DYNAMIC CLINICAL STUDIES WITH RADIOISOTOPES AND THE SCINTILLATION CAMERA: IV. ^{99m}Tc-SODIUM PERTECHNETATE CARDIAC BLOOD-FLOW STUDIES

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The recent availability of short-lived radionuclides such as ^{99m}Tc-sodium pertechnetate and the demonstrated (*1–3*) ability of the scintillation camera to perform dynamic clinical studies with radioisotopes has led us to consider techniques with which perfusion of major organs can be studied without risk to the patient.

Rosenthall (*4*) has suggested that scintillation-camera studies with ^{99m}Tc might be of value for visualizing cardiac blood flow. The present investigation has been directed toward determining cardiac chamber size and delineating normal and abnormal blood-flow patterns through the heart and great vessels. In addition, correlative studies have been performed to obtain comparisons between visually determined right heart-to-left heart transit times and those obtained by conventional dual-probe radiopulmonary cardiography (*5*). The results validate the clinical utility of this approach and are presented in detail.

MATERIALS AND METHODS

The scintillation camera used in this study has been described in detail elsewhere (*1*). The instrument is now equipped with a 70-mm stop-motion camera replacing the conventional viewing port. The camera uses an electronic film advance, permitting accurate exposures ranging from 1 sec to 20 min.

The supine patient was positioned under the 11.5-in. camera crystal so that the entire heart and a significant portion of the lung fields were located in the field of view. To ensure proper positioning and to obtain anatomical landmarks for the study, ^{99m}Tc point-source markers were placed at the suprasternal notch, the fifth left intercostal space in the midclavicular line and the fifth right intercostal space at the right sternal border. A photograph of the markers in place was obtained on the 70-mm film (Fig. 1), the markers were removed and 30 mCi ^{99m}Tc was administered intravenously in a "concentrated" bolus as described previously (*3*). At the time of release of the blood pressure cuff (i.e., the time of entry of the bolus), the 70-mm camera was activated, and a ^{99m}Tc point-source marker was inserted momentarily into the field of view of the camera to record on film the starting time of the study. The film was electronically advanced every second for approximately 30 sec. When determination of individual chamber size rather than measurement of transit time was the object of the study, left anterior oblique and right anterior oblique projections have also been used.

Patients with no clinical or laboratory evidence of heart disease were selected as controls, and informed consent was obtained. Patients with a variety of cardiac and extracardiac intrathoracic lesions were also studied as described below.

Corollary ^{99m}Tc studies using a modification of the double-probe technique (radiopulmonary cardiography) of Johnson *et al* (*5*) were also performed in a number of these patients immediately before the scintillation-camera study. For this purpose, matched scintillation probes with wide-angle collimation were used. The cardiac probe was placed in the fifth intercostal space midway between the point of maximal impulse and the sternum while the lung monitor was placed in the fifth intercostal space immediately to the right of the midclavicular line. Both probes were perpendicular to the skin surface. A dose of 1 mCi ^{99m}Tc was injected using the concentrated bolus injection technique (*3*). A scale range of 300 K, time constant of 0.3 sec and a chart speed in 12 in./min were uniformly used.

CLINICAL APPLICATION

Correlative scintillation-camera cardiac blood-flow studies and dual-probe radiopulmonary cardiography with ^{99m}Tc. To date 25 subjects with no clinical or laboratory evidence of heart disease have been studied in this fashion. A representative film sequence is

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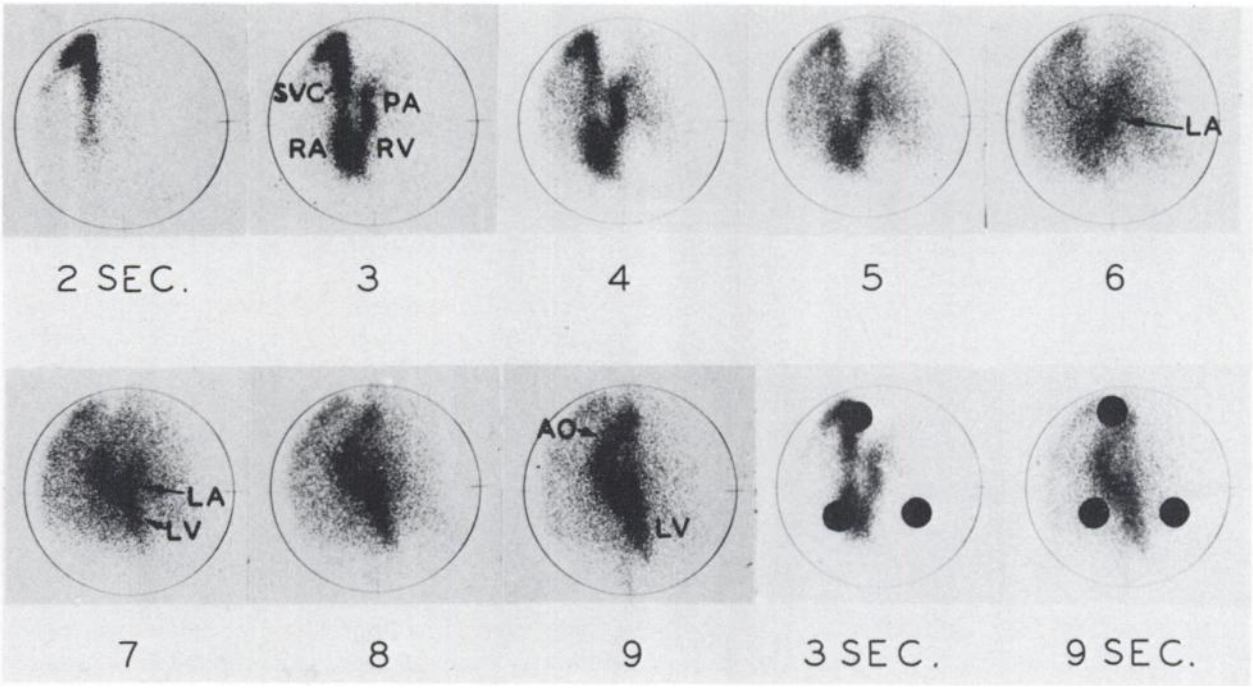

FIG. 1. Scintillation-camera ^{99m}Tc cardiac blood-flow study in normal subject. SVC = superior vena cava, RA, LA = right, left atrium, RV, LV = right, left ventricle, PA = pulmonary artery, AO = ascending aorta. Solid circles in last two frames represent sites of ^{99m}Tc point-source markers used in positioning patient.

shown in Fig. 1. The radioactive bolus is seen entering the superior vena cava at 2 sec postinjection, and in the next frame the right atrium and ventricle are delineated. The radionuclide is seen entering the lung fields at 4 sec; 2 sec later its first appearance in the left atrium is noted and at 7–9 sec the left ventricle and ascending aorta are well delineated. This film sequence indicates that the transit time of the radioactive bolus from the right heart to lung is 1 sec and from the lung to left heart 2 sec.

