

# New Universal Strain Software Accurately Assesses Cardiac Systolic and Diastolic Function Using Speckle Tracking Echocardiography

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**Background:** We have developed new universal strain software (USS) that can be used to perform speckle tracking of any Digital Imaging and Communications in Medicine (DICOM) image, regardless of the ultrasound system used to obtain it. **Methods:** Fifty patients prospectively underwent echocardiography immediately prior to cardiac catheterization. Biplane peak global longitudinal strain (GLS), peak systolic longitudinal strain rate (SSR), peak early diastolic longitudinal strain rate (DSR), and peak early diastolic circumferential strain rate (DCSR) were determined using conventional strain software (CSS) that uses raw data, and using the new USS applied to DICOM images. **Results:** Universal strain software correlated with CSS for GLS ( $r = 0.78$ ,  $P < 0.001$ ), SSR ( $r = 0.78$ ,  $P < 0.001$ ), DSR ( $r = 0.54$ ,  $P < 0.001$ ), and DCSR ( $r = 0.43$ ,  $P = 0.019$ ). GLS and SSR using USS correlated with left ventricular ejection fraction (LVEF) ( $r = -0.67$  and  $-0.71$ , respectively) as well as using CSS ( $r = -0.66$  and  $-0.71$ ). Patients with diastolic dysfunction had significantly lower DSR (0.61 vs. 0.87/sec,  $P = 0.02$ ) and DCSR (0.89 vs. 1.23/sec,  $P = 0.03$ ), and less negative GLS ( $-10.8$  vs.  $-16.1\%$ ,  $P = 0.002$ ) using USS in all patients, as well as among those with LVEF  $\geq 50\%$ . Receiver-operating characteristic (ROC) analysis for detection of diastolic dysfunction revealed a sensitivity and specificity of 82% and 83% for DCSR  $< 1.09$ /sec (area under the curve [AUC = 0.80]) and 85% and 83% for GLS  $> -13.7\%$  (AUC = 0.84) using USS. **Conclusion:** Universal strain software can be used to accurately assess LV systolic and diastolic function using speckle tracking echocardiography. (Echocardiography 2014;31:947–955)

**Key words:** speckle tracking echocardiography, strain, strain rate, systolic function, diastolic function

Strain and strain rate imaging using speckle tracking echocardiography are newer imaging modalities which allow detailed analysis of cardiac mechanics.<sup>1,2</sup> These techniques allow for more sensitive and earlier detection of cardiac disease in a variety of clinical conditions.<sup>3–10</sup> Because they use speckle tracking rather than Doppler methodology, they are not limited by angle dependence as tissue Doppler methods are, and can be measured in any direction within the two-dimensional (2D) imaging plane.<sup>11</sup>

Current conventional techniques for speckle tracking have significant limitations that have impeded their widespread adaptation. Currently,

several ultrasound system vendors have developed their own speckle tracking software techniques to measure strain and strain rate. In the majority of cases, however, the software can only be used with images obtained from their own hardware platform. Furthermore, strain and strain rate values obtained from one hardware/software platform are often different from those obtained on the same patient using a different hardware/software system.<sup>12–15</sup> A third limitation is that images that have not been saved in the raw data format (which is often the case for images archived to a Picture Archiving and Communication System (PACS) in Digital Imaging and Communications in Medicine [DICOM] format) cannot then be analyzed using most conventional speckle tracking software packages, which precludes serial comparisons retrospectively.

To address these limitations, we have developed a new universal strain software (USS) system which can be used to perform speckle tracking of any digital echocardiographic imaging clip that

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has been saved in the standard DICOM format, regardless of the ultrasound system from which it has been obtained. This new software uses a proprietary method to convert the DICOM B-mode data back to a radiofrequency-like signal, which has significant advantages in improving the accuracy of tracking the speckles. In addition, this new software uses the normalized cross-correlation method of tracking, in contrast to the more common, and less computationally intensive sum-of-absolute difference method or other “feature tracking” algorithms that are commonly used in current commercial systems. This normalized cross-correlation method performs better in the presence of noise and is not as affected by signal magnitude.<sup>16</sup> Its limitation has been greater computational demand compared to other methods, but with newer faster computer processors, it is now feasible to perform this technique in real time.

