

# Left Ventricular Dyssynchrony Parameters Measured by Phase Analysis of Post-stress and Resting Gated SPECT Myocardial Perfusion Imaging

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## Abstract

Phase analysis has been validated to measure left ventricular (LV) dyssynchrony from resting gated SPECT myocardial perfusion imaging (MPI). In 1-day rest/stress protocols, often only post-stress gated data are acquired. The purpose of this study was to determine whether LV dyssynchrony parameters measured at post-stress significantly differ from those measured at rest. Sixty normal subjects, 40 patients with stress-induced ischemia but normal LV function, and 29 patients with LV dysfunction were included in this study. All patients were scanned using a 2-day Technetium-99m sestamibi (MIBI) MPI protocol, where gated SPECT data were acquired at 60 min post injection of the radiotracer. LV dyssynchrony parameters at post-stress and at rest were calculated and compared using paired *t*-test. There were no significant differences in the LV dyssynchrony parameters between post-stress and resting in all cohorts. No patient showed differences in the LV dyssynchrony parameters between the post-stress and resting scans significantly greater than the reported variations in these parameters between serial resting scans. There was no significant difference in dyssynchrony parameters measured at rest and 60 min after stress on MPI gated images.

**Keywords:** Left ventricular dyssynchrony, myocardial perfusion imaging, phase analysis

## Introduction

Phase analysis has been developed to assess left ventricular (LV) dyssynchrony based on gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI).<sup>[1]</sup> It has been shown that the LV dyssynchrony parameters (phase standard deviation (PSD) and phase histogram bandwidth (PHB)) measured by phase analysis correlate well with those measured by tissue Doppler imaging,<sup>[2-4]</sup> and predicted response to cardiac resynchronization therapy (CRT) in heart failure (HF) patients.<sup>[5]</sup> Recently, phase analysis has shown to be able to identify the site of latest mechanical

activation as the optimal LV pacing lead position.<sup>[6]</sup> In the above validation studies, all gated SPECT images were acquired using resting Technetium-99m (Tc-99m) gated SPECT MPI protocols.

In practice, most of the Tc-99m MIBI SPECT MPI scans are performed using same-day resting/stress protocols, where the resting data are acquired using a relatively low dose as compared to the stress data, and many centers only acquire gated SPECT data at stress. Presumably, the high-count gated SPECT data acquired post-stress can provide better quantification of LV function. However, it has been shown that in patients with an earlier myocardial infarction, LV function post-stress might not represent the true resting LV function.<sup>[7]</sup> Consequently, this study suggested the stratification of patients before starting gated SPECT MPI, meaning in patients with an earlier myocardial infarction, the gated acquisition should be performed during the resting study. In another study, post-stress LV ejection fraction (LVEF) reduced and end-systolic

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volume and end-diastolic volume increased in patients with stress-induced ischemia.<sup>[8]</sup> However, the effect of ischemia on the difference between post-stress and resting LV function measurements was modest and rarely exceeded the confidence limits in normal patients undergoing 2-day protocols.<sup>[9]</sup> There is a recent study enrolling 20 patients with reversible perfusion defects involving >10% of the LV myocardium and 20 normal subjects to show that there was no significant change from rest to stress in the LV dyssynchrony parameters between the two groups.<sup>[10]</sup> It is important to note that all of the subjects in this study had normal LVEF. The impact of stress on LV dyssynchrony parameters was not evaluated in patients with LV dysfunction.

The purpose of this study was to determine whether LV dyssynchrony parameters (PSD and PHB) measured at post-stress significantly differ from those measured at rest in normal subjects, patients with stress-induced ischemia but normal LVEF, and patients with LV dysfunction.

## Materials and Methods

### Patients

The study retrospectively analyzed gated SPECT MPI data acquired from July 2008 to January 2010. Sixty normal subjects (30 underwent exercise stress and 30 underwent adenosine stress), 40 patients with stress-induced ischemia but normal LV function (LVEF >50%, 20 underwent exercise stress and 20 underwent adenosine stress), and 29 patients with LV dysfunction (LVEF <50%, 19 underwent exercise stress and 10 underwent adenosine stress) were included in this study. Table 1 summarizes the characteristics of the three cohorts. Stress-induced ischemia was considered in the presence of reversible myocardial perfusion defect at stress. Among the 29 patients with LV dysfunction, 14 had ischemic cardiomyopathy (including 10 patients with myocardial infarction) and 15 patients had non-ischemic cardiomyopathy. The study protocol was approved by the institutional review board (IRB).

