Assessment of Left Ventricular Volume Using ECG-Gated SPECT with Technetium-99m-MIBI and Technetium-99m-Tetrofosmin

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We evaluated ECG-gated SPECT (g-SPECT) in the measurement of absolute left ventricular (LV) volume by comparing it with left ventriculography (LVG) and with cine-MRI. **Methods:** Projection data from 31 patients were acquired with a three-headed SPECT system in 12 min using a 64 × 64 matrix with 1.5 zoom (1 pixel = 4.27 mm). The R-R interval from simultaneously acquired ECG was divided into eight frames. The end-diastolic and end-systolic volumes (EDV; ESV) and LV mass were assessed by an area-length method with manual delineation of the epi- and endocardial LV borders using midventricular vertical and horizontal long-axis images. The stroke volume, LVEF and cardiac output (CO) were generated from the EDV, ESV and heart rate during the study. The g-SPECT LV values were compared with those of LVG (25 patients) and cine-MRI (18 patients). **Results:** The g-SPECT values correlated well with those from LVG ($r = 0.83$ to 0.92; $p < 0.001$) and cine-MRI ($r = 0.76$ to 0.99; $p < 0.001$). The g-SPECT technique provides an assessment of LV volumes (EDV, ESV, stroke volume, LVEF, CO, LV mass). **Conclusion:** Despite potential problems that may cause inaccuracy and require improvements such as an accurate and reproducible automatic edge detection algorithm, g-SPECT has clinical utility in assessing global LV volumes and function.

Key Words: ECG-gated SPECT; left ventricular volume; technetium-99m-sestamibi; technetium-99m-tetrofosmin

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The ^{99m}Tc-labeled myocardial perfusion imaging agents, ^{99m}Tc-hexakis 2-methylisonitrile (^{99m}Tc-MIBI) (*1,2*) and ^{99m}Tc-1, 2-bis-[bis(2-ethoxyethyl) phosphino] ethane (^{99m}Tc-tetrofosmin) (*3–6*) have made ECG-gated myocardial SPECT (g-SPECT) more practical in the clinical setting. The g-SPECT technique has several advantages over nongated SPECT, i.e., the ability to assess wall motion and systolic thickening as functional information. We previously reported the merits of g-SPECT in relation to wall motion (*7*) and systolic thickening (*8*). The present study was performed to evaluate another aspect of g-SPECT: the ability to assess LV volumes. Theoretically, the known pixel size-based SPECT data should be able to measure absolute volumes. Therefore, we hypothesize that g-SPECT can assess end-diastolic, end-systolic LV volumes (EDV, ESV, respectively) and LV mass. From the EDV and the ESV, stroke volume and LVEF were calculated. By adding the heart rate to the study, cardiac output (CO) was generated.

This work was performed to evaluate the ability of g-SPECT to measure absolute LV volumes by comparing its values with those generated from left ventriculography (LVG) and cine-MRI.

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MATERIALS AND METHODS

Patients

Forty-three patients were referred for g-SPECT from April 1994 to April 1995. Thirty-one of these patients received LVG and/or cine-MRI (13 LVG only, 6 MRI only and 12 both) and were entered into the study (23 men, 8 women; aged 32–87 yr; mean age 62 yr). Technetium-99-MIBI was administered to 26 patients and ^{99m}Tc-tetrofosmin to 5. Twenty-one patients had coronary artery disease (CAD), four had cardiomyopathy with ventricular dilatation (DCM), two had hypertrophic cardiomyopathy (HCM), three had valvular disease, one had chest pain with negative studies (stress ECG, coronary angiography, LVG and cine-MRI). In the 21 CAD patients, 13 had previous myocardial infarction [five in the subacute phase (3–5 wk), eight with old phase (>5 wk)] and eight with angina pectoris. The mean interval between g-SPECT and LVG was 22.6 days, ranging from 1 to 95, and the mean interval between g-SPECT and cine-MRI was 18.9 days, ranging from 1 to 118. All patients were clinically stable with no documented new cardiac event, surgery or interventional therapy.

