Accurate identification of regional myocardial dysfunction is pivotal to the diagnosis and management of patients with coronary artery disease. However, present methods for the assessment of regional myocardial function rely on semiquantitative visual gradation of endocardial excursion and wall thickening and are therefore highly subjective. In addition, visual assessment cannot easily distinguish the contribution of rigid body translational motion affecting the entire heart from regional contractility, nor can it differentiate wall motion abnormalities generated by passive tethering from those caused by active intrinsic contraction.

Tissue Doppler imaging (TDI) recently has been introduced as a method to quantitatively assess regional myocardial function by providing a map of color-encoded tissue velocities. TDI offers no solution, however, to the issue of distinguishing local velocity from translational motion and tethering effects from other regions. A potentially more specific measure of regional function would be quantification of regional deformation or strain. The concept of myocardial strain was defined by Mirsky and Parmley as fractional tissue deformation in response to applied force (stress). Quinones et al suggested measuring myocardial strain rate from M-mode echocardiographic data, but this principle has not been implemented in clinical routine. More recently, Heimdal et al introduced TDI-derived real-time strain rate, from which regional myocardial strain may be derived as the time integral of regional Doppler velocity gradients.

In principle, myocardial strains are independent of translational motion and other through-plane motion effects and should be relatively uniform throughout the normal left ventricular (LV) myocardium. In contrast, myocardial velo-
ites show marked nonuniformity in the normal ventricle, and this complicates data interpretation. The assessment of myocardial strain by tissue Doppler imaging (SDE) could simplify the analysis of regional contractile function by providing a more objective and uniform parameter of myocardial function. However, the validity and relevance of this novel parameter has not been established clinically. Therefore, the aim of the present study was to validate the measurements of peak systolic myocardial strains from regional velocity gradients against strains obtained by 3-dimensional tagged MRI. Additionally, we sought to compare the regional distribution of myocardial strains to that of regional myocardial velocities to establish which parameter might be more useful for clinical assessment of regional contractility.

Methods

Study Population

Three groups of subjects were studied. Thirty-three healthy volunteers (24 men, 9 women, 41 ± 13 years of age) and 17 patients (11 men, 6 women, 56 ± 15 years of age) with recent acute myocardial infarction (10 anterior and 7 inferior) were studied during resting conditions. Eleven volunteers and all infarct patients underwent both SDE and magnetic resonance tagged-cine imaging within the same day, typically with <2 hours between both investigations. In addition, 8 patients (4 men, 4 women, 65 ± 12 years of age) with suspected coronary artery disease were studied by SDE both at rest and during maximum dose of dobutamine infusion while undergoing a dobutamine stress echo mandated clinically to evaluate chest pain. 

Study Population

Four of the subjects agreed to repeat the dobutamine stress test with SDE and magnetic resonance tagged-cine imaging within the same day, typically with <2 hours between both investigations. In addition, 8 patients (4 men, 4 women, 65 ± 12 years of age) with suspected coronary artery disease were studied by SDE both at rest and during maximum dose of dobutamine infusion while undergoing a dobutamine stress echo mandated clinically to evaluate chest pain. β-Blockers (3 subjects) were withdrawn 24 hours before the study. Four of the subjects agreed to repeat the dobutamine stress test with the use of MRI on a separate day, having had no changes in medication regimen and clinical status in the meantime. The Institutional Review Board of the Johns Hopkins University approved the study protocol, and all subjects gave informed written consent to participate in this study.

Echocardiography

All studies were acquired with the use of a System Five digital ultrasound scanner (GE Medical Systems). After views were optimized in fundamental mode, images were acquired in TDI mode. Both myocardial velocities and strain values could be assessed from the same heartbeat. Frame rates varied from 56 to 134 frames per second, with a mean value of 92. Analysis of SDE and TDI images was performed offline on a personal computer with the aid of a customized software package (Echopac, GE Medical Systems). For tissue velocity measurements, we used a 2-dimensional multiregion technique, which allowed simultaneous processing of multiple velocity traces as described earlier. Peak systolic myocardial velocity was assessed from the apical, mid, and basal segments, using the same regions as for strain measurements.