The curves obtained in the dual-probe radiopul-

TABLE 1. ARTERIAL AND VENOUS SEGMENTS OF CENTRAL TRANSIT TIME DETERMINED BY COMPUTATION (RADIOPULMONARY CARDIOGRAM) AND BY INSPECTION OF SCINTILLATION-CAMERA FILM SEQUENCE IN 25 NORMAL SUBJECTS

	Radiopulmonary cardiogram Mean transit time (sec)			Scintillation camera Transit time (sec)		
	RH → LH	RH → lung	lung → LH	RH → LH	RH → lung	lung → LH
Mean	5.48	3.19	2.29	3.6	1.2	2.4
s.d.	1.23	0.94	0.97	0.68	0.35	0.68
Range	3.26–8.32	2.09–5.97	0.59–3.96	2.0–5.0	0.5–2.0	1.0–4.0

TABLE 2. COMPARISON OF CENTRAL TRANSIT TIMES IN NORMAL SUBJECTS AND PATIENTS WITH LEFT-SIDED VALVULAR LESIONS

	Computed mean transit time (sec)			Camera transit time (sec)		
	RH → LH	RH → lung	lung → LH	RH → LH	RH → lung	lung → LH
Normal (N = 25)	5.5 ± 1.2	3.2 ± 0.9	2.3 ± 1.0	3.6 ± 0.7	1.2 ± 0.4	2.4 ± 0.7
Abnormal* (N = 11)	10.1 ± 3.6	4.7 ± 1.4	5.5 ± 2.7	5.0 ± 1.3	1.6 ± 0.5	3.5 ± 1.0
p for difference normal-abnormal	< 0.001	< 0.01	< 0.001	< 0.01	< 0.01	< 0.01

* Patients with stenosis and/or insufficiency of mitral or aortic valve.

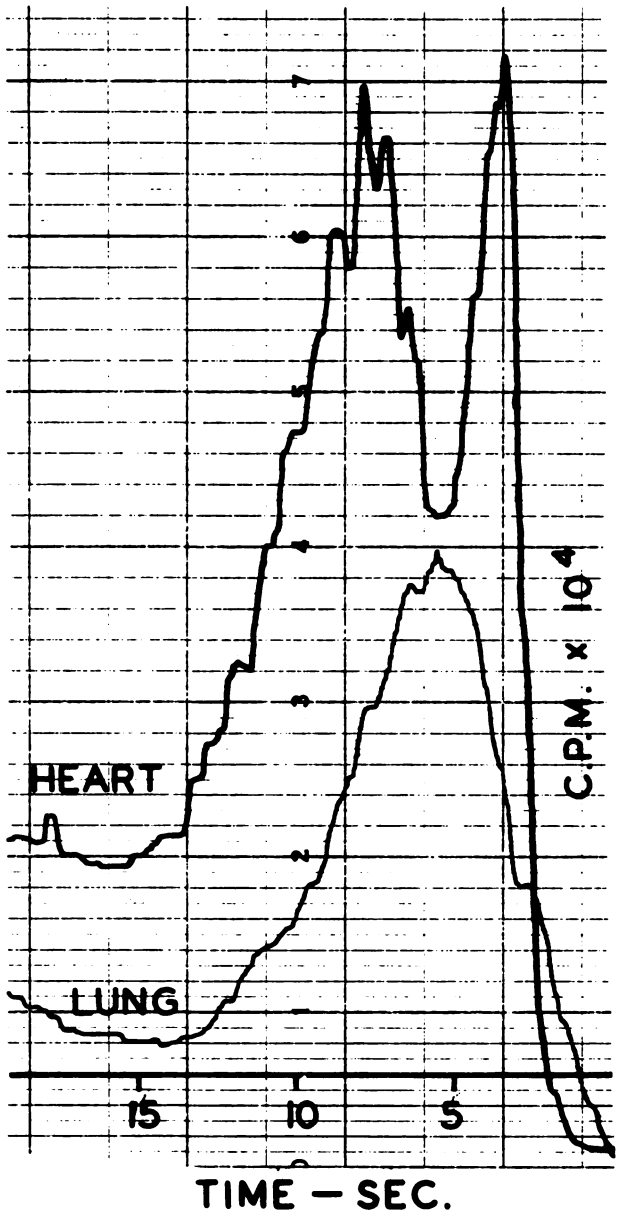

FIG. 2. Radiopulmonary cardiogram in normal subject.

monary cardiogram on the same patient are shown in Fig. 2. The right-heart curve has a rapid rise and fall and is followed immediately by the more gradual left-heart curve. The peak of the lung curve falls midway between the peaks of the right- and left-heart curves.

Mean transit time between the various segments of the central circulation was calculated by applying the Hamilton formula (*6*) to the analysis of the dilution curves recorded simultaneously over the right heart, lung and left heart (*5*). The average time M taken by an indicator (dye or radionuclide) to go through a system can be calculated from the time-concentration curve by the formula

$$M = \frac{T_1C_1 + T_2C_2 + \ldots + T_nC_n}{C_1 + C_2 + \ldots + C_n}$$

in which the concentration readings are C_1, C_2, . . . C_n at times T_1, T_2, . . . T_n. M is the T coordinate of the center of gravity of the curve. Mean transit times from right heart to lung and lung to left heart calculated from curves in Fig. 2 were 2.6 and 2.1 sec, respectively.

A detailed comparison between computed mean transit time (dual-probe radiopulmonary cardiography) and transit-time estimates obtained by inspecting the film sequence (scintillation camera) is seen in Table 1. Note that the computed right-heart-to-lung transit time (mean = 3.19 sec ± 0.94 s.d.) significantly exceeds that derived visually (mean = 1.2 sec ± 0.35 s.d.) while the lung-to-left heart transit times are virtually identical in both studies.

A comparison of computed mean transit times and those obtained by inspecting the scintillation-camera film sequence in patients with acquired hemodynamically significant mitral or aortic valvular lesions is detailed in Table 2. There was no clinical evidence of congestive failure in any of the patients at the time of study.

Comparison of these data to those in normal subjects indicates that the prime factor in increased central mean transit time in patients with left-sided valvular lesions is a differential prolongation of lung-to-left heart transit time. As in normal subjects, the major difference between computed and camera transit times is occasioned by the much shorter right heart-to-lung transit time in the camera studies. As Table 2 shows, the transit-time differences between normal subjects and patients with mitral and/or aortic valve disease are highly significant with *both* techniques.

Scintillation-camera ^{99m}Tc cardiac blood-flow studies in patients with congenital heart disease. Four patients with atrial septal defects (ASD) and hemodynamically significant left-to-right shunts have been studied; the following case is illustrative of the findings obtained:

Case 1. A 34-year-old woman with a suspected interatrial septal defect was admitted to Michael Reese Hospital for cardiac evaluation. At right-heart catheterization, the catheter passed easily from the right atrium to the left atrium and into the left ventricle. Veno-arterial dye-dilution curves and selective left-atrial cineangiocardiography confirmed the presence of an atrial-septal defect giving rise to a left-to-right shunt contributing approximately two-thirds of total pulmonary flow.

