Reversibility Bull's-Eye: A New Polar Bull's-Eye Map to Quantify Reversibility of Stress-Induced SPECT Thallium-201 Myocardial Perfusion Defects

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Myocardial ischemia is currently interpreted from SPECT thallium-201 (^{201}Tl) tomograms by the subjective visual finding of stress-induced perfusion defects which "normalize" or "reverse" by 4 hr. Thus, we have developed a computer method to quantify and display the three-dimensional distribution of reversible segments. Circumferential profiles generated from the short axis slices are normalized to the reference area in the stress study. The stress is subtracted from the normalized delayed data, and then displayed as a polar bull's-eye plot so that positive values show areas that have "reversed" or "improved." Patient profiles are compared to means and standard deviations of reversibility for all pixels determined from the Emory normal male files. Criteria for reversibility were developed from studies of 42 male patients found to have 48 defects, as determined by the consensus of five blinded expert observers. There was computer agreement with the experts on 25 of 31 relatively fixed and 14 of 17 reversible defects. Our preliminary results indicate that this new method promises to aid observers to more consistently identify and quantify the reversibility of SPECT ^{201}Tl myocardial perfusion defects.

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Thallium-201 (^{201}Tl) myocardial perfusion imaging has become an important diagnostic modality for the evaluation of cardiac patients. It is invaluable to clinicians to raise or lower the suspicion for coronary artery disease in a given patient. It is currently the procedure of choice in the assessment of the "significance" of a coronary artery stenosis. Whether a defect is fixed or reverses several hours after exercise has important clinical implications. Based on the thallium findings, invasive testing or procedures may be ordered or deemed unnecessary.

Currently, regions of myocardial ischemia are suggested from a SPECT ^{201}Tl tomographic study by the visual findings of a stress-induced perfusion defect that "normalizes" or "reverses" after several hours. Visual interpretation of thallium tomographic studies is time consuming and limited by interobserver variability and the inability to quantify the extent of normalization. Although quantitative techniques are being utilized for detection and localization of abnormalities (*1–3*), no satisfactory technique for quantifying reversibility of SPECT thallium studies has been achieved. Thus, we developed a computer method to quantify and display the degree that tomographic thallium myocardial perfusion defects "reverse" or "normalize."

METHODS

This study consisted of four main steps:

1. To develop the computer algorithm to display areas of reversibility using a polar display.
2. To quantitate, using existing normal patient studies, the normal amount of reversibility one could expect to see in patients considered unlikely to have significant coronary artery disease.
3. To take a test group of patients and process their studies using the newly developed computer algorithm and to compare the amount of reversibility in these patients versus the amount of reversibility in normals as determined from the normal files.
4. To use expert observers' standard interpretation of the test group studies to develop criteria for significant reversibility and to test and modify the criteria as necessary.

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Our procedure for SPECT exercise stress thallium studies has been recently described (*1*). Using standard acquisition and reconstruction protocols oblique angle images are generated in the short axis, vertical long axis, and horizontal long axis. Quantification consists of extracting maximal count circumferential profiles on each of the short axis slices in 9° arcs, ranging from apex to base, yielding 40 data points for each slice. The data is then interpolated to the equivalent of 15 slices and stored in two 15 × 40 arrays, one for the stress data and one for the delayed data. These data are then transformed into a polar plot known as the bull's-eye map.

Computer Algorithm

When interpreting bull's-eye for differentiating reversible versus fixed defects, physicians frequently compare the relative counts in a defect to the counts in a normal region. If the relative ratio of defect to normal counts is unchanged in the delayed study then the defect is considered to be fixed. If the relative counts of the defect increases relative to the normal area, then the defect is considered reversible. For example, in the stress bull's-eye seen in Figure 1A, there are decreased counts in the anterior region as compared to the lateral wall. Figure 1B confirms that this area of decreased counts is abnormal by "blacking out" areas that exceed 2.5 standard deviations (s.d.s) from the mean of normal distribution. Figure 1C shows via color scale the number of s.d.s any given area differs from the mean. In order to determine if there has been improvement, the reviewing physician compares the relative counts of the anterior to lateral regions in the delayed study (Fig. 1D). In this fairly obvious example, the delayed images show that several hours after exercise the anterior wall activity is much more comparable to the lateral wall than it was at stress, indicating reversibility. We designed our algorithm to use similar logic and to compare the counts in different regions of the image.

Using the stress 15 × 40 array representing the entire three-dimensional myocardial ^{201}Tl distribution, the 5 × 5 area with the greatest counts, and therefore presumably the most normal area, is identified. The array is normalized so that this area now has a maximal count of 1,000. The same reference area is identified in the delayed array and this array is normalized to make the same area in the delayed array 1,000 as well. Each point in the normalized stress array is subtracted from the corresponding point in the normalized delay array yielding a new 15 × 40 array of reversibility. This is then plotted in polar form to yield the reversibility bull's-eye (Fig. 1E). These are plotted so that areas which reverse are colored from blue to white depending on how great the relative improvement is. Areas that have not reversed or have relatively gotten worse are seen in black.

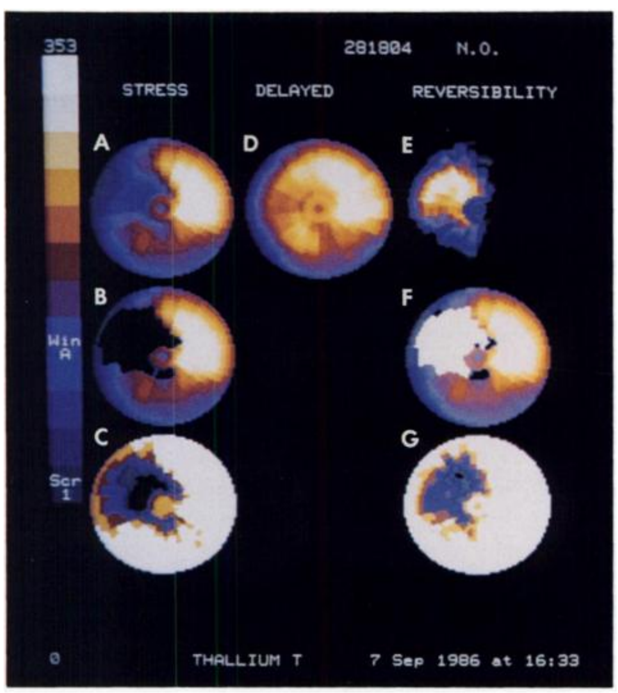

FIGURE 1
Example of a patient with an anteroseptal stress perfusion defect which completely reverses by four hours. See text for explanation of display. Refer to Table 1, defect number 27.

Normal Files

In order to evaluate this technique and develop criteria for significant reversibility, in a quantitative fashion, the male normal file patients were processed using this new computer algorithm. Mean values and s.d.s of reversibility for each point of the 15 × 40 array were generated to define normal limits of reversibility. The normal file consisted of 20 men (mean age of 41 yr) considered to have <5% likelihood of coronary artery disease by Bayesian analysis of age, sex, symptoms, and risk factors (*4*). They all had normal resting electrocardiograms, and did not have chest pain or EKG changes on electrocardiographic stress test while achieving >85% of their age predicted maximal heart rate. The same procedure was followed to generate a female normal file consisting of 16 women.

Pilot Group

A pilot population consisting of 42 male patient studies was then processed. This test population was selected to be fairly representative of the range of studies seen in routine clinical practice. These included studies with fixed and/or reversible defects, large, small, or multiple defects. Using the newly developed algorithm, reversibility bull's-eyes were created for each study. In addition, a comparison against normal files of reversibility were performed to measure the reversibility against a normal standard.

Expert Review of Pilot Group

In order to develop criteria for significant reversibility, five physicians experienced in the interpretation of SPECT thallium myocardial perfusion studies were asked to review the standard stress and delay bull's-eyes for each of the patients in the pilot population. These bull's-eyes included comparisons with normal files but did *not* include the reversibility bull's-eyes. The studies were reviewed independently with each reviewer asked to identify all stress abnormalities and then grade the improvement in the delayed study using the following scoring; 0 for fixed, 1 for minimal reversal, 2 for nearly complete reversal, and 3 for complete reversal. Abnormality and reversal was determined by the agreement of the majority of reviewers. Areas graded as 0 or 1 were considered relatively fixed and defects scored 2 or 3 were considered relatively reversible. This consensus opinion using routine review of studies would serve as our standard in order to further develop and refine the rules for the interpretation of the reversibility bull's-eyes in patients.

