

# Endocardial Surface Area Tracking for Assessment of Regional LV Wall Deformation With 3D Speckle Tracking Imaging

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**OBJECTIVES** The aim of this experimental study was to validate area tracking by 3-dimensional (3D) speckle tracking imaging (STI) as a method to measure changes in regional left ventricular (LV) endocardial surface area with sonomicrometry and to assess the usefulness as a wall motion evaluation method compared with 1-dimensional strain parameters.

**BACKGROUND** A 3D-STI allows for tracking a regional endocardial surface area during a cardiac cycle. Area tracking is a new concept that regional wall motion is quantified through the magnitude of deformation in an endocardial surface area.

**METHODS** In each of 8 anesthetized sheep, sonomicrometry crystals were implanted on the endocardium at the LV mid and apical anterior walls. Area change ratio (ACR) that was a novel parameter obtained by area tracking was measured as percentage change in a segmental area during systole. Segmental longitudinal (LS) and circumferential strain (CS) also were measured by 3D-STI. The ACR, LS, and CS were compared with those by sonomicrometry at baseline and during pharmacological stress tests (dobutamine and propranolol infusion) and acute myocardial ischemia induced by occlusion of mid-left ascending artery.

**RESULTS** The strong correlation was observed between ACR measurements by 3D-STI and those by sonomicrometry ( $Y = -4.20 + 0.84X$ ,  $r = 0.87$ ,  $p < 0.001$ ). The ACR showed significant relations with both LS and CS (LS:  $Y = -15.1 + 1.73X$ ,  $r = 0.73$ ,  $p < 0.001$ ; CS:  $Y = -5.85 + 1.06X$ ,  $r = 0.79$ ,  $p < 0.001$ ). ACR showed significant differences among baseline, pharmacological stress, and acute myocardial ischemia. In contrast, LS and CS were reduced significantly during acute ischemia studies compared with those during the other studies; no differences were observed among baseline, propranolol infusion, and dobutamine infusion studies.

**CONCLUSIONS** Area tracking by 3D-STI can estimate changes in LV regional area and might be promising for regional wall motion evaluations. (J Am Coll Cardiol Img 2011;4:358–65) © 2011 by the American College of Cardiology Foundation

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Left ventricular (LV) regional wall motion has been assessed by regional deformation measurements, which are separated into 3 components: longitudinal, circumferential, and radial strain. Speckle tracking imaging (STI) has been focused as a useful modality to assess myocardial deformation (1–4). Because of complex 3-dimensional (3D) wall deformations including longitudinal entire heart motion and circumferential rotation during the cardiac cycle, a 3D-STI system might have an advantage in assessing accurate regional deformation. Recently, a robust 3D-STI system was developed and introduced on a commercially available ultrasound system (5,6). We previously validated strain measurements by the 3D-STI system against data obtained by sonomicrometry to assess regional myocardial function (7). In addition, this system allows tracking a regional endocardial surface area during a cardiac cycle. Area tracking is the new concept that regional wall motion is quantified through the magnitude of deformation in an area. Area tracking has combined data for 2 directional deformations, longitudinal and circumferential components, which might decrease the tracking error and emphasize synergistically the magnitude of deformation. Therefore, area tracking might be more sensitive in assessing LV regional deformation compared with 1-dimensional (1D) strain parameters. This experimental study aimed to validate area tracking as a novel method to measure changes in regional LV endocardial surface area with sonomicrometry and to assess the usefulness of area tracking as a wall motion analysis method compared with 1D strain parameters.

## METHODS

**Animal preparation.** Eight male hybrid Suffolk sheep (Japan Lamb, Ltd., Hiroshima, Japan) were used for this study. After receiving approval from the Institutional Animal Experiment Committee of the University of Tsukuba, we carried out all experiments in a humane manner and in accordance with the “Regulation for Animal Experiments” of our university and the “Fundamental Guideline for Proper Conduct of Animal Experiment and Related Activities in Academic Research Institutions” under the jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology. Anesthesia was induced with thiopental sodium (10 to 15 mg/kg IV), and the animals were intubated. Anesthesia was maintained with isoflurane (1.5% to 2%) and oxygen. All animals underwent left thoracot-

omy under aseptic conditions. Polypropylene snares were loosely placed around the appropriate coronary arteries. A fluid-filled catheter was inserted via a femoral artery for continuous monitoring of systemic arterial pressure and heart rate.

