Detection of Severe Coronary Heart Disease with Tl-201: Comparison of Resting Single Photon Emission Tomography with Invasive Arteriography

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To investigate the application of Tl-201 single photon emission computed tomography (SPECT) at rest in the confirmation of coronary heart disease (CHD), we studied 95 patients who had all undergone coronary angiography and cineventriculography. We separated three groups, patients with (a) prior myocardial infarction (MI) (n = 45), (b) no history of MI (n = 40), and (c) no abnormality of coronary angiogram (n = 23). The results of planar imaging with computer-assisted evaluation (scintimetry, SCM) and of SPECT with a three-plane reconstruction (transverse, sagittal, frontal) were compared with the invasive, arteriographic findings. SPECT yielded a higher sensitivity (93%) than SCM (68%) in the detection of defects in both infarcted and noninfarcted groups. The specifity was found to be almost equal in the two imaging modalities. A significant ($p \leq 0.01$) increase in accuracy was found in SPECT in the assessment of the posterior wall (54% compared with 88%) as well as in the general detection of defects (68% compared with 88%). Applying the SPECT imaging technique increases both the diagnostic accuracy of Tl-201 myocardial imaging and the anatomical association of CHD.

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Conventional planar imaging using gamma cameras and an on-line computer system has provided a useful tool in assessing changes in regional Tl-201 uptake (*1–3*). A variety of methods have been developed to quantify relative changes in thallium uptake following alterations in blood supply during stress or pharmacological intervention (*1,3,5*). These methods have all been hampered by the constraints imposed by two-dimensional imaging. In conventional camera imaging the superimposition of structures of the object, as well as background activity, restrict the value of scintigraphy to areas of the heart that project unequivocally or present low background.

In the past two years tomographic systems such as the seven-pinhole collimator (limited-angle tomography) and systems for transaxial tomography, such as rotating gamma cameras, have become readily available (*6*). Only transaxial tomographic systems, however, have the capability of actually displaying the total three-dimensional radionuclide distribution independent of position.

Holman and co-workers (*7*) showed the feasibility of using Tl-201 with a SPECT instrument to image myocardial infarction. More recently, other investigators (*6,8*) compared the results of conventional and SPECT imaging for the confirmation of myocardial infarction.

The objective of our study was to extend the use of Tl-201 SPECT imaging to the diagnostic assessment of coronary heart disease (CHD). We compared the evaluation of (a) quantified negative contrast in the computer-processed planar images, (b) scintimetry (*2,4*), and (c) the visual assessment in SPECT presenting a full three-dimensional reconstruction (transverse, sagittal, and frontal planes) with the results of invasive diagnostic procedures: coronary angiography and cineventriculography.

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The patients were kept at rest to have the boundary conditions constant, which is needed for validating the method.

MATERIALS AND METHODS

Description of systems. Planar imaging was performed with a large-field gamma camera equipped with a low-energy high-resolution collimator. The data were recorded on-line with a nuclear medicine computer system.

The SPECT system used in this study consists of a large-field-of-view (40 cm) gamma camera with a high-resolution, parallel-hole collimator mounted on a gantry in a tunnel configuration and an integrated computer system with software provided by the manufacturer. Data were acquired as 64-by-64 images in 64 angular projections over 360°, with the camera rotating continuously around the patient rather than in a "step-and-shoot" mode. The first projection image is acquired during the first 5.625 degrees of rotation, the second during rotation from 5.625° to 11.25°, and so forth. The time for a full rotation was set to 22 min. The spatial resolution of the system is 16 mm in the tomographic plane and 20 mm between the planes (adding two lines of pixels in each projection image) using Tc-99m. On the average 2 million counts were recorded for each study. The transverse sections, containing between 80,000 to 100,000 counts, were reconstructed using a filtered back-projection algorithm with a subsequent computation of sagittal and frontal planes. No correction for internal absorption (attenuation) was incorporated.