In this study, we sought to test this new USS and to determine if it can be used to accurately assess left ventricular systolic and diastolic function. We tested it in patients enrolled in the RF-SPEED (Radiofrequency-based Speckle Tracking Echocardiography to Evaluate Diastolic Function) study, which was a single center study designed to evaluate speckle tracking echocardiographic techniques for the assessment of diastolic function.

### Methods:

Fifty patients scheduled to undergo a left heart catheterization and coronary arteriography were prospectively enrolled in the RF-SPEED study. Patients were enrolled on the day of their catheterization procedure while waiting in the preprocedure prep area or on the inpatient ward, and each subject provided informed consent prior to participation in the study. Patients were excluded if they had any of the following: suspected acute ST elevation myocardial infarction, acute coronary syndrome with active ongoing chest pain, known or suspected acute aortic dissection, known or suspected cardiac tamponade, known history of unoperated constrictive pericarditis, known or suspected severe aortic stenosis or severe mitral regurgitation, any history of valve surgery, heart rhythm other than sinus rhythm on precath EKG, age less than eighteen years old, or unable to provide informed consent. The protocol was approved by the Institutional Review Board of the University of Michigan.

As part of the study, each subject underwent an echocardiogram using a latest generation commercially available echocardiography system (Vivid E9; GE Healthcare, Waukesha, WI, USA). A 2D apical four-chamber view was obtained,

followed by pulse-wave Doppler of the mitral inflow with the sample volume placed at the level of the tips of the mitral valve leaflets in diastole. Subsequently, pulse-wave tissue Doppler was performed of the septal annulus and lateral annulus. This was followed by 2D imaging of the apical two-chamber and long-axis views, and then parasternal long and short-axis views were obtained. The following ultrasound system acquisition settings were kept standard for all fifty subjects: the “UD clarity” was set to zero, to maintain speckle and avoid any electronic speckle reduction; the reject level was set to zero; the compress level was set to the minimum at 5; and the HD setting was turned off. The frame rate (average  $\pm$  standard deviation [SD]) was  $72 \pm 6$  frames per second.

Raw data echocardiography files were transferred to an offline analysis system for strain and strain rate analysis using commercially available conventional strain software (CSS) that can be used to analyze data from the echocardiography system used for acquisition (2D Strain, EchoPAC PC Workstation; GE Healthcare). DICOM files of the same images were also transferred to a separate computer using minimal lossy compression (95%) for analysis with the new USS (EchoInsight; Epsilon Imaging Inc., Ann Arbor, MI, USA). The USS settings were set to track and measure across the entire myocardium and to provide averaged mid-myocardial strain and strain rate values.

Strain and strain rate analysis was performed using both sets of software. The following parameters were obtained in both the apical four-chamber and apical two-chamber views: peak global longitudinal strain (GLS), peak systolic global longitudinal strain rate (SSR), and peak early diastolic global longitudinal strain rate (DSR). The values from the four-chamber and two-chamber views were averaged together to give a biplane global value, and these averages were used in subsequent analyses. In addition, peak early diastolic circumferential strain rate (DCSR) was obtained from the parasternal short-axis view.

Standard echo measurements were also performed on the echocardiographic images, including mitral inflow peak E- and A-wave velocities and tissue Doppler measurements of early diastolic mitral annular velocities. Left ventricular ejection fraction (LVEF) was determined visually by an expert echocardiographer blinded to all other data using all views available. In addition, ejection fraction (EF) was also measured using the Simpson’s method to determine the left ventricular end-diastolic and end-systolic volumes from the apical four-chamber view.

Subjects underwent left heart catheterization and coronary arteriography immediately after

echocardiography. Left ventricular pressure tracings were recorded during the heart catheterization using standard fluid-filled angiographic catheters connected to a pressure transducer. All tracings were reviewed off line by a single interventional cardiologist blinded to the echocardiography results, and the left ventricular end-diastolic pressure (LVEDP) was recorded.

Diastolic function was characterized based on the E/A ratio from the mitral inflow pattern obtained using pulse-wave Doppler, together with the invasively derived LVEDP to distinguish a pseudonormal from a normal pattern. Normal diastolic function was defined as an E/A  $\geq$  1.0 and  $\leq$  2.0, with an LVEDP  $\leq$  15 mmHg. Grade 1 diastolic dysfunction was defined as E/A  $<$  1.0; Grade 2 diastolic dysfunction as an E/A  $\geq$  1.0 and  $\leq$  2.0, with an LVEDP  $>$  15 mmHg; and Grade 3 diastolic dysfunction as an E/A  $>$  2.0.