Display of Results

In addition to the new reversibility polar plot, two other reversibility plots are generated, a "white out" map and a s.d. map. The "white out" bull's-eye (Fig. 1F) duplicates the results of the stress blackout bull's-eye in which the areas which fall below stress normal limits, previously determined to be 2.5 s.d.s from the mean, are blacked out. In addition, the regions which have significantly reversed by the time of delayed imaging are whited-out as determined from the application of normal limits and criteria for reversibility developed during these investigations. The s.d. reversibility bull's-eye (Fig. 1G) indicates the number of s.d.s from the mean of normal reversibility, using a varying color scale, that any given area reverses.

A numerical report accompanies this reversibility white-out bull's-eye map which includes for each defect, the extent (number of pixels) of both the stress perfusion defect (blacked-out area) and the sub-region (white-out area) within this defect which reverses by 4 hr. A severity score is also reported as the sum of the number of s.d.s from the mean of the pixels in the stress map which have been blacked-out and those in the reversibility map which have been whited-out. These scores are determined for each defect by using a feature extraction algorithm on the blacked-out and whited-out regions as previously reported (*5*). Briefly, this feature extraction algorithm identifies contiguous blacked-out pixels which form an individual defect.

Reproducibility of Reversibility

In order to test the reproducibility of the reversibility method, studies from a subset of 14 randomly selected patients were processed from the initial, raw tomographic data by two independent research technologists. Comparisons were made between the two independently processed reversibility bull's-eyes to see if there was reproducibility of the presence and extent of reversibility.

RESULTS

Upon review of the reversibility bull's-eyes generated from the normal files, it was observed that only one of the twenty normal patients showed areas of reversibility >1.5 s.d.s associated with a stress blackout region on their reversibility plots. An additional four patients had areas of reversibility >1.5 s.d.s that were not associated with a blackout stress perfusion defect, with three of them showing areas of reversibility confined to the apex or base. Thus, it was empirically determined that significant reversibility criterion should only be applied to a region that exhibits a stress perfusion defect and is not located at the extreme base or apex. Because the reversibility data looks at an improvement or increase in the relative counts, the data is described as a mean *plus* 1.5 s.d.s rather than mean *minus* 1.5 s.d.s.

After these initial observations, the physicians' review of the pilot coronary artery disease population was assessed. The five physicians who reviewed the studies of patients in the pilot population identified 48 stress defects. Using the consensus of the majority of the reviewers, 17 of the defects were considered to be relatively reversible and 31 of the defects were evaluated as relatively fixed. Based on these findings, criteria for evaluating the reversibility bull's-eyes were further developed and refined by empiric observation. For a blackout defect identified in a stress study to be considered reversible, it should meet the following three criteria:

1. The reversibility should be a minimum of 1.5 s.d.s greater than the mean of normal reversibility as seen on the reversibility s.d. bull's-eye.
2. The size of the area identified as reversible in the reversibility bull's-eye should be at least 15% of the area of the defect identified in the original stress bull's-eye (although some regions as small as 5% were perceived by the experts as having minimal or partial reversibility).
3. The reversible area is not located at the extreme apex or base of the bull's-eye.

Applying these criteria of significant reversibility to the 48 defects seen in the pilot group, the reversibility bull's-eye algorithm identified 28 defects as fixed and 20 as reversible. There was agreement between reversibility criteria and the experts on 25 of the 31 (81%) defects considered fixed by the experts and 14 of the 17 (82%) defects that were graded reversible.

Table 1 summarizes the findings of the experts and computer algorithm with regard to the 48 defects. From this it can be seen that even experts show variability in the interpretation of defect reversibility. Any one of the five experts disagreed with the majority decision as to whether a defect was fixed or reversed in 12 of the 48 defects. On five defects, any two of the five reviewers disagreed with the majority decision. Thus, there were 17 disagreements out of 239 total interpretations for an agreement rate of 93%.