### Acquisition and processing

A 2-day MIBI SPECT MPI protocol was used in this study. Patients who had exercise stress underwent a symptom-limited treadmill test using standard Bruce protocol. MIBI was intravenously injected when a  $\geq 85\%$  heart rate was achieved. Exercise was continued at the workload for 1.5-2.0 min when possible. Patients who had adenosine stress were infused with adenosine at 140  $\mu\text{g}/\text{kg}/\text{min}$  for 5 min and MIBI was injected at the end of the second minute. Tc-99m Sestamibi doses ranged from 25 to 30 mCi depending on the patients' weight or body mass indices.

A Philips CardioMD system (Philips Medical Systems, Milpitas, CA, USA) was used to acquire all post-stress and resting scans with 20% energy windows around 140 keV. A total of 64 projections (24 sec/projection, total acquisition time of 14 min) were obtained over a 180° circular orbit. The gated SPECT data were acquired as eight frames per cardiac cycle. Data were stored in a 64-64 matrix with 6.4 mm/pixel.

All of the gated SPECT data were reconstructed using a manufacturer-provided filtered backprojection program (AutoSPECTPlus™, Philips Medical Systems). All reconstructed data were reoriented to generate gated short-axis images and then submitted to phase analysis to calculate PSD and PHB.<sup>[1]</sup> The post-stress and resting images were processed side-by-side by an experienced technologist, who was blinded from this research project.

### Statistical analysis

Paired *t*-test (two-tailed) and Bland-Altman plot were used to compare the post-stress and resting PSD and PHB in the three cohorts, respectively. A  $P < 0.05$  was considered statistically significant.

## Results

Table 2 shows the LV dyssynchrony parameters in the three cohorts. In normal subjects, although it showed a trend that LV dyssynchrony parameters acquired from stress scans were smaller than those from resting

Table 1: Patient characteristics

	Normal subjects (n=60)	Patients with ischemia (n=40)	Patients with LV dysfunction (n=29)
Age (years)	60.3±18.3	60.9±10.2	61.8±9.5
Male (%)	55	67.5	82.5
Diabetes mellitus (%)	8.9	17.5	12.5
Hypertension (%)	45	63	57.5
MI/non-MI (%)	NA	7.5/92.5	34.5/65.5
Ischemic/non-ischemic (%)	NA	NA	48.2/52.8
QRS duration (msec)	100±18.7	101.5±20.9	102.5±20.9
SSS	NA	6.1±3.9	13±12
SDS	NA	4±2.9	1.9±2.1

MI: Myocardial infarction; SSS: Summed stress score; SDS: Summed difference score

scans, the differences were not significant. Figure 1a-c shows the Bland-Altman plots that compared the LV dyssynchrony parameters between the post-stress and resting scans in the three cohorts. The mean differences in the LV dyssynchrony parameters were very small, indicating there were no systemic differences in these parameters between the post-stress and resting scans. There were no outliers that showed clinically important differences in the LV dyssynchrony parameters between

the post-stress and resting scans, indicating the two scans yielded equivalent results. Figure 2a and b shows two example patients with anterior and inferior ischemia post-stress, respectively. Both patients had comparable LV synchrony at post-stress and at rest. Figure 3 shows an example patient with severe LV dysfunction (LVEF = 24%) and myocardial infarction (summed stress score = 33). Even though severe reduction in perfusion uptake in the infarct region might impact the phase measurement, the global LV dyssynchrony parameters were not significantly different between the post-stress and resting scans, indicating that phase analysis was a robust tool to measure LV dyssynchrony in patients with severe LV dysfunction and myocardial infarction.