The scintillation-camera study is shown in Fig. 3. Slight right-atrial and moderate right-ventricular en-

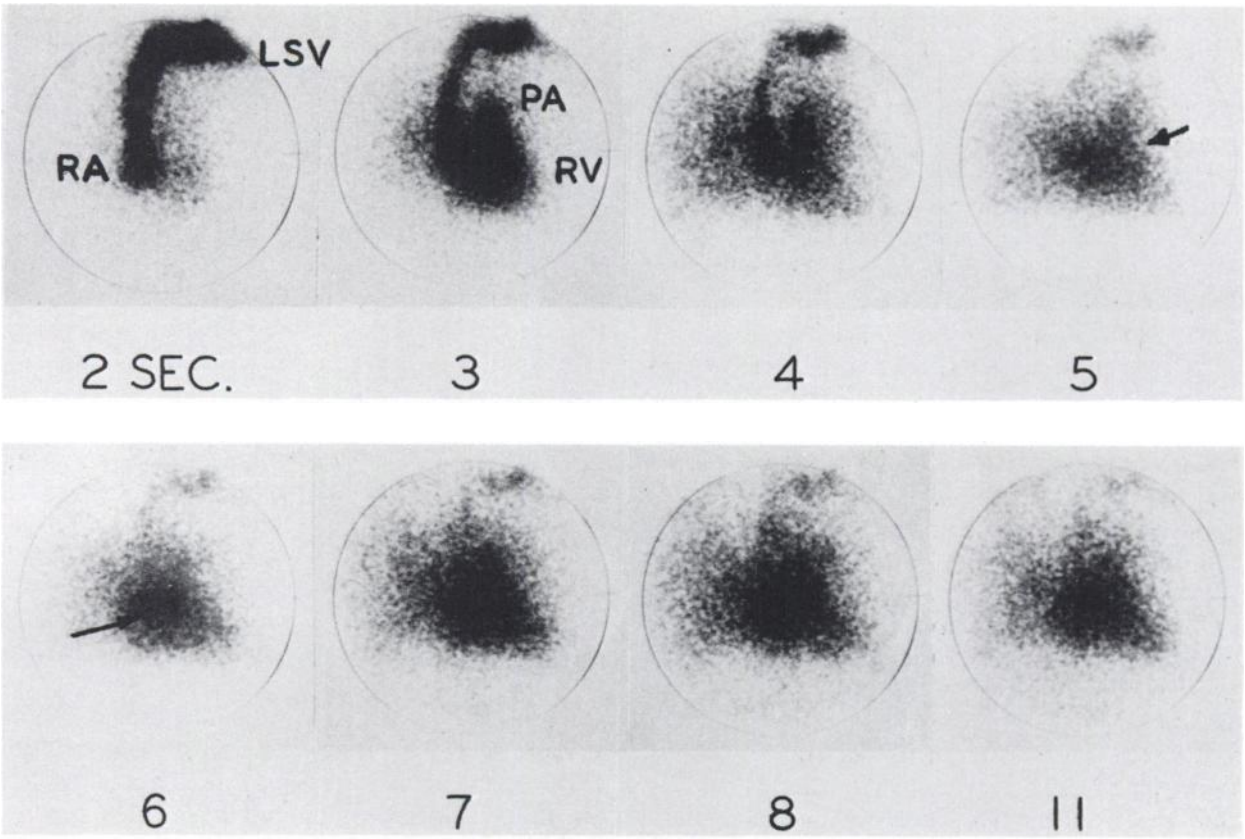

FIG. 3. Cardiac blood-flow study in patient with interatrial septal defect (Case 1). Arrow at 5 sec indicates return of labeled blood to left heart, that at 6 sec shunting of blood to right atrium (see text). LSV = left subclavian vein.

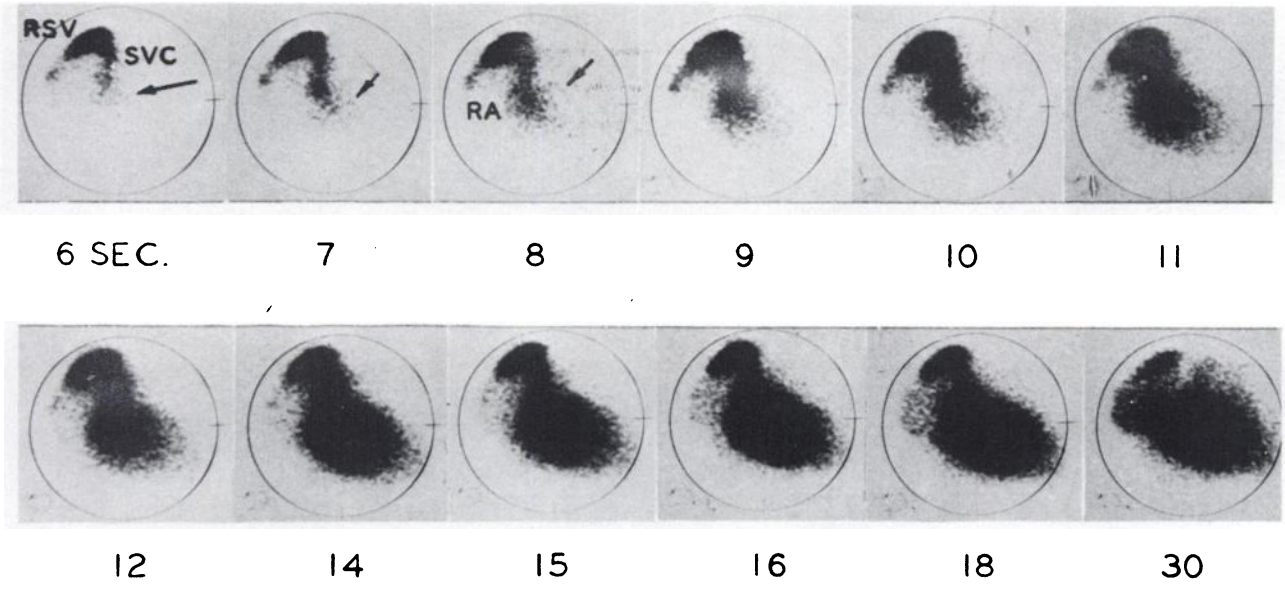

FIG. 4. Cardiac blood-flow study in patient with Ebstein's anomaly (Case 2). Arrows in 6–8-sec films indicate shunting of labeled blood to left atrium (see text). RSV = right subclavian vein.

largement are evident at 2 and 3 sec postinjection, respectively. Radioactivity is seen in the lung fields at 4 sec; in the next film there is increased radioactivity in the area corresponding to the location of the left atrium and left ventricle. Although significant decrease in lung radioactivity is evident at 6 sec, there is now a reaccumulation of radioactivity in the area corresponding to the right atrium, and at 7–8 sec an *increase* in lung radioactivity is evident. At 11 sec postinjection the lung fields are rela-

tively clear; although there is considerable cardiac radioactivity at this time (presumably due to repeated shunting of blood from left to right), left-ventricular filling is never clearly delineated.

One patient with Ebstein's disease was studied:

Case 2. A 54-year-old man was admitted to Michael Reese Hospital for cardiac catheterization. A heart murmur had been present since birth, but the patient had been asymptomatic until the past year when he developed exertional dyspnea.

At right-heart catheterization and selective cineangiocardiography a markedly dilated right atrium was found. Veno-arterial dye-dilution curves indicated a right-to-left shunt at the atrial level in the presence of tricuspid insufficiency; there was systemic arterial desaturation, and it was estimated that the right-to-left shunt constituted approximately 38% of the systemic flow.

The ^{99m}Tc cardiac blood-flow study is shown in Fig. 4. Between 6 and 12 sec postinjection progressive filling of the massive right atrium is seen. In the early films (6–8 sec) spotty isotope accumulation is seen in the region of the left atrium. The first appearance of radioactivity in the lungs is not seen until 15 sec; thereafter there is a gradual increase in lung radioactivity for the remainder of the study, but it remains well below normal in magnitude. No ventricular filling was seen at any time in the study.

