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Seven-Pinhole Emission Tomography with Thallium-201 in Patients with Prior Myocardial Infarction

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Thirty-six patients with prior myocardial infarction, and 14 patients without, had myocardial imaging at rest using both seven-pinhole emission tomography and planar imaging with thallium-201. The sensitivity and specificity of the two approaches for the detection of prior myocardial infarction were compared. Qualitatively, planar imaging yielded sensitivities of 69% (25 of 36) and 80% (29 of 36) with Polaroid and video display formats, respectively. A semiquantitative analysis gave a sensitivity of 75% (27 of 36). Specificities for these three planar approaches were, respectively, 100% (14 of 14), 93% (13 of 14), and 71% (10 of 14) for the Polaroid, video, and semiquantitative analyses.

Seven-pinhole tomography had a sensitivity of 83% (30 of 36) by qualitative or visual inspection and 86% (31 of 36) by semiquantitative analysis. Specificities by these two techniques were 71% (10 of 14) and 57% (8 of 14). There were no statistically significant differences in either sensitivity or specificity between the planar and tomographic approaches. Repeat seven-pinhole images were identical in 95% (46 of 48) of patients, showing that reproducibility was satisfactory. We conclude that the seven-pinhole tomographic approach has no advantage over standard planar imaging in the detection of prior myocardial infarction.

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Thallium-201 is the radionuclide of choice for delineating myocardial perfusion in the detection of myocardial ischemia or remote myocardial infarction. Experimental studies have shown a good correspondence between myocardial tracer deposition and myocardial blood flow (*1,2*), and a variety of clinical studies have proved the efficacy of imaging with this agent in detecting myocardial ischemia or scar (*3–5*). With the detection of myocardial ischemia, either exercise or pharmacologic stress have been used, and most investigators have shown that the detection of exercise-induced ischemia with this technique is improved over that of the exercise tolerance test alone (*3,4,6–8*). Similarly, in patients with prior myocardial infarction, scar tissue with little residual blood flow extracts relatively little tracer, and perfusion defects present at rest have been shown to correlate with the presence and extent of abnormally contracting segments seen on the contrast ventriculogram, as well as with other indicators of prior myocardial infarction (*5,9*).

Nevertheless, the clinical application of thallium-201 imaging to patient studies is fraught with some limitations. These include the fact that organs contiguous to the heart also accumulate tracer, such that the net external ratio of myocardial activity to adjoining background, when imaged externally on a gamma camera, ranges from 2 to 2.5 (*9*). Additionally, the predominant photon energy of 80 keV is associated with considerable soft-tissue attenuation, such that areas of the heart more distant from the gamma camera are under-represented

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in a planar image. Tomographic imaging, in which out-of-plane activity can be partially or largely eliminated, should obviate these problems in that reconstruction of discrete slices of myocardium minimizes the contribution of background in any one slice, and similarly reduces the problem of overlapping normal and abnormal regions of myocardium. The recent introduction of a commercially available seven-pinhole tomographic collimator, which can be attached to a conventional scintillation camera (*10,11*), allows for the potentially widespread use of this tomographic approach. The present study of this tomographic system in patients addresses the following questions: (a) is the sensitivity or specificity in the detection of perfusion abnormalities improved over planar imaging?; and (b) what is the reproducibility of the seven-pinhole technique? To learn the answer, we studied patients with and without remote myocardial infarction and performed tomographic and planar imaging only at rest.

