ORIGINAL ARTICLE

Left ventricular mechanical synchrony from stress and rest ^{82}Rb PET myocardial perfusion ECG-gated studies: Differentiating normal from LBBB patients

C. David Cooke, MSEE, Fabio P. Esteves, MD, Ji Chen, PhD, and Ernest V. Garcia, PhD

Background. We have previously reported normal values for LV mechanical synchrony from post-stress exercise ^{99m}Tc SPECT studies; the goal of this study was to develop normal values for mechanical synchrony from pharmacologic stress and rest ^{82}Rb PET studies and compare these values to a population of LBBB patients.

Methods and Results. The normal population consisted of 40 patients with a low likelihood of coronary artery disease. The LBBB population consisted of 23 patients with ECG evidence of LBBB. All patients were imaged with pharmacologic stress and processed using SyncTool^{TM} (Emory Cardiac Toolbox^{TM}). Means and standard deviations were calculated for the stress and rest phase parameters. Normal male and female phase standard deviation were 15.0 ± 7.0 and 13.2 ± 7.7, respectively, for stress (P = NS), and 22.7 ± 13.2 and 16.6 ± 14.3 for rest (P = NS). Normal male and female histogram bandwidth were 38.1 ± 13.3 and 32.0 ± 13.5, respectively, for stress (P = NS) and 50.8 ± 18.7 and 44.4 ± 44.9 for rest (P = NS). ROC analysis yielded a sensitivity/specificity as high as 80%/90% for males, and 92%/75% for females (P = NS).

Conclusions. Normal values for LV mechanical synchrony have been developed for ^{82}Rb pharmacologic stress and rest PET studies; furthermore, the stress pharmacologic values do not differ significantly from our previously reported exercise post-stress SPECT normal values. Finally, ROC analysis confirmed that these normal values were able to differentiate normal and LBBB populations. (J Nucl Cardiol 2011;18:1076–85.)

Key Words: Left ventricular function • myocardial perfusion imaging: PET • pharmacologic stress • phase analysis

INTRODUCTION

Left ventricular (LV) mechanical synchrony has been shown to be useful in predicting a patient's response to cardiac resynchronization therapy (CRT).[1] To this end, it is useful to know the normal values for mechanical synchrony. We have previously reported the normal values of LV mechanical synchrony for ^{99m}Tc post-stress exercise SPECT studies.[2] In this current study we investigated the normal values of LV mechanical synchrony for ^{82}Rb PET pharmacologic stress (regadenoson) and rest studies. Li et al[3] have shown that different reconstruction methodologies (i.e., filtered back-projection vs iterative) do not significantly impact LV dyssynchrony indices. However, we anticipated there might be additional differences in the normal values derived from PET vs SPECT because PET studies are typically reconstructed with attenuation and scatter correction, PET studies typically use different filters from SPECT (filtering can cause the ventricle to look more or less synchronous, depending on the degree of filtering), PET and SPECT studies typically have different count densities, statistical noise and spatial resolution, and there are differences in LV function between stress SPECT (usually imaged 15-60 minutes post-stress) and stress ^{82}Rb PET (imaged during pharmacologic stress). Therefore, the goal of this study was to develop normal values for mechanical synchrony

from pharmacologic stress and rest ^{82}Rb PET studies, and compare these normal values to a population of left bundle branch block (LBBB) patients and to our previously determined normal values from a SPECT population.[2]

METHODS

Patient Populations

We retrospectively identified 40 sequential patients (20 males, 20 females) with a low likelihood (LLK) of coronary artery disease based on non-cardiac chest pain, a normal ECG and absent coronary artery calcium. All 40 patients were imaged with regadenoson and at rest. The demographics for these patients are listed in Table 1. In addition, we also retrospectively identified 23 sequential patients (13 females, 10 males) with ECG evidence of LBBB (QRS ≥ 120 ms) at the time of the imaging study; 6/23 (5 males) were stressed using adenosine instead of regadenoson. The demographics of this LBBB population are also shown in Table 1. Of these 23 patients, 10 (4 males) had prior CAD and 3 (2 males) had an abnormal PET scan.

Acquisition and Processing

All patients were imaged on a Siemens Biograph-40 3D PET/CT scanner (Knoxville, TN) comprised of a lutetium oxyorthosilicate (LSO) block detector ring of 162 mm field-of-view operating in 3D mode. All images were acquired in listmode and rebinned to 8 frames per cardiac cycle. Pharmacologic stress (regadenoson or adenosine) was used with an average injection of 50.0 mCi of ^{82}Rb. Regadenoson (0.4 mg) was administered as a bolus injection over 10 seconds and was followed by a 5-mL saline flush; the ^{82}Rb generator was started immediately after the saline flush. If adenosine was used as the stress agent instead of regadenoson, it was administered using a 4-minute infusion (140 µg/kg/minute); the ^{82}Rb generator was started at the beginning of the third minute of the

adenosine infusion. Regardless of the stress agent, the acquisition was started 2 minutes after the start of the ^{82}Rb infusion and images were acquired for 5.5 minutes. The studies were reconstructed into a 128×128 matrix using the iterative ordered-subsets expectation maximization (OSEM) algorithm (4 iterations, 16 subsets) with attenuation correction, and post-filtered with a Gaussian spatial filter at 7 mm FWHM. Studies were subsequently reoriented into short-axis slices and then processed with SyncTool^{TM} (Emory Cardiac Toolbox^{TM}); the algorithms used for measuring mechanical synchronicity in this present study were the same as those used in previously published studies for SPECT.[2] As part of the Emory Cardiac Toolbox processing, all gated studies were additionally filtered with a 9-point spatial filter and a 3-point temporal filter with wrap-around from frame 8 to frame 1. Automatic processing was used for all studies with manual override needed for 9% of the automatically determined parameters.

