

Gated blood pool SPECT improves reproducibility of right and left ventricular Fourier phase analysis in radionuclide angiography

Itaru ADACHI,* Hiroyuki AKAGI,* Tatsuya UMEDA,** Michihiro SUWA,** Tsuyoshi KOMORI,*
Yasuharu OGURA,* Keita UTSUNOMIYA,* Yasushi KITAJIMA** and Isamu NARABAYASHI*

*Department of Radiology and **Third Department of Internal Medicine, Osaka Medical College

Objectives: The ventricular phase angle, a parametric method applied to Fourier phase analysis (FPA) in radionuclide ventriculography, allows the quantitative analysis of ventricular contractile synchrony. However, FPA reproducibility using gated blood pool SPECT (GBPS) has not been fully evaluated. The present study evaluates whether by using GBPS, the reproducibility of FPA could be improved over that in planar radionuclide angiography (PRNA). **Methods:** Forty-three subjects underwent both GBPS and PRNA, of which 10 subjects were normal controls, 25 had dilated cardiomyopathy, and 8 had various heart diseases. Interventricular contractile synchrony was measured as the absolute difference in RV and LV mean ventricular phase angle as $\Delta\theta$ (RV – LV). Intraventricular contractile synchrony was measured as the standard deviation of the mean phase angle for the RV and LV blood pools (RVSD θ , LVSD θ). Two nuclear physicians processed the same phase images of GBPS to evaluate the interobserver reproducibility of the phase angles using data from the 43 study participants. Phase images acquired from PRNA were processed in the same manner. **Results:** Excellent reproducibility of $\Delta\theta$ (RV – LV) was obtained with both GBPS ($Y = -3.10 + 0.89 \cdot X$; $r = 0.901$) and PRNA ($Y = -4.51 + 0.81 \cdot X$; $r = 0.834$). In regard to RVSD θ reproducibility was not adequate with PRNA ($Y = 18.56 + 0.35 \cdot X$; $r = 0.424$), while it was acceptable with GBPS ($Y = 5.22 + 0.85 \cdot X$; $r = 0.864$). LVSD θ reproducibility was superior using both GBPS ($Y = 4.15 + 0.97 \cdot X$; $r = 0.965$) and PRNA ($Y = -0.55 + 0.98 \cdot X$; $r = 0.910$). **Conclusion:** Our results demonstrate FPA obtained using GBPS to be highly reproducible for evaluating $\Delta\theta$ (RV – LV), RVSD θ and LVSD θ , in comparison with the PRNA method. We thus consider GBPS appropriate for evaluating ventricular contractile synchrony.

Key words: Fourier phase analysis, reproducibility, blood pool scintigraphy

INTRODUCTION

PLANAR RADIONUCLIDE ANGIOGRAPHY (PRNA) is considered to be the gold standard for quantifying ejection fraction as well as ventricular synchronous motion by Fourier phase analysis (FPA), which is an objective parametric method of planar imaging that can be useful for detecting abnormal right ventricular (RV) and left ventricular (LV) contraction.^{1–3} Although applied since the 1970s, PRNA presents inherent limitations, such as the overlap of adja-

cent cardiac structures and the imprecise localization of LV and RV abnormalities.^{4,5} Gated blood pool single photon emission tomography (GBPS) is a three-dimensional analog of conventional PRNA, in which many of the limitations of planar PRNA are overcome because of the improved separation of cardiac structures and localization of ventricular abnormalities.^{6–8} Yet, lengthy acquisition and processing times, as well as large data sets have limited the clinical applicability of GBPS. Advances in multidetector gamma cameras and high performance computer systems have recently increased system sensitivity, and have decreased acquisition and processing times to within clinically acceptable limits. In addition, automatic algorithms to calculate LV ejection fraction (LVEF) have been validated. Nevertheless, the

Received June 27, 2003, revision accepted October 14, 2003.

For reprint contact: Itaru Adachi, M.D., Department of Radiology, Osaka Medical College, 2–7 Daigakumachi, Takatsuki 569–8686, JAPAN.

reproducibility of FPA using GBPS has not been fully evaluated. The present study therefore examines whether GBPS can help to improve FPA reproducibility compared with PRNA.

