"Circumferential Profiles:" A New Method for Computer Analysis of Thallium-201 Myocardial Perfusion Images

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A method for computer analysis of thallium-201 scintigrams is described, in which the left-ventricular activity is measured along radii constructed from the center of the left ventricle (LV) to each point on the LV circumference. Data are then displayed graphically as a "circumferential profile" of normalized activity against radial location. Thallium defects are identified and scored by comparison of the profile curve with empirically determined normal limits. In patients with coronary artery disease, defect scores were found to be quantitative and reproducible, and to agree generally with subjective visual analysis.

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Thallium-201 scintigraphy is being used increasingly for evaluation of regional myocardial perfusion (*1*). Currently, most myocardial perfusion images are interpreted subjectively by visual identification of areas of abnormally reduced activity. Unfortunately, subjective interpretations of myocardial images are strongly influenced by the experience of the observers, the quality of the images, the ratio of myocardial to background activity, the characteristics of the display system, and many other factors inherent in subjective interpretations and evaluations. We have therefore devised a computer-assisted technique for analyzing thallium images; it is objective, reproducible, and independent of observer bias. This report describes our method and presents early results in normal subjects and patients with coronary artery disease.

METHODS

Patients. Three groups of patients were studied. Group 1 consisted of 13 normal volunteers (ages 23–46) who had no history of cardiac symptoms and normal cardiac examination, chest radiograph, resting electrocardiogram, and exercise electrocardiogram. Group 2 consisted of 74 patients with coronary artery disease. Forty patients (Group 2A) were imaged at rest within 12 hr of onset of an acute myocardial infarction. The diagnosis of infarction was based on a typical history of chest pain, characteristic electrocardiographic changes, and/or a typical rise in serum creatine kinase. Eleven patients had acute anterior transmural infarctions, 21 had inferior or posterior transmural infarctions, and six had subendocardial infarctions. Thirty-four other patients with angina pectoris (Group 2B) had angiographically proven coronary artery disease, with 30% or less of the luminal diameter remaining in at least one major coronary artery. These patients were imaged both at rest and after exercise. Sixteen had a history of prior myocardial infarction.

Thallium scintigrams were acquired using standard techniques. For rest studies, 1.5–2.0 mCi Tl-201 were injected i.v., and 10 min later imaging was performed in anterior, 40° left anterior oblique (LAO), and 60° LAO views, using a scintillation

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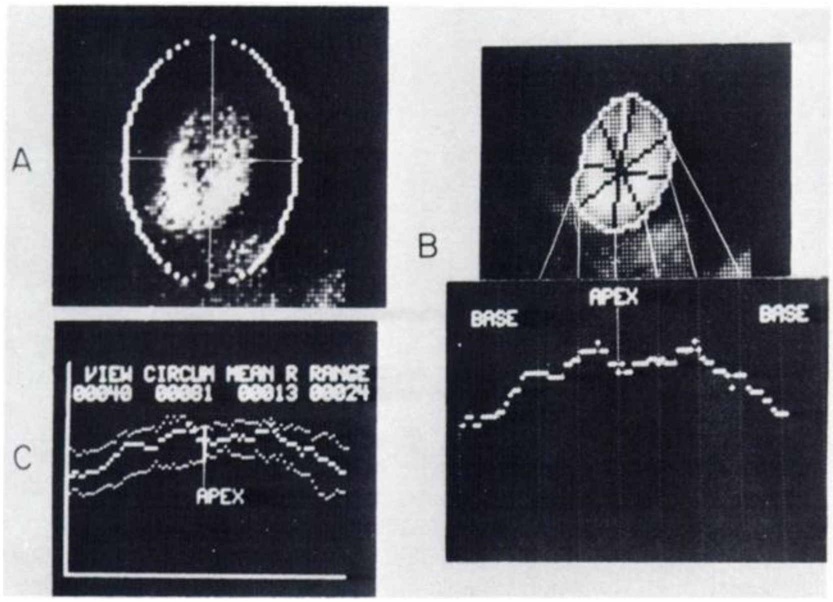

FIG. 1. Circumferential profile technique. In (A) an ellipse is placed around left ventricle (LV) of normal subject imaged in 60° LAO view. In (B), computer has generated an isocount LV edge and radii from center of LV to each circumference point. Every tenth radius is shown in black, with starting radius in white. Below the image is curve of normalized thallium activity vs radial location, starting with white radius and proceeding counterclockwise. Activity is lowest in basal region. In (C), curve is superimposed on predetermined normal limits (see text). Apex is marked for orientation, and computer text gives the view, number of circumference points, mean radius in pixels, and range of normalized thallium activity.

camera and a general-all-purpose parallel-hole collimator. Images contained 400,000 counts full field and were stored on magnetic disk in a 128 × 128 matrix. For exercise studies, patients performed graded exercise on a bicycle ergometer or treadmill using standard protocols. Exercise was terminated when chest pain or ischemic ST segment changes occurred, or when the patient became exhausted, or the heart rate reached 90% of the maximum predicted value. Thallium was injected intravenously 1 min before the end of exercise, and the patient was imaged 5 min later as described above.