Continuous data are expressed as mean  $\pm$  SD, and categorical variables are presented as numbers or percentages. Pearson correlation and Bland–Altman analysis<sup>17</sup> was used to compare the 2 methods (USS and CSS) of strain and strain rate imaging. In addition, Pearson correlation analysis was used to determine the correlation between GLS and EF, and between SSR and EF using each method. *t*-testing was used to compare GLS in patients with and without diastolic dysfunction, as well as to compare DSR and DCSR in patients with and without diastolic dysfunction using each method. Receiver-operating characteristic (ROC) curves were developed for detection of diastolic function using parameters obtained from each method, and the results were expressed as the area under the curve (AUC). Intra- and inter-observer reproducibility was assessed in a subset of 9 patients using the coefficient of variation.<sup>18</sup> Statistical calculations were performed using IBM SPSS version 20 (IBM Corporation, Armonk, NY, USA).

**Results:**

The clinical characteristics of the patients in the study are shown in Table I. Forty-five (90%) of the 50 patients had adequate images for analysis

using the new USS (41 had adequate apical views, and 29 had adequate short-axis views). Figure 1 shows an example of the USS used to analyze the apical four-chamber view of a patient in the study. Forty-eight patients had invasive measurement of their LVEDP. Nine patients had normal diastolic function, 28 had Grade 1 diastolic dysfunction, 11 had Grade 2 diastolic dysfunction, and 1 had Grade 3 diastolic dysfunction, with 1 patient having indeterminate diastolic function. The mean EF was  $50 \pm 17\%$ , and 31 (62%) had an EF  $\geq 50\%$ .

Figures 2 and 3 show the correlations and Bland–Altman comparisons between USS and CSS for measurement of GLS, SSR, DSR, and DCSR. There was a fairly tight correlation between USS and CSS for GLS ( $r = 0.78$ ,  $P < 0.001$ ) and SSR ( $r = 0.78$ ,  $P < 0.001$ ), with a bit weaker correlations for DSR ( $r = 0.54$ ,  $P < 0.001$ ) and DCSR ( $r = 0.43$ ,  $P = 0.019$ ).

Global longitudinal strain using USS correlated well with LVEF ( $r = -0.67$ ,  $P < 0.001$ ), as did SSR using USS ( $r = -0.71$ ,  $P < 0.001$ ). GLS and SSR using CSS also correlated with LVEF ( $r = -0.54$  and  $-0.62$ , respectively, when all patients who underwent analysis by CSS were included ( $n = 50$ ), and  $r = -0.66$  and  $-0.71$ , respectively, when limited to the 41 patients analyzed using the USS,  $P < 0.001$  for all 4 correlations). Alternatively, if Simpson’s method or the clinical catheterization report were used for determination of LVEF, the results were similar ( $r = -0.59$  by Simpson’s method and  $-0.51$  by catheterization for GLS using USS,  $r = -0.59$  by Simpson’s method and  $-0.48$  by catheterization for GLS using CSS).