PARTICIPANTS

The study population comprised 10 normal controls and 33 consecutive patients (31 men and 12 women), with a mean age of 52 years (range, 19–75 years) who underwent both GBPS and PRNA. The ten controls had no clinical or electrocardiographic evidence of heart disease. The spectrum of heart disease in the patients included dilated cardiomyopathy ($n = 25$), conduction disturbance ($n = 4$), old myocardial infarction ($n = 2$) and valvular heart disease ($n = 2$). Diagnoses were based on complete evaluations that included electrocardiography, chest X-rays, echocardiography, cardiac catheterization and endomyocardial biopsy. All the patients gave written informed consent to undergo all the procedures associated with the study.

METHODS

All participants were given an injection of 740 MBq technetium 99m-labeled human serum albumin diethylenetriamine-pentaacetic acid (HSA-D, Nihon Medi-Physics Co., Ltd, Japan), following which PRNA and GBPS images were consecutively acquired in a random sequence using the same 3-head gamma camera (GCA-9300; Toshiba, Tokyo, Japan). The GBPS images were acquired using the camera equipped with low-energy, high-resolution collimators. We obtained GBPS data from 64 projections over a 360° full rotation in a 64 × 64 matrix under the following conditions: 1 minute per projection, no acquisition zoom, 140 keV ± 10% energy-acquisition window, 24 gated intervals per cardiac cycle, and ±20% R-R interval-acceptance window. The pixel size at acquisition was 6.8 mm. The projection data were reconstructed by filtered back projection using a Butterworth filter (cutoff frequency, 0.30 cycles/cm; order, 5). Reconstructed slices were reoriented according to the left ventricular long axis. Oblique slices were used as input for both automatic programs and a series of 24 consecutive horizontal long-axis slices was obtained through one cardiac cycle. We performed PRNA with 24 electrocardiography-gated frames, and the beat acceptance window was set at 20% of the average R-R interval obtained just before the start of the acquisition. A left anterior oblique projection (best septal view) was obtained with one head of the 3-head gamma camera used for GBPS. Data were acquired in a 64 × 64 format without a zoom (pixel size, 6.8 mm) until a total density of 4.5 million counts was reached. The images were transferred to a GMS-5500 processing workstation (Toshiba, Tokyo, Japan).

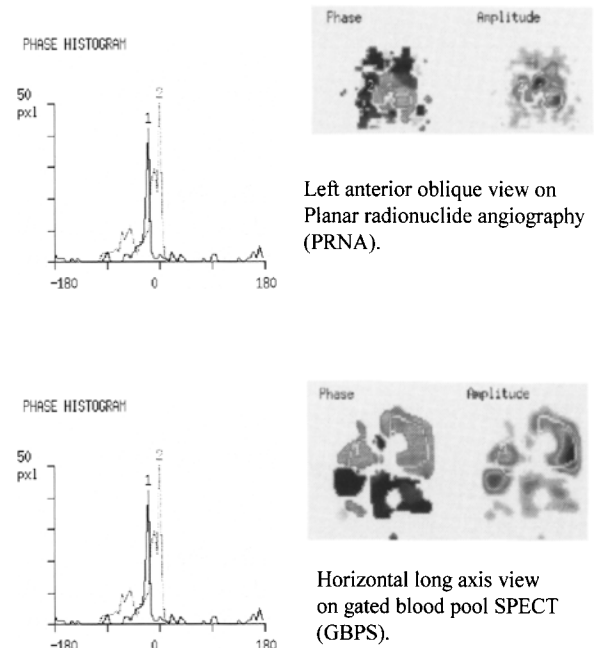


Fig. 1 Examples of Fourier phase analysis with planar radionuclide angiography (PRNA) and with gated blood pool SPECT (GBPS). Upper panel: histogram and right and left ventricular ROIs in PRNA; Lower panel: histogram and right and left ventricular ROIs in GBPS.

