Echocardiography and Cardiac Magnetic Resonance-Based Feature Tracking in the Assessment of Myocardial Mechanics in Tetralogy of Fallot: An Intermodality Comparison

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We investigated intermodality agreements of strains from two-dimensional echocardiography (2DE) and cardiac magnetic resonance (CMR) feature tracking (FT) in the assessment of right (RV) and left ventricular (LV) mechanics in tetralogy of Fallot (TOF). Patients were prospectively studied with 2DE and CMR performed contiguously. LV and RV strains were computed separately using 2DE and CMR-FT. Segmental and global longitudinal strains (GLS) for the LV and RV were measured from four-chamber views; LV radial (global radial strain [GRS]) and circumferential strains (GCS) measured from short-axis views. Intermodality and interobserver agreements were examined. In 40 patients (20 TOF, mean age 23 years and 20 adult controls), LV, GCS showed narrowest intermodality limits of agreement (mean percentage error 9.5%), followed by GLS (16.4%). RV GLS had mean intermodality difference of 25.7%. GLS and GCS had acceptable interobserver agreement for the LV and RV with both 2DE and CMR-FT, whereas GRS had high interobserver and intermodality variability. In conclusion, myocardial strains for the RV and LV derived using currently available 2DE and CMR-FT software are subject to considerate intermodality variability. For both modalities, LV GCS, LV GLS, and RV GLS are reproducible enough to warrant further investigation of incremental clinical merit. (Echocardiography 2012;0:1-8)

Key words: feature tracking, adult congenital heart disease, pediatric cardiology, tetralogy of Fallot, echocardiography, cardiac magnetic resonance

Quantification of myocardial function is of critical importance in the management of the patient with heart disease. Assessment of global and regional myocardial contractile properties by measurement of strain and strain rate are increasingly utilized in clinical practice.1 Several studies have demonstrated the feasibility of strain imaging by two-dimensional speckle tracking echocardiography (2DE), and its potential superiority compared with conventional visual assessment of regional wall motion.2 Feature tracking (FT) is a relatively new ultrasonic tool analogous to speckle tracking for deriving objective information about myocardial performance.3,4 FT algorithms combine speckle tracking, atrioventricular valve annulus motion, myocardial blood interface, and myocardial structure over a sequence of steps to improve tracking results. The frame-to-frame displacement of features tracked on FT algorithms equates to the evaluation of the local velocity (ratio between displacement and time interval), thereby allowing automated measurement of tissue motion during the cardiac cycle. Myocardial strain measurements can be derived from 2DE-FT and the newly introduced cardiac magnetic resonance (CMR)-based FT.

Right ventricular (RV) dysfunction5,6 and less frequently left ventricular (LV) dysfunction7,8 are prevalent in children and adults with repaired
tetralogy of Fallot (TOF). Dyskinesis of the outflow patch, RV fibrosis, impaired RV diastolic function, and LV dysfunction contribute to adverse RV and LV mechanics in TOF. Strain function, and LV dysfunction contribute to measurements obtained using the two FT techniques is clinically relevant, and validation of reproducibility of measures between modalities is of practical importance. We therefore sought to investigate the intermodality agreement of measurements from 2DE-FT and CMR-FT algorithms in the assessment of RV and LV mechanics in TOF.

Methods:

Patients:
We prospectively enrolled patients with repaired TOF and normal controls for this investigation. 2DE and CMR were performed contiguously on the same day in all patients. Exclusion criteria were any residual intracardiac shunt, pulmonary atresia, pacemaker or defibrillator implantation, or claustrophobia. Clinical data including demographics, age at surgical repair, height, and weight were obtained from the medical records. Body surface area was calculated using the Haycock formula. The Institutional Review Board of the University of Nebraska Medical Center approved the study protocol and all enrolled subjects signed informed consent.

Echocardiography:
Two-dimensional echocardiograms were obtained using Sequoia 512 system (Siemens Medical, Mountain View, CA, USA). Images were optimized for gain, compression, depth, and sector width and acquired at frame rates of 50–80 frames/sec. Apical four-chamber and parasternal mid-ventricular short-axis images were acquired during quiet respiration. All patients had satisfactory images suitable for 2DE-FT analysis.

Cardiac MR:
Cardiac magnetic resonance studies were performed using a 1.5 Tesla Philips Intera scanner (Philips Medical Systems, Best, the Netherlands). Ventricular dimensions and function were assessed with electrocardiogram-gated steady-state free-precession cine CMR pulse sequences during brief periods of breath holding in the following planes: ventricular two-chamber (vertical long-axis), four-chamber (horizontal long-axis), and short-axis planes (perpendicular to the ventricular long-axis plane based on the previous four-chamber images), with 12–14 equidistant slices (slice thickness 6–8 mm; interslice space 0–2 mm) completely covering both ventricles. The acquisition parameters were repetition time 2.8–3.2 ms, echo time 1.4–1.7 ms, field of view (tailed to the patient’s size) average 360 × 360 mm, and matrix size 196 × 172. The effