

Estimates of Left-Ventricular Volumes by Equilibrium Radionuclide Angiography: Importance of Attenuation Correction

Mark R. Starling, Louis J. Dell'Italia, Martin L. Nusynowitz, Richard A. Walsh, William C. Little,
and Anthony R. Benedetto

The University of Texas Health Science Center, San Antonio, Texas

To compare the accuracy of attenuated and attenuation-corrected equilibrium radionuclide angiographic (RNA) left ventricular (LV) volume estimates, we studied 23 consecutive patients with biplane contrast cineangiography (CINE). Attenuated RNA end-diastolic (ED) and end-systolic (ES) volumes were calculated from background-corrected ED and ES counts obtained from hand-drawn regions of interest that were normalized to cardiac cycles processed, frame rate, and blood activity. A simple, geometric attenuation correction was performed to obtain attenuation-corrected RNA LV volumes. The attenuated and attenuation-corrected RNA LV EDV estimates correlated with the CINE LV EDVs; however, the attenuation-corrected RNA LV EDV estimates correlated more closely. Also, the average attenuation-corrected RNA LV EDV did not differ significantly from the mean CINE LV EDV. Attenuated and attenuation-corrected RNA LV ESV estimates also correlated with the CINE LV ESVs, but the attenuation-corrected RNA LV ESV estimates correlated more closely. Also, the average attenuation-corrected RNA LV ESV did not differ significantly from the mean biplane CINE LV ESV.

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Several methods of estimating cineangiographic left-ventricular (LV) volumes by equilibrium radionuclide angiography (RNA) have been reported (1-8). Massie and co-workers have shown a method based on RNA count to be more accurate than geometric methods of estimating LV volumes (7). Early RNA methods of estimating LV volumes did not apply an attenuation correction (5-7). However, there are theoretic advantages to correcting for attenuation, since attenuated RNA LV volume calculations depend strongly on correction by regression equation to obtain LV volume estimates (8). Such corrections may not be accurate in individual patients, since each patient may attenuate differently depending upon the distance from the LV to the gamma detector. However, this systematic study compares in the same patients uncorrected and attenu-

ation-corrected RNA estimates with biplane cineangiographic LV volumes to determine whether the correction is worthwhile.

METHODS

Patient population. This consisted of 23 consecutive patients, nine men and 14 women with age range 38-68 yr (mean 50), who gave written informed consent for biplane LV cineangiography, coronary arteriography, and an equilibrium RNA study within 24 hr. The underlying cardiac disease was coronary artery disease in ten patients, aortic stenosis in one, mitral regurgitation in three, aortic regurgitation in one, congestive cardiomyopathy in three, hypertrophic obstructive cardiomyopathy in one, tetralogy of Fallot with cardiomyopathy in one, and atypical chest-pain syndrome with normal coronary arteries in three patients. Abnormal segmental wall motion was present in eight of the ten

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For reprints contact: Mark R. Starling, MD, The University of Texas Health Science Ctr., Dept. of Medicine, Division of Cardiology, 7703 Floyd Curl Dr., San Antonio, TX 78284.

with coronary artery disease. There was no change in clinical status or medical therapy during the 24 hr between the two studies.

Cineangiography. Left-heart catheterization was performed using brachial- or femoral-artery approaches. Simultaneous biplane LV cineangiograms were obtained in the 30° RAO projection and 60° LAO with 20° caudal tilt, using CGR biplane cineangiographic equipment after 500-PSI injection of 40–60 cc of Renografin-76 at 10–15 cc/sec. In addition, correction factors from each image intensifier to the LV geometric center of mass were recorded for correction of magnification and pincushion distortion. The LV end-diastolic images in both projections were outlined at the peak of the R wave, determined from the simultaneously recorded electrocardiogram, and the LV end-systolic images in both projections were traced at maximal inward motion of the LV. The left-ventricular long axis was measured from the plane of the aortic valve to the LV apex in both projections. LV end-diastolic and end-systolic volumes were calculated using a modified biplane formula (9).

