JACC Vol. 26, No. 4
October 1995:870–8

Evaluation of Myocardial Ischemia Using a Rest Metabolism/Stress Perfusion Protocol With Fluorine-18 Deoxyglucose/Technetium-99m MIBI and Dual-Isotope Simultaneous-Acquisition Single-Photon Emission Computed Tomography

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Objectives. **This study sought to develop a dual-isotope single-acquisition single-photon emission computed tomographic (SPECT) protocol using a multihead SPECT camera equipped with an ultra-high energy collimator to evaluate rest metabolism/stress perfusion simultaneously with fluorine-18 (F-18) deoxyglucose/technetium-99m (Tc-99m) 2-hexakis-2-methoxy-2-methylpropyl isonitrile (MIBI).**

Background. **The most accurate and logistic method of identifying injured but viable myocardium remains a diagnostic challenge.**

Methods. **Sixty-five patients were given 25 to 50 g of glucose and, after ~60 min, an injection of 370 MBq (10 mCi) of F-18 fluorodeoxyglucose. After a 35-min distribution phase, patients underwent exercise or pharmacologic stress followed by administration of 925 MBq (25 mCi) of Tc-99m MIBI. Five patients underwent F-18 fluorodeoxyglucose positron emission tomography before dual-isotope SPECT.**

Results. **With a window of 20% for both photopeaks and a technetium-99m/fluorine-18 concentration of 3.2:1, the "spillover" from fluorine-18 into the technetium-99m window is <6% of the total counts in the window in patients with a normal distribution of both radiopharmaceuticals. Phantom images clearly demonstrated cardiac defects measuring 2 × 1 and 2 × 0.5 cm. There was no significant difference in the images of the five patients who underwent both positron emission tomography and SPECT. Fifty-seven patients (mean [±SD] age 55 ± 15 years, range 25 to 83; 38 men, 19 women) had satisfactory images and were included in the study. Twenty-one patients had normal study results; 15 had mismatched defects; 14 had matched defects; and 7 had both matched and mismatched defects. Twenty-three patients (mean age 54 ± 6 years, range 30 to 83; 14 men, 9 women) underwent coronary angiography within 3 months of dual-isotope SPECT. There were seven normal studies, eight with mismatched defects, one with a matched defect and seven with matched and mismatched defects. When stenosis >70% was used as the criterion for a diagnosis of coronary artery disease, dual-isotope SPECT had a sensitivity of 100%, specificity of 88%, positive predictive value of 93%, negative predictive value of 100% and an accuracy of 96%.**

Conclusions. **Dual-isotope SPECT may provide an alternative, accurate, cost-effective method to nitrogen-13 ammonia/F-18 fluorodeoxyglucose positron emission tomography or thallium-201 reinjection for identifying injured or dysfunctional but viable myocardium.**

(J Am Coll Cardiol 1995;26:870–8)

Myocardial perfusion can be evaluated with thallium-201 chloride, technetium-99m (Tc-99m) 2-hexakis-2-methoxy-2-methylpropyl isonitrile (MIBI) single-photon emission tomography (SPECT) or with nitrogen-13 (N-13) ammonia positron emission tomography (1). Myocardial glucose metabolism can be evaluated with fluorine-18 (F-18) fluorodeoxyglucose, fatty acid metabolism with carbon-11 (C-11) palmitate and oxidative metabolism with C-11 acetate (1).

Recent modifications of thallium-201 SPECT protocols that include 24-h delayed imaging or imaging after reinjection of thallium-201 up to 24 h have improved the detection of viable myocardium when F-18 fluorodeoxyglucose positron emission tomography is not available (1). However, these protocols have been shown (2,3) to underestimate myocardial viability.

The feasibility of performing cardiac SPECT with F-18 fluorodeoxyglucose has been demonstrated by several investigators (4–7). The purpose of the present study was to develop a simultaneous dual-isotope single-acquisition protocol using a

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Manuscript received November 11, 1994; revised manuscript received May 18, 1995, accepted May 25, 1995.

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0735-1097/95/$9.50
0735-1097(95)00295-F

multihead SPECT camera equipped with ultra-high energy collimators to simultaneously evaluate rest cardiac metabolism with F-18 fluorodeoxyglucose and stress cardiac perfusion with Tc-99m MIBI.

Methods

Equipment and physical measurements. Dual-isotope (fluorine-18 and technetium-99m) SPECT imaging was performed using an Apex Helix dual-head, rectangular field-of-view digital scintillation camera (Elscint, Inc.) modified by the manufacturer to permit imaging of 511-keV photons in the single noncoincidence mode (7). Positron emission tomography was performed with a Siemens 933/08/16 tomograph with previously described specifications (7).

A set of ultra-high energy collimators were designed to support ultra-high energy, general-purpose whole-body and SPECT applications (7). Methods of measurements of system planar and SPECT sensitivity and spatial resolution have been described previously (7).

