DIAGNOSTIC NUCLEAR MEDICINE

Simultaneous Display of Gated Technetium-99m Stannous Pyrophosphate and Gated Blood-Pool Scintigrams

James R. Corbett, Samuel E. Lewis, Gregory Dehmer, Frederick J. Bonte, Robert W. Parkey, L. Maximilian Buja, and James T. Willerson

University of Texas Health Science Center and Parkland Memorial Hospital, Dallas, Texas

We have developed a method by which any two sets of R-wave-synchronized radionuclide images may be registered, color-coded, and displayed in cinematic fashion so that the image sets are superimposed and shown simultaneously in contrasting colors. The technique has been applied to technetium-99m stannous pyrophosphate (Tc-99m PPi) and equilibrium blood-pool images. Gated Tc-99m PPi and gated blood-pool image sets (16 frames per cardiac cycle) were acquired in identical projections. Image sets were then registered, if necessary, and color-coded by a computer algorithm. Our initial experience suggests that this overlay technique may be of value to: (a) detect right ventricular infarction with greater precision; (b) provide a better estimate of anatomic location and circumferential extent of Tc-99m PPi myocardial uptake relative to the ventricular blood pool; and (c) distinguish between segmental contraction abnormalities caused by recent infarction (identified by abnormal Tc-99m PPi uptake) and segmental contraction abnormalities caused by ischemia or previous myocardial infarction.

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R-wave-synchronized equilibrium blood-pool imaging provides a means for noninvasive characterization of global and segmental ventricular function. However, in patients with ischemic heart disease, alterations in ventricular function may be the result of myocardial ischemia, prior myocardial infarction, and/or recent myocardial infarction. Technetium stannous pyrophosphate (Tc-99m PPi) myocardial scintigraphy provides a means to identify, localize, and estimate the size of certain acute myocardial infarcts (*1–6*). The combination of focal myocardial increased activity using Tc-99m PPi with R-wave synchronized equilibrium blood-pool imaging should provide a potential means of differentiating possible causes of global or regional ventricular dysfunction (*7–10*). If sites of myocardial accumulation of Tc-99m PPi could be superimposed over gated images of the cardiac blood pool, it should be possible not only to assess global and segmental ventricular function but to identify and assign regional functional alterations to either acute myocardial infarction, prior myocardial infarction, or myocardial ischemia. The purpose of this communication is to describe the development and application of the method that allows this approach.

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For reprints contact: James R. Corbett, MD, Ischemic Heart Center, Room L5.134, The University of Texas Health Science Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX 75235.

MATERIALS AND METHODS

We have studied 21 patients in whom acute myocardial infarction was suggested by clinical history and confirmed by diagnostic or consistent electrocardiographic alterations, serial alterations in cardiac enzymes (including CK-B iso-enzyme) (*11,12*), and abnormal Tc-99m-PPi myocardial scintigrams (*1–6*).

Superimposed, histogram-specified, and color-coded Tc-99m PPi and Tc-99m RBC blood-pool image sets

