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Noninvasive Myocardial Strain Measurement by Speckle Tracking Echocardiography

Validation Against Sonomicrometry and Tagged Magnetic Resonance Imaging

Brage H. Amundsen, MD,* Thomas Helle-Valle, MD,† Thor Edvardsen, PHD, MD,† Hans Torp, DRTECHN,* Jonas Crosby, MSC,* Erik Lyseggen, MD,† Asbjørn Støylen, MD, PHD,*‡ Halfdan Ihlen, MD, PHD,† João A. C. Lima, MD, FACC,§ Otto A. Smiseth, MD, PHD, FACC,† Stig A. Slørdahl, MD, PHD*‡

Trondheim and Oslo, Norway; and Baltimore, Maryland

OBJECTIVES The aim of this study was to validate speckle tracking echocardiography (STE) as a method for angle-independent measurement of regional myocardial strain, using sonomicrometry and magnetic resonance imaging (MRI) tagging as reference methods.

BACKGROUND Tissue Doppler imaging allows non-invasive measurement of myocardial strain in the left ventricle (LV), but is limited by angle dependency.

METHODS Strain measurements with STE were obtained by a custom-made program that allowed tracking of two-dimensional motion of speckle patterns in a B-mode image. In anesthetized dogs, we compared LV long- and short-axis measurements by STE to sonomicrometry during preload changes and regional myocardial ischemia. Measurements in the two orthogonal axes were obtained simultaneously in a single imaging plane. In human subjects, long-axis strain by STE and MRI tagging were compared in multiple segments of the LV.

RESULTS In the experimental study there was good correlation and agreement between STE and sonomicrometry for systolic strain in the long axis ($r = 0.90$, $p < 0.001$; 95% limits of agreement −4.4% to 5.0%) and systolic shortening in the short axis ($r = 0.79$, $p < 0.001$; −5.6% to 5.1%). In the clinical study, 80% of the segments could be analyzed, and correlation and agreement between STE and MRI tagging were good ($r = 0.87$, $p < 0.001$; −9.1% to 8.0%).

CONCLUSIONS Speckle tracking echocardiography provides accurate and angle-independent measurements of LV dimensions and strains and has potential to become a clinical bedside tool for quantifying myocardial strain. (J Am Coll Cardiol 2006;47:789–93) © 2006 by the American College of Cardiology Foundation

Myocardial strain calculated from tissue Doppler imaging (TDI) has been shown to be superior to myocardial velocities by TDI and wall motion score in assessment of ischemia in experimental and clinical studies (1–4). However, TDI-based strain measurements are angle dependent owing to use of the Doppler effect and simultaneous opposite deformation in the long and short axes (1,2). Speckle tracking is an echocardiographic method based on tracking of characteristic speckle patterns created by interference of ultrasound beams in the myocardium (5). As the tracking is based on grayscale B-mode images, it is in principle angle independent. Different speckle tracking methods have been applied in vivo previously, but systematic validation studies are sparse (6,7).

We have developed a speckle tracking echocardiography (STE) application for B-mode images that tracks the displacement of segment end points and calculates strain from the change of length between them. In contrast, a different speckle tracking application that has recently been made commercially available (2D Strain, GE Vingmed, Horten, Norway) tracks a larger number of small regions and averages their motion with spline interpolation before regional curves can be extracted (6). The aim of the present study was to validate STE against sonomicrometry in an experimental study and against magnetic resonance imaging (MRI) tagging in a clinical study.

METHODS

Experimental study. Nine mongrel dogs of either gender (23 ± 2 kg) were anesthetized and instrumented as previously described (2). Recordings were done at baseline ($n = 9$), during intravenous loading with 1,000 ml saline ($n = 9$), and during 5 to 15 min occlusion of the left anterior descending coronary artery (LAD) ($n = 9$). The study protocol was approved by the National Animal Experimental Board.