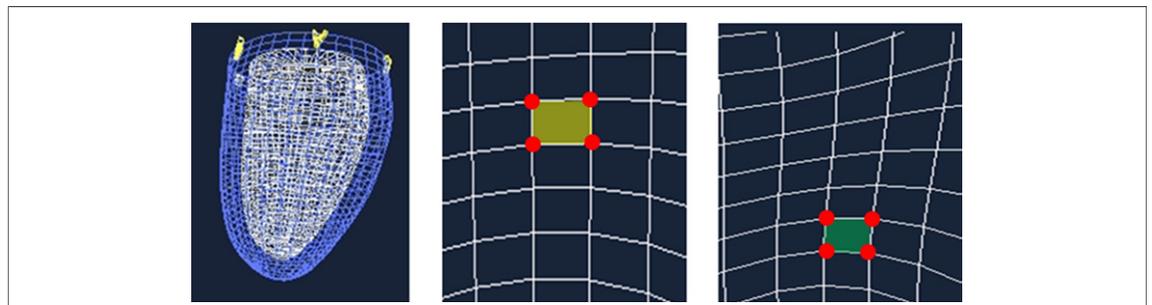
**Echocardiography.** Echocardiographic examinations were performed with an Artida ultrasound system (Toshiba Medical Systems, Tochigi, Japan). Full-volume, electrocardiography-gated, 3D datasets were acquired from apical positions with a matrix array 2.5-MHz transducer, which was fixed in an ultrasound gel-filled latex bag and placed on the apical epicardium. To obtain these datasets, 4 or 6 sectors were scanned and automatically integrated into a wide-angle ( $70^\circ \times 70^\circ$ ) pyramidal data image covering the entire LV. Frame rate of each image was set at approximately 30 Hz.

The data were stored and transferred to a computer (INSPIRON 1300, Dell, Inc., Round Rock, Texas) for offline analysis. The images were analyzed with software (3D Wall Motion Tracking, Toshiba Medical Systems) specific for the analysis of data acquired by the Artida. First, the endocardial border of the 4-chamber image at end-diastole was traced manually, followed by manual tracing of the epicardial border. Second, the same tracing processes were repeated in the 2-chamber image. After these long-axis tracings were complete, 3D myocardial surfaces were automatically reconstructed, and fine adjustments were made to the traced borders on the short-axis images.

**Wall motion tracking algorithm.** First, the tracking points are distributed on the 3D curved surfaces (Fig. 1). Alternatively, motion estimation points where the image has features appropriate for tracking are located automatically in a region of myocardium in each volume frame. Each tracking point is moved on the basis of the motion information obtained from nearby motion estimation points. The motion vector for each motion estimation point between consecutive volume frames is detected by template matching technique. In the template matching process, the template volume in the current frame is generated from an approximately  $10 \times 10 \times 10$ -mm cube in which the motion estimation point is centered. The most similar point in the next volume is searched for by comparing a template volume with the cube in the next volume. We used the 3D sum of squared differences method to test image similarity. Finally,

### ABBREVIATIONS AND ACRONYMS

<b>ACR</b>	= area change ratio
<b>CS</b>	= circumferential strain
<b>LAD</b>	= left anterior descending coronary artery
<b>LS</b>	= longitudinal strain
<b>LV</b>	= left ventricle/ventricular
<b>STI</b>	= speckle tracking imaging



