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

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SUMMARY
The recent development of the instantaneously sensing Anger scintillation camera, capable of recording wide-field radioisotope images from the precordium, and a system for video storage and analysis has provided a means of visualizing the anatomic and hemodynamic features of the heart and great vessels without the hazards involved in introducing a radiopaque agent. Sodium pertechnetate (99mTcO4-) produces no cardio-circulatory effects or untoward actions and delivers only 0.13 rads of total body radiation. Following injection, the rapidly changing distribution of radioactivity within the heart is recorded by the scintillation camera-television system which includes no inherent dead time or overlap of the scanned field from frame to frame. Video tape replay is available immediately and sequential integrated pictures are possible at any rate up to 60 sec. Radioisotope images of longer intervals are easily obtained by the integration of successive stop-action fields reproduced on a high resolution television monitor and photographed on rapidly developed film. In addition, the replay may be gated and tracked, allowing selected phases to be integrated and time-concentration curves of blood flow.

Five to 10 millieuries of 99mTcO4- in 2 to 8 cc were rapidly injected into selected cardiac chambers at the time of diagnostic catheterization in 50 patients with a variety of congenital and acquired forms of heart disease. Movement of radioisotope closely reflected the hemodynamic alterations caused by these conditions, as determined by standard contrast angiocardiography. The radioisotope-angiocardiogram provides a new approach for visualization of the cardiovascular system, does not require the use of radiopaque medium, is safer than angiography, and does not disturb circulatory function.

Additional Indexing Words:
Cardiac catheterization Congenital heart disease Rheumatic heart disease
Ventricular volume Regional blood flow Cardiac output

Visualization of the cardiovascular system by standard angiographic techniques requires the rapid administration of large volumes of radiopaque dyes into the circulation under high pressure, a procedure

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Circulation, Volume XXXIX, January 1969

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which disturbs circulatory function and is not without hazard and discomfort to the patient. The recent development of the instantaneously sensing Anger scintillation camera, capable of recording wide-field radioisotope images from the precordium provides a new and safe means for viewing the cardiovascular system.\textsuperscript{3,4} By the use of this technique, scintiphotographic images produced by trace concentrations of gamma-emitting radioisotopes can be recorded in rapid sequence as the isotope flows through the circulation. It was considered that the radioisotope-picture produced following injection of technetium-99m (\textsuperscript{99m}Tc) might prove useful for visualizing the anatomic features of the heart and great vessels in patients, without some of the disadvantages inherent in the use of radiopaque agents. The technique employs a system developed for permanently recording dynamic radioisotope studies which permits replay and special analysis without loss or distortion of the original data.\textsuperscript{4} The present report describes the clinical applications of this new technique, the radioisotope-angiocardio gram.

**Methods**

The scintillation detector employed was the commercial model of the Anger scintillation camera (Pho-Gamma III, Nuclear-Chicago). The details of operation of this scintillation camera have been fully described.\textsuperscript{1,2} The data retrieval system and method of analysis have been described elsewhere,\textsuperscript{4} and the essential elements are shown diagrammatically in figure 1. The patient is positioned beneath the detector so that the area of interest is subtended by the 11-inch crystal. Gamma rays from the injected isotope strike the crystal, are converted to electronic signals, and recorded as flashes of light on a remote cathode ray tube in a pattern corresponding precisely to the isotope location within the body. As the isotope bolus flows through the heart and great vessels, the rapidly changing image is recorded at 1/60-sec intervals by a television camera which is focused on the face of the cathode ray tube and recorded on video tape.

On replay of the tape, the video signal is displayed on a high resolution television monitor from which photographs are taken with a Polaroid camera. The stop-action mode of the video recorder permits photographing serial video fields (each field representing 1/60 sec of live recording) in any sequence of exposures up to a maximum rate of 60/sec. For example, when exposures of 4/sec are desired, 15 serial stop-action fields are integrated on the same Polaroid film.

Physiological information can be recorded on the audio channel of the video tape and used to gate the video signal going to the television monitor on tape replay (middle row in figure 1). This is done by allowing the video signals to pass only during selected periods of the cardiac cycle.

**Figure 1**

Diagram of the scintillation camera and recording system (top row) and the tape retrieval system (middle row = gate discriminator; bottom row = gate generator) described in the text. In the bottom line the radioisotope image on the television monitor is an abdominal aortogram; cursors are over the left iliac artery. CRT = cathode ray tube, OSC = oscilloscope.
without interruption of the associated television pulses. For example, the gate may be triggered by the R-wave deflection of the electrocardiogram, thereby obtaining selected video scintillation pictures at particular times, such as during cardiac systole or during any phase of the respiratory cycle, without losing the total original information.