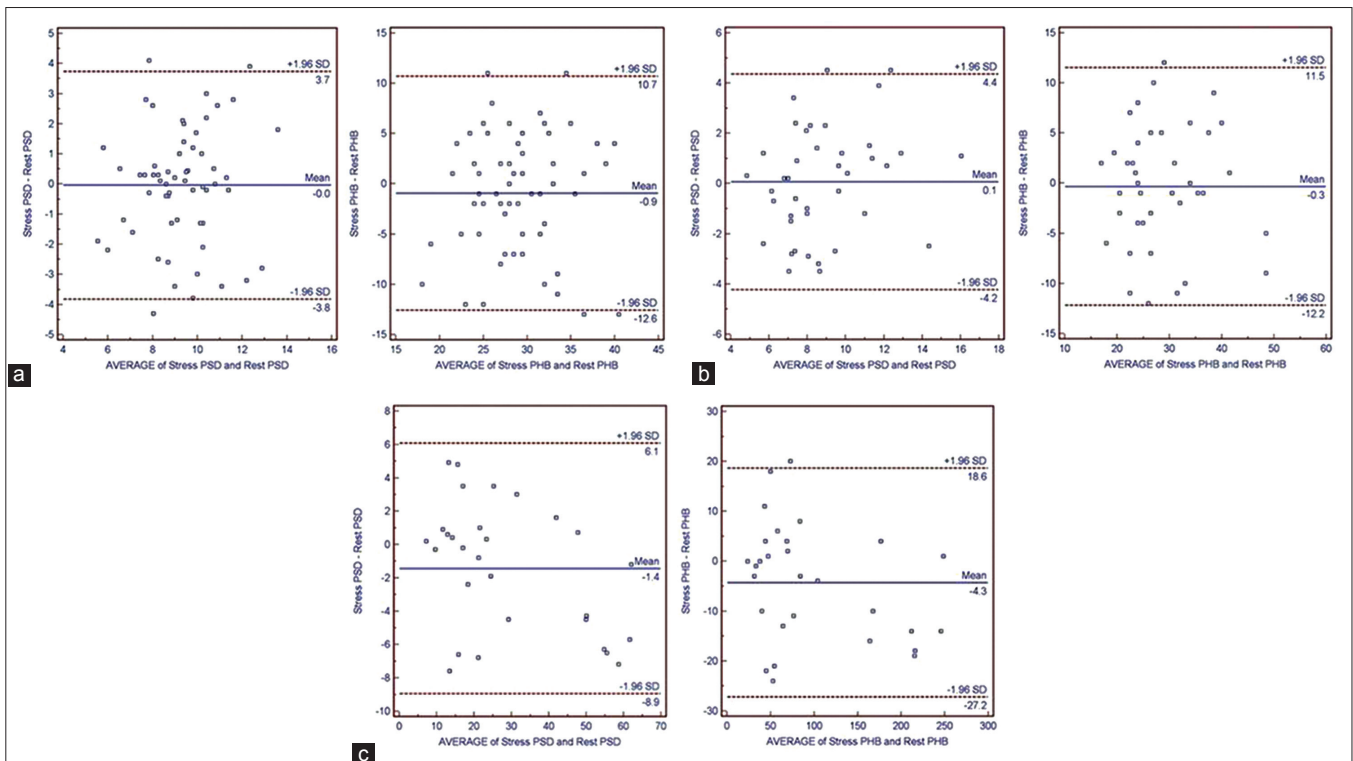
**Table 2: Post-stress and resting LV function parameters**

	Normal subjects (n=60)		Patients with ischemia (n=40)		Patients with LV dysfunction (n=29)	
	Stress	Rest	Stress	Rest	Stress	Rest
<b>PSD</b>						
Mean	9.3	9.3	8.9	8.8	28.5	29.9
SD	2.0	1.9	2.9	2.4	17.1	18.8
P value	0.89		0.82		0.05	
<b>PHB</b>						
Mean	28.5	29.5	28.4	28.8	95.6	99.9
SD	5.9	5.7	8.3	8.3	70.4	74.0
P value	0.23		0.74		0.06	
<b>EF</b>						
Mean	76.1	76.2	61.5	64.8	33.5	35.4
SD	6.4	6.4	9.7	7.5	10.1	10.9
P value	0.83		0.004		0.12	

PSD: Phase standard deviation; PHB: Phase histogram bandwidth; SD: Standard deviation; LV: Left ventricular