Figure 1, discussed previously, shows an example of a study in which there was agreement by the computer and the experts that the large anteroseptal defect is reversible. Figure 2 shows an example of agreement by the majority of experts with the computer interpretation on both a reversible and a fixed defect. Figure 2A–C shows the standard series of stress bull's-eye plots, identifying significant anteroseptal and inferolateral defects. Figure 2D shows the delayed bull's-eye. Figure 2E–G shows the new reversibility bull's-eye plots. Figure 2E shows which areas have relatively reversed. Figure 2F identifies the anteroseptal defect as reversible since at least 15% of the original defect is whited out (in this

TABLE 1
Comparison Between Visual and Computer Assessment of Reversibility for Each Defect

Defect no.	Patient no.	Location	% reversed	Scores	R/F	No. disagree	Experts	Computer
1	1	AS	70	33323	RRRRR	0	R	R+
2	1	IL	0	22213	RRRFR	1	R	F−
3	2	L	3	00000	FFFFF	0	F	F+
4	3	AS	90	22222	RRRRR	0	R	R+
5	3	I	21	01102	FFFFR	1	F	R−
6	4	AS	0	00000	FFFFF	0	F	F+
7	4	IS	0	10110	FFFFF	0	F	F+
8	4	L	40	10100	FFFFF	0	F	R−
9	5	A	40	22222	RRRRR	0	R	R+
10	5	IL	0	00100	FFFFF	0	F	F+
11	6	IS	0	10100	FFFFF	0	F	F+
12	9	I	17	13212	FRRFR	2	R	R+
13	10	AS	0	00000	FFFFF	0	F	F+
14	10	I	0	00000	FFFFF	0	F	F+
15	11	S	100	23323	RRRRR	0	R	R+
16	11	IL	0	22110	RRFFF	2	F	F+
17	12	S	97	23213	RRRFR	1	R	R+
18	16	IL	0	11100	FFFFF	0	F	F+
19	17	L	0	00000	FFFFF	0	F	F+
20	18	A	33	21211	RFRFF	2	F	R−
21	18	IL	0	10101	FFFFF	0	F	F+
22	22	A	58	23323	RRRRR	0	R	R+
23	22	IL	0	21211	RFRFF	2	F	F+
24	23	I	0	00000	FFFFF	0	F	F+
25	24	AS	0	10110	FFFFF	0	F	F+
26	24	IL	0	00100	FFFFF	0	F	F+
27	25	AS	96	33323	RRRRR	0	R	R+
28	26	AL	0	00000	FFFFF	0	F	F+
29	27	A	0	00000	FFFFF	0	F	F+
30	27	I	0	11110	FFFFF	0	F	F+
31	28	IL	0	00000	FFFFF	0	F	F+
32	29	AS	41	21212	RFRFR	2	R	R+
33	29	I	0	10000	FFFFF	0	F	F+
34	31	IL	17	21101	RFFFF	1	F	R−
35	32	A	79	23323	RRRRR	0	R	R+
36	32	I	0	11211	FFRFF	1	F	F+
37	33	AS	0	22222	RRRRR	0	R	F−
38	34	AL	85	22222	RRRRR	0	R	R+
39	35	I	0	00000	FFFFF	0	F	F+
40	36	IL	0	10110	FFFFF	0	F	F+
41	37	A	44	23323	RRRRR	0	R	R+
42	38	AL	0	00000	FFFFF	0	F	F+
43	38	IL	63	10112	FFFFR	1	F	R−
44	39	AS	0	00100	FFFFF	0	F	F+
45	39	IS	90	22322	RRRRR	0	R	R+
46	40	S	18	21322	RFRRR	1	R	R+
47	41	AL	0	22322	RRRRR	0	R	F−
48	42	IL	17	1010*	FFFF*	0	F	R−
						Total rev	17	20
						Total fix	31	28
						Agree rev	14/17	
						Agree fix	25/31	

* Reviewed by only four experts.

The location column notes in which part of the bull's-eye the defect was seen (A = anterior, AL = anterolateral, L = lateral, IL = inferolateral, I = inferior, IS = inferoseptal, S = septal, and AS = anteroseptal). The % reversed column notes the extent of significant reversal relative to the number of pixels in the original stress defect. The scores column shows a five digit number with each digit indicating the score given to a defect by each individual reviewer. The R/F column shows the conversion of the numeric score to a grade of reversibility (R) or fixed (F) for each reviewer. The No. disagree column identifies the number of reviewers whose defect grade disagreed with the majority decision. The experts column gives the final grade (R or F) given to the defect by the majority of reviewers. The computer column shows the grade (R or F) and whether there was agreement (+) or disagreement (−) with the experts.