Analogue tracings of radioisotope flow through any selected area of interest can be obtained during video tape replay. Thus, the gating generator produces marker pulses which appear as two wide vertical bars or cursors superimposed on the television monitor (bottom row in figure 1). The region contained within the cursors thereby becomes the area of interest. These cursors can be positioned electronically anywhere over the television image, and the total area to be analyzed can be varied by independently controlling the height and distance between the cursors. When the electron beam sweep is between these two marker pulses, a video level differentiating circuit (referred to as the black/white differentiator in figure 1) produces a pulse for each discrete flash on the television monitor. These pulses are registered on a high speed binary counter and converted to an analogue voltage proportional to the accumulated counts in each 1/60-sec interval of recorded image. Variable amounts of capacitance may be used to increase the time constant above 1/60 sec when smoothing of the time concentration curves of blood flow are desired.

It is important to consider the details of the cathode ray tube of the scintillation camera and the television camera and monitor which converts the random flashes on the cathode ray tube into a fixed high-speed television format. The standard television picture consists of a sequence of horizontal sweeps in 1/30 sec, 505 of which are used to produce the picture. Each of these television frames actually consists of two sequential 1/60-sec complete fields of which 252-half lines contribute to the video picture. Thus, the video picture is obtained by the television camera at 1/60-sec intervals and on tape replay the recorded 1/60-sec fields are reconstituted in proper sequence. In this manner, the rapidly changing distribution of radioactivity within the cardiovascular system is registered and displayed in a synchronous fashion by the scintillation-television system which includes no inherent dead time or overlap of the scanned field from frame to frame.

Technetium-99m as sodium pertechnetate \((^{99m}\text{TcO}_4^-)\) was used throughout this investigation. Because of this isotope's short half-life of 6 hours, it is necessary that the substance be obtained daily by eluting a commercially supplied isotope generator system which consists of an alumina column onto which the parent radioisotope, molybdenum-99 \((^{99}\text{Mo})\) is firmly bound. As the \(^{99}\text{Mo}\) undergoes radioactive decay to become \(^{99m}\text{Tc}\), the solution for injection is collected by passing sterile sodium chloride through the column, thereby removing the \(^{99m}\text{Tc}\) in the form of sodium \(^{99m}\text{TcO}_4^-\).

In these studies, 5 to 10 \(\mu\)c of \(^{99m}\text{TcO}_4^-\) in 2 to 8 cc were injected rapidly into selected cardiac and vascular chambers at the time of diagnostic catheterization. \(^{99m}\text{TcO}_4^-\) causes no hemodynamic effects or untoward actions. The total body absorbed radiation dose is only 0.13 rads when 10 \(\mu\)c of the isotope are employed. By way of comparison, it is estimated that during standard contrast-dye cineangiography at least 3 rads are absorbed.

**Figure 2**

Serial scintiphotos, integrated for 1 sec in the frontal view, of the right, and then the left, heart in a normal subject following injection of \(^{99m}\text{TcO}_4^-\) into the right atrium (RA). In this and all subsequent figures, the diagrams on the right represent the areas visualized by the corresponding isotope image. The events illustrated in this figure and the figures which follow are discussed in detail in the text. RV = right ventricle, PA = pulmonary artery, LA = left atrium, LV = left ventricle, Ao = ascending aorta.
within the field of view, although the gonadal radiation from scattered x-rays is substantially less.

Results

The radioisotope-angiocardiogram has been employed in more than 50 patients in whom the diagnoses have included a variety of congenital and acquired forms of heart disease. The radioisotope images have closely reflected the hemodynamic and anatomic conditions, as determined by standard contrast angiocardiography prior to administration of $^{99m}$TcO$_4^-$.

Figures 2 and 3 illustrate the scintiphotos obtained following the injection of radioisotope into the right atrium of a patient without heart disease. Figure 2 is a continuous sequence of the radioisotope images, each picture representing 1-sec integrations. In the first exposure, the isotope is observed in the right atrium, right ventricle, and main pulmonary artery. In the second and third exposures, flow of the radioisotope reaches both lung fields, and in the third, the isotope has been cleared from the right atrium. On the bottom row, in the fourth exposure, the isotope completely fills both lungs. The left ventricle is visualized in the last two exposures and, at the end of the sequence, the isotope has circulated almost completely out of the lungs. During this sequence of images, there was no dead, or lost exposure, time.

