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Real-Time Three-Dimensional Echocardiography as a Novel Approach to Quantify Left Ventricular Dyssynchrony: A Comparison Study with Phase Analysis of Gated Myocardial Perfusion Single Photon Emission Computed Tomography

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Abstract

Background—Different imaging modalities have been explored for assessment of left ventricular (LV) dyssynchrony. Gated myocardial perfusion single photon emission computed tomography (GMPS) with phase analysis is a reliable technique to quantify LV dyssynchrony and predict response to cardiac resynchronization therapy.

Objective—Real-time 3-dimensional echocardiography (RT3DE) is a novel imaging technique that provides a LV systolic dyssynchrony index, based on regional volumetric changes as a function of time and calculated as the SD of time to minimum systolic volume of 16 standard myocardial segments expressed in percentage of cardiac cycle. The aim of this study was to compare LV dyssynchrony evaluated with GMPS with LV dyssynchrony assessed with RT3DE.

Methods—The study population consisted of 40 patients with heart failure who underwent both GMPS and RT3DE.

Results—Good correlations between LV dyssynchrony assessed with RT3DE and GMPS were demonstrated ($r = 0.76$ for histogram bandwidth, $r = 0.80$ for phase SD, $P < .0001$). Patients with substantial LV dyssynchrony on GMPS (defined as ≥ 135 degrees for histogram bandwidth and ≥ 43 degrees for phase SD) had significantly higher LV systolic dyssynchrony index than patients without substantial LV dyssynchrony.

Conclusions—The good correlations between LV dyssynchrony assessed with GMPS and with RT3DE provide further support for the use of RT3DE for reliable assessment of LV dyssynchrony.

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Keywords

Three-dimensional echocardiography; Left ventricular dyssynchrony; Heart failure; Left ventricular function; SPECT

Patients with heart failure, depressed left ventricular (LV) function, and wide QRS complex may benefit from cardiac resynchronization therapy (CRT). Previous studies have shown that the presence of LV dyssynchrony is important for the response to CRT.¹ Different imaging modalities have been explored for assessment of LV dyssynchrony, including echocardiography,^{2,3} magnetic resonance imaging (MRI),⁴ and gated myocardial perfusion single photon emission computed tomography (GMPS) with phase analysis.^{5,6} A 3-dimensional (3D) technique may be preferred because these techniques provide information on LV dyssynchrony in the entire LV. In addition, reliable information on LV ejection fraction (LVEF) can simultaneously be obtained. Recently, a novel echocardiographic technique has emerged for the assessment of LV dyssynchrony: real-time 3D echocardiography (RT3DE).⁷ This technique allows accurate quantification of LV volumes and LVEF⁸⁻¹⁰ and functional assessment of 16 LV segments. In addition, a LV systolic dyssynchrony index (SDI), based on analysis of regional volumetric changes, can be derived from RT3DE to quantify the severity of LV dyssynchrony.⁷

Initial results with RT3DE for assessment of LV dyssynchrony are promising but further validation is needed. In the current study, assessment of LV dyssynchrony by RT3DE was compared with GMPS using phase analysis. Phase analysis is a count-based method that extracts the phase from the regional LV count changes during the cardiac cycle. Phase information is related to the onset of mechanical contraction in the 3D myocardial wall and, therefore, provides information on the synchrony of the contraction of the LV.¹¹⁻¹³ This approach provides important information on the presence of LV dyssynchrony in patients with heart failure and can predict response to CRT.^{5,6}

The aim of the current study was to investigate how LV dyssynchrony as evaluated with phase analysis with GMPS relates with LV dyssynchrony as assessed with RT3DE. Assessment of LVEF with both techniques was also compared.

METHODS

Patients and Study Protocol

The study population consisted of 40 consecutive patients with drug-refractory heart failure, who were referred to our heart failure outpatient clinic for evaluation of therapeutic options (eg, medical therapy, surgery, CRT).

In all patients, GMPS was performed to exclude inducible ischemia or viability, and to refer patients to revascularization if indicated.^{14,15} In addition, phase analysis was used to evaluate the presence of LV dyssynchrony. All patients also underwent RT3DE for assessment of LV volumes and function, and LV dyssynchrony. Thereafter, LV dyssynchrony measured with RT3DE was compared with LV dyssynchrony measured with phase analysis.

