Radionuclide Angiographic Measurement of Left Ventricular Volume and Ejection Fraction*

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In recent years a number of different radionuclidic techniques have been developed to measure left ventricular volume and ejection fraction. Area-measurement concepts have been applied to static and electrocardiographically gated radionuclide images which have resulted in accurate measurement of left ventricular end-diastolic volume (LVEDV) and ejection fraction (LVEF). Gated (end-diastolic and end-systolic) image analysis has also proven capable of detecting regional left ventricular wall-motion abnormalities in patients with coronary disease.

Radioisotopes have been used to define cardiac performance for several decades. Scintillation probes were initially used with radioisotopes such as radioactive 131iodine to measure cardiac output and various transit times across the central circulation. With the invention of the Anger camera and the development of radionuclides with suitable energies and half-lives, such as radioactive 99mtechnetium, cardiac images could be obtained.

Dynamic imaging of the heart and great arteries has been successfully undertaken for a number of years. In this technique, sequential images are obtained following intravenous injection of 99mtechnetium (5 to 20 millicuries) with the patient positioned under an Anger camera. Scintiphotographs of the tracer are obtained as it courses through the right side of the heart, the lungs, and the left side of the heart; and these scintiphotographs have proven to be of value as a screening test in young patients suspected of having congenital heart disease, in patients with acquired cardiovascular diseases, and in patients with pericardial effusion. By application of data storage and playback capability, cine imaging can be performed.

A number of techniques have been developed in recent years to extend radionuclide angiocardiography to quantification of the cardiac image for measurement of left ventricular volume. These techniques include (1) analysis of the static of summed end-diastolic image of the left ventricle utilizing area-length concepts, (2) electrocardiographically gated left ventricular imaging to acquire an end-diastolic and end-systolic image for area-length analysis, and (3) dynamic imaging for extraction of a time-activity curve from an area of interest coincident with the left ventricle. This report will review these various methods of measuring left ventricular volume and ejection fraction from radionuclide data.

**Static Left Ventricular Imaging**

Sullivan and associates developed a method for determining left ventricular end-diastolic volume (LVEDV) following intravenous injection of 99mtechnetium. Scintiphotographs at two-second intervals were obtained during the left cardiac phase of the study. The images were obtained in the right anterior oblique projection; and as they represented two seconds of imaging data, they visualized the left ventricle at the end of diastole. These static images were analyzed using area-length concepts which have been successfully applied to contrast ventriculograms. Two point sources of radioactivity were used to correct for minification in a fashion similar to the grid correction used for estimation of end-diastolic volume from cineventriculograms. Using this radionuclide technique, an accurate mea-

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measurement of LVEDV was obtained, as compared to that obtained with contrast left ventriculographic studies \( (r = 0.99; n = 10) \). Several advantages of this method for measuring left ventricular volume are apparent: (1) left cardiac catheterization is not necessary; (2) the radionuclide, \(^{99}\)Tc-technetium as pertechnetate, is readily available; and (3) the technique utilizes the standard, commercially available Anger camera. The major drawbacks of the method are the relatively poor spatial resolution of such a left ventricular image and the inability to measure end-systolic volume; however, left ventricular end-systolic volume can be measured by complexing \(^{99}\)Tc-technetium to albumin\(^{15}\) and using this radionuclide for ventricular imaging and also for extraction of time-activity curves for determination of cardiac output and stroke volume.\(^{16}\) With cardiac output and LVEDV, the end-systolic volume can be calculated, although this calculation would not be accurate in patients with valvular regurgitation.

**Gated Left Ventricular Imaging**

Strauss and associates\(^{17}\) developed a radionuclide technique for measuring left ventricular volume using a gated system. Following an intravenously administered dose of \(^{99}\)Tc-technetium complexed to albumin, cumulative end-diastolic and end-systolic images (each containing approximately 300,000 counts) were obtained using the electrocardiogram as a gate. The cumulative end-diastolic and end-systolic images were used to calculate ejection fraction by the same area-length method used by Sullivan et al.\(^{11}\) In the right anterior oblique projection an accurate estimate of left ventricular ejection fraction (LVEF) was obtained \( (r = 0.92; n = 20) \).