Circumferential profiles. Each image was smoothed using a nine-point averaging algorithm, and displayed on a video screen. No background was subtracted from the image. An observer selected the center point and the lengths of the major and minor semi-axes of an ellipse that contained the area of the left ventricle and isolated it from the remainder of the image (Fig. 1A). Based on a threshold percentage of maximum supplied by the user, an isocount contour was determined by searching from the edge of the ellipse toward the center. A threshold value of 50% was generally selected first, followed by adjustments up or down until the isocount contour best approximated the outer edge of the left ventricle as assessed visually by the user. In cases where high adjacent background or very low thallium uptake, or both, resulted in obscure edge definition, the ellipse was positioned so that a portion of its edge approximated the outer border of the left ventricle and formed part of the isocount contour. The centroid was then determined and radii constructed to each point on the isocount contour (normally 70–100 points). The distribution of Tl-201 activity was determined by calculating the average activity per pixel along each radius and normalizing the data to the radius with the highest average activity. These data were then displayed as a "circumferential profile" curve by plotting normalized thallium activity against angular position, beginning with the "highlighted" radius and proceeding counterclockwise around the circumference (Fig. 1B). Individual circumferential profiles were generated using this technique for each of the three views in each study. The time required for computer processing averaged 2–3 min per view.

Definition of normal limits. Circumferential profiles for the 13 normal volunteers were categorized by view and whether they represented rest or exercise studies. The profiles for each of the six categories were aligned on the point corresponding to the scintigraphic apex and were normalized for size. A mean normal profile and curves representing two standard deviations from the mean were calculated by averaging the profiles point by point. The curve representing two standard deviations below the mean was taken as the lower limits of normal.

Scoring of defects. Computer-generated circumferential profiles of images from patients with coronary disease were scored by comparing each curve with empirically determined normal limits. We displayed the original unprocessed myocardial perfusion scintigram and the computer-smoothed image, with the left-ventricular isocount edge and every tenth radius superimposed. The number of the radius corresponding to the apex, the patient position, and whether the study was rest-injected or exercise-injected were entered into the program. The appro-

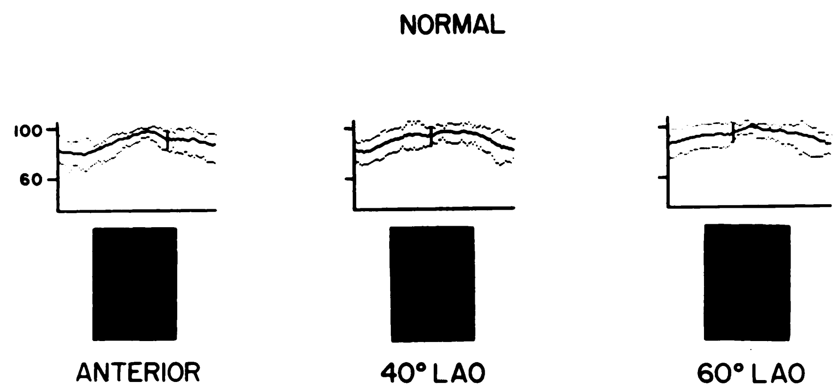

FIG. 2. Mean thallium profile curves (darker lines) of 13 normal volunteers, with ± 2 standard deviations (lighter lines) for the three views. Vertical scale is radial thallium activity per pixel as percentage of highest value. Note greater variability in basal regions.