Patients' clinical status was evaluated by assessment of New York Heart Association (NYHA) functional class, exercise capacity (using the 6-minute walk test), and quality-of-life score (using the Minnesota quality-of-life questionnaire).

GMPS

Resting GMPS with technetium-99m tetrofosmin (500 MBq, injected at rest) was performed using a triple-head single photon emission computed tomography camera system (GCA 9300/HG, Toshiba Corp, Tokyo, Japan) equipped with low-energy high-resolution collimators. A 20% window around the 140-keV energy peak of technetium-99m tetrofosmin was used. A total of 90 projections (step and shoot mode, 35 s/projection, imaging time 23 minutes) was obtained over a 360-degree circular orbit. GMPS acquisition involved 16 frames per cardiac cycle with an average temporal resolution of 45 milliseconds. Data were stored in a 64×64 matrix. Data were reconstructed by filtered back projection and then reoriented to yield gated short-axis images. The reconstruction was performed over 360 degrees and took generally 3 to 5 minutes. LVEF was assessed from the gated short-axis images using previously validated and commercially available automated software (quantitative gated single photon emission computed tomography, QGS, Cedars-Sinai Medical Center, Los Angeles, CA).¹⁶

All studies were then submitted to the Emory Cardiac Toolbox for phase analysis.¹¹ A phase distribution was extracted from a GMPS study, representing the regional onset of mechanical contraction of the LV. It can be displayed in a polar map or in 3D and used to generate a phase histogram.

Two quantitative indices have been recently validated to assess LV dyssynchrony with phase analysis and to predict response to CRT^{5,6}: (1) histogram bandwidth, which includes 95% of the elements of the phase distribution; and (2) phase SD, which is the SD of the phase distribution. In a normal heart LV contraction is homogeneous and phase distribution is nearly uniform with a highly peaked distribution. As the LV mechanical synchrony worsens, histogram bandwidth and phase SD are expected to increase. Based on previous work,⁶ we applied a cut-off value of 135 degrees for histogram bandwidth and of 43 degrees for phase SD to define substantial LV dyssynchrony.

RT3DE

Acquisition of the 3D data set—Patients were imaged in left lateral decubitus position with a commercially available system (iE33, Philips Medical Systems, Bothell, WA) equipped with X3, fully sampled matrix transducer. Apical full-volume data sets were obtained in all patients. The acquisition of all images could be completed in approximately 5 minutes in all patients.

For the evaluation of LV volumes and LVEF, the lowest scan line density was used and gain and compression were adjusted to obtain a good image quality and a clear endocardial border. With dedicated software (Large Volume Size, Vision 2007, Philips Medical Systems) 4 small real-time subvolumes were acquired from alternate cardiac cycles and combined to provide a larger pyramidal volume (up to 103×103 degrees) and to ensure a complete capture of the LV. The acquisition was performed during end-expiratory phase of one breath hold and with a relatively stable heart rate to minimize translation artefacts among the 4 subvolumes.

For the evaluation of LV dyssynchrony the frame rate was optimized by reducing the depth and by the acquisition of a full-volume data set of 7 subvolumes with an average temporal resolution of 30 milliseconds.

Assessment of LV volumes and LVEF—RT3DE data sets were stored digitally and quantitative analysis of the 3D data was performed offline using a semiautomated contour tracing algorithm (Q-Lab, Version 5.0, Philips Medical Systems) over a complete heart

cycle. The echocardiographic examination and the offline analysis were performed by the same experienced echocardiographer, blinded to the GMPS and clinical data.

After first identifying the apex and mitral annulus on end-diastolic and end-systolic slices, a preconfigured ellipse was fitted to the endocardial border for each frame. The endocardial border definition was optimal in most of patients and, in case of a suboptimal automated contour tracing, manual adjustments were performed (in 12 of 40 patients). A 3D model of the LV was then generated and LV volumes and LVEF fraction were provided (Figure 1). Papillary muscles were included in the LV cavity. The postprocessing of the images required between 2 and 5 minutes.

