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Right Anterior Oblique First-Pass Radionuclide Ejection Fractions: Effects of Temporal Smoothing and Various Background Corrections

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Thirty-seven patients undergoing contrast left ventriculography were studied by first-pass radionuclide angiography (FPRA) in the right anterior oblique view. Ejection fraction (LVEF) was calculated from FPRA using (a) a spatially and temporally varying background correction (BGC) based on a matrix of activity in lung and left atrium and (b) BGC with temporal fluctuation but with no allowance for spatial variations. The two methods were performed on both raw and temporally smoothed data.

All four LVEFs correlated well with contrast LVEF (r = 0.90–0.94). Absolute values differed significantly from contrast values except for the method using the spatially and temporally varying BGC on smoothed data, which provided the closest overall agreement at all levels of LVEF, despite occasional large individual variations. The same method on raw data overestimated low LVEFs, and the method applying only temporal fluctuation in background underestimated high LVEFs. Allowance for spatial and temporal variations in background is therefore important when first-pass radionuclide angiography is performed in the RAO view.

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Left-ventricular ejection fraction is one of the most useful indices of left-ventricular function, and as a single measurement it is considered more useful for prognosis than cardiac output or left-ventricular end-diastolic pressure (*1*). Radionuclide ventriculography has come to occupy a major clinical role in the noninvasive assessment of ejection fraction, following the discovery that the left-ventricular change in radioactive counts with time could be exploited to provide a geometry-independent ratio of stroke volume to end-diastolic volume (*2*). A prerequisite for the determination of ejection fraction by radionuclide techniques is the accurate assessment of background, nonventricular counts. Methods used for background correction have varied. Most workers with the first-pass technique have used modifications of the method of Van Dyke et al. (*3*), involving an anatomically selected background zone surrounding the left-ventricular region of interest, and good correlations between contrast and radionuclide ejection fraction have been obtained (*4*,*5*). The potential of using the right anterior oblique (RAO) projection, a major advantage of the first-pass technique, imposes additional demands on the background correction used. The spatial overlap of right and left ventricles must be considered, even though the first-pass method theoretically separates the chambers in time. To overcome this, some workers have used pulmonary artery injections of radionuclide to avoid the right heart (*6*), and others have applied background corrections on a trial-and-error basis in search of the closest agreement with ejection fraction measured in the left-anterior oblique in the same patients (*7*). In addition to differences in the approach to background, the influence of other variables in data processing, such as temporal smoothing to reduce statistical errors, has not been clearly defined.

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TABLE 1. CLASSIFICATION OF PATIENTS STUDIED

Reason for study	Number	Range of LVEF from contrast angiogram (%)
Chest pain	15	40–84
Recurrent angina following documented myocardial infarction	5	29–43
LVF or CCF	10	12–33
Aortic stenosis	4	71–83
IHSS	2	80–84
Recurrent VT	1	28

Abbreviations: LVF = left-ventricular failure; CCF = congestive cardiac failure; IHSS = idiopathic hypertrophic subaortic stenosis; VT = ventricular tachycardia.

The purpose of this study was to examine the effects (a) of different background-correction techniques and (b) of temporal smoothing of dynamic data, on the accuracy of left-ventricular ejection fractions calculated from first-pass radionuclide angiograms performed in the RAO view.

PATIENTS AND METHODS

A total of 37 patients undergoing routine diagnostic cardiac catheterization and left-ventricular cineangiography were studied. There were 32 males and five females, whose ages ranged from 42 to 66 yr (mean 52 yr). The classification of the patients according to diagnosis is shown in Table 1. All patients were in sinus rhythm, and all underwent radionuclide ventriculography within 24 hr of cardiac catheterization. Informed consent was obtained from each patient.

CONTRAST ANGIOGRAPHY

Contrast left ventriculography was performed in the 30° right anterior oblique (RAO) projection. Fully opacified beats that neither were ventricular extrasystoles nor immediately followed one were visually identified. End-diastolic and end-systolic frames were selected and the ventricular silhouettes were traced. Volumes were calculated using the area-length formula modified for the RAO projection (*8*).