Sonomicrometry. Four ultrasonic crystals were implanted in the left ventricular (LV) wall (Sonometrics Corp., London, Ontario, Canada) to allow simultaneous measurements

From the *Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway; †Institute for Surgical Research/Department of Cardiology, Rikshospitalet University Hospital, Oslo, Norway; ‡Department of Cardiology, St. Olavs Hospital/Trondheim University Hospital, Trondheim, Norway; and §Department of Cardiology, Johns Hopkins University, Baltimore, Maryland. Dr. Amundsen and Mr. Crosby were recipients of grants from the Research Council of Norway, Oslo, Norway. Drs. Helle-Valle and Lyseggen were recipients of grants from the Norwegian Council of Cardiovascular Diseases, Oslo, Norway. Dr. Torp has received consultant fees from GE Vingmed Ultrasound, Norway.

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Abbreviations and Acronyms

COR = coefficient of repeatability
LAD = left anterior descending artery
LV = left ventricle/ventricular
MRI = magnetic resonance imaging
ROI = region of interest
STE = speckle tracking echocardiography
TDI = tissue Doppler imaging

of long-axis strain (in the septum and lateral wall) and LV short-axis systolic shortening (at the apical and mid-ventricular levels) (Fig. 1A). The traces were analyzed in SonoVIEW (Sonometrics Corp.). Lagrangian strain was calculated as: strain = $(L - L_0)/L_0$, where L_0 is segment length at the onset of the QRS.

Echocardiography. B-mode second-harmonic images (frame rate 68 ± 31 s^{-1}) were recorded from the apical four-chamber view (Vivid 7, 2.0 MHz transducer, GE Vingmed, Horten, Norway). The imaging plane was matched to the crystal positions. Images were analyzed in a Matlab-based custom-made program (MathWorks Inc., Natick, Massachusetts), which uses the "sum of absolute differences" method to find the most similar speckle pattern in two subsequent frames (5) (Fig. 2). Four 5 × 5 mm regions of interest (ROI) were placed corresponding to the crystal positions. Maximum tracking velocities were ±16 cm/s in the beam direction and ±12 cm/s laterally, and forward and backward tracking were averaged (weighted). Strain and shortening were calculated from the change of length between pairs of ROIs and averaged over three cycles. No temporal averaging was applied.

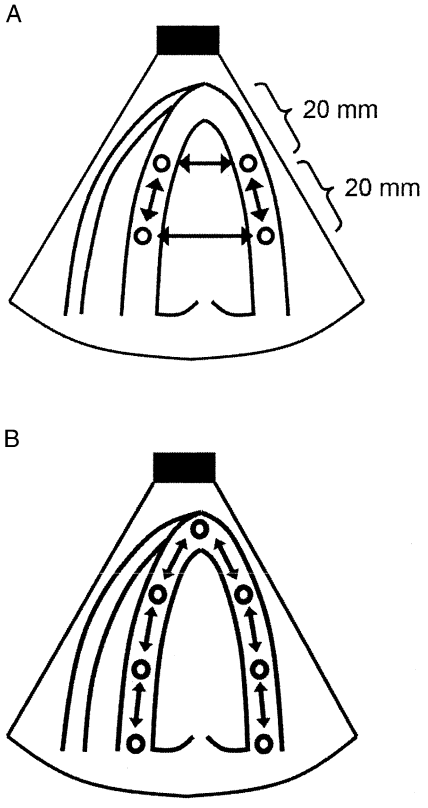

Figure 1. (A) Figure from the experimental study showing an apical four-chamber view with crystal positions **(circles)** and directions for strain and shortening measurements **(arrows)**. **(B)** Figure from the clinical study showing an apical four-chamber view with the positions of the seven regions of interest **(circles)** and **arrows** to indicate where strain was measured.

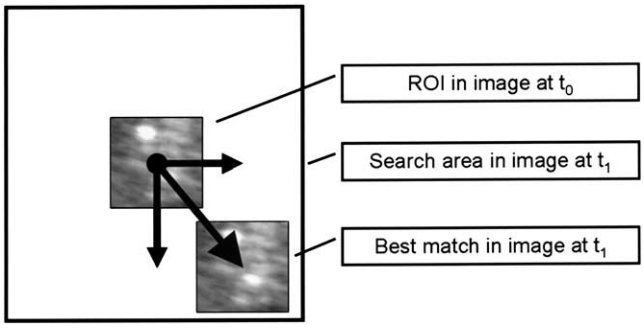

Figure 2. Speckle tracking: the motion of the region of interest (ROI) from one frame (t_0) to the next (t_1) can be quantified in two dimensions, allowing angle-independent measurements. t = time.