Measuring Synchronicity

We have previously shown that the change in counts in the myocardium over the cardiac cycle is proportional to wall thickening.[4] Using Fourier harmonic analysis, it has also been shown that this change in counts can be used to accurately detect the onset of mechanical thickening (contraction), also called myocardial synchronicity.[5,6] Figure 1 shows how myocardial synchronicity is measured from an 8-frame gated study. Across the top of this figure are representative models of the ventricle at each frame of the 8-frame study. The graph shows the counts extracted from 1 inferior-wall pixel, from each frame of the study (squares connected by a thin line). The thick, smooth line represents the first harmonic from the Fourier transform of these 8 points. The dashed straight line represents the DC component of the Fourier transform. Note where the first harmonic curve crosses the DC component, this phase offset from the first frame of the study, measured in degrees, is the onset of mechanical contraction, for this particular pixel. This methodology is then repeated for all pixels in the myocardium and the resultant collection of these phase offsets can then be analyzed and displayed. Figure 2 shows a

Table 1. Patient demographics

	Normal regadenoson		LBBB	
	Male (N = 20)	Female (N = 20)	Male (N = 10)	Female (N = 13)
Age	49.4 ± 10.3	49.5 ± 10.5	69.1 ± 10.7*	67.0 ± 13.2*
BMI (kg/m^2)	31.2 ± 6.9	30.3 ± 11.6	28.6 ± 6.2	30.3 ± 6.9
Resting systolic BP (mmHg)	138.8 ± 20.3	134.3 ± 29.4	142.3 ± 22.1	147.9 ± 20.1
Resting diastolic BP (mmHg)	84.1 ± 14.0	75.4 ± 14.0	78.6 ± 13.0	77.5 ± 15.8
Stress PET EF	65.3 ± 7.8§	72.9 ± 7.1§	39.7 ± 15.4*	52.2 ± 16.9*
Rest PET EF	60 ± 6.5§	64.7 ± 6.2§	37.5 ± 14.2*	50.8 ± 16.2*
Stress ^{82}Rb injected dose (mCi)	49.6 ± 5.0	48.4 ± 6.9	51.9 ± 6.8	51.4 ± 6.3
Rest ^{82}Rb injected dose (mCi)	49.8 ± 5.2	48.6 ± 6.8	52.3 ± 6.4	51.8 ± 6.2

LBBB, Left bundle branch block; *BMI*, body mass index; *BP*, blood pressure; *EF*, ejection fraction.
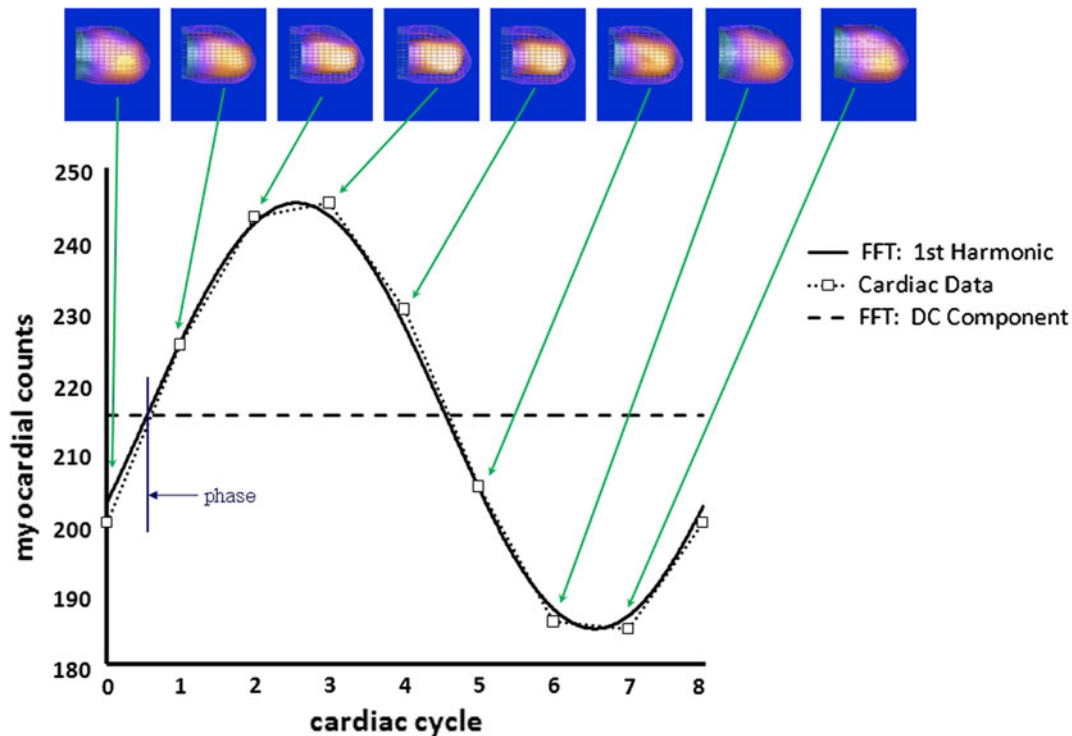§ *P* < .05 male vs female, * *P* < .05 LBBB vs normal.