Nuclear phase imaging

Phase images were generated from the scintigraphic data derived from the reconstructed GBPS and PRNA images using commercially available software (Toshiba, Tokyo, Japan). Identical scintigraphic data were digitally processed to display the phases for each pixel overlaying the equilibrium blood pool and gated to the ECG R wave. The phase program assigns a phase angle (θ) to each pixel of the phase image, derived from the first Fourier harmonic of the time versus radioactivity curve (a parallel of the ventricular volume curve) fitted to the cardiac cycle. The phase angle corresponds to the relative sequence and pattern of ventricular contraction during the cardiac cycle. Color-coded phase images with corresponding histograms were generated for each participant. Scintigrams were intensity-coded for amplitude, a parameter related to stroke volume, setting background pixels to black (zero amplitude) and providing clear edges to ventricular regions of interest. Pixels overlying cardiac regions below amplitude threshold, corresponding to a low stroke volume, were also set to black. Phase images were generated for cardiac regions above amplitude threshold using a continuous rainbow color wheel corresponding to phase angles from 0 to 360 degrees. To avoid discontinuities of the phase angle display, the entire scale was shifted 180 degrees, placing ventricular ejection at the center of the histogram display. Mean phase angles were computed for RV and LV blood pools as the arithmetic mean phase angle for all pixels in the ventricular region of interest

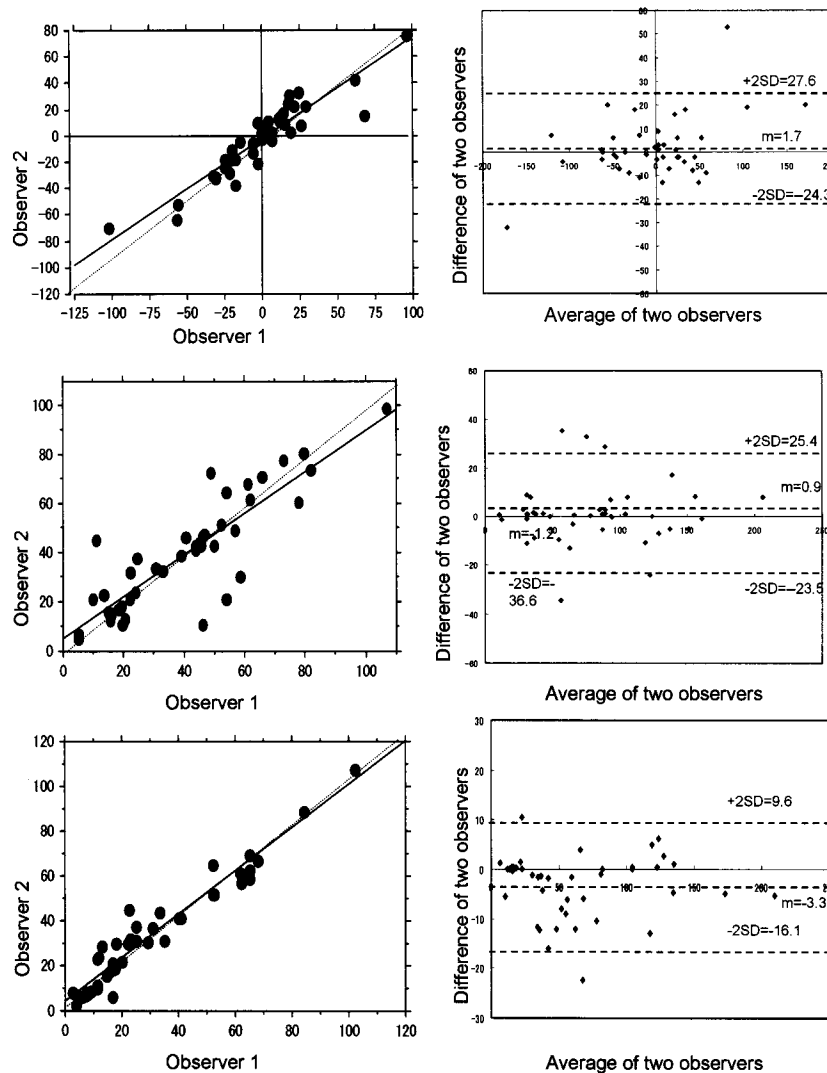


Fig. 2 Linear regression analysis (*left column*) and analysis of the Bland-Altman plots (*right column*) are shown to compare the reproducibility of observations between observers 1 and 2 in GBPS. Upper panel: $\Delta\phi$ (RV - LV); middle panel: RVSD ϕ ; lower panel: LVSD ϕ .