Image acquisitions of 30-min duration were performed on the SPECT and positron emission tomographic systems using a Data Spectrum cardiac phantom containing 300 μCi of fluorine-18 and placed in a 22-cm diameter water-filled cylindric phantom. A 13-cm radius of rotation was used for SPECT imaging. The phantom contained two simulated 45° defects: one 2 × 1 cm and the other 2 × 0.5 cm. Data were collected separately for the two heads of the camera system using the dual-isotope technique, which enables simultaneous acquisition in two energy windows and a 360° rotation. The SPECT reconstruction was accomplished from the fluorine-18 window for the single anterior detector alone (180° acquisition) and for both detectors together (360° acquisition). Image comparisons were performed to determine the optimal acquisition protocol. In addition, SPECT image reconstruction was also accomplished from the technetium-99m window to evaluate the contribution of scatter from fluorine-18 into the technetium-99m window. Total counts from the heart phantom were determined for both windows. A solution of technetium-99m was then added to the phantom, and the dual-isotope SPECT image acquisition was repeated. The activity of technetium-99m was calculated to provide a technetium-99m/fluorine-18 ratio of 3.2:1 to simulate the ratio of activities in the myocardium at the time of imaging after the dual-isotope SPECT protocol. This ratio was calculated by decaying the administered doses of fluorine-18 and technetium-99m to the start of acquisition in the clinical protocol and assuming identical percent uptakes for the two radiopharmaceuticals. The ratio was verified by collecting an energy spectrum from the phantom and from a patient with the scintillation camera positioned for an anterior view. Reconstructed SPECT images were compared for the two windows to evaluate the potential diagnostic quality of the dual-isotope technique with the ultra-high energy collimator.

Total counts from the heart recorded in the two windows were determined in five patients who underwent imaging using the dual-isotope protocol and were reported to have normal distributions of both radiopharmaceuticals with normal findings on coronary angiography so as to determine the contribution of downscatter from the fluorine-18 to the technetium-99m window.

An additional set of data was obtained to evaluate the effects of fluorine-18 downscatter in a region of ischemia in a heart where the global perfusion is reduced. Two-centimeter diameter vials were filled with solutions of technetium-99m and fluorine-18 to simulate normal (technetium-99m/fluorine-18 3.2:1), 75% normal (technetium-99m/fluorine-18 2.4:1), 50% normal (technetium-99m/fluorine-18 1.6:1) and 25% normal (technetium-99m/fluorine-18 0.8:1) global perfusion (vial A). For each of these conditions, additional vials were filled with solutions of technetium-99m and fluorine-18 to represent regions of 100%, 75%, 50%, 25% and 0% ischemia (vial B). A constant activity of fluorine-18 (100 μCi) was used in all vials representing normal myocardial metabolism. These vials were then imaged at a constant time using the dual-isotope technique, and technetium-99m window counts were determined from each vial using a circular region of interest that just included the vial. Measured percent contrast between the simulated ischemic and normal myocardium [(technetium-99m window counts in vial B/technetium-99m window counts in vial A) × 100] was calculated from each of the samples. Data for different activities of fluorine-18 (up to four times normal) were then extrapolated from this data set to simulate increased amounts of metabolism in the presence of varying degrees of ischemia.

Patients. Rest F-18 fluorodeoxyglucose/stress Tc-99m MIBI dual-isotope SPECT imaging was performed on 65 patients referred for evaluation of myocardial ischemia. Eight patients were excluded because of movement artifact (n = 2), poor image quality secondary to massive obesity (n = 1) and poor F-18 fluorodeoxyglucose uptake secondary to diabetes (n = 5). The demographic data for the 57 patients included in the study are summarized in Table 1. A subgroup of 23 patients underwent coronary angiography within 3 months of dual-isotope SPECT. Five patients underwent rest F-18 fluorodeoxyglucose positron emission tomographic imaging before

Table 1. Patient Demographics

	All Patients (n = 57)	Patients With Angiography (n = 23)
Men	38 (67)	14/9 (61/39)
Women	19 (33)	
Age (yr)		
Mean ± SD	55 ± 15	54 ± 16
Range	25–83	30–83
History of CAD	43 (75)	20 (87)
Bypass graft	14 (25)	6 (26)
Beta-blockers	20 (35)	8 (35)
Exercise	39 (68)	16 (70)
Dipyridamole	17 (30)	7 (30)

Data presented are number (%) of patients, unless otherwise indicated.

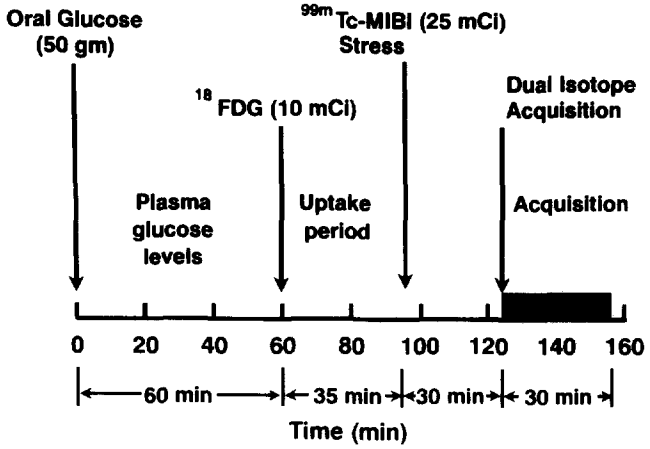

Figure 1. Schematic of the rest/stress dual-isotope single-acquisition SPECT protocol for fluorine-18 fluorodeoxyglucose (^{18}FDG)/technetium-99m (^{99m}Tc) MIBI.

stress and imaging with dual-isotope SPECT. This protocol was approved by the Vanderbilt University Medical Center Institutional Review Board, and all participants gave written informed consent.