Patients. Our study population comprises a total of 108 patients, all of whom had undergone left-ventricular cardiac catheterization, including cineventriculography and coronary angiography. Out of these, CHD was confirmed in 85 individuals and excluded in 23. The latter presented either no pathologic findings in the coronary arteries or revealed cardiomyopathy, and therefore served as the control group for the assessment of the specificity (true negative over false positive plus true negative) of the technique in the detection of CHD by defects. Forty-five patients of the CHD group had prior myocardial infarction, clinically proven by history, EKG changes, and elevated enzymes. No patients with acute myocardial infarction were studied. The time lapse between the infarct and our examination was at least 2 wk.

Coronary angiography and cineventriculography were carried out as part of the routine diagnostic work-up. For coronary angiography the technique of Judkins was used, with manual injections (3–5 ml) of 76% meglumine sodium diatrizoate in various projections. CHD was assumed if a vessel revealed stenosis.

Cineventriculography was acquired at a rate of 50 frames per sec in a single plane projection (30° RAO). Contrast agent (40–60 ml) was applied using power injection.

Shortly before or after cardiac catheterization, the nuclear medicine examination was carried out according to the following protocol. Patients received 2 mCi (74 MBq) of Tl-201 chloride into an antecubital vein at rest. Ten minutes later, planar images were acquired in a 45° LAO and 90° LL projections for 6 min each, collecting between 300,000 and 400,000 counts per image. Following this, the patients were transferred to the rotating gamma camera system and positioned comfortably supine on the couch inside the gantry. The center of rotation was adjusted to the backbone of the patient and the diameter of rotation was minimized. Data collection began ~30 min after injection.

Nuclear evaluation. Scintimetric evaluation of the planar images was performed according to the method described by Buell and co-workers (*4*). In each projection (45° LAO and 90° LL) the relative decrease in activity of a defect within the left-ventricular region of interest was assessed with respect to the maximum uptake of Tl-201 in the left ventricle. A regional decrease of two standard deviations from normal values, as determined in a group of normal subjects (*9*), was considered to be pathologic.

Since the problems of correction for internal self-absorption have not been solved satisfactorily at this time, a quantification similar to that in scintimetry is not possible. Therefore, the SPECT studies were evaluated by two independent observers without knowledge of the angiographic findings. In case of discord the images were viewed together and final interpretation was reached by agreement. A visual scheme was developed relating the maximum uptake to the decreased uptake in a section. The criterion for diagnosing decreased perfusion in the SPECT studies was met if a defect or decreased uptake was present in at least two contiguous slices in two of the three reconstructed planes.

The clinical presentation and the results of coronary angiography—and cineventriculography in particular—served as the "gold standard" for validation of the findings of SPECT and scintimetry. Both wall motion (normo-, hypo-, dys- and akinesis) and the results of angiography were used as criteria. If a normokinetic myocardial wall was found with coronary artery stenosis, the stenosis was used for reference. If a hypokinetic segment was found and a stenosis of, for instance, less than 50%, the wall-motion abnormality was used.

RESULTS

The results of applying both methods—SPECT and scintimetric evaluation of planar images—are listed in Tables 1 and 2. For either method we divided the total number of patients (n = 85) into two subgroups, one comprising all the patients having a history of myocar-

TABLE 1. RESULTS OF Tl-201 SPECT SEARCHING FOR CHD*

		Location		
		Anterior	Posterior	CHD†
Sensitivity				
overall	(n = 85)	81%	90%	93%
infarct	(n = 45)	86%	95%	100%
no inf.	(n = 40)	76%	84%	85%
Specificity (n = 23)		91%	74%	70%
Accuracy				
overall	(n = 108)	84%	88%‡	88%‡
infarct	(n = 68)	88%	87%‡	90%
no inf.	(n = 63)	83%	80%‡	79%

* At rest, selected patients, also invasively examined.
† Found to have (no) defects most probably due to CHD.
‡ Significantly ($p \leq 0.01$) different from results in Table 2.

dial infarction (n = 45) and the other those patients with no such history (n = 40). The specificity was assessed in the 23 subjects.

Coronary angiography revealed three-vessel disease in 20 of the 40 patients of the noninfarct group, two-vessel disease in eight, and one-vessel disease in 12 patients; three patients in this group had hypokinesia with stenosis of less than 50%, four had 50 to 75% stenosis, 20 had more than 75%, and 13 had occlusion. Seventeen patients had normal wall motion, and 23 abnormal.

