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Effects of Region of Interest (ROI) Tracking on the Diagnosis of Left Ventricular Dyssynchrony from Doppler Tissue Images

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Abstract

Background—Left ventricular dyssynchrony is often diagnosed by comparing velocity curves from Doppler tissue images (DTI) of 2 or more myocardial regions. Velocity curves are generated by placing sample volumes or "regions of interest" (ROIs) within the myocardium. ROIs need to be manually relocated to maintain a mid-myocardial location as the heart moves, but are frequently left in a stationary position. The error caused by use of a stationary ROI may affect the diagnosis of dyssynchrony, but this has *not* been quantified.

Hypothesis—We *hypothesized* that using a stationary ROI to quantify dyssynchrony from DTI would affect the diagnosis of dyssynchrony in patients with heart failure.

Methods—We quantified dyssynchrony in 18 heart failure patients using 4 published dyssynchrony parameters: septal-to-lateral delay (SLD), maximum difference in the basal 2- or 4-chamber times-to-peak (MaxDiff), SD of the 12 basal and mid-wall times-to-peak (Ts-SD) and cross-correlation delay (XCD). Each dyssynchrony parameter was measured using both tracked and stationary ROIs.

Results—Use of a stationary ROI did *not* change the diagnosis of dyssynchrony when using XCD. However, ROI tracking changed the diagnosis of dyssynchrony in 17, 11 and 17% of patients when using SLD, MaxDiff and Ts-SD, respectively. XCD showed the lowest percent difference between tracked and stationary ROIs (4±9% versus 22±53%, 50±167% and 12±30%, respectively, for SLD, MaxDiff and Ts-SD).

Conclusion—Manual region of interest tracking is required when using conventional time-to-peak parameters to diagnose dyssynchrony. Cross-correlation delay diagnosis of dyssynchrony can be performed accurately with a stationary region of interest.

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Disclosures
None.

INTRODUCTION

Accurate diagnosis of mechanical dyssynchrony in the heart is becoming increasingly important in clinical practice for two reasons. First, the presence of left ventricular (LV) mechanical dyssynchrony has been shown to be a predictor of severe cardiac events in heart failure patients.[1] Second, LV dyssynchrony can be treated successfully with cardiac resynchronization therapy (CRT) utilizing biventricular pacemaker implantation.[2]

Left ventricular mechanical dyssynchrony can be diagnosed using Doppler tissue imaging (DTI) of the myocardium.[3] Diagnosis of dyssynchrony with DTI requires two main postprocessing steps which have not been standardized. First, velocity-time curves are generated from myocardial segments by placing regions of interest (ROIs) within both the mid-ventricular and basal segments of the LV walls.[4] Manual "tracking" of the ROI throughout the cardiac cycle is performed to ensure that the ROI remains in a mid-myocardial location. Tracking is required to generate the true shape of the myocardial velocity curve, but is time consuming and typically not performed when diagnosing dyssynchrony.[5] Importantly, many authors have omitted the description of whether or not ROI tracking was employed.[6–15]

The second post-processing step required to diagnose dyssynchrony using DTI is to compare the velocity-time curves from different myocardial walls to generate a quantitative value of dyssynchrony. Unfortunately, there is no accepted parameter for calculating dyssynchrony. Most methods utilize parameters based on a time-to-peak analysis where the time from the electrocardiogram Q-wave to the peak systolic velocity is measured in each segment of the LV. A simple difference in this time-to-peak ≥60ms between the basal septal and lateral segments can be used to define dyssynchrony.[10] Cross-correlation delay (XCD) is a new dyssynchrony parameter which utilizes all velocity data points from 3 consecutive beats (~420 points) to quantify dyssynchrony using a linear cross-correlation function.[16] A threshold XCD of 31ms was recently shown to discriminate between positive and negative control groups with 100% accuracy.[16]

Dyssynchrony parameters are typically calculated from velocity-time curves generated from a stationary ROI. A stationary ROI generates a slightly different velocity-time curve than a tracked ROI because the stationary ROI includes regions of the ventricular cavities (outside the myocardial segment of interest) during part of the cardiac cycle (Figure 1 and Movie 1, supplemental materials). This may lead to a change in the location of the peak systolic velocity, which may affect the diagnosis of dyssynchrony. No study to date has examined the effect of manual ROI tracking on the diagnosis of dyssynchrony.