Fluorine-18 fluorodeoxyglucose positron emission tomographic imaging. Positron emission tomographic imaging was performed in five patients before dual-isotope SPECT, as previously described (7). After completion of positron emission tomographic imaging, the patients underwent stress testing and then imaging with the dual-isotope simultaneous acquisition protocol, as described later (Fig. 1).

Fluorine-18 fluorodeoxyglucose/Tc-99m MIBI dual-isotope rest/stress cardiac protocol. *Rest F-18 fluorodeoxyglucose administration.* Patients fasted for a minimum of 4 h before the study. All patients were given 25 to 50 g of oral glucose ~60 min before injection of 370 MBq (10 mCi) of F-18 fluorodeoxyglucose, and soluble insulin was administered if necessary according to blood glucose levels. After a 45-min uptake phase, patients underwent stress testing using a standard graded exercise treadmill test or pharmacologic stress testing with dipyridamole (0.72 mg/kg body weight infused over 5 min).

Technetium-99m MIBI administration. A dose of 925 MBq (25 mCi) Tc-99m MIBI was administered intravenously at peak exercise or 2 min after dipyridamole infusion. Dual-isotope SPECT was started 15 to 30 min after administration of Tc-99m MIBI.

Dual-isotope single-acquisition SPECT protocol. The acquisition protocol included a single head rotating 180° from the right anterior oblique to the left posterior oblique projection for 60 stops at 30 s/stop. The images from the two energy windows (20% from both photopeaks) were collected in separate 64 × 64 matrices using word mode and then reconstructed using a Butterworth filter and temporal smoothing along the short axis, horizontal long axis and vertical long axis of the heart. Thus, two separate sets of slices mapping the Tc-99m MIBI and F-18 fluorodeoxyglucose distributions were obtained with one-to-one correspondence in spatial registration.

Image analysis. Positron emission tomographic and SPECT images were reoriented along the short axis of the heart with slices of the same thickness. As with the phantom studies, images were normalized to the pixel containing the maximal number of counts in each radionuclide data set. The rest F-18 fluorodeoxyglucose/stress Tc-99m MIBI images were interpreted independently by two experienced observers without previous knowledge of other study results, including electrocardiography, clinical and hemodynamic response to the functional study as well as recent cardiac angiography if this had been done. Qualitative analysis was performed using a nine-segment model/study: an apical segment as well as distal and proximal (basal) segments of the anterior, inferior, lateral and septal walls. Segments were classified into three categories: 1) *normal* = good F-18 fluorodeoxyglucose and Tc-99m MIBI uptake; 2) *mismatched defect* = moderate to severe decreased uptake of Tc-99m MIBI but adequate F-18 fluorodeoxyglucose uptake, suggesting either acute ischemia or hibernating myocardium; 3) *matched defects* = moderate to severe decreased uptake of both Tc-99m MIBI and F-18 fluorodeoxyglucose indicative of scar.

Coronary angiography. Coronary angiography was performed in multiple orthogonal projections, and single and biplane left ventriculograms were obtained. Cineangiograms were assessed by an experienced angiographer unaware of both clinical and scintigraphic data. Extent of coronary artery disease was defined as number of vessels with a stenosis >70%, or in patients with coronary artery bypass graft surgery, both the native vessel as well as the graft supplying that vascular distribution required >70% stenosis to be considered a hemodynamically significant stenosis.

Interpretation of data. The ability of F-18 fluorodeoxyglucose/Tc-99m MIBI dual-isotope SPECT to predict involvement of individual coronary vessels was assessed by ascribing the septum and anterior walls to the left anterior descending coronary artery, the lateral wall to the left circumflex coronary artery and the inferior wall to the right coronary artery, except in cases where coronary angiography revealed a left-dominant system. In these cases both inferior and lateral walls were ascribed to the left circumflex vessel. The apex was allocated to any other involved territory. However, if the apex alone was involved, the left anterior descending coronary artery was implicated.

Statistical analysis. Patient demographic data are expressed as mean value ± SD. Sensitivity, specificity, positive and negative predictive values and accuracy of results were determined using standard formulas.

Results

Physical measurements. The single-detector system sensitivity for the dual-head camera with the ultra-high energy collimator was measured to be 129 cpm/μCi, including penetration, for fluorine-18 and 114 cpm/μCi for technetium-99m. Excluding penetration, the system sensitivity was calculated to

