Factors Affecting Ventricular Volumes Determined by a Count-Based Equilibrium Method

Edgar C. Fearnow III, James A. Stanfield, Ronald J. Jaszczak, C. Craig Harris, and R. Edward Coleman

Department of Radiology, Duke University Medical Center, Durham, North Carolina

Using a ^{99m}Tc-filled source ("ventricle") in an elliptical torso phantom, we analyzed the effect of source depth, region of interest (ROI) size, background concentration and source shape on volumes determined by an attenuation-corrected count-based equilibrium method. The calculated volume of a 96 cc sphere decreased linearly from 103 to 82 cc with increasing depth from 4 to 18 cm [vol = −1.48 · depth (cm) + 109, r = 0.99]. The calculated volume of the same sphere imaged at a depth of 9 cm increased from 98 to 117 cc with ROI sizes increasing from 161 to 1,369 pixels (1 pixel = 0.17 cm^2). With increasing background concentration from 0–2 μCi/ml calculated volumes decreased from 95 to 85 cc (vol = −5.3 · background concentration (μCi/ml) + 95, r = 0.97). However, with correction for over-subtraction of background, increasing background activity caused no decrease in calculated volume (mean = 95 cc, s.d. = 1). Calculated volumes for the sphere and various cylinders were accurate, while those for cones were up to 37% lower for actual volumes ranging from 56–608 cc. This study demonstrates that multiple factors produce variability in count-based determination of phantom volumes. A careful consideration of the interaction of these factors with the edge-detection and computational algorithms is required.

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The problems associated with the determination of accurate ventricular volumes are formidable. However, several investigators (*1–5*) have reported on the determination of ventricular volumes from equilibrium blood-pool studies. Slutsky et al. (*1*) correlated left ventricular (LV) counting rates with angiographic volumes (CINE) and used a regression equation to calculate LV volumes. This method required the use of geometric assumptions to calculate CINE volumes used in the regression equation. Attenuation-corrected count-based equilibrium methods for volume determination were introduced in 1980 by Links et al. (*2*) and Jaszczak et al. (*3*). These methods corrected for thoracic attenuation of photons and did not require the use of regression equations. Links et al. (*2*) used a theoretical attenuation coefficient of 0.15 cm^{-1}. The method described by Jaszczak et al. (*3,4*) assumes exponential photon attenuation with an empirically derived attenuation coefficient of 0.13 cm^{-1}. Correction for background oversubtraction is also accomplished using this method.

Factors that affect LV volumes obtained from equilibrium blood-pool methods have not been well studied. The purpose of this study was to evaluate the effects of source depth, region of interest (ROI) size, background concentration, and source shape on attenuation corrected count-based volumes using the method of Jaszczak et al. (*3*) and a modification of the method proposed by Links et al. (*2*).

MATERIALS AND METHODS

Volume determination at increasing depth

A 96-cc hollow acrylic sphere, 6 cm in diam, filled with 1.5 mCi of technetium-99m (^{99m}Tc) pertechnetate, was imaged in a water-filled phantom at depths to the center of the sphere of 4–18 cm (Fig. 1). There was

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For reprints contact: R. E. Coleman, MD, Box 3949, Duke University Med. Ctr., Durham, NC 27710.

no background activity in the water-filled phantom. A gamma camera* with a low energy, high resolution collimator and a 20% window centered on the 140 keV photopeak was used for all experiments. Unless noted data were collected for 200K counts in a 64 × 64 word matrix in static acquisition mode using a standard computer system.† Semiautomatic ROIs were generated around the image of each sphere using a second derivative edge-detection algorithm. Total counts and total pixel numbers were recorded for each region. Background regions adjacent to the sphere's image were automatically generated using the ejection fraction algorithm supplied with the computer system, and background counts per pixel were recorded.

A 1-cc sample was taken from the sphere, placed in a test tube 2.5 cm above the collimator face and imaged for 50k counts. Total counts in a 721 pixel ROI were recorded, and background counts per pixel were determined for an adjacent background region.

Counting rates (decay corrected) for the sphere at all depths and the point source were determined using the following equation.

$$\text{bkg cor ct rt} = \frac{\text{ROI counts} - \text{background counts}}{\text{acquisition time}} \cdot e^{kt}, \quad (1)$$

where bkg cor ct rt = background corrected counting rate,
ROI counts = counts in ROI of size y pixels,
bkg counts = (background count/pixel)·y pixels,
$k = 1.925 \times 10^{-3}\ \text{min}^{-1}$ (decay const. for ^{99m}Tc)
t = time from start of experiment to data acquisition.

