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Distribution of dyssynchrony in subjects with no known cardiac disease and comparison of velocity vector imaging to color coded tissue Doppler imaging.

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Running head: Dyssynchrony in subjects with no known cardiac disease

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Key Words: Dyssynchrony, Velocity Vector Imaging, color coded tissue Doppler imaging

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Abstract

Data on the distribution of dyssynchrony in subjects with normal ejection fraction and normal QRS are scarce. We studied 100 subjects with no known cardiac disease (52% male, mean age 60 ± 17 years) using velocity vector imaging. Seventeen percent had septal to lateral (S-L) wall longitudinal delay >75 ms, 63% of subjects had S-L wall radial delay >75 ms and 25% had a circumferential opposing wall delay >100 ms. Those with circumferential opposing wall delay of >100 ms had a lower ejection fraction (57 ± 5 % vs. 62 ± 5 %, $p < 0.05$). In an additional group of 33 patients we compared the longitudinal dyssynchrony parameters as assessed by velocity vector imaging and tissue Doppler imaging and found them to be comparable. In conclusion, we find significant variation in time to peak velocities in subjects with no known cardiac disease, who had a normal left ventricular ejection fraction and QRS duration. Velocity vector imaging is comparable to tissue Doppler imaging.

Introduction:

Cardiac resynchronization therapy (CRT) is the current standard of care for patients with left ventricular ejection fraction (LVEF) of 35% or less, New York Heart Association (NYHA) functional class III-IV, and QRS duration $> 120\text{ms}$ ¹. CRT has been shown to improve NYHA functional class, mortality, mitral regurgitation and left ventricular remodeling^{2,3}. A wide QRS is used as a screening tool for mechanical dyssynchrony. However, not all patients with a wide QRS complex have mechanical dyssynchrony assessed by non-invasive echocardiographic (echo) techniques⁴ and further 30% of patients receiving CRT do not show significant improvement^{2,5}. Importantly, those with a narrow QRS complex can also have evidence of mechanical dyssynchrony⁴. In a recent multi-center trial 'Results of the Predictors of Response to CRT (PROSPECT) trial', color coded tissue Doppler imaging (TDI), among several other echo parameters was found not to be useful in real-world clinical settings for assessing mechanical dyssynchrony⁶.

Myocardial contraction and relaxation are complex processes involving longitudinal, circumferential, radial and torsional forces, among others. There is inherent electrical and mechanical inhomogeneity in the normally functioning heart⁷⁻¹⁰. Several studies have shown that the normal heart has regional variations in ejection fraction, wall thickening and timing of contraction of segments⁷⁻¹⁰. Although data on echo criteria for dyssynchrony in patients with left ventricular dysfunction are abundant, data on the variations in subjects with no known cardiac disease are scarce. Knowledge of the variations in timing of contraction of various segments will serve as a reference when studying the diseased heart. For example, variations in time to peak

(TTP) velocities in subjects with no known cardiac disease could account for why TDI did not predict response to CRT in the PROSPECT trial⁶.

Unlike color-coded TDI which is dependant on the angle of the transducer and can only assess longitudinal velocities, a new B-mode echo technique called velocity vector imaging (VVI) is available¹¹. VVI is angle independent and can assess longitudinal, circumferential and radial velocities, and strain. The purpose of this study is two fold: 1) To assess whether variations are present in TTP velocities and strain among subjects without any known cardiac heart disease using VVI and 2) to directly compare color-coded TDI with VVI.

Materials and Methods:

Three hundred and forty consecutive subjects who underwent 2D echocardiography at Albert Einstein Medical Center in Philadelphia between September 2007 and November 2007 on an Acuson Sequoia C512 (Siemens Medical Solutions, Inc.) were screened. Two hundred and forty subjects were excluded with the following exclusion criteria (1) history of coronary artery disease; (2) LVEF <55%; (3) diastolic dysfunction greater than grade 1 (mitral early to late diastolic inflow peak velocity ratio >0.8, deceleration time of the mitral inflow <200msec, isovolumetric relaxation time <60 msec, pulmonary venous systolic to diastolic peak velocity ratio <1, and mitral early inflow to early diastolic annular septal tissue peak velocity ratio >9, as listed in American Society of Echocardiography criteria ¹²; (4) QRS duration >120 msec; (5) moderate or severe valvular heart disease (using Doppler echocardiographic parameters: central jet >4 cm² or jet area >20% of left atrial area for mitral regurgitation, central jet width >25% or vena contracta >0.3 cm² or pressure half-time <500 msec for aortic regurgitation, central jet area >5 cm² or proximal isovelocity surface radius >0.5 cm for tricuspid regurgitation, jet size by color Doppler >10 mm for pulmonary regurgitation for regurgitant lesions ¹³; mean gradient >20 mm Hg or aortic valve area <1.5 cm² or aortic jet velocity >3 m/sec for aortic stenosis, mitral valve area <1.5 cm² or mean gradient >5 mm Hg for mitral stenosis, tricuspid valve area <1 cm² or mean gradient >5mm Hg or inflow time-velocity time integral >60 cm or pressure half-time >190 msec for tricuspid stenosis, peak velocity >3 m/sec or peak gradient >36 mm Hg for pulmonic stenosis for stenotic lesions ¹⁴; (6) pacemaker; (7) arrhythmias (8) hypertrophic cardiomyopathy; (9) pericardial effusion or disease; (10) poor-quality images in which the myocardium was not visible; and (11) admission to the intensive care unit.

Additional echocardiograms of 35 consecutive patients (all-comers), who were not subjected to the above mentioned exclusion criteria, were studied to compare TDI and VVI measurements. The details of the VVI and TDI measurements are described below.

Patient demographics, clinical characteristics, laboratory data and QRS duration were collected (Table 1). Patient demographics collected were age, gender, and race. Clinical characteristics collected were any history of hypertension (blood pressure $>140/90$ mm Hg as defined by the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure¹⁵ or use of antihypertensive agents); diabetes mellitus (fasting plasma glucose >126 mg/dL per the American Diabetes Association¹⁶ or receipt of antidiabetic treatment); hypercholesterolemia (low-density lipoprotein level > 130 mg/d per the National Cholesterol Education Program¹⁷ or statin use) and smoking history. The longest QRS duration was recorded from the electrocardiogram. LVEF was calculated using the modified Simpson's rule¹⁸. Laboratory data obtained were hemoglobin and creatinine, which were measured closest to the time of echocardiography. This study was approved by the institutional research board of Einstein Medical Center, Philadelphia, PA.

The Acuson Sequoia C512 echo machine (Sequoia, Siemens Medical Solutions Inc., Mountain View, California), which has capabilities for both TDI and VVI, was used for the study. Images were captured using frame rates used for traditional 2D echocardiography (30–60 frames/sec). VVI uses a series of tracking algorithms whose details are described elsewhere¹¹. In brief, the endocardial-myocardial interface is traced manually in a single frame on a digital cine loop. When the image is processed, a complex algorithm tracks each pixel, and the myocardial velocity vectors are displayed in cine format. The lengths of the vectors are proportional to the

magnitude of velocity, and the direction of the arrows corresponds to the direction of myocardial motion. One cardiac cycle was analyzed if the RR intervals were regular, and an average of three beats was used if RR intervals were irregular (none of the study subjects had irregular RR intervals). Apical four-chamber, two-chamber, and short-axis views at the papillary muscle level were studied offline. In the apical four-chamber and two-chamber views, a trace was made (along the endocardial-myocardial interface) from the septal to lateral mitral annulus and from the inferior to anterior mitral annulus, respectively. In the short-axis view at the level of papillary muscles, a circumferential trace was made starting at the 12 o'clock position and ending at the same point in a clockwise direction, excluding the papillary muscles. Approximately one point per myocardial segment was used to draw the trace. A point of reference was placed at the apex in the two-chamber and four-chamber views to calculate longitudinal velocities and strain. The point of reference was moved to the LV cavity to calculate radial velocities. In the short-axis view, the point of reference was at the center of the left ventricle to calculate circumferential velocities and strain. Longitudinal velocity, longitudinal strain, and radial velocities were measured at the basal septal, basal lateral, basal anterior, and basal inferior walls in the apical four-chamber and two-chamber views. The circumferential velocities and strain were measured in the short-axis view at the papillary muscle level. Time to peak velocities and strain were calculated from the onset of the QRS complex to the peak systolic velocity or peak strain, respectively, during the ejection phase. We defined mechanical dyssynchrony as longitudinal opposing wall delay >75 msec by VVI on the basis of a prior study¹⁹. Because there are no published criteria for circumferential dyssynchrony and because we were looking at the maximum delay between all six segments in the short-axis view, not just the opposing wall delays, we used a higher number (maximum delay >100 msec) to define circumferential dyssynchrony. We used a value of 75 msec for septal-to-lateral wall radial delay. Examples of

longitudinal and circumferential LV dyssynchrony analysis using the above-mentioned VVI technique are illustrated in Figures 2 and 3, respectively.