Equilibrium radionuclide angiography. Following the i.v. administration of 20 mCi technetium-99m-labeled human serum albumin (HSA), the distance from the LV to the scintillation detector in the LAO position was obtained for attenuation correction, using a simplification of the geometric method validated by Links and co-workers (8). Briefly, with the camera in the 45° LAO position, a capped 3-cc syringe with residual Tc-99m HSA in the tip was placed over the LV such that the source was equidistant from the LV borders, and a mark was placed on the anterior chest wall. The camera was repositioned in the anterior projection, and the point source was placed over the LV midway between the left margin of the pulmonary artery and the LV apex, equidistant from the anterior and inferior LV borders, and a mark was placed on the anterior chest wall. The horizontal distance (d) between the two marks was then measured. Each value for d is the average of three measurements made by each of two investigators. The maximum difference between these individual marks was 4 mm. The distance (d') to the LV from the detector in the LAO position was calculated as:

$$d' = \frac{d}{\sin 45^\circ} .$$

Gated equilibrium radionuclide cardiac images were then acquired in the anterior projection and the 45° LAO with 10° caudal tilt, using a 37-photomultiplier single-crystal gamma camera (25 cm FOV) equipped with a low-energy, all-purpose, parallel-hole collimator. Consecutive 30-msec frames, gated by R wave, were acquired in 64 × 64 byte mode and stored in the computer's remote memory until counts from 1,000 R-R intervals had been acquired. Midway through the LAO

image acquisition, a 2-ml blood sample was drawn and the time recorded. After the image acquisition, the 2-ml blood sample was counted for 2 min on the collimator and the time recorded.

Left-ventricular ED and ES counts were obtained from the 45° LAO image using a hand-drawn region of interest (ROI). Briefly, the ED frame, as determined from the semiautomated variable time-activity curve, was displayed. Background was obtained manually from a LV ED paraventricular ROI two pixels wide, placed inferior and lateral to the LV and two to three pixels away from the LV border.

The net ED image received a nine-point smoothing, and the operator then outlined manually a LV ED ROI that totally encompassed the LV but included no adjacent structures. The LV ES image was processed similarly. From these hand-drawn ROIs, the LV ED and ES counts were obtained. Finally, the static image of the blood sample was displayed, the operator placed a 10-by 15-pixel ROI around it, and the blood count was obtained. No background subtraction was considered necessary.

Left-ventricular ED and ES volumes were calculated as:

$$\frac{\text{background-corrected LV counts}}{\text{blood sample counts}} \times A;$$

where the numerator is the net LV ED or ES count, normalized in the following manner:

$$\frac{\text{net LV counts} \times 60 \text{ sec/min}}{1,000 \text{ beats} \times 0.03 \text{ sec/beat}}$$

(1,000 beats is the number of R-R intervals processed, 0.03 sec/beat is the frame rate during acquisition, and the 60 converts cps to cpm.) The blood-sample counts were corrected for decay, using 360 min as the half-life of Tc-99m and the time from the drawing of the blood sample until it was counted. This results in uncorrected LV ED and ES volume estimates in ml. The result can be multiplied by A to correct for photon attenuation, where A is:

$$e^{-\mu d'}$$

where $\mu = 0.15 \text{ cm}^{-1}$ represents the linear attenuation coefficient for the 140-keV photon of Tc-99m in water (8,10), and d' represents the calculated distance in cm. After multiplying by A, the result is attenuation-corrected RNA ES or ED volume in ml.

Data analysis. The uncorrected and attenuation-corrected RNA LV volume estimates were compared with the corresponding biplane cineangiographic LV volumes by least squares linear regression analysis to obtain correlation coefficients, regression equations, and standard errors of the estimate (s.e.e.). In addition, to test for the strength of these relationships, the correlation coefficients were compared by Fischer's Z-transfor-