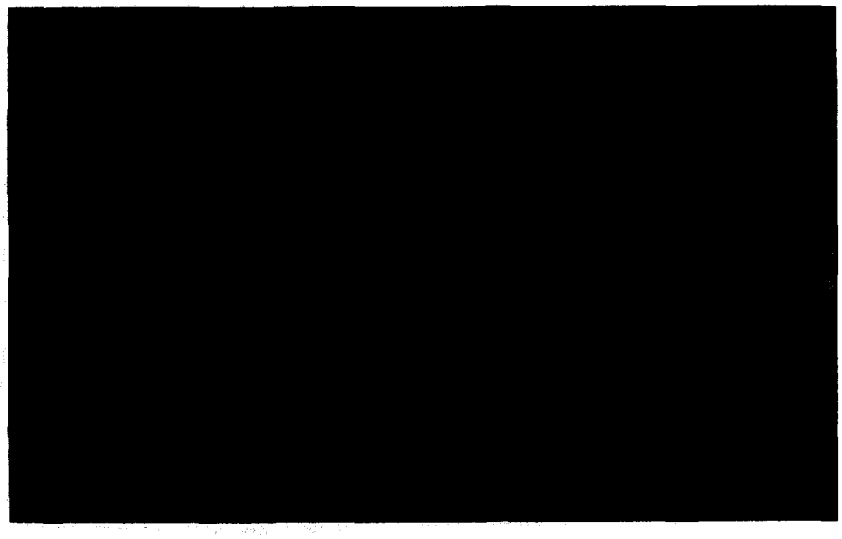

Figure 2. Single-photon emission computed tomographic images using the ultra-high energy collimator of the Data Spectrum cardiac phantom containing a solution of F-18 fluorodeoxyglucose alone and embedded in a 22-cm diameter water-filled phantom and with a solution of technetium-99m added in a concentration of 3.2:1. **A,** Fluorine-18 in fluorine-18 window. **B,** Fluorine-18 in technetium-99m window. **C,** Technetium-99m and fluorine-18 in technetium-99m window. Simulated lesions are indicated by **arrows.**

be 62 cpm/μCi for fluorine-18. Planar system spatial resolution measurements at 10 cm in air indicated that the spatial resolution for technetium-99m (11.1 mm) was superior to that for fluorine-18 (14.5 mm) using the ultra-high energy collimator. However, the spatial resolution for technetium-99m was inferior to that routinely obtained with the low energy, high resolution collimator (8.4 mm). The SPECT spatial resolution measurements with scatter yielded measurements of 14.6 and 17.0 mm for technetium-99m and fluorine-18, respectively for the ultra-high energy collimator. The SPECT dual-head volume sensitivity measurements yielded values of 125 and 270 cpm/μCi for technetium-99m and fluorine-18, respectively.

For the positron emission tomographic scanner, spatial resolution with fluorine-18 within an 8-mm slice was measured and found to be 6.5 mm, yielding a voxel size of 6.5 × 6.5 × 8 mm. Volume sensitivity was measured and found to be 2,238 cpm/μCi. When dual-head SPECT was compared with positron emission tomography for 511-keV imaging, it was apparent that the measured reconstructed spatial resolution was lower by a factor of 2.6, and volume sensitivity was lower by a factor of 8.

With the Data Spectrum cardiac phantom, a comparison of reconstructed images from the single anterior detector of the dual-head SPECT system (180° acquisition) versus both detectors together (360° acquisition) shows the image quality to be slightly superior for the single-head acquisition. Comparable images of 8-mm thick slices in the short-axis view of the phantom using the positron emission tomographic scanner and the SPECT camera with a single-head 180° acquisition demonstrated the superior spatial resolution of positron emission tomography. This was apparent in the thin, well defined walls of the phantom (1 cm thick) and in the definition of the two lesions. However, the image from the SPECT camera with the ultra-high energy collimator demonstrated that F-18 fluorodeoxyglucose SPECT can resolve cold defects of 2 × 0.5 cm in the heart (7).

Figure 2 shows selected SPECT images of the cardiac phantom containing fluorine-18 alone and imaged with the dual-isotope technique. The first set of images was obtained with the fluorine-18 window and the second set from the technetium-99m window. Images were normalized to the pixel containing the maximal number of counts in the complete study. Measurements of total counts from the heart phantom in the two windows indicated that downscatter into the technetium-99m window for the Apex Helix was 31% of the counts recorded in the fluorine-18 window. The third set of images was obtained after adding a solution of technetium-99m to the phantom in a concentration 3.2 times that of fluorine-18 and independently normalized to the maximal count in the technetium-99m image. The high quality of the reconstructed images is evident for both windows (first and third image sets), with both simulated lesions being clearly defined. The two data sets also clearly indicate the direct image comparison capability with the one to one correspondence of comparable slices provided by the simultaneous dual-isotope imaging technique. By measuring the total counts in the technetium-99m window from the cardiac phantom and assuming that 31% of the counts from the fluorine-18 peak appear in the technetium-99m window, it was determined that only 5.9% of the counts in the technetium-99m window represented downscatter from fluorine-18. Figure 3 shows an energy spectrum from technetium-99m and fluorine-18 in the 3.2:1 concentration ratio clearly indicating the ability to resolve the technetium-99m photopeak from the other structures in the spectrum. Energy spectra from the cardiac phantom and a patient with normal global perfusion and normal cardiac metabolism were virtually identical when superimposed, verifying the 3.2:1 ratio in normal global perfusion and metabolism.