RADIONUCLIDE VENTRICULOGRAPHY

This was performed using a computerized multicrystal scintillation camera* and a 1½-in.-thick parallel-hole collimator. Patients were given 400 mg of potassium perchlorate orally. An 18-gauge indwelling cannula was placed in an antecubital vein, and the detector was positioned in 30° RAO with the patient supine. A 15-mCi bolus of technetium-99m as high specific-activity pertechnetate was injected intravenously with a rapid 20-ml saline flush. Counts were recorded at 20 frames per second for 50 sec during the first pass of the radionuclide through the central circulation. Data were acquired in the 14 × 21 matrix format of the multicrystal detector, and recorded on computer disk. All data were corrected for flood field nonuniformity and for the deadtime of the instrument, and stored on magnetic tape. The 14 × 21 format was maintained for all ejection-fraction calculations.

ANALYSIS OF RADIONUCLIDE DATA

The corrected data were first replayed as a series of twelve frames, each being the sum of 30 individual 50-msec frames. This series of images showed the position of the bolus at 1.5-sec intervals and enabled the left-ventricular phase to be identified (*9*). A left-ventricular region of interest was selected and a high-frequency (100 frames per 5 sec) time-activity curve was generated displaying the counts per frame registered by the chosen crystals. From the time-activity curves, ejection fraction was calculated using two methods of background correction, each method in addition being tested on raw data and temporally smoothed data. This latter comparison was made to assess the net effect, on estimates of ejection fraction, of improving statistics with a concomitant decrease in temporal resolution, both of which are affected by smoothing. Each frame of the study was thus smoothed with its nearest neighbor in time so that Frame 2 of the temporally smoothed study would be

$$\frac{(\text{Frame 1}) + (2 \times \text{Frame 2}) + (\text{Frame 3})}{4}.$$

BACKGROUND CORRECTIONS

Method A. Here, background frames were chosen directly from the raw left-ventricular time-activity curve, and background corrections were performed with the manufacturer's software. The background frames were those on the flat portion of the curve, immediately before the phasic fluctuations of the levophase. At this point, the bolus of radionuclide is distributed in the lungs and left atrium, but not yet in the left ventricle. The frames corresponding to the peaks and troughs of the individual cardiac cycles in the levophase were then identified, fed into the computer, and summed there to produce a representative cardiac cycle with good statistics (*9,10*). Only cycles with obvious phasic fluctuations were selected, and usually there were between three and eight per study. If seven cardiac cycles were used, seven individual background frames from the prelevophase plateau of the curve were summed by computer. The final background

frame thus consisted of the sum of the same number of individual background frames as cardiac cycles used. The rationale for this was twofold. First, it automatically normalized the sampling time for background to the end-diastolic sampling time, so the summed background frame was weighted according to the number of end-diastoles involved in the first pass. Second, it achieved a compromise between a long background sampling time for statistical advantage, yet maintained the background acquisition temporally within the lung phase. This two-dimensional matrix of summed background frames represented the spatial distribution of the tracer when the bolus was in left lung and left atrium but not yet in the left ventricle, and hence defined the spatial distribution of background.

Such a distribution is not uniform but varies with individual anatomy. The background at the base of the left ventricle is higher than that at the apex. The spatial inhomogeneity is exaggerated in the RAO, where the hilum of the left lung lies directly behind the base of the left ventricle, so observed counts from this region have a higher background contribution than those from the distal portions of the left ventricle. To illustrate this point, Fig. 1 shows the end-diastolic outline of the left ventricle superimposed on the summed background frame.

Once the spatial distribution of background was defined, a correction was applied to the summed background frame to ensure that the counts in the extraventricular region of that frame were equal to those in the same extraventricular region during the levophase. The computer determined the total counts in this region for the summed lung-background frame just before the beginning of the levophase, and for the same region in the summed end-diastolic frame during the levophase. This gave the total remaining counts within a 6 × 9 in. region of interest, once the pixels of the left ventricle and aorta at end-diastole had been subtracted from each frame. The ratio of the total counts in the extraventricular region of the summed end-diastolic frame to the total counts in the same region just before the levophase was defined as the lung washout factor. This adjustment takes into account the decrease in counts in the background structures that occurs between the lung phase and the levophase of a first-pass study. The final background matrix was thus the initial lung background frame multiplied by the washout factor, and this matrix was then subtracted from the summed cardiac cycles. This technique thus permitted background to vary both spatially and temporally.