**Figure 1. Area Tracking of Endocardial Surface**

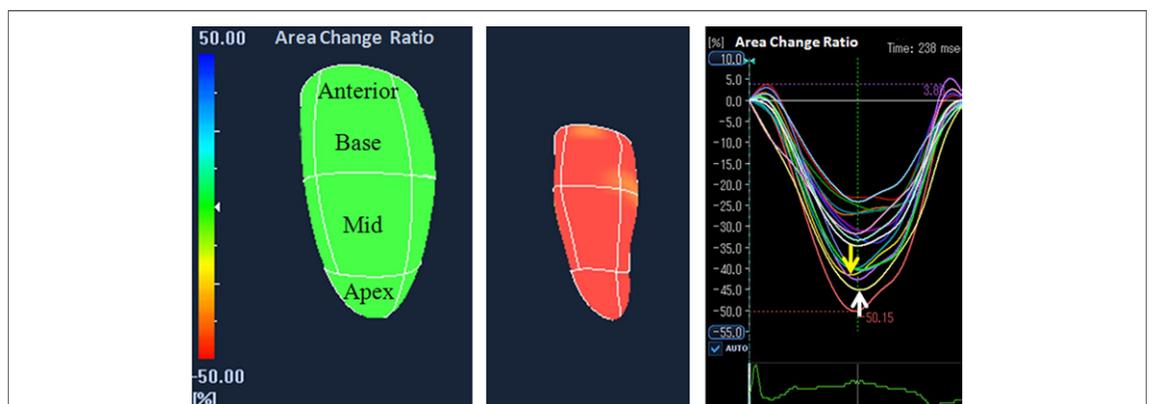
A 3-dimensional speckle tracking image called “mesh” (left panel) is shown. A unit segment image of endocardial sight at end-diastole (center panel) and 1 at end-systole (right panel); the yellow area in the center panel corresponds to the green area in the right panel. The red points located at intersection points show tracking points. Note the apparent area deformation between the yellow region and the green region, showing apical translation and rotation through systolic phase.

interpolation of the motion vectors is performed with a 3D interpolation algorithm. After these steps, arbitrary points of interest on the cardiac wall can be tracked by integrating the interpolated motions over all frames during 1 cardiac cycle. We identified the tracking quality by eye on the basis of the tracking quality of both endomyocardial and epimyocardial trace lines on multiplanar reconstruction images (6).

**Area change ratio.** Figure 1 shows area tracking images in a unit segment that is defined by 4 tracking points. The area in a unit segment is calculated frame-by-frame. Then, area change in a unit segment is calculated as follows:  $(A - A_0)/A_0$ , where  $A(t)$  is the area at time  $t$ , and  $A_0$  is the corresponding area at the peak of the R-wave of the QRS complex. Area change ratio (ACR), which is a parameter of systolic area change in a LV seg-

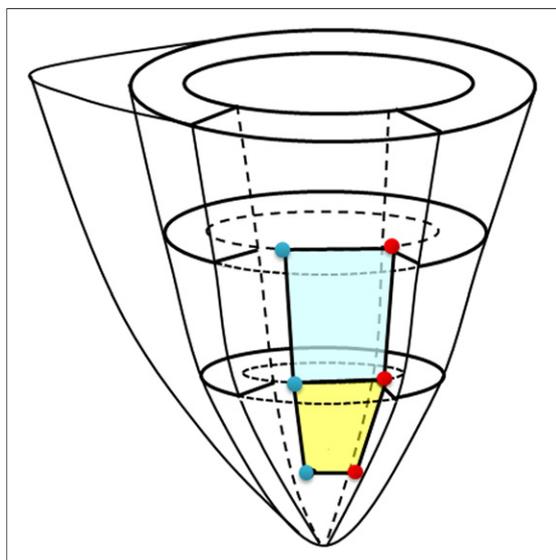
ment, is calculated as an average value of all unit segment data in each LV segment (Fig. 2).

**Sonomicrometry study.** In all sheep, 6 sonomicrometry crystals (2 mm in diameter, Sonometrics Corporation, London, Ontario, Canada) were implanted in LV anterior subendocardium (Fig. 3). Basal crystals were implanted at the border between the basal and mid segments, mid crystals were implanted at the border between the mid and apical segments, and apical crystals were implanted in the mid portion of the LV apical segment. Of 6 crystals, 3 were implanted at the septal side, and the other 3 were implanted at the border between the anterior wall and lateral wall. The crystals were introduced in an oblique way to avoid damage to the myocardium to be studied. After each implant procedure, appropriate positioning of each crystal was confirmed by 2-dimensional echocardiographic imag-



**Figure 2. Assessment of Area Change Ratio**

A 3-dimensional speckle tracking image called “plastic bag” at end-diastole (left panel) and end-systole (center panel) and area change ratio-time curves corresponding to data in 16 regional segments of the left ventricle (right panel) in a baseline study is shown. The yellow arrow shows the area change ratio-time curve in mid-anterior wall (upper yellow curve), and the white arrow shows the curve in apical anterior wall (lower yellow area).