Clinical study. Eleven subjects, seven with previous myocardial infarction (65 ± 7 years) and four healthy volunteers (37 ± 13 years) were included after having given written informed consent. The study protocol was approved by the Institutional Review Board of the Johns Hopkins University.

MRI tagging. Tagged MRI images were recorded using a 1.5-T magnet with a phased-array cardiac coil (Signa, GE Healthcare, Waukesha, Wisconsin) applying an electrocardiogram-triggered segmented k-space fast gradient-echo sequence (DANTE-SPAMM) (8). Four to five contiguous stacks of short-axis images were prescribed from base to apex, and six long-axis slices were prescribed radially every 30°. Lagrangian strain was analyzed from this three-dimensional data using a displacement field-fitting method (8). Long-axis strain was measured in the basal, mid, and apical segments of the septum, lateral, anterior, and inferior walls (9).

Echocardiography. B-mode second-harmonic images (frame rate 84 ± 18 s^{-1}) were recorded from the apical two- and four-chamber views (System Five, 2.0 MHz transducer, GE Vingmed). Seven ROIs were positioned to measure strain in six segments in each image (Fig. 1B).

Statistics. Strain values were compared using paired-sample *t* test and by calculating the 95% limits of agreement (10). Bonferroni post-hoc correction of p values was used for comparison of baseline with loading and LAD occlusion values (number of comparisons = 2). Intra- and interobserver variability was measured by the coefficient of repeatability (COR) (10). A $p < 0.05$ was considered statistically significant. Values are reported as mean ± SD.

RESULTS

Experimental study. Long-axis strain measured by STE and sonomicrometry correlated well ($r = 0.90$, $p < 0.001$), as did the measurements of short-axis systolic