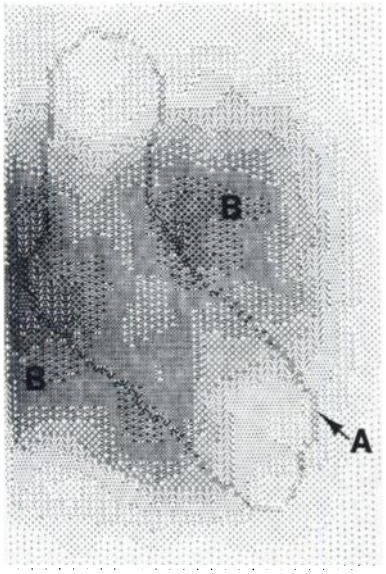

FIG. 1. Composite RAO image of summed lung background (B) with left-ventricular end-diastolic silhouette (A) superimposed. Spatial variations in counts outside left ventricle are evident, with higher background at base than at apex.

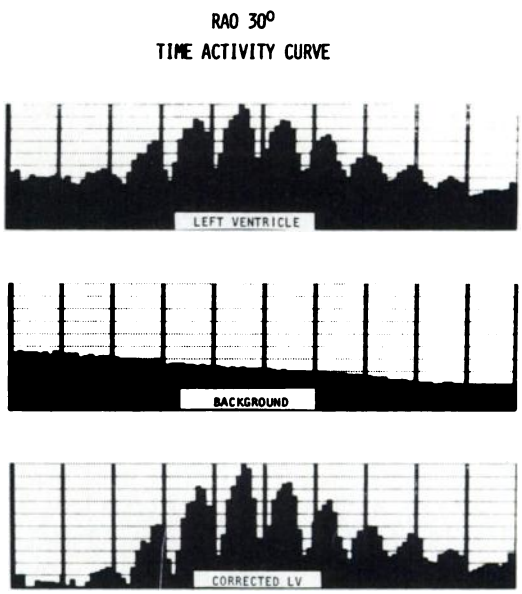

FIG. 2. Time-activity curves. Top: left ventricle, uncorrected. Middle: uncontaminated background curve, normalized (see text). Bottom: left-ventricular curve with background subtracted.

Method B. Method B used the same method on temporally smoothed data.

Method C. As with Method A, a time-activity curve was generated from a left-ventricular region of interest. The end-diastolic frames were identified from the peaks of the curve, and were summed. Similarly, the background frames before the levophase were summed as in Method A. However, instead of proceeding with the computer program described above, the operator isolated the extraventricular region by deleting the pixels in the left ventricle and aorta from the summed background frame. This was done by creating a mask (defined as a matrix of ones) of the left ventricle and aorta at end-diastole and using this mask to zero the pixels of the left ventricle and aorta. A second region of interest was then entered in the extraventricular region of the uncontaminated background frame. New time-activity curves