METHODS

Patient selection. Thirty-six male patients (ages 41-67, mean age 54) were identified from a clinic devoted to follow-up of patients with cardiovascular diseases. All patients were New York Heart Association (N.Y.H.A.) Class I or II for either angina or congestive heart failure. All patients had documentation of myocardial infarction one or more months before imaging by the following: (a) new electrocardiographic Q waves of 0.04 sec or more, or ST-T wave changes associated with substernal chest pain refractory to nitrates and persisting for 0.5 hr or longer; and (b) characteristic enzyme changes elevated to at least twice the normal level. Patients who fulfilled the above criteria were selected as those seen serially by one of the authors and who agreed to have the imaging procedure. Fourteen patients were similarly identified who lacked all the above criteria for myocardial infarction and who, in addition, had undergone cardiac catheterization within 6 mo of the time of study. Five of these patients had either normal coronary arteries or stenoses of less than 50% diameter. The remainder had coronary artery disease without prior myocardial infarction and had, in addition, a normal biplane contrast cineventriculogram and a normal ejection fraction. All patients were advised of the experimental nature of the study and gave informed consent approved by the University's Human Subjects Review Committee.

Imaging procedures. All patients were studied in the fasting state following a single 1.5-2.0-mCi intravenous injection of Tl-201 in the standing position. Seven-pinhole tomographic imaging began 15 min after injection and utilized a wide-field-of-view scintillation camera.* Point- and flood-source calibrations, as described by Vogel et al. (*10*), were made before clinical imaging for each patient studied. A commercial seven-pinhole collimator and reconstruction algorithm were used.† Patient positioning for the tomography followed the recommendation of Vogel et al. (*10*) and consisted of beginning at a 45° left anterior oblique (LAO) angulation with repositioning as necessary to ascertain that no images in the peripheral six pinholes were incomplete, i.e., that the heart was always within the outer border of all seven fields of view. Additionally, positioning was adjusted until the central pinhole image most closely approached the "doughnut" pattern characteristic of a true LAO image. A 30%, symmetric energy window, set up in air on the 80-keV peak, was used. A two-million-count image was then obtained and 12 planes were reconstructed, with the central plane identified as that halfway through the series beginning with the first plane that showed discrete apical activity. At the termination of the first tomographic image acquisition, patients were moved to a second gamma camera (standard-field-of-view) equipped with an all-purpose, low-energy collimator. Standard 300,000-count planar myocardial images were obtained in the anterior, 30° LAO, 45° LAO, and 60° LAO positions and recorded both on triple-lens Polaroid film and on a digital computer in a 128 × 128 format. Following the planar studies, which averaged 40 min, the patient was immediately returned to the large-field camera for a second tomographic acquisition, performed in a manner identical to that for the first tomographic studies. Patient repositioning was based on direct visual comparison with the initial view data. Also, for the first 25 patients, a number of wood spacing blocks were used to control precisely the distance from the patient's chest wall to the collimator face, so that this distance would be identical between the initial and repeat tomographic studies. For the subsequent 25 studies, these spacing blocks were no longer felt to be required and their use was discontinued.

All planar and tomographic images were interpreted qualitatively and independently by a panel of three experienced observers, with patient identity and clinical information withheld. A perfusion defect was considered to be present when a discrete regional count deficit, visually estimated at 50% or greater and encompassing at least 20% of the circumference of the myocardium, was present in two views (*9*). In cases of observer disagreement, the reading of the two observers who agreed was used. For planar studies, the Polaroid images were initially interpreted by the reader panel. The interpretation of Tl-201 images from the triple-lens Polaroid film format without any computer display represents our standard clinical practice. Subsequently, these same images were reinterpreted 2 mo later by the same panel using only the computer display. In this video system, images were displayed in both black and white and color, in a 128 × 128 matrix with 64 gradations of intensity or color, and a potentiometer was adjusted such that 0-100% background subtraction could be applied to the display of each image. Each observer manipulated the display controls to obtain a satisfactory visual presentation of every image. Images were interpreted as being either normal or showing discrete perfusion defects, as previously defined. For the tomographic studies, a pilot series of 20 patients with known perfusion defects, or a lack thereof, on planar images were reviewed in an unblinded fashion to establish criteria for the presence or absence of perfusion defects. These criteria were the same as those applied to the LAO planar image as described above. Two months later, the entire 50 tomographic images, as well as the repeat studies in 48 of the 50 patients,[‡] were randomly mixed and intepreted in a blinded fashion. Since no analog images were obtained for the tomograms, all tomographic studies were read from the computer-generated display, as noted above. Finally, the 50 initial tomographic images were transferred by magnetic tape to the computer system at another institution and reviewed there by one of the developers of the seven-pinhole technique (R.A.V.), for a qualitative or visual interpretation without clinical information.

