Radionuclide Cardiac Volumes: Effects of Region of Interest Selection and Correction for Compton Scatter Using a Buildup Factor

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The effects of region of interest (ROI) selection and correction for Compton-scattered photons using a buildup factor on radionuclide left ventricular volumes calculated by the Links method were compared in 19 humans with contrast ventriculography and in phantoms. Three different methods of ROI selection were compared: a manual ROI, a second derivative ROI and a 50% count-threshold ROI. In phantoms without Compton scatter correction, volumes were overestimated by 30% (manual ROI), 20% (derivative ROI) and 1% (count threshold ROI). In subjects, results without Compton scatter correction were similar with overestimates of 50% (manual ROI) and 20% (derivative ROI) and an underestimate by 3% (count threshold method). Correction for Compton-scattered photons with the use of a phantom-derived buildup factor resulted in improved accuracy for the manual ROI (+15%) and the derivative ROI (0%). A 50% count threshold ROI following interpolative background subtraction allows the accurate calculation of cardiac volumes without the need for scatter correction, while a second derivative ROI method requires a correction for Compton scatter with the use of a buildup factor.

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Cardiac volumes are frequently used to initially assess and follow patients with cardiac disease. The end-systolic volume is as important as the ejection fraction in assessing prognosis following a myocardial infarction (*1-3*). The end-systolic volume has also been used for the timing of cardiac surgery in patients with valvular heart disease (*4, 5*). Numerous radionuclide methods have been proposed to determine cardiac volumes, including count-based distance methods (*6-10*), count-based ratio methods (*11,12*), SPECT (*13-15*) and geometric methods (*16-17*).

Two factors that influence the determination of absolute cardiac volumes by radionuclide angiography are the methods used to define the ventricular region of interest (ROI) and the contribution of Compton-scattered photons. Most of these have used manual methods to define the ROI (*6,7,9,11*), although some have used automated algorithms (*8,10*). Most (*6-11*), but not all (*18,19*), investigators have ignored the contribution of Compton-scattered photons in quantitative cardiac volumes.

Ideally, only primary photons would be accepted by the gamma camera. However, due to the poor energy resolution of the gamma camera, wide photopeaks are used to enhance counting statistics and result in a large contribution of Compton-scattered photons. These scattered photons degrade the image quality and more importantly cause a significant overestimation of quantitative cardiac volumes unless a correction is made for these additional counts (*18,19*).

Radionuclide count-based distance methods (*6-10*) correct for photon attenuation with the equation, $A = A_o e^{-\mu d}$ (Equation 1) (*6*), whereas A = attenuated count rate, A_o = source count rate, $\mu = 0.15\ cm^{-1}$, which is the linear attenuation coefficient of water for ^{99m}Tc, and d = distance to the center of the left ventricle. The use of a multiplicative buildup factor (B), $A = BA_o e^{-\mu d}$ (Equation 2) (*20,21*) has been suggested as a method for correction of Compton scatter, and although it has been used with other methods (*18,19*), its use has not been reported with a count-based distance method of volume determination.

The first purpose of the present study was to compare the cardiac volumes determined by a count-based distance method introduced by Links et al. (*6*) in a phantom and in humans using three different methods to define the ROI: a manual ROI, an automated second derivative ROI and an automated count-threshold ROI developed in our laboratory (*12*). Contrast angiographic determination of left ventricular volume was used as the reference method for evaluation of the radionuclide techniques. The second purpose of this study was to determine if correction for Compton scatter using a phantom-derived buildup factor would improve the accuracy of cardiac volumes determined by radionuclide angiography (RNA).

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METHODS

Patient Selection

We prospectively studied 19 men who were undergoing clinical diagnostic cardiac catheterization and had good quality contrast ventriculograms. This study was approved by the Human Subjects Committee of the University of Washington and all patients gave informed consent.

Contrast Ventriculography

Left heart catheterization and coronary arteriography were performed by standard techniques. Following coronary arteriography, contrast ventriculography was performed in the 30° RAO view at 30 frames/sec using Renografin 76 or Isovue. Left ventricular volumes were calculated using the single plane area-length method with the Kennedy regression equation (*22*).