(ROI) which was drawn manually. Interventricular contractile synchrony ($\Delta\phi$ (RV - LV)) was measured as the absolute difference in RV and LV mean phase angles. Intraventricular contractile synchrony was measured as the standard deviation of the mean phase angle for the RV and LV blood pools (RVSD ϕ , LVSD ϕ).⁹ Two nuclear physicians processed the same phase images and positioned the ROIs for both the RV and LV blood pools to evaluate GBPS reproducibility. The phase images obtained by PRNA were also processed, and ROIs were drawn by the same physicians for comparisons of reproducibility of the FPA between GBPS and PRNA. Figure 1 shows examples of phase analysis of PRNA and GBPS.

Data analysis

The interobserver reproducibilities of $\Delta\phi$ (RV - LV), RVSD ϕ and LVSD ϕ were analyzed using linear regression and Bland-Altman plots for the GBPS and PRNA

methods, respectively. Values of $\Delta\phi$ (RV - LV), RVSD ϕ , and LVSD ϕ were compared between GBPS and PRNA using linear regression analysis. A p value <0.05 was considered to denote statistical significance.

RESULTS

Figures 2 and 3 show linear regression analyses of the reproducibility of FPA in GBPS and PRNA, respectively. The reproducibility of $\Delta\phi$ (RV - LV) obtained with both GBPS ($Y = -3.10 + 0.89 \cdot X$; $r = 0.901$) and PRNA ($Y = -4.51 + 0.81 \cdot X$; $r = 0.834$) was excellent. With regard to RVSD ϕ reproducibility, while it was acceptable with GBPS ($Y = 5.22 + 0.85 \cdot X$; $r = 0.864$), it was not adequate with PRNA ($Y = 18.56 + 0.35 \cdot X$; $r = 0.424$). On the other hand, LVSD ϕ reproducibility was excellent with both GBPS ($Y = 4.15 + 0.97 \cdot X$; $r = 0.965$) and PRNA ($Y = -0.55 + 0.98 \cdot X$; $r = 0.910$). Bland-Altman plots did