Equipment and Data Processing

Patients were injected with 740–1110 MBq (20–30 mCi) ^{99m}Tc-MIBI or ^{99m}Tc-tetrofosmin at rest or during exercise. Thirty minutes later, the patients ate a meal or drank 200 ml of whole milk. Thirty minutes after that, projection data were acquired with a three-headed SPECT system equipped with low-energy, high-resolution collimators (FWHM = 12 mm). The projection data were acquired in 60 steps (30 sec/step in 20 steps for each detector, 12 min total, including rotational deadtime) using a 64 × 64 matrix with a 1.5 zoom (1 pixel = 4.27 mm). The mean radius of rotation was 220 mm. The R-R interval was divided into eight frames. All eight frames of the projection data were reconstructed into transaxial images using the backprojection technique without attenuation correction. The two-dimensional filter was a 15 × 15 Butterworth (order = 8, 0.15 cycles/pixel) and the ECT filter was a Shepp-Logan.

The vertical and horizontal long-axis and short-axis images were reconstructed (1 slice = 1 pixel). Two long-axis slices of the midleft ventricle were added to make a two-pixel thick (8.54 mm) midventricular slice in each of the vertical and horizontal long axes for the preparation of the cinematic display. These midventricular slices of the vertical long-axis and horizontal long-axis were used for the LV volume measurement. Two short-axis slices near the base (one-third from the base) and two short-axis slices near the apex (one-third from the apex) were also added for the cinematic display. Then four tomographic slices of the eight frames were displayed cinematically on the CRT (Fig. 1). For most patients, the first or the eighth (=last) frame was the end-diastolic phase and the third or the fourth frame was the end-systolic phase. The ED and ES frames were detected visually with the help of the cinematic

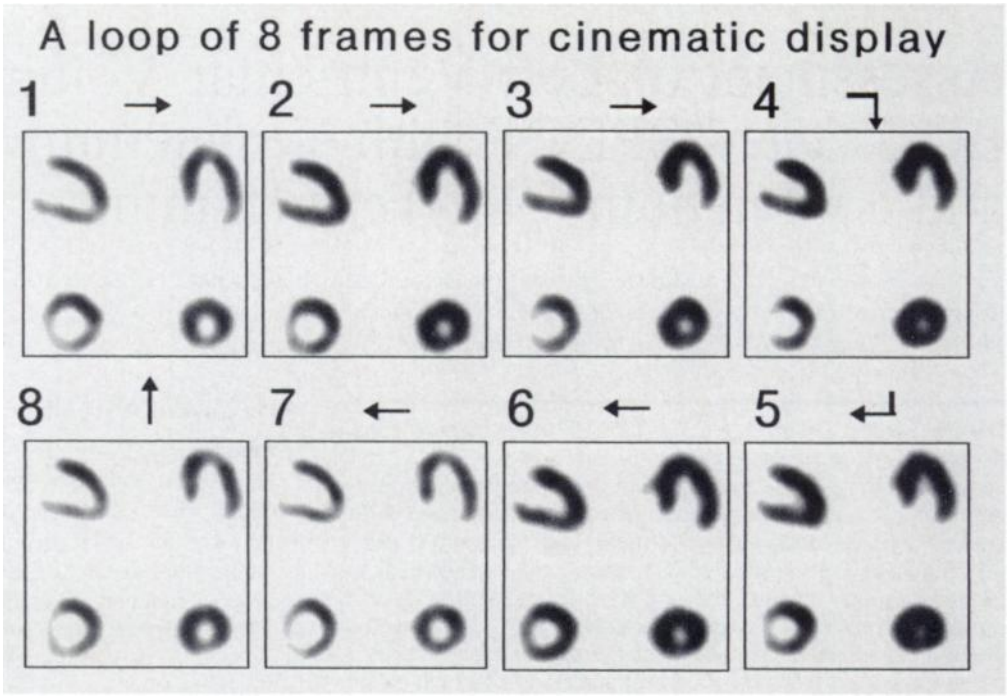

FIGURE 1. An eight-frame loop for cine-mode display in a 79-yr-old woman with aortic stenosis. Sufficient pixel counts in each frame allow clear perfusion images, which provide information about wall motion and systolic thickening.

display. After detection of the ED and ES frames, EDV and ESV were calculated by the area-length method:

$$\text{Volume} = (8A^2)/(3\pi L),$$

where A is the area of the LV cavity and L is the length of the LV in the long-axis, by tracing the inner LV borders of the vertical long-axis and horizontal long-axis images using both color and black and white monitors and 65% of a maximum myocardial pixel count as a guide for manual edge delineation. The LV mass was calculated in the same manner by tracing the outer LV borders of the vertical long-axis and horizontal long-axis images in the ED phase and then the EDV was subtracted from the outer volume. The stroke volume and the LVEF were calculated from the EDV and the ESV. The CO was also generated by inputting the heart rate to the volume data (Fig. 2).