From tissue Doppler data, incremental strain rate (SR) can be estimated by calculating the velocity gradient, as follows:

$$SR = \frac{v(r) - v(r + \Delta r)}{\Delta r}$$

where $v$ is the tissue velocity at different range depths $r$. The time integral of incremental strain rate yields logarithmic strain $e = \log(L/L_0)$:

$$e = \log \left( \frac{L}{L_0} \right) = \int_{t_0}^{t} SR \, dt.$$

Strain Doppler Echocardiography Versus MRI

where $L$ is the instantaneous segment length and $L_0$ is the segment length at time $t_0$. In this study, the logarithmic strain was converted to Lagrangian strain $e = (L/L_0)$:

$$e = \frac{L - L_0}{L_0} = \exp(e) - 1.$$

The velocity gradient was estimated between two points ($r$ and $r + \Delta r$) with a distance of 8 mm. This spatial offset ($\Delta r$) was selected as a compromise between acceptable signal-to-noise ratio and longitudinal spatial resolution.

MRI Tagging

MRI was performed on a 1.5-T whole-body magnet (Signa, GE Medical Systems) with a phased-array cardiac coil. Tagged images were acquired with the use of an ECG-triggered segmented k-space fast gradient-echo sequence with spatial modulation of magnetization (DANTE-SPAMM) during breath holds. Four to 5 contiguous stacks of short-axis images were prescribed to cover the entire heart from base to apex. From these short-axis slices, 6 long-axis slices were prescribed radially every 30 degrees. Imaging parameters were as follows: tag separation, 7 mm; field of view, 36 cm; slice thickness, 8 mm; matrix size, 256 × 160; TR, 6.2 ms; TE, 2.3 ms; and flip angle, 15 degrees.

Dobutamine Stress

Similar dobutamine stress tests were performed in the echocardiographic laboratory and in the MRI environment. ECG was monitored continuously, and blood pressure was recorded every 3 minutes throughout the procedure. After baseline acquisitions, dobutamine was increased stepwise by 10 μg · kg\(^{-1}\) · min\(^{-1}\) every 3 minutes, using a standard protocol up to 50 μg · kg\(^{-1}\) · min\(^{-1}\) or until 85% of maximal predicted heart rate was reached. Full SDE and 3-dimensional MRI sets were acquired at baseline and at peak dobutamine stress.

Coregistration of Myocardial Strains by Both Techniques

Analysis of 3-dimensional strains from tagged MRI data sets was performed with a displacement field-fitting method to estimate the Lagrangian strain. Strains by MRI were computed in the 3 normal orthogonal directions (radial, circumferential, and longitudinal) and reported as a strain map consisting of 12 circumferential angular sectors and 4 to 5 longitudinal planes. They were expressed as percent change in segment length between end-diastole and end-systole.

Longitudinal strains were obtained by SDE with apical 4- and 2-chamber views, respectively, and were compared with longitudinal shortening strain by MRI from the same segments. The midmyocardial layer was chosen from both methods. From the parasternal short-axis view, we measured radial strains by SDE in the anteroseptal and posterior walls. Two different investigators unaware of each other’s results analyzed MRI tagging and Doppler measurements.

Statistical Analysis

Values are expressed as mean ± SD. Comparisons between peak systolic strain values by SDE and MRI were performed by linear regression analysis. Differences between myocardial peak systolic strains, strain rates, and velocities in each myocardial segment were analyzed with 2-way ANOVA methods. Comparisons of myocardial peak systolic strains, strain rates, and velocities at baseline and peak dose of dobutamine were analyzed with paired Student’s $t$ tests. The agreement between the 2 methods (peak systolic strain by MRI and Doppler) was expressed as 95% limits of agreement, as recommended by Bland and Altman. A value of $P < 0.05$ was considered statistically significant.