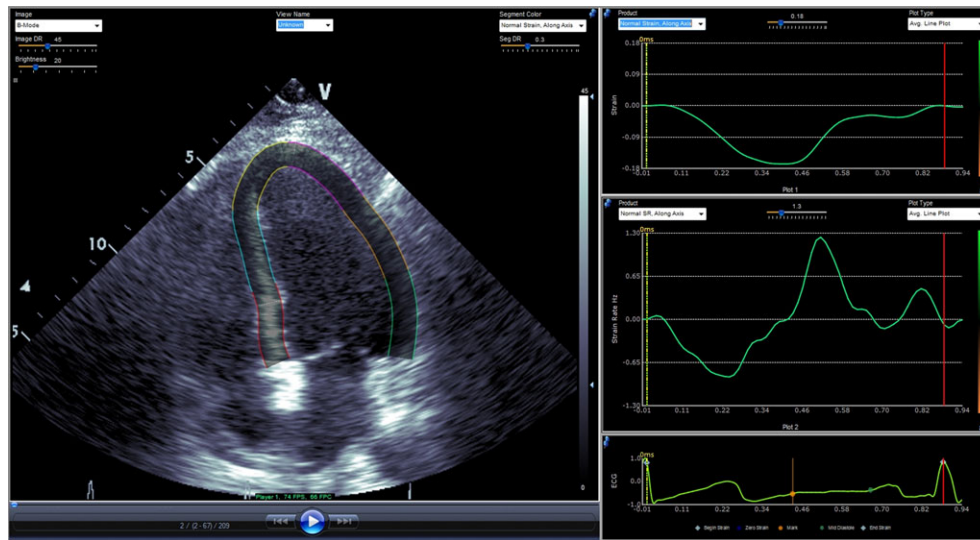
Figure 4 shows the deformation parameters of patients with and without diastolic dysfunction obtained using USS. Patients with diastolic dysfunction had significantly lower DSR ( $0.61 \pm 0.21$  vs.  $0.87 \pm 0.40$ /sec,  $P = 0.018$ ) and DCSR ( $0.89 \pm 0.28$  vs.  $1.23 \pm 0.42$ /sec,  $P = 0.026$ ), and less negative GLS ( $-10.8 \pm 3.5$  vs.  $-16.1 \pm 4.7\%$ ,  $P = 0.002$ ) using USS when all patients were included in the analysis (left panel). Furthermore, among patients with LVEF  $\geq 50\%$  (right panel), those with diastolic dysfunction had significantly lower DSR ( $0.68 \pm 0.22$  vs.  $0.95 \pm 0.38$ /sec,  $P = 0.039$ ) and DCSR ( $0.90 \pm 0.27$  vs.  $1.40 \pm 0.23$ /sec,  $P = 0.004$ ), and less negative GLS ( $-12.4 \pm 2.6$  vs.  $-17.6 \pm 3.4\%$ ,  $P = 0.001$ ) using USS.

Figure 5 demonstrates the ROC curve analysis for detection of diastolic dysfunction. For detection of diastolic dysfunction using USS, the optimal DCSR threshold (for combined sensitivity and specificity) of  $<1.09$ /sec produced a sensitivity of 82% and a specificity of 83% (AUC = 0.80,  $P = 0.025$ ). Likewise, a GLS of  $>-13.7\%$

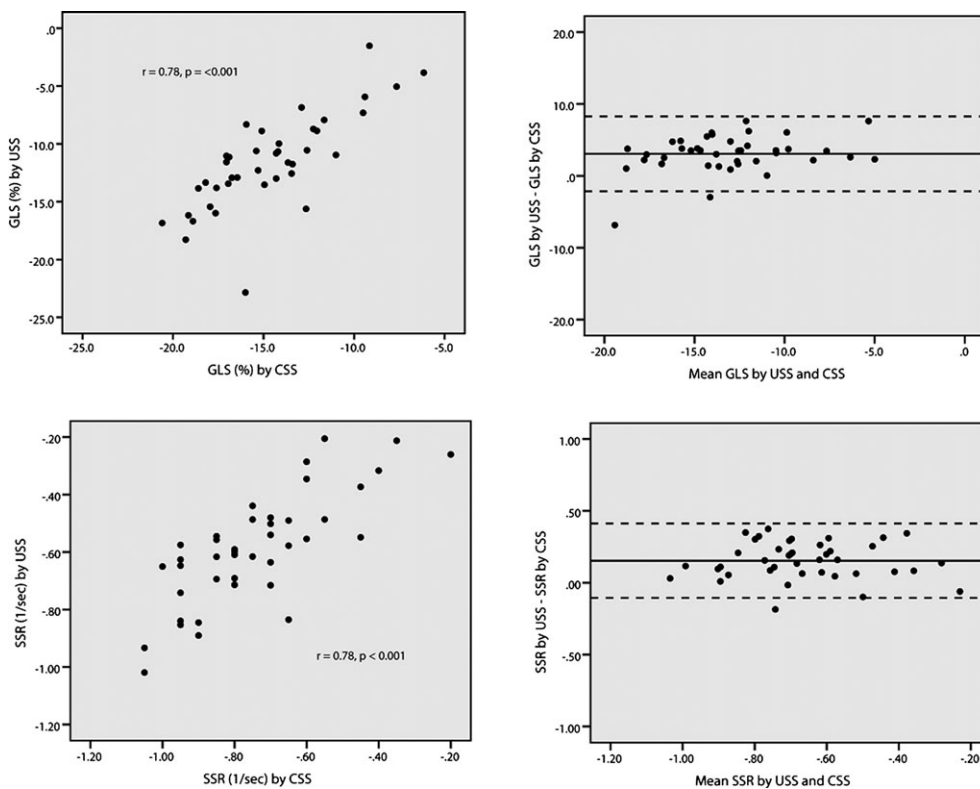
**TABLE I**

Clinical Characteristics of Patients in the Study

Age	50 $\pm$ 10 Years
Female	52%
History of hypertension	60%
History of diabetes	24%
History of congestive heart failure	16%
History of coronary artery disease	40%