Sphere volumes were calculated using Eq. (2):

$$\text{"First-order" vol} = \frac{\text{bkg cor ct rt for sphere}}{\text{bkg cor ct rt, 1 cc source}} \cdot e^{\mu d}, \quad (2)$$

where $\mu = 0.13\ \text{cm}^{-1}$
d = depth of center of sphere in phantom.

This equation is a simplified form of Equation 3 (described later), corresponding to the "first order" volume calculation which assumes no background activity. This equation is equivalent to the method proposed by Jaszczak et al. (*3,4*), if background activity is absent. This equation is also essentially the method proposed by Links et al. (*2*) except that an attenuation coefficient of $0.13\ \text{cm}^{-1}$ is used rather than a value of $0.15\ \text{cm}^{-1}$ as proposed by Links.

Volume determination at increasing ROI size

The 96-cc sphere was placed inside the water-filled elliptical phantom at a depth of 9 cm as shown in Fig. 2. The phantom was imaged at a 45° angle to simulate left anterior oblique geometry. There was no background activity in the phantom. Regions of interest of variable size were placed around the sphere image. The smallest ROI (161 pixels) was computer generated by the semiautomatic second derivative method. Two ROIs (269 and 387 pixels) were manually drawn circular ROIs. The next seven were manually drawn square ROIs. A background region was selected outside and adjacent to the largest region. The counting rate for this background ROI was used in calculating volumes at all ROI sizes. A 1-cc sample was withdrawn from the sphere and imaged as described in the previous experiment. Background corrected counting rates were determined for the sphere at each region size and for the 1-cc sample using Eq. (1). Sphere volumes for each region size were calculated using Eq. (2).

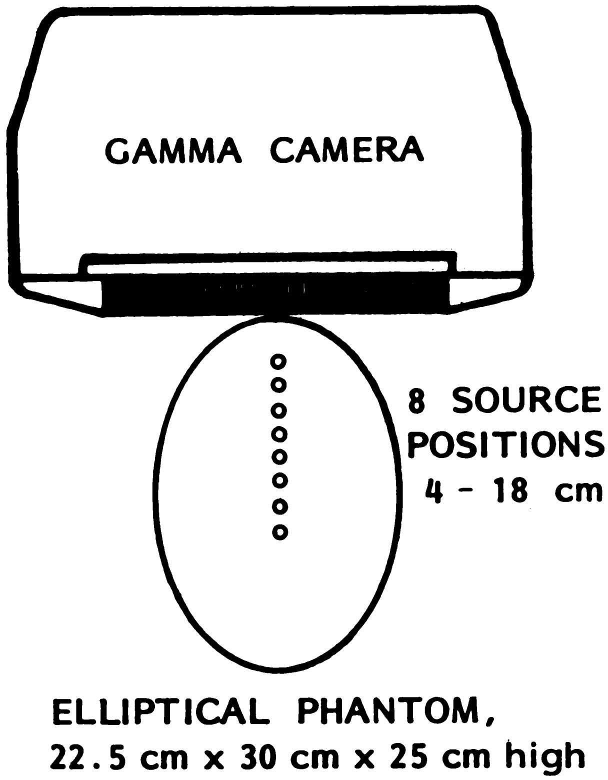

FIGURE 1
Phantom configuration used for depth experiment

Volume determination at increasing background concentration

Using the phantom configuration shown in Fig. 2, the 96-cc sphere containing 1.5 mCi [^{99m}Tc]pertechnetate was imaged with background concentrations of [^{99m}Tc]pertechnetate of 0–2.0 μCi/ml. Computer-generated ROIs were used for the sphere at each background concentration. Adjacent background regions were automatically generated using an ejection fraction algorithm and background corrected counting rates were calculated by Eq. (1). A 1-cc sample was taken from the sphere and imaged in air with the background and decay-corrected counting rate being deter-