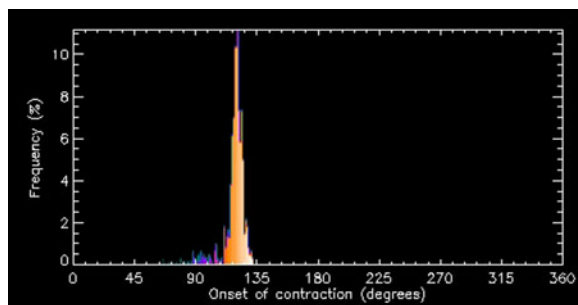**Figure 1.** Measuring myocardial synchronicity.

Figure 2. Colorized phase histogram for a normal study.

colorized histogram of the phase offsets (or onset of mechanical contraction) for one of the normal female patients, using the scale shown at the right of Figure 3. A colorized, normalized polar map of the phase offsets for this same study is shown in Figure 3, where darker colors (black, green blue, …) indicate early phases and lighter colors (purple, gold, white) indicate later phases; a color scale is shown at the right of this figure indicating the phase associated with each color. The normalization process limits the range of the polar map to the range of phases found in the study, with black corresponding to the earliest phase (56 in this study) and white corresponding to the latest phase (131 in this study). Finally, a movie can be constructed of the wave of contraction as it moves across the myocardium. Figure 4 shows 6 consecutive frames from the stress movie for this same study, for phases: 111°, 115°, 119°, 123°, 127°, and 131°. The blacked-out areas represent all of the
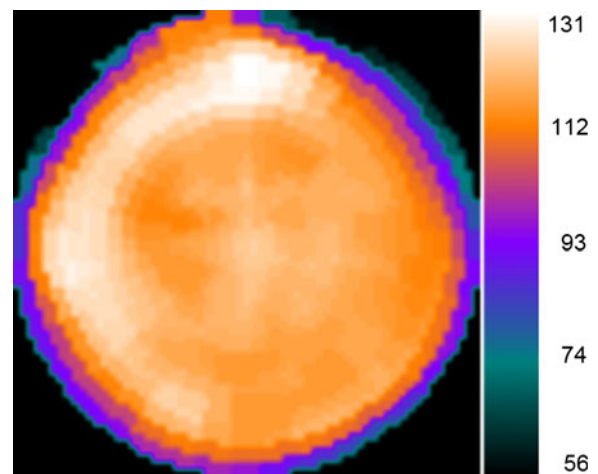

Figure 3. Colorized, normalized phase polar map for the same study as shown in Figure 2. The *color scale to the right* of the polar map indicates the phase associated with each color.

regions that share the same phase; these blacked-out regions are then super-imposed over the stress ore rest [82]Rb perfusion. In addition, there are several quantitative parameters that can be extracted from the histogram or phase distribution; currently, there are 2 that have shown clinical utility,[1,7] these are the phase standard deviation (SD, the standard deviation of the phase distribution) and the histogram bandwidth (BW, bandwidth that includes 95% of the phase distribution). These
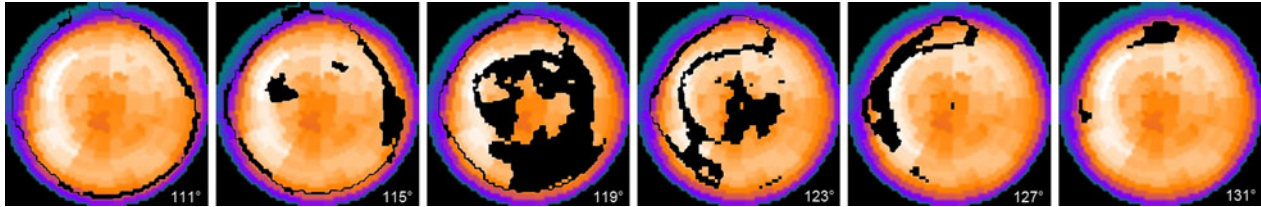
Figure 4. Six consecutive frames from a movie of the wave of contraction for the same study as shown in Figure 2. The blacked-out areas represent all of the pixels that share the same phase, super-imposed over the stress ^{82}Rb perfusion (the phase is indicated in the *lower right-hand corner* of each frame).

quantitative measures for the normal patient shown in Figures 2, 3, and 4 are: phase SD: 10.94° and histogram BW: 29.0°.

Data Analysis

All values are reported as the mean ± 1 standard deviation. The statistical tests were performed using unpaired, 2-tailed t tests, with a probability value <.05 considered to be statistically significant.

RESULTS

Table 1 compares the demographics of the normal and LBBB populations. For the normal population, there were significant differences between male stress and rest PET EF's and female stress and rest PET EF's (females had higher stress and rest EF's). For the LBBB population, there were no significant differences found between male stress and rest PET EF's and female stress and rest PET EF's. Comparing the normal population with the LBBB population, there were significant differences in age (the LBBB population was older) and stress and rest PET EF's (the LBBB population had lower EF's).

The quantitative values for regadenoson stress and rest ^{82}Rb PET onset of mechanical contraction for the low likelihood and LBBB populations are shown in Table 2. There were no significant differences between stress and rest for both the LLK and LBBB populations, except the male LLK phase SD and BW. There were significant differences ($P < .05$) between the LLK and LBBB populations for all parameters except the female rest histogram bandwidth.