Assessment of LV dyssynchrony—The LV 3D model was subdivided in 16 pyramidal subvolumes based around a nonfixed central point (6 basal segments, 6 mid segments, and 4 apical segments). For the whole LV and for each volumetric segment, it was possible to derive time-volume data for the entire cardiac cycle and assess the time taken to reach the minimum systolic volume (Tmsv). As previously described by Kapetanakis et al,⁷ the SD of 16-segment Tmsv expressed in percentage of cardiac cycle (SDI) was calculated. Parametric images, derived from more than 800 virtual waveforms, were also provided by the software (Q-Lab, Version 5.0, Philips Medical Systems) with a visual presentation (polar plot) of LV regional contraction timings. The global Tmsv was used as timing reference and coded in green. Early segments were coded in blue, whereas late segments were coded in red/yellow (Figure 2) allowing a rapid identification of the area of latest activation.

Reproducibility of the RT3DE measurements—Twenty patients were selected to evaluate the interobserver and intraobserver agreement for the analysis of LVEF and LV dyssynchrony. Bland-Altman analysis was performed to evaluate agreement between observer 1 and observer 2 to determine interobserver agreement. An excellent agreement was found with a mean difference for SDI and LVEF of $0.1 \pm 2\%$ ($P =$ not significant [NS]) and $0.4 \pm 3\%$ ($P =$ NS), respectively. Similarly, the 3D measurements derived by the first observer were compared (Bland-Altman analysis) with the results calculated by the same operator 1 month later. The intraobserver agreement was excellent with average differences of $0.03 \pm 0.4\%$ ($P =$ NS) for SDI and $0.8 \pm 2\%$ ($P =$ NS) for LVEF.

Statistical Analysis

Continuous data are presented as mean $\pm$ SD. Categorical data are presented as absolute number or percentages. Unpaired and paired Student t test, Mann-Whitney test, and χ^2 test were used for appropriate comparisons. Pearson's correlation analysis was performed to evaluate the relation between LV dyssynchrony (SDI) by RT3DE and histogram bandwidth and phase SD by the phase analysis of GMPS. A similar approach was used to compare assessment of LVEF by RT3DE and GMPS together with the Bland-Altman analysis that was performed to evaluate the mean difference between the two techniques. A P value less than .05 was considered to be statistically significant. A statistical software program (SPSS 12.0, SPSS Inc, Chicago, IL) was used for statistical analysis.

RESULTS

Patient Characteristics

Baseline characteristics of the study population (32 men; mean age 62 ± 10 years) are summarized in Table 1. Most patients had ischemic cause of cardiomyopathy (75%) and 68% of patients were in NYHA functional class III. Mean QRS duration was 135 ± 33 milliseconds. Patients had severe LV dysfunction and dilatation (mean LVEF $29 \pm 7\%$, mean LV end-diastolic volume 223 ± 70 mL).

The correlation between LVEF assessed with GMPS and RT3DE was good ($r = 0.84$ [$r^2 = 0.7$, $P < .0001$]). The Bland-Altman analysis revealed a small, but nonsignificant difference in the value of LVEF measured with RT3DE and GMPS: GMPS LVEF was $0.8 \pm 8\%$ lower than RT3DE LVEF ($P = \text{NS}$) (Figure 3).

LV Mechanical Dyssynchrony

The mean value of SDI in the study population was $7.8 \pm 4.8\%$, whereas from phase analysis the mean value of histogram bandwidth was 149 ± 73 degrees and the mean value of phase SD was 46.0 ± 21.7 degrees. A good correlation was observed between SDI and LV dyssynchrony assessed with phase analysis. Pearson's correlation coefficient was 0.76 ($r^2 = 0.58$) for histogram bandwidth ($P < .0001$) and 0.80 ($r^2 = 0.64$) for phase SD ($P < .0001$) (Figure 4). Based on previous work,⁶ we applied a cut-off value of 135 degrees for histogram bandwidth and of 43 degrees for phase SD to define substantial LV dyssynchrony. Considering the value of histogram bandwidth, 21 patients (52%) had substantial LV dyssynchrony (defined as ≥ 135 degrees). No significant differences in baseline echocardiographic characteristics were found between patients with and without substantial LV dyssynchrony (Table 2), except that SDI was higher in patients with histogram bandwidth greater than or equal to 135 degrees: $10.4 \pm 5.1\%$ versus $4.8 \pm 1.8\%$ ($P < .0001$) (Figure 5, A). Considering phase SD, 19 patients (48%) had substantial LV dyssynchrony (defined as ≥ 43 degrees) and these patients had a significantly higher value of SDI as compared with patients without substantial LV dyssynchrony: $11.2 \pm 4.8\%$ versus $4.7 \pm 1.9\%$ ($P < .0001$) (Figure 5, B).