One patient with congenital stenosis of the pulmonary valve was studied:

Case 3. A 26-year-old woman was admitted to Michael Reese Hospital for cardiac catheterization. Although a heart murmur had been present since birth, growth and development had been entirely normal and she was asymptomatic.

Chest x-ray revealed a normal-sized heart with aneurysmal dilatation of the pulmonary artery (Fig. 5). The patient underwent right-heart and retrograde left-heart catheterization with pulmonary arteriography; the findings were consistent with severe pulmonary valvular stenosis and revealed poststenotic dilatation of the left pulmonary artery at its origin.

The ^{99m}Tc cardiac blood-flow study is shown in Fig. 5. Moderate right-atrial and right-ventricular enlargement are evident at 2–3 sec postinjection. The marked poststenotic dilatation of the pulmonary artery and retention of radionuclide in this area are clearly evident from 3–7 sec. Maximal uptake of radioactivity in both lung fields is not evident until 7–8 sec.

Left anterior oblique scintillation-camera ^{99m}Tc cardiac blood-flow studies in normal subjects. Because of the inability to clearly delineate the left atrium on the anteroposterior scintillation-camera study, a number of studies were carried out in the standard radiologic left anterior oblique projection. A study of this kind in a normal subject is shown in Fig. 6. The injection was made in the left antecubital vein, and at 1 sec postinjection the left sub-

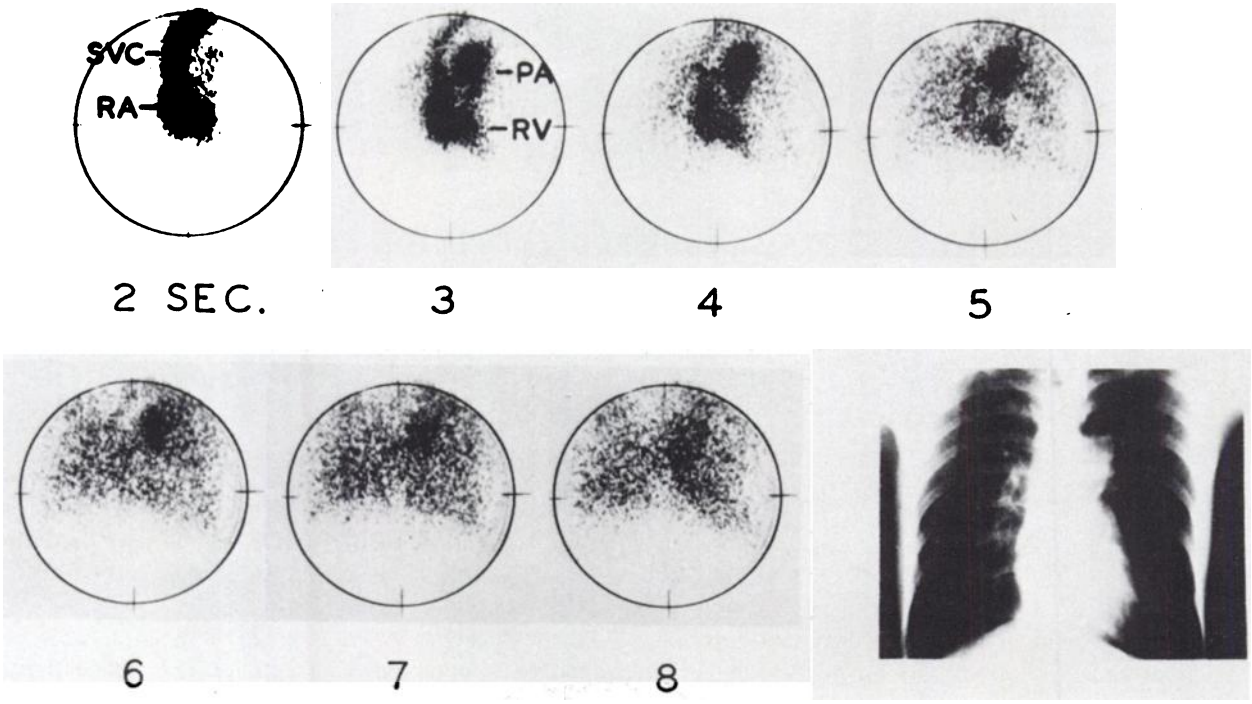

FIG. 5. Cardiac blood-flow study and chest film in 26-year-old woman admitted for cardiac catheterization (Case 3) with congenital pulmonic stenosis and aneurysmal dilatation of pulmonary artery.

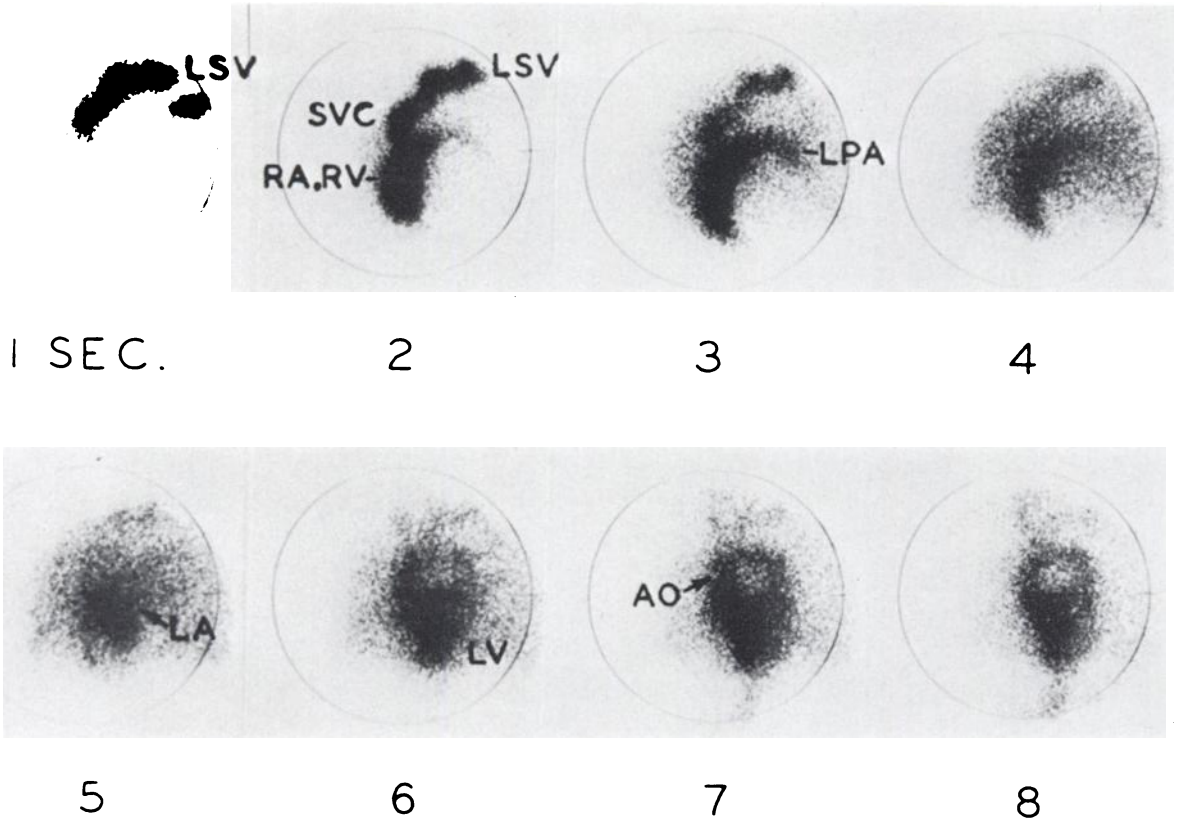

FIG. 6. Left anterior oblique (LAO) scintillation-camera cardiac blood-flow study in normal subject. LPA = left main pulmonary artery.

clavian vein and superior vena cava are seen. At 2 sec the right atrium, right ventricle and left main pulmonary artery are clearly delineated; the latter is best seen at 3 sec. Pulmonary isotope accumulation is evident at 3 and 4 sec postinjection. Filling of the left atrium and ventricle is seen at 5 sec, and the delineation between these chambers is evident at 6 sec. The aortic arch and descending aorta are seen well in the later films.