A comparison of our previously determined post-stress exercise ^{99m}Tc Sestamibi SPECT normal values[2] with the current ^{82}Rb pharmacologic stress and rest low likelihood values is shown in Table 3. There were no significant differences ($P > .4$) between the male and female post-stress SPECT normal values and the ^{82}Rb regadenoson stress LLK values for phase SD or histogram BW. There were significant differences between the male post-stress SPECT normal values and the ^{82}Rb rest LLK values for both phase SD and histogram BW. There were also differences between the female post-stress SPECT normal values and the ^{82}Rb rest LLK values for both phase SD and histogram BW, though they did not quite reach significance ($P = .052$ and $P = .053$, respectively).

Table 4 summarizes the ROC analysis results for phase SD and histogram BW, for both pharmacologic stress and rest. There were no significant differences in the area under the curve (AUC, stress vs rest, phase SD vs histogram BW or male vs female), though the histogram BW trended toward having a higher AUC. Optimum thresholds and associated sensitivities and specificities are also shown in this table. Figure 5 shows the ROC curves for histogram BW vs phase SD for the males (top row) and females (bottom row). Note that in all 4 cases, the histogram BW has a slightly larger, though not significant, AUC. The greatest AUC for both males and females was for stress histogram BW, yielding a sensitivity/specificity of 80%/90% for males and 92%/75% for females; there was no significant difference ($P > .1$) between these male/female sensitivities/specificities.

Figure 6 shows a comprehensive display for one of the female LLK patients. Note the uniform phase polar map and narrow phase histogram with a normal phase SD of 11.1 and histogram BW of 29, indicating that the left ventricle is contracting normally and uniformly. In contrast, Figure 7 shows a comprehensive display for one of the female LBBB patients with very similar perfusion and function results. However, the phase polar map is no longer uniform with the wave of contraction starting in the septal wall and traversing around the left ventricle to the lateral wall. The phase histogram is also broader with an abnormal phase SD of 15.1 and histogram BW of 52; both outside the optimal threshold for normal as identified by ROC analysis (normal female stress phase SD threshold is 13.7 and histogram BW is 33).

Table 2. Regadenoson stress ^{82}Rb PET normal values of onset of mechanical contraction vs stress ^{82}Rb PET LBBB

	Males			Females		
	^{82}Rb LLK (N = 20)	^{82}Rb LBBB (N = 10)	*P*, LBBB vs LLK	^{82}Rb LLK (N = 20)	^{82}Rb LBBB (N = 13)	*P*, LBBB vs LLK
Stress phase SD	15.0 ± 7.0	38.1 ± 24.7	<.05	13.2 ± 7.7	24.1 ± 18.9	<.05
Rest phase SD	22.7 ± 13.2	40.3 ± 25.6	<.05	16.6 ± 14.3	33.3 ± 31.2	<.05
P, stress vs rest	<0.05	>0.1		>0.1	>0.1	
Stress histogram BW	38.1 ± 13.3	121.8 ± 83.0	<.05	32.0 ± 13.5	67.5 ± 54.1	<.05
Rest histogram BW	50.8 ± 18.7	92.2 ± 42.0	<.05	44.4 ± 44.9	68.8 ± 40.7	>.1
P, stress vs rest	<0.05	>0.1		>0.1	>0.1	

LLK, Low likelihood; *LBBB*, left bundle branch block; *SD*, standard deviation; *BW* bandwidth.
P = NS males vs females for both LLK and LBBB.

Table 3. Normal values from previous post-stress exercise ^{99m}Tc SPECT compared to regadenoson stress and rest ^{82}Rb PET

	Males			Females		
	Post-stress SPECT (N = 45)	Stress PET (N = 20)	Rest PET (N = 20)	Post-stress SPECT (N = 45)	Stress PET (N = 20)	Rest PET (N = 20)
Phase SD	14.2 ± 5.1[§]	15.0 ± 7.0	22.7 ± 13.2[§]	11.8 ± 5.2	13.2 ± 7.7	16.6 ± 14.3
Histogram BW	38.7 ± 11.8[§]	38.1 ± 13.3	50.8 ± 18.7[§]	30.6 ± 9.6	32.0 ± 13.5	44.4 ± 44.9

SD, Standard deviation; *BW*, bandwitdh.
P = NS, post-stress SPECT vs stress PET (SPECT normal data is from a previous publication[2]).
P = NS, female post-stress SPECT vs female rest PET.
[§] *P* < .05, male post-stress SPECT vs male rest PET.

Table 4. ROC analysis for phase SD and histogram BW

	Phase SD				Histogram BW			
	Stress ^{82}Rb		Rest ^{82}Rb		Stress ^{82}Rb		Rest ^{82}Rb	
	Males	Females	Males	Females	Males	Females	Males	Females
Threshold	26.1	13.7	22.1	15.7	52	33	49	50
AUC	0.870	0.788	0.750	0.781	0.915	0.863	0.823	0.846
Sensitivity (%)	80	85	90	85	80	92	90	77
Specificity (%)	90	75	60	80	90	75	65	95

AUC, Area under the ROC curve; *SD*, standard deviation; *BW*, bandwidth.
P = NS, male vs female, stress vs rest, phase SD vs histogram BW.