TABLE 1. NORMAL VALUES

	Circumference (points)		Range (% of maximal Tl activity)		Mean radius (points)	
View	Rest (n = 12)	Stress (n = 13)	Rest (n = 12)	Stress (n = 13)	Rest (n = 12)	Stress (n = 13)
Anterior	83 ± 6	87 ± 8	22 ± 4	22 ± 3	13 ± 1	13 ± 1
LAO 40°	78 ± 6	78 ± 9	24 ± 5	25 ± 4	12 ± 1	12 ± 1
LAO 60°	81 ± 6	81 ± 7	20 ± 5	21 ± 4	12 ± 1	12 ± 1

Values are mean ± s.d.

priate curves for normal limits were then aligned about the chosen apex point of the profile, normalized to the length of the profile, and displayed as a composite image (Fig. 1C). For each image the following characteristics were determined:

1. Number of points on the circumference (C).
2. Mean radius (R).
3. Range of activity: the lowest activity in the normalized profile (the highest was always 100%).
4. The percent circumference defect (%C): the percentage of circumference points falling below the −2 s.d. normal-limits curve.
5. A score (S) for the image: the area of abnormality, found by multiplying %C by the average reduction in thallium activity below the −2 s.d. normal curve.

A total score for each patient was obtained by summing the scores of the three individual views.

Subjective scoring. The images of the 40 patients with acute myocardial infarction (Group 2A) were subjectively scored by at least two independent observers for comparison with the computer-generated defect scores. The left ventricle in each view was divided into five equal segments, each of which was scored for intensity of defect (0 = normal, 1 = slightly but definitely abnormal, 2 = moderately abnormal, and 3 = severely abnormal). The image score was obtained by summing the individual segment scores, and a total score was obtained for each patient by adding the scores for three views.

RESULTS

Normal curves. (Fig. 2). The circumferential pro-

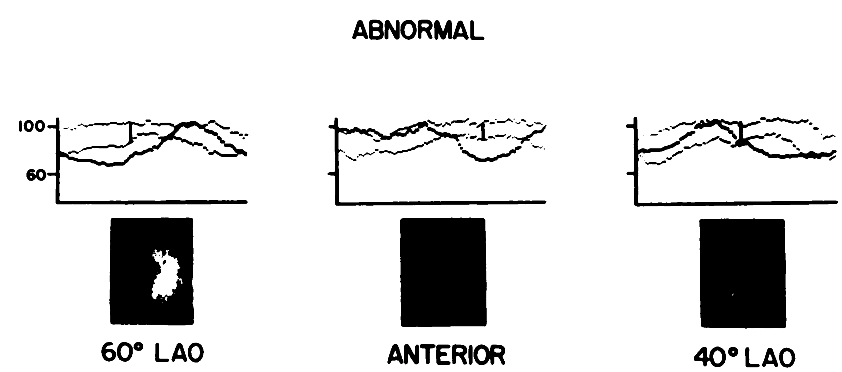

FIG. 3. Examples of abnormal circumferential profiles. Normal limits are shown by lighter lines, with location of apex marked by short vertical line. The 60° LAO image is from patient with large anteroseptal defect. Anterior and 40° LAO images are from other patients with apical and lateral-wall abnormalities, respectively. Corresponding profile curves are shown for each image by darker lines, and defects correspond to where image curve falls below normal limits.

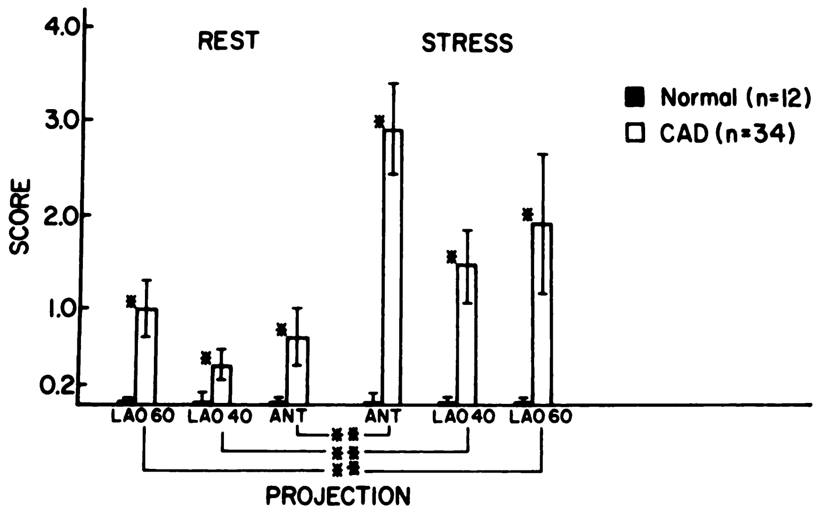

FIG. 4. Mean defect scores for 12 normal subjects and 34 patients with coronary disease shown for three standard views for rest and stress studies. * = that difference between normal and CAD is statistically significant ($p < 0.05$). ** = significant difference ($p < 0.05$) between rest and stress for CAD patients.