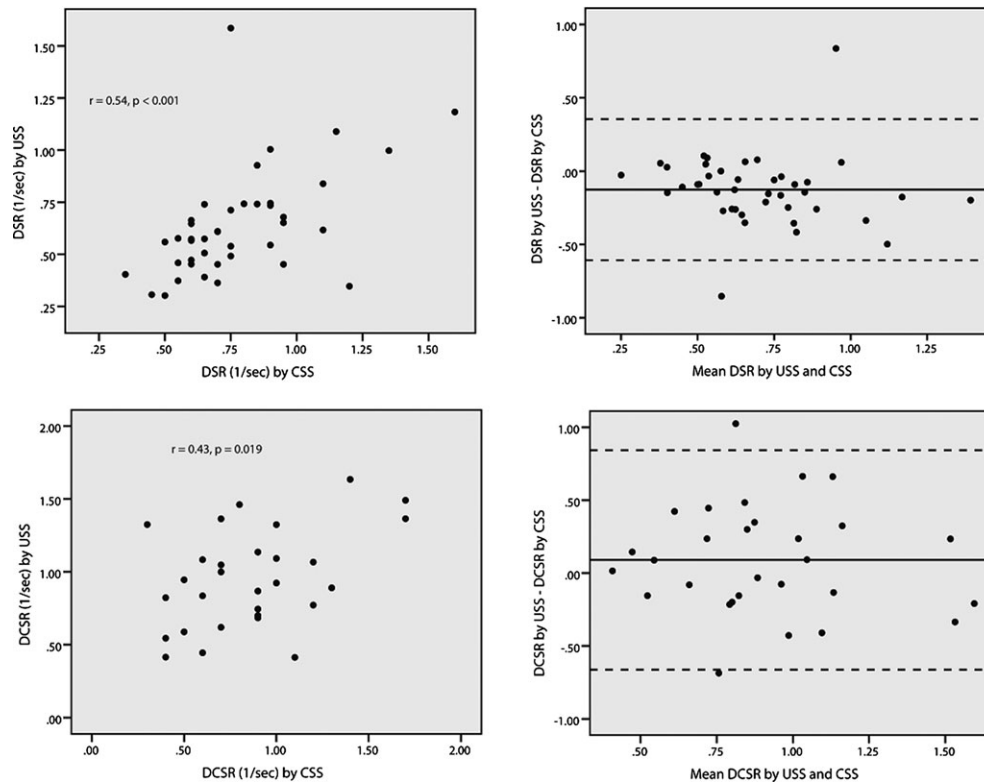
**Figure 1.** Strain and strain rate analysis using the universal strain software (USS). The figure shows an example of an image analyzed using the new USS. The global longitudinal strain (GLS) curve is displayed on the upper right panel, and the strain rate curve is displayed in the middle right panel of the image. The lower right panel is the electrocardiogram tracing.



**Figure 2.** Comparison of universal strain software (USS) and conventional strain software (CSS) for determination of strain and systolic strain rate. Correlation graphs (left panels) and Bland–Altman graphs (right panels) are shown comparing USS and CSS for the parameters global longitudinal strain (GLS) and SSR. The *r* values displayed represent the Pearson correlation. The solid horizontal lines in the Bland–Altman charts represent the line of bias, and the dotted lines represent the 95% limits of agreement.

obtained using USS had a sensitivity of 85% and a specificity of 83% for the detection of diastolic dysfunction (AUC = 0.84, P = 0.009). DSR was

less effective at discriminating between normal and abnormal diastolic function (AUC = 0.74, P = 0.069).