We *hypothesized* that using a stationary ROI to quantify dyssynchrony from DTI would affect the diagnosis of dyssynchrony in patients with heart failure. We tested our hypothesis by quantifying dyssynchrony using both tracked and stationary ROIs in 18 patients with heart failure who were being evaluated for CRT. We examined the effect of ROI tracking on 4 published dyssynchrony parameters.

METHODS

Patient population

Consecutive patients referred to Emory University Crawford Long Hospital for potential treatment with CRT were evaluated for inclusion. Inclusion criteria were: 1) left ventricular ejection fraction <35%, 2) QRS duration > 120ms, and 3) New York Heart Association (NYHA) class III or IV heart failure. Twenty patients satisfied criteria and were enrolled initially. However, subsequent testing revealed that one patient had a QRS duration of 96 ms

and another had an ejection fraction of 57%. These two patients were excluded. Characteristics of the final 18 patients are shown in Table 1. All patients gave informed consent under guidelines established by the institutional review board.

Tissue Doppler data acquisition

Apical 2-, 3- and 4-chamber DTI of the myocardium were acquired with the patient lying in the lateral decubitus position using a commercial system (Vivid 7, GE Vingmed, Horten, Norway). The myocardial walls were aligned as parallel to the Doppler beam as possible to minimize the angle of insonation, and frame rate was optimized from 100 to 140 Hertz. Pulsed Doppler spectral recordings of the aortic outflow tract were acquired for definition of systole.

Tissue Doppler post-processing

Four dyssynchrony parameters were calculated during post-processing using commercially available software (EchoPAC PC, Version 4.0.3, GE Vingmed):

1. basal septal-to-lateral delay in time-to-peak systolic velocity (SLD)[10]
2. maximum difference in times-to-peak systolic velocity between any 2 of the basal septal, lateral, anterior and inferior LV segments (MaxDiff)[1]
3. the standard deviation of times-to-peak systolic velocity in the 12 basal and mid-wall segments of the LV (Ts-SD)[17]
4. cross-correlation delay (XCD).[16] Briefly, a time delay was calculated between velocity curves from the basal sections in apical 2-, 3- and 4-chamber views. One velocity curve was shifted relative to the other curve, and the cross-correlation value was computed for each time shift. The time shift between the two curves that resulted in the maximum correlation value was defined as the delay between the two curves. One delay was measured from each of the three apical views, and XCD was defined as the maximum of these three delays.[16] Inter and intra-observer variabilities for XCD were previously reported to be ~6% in patients with heart failure and <1% in normal volunteers.[16]

Velocity data was exported from the 12 basal and mid-wall segments of the 6 standard LV walls (septum and lateral walls in 4-chamber view, anteroseptal and posterior walls in 3-chamber view, and anterior and inferior walls in 2-chamber view). Velocity data was exported using two methods for comparison:

1. Tracked ROIs: A 30×6-millimeter ROI was located over the mid-wall of the myocardium and was moved manually throughout the cardiac cycle to maintain this mid-wall location within the ventricular segment of interest.
2. Stationary ROIs: A 30×6-millimeter ROI was placed at the center of motion of the ventricular segment of interest.

Each dyssynchrony parameter was calculated twice for each patient: first using velocity curves from the tracked ROIs and second using velocity curves from the stationary ROIs. An average velocity curve was generated from three cardiac cycles of velocity data prior to measuring dyssynchrony parameters. Pulsed Doppler of the aortic outflow tract was used to define systole for identification of the peak systolic velocity.

Statistics

Bland-Altman and mean percent difference plots were generated to demonstrate the agreement between calculating dyssynchrony using tracked versus stationary ROIs for each of the 4 dyssynchrony parameters. Paired student's t-tests were used to compare

dyssynchrony derived from tracked versus stationary ROIs for each of the 4 dyssynchrony parameters. A value of $p<0.05$ was defined as statistically significant. Threshold values to diagnose dyssynchrony were used to determine whether use of a stationary ROI changed the diagnosis of dyssynchrony for any patients.

RESULTS

Mean differences between tracked and stationary ROIs

Results for each patient are shown (Table 2). XCD had the lowest mean percent error when using a stationary ROI compared to a tracked ROI (4±9% versus 22±53%, 50±167% and 12±30%, respectively, for SLD, MaxDiff and Ts-SD) (Figure 2). There was no significant difference in mean values for tracked versus stationary ROI analysis for any dyssynchrony parameter (Table 3). Bland-Altman analysis (Figure 3) demonstrated excellent agreement between stationary and tracked ROIs for XCD (2*SD of the mean difference = 11 ms). The agreement was poor for the time-to-peak dyssynchrony parameters (2*SD of the mean difference = 74, 71 and 18 ms, respectively, for SLD, MaxDiff and Ts-SD).