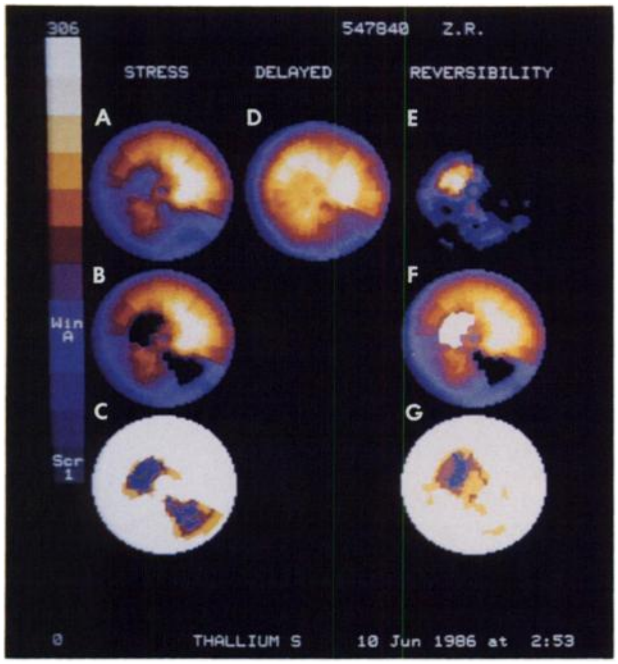

FIGURE 2
Example of a patient with an anteroseptal stress perfusion defect which completely reverses and an inferolateral defect which remains fixed at four hours. See text for explanation of display. Refer to Table 1, defect numbers 15 and 16.

case, 100%). The inferolateral defect is identified as fixed since <15% of that defect is whited out (in this case, 0%). Figure 3 shows an example of the subjectivity involved in the visual interpretation of the reversibility of stress perfusion defects. Among the five experts, there was considerable variability in assessing the reversibility of the inferolateral stress perfusion defect. As seen from Table 1, three of the experts assessed the defect to be "minimally or partially" reversible (score of 1) while another deemed the defect to be nearly completely reversible (score of 2), while the remaining expert evaluated the defect to be fixed (score of 0) with a partially reversible border zone. The majority of these scores resulted in a relatively fixed perfusion defect visual score which disagreed with the application of the quantitative reversibility criteria which suggested that there was significant reversibility. Figure 3F shows a partial (17%) white out of the original stress perfusion defect.

Table 2 shows the results of the independent processing of 14 studies by the two research technologists. In these studies, 19 defects were identified. Using the criteria for significant reversibility, there was agreement in all 19 cases, which included 12 fixed and 7 reversible defects. The agreement of the % reversibility of defects was analyzed using linear regression and correlated with an r value of 0.95 for fixed and reversible defects. For the reversible defects alone, there was a correlation of 0.80.

DISCUSSION

In this project we have developed a technique to determine the presence and magnitude of reversibility that a stress-induced thallium defect improves and the extent of improvement. This method is unique in that its algorithm emulates the logic used by expert observers, in the interpretation of SPECT thallium myocardial perfusion studies, by comparing the relative activity of the defect to the most normal area of the tomographic data and by observing how this ratio changes over time, from stress to delay. A ratio that remains relatively constant would be interpreted by the experts as "fixed" and displayed by the reversibility bull's-eye in black. If the ratio improves, the experts would interpret this as some degree of "reversibility" or ischemia. The degree of reversibility would be graded using subjective criteria such as partial, nearly complete, or complete. The reversibility bull's-eye shows regions which have relatively reversed, plotted with different colors depending on the degree of reversibility. This extent of reversibility is then measured and displayed against a normal standard and is, thus, objective. The agreement of interpretations by the computer and the experts in this test population is good, with agreement on 82% of reversible defects, and 81% of fixed defects. Of course, the