Total counts from the heart were determined for the two energy windows in five patients imaged with the dual-isotope protocol and who were reported as having normal distribution of both radiopharmaceuticals. Assuming 31% downscatter from fluorine-18 as measured from the phantom study, the

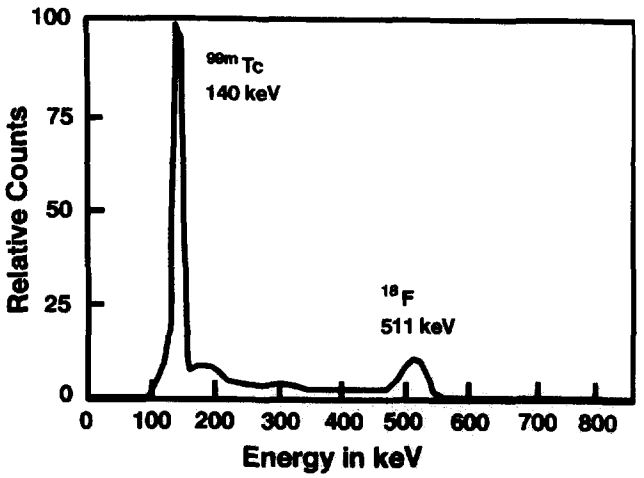

Figure 3. Energy spectrum from technetium-99m (^{99m}Tc) and fluorine-18 (^{18}F) in a 3.2:1 ratio of activities, respectively, obtained with the dual-head SPECT camera.

average contribution to the technetium-99m window was measured to be 3.7% to 6.6% of the total counts measured in the technetium-99m window, which agreed with the phantom measurements.

In imaging situations where global perfusion is reduced and regions of ischemia are identified, the percent contribution of fluorine-18 downscatter to the technetium-99m window will be >5.9%. Table 2 shows the results of the sample counting experiment to evaluate this effect. For the four global perfusion rates chosen (normal to 25% normal), five data sets representing 100% to 0% ischemia were evaluated. In each of these cases, the effect of fluorine-18 downscatter was measured or calculated from the measurements for a range of up to four times the activity representing normal metabolism. (Note that for this experiment, 100 μCi of fluorine-18 represents normal metabolism, and 320 μCi of technetium-99m represents normal perfusion, i.e., 3.2:1). The measured percent contrast values (ischemic region/normal myocardium × 100 based on technetium-99m window counts) are shown for the case of normal metabolism along with the range of values for up to four times normal. These values can be compared with the actual values that are determined by the ratio of technetium-99m activities in the two samples.

Clinical results. Rest F-18 fluorodeoxyglucose positron emission tomographic images obtained before stress testing and Tc-99m MIBI injection were compared with F-18 fluorodeoxyglucose SPECT images obtained with the dual-isotope protocol in five patients. These two sets of images showed no significant difference, confirming that the F-18 fluorodeoxyglucose distribution was not qualitatively altered by stress.

Of the 57 patients, 21 had normal F-18 fluorodeoxyglucose/Tc-99m MIBI study results, 15 patients had only mismatched

Table 2. Measurement of the Effect of Fluorine-18 Downscatter Into the Technetium-99m Window in Simultaneous Dual-Isotope Study

Global Perfusion Tc-99m Activity (μCi) in A	Simulated Ischemia in B	Actual %B/A Determined by Percent of Tc-99m Activity (A) in B	Measured %B/A for Normal Metabolism (100 μCi of F-18 in A and B)	Calculated %B/A for Range of Metabolism (100–400 μCi of F-18 in A and B)
320 (normal)	100%	0%	5%	5–17%
	75%	25%	28%	28–37%
	50%	50%	54%	54–60%
	25%	75%	76%	76–79%
	0%	100%	100%	100%
240 (75% normal)	100%	0%	6%	6–21%
	75%	25%	30%	30–42%
	50%	50%	54%	54–61%
	25%	75%	78%	78–81%
	0%	100%	100%	100%
160 (50% normal)	100%	0%	9%	9–28%
	75%	25%	33%	33–47%
	50%	50%	52%	52–62%
	25%	75%	76%	76–81%
	0%	100%	100%	100%
80 (25% normal)	100%	0%	17%	17–45%
	75%	25%	41%	41–61%
	50%	50%	63%	63–76%
	25%	75%	85%	85–89%
	0%	100%	100%	100%

Vial A represents the myocardium, and vial B represents an area of ischemia. Percent contrast (ischemic area to normal myocardium) is measured by %B/A determined by detected counts in the technetium-99m (Tc-99m) window. The column labeled "Actual" is determined by the ratio of technetium-99m activities and corresponds to 100% to 0% ischemia. Percent contrast was measured for a simulation of normal metabolism (100 μCi of fluorine-18 [F-18] in vials A and B). Percent contrast was calculated for up to four times normal metabolism. These values are measured/calculated for four simulated conditions of global perfusion: normal, 75% normal, 50% normal and 25% normal. The normal ratio (3.2:1) is represented by 320 μCi of technetium-99m and 100 μCi of fluorine-18 in vials A and B.