DISCUSSION

In this study we retrospectively identified 40 ^{82}Rb patients (20 males and 20 females) who had a low likelihood of coronary artery disease based on non-cardiac chest pain, a normal ECG and absent coronary artery calcium. Normal values for mechanical synchronicity were established using these 40 patients for both regadenoson stress and rest. An additional 23 patients (10 males, 13 females) with ECG evidence of LBBB (QRS ≥ 120 ms) at the time of the imaging study were
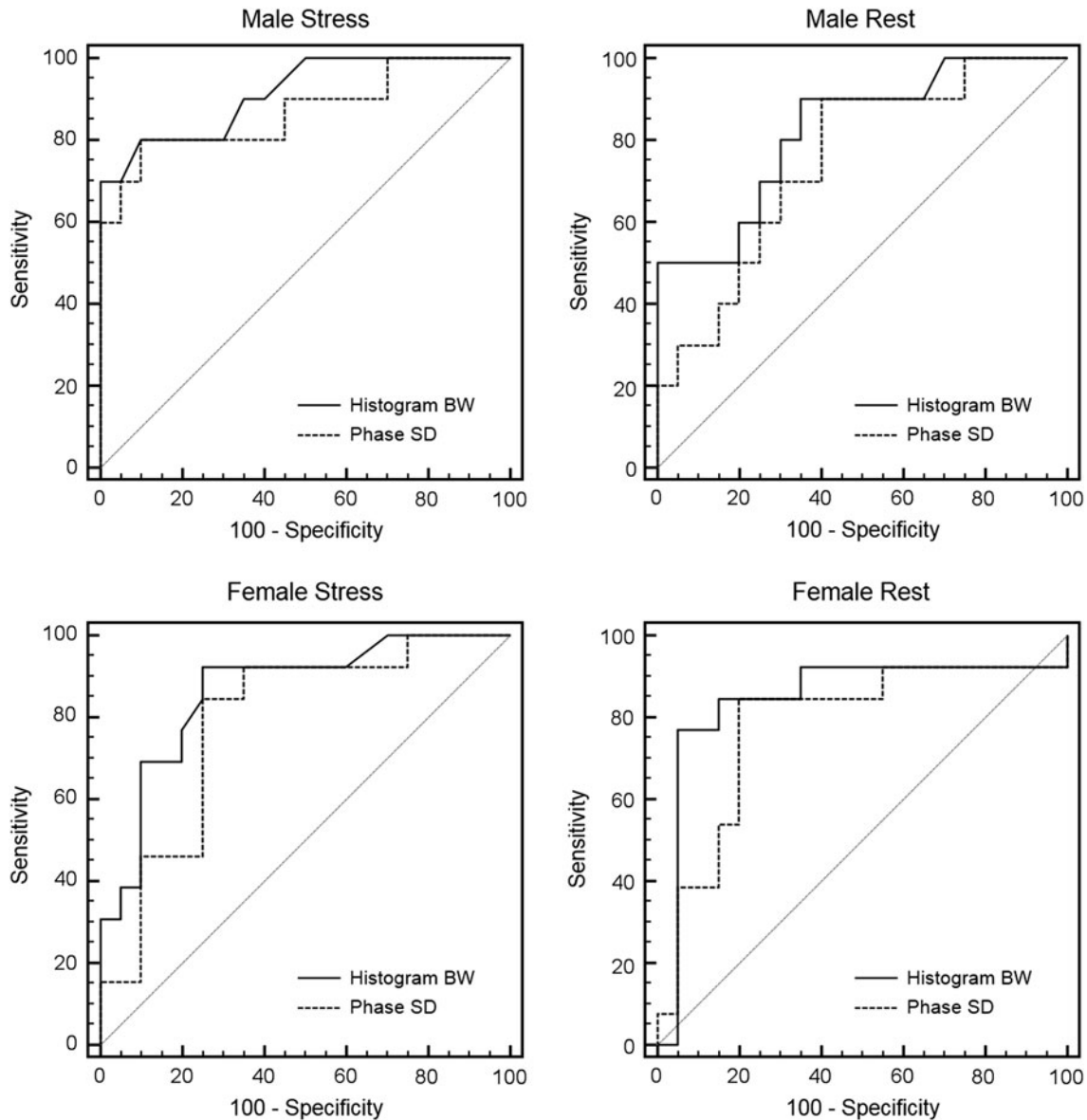
Figure 5. ROC curves for histogram BW vs phase SD for males (*top row*) and females (*bottom row*). Area under the curve, thresholds, and associated sensitivities and specificities are presented in Table 4.

compared to these normal limits and found to be significantly different for all parameters except resting female histogram bandwidth.

Taking a closer look at the female low likelihood patients, it was noticed that one obese female patient had a much larger resting phase SD (72 vs the average of 16.6) and histogram BW (233 vs the average of 44.4) than the other low likelihood patients. When this patient was removed from the analysis, the resting female histogram bandwidth reached significance between the low likelihood population and the LBBB population, with $P = .001$.