TABLE 1. LEFT VENTRICULAR VOLUMES

Patients	CINE		Uncorrected RNA		Corrected RNA	
	EDV*	ESV†	EDV	ESV	EDV	ESV
1	256	138	90.0	55.9	249	155
2	137	36	38.7	14.7	163	62
3	131	47	26.1	10.0	151	58
4	139	85	46.2	27.1	149	87
5	77	18	28.1	10.0	105	37
6	89	20	30.3	10.3	108	37
7	149	26	33.3	11.9	126	45
8	179	76	51.9	15.5	186	56
9	234	86	56.9	24.6	228	99
10	361	310	99.5	87.1	390	341
11	251	156	58.2	39.9	221	152
12	271	145	50.9	35.7	199	140
13	200	105	40.0	25.7	176	103
14	339	168	52.5	22.8	286	124
15	87	18	21.5	6.9	110	35
16	167	99	56.8	22.8	203	82
17	217	153	36.2	23.8	181	119
18	311	231	114.9	90.0	318	249
19	281	178	48.7	33.9	283	196
20	169	127	39.8	29.0	155	116
21	522	444	90.3	83.0	551	507
22	166	81	65.2	26.6	176	72
23	268	191	59.5	44.0	226	167
Mean	217	128	54	33	215	132
±1 s.d.	±104	±101	±24	±25	±102	±110

* EDV = end-diastolic volume.
† ESV = end-systolic volume.

mation. Group mean data were expressed as the mean \pm 1 s.d. and compared by a paired t-test. A significant difference was considered present if its probability was 0.95 or more. The interobserver reproducibility for the calculated distance d' and blood-sample counts, and the intra- and interobserver reproducibility of the LV ED and ES counts were evaluated from the determinations by two independent observers.

RESULTS

Left ventricular end-diastolic volumes (Table 1 and 2). The uncorrected ED volume estimates correlated with the CINE LV EDVs ($r = 0.74$, Fig. 1). The corrected RNA absolute LV EDV estimates also correlated with the CINE LV EDVs ($r = 0.96$, Fig. 1), this correlation being considerably better ($p < 0.001$). Moreover the average corrected LV EDV of 215 ± 102 ml did not differ significantly from the mean cineangiographic LV EDV of 217 ± 104 ml.

In the nine men the attenuation-corrected LV EDV estimates showed an improved correlation compared with the uncorrected data. The findings were similar for the 14 women (Table 2). The average attenuation-cor-

rected RNA LV EDV for the men of 257 ± 69 ml did not differ significantly from the mean CINE LV EDV of 270 ± 63 ml, and the average corrected RNA LV EDV for the women of 188 ± 112 ml also did not differ significantly from the mean CINE LV EDV of 184 ± 112 ml.

Left ventricular end-systolic volumes (Table 1 and 2). The uncorrected RNA LV ES volumes (ESV) correlated with the CINE LV ESVs ($r = 0.87$, Fig. 2). The attenuation-corrected RNA LV ESV estimates also correlated with the CINE LV ESVs ($r = 0.98$, Fig. 2), with the correlation closer for the corrected estimates ($p < 0.01$). Also, the average corrected RNA LV ESV of 132 ± 110 ml did not differ significantly from the mean biplane cineangiographic LV ESV of 128 ± 101 ml.

Within the set groups, the corrected RNA LV ESVs in the nine men correlated better with the LV ESVs than the uncorrected RNA LV ESV estimates. Similar improvement in correlation was observed in the group of 14 women (Table 2). The average corrected RNA LV ESV for the men of 168 ± 71 ml did not differ significantly from the mean CINE LV ESV of 167 ± 84 ml, and the same held for the women: 102 ± 111 compared with 110 ± 122 .

TABLE 2. LEFT VENTRICULAR VOLUME COMPARISONS

Patients	LV volume		Correlation coefficient (r)	Regression equation	s.e.e.
All patients (n = 23)	EDV*	A†	0.74	$y = 0.17x + 16$	17
		AC§	0.96	$y = 0.94x + 10$	30
	ESV‡	A	0.87	$y = 0.21x + 5$	12
Men (n = 9)	EDV	A	0.55	$y = 0.22x + 4$	22
		AC	0.85	$y = 0.92x + 8$	39
	ESV	A	0.87	$y = 0.33x - 12$	14
		AC	0.97	$y = 1.14x - 24$	23
Women (n = 14)	EDV	A	0.81	$y = 0.16x + 18$	14
		AC	0.98	$y = 0.98x + 8$	23
	ESV	A	0.93	$y = 0.18x + 8$	8
		AC	0.98	$y = 1.08x + 0.1$	23

* EDV = end-diastolic volume.
† A = attenuated.
‡ ESV = end-systolic volume.
§ AC = attenuation-corrected.

Attenuation-correction error analysis. The improved correlation and accuracy in LV volume estimates using attenuation correction of RNA count data depend upon the variable distance d' from the LV to the scintillation detector in the LAO position in each patient, since μ , the linear attenuation coefficient of Tc-99m gammas in water, is assumed to be constant at 0.15 cm^{-1} . The individual values of d' in the present investigation ranged widely from 6.7 to 12.1 cm; and thus the attenuation correction factor (A) ranged from 2.8 to 6.1, empha-

sizing the importance of this determination in an individual patient. Also, the reproducibility of d' was $r = 0.99$ (Fig. 3), and the interobserver difference in individual determination of d' ranged from 0 to only 0.4 cm. Using $\pm 0.4 \text{ cm}$ as the maximum variability of d' , the attenuation correction factor, A, varied by only ± 0.2 . Thus, the average attenuation-corrected RNA LV EDV of 215 ml varied by only $\pm 11 \text{ ml}$, due to the variability of d' , and the average ESV of 132 ml similarly varied by only $\pm 6 \text{ ml}$.

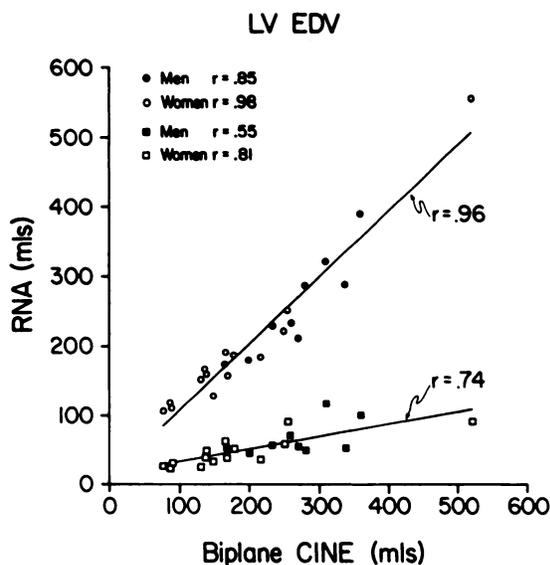


FIG. 1. Relation between uncorrected ($\square =$ women, $\blacksquare =$ men) and attenuation-corrected ($\circ =$ women, $\bullet =$ men) gated equilibrium radionuclide angiographic (RNA) left-ventricular (LV) end-diastolic volumes (EDV), on ordinate, and biplane contrast cineangiographic (CINE) LV EDV measures, on abscissa. Regression lines and correlation coefficients are shown.

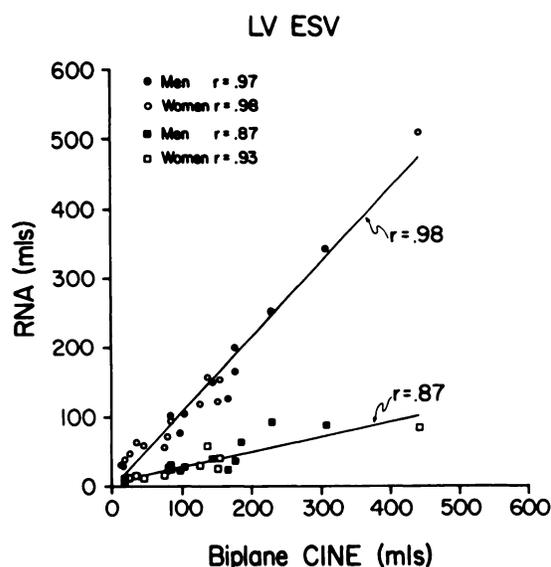


FIG. 2. Corrected and uncorrected end-systolic RNA volumes are shown as in Fig. 1, plotted against cineangiographic measurements. LV end-systolic volumes (ESV), on ordinate, and corresponding biplane cineangiographic (CINE) LV ESV measures, on abscissa, are shown as in Fig. 1.