The relatively low percentage of patients with substantial LV dyssynchrony may be partially explained by the characteristics of the study population that consists of patients with heart failure and varying degrees of LV dysfunction and both wide and narrow QRS complexes.

LV Systolic Function Versus LV Mechanical Dyssynchrony

Of the 40 patients included, 22 (55%) had LVEF less than or equal to 30%, assessed by RT3DE, whereas 18 patients (45%) had LVEF greater than 30%. No significant difference in LV dyssynchrony, measured with both RT3DE and phase analysis, was noted between the two groups. Histogram bandwidth was 148 ± 67 degrees in patients with LVEF less than or equal to 30% and 150 ± 81 degrees in patients with LVEF greater than 30% ($P = \text{NS}$); phase SD was 45.1 ± 18.3 degrees in patients with LVEF less than or equal to 30% and 47.0 ± 25.8 degrees in patients with LVEF greater than 30% ($P = \text{NS}$); accordingly SDI was $6.9 \pm 3.0\%$ in patients with LVEF less than or equal to 30% and $8.8 \pm 6.3\%$ in patients with LVEF greater than 30% ($P = \text{NS}$).

Correlations between GMPS variables histogram bandwidth and phase SD, and SDI were slightly better for patients with LVEF greater than 30% (histogram bandwidth: $y = 0.0662x - 1.1875$, $r = 0.85$ [$r^2 = 0.72$]; and phase SD: $y = 0.2101x - 1.1238$, $r = 0.86$ [$r^2 = 0.74$]) as compared with patients with LVEF less than or equal to 30% (histogram bandwidth: $y = 0.0305x + 2.4374$, $r = 0.69$ [$r^2 = 0.48$]; phase SD: $y = 0.1185x + 1.5864$, $r = 0.73$ [$r^2 = 0.53$]).

DISCUSSION

The findings in the current study support the use of RT3DE for assessment of LV dyssynchrony; assessment of LV dyssynchrony according to RT3DE using SDI correlated well with previously validated nuclear imaging techniques for assessment of LV dyssynchrony. In particular, SDI by RT3DE correlated well with histogram bandwidth and phase SD by GMPS phase analysis.

In addition, both techniques can assess the LVEF with high accuracy, and the correlation between both modalities for assessing LVEF in the current study was good ($r = 0.84$, $P < .0001$) with a small, nonsignificant difference (mean difference $0.8 \pm 8\%$).

LV dyssynchrony appears important in the response to CRT. Many techniques have been used to assess LV dyssynchrony and to predict response to CRT. For example, Doppler tissue imaging has been used for assessing longitudinal myocardial velocities and strain, and speckle tracking focuses on the evaluation of radial strain.^{2,17} Other nonechocardiographic techniques for assessment of LV dyssynchrony include GMPS with phase analysis^{5,6} and velocity-encoded MRI.⁴ However, all these techniques have their disadvantages: echocardiographic techniques only allow assessment of dyssynchrony in a 2-dimensional setting, GMPS with phase analysis involves radiation, and velocity-encoded MRI cannot be applied after CRT implantation. The optimal modality would be a 3D approach that combined all the different components of myocardial contraction (longitudinal, radial, circumferential) that is also suitable for repeated imaging without imposing a radiation burden. RT3DE is a novel echocardiographic technique that appreciates radial, longitudinal, and circumferential timing of the myocardium. Moreover, it permits identification of the area of latest mechanical activation and accurate assessment of LV function and size without imposing a radiation burden. Recently, Kapetanakis et al⁷ studied the feasibility of LV dyssynchrony assessment with RT3DE in a large group of patients and control subjects. The authors developed an index (SDI) to quantify LV dyssynchrony with RT3DE by calculating the time to reach minimum regional volume for each segment as a percentage of the cardiac cycle. The SDI was defined as the SD of the timings of all 16 segments. After classifying patients according to their LV systolic function or dysfunction (normal with LVEF $>50\%$, mild dysfunction with LVEF $40\%–49\%$, moderate dysfunction with LVEF $30\%–39\%$, and severe dysfunction with LVEF $<30\%$), the authors were able to show significant differences in SDI among these 4 groups. In addition, 26 patients were referred for CRT implantation. It was observed that responders to CRT had significantly higher SDI at baseline than the nonresponders ($16.6 \pm 1.1\%$ vs $7.1 \pm 2.0\%$, $P < .001$). After a mean follow-up of 10 ± 1 months, a reduction in SDI could be demonstrated in the responders to CRT, whereas an increase in SDI was observed in the nonresponders. Although these results are promising, only a moderate correlation could be detected for SDI and the SD of the maximum sustained systolic velocity as assessed with Doppler tissue imaging ($r = 0.38$). These observations are in line with data reported by Burgess et al,¹⁸ who compared RT3DE and TDI for the assessment of LV dyssynchrony in 100 patients with ischemic cardiomyopathy. The authors hypothesized that the poor correlation between these two techniques could be in part explained by the respective assessment of longitudinal versus radial timing.