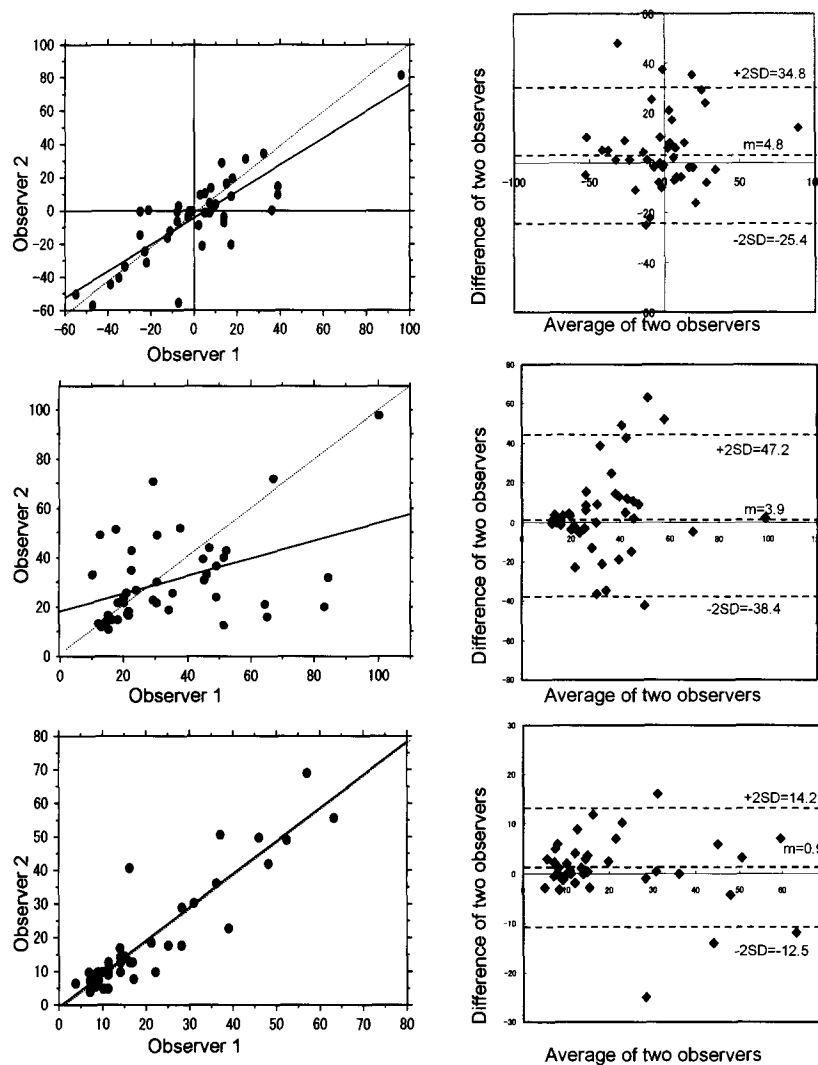


Fig. 3 Linear regression analysis (*left column*) and analysis of the Bland-Altman plots (*right column*) are shown to compare the reproducibility of observations between observers 1 and 2 in PRNA. Upper panel: $\Delta\theta$ (RV – LV); middle panel: RVSD; lower panel: LVSD. Adequate RVSD reproducibility could not be obtained.

not reveal any apparent trends across the complete range of $\Delta\theta$ (RV – LV).

DISCUSSION

We compared the $\Delta\theta$ (RV – LV), RVSD, and LVSD values obtained using GBPS and PRNA, and evaluated the reproducibility of these parameters using FPA. The correlation between the results obtained by GBPS and PRNA was close in terms of the $\Delta\theta$ (RV – LV) and LVSD values obtained, but inadequate in terms of the RVSD values. The reproducibility of each parameter was superior excellent using GBPS.

Applicability of GBPS

PRNA has been in use as the standard method of noninvasive cardiac function assessment since the 1970s.

This noninvasive scintigraphic method is useful for measuring LVEF and ventricular function including RVEF,¹⁰ as well as for detecting regional wall motion in humans without cardiac catheterization over long periods.^{4,5} The three-dimensional analog of conventional PRNA, which is GBPS, can overcome some limitations by improving the separation of cardiac structures and the localization of ventricular abnormalities. Despite these advantages, the clinical use of GBPS has been limited to feasibility studies, mostly because data acquisition is more complex, the amount of data is considerable (compared with planar imaging), and the availability of processing software is limited. However, recent technical refinements in multihead cameras and computers have helped to overcome these technical limitations. The inherently 3-dimensional (3-D) GBPS could replace PRNA for measuring left ventricular ejection fraction (LVEF),

as well as analyzing regional wall motion and right heart function.^{6-8,12-14} Bartlett et al. reported that GBPS-determined LVEF values correlated well with PRNA-determined LVEF values, but in those LVEF values, the former was significantly higher than the latter. This discrepancy is caused by atrial overlap in the planar image and disappears when SPECT slices are reprojected at the same angle of view as the planar images.⁷ Van Kriekinge et al. developed a new algorithm that determined an ellipsoidal coordinate system for the left ventricle and then computed a static estimate of the endocardial surface using counts and count gradients. This algorithm agrees with conventional radionuclide measurements of LVEF and provides the basis for a 3-D analysis of wall motion. This technique is currently the most popular for clinically measuring LVEF, which is considered the most powerful prognostic measure of cardiac function over the spectrum of heart diseases.¹⁵