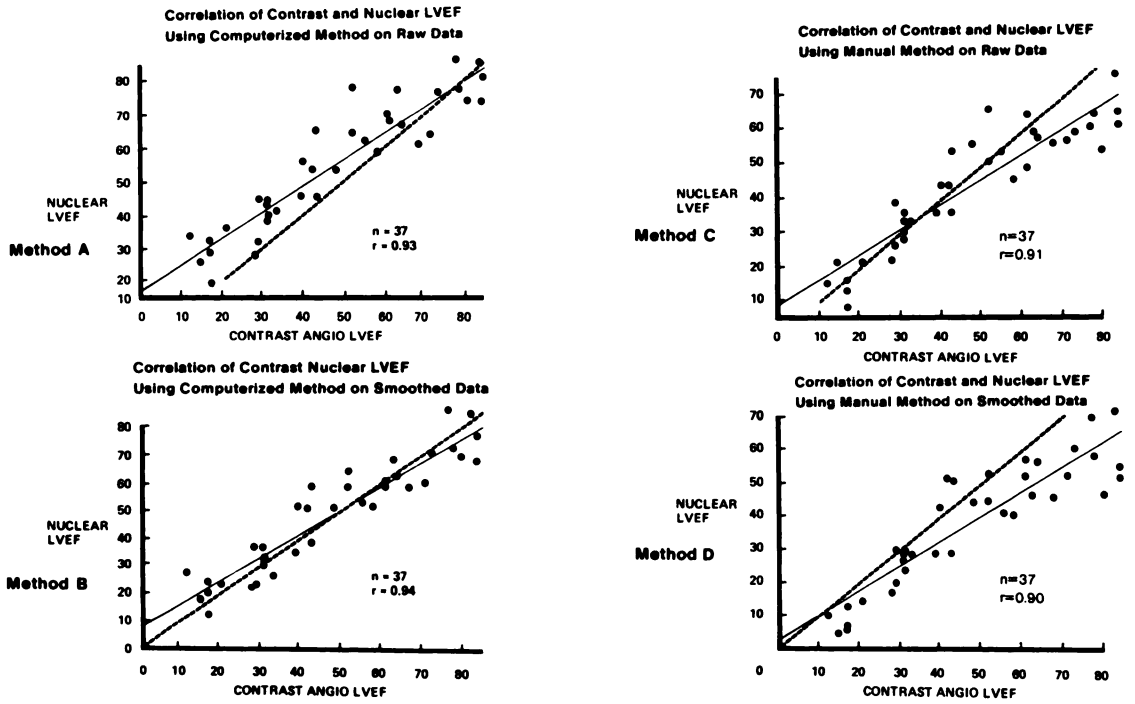

FIG. 3. (a–d): Correlations between contrast and radionuclide angiographic ejection fraction for each method A–D. In each case solid line represents slope of regression and broken line is line of identity. LVEF = left-ventricular ejection fraction.

from the two zones were generated, representing left ventricle and background (Fig. 2). To correct for the difference in absolute counts from the two regions, each point in the background curve was divided by a constant (always greater than unity in these studies) so that the lowest counts in the immediate prelevophase portion of the left-ventricular curve equalled the counts in the same frame of the background curve. The latter was then subtracted point by point from the ventricular curve to produce a background-corrected ventricular curve, with no counts in the low-point frame. Ejection fraction was then computed as

$$\frac{\text{End-diastolic counts} - \text{End-systolic counts}}{\text{End-diastolic counts}}.$$

Method D. Method D used the same steps on temporally smoothed data.

STATISTICAL ANALYSIS

Correlations were assessed by standard linear regression, and differences between techniques were assessed by analysis of variance for a repeated-measures design and the paired *t* test. Results are expressed as mean ± standard deviation.

RESULTS

Mean left-ventricular ejection fraction from contrast angiographic silhouettes was 47.6 ± 22.3%, with a range from 12% to 84%. Figures 3a–3d show the correlations between contrast and radionuclide ejection fractions for each data-processing technique A–D. Correlation coefficients were r = 0.93 for Method A, 0.94 for B, 0.91 for C, and 0.90 for D. Regression equations and standard

TABLE 2. COMPARISON OF CONTRAST AND RADIONUCLIDE LVEF FOR ALL METHODS FOR ENTIRE PATIENT GROUP (n = 37)

	Contrast angiographic LVEF	Method A	Method B	Method C	Method D
Mean	47.6%	55.5%	48.1%	42.9%	38.6%
Standard deviation	22.3%	19.4%	20.3%	17.5%	18.7%
Mean difference between contrast and nuclear LVEF		7.9% ± 8.2%	0.5% ± 7.3%	−4.7% ± 9.4%	−8.8% ± 9.4%
P value of difference		<0.001	ns	<0.001	<0.001

errors of the estimate (s.e.e.) were:

$y = 0.81x + 16.9$, s.e.e. 7.2% for Method A;

$y = 0.86x + 7.1$, s.e.e. 6.8% for Method B;

$y = 0.72x + 8.7$, s.e.e. 7.1% for Method C;

$y = 0.76x + 2.3$, s.e.e. 7.9% for Method D.