Emerging from the studies, two categories were formed: an anterior location containing anterior-wall and septal defects, and a posterior location with the posterior-wall and inferior defects.

In the SPECT studies, a higher sensitivity for the anterior and posterior walls was found in the infarct group. In the third column of Table 1, CHD represents the true-positive or true-negative finding of a defect being due to the presence or absence of CHD. The finding of coronary heart disease was correct in all of the cases in the infarct group (sensitivity 100%). In the group of patients with no history of infarction, the sensitivity was lower (85%). Using SPECT, the overall accuracy ranges between 79% and 90%.

Looking at the results obtained by planar imaging with subsequent scintimetric evaluation, and comparing the anterior and the posterior wall, a significant decrease in the overall sensitivity is found ($p \leq 0.01$). No major

TABLE 2. RESULTS OF Tl-201 SCINTIMETRY SEARCHING FOR CHD*

		Location		
		Anterior	Posterior	CHD‡
Sensitivity				
overall	(n = 85)	64%	40%	68%
infarct	(n = 45)	70%	50%	78%
no inf.	(n = 40)	59%	27%	58%
Specificity (n = 23)		83%	96%	78%
Accuracy				
overall	(n = 108)	70%	54%	68%
infarct	(n = 68)	75%	67%	78%
no inf.	(n = 63)	69%	57%	65%

† At rest selected patients, also invasively examined.
‡ Found to have (no) defect most probably due to CHD.

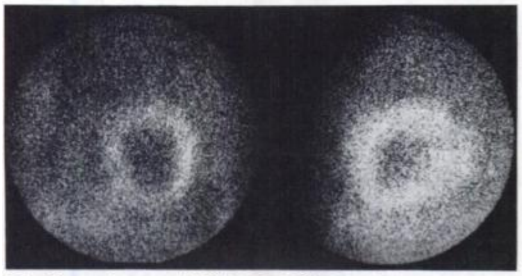

FIG. 1A. Planar images (45° LAO, 90° LL) of 64-yr-old patient with episodes of severe angina (at rest, 10–25 min after injection).

difference in sensitivity occurred in either group regarding the anterior wall. In the posterior wall a considerable decrease in sensitivity must be admitted for the infarct group. The specificity was found to be slightly higher than in SPECT. The overall accuracy ranged between 69% and 75% for the anterior wall and 54% and 67% for the posterior wall. Again an increase was found in the infarct group.

Figure 1A shows the planar images in 45° LAO and 90° LL projection of a 64-yr-old male patient suffering

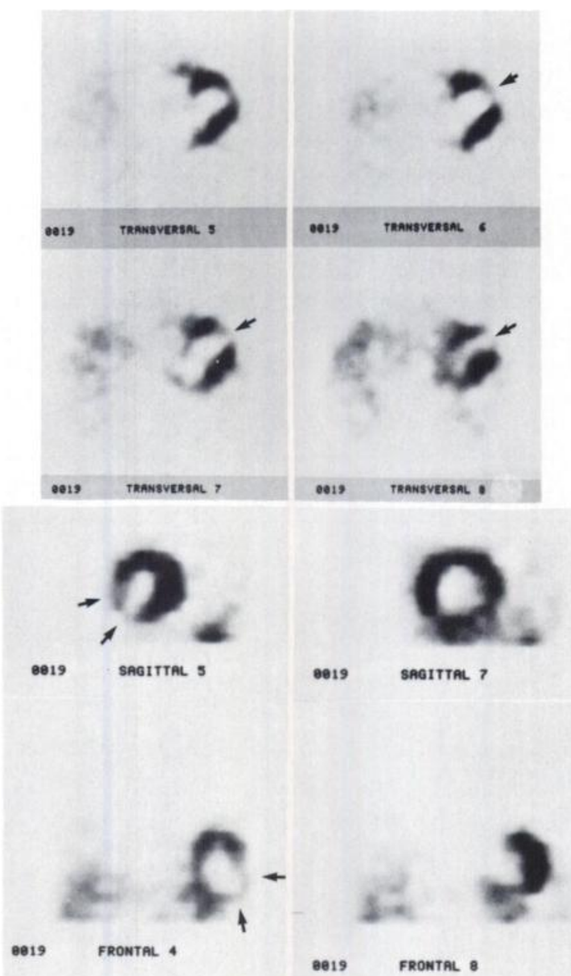

FIG. 1B. Transverse SPECT images (upper) of same patient, showing decreased uptake in apex and anterior wall (arrows). Findings confirmed in sagittal and frontal slices (lower, arrows).