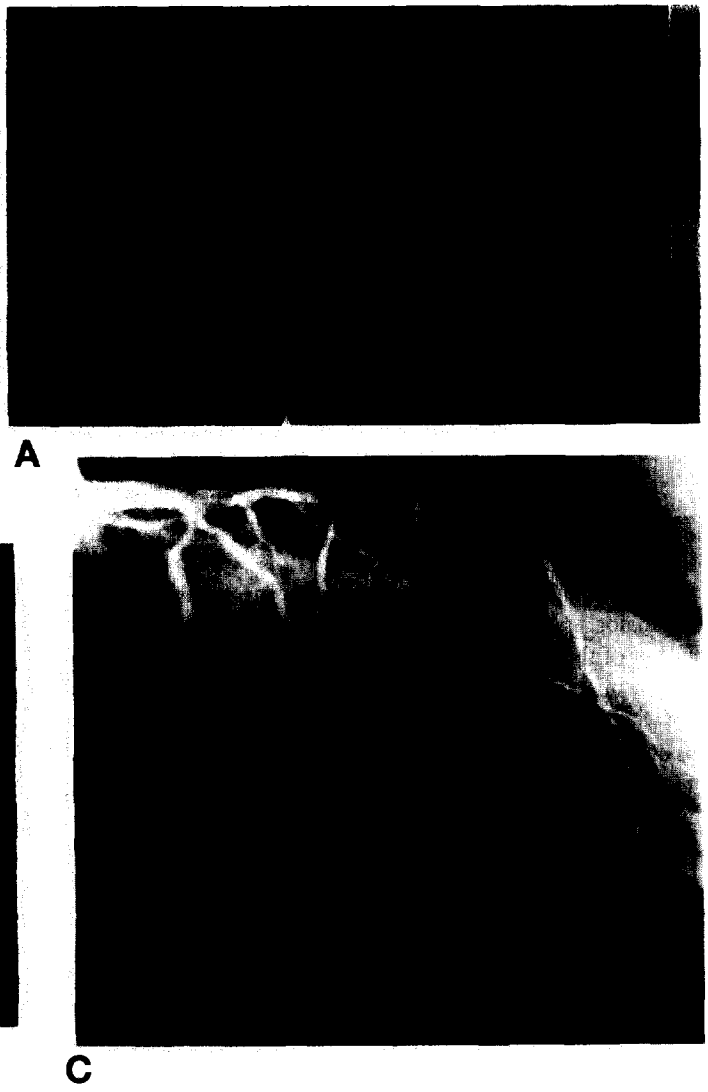

Figure 4. Images from a 34-year old man with unstable angina and severe two-vessel disease with a previous history of anterior myocardial infarction. **A,** Short-axis F-18 fluorodeoxyglucose (FDG)/Tc-99m MIBI dual-isotope SPECT images demonstrate ischemia of the anteroseptal and inferior walls of the left ventricle (**arrowheads**). **B,** Horizontal long-axis F-18 fluorodeoxyglucose/Tc-99m MIBI dual-isotope SPECT images demonstrate nonviable tissue in the apex of the left ventricle (**arrowheads**) and septal ischemia. **C,** Coronary angiogram in the right anterior oblique view identifying a severe proximal left anterior descending coronary artery stenosis and an attenuated distal left anterior descending coronary artery with Thrombolysis in Myocardial Infarction grade 2 flow. Collateral vessels are seen from the left anterior descending and left circumflex coronary artery distribution supplying the posterior descending branch of an occluded right coronary artery.

defects indicative of ischemia, 14 patients had only matched defects indicative of scar, and 7 patients had both matched and mismatched defects. A typical scan of a patient with both matched and mismatched defects is shown in Figure 4.

Table 3 shows the correlation between F-18 fluorodeoxyglucose/Tc-99m MIBI scintigraphy and angiography in the 23 patients who underwent coronary angiography. Among the seven patients with normal F-18 fluorodeoxyglucose/Tc-99m MIBI scan results and no significant lesions on the angiogram, two had no known coronary artery disease but presented with chest pain on several occasions. Although four other patients had known coronary artery disease, angiography demonstrated mild coronary artery disease in one patient (<50% stenosis); one patient had a patent vessel in a region of previous successful percutaneous transluminal angioplasty; and two patients had patent coronary bypass grafts. The patient with a matched defect (inferior wall) had a documented recent inferior myocardial infarction with follow-up lytic therapy. The angiogram revealed a residual 60% stenosis of the right coronary artery and severe inferior wall hypokinesia. Eight patients had mismatched defects only. Of these eight patients, one had no documented history of coronary artery disease, and seven had known coronary artery disease. The single patient with a mismatched defect (anterior wall) and no significant coronary artery disease on the angiography (false positive result) had a history of anteroseptal myocardial infarction with a patent graft to the left anterior descending coronary artery.

Table 3. Correlation Between Fluorine-18 Fluorodeoxyglucose/Technetium-99m MIBI Scan and Angiography

	Negative Results on Angiography	Positive Results on Angiography	Total
Normal	7 TN	0 FN	7
Mismatched defects only	1 FP	7 TP	8
Matched defects only	1 TN	0 FN	1
Mismatched and matched defects	0 FP	7 TP	7
Total	9	14	23

FN = false negative; FP = false positive; TN = true negative; TP = true positive.

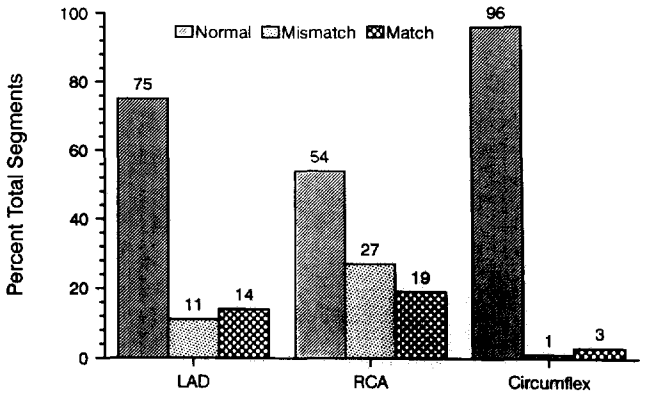

Figure 5. Angiographic distribution of the segmental pattern of uptake according to coronary artery distribution for 23 patients. LAD = left anterior descending coronary artery; RCA = right coronary artery.