Results

Healthy Volunteers

Typically, normal LV myocardium shortens in the longitudinal direction and thickens along the radial direction during systole. Because SDE records intrinsic deformation of the
myocardium only along the orientation of the Doppler beam, longitudinal shortening is measured from apical views. Shortening or thinning strains and strain rates (ie, compression) are by convention shown by negative signs. Thickening or lengthening strains and strain rates (ie, expansion) are shown with positive signs. An example of an apical 4-chamber and a parasternal short-axis SDE image with corresponding strain rates and strains obtained in a healthy volunteer is shown in Figure 1. In short-axis views, myocardial shortening is perpendicular to the direction of the Doppler beam and, therefore, SDE measurements of strains in the anteroseptal and posterior walls reflect radial thickening (lower right panel). Mean values of Doppler strain and strain rate in the healthy volunteers are reported in Tables 1 and 2.

Figure 2 illustrates the distributions of regional myocardial velocities by TDI and strains by SDE in healthy volunteers. Longitudinal tissue velocities were heterogeneously distributed in the normal LV, showing progressive decrease from the base toward the apex, mainly attributable to the through-plane motion of the heart. By contrast, values of myocardial strain and strain rate were found to be relatively homogeneous in all regions of the heart, reflecting independence from rigid body motion of the entire heart. Peak negative systolic longitudinal strains from all longitudinal segments assessed by both methods were $-18.7\pm3.7\%$ by SDE and $-18.1\pm3.6\%$ by MRI (Tables 1 and 2). Peak systolic radial strains were $18.0\pm5.3\%$ and $17.8\pm7.5\%$. The ranges of strain values in healthy subjects were $9\%$ to $30\%$ and $9\%$ to $28\%$ by SDE and MRI, respectively.

### Regional Myocardial Deformation in Postinfarct Patients

In contrast to normal hearts, the left ventricle of postinfarct patients was characterized by marked nonuniformity of myocardial velocities and strains. Tissue Doppler velocities at basal and apical levels were $6.5\pm1.6\,\text{cm/s}$ and $6.7\pm1.4\,\text{cm/s}$ for the anterior septal segment, respectively. Strain rates were $-1.7\pm0.4\,\text{1/s}$ and $-1.6\pm0.4\,\text{1/s}$ for the anterior septal segment, respectively. Strains were $-19\pm4\%$ and $-18\pm5\%$ for the anterior septal segment, respectively. MRI strain values were $-17\pm3\%$ and $-18\pm4\%$ for the anterior septal segment, respectively.

<table>
<thead>
<tr>
<th>Segments</th>
<th>Anterior Base</th>
<th>Anterior Apex</th>
<th>Septal Base</th>
<th>Septal Apex</th>
<th>Posterior Base</th>
<th>Posterior Apex</th>
<th>Lateral Base</th>
<th>Lateral Apex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue Doppler velocities, cm/s (n=33)</td>
<td>6.5±1.6</td>
<td>2.8±1.0*</td>
<td>6.7±1.4</td>
<td>2.8±1.1*</td>
<td>6.5±1.4</td>
<td>2.9±1.3*</td>
<td>6.7±1.5</td>
<td>3.2±1.6*</td>
</tr>
<tr>
<td>Doppler strain rate, 1/s (n=33)</td>
<td>$-1.7\pm0.4$</td>
<td>$-1.6\pm0.4$</td>
<td>$-1.6\pm0.4$</td>
<td>$-1.7\pm0.3$</td>
<td>$-1.6\pm0.3$</td>
<td>$-1.7\pm0.3$</td>
<td>$-1.6\pm0.3$</td>
<td>$-1.6\pm0.3$</td>
</tr>
<tr>
<td>Doppler strain, % (n=33)</td>
<td>$-19\pm4$</td>
<td>$-18\pm5$</td>
<td>$-17\pm3$</td>
<td>$-19\pm4$</td>
<td>$-20\pm4$</td>
<td>$-21\pm2$</td>
<td>$-18\pm4$</td>
<td>$-17\pm3$</td>
</tr>
<tr>
<td>MRI strain, % (n=11)</td>
<td>$-17\pm3$</td>
<td>$-18\pm4$</td>
<td>$-17\pm3$</td>
<td>$-19\pm5$</td>
<td>$-18\pm4$</td>
<td>$-19\pm3$</td>
<td>$-18\pm4$</td>
<td>$-17\pm4$</td>
</tr>
</tbody>
</table>
cardiac systolic strains (Table 3). This is illustrated in Figure 3, which displays myocardial strains from an infarcted region. In the longitudinal direction, both SDE and MRI demonstrated reduced shortening or stretching in infarcted segments (1.5±4.3% and 0.4±4.9%, respectively). This was in contrast to the nonischemic region, where near-normal shortening was observed (−15.0±3.8% and −15.7±3.6% by Doppler and MRI, respectively). The ranges of longitudinal strain values in ischemic myocardium were −8% to +11% and −9% to +10% by SDE and MRI, respectively.