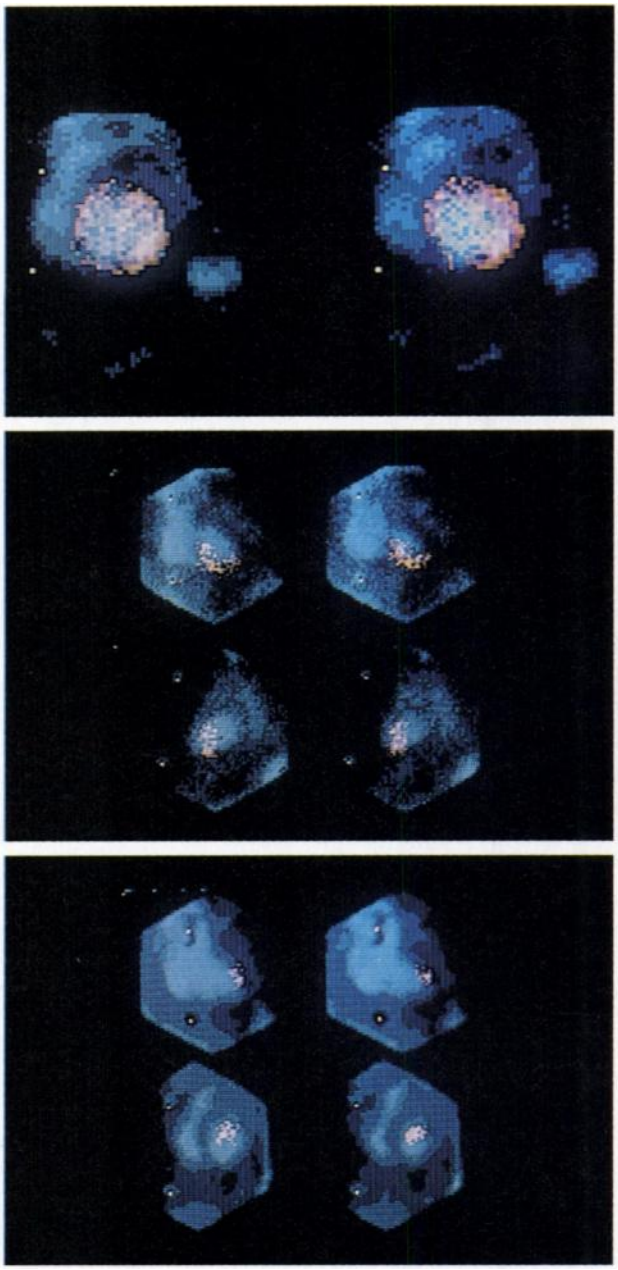

FIG. 1. (Top, left) Tc-99m PPi myocardial scintigrams superimposed on blood-pool scintigrams are shown in patient with "donut" Tc-99m PPi pattern of uptake. Note intense Tc-99m PPi uptake (orange) with central defect (white) superimposed on cardiac blood pool (blue). Diastole is shown at left and systole at right.

FIG. 2. (Center, left) Tc-99m PPi myocardial scintigram obtained from patient with acute anteroseptal myocardial infarction is superimposed on blood-pool scintigram. Note septal uptake of Tc-99m PPi (orange-white) shown in 30° LAO projection during diastole (upper left) and systole (upper right) and in left lateral projection in diastole (bottom left) and systole (bottom right).

FIG. 3. (Bottom, left) Tc-99m PPi myocardial scintigram obtained from patient with anterolateral subendocardial infarction is superimposed on blood-pool scintigram. Upper panels are anterior views in diastole (left) and systole (right). Small, well-defined site of Tc-99m PPi activity is seen along anterolateral wall. Bottom panels show modified LAO views in diastole (left) and systole (right).

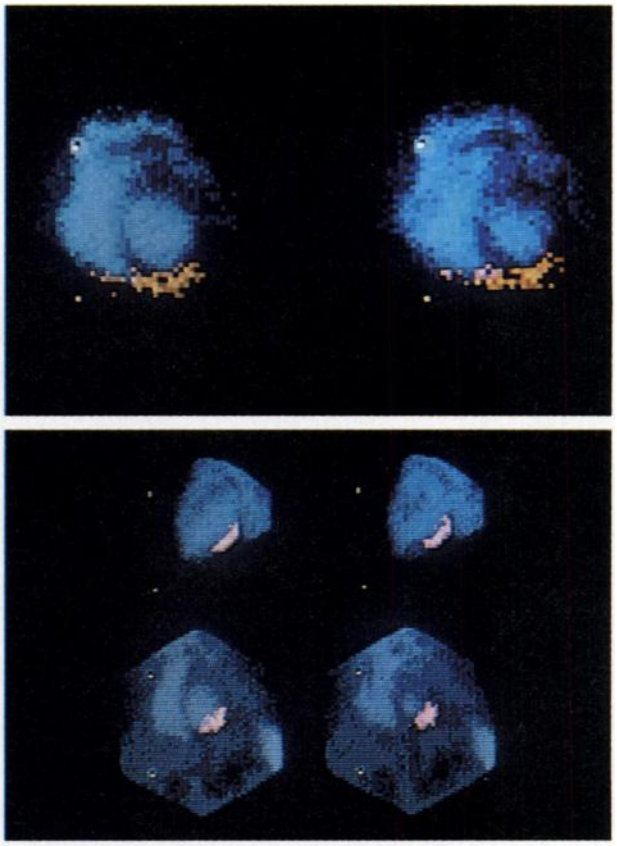

FIG. 4. (Top, right) Tc-99m PPi myocardial scintigram obtained from patient with mild biventricular dysfunction is superimposed on blood-pool scintigram. LAO projections in diastole (left) and systole (right) show Tc-99m PPi uptake (orange) at lower portion of the ventricular septum, inferior and inferolateral portions of left ventricle, and apical aspect of right ventricle.