For color coded TDI, the highest possible frame rate was used (>100 mHz). The average of three beats was analyzed. Longitudinal velocities at the basal anterior, inferior, lateral and septal walls using TDI were measured. Care was taken to ensure that there was a distinct positive velocity in the systolic phase. If there was no positive velocity recorded, that trace was excluded. If there was more than one peak, the earliest peak was used to calculate TTP velocities. We defined mechanical dyssynchrony as an opposing wall delay >75 ms by VVI (longitudinal and radial) based on a prior study¹¹. Since there are no published criteria for circumferential dyssynchrony and since we were looking at the maximum delay between all 6 segments in the short axis view, and not just the opposing wall delays, we used a higher number (maximum delay >100 ms) to define circumferential dyssynchrony. Patients with poor color-coded TDI curves and patients with poor acoustic windows were excluded from the study.

Statistical analysis:

Data were analyzed using the SPSS 10 (Chicago, IL, USA). Continuous data are presented as mean $\pm$ SD. Means were compared using a two-tailed student t test. Chi-square test was used to compare categorical variables. A p value less than 0.05 were considered significant. Co-efficient of variation (COV) was used to measure the inter and intra-observer variability on 20 random obese and non-obese subjects.

Results:

Description of subjects with normal EF and QRS<120 ms

The final cohort consisted of 100 patients with complete data. 52% were male, mean age 60 ± 17 years, mean QRS duration 86 ± 12 ms and mean ejection fraction (EF) was $61 \pm 6\%$ (Table 1.)

Longitudinal velocity:

There were no significant differences in time to peak septal-lateral wall longitudinal velocities and time to peak inferior- anterior wall longitudinal velocities. The average septal to lateral wall and inferior-anterior wall delays were 34 ± 55 ms and 18 ± 35 ms, respectively.

Radial velocity:

The radial time to peak lateral wall velocity was significantly earlier than the time to peak radial septal velocity (271 ± 147 ms vs. 211 ± 116 ms, $p < 0.001$). The absolute radial velocity of contraction of the anterior wall was significantly greater than the inferior wall (2.2 ± 1.4 cm/s vs. 1.5 ± 1.2 cm/s, $p < 0.05$).

Circumferential velocity:

There were no significant differences in time to peak circumferential velocities among opposing walls in the short axis view. The average maximum delays between all the walls were 79 ± 68 ms. The average delay between anterior-inferior, anteroseptal-inferolateral and anterolateral – inferoseptal walls were 43 ± 58 ms, 49 ± 53 ms and 50 ± 58 ms, respectively.

Variation in time to peak velocities:

Although there were no significant differences in overall time to peak velocities between opposing walls (except for radial septal- lateral wall time to peak velocities), there were

significant variations in individual subjects. Of the 100 subjects only 22 had no longitudinal, radial or circumferential dyssynchrony. 3 subjects had longitudinal, radial and circumferential dyssynchrony. Those with all three forms of dyssynchrony had a significantly lower ejection fraction compared to those who did not have any dyssynchrony ($63 \pm 6\%$ vs. 55% , $p < 0.05$). When the contribution of circumferential dyssynchrony was removed, the results were no longer significant. The remaining subjects had longitudinal, circumferential or radial dyssynchrony.

Variation in radial velocity:

There were significantly more variations in radial velocities when compared with longitudinal velocities (Fig 3). 63% of subjects had S-L wall delay of radial velocities > 75 ms. There were no significant differences in ejection fraction, age, QRS duration, longitudinal or circumferential velocities among those subjects with S-L wall delay of ≤ 75 ms compared to those with S-L wall delay > 75 ms.