In the current study, the performance of RT3DE for assessment of LV dyssynchrony was compared with phase analysis with GMPS in patients with heart failure and varying degrees of LV dysfunction and both wide and narrow QRS complexes.

Table 3 provides a head-to-head comparison between the two techniques from a technical point of view. The temporal resolution of GMPS is perceived to be slightly lower as compared with echocardiography. Both techniques use the first harmonic Fourier approximation to improve the temporal resolution. The first harmonic Fourier approximation can enhance phase calculation if it is applied to data with lower temporal resolution by transforming discrete data points into a continuous curve. For GMPS phase analysis only the systolic portion of the data is used to determine the phase. By fitting the curve closely with the systolic data points, the artifactual phase difference resulting from a lower temporal resolution is importantly reduced.⁶

Although phase analysis with GMPS measures the regional onset of mechanical contraction and RT3DE the regional Tmsv, both techniques evaluate the regional changes with a 3D approach, combining all the different components of myocardial contraction. A good correlation between RT3DE and phase analysis with GMPS was demonstrated for the assessment of LV dyssynchrony ($r = 0.76$ for histogram bandwidth, $r = 0.80$ for phase SD).

A good correlation between the two techniques was also found for LVEF assessment. However, the correlation coefficient ($r = 0.84$) was somewhat lower as compared with other validation studies between RT3DE and cardiac MRI ($r = 0.9$),^{19,20} although Jenkins et al²¹ found a correlation coefficient of 0.81, which is fairly in line with our results.

Several limitations of the current study need attention. The patient cohort was relatively small, and larger populations need to be studied.

Moreover, as we compared two different techniques, the basis of regional myocardial dyssynchrony was fundamentally different: GMPS considers the onset of mechanical contraction whereas RT3DE assesses the timing of minimum systolic volume. Regardless of this difference, the current study shows that both techniques seem to correlate fairly well ($r = 0.76$ for histogram bandwidth and $r = 0.80$ for phase SD).

In the current study, follow-up data after CRT implantation were not available.

A more general limitation is the radiation burden of GMPS, which renders the technique less suitable for repeated imaging.

CONCLUSIONS

The current findings demonstrate that LV dyssynchrony assessed by RT3DE correlated well with histogram bandwidth and phase SD derived from phase analysis and GMPS. The correlation between LVEF derived from both techniques was also good. These findings provide further support for the use of RT3DE for reliable assessment of LV dyssynchrony.

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Figure 1.
Example of 3-dimensional (3D) left ventricular (LV) volumes and LV ejection fraction generated by postprocessing of real-time 3D echocardiography data set, acquired in patients with heart failure.

Figure 2.

Example of patient with severe left ventricular dyssynchrony on both real-time 3-dimensional echocardiography (RT3DE) and phase analysis with gated myocardial perfusion single photon emission computed tomography. (A), Polar map generated by postprocessing of RT3DE data set. Early activated segments are coded in *blue*, whereas late activated segments are coded in *red/yellow*, allowing rapid identification of area of latest activation. This patient had systolic dyssynchrony index of 16.4%. (B), In same patient, histogram distribution generated by phase analysis displaying nonuniform and widespread distribution (early activated segments in *blue*, late activated segments in *yellow*). This patient had histogram bandwidth of 257 degrees and phase SD of 77.7 degrees.

Figure 3.