FIG. 5. (Bottom, right) Increased Tc-99m PPi uptake (light orange) in posterior aspect of left ventricle is shown superimposed on dynamic myocardial scintigram (blue). Top two panels are lateral projections in diastole and systole, respectively; bottom two are LAO projections in diastole and systole.

were obtained as follows. Standard Tc-99m PPi myocardial scintigrams were acquired in anterior, 30° left anterior oblique (LAO), 70° left anterior oblique, and left lateral projections using methods we have previously described (*1–3*). Cobalt-57 point-source markers (25 μCi/marker) were affixed temporarily with adhesive tape to the skin over the manubrium and xyphoid process. The patient was positioned so that his long axis while supine was parallel to the face of the gamma scintillation camera and parallel to its y axis. The latter condition was ensured by requiring that activity from the two point sources appear in the same column of the digitized 64 × 64 image. R-wave synchronized Tc-99m PPi myocardial scintigrams were acquired at a temporal resolution of 16 frames per cardiac cycle for a total acquisition time of approximately 10 min, yielding an image density of 75,000–125,000 counts per frame. Image sets were acquired in multiple projections. The

patient's red blood cells were labeled with 15 mCi of [^{99m}Tc] pertechnetate by a combination in vivo/in vitro method (*13*). Gated equilibrium blood-pool image sets were acquired at a temporal resolution of 16 frames per cardiac cycle to an average pixel density of 200 counts/pixel in the center of the left ventricle in projections identical to those used for the gated Tc-99m PPi image sets. All gated acquisitions were performed on a dedicated nuclear medicine computer system. The same orientation of the patient's long axis to detector's y axis was maintained throughout the study as described above. The various image projections were obtained by rotating the camera head about its y axis only, with the degree of obliquity measured and reproduced with the aid of a precision protractor.

Corresponding gated Tc-99m PPi and gated blood-pool image sets were registered and color-coded for subsequent cinematic display by a BASIC language algorithm. The algorithm identified the x,y location of the point-source markers by searching for the maximum pixel values within an operator-defined region containing the point source. Possible sampling errors were reduced by image smoothing with a 9-point, center-weighted, filter kernel before locating the point sources. The sources should have identical x coordinates. An error of ±1 pixel was allowed. Registration of images was accomplished by shifting one image set so that the x,y coordinates of its more inferior marker were identical to those of the corresponding marker in the other set. Color-coding of the image sets was achieved by mapping pixel values in the gated blood-pool study into the count range 0–127 for display in the lower half of the color table, and pixel values in the gated Tc-99m PPi study into the count range 128–255 for display in the upper half of the color table. These operations were carried out by operator interaction. The operator identified the center of the left-ventricular activity on the end-diastolic frame of the gated blood-pool study. The algorithm averaged the values of the center pixel and its eight nearest neighbors. This average was mapped to a display value of 115 (90% of the maximum display value) and all other pixels in each of the 16 gated blood-pool frames were scaled appropriately. Similarly, the average value in the region of greatest Tc-99m PPi myocardial uptake was mapped to a display value of 255 and all other pixels in each of the 16 gated Tc-99m PPi frames were scaled appropriately. A color table was constructed for best display of the contrast between blood-pool and Tc-99m PPi images. This color table consisted of twenty distinct colors. Count values in the range 0–127 (blood-pool images) were displayed as ten distinct colors. The three lower levels were displayed as black and the seven upper levels as increasing monochromatic blue. Count values in the range 128–255 (Tc-99m PPi images) were also displayed as ten distinct colors. The five lower levels were displayed as black and the five upper levels as increasing monochromatic red. This mapping suppressed low-intensity activity in both image sets. Cinematic display of the registered and color-coded image sets was achieved by reading the first frame of the gated blood-pool study into the first frame of the image memory, and alternating corresponding frames of the two studies. Sequential display of the image memory in an endless-loop cinematic format produced the desired superimposition of moving images. The pure bichromatic color scale is suppressed in the cinematic display, since color mixing occurs at sites of overlap. Thus some Tc-99m PPi activity may appear orange or orange-white in the final display.

