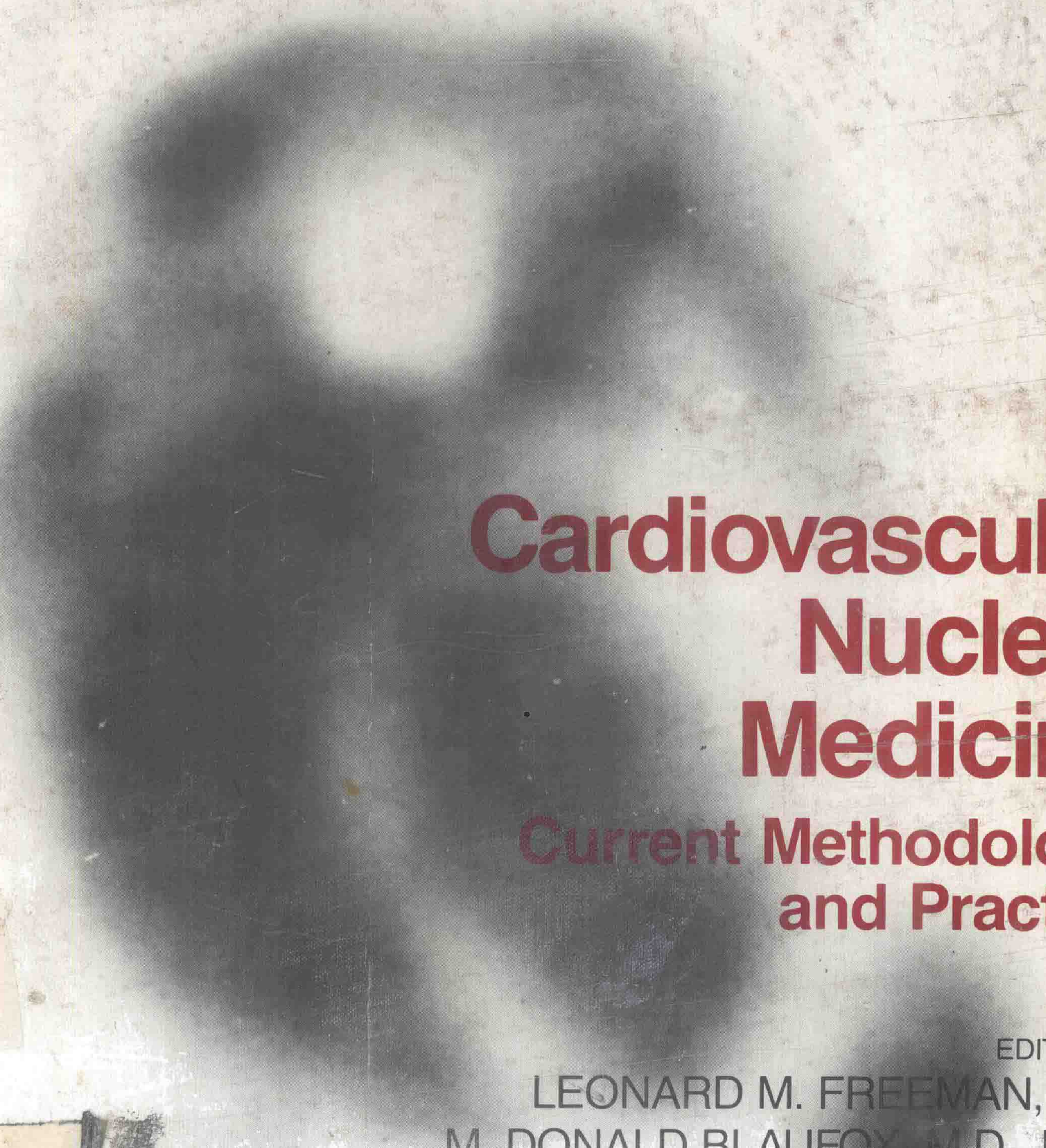

# Cardiovascular Nuclear Medicine

## Current Methodology and Practice

EDITED BY
LEONARD M. FREEMAN, M.D.
M. DONALD BLAUFOX, M.D., Ph.D.

