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Comparison of gating methods for the real-time analysis of left ventricular function in nonimaging blood pool studies

Brian B. Beard, PhD, James R. Stewart, MD, Richard G. Shiavi, PhD, and Christine H. Lorenz, PhD

Departments of Biomedical Engineering and Radiology and Radiological Sciences, Schools of Medicine and Engineering, and the Department of Cardiac and Thoracic Surgery, School of Medicine, Vanderbilt University, Nashville, Tenn

Abstract

Background—Gating methods developed for electrocardiographic-triggered radionuclide ventriculography are being used with nonimaging detectors. These methods have not been compared on the basis of their real-time performance or suitability for determination of load-independent indexes of left ventricular function. This work evaluated the relative merits of different gating methods for nonimaging radionuclide ventriculographic studies, with particular emphasis on their suitability for real-time measurements and the determination of pressure-volume loops.

Methods and Results—A computer model was used to investigate the relative accuracy of forward gating, backward gating, and phase-mode gating. The durations of simulated left ventricular time-activity curves were randomly varied. Three acquisition parameters were considered: frame rate, acceptance window, and sample size. Twenty-five studies were performed for each combination of acquisition parameters. Hemodynamic and shape parameters from each study were compared with reference parameters derived directly from the random time-activity curves. Backward gating produced the largest errors under all conditions. For both forward gating and phase-mode gating, ejection fraction was underestimated and time to end systole and normalized peak ejection rate were overestimated. For the hemodynamic parameters, forward gating was marginally superior to phase-mode gating. The mean difference in errors between forward and phase-mode gating was 1.47% (SD 2.78%). However, for root mean square shape error, forward gating was several times worse in every case and seven times worse than phase-mode gating on average.

Conclusions—Both forward and phase-mode gating are suitable for real-time hemodynamic measurements by nonimaging techniques. The small statistical difference between the methods is not clinically significant. The true shape of the time-activity curve is maintained most accurately by phase-mode gating.

Keywords

comparative study; computer simulation; gated blood pool imaging; left ventricular function

Variations in the length of cardiac cycles occur normally in all individuals and have been shown to cause errors in quantitating parameters of left ventricular function from electrocardiographic-gated equilibrium blood pool studies.^{1,2} A number of gating methods have been used for radionuclide scintigraphy: forward gating, backward gating, and various combinations of forward-backward gating. Average time-activity curves are created that reflect changes in left ventricular volume.

These gating methods, which were developed and tested for radionuclide scintigraphy, have also been used for nonimaging detectors with little regard to differences in the methods.^{1,3,4} With nuclear imaging, hundreds of beats are averaged to accumulate a significant number of counts in each pixel of the image. For nonimaging techniques, counts are simultaneously accumulated over the entire left ventricle so a significant number of counts can be reached in a much shorter time. This makes the use of nonimaging techniques feasible for real-time measurement of hemodynamic and pressure-volume relationships.

This work was performed to evaluate the relative merits of forward, backward, and phase-mode gating, used with nonimaging equilibrium blood pool techniques in the presence of heart rate variation. Particular emphasis was placed on their suitability for real-time measurements and the determination of pressure-volume loops. Linear combinations of forward and backward gating are often used in radionuclide scintigraphy to combine the most accurate regions of each. We used pure forward and backward gating in this simulation to help determine those regions. The method of this simulation replicates that used by Juni and Chen⁵ in their study of gating modes for radionuclide scintigraphy; in turn, they relied on approximations of left ventricular time-activity curves presented by Bacharach et al.⁶

MATERIAL AND METHODS

Computer Simulation

Left ventricular time-activity curves were approximated as a series of linear segments (Figure 1, A) with count values every millisecond. These piecewise linear functions were then passed through a 6.3 Hz low-pass filter to produce smooth curves approximating ideal time-activity curves. As with the previous simulation studies for radionuclide scintigraphy, statistical counting noise was not included.^{5,6}

The durations of individual time-activity curves were varied randomly in a normal distribution around a mean of 800 msec, 75 beats/min, with an SD of 10%, 80 msec. This reflects a heart rate variability of approximately 10% of the mean cycle duration.⁷⁻⁹ Based on the work of Hammermeister et al.^{7,8} and Juni and Chen,⁵ 90% of the variation was placed in diastasis (T_4 to T_5) and 10% in the rapid-filling phase (T_3 to T_4). All cycle durations were rounded to the nearest millisecond.