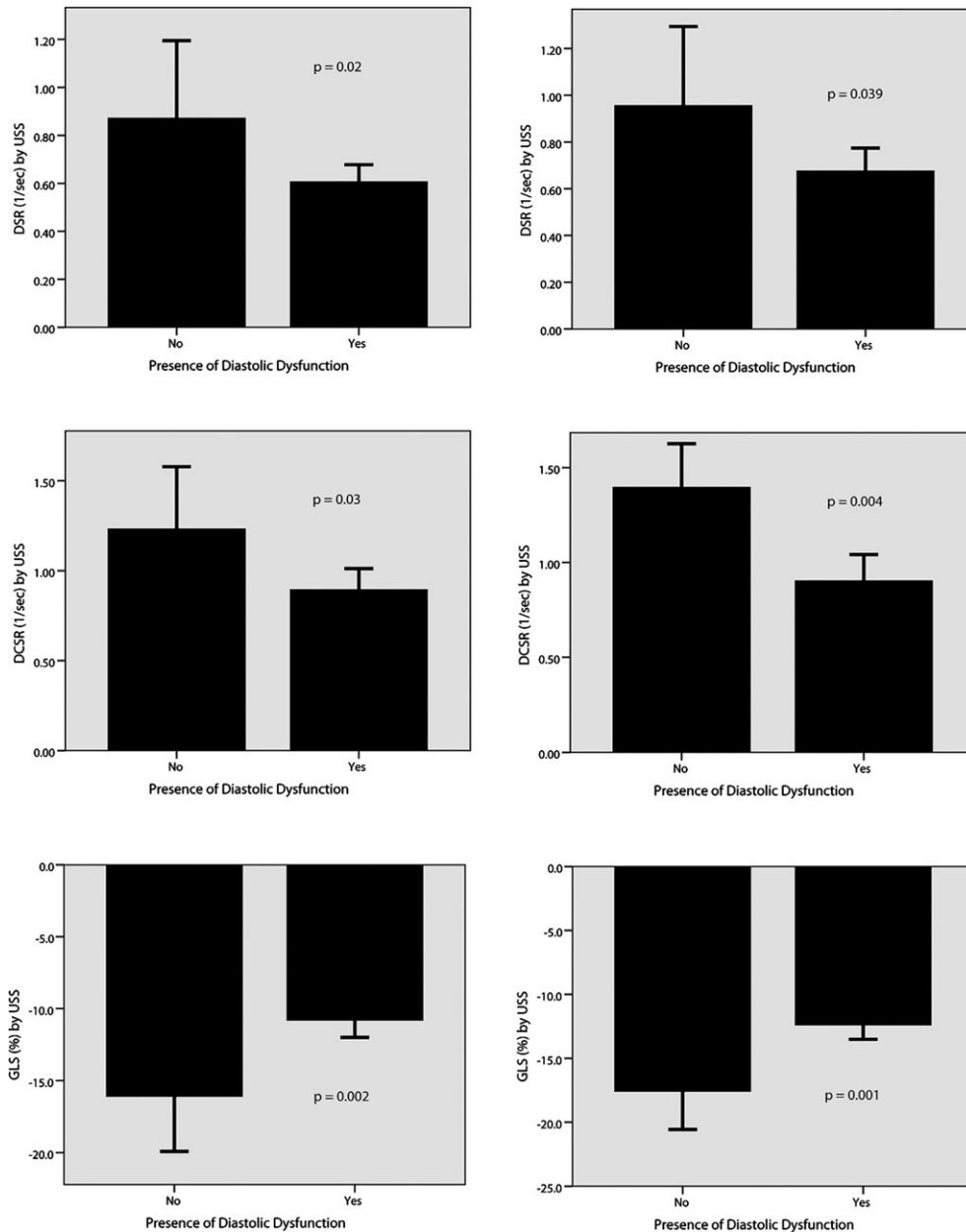
**Figure 3.** Comparison of universal strain software (USS) and conventional strain software (CSS) for determination of diastolic longitudinal and diastolic circumferential strain rate. Correlation graphs (left panels) and Bland–Altman graphs (right panels) are shown comparing USS and CSS for the parameters DSR and DCSR. The  $r$  values displayed represent the Pearson correlation. The solid horizontal lines in the Bland–Altman charts represent the line of bias, and the dotted lines represent the 95% limits of agreement. Global longitudinal strain (GLS) and SSR (shown in Fig. 2) had stronger correlations and narrower limits of agreement compared to DSR and DCSR. DSR = peak early diastolic longitudinal strain rate; DCSR = peak early diastolic circumferential strain rate.

The intra-observer and inter-observer reproducibility of the USS is shown in Table II.