The gated radionuclide angiogram can be obtained in multiple projections, such that biplane images can be used to calculate LVEF. This would be a potential advantage, particularly in patients with coronary disease in which localized areas of left ventricular wall-motion disturbance occur.\(^{19}\) A further advantage of the gated system is that regional wall-motion abnormalities can be demonstrated\(^{19,20}\) in a manner similar to contrast ventriculographic studies.\(^{21}\) The gated method requires a tracer that remains in the circulation, and \(^{99}\)Tc-technetium-labelled albumin is a convenient radionuclide for this use but requires some lead time to prepare prior to performance of the study. The patient’s cooperation is necessary, as it takes 20 to 30 minutes to complete the imaging; and during this time, the patient must lie still, which limits the technique to relatively well patients.

The gating equipment is relatively inexpensive, costing about $2,000, and is commercially available. An Anger camera costs about $56,000 but is universally available in nuclear medicine departments. Thus, gated radionuclide angiographic studies can be performed in most existing departments of nuclear medicine for only about $2,000 of additional expense.

Ashburn and associates\(^{22}\) have utilized a gated system with video magnetic tape for data storage and subsequent \textit{a posteriori} gating. These investigators successfully used the left lateral projection for imaging, with LVEF and LVEDV calculated by area-length methods. The reduced patient-to-colimator distance of the left lateral projection, as compared to the right or left anterior oblique, improves the spatial resolution of the left ventricular image.

Count-rate from a tracer mixed in the left ventricle is proportional to the volume of that chamber, regardless of chamber geometry. This concept was first applied to the measurement of LVEDV and LVEF by Van Dyke et al.\(^{23}\) Secker-Walker and co-workers\(^{24}\) have applied this concept to gated radionuclide angiography. Following injection of \(^{99}\)Tc-technetium-labelled albumin, images were recorded in the left anterior oblique projection. The Anger scintillation camera was interfaced to a digital computer to extract a count-rate from the end-diastolic and end-systolic images, and LVEF was computed as:

\[
LVEF = \frac{\text{counts end-diastole} - \text{counts end-systole}}{\text{counts end-diastole} - \text{background counts}} \tag{1}
\]

The background counts were obtained from the area between the left ventricular end-diastolic and end-systolic outlines and represent radiation scattered from adjacent radionuclide-containing tissues. Correction for scattered radiation and background activity is not a completely understood concept, but some method of correction must be applied to radionuclide count-rate data to obtain volumes which correlate with contrast angiograms. Utilizing this method, Secker-Walker et al\(^{24}\) obtained an accurate measurement of LVEF in ten patients \( (r = 0.87) \).

**Dynamic Left Ventricular Imaging**

Van Dyke et al\(^{25}\) developed a dynamic radionuclide method for measuring LVEF and LVEDV. The radionuclide \((^{99}\)Tc-technetium-labelled albumin\) was injected either intravenously or into the superior vena cava, and a time-activity curve was recorded from an area of interest coincident with the left ventricle. The fractional fall in count-rate from the end of diastole to the end of systole was divided by the end-diastolic count-rate and ejection fraction computed on a beat-to-beat basis. Van Dyke et al\(^{25}\) recognized the contribution of scattered radiation to
the left ventricular time-activity curve and developed an empirical correction so that LVEF calculated from time-activity curves was comparable to that obtained with left cineventriculographic studies. This correction consisted of subtraction from the left ventricular time-activity curve of a time-activity curve obtained from a ring area placed around the end-diastolic area of the left ventricle (right anterior oblique projection). Using this method, an accurate measurement of LVEF was obtained ($r = 0.85; n = 16$). This method has been successfully applied by Weber et al., and they have developed a computer technique to simplify the calculations.

The LVEDV can be obtained from the LVEF, the cardiac output (CO), and the heart rate (HR) as:

$$LVEDV = \frac{CO/HR}{LVEF}$$

which is, however, accurate only in patients without valvular regurgitation. If LVEDV is not desired (that is the tracer need not remain within the vascular compartment), this method can use $^{99}$technetium as pertechnetate, which is readily available in all nuclear medicine departments. This dynamic radionuclide study requires only a few minutes of the patient’s time; and with the type of dedicated computers available in many laboratories, the calculations can be easily and quickly performed.