LVG was performed with a biplane angiography system with a frame rate of 60 per second. After the LVG data had been transferred to a cardiac function analyzing system, LV volumes were measured by tracing the LV contour using the right anterior oblique data.

Cine-MRI transaxial and short-axis localizer slices were imaged to define the vertical long-axis and horizontal long-axis angles and the positions. The sequence used was FISP-2D (FA/TR/TE/NEX, 30/50/12/3). The slice thickness was 7 mm and the R-R interval was divided into 12 frames. The acquisition time for vertical long-axis or horizontal long-axis data was about 4–6 min. After detection of the ED and ES frames, the EDV, ESV and the LV mass were measured by tracing the LV borders with the area-length method using the software packaged in the standard machine. The horizontal long-axis data were not obtained in 4 of 18 patients who underwent MRI because of scheduling constraints: Because cine-MRI was usually acquired after T1-weighted images with and without Gd-DTPA in at least two tomographic sections, sometimes we could not arrange enough time for cine-MRI.

The LV volumes were measured independently by the operators who were blind to the results of other procedures.

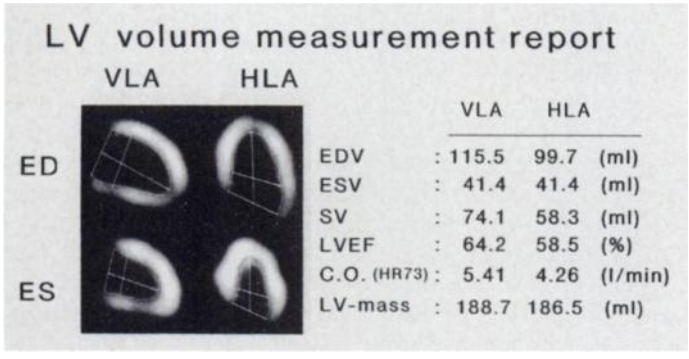

FIGURE 2. Representative LV volume report in the same patient depicted in Figure 1. VLA= vertical long-axis; HLA= horizontal long-axis; ED = end-diastole, ES = end-systole; EDV = end-diastolic volume; ESV= end-diastolic volume; SV = stroke volume; LVEF = left ventricular ejection fraction; C O = cardiac output; HR = heart rate; LV mass = volume of LV mass assessed with ED images.

Statistical Analysis

Statistical differences between the two groups (g-SPECT versus LVG values and g-SPECT versus MRI values) were determined by Student's t-test. Linear regression analysis was used to examine the relation between the two variables. A probability value of <0.05 was considered significant.

RESULTS

LV volume data derived from the g-SPECT technique were compared with those from LVG (n = 25 patients) and cine-MRI (n = 18 patients; 4 patients were studied only in vertical long-axis;12 patients had both LVG and MRI). The r values and regression lines are summarized in Tables 1 and 2.

The r values compared with the LVG of EDV, ESV, LVEF in the vertical long-axis and EDV, ESV, LVEF in the horizontal long-axis were 0.92, 0.90, 0.83 and 0.86, 0.91, 0.87, respectively (n = 25, $p < 0.001$ in all values). The g-SPECT tends to underestimate the EDV and ESV compared with LVG {"g-SPECT − LVG" = −12.5 ± 27.0 ml; mean ± s.d., n = 100 (25 × 4)}. The r values compared to cine-MRI of EDV, ESV, LVEF in the vertical long-axis and EDV, ESV, LVEF in the horizontal long-axis were 0.94, 0.90, 0.89 and 0.99, 0.96, 0.89, respectively (n = 18 in the vertical long-axis and n = 14 in the horizontal long-axis, $p < 0.001$ in all values). The g-SPECT EDV and ESV values tend to be larger than those of the MRI {"g-SPECT − MRI" = 12.2 ± 21.9 ml; mean ± s.d., n = 64