files from normal volunteers had a characteristic shape: activity was lower at the two ends corresponding to the base, and higher in the middle (Fig. 1B, lower). There was usually a small reduction of activity at the apex. The mean normal values for circumference, range, and radius are shown in Table 1. There were no significant differences in these values between the three patient views or between rest and stress for each view. The minimum value for thallium activity in the normal profiles averaged 80–84% of the maximum. The area between the curves for the normal limits (2 standard deviations above and below the normal mean curve) showed regional variations in width. The greatest variability in normal subjects occurred in the basal regions, where the s.d. was 7% in all three views. The minimum variability occurred a) just inferior to the apex in the anterior view (s.d. = 2%), b) in the lateral wall just superior to the apex in the LAO 40° view (s.d. = 2%), and c) in the distal posterolateral wall in the LAO 60° view (s.d. = 2%).

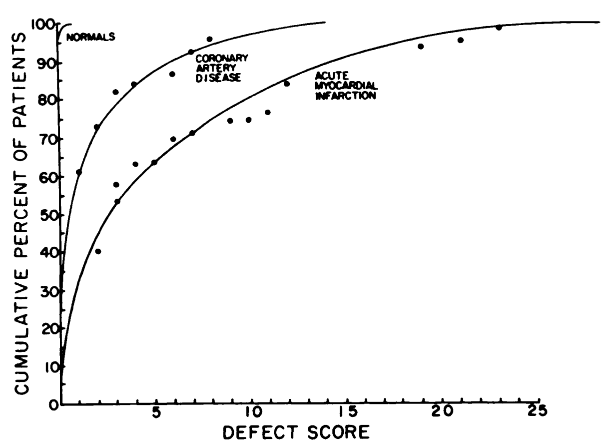

FIG. 5. Cumulative distribution of total defect scores in resting studies of normal subjects, patients with chronic CAD (Group 2B), and patients with acute myocardial infarction (Group 2A).

Coronary artery disease. Most patients with coronary artery disease (CAD) showed a portion of their circumferential profile at rest or exercise falling below the −2 s.d. normal-limits curve. Examples are given in Fig. 3. Patients with chronic CAD had significantly greater mean percentage circumference defects and defect scores than normal subjects in all three views at rest and exercise (Fig. 4). CAD patients also had significantly higher defect scores in exercise images than in rest images for all three views (Fig. 4). Mean values for circumference (82–86) and radius (12–14) in CAD patients did not differ significantly from normal.

Figure 5 shows the cumulative distributions of total defect score for the rest studies from the three groups of subjects. All of the normal individuals had scores of less than unity. The distributions for patients with CAD and acute myocardial infarction were shifted to the right, indicating larger scores in these groups, although there was some overlap with the normal group. The cumulative distribution of scores for the exercise studies in chronic CAD patients is not shown; it was displaced to the right as in the acute myocardial infarction group; 50% of the patients had scores of 3.0 or more, and 82% had scores > 1.0.

Interobserver variability of computer analysis. Thallium-201 perfusion scintigrams from nine patients having a variety of defects were analyzed by six independent observers using the circumferential profile method. Table 2 shows the total defect scores obtained for the exercise studies in these nine patients. Inspection of the table shows low interobserver variability in most patients. Analysis of variance revealed no significant difference between

TABLE 2. INTEROBSERVER VARIABILITY OF DEFECT SCORES

	Observers							
Patients	1	2	3	4	5	6	Mean	s.d.
1	24.92	17.86	26.07	17.54	26.01	25.29	22.95	4.09
2	0.01	0.00	0.02	0.01	0.08	0.00	0.02	0.03
3	9.17	9.68	9.93	10.17	9.44	9.85	9.71	0.36
4	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00
5	34.83	31.18	34.01	34.91	33.31	33.47	33.62	1.37
6	22.38	23.98	20.19	21.15	21.24	19.79	21.46	1.53
7	3.96	3.95	6.62	3.96	3.69	4.29	4.41	1.10
8	0.05	0.04	0.11	0.95	0.22	0.00	0.23	0.36
9	0.00	0.01	0.00	0.00	0.00	0.05	0.01	0.02
Mean	10.59	9.63	10.77	9.65	10.44	10.31		
s.d.	13.35	11.94	12.95	12.22	13.03	12.80		

ANALYSIS OF VARIANCE

Source	Sum of squares	D.F.	Mean square	F	
Patients	7648.2	8	956.0	309.00	p < .001
Observers	10.5	5	2.1	0.67	N.S.
Residual	123.8	40	3.1		
Total	7782.5				