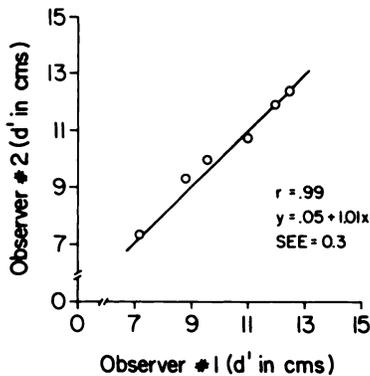


FIG. 3. Showing interobserver reproducibility of calculated distance d' .

Accuracy of individual absolute LV volume estimates. The relative accuracy of uncorrected RNA LV volume and attenuation-corrected RNA LV volume estimates for individual cineangiographic LV volumes was evaluated using the 95% confidence intervals for the uncorrected and corrected RNA data. Using cineangiographic LV ED and ES volumes in 50-ml increments between 50 and 600 ml, the corresponding 95% confidence interval values for the uncorrected and corrected RNA data were determined and corrected using the corresponding EDV or ESV regression equations to obtain a range of individual RNA LV volume estimates. Then, the resulting range of absolute LV volume estimates for the uncorrected and corrected RNA data were plotted for the LV ED and ES volumes (Figs. 4 and 5, respectively). For both the cineangiographic LV ED and ES volumes, the range of LV volume estimates corrected by regression equation using the attenuation-corrected RNA LV volume data was substantially narrower than that ob-

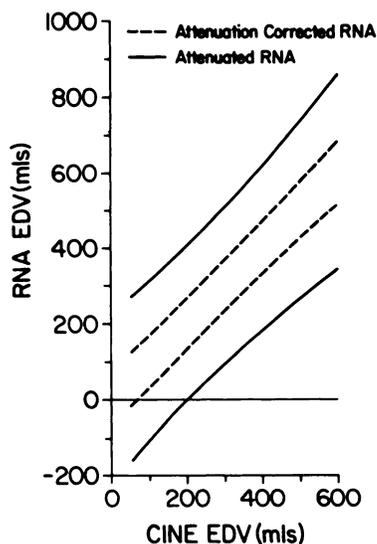


FIG. 4. Comparison of range of 95% confidence intervals, corrected by regression equation, computed for uncorrected (—) and attenuation-corrected (---) radionuclide LV ED volume estimates for predicting individual cineangiographic (CINE) EDVs. Range of RNA corrected LV EDV estimates is significantly smaller.

tained from the uncorrected RNA LV volumes. Also, the average percent relative errors in the calculated individual absolute LV EDV and ESV attenuation-corrected RNA data (13 ± 9 and $27 \pm 23\%$, respectively) were significantly less than those obtained using the uncorrected RNA data (30 ± 23 and $143 \pm 99\%$, respectively).

Reproducibility. The intra- and interobserver reproducibility for hand-drawn ROI ED and ES counts in ten studies each were $r = 0.98$ and 0.97 , respectively; and the interobserver reproducibility for the blood sample count data was $r = 0.99$.

DISCUSSION

Several studies have attempted to estimate LV volumes using data from equilibrium RNA images (5-8). Initially, Slutsky and co-workers observed correlations between RNA LV ED and ES volumes and the corresponding biplane cineangiographic LV volumes ($r = 0.97$ and 0.98 , respectively) (5). Dehmer and co-investigators also observed a correlation between uncorrected RNA LV ED and ES volumes compared with 30° RAO single-plane cineangiographic LV volumes ($r = 0.99$ for both) (6). However, both of these early RNA studies rely heavily on correction of RNA LV volumes by regression equation to obtain absolute LV ED and ES volumes. This correction may be inaccurate in individual patients, since RNA absolute LV volume calculations will vary according to the amount of photon attenuation and the distance from the LV to the scintillation camera through which the photon passes (8).