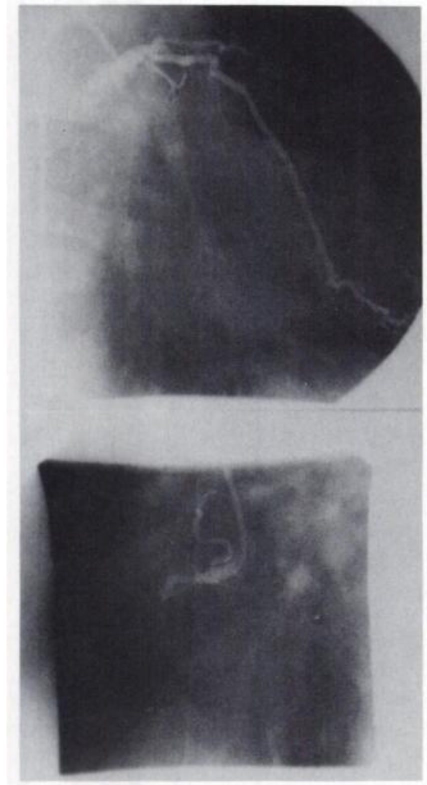

FIG. 1C. Angiogram of same patient, showing occlusion of LAD, CFA, and RCA.

from severe angina. Cineventriculography revealed akinesia in the supra-apical part of the anterior wall, the apex, and the inferior part of the posterior wall, with an ejection fraction of 24%. These planar views do not present any major diagnostic information except for an enlarged ventricle. With the help of scintimetric evaluation, a decreased uptake in the anterior wall and the apex can be found. The transaxial slices, shown in Fig. 1B (upper), also display a markedly reduced uptake of Tl-201 in the anterior wall and the apical area (arrows). The subsequently generated sagittal slices (Fig. 1B, lower) confirm that finding. In addition it is found that the defect in the apex extends into the inferior part of the posterior wall. According to our criteria, the same

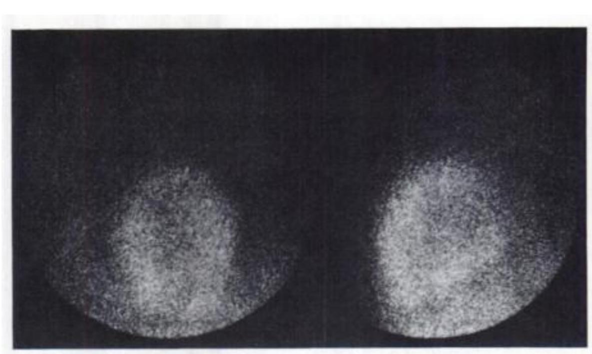

FIG. 2A. Planar images (45° LAO, 90° LL) of 41-yr-old patient with arterial hypertension and LV hypertrophy (at rest, 10–25 min after injection).