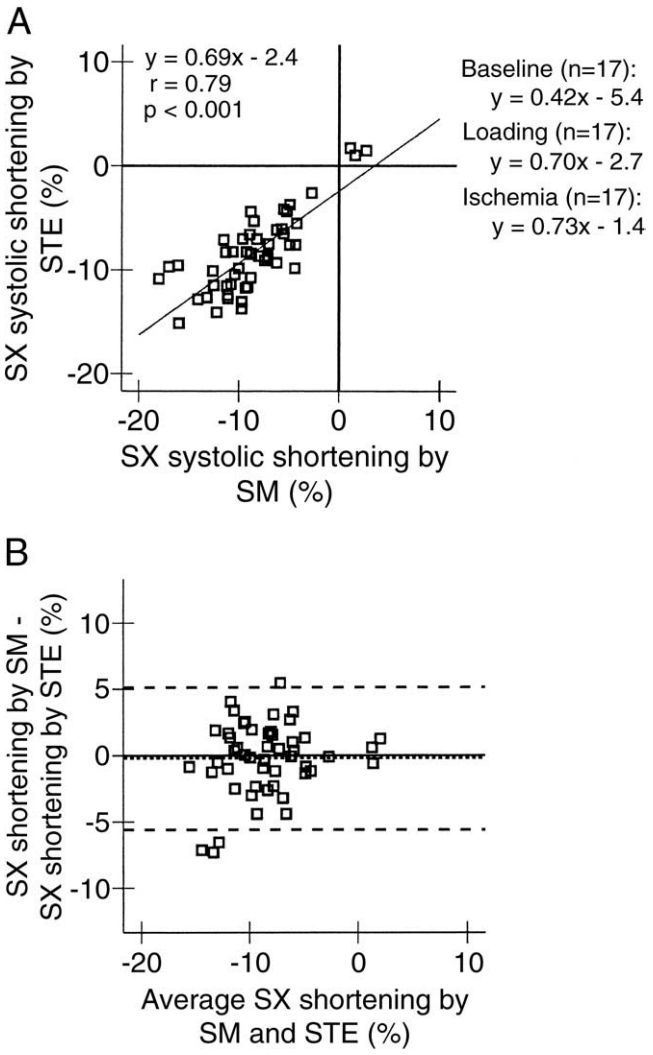

Figure 3. **(A)** Plot showing the relation between left ventricular short-axis (SX) shortening by sonomicrometry (SM) and speckle tracking echocardiography (STE). **(B)** Bland-Altman plot showing the mean difference **(dotted middle line)** and 95% limits of agreement **(dashed lines)**.

shortening ($r = 0.79$, $p < 0.001$) (Figs. 3A and 4A). The 95% limits of agreement for long- and short-axis measurements were not significantly different (−4.4 to 5.0% vs. −5.6 to 5.1%, respectively; $p = 0.28$) (Figs. 3B and 4B). Saline loading increased long-axis septal strain and midventricular systolic shortening, whereas LAD occlusion reduced apical short-axis shortening and lateral wall strain (Table 1). Speckle tracking echocardiography and sonomicrometry measurements were not significantly different in any of the measurement conditions. Intra- and interobserver COR for STE measurements were 4.6% and 7.0%, respectively, for shortening and 6.0% and 6.4%, respectively, for strain. A representative example of traces is shown in Figure 5.

Clinical study. Twenty-six of 132 segments (20%) were excluded from STE analysis (7 because of reverberations, 19 because of drop-outs). Strain measured by STE and MRI tagging correlated well ($r = 0.87$, $p < 0.001$) (Fig. 6A). The 95% limits of agreement were −9.1 to 8.0% (Fig. 6B). Intra- and interobserver COR for strain by STE was 5.2% and 8.6%, respectively. Heart rate was 84 ± 18 beats/min.

DISCUSSION

The present study demonstrates that STE can quantify regional myocardial deformation independent of insonation angle and thus simultaneously assess systolic long-axis strain and short-axis shortening. The accuracy of STE was confirmed using sonomicrometry and MRI tagging as reference methods.

A recent experimental study with a different speckle tracking application found agreement with sonomicrometry comparable to our results (7); however, the researchers used frequencies and depths that are less relevant for a clinical setting. In the experimental part of the present study, STE appeared to underestimate shortening at higher values of short-axis shortening (Figs. 3A and 3B). Poorer lateral than