**Figure 3. Scheme of Implanted Positions of Sonomicrometry Crystals**

Red and blue dots show each crystal position, the blue area is a region of the mid anterior wall, and the yellow area is a region of the apical wall.

ing. Crystals in the apical regions were implanted in the segments corresponding to territories supplied by the distal left anterior descending coronary artery (LAD). Implant locations for mid crystals were in borderline areas at risk of ischemia, which was dependent on individual differences in bifurcation patterns of the diagonal artery branch. Sonomicrometry recordings were made with CardioSOFT Pro (Sonometrics Corporation).

Two LV anterior regions that consisted of 4 crystals were assessed to measure area deformation; 1 consisted of 2 basal and 2 mid crystals corresponding to a LV mid region of interest, and another consisted of 2 mid and 2 apical crystals corresponding to a LV apical region of interest. Each region of interest was approximated as a trapezoid section. A baseline area at mid anterior wall was calculated from the trapezium rule with the width between 2 basal crystals and 2 mid crystals and height between the basal and mid crystals in the lateral side at the onset of the QRS. Similarly, a baseline area at the apical anterior wall was calculated with the width between 2 mid crystals and 2 apical crystals and height between the mid and apical crystals in the lateral side at the onset of the QRS. Consequently, an end-systolic area at the mid anterior and apical wall was calculated in the same manner. Then, change in an area was obtained from 1 at baseline and at end-systole. Strain was calculated as:  $\text{strain} = L(t) - L_0/L_0$ , where

$L(t)$  is the segment length at time  $t$ , and  $L_0$  is the segment length at the onset of the QRS. Longitudinal strain (LS) of the LV mid segment was measured as the mean between the basal and mid crystals in each anterior and lateral wall, and the LS of the LV apical segment was measured between mid and apical crystals. Circumferential strain (CS) of the LV mid wall were assessed as the mean of basal paired and mid paired crystals, and apical anterior segments were measured as the mean of mid paired and apical paired crystals. All strain data were calculated by averaging data from 10 consecutive heart beats.

**Experimental protocol.** Sonomicrometric and echocardiographic measurements were obtained sequentially.

After baseline studies, datasets were recorded under continuous intravenous dobutamine infusion (2 to 3  $\mu\text{g}/\text{kg}/\text{min}$ ). After the end of dobutamine infusion and when vital signs had returned to resting conditions, recordings were repeated under intravenous infusion of propranolol (1 mg/min, total dose 6 to 10 mg). After baseline recordings and pharmacological stress tests, ligation of the LAD coronary artery and its second diagonal branch was performed at 40% of the distance from the apex to the base of the heart. Recordings were repeated at 10 min after LAD occlusion. The mechanical ventilator was stopped for no more than 30 s to minimize the effects of variation in heart position caused by breathing while acquiring the 3D dataset, because tracking quality can be affected by stitching artifacts appearing at the sector borders.

**Reproducibility.** Ten studies composed of 2 studies each of baseline, dobutamine infusion, and ischemic procedures were selected for the assessment of intraobserver and interobserver reproducibility of ACR, CS, and LS measurements. To test intraobserver variability, a single observer analyzed the data twice on occasions separated by an interval of 1 month. To test interobserver variability, a second observer analyzed the data without knowledge of the measurements of the first observer.