All tomographic images were also analyzed by the semiquantitative "CIRCLE" approach described by Vogel et al. (*10*). In brief, the geometric center of the left ventricle was identified visually and a series of 60 radii, equally spaced in angle, projected outward from this point to a maximum radius specified by the operator. A search was made along each radius and the maximum count value ascertained. A plot was then constructed of the peak count found along each radius against angle over the 360° circumference of the myocardium, normalized to the maximum count value in a given patient. The circumferential plot for each tomogram was rated against a lower limit of normal, previously established from circumferential analysis of the tomograms from (a) five patients with normal coronary arteries, and (b) the larger group of 14 patients that included the five normals plus nine patients without prior myocardial infarction. These plots were statistically identical. Our curve for the lower limit of normal was obtained from the 14-patient average by establishing the mean minus 2 s. d. value at each of the 60 angles, then smoothing the resulting plot with a Hanning filter. For use as a standard for interpreting a patient's tomogram, we considered as abnormal any radial value that fell below the lower limit of normal for that angle. We also compared our study population with the lower-limit-of-normal curve defined by Vogel et al. (*10*) for exercise studies. For the 45° LAO planar images, a similar lower-limit-of-normal curve was defined, and all 50 planar images were similarly analyzed in the 45° LAO view.

RESULTS

Image interpretation, interobserver variability. For the planar studies, interpreted from the analog Polaroid triple-lens images, all three observers agreed to the presence or absence of a defect in 45 of 50 patients (90%). In the remaining five, one reader disagreed and the reading of the other two observers was accepted as the consensus. In all cases (both planar and tomographic), the location of the defect, as previously described by us (*9*), was agreed upon by all observers. When the planar images were interpreted in the video (computer) display, there was similar agreement (44 of 50 = 88%, p = NS). For the tomographic images, all three readers agreed as to the presence or absence of a defect in 36 of the 50 patients (72%, $p < 0.05$ McNemar test of correlated proportions compared with agreement for planar studies).

Sensitivity and specificity of planar and tomographic images for prior myocardial infarction. The qualitative interpretation of the planar images yielded 69% (25 of 36) and 80% (29 of 36) sensitivities for the Polaroid and video interpretations, respectively, for the detection of prior myocardial infarction (Fig. 1A). Specificities were 100% (14 of 14) and 93% (13 of 14) for Polaroid and video displays (Fig. 1B). The semiquantitative "CIRCLE" analysis of the planar images gave a sensitivity of 75% (27 of 36) and specificity of 71% (10 of 14). None of these differences was statistically significant.

The qualitative interpretation of the tomographic images gave a sensitivity of 83% (30 of 36) and specificity of 71% (10 of 14) (Fig. 1). The use of the semiquantitative "CIRCLE" analysis, based on the normal range derived from our own patients, gave a sensitivity of 86% (31 of 36) and specificity of 57% (8 of 14) (Fig. 1). The use of the normal quantitative range derived by Vogel et al. was similar (although derived from exercise studies), giving a sensitivity of 83% (30 of 36) and specificity of 43% (6 of 14). None of these sensitivities or specificities obtained with the tomographic approach differed significantly from those obtained from the planar images (McNemar test).