Variation in longitudinal velocity:

Thirteen percent of subjects had S-L wall delay > 75 ms in longitudinal velocities by VVI (Fig. 4). These patients also had a significantly lower absolute velocity of contraction in the septum compared with the lateral wall (2.7 ± 1.2 cm/s vs. 3.7 ± 1.4 cm/s, $p < 0.05$). There were no significant differences in ejection fraction, age, QRS duration, radial or circumferential velocities among those subjects with S-L wall delay of ≤ 75 ms compared to those with S-L wall delay > 75 ms.

Variation in circumferential velocity:

Twenty five percent of subjects had > 100 ms delay between time to peak circumferential velocities among all the walls in the short axis view. Those with > 100 ms delay had a significantly lower ejection fraction compared to those with < 100 ms delay ($58 \pm 5\%$ vs. $62 \pm 6\%$,

$p < 0.05$), although both ejections fractions were still in the normal range (Fig. 5, Table 2.). There were no significant differences in age, QRS duration, radial or longitudinal velocities among those subjects with a maximum delay of < 100 ms compared to those with a delay > 100 ms.

Variation in time to peak longitudinal and circumferential strain:

The difference in time to peak longitudinal strain between the septal and lateral walls showed a similar pattern of variability when compared to longitudinal velocities. The mean difference in time to peak strain between the S and L walls were 49 ± 89 ms compared with 34 ± 54 ms for time to peak S-L velocities ($p > 0.05$). However, the maximum difference in time to peak circumferential strain between all the walls showed less variability than maximum difference in time to peak circumferential velocities. (59 ± 57 ms vs. 79 ± 68 ms, $p < 0.05$).

Variation in time to peak velocities among those with no cardiac risk factors:

Only 23% ($n=23$) of patients in the cohort did not have any history of hypertension, diabetes, hypercholesterolemia and were non-smokers. Since these risk factors could potentially influence the distribution of dyssynchrony, we separately analyzed this group (mean age 47 ± 19 years, 26% male). Even in this healthy group, with normal EF, QRS < 120 ms and no cardiovascular risk factors, 13% had S-L wall longitudinal delay > 75 ms, 69% had radial S-L wall delay > 75 ms and 17% had circumferential maximum delay > 100 ms. This mirrored the general distribution of dyssynchrony in the whole cohort of 100 patients.

Comparison of VVI with TDI:

We studied an additional 35 consecutive patients who underwent both VVI and TDI imaging. In two patients adequate TDI could not be obtained even after multiple attempts, due to inadequate frame rates or due to inconsistent TDI tracings, and were excluded. VVI could be performed and

interpreted in all patients. This final cohort consisted of 33 patients with complete data. Sixty-two percent were male, mean age 63 ± 16 years, mean QRS duration 76 ± 40 ms and 22% had ejection fraction(EF) $<55\%$. All patients (four) with S-L wall delay >65 ms by TDI also had S-L wall delay by VVI (all greater than 75 ms). Among the 27 patients with S-L wall delay <65 ms by TDI (mean 24.7 ± 22 ms), 26 patients had S-L wall delays <75 ms by VVI (mean 18.8 ± 20 ms). Although the other patient had a S-L wall delay <65 ms, there was an antero-posterior wall delay of >65 ms by TDI.

Inter- and intra-observer variability was calculated for all VVI measurements in 20 random subjects. The coefficients of variation for longitudinal, radial, and circumferential time to peak velocities were 5%, 6%, and 6%, respectively, for interobserver variability and 5%, 5%, and 6%, respectively, for intraobserver variability. The coefficients of variation for longitudinal and circumferential strain were 8% and 8%, respectively, for interobserver variability and 7% and 8%, respectively, for intraobserver variability.

Discussion:

Although several single center studies have shown the utility of using echo criteria for assessing mechanical dyssynchrony²⁰⁻²³, it has not found wide clinical use. Part of the reason for this is that there are several different methods to assess mechanical dyssynchrony and several criteria have been proposed by different authors. Color coded TDI has been shown in several studies to predict left ventricular remodeling and response to CRT²⁰⁻²³. However, a recent multi-center trial (PROSPECT) failed to show the utility of CRT based on several echo criteria, including TDI⁶. This could be due to lack of strict standardization and uniformity in performing measurements, unlike in a single center study. Also, TDI may not be the best technique to predict response to CRT. While data on timing of regional contraction in those with LV dysfunction is abundant, similar data on subjects with normal EF is scarce. There is normal apex to base spread of electrical activity and a similar apex to base spread of myocardial contraction²⁴. There can be significant regional heterogeneity in electrical and mechanical activation of the normal heart^{9, 24, 25}. The degree of heterogeneity can vary and some normal healthy subjects could meet criteria for LV dyssynchrony. Therefore, it is important to know what the baseline variations in regional timing of contraction of the normal heart are in order to be able to establish criteria in the diseased state. Although initial studies by Yu et. al.²⁶ found low variability in TDI measurements in healthy patients, other studies found more variations in normal subjects²⁷. Zwanenburg et al, studied MRI derived time to peak strain and time to onset of contraction in healthy volunteers and found that there is heterogeneity in contraction between different segments of the heart, with the range being between 200-400 ms for onset of time to peak contraction¹⁰. A recent study by Miyazaki et. al. found significant overlap of TDI measurements in four groups of subjects: those with normal LV function and a narrow QRS, subjects with

normal LV function and left bundle branch block, subjects with LV dysfunction and narrow QRS, and subjects with wide QRS and depressed LV function²⁸.

In our study of 100 subjects with normal LVEF and narrow QRS, the average S-L wall delay for longitudinal velocities were 34 ± 55 ms, for radial velocity, 141 ± 125 ms and for circumferential velocities, the average opposing wall delays were 43 ± 58 ms between the anterior and inferior wall, 49 ± 53 ms between the anteroseptal and inferolateral wall and 50 ± 58 ms between the anterolateral and inferoseptal walls. Using the prior published criteria for dyssynchrony by VVI¹⁹ (S-L wall delay >75 ms for longitudinal velocities), 13% of subjects met criteria for longitudinal dyssynchrony. There were no significant differences between the groups with and without dyssynchrony suggesting that this may be the normal spread of opposing wall delay values. The spread of opposing wall time to peak radial velocities were even wider. Sixty three percent of subjects had S-L wall radial delay >75 ms. Criteria for dyssynchrony for time to peak radial velocities have not been established. This wide spread would suggest that the cut off value for dyssynchrony for radial velocities would be higher than for longitudinal velocities. The spread of values for circumferential time to peak velocities were in-between those for radial and longitudinal velocities. Twenty-five percent of subjects had maximum opposing wall delay >100 ms. In contrast to the subjects above who despite significant variation in velocities demonstrated no differences between groups, subjects with a maximum opposing delay >100 ms. These subjects also had a significantly lower left ventricular ejection fraction (58 ± 5 % vs. 62 ± 5 %; $p=0.001$) compared to those with maximum opposing wall delay <100 ms. Although both these ejection fractions were still within the normal range, the results were statistically significant. It is well known that one of the major contributors to robust left ventricular emptying is the twisting or wringing motion of the heart²⁵. It is conceivable that those with greater degrees of inhomogeneity in circumferential twist would have lower left ventricular ejection fractions.

Whether these patients have a greater chance of progression to significant left ventricular dysfunction is not known and requires further study.

We also compared those patients who did not have any evidence of radial, longitudinal or circumferential dyssynchrony (22 subjects) with those who had evidence of all three forms of dyssynchrony (3 subjects). The only statistically significant difference between these groups was a lower ejection fraction in those with all three forms of dyssynchrony ($63 \pm 6\%$ vs. $55 \pm 0\%$, $p < 0.05$). Once the contribution of circumferential dyssynchrony was removed, the results were no longer statistically significant. Again, it is unclear whether these subjects will go on to have significant left ventricular dysfunction in the future. Although the difference in time to peak longitudinal strain between opposing walls showed a similar spread to TTP longitudinal velocities, the difference in time to peak circumferential strain showed significantly less variation. Thus, as suggested by Miyazaki et al²⁸, it is possible that time to peak strain measurements may be more accurate to assess dyssynchrony. However, additional trials are needed to answer this question.