Technetium-99m PPi activity not associated with the myocardium was eliminated from the final display as follows. Conventional static and gated Tc-99m PPi images, gated blood-pool images, and superimposed image sets were reviewed by two experienced observers. The location and extent of Tc-99m PPi myocardial activity was determined by careful observation. The position and periodic motion of the Tc-99m PPi activity relative to the cardiac blood pool facilitated the perception of abnormal activity. Computer-assisted manual construction of a region of interest over the myocardial Tc-99m PPi activity created a masking image. Subtraction of the inverse masking image from each frame of the gated Tc-99m PPi study removed nonmyocardial activity. Although this procedure was used in the preparation of the figures in this report, we have subsequently found it unnecessary. Indeed, we have discovered that the presence of the osseous activity improves the perception of spatial orientation.

RESULTS

Twenty-one patients with proven acute myocardial infarcts were studied with the technique described above for overlaying gated Tc-99m PPi and gated blood-pool images. Table 1 gives complete patient data and the general contribution of the overlay technique to interpretation: improved anatomic definition, more precise differentiation of abnormal myocardial accumulation of Tc-99m PPi from other causes of apparent myocardial uptake, or qualitative increase in extent of myocardium involved by acute infarction. Fifteen of the 21 patients had acute transmural infarcts, while six had acute nontransmural infarcts. Three of eight patients with anterior myocardial infarcts had "donut" patterns of uptake on planar Tc-99m PPi scintigrams (Fig. 1) (*4*). Two patients had acute anteroseptal infarcts and one infarct was apical in location. One patient had a true posterior infarct, and three had acute right-ventricular infarcts.

Several brief case presentations provide representative examples of the clinical presentations of these patients in relation to the scintigraphic findings obtained with the overlay technique.