To evaluate the effectiveness of the gating methods in a variety of conditions, three acquisition parameters were considered. The first variable was framing rate or frames per beat. Frame rates of 16, 24, 32, and 40 were considered. The second variable was acceptance window size. Acceptance windows of 10%, 15%, and 20% were considered. The center of the acceptance window was always 800 msec. The third variable, sample size, was the

number of individual time-activity curves (heart beats) summed to compute the average time-activity curve for a study. Only time-activity curves falling within the acceptance window were counted. Sample sizes of 4, 8, 12, 16, and 20 were considered. Studies of all sample sizes were independent in that no study was a subset of any other.

Each randomly generated time-activity curve was provided as an input for all three gating algorithms. Therefore for any combination of acquisition parameters, all the gating algorithms processed the same time-activity curves. For each combination of acquisition parameters, 25 studies were completed for each gating method; this yielded 4500 total studies.

Gating Algorithms

The frame size in any study for both forward and backward gating is a constant time increment. Frame size is determined by dividing the center time of the acceptance window by the frame rate. For forward gating the first frame begins at the R wave trigger, whereas for backward gating the last frame ends at the R wave trigger of the next beat. Each frame's total counts were obtained by summing the simulated counts falling within the frame.

Phase-mode gating was first proposed in 1976 by deGraaf and van Rijk¹⁰ and Leger and Valli¹¹ and investigated by Bacharach et al.¹² in 1990. Phase-mode gating does not maintain a fixed frame size from beat to beat. Frame size is recalculated for each beat by dividing the actual duration of the beat by the frame rate. Instead of each frame being a constant time, it is a constant fraction, or phase, of the cardiac cycle. The assumption implicit in this method is that short beats are linearly compressed copies of longer beats. Although this assumption is violated, in fact^{7,8} and in this simulation,⁵ the effect of the violation is minimal under normal conditions.¹²

All the algorithms produce an averaged time-activity curve, referred to here as the “gated” time-activity curve. The gated time-activity curve has one data point per frame, making its temporal resolution equivalent to the duration of a single frame. A frame rate of 16 produces a gated time-activity curve with values 50 msec apart, because we simulated an average cardiac cycle of 800 msec. It should also be noted that when fluctuations in cardiac cycle length are absent, all three methods produce identical gated time-activity curves.

Hemodynamic Parameters

The following systolic parameters were calculated from the gated time-activity curve for each gating method: time to end systole, ejection fraction, peak ejection rate, and time to peak ejection rate. The calculated diastolic parameters were peak filling rate and time to peak filling rate.

The temporal resolution of the gated time-activity curves was too coarse to calculate the hemodynamic parameters accurately. We increased the temporal resolution to 1 msec by applying a cubic spline curve fit¹³ to the gated time-activity curves. Figure 1, *B* and *C*, illustrates how the parameters were calculated from a curve fit and its derivative. End-systolic count was considered the minimum data point on the time-activity curve, and time to endsystole was its time index. End-diastolic count was considered the maximum data

point on the time-activity curve. All timing parameters were calculated to the nearest millisecond. All rate parameters were normalized to end-diastolic counts.

Error Analysis

Although count rates are not high enough to measure individual beats accurately in real life, it is possible in a simulation with no noise. This simulation computed the actual hemodynamic parameters for every random time-activity curve. Because the simulation did not include noise, calculations could be made safely from the derivative of any random time-activity curve. The means of these actual measurements, for all the random time-activity curves in a study, were used as the reference values for that study. Thus the reference values were not constant but were potentially different for every study. Indeed, with sample sizes as small as 4 beats, the reference values often varied from study to study.

For all three gating methods, the parameters derived from the gated time-activity curves were compared with the reference values. Differences were expressed as percent-ages of the reference values and converted to root mean squared error (RMSE) and bias according to the following formulas:

$$e_i = \frac{p_i - r_i}{r_i} \times 100\%$$

$$\text{Bias} = \frac{1}{N} \left[\sum_{i=1}^N e_i \right]$$

$$\text{RMSE} = \text{SQRT} \left[\frac{1}{N} \left[\sum_{i=1}^N e_i^2 \right] \right]$$

where i = i 'th study for unique combination of acquisition parameters, N = total studies, 25 for each combination of acquisition parameters, e_i = percent error for parameter p in study i , p_i = parameter calculated from study i , r_i = reference value for parameter p in study i , and Bias = error bias.