Seminars in Nuclear Medicine Reprint
October 1979, January 1980, April 1980

# CARDIOVASCULAR NUCLEAR MEDICINE

## Current Methodology and Practice

**Edited by**

**Leonard M. Freeman, M.D.**
Professor of Radiology
Co-director, Divisions of Nuclear Medicine
Albert Einstein College of Medicine
Chief, Montefiore Hospital and Medical Center Division
Bronx, New York

**M. Donald Blaufox, M.D., Ph.D.**
Professor of Radiology (Nuclear Medicine)
and Professor of Medicine
Director, Divisions of Nuclear Medicine
Albert Einstein College of Medicine
Bronx, New York

GRUNE & STRATTON
*A Subsidiary of Harcourt Brace Jovanovich, Publishers*
New York London Toronto Sydney San Francisco

The chapters of this book originally appeared in the October 1979, January 1980, and April 1980 issues (Volume IX, Number 4; Volume X, Numbers 1 and 2) of *Seminars in Nuclear Medicine,* a quarterly journal published by Grune & Stratton, Inc., and edited by Leonard M. Freeman, M.D., and M. Donald Blaufox, M.D., Ph.D.

**Library of Congress Cataloging in Publication Data**
Main entry under title:

Cardiovascular nuclear medicine.

Reprinted from Seminars in nuclear medicine, v. 9, no. 4, Oct. 1979 and v. 10, no. 1 and 2, Jan. and Apr. 1980.
Includes bibliographical references and indexes.
1. Radioisotopes in cardiology—Addresses, essays, lectures. 2. Nuclear medicine—Addresses, essays, lectures. 3. Angiocardiography—Addresses, essays, lectures. I. Freeman, Leonard M., 1937– II. Blaufox, M. Donald. III. Seminars in nuclear medicine.
RC683.5.R33C38 1980 616.1'07575 80-16126
ISBN 0-8089-1292-5



**Grune & Stratton, Inc.**
**111 Fifth Avenue**
**New York, New York 10003**

Distributed in the United Kingdom by
**Academic Press, Inc. (London) Ltd.**
**24/28 Oval Road, London NW 1**

Library of Congress Catalog Number 80–16126
International Standard Book Number 0-8089-1292-5

Printed in the United States of America

# CARDIOVASCULAR NUCLEAR MEDICINE

# DEDICATION

This volume is dedicated to the memory of three Nuclear Medicine Physicians who passed away in 1979; Philip M. Johnson, George V. Taplin, and Marc R. Tetalman. Tapey and Phil had long distinguished careers in Nuclear Medicine that contributed heavily to our specialty. Marc, in his relatively brief career, was highly regarded and showed great promise of future achievements. They will all be missed by their friends and colleagues.

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# CARDIOVASCULAR NUCLEAR MEDICINE

# Letter From the Editors

FEW EXAMPLES of the dynamism and excitement of nuclear medicine demonstrate this field's vitality in the way that cardiovascular nuclear medicine does. No other branch of diagnostic medicine offers the incredible potential to demonstrate the function of the body and its organs in a noninvasive manner as does nuclear medicine. The development of transmission computerized tomography to many shortsighted individuals was a severe blow to the growth and development of this field. In fact it has turned out that the development of this incredibly powerful radiologic tool was a very positive force in nuclear medicine. The resolution achieved by radiographic techniques will undoubtedly be superior to nuclear medicine techniques for many years to come. The ability to use radiotracers to depict function with images, curves, graphs and a variety of other displays, however, remains unrivaled by any other diagnostic modality. Nowhere has this been more apparent than in the cardiovascular area. Because of the lack of safe, noninvasive technology, cardiologists have long sought alternative means of evaluating the heart. This is exemplified by the great interest they have shown in echocardiography. With the availability of radionuclide techniques, the potential for evaluation of wall motion and the on-line measurement of cardiac function in coronary artery disease and other congenital and acquired diseases of the heart, as well as during various medical intervention procedures, has begun to be realized. The combined use of echocardiography and cardiovascular nuclear medicine permits the cardiologist to delineate parameters of the heart that previously could be obtained only at cardiac catheterization. Because of the availability of these new techniques, the potential for defining the characteristics of a wide variety of diseases as well as their natural history has now come within reach.

Further, the requirements of cardiovascular nuclear medicine and its cost justification have now made highly advanced computer technology available to many nuclear medicine laboratories that could not previously justify it. An anticipated spin-off of this technology will be its application to organ systems other than the heart so that the model that the cardiologist has available to him can be extended to the nephrologist, pulmonary physician, neurologist, gastroenterologist, and other disciplines where in vivo evaluation of organ function and its response to disease and therapeutic modalities are desperately needed.

In this volume dynamic function procedures as well as the static imaging techniques are reviewed. The discussions of physiological considerations related to thallium and phosphate myocardial imaging help clarify these procedures to some extent, but they also show that there still is a need for significantly more research in order to fully understand how and why they work.