The remaining seven patients with only mismatched defects had angiographic stenosis corresponding to the regional distributions of these defects. All seven patients with both matched and mismatched defects had documented myocardial infarction with wall motion abnormalities on the left ventriculogram (in one patient, the left ventriculogram was not obtained). Six of these patients had evidence of ischemia in the same vascular distribution as the previous myocardial infarction, and one in another vascular distribution.

A total of 513 segments were analyzed, and the segmental patterns of uptake (normal, matched defects and mismatched defects) according to the three individual coronary artery distribution were similar for all patients (n = 57) and for the patients who underwent coronary angiography (n = 23) (Fig. 5). The one false positive scan was in the left anterior descending coronary artery distribution, with the coronary angiogram showing no evidence of left anterior descending coronary artery stenosis despite the presence of a mismatched defect on the F-18 fluorodeoxyglucose/Tc-99m MIBI scan.

The interpretation by the two independent observers agreed in 489 (95%) of 513 segments. In all but one of the patients, the disagreement was related to the extent of the defects but not to the vascular territory involved. In only one patient did the two observers differ on the diagnosis.

In the 23 patients who had coronary angiography, the sensitivity and specificity of F-18 fluorodeoxyglucose/Tc-99m MIBI dual-isotope single acquisition SPECT protocol to detect coronary artery disease were 100% and 88%, respectively, with a positive predictive value of 93%, a negative predictive value of 100% and an accuracy of 96%.

Discussion

Previous work in our laboratory (7) has demonstrated the ability of the modified Apex dual-head helix (Elscint, Inc.) fitted with ultra-high energy collimators to provide excellent quality images of the heart using F-18 fluorodeoxyglucose.

Sequential acquisition cardiac studies to evaluate for hibernating myocardium with F-18 fluorodeoxyglucose SPECT, thallium-201 or Tc-99m MIBI SPECT have been performed and appear to supply comparable diagnostic quality images and adequate clinical information compared with that for N-13 ammonia/F-18 fluorodeoxyglucose positron emission tomography (4–7). In the present study we developed a new methodology using a rest metabolism/stress perfusion protocol with F-18 fluorodeoxyglucose/Tc-99m MIBI followed by dual-isotope SPECT that can identify both acute cardiac ischemia and hibernating myocardium in patients with left ventricular dysfunction. Experimental data from the present study using simulated myocardial distributions of technetium-99m/fluorine-18 revealed that the downscatter contribution from fluorine-18 into the technetium-99m image becomes theoretically significant in regions of severe ischemia (75% to 100%), with a fourfold increase in metabolism when associated with a twofold decrease in global perfusion.

The data in the present study from the 23 patients who underwent coronary angiography demonstrated a sensitivity of 100%, specificity of 88% and accuracy of 96% for a diagnosis of coronary artery disease >70% stenosis. These data are comparable to those reported (8,9) for thallium-201 stress SPECT imaging (sensitivity 96%, specificity 70% to 85%) for the diagnosis of coronary artery disease.

Advantages of rest F-18 fluorodeoxyglucose/stress Tc-99m MIBI dual-isotope SPECT. The ability to identify hibernating myocardium or chronic coronary artery disease, or both, by evaluating myocardial metabolism directly with F-18 fluorodeoxyglucose SPECT using the dual-isotope SPECT protocol is a significant advantage over either thallium-201 or technetium-99m MIBI stress/rest protocols.

Several studies have shown that 38% to 50% of the irreversible defects on stress/4-h redistribution thallium-201 studies show metabolic activity with positron emission tomography and improve after revascularization. Delayed 24-h imaging shows redistribution in 21% to 61% of the segments with a fixed stress/4-h redistribution defect. Among the segments with late redistribution, 95% improve after revascularization. However, 37% of the segments with a fixed defect on both 4- and 24-h images also improve after revascularization, indicating that 24-h images still underestimate the presence of viable myocardium (1). Reinjection of thallium-201 before redistribution imaging demonstrates reversibility in 31% to 49% of segments with fixed defects on stress/4-h redistribution images (1). Most of the segments (80% to 87%) showing reversibility on reinjection images improved after revascularization, whereas only 0% to 18% of irreversible defects on both 4-h and reinjection images improved after revascularization (1).

Numerous groups of investigators have confirmed these data but have also demonstrated F-18 fluorodeoxyglucose metabolism (2,3) and regional wall motion improvement after revascularization in 25% of segments with a fixed defect using thallium-201 reinjection (4) and most segments with persistent 24-h thallium-201 defects (3).

Several studies (10) have reported that Tc-99m MIBI may be an accurate marker of viability in the setting of stunned

myocardium after reperfusion after acute myocardial infarction. With respect to evaluation of myocardial viability in patients with chronic ischemia and left ventricular dysfunction, more recent data (11) show that regions with severe reduction of Tc-99m MIBI uptake on both stress and rest images may have a reversible defect on thallium-201 reinjection and therefore contain viable myocardium. Preliminary data have shown F-18 fluorodeoxyglucose uptake in regions that had reversible thallium-201 uptake with a fixed Tc-99m MIBI defect (12). Therefore at present, it appears that stress/rest Tc-99m MIBI studies underestimate the presence of viable myocardium in patients with chronic ischemic heart disease and left ventricular dysfunction.