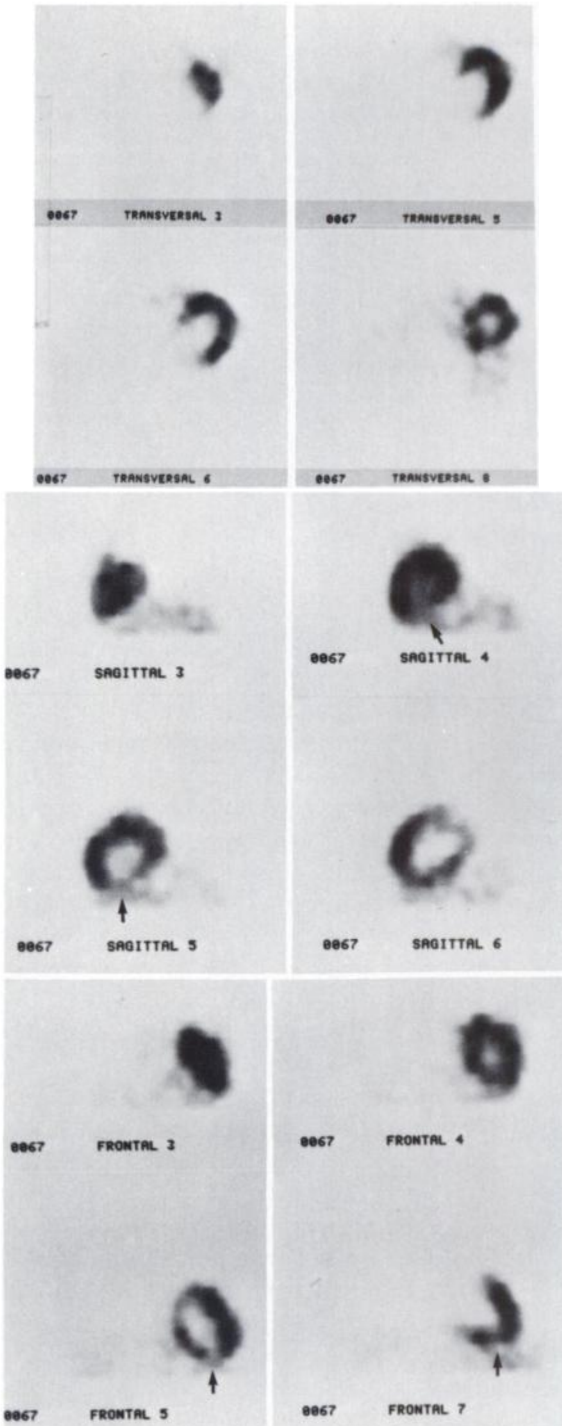

FIG. 2B. Selected transverse SPECT images of patient of Fig. 2A, with no defects (upper). Contiguous series of sagittal slices (3–6) (center) showing decreased uptake in inferior portion of posterior wall (arrows). Confirmation of defect (lower) in frontal cuts (arrow). Computer-processed image (isocount plot) of 90° LL projection, with decrease in apical region (arrow).

finding can be claimed in the frontal views, with a further suggestion that the defect also extends into the posterior lateral region. All these findings can be explained by the angiogram shown in Fig. 1C. The left anterior descending coronary artery is occluded, and so is the cir-

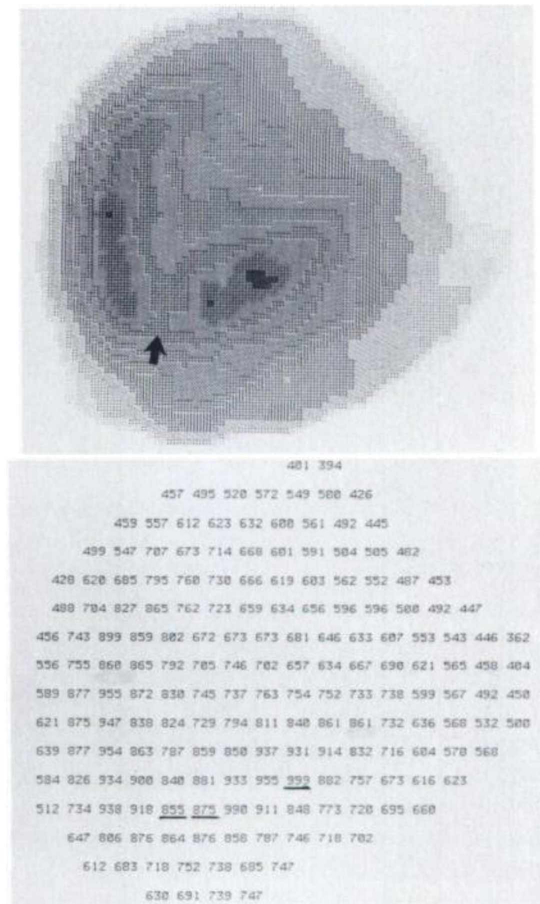

FIG. 2C. Computer-processed image (isocount/plot) of 90° LL projection, with decrease in apical region (arrow). Image 2e in digital print-out, as mean of 4 neighboring pixels (underlined) normalized to maximum pixel value of "999". Minimum uptake (underlined) does not exceed normal range (67.5% to 100%) for this anatomical area in 90° LL projetion.

cumflex. Furthermore, the right coronary artery is occluded beyond the first third. This patient did not have any hint of myocardial infarction in his history.