As is true for most other areas of nuclear medicine, the cardiovascular techniques span many fields. Application in pediatric and adult medicine and in congenital and acquired heart disease and interrelationships with echocardiography are of major importance in the daily practice of cardiovascular nuclear medicine. Emission tomography and short-lived nuclides that have not achieved general clinical use have applications in the heart as well.

It is a challenge to the nuclear medicine physician to learn cardiology as in the past he has had to learn aspects of neurology, gastroenterology, and other subspecialities of medicine. But this is the excitement and challenge of the field. Few areas of medicine offer the vast diversification and opportunity to deal with all aspects of medical practice as does nuclear medicine.

The thallium-201 chloride perfusion study is probably the most difficult radionuclide imaging study to interpret. Its low myocardial concentration (5% of injected dose), poor imaging photopeak (70–80 KeV mercury x-ray), poorly understood localization and redistribution mechanisms, diminished sensitivity in cases of global ischemia, and significant variability in intraobserver interpretation all contribute to the problems faced by the nuclear medicine physician. Factors related to performance of stress testing also affect the thallium study and impose limitations similar to that encountered by the ECG. In any event, early results clearly indicate that the combination of stress electrocardiography and myocardial perfusion imaging yield a sensitivity greater than either procedure can achieve by itself. Quantitation of the thallium study is difficult; yet several of the approaches are currently under intense investigation and appear promising.

An important question that must be answered relates to the relative roles of wall motion studies (first pass or gated blood pool) and myocardial perfusion imaging in the screening of patients for ischemic coronary artery disease. Although different functions are being studied, the underlying pathology being sought is the same. It is clear that the early 1980s should yield some useful information concerning this problem.

The tremendous amount of research success and clinical acceptance of cardiovascular nuclear medicine have been due to the combined efforts of the nuclear medicine physician and cardiologist. The technical expertise and interpretive skills of the former have blended well with the clinical acumen of the latter. As highlighted by the survey published in the May 1979 issue of the *Journal of Nuclear Medicine*, this "team" approach is overwhelmingly utilized in the many institutions surveyed. A unilateral approach to the problem undoubtedly will lead to mediocrity and a disservice to the patient. The rare exception to this statement might exist when one physician possesses dual expertise, e.g., a nuclear medicine physician with a cardiology background. "Turf" battles, in general, should be avoided by encouraging cooperative effort in this important area of patient care.

The introduction of cardiovascular nuclear medicine techniques is truly one of the most impressive advances in nuclear medicine. We await the extension of this technology to other areas of nuclear medicine. Nuclear medicine began as a function-oriented discipline which, in its second phase, moved strongly toward imaging where there were few competitive techniques. During its imaging phase, much of the potential functional evaluation in nuclear medicine was neglected. We have now gone full cycle and have begun to utilize all of the potential information capabilities of nuclear medicine with a combination of functional studies applied in parallel with organ imaging.

Leonard M. Freeman, M.D.
M. Donald Blaufox, M.D., Ph.D.

# Cardiovascular Nuclear Medicine: An Overview

Richard N. Pierson, Jr., Marvin I. Friedman, William A. Tansey, Frank S. Castellana, Derek Enlander, and Por J. Huang

**Some of the available cardiovascular nuclear medicine methods are incompletely validated, and others are incompletely developed. They are, however, of very great potential in diagnostic cardiology, and in patient management. A new era of clinical research and acute care monitoring has been opened by serial, noninvasive, hemodynamic measurements of right ventricular as well as left ventricular function. Stress testing has become more specific, and should, with future developments, become more sensitive, using radionuclide procedures. Serious quality control and validation questions concerning thallium stress testing must be addressed. Intracoronary injection of radiogases has great potential, although minimal present application. Emission computerized tomography will be an important research tool. Compartmental analysis modeling of first pass tracer injections has much to offer, but is not yet validated. Present growth rate of these procedures is very rapid. Fully developed, cardiovascular nuclear medicine may become the largest component of clinical nuclear medicine practice.**

NUCLEAR CARDIOLOGY has come of age in concept, instrument development, and clinical application. However "coming of age" and "reaching maturity" are neither biologically nor legally identical stages, and the authors of this overview take pleasure in this opportunity to discuss present status and to consider the implications for an apt definition of maturity. This definition will take several dimensions in our construction, or "evaluation matrix." We will consider aspects of physiologic concept, equipment and materials design, and the diagnostic needs of cardiology. We will discuss the special methods and disciplines represented by the authors in this journal. For each method, we will consider stages of development, which may imply time tables, or at least developmental sequences. Finally, we will indulge in all the license implied in the title to speculate, to prick balloons, and to dream, based on our experience and our wits. For "in dreams begin responsibility."[1] Figure 1 presents two types of judgments about each of the measurement methods. The theoretical validity is rated by the authors on a scale of A through X. The present level of acceptance is indicated by a number, 1 to 4. The reasons for the alphabetical ratings are given in further detail in the section describing each method.