Bland-Altman scatter plot of differences in left ventricular ejection fraction (*LVEF*) between real-time 3-dimensional echocardiography (*RT3DE*) and gated myocardial perfusion single photon emission computed tomography (*GMPS*) and average LVEF between two techniques: GMPS LVEF is $0.8 \pm 8\%$ lower than RT3DE LVEF ($P =$ not significant).

Figure 4.

(A), Correlation between histogram bandwidth assessed with phase analysis of gated myocardial perfusion single photon emission computed tomography (GMPS) and left ventricular (LV) dyssynchrony assessed with real-time 3-dimensional echocardiography (RT3DE) (systolic dyssynchrony index [SDI]). (B), Correlation between phase SD by phase analysis of GMPS and LV dyssynchrony assessed with RT3DE (SDI).

Figure 5.

(**A**), Left ventricular (LV) dyssynchrony assessed with real-time 3-dimensional echocardiography (RT3DE) (systolic dyssynchrony index [SDI]) is significantly higher in patients with substantial LV dyssynchrony on phase analysis, using cut-off value for histogram bandwidth of 135 degrees as previously described.⁶ (**B**), LV dyssynchrony assessed with RT3DE (SDI) is significantly higher in patients with substantial LV dyssynchrony on phase analysis, using cut-off value for phase SD of 43 degrees as previously described.⁶

Table 1

Baseline characteristics of the study population (n = 40)

Age (y)	62 ± 10
Male/female	32/8
NYHA class, n (%)	2.7 ± 0.5
I	0
II	13 (32)
III	27 (68)
IV	0
6-MWT (m)	354 ± 118
QoL score	29 ± 15
QRS duration (ms)	135 ± 33
Origin, n (%)	
Ischemic	30 (75)
Idiopathic	10 (25)
LVEF (%)	29 ± 7
LVEDV (mL)	223 ± 71
LVESV (mL)	159 ± 61
Histogram bandwidth (degrees)	149 ± 73
Phase SD (degrees)	46 ± 22

LVEDV, Left ventricular end-diastolic volume; *LVEF*, left ventricular ejection fraction; *LVESV*, left ventricular end-systolic volume; *6-MWT*, 6-minute walk test; *NYHA*, New York Heart Association; *QoL*, quality of life.

Table 2

Baseline characteristics of patients with and without substantial left ventricular dyssynchrony assessed by histogram bandwidth and phase SD from phase analysis

	Histogram bandwidth <135 degrees (n = 19)	Histogram bandwidth ≥135 degrees (n = 21)	P value
Ischemic origin, n (%)	12 (63)	18 (86)	NS
LVEF (%)	29 ± 7	30 ± 8	NS
LVEDV (mL)	229 ± 69	219 ± 74	NS
LVESV (mL)	164 ± 59	155 ± 63	NS
SDI (%)	4.8 ± 1.8	10.4 ± 5.1	<.0001
	Phase SD <43 degrees (n = 21)	Phase SD ≥43 degrees (n = 19)	
Ischemic origin, n (%)	13 (62)	17 (89)	NS
LVEF (%)	29 ± 7	30 ± 8	NS
LVEDV (mL)	224 ± 68	223 ± 76	NS
LVESV (mL)	161 ± 59	157 ± 64	NS
SDI (%)	4.7 ± 1.9	11.2 ± 4.8	<.0001

LVEDV, Left ventricular end-diastolic volume; *LVEF*, left ventricular ejection fraction; *LVESV*, left ventricular end-systolic volume; *NS*, not significant; *SDI*, systolic dyssynchrony index assessed with real-time 3-dimensional echocardiography.

Table 3

Head-to head comparison between gated myocardial perfusion single photon emission computed tomography and real-time 3-dimensional echocardiography from a technical point of view

	GMPS	RT3DE
Mean imaging time	23 min	5 min
Mean postprocessing time	3–5 min	2–5 min
Mean temporal resolution	45 ms	30 ms
Mean frame rate	16 frames/cycle	20–35 frames/s
LV dyssynchrony assessment	Regional time-to-onset of mechanical contraction	Regional time-to-minimum systolic volume
LV dyssynchrony parameter	Histogram bandwidth Phase SD	SDI

GMPS, Gated myocardial perfusion single photon emission computed tomography; *LV*, left ventricular; *RT3DE*, real-time 3-dimensional echocardiography; *SDI*, systolic dyssynchrony index.