Fourier phase analysis

FPA is an established, objective parametric means of detecting abnormal RV and LV contraction in PRNA.¹⁻³ The first harmonic Fourier phase of a voxel is closely correlated to the moment at which ejection ends. This parameter is significantly influenced by both the time to myocardial activation and the time to the end of myocardial contraction. The homogeneity of the overall ventricular phase distribution histogram is largely dependent on these two variables, which make a useful objective parametric method with which to detect abnormal ventricular activation or contraction.^{9,16,17} The FPA applicability to planar imaging however, is also limited by overlapping adjacent cardiac structures, and the imprecise localization of LV and RV abnormalities.¹⁸ Many of these limitations can be overcome by improving the separation of cardiac structures and the localization of ventricular abnormalities by GBPS. Therefore, using FPA with GBPS instead of planar imaging might improve its overall diagnostic performance. In the same way that gated tomographic myocardial perfusion imaging is a logical extension of planar myocardial perfusion imaging, GBPS is a logical 3-D extension of PRNA. The present study discovered that the reproducibility of GBPS is superior to that of optimized, high-resolution PRNA in detecting wall motion abnormalities or for measuring FPA. In addition, GBPS can reveal the extent of wall motion abnormalities without the superimposition of other cardiac cavities, adjacent ventricular segments, or vascular structures. Moreover, GBPS can examine the right ventricle, which is impossible with PRNA. Automatic 3-D methods have already been applied to quantitative FPA in GBPS. Vilain et al. have reported that the hybrid or cylindrical and spherical methods with fixed thresholding for the left and right ventricles, respectively, are the optimal means of automatic 3-D FPA measurement in GBPS.¹⁹

Study limitations

Acquisitions of GBPS data could not be performed twice due to the lengthy protocol of both GBPS and PRNA acquisition. Consequently, reproducibility in this study could progress only as far as processing by two observers. We manually positioned ROIs over RV and LV using GBPS images to measure their FPA values. This two-dimensional method was similar to the usual measurement for FPA in PRNA. We decided to not use the automatic 3-D FPA, including automatic contour detection of the ventricle for GBPS, because we wished to assess whether GBPS was superior in terms of the FPA reproducibility to PRNA using the same FPA software. However, we found that the ventricular phase angle for evaluating $\Delta\phi$ (RV - LV), RVSD ϕ and LVSD ϕ obtained using GBPS was more highly reproducible than that obtained using PRNA. While our 2-D processing software was compatible with both PRNA and GBPS, an accurate tracing of the RV could not be obtained to recreate the complex cardiac structure in PRNA. The reproducibility of RVSD ϕ determined by PRNA was poorer, because manual tracing of the ventricular contour and valve planes of the RV was not possible with the software. Elaborate sophisticated techniques for RV and LV surface determination are not required in GBPS unlike in PRNA, because the cardiac surface is easily detected on the functional amplitude and phase images in this technique.

CONCLUSIONS

Our results demonstrated that evaluating $\Delta\phi$ (RV - LV), RVSD ϕ and LVSD ϕ with the FPA value obtained from GBPS is more reproducible than by PRNA. We therefore considered that GBPS is the superior means of evaluating inter and intraventricular dys-synchrony.

REFERENCES

1. Swiryn S, Pavel D, Byrom E, Bauernfeind RA, Strasberg B, Palileo E, et al. Sequential regional phase mapping of radionuclide gated biventricular tachycardia: close correlation with electrophysiologic characteristics. *Am Heart J* 1982; 103: 319-332.
2. Nakajima K, Bunko H, Tada A, Tonami N, Taki J, Nanbu I, et al. Length-based Fourier analysis in the pre-excitation syndrome. *J Nucl Med* 1986; 27: 1131-1137.
3. Links JM, Raichlen JS, Wagner HN Jr, Reid PR. Assessment of the site of ventricular activation by Fourier analysis of gated blood-pool studies. *J Nucl Med* 1985; 26: 27-32.
4. Strauss HW, Zaret BL, Hurley PJ, Natarajan TK, Pitt B. A scintiphotographic method for measuring left ventricular ejection fraction in man without cardiac catheterization. *Am J Cardiol* 1971; 28: 575-580.
5. Zaret BL, Strauss HW, Hurley PJ, Natarajan TK, Pitt BN. A noninvasive scintiphotographic method for detecting regional ventricular dysfunction in man. *Engl J Med* 1971;