*From the Divisions of Nuclear Medicine and Cardiology St. Luke's Hospital Center, and Department of Chemical Engineering, Columbia University.*

*Address reprint requests to Richard N. Pierson, Jr., Divisions of Nuclear Medicine and Cardiology, St. Luke's Hospital Center, New York, N.Y. 10025*



*0001-2998/79/0904-0001$0200/0*

## FIRST PASS STUDIES

First pass studies may be carried out with either an Anger or a multicrystal camera. A larger field of view, inherently higher spatial resolution, and possible biplane[2] (two angle) viewing of a single injection bolus favor the Anger camera, while higher count rate capability and a highly developed software in a built-in computer favor the multicrystal camera, especially where less local programming capability makes a turn-key system desirable. Almost identical readouts, in terms of cinematic ventriculograms and the reported parameters of regional wall motion and ejection fraction of both ventricles, and cardiac output and pulmonary blood volume, are available from both systems, and the first pass studies available with either will be considered together, with the important proviso that the 3–4-fold higher count rates with the multicrystal system may be an important difference for some purposes.

### Pros and Cons

#### *Pros*

*RAO ventriculogram.* The most important of the advantages of the first pass method is its access to the right anterior oblique (RAO) ventriculogram. Of the eight segments of the left ventricle to which conventional angiography gives access, five are best imaged in this view. The left anterior oblique (LAO) view, representing the septal and posterior segments, images three segments. Of course either view may, in a given case, best locate a contraction abnormality. Measurement of ventricular volume by the area-length method is only possible in the RAO view.[3,4] The RAO first pass study

| | EQUILIBRIUM GATED | | FIRST PASS Gated | | Time-Activity | | Single Probe | Model Based Analysis | ECAT | Thallium | Pyrophos-phate |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | RWM | EF | RWM | EF | PBV | EF | EF | | | | |
| CONCEPT LAO | A1 | B1 | A1 | B1 | A3 | C2 | | | | | |
| Anterior | A2 | X | A1 | C2 | A3 | B1 | A1 | A3 | B3 | A1 | A1 |
| RAO | C2 | X | A1 | A1 | A3 | A1 | | | | | |
| TECHNIQUE | A1 | B2 | A1 | B2 | B2 | A1 | A1 | B1 | B3 | B2 | A1 |
| INSTRUMENT DESIGN | A1 | B2 | B1 | A1 | B2 | A1 | A1 | A1 | B3 | B2 | A1 |
| CARDIO-LOGIC NEED CAD | A1 | B1 | A1 | A1 | A3 | A2 | A1 | D4 | B4 | A1 | A1 |
| Myopathy | A1 | B1 | A1 | A1 | A2 | A2 | A1 | B4 | C4 | X | C3 |
| Valve Disease | B3 | B3 | B2 | A1 | B2 | A1 | C3 | B3 | D4 | X | X |
| Shunt | X | X | D4 | A1 | A1 | A1 | B2 | A3 | X | X | X |
| Exercise | A1 | B1 | A1 | A1 | A3 | A1 | A1 | A3 | X | A1 | X |

Legend

- A Conceptually sound. Well validated and calibrated.
- B Promising. Advanced in development.
- C Possible
- D Doubtful
- X Inappropriate

- 1 Widely accepted.
- 2 Accepted by some.
- 3 Experimental.
- 4 Untested.

A, B, C, D, and X represent a judgment by the authors on the level of development of a technique, in a particular application.

1 - 4 represents a review of the literature

**Fig. 1. An evaluation matrix for nuclear cardiological procedures and their applications to clinical cardiology, as of July 1979.**

with tagged albumin or red blood cells (RBC) may be followed by an LAO equilibrium gated study, permitting definition of all eight traditional angiographic segments of the left ventricle. For imaging the function of the right ventricle, the RAO view is even more critical, since the most mobile segments are not defined at all in the LAO view.

*Temporal separation.* The first pass view images the ventricles when the radioactive bolus in the chamber of interest (right or left ventricle, or each in turn) is maximal, and the background minimal. This temporal separation is best with good bolus injection in a central vein; in a high output state; and in a normal heart; and least effective with peripheral injections; in low output states; and in patients with congestion and pooling of increased blood volumes. Sharp and accurate description of the aortic valve plane is usually, although not always, possible. When it is possible, the quality of the resulting study often is highly significant clinically by its contribution to diagnostic accuracy. The mitral valve plane is less clearly seen, but when the left atrium is enlarged, mitral insufficiency may be suggested by atrial enlargement in systole.