Effects of tracking on the diagnosis of dyssynchrony

ROI tracking did *not* affect the diagnosis of dyssynchrony when using the XCD parameter (Table 3). However, ROI tracking changed the diagnosis of dyssynchrony in 17, 11 and 17% of the patients when using SLD, MaxDiff and Ts-SD, respectively (Table 3). For example, Figure 4A shows velocity curves from the basal septum and lateral wall of patient number 10 using tracked ROIs. Figure 4B shows velocity curves from the same patient using stationary ROIs placed in the same segment as the tracked ROIs. The patient had a SLD of 0 ms using tracked ROIs compared to a SLD of 141 ms using stationary ROIs. Since the threshold value for diagnosing dyssynchrony with SLD is 60 ms, the stationary ROI suggested that the patient had dyssynchrony while the tracked ROI demonstrated that the patient did not have dyssynchrony.

DISCUSSION

Doppler tissue imaging (DTI) of the myocardium is a powerful tool to diagnose LV mechanical dyssynchrony.[3] Dyssynchrony is diagnosed by placing sample volumes, or regions of interest (ROIs), in several ventricular segments and comparing the velocity tracings from these segments. Manual tracking of the ROIs needs to be performed to maintain the location of the ROI within the segment of interest as the heart moves. However, the process of manual tracking is time-consuming and not typically done.[5] We showed that using a *stationary* ROI changed the diagnosis of dyssynchrony in 11–17% of patients with advanced heart failure using time-to-peak dyssynchrony parameters while use of a stationary ROI did *not* affect the diagnosis using cross-correlation delay analysis. This is the first study to report the effects of ROI tracking on the diagnosis of dyssynchrony.

Region of interest tracking in other DTI dyssynchrony studies

The significance of ROI tracking on dyssynchrony indices has been largely ignored in the literature. Ten of the most commonly cited studies using color DTI to measure ventricular dyssynchrony[6–15] failed to specify whether the authors used a tracked or stationary ROI. (However, in a correspondence letter, Yu et al stated that their group always uses a tracked ROI.[18]) Studies using pulsed DTI to quantify dyssynchrony[1, 19–21] all use stationary ROIs as software has not been developed to reconstitute velocity tracings with a tracked pulsed Doppler ROI. Our study suggests that ROI tracking is critically important and should be addressed in future DTI dyssynchrony studies such as the recently completed PROSPECT trial.[22]

Studies using strain rate imaging to quantify dyssynchrony have reported using a tracked ROI for analysis.[23, 24] Since Doppler-derived strain rate is calculated with a velocity gradient, velocity must be measured accurately in two places within the myocardium. Thus, we expect that strain rate imaging will be *more* susceptible to ROI tracking than velocity-based measures of dyssynchrony, and this is currently being studied in our laboratory.

Comparison to existing studies

The mean values of dyssynchrony in our study compare well with previous reports. Yu et al[17] reported a Ts-SD of 38 ± 11 ms in a group of 25 patients undergoing CRT compared to 40 ± 12 ms in our group of 18 patients. Bax et al[8] reported a value of 73 ± 49 ms for MaxDiff in a group of 85 patients receiving CRT, which was identical to that seen in our study. SLD shows variability in the literature as Bax et al reported a value of 71 ± 38 ms in 25 patients with heart failure[10] and 97 ± 35 ms in a different group of 22 patients.[11] In another study, Yu et al[9] reported a mean SLD of 36 ms in a group of 30 heart failure patients, which compares well with the value of 40 ± 37 ms in our group of patients.

Cross-correlation delay versus time-to-peak parameters for quantification of dyssynchrony

The majority of techniques to assess LV dyssynchrony utilize “time-to-peak” analysis where the time from the QRS onset to the peak velocity of a ventricular wall is compared to that of a different ventricular wall.[10] Using DTI, it is possible to obtain velocity curves from two ventricular walls simultaneously at frame rates over 140 Hertz. Therefore, when analysis is limited to time-to-peak systolic myocardial velocity, only one of approximately 140 data points per heart cycle is utilized. XCD analysis overcomes this limitation by utilizing all data (~420 points from 3 consecutive heart beats) from the myocardial velocity curves to quantify dyssynchrony as opposed to just peak values. Therefore it is not surprising that XCD is less vulnerable to the slight errors caused by the myocardium being outside of the stationary ROI for brief periods during the cardiac cycle.