**Statistical analysis.** Results are expressed as the mean  $\pm$  SD. A mixed model analysis was used to compare results among the variables obtained under the various conditions and among regions. When significant differences between groups were present, Bonferroni test was used to compare individual groups. Agreement between sonomicrometry and 3D-STI-derived area tracking data was assessed by linear regression analysis with the Bland-Altman method. Comparisons between STI and corresponding sonomicrometry data were performed with a paired student  $t$  test. Reproducibility was

**Table 1. Hemodynamic and Echocardiographic Parameters**

	Baseline	Dobutamine	Propranolol	CA Occlusion	p Value
SBP, mm Hg	103 ± 12*†	110 ± 15‡	95 ± 14*	81 ± 12	<0.001
DBP, mm Hg	74 ± 11*	72 ± 14	66 ± 10	58 ± 14	0.01
HR, beats/min	108 ± 11	132 ± 10‡	102 ± 9	107 ± 17	<0.001
LVEDV, ml	37 ± 7	35 ± 4	39 ± 9	40 ± 5	0.13
LVESV, ml	18 ± 4§	15 ± 2	20 ± 5§	24 ± 3‡	<0.001
LVEF, %	50 ± 2*	56 ± 5‡	47 ± 5*	37 ± 4	<0.001

Data are presented as mean ± SD. p value means the overall p value from the mixed model analysis. \*p < 0.01 versus CA occlusion; †p < 0.01 versus propranolol; ‡p < 0.01 versus dobutamine; §p < 0.01 versus other groups.  
CA = coronary artery; DBP = diastolic blood pressure; HR = heart rate; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; SBP = systolic blood pressure.

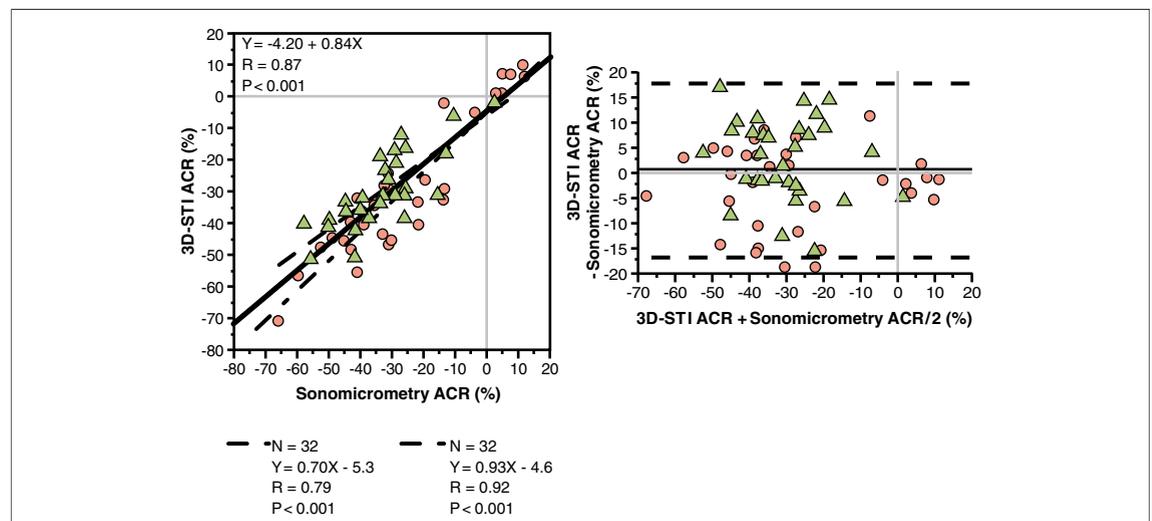
assessed as the mean percentage error (absolute difference divided by the mean of the 2 observations). A p value <0.05 was considered to indicate statistical significance. All calculations were performed with the SPSS 17 for Windows statistical program (SPSS, Inc., Chicago, Illinois).

## RESULTS

**Hemodynamic and echocardiographic data.** Hemodynamic and echocardiographic data obtained at baseline and during pharmacological stress and coronary artery occlusion studies for the 8 sheep (body weight  $31.9 \pm 7.4$  kg, range 26 to 50 kg) are summarized in Table 1. During dobutamine infusion tests, heart rate and LV ejection fraction were significantly higher than during other test condi-

tions. During coronary artery occlusion tests, systolic blood pressure and LV ejection fraction were reduced compared with values recorded during the other test conditions.