TABLE 1
Comparison of g-SPECT and LVG r Values and Regression Lines

	g-SPECT vs. LVG			
	Vertical long-axis (n = 25)		Horizontal long-axis (n = 25)	
	r value	Regression line	r value	Regression line
EDV	0.92	y = 0.72x + 28.0	0.86	y = 0.69x + 26.0
ESV	0.90	y = 0.81x + 8.00	0.91	y = 0.85x + 4.20
SV	0.91	y = 0.69x + 16.9	0.90	y = 0.52x + 27.8
EF	0.83	y = 0.81x + 10.2	0.87	y = 0.81x + 10.3
CO	0.88	y = 0.78x + 0.71	0.87	y = 0.62x + 1.36

These values correspond to Figure 3. All values are $p < 0.001$. LVG = left ventriculography; EDV = end-diastolic volume; ESV = end-systolic volume; SV = stroke volume; EF = ejection fraction; CO = cardiac output.

$(18 \times 2 + 14 \times 2)\}$. The EDV and ESV in vertical long-axis and horizontal long-axis assessed by g-SPECT correlated well with those by cine-MRI.

The scattergrams are shown in Figure 3 (g-SPECT versus LVG) and Figure 4 (g-SPECT versus cine-MRI). The g-SPECT values correlated well with the LVG and MRI data.

DISCUSSION

General Consideration

Tauxe and co-workers (*9*) proposed a computerized technique to assess organ volume with SPECT and suggested its use in g-SPECT to estimate cardiac chamber volumes. Faber et al. (*10,11*) have developed an edge detection algorithm for gated blood-pool SPECT. Studies on myocardial volume assessment have also been reported. Holman et al. (*12*), Corbett et al. (*13*), Fujiwara et al. (*14*) assessed acute myocardial infarct volume using ^{99m}Tc-pyrophosphate and nongated SPECT; their results, suggest a reasonable cutoff level as 65% to 70% of the maximum pixel counts.

Though there have been few studies published about LV volume measurement using gated myocardial SPECT, DePuey et al. (*15*) and Germano et al. (*16*) measured LVEF, relative LV volume with g-SPECT and ^{99m}Tc-MIBI. They demonstrated good LVEF correlation between g-SPECT and radionuclide ventriculography. Germano et al. (*16*) have developed an automatic computer-driven method for LVEF quantification. Their data support the potential ability of g-SPECT to measure LV volume. A computer-driven method may have better reproducibility of volume calculation than manual edge delineation, but it requires a sophisticated edge detection algorithm and software. Edge detection using a certain cutoff level may fail to delineate the proper LV edge in patients with a large defect or in patients with nonuniform myocardial perfusion such as HCM. A proper cutoff level is dependent on the resolution of the SPECT camera used, data processing protocol (filtering, attenuation correction, etc.) and probably assessment of volume or thickness. Our manual edge detection method is simple, as it only uses midventricular slices. Based on the phantom study, our experiences (*14*) and data reported by Holman (*12*) and Corbett (*13*), we used 65% of maximum myocardial pixel counts as a guide for manual edge delineation. In the area with a large defect, a black and white scale was used to delineate the smooth edge using a lower cutoff level (i.e., manual or visual smoothing). Germano et al. (*16*) reported that their automatic algorithm successfully detected the LV edge even with a large defect. Since accurate and reproducible edge detection is the major limitation of LV volume measurement using g-SPECT, further research is needed.

Comparison with LVG Data

End-diastolic volume in vertical long-axis and horizontal long-axis measured by g-SPECT correlated well with the LVG data. ECG-gated SPECT tends to underestimate EDV compared with LVG. This may have been caused by the following potential problems:

1. Summation of the two midventricular slices (4.27 2 = 8.54 mm thick) and partial volume effect are likely to reduce the LV volumes and increase the thickness of the LV wall.
2. Eight R-R fractions may not be enough to obtain an accurate ED phase.
3. The inner LV border may have been detected far inside from the true edge.