### Discussion:

This study demonstrates that the newly developed USS can be used to accurately assess left ventricular systolic and diastolic function using speckle tracking echocardiography. This new technique has several advantages. Like a universal remote that can be used with multiple different electronic components from different manufacturers, the USS can be applied to any DICOM echocardiographic image regardless of the ultrasound system it was obtained on. In addition, it can be applied retrospectively to images obtained previously, which may be important for comparing serial studies, particularly to evaluate the effect of drug therapy. Finally, because it can be applied to images obtained from different vendors, it has potential to decrease the variability in results that can often occur when multiple different analysis software programs are used; this effect has recently been seen in another study using vendor-independent software.<sup>19</sup>

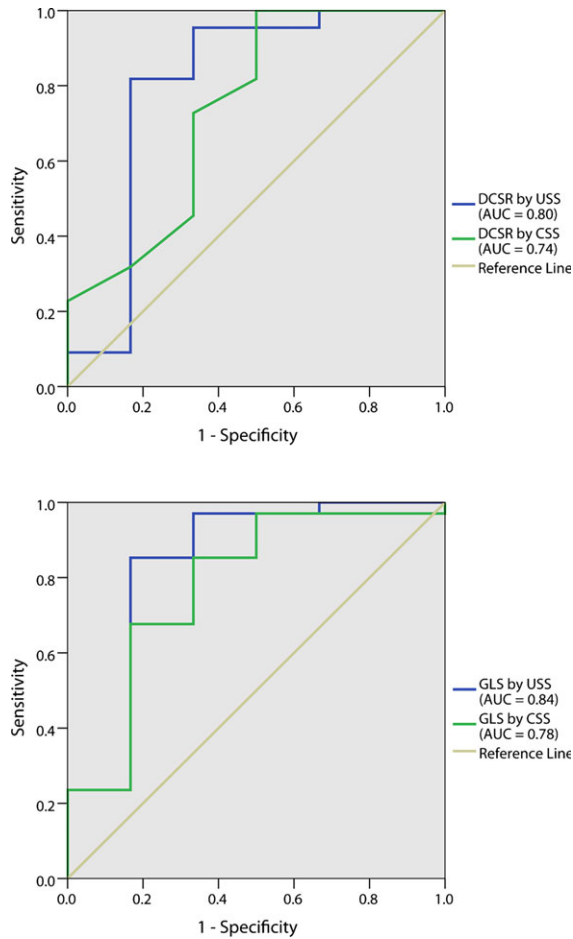
There were strong correlations seen between the USS and CSS for the measures of systolic function (GLS, SSR). There was a slight bias toward higher values for CSS, the etiology of which is likely multifactorial. There are several technical differences between the 2 methods of speckle tracking. The speckle tracking algorithm used by this particularly CSS uses the sum-of-absolute differences method of block matching, whereas the USS uses the normalized cross-correlation method. The normalized cross-correlation method is less affected by noise in the signal, but is more computationally intensive. Second, the CSS used the raw data, as opposed to the processed DICOM images used by the USS, and therefore there may be additional tracking information utilized by the CSS compared to the USS. Finally, the USS calculates the natural strain, as opposed to the Lagrangian strain calculated by the CSS. A potential advantage of the natural strain parameter is that it is calculated instantaneously at each time point, and is not relative to a single measurement at end-diastole; as such, it is less prone to error if the end-diastolic measurement is inaccurate.



**Figure 4.** Comparison of strain and strain rate parameters in patients with and without diastolic dysfunction. DSR, DCSR, and GLS all were significantly reduced in patients with diastolic dysfunction compared to those without diastolic dysfunction, both in the whole cohort studied (left panels) as well as in patients with LVEF  $\geq$  50% (right panels). DSR = peak early diastolic longitudinal strain rate; DCSR = peak early diastolic circumferential strain rate; GLS = global longitudinal strain; LVEF, left ventricular ejection fraction.