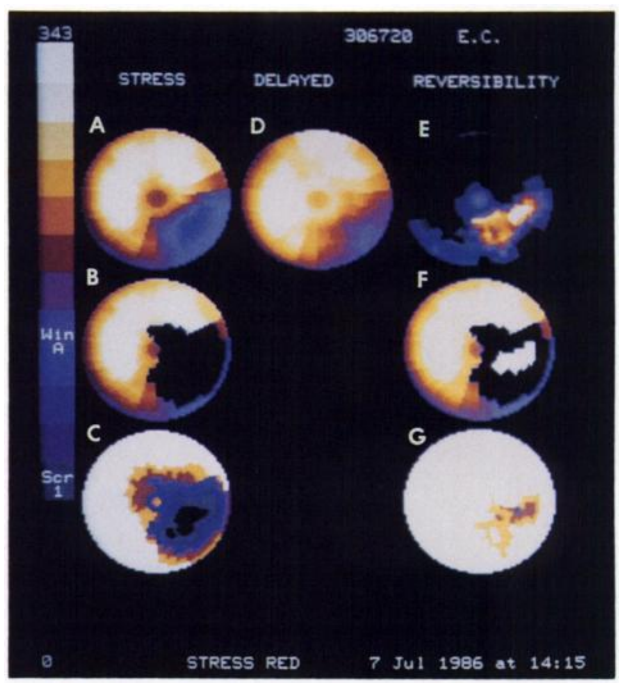

FIGURE 3
Example of a patient with an inferolateral stress perfusion defect which was visually scored by the majority of the experts as being relatively fixed. The reversibility algorithm found a 17% extent of reversibility. This serves as an example of disagreement between the experts and the computer. See text for explanation of display. Refer to Table 1, defect number 34.

TABLE 2
Reproducibility of Reversibility by Two Processors*

Defect no.	Processor A	Processor B
1	F - 0	F - 0
2	F - 0	F - 0
3	R - 99	R - 99
4	R - 22	R - 27
5	R - 51	R - 51
6	F - 0	F - 0
7	F - 0	F - 0
8	F - 0	F - 0
9	F - 0	F - 0
10	R - 82	R - 97
11	R - 83	R - 80
12	F - 0	F - 0
13	R - 90	R - 56
14	F - 0	F - 0
15	F - 0	F - 0
16	F - 0	F - 0
17	R - 88	R - 92
18	R - 19	R - 24
19	F - 0	F - 0

* Table identifies by defect number for operator A and B the grade obtained for a defect using the reversibility criteria (R = reversible; F = fixed) and % reversibility for the defect.

agreement was expected to be good, since the criteria for reversibility were developed using this same test population. Further evaluations of the algorithm on other prospective populations need to be done to test the applicability of the program.

Many quantitative techniques have been developed and proven to be helpful in the interpretation of planar thallium studies (*6,7,8,9*), but have not been tested or found to be useful in tomographic studies. Kaul et al. (*6*) developed a technique using an algorithm somewhat similar to ours. However, their approach was applied only to planar studies. In order to define a normal amount of reversibility, they did compare their findings against normal files. A defect was considered to redistribute if a normalized segment's change in relative counts exceeded a certain threshold established from the normal files. However, they did not further quantify the degree of reversibility in terms of s.d.s from the normal amount of reversibility as is done in our algorithm. Others have developed and used quantitative techniques with myocardial perfusion SPECT imaging, but to date, none have quantified and displayed reversibility of perfusion defects. DePasquale and Garcia (*1,3*) reported on the quantitative bull's-eye technique. This method was used only to identify the presence and location of defects and did not address the reversibility of defects.

Besides identifying reversible defects, our new technique may also provide additional quality control in the processing of SPECT studies. A reversibility bull's-eye demonstrating reversible areas at the very base or apex should arouse suspicion that dissimilar apical or basal short-axis slices were chosen during reconstruction for the stress and delayed bull's-eye processing. Although the criteria for abnormality was developed from a group of male patients, we have observed similarity between the male and female normal files indicating that the same criteria could be used in assessing reversibility from a female patient's study. Nevertheless, this is yet to be established.

The reproducibility of the presence and extent of reversibility proved to be excellent when processing was performed by our two independent research technologists. It should be noted, however, that both technologists have had considerable experience in processing tomographic thallium studies and consistently make appropriate decisions in the choice of axes and slice selection in bull's-eye processing. Whether less experienced technologists would demonstrate this extreme degree of consistency is uncertain, but with appropriate training similar results should be expected.

CONCLUSIONS

In summary, we have developed a computer method which can define and quantitate regions of reversibility in SPECT thallium studies. The reversibility plot may also identify improperly processed studies and therefore be useful in quality control. The technique agrees well with expert observers and will hopefully decrease interobserver variability in the interpretation of SPECT thallium studies. Further prospective evaluation of the technique is needed in a larger patient population to see if the criteria developed in our pilot group not only agrees with expert interpretation of defect reversibility, but also if it may help to truly differentiate ischemia from infarcted regions of myocardium.

ACKNOWLEDGMENTS

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