When used with a left ventricular pressure catheter, equilibrium blood pool studies can be used for pressure-volume loop analysis. However, distortions in the shape of the gated time-activity curve translate directly into distortions in the volume component of the pressure-volume loop. To evaluate the relative distortion caused by the different gating methods, a quantitative measure of distortion had to be devised. This was done as follows: A reference time-activity curve, with one data point per frame, was created by taking the center value from each frame in the average (800 msec) cycle. The reference and gated time-activity curves were normalized by their respective end-diastolic counts, preventing any change in scale from being interpreted as shape distortion. The difference between the normalized time-activity curves in each frame was computed, squared, and summed. The total squared error was divided by the number of frames per beat to yield the squared error per frame. The

square root of the mean squared error per frame produces the shape RMSE as a fraction of end-diastolic counts per frame.

Analysis of variance was carried out to determine which hemodynamic parameters were significantly affected by choice of gating method and which acquisition parameters significantly affected different measured parameters for a given gating method. Multiple linear regressions were done to determine the significance of the effect of the acquisition parameters on the RMSE for the measurement parameters.

RESULTS

Comparing the reference values and all three gating methods, analysis of variance showed an overall significant difference ($p < 0.001$) in the means for all measurement parameters. Further analysis compared the parameter reference values to the means determined by each gating method. For forward and phase-mode gating, the means of all measurement parameters differed significantly from the reference values. For backward gating, the means of all measurement parameters, except time to peak filling rate, differed significantly from the reference values.

Tables 1 and 2 show the mean error and RMS errors for all parameters by the gating method. Not only did backward gating have the highest average error but also for each of the 60 combinations of acquisition parameters, RMSE for all parameters was largest for backward gating. Magnitude of backward gating bias exceeded that of forward gating in 88% of the studies and that of phase-mode gating in 86% of the studies. Therefore further analysis was confined to the difference between forward and phase-mode gating.

The levels of the acquisition parameters were compared by analysis of variance to determine whether the magnitude of an acquisition parameter resulted in a significant difference in any measurement parameter. These results are summarized in Table 3. Frame rate had a significant influence on all measurement parameters for both forward and phase-mode gating.

Tables 4 and 5 summarize the results of the multivariate linear regression analysis for forward and phase-mode gating. This shows the acquisition parameters that have significant effect (regression coefficient less than or more than 0, $p < 0.001$) on the RMSE for each of the output parameters and the direction of that effect (sign of the coefficient).

For the hemodynamic parameters, forward gating was marginally superior to phase-mode gating. The mean difference in errors between forward and phase-mode gating was 1.47%, with an SD of 2.78%.

For shape RMSE, phase-mode gating was the best in every study. The average shape RMSEs, expressed as percent of end-diastolic counts per frame, were: phase mode, $1.51\% \pm 0.52\%$; forward, $10.64\% \pm 1.34\%$; and backward, $12.5\% \pm 1.88\%$.

DISCUSSION

When gating forward from the R wave, time-activity curve distortion occurs at the end of diastole.^{1,2} Gating backward in time from the R wave reduces this problem; however, when gating backward, time-activity curve distortion occurs at the beginning of systole. Phase-mode gating was proposed to spread the distortion caused by heart rate variability evenly over the entire time-activity curve rather than concentrating it at one end of the curve. Figure 2 shows representative time-activity curves formed by each of the gating methods. We hoped phase-mode gating would produce gated time-activity curves that faithfully maintained the shape of the original time-activity curves while producing hemodynamic measurement errors roughly equivalent to those obtained with forward gating.

Ejection fraction was underestimated by all gating methods. This is to be expected because any averaging process, including all three gating methods, flattens out both peaks and valleys.

Our methods of calculating reference values and hemodynamic parameters differed slightly from those used by Juni and Chen.⁵ They used the hemodynamic parameters measured on a single time-activity curve of exactly 800 msec as their reference values.⁵ However, the true mean of any measurement parameter is that formed from the collection of all single-beat values and not that measured from one beat whose duration equals the center of the acceptance window.¹ We used the actual means computed from the random time-activity curves in a study as our references. Juni and Chen determined hemodynamic parameters by applying a second-order (quadratic) curve fit to the gated time-activity curves.⁵ However, Bacharach and Green² note that a third-order (cubic) curve fit captures more information than a quadratic curve fit, whereas increasing the fit to fourth-order curve offers no significant improvement over third-order curves. We applied a cubic spline curve fit to the gated time-activity curves.