The same radioisotope study shown in figure 2 at 1-sec intervals is displayed in figure 3 at $\frac{1}{3}$-sec intervals. Now each horizontal column of four exposures represents 1 sec, and the entire figure represents 3 sec. Each $\frac{1}{3}$-sec field consists of 15 integrated, 1/60-sec, stop-motion fields on video replay; the integration of four of these fields produces one of the pictures shown in figure 2. In the upper row, the isotope is observed successively in the right atrium, the right ventricle, and the pulmonary artery. In the second row, the isotope appears gradually in both lung fields. In the bottom row, the isotope has circulated more completely into the pulmonary vascular bed.

Radioisotope-pictures, integrated for 1 sec, are shown in figure 4, of three patients following injection into a systemic vein or the right atrium. Panel A is a scintiphoto obtained from a normal subject 2 sec after injection into the superior vena cava. The right heart and pulmonary arteries are shown. Panel B shows a greatly enlarged right atrium in a patient with Ebstein's anomaly of the tricuspid valve, 4
**Figure 4**

Radioisotope pictures of the right heart in a normal subject (A), in a patient with Ebstein's abnormality (B), and in a patient with a dissecting aneurysm of the ascending aorta (As.Ao.). In this figure and through figure 11, the site of injection and the view exposed are given next to each image. SVC = superior vena cava, IV = peripheral system vein, AP = posteroanterior or frontal view. The arrow in diagram C indicates encroachment of the aneurysm on the right ventricular outflow tract.

**Figure 5**

Scintiphotos of the left heart following injection into the left atrium in aortic stenosis (AS), mitral stenosis (MS), atrial septal defect (ASD), and mitral regurgitation (MR). LAT. = lateral projection, RAO = right anterior oblique projection. The arrow in diagram C represents isotope flow across the atrial septal defect.
sec following injection into a peripheral vein. Panel C is a scintiphoto taken 2 sec after injection into the right atrium in a patient with an aneurysm of the ascending aorta. The right ventricular outflow tract is deformed and displaced to the left, and there is obstruction to flow into the right pulmonary artery with a 20-mm Hg systolic pressure gradient. This is reflected in the greater isotope concentration in the left, as compared to the right, pulmonary artery.

In figure 5 are displayed scintiphotos following injection into the left atrium in four patients with different forms of heart disease. Panel A was obtained from a patient with aortic stenosis, 3 sec after injection through a transseptal left heart catheter. The isotope has cleared the atrium and is in the left ventricle and aorta. In panel B, obtained from a patient with mitral stenosis, also 3 sec following injection, a large portion of the isotope remains in the enlarged left atrium. In panel C, from a patient with an atrial septal defect, the isotope circulates across the defect into the right atrium and right ventricle, as well as across the mitral valve into the left ventricle and aorta. In panel D, from a patient with severe mitral regurgitation, the enlarged left atrium is observed to be persistently filled 3 sec after injection into the left atrium.

Some additional examples of the usefulness of this technique are shown in figure 6. Scintiphotos of the cardiac chambers exposed for 1 sec are illustrated in six patients following selective injection of $^{99m}$TcO$_4^-$. In panel A, obtained from a patient without heart disease, the left ventricle and aorta are shown following left ventricular injection. In panel B the left atrium and ventricle, and the aorta are visualized after left atrial injection in a patient with mitral stenosis; the left atrium is well outlined. In contrast, in panel C, obtained from a patient with aortic stenosis after left atrial injection, the isotope fills the left ventricle and aorta but has cleared the left atrium. Panel D was obtained from a patient with mitral regurgitation 3 sec following left ventricular injection. Here the isotope regurgitates into the left atrium, as well as filling the left ventricle and aorta. In panel E, 3 sec after left atrial injection in a patient with idiopathic hypertrophic subaortic stenosis, the isotope is in the left atrium, left ventricle, and aorta. A filling defect in the outflow tract of the left ventricle is produced by the septal hypertrophy characteristic of this condition. In panel F, the isotope is observed in

**Figure 6**

Scintiphotos illustrating various cardiac defects. IHSS = idiopathic hypertrophic subaortic stenosis. The arrow in diagram E indicates the filling defect due to ventricular septal hypertrophy. VSD = ventricular septal defect, LAO = left anterior oblique projection.
Figure 7

Isotope-ascending aortogram in a patient without heart disease. inj. = injection site, D.Ao. = descending aorta.

Figure 8

Serial scintiphotos following aortic root injection in a patient with aortic regurgitation (AR).
both the left and right ventricles 4 sec following injection into the pulmonary artery in a patient with a ventricular septal defect, the scintiphoto is compatible with the diagnosis of a left-to-right shunt across the ventricular septum.

In figure 7, 1-sec integrations are displayed serially in a patient without heart disease following injection of $^{99m}$TcO$_4$ into the ascending aorta. The isotope rapidly circulates from the aorta and has disappeared completely after 3 sec. In contrast, figure 8 shows an identical sequence following injection into the aortic root in a patient with aortic regurgitation. The isotope has refluxed into the left ventricle and continues to fill the left ventricle and aorta 6 sec following injection.