In a similar study from 2007, Trimble et al[8] reported combined post-stress SPECT results from 157 normal patients (52% male) and 33 with LBBB (39% male), using SyncTool™ and acquiring at 8 frames/cardiac cycle. Though there was not enough information for a statistical comparison of the demographics of the two normal populations; however, in general, the ages and EF's were similar. Comparing the phase parameters of the two normal populations, there were no significant differences in phase SD or histogram BW. Likewise, no significant differences were found when comparing the two LBBB populations for phase SD or histogram BW.
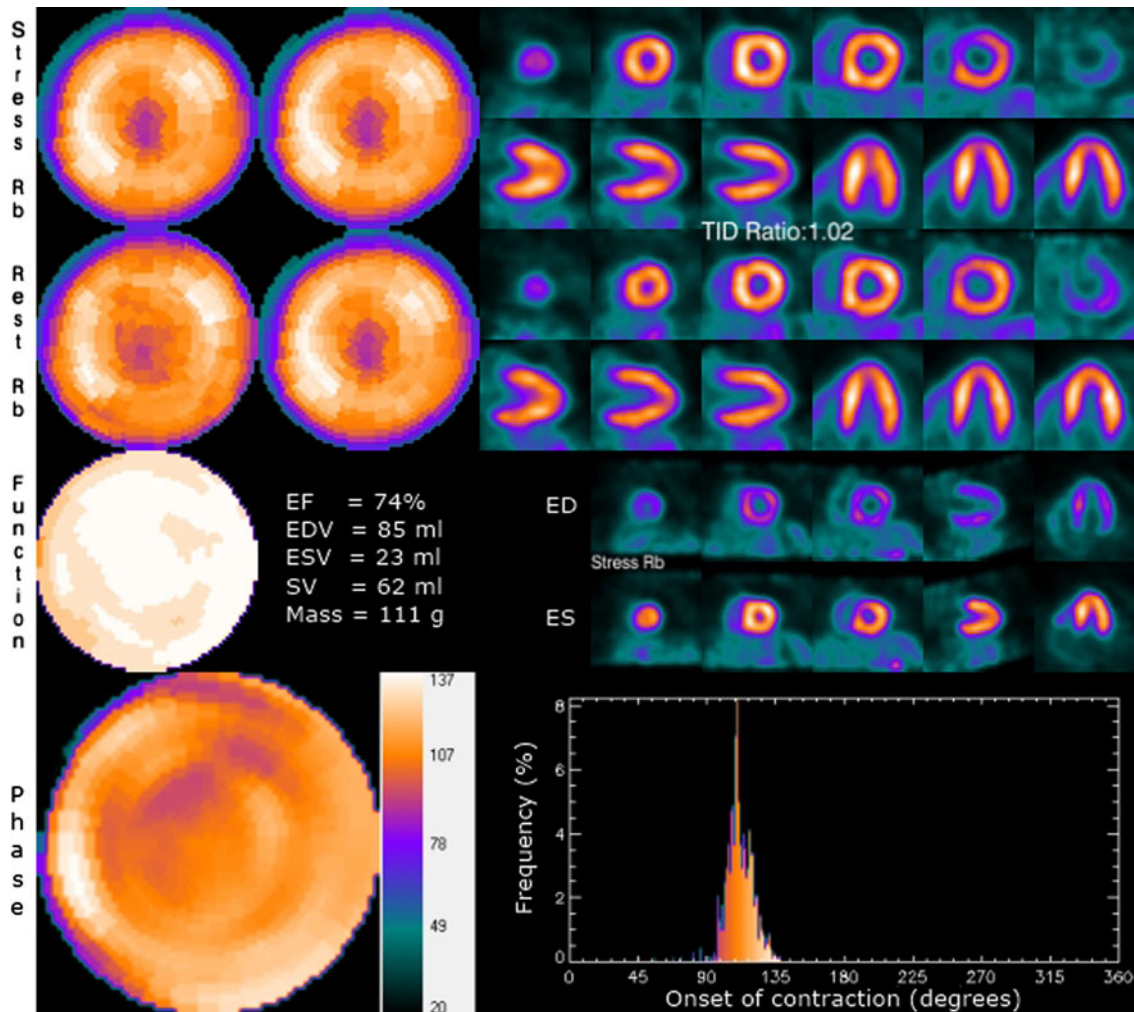
Figure 6. Stress and rest perfusion, stress function and stress phase information for a normal female with a phase SD of 11.1 and a histogram BW of 29.0. The *top row* shows the stress ^{82}Rb raw perfusion and blackout polar maps along with the stress short-axis, vertical long-axis, and horizontal long-axis slices (there are no blacked-out defects). The *second row* shows the rest ^{82}Rb raw perfusion and reversibility polar maps along with the rest short-axis, vertical long-axis, and horizontal long-axis slices. The *third row* shows the stress ^{82}Rb percent-thickening polar map (*white* $\geq$ 40% thickening, *light tan* > 25%, and *dark tan* > 10%), the functional parameters for the stress study and representative end-diastolic and end-systolic short-axis, vertical long-axis, and horizontal long-axis slices. The *fourth row* shows the normalized phase polar map and the associated phase histogram.

Note that though there are the typical PET vs SPECT methodological differences between the two studies (type of stress, attenuation and scatter correction, reconstruction protocol, count density, statistical noise, and spatial resolution), there were no differences in phase SD or histogram BW.