In the short-axis view, instead of apparently normal radial thickening strain as found in remote noninfarcted myocardium (14.3±5.0% and 15.1±6.0%), infarcted segments demonstrated marked reduction in thickening or systolic thinning (−6.9±4.1% and −5.3±4.4% by both SDE and MRI, respectively).

**TABLE 2. Myocardial Velocities, Strain Rates, and Strains in Healthy Volunteers: Radial Measures From 2 Segments (Parasternal Short-Axis View)**

<table>
<thead>
<tr>
<th>Segments</th>
<th>Tissue Doppler velocities, cm/s (n=33)</th>
<th>Doppler strain rate, 1/s (n=33)</th>
<th>Doppler strain, % (n=33)</th>
<th>MRI strain, % (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>−3.5±0.8</td>
<td>1.6±0.2</td>
<td>18±6</td>
<td>19±4</td>
</tr>
<tr>
<td>Posterior</td>
<td>4.4±0.6</td>
<td>1.8±0.4</td>
<td>18±9</td>
<td>17±6</td>
</tr>
</tbody>
</table>

*P<0.05 vs the basal segment within the same region.

**TABLE 3. Peak Systolic Strains in Patients With Myocardial Infarction (n=17)**

<table>
<thead>
<tr>
<th>Region</th>
<th>SDE</th>
<th>MRI</th>
<th>SDE</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior infarct (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarct</td>
<td>−5.9±3.3</td>
<td>−4.6±4.5</td>
<td>1.1±4.5</td>
<td>1.0±4.7</td>
</tr>
<tr>
<td>Remote</td>
<td>10.0±3.4</td>
<td>12.5±7.9</td>
<td>−15.1±3.5</td>
<td>−15.3±3.6</td>
</tr>
<tr>
<td>Posterior infarct (n=7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarct</td>
<td>−9.2±5.1</td>
<td>−6.8±4.3</td>
<td>2.3±3.9</td>
<td>0.8±5.2</td>
</tr>
<tr>
<td>Remote</td>
<td>16.4±4.2</td>
<td>16.3±4.6</td>
<td>−14.9±4.3</td>
<td>−16.2±3.9</td>
</tr>
</tbody>
</table>

Alterations of Intrinsic Deformation During Dobutamine Stress

The maximum dobutamine dose reached during the stress test was 41±9 μg · kg⁻¹ · min⁻¹ (range, 20 to 50). Atropine (1 mg) was given to 1 patient to additionally increase heart rate. Dobutamine infusion significantly increased heart rate from 72±13 to 121±16 bpm (82±16% of maximal predicted heart rate, P<0.001) and tended to increase systolic blood pressure (from 118±16 to 157±59 mm Hg; not significant). Longitudinal shortening and radial thickening increased significantly between baseline and dobutamine infusion, illustrating the positive inotropic effect of this drug. Changes in maximal end-systolic strain from longitudinal view by SDE and MRI during dobutamine infusion were from −13.5±3.1 to −23.8±4.2% (P<0.05) and from −12.5±4.8 to −20.5±2.9% (P<0.01), respectively.