Case 1 (C.J.). A 46-year-old male with no previous

TABLE 1

Patient	Age, sex	Previous MI	Location and type of MI*	Tc-99m PPi scintigram†	LV dynamic scintigram	Overlay contribution	Clinical course and/or complications
ES	64, M	+‡	Anterior TM	4+ Donut	Extensive Ant (Sep and Lat) and Inf WMA, LVEF 15%	Extensive LV uptake exclusive of Hypo Inf wall	Killip III, died
CJ	46, M	0	Anterior TM	2+ Ant Sep	Ap, Ant, Sep–Hypo, LVEF 41%	Better definition	Uncomplicated
HZ	47, M	0	Anterior TM	3+ Donut	Ap, Ant, Sep–AK and Lat Hypo, LVEF 34%	Ap and basal septal and lateral uptake	Killip II, CAB
JG	39, M	0	Anterior TM	3+ Donut	Extensive Ant (Sep and Lat) WMA, LVEF 22%	Increased extent of uptake	Killip III, recovered
JJ	78, M	0	Anterior TM	2+ Ap Ant Sep	Ap, Ant Sep AK and Hypo, LVEF 60%	Better definition and extent	Uncomplicated
WS	78, M	0	Anterior TM	2+ Ant Lat	Ap, Ant aneurysm, LVEF 20%	Donut pattern, Sep and Lat uptake and WMA	Killip III, arrhythmias
MC	63, F	+	Anterior TM	3+ Ap Ant Lat	Ap, Ant aneurysm, LVEF 29%	Increased extent of uptake	Killip III, arrhythmias, died
DS	71, M	0	Anterior TM	4+ Ap Ant Lat and Inf	Ap, Ant, Sep and Lat WMA, LVEF 30%	Sep involvement, increased extent	Killip IV, arrhythmias, died
WZ	43, M	0	Inferior TM	3+ Inf Pos Lat	Inf, Pos, Lat–Hypo, LVEF 39%	Increased extent of uptake	Recurrent angina
LW	70, F	0	Inferior TM	3+ Inf Pos Lat	Ap, Inf, Pos–Hypo, RV Ap Lat-AK, LVEF 41%, RVEF 20%	Better definition including RV	Hypotension, recovered
RB	49, M	0	Inferior TM	2–3+ Inf Pos	Pos–Hypo, LVEF 63%	Better definition	Uncomplicated
JM	43, M	0	Inferior TM	2+ Pos	Inf, Pos, Lat Hypo, LVEF 66%	Better definition to Inf and Lat	Uncomplicated
GO	71, M	0	Inferior TM	3+ Inf Pos Lat	Inf Pos Lat Hypo, LVEF 48%	Increased extent of uptake	Killip II, recovered
SW	54, F	0	Inferior TM	2+ Inf Ap	Ant–Hypo and Ap Inf Pos–Hypo, LVEF 49%, RV Ap Lat Hypo	RV and Pos involvement	Killip II, hypotension, CHB
CS	51, M	0	Inferior TM	4+ Inf Lat	Ap, Inf, Pos Lat WMA, RV Ap Lat Hypo, LVEF 47%, RVEF 41%	Ap Pos and RV involvement	Killip II, CHB, CAB
DW	59, F	0	Anterior NT	2+ Ap Lat	Lat–Hypo, LVEF 61%	Better definition	Uncomplicated
HW	72, M	0	Anterior NT	3+ Ap Inf Pos Lat	Ap, Ant, Lat and Pos WMA, LVEF 31%	Better definition and extent	Killip II, died
PS	54, M	+	Anterior NT	Equivocal Ant	Ant, Lat, Hypo, LVEF 55%	Better definition	Recurrent angina
ES	35, M	+	Anterior NT	3+ Ant	Ant, Lat and Inf Pos Hypo, LVEF 37%, RVEF 55%	Distinguished new WMA	Killip II, recovered
JR	49, M	+	Indeterminate	4+ Ap	Ap, Ant, Lat and Inf Sep Hypo, LVEF 29%	Increased extent, new WMA	Killip II, recovered
SR	73, F	+	Indeterminate	2+ poorly defined	Ant, Lat and Inf, Pos–Hypo, LVEF 38%	Better definition, new WMA	Killip II, recovered

* By ECG criteria.

† Ungated scintigram.

‡ Abbreviations: + = present; 0 = absent; TM = transmural; NT = nontransmural; LV = left ventricular; RV = right ventricular; Ap = apical; Ant = anterior; Sep = septal; Lat = lateral; Inf = inferior; Pos = posterior; EF = ejection fraction; Hypo = hypokinesis; AK = akinesis; CAB = coronary artery bypass; CHB = complete heart block; WMA = wall-motion abnormality.

history of heart disease presented with symptoms suggestive of acute myocardial infarction and Killip Class II congestive heart failure. Evolution of the patient's EKGs and cardiac enzymes (CK and CK-B) demonstrated classic changes diagnostic of acute anteroseptal infarction. The gated blood-pool study showed severe hypokinesis of the apex and apical anteroseptal segments of the left ventricle. The global left-ventricular ejection fraction was 41%. The Tc-99m PPi overlay revealed abnormal accumulation in the apex and apical portion of the septum in the 30° LAO projection and in the apical-anterior and apical segments of the left ventricle in the 70° LAO projection (Fig. 2). Thus, the septal and apical wall-motion abnormalities identified on the gated blood-pool study were most likely due to recent myocardial necrosis. Following initial treatment, the patient had an uncomplicated course.

Case 2 (E.S.). A 64-year-old male with a history of previous inferior myocardial infarction presented with 3 hr of chest pain, Killip Class III heart failure, and ECG findings of ST elevation in leads V2–V4, and significant Q waves in leads 2,3, and AVF. Evolution of cardiac enzymes (CK and CK-B) and ECGs documented an acute anterolateral transmural infarction. Gated

blood-pool imaging demonstrated severe hypokinesis of the ventricular septum and akinesis of the apical, anterolateral, and inferolateral segments of the left ventricle. Global left-ventricular ejection fraction was 15%. The Tc-99m PPi overlay demonstrated abnormal uptake over the anterior surface of the left ventricle from septum to lateral wall, with a "donut" pattern (Fig. 1). There was no Tc-99m PPi uptake over the inferior aspect of the left ventricle. Thus the patient had recent extensive infarction of the anterolateral wall of the left ventricle as the major cause of his severe congestive heart failure. He remained in congestive heart failure and died 3 mo later.