We showed in a previous study using positive and negative control groups that cross-correlation delay was superior to time-to-peak dyssynchrony parameters at diagnosing dyssynchrony.[16] In addition, we showed in our previous study how calculation of XCD does not require identification of systole or manual selection of peak velocities (which are required for time-to-peak dyssynchrony parameters and require additional time and add potential operator error). The results of this study show an additional advantage of XCD while at the same time highlighting a weakness in conventional time-to-peak parameters. XCD dyssynchrony can be diagnosed with a stationary ROI while a tracked ROI should be used to measure conventional time-to-peak parameters. Thus, XCD can be calculated approximately 30 minutes faster per patient than time-to-peak parameters when using current commercially-available software platforms.

Automation of region tracking

The main deterrent from performing ROI tracking is the prolonged time required to complete the analysis. Manual ROI tracking added approximately 30 minutes of post-processing time per patient in our study. However, new speckle tracking technology which enables manual tracking of the myocardium in 2 dimensions[25] could be utilized to perform automated ROI tracking in future DTI post-processing software platforms. A recent study implemented this technique and showed its feasibility.[26]

Study limitations

Since there is no gold standard for diagnosing dyssynchrony, a limitation of our study is that it was unknown whether or not each patient in this study did or did not have dyssynchrony. Thus, we could not compare the performance of the 4 dyssynchrony parameters in diagnosing dyssynchrony. However, we have previously done this in a positive and negative control study where we showed that XCD and Ts-SD showed significantly better discrimination between patients with known dyssynchrony and volunteers with normal function than MaxDiff and SLD.[16] Further comparison studies of the ability of these parameters to predict clinical outcomes of CRT are needed to determine which parameter should become the gold standard for quantifying dyssynchrony.

The true impact of ROI tracking on dyssynchrony assessment may be underestimated in this study as we only included patients with severe heart failure. These patients may have different or less myocardial motion than patients with either normal hearts or less severe disease. Further studies are needed to determine whether the amplitude of myocardial motion causes differing errors when stationary ROIs are used to diagnose dyssynchrony.

Five patients in our study had a left ventricular ejection fraction less than 35% quantified by short-axis M-mode but between 35 and 41% as quantified by a Simpson's bi-plane analysis. We chose *not* to exclude these patients since inclusion criteria for CRT include ejection fraction < 35% typically quantified by M-mode. However, we reported ejection fractions in Table 1 using Simpson's method since this is usually done in the research setting.

Conclusions

Use of a stationary region of interest (ROI) changes the diagnosis of dyssynchrony 11–17% of the time when using conventional Doppler tissue imaging time-to-peak parameters such as septal-to-lateral delay. Cross-correlation delay (XCD) diagnosis of dyssynchrony is unaffected by use of a stationary region of interest. These data demonstrate that region of interest tracking should be used and should be specified when using time-to-peak parameters to quantify dyssynchrony. However, cross-correlation delay dyssynchrony can be diagnosed using stationary regions of interest, which saves post-processing time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

CRT	cardiac resynchronization therapy
LV	left ventricular (or left ventricle)
MaxDiff	maximum difference in times-to-peak systolic velocity between any 2 of the basal septal, lateral, anterior and inferior left ventricular segments
NYHA	New York Heart Association
SLD	septal-to-lateral delay in peak systolic velocity

DTI	Doppler tissue imaging
Ts-SD	standard deviation of times-to-peak systolic velocity of the 12 basal and mid left ventricular segments
XCD	cross-correlation delay