Similar to the wide spread of opposing wall delays in subjects without heart disease, those with left ventricular dysfunction may also have a normal spread of opposing wall delays, and thus all of them may not respond to CRT. If a subject with normal left ventricular function and evidence of dyssynchrony at baseline develops left ventricular dysfunction and the degree of dyssynchrony persists, it is unclear whether this patient will respond to CRT. On the other hand, if someone with preserved left ventricular function and no dyssynchrony at baseline develops left ventricular systolic dysfunction and dyssynchrony subsequently develops, they may derive benefit from CRT. Since cardiac mechanics are complex, defining dyssynchrony by opposing wall delays in one dimension may be too simplistic. Some degree of dyssynchrony may be of no hemodynamic consequence to one individual, but may cause significant hemodynamic

disturbance in other subjects. Thus, using a blanket cut off value to define response to dyssynchrony may not be ideal. Costa et al. also showed that a significant fraction of their study group with preserved ejection fraction and normal QRS width had dyssynchrony by M-Mode and tissue Doppler echocardiography²⁹. With the increasing use of 3-dimensional echocardiography in the assessment of left ventricular dyssynchrony and cardiac resynchronization therapy, it would be interesting to see if similar results are obtained when using this modality^{30, 31}. Sengupta et. al have studied blood flow hemodynamics and have shown characteristic filling and emptying patterns of left ventricular blood flow using ultrasonic digital particle imaging velocimetry³². Thus, looking at the end result of left ventricular mechanics, namely efficient patterns of blood flow within the left ventricle may be a more ideal way to assess left ventricular synchrony than looking at the mechanical delay between LV walls.

Comparison of VVI with TDI:

VVI is angle independent, and can be performed without the need for very high frame rates. It also allows assessment of radial and circumferential dyssynchrony in addition to longitudinal dyssynchrony. Data on the use of VVI for dyssynchrony are scarce. Cannesson and colleagues have shown that an opposing wall delay > 75 ms by VVI predicts LV remodeling after CRT¹⁹. They however did not make a direct comparison between TDI and VVI. Based on that study, we used a cut off of 75 ms between septal and lateral wall TTP longitudinal velocities to define dyssynchrony. Among those patients whose TDI could be analyzed, everyone with septal to lateral wall delay >65 ms also had S-L wall delay > 75 ms by VVI. Similarly, all but one patient with S-L wall delay <65ms by TDI had no longitudinal dyssynchrony by VVI. This patient had anterior to posterior wall delay by TDI (> 65 ms) and thus technically has mechanical

dyssynchrony. Two patients had poor quality TDI tracings that could not be analyzed. VVI could be performed and interpreted in all patients studied. Thus VVI is an attractive alternative to TDI for assessing mechanical dyssynchrony, and does not carry some limitations of TDI.

Limitations:

Although consecutive patients undergoing echocardiography with normal EF and QRS duration were studied, this cohort does not represent a truly healthy population with a significant number of patients having cardiovascular risk factors. It is possible that these risk factors could have influenced the distribution of dyssynchrony. However, we separately analyzed 23 subjects without any cardiovascular risk factors and the distribution of dyssynchrony in this healthy group was similar to the overall cohort of patients. Even in the 23 healthy subjects, given the older age of the population, it is possible that unaccounted confounders, such as occult coronary artery disease could influence dyssynchrony. The effect of body mass index on the distribution of dyssynchrony was not assessed in this study. We have shown in one of our previous studies that there was an increased prevalence of dyssynchrony among the obese with no known history of significant cardiac disease³³. Since a lower frame rate was used for VVI, it is conceivable that some very rapid velocities seen with TDI may not be recorded. However, comparison between the time to peak velocities between two walls should still be valid. MRI studies looking at the heterogeneity in LV contraction used frame rates ranging from 14 – 35 ms^{7, 10}. This is comparable with the 30-60 f/s (16-33 ms) used in this study. However, it is lower than frame rates used for TDI (>100 f/s or <10 ms).

Conclusions:

In summary, there appears to be normal heterogeneity in opposing wall delays in adult subjects without apparent heart disease. The variation in opposing wall delay seems to be highest for radial velocities and least for longitudinal velocities. Even in the normal range of left ventricular ejection fractions, those with circumferential dyssynchrony seems to have lower ejection fractions, highlighting the contribution of left ventricular twist towards the overall left ventricular function. Knowing the normal spread of velocities is important in order to be able to set appropriate limits in the diseased state. Since there is a normal heterogeneity in opposing wall delays, and since a recent large trial has shown that echo-guided resynchronization was not able to predict response to CRT, it may be worthwhile to explore alternative indicators of dyssynchrony such as left ventricular blood flow dynamics. Alternatively, instead of focusing on longitudinal velocities, it may be useful to integrate multiple measures of dyssynchrony as radial and circumferential time to peak velocities. Another area that will be interesting to study is whether healthy subjects with mechanical dyssynchrony will eventually develop left ventricular dysfunction. When comparing VVI with TDI, VVI appears as good as TDI for assessing longitudinal dyssynchrony, and may be useful in evaluating patients with poor quality TDI images. In addition, VVI can be used to detect circumferential and radial dyssynchrony. VVI is an attractive alternative to TDI for assessing mechanical dyssynchrony and does not carry some of the technical limitations of TDI.