Despite these potential problems, the differences between g-SPECT and LVG are small enough for clinical application. Germano et al. (*16*) reported that an average LVEF value

TABLE 2
Comparison of g-SPECT and MRI r Values and Regression Lines

	g-SPECT vs. MRI			
	Vertical long-axis (n = 18)		Horizontal long-axis (n = 14)	
	r-value	Regression line	r-value	Regression line
EDV	0.94	y = 1.28x − 18.2	0.99	y = 1.14x − 6.50
ESV	0.90	y = 1.29x − 9.10	0.96	y = 1.12x − 1.30
SV	0.87	y = 1.74x − 41.1	0.86	y = 0.84x + 16.6
EF	0.89	y = 1.05x − 2.90	0.89	y = 0.79x + 11.0
CO	0.79	y = 1.36x − 1.00	0.92	y = 0.98x − 0.60
LV mass	0.85	y = 0.73x + 53.5	0.92	y = 0.73x + 59.3

These values correspond to Figure 4. All values are $p < 0.001$. See Table 1 for abbreviations.

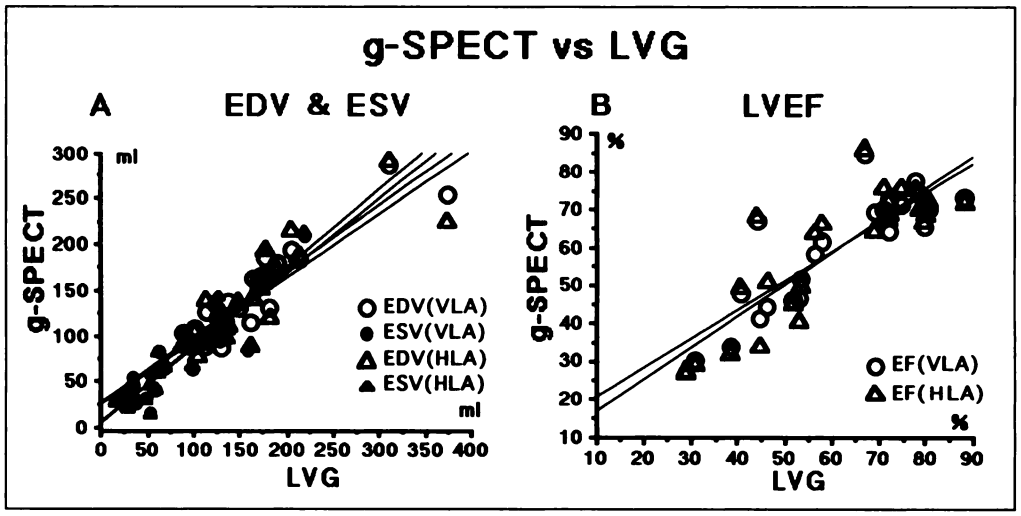

FIGURE 3. Correlation between g-SPECT and LVG. (A) Comparison of g-SPECT and LVG, EDV and ESV. Open circles show EDVs and closed circles are ESVs in the vertical long-axis (VLA). Open triangles show EDVs and closed triangles are ESVs in the horizontal long-axis (HLA). (B) LVEF of g-SPECT and LVG are compared in VLA (open circle) and HLA (open triangle). See Table 1.

assessed by 8 framing was 3.7% lower than that of 16 framing. Since the difference was small and predictable, they recommended eight frames for quantitative g-SPECT.

The ESV in vertical long-axis and horizontal long-axis measured by g-SPECT also correlated well with those by LVG. The resolution of g-SPECT may not be suitable to measure small ESV, but the relation was good enough for clinical application.

Comparison with Cine-MRI

EDV and ESV in vertical long-axis and horizontal long-axis assessed by g-SPECT correlated well with those assessed by cine-MRI. LVG may be a better technique for comparison as a gold standard, but cine-MRI assesses LV volumes by similar tomographic slices using the same area-length method with higher resolution. Cine-MRI can assess LV mass easily using the same technique. Therefore, we tried to evaluate the resolution of g-SPECT for assessing LV volume by comparing its data with cine-MRI data.

Although the resolution of MRI is much higher than that of g-SPECT, we encountered some difficulties in detecting accurate slice positions and angles to obtain a midventricular slice from the limited number of the localizer slices with MRI. This may have caused some underestimation of EDV and ESV. Even though g-SPECT resolution is lower than that of MRI, the detection and arrangement of the slice positions and angles with g-SPECT are easy, accurate and can be corrected after data acquisition for inappropriate positioning.

Other Technical Considerations

We used the area-length method instead of three-dimensional volume measurement or Simpson's method because:

1. It is simple and requires only one slice (midleft ventricular slice).
2. The images for cinematic display can be used for volume measurement. No additional procedures require preparation to assess volumes.
3. The three-dimensional method requires edge detection in all slices and edge detection is difficult or complicated near the apex or the base on the short-axis and requires a sophisticated edge detection algorithm and software.