Despite the high correlation coefficients, a close inspection of the data showed significant differences between the contrast and radionuclide data, depending upon the method used. As shown in Table 2, there were significant differences between the mean ejection fraction from contrast and radionuclide studies for all except Method B. Figures 4a–4d show the contrast angiographic ejection fraction on each abscissa plotted against the difference between contrast and radionuclide values on each ordinate. Data below the horizontal dotted line indicate an overestimate of ejection fraction by the radionuclide methods, and data above an underestimate, all compared with contrast angiography. Method A overestimated ejection fractions in 31/37 patients ($p < 0.001$), and the degree of overestimate was greater at lower levels of ejection fraction. Method B did not significantly miscalculate ejection fraction for the entire group of patients, although Fig. 4b shows that there was not perfect agreement between the two techniques, with the scatter being evenly spread around the vertical line. Method C produced good agreement at the lower ejection fractions, but markedly underestimated the higher ones. For the group as a whole, the differences between contrast and radionuclide values were significant ($p < 0.001$). Method D produced an underestimate of ejection fraction in 32/37 patients ($p < 0.001$), again with the most severe underestimation occurring in patients with higher ejection fractions.

This apparent influence of biological variability in the patient group on the closeness of agreement of ejection fraction was further tested by subdividing the patients into two groups, those with contrast ejection fractions of 50% or more (n = 17) and those with less than 50% (n = 20). The results are shown in Table 3 as the mean difference between contrast and radionuclide data for each group. Method A significantly overestimated lower ejection fractions ($p < 0.001$), but not those greater than 50%. Method B produced no statistically significant

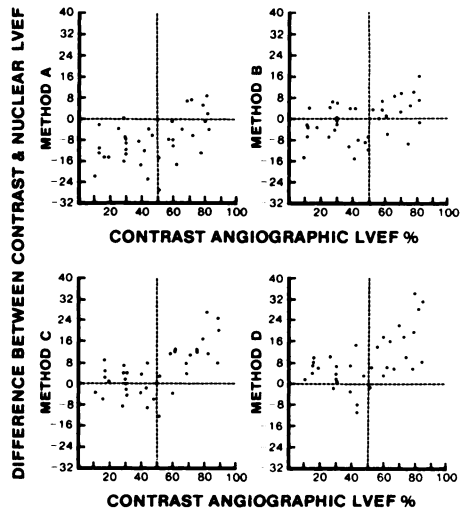

FIG. 4. (a–d): Individual differences between contrast and radionuclide ejection fractions plotted against absolute values of contrast ejection fraction, for each method A–D. Dotted horizontal line represents complete agreement between the two; vertical dotted line represents contrast ejection fraction of 50%. LVEF = left-ventricular ejection fraction.

disagreement at higher or lower levels. Method C produced excellent agreement at low levels, but significantly underestimated ($p < 0.001$) at high levels. Method D consistently underestimated ejection fractions at all levels, although the underestimation of the lower values was of marginal statistical significance.

DISCUSSION

These results suggest that significant, consistent errors occur in the calculation of ejection fraction from RAO radionuclide angiograms, depending upon the background correction applied or the use of temporal smoothing. Significant differences may thus exist between contrast and radionuclide ejection fractions despite the fact that correlations between the two techniques may be similar.

The background correction based on the spatial distribution of radionuclide before the levophase and the use of a lung washout factor have been shown previously to produce good correlations with contrast angiography in the anterior and left anterior oblique projections (*7,10*). Our method makes the major assumption that