The differences seen between the 2 techniques were relatively small, and when each technique was compared to an external measurement of systolic function (EF), they correlated equally well. More patients were analyzed with the CSS (49) than the USS (41), and when all patients analyzed using the CSS were included, the correlation between GLS and EF using CSS

was worse than using USS. This was likely because the additional 8 patients had poorer images, and were included because the automatic quality indicator of the CSS suggested that there was adequate tracking. When those 8 patients were excluded, the correlation between GLS and EF was the same for both CSS and USS; the same held true for SSR. This highlights the



**Figure 5.** ROC analysis for detection of diastolic dysfunction. ROC analysis revealed that DCSR (upper panel) and global longitudinal strain (GLS) (lower panel) obtained using universal strain software (USS) was at least as good as using CSS for the detection of diastolic dysfunction. Using USS, DCSR < 1.09/sec had a sensitivity of 82% and a specificity 83%, and GLS > -13.7% had a sensitivity of 85% and a specificity of 83% for detection of diastolic dysfunction. DCSR = peak early diastolic circumferential strain rate; ROC, receiver-operating characteristic.

**TABLE II**

Intra- and Inter-Observer Reproducibility of USS

	Intra-observer COV	Inter-Observer COV
GLS	7.5%	7.1%
SSR	8.0%	10.5%
DSR	5.2%	12.9%
DCSR	9.4%	12.0%

GLS = peak global longitudinal strain; SSR = peak systolic longitudinal strain rate; DSR = peak early diastolic longitudinal strain rate; DCSR = peak early diastolic circumferential strain rate; COV = coefficient of variation; USS = universal strain software.

important role that image quality plays in the accuracy of speckle tracking.

Of the 2 diastolic strain rate parameters evaluated, the circumferential parameter DCSR was better at distinguishing between patients with normal and abnormal diastolic function compared to the longitudinal parameter DSR, although DSR was obtainable in more patients. ROC curve analysis demonstrated that DCSR obtained using USS was at least as good as that obtained using CSS for detecting diastolic dysfunction. Furthermore, DCSR obtained using USS was significantly decreased in patients with diastolic dysfunction even if they had normal EF; this suggests that it can play an important role in the evaluation of patients with heart failure and preserved EF, who make up a large percentage of all heart failure patients.<sup>20</sup>

An important and significant finding was that GLS itself was a sensitive parameter that was able to distinguish patients with diastolic dysfunction. In fact, GLS had a slightly better sensitivity (85%) with equally good specificity (83%) for the detection of diastolic dysfunction. The difference seen in GLS between those with and without diastolic dysfunction remained even if the patients with decreased EF were excluded. This finding is consistent with prior studies showing that GLS is decreased in patients with heart failure with preserved EF.<sup>21-23</sup> Furthermore, this finding has several potential implications: first, it suggests that there may be an intricate association between systolic and diastolic function. Second, it also raises the possibility that patients with diastolic dysfunction may have subclinical systolic dysfunction, even if they have preserved EF. A third implication deserving consideration is that the measurement of strain itself may not be a measure of only systolic function, but may also incorporate diastolic characteristics of the myocardium. At the very least, these data suggest that evaluation of GLS should be considered for the complete assessment of patients with suspected diastolic dysfunction.

Finally, the intra-observer and inter-observer reproducibility of the USS was quite good. GLS was the most reproducible parameter, but the systolic and diastolic strain rate parameters also had reasonably good reproducibility.

**Limitations:**

This was an initial study evaluating the newly developed USS, and as such, it has a limited number of patients. In addition, all the patients were undergoing clinically indicated heart catheterizations, so there is some selection bias; this was also likely responsible for the relatively fewer number of patients with normal versus abnormal

diastolic function. Another limitation is that the echocardiograms were performed right before, but not during the heart catheterization. The patients typically receive mild intravenous sedation medicine during the catheterization, which could mildly impact the measures of left ventricular filling pressure. The effect of this was likely small, however, and if anything, would make the echocardiographic measurements appear less accurate than they truly are. In addition, the comparison of the 2 methods (USS and CSS) should not be significantly affected, as any confounding effect would be similar on the results from either method. Finally, the comparison of strain to EF is not a pure comparison, as they do not measure the same thing. For this reason, it is not surprising that the correlations are not extremely tight between the 2, but as EF is the most common clinically used measure of systolic function currently, we believe it is useful to see how well strain and strain rate by each technique correlates with it, as has been done previously.<sup>24</sup>

### Conclusions:

Newly developed USS can be used to accurately assess left ventricular systolic and diastolic function using speckle tracking echocardiography. This new technique can be applied to DICOM images obtained from any echocardiographic image. In addition, GLS obtained using this technique was a sensitive marker for the detection of diastolic dysfunction, even in patients with preserved EF.

### Disclosures:

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