Left anterior oblique scintillation-camera ^{99m}Tc cardiac blood-flow studies in patients with left-atrial enlargement.

Case 4. A 36-year-old woman was admitted to Michael Reese Hospital for cardiac catheterization. She had been well until 1 year before admission when she developed exertional dyspnea, orthopnea and leg edema. Right-heart and retrograde left-heart catheterization indicated mitral stenosis with trivial mitral insufficiency and aortic insufficiency.

The ^{99m}Tc cardiac blood-flow study is shown in Fig. 7. Of particular interest is the large left atrium seen at 9 and 10 sec postinjection because none of the nonisotopic studies suggested enlargement of this chamber.

Case 5. A 39-year-old woman with atrial fibrillation secondary to long-standing rheumatic heart disease was admitted to Michael Reese Hospital for cardioversion. Cardiac catheterization revealed severe mitral insufficiency with marked dilatation of both atria and slight left-ventricular enlargement.

The first ^{99m}Tc cardiac blood-flow study was performed in the right anterior oblique projection at a time when the patient was still in atrial fibrillation (Fig. 8). Note the enlarged right atrium (4 sec); return of labeled blood to a grossly enlarged left atrium is seen at 12 sec. Subsequent left-ventricular filling is somewhat delayed (12–18 sec).

The cardiac blood-flow study was repeated 2 months later when sinus rhythm had been restored and a left anterior oblique view was used (Fig. 9). The enlarged right atrium is again seen at 3–4 sec postinjection; the enlarged left atrium is first seen at 8 sec but compared with the initial study, left-ventricular filling occurs promptly thereafter. Note the delineation between the left and right ventricles in the 9-sec film. Inspection of the 11-sec film reveals that the left ventricle is slightly to moderately increased in size.

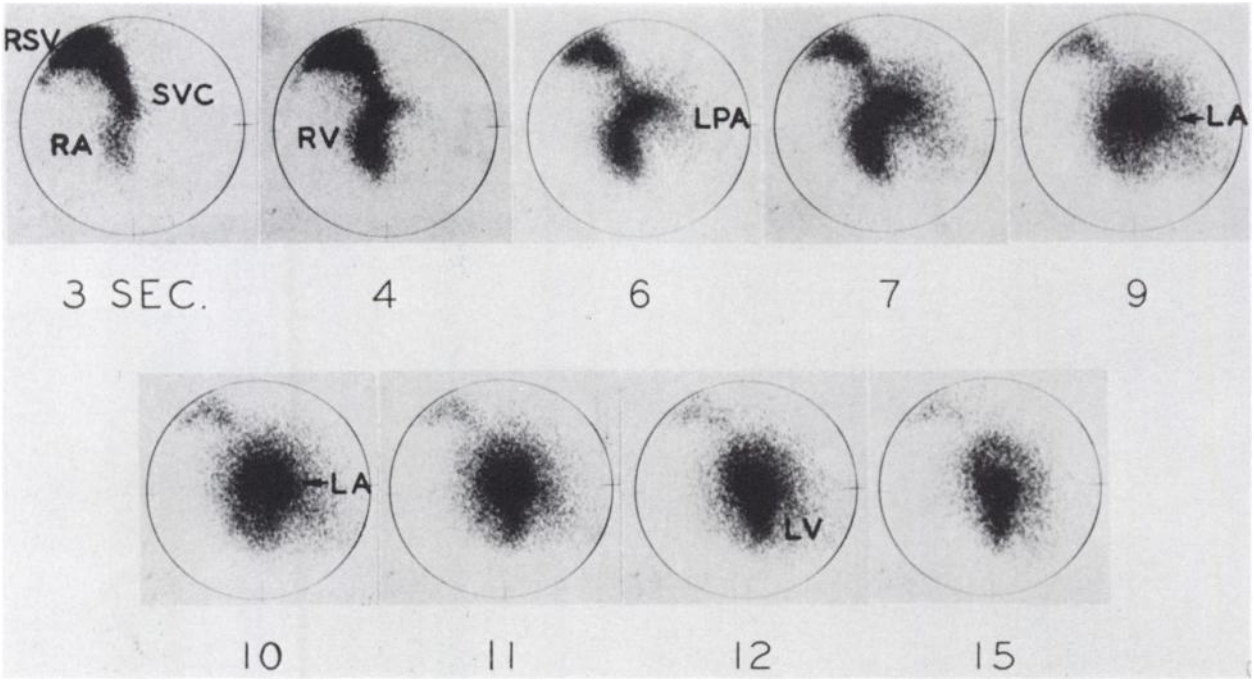

FIG. 7. LAO cardiac blood-flow study in patient with mitral stenosis (Case 4).

Scintillation-camera ^{99m}Tc cardiac blood-flow studies in patients with pericardial effusion.

Case 6. A 30-year-old man was admitted to Michael Reese Hospital with a 4-day history of precordial chest pain, exacerbated by recumbency with subsequent development of marked dyspnea.

An electrocardiogram on admission was compatible with acute pericarditis. A diagnostic pericardiocentesis yielded 160 cc of grossly bloody fluid. A cardiac angiogram revealed a 4.5-cm distance between the internal and external cardiac borders.