**Correlations and Agreement Between Strains Assessed by SDE and MRI Tissue Tagging**

Figure 4 demonstrates correlations between longitudinal systolic strain measurements by tagged MRI and SDE in each group of patients and healthy subjects. The overall correlation between SDE and MRI for pooled measurement of myocardial strain in healthy volunteers, postinfarct patients, and during dobutamine infusion was excellent (r=0.92 and r=0.84 for radial and longitudinal strain, respectively; both P<0.001). There were also good correlations within each group of study subjects.

Figure 5 shows a Bland-Altman plot of differences between strain values obtained from MRI and SDE in healthy subjects and patients with myocardial infarction. The mean difference±2 SD was 0.4±6.8, −0.7±6.6, and 0.4±4.1 in healthy subjects, in patients with myocardial infarcts, and during stress echo, respectively. In the subgroup of healthy subjects, the regression data are calculated from strain values that are clustered over a very narrow range of strains. As indicated by the Bland-Altman plots in Figure 5, however, the
agreement between the 2 methods in healthy subjects is similar to that in the patient groups.

Discussion
With tagged MRI as reference method, we have demonstrated the ability of strain Doppler echocardiography to quantify regional myocardial strains in a clinical setting, in all coronary perfusion territories and in patients with different degrees of myocardial function. In normal hearts, systolic strain values were essentially homogeneous throughout the left ventricle, which was in contrast to the distribution of myocardial velocities. The latter observation relates to the relative independence of strains from motions caused by tethering to other structures or cardiac translation.

Strain Versus Strain Rate
In principle, systolic strain reflects the extent of myocardial fiber shortening, whereas strain rate reflects velocity of shortening. Therefore, myocardial strain and strain rate reflect somewhat different aspects of myocardial function, and the 2 methods may provide complementary information. Strain and strain rate were measured, providing detailed information about regional LV function within normal and ischemic myocardium in humans. The recent study by Greenberg et al suggests that strain rate may be a sensitive marker of inotropy.

Strain Versus TDI
In opposition to tissue velocities, our study indicated that myocardial strains in the normal human heart, as measured by Doppler and MRI, were homogeneously distributed from base to apex of the LV. This difference relates to the fundamental difference between deformation and velocities and to the fact that the LV apex is relatively stationary during the cardiac cycle. Our observation is consistent with recent MRI studies showing uniformity of strains within different regions of the heart. This characteristic of myocardial strain reflects the fact that regional contractility of individual myocardial regions is relatively uniform and will facilitate the differentiation of normal from abnormal contractility in different regions of the heart. Conversely, the marked non-uniformity of myocardial velocities that showed a progressive decrease when moving the sample volume from the base toward the apex may limit the ability of TDI to separate normal from abnormal regions with the use of this parameter. Regional myocardial velocities are generated in part by local fiber shortening and in part by motion caused by tethering from other regions. It remains to be determined, however, if these limitations of TDI are of clinical significance.
MRI Versus Doppler

The present study demonstrates the feasibility of Doppler-derived strain measurement in humans under different conditions and validates it against MRI as an independent gold standard. The MRI method relies on deformation of tag lines to assess strain in 3 dimensions. Both methods were used to calculate the Lagrangian strain value from a given region of interest.\textsuperscript{12,14}

The first validation of the SDE-derived strain measurement was performed in an animal model and compared SDE with sonomicrometry.\textsuperscript{12} This experimental validation model was limited to one region per animal. The present study, however, extends the findings in animals to clinical imaging in humans. Furthermore, we demonstrate that SDE is accurate in all regions of the left ventricle and for strains in both longitudinal and radial directions.