Case 3 (E.S.). A 35-year-old male was admitted to the coronary care unit after awakening with chest pain. Relevant historical data included the presence of systemic arterial hypertension and a documented inferior-wall myocardial infarction 1 yr before this admission. Serum cardiac enzymes (CK and CK-B) evolved in a manner classical for acute infarction. ECG changes were compatible with an acute nontransmural infarct. The gated blood-pool study showed mild hypokinesis of the anterolateral segments of the left ventricle and severe hypokinesis of the inferoposterior segments. Global left-ventricular ejection fraction was 37%; right-ventricular ejection fraction was 55%. The Tc-99m PPi overlay revealed a relatively small area of abnormal uptake of Tc-99m PPi over the anterolateral aspect of the left ventricle (Fig. 3). Thus the patient's prior inferior infarction had resulted in important segmental left-ventricular dysfunction, and the reduction in LVEF was the result of the combined effects of the recent anterolateral subendocardial infarction and the earlier inferior infarction.

Case 4 (C.S.). A 51-year-old male awoke with severe substernal chest pain following 1 wk of increasing angina. Upon admission to the coronary-care unit, he had jugular venous distension and bibasilar rales, which cleared with diuretics and digoxin. ECG changes were diagnostic for acute inferior transmural myocardial infarction. The gated blood-pool study showed mild right-ventricular dysfunction with a global right-ventricular ejection fraction of 41% ("gated first-pass" measurement) (*14*). The apex and diaphragmatic regions of the right ventricle were akinetic. The left-ventricular ejection fraction was 47%. Severe hypokinesis of the inferoposterolateral segments of the left ventricle was noted. The Tc-99m PPi overlay showed abnormal myocardial uptake over the apical portion of the right ventricle and the inferoposterolateral regions of the left ventricle (Fig. 4). Thus the overlay image allowed one to establish that the segmental right- and left-ventricular wall-motion abnormalities were due to recent myocardial infarction. Right-ventricular infarction was identified as the cause of the mild right-ventricular dysfunction. The apical and posterior extent of infarction of the left ventricle were clearly documented by the overlay. Even in retrospect, the posterior aspect of the LV infarct was not apparent on the ECG.

Case 5 (J.M.). A 43-year-old male presented with severe chest pain. Electrocardiographic changes consisted of ST elevation in leads II, III, and aVF, with evolution of significant Q waves in those leads. Cardiac enzymes (serum CK and CK-B values) were elevated and evolved in a manner consistent with acute myocardial infarction. Despite a LVEF of 66%, the gated blood-pool study showed severe hypokinesis of the inferolateral and posterior regions of the left ventricle. Right-ventricular function was normal. The Tc-99m PPi overlay showed abnormal Tc-99m PPi uptake over the posterior segments of the left ventricle in the 70° LAO projection and over the inferoposterior and lateral segments in the 40° LAO view (Fig. 5). In the 70° projection, one can see the margins of the uptake pulled centrally by more normal adjacent segments, whereas the center of the infarct is nearly motionless. No significant right-ventricular uptake of Tc-99m PPi was identified. Again, the ECG did not evolve changes that would allow detection of the posterior-wall involvement.

DISCUSSION

Currently available radionuclide imaging procedures can provide considerable information concerning myocardial metabolism, relative segmental perfusion of the left- and right-ventricular muscle masses, site and extent of acute myocardial infarction, blood flow, and mechanical function. Unfortunately, the precise relationship between these physiologic, anatomic, and mechanical parameters in a particular patient often remains unclear because of an inability to correlate accurately the information provided by different imaging procedures. We have developed a method by which any two sets of R-wave-synchronized radionuclide images can be registered, color-coded, and displayed in cinematic fashion so that both image sets are displayed simultaneously, one image set being superimposed over the other in contrasting colors. This technique may be extended to allow the display of superimposed data from more than two imaging procedures. The present study illustrates the potential clinical value of combining information from multiple imaging studies in a direct fashion.