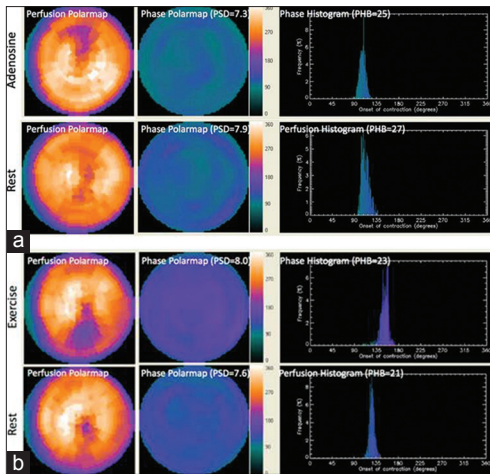
### Discussion

This study compared LV dyssynchrony parameters measured by phase analysis of gated SPECT MPI between post-stress (either adenosine or exercise) and resting scans. No significant differences in these parameters were observed in normal subjects, patients with stress-induced ischemia but normal LV function, and patients with LV dysfunction. As the majority of clinical MPI data are acquired using 1-day Tc-99m protocol, where usually gated SPECT data are acquired only at post-stress, this finding supports the application

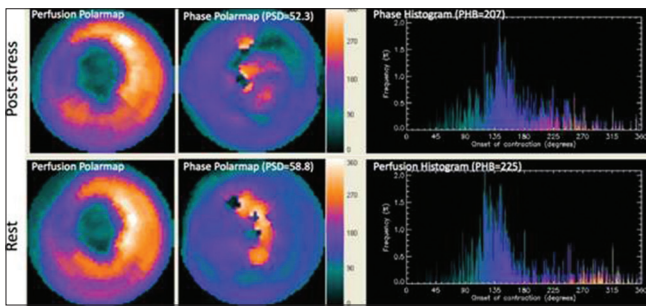


**Figure 1:** Bland-Altman plots for comparisons of the post-stress and resting LV dyssynchrony parameters in the (a) normal subjects, (b) patients with stress-induced ischemia but normal LV function, and (c) patients with LV dysfunction





**Figure 2:** Two example patients. One with adenosine stress in (a) and the other with exercise stress in (b). Both patients showed comparable LV synchrony at post-stress and at rest



**Figure 3:** An example patient with severe LV dysfunction (LVEF = 24%) and myocardial infarction (summed stress score = 33). Even though severe reduction in perfusion uptake in the infarct region might impact the phase measurement, the global LV dyssynchrony parameters were not significantly different between the post-stress and resting scans

of phase analysis to post-stress Tc-99m gated MIBI SPECT MPI data to measure LV dyssynchrony, which is equivalent to that measured at rest.

Stress-induced ischemia is associated with post-stress reduction in LVEF and increased post-stress EDV and ESV.<sup>[11]</sup> Stress-induced severe ischemia may lead to myocardial stunning and transient LV dilation, and possibly LV dyssynchrony. A few studies showed that physical effort might further increase LV dyssynchrony in patients with HF assessed by echocardiography during exercise.<sup>[12-14]</sup> However, a recent study reported that even a large reversible perfusion defect does not alter the indices of mechanical dyssynchrony by phase analysis in patients with coronary artery disease and normal LVEF, when all post-stress data were acquired 60 min post injection of Tc-99m Sestamibi.<sup>[10]</sup> This study confirmed that finding, and indicated that the post-stress LV dyssynchrony was equivalent to that at the resting state in patients with LV dysfunction.

For Tc-99m Sestamibi, the post-stress image acquisition

minimum delay is 15-20 min for exercise stress, 45-60 min for resting, and 60 min for pharmacologic stress,<sup>[15]</sup> in order to avoid the influence of liver and gut uptake. We uniformly acquire the stress imaging 60 min after tracer injection. As we all know, the parameters of the wall motion and dyssynchrony are derived from the gated images that are acquired at the time of imaging, not at the time the tracer injection. So, the timing of acquisition may affect the function and dyssynchrony parameters.

There are two limitations of this study. First, there are only 14 ischemic and 15 non-ischemic HF patients in this study, which may suggest limited statistical power. Secondly, to clarify the difference of LV dyssynchrony parameters between the post-stress and resting scans, different stage post injection of Tc-99m Sestamibi will be observed in our further study.

## Conclusion

The LV dyssynchrony parameters measured at 60 min after stress did not significantly differ from those measured at rest in normal subjects, patients with stress-induced ischemia but normal LV function, and patients with LV dysfunction, in a 2-day Tc-99m MPI protocol. Phase analysis can be applied to post-stress Tc-99m gated SPECT MPI data to measure LV dyssynchrony, which is equivalent to that measured at rest.

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