Radionuclide Angiography

RNA was performed 1–3 days following cardiac catheterization in 18 patients and 3 days prior to cardiac catheterization in one patient. No subject had a change in medications or clinical status between studies. Red blood cells were labeled with approximately 1100 MBq [^{99m}Tc]pertechnetate using the modified in-vivo technique of Callahan et al. (*23*).

Imaging was performed in the left anterior oblique (LAO) projection to provide the best septal separation of the ventricles. Frame mode studies were acquired for a total of 4 million counts (20 frames/cycle) using a GE300 A/M camera with a general all-purpose collimator, a software zoom of 1.5, a 64 × 64 pixel word image, a 20% energy window and a beat rejection window of ± 10%.

Following completion of the gated acquisition, and with the camera still in the LAO projection, a ^{57}Co point source was placed over the center of the left ventricle as visually estimated on the camera persistence scope. The camera was then repositioned and anterior images of the heart were acquired for 60 sec at the 140% ± 10% keV peak for ^{99m}Tc and at the 122% ± 10% keV peak for ^{57}Co. Subsequently, duplicate 3-ml blood aliquots, drawn at the end of the gated acquisition, were positioned 5 cm from the collimator and counted for 5 min. A separate 5-min acquisition without any radioactivity was made to correct for background activity.

Phantom

A 4-cm cylindrical phantom with a volume of 94.6 ml was filled with 50 MBq of ^{99m}Tc in water. The phantom was imaged perpendicular to the long-axis in a 30-cm diameter water bath at depths of 5–16 cm to the center of the phantom.

Data Processing

ROI Selection. The frame mode RNA images were nine-point spatially smoothed and three-point temporally smoothed using commercial software. The three methods of ROI determination were as follows:

1. A manual ROI was hand drawn by an experienced technologist. A hand drawn region inferior and lateral to the left ventricle was used for manual background correction.
2. An automated ROI was drawn by a commercial second derivative edge detection program (Version 7.1, Siemens Microdelta/Maxdelta Imaging System, Des Plaines, IL). An automated paraventricular background ROI was used for background correction.
3. A 50% count-threshold method, developed in our laboratory (*12*) (Fig. 1) was used. The background constant (V) (i.e., not the interpolative background) was used for a uniform background correction.

The ROIs for each method described above were applied to the unfiltered images and the background-corrected count rates were used to calculate left ventricular volumes using the formulas described by Links et al. (*6*).

Determination of Compton Scatter Corrections-Buildup Factor. With the use of a phantom, the buildup factor (B), which corrects for Compton scatter, was calculated for the three methods of ROI selection as follows. Phantom images were processed in the same manner as radionuclide angiograms. The counts obtained were used to calculate the buildup factor at various depths by solving Equation 2 for B, $B = A/A_o\, e^{-\mu d}$ (Equation 3), where A is the attenuated counts from the ROI, A_o is the source counts calculated from the results for the 3-ml aliquots and the known volume of the phantom, $\mu = 0.15\ cm^{-1}$, is the linear attenuation coefficient of water and d is the distance to the center of the phantom.

Volume Determination. For all three methods of ROI selection, cardiac volumes were next calculated using the method of Links et al. (*6*). The distance from the chest wall to the center of the left ventricle was estimated as described by Links (*6*).

The attenuation corrected source count rate (A_o) was calculated by solving Equation 2 for A_o, $A_o = A/(Be^{-\mu d})$ (Equation 4), where A = count rate measured at the chest wall, B = 1.0 (i.e., no correction for Compton scatter) and $\mu = 0.15\ cm^{-1}$. Absolute cardiac volumes (V_{abs}) were calculated by $V_{abs} = A_o/C_{ba}$ (Equation 5), where C_{ba} was the decay-corrected count rate/ml of the blood aliquot.

To determine if correction for Compton scatter using the buildup factor would improve the accuracy or the precision of the method, volumes were also calculated using the phantom-derived buildup factor for each of the three methods used to define the ROIs with Equation 2.