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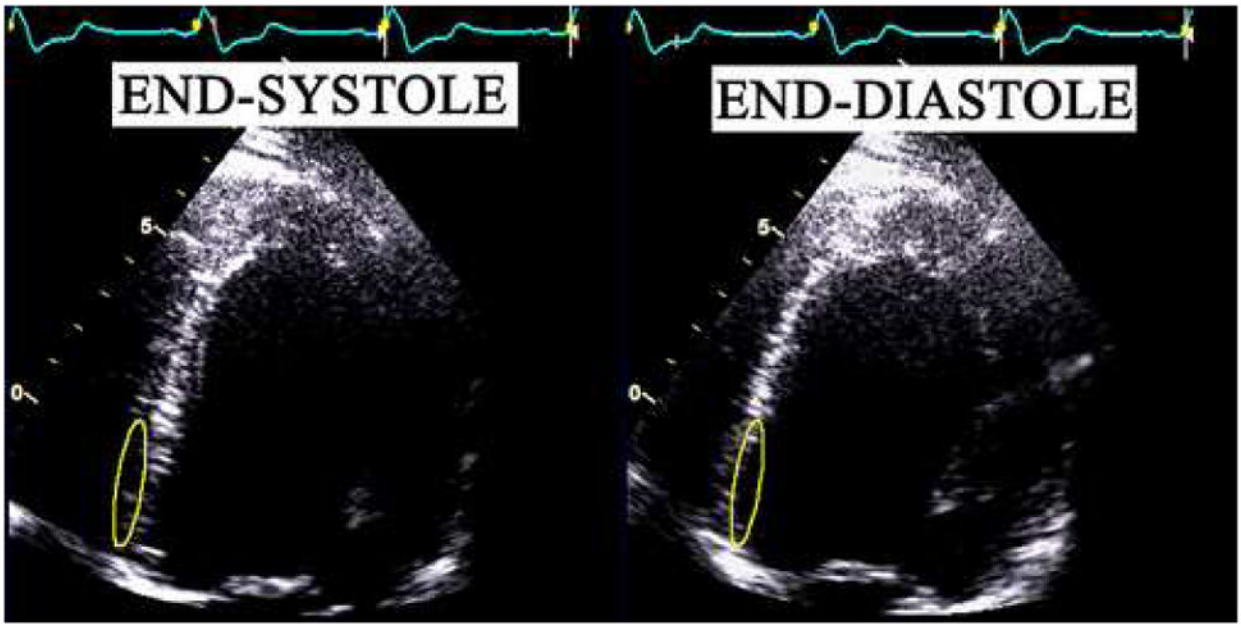

Figure 1.
The myocardium moves into and out of a stationary region of interest during the cardiac cycle. The oval region of interest was placed in the basal septum of a patient with heart failure. The region of interest includes some of the right ventricular cavity at end-systole and some of the left ventricular cavity at end diastole, potentially leading to erroneous myocardial velocity quantification.