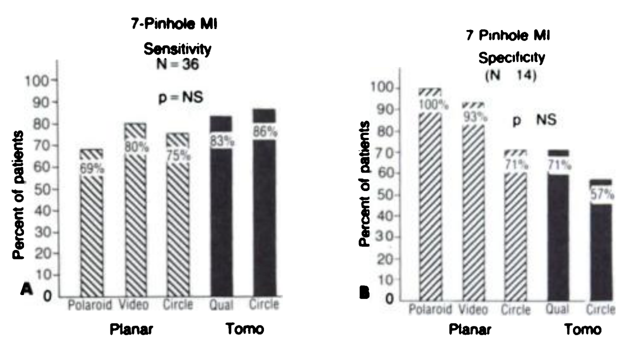

FIG. 1. Sensitivity (1A) and specificity (1B) data for planar (striped bars) and seven-pinhole tomographic (solid bars) images. There were no significant differences in sensitivities or specificities between tomographic and planar approaches. Polaroid = analysis of Polaroid display; video = analysis of video display; circle = semiquantitative anlysis; and Qual = visual analysis of seven-pinhole images by video display.

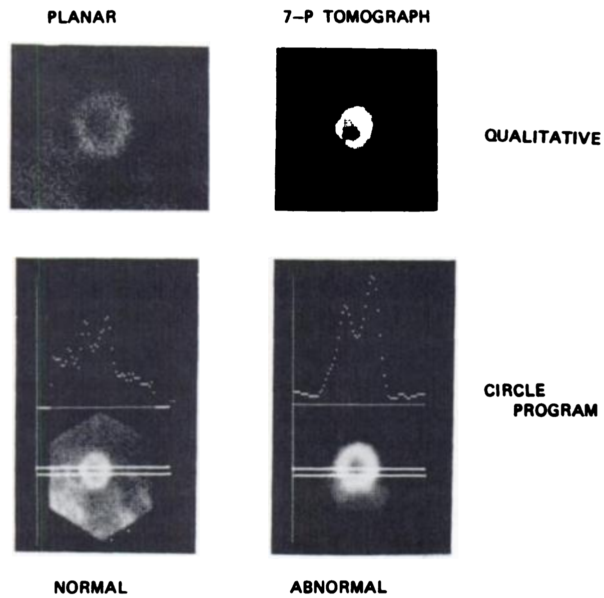

FIG. 2. Patient with antero-apical infarction by electrocardographic Q wave. Planar studies (left) were considered normal, although tomograms (right) were abnormal to both visual or qualitative and semiquantitative "CIRCLE" analysis. Bottom panel shows horizontal profile of count activity, demonstrating reduced anterior-wall activity in tomogram, not seen in similar 45° LAO planar study.

A highly experienced reader (R.A.V.), from the institution developing the seven-pinhole approach, recorded a sensitivity of 85% (29 of 34) and specificity of 58% (7 of 12). He felt that four studies were technically inadequate (two in the infarction group and two in the normal group) and excluded these from his readings. His results were not significantly different from our own. The repeat analysis of our data excluding these four cases similarly did not modify the initial results. Examples of studies in which defects were identified only in the to-

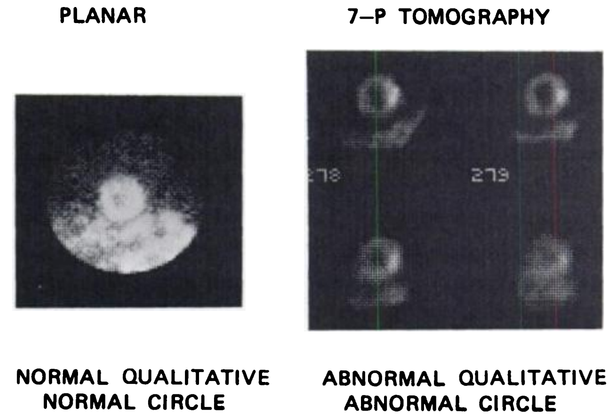

FIG. 3. Patient with normal coronary arteries and without prior myocardial infarction. Planar study (left, 45° LAO image) was entirely normal, whereas tomograms showed an inferior defect in two planes (top right) both qualitatively and by "CIRCLE" analysis.

mographic image, or misidentified in the tomographic image, are shown in Figs. 2 and 3.