Statistics. Radionuclide volumes were compared with contrast

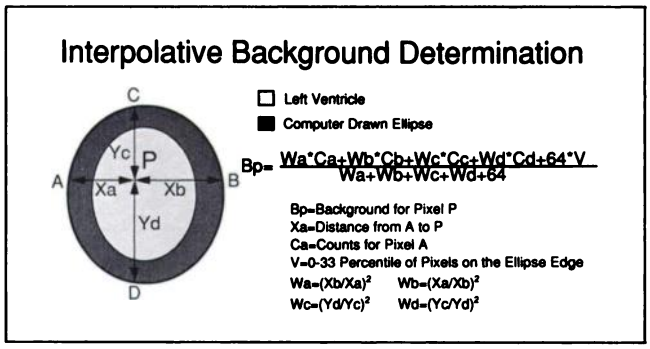

FIGURE 1. A generous user-defined, computer-drawn ellipse is placed around the left ventricle on the end-diastolic image. The pixels on the end-diastolic image, computer-drawn ellipse are sorted from the lowest to the highest. The lowest 33% are averaged to calculate the background constant (V). An interpolative background is calculated for each pixel inside the ellipse for each image, using the above formula, and is subtracted from the temporally and spatially smoothed images to provide an isolated left ventricle. A 50% count threshold is then applied to define the ventricular ROI. The background constant (V) is held constant for the interpolative background calculation for the cardiac cycle. Reprinted with permission from (*12*).

TABLE 1
Counts, Background, and Pixels for Different ROIs

	Manual	Derivative	Count-Threshold
Ejection fraction (Contrast = 46.3)	48.2	49.2	47.6
End-Diastolic counts – Total	41,780	32,991	26,042
End-Systolic counts – Total	25,005	19,654	15,676
End-Diastolic pixels	419	310	226
End-Systolic pixels	284	208	153
Background/Pixel	38.3	40.6	42.0
EDC – Background corrected	25,760	20,669	16,734
ESC – Background corrected	14,183	11,354	9,395

volumes by linear regression and root mean square deviation (RMSD) (*26*). The RMSD is similar to the s.e.e., except that it measures how well the data fit the line of identity (slope 1 and intercept of 0) rather than the fitted regression line. The method with the lowest RMSD should estimate the contrast volumes with the best accuracy. Values are expressed as mean ± 1 s.d. Students t-test was used for paired data, with significance defined as $p \leq 0.05$.

RESULTS

Patients—No Correction for Scatter

The mean value for the 38 contrast ventriculographic volumes was 127 ± 61 ml, with a mean end-diastolic volume of 162 ± 53 ml (range 79–292 ml) and a mean end-systolic volume of 91 ± 49 ml (range 26–225 ml). The mean distance from the chest wall to the center of the left ventricle was 9.7 ± 1.5 cm with a range of 6.5–12.7 cm.

Manually defined ROIs contained 86% more pixels than the count threshold method, and derivative ROIs contained 37% more pixels (Table 1). The end-diastolic and end-systolic counts were also proportionately larger for the manual and derivative methods than the count-threshold method. The background counts/pixel were significantly less for the manual method ($p < 0.01$) than for the automated methods but did not differ significantly between the two automated methods.

Only obvious errors or discontinuities in the automated ROI were corrected. This occurred in 11 of the 38 regions for the derivative method, but in only 1 of 38 regions for the count threshold method ($\chi^2 = 9.90$, $p < 0.01$).

Table 2 and Figure 2 show the 38 calculated cardiac volumes (19 end-diastolic and 19 end-systolic) for the different ROIs. The manual and derivative methods overestimated the contrast volumes by 50% and 20%, respectively ($p < 0.0001$ versus contrast angiography), while the count-threshold method underestimated the contrast volumes by 3% (p = ns versus contrast angiography).