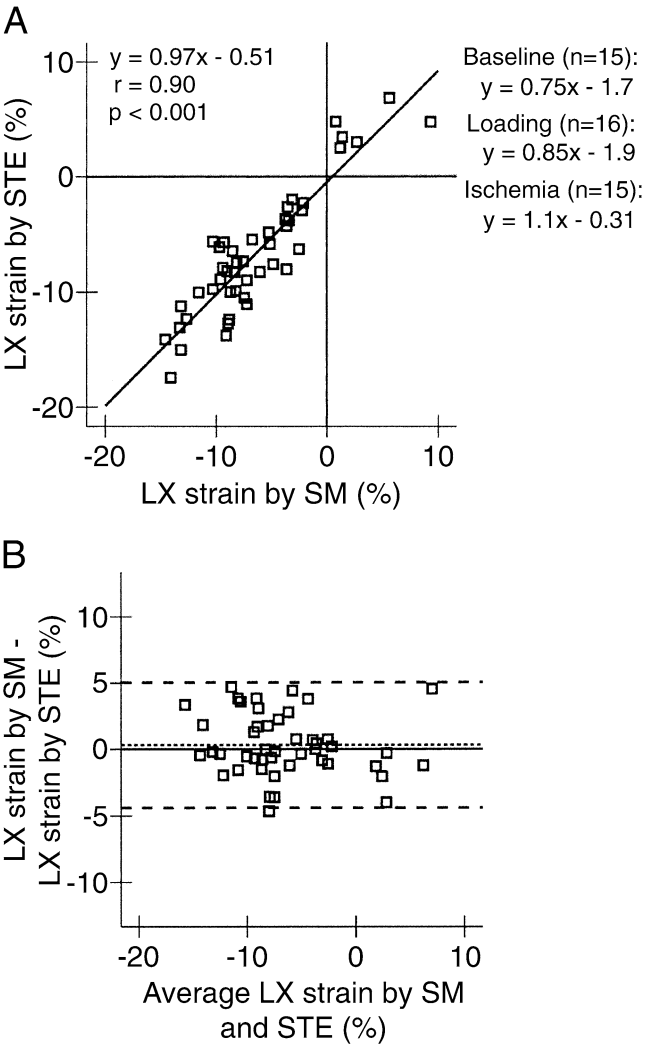

Figure 4. **(A)** Plot showing the relation between long-axis (LX) strain by sonomicrometry (SM) and speckle tracking echocardiography (STE). **(B)** Bland-Altman plot showing the mean difference **(dotted middle line)** and 95% limits of agreement **(dashed lines)**.

Table 1. Results From the Experimental Study

	Baseline	Loading	p Value	Ischemia	p Value
Long-axis strain (%)					
Septum					
STE	−9.0 ± 3	−12 ± 3*	0.032	−10 ± 2	1.0
SM	−9.4 ± 2	−12 ± 2*	0.034	−7.9 ± 2	0.27
Lateral wall					
STE	−5.1 ± 2	−5.9 ± 2	1.0	3.2 ± 3*	0.001
SM	−5.0 ± 2	−5.3 ± 3	1.0	2.5 ± 4*	0.003
Systolic shortening in LV short axis (%)					
Apex					
STE	−8.6 ± 3	−7.9 ± 3	0.81	−4.0 ± 5	0.13
SM	−8.1 ± 3	−8.2 ± 3	1.0	−4.0 ± 5	0.16
Mid-ventricle					
STE	−9.7 ± 2	−11 ± 3	0.13	−8.3 ± 3	0.46
SM	−10 ± 4	−12 ± 4*	0.016	−9.1 ± 4	1.0
Heart rate (min^{-1})	94 ± 13	106 ± 13*	0.042	108 ± 9*	0.042

All values are mean ± SD. The p values are for comparison with baseline values. All p values are adjusted for multiple comparisons (Bonferroni, n = 2). *Significantly different from baseline.
LV = left ventricle; SM = sonomicrometry; STE = speckle tracking echocardiography.

axial resolution might explain this, as there was no such trend in the long-axis strain measurements.

In the clinical study STE was tested against MRI tagging, which is currently the non-invasive gold standard for evaluation of systolic deformation (11). Reduced systolic strain was found in infarcted areas, whereas remote myocardium had normal values. The agreement was comparable to what has previously been reported for TDI-based strain and MRI tagging (8), as was the percentage of analyzed segments (3).

The number of beams covering the sector determines the lateral resolution, and in TDI recordings for strain measurements, this number is three to four times lower than in B-mode images, which are used in STE. Even though strain can be measured only in the beam direction with TDI methods, the lateral resolution is important, as lower resolution increases the likelihood for inclusion of noise from for instance the pericardium. In TDI-based