Recently, Links and co-investigators used an attenuation correction of RNA count data and observed a correlation between RNA LV ED and ES volume esti-

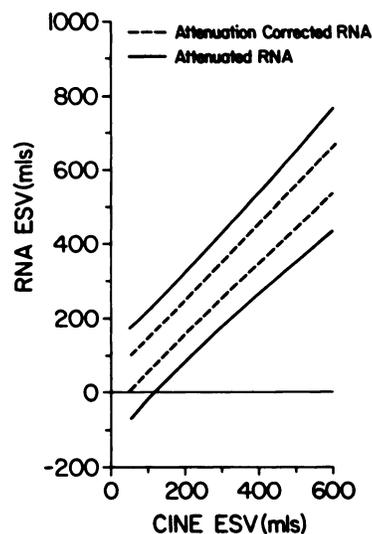


FIG. 5. Comparison of range of 95% confidence intervals, corrected by regression equation, computed for uncorrected and attenuation-corrected RNA estimates of end-systolic volume (ESV) for predicting individual cineangiographic (CINE) ESVs, illustrated as in Fig. 4.

mates and the corresponding 30° RAO single-plane cineangiographic LV volumes: $r = 0.95$ for both (8). Burow and co-investigators also observed a correlation between simultaneous attenuation-corrected RNA determinations of LV stroke volume and thermodilution stroke-volume measurements ($r = 0.94$) (11). Although corrected RNA LV ED and ES volumes and LV stroke-volume measurements were obtained, these correlations were not better than those previously reported using only uncorrected RNA LV volumes. By contrast, Burow and co-authors reported a correlation coefficient of only 0.80 between simultaneous uncorrected RNA LV stroke volumes and thermodilution stroke-volume measurements. This suggests that attenuation correction improved the correlation with an independent measure of LV stroke volumes. However, despite this observation and the theoretical advantage of attenuation correction, the importance of attenuation correction of uncorrected RNA LV volumes to obtain absolute LV volumes remains unclear, as does the relative accuracy of these RNA LV volume estimates compared to those obtained by contrast biplane cineangiography.

The present investigation systematically evaluated the importance of attenuation correction of attenuated RNA LV volumes for obtaining individual LV volumes. The corrected RNA LV ED and ES volume estimates correlated more closely with the corresponding biplane cineangiographic LV volume measures than did the uncorrected RNA LV volumes. Also, the average corrected RNA LV ED and ES volume measurements did not differ significantly from the corresponding mean biplane cineangiographic LV volumes. Using the 95% confidence intervals, corrected by regression equation, for the uncorrected and corrected RNA LV volume data, the range of attenuation-corrected RNA LV ED and ES volume estimates for individual biplane cineangiographic LV volumes was substantially less than that for the uncorrected RNA LV volumes. Also, the average percent relative errors for LV ED and ES volumes were significantly smaller for the corrected LV volume estimates compared with the uncorrected RNA volumes. Therefore, compared with uncorrected RNA LV volumes, attenuation-corrected RNA LV volumes provide more accurate estimates of individual biplane cineangiographic absolute LV volumes.

The improved correlation between the corrected and uncorrected RNA LV volume estimates and the biplane cineangiographic LV measurements observed in the present study depended upon the individual correction factors (A), which include the linear attenuation for the 140-keV photon of Tc-99m, and the distance (d') from the LV to the scintillation detector in the LAO position. In the present investigation, we considered μ to be a constant (0.15 cm^{-1}) and we calculated the distance d' for each patient (8). Importantly, the individual calculated values of d' varied in our 23 patients from 6.7 to

12.1 cm, which resulted in values of A ranging from 2.8 to 6.1. Consequently, depending on the individual distance measurement, the factor A raised the uncorrected RNA LV volumes up to the corrected RNA LV volumes, improving the correlation with the corresponding biplane cineangiographic LV volumes. Moreover, the range of individual attenuation-corrected RNA LV ED and ES volumes was smaller for each cineangiographic LV volume studied than that for the uncorrected RNA LV volumes, which suggested that individual LV volumes can be estimated more accurately using an attenuation correction.