Determination of Buildup Factors in Phantoms

The relative count profile of the cylinder at a depth of 10.4 cm to the center of the phantom is shown in Figure 3, with the buildup factor for each pixel. The maximum buildup factor is 1.18 at the center of the cylinder and decreases to 0.55 at the edge of the cylinder. Counts outside the projected area of the cylinder reflect both Compton-scattered photons and the point spread function (PSF) of the gamma camera. The area of the manual ROI was 120% larger, the derivative method 43% larger and the count-threshold method 1% larger than the true cross-sectional area of the cylinder, which was similar to the in-vivo differences.

The buildup factor varied for each method used to define ROIs (Fig. 4) and was 1.30 ± 0.05 for the manual ROI, 1.20 ± 0.02 for the derivative ROI and 1.01 ± 0.02 for the count-threshold ROI.

Patients—Correction for Compton Scatter

When the phantom-derived buildup factor is used to correct for in-vivo Compton-scattered photons (Tables 3 and 4), the cardiac volumes calculated with the manual method still resulted in a 15% overestimation ($p < 0.005$ versus contrast angiography). However, use of the phantom-derived buildup factor with the derivative ROI improved the results in that the estimated cardiac volumes

TABLE 2
Comparison of Radionuclide with Contrast Volumes Without Scatter Correction

	Mean (ml)	r	Slope	Intercept	s.e.e.	RMSD
Contrast angiography (EDV and ESV)	126.6					
Manual	189.5*	0.88	1.36	17.4	45.6	82.2
Derivative	151.9*	0.89	1.12	9.5	36.3	45.3
Count-Threshold	123.4	0.89	0.91	8.8	29.0	29.8

* $p < 0.0001$ vs. contrast.
r = correction coefficient and s.e.e. = standard error of the estimate.

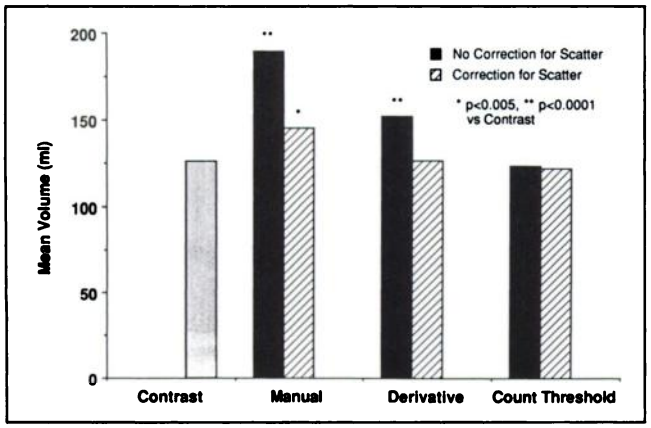

FIGURE 2. Contrast volumes are compared with radionuclide volumes obtained with the manual, derivative and count-threshold ROI, with and without the use of a phantom-derived buildup factor to correct for Compton scatter.

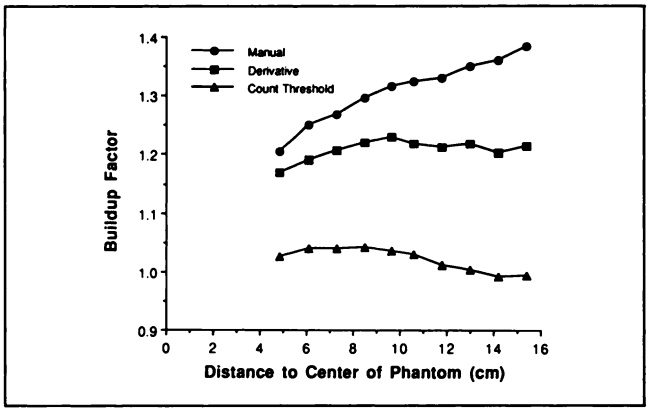

FIGURE 4. The buildup factor for the 4-cm cylinder at depths of 5–16 cm in the water phantom is shown using the ROIs defined by the manual, derivative and count-threshold methods.

were no longer significantly different from contrast angiography. The Compton-corrected count-threshold volumes were essentially the same as the non-Compton corrected volumes and were *not* significantly different from contrast angiography.