We used both vertical long-axis and horizontal long-axis because:

1. Averaging of the vertical long-axis and horizontal long-axis may reduce underestimation or overestimation of global LV volumes.
2. Both vertical long-axis and horizontal long-axis images were already reconstructed for cinematic display.

We tried not to increase the acquisition time of g-SPECT in comparison with nongated SPECT. Therefore, the minimal R-R interval of eight frames was chosen; this allowed enough radionuclide counts for each frame. The 64 × 64 matrix with a 1.5 zoom (1 pixel = 4.27 mm) allowed higher resolution compared to that without zoom (1 pixel = 6.4 mm). The eight fractions of the R-R interval offered smooth movement for

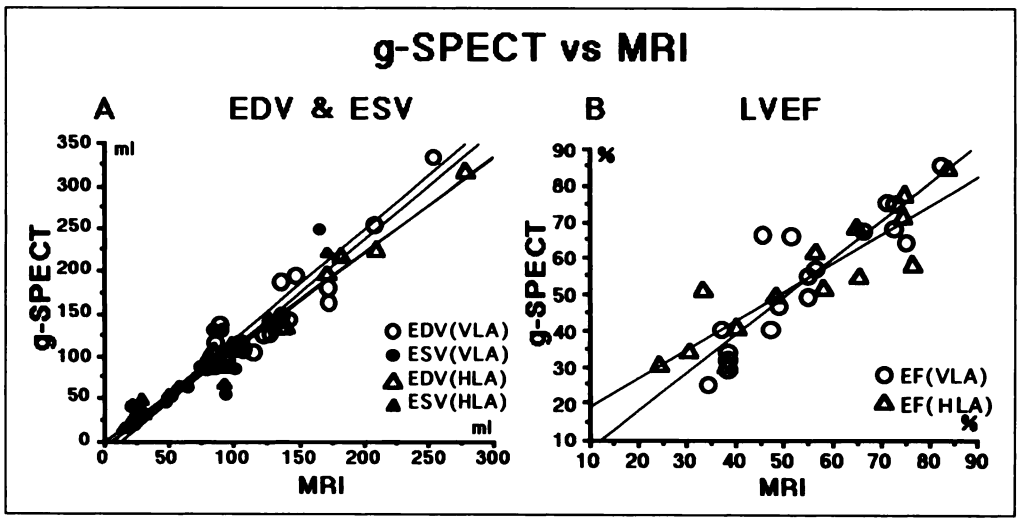

FIGURE 4. Correlation between g-SPECT and cine-MRI. (A) Comparison of g-SPECT and LVG, EDV and ESV. Open circles are EDV and closed circles are ESV in the vertical long-axis (VLA). Open triangles are EDV and closed triangles are ESV in the horizontal long-axis (HLA). (B) Comparison of g-SPECT and cine-MRI LVEF in the VLA (open circle) and in HLA (open triangle). See Table 2.

cinematic display and was sufficient for visual analyses of wall motion and systolic thickening.

Although evaluation of the usefulness of cinematic display was not the main purpose of this study, cinematic display of the four tomographic slices offered an excellent method for evaluating both wall motion and systolic thickening of the whole left ventricle.

Clinical Implications

We believe that the ability to assess reasonable absolute LV volumes is only one of the merits of g-SPECT. ECG-gated SPECT has all the merits of a nongated myocardial perfusion imaging test since nongated images with higher pixel counts can also be reconstructed from the g-SPECT projection data by adding all the frames. Clearer diastolic SPECT images can also be reconstructed by avoiding the ES (e.g., adding first, sixth, seventh, eighth frames for the diastolic phase).

CONCLUSION

We assessed LV volume measurements (EDV, ESV, stroke volume, LVEF, CO and LV mass) using g-SPECT by manual edge delineation of the vertical long-axis and horizontal long-axis midventricular slices and the area-length method. ECG-gated SPECT LV values correlated well with LVG and MRI values. There are several potential problems that may cause inaccuracy and require improvement such as accurate and reproducible automatic edge detection algorithm, but g-SPECT has proven to have sufficient ability to assess global LV volumes and function.

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