When attenuation correction of RNA count data is performed to obtain LV volume estimates, two additional variables, which have limitations, are included in the calculation. First, the assumption that $\mu = 0.15 \text{ cm}^{-1}$ from the LV center of mass to the scintillation detector in the LAO position is only an approximation. Since several tissues with different linear attenuation coefficients for the 140-keV photon of Tc-99m intervene, some variability in the LV volume calculations using the corrected RNA count data might be expected. Nevertheless, the improved correlations and accurate estimates of LV volumes using this method suggest that this is an acceptable assumption. Second, the calculated distance d' from the gamma camera in the LAO position to the left ventricle is an approximation of the distance through which the 140-keV photon of Tc-99m must pass and be subject to attenuation. The method used in the present investigation to determine this distance was an attempt to simplify the geometric method previously validated by Links and co-workers (8). We used anatomic landmarks to obtain this distance. The principal variability in the measurement is in determining the appropriate point over the LV in the anterior camera position. Choosing the distance from LV apex to pulmonary artery as the long axis of the LV was an approximation taken from prior first-transit radionuclide studies where the pulmonary artery was observed to overlie the aortic valve plane (3). Therefore, bisecting this distance would provide a reasonable determination of the LV center of mass in the anterior camera position. The distance d' could then be calculated as described. The reproducibility of this measurement was excellent and the interobserver variability was small. Thus, individual corrected RNA LV volume estimates were significantly more accurate than the uncorrected volumes for estimating the corresponding LV volumes by biplane contrast cineangiography.

Therefore, uncorrected RNA LV volume indices should be attenuation-corrected to obtain accurate estimates of individual LV volumes. These can be obtained in each patient without depending strongly on corrections by regression equation. Moreover, the range of attenuation-corrected RNA LV ED and ES volume estimates of the corresponding individual cineangiographic LV

volumes was small relative to that obtained from uncorrected RNA LV volumes. Consequently, this method of obtaining LV volumes should be useful for following disease progression and therapeutic interventions in individual cardiac patients.

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The Education and Research Foundation of the Society of Nuclear Medicine Fellowship/Pilot Research Grant

The Education and Research Foundation of the Society of Nuclear Medicine welcomes applications for Student Fellowships and Pilot Research grants. These awards are made possible through donations from SNM members as well as from various commercial firms whose products are used in the practice of Nuclear Medicine. Applications received prior to December 15 of any year will be evaluated by the ERF Board on a competitive basis. Awards will be announced on or about February 15 of the following year.

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These awards are designed to stimulate interest among students in the United States and Canada in the field of Nuclear Medicine. The awards are intended to provide an opportunity to spend elective quarters and/or summers in active departments working and associating with experts in the field. Maximum grant: \$1,500. Letters of application should be submitted in duplicate and should contain the following: applicant's name, address, birth date, period for which support is requested, name and institution of sponsor, previous education, previous research, and brief summary of the proposed project, including an appropriate bibliography. Application forms should be requested from the office of the E&R Foundation. Additional applications may be submitted prior to May 1, 1984.

PILOT RESEARCH GRANTS

The goal of this research support is to provide money to young scientists working in Nuclear Medicine who desire support for a research project. Priority will be given to those proposals that are of a pilot nature in either clinical or basic research. The grants are not intended to support salaries, purchase major equipment, or for travel, but are designed to provide essential materials so that innovative ideas can be quickly tested. Maximum grant: \$3,000. Additional applications may be submitted prior to May 1, 1984.

SPECIAL ANNOUNCEMENT: FOURTH TETALMAN MEMORIAL AWARD

A fund has been established in the ERF by friends of Marc Tetalman, M.D., who was a tragic homicide victim while attending the SNM meeting in Atlanta in June 1979. This fund will permit an award of \$3,000 to be made in June, 1984 to a young investigator (35 years of age or younger) who is pursuing a career in Nuclear Medicine. This award is to be repeated annually. It is possible that additional contributions to our fund will permit the stipend to be increased in future years. Applicants should submit prior to March 1, 1984 a curriculum vitae together with data supporting current research efforts.

All letters and applications should be addressed to:

Walter Wolf, Ph.D.
President, E&R Foundation
c/o Society of Nuclear Medicine
475 Park Avenue South
New York, NY 10016