DISCUSSION

Most (*6–10*), but not all (*18,19*), previous reports have generally ignored the effects of Compton scatter on quantitative cardiac volumes. In this report, we have estimated the effects of three different methods of ROI selection and the contribution of Compton scatter on quantitative cardiac volumes. The automated count-threshold method described in this report provided accurate cardiac volumes without the need for Compton scatter correction, since the phantom-derived buildup factor is negligible (1.01). The automated second derivative method required scatter correction, with the use of a phantom-derived buildup factor (1.20), to provide accurate volumes. The manual method overestimated the contrast volumes by 15% even after correction for Compton scatter with the phantom-derived buildup factor (1.30).

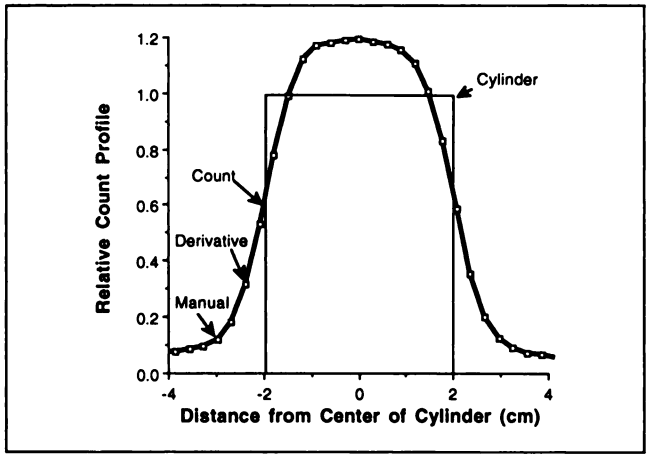

FIGURE 3. The relative count profile is shown for the 4-cm cylinder at a depth of 10.4 cm in the water phantom. The ideal count profile of the cylinder if there were no Compton scatter or point spread function is also shown (labeled cylinder). The count profile is corrected for attenuation so that any increase within the projected area of the cylinder represents the increase due to the contribution of Compton-scattered photons (buildup factor). The edge of the ROI defined by the manual, the second derivative and the count-threshold methods are marked by arrows on the count profile curve relative to the actual size of the cylinder.

Effect of ROI Selection

The larger cardiac volumes obtained with the manual methods presumably reflect the larger ROIs defined by this method. Manual methods of edge detection overestimate the left ventricular end-diastolic diameter due to the PSF of the gamma camera (*27*). Whether in a phantom or a patient, an increase in the size of the ROI beyond the edge of the volume of interest will increase the total counts due to a greater contribution of scattered photons. In patients, there may be an additional increase in Compton-scattered photons arising from the right ventricle or from adjacent overlapping structures.

Count Threshold Method. In the phantom, the 50% automated count threshold method identifies a ROI that is very close to the true object size and is relatively constant with depth. The number of primary photons that are detected outside this ROI due to the PSF of the gamma camera almost exactly counterbalances the Compton-scattered photons detected inside the ROI. Thus, no correction for scatter is necessary with this method. In comparison, the derivative and manual ROIs include all of the primary photons from the phantom and many more Compton-scattered photons, resulting in a buildup factor significantly greater than 1.00.

Derivative Method. Our derivative method yielded a 20% overestimation of cardiac volumes in comparison to contrast angiography, similar to the 24% overestimation reported by Petru et al. (*8*) with a second derivative method. However, other investigators report that a derivative ROI resulted in significantly smaller cardiac volumes in comparison to contrast angiography by 14% (*7*), 15% (*9*) and 41% (*6*).

TABLE 3
Comparison of RNA with Contrast Volumes with the Use of a Buildup Factor to Correct for Scatter

	Buildup factor	Mean (ml)	r	Slope	Intercept	s.e.e.	RMSD
Contrast angiography (EDV and ESV)		126.6					
Manual	1.30	145.8*	0.88	1.05	13.4	35.1	40.3
Derivative	1.20	126.6	0.89	0.94	7.9	30.3	30.5
Count-Threshold	1.01	122.2	0.89	0.90	8.7	28.8	29.8

* $p < 0.005$ vs contrast.
r = correlation coefficient and s.e.e. = standard error of the estimate.