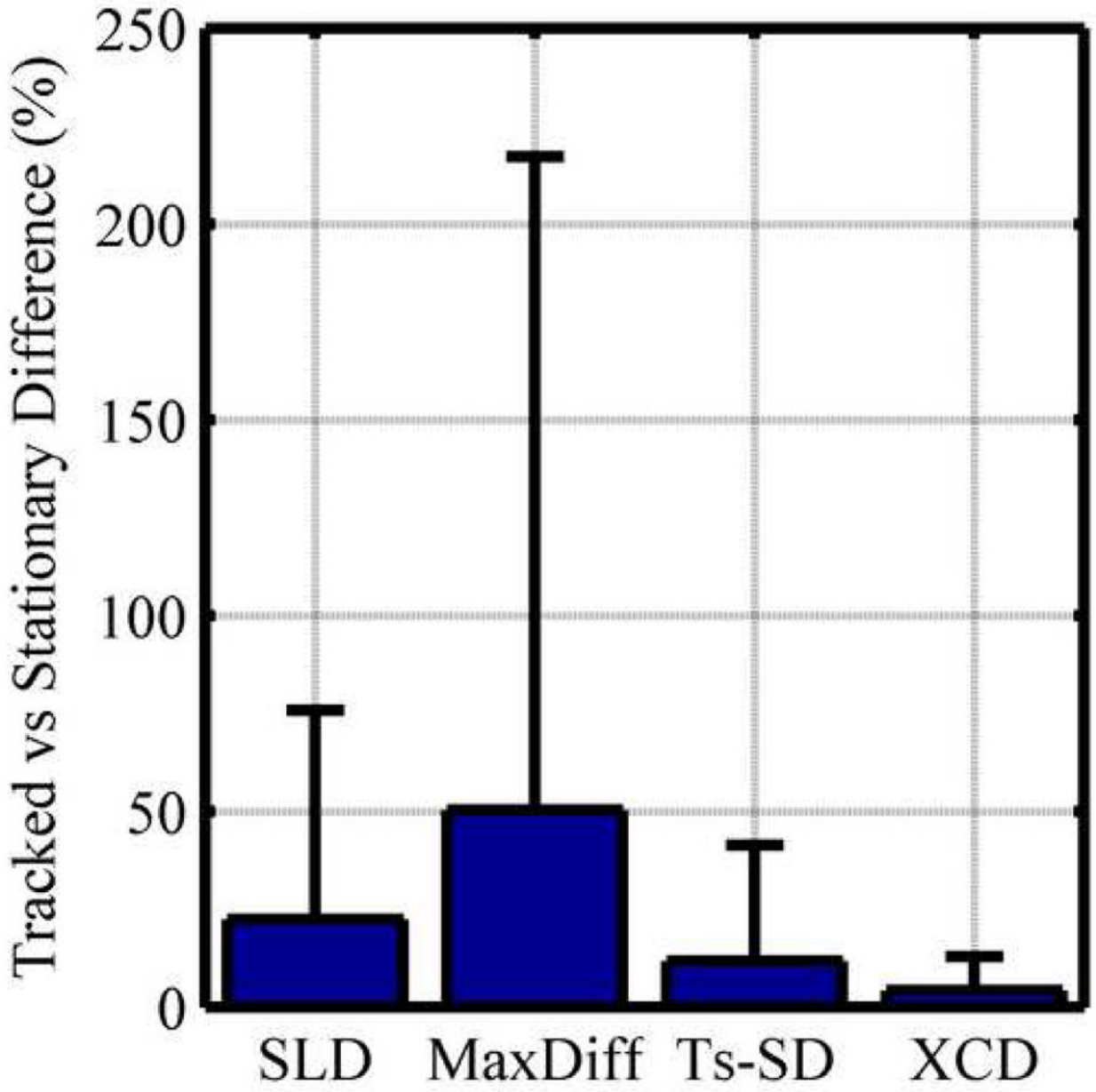

Figure 2.

Cross-correlation delay shows the smallest percent difference between tracked and stationary region of interest quantification of dyssynchrony. *MaxDiff*, maximum difference in times-to-peak systolic velocity between any 2 of the basal septal, lateral, anterior and inferior left ventricular segments; *SLD*, septal-to-lateral delay in peak systolic velocity; *Ts-SD*, standard deviation of times-to-peak systolic velocity in the 12 basal and mid-wall segments of the left ventricle; *XCD*, cross-correlation delay.