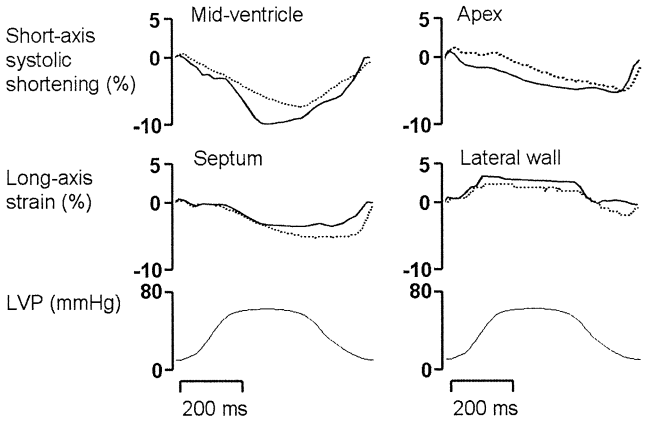

Figure 5. Recordings from a single experiment during left anterior descending artery occlusion. **(Upper panels)** Left ventricular (LV) short-axis shortening at mid-ventricular level **(left)** and apical level **(right)**. **(Middle panels)** Long-axis strain in the septum **(left)** and lateral wall **(right)**. **(Lower panels)** LV pressure (LVP) for timing. Reduced short-axis systolic shortening and lateral wall strain indicate ischemic dysfunction. **Dashed line** = sonomicrometry, **solid line** = speckle tracking echocardiography.

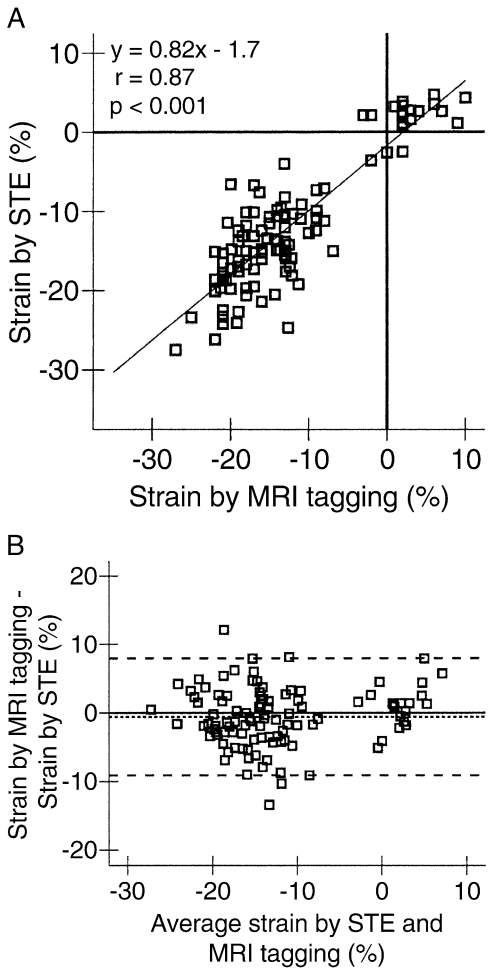

Figure 6. (A) Long-axis strains measured by magnetic resonance imaging (MRI) tagging and speckle tracking echocardiography (STE). **(B)** Bland-Altman plot showing the mean difference **(dotted middle line)** and 95% limits of agreement **(dashed lines)**.

methods, such noise can be included without the user's knowledge, whereas the accuracy of STE can be inspected by the user because the tracking result is displayed in the image.

Study limitations. Sonomicrometry measures the motion of material points in the myocardium, while STE measures motion in the image plane. Thus, misalignment between the ultrasound plane and the crystals and out-of-plane motion were probably the most important sources of variation between the methods. High B-mode frame rates were used to minimize speckle decorrelation.

In the clinical study, misaligned image planes and segment boarders in MRI tagging and STE might explain some of the variation. As strain by MRI tagging was calculated by a three-dimensional technique, whereas STE is two-dimensional, out-of-plane movement in STE could also have contributed to the variation.

The ROI size must be considerably larger than the image resolution to allow robust tracking, but also small enough to allow accurate positioning. We did not perform systematic comparisons of the effects of different ROI sizes on tracking quality, but preliminary testing showed that 5 × 5 mm was a reasonable compromise between robust tracking and accurate positioning.

The Vivid 7 scanner used in the experimental study has better resolution than the System Five scanner used in the clinical part, and using Vivid 7 in the clinical study as well might have improved our results.

Conclusions. The present study demonstrates that STE can provide accurate and angle-independent measurements of regional myocardial strain and has potential to become a clinical bedside tool to quantify regional myocardial function.

Reprint requests and correspondence: Dr. Brage H. Amundsen, Department of Circulation and Medical Imaging, NTNU, MTFS, N-7489 Trondheim, Norway. E-mail: brage.h.amundsen@ntnu.no.

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