Conventional planar Tc-99m PPi myocardial scintigrams provide a sensitive means to detect acute myocardial infarction (*1–4*). Dead and dying myocardial muscle cells accumulate increased levels of Tc-99m PPi (*6*) compared with normal myocardial cells, blood, and adjacent soft tissues. When at least 3 g of irreversible cellular damage exist and multiple image sets are obtained in serial fashion 1–7 days after injury, Tc-99m PPi myocardial scintigrams are usually abnormal (*15,16*). Accurate interpretation of planar Tc-99m PPi images,

however, may be marred by such factors as tracer activity in the chest wall overlying the heart, inability to distinguish confidently residual activity in the cardiac blood pool from true myocardial accumulation of Tc-99m PPi, and lack of information regarding heart size and orientation of the heart within the thorax. Berman et al. have shown that computerized selective blood-pool subtraction may improve the accuracy of Tc-99m PPi myocardial scintigraphy for the diagnosis of acute infarction (*17*). We have found that the acquisition and cinematic display of gated images appear to improve both the sensitivity and specificity of infarct-avid imaging for the detection of acute infarction (*18*). Residual activity in the cardiac blood pool is usually easily distinguished from abnormal activity by its characteristic appearance and cyclic motion. Small infarcts—especially those located in regions of relatively normal wall motion—may be better visualized because the blurring effect of cardiac motion is nullified. The superimposition of gated Tc-99m PPi images and gated blood-pool images appears to have additional value. The exact registration of questionable Tc-99m PPi activity with the cardiac blood pool offers further strong evidence of nonmyocardial activity. Cyclic motion of all or part of an area of localized activity adjacent to or only partially overlapping the ventricular blood pool is further evidence for the presence of abnormal myocardial uptake. We believe the ability to superimpose gated Tc-99m PPi images over gated blood-pool images acquired in identical projections does permit the differentiation of true myocardial uptake of Tc-99m PPi from other activity and allows accurate anatomic localization of sites of acute infarction.

Radionuclide imaging of the cardiac blood pool has gained wide popularity as a noninvasive means to characterize the anatomic and functional relationships of the cardiac chambers in patients with various cardiovascular disorders. First-transit or equilibrium techniques provide characterizations of global and regional ventricular function that show excellent correlation with similar angiographic measurements (*7,9,10,19-21*). Such techniques do not alter ventricular function, may be repeated with reasonable frequency, and may be applied at the patient's bedside. The assessment of global and segmental ventricular function in patients with acute and chronic ischemic heart disease may allow one to assess prognosis (*20*) and to estimate the location and functional severity of pathologically important coronary artery disease (*20,21*). However, in patients with suspected acute infarction, the information that can be extracted from these studies alone can be limited. It is currently impossible, for example, to differentiate regional alterations of wall motion caused by acute infarction from those resulting from remote infarction. In addition, it is impossible to distinguish functional alterations due to ischemia from those due to infarction without using some intervention to determine whether such alterations can be reversed (*22,23*). Such intervention is not always possible nor is it always practical in patients with suspected myocardial infarcts. The ability to superimpose Tc-99m PPi and gated blood-pool images provides considerable information concerning the relationship between recent infarction and global and segmental ventricular function.

In our 21 patients we have found that the superimposition of these images allows more confident interpretation of Tc-99m PPi distribution patterns. Nonmyocardial Tc-99m PPi activity is more easily distinguished from true myocardial uptake. The technique provides precise anatomic localization of sites of recent infarction in relation to the blood pool of the cardiac chambers. Right-ventricular infarction is clearly identified. The extent of ventricular involvement is often greater than one would estimate from the ungated scintigrams alone. Using this overlay method, a decision can be made as to whether segmental alterations in ventricular function result from recent infarction or from an old infarct or ischemia.

The combination of information regarding myocardial metabolism, relative myocardial perfusion, and acute myocardial necrosis, together with quantitative assessments of segmental mechanical function, should allow accurate characterization of the relationships between these parameters. We propose that the superimposition technique described in this report is a means to evaluate these relationships.

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