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Legends:

Figure 1. Velocity vector imaging in the apical four-chamber view.

Figure 2. Velocity vector imaging in the short axis view.

Figure 3. Variation in time to peak velocities.

Figure 4. Distribution of longitudinal time to peak septal to lateral wall delays.

Figure 5. Left ventricular ejection fraction in those with and without circumferential dyssynchrony.

Table 1. Baseline characteristics of 100 people with normal ejection fraction and normal QRS duration.

Males	52 %
Age	60±17 years
QRS Duration	86.2±12.6 ms
Ejection Fraction	61±6 %
Hypertension	63%
Diabetes	30%
Hypercholesterolemia	26%
Smoker	11%
Hemoglobin (g/dL)	12.5±2.1
Creatinine (mg/dL)	1.6±1.5
Radial maximum TTP delay	241.5±139 ms
Radial TTP S-L delay	141.8±125 ms
Radial TTP A-I delay	120.4±100 ms
Circumferential TTP maximum delay	79±68 ms
Circumferential TTP delay between A and I walls	43.3±58 ms
Circumferential TTP delay between IS and AL walls	49.7±53 ms
Circumferential TTP delay between AL and IS	50.1±58 ms
Longitudinal maximum delay	95.9±70 ms
Longitudinal TTP delay between S and L walls	34.6±55 ms
Longitudinal TTP delay between A and I walls	18.2±35 ms

TTP- Time to peak

S, L, A, I, AS, AL, IL, IS- Septal, Lateral, Anterior, Inferior, Anteroseptal, Anterolateral, Inferolateral and Inferoseptal walls respectively.

Table 2. Relationship of left ventricular ejection fraction (EF) with time to peak (TTP) opposing wall delays.

Left ventricular EF in those with circumferential maximum TTP delay (CVVI) >100 ms vs. ≤ 100 ms

	N	Mean EF $\pm$ SD	P value
CVVI>100	27	58.2 $\pm$ 5 %	0.001
CVVI $\leq$ 100	73	62.5 $\pm$ 6 %	

Left ventricular EF in those with longitudinal TTP septal –lateral wall delay (LVVI) >75 ms vs. ≤ 75 ms

	N	Mean EF $\pm$ SD	P value
LVVI $\leq$ 75	87	61.4 $\pm$ 5	0.7
LVVI>75	13	60.7 $\pm$ 7	

Left ventricular EF in those with radial TTP septal –lateral wall delay (RVVI) >75 ms vs. ≤ 75 ms

	N	Mean $\pm$ SD	P value
RVVI $\leq$ 75	36	61.5 $\pm$ 6	0.8
RVVI>75	64	61.2 $\pm$ 5	

Figure1

Top left: Myocardial longitudinal velocity vectors in the apical 4-chamber view are shown. The direction of the arrows correspond to the direction of contraction and the length of arrows is proportional to the velocity of contraction. Bottom left: Velocity curves for the basal septal and basal lateral walls are shown. Top right: The time to peak delay between these walls is shown in graphic format. Note that there is no delay between the basal septal and lateral walls.

Figure 3

Distribution (mean $\pm$ 95% confidence interval) of longitudinal (LVVI s-l delay) and radial (RadialVVI s-l delay) time to peak septal-lateral wall delays. The circumferential (CircVVI Max delay) time to peak delay is the maximum delay between all opposing walls in the short axis view. The radial and circumferential time to peak velocities show more variation than longitudinal time to peak velocities.

Figure 4

Fig. 4

Distribution of longitudinal time to peak septal - lateral (S-L) wall delays. Note that in 13% of healthy subjects, the S-L wall delay is > 75 ms. In 48%, the S-L wall delay is zero.

Figure 5

Fig. 5

Left ventricular ejection fraction in those with circumferential maximum delay (VVI) <100 ms vs >100 ms. Note that in those with VVI <100 ms, the ejection fraction is higher (p=0.001).