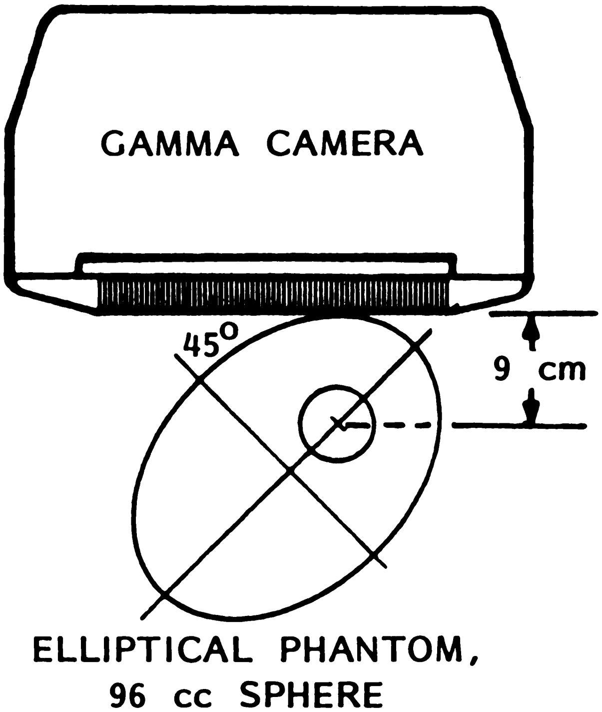

FIGURE 2
Phantom configuration used for ROI and background activity experiments

mined as described in the first experiment. Volumes were calculated using the method proposed by Jaszczak et al. (*3,4*):

$$\text{Vol.} = \frac{\text{bkg cor ct rt, sphere}}{\text{bkg cor ct rt, 1 cc}} \cdot e^{\mu z}(1 + R^{-1}), \quad (3)$$

where $\mu = 0.13\ \text{cm}^{-1}$
z = ventricular depth (9 cm)
R^{-1} = body-to-ventricle concentration ratio.

The inclusion of the variable R^{-1} is based on the theoretical assumption that at increasing background concentrations background counts are oversubtracted (*3,4*). The value of R^{-1} can be estimated if the diameter of the body and the diameter of the heart at the imaging angle are known. The derivation of R^{-1} is based on the use of a model containing uniform, but differing, activities within the ventricle and the body. The expression $(1 + R^{-1})$ results from an analysis of the integral equations representing the activities measured by the gamma camera over regions viewing the ventricle and surrounding background. The value of R^{-1} is zero with no background activity. Volumes are considered to be first order if they were calculated with $R^{-1} = 0$, and in this case, Eq. (3) is identical to Eq. (2). The volumes are "second order" if R^{-1} is greater than zero. More detailed consideration of the concentration ratio R has been presented previously (4).

Volume determination of different source shapes

Polyethylene Erlenmeyer flasks ("ventricles") of volume 56 cc, 134 cc, 230 cc, and 608 cc and polyethylene cylinders ("ventricles") of volume 135 cc, 286 cc, and 540 cc were filled with [^{99m}Tc]pertechnetate in a concentration of 20 μCi/ml and were sealed with cork stoppers. The ventricles were imaged in the elliptical phantom at a 45° LAO view with the long axis of the ventricle perpendicular to the collimator face. A background concentration of 1.6 μCi/ml was used. Computer generated ROIs were placed around the LAO image of each cone and cylinder, and background regions were automatically selected. Counting rates were then determined using Eq. (1). A line source was placed on the elliptical phantom superimposed over the center of the ventricle in the 45° LAO view. The phantom was then imaged from a 45° RAO angle and measurements were taken of the distance from the line source to the back of the ventricle (d_b) and from the line source to the front of the ventricle (d_f). A 1-cc sample taken from the ventricle was imaged and the background corrected counting rate was determined as described in the first experiment. "First order" and "second order" volumes were calculated for each ventricle using Eq. (3). The value of z, the ventricular depth, is defined by the following:

$$z = d_f + \lambda(d_b - d_f), \quad (4)$$

where d_f = distance (cm) from line source to front of ventricle at 45° RAO angle
d_b = distance (cm) from line source to back of ventricle at 45° RAO angle
λ = shape-dependent parameter (0.5).

When $\lambda = 0.5$, z is the depth to the linear center of the ventricle. This linear center is nearly equal to the geometric center or centroid of counts of a sphere or cylinder; however, it is short of the geometric center of a cone. Thus, the objective of this experiment was to determine the error resulting from the use of a value of 0.5 for the shape-dependent parameter when imaging cone-shaped ventricles.