Strain measurements by SDE are confined to a 1-dimensional space. The 3-dimensional MRI technique accounts for through-plane motion effects occurring perpendicularly to the imaging plane, whereas no such corrections could be applied for the SDE strain measurements. The longitudinal spatial resolution of SDE is related to the distance between the 2 sampling points for velocity gradient calculation. This offset was set to 8 mm as a compromise between demand for high spatial resolution and acceptable signal-to-noise ratio. In our experience, offsets <8 mm may give unacceptable noise levels in the strain rate signals. The present SDE method has very limited lateral resolution and in this regard is inferior to tagged MRI. Furthermore, the present Doppler method could hardly be used to measure longitudinal strains in different myocardial layers such as endocardium, myocardium, and epicardium. An improvement of the SDE acquisition technology with higher density of ultrasonic beams could make it possible to interpret the different cardiac layers in more detail.

Despite the fact that there are some differences in strains obtained from MRI and SDE, the limits of agreement between the techniques were relatively small, indicating that the impact of these potential errors is likely to be modest (Figure 5). Therefore, the present study gives foundation for the use of this technique to measure 3-dimensional strains in humans.

Clinical Implications

The results of this study suggest that quantitative measurement of myocardial strain by Doppler may provide an important advance over visual assessment of regional contractile function. For instance, SDE could be particularly...
valuable to facilitate the interpretation of echocardiograms during stress. The exact place of SDE and TDI versus visual assessment of wall motion abnormalities, however, still has to be defined for stress echocardiography as well as for other clinical applications.

Deviation from normal function might be easier to define with SDE than TDI because of the homogeneity of strain measurements in normal myocardium. This would possibly result in greater specificity for this technique compared with TDI. Shortening strains in normal myocardium were between 9% and 30%. Shortening strains <9% were not found in any of the healthy individuals included in this study, which suggests that strains below this value are a marker of myocaridal injury. We previously have demonstrated acceptable intraobserver and interobserver variabilities for strain measurements.\(^{15}\)

**Limitations**

Like other Doppler modalities, strain measurements are dependent on the direction of the Doppler angle of incidence in relation to myocardial motion.\(^{12}\) To overcome this limitation, longitudinal shortening was measured from long-axis views and radial thickening from short-axis views. For each segment, care was taken to keep the angle between the direction of the Doppler beam and that of tissue deformation as small as possible.

Strain profiles and curves do not always return to baseline (zero) at end-diastole. This may in part be because of the mathematical integration algorithm but may also be caused by the fact that the myocardium itself does not return to exactly the same state of deformation at the end of the cycle as was the case at the start. Several factors, including the normal beat-to-beat variation in stroke volume, may contribute to this.

**Conclusions**

The present study demonstrates the ability of tissue Doppler echocardiography to measure myocardial strains in a clinical setting and validates its accuracy against MRI tissue tagging. This novel technique may lead to improved noninvasive quantification of regional myocardial function in humans.

**Acknowledgments**

This study was supported in part by National Heart, Lung and Blood Institute grants HL-45090 and R29HL-47405 (National Institutes of Health, Bethesda, Md). Dr Edvardsen was a recipient of a clinical research fellowship from the Norwegian Council on Cardiovascular Diseases and was also supported by a grant from Stokbak’s Heart Foundation, Johan H. Andresen’s Medical Foundation, and Nathalia and Knut Juul Christiansen’s Foundation (Oslo, Norway). Dr Gerber was supported by a grant in aid from the Fulbright-Hayes Foundation of the United States Government. Dr Garot was supported by a grant from the Institute Roche Cardiovasculaire (Paris, France) and the Boehringer-Ingelheim grant of the Fédération Française de Cardiologie (Reims, France). We thank Sharon Cassidy, RCVT, for help with echocardiographic acquisitions and Elisabeth Brady, RN, for patient recruitment.

**References**

Quantitative Assessment of Intrinsic Regional Myocardial Deformation by Doppler Strain Rate Echocardiography in Humans: Validation Against Three-Dimensional Tagged Magnetic Resonance Imaging
Thor Edvardsen, Bernhard L. Gerber, Jérôme Garot, David A. Bluemke, João A.C. Lima and Otto A. Smiseth

Circulation. 2002;106:50-56; originally published online June 10, 2002;
doi: 10.1161/01.CIR.0000019907.77526.75
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/106/1/50

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/