Another marker of myocardial viability that is being investigated clinically to detect hibernating myocardium is the evaluation of regional systolic wall thickening using dobutamine echocardiography because recent reports (13) indicate that isotropic reserve is maintained in hibernating myocardium. Preliminary studies (13) with a small number of patients support the possibility of dobutamine echocardiography to predict postvascularization recovery, with a sensitivity and specificity comparable to that of delayed thallium-201 imaging.

The choice of Tc-99m MIBI over thallium-201 for the stress part of the dual-isotope SPECT protocol relates to the fact that the 140-keV photons from the technetium-99m component and injectable doses of up to 925 MBq/70 kg result in improved count density and image resolution compared with that for thallium-201 when imaging is done with ultra-high energy collimators. A further advantage of using Tc-99m MIBI is the ability to perform gated cardiac images with dual-isotope SPECT to assess wall motion as well as the potential to obtain volume-determined ejection fraction values.

Other advantages of dual-isotope SPECT include patient convenience, shorter length of image acquisition and perfect registration of the two sets of images. The larger axial field of view of most gamma cameras (40 cm for the Apex Helix) compared with positron emission tomography (13 to 15 cm) is a relative advantage for imaging patients with cardiomegaly. In addition, because imaging is performed with F-18 fluorodeoxyglucose, there is no need to perform 24-h delayed imaging, as may be necessary for fixed defects when thallium-201 reinjection is used to evaluate patients for the presence of hibernating myocardium.

Limitations of rest F-18 fluorodeoxyglucose/stress Tc-99m MIBI dual-isotope SPECT. With the present protocol, stress-induced ischemia cannot be differentiated from hibernating myocardium. However, all patients with ischemic myocardium might benefit from revascularization whether it is stress induced or chronic in nature (14,15).

One potential limitation of using F-18 fluorodeoxyglucose is encountered in patients with diabetes or a prediabetic condition. Although administration of soluble insulin improves F-18 fluorodeoxyglucose uptake by the myocardium, a significant number of patients with coronary artery disease are diabetic or prediabetic and demonstrate poor F-18 fluorodeoxyglucose uptake by the myocardium. Implementation of the euglycemic hyperinsulinemic clamp, which utilizes a simultaneous infusion of soluble insulin with a 10% dextrose solution to stimulate myocardial uptake of F-18 fluorodeoxyglucose, has resulted in excellent quality metabolic images in diabetic patients undergoing dual-isotope SPECT in our laboratory (16). Utilization of the euglycemic hyperinsulinemic clamp increases both the cost and complexity of dual-isotope SPECT. However, this technique is equally applicable to diabetic patients undergoing cardiac F-18 fluorodeoxyglucose positron emission tomography to identify regions of injured but viable myocardium.

Another limitation of the present study was that patients undergoing dual-isotope SPECT were not evaluated with thallium-201 reinjection scintigraphy for up to 24 h. In a recent study by Dreyfus et al. (15), among 50 patients initially referred for heart transplantation, 46 were identified as having myocardial viability and underwent coronary artery bypass grafting. All patients underwent initial evaluation with thallium-201 reinjection scintigraphy for up to 24 h to identify injured but viable myocardium (25 of 46). Thirty-nine percent of patients with fixed thallium defects (18 of 46) were identified as having hibernating myocardium in at least two different vascular distributions by positron emission tomography and underwent successful coronary artery revascularization.

The difference in attenuation between Tc-99m MIBI and F-18 fluorodeoxyglucose, especially by the diaphragm, should be recognized as a potential source of false positive study results with dual-isotope SPECT. In our experience, attenuation of F-18 fluorodeoxyglucose with dual-isotope SPECT has been insufficient to cause false positive metabolic study results. We are presently developing a method of attenuation correction for Tc-99m MIBI for dual-isotope SPECT imaging. As a temporary solution, patients are imaged in the prone position whenever possible to minimize the number of false positive study results with dual-isotope SPECT secondary to diaphragmatic attenuation.

A limitation of the data provided from this study is the absence of outcome data. However, Bax et al. (17) recently demonstrated improved regional wall motion in 77% of mismatched segments after revascularization in 15 patients who underwent both F-18 fluorodeoxyglucose SPECT and rest thallium-201 imaging. In the same study, 89% of matched defects showed no improvement in wall motion after revascularization.

Conclusions. The results of the present study need to be confirmed in a larger series of patients with outcome monitoring. However, the use of rest F-18 fluorodeoxyglucose/stress Tc-99m MIBI dual-isotope SPECT may provide a cost-effective alternative to N-13 ammonia/F-18 fluorodeoxyglucose cardiac positron emission tomography and a more accurate logistic method than thallium-201 reinjection to identify injured or dysfunctional but viable myocardium. Although the data from the present study are comparable to those from other radiopharmaceuticals for detecting acute myocardial ischemia, the present availability and cost of F-18 fluorodeoxyglucose will initially limit the utilization of dual-isotope SPECT to identifying those patients with injured but viable myocardium.

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