Manual Method. In our subjects, manual ROIs resulted in a 50% overestimation of cardiac volumes compared to contrast angiography. Links (*6*) and Starling (*7*) both found that manual ROIs provided accurate cardiac volumes in comparison to contrast angiography.

The explanation for the 50% overestimation of volumes we found with manual ROIs in comparison to accurate cardiac volumes in prior reports is uncertain (*6,7,9*). The 9.7-cm mean depth to the center of the left ventricle in this report is similar to the 8.9–10.2-cm (*6,7,26*) mean depths previously reported and is probably not contributory. Links et al. (*6*) and Rabinovitch et al. (*9*) used in-vivo labeling of RBCs while Starling et al. (*7*) used technetium-labeled albumin. These methods resulted in a high background activity, 48%–51% versus 40% with the modified in-vivo method of labeling RBCs. It is probable that the ~25% higher background activity obtained with the use of an in-vivo method of labeling of RBCs resulted in an oversubtraction of the left ventricular counts, which, at least partially, compensated for the buildup due to Compton-scattered photons in the previous reports.

Compton Scatter Correction-Buildup Factor

Investigators have measured a 22% scatter fraction using a cylindrical phantom with a germanium detector and a 25% scatter fraction with Monte Carlo simulation (*28*), similar to the 18% buildup due to Compton scatter over the center of the cylinder in this report. Siegel measured in-vitro buildup factors in the range of 1.21–1.27 using a second derivative edge detection program (*20,21*) with a 20% energy window, similar to the 1.20 phantom-derived buildup factor we determined.

Several previously reported methods of cardiac volume determination have attempted to correct for Compton scatter (*18,19*) using an intraesophageal source or an individual buildup factor estimated from opposed LAO and RPO images (*19*). However, when both methods were performed in the same subjects, there was a 24% mean difference in the calculated transmission factor (*19*). We doubt that the use of an individually derived transmission factor or buildup factor would provide significantly more accurate absolute cardiac volumes than the method proposed here.

Limitations

Contrast ventriculography is used as a reference method because of the validation performed in postmortem studies with AP-lateral biplane angiocardiograms (*29*). It is, however, influenced by geometric assumptions, prior contrast load, fluctuating hemodynamics and represents a single ventricular contraction. Differences between the contrast and radionuclide volumes may be due to variations of the attenuation coefficient between individuals (*30–33*) or of the cardiac volumes between the two studies. Our phantom was not designed to simulate a left ventricle with adjacent structures and background activity. We chose a simpler

TABLE 4
Comparison of RNA with Contrast Volumes with the Use of a Buildup Factor to Correct for Scatter

	Buildup Factor	Mean (ml)	r	Slope	Intercept	s.e.e.
EDV contrast angiography		162.0				
Manual	1.30	188.9*	0.73	0.85	50.5	43.4
Derivative	1.20	164.8	0.76	0.81	33.2	38.5
Count-Threshold	1.01	157.7	0.77	0.79	30	36.3
ESV contrast angiography		91.2				
Manual	1.30	102.6*	0.92	1.08	3.9	22.8
Derivative	1.20	88.4	0.93	0.93	3.6	18.7
Count-Threshold	1.01	86.6	0.92	0.90	4.1	19.1

* $p < 0.05$ vs. contrast.
r = correlation coefficient and s.e.e. = standard error of the estimate.

model because it provided results consistent with reports in the literature and could be implemented in other laboratories.

Until current research methods (*34–36*) that allow pixel estimates of Compton scatter reach clinical utility, the use of a buildup factor with a derivative ROI or a 50% count-threshold method can be used to provide accurate cardiac volumes.

CONCLUSION

Accurate cardiac volumes can be calculated using derivative methods to define the ROI, but they require the use of a buildup factor to correct for the contribution of Compton-scattered photons. The 50% count-threshold method, utilizing an interpolative background subtraction, effectively counterbalances the contribution of Compton scatter in radionuclide volume determinations. This allows for the accurate calculation of cardiac volumes without the need for scatter correction with a buildup factor.

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