Steele et al. modified the technique of Van Dyke and associates by using a wedged pulmonary arterial catheter to deliver radionuclide. With the patient in the 40° right anterior oblique projection, 10 to 15 millicuries of $^{99}$technetium as pertechnetate was injected, and the study was recorded at 20 frames per second with an Anger camera interfaced to a digital computer. For generation of time-activity curves, an area of interest coincident with the left ventricle at the end of diastole was constructed with the computer (Fig 1). A semiannular ring surrounding the left ventricle was also constructed as a background area (Fig 1). Time-activity curves were obtained from each area; and following subtraction of the background curve from the left ventricular curve, a corrected left ventricular time-activity curve was generated (Fig 2).

The LVEF was calculated from the beat-to-beat fractional fall in count-rate (end of diastole to end of systole) divided by the background-corrected end-diastolic count-rate (Fig 2). In 29 patients, the LVEF determined in this way correlated ($r = 0.84$) with that obtained by contrast cineventriculographic studies.

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activity curve can be fitted with an exponent and LVEDV calculated as:

$$\text{LVEDV} = \frac{\text{SV}}{(1-a^t)} \quad (3)$$

where $\text{SV}$ is stroke volume, $a$ is the rate constant from a least-squares fit, and $t$ is 60/heart rate (Fig 2). The LVEDV can also be calculated using the relationship in equation 2, where computation of LVEF is made from the fractional fall of beat-to-beat count-rate data. A more accurate measurement of LVEDV was obtained using the method of equation 3 ($r = 0.95; n = 23$).

Some additional advantages of the wedge-injection radionuclide technique with its resultant bolus entry into the left side of the heart include the ability to calculate regurgitant ejection fractions for the mitral and aortic valves, in addition to total and forward LVEF. The high count-rate from the left ventricular area of interest also allows a time-activity curve to be obtained from an area coincident with the minor axis (in the right anterior oblique projection) of the left ventricle; and from this time-activity curve, the mean circumferential fiber-shortening velocity can be recorded.\(^{27}\)

Computerized analysis of dynamic radionuclide images requires a computer system (approximately $50,000) in addition to the cost of the Anger camera (approximately $56,000), which makes this technique an inherently expensive endeavor. A baseline system for hardwired acquisition of data at 40 frames per second and for curve extraction can be obtained for $21,000, but the more expensive and flexible analytic ability of a computer system is certainly desirable.

Experience with systems using an Anger camera and a computer suggested that a scintillation probe which was properly collimated and equipped with high-response recording equipment could generate time-activity curves from the left ventricle.\(^{30}\) Utilizing the area of interest and background concepts of Van Dyke et al.,\(^{28}\) lead collimators were attached to the scintillation-probe face placed at the midpoint of the left ventricle. Through a central venous catheter, radioactive $^{113}$indium was injected, and a high-frequency time-activity curve was recorded (Fig 3). The LVEF was measured in a similar fashion to that described above (beat-by-beat analysis of the fractional fall in count-rate), following recording of a baseline correction curve (background) using the eclipse collimation. The LVEF was correlated with contrast cineventriculographic studies ($r = 0.90; n = 36$).

The advantages of the method using the scintillation probe are its low cost (approximately $7,000; $600 to modify most existing renographic or thyroid-uptake probes); its portability, such that it can be easily transported to the bedside; the rapid availability of information in respect to calculation of LVEF;

\[\text{Figure 3. High-frequency precordial time-activity curve obtained with collimated scintillation probe following injection of radionuclide into superior vena cava. Right ventricular peak (RV) and left ventricular peak (LV) are identified. The LVEF is calculated as fractional fall in counts from end of diastole (ED) to end of systole (ES) divided by end-diastolic count-rate. Eclipse record is noted. Ejection fraction averages 0.74 for three beats beginning with ED-ES.}\]
and the fact that the radionuclide (113m-Indium) is easily and quickly prepared from a commercially available generator and has a short half-life (1.7 hours) to allow frequent serial study.

The probe cannot be used to assess left ventricular wall motion, but portable scintillation cameras have been developed which will permit gated or dynamic left ventricular imaging at the patient's bedside in intensive care areas.

DISCUSSION

A variety of radionuclide techniques have been developed in recent years which can accurately describe left ventricular performances. Left ventricular images generated as static images or as electrocardiographically gated images can be analyzed using area-length measurement to obtain LVEF and LVEDV. Left ventricular time-activity curves can be obtained in several ways and also yield accurate measurement of LVEF and LVEDV. The gated systems and the scintillation-probe method have the distinct advantage of low cost and consequently should be easy to undertake in most hospitals. The dynamic computerized systems require a substantial commitment in terms of the equipment's cost and technical personnel.

REFERENCES