An example of a false-positive finding is given in Fig. 2A, showing the planar images (45° LAO and 90° LL) with a suspected decrease in uptake in the apical area (arrows). The patient, a 41-yr-old male, has a history of arterial hypertension (intra-aortic pressure 176/101 mm Hg), with hypertrophy of the left ventricle. Figure 2B (upper) shows some selected transverse slices presenting no defect. Looking at the contiguous series of sagittal cuts (Fig. 2B, center), however, one clearly finds decreased uptake in the inferior portion of the posterior wall (arrow). This finding is confirmed in the frontal views of Fig. 2D, lower (arrows). In the invasive examination the patient had a normokinetic left ventricle with an ejection fraction of 67%, and did not present any abnormalities in the coronary angiogram. Evaluating the planar images, scintimetry of the 90° LL projection (Fig. 2C) displays the computer-processed images, which show a slight decrease in uptake in the apical region

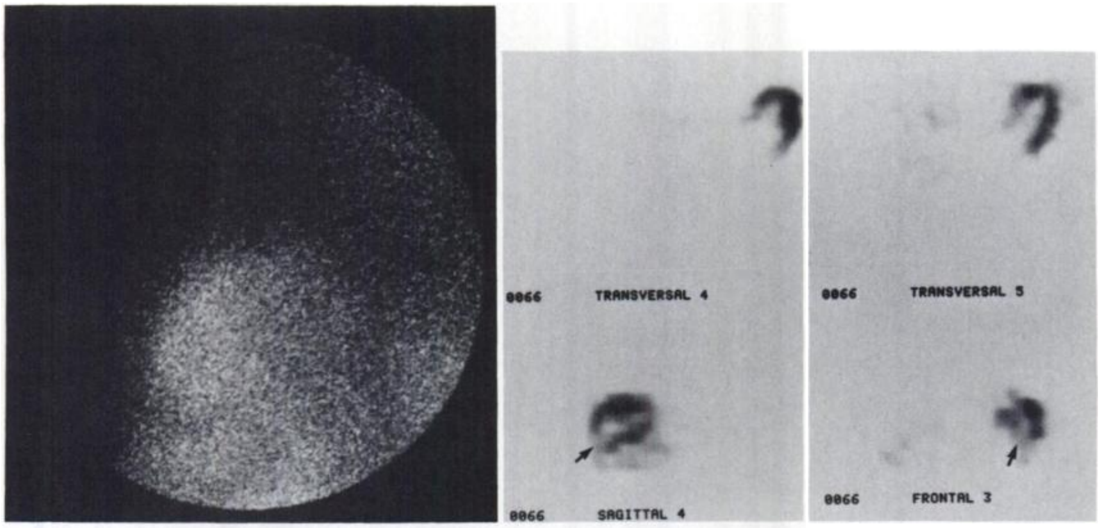

FIG. 3. Left: Planar image (90° LL) from 46-yr-old patient with 40% stenosis of LAD and hypokinetic apex (at rest). Right: Selected images of same patient's SPECT study, showing decreased uptake in apical region (arrows).

(arrow). This decrease, however, does not exceed the standard range (100.0–65.5%) set for normals. Therefore, no pathologic finding is stated.

The third example illustrates the high sensitivity of the method. Evaluation of the planar view at 90° LL by scintimetry (Fig. 3, left) reveals no abnormality. Figure 3 (right) shows selected slices from the three planes in the SPECT study. A decrease in uptake can be found in the apical region (arrows). Upon cardiac catheterization, this patient, a 46-yr-old male, presents a 40% stenosis in the LAD and a hypokinetic apex.

DISCUSSION

Our study shows good sensitivity for SPECT in the detection of myocardial defects, most probably due to CHD already suspected by history and EKG on this selected group of patients. The goal was to extend the use of Tl-201 beyond the confirmation of defects such as infarction. Even though our examinations were performed under resting conditions, the sensitivity of SPECT proved superior to that of the computer-assisted planar images, i.e., scintimetry. One constraint is imposed on these two methods, however. In both the observer compares the maximum uptake with areas showing decreased uptake. A general decrease in uptake would therefore be missed if due to the involvement of all vessels and/or the myocardium to a similar degree.