TABLE 3. MEAN DIFFERENCE BETWEEN CONTRAST AND RADIONUCLIDE LVEF

	Contrast LVEF < 50%		Contrast LVEF ≥ 50%	
Method A	10.7 ± 6.3%	$p < 0.001$	4.7 ± 9.2%	p.ns
Method B	2.7 ± 6.8%	p.ns	−2.2 ± 7.5%	p.ns
Method C	0.3 ± 5.3%	p.ns	−10.5 ± 9.9%	$p < 0.001$
Method D	−4.3 ± 6.3%	$p < 0.01$	−14.3 ± 9.6%	$p < 0.001$

the spatial fluctuations in left-ventricular background counts can be represented accurately by the pulmonary-phase distribution of background before the levophase. This in turn requires that the shape of the background curve must be temporally consistent during the pulmonary phase and during the levophase. Whereas this has been shown to be a reasonable assumption for the anterior projection (*10*, and personal communication with D.W. Heyda), it could possibly be violated in the RAO, owing to additional right-heart background components caused by lag of the bolus in the right ventricle. A second assumption that has been suggested is that the background remains relatively constant during the levophase compared with the large phasic fluctuations in counts between diastole and systole (*10*). Although this assumption is probably correct (*3*), any such changes occurring in background are also considered by our technique, since the background contribution to the observed counts in each individual peak on the time-activity curve is summed into the representative end-diastolic image, and the total background in this image is used for calculation of the lung washout factor.

The overestimate of ejection fraction by Method A could possibly be caused by oversubtraction of background by including right-ventricular counts in the background matrix, as mentioned above. Another possible cause for the overestimate is the effect of Poisson noise on the calculations. Twieg et al. (*11*) have shown that the error introduced by such noise leads to an overestimate of ejection fractions calculated from time-activity curves. In addition, it has been shown that statistical errors due to noise are more likely to occur at lower levels of ejection fraction (*12*). The results from Method A did produce significant overestimates of lower but not higher ejection fractions, and suggest that noise is an important factor, even with the count rates obtained with a multicrystal gamma camera. The finding that Method B, the same technique applied to statistically smoothed data, produced no consistent errors in ejection fraction at high or low levels, is further evidence that the errors in Method A were related to noise. The smoothing technique lowered the mean radionuclide ejection fraction by 7.4% overall, which is similar to the reduction caused by the five-point temporal smoothing applied by Ashburn et al (*13*). The fact that temporal smoothing reduced the overestimates of the lower ejection fractions in Method A, while not significantly altering the accuracy of the higher values (Table 3) is further support for the concept of noise being a major factor in errors at low ejection fractions. Despite the occasionally large differences between contrast and radionuclide values, the good overall agreement in ejection fractions obtained by Method B suggests that the assumptions pertinent to that method are not significantly violated in the RAO view.

Method C underestimated the values of the group as a whole, although it provided excellent agreement at lower ejection fractions. Folland et al. (*5*), using a similar technique for background-curve subtraction in first-pass studies, found a consistent underestimation of ejection fractions compared with contrast angiograms, the closest fit occurring at lower ejection fractions, as in our present data. The major assumption made in the curve-subtraction approach is that the background contribution to left-ventricular counts may be accurately represented by the global average of the counts outside the left ventricle. Although background fluctuates temporally, this method does not take spatial variations in background into account. Thus undersubtraction of background may occur. As discussed earlier, spatial variations in background may be particularly important in the RAO projection, where the background behind the base of the left ventricle is higher than at the apex. The more significant underestimation of high ejection fractions than low ones by this technique is consistent with the previous observation that errors due to background have their major impact at normal or high ejection fractions, not at low ones (*12*).

The temporal smoothing in Method D led to underestimates of ejection fraction at all levels, although again the mean error in the low group was smaller than in patients with high ejection fractions.

Our findings indicate that spatial fluctuations in background must be considered as well as the temporal variations that occur from the beginning to the end of the levophase, if accurate values for ejection fraction are to be obtained from first-pass radionuclide angiograms carried out in the RAO view. In addition, there may be nonanatomical contributions to background counts, primarily due to Compton scatter, that could also introduce inaccuracy into the results. Certainly the slopes of the regression equations for all four methods of data processing were less than unity (mean 0.79 ± 0.06) and a missing background component would be one possible explanation for this. However, it is also possible that errors in the contrast ejection fraction may have contributed. Apart from the possible errors inherent in tracing the angiographic silhouettes, the use of single-plane RAO angiograms alone may have overestimated ejection fraction compared with biplane values. This is particularly likely to occur in patients with normal ventricular function (*14*), and this may have contributed to the apparent underestimation of ejection fraction by the radionuclide techniques. In addition, the radionuclide and contrast studies were not performed together, although within 24 hr of each other, so spontaneous variations in ventricular function could also have contributed to differences.