*Short term measurement.* The measurements from a first pass study reflect function during a relatively brief period of 10–30 sec, as opposed to an average function over a much longer (2–10-min) period with equilibrium studies. Individual beats may be studied by time-activity curves, as shown in Fig. 2. Markedly irregular rhythms, as in the figure, can only be characterized by first pass time-activity curves.

*Ejection fraction, blood volume, chamber volumes, cardiac output, and regurgitant flows.* The time activity curves produced from first pass studies provide an accepted method of measuring ejection fraction by the Schelbert method.[5] Of potentially even greater importance, the indicator dilution signal from the tracer bolus transit through the heart can be analyzed by compartmental analysis to give pulmonary

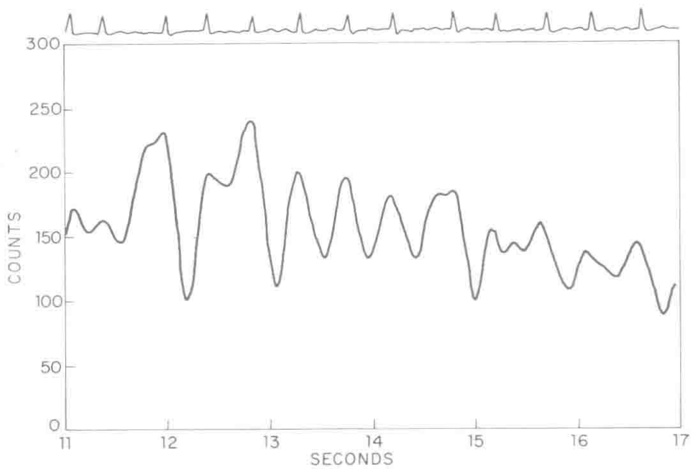


**Fig. 2. A time activity curve in which the y-axis represents ventricular volume changes in relationship to varying cycle lengths, indicated by the ECG tracing (top). Longer R-R intervals appear to result in larger stroke volumes, although other variables, such as respiration also affect filling.**

blood volume, chamber volumes, cardiac output, and regurgitant flows.[6,7] These calculations have not yet been validated, and progress in rationalizing the adequacy of mixing, and background and crosstalk corrections, must be accomplished before this goal can be achieved. However, the data are inherently available, and the computers used to take the data are inherently programmable, to make this calculation. This potential for acquisition of physiologic measurements from the tracer injection represents a potential advantage for this method. An additional motivation to examine carefully the time activity curve, and the first pass gated images, is the identification and quantification of mitral regurgitation, which is a finding of great clinical significance. This may be done either by quantifying a difference between forward stroke volume and total strole volume, or by finding the accentuated filling of an enlarged atrium during ventricular systole.

*Cons*

*Placement of the tracer injection is more critical.* A right atrial pulse injection during systole is ideal, and a small vein delayed injection is least adequate, the quality deficit being more marked as the patient has a more congested circulation.

*Coordination.* More coordination is required in operating the equipment than for an equilibrium study. Technical failure to start the counting system promptly may lose a critical part of the study.

*Data processing.* Data processing is much more time consuming, and more demanding, for proper region and time selection in first pass studies, since temporal separation of right and left heart phases is required. Highly developed software for the multicrystal camera simplifies this problem, and it is expected that similar programs will become more widespread for application to Anger camera data.

*Number of counts.* The total number of counts available for image definition is inherently limited on first pass studies by Anger camera systems by the maximum processing rate of the instrument. These constraints in fact result in "just enough" or "not quite enough" count density compared with what could be desired. This results in confidence limits about the chamber count rates, which are in the 5%–10% range, a number considered applicable to most flow and volume measurements in clinical cardiology. By contrast, equilibrium studies can be collected over much longer patient study times, reducing the statistical variations that depend on total count rates, while adding uncertainties based on patient motion.

*Camera placement.* Camera placement is always critical in first pass studies, even more so with the multicrystal camera, which has a smaller field of view. Partly for this reason, the anterior view has been favored with this instrument.

*Repeated injections.* Finally, repeated studies require repeated injections. When a single, or only two injections are required, the first pass method advantages may be substantial. When repeated studies over a period of several hours are required, equilibrium gated methods have a distinct advantage.

## SINGLE PROBE STUDIES

Single probe radiocardiography, measuring a time-activity curve from the entire heart or any chosen region, was the original technique with Blumgart and Weiss in 1929,[8] and again with Corday and Prinzmetal in 1949.[9] The precordial time-activity curve was conceptualized, approximately, by Lammerant in 1950,[10] and very precisely by Donato working with Cournand in 1962.[11] Clinical applications have been of merit, although limited in number.[12-14] This very viable methodology provides much less data than the spatially resolving gamma cameras, but it provides the measurements at much less cost and complexity.