RESULTS

Volume determination at increasing depth (Fig. 3)

The calculated volumes decreased in a linear fashion from 103 cc at 4 cm to 82 cc at 18 cm, a decrease in calculated volume of 20% over this distance (vol = $-1.48 \cdot \text{depth(cm)} + 109$, r = 0.99). At a depth of 9 cm (typical of the depth of the ventricle within the human thorax) the calculated volume was equal to the actual volume of the sphere (96 cc). ROI size increased from 159 to 168 pixels and the background counting rate increased from 7 to 58 counts per pixel with increasing source depth. Note that this increasing "background" is the result of (a) degrading collimator resolution with

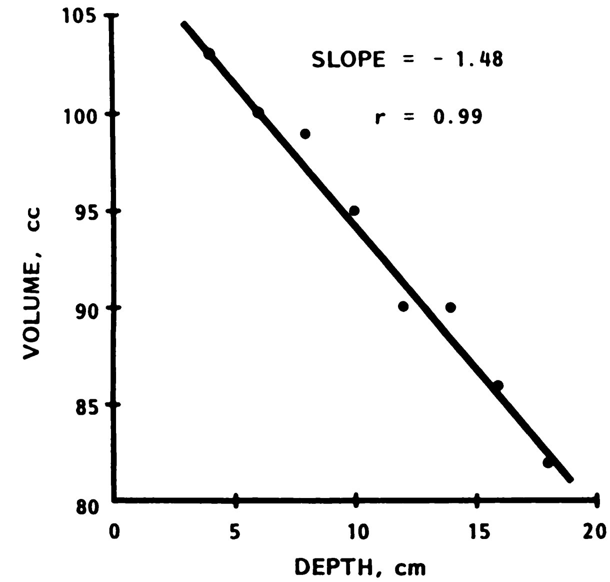

FIGURE 3
Calculated volume of 96 cc sphere at various depths in phantom. Slope = −1.48, r = 0.99

depth and (b) increasing detection of scattered photons, since no background activity was used for this experiment.

Volume determination with increasing ROI size (Fig. 4)

The calculated volumes increased nonlinearly from 98 cc to 117 cc with ROI sizes increasing from 161 pixels to 1,369 pixels, an increase in volume of 19%. The use of a fixed background region located outside the largest ROI in this experiment resulted in a slightly larger volume (98 cc) for the smallest ROI as compared with the volume determined at 9 cm in the previous experiment where an automatic background ROI was used. The rate of increase in calculated volume was greatest at smaller region sizes. The actual volume for the sphere was 96 cc.

Volume determination with increasing background concentration (Fig. 5)

First order volumes (Eq. 2) for the 96 cc sphere decreased linearly from 95 to 85 cc with background concentration increasing from 0–2.0 μCi/ml [y = −5.3 · background concentration (μCi/l) + 95, r = 0.97]. Second order volumes (Eq. 3) did not change with increasing background concentration (range 94 cc − 97 cc, mean 95 cc, s.d. = 1).

Volume determination of different source shapes (Table 1)

Second order volumes for cylinders differed from actual volumes by 1 to 5%. Using a value of 0.5 for the shape-dependent parameter λ, second order volumes for cones were 5 to 37% below actual volume with the greatest error occurring with the 608 cc cone (second order volume = 384 cc).

DISCUSSION

Radionuclide methods of evaluating cardiac function are widely utilized in patent evaluation. A simplified and accurate determination of ventricular volume would be important in evaluating certain patients such as those with aortic insufficiency. A good correlation between ventricular volumes obtained by angiography and equilibrium blood-pool techniques has been reported. Links et al. (*2*) compared LV volumes obtained from attenuation corrected blood-pool studies with angiographic volumes in 35 patients and reported a correlation coefficient of 0.95 with a standard error of estimate (s.e.e.) of 36 ml. Burow et al. (*6*) used attenuation corrected LV volumes to calculate stroke volumes. These stroke volumes correlated well with thermodilution stroke volumes (r = 0.96, s.e.e. = 6 ml). Our method for determining volumes differs from those previously reported in several important ways. An empirically determined attenuation coefficient of 0.13 cm^{-1} is used instead of the theoretical value of 0.15 cm^{-1} (*7,8*). This lower value is used since scattered events are included in the primary photopeak and is based on measurement of a point source in a water-filled phantom. A body-to-ventricle concentration ratio (R^{-1}) is used to calculate second order volumes (Eq. 3) that are corrected for oversubtraction of background activity. The ventricular depth is measured directly from a RAO view rather than calculated trigonometrically from an anterior projection (*2*). In clinical studies, the back of the left ventricle is assumed to lie at the atrio-ventricular groove. This is easily seen on a 45° RAO view. The front of the left ventricle is the cardiac apex. It is also easily seen on a 45° RAO view. Our