An example of the usefulness of the gating

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Figure 9

Serial scintiphotos illustrating changes in the size of the left ventricular cavity at end-systole (A) and end-diastole (B), following left ventricular injection in a patient without heart disease. The images were exposed at ½-sec intervals for four consecutive cardiac cycles from the video tape replay by the use of the gating discriminator. The time of exposure is indicated by the horizontal bar beneath each electrocardiogram.

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Figure 10

Isotope-abdominal aortogram in a normal subject. Abd.Ao. = abdominal aorta, RRA = right renal artery, LRA = left renal artery, CA = celiac artery, IVC = inferior vena cava, RK = right kidney, LK = left kidney, RRV = right renal vein, LRV = left renal vein.
RADIOISOTOPE ANGIOGRAPHY

Figure 11

(A) Time-activity curves of isotope flow through the kidneys obtained by the gating generator technique from the abdominal aortogram shown in figure 10. The cursors are over the left renal parenchyma. CPM = radioactivity in counts per minute. (B) Analogue curve of isotope flow through the renal vascular pedicle from the same injection in the patient illustrated in figure 10. With the cursors over the right renal artery and vein, a biphasic flow pattern was observed, indicating blood flow into and out of the kidney.

discriminator for obtaining selected portions of the cardiac cycle is illustrated in figure 9 in a patient without heart disease following left ventricular injection of $^{99m}$TcO$_4^-$. The horizontal bar beneath the simultaneously recorded electrocardiogram in both films represents the period that the video signal was allowed to be recorded on the television monitor at the time of the tape replay. In each instance, the time of exposure is ¾ sec for four consecutive cardiac cycles, and thus comprises 30 integrated, 1/60-sec fields. At end-systole (A), the ventricular volume is substantially less than at end-diastole (B). The application of this technique in the accurate determination of left ventricular end-diastolic and end-systolic volumes in experimental animals has been reported from our laboratories.$^7$

A radioisotope-angiogram of the abdominal aorta is recorded in figure 10 at 1-sec intervals following injection of isotope into the
aorta at the level of the diaphragm in a normal subject. In panel A, the isotope fills the entire abdominal aorta, the renal, celiac, and iliac arteries. In the remainder of the fields shown on the top row, the isotope has entered the intrarenal circulation. By placing the cursors over the renal parenchyma on video tape replay, analogue tracings of the activity were recorded on a strip chart recorder (fig. 11A). In the bottom row (fig. 10), the isotope has flowed from the kidneys into the renal veins, thus permitting the arterial and venous phase of the renal circulation to be observed. When the cursors were placed over the renal vascular pedicle, analogue curves of these phases were recorded on a strip chart recorder (fig. 11B).

A further application of analogue tracings of radioisotope flow obtained from radioisotope-pictures is illustrated in figure 12 in a normal subject following injection into the superior vena cava. At the time of tape replay, the cursors of the gating generator were placed over the pulmonary artery in order to record a time-activity curve of $^{99m}$TcO$_4^-$ flow through this vessel. The pulmonary artery can be located precisely on the video tape, and this area of interest does not overlie the cardiac chambers or great vessels. Thus a valid time-concentration curve of total blood flow is provided and cardiac output may be determined, if the measurement of blood volume also is carried out.$^8$

**Discussion**

A new technique has been described in which the gamma radiation emitted from circulating isotopes can be detected instantaneously from the precordium or other vascular areas by the wide-field Anger scintillation camera and recorded on video magnetic tape for subsequent replay and study. The radioisotope-angiocardio gram obtained in this manner can be used to study anatomic and physiological features of the heart and circulation. Thus, as shown in this investigation, scintiphotos correlate closely with the hemodynamic and anatomic alterations caused by abnormalities of the cardiovascular system. Although the images obtained in this fashion do not yet provide as precise a definition of structures as does contrast angiography, the isotope image provides sufficient detail to warrant the use of this technique in special situations, especially when the patient may be too critically ill to tolerate contrast medium. In addition, the isotope can be injected into a peripheral or central vein, or into an easily accessible chamber of the right heart, and thus serves as an innocuous screening test in some clinical settings. Further extensions of the use of this method under continued investigation include the study of regional blood flow, cardiac output, and ventricular volumes. In conclusion, the radioisotope-angiocardio gram provides a new and potentially valuable approach to the visualization of the heart and circulation which can be applied without hazard to patients and which does not disturb circulatory function.

**References**

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Circulation. 1969;39:19-28
doi: 10.1161/01.CIR.39.1.19

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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