*Pros*

*Simplicity.* A single well-collimated crystal and a ratemeter readout are relatively portable, inexpensive, and simple to maintain and operate. A physician, without need for a technologist, can draw up a dose, place the probe, and carry out a study in 10–15 min, and then provide a result (cardiac output, ejection fraction, and approximate pulmonary blood volume) within 10 min after the study, without a computer.

*Repeated studies.* Using short half-lived tracers ($^{113m}$In is ideal[15]), studies can be repeated at almost any desired frequency.

*Cons*

*Placement.* Careful probe placement is critical for LV ejection fraction measurements. It is difficult (but not impossible) to know from the output tracing whether placement was acceptable.

*Simplicity versus believability.* Who will believe that such a simple measurement could be accurate or useful?

### Conclusions

High technology laboratories will not settle for a time-activity curve, when two- and three-dimensional cine studies can be provided. But there are environments, such as the intensive care unit, where gamma cameras cannot easily be applied in the study of very sick patients. Here, the more qualitative single probe study could be invaluable. We look forward to seeing the necessary validation for such an application.

The nuclear stethoscope[16] is an intriguingly simple and relatively inexpensive instrument that creates a representative volume cycle by an equilibrium gated logic of summing small signals from recurring beats (v.i.) using an ECG trigger. An average time-activity curve results, which may be processed (by estimating background) to give an ejection fraction. The output of this instrument, ejection fraction, and an "average volume cycle," could be useful in serial measurements with intervention. (The first pass and gated "nuclear stethoscope" approaches are discussed in detail in this seminar and the reader should look there for a detailed pro and con discussion.)

## SHUNT DETECTION

Simple,[17] more complex empiric,[18] and totally explicit model-based methods[6] have been used to estimate shunt size from external counting of regional time-activity curves. The principal of locating, quantifying, and calculating the recirculation of tracer from left to right shunts is highly satisfactory using any of these methods for shunts in which pulmonary flow is between 115% and 300% of systemic flow. Below 15% shunt fraction, the recirculating tracer may be missed in noise. Beyond 300%, the presence of the shunt is apparent, but doubtful mixing assumptions and difficulty in separation of secondary from primary curves prevent accurate quantitation.

These techniques are primarily used in children with congenital heart disease, and they are excellent. Analytic problems are so well in hand in this area, that further developments tend to outstrip the cardiologic need. The principal problem in adult nuclear cardiology is the infrequency with which shunts are seen in practice. The search for better techniques is a restless and permanent reality in research, as indicated in the second part of this review series. However more than in any other area of cardiovascular nuclear medicine, current technology in shunt detection works very well; new and perhaps more complex solutions may be in advance of the problems.

## EQUILIBRIUM GATED STUDIES

Equilibrium gated studies in the LAO view, both at rest and during exercise, have been widely popularized since 1976.[19-21] Multiframe computer-reconstructed ECG gated images created from as few as 100 cardiac cycles (better images result from 350 to 500 cycles) can be produced using programs available from most of the commercially available nuclear cardiology computer systems. Anterior, RAO, and LPO views have also been recorded, to increase the range of the equilibrium technique to visualize other regions of the heart not visualized in the LAO view. The uses of the equilibrium gated technique may be summarized in the form of two pros and two cons.

## Pros and Cons

### *Pros*

*Number of "steady states."* Any number of "steady states" (a period of 100 or more beats) can be studied after a single tracer administration. Several levels of exercise, serial responses to drug therapy, pacing, volume alteration, or any other physiologic stimulus may be analyzed over a period up to 6 hr. It is only required that the subject be at steady state for 1½–5 min, and that motion of the subject with regard to the gamma camera be very limited. Although these restrictions would appear to favor passive physiologic changes such as drug or volume intervention, supine exercise has been studied most widely,[19] and advantage has been taken of the potential of the the exercise stress technique to evaluate both coronary flow and myocardial reserve by increasing myocardial work.

*Simplicity.* The technique is extremely simple to carry out, given the computer and appropriate programs. There is virtually no processing time between performance of the study and its availability for interpretation.