Although a particular acquisition parameter may have a significant impact on the mean value of a measurement parameter (Table 3), the same may not be true for the error associated with that parameter (Tables 4 and 5). When we select the acquisition parameters, we are affecting the reference values, as well as the gated time-activity curves. Beats outside the acceptance window are removed from the reference and gated time-activity curves. Framing rate determines the number of data points per beat for all computations, and the same sample size applies to both reference averages and gated time-activity curves. Therefore our reference values are also affected by the acquisition parameters, and the variability in error is reduced. Consider the frame rate: it has a significant effect on all parameters for forward gating, whereas it only has a significant effect on the RMSE for ejection fraction, time to peak ejection rate, and peak filling rate.

As summarized in Table 4, the error performance of forward gating is interesting. The RMSE for three parameters (time to end systole, time to peak filling rate, and peak filling rate) is not significantly affected by any of the acquisition parameters; the error hovers around the values given in Tables 1 and 2. The only acquisition parameter that affects any of the hemodynamic parameters' RMSE is frame rate. Shape error is unaffected by frame rate

but is affected by window and sample size. The effect of the acquisition parameters on the RMSEs for phase-mode gating (Table 4) is more complex. Each of the acquisition parameters has a significant effect on RMSE for three hemodynamic parameters and shape. RMSE for each of the hemodynamic parameters is significantly affected by one or two of the acquisition parameters.

The acquisition parameters in this simulation covered a range of values suitable for real-time measurement according to nonimaging techniques. Real-time measurement should not be confused with instantaneous measurement. By their nature, nuclear measurements must be made over some period and cannot be instantaneous. By real-time measurement we refer to an average over time extending backward from the present. We set the minimum sample size based on experience with our nonimaging detectors, which can achieve 10% counting accuracy in all frames with four beats when count rates are high. Even though other detectors' sensitivities may differ, we thought four beats was a reasonable minimum.

Data accumulation time for real-time measurements should be as short as possible while maintaining acceptable accuracy. Narrow acceptance windows generally decrease error, but they extend the time required to accumulate adequate data. Increased sample size has the same effect. Therefore selection of the acquisition parameters usually involves a compromise between timeliness and accuracy. For forward gating this is not a problem because window and sample size do not have a significant effect on RMSE for any of the hemodynamic parameters. For phase-mode gating, reducing sample time will result in a statistically significant increase in RMSE for all the hemodynamic parameters except time to peak ejection rate; however, for the range of variables used in this simulation, the magnitude of this increase will only be 2% to 5%, within the normal range of clinical accuracy. For pressure-volume loops the compromise between accuracy and timeliness cannot be avoided, because reduced sample time increases shape error for both forward and phase-mode gating.

The difference in RMSE between forward and phase-mode gating is small for all parameters except peak filling rate, where phase-mode gating error predominates. As shown in Table 2, the 1σ error bars overlap for all parameters except peak filling rate. Because statistical counting noise was not included, clinical sample sizes will need to be larger than those implied by this study. Further, in the measurement of hemodynamic parameters, it is likely that counting noise will mask the small statistical differences in these two methods, producing no observable clinical difference.

Leger and Valli¹¹ and deGraaf and van Rijk¹⁰ compared forward and phase-mode gating based on ejection fraction measurements from patient scintigraphic studies. They found that there was no significant difference between the methods. Bacharach et al.¹² also used patient scintigraphy to compare forward and phase-mode gating based on ejection fraction, peak ejection rate, peak filling rate, time to peak ejection rate, and time to peak filling rate. They found that the differences between the methods were not of clinical significance, except for peak filling rate where phase-mode gating produced a greater error than forward gating. They concluded that forward gating is preferred for diastolic measurements when abnormal variations in heart rate are present because the assumption of linearly compressed beats is violated. Our findings are consistent with these conclusions.

No previous investigation has considered the effect of gating mode on the pressure-volume loop. The fall-off seen at the end of forward gating time-activity curves produces a discontinuity in the pressure-volume loop. Phase-mode time-activity curves do not exhibit this fall-off and pressure-volume loops plotted from them are smooth and continuous.

