is further corroborated by paired t-test: $t = -1.25$, at 90% confidence level $-2.015 < t < 2.015$. The sensitivity of the isotopic method to change in cardiac output is attested to by sequential dye and radionuclide output measurements before and after 200 cc phlebotomy in one of the study dogs, viz, control output: cardiogreen, 2.7 liters/min, ^{99m}Tc, 2.3 liters/min; postphlebotomy output: cardiogreen, 1.9 liters/min, ^{99m}Tc, 1.4 liters/min.

Seven patients (Table 2) undergoing cardiac catheterization were also studied by the isotopic technique. In two instances, the isotopic study was carried out with the catheter still in place; in the remainder, the study was performed with a concentrated bolus injection into an antecubital vein (*1,2*) 1 day after cardiac catheterization. All studies were carried out in the anterior projection. To delineate the field of view, three ^{99m}Tc markers were placed on the chest at the suprasternal notch, the 5th intercostal space at the right sternal border, and at the point of maximum impulse. Three to 5 mCi ^{99m}Tc-albumin were injected either directly into the cardiac catheter or into an antecubital vein (*1,2*). Figure 4 shows the first 2.5 sec of a typical study. Note the cursors in position over the enlarged right atrium. Cardiac output was determined in the same manner as described for the dog studies. Figure 5 indicates the excellent correlation between cardiac output in the seven patients studied to date as determined by the cardiogreen procedure and that determined by the isotopic technique (correlation coefficient 0.8, $p < 0.05$). Analysis of these data by paired t-test again confirms their statistical identity ($t = -0.52$, at 90% confidence level $-1.943 < t < 1.943$).

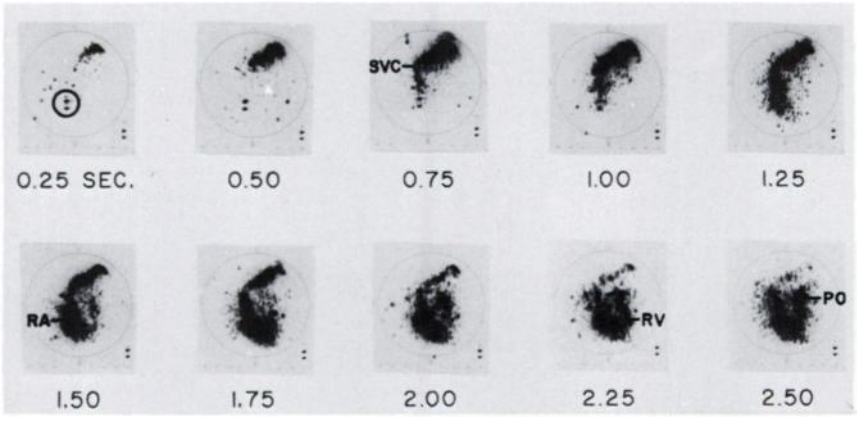

FIG. 4. Image-intensifier scintillation camera ^{99m}Tc-albumin cardiac blood-flow study in patient LP. SVC = superior vena cava; RA = right atrium; RV = right ventricle; PO = pulmonary outflow tract. Small solid circle in 0.25-sec photo encloses cursors placed over (enlarged) right atrium.

TABLE 2. DIAGNOSES AND WAY IN WHICH ISOTOPIC STUDY WAS PERFORMED IN SEVEN PATIENTS STUDIED

Patient	Diagnosis	Site of isotope injection
JP	No confirmed cardiac disease	Catheter in inferior vena cava
JC	Mitral stenosis; aortic regurgitation	Left antecubital vein
JM	Aortic stenosis and regurgitation	Left antecubital vein
PM	Aortic regurgitation, severe	Right antecubital vein
LP	Status postsurgical closure of left-to-right atrial shunt	Catheter in superior vena cava
CP	Pseudo-coarctation of aorta	Left antecubital vein
GW	No confirmed cardiac disease.	Left antecubital vein

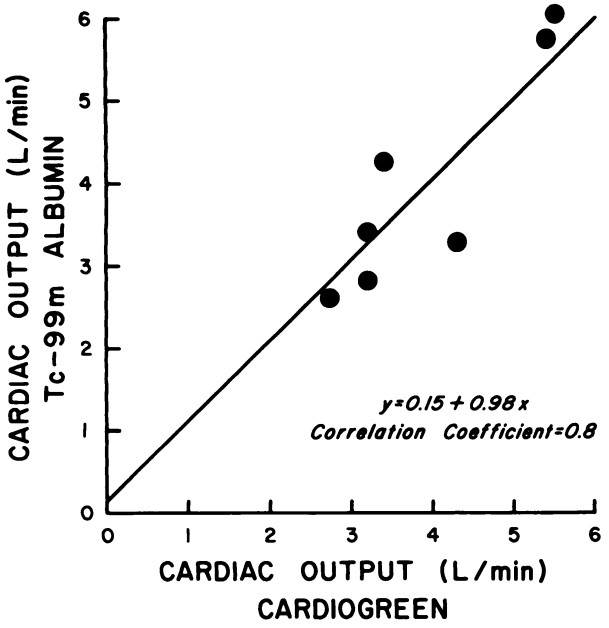

FIG. 5. Correlation between cardiac outputs in seven patients as determined by cardiogreen technique and by ^{99m}Tc-albumin procedure.