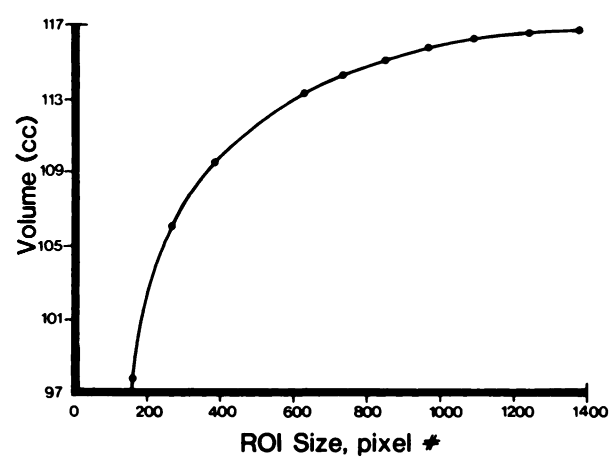

FIGURE 4
Calculated volume of 96 cc sphere at various ROI sizes

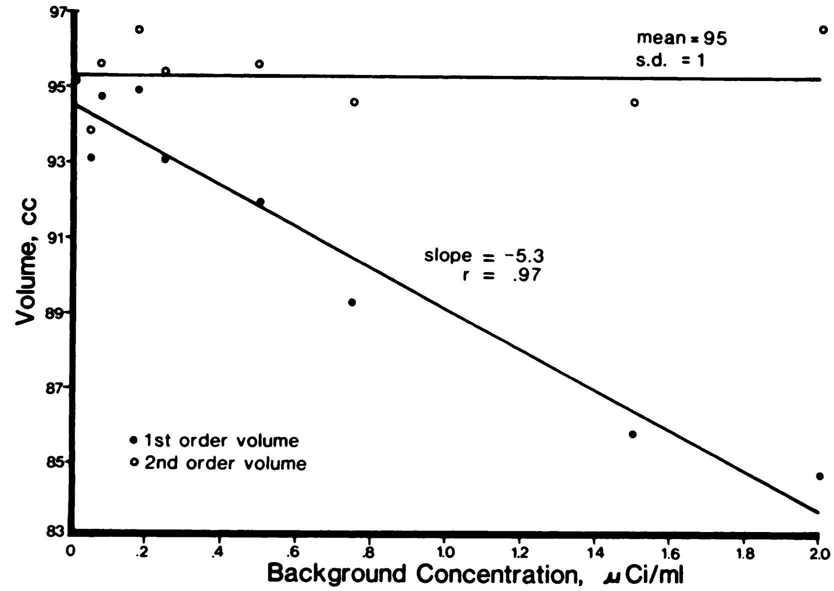

FIGURE 5
"First order" (●) and "second order" (O) volumes of 96 cc sphere at different background concentrations. Slope = −5.3, r = 0.97, mean = 95, s.d. = 1

methods also include a shape-dependent parameter whose value may be estimated for each patient based on a classification of the shape of the patient's ventricle.

Although several studies have evaluated attenuation corrected LV volumes, little attention has been directed at potential sources of error in these calculated volumes. The factors investigated in this study may explain some of the variability in quantitating ventricular volumes and delineate several sources of error.

Increasing source depth resulted in progressively lower calculated volumes. This finding occurs because an increasing number of photons are scattered out of the computer generated "ventricular" ROI at greater depths. The computer chose larger regions at greater depths, but this size increase was not enough to compensate for the effects of degrading collimator resolution with depth and increased scatter into the background ROI. Links et al. (*2*) reported a range of ventricular depths of 6.4–13.2 cm in 35 patients. Starling et al. (*5*) reported a range of 6.7–12.1 cm in 23 patients. Over a similar depth range (6–12 cm), we recorded a 10% loss in volume.