Although this study was conducted using a multicrystal gamma camera, the principles should be equally applicable to single-crystal instruments, especially since the use of such instruments for first-pass studies is likely

to increase as count-rate capabilities increase. In clinical practice, the presence of errors due to variations in data processing may mean only that lower limits of normal should be established for each laboratory and adjusted appropriately. However, it is possible that errors having a significant impact only at one range of ejection-fraction values could cause artifactual results in patients undergoing resting and postintervention studies. Thus, rest-to-exercise response could be falsely blunted or exaggerated, for example, and further studies are being conducted to investigate this possibility.

The identification and elimination of sources of such errors should improve the accuracy of radionuclide angiography, and enhance the acceptability of the technique in the medical community.

FOOTNOTE

* Baird Corporation, System 77.

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REFERENCES

1. COHN PF, GORLIN R, COHN LH, et al: Left ventricular ejection fraction as a prognostic guide in surgical treatment of coronary and valvular heart disease. *Am J Cardiol* 34: 136-141, 1974
2. PARKER JA, SECKER-WALKER RH, HILL R, et al: A new technique for the calculation of left ventricular ejection fraction. *J Nucl Med* 13:649-651, 1972
3. VAN DYKE D, ANGER HO, SULLIVAN RW, et al: Cardiac evaluation from radioisotope dynamics. *J Nucl Med* 13: 585-592, 1972
4. SCHELBERT HR, VERBA JW, JOHNSON AD, et al: Non-traumatic determination of left ventricular ejection fraction by radionuclide angiocardiography. *Circulation* 51:902-909, 1975
5. FOLLAND ED, HAMILTON GW, LARSON SM, et al: The radionuclide ejection fraction: a comparison of three radionuclide techniques with contrast angiography. *J Nucl Med* 18:1159-1166, 1977
6. JENGO JA, MENA I, BLAUFUSS A, et al: Evaluation of left ventricular function (ejection fraction and segmental wall motion) by single pass radioisotope angiography. *Circulation* 57:326-332, 1978
7. BODENHEIMER MM, BANKA VS, FOOSHEE CM, et al: Quantitative radionuclide angiography in the right anterior oblique view: comparison with contrast ventriculography. *Am J Cardiol* 41:718-725, 1978
8. KENNEDY JW, TRENHOLME SE, KASSER IS. Left ventricular volume and mass from single plane cineangiocardiogram. A comparison of anteroposterior and right anterior oblique methods. *Am Heart J* 80:343-352, 1970
9. DYMOND DS, JARRITT PH, BRITTON KE, et al: Detection of post infarction left ventricular aneurysms by first pass radionuclide ventriculography using a multicrystal gamma camera. *Br Heart J* 41:68-78, 1979
10. MARSHALL RC, BERGER HJ, COSTIN JC, et al: Assessment of cardiac performance with quantitative radionuclide angiocardiography. Sequential left ventricular ejection fraction, normalized left ventricular ejection rate, and regional wall motion. *Circulation* 56:820-829, 1977
11. TWIEG DB, STOKELY EM, PARKEY RW, et al: Effects of noise on the determination of ejection fraction from left ventricular time-activity curves. *J Nucl Med* 18:180-182, 1977
12. WILLIAMS DL, HAMILTON GW: The effect of errors in determining left ventricular ejection fraction from radionuclide counting data. In *Nuclear Cardiology: Selected Computer Aspects.* Sorenson JA, Ed. New York, Society of Nuclear Medicine, 1978, pp 107-117
13. ASHBURN WL, SCHELBERT HR, VERBA JW. Left ventricular ejection fraction—A review of several radionuclide angiographic approaches using the scintillation camera. *Prog Cardiovasc Dis* 20:267-284, 1978
14. COHN PF, GORLIN R, ADAMS DF, et al: Comparison of biplane and single plane left ventriculograms in patients with coronary artery disease. *Am J Cardiol* 33:1-6, 1974