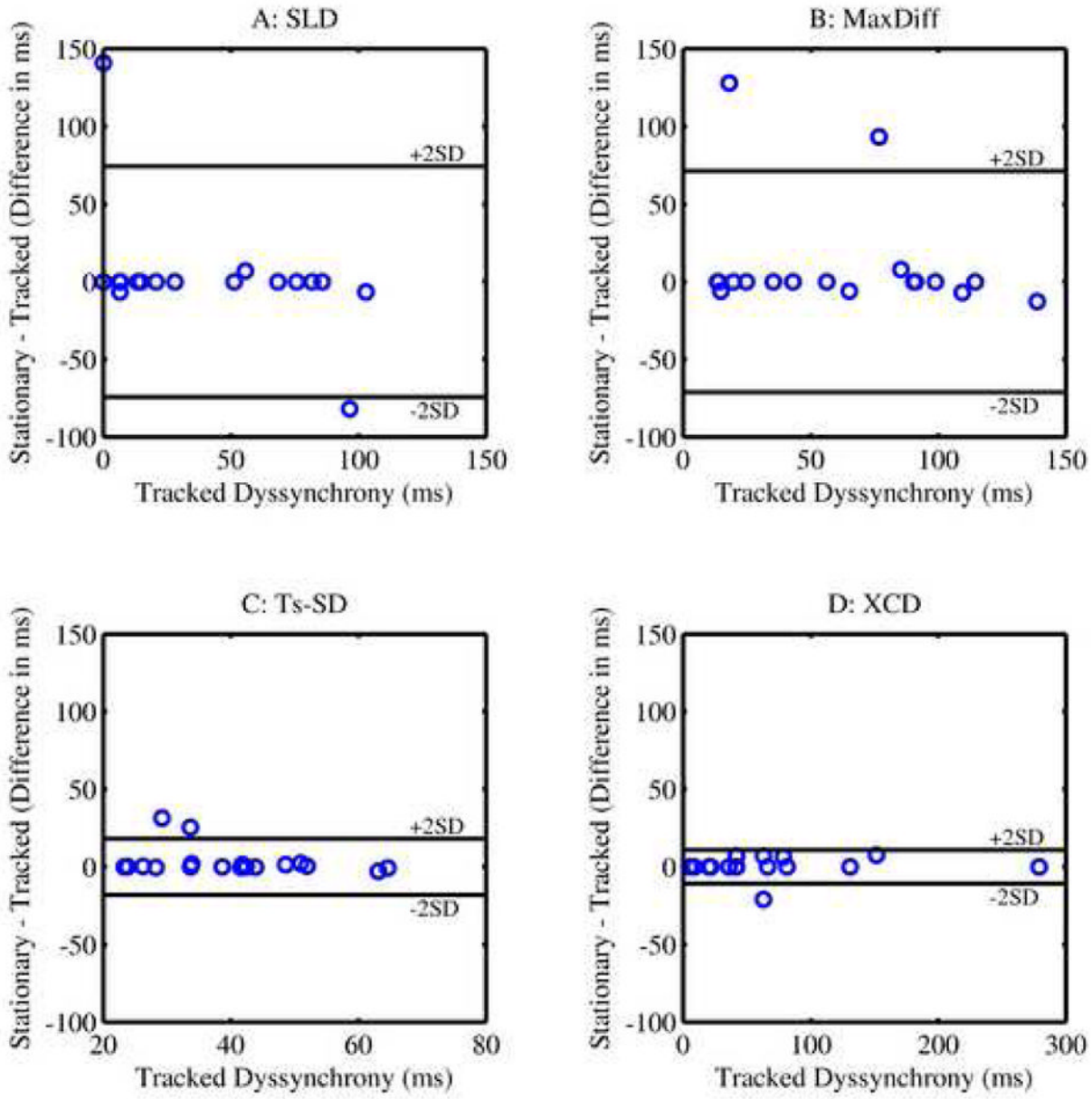

Figure 3.

Cross-correlation delay shows the closest agreement between tracked and stationary region of interest quantification of dyssynchrony. Bland-Altman plots show the difference between using a stationary region of interest and a manually tracked region of interest to quantify dyssynchrony in patients with heart failure. Bars showing ±2*SD are plotted in each figure. **A,** Septal-to-lateral delay (SLD) in peak systolic velocity. **B,** Maximum difference in times-to-peak systolic velocity between any 2 of the basal septal, lateral, anterior and inferior left ventricular segments (MaxDiff). **C,** The standard deviation of times-to-peak systolic velocity in the 12 basal and mid-wall segments of the left ventricle (Ts-SD). **D,** Cross-correlation delay (XCD).

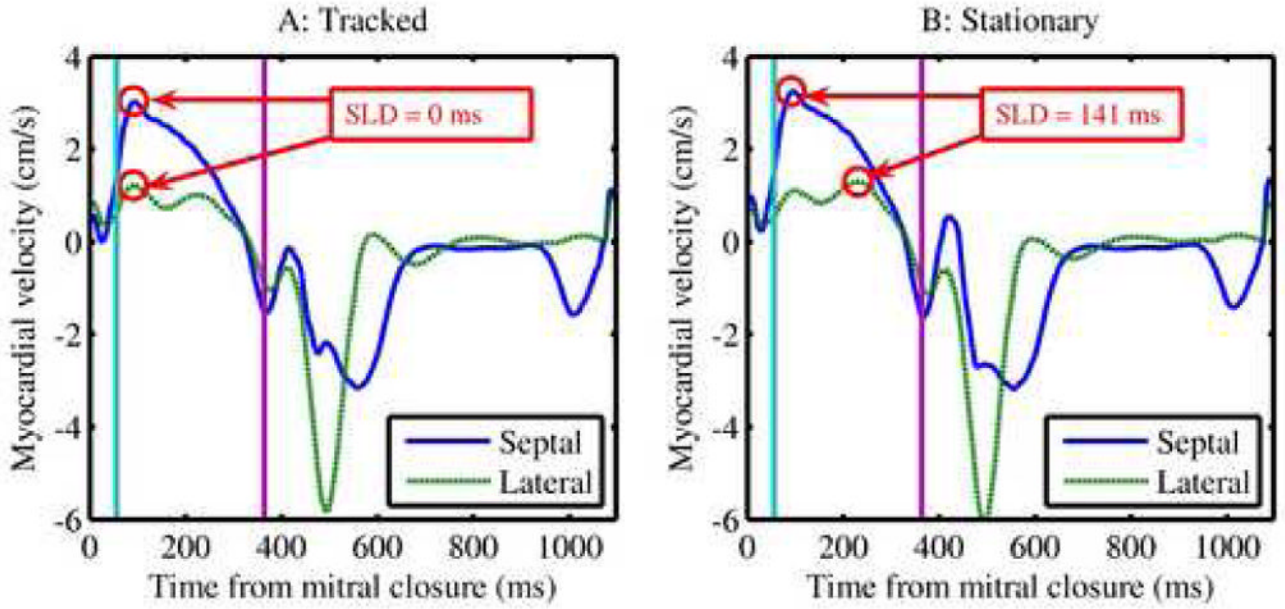

Figure 4.