Serial tomographic images. Of the 48 serial or repeat seven-pinhole tomographic images, the blinded interpretation as to the presence or absence of a defect differed in eight patients (17%). However, direct comparison of the initial and repeat tomogram in a side-by-side fashion showed that all but two were in fact identical. That is, in 95% of cases, the repeat study was the same as the initial study. Neither of the two patients whose tomography differed had prior myocardial infarction. In one, the initial tomogram showed a defect both qualitatively and quantitatively, whereas the repeat tomogram was entirely normal. In retrospect only, the apex of the heart was minimally clipped or not entirely within the field of view in the inferior seven-pinhole image, as shown in Fig. 4, presumably creating an artifactual de-

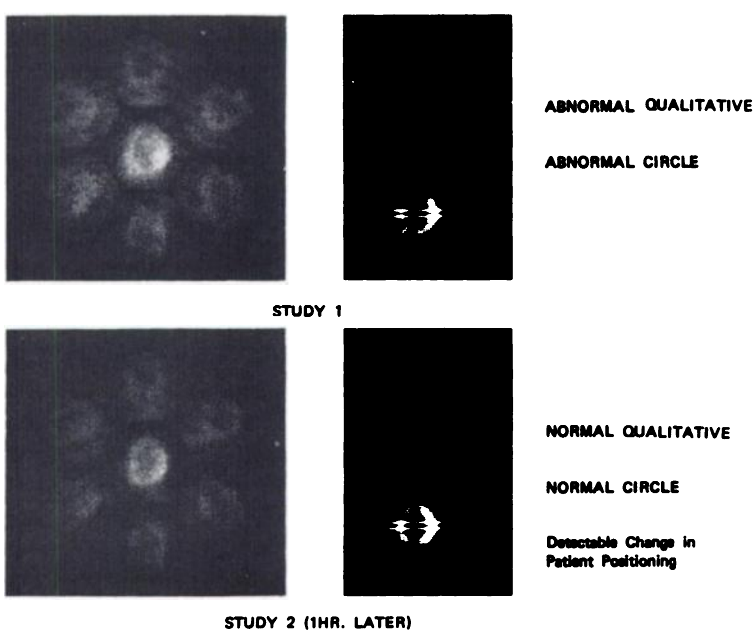

FIG. 4. Individual seven-pinhole views in a patient with no prior infarction are at left, and a reconstructed slice at right. In initial image (top), a defect was identified by both qualitative, visual inspection and by the "CIRCLE," semiquantitative analysis. Repeat image (bottom) was entirely normal. In retrospect, it was noted that the 6 o'clock seven-pinhole view (top panel) was improperly positioned, with apex of heart extending slightly beyond field of view. This positioning error presumably created the false perfusion defect.

fect. In the second patient, the initial tomogram was strikingly abnormal, whereas both the planar and repeat tomograms in this patient without prior myocardial infarction were entirely normal. No changes in patient positioning between the two studies were evident, and the explanation for the difference in the pair of tomographic studies is unknown.

DISCUSSION

Initial reports suggested that seven-pinhole tomography had improved sensitivity and specificity in detecting exercise-induced perfusion abnormalities (*10,11*). In these reports, however, the tomographic imaging had been performed before the planar images were obtained, and redistribution of Tl-201 into the area of the perfusion defects may have taken place, possibly masking the presence of such defects in the planar images. Both experimental-animal and clinical studies have demonstrated substantial redistribution over a 15–60 min time period (*12–15*). By studying patients at rest who had remote myocardial infarctions and no more than N.Y.H.A. Class I or II angina, the present study largely eliminated this problem of exercise redistribution. Although patients with unstable pain patterns may show changes in the resting Tl-201 image over time (*16,17*), such would not be anticipated in the chronic setting and was so documented in that a repeat tomogram following the planar study was identical in all but two cases. Moreover, the early reports of seven-pinhole tomography involved a large-field scintillation camera for the planar Tl-201 images. These cameras often have poorer intrinsic spatial resolution than standard 10-in.-crystal cameras that are routinely employed in planar Tl-201 imaging, thus constituting a bias against the planar images. In the present study, a standard camera with 10-in. crystal and collimator was used for planar imaging. Note that in the initial clinical report on seven-pinhole tomography (*11*) the improvement in detection of defects occurred exclusively among patients with normal left-ventricular function, i.e., the patient population studied probably differed from that reported herein. A recent multicenter trial of exercise seven-pinhole imaging confirmed that it was the quantitation of the seven-pinhole tomogram, rather than the qualitative or visual inspection, that accounted for the improvement in defect detection (*18*). Recent reports of quantitative approaches in planar exercise studies suggest a very high sensitivity and specificity in detecting both coronary artery disease per se as well as disease of individual coronary arteries. A quantitative analysis of the planar images obtained at rest in this study did not, however, improve detection of defects.