**Correlations between STI- and sonomicrometry-derived data.** We obtained 64 ACR datasets in the 3D-STI and the sonomicrometry studies. The correlation of all ACR data under baseline, pharmacological stress, and coronary artery occlusion conditions between 3D-STI and sonomicrometry are summarized in Figure 4. Strong correlations between 3D-STI- and sonomicrometry-derived ACR data were observed. The Bland-Altman plot shows no significant proportional bias ( $p = 0.52$ ). The fixed bias was 0.45%, and the 95% confidence interval was from -16.9% to 17.8%. The correlations of ACR with CS or LS by 3D-STI are shown

**Figure 4. Relation Between ACR by Echocardiography and by Sonomicrometry**

(Left panel) scatter plot showing the relation between all measurements of area change ratio (ACR) by sonomicrometry and 3-dimensional speckle tracking imaging (3D-STI). The solid line shows a regression line of all measurements. The dashed dotted line shows a regression line at apex area (pink circles). The dashed line shows a regression line at mid area (green triangles). (Right panel) Bland-Altman plots for the comparison of all measurements of ACR as measured with the 2 methods showing the mean differences (solid line) and 95% limits of agreement (dashed lines).

in Figure 5, and similar correlations were observed, respectively.

**Comparison of ACR data.** Both 3D-STI- and sonomicrometry-derived ACR and strain data obtained during baseline, pharmacological stress, and coronary artery occlusion studies are shown in Figure 6. ACR clearly distinguished changes in myocardial function induced by pharmacological stress and acute ischemia in both mid and apical anterior wall. In 1D strain data, a significant difference in LV mid wall was observed between CS at acute ischemia and at dobutamine infusion only. Although LS and CS of the apical anterior walls were reduced significantly during acute ischemia studies compared with those during the other studies, no differences were observed among baseline, propranolol infusion, and dobutamine infusion studies, unlike in ACR studies in the apical anterior wall.

**Reproducibility.** Intraobserver and interobserver variability was 7.2% and 8.5%, respectively, for ACR measurements; 9.0% and 9.7%, respectively, for CS measurements; and 8.1% and 8.9%, respectively, for LS measurements.

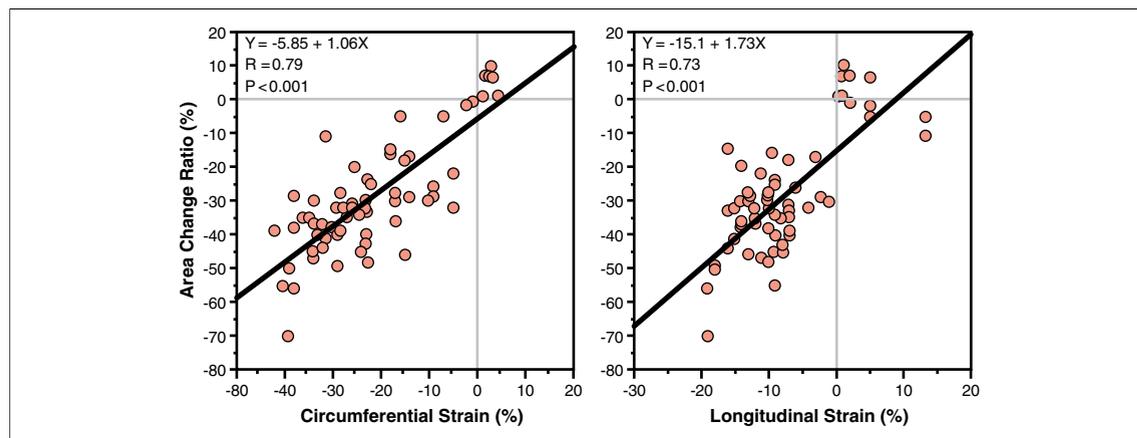
## DISCUSSION

This experimental study first demonstrated feasibility of a novel echocardiographic parameter that represented regional deformation measured as change in an endocardial area. The parameter, which had significant correlations with both LS and CS components, showed greater changes in ACR compared with 1D strain.