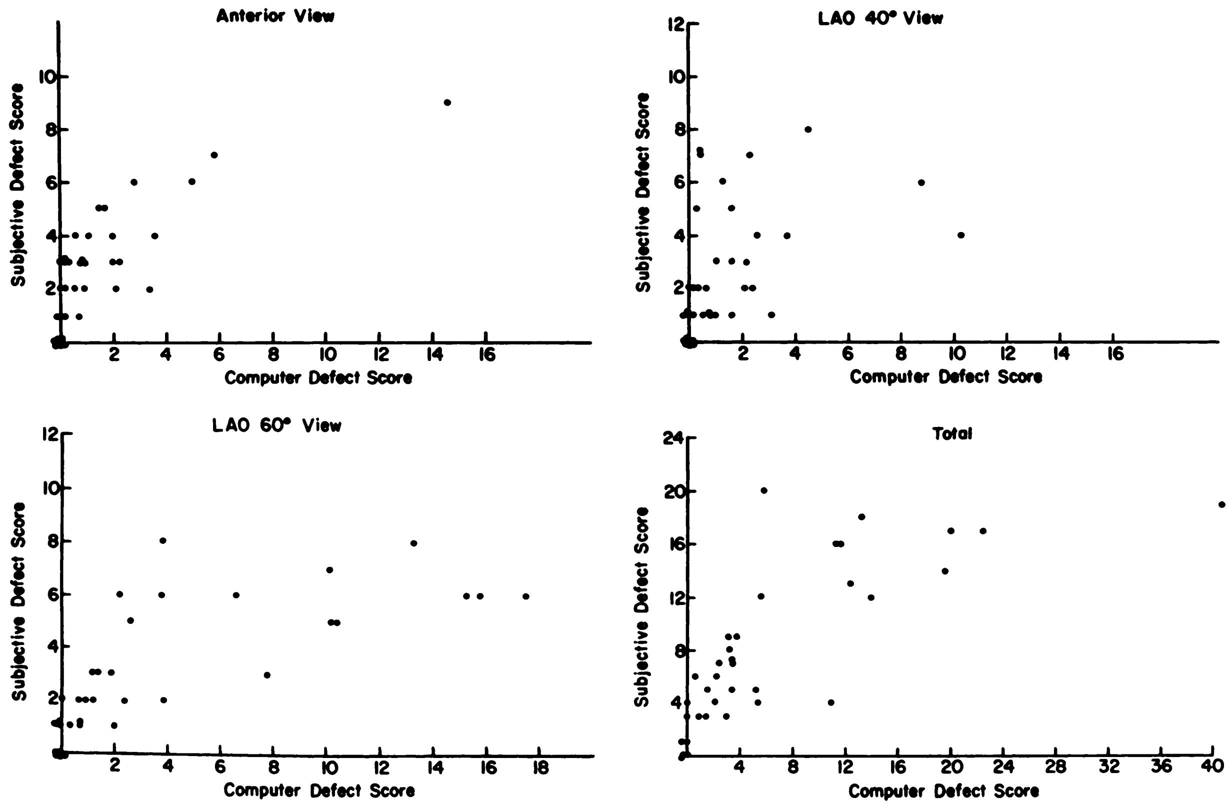

FIG. 6. Comparison of subjective and computer-generated defect scores for individual views and for total score in patients with acute myocardial infarction. Note that computer tends to be "conservative" for small visual defects.

observers after correction for interpatient differences. Similar results were found for total defect scores in rest images, and for defect scores in individual views in both rest and stress studies. Low interobserver variability was also found for circumference, range, and percentage circumference defect measurements.

Comparison of visual and computer analysis. Figure 6 compares the computer-generated defect scores with a semiquantitative visual scoring system for the 40 patients imaged within 12 hr of onset of an acute myocardial infarction (Group 2A). In all three individual views, the computer tended to be "conservative" when defects were small. Com-

TABLE 3. COMPARISON OF REGIONAL DEFECTS IDENTIFIED BY VISUAL AND COMPUTER METHODS

	Anterior view			40° LAO view			60° LAO view		
	Anterior	Apical	Inferior	Septal	Apical	Lateral	Ant-Septal	Apical	Post-Lat
Visual defect	11	26	16	15	16	17	16	16	20
Computer defect where visual defect present	8	21	16	9	14	15	15	15	17
Computer defect where no visual defect present	0	0	0	0	2	0	1	1	0