In another similar study from 2008, Van Kriekinge et al[9] reported post-stress SPECT results from 86 normal patients (38% male) and 72 with LBBB (57% male), using their own algorithms and acquiring the data at 16 frames/cardiac cycle. Comparing the demographics of the two normal populations, there were no significant differences in age or LVEF. Comparing the phase parameters of the two normal populations, there were no significant differences in female phase SD; however, there were significant differences in male phase SD (15.0 ± 7.0 Emory vs 22.4 ± 12.4 Kriekinge) as well as male and female histogram BW (males: 38.1 ± 13.3 Emory vs 80.2 ± 46.6 Kriekinge, females: 32.0 ± 13.5 vs 59.1 ± 39.3). Comparing the LBBB populations, there were no significant differences in phase SD or histogram BW. Given that Van Kriekinge and
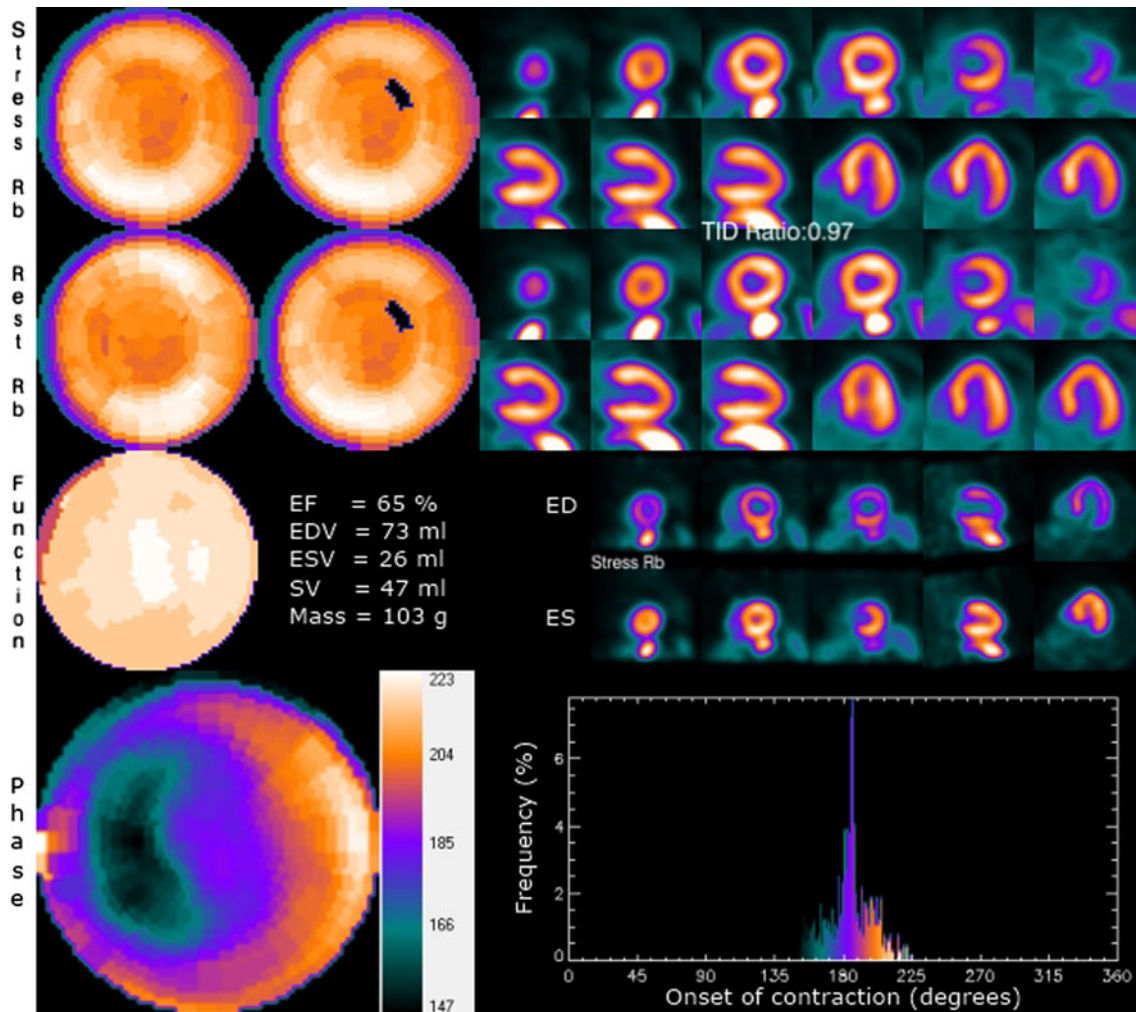
Figure 7. Stress and rest perfusion, stress function, and stress phase information for a LBBB female with a phase SD of 15.1 and a histogram BW of 52.0. The figure setup is the same as that described in Figure 6.

colleagues used a different program to calculate phase SD and histogram BW, it is surprising that there are not more significant differences between the two studies.

In another similar study from 2009, Nichols et al[10] reported post-stress SPECT results from 20 subjects (56% male) with confirmed LBBB along with 9 controls (65% male), using SyncTool™ and acquiring at 16 frames/cardiac cycle. Comparing the demographics of the two normal populations, there were no significant differences in LVEF; however, there were significant differences in age (combined: 49.4 ± 10.3 Emory vs 73 ± 13 Nichols). Comparing the phase parameters of the two normal populations, there were no significant differences in phase SD; however, there were significant differences in histogram BW (combined: 35.0 ± 13.6 Emory vs 59 ± 34 Nichols). Comparing the LBBB populations, there were no significant differences in

phase SD or histogram BW. It is again interesting to note that although there are the same typical PET vs SPECT methodological differences between the two studies, only the normal histogram BW showed a significant difference between the two studies.

It seems that both phase SD and histogram BW are particularly robust measures of LV mechanical synchrony across different forms of stress, different physiologic states, different acquisition, and reconstruction methodologies and perhaps even across different processing algorithms.