Stationary region of interest quantification of dyssynchrony with time-to-peak parameters results in a different diagnosis relative to tracked analysis of the same patient. Peak systolic velocities are labeled with red arrows. Pulsed Doppler-derived aortic valve opening (light blue) and closure (magenta) are shown as vertical lines. **A,** Velocity curves from the basal septum and lateral wall reconstituted from manually tracked regions of interest. **B,** Velocity curves from the basal septum and lateral wall reconstituted from stationary regions of interest.

Table 1

Characteristics of the patient population.

Variable (units)	Value*
Age (years)	58 ± 16
Male gender (%)	9 (50%)
LV end systolic volume (ml)	115 ± 51
LV end diastolic volume (ml)	165 ± 64
LV ejection fraction (%)	31 ± 10
QRS duration (ms)	183 ± 36

* Values are means ± SD, $n = 18$.

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Table 2

Dyssynchrony values using tracked versus stationary regions of interest.

Patient Number	SLD (threshold = 60ms)		MaxDiff (threshold = 65ms)		Ts-SD (threshold = 34.4ms)		XCD (threshold = 31ms)	
	Tracked	Stationary	Tracked	Stationary	Tracked	Stationary	Tracked	Stationary
1	86	86	99	99	42	43	20	20
2§	28	28	77	170	29	61	9	9
3*	56	63	90	90	52	52	131	131
4†	51	51	65	59	39	39	36	36
5	82	82	91	91	49	50	81	81
6	76	76	114	114	51	53	5	5
7	0	0	14	14	42	41	41	41
8*	97	15	109	102	63	60	22	22
9	103	96	139	126	65	64	79	85
10*†§	0	141	18	146	34	59	63	42
11	68	68	85	93	42	42	152	159
12	0	0	43	43	24	24	66	66
13	6	6	20	20	34	34	63	70
14	21	21	56	56	44	44	20	20
15	15	15	25	25	26	27	42	42
16§	7	7	35	35	34	36	20	20
17	13	13	13	13	23	23	42	49
18	7	0	15	9	28	28	279	279

All values are dyssynchrony in milliseconds. Published threshold values for diagnosing dyssynchrony are given in the column headers for each parameter.[8,10,13,16]

*Use of a stationary region of interest changed the diagnosis of dyssynchrony according to SLD.

†Use of a stationary region of interest changed the diagnosis according to MaxDiff.

§Use of a stationary region of interest changed the diagnosis according to Ts-SD. *MaxDiff*, maximum difference in times-to-peak systolic velocity between any 2 of the basal septal, lateral, anterior and inferior left ventricular segments; *SLD*, septal-to-lateral delay in peak systolic velocity; *Ts-SD*, standard deviation of times-to-peak systolic velocity in the 12 basal and mid-wall segments of the left ventricle; *XCD*, cross-correlation delay.

Table 3

Comparison of dyssynchrony values using tracked versus stationary regions of interest.

Parameter	Tracked (ms)*	Stationary (ms)*	p†	Dyssynchrony Threshold (ms)‡	Disagreement on Diagnosis between Tracked and Stationary
SLD	40 ± 37	43 ± 42	0.76	60	17 %
MaxDiff	62 ± 40	73 ± 49	0.23	65	11 %
Ts-SD	40 ± 12	43 ± 13	0.14	34.4	17 %
XCD	65 ± 66	65 ± 67	0.79	31	0 %

*Values are means ± SD, $n = 18$.

†Paired t-test comparing tracked and stationary values.

‡Published reference values.[8,10,13,16] *MaxDiff*, maximum difference in times-to-peak systolic velocity between any 2 of the basal septal, lateral, anterior and inferior left ventricular segments; *SLD*, septal-to-lateral delay in peak systolic velocity; *Ts-SD*, standard deviation of times-to-peak systolic velocity in the 12 basal and mid-wall segments of the left ventricle; *XCD*, cross-correlation delay.