- 284: 1165–1170.
6. Mate E, Mester J, Csernay L, Kuba A, Madani S, Makay A. Three dimensional presentation of the Fourier amplitude and phase: a fast display method for gated cardiac blood-pool SPECT. *J Nucl Med* 1992; 33: 458–462.
 7. Bartlett ML, Srinivasan G, Barker WC, Kitsiou AN, Dilsizian V, Bacharach SL. Left ventricular ejection fraction: comparison of results from planar and SPECT gated blood-pool studies. *J Nucl Med* 1996; 37: 1795–1799.
 8. Nichols K, Saouaf R, Ababneh AA, Barst RJ, Rosenbaum MS, Groch MW, et al. Validation of SPECT equilibrium radionuclide angiographic right ventricular parameters by cardiac magnetic resonance imaging. *J Nucl Cardiol* 2002; 9: 153–160.
 9. Kerwin WF, Botvinick EH, O'Connell JW, Merrick SH, DeMarco T, Chatterjee K, et al. Ventricular contraction abnormalities in dilated cardiomyopathy: effect of biventricular pacing to correct interventricular dyssynchrony. *J Am Coll Cardiol* 2000; 35: 1221–1227.
 10. Maddahi J, Berman DS, Matsuoka DT, Waxman AD, Stankus KE, Forrester JS, et al. A new technique for assessing right ventricular ejection fraction using rapid multiple-gated equilibrium cardiac blood pool scintigraphy: description, validation and findings in chronic coronary artery disease. *Circulation* 1979; 60: 581–589.
 11. Groch MW, DePuey EG, Belzberg AC, Erwin WD, Kamran M, Barnett CA, et al. Planar imaging versus gated blood-pool SPECT for the assessment of ventricular performance: a multicenter study. *J Nucl Med* 2001; 42: 1773–1779.
 12. Daou D, Harel F, Helal BO, Fourme T, Colin P, Lebtahi R, et al. Electrocardiographically gated blood-pool SPECT and left ventricular function: comparative value of 3 methods for ejection fraction and volume estimation. *J Nucl Med* 2001; 42: 1050–1052.
 13. Groch MW, Schippers DJ, Marshall RC, Groch PJ, Erwin WD. Quantitative gated blood pool SPECT: Analysis of 3-dimensional models for the assessment of regional myocardial wall motion. *J Nucl Cardiol* 2002; 9: 271–284.
 14. Mariano-Goulart D, Collet H, Kotzki PO, Zanca M, Rossi M. Semi-automatic segmentation of gated blood pool emission tomographic images by watersheds: application to the determination of right and left ejection fractions. *Eur J Nucl Med* 1998; 25: 1300–1307.
 15. Van Krieking SD, Berman DS, Germano G. Automatic quantification of left ventricular ejection fraction from gated blood pool SPECT. *J Nucl Cardiol* 1999; 6: 498–506.
 16. Le Rest C, Couturier O, Turzo A, Guillo P, Bizais Y, Etienne Y, et al. Use of left ventricular pacing in heart failure: evaluation by gated blood pool imaging. *J Nucl Cardiol* 1999; 6: 651–656.
 17. Santomauro M, Fazio S, Ferraro S, Maddalena G, Papaccioli G, Pappone C, et al. Fourier analysis in patients with different pacing modes. *Pacing Clin Electrophysiol* 1991; 14: 1351–1358.
 18. Casset-Senon D, Philippe L, Babuty D, Eder V, Fauchier L, Fauchier JP, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy by Fourier analysis of gated blood pool single photon emission tomography. *Am J Cardiol* 1998; 82: 1399–1404.
 19. Vilain D, Daou D, Casset-Senon D, Faraggi M, Le Guludec D. Optimal 3-dimensional method for right and left ventricular Fourier phase analysis in electrocardiography-gated blood-pool SPECT. *J Nucl Cardiol* 2001; 8 (3): 371–378.