In conclusion, the results of this study indicate that both forward and phase-mode gating are suitable for real-time measurements by nonimaging techniques. Although forward gating is statistically superior for measurement of hemodynamic parameters, this difference is not clinically significant. However, if pressure-volume loops are the main concern the choice is less clear. Phase-mode gating is a more complex algorithm than forward gating; as such it is harder to implement and requires more computer time. The actual effect of time-activity curve distortion on parameters derived from the pressure-volume loop, such as stroke-work and preload recruitable stroke-work, is unclear. It is possible that the relative shape accuracy of phase-mode gating may not provide a clinically significant improvement in the measurement of these secondary parameters. Further study in this area is needed.

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Figure 1.

Time-activity curves used for simulation. Curve *A* is piecewise linear simulated time-activity curve. Smoothing curve *A* with 6.33 Hz low-pass filter creates curve *B*, standard cycle-length (800 msec) curve. Curve *C* is first derivative of curve *B*. Parameters of left ventricular function are calculated from curves *B* and *C*. (*TPER*, time to peak ejection rate; *TPFR*, time to peak filling rate; *TES*, time to end systole; *EF*, ejection fraction; *PFR*, peak filling rate; *PER*, peak ejection rate.)

Figure 2.
Cubic spline curve fits to gated time-activity curves for same acquisition parameters: 24 frames/beat, 15% window, and 12 beats.

Table 1

Bias errors by gating method, over all acquisition parameters

Gating method	Hemodynamic parameters					
	EF	TES	TPER	TPFR	PER/edc	PFR/edc
Phase mode						
Mean (%)	-1.17	2.19	-2.89	-1.16	1.50	-6.76
SD (%)	0.44	0.76	4.90	0.88	1.24	3.86
Forward						
Mean (%)	-0.76	3.04	-2.60	0.29	2.08	1.27
SD (%)	0.46	0.51	5.89	0.94	1.24	3.18
Backward						
Mean (%)	-6.70	4.37	2.47	0.15	-16.62	-24.75
SD (%)	2.74	2.61	15.87	1.50	12.65	7.60

EF; Ejection fraction; TES, time to end systole; TPER, time to peak ejection rate; TPFR, time to peak filling rate; PER/edc, peak ejection rate normalized by end-diastolic counts; PFR/edc, peak filling rate normalized by end-diastolic counts.

Table 2

RMS errors by gating method, over all acquisition parameters

Gating method	Hemodynamic parameters					
	EF	TES	TPER	TPFR	PER/edc	PR/edc
Phase mode						
Mean (%)	1.20	3.44	6.87	3.33	3.30	8.47
SD (%)	0.45	0.87	3.53	1.23	1.14	3.52
Forward						
Mean (%)	0.78	3.07	6.74	1.52	2.62	3.04
SD (%)	0.45	0.51	3.61	1.06	0.86	1.92
Backward						
Mean (%)	7.26	9.46	26.92	6.97	22.46	26.10
SD (%)	2.98	4.04	10.02	2.85	9.89	7.48

See Table 1 for abbreviations.

Table 3

Significance ($p < 0.001$) of differences in measurement parameter means

Analysis groups	Measurement parameters						
	EF	TES	TPER	TPFR	PER/edc	PFR/edc	SHAPE
Forward gating							
Frame rates	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Windows	No	Yes	No	No	No	No	Yes
Sample sizes	No	No	No	No	No	No	Yes
Phase-mode gating							
Frame rates	Yes	Yes	Yes	Yes*	Yes	Yes	Yes
Acceptance windows	Yes	Yes*	No	Yes	No	Yes	Yes
Sample sizes	Yes	Yes	No	Yes	Yes	Yes	Yes

See Table 1 for abbreviations.

* Significant at $p < 0.01$ but not at $p < 0.001$.

Table 4

Significance ($p < 0.001$) of RMSE regression coefficients for forward gating

Acquisition parameters	Measurement parameters						
	EF	TES	TPER	TPFR	PER/edc	PFR/edc	SHAPE
Frame rate	-	0	+	0	0	+	0
Window	0	0	0	0	0	0	+
Sample size	0	0	0	0	0	0	-

See Table 1 for abbreviations.

+, Significant positive coefficient; -, significant negative coefficient; 0, coefficient was not significant.

Table 5

Significance ($p < 0.001$) of RMSE regression coefficients for phase mode

Acquisition parameters	Measurement parameters						
	EF	TES	TPER	TPFR	PER/edc	PFR/edc	SHAPE
Frame rate	-	0	+	0	0	-	-
Window	+	0	0	+	0	+	
Sample size	0	-	0	-	-	0	-

See Tables 1 and 4 for abbreviations.