### *Cons*

*Nonidentity of successive heart volume cycles.* The requirement of steady state presents limitations. Sharp images created by the summing of many low signal events is essentially the well recognized electrical engineering technique of "computation of average transients."[22] It depends heavily on the assumption of the near-identical nature of the recurring transient signal. Nonidentity of successive heart volume cycles occurs from four sources. (1) Respiratory cycling results in phasically increasing and decreasing venous return (and stroke volume) with a frequency of 0.2–0.5/second, or 0.1–0.5 of the cardiac frequency. Respiration phased changes in stroke volume are maximal in healthy athletes, and minimal in older cardiac patients, and are usually less than ±10% of mean. (2) Varying cycle length, as in atrial fibrillation with marked variation in R-R interval (Fig. 2), results in widely varying end diastolic volume(EDV) and ejection fraction (EF).[23] Sinus arrhythmia and fairly regular atrial fibrillation introduce only minor changes in stroke volume, which may be less than 10% in magnitude, and fall within the envelope of precision available from the method. Premature ventricular beats can be excluded from summation by use of recognition and buffering circuits, which are readily available. (3) Exercise steady states should await the 3rd min of a newly imposed stress level, as most patients "hunt" a steady heart rate and stroke volume during the first 2 min.[24] (4) Patient motion with regard to the gamma camera is always a problem at exercise, and increases with increasing levels of exercise. It must be prevented by vigilance, and should be monitored by a fixed radioactive marker on the patient's chest.[25] Patient motion will artifactually increase apparent EDV, and reduce apparent regional wall motion. Both errors have substantial effect on the utility of the study.

*Limitations of viewing angle.* Limitations of viewing angle are severe in the LAO position, from which only three of the classical regional segments are seen on tangent. Addition of anterior, RAO, and LPO views in some (a minority) of reports[26] increases the specificity of the equilibrium technique for defining regional wall motion. However, the anterobasal and posterobasal segments are rarely convincingly demonstrated because of the overlying right ventricular and pulmonary blood volumes. The limitation of viewing angle presents no problem when the purpose of the study is limited to global ejection fraction, or its reserve in response to exercise. For the most sensitive measurements of regionally developing contraction abnormalities, the RAO first pass methods (v.s.), which have the capacity to image a larger number of cardiac segments, may be required.

## Pros Versus Cons: Conclusions

The advantages of the multiple gating equilibrium method listed above present a powerful motivation to overcome the disadvantages, because of the great importance of intervention studies in cardiology. Accordingly, we predict that it will be developed further, using strict attention to multiple chest wall markers to warn of patient motion or, conceivably, to correct for motion by aligning images in a processing buffer according to the positions of the markers. Respiratory phase gating also is possible, but it is not likely to be necessary for the average patient, and its use would probably double or treble the time required for the study, which would rarely be tolerable in the clinical environment. A biplane measurement, capable of producing LAO and anterior views simultaneously,[2] would be a very useful development with widespread utility in exercise testing, and in intervention evaluation of cardiac reserve in the acute care environment. Accurate measurements of end-diastolic and end-systolic volumes are not available now from equilibrium gating techniques, and we consider it unlikely that quantitative measurements will evolve from this method.

## QUANTITATIVE MEASUREMENT OF EJECTION FRACTION:

Accurate quantitative measurement of ejection fraction using the counts method has been claimed for some years, and many studies have compared this technique with contrast angiography in the same patients.[27-29] In the LAO view, on theoretical grounds we would expect only approximately correct results from this method, because the left atrium, which contains a volume of blood approximately equal to that of the end-diastolic left ventricle, has about 30% overlap with the upper and posterior portion of the ventricle. This nonventricle source of counts, combined with Compton scatter counts from other nearby cardiac structures, is compensated for by subtracting an arbitrary background, usually selected by choosing a region over the lung, some arbitrary distance from the heart, and assuming that the count rate in this region is similar to that behind the left ventricle. The probability that lung counts would just match, in timing and quantity, both left atrial and Compton scatter counts seems to us quite low, but by fortuitous arrangement of the regions-of-interest, a matching count for any given time point can of course be produced. Its stability over time, and its stability from one patient to another, are in question. Operator experience in choosing these regions, particularly when a number of angiographic studies are available during the learning phase, results in numbers that are on average reasonable, particularly when they are evaluated as a group, using the blunt statistical tool of correlation coefficient rather than its more appropriate first cousin, the standard error of the estimate.[30]

Divergences between radionuclide and contrast studies are most apparent at high and low levels. The occasionally reported ejection fractions of less than 10%, are incompatible with life. The regression slope is characteristically between 0.8 and 0.85, with convexities to a best fit function at either end. Since most measurements fall between 20% and 75%, the actual errors are not very visible by regression analysis. Fortunately however, in the exercise stress studies, the direction of change if EF is far more important than an absolute measurement, since in any given patient the unknown contribution of counts into the LV from the left atrium and other chambers should remain approximately constant before and after the intervention, and the measured change in EF should be directionally accurate.