The scintillation-camera ^{99m}Tc cardiac blood-flow

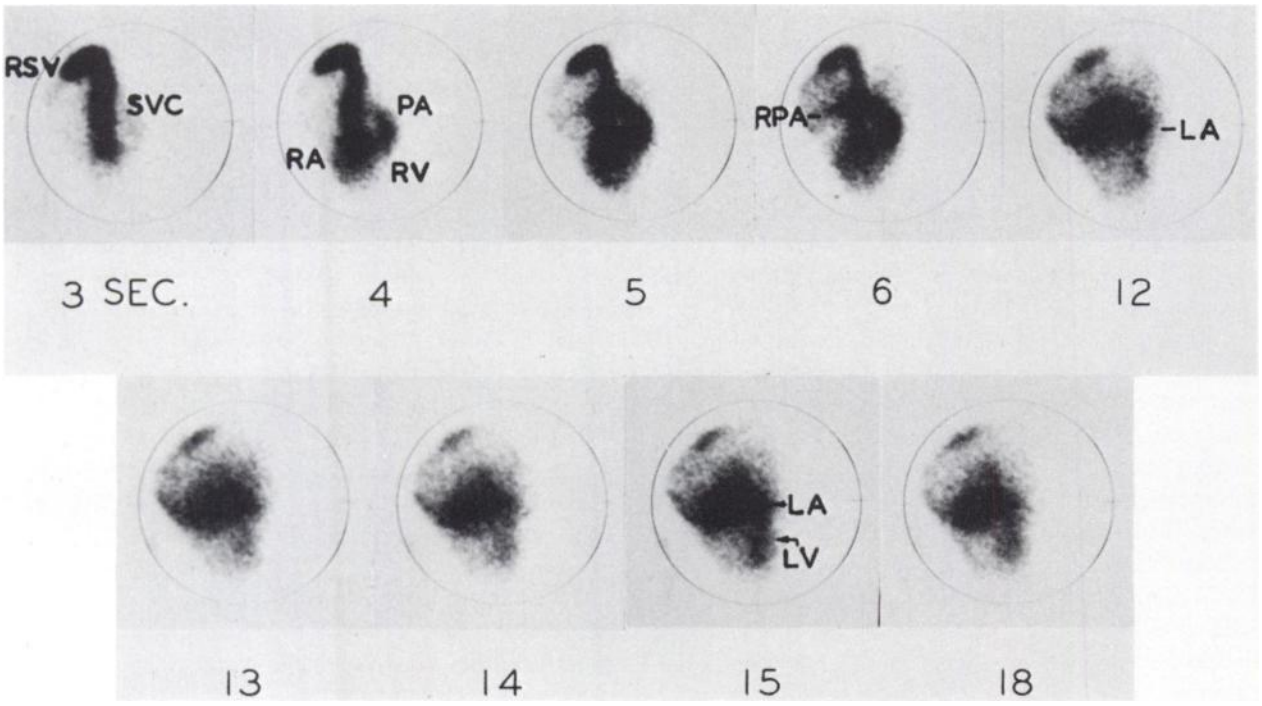

FIG. 8. Right anterior oblique cardiac blood-flow study in patient with mitral insufficiency (Case 5) performed when patient was in atrial fibrillation. RPA = right main pulmonary artery (see text).

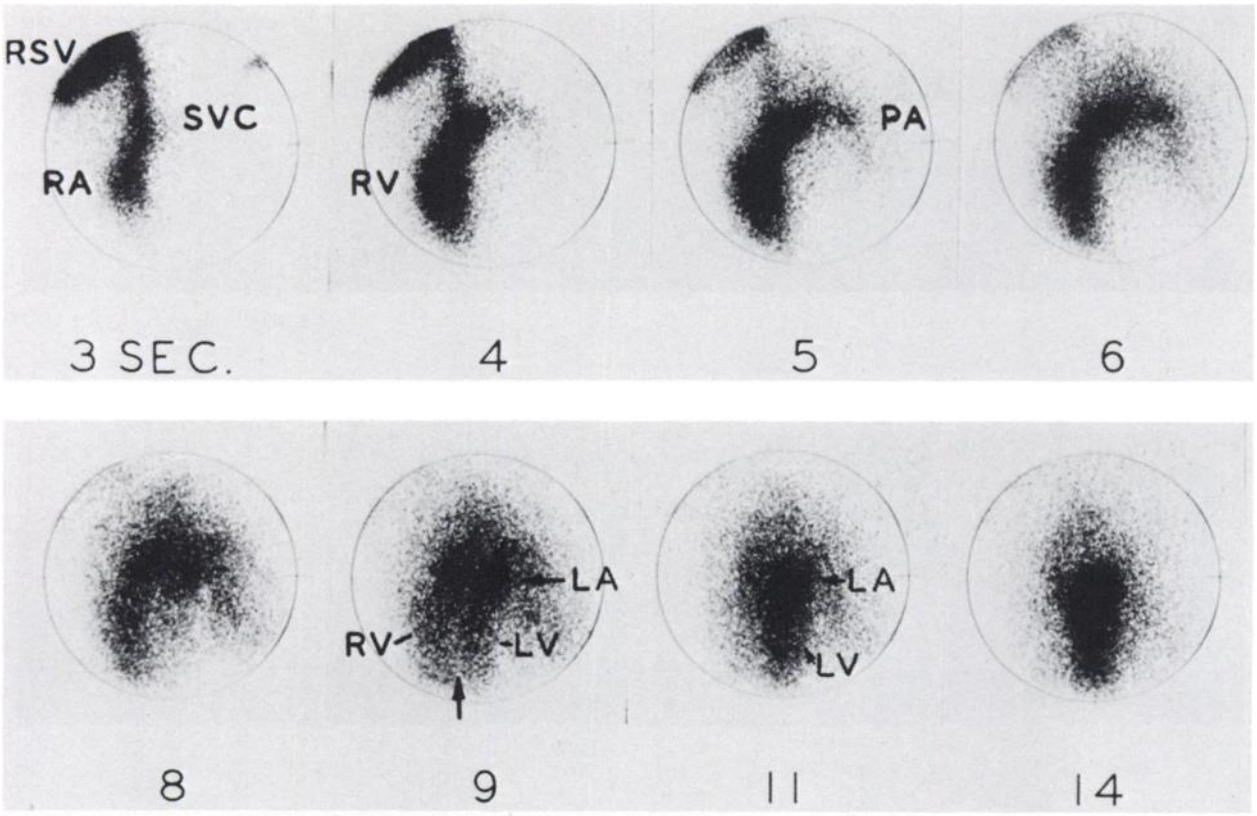

FIG. 9. LAO cardiac blood-flow study in Case 5 performed after cardioversion. Arrow at 9 sec indicates interventricular septum (see text).

study is shown in Fig. 10. Of particular interest is the "cold" area separating the right-lung field from the right atrium (5–6 sec). Filling of the left ventricle is seen at 10 sec; at this time there is clear separation between the accumulation of ^{99m}Tc in both lung fields and intracardiac radioactivity.

Scintillation-camera ^{99m}Tc cardiac blood-flow studies in patients with superior vena caval syndrome.

Case 7. A 55-year-old man was admitted to Michael Reese Hospital with a 3-week history of face and neck swelling and cyanosis. Chest x-ray revealed a large right hilar mass with irregular borders consistent with carcinoma and a right-sided pleural effusion.

The ^{99m}Tc cardiac blood-flow study is shown in Fig. 11. The films from two 2–11 sec reveal only collateral venous circulation because of complete occlusion of the right subclavian vein; at 11 sec postinjection no isotope has yet entered the lungs.

Six weeks after the start of radiation therapy to the right hilum and mediastinum no clinical manifestations of intrathoracic venous obstruction were evident, and the isotopic blood-flow study was entirely normal (Fig. 11).

Case 8. A 73-year-old woman was admitted to Michael Reese Hospital with a 10-day history of swelling of the right upper extremity and right breast. A superior vena cavagram showed obstruction of the right innominate vein (Fig. 12).

The ^{99m}Tc cardiac blood-flow study performed 10 days later (Fig. 13) shows complete occlusion of the right innominate vein. Of interest is the finding of significant right-atrial enlargement seen from 6 to 11 sec. The first appearance of radioactivity in the lungs is not noted until 23 sec postinjection.

The patient died suddenly 2 weeks later; autopsy revealed thrombotic occlusion of the right subclavian and innominate veins with thrombus extending into the superior vena cava.

DISCUSSION

Although improvement in skills, equipment and materials have materially reduced the hazards of cardiac catheterization (*7*), a need has long existed in clinical medicine for a technique using an intravenously administered radionuclide which would permit delineation of the various cardiac chambers as well as of abnormalities in cardiac blood flow.