All three of the studies above were reported with post-stress SPECT data; we believe our study is the first to report normal values for both pharmacologic stress and rest PET. It is important to understand how normal values for mechanical synchronicity might vary depending on the imaging modality and stress condition

of the patient. As we have shown in this study, there are no significant differences between normal patients acquired with regadenoson stress PET vs post-stress SPECT for phase SD or histogram BW, though there were significant differences in males between rest PET and post-stress SPECT (and nearly significant differences in females between rest PET and post-stress SPECT). While there are indications for acquiring a patient by PET vs SPECT, we are not advocating one method over the other. Instead, the purpose of this study was to show that phase analysis is an easy (and essentially free) addition to any gated PET or SPECT study, and this analysis of mechanical synchronicity can have important clinical ramifications for patient management and care. There have been several papers published indicating the clinical utility of phase analysis, such as: in predicting a patients response to cardiac resynchronization therapy[1]; in predicting cardiac death and inappropriate shocks in patients with implantable cardiac defibrillators[7]; and in using dyssynchrony by FDG PET as a marker for survival in patients with ischemic cardiomyopathy[11]. Similar clinical results would be expected from using phase analysis of ^{82}Rb PET cardiac studies. In all of these papers, both phase SD and histogram bandwidth appear to have similar statistical power. In this study, there were no significant differences in sensitivity or specificity between phase SD and histogram bandwidth in distinguishing LLK from LBBB, though histogram bandwidth did have a slightly higher AUC in ROC analysis.

Finally, in our study we utilized gated data that had been acquired at 8 frames per cardiac cycle. We have shown that using our phase analysis technique of converting the discrete thickening curves to continuous curves utilizing the first harmonic of the Fourier transform, we can actually measure phase shifts as if the study had been acquired at 64 frames per cardiac cycle.[6] Thus, acquiring a study at 8 frames/cardiac cycle or 16 frames/cardiac cycle will not yield any clinically significant differences using our phase analysis technique, as was also shown by Trimble et al.[8]

LIMITATIONS

The current study reports the normal values from 20 male patients and 20 female patients (the SPECT normal values were derived from a different population of 45 males and 45 females), and the criteria for normality were slightly different between the PET and SPECT cohorts. Furthermore, there was a significant difference in age between the LLK and LBBB populations which may account for some of the differences in phase SD and histogram BW between these populations; however, other studies with age matched controls showed a

similar significant difference in these parameters comparing LLK vs LBBB.[10]

CONCLUSIONS

We have developed normal values for LV mechanical synchrony for ^{82}Rb regadenoson stress and rest PET studies. In comparison with our previously published ^{99m}Tc post-stress exercise SPECT normal values, there were no significant differences in phase SD or histogram BW for regadenoson stress; however, there were differences between the SPECT values and the PET rest values. In addition, ROC analysis confirmed that these new normal values were able to successfully distinguish between LLK and LBBB populations with a sensitivity/specificity as high as 80%/90%, respectively, for males, and 92%/75% for females ($P = NS$).

References

1. Henneman MM, Chen J, Dibbets-Schneider P, Stokkel MP, Bleeker GB, Ypenburg C, et al. Can LV dyssynchrony as assessed with phase analysis on gated myocardial perfusion SPECT predict response to CRT? J Nucl Med 2007;48:1104-11.
2. Chen J, Garcia EV, Folks RD, Cooke CD, Faber TL, Tauxe EL, et al. Onset of left ventricular mechanical contraction as determined by phase analysis of ECG-gated myocardial perfusion SPECT imaging: Development of a diagnostic tool for assessment of cardiac mechanical dyssynchrony. J Nucl Cardiol 2005;12:687-95.
3. Li D, Zhou Y, Feng J, Yuan D, Cao K, Garcia EV, et al. Impact of image reconstruction on phase analysis of ECG-gated myocardial perfusion SPECT studies. Nucl Med Commun 2009;30:700-5.
4. Galt JR, Garcia EV, Robbins WL. Effects of myocardial wall thickness on spect quantification. IEEE Trans Med Imaging 1990;9:144-50.
5. Cooke CD, Garcia EV, Cullom SJ, Faber TL, Pettigrew RI. Determining the accuracy of calculating systolic wall thickening using a fast Fourier transform approximation: A simulation study based on canine and patient data. J Nucl Med 1994;35:1185-92.
6. Chen J, Faber TL, Cooke CD, Garcia EV. Temporal resolution of multiharmonic phase analysis of ECG-gated myocardial perfusion SPECT studies. J Nucl Cardiol 2008;15:383-91.
7. Aljaroudi WA, Hage FG, Hermann D, Doppalapudi H, Venkataraman R, Heo J, et al. Relation of left-ventricular dyssynchrony by phase analysis of gated SPECT images and cardiovascular events in patients with implantable cardiac defibrillators. J Nucl Cardiol 2010;17:398-404.
8. Trimble MA, Borges-Neto S, Smallheiser S, Chen J, Honeycutt EF, Shaw LK, et al. Evaluation of left ventricular mechanical

dyssynchrony as determined by phase analysis of ECG-gated SPECT myocardial perfusion imaging in patients with left ventricular dysfunction and conduction disturbances. J Nucl Cardiol 2007;14:298-307.

9. Van Kriekinge SD, Nishina H, Ohba M, Berman DS, Germano G. Automatic global and regional phase analysis from gated myocardial perfusion SPECT imaging: Application to the characterization of ventricular contraction in patients with left bundle branch block. J Nucl Med 2008;49:1790-7.

10. Nichols KJ, Van Tosh A, Siddiqi S, Chen J, Garcia EV, Palestro CJ, et al. Gated myocardial perfusion SPECT asynchrony measurements in patients with left bundle branch block. Int J Cardiovasc Imaging 2009;25:43-51.

11. Santana C, Verdes L, Chen J, Esteves F, Cooke CD, Faber T, et al. Left ventricular (LV) dyssynchrony measured by phase analysis of gated FDG PET studies predicts cardiac death in patients with ischemic cardiomyopathy. J Nucl Med Supplement 1 2008;49:188.