## EVALUATION OF THE RIGHT VENTRICLE

The right ventricle is imaged by equilibrium studies in the LAO position for motion of the septal, inferior, and lateral free walls. Since the RV volume is best described as a three-dimensional crescent wrapped around one-third of the surface of the left ventricle, this view is very limiting, being restricted to showing the width of the crescent, and its base in the narrowest view. Motion of the septal surface reflects LV more than RV muscle contraction. Thus, marked abnormalities of RV contraction, especially in diffuse processes such as cardiomyopathy, may be visualized by the gated LAO view, but for appreciation of regional contraction, the RAO angle provides a substantially better view of the right ventricle. This cannot be accomplished in the equilibrium gated method because of the chamber overlap previously described. The "thickness," or third dimension, of the right ventricle is much less than that of the more spherical left ventricle, which dominates the "count image" in any view in which these volume images overlap.[31] The anterior view may improve the odds of imaging the inferior left ventricle, and the anterior right ventricle wall, and may thus permit sufficient visualization of both ventricles to allow clinical judgments to be made. However, rendering of quantitative measurements from this view seems extremely unlikely.

The first pass method, using the 30° RAO view, images the right ventricle in its widest horizontal dimension, showing the chord or waist of the three-dimensional crescent extending from the tricuspid valve plane (on edge in this view) to the anteroseptal free wall. Both types of gamma cameras have provided excellent representation of regional wall motion, and either by count change[32] or area-volume formulation,[33,34] estimation of RV ejection fraction has been made using this view. The effects of predominant right ventricular infarction,[35] pulmonary hypertension, obstructive airway disease, and left ventricular disease on right ventricular function have been for the first time critically studied in vivo, since angiographic methods are applied only with difficulty in the right ventricle. We predict new, basic, and major contributions to the understanding of right ventricular function using radiocardiographic techniques. More new and undiscovered territory is apparent here than in any other area of hemodynamic cardiology.

## STRESS EXERCISE MEASUREMENTS BY RADIOCARDIOGRAPHY

Gated blood pool imaging by either first pass or equilibrium methods is inherently applicable to stress testing, and extensive experiences have been reported. Borer and colleagues have used equilibrium measurements;[19] Jones,[36] Zaret[37] and others have used multicrystal cameras; and Jengo[38] has used the Anger camera to measure regional wall motion in exercising patients. The stimulus of exercise has been used both in electrocardiography and radiocardiography because it is physiologic; becuase it can often be pushed to levels associated with maximum cardiac work; and because it has the tendency to avoid an excessive, morbid, or fatal stress through self-limitation, although, as the runner of the original marathon established, death occasionally may result from extreme exercise. Other stresses, such as isometric handgrip,[39] intravenous catecholamine stimulation,[40] and atrial pacing[41] do not require patient cooperation to the same degree, but they also lack the inherent safety of graded application and a self-limited maximum level, and they all have disadvantages for routine application, although they clearly do have special applications, usually in hospital.

Exercise may be performed by supine cycling, which has the advantage of fixing the chest vis-à-vis the camera for stable imaging during leg exercise, and the disadvantage of requiring a somewhat clumsy and unaccustomed exercise.

Sitting cycling is easier for the subject, and more difficult for stability in imaging, particularly in the gated equilibrium method, where an image requires 2–5 min. The 10–30 sec required for a first pass study at exercise requires close attention to detail, but such studies have been successfully carried out in great numbers of subjects, with over 90% technical success rates, by Jones and colleagues at Duke.[36]

It has not yet been definitively established that exercise quantitative radiocardiography is more sensitive than exercise thallium in disclosing early or single vessel coronary artery disease. In a limited experience, we believe wall motion techniques to provide earlier and more reliably interpretable evidence of coronary artery disease. For example, it is possible to see delayed diastolic filling confined to one segment of the ventricle, with no change in end-diastolic or end-systolic volume, or ejection fraction. If this is the earliest contractile abnormality in ischemia, it clearly precedes changes in ejection fraction, and it may well precede measurable changes in the thallium-concentrating pump, given the currently approximate nature of the art of thallium imaging.

Measuring ejection fraction alone in response to stress seems a crude, global, and inherently interim technology, when the capacity to measure regional wall motion mechanics is available with the same instruments, at the dual needs of increased image processing, and the cardiologic skills to interpret a ventriculogram instead of a single number readout. The opportunity for laboratory error is much greater in producing one number, than with a cine that shows end-diastolic and end-systolic volumes and regional contraction patterns. Self-evident as this observation seems, we recognize the impetus to the growth of this field that has been