The full three-dimensional representation of myocardial Tl-201 uptake in SPECT overcomes the restriction imposed by planar imaging. This can be shown in particular in the assessment of Tl-201 uptake in the posterior wall, where the sensitivity of SPECT is 90% compared with 40% for planar imaging. Since the anterior wall projects without major background overlay—relative to the posterior wall, where stomach, liver, and spleen activity may interfere—the advantage is not quite as striking: 81% compared with 64%.

The subdivision of the total number of patients into two groups, those who had myocardial infarction and those who had not, allows the comparison with respect to the goal of our study. We found, as can be expected, a higher sensitivity in the infarct group. Even though we studied a highly selected group of patients, some with advanced CHD, the sensitivity (85%) and accuracy (79%) in the noninfarct group in detecting the presence of CHD is high enough to support the idea of investigating the degree of CHD with Tl-201 SPECT. We believe that myocardial uptake of Tl-201 depends on a number of factors, such as myocardial perfusion, metabolism, and muscle mass (*9*). Chronically diminished perfusion is able to change one or more of these parameters. Thus the myocardial distribution pattern can be altered at rest, revealing a defect even without previous myocardial infarction. The specificity assessed in our study cannot be compared with the results of other investigators (*6,8*), since we did not study healthy individuals. Our "specificity" is therefore lower. Using the criterion "clean coronary arteries" does not reflect the state of the myocardium, which can be altered by other factors influencing Tl-201 uptake (*9*).

Using ungated data acquisition, the resulting image is "blurred" by approximately 1200 heart cycles. This fact should faciliate the imaging of enlarged ventricles with reduced motion and ejection fraction. We found the limitations of SPECT to appear in small hearts with high ejection fraction and in small hypertrophic hearts, which led to false-negative results, as well as in large hypertrophic hearts and patients with cardiomyopathy prone to false-positive findings.

Cardiomyopathy appears as a "patchy" uptake suggesting reduced perfusion and/or altered myocardial cells in various parts of the heart. The pattern found was finally considered so typical as to allow the diagnosis of disease other than CHD. With respect to the criteria for a diagnosis of CHD, these findings have to be seen as false positive, however.

The SPECT images were reconstructed without correction for the effects of attenuation within the body. The only "processing" of the projection data before the convolution-backprojection reconstruction was the summation of opposing views during the acquisition (*10*), which cannot be switched off. The accuracy in assessing the posterior wall must be qualified by the influence of attenuation. The increase in sensitivity (90%) and the decrease in specificity (74%) confirm the suspicion that the higher number of "true positives" as well as "false positives" are due to the effects of attenuation. The projection path to the anterior wall leads primarily through lung tissue and the rib cage, whereas the inferior portion of the posterior wall may project through liver, stomach, and spleen, all with higher attenuation than air-filled lung tissue. This implies trading the problem of superimposition of structures in planar imaging for the difficulties imposed by attenuation in SPECT, which seem to be the less restricting.

In conclusion, we found that the application of the SPECT imaging technique with the subsequent reconstruction of transverse, sagittal, and frontal sections provides higher accuracy compared with the computer-assisted evaluation of planar images (scintimetry), even with the patient at rest. Although in theory all the information is present in the transverse slices, we want to emphasize that the generation of frontal, and in particular sagittal, cuts is crucial for a precise location of the lesion. This is especially important for the posterior wall, the state of which can hardly be judged using the transverse planes only.

In the future, exercise testing might increase the accuracy of the method, to detect and confirm even less pronounced CHD. The relatively long time of data acquisition (20 min) raises the question whether redistribution effects during the SPECT study might possibly distort the data and result in irreproducible results. The preliminary results of MacIntyre (*11*) and our own investigations including exercise, however, suggest that the effect of redistribution is less than anticipated and that valuable information can be gained from these studies. This certainly increases the usefulness of Tl-201 SPECT. Those results will be published in a paper currently in preparation.

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