DISCUSSIONS AND CONCLUSIONS

There have been a number of publications (*14–17*) reporting the determination of cardiac output by external monitoring of cardiac output of radionuclides using collimated scintillation probes. Accuracy of probe placement is critical to each of these methods, and our own experience (*2*) suggests that use of a scintillation camera obviates this potential source of serious error. In addition, the instantaneous visualization of the passage of the radioactive bolus through the cardiac chambers affords substantive qualitative information and offers the potential for measurement of, e.g., ventricular volume (*4*).

Herbert et al (*18*) have reported an initial rapid breakdown of ^{99m}Tc-albumin in vivo. The present studies confirm their findings but suggest that continued breakdown does not occur beyond 5 min. It must be noted, however, that our data do not preclude the possibility that the subsequent constancy of the ratio of labeled albumin to $^{99m}TcO_4^-$ might, in part, reflect passage of $^{99m}TcO_4^-$ from the intravascular compartment to the extravascular space.

The findings reported herein indicate that accurate quantitative assessment of cardiac output can be obtained by an external monitoring isotopic method with a scintillation camera which need not involve cardiac catheterization. Use of ^{99m}Tc-albumin by systemic injection in this manner has caused no untoward side effects of hemodynamic disturbances. Studies are presently under way in patients with intracardiac shunts to determine the potential and limitations, if any, of this approach.

REFERENCES

1. BURKE G, HALKO A, GOLDBERG D: Radiopulmonary cardiography with the scintillation camera and ^{99m}Tc-pertechnetate. *J Nucl Med* 9: 306–307, 1968

2. BURKE G, HALKO A, GOLDBERG D: Dynamic clinical studies with radioisotopes and the scintillation camera: IV. ^{99m}Tc-sodium pertechnetate cardiac blood flow studies. *J Nucl Med* 10: 270–280, 1969

3. MASON DT, ASHBURN WL, HARBERT JC, et al: Rapid sequential visualization of the heart and great vessels in man using the wide-field Anger scintillation camera. Radioisotope angiography following the injection of technetium-99m. *Circulation* 29: 19–28, 1969

4. MULLINS CB, MASON DT, ASHBURN WL, et al: Determination of ventricular volume by radioisotope angiography. *Amer J Cardiol* 24: 72–78, 1969

5. STRAUSS HW, HURLEY PJ, ZARET BL, et al: Measurement of systolic and diastolic cardiac chamber volumes without cardiac catheterization. *J Nucl Med* 11: 364–365, 1970

6. TREVES S, LANGE RC, FREEDMAN GS: Study of cardiopulmonary hemodynamics using a gamma camera and a computer. *J Nucl Med* 11: 369–370, 1970

7. TER-POGOSSIAN MM, NIKLAS WF, BALL J, et al: An image tube scintillation camera for use with radioactive isotopes emitting low-energy photons. *Radiology* 86: 463–469, 1966

8. FREEDMAN GS, GOODWIN PN, JOHNSON PM, et al: An evaluation of the image-intensifier scintillation camera with some comparisons to the single crystal camera. *Radiology* 92: 21–29, 1969

9. GUYTON AC: *Circulatory Physiology: Cardiac Output and its Regulation.* Philadelphia, WB Saunders Co, 1963, pp. 40–59

10. KAZEM I, MAIER-BORST W: Preparation of human serum albumin labeled with ^{99m}Tc. *J Nucl Med* 5: 285–288, 1964

11. GORTEN RJ, STAUFFER JC: A study of the techniques and sources of error in the clinical application of the external counting method of estimating cardiac output. *Amer J Med Sci* 238: 274–279, 1959

12. WILLIAMS JA, GRABLE E, FINE J: A semi-automatic instrument for measuring blood volume. *JAMA* 178: 1097–1098, 1961

13. BLAHD WH: *Nuclear Medicine,* New York, McGraw-Hill Book Co, 1965, pp. 531–534

14. MACINTIRE WJ, STORAASLI JP, KRIEGER H, et al: I^{131}-labeled serum albumin: its use in the study of cardiac output and peripheral vascular flow. *Radiology* 59: 849–857, 1952

15. SHREINER BF, LOVEJOY FW, YU PN: Estimation of cardiac output from precordial dilution curves in patients with cardiopulmonary disease. *Circ Res* 7: 595–601, 1959

16. GLICK G, SCHREINER BF, LURIA MN, et al: Determination of cardiac output by means of radioisotope dilution technique. *Progr Cardiovasc Dis* 4: 586–614, 1962

17. RAZZAK MA, BOTTI RE, MACINTIRE WJ, et al: Consecutive determination of cardiac output and renal blood flow by external monitoring of radioactive isotopes. *J Nucl Med* 11: 190–195, 1970

18. HERBERT RJT, HIBBARD BM, SHEPPARD MA: Metabolic behavior and radiation dosimetry of ^{99m}Tc-albumin in pregnancy. *J Nucl Med* 10: 224–232, 1969