The increase in calculated volume with increasing ROI size is caused by the increased number of scattered photons detected in the larger regions. Some investigators (*2*) use regions larger than the computer generated regions for clinical calculation of LV volumes. The reason for this method will be discussed below.

With increasing background concentration first order volumes were found to decrease by 11% while second order volumes remained constantly independent of background concentration. Our method of correction for background oversubtraction works well over a wide range of background concentrations and at background count rate to source count rate ratios equal to those obtained in patient studies. The typical background count rate to source count rate ratio we obtain in patient studies using 25 mCi ^{99m}Tc-labeled RBCs is equivalent to that obtained in our phantom study with a background concentration of ~2.0 μCi/ml (i.e., with a ventricle-to-body concentration ratio equal to 7.8:1).

The above data suggest that if one does not use a correction for background oversubtraction, clinically calculated LV volumes could be considerably less true LV volume. If, however, ROIs larger than the computer generated ROIs were used, accurate volumes might be obtained without correction for background oversubtraction. This may explain the excellent results obtained by Links (*2*) who did not correct for background oversubtraction, but who did use an attenuation coefficient equal to 0.15 cm^{-1} and manually drawn ROIs that were larger than the computer generated ROIs. Although the justification presented by Links et al. (*2*) for arbitrarily increasing the ROI size is not completely clear, it is reasonable to assume that several of these factors may interact to produce accurate ventricular volumes, at least over a limited range of measurements.

The volumes calculated for the sphere and the cylinders were accurate. The calculated cone volumes were low for several reasons. With the large cones the se-

TABLE 1
Volumes of Cones and Cylinders

Cones			Cylinders		
Actual vol. (cc)	Second order volume (cc)	% Diff. from actual vol.	Actual vol. (cc)	Second order volume (cc)	% Diff. from actual vol.
608	384	37	540	555	3
230	188	18	286	271	5
134	108	19	135	133	1
56	53	5	—	—	—

miautomatic second derivative edge detection algorithm had great difficulty choosing the outer margin of the cones. This computer-generated region visually appeared to be much smaller than the true margin. Furthermore, for all cones the centroid of counts is much closer to the base than the apex. For the experiment described in the text, a single shape dependent parameter (λ) of 0.5 was used for all phantom shapes. This parameter gave a distance (z) to the linear center of the cone, far short of the cone's centroid of counts. For example, for a 45° cone in the absence of attenuation, a shape-dependent parameter (λ) of 0.7 gives the true centroid of counts. A simple calculation indicates that the volumes of "cone-shaped" ventricles may be underestimated by 25 to 30% if a shape-dependent parameter of 0.5 is used in calculating their volumes. The shape of the human heart varies greatly from person to person. In some individuals it may approach a conical shape. To arrive at the correct centroid of counts and to avoid underestimating ventricular volumes a value of λ may need to be estimated for each patient based on a standard method for classification of ventricle shapes.

The accuracy of ventricular volumes determined by using gated blood-pool imaging is directly influenced by the factors described in this paper. It is also influenced clinically by other factors such as nonuniform attenuation resulting from overlying lung and bone tissue, and superposition of source activities from structures in close proximity to the LV such as the left atrium, descending aorta, and right ventricle. While these later factors may ultimately limit the accuracy of clinical quantification of LV volumes using planar imaging, it is, nevertheless, essential to understand the specific factors that affect volume quantification using an idealized phantom situation. The factors investigated in this phantom study will be equally important in patient studies.

The results of this research provides an impetus for the development of improved approaches for determination of LV volumes. For example we have shown that the shape of the ventricle affects its calculated volume. Thus, an improved algorithm should account for this factor by including a shape-dependent parameter. An improved algorithm should also include compensation for variable body-to-ventricle concentration ratios and for the effect of scattered photons. If after compensation for these effects accurate volumes cannot be determined using a range of phantom source geometries, it is unlikely that accurate results will be possible within the clinical environment.

We have shown that multiple factors influence volumes determined by attenuation corrected count-based methods. An understanding of these sources of variability is essential to the intelligent interpretation of LV volumes obtained by this technique.

FOOTNOTES

* Siemens LEM., Siemens Medical Systems, Inc., Iselin, NJ.

† MDS A², Medtronic/MDS, Ann Arbor, MI.

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