The present study suggests that the seven-pinhole tomographic approach does not substantially improve the sensitivity or specificity in the detection of abnormal myocardial perfusion with Tl-201. This series is relatively small and slight, but possibly significant changes might not be detected. Also, an ideal control group—e.g., middle-aged patients without myocardial infarction or chest-pain syndromes and with normal coronary arteries—is not available, since such patients do not undergo angiography. The greater interobserver variability seen in the readings of the seven-pinhole tomograms may reflect our relative inexperience with this format. However, the fact that an experienced reader from another institution obtained a similar sensitivity and specificity supports the overall conclusion of the study. This result is that the seven-pinhole approach had no clear advantage over planar imaging in the detection of defects in the image performed at rest. For clinical purposes, it is of particular interest that simple video display of the planar images resulted in a sensitivity essentially identical to that for the tomographic approach. It is also of clinical importance to emphasize that minor errors in patient positioning may introduce artifact, as shown in Fig. 4. Overall, however, the reproducibility of repeat seven-pinhole tomograms in this series was satisfactory.

Other clinical reports using the seven-pinhole system have been in preliminary form only. Berman et al., using exercise testing and seven-pinhole Tl-201 imaging, found no improvement in the detection of coronary disease per se over that with planar imaging, but suggested that the detection of individual diseased vessels was enhanced (*19*). Francisco et al. (*20*), stressing with intravenous dipyridamole rather than exercise, reported improved sensitivity with the seven-pinhole approach for the detection of coronary disease. In that series, however, a qualitative interpretation of the planar images was compared with a quantitative analysis of the seven-pinhole tomograms. The clinical findings in the present study are in basic accord with a detailed cardiac-phantom study performed by us using seven-pinhole tomography (*21*). In that study, we employed a heart phantom designed at the University of Iowa (*22*) and suspended it within a tank filled with Tl-201 and water to mimic contiguous noncardiac background. A 24-g transmural, area of decreased activity in the myocardial wall showed a reduction in activity to 50% of the opposing normal wall by seven-pinhole emission tomography (the true figure being zero), compared with a reduction to 70% with planar imaging. That is, contrast was slightly improved with the seven-pinhole tomography. However, the area of decreased activity, geometrically 3 cm in depth, was seen throughout all 12 of the 1-cm-thick tomographic slices; i.e., there was no depth localization. Thus in a controlled experimental setting, the tomography improved contrast but was not quantitative as to either the magnitude of activity or its geometric location. This follows from the fact that the seven-pinhole tomographic samples from a limited angle rather than the full 180°

minimum angular coverage required for true tomography (*23,24*). Preliminary studies on this same cardiac phantom, using 180° tomography with a rotating gamma-camera system, suggest improved quantitative capability, but clinical trials have yet to be performed (*25*).

In summary, seven-pinhole tomography, performed at rest in patients with remote myocardial infarction, was neither more sensitive nor more specific than traditional planar imaging in the identification of perfusion defects.

FOOTNOTES

* Sigma 410.

† CMS Company and Medical Data Systems, Ann Arbor, MI.

‡ Two patients declined repeat tomograms because of time constraints.

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