The studies reported in this communication clearly show the clinical utility of cardiac blood-flow studies with ^{99m}Tc and the scintillation camera. Visualization of the atria and ventricles, documentation of chamber enlargement and delineation of great vessel abnormality compare favorably with that obtained on conventional and intravenous (*8*) angiocardiography. Indeed, in a number of the cases reported here, demonstration of atrial and/or ventricular hyper-

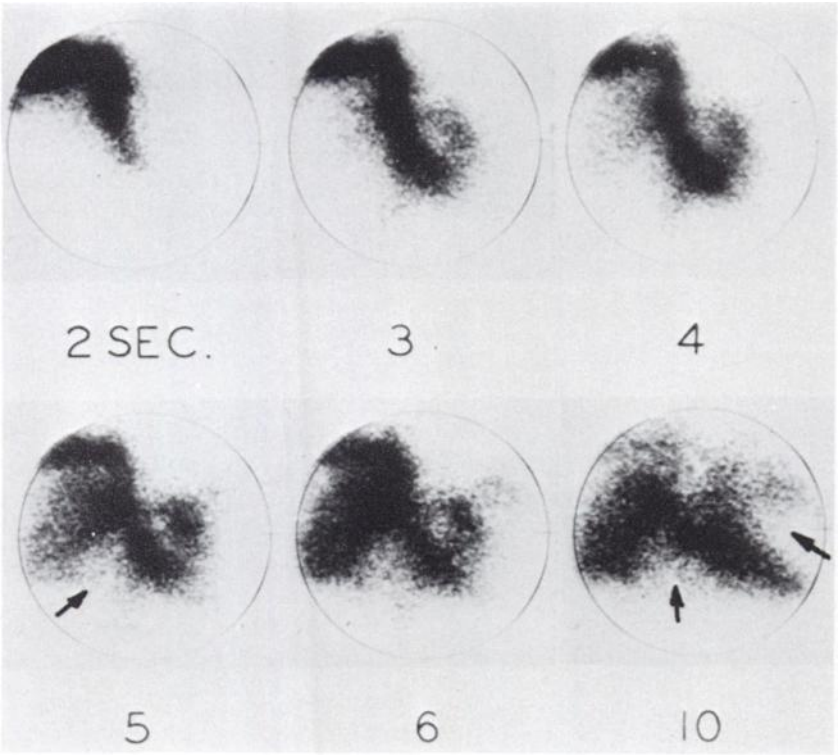

FIG. 10. Anteroposterior cardiac blood-flow study in patient (Case 6) with pericardial effusion. Arrows indicate "cold" areas separating cardiac and pulmonary radioactivity.

trophy was most evident in the isotopic camera study. Although no quantitative criteria for specific chamber enlargement have as yet been determined, it is expected that these will be forthcoming as the study group continues to expand.

Study of cardiac blood flow with the scintillation camera may be of value for detecting intracardiac shunts. In cases of suspected atrial septal defect with left-to-right shunt, for example, the demonstration of right atrial enlargement in the presence of delayed clearing of pulmonary radioactivity and poor delineation of left-ventricular filling is very suggestive. Although we have studied only four cases of this type so far, we have been able to visualize actual shunting of labeled blood from left-to-right atrium in two instances of which Case 1 (Fig. 3) is an example. It must be pointed out, however, that in each of these four patients the left-to-right shunt was of great magnitude, representing approximately ½–⅔ of the total pulmonary flow. Clearly, systematic study of large numbers of patients with shunts of varying hemodynamic significance will be required before a definitive assessment of the diagnostic sensitivity of the camera technique in this clinical situation can be made.

The determination of right heart-to-left heart transit time and its subdivisions from inspection of the film sequence reported here is analogous to the method used in cardiac catheterization because both techniques use "first" appearance of the isotope or dye to determine transit time. Johnson and his associates (*5*) described a dual-tracer technique for measuring the arterial and venous subdivisions of the pulmonary circulation separately by registering an ^{125}I lung dilution curve simultaneously with an ^{131}I radiocardiogram. Mean transit times were calculated by applying the Hamilton-Stewart formula to the curves obtained. We compared scintillation-camera transit-time data with those obtained from dual-probe radiopulmonary cardiograms to determine whether the two techniques would yield analogous data both in normal subjects and in patients with cardiac disease. If this were the case, the time-consuming computation of mean transit time inherent in radiopulmonary cardiography could legitimately be obviated. The data presented in this report suggest that, although discrepancies exist, such is indeed the case.

Thus, in normal subjects, computed and camera lung-to-left heart transit times were virtually identical; the computed right heart-to-lung transit time was significantly greater than that derived visually. This discrepancy is not unexpected, however, because the latter is determined by first appearance of the radionuclide in the lung field which would not be detected by the smaller and far less sensitive detector used in the double-probe study.

Although *both* right heart-to-lung as well as lung-to-left heart computed transit times in patients with mitral or aortic valvular lesions significantly exceeded those obtained from inspection of the camera-film sequences (Table 2), there was clear-cut dif-

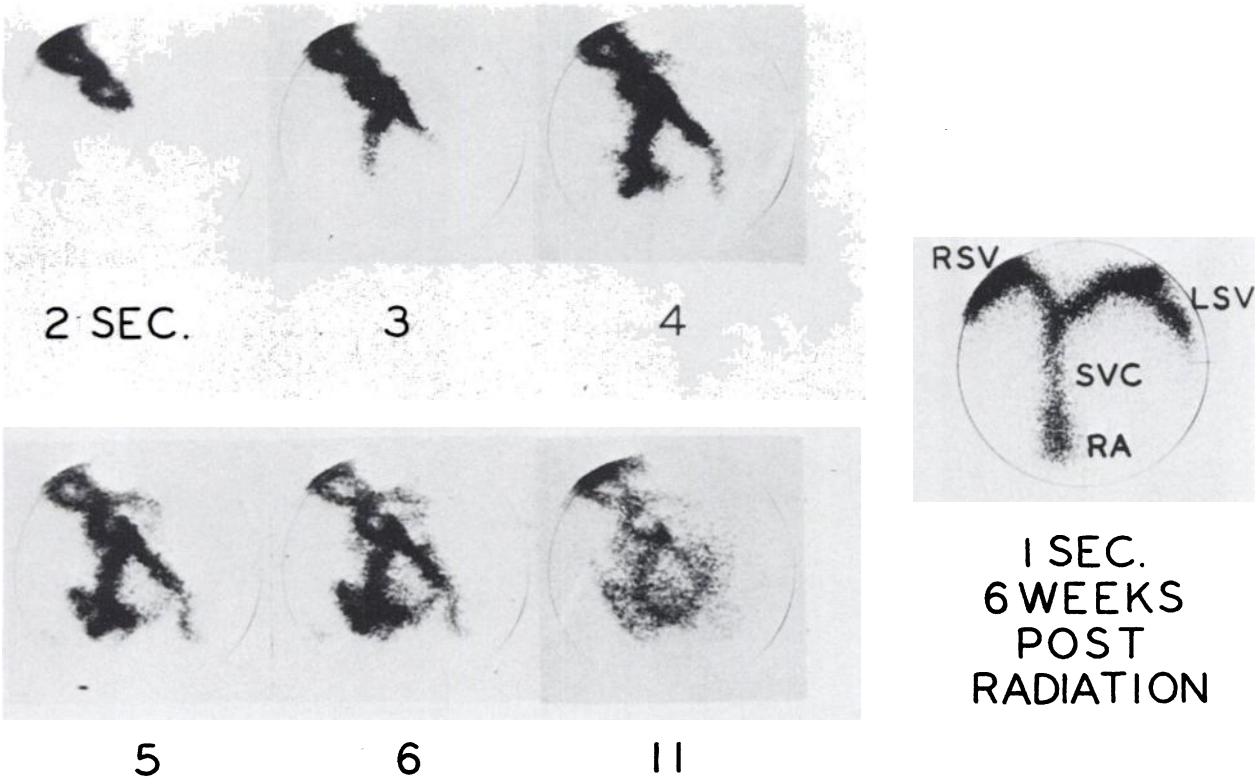

FIG. 11. ^{99m}Tc cardiac blood-flow study in patient (Case 7) with superior vena caval syndrome secondary to bronchogenic carcinoma. Preradiation therapy study was performed with right-sided injection only; in followup study, simultaneous bilateral antecubital vein injections (15 mCi each) were used.

ferentiation between normal and abnormal with *either* technique, and in both instances the predominant prolongation was in lung-to-left heart transit time.