Recently introduced 3D-STI is a robust technology for strain measurements and can provide regional 1D strain (6,7). In addition, the usefulness of 3D-STI in assessing regional wall displacement and strain, LV volume measurements, and LV dyssynchrony has been reported in clinical studies (8-10). In addition, the 3D-STI can track regional endocardial area and calculate changes in an area through the cardiac cycle, because of a 3D imaging system. The unique parameter, ACR, can be measured on the basis of the deformation of regional rectangular or trapezoidal area measured by orthogonal directional data, just as the present study has confirmed that area tracking had significant relations with both components of CS and LS. In addition, 3D-STI-derived ACR data were accurately tracking the area deformation as shown in significant correlation between 3D-STI and sonomicrometry data. Therefore, this method is considered to be feasible for area deformation.

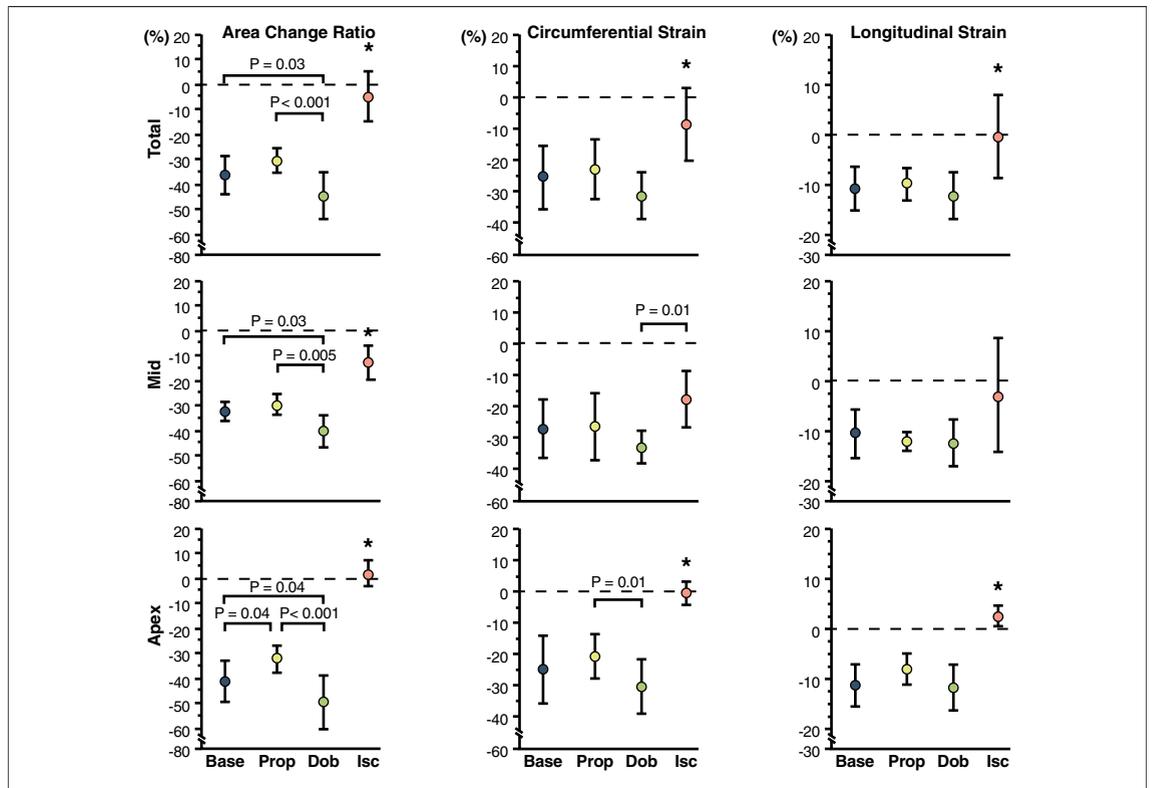
In contrast, the limits of agreement in the Bland-Altman analysis were relatively wide. The differences between sonomicrometry and 3D-STI measurements might be synergistically increased, because the area tracking was based on a 2-dimensional component. In addition, some misplacements of the area of interest between 3D-STI and sonomicrometry studies, the methodological difference in calculating ACR between the 2 methods, and the underestimation of ACR on the basis of the limited temporal resolution of 3D-STI might affect the discrepancy.