TABLE 4. PREDICTION OF CORONARY ARTERY DISEASE FROM THALLIUM-201 DEFECT SCORES

Upper limit of normal for defect score	Sensitivity			Specificity
	CAD rest	CAD stress	Acute M.I.	Normals
1.0	44%	72%	70%	100%
0.5	56%	88%	92%	92%

Sensitivity is defined as the frequency of abnormal scores in each of the three patient groups. Specificity is the frequency of normal scores in the normal volunteer group. CAD refers to the chronic coronary artery disease group (2B) and acute M.I. to group 2A.

puter scores were generally zero when "defects" were mild and visually involved only a single segment in a single view. On the other hand, when defects were large, the computer was able to measure a wide range of scores that appeared similar by visual analysis.

Table 3 compares the frequency of detection of perfusion defects in these 40 patients by visual and computer methods for specific regions of the heart. Using the current normal limits, the computer analysis generally appeared to be less sensitive than visual interpretation, particularly for the anterolateral wall and apex in the anterior view, and the septum in the 40° LAO view.

DISCUSSION

Despite the rapid expansion of thallium perfusion scintigraphy and increasing availability of computers for data acquisition and storage, interpretation of thallium studies has generally remained at a subjective and qualitative level. The method of "circumferential profiles" that we have described utilizes a computer to measure and display normalized thallium activity along radii constructed from the center of the left ventricle to each point on the circumference. A quantitative score is then generated, based on the deviation of the profile curve below previously established normal limits.

Several other investigators have described computer-assisted methods for analyzing thallium scintigrams, but in most cases the computer was used for image enhancement rather than defect identification and scoring (*2-4*). Some investigators have used hand-drawn light-pen outlines of defect area to estimate the size of acute myocardial infarctions (*5,6*), but this approach is merely an extension of subjective interpretation. One group has used a "heterogeneity index" to express the nonuniformity of thallium uptake in the left ventricle (*7*); compared with normals, patients with coronary disease were found to have more matrix points with activity below a given percentage of the maximum.

Two other groups have described methods similar to ours using computer-measured radial thallium activities (*8,9*). The method of Meade et al. (*8*) uses analysis of images enhanced by fast Fourier transform methods. Profiles of rest and exercise images are visually compared, but there are no experimentally determined criteria for abnormality. The method of LeFree, Vogel et al. (*9*) compares radial thallium activity with normal limits determined from profiles of normal volunteers. As with our method, normal limits are determined from the mean ± 2 standard deviations of the normal curve, averaged point by point around the LV circumference. What is "normal" therefore varies with the particular anatomic region in a particular view. A feature of our program is that the apices of each profile and the mean normal curve are superimposed, allowing us to correct at least partially for variations in heart position.

In addition, we have quantified thallium defects using a score that takes into account both the extent and intensity of the defect. In patients with acute myocardial infarction, the defect score may be expected to reflect the extent of infarcted and/or ischemic myocardium, and should therefore be useful for assessing prognosis and the effect of intervention therapy. The defect score may also prove useful for differentiating patients with and without coronary artery disease. A score can be arbitrarily established to represent the upper limits of "normal"—for example, 1.0. All of our normal volunteers had scores < 1.0, whereas the majority of patients with ischemic heart disease had higher scores (Fig. 5). With the upper normal value reduced to 0.5, one of the 13 normal subjects became "abnormal," but more patients with CAD were correctly identified. Table 4 indicates values for the specificity and sensitivity of this technique in our population, using the arbitrary upper normal scores of 1.0 and 0.5. We wish to emphasize, however, that our patients and normal volunteers were selected groups, and it is therefore uncertain to what extent the indicated values are applicable to a general population. In addition, we must caution that our normal limits, against which the circumferential profiles were compared, was based on only 13 subjects. As more normals are added—especially subjects closer in age to CAD patients—the normal limits may change, along with what constitutes a "normal" defect score, as well as values for sensitivity and specificity.

We performed our analyses without background subtraction and without image enhancement except for a single smoothing. We did not wish to distort the image by applying enhancement techniques, and felt that no adequate method currently exists for background correction. We found that in images without background subtraction the minimum thallium activity in normal subjects was 75–80% of the maximum. This is similar to the 71% minimum value obtained by Vogel and colleagues for standard thallium images in normals (*10*). These authors found lower minimum values in normals (46%) using a tomographic method with background subtraction. We anticipate that when a suitable background correction method is developed and applied to standard images, the normal limits may need to be altered and the sensitivity and specificity of computer analysis redefined.

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