In addition to its inherent simplicity, transit-time determination with the scintillation camera avoids a major limitation inherent in the double-probe techniques: that of inaccurate probe placement. Carter *et al* (*9*) have noted that positioning of the cardiac detector is critical because even small errors in probe placement markedly distort the cardiac dilution curves.

As reported in this paper, study of cardiac blood flow with ^{99m}Tc and the scintillation camera is also of considerable diagnostic value in the detection of pericardial effusions and in the presence of superior vena caval syndrome. Delineation of intrathoracic venous obstruction with this technique compares favorably with that obtained with phlebography, and serial studies may be of value in characterizing response to radiation therapy when the underlying etiology is a malignancy.

Use of ^{99m}Tc by systemic injection in this manner has not resulted in any untoward side effects or hemodynamic disturbances. The technique offers a potential means for detailed studies of regional blood flow, cardiac output and ventricular volumes. On the basis of the studies outlined in this presentation, it appears that the scintillation-camera ^{99m}Tc study

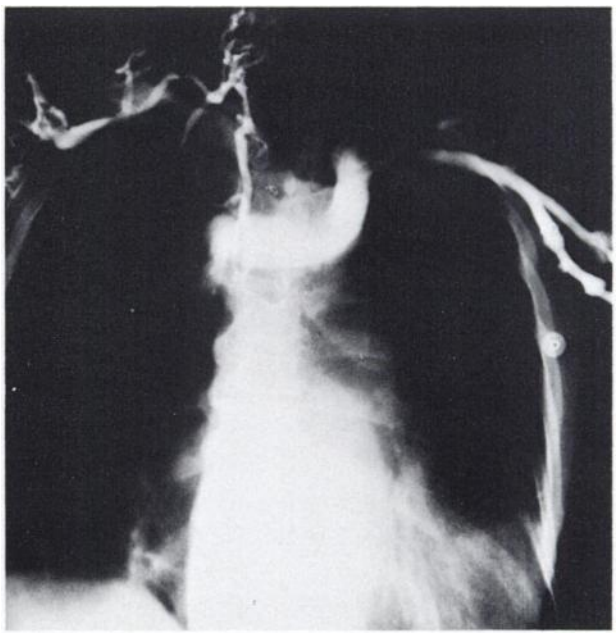

FIG. 12. Superior vena cavagram in patient (Case 8) with superior vena caval syndrome demonstrating obstruction of right innominate vein.

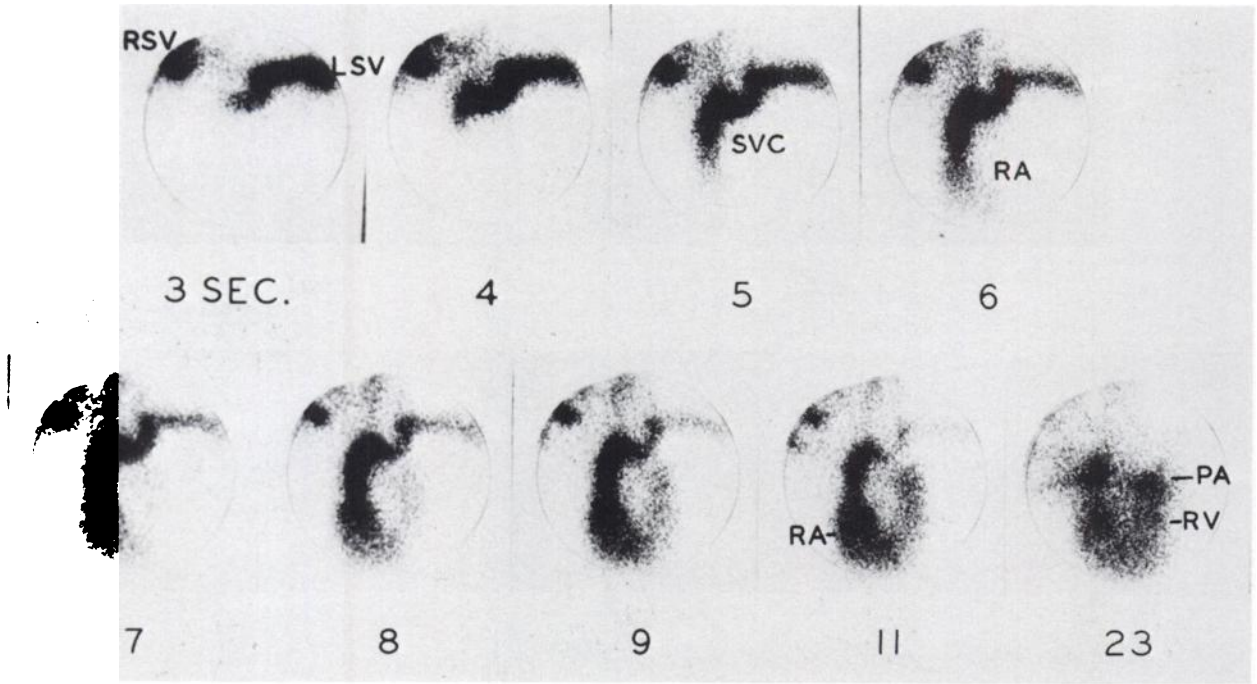

FIG. 13. ^{99m}Tc cardiac blood-flow study with simultaneous bilateral intravenous injections in Case 8; findings are entirely analogous to those demonstrated in phlebogram. Note right atrial enlargement (6–11 sec).

of cardiac blood flow provides a very useful adjunct in the clinical assessment of heart disease and merits continued investigation.

SUMMARY

The scintillation camera has been used for dynamic studies of cardiopulmonary blood flow with ^{99m}Tc-sodium pertechnetate. Visualization of the cardiac chambers achieved with this method compares favorably with that obtained on conventional angiocardiography. The technique has been found of value in determining relative cardiac chamber size, detection of intracardiac shunts and demonstration of pericardial effusions as well as in the diagnosis of superior vena caval syndrome.

Determinations of central mean transit time and its arterial and venous subdivisions from inspection of the scintiphoto sequence yield data entirely analogous to those obtained by the more tedious mathematical analysis of dual-probe radiopulmonary cardiogram curves in normal subjects and patients with cardiac disease. Cardiac blood-flow study with the scintillation camera is without hazard to the patient and is of significant diagnostic value in a variety of cardiac disorders.

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