The parameter, ACR, mainly uses endocardial tracking data, and not epicardial tracing. In our 3D-STI system, CS and LS also are measured by



**Figure 5. Relation Between ACR and 1-Dimensional Strain**

(Left panel) scatter plot showing the relation between all measurements of ACR and circumferential strain by 3D-STI. (Right panel) scatter plot showing the relation between all measurements of ACR and longitudinal strain by 3D-STI. Abbreviations as in Figure 4.



**Figure 6. Comparisons of ACR and 1-Dimensional Strain**

Comparisons of ACR, circumferential strain, and longitudinal strain by 3D-STI during baseline (Base), propranolol infusion (Prop), dobutamine infusion (Dob), and acute ischemia (Isc). **Upper panels** correspond to total data (Total), **middle panels** correspond to mid anterior wall (Mid), and **bottom panels** correspond to apical anterior wall (Apex). \* $p < 0.001$  versus others. Abbreviations as in Figure 4.

endocardial speckle tracking data. Among 3 components of 1D strain, CS and LS obtained by 3D-STI have more accuracy—on the basis of our previous research—in assessing regional deformation compared with radial strain (7). This is caused by limitation of spatial resolution of 3D-STI—namely, epicardial tracking precision might be less than that in the endocardial tracking. Radial strain depends on not only endocardial tracking qualities but also epicardial tracking qualities, because radial strain is estimated by both endocardial and epicardial speckle tracking data. Then, accuracy of radial strain measurements might be less compared with those of the CS and LS components. Consequently, endocardial surface tracking with CS and LS can provide more accurate data among combinations of 3 strain components.

The present study showed greater changes in ACR compared with 1D strain in pharmacological stress and acute myocardial ischemia induced by coronary occlusion. In particular, ischemic

change of LV mid deformation—where myocardial ischemia was induced depending on extension of diagonal branch—varied in the individual sheep as compared with apical area. Therefore, deterioration in mid LV contraction might be too slight to detect by 1D strain. In addition, although pharmacological-induced changes in myocardial contraction were more slight as compared with those by ischemia, the slight changes could be well-distinguished by ACR compared with 1D strain. First, combined deformation data in 2 orthogonal directions may provide these greater changes in ACR. Although 1D data might cause tracking error, combined data for 2 directional deformations can decrease the tracking error, because of higher signal-noise ratio compared with that of 1D strain parameter. Because ACR has 2 directional deformation data, the magnitude of deformation might be emphasized synergistically. In addition, the endocardial site is more sensitive for myocardial ischemia than the epicardial site, and

our colleagues recently reported loss of myocardial strain gradient in experimental ischemic studies with 2-dimensional STI (11). The endocardial ACR has an advantage, in view of the myocardial ischemic cascade. Thus, regional deformation assessment with a change in endocardial surface area, which can be assessed by 3D imaging only, seems to be a promising parameter to assess regional cardiac function in detail.

**Study limitations.** Because each study was performed at relatively high heart rate, the low frame rate of 3D-STI could cause miscorrelation between frames and possibly might have affected tracking quality and strain data. Because we assessed only the anterior walls, evaluation of these limited regions might be insufficient to estimate regional deformations in other regions. Our experimental studies were performed with open chest models. Therefore, strain data might differ from those under closed chest conditions.

In the present study, because sonomicrometry and 3D-STI studies were evaluated only in the

ischemic area, the sensitivity and specificity to detect risk areas at ischemic condition were not assessed. Therefore the superiority of area tracking over 1D strain cannot be concluded.

## CONCLUSIONS

Area tracking by 3D-STI can estimate changes in LV regional area and might be promising for regional wall motion evaluations.

### Acknowledgments

The authors thank Mr. Yasuhiko Abe and colleagues (Toshiba Medical Systems) for technical advice on 3D-STI technology and operation techniques.

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**Key Words:** 3D echocardiography  
■ area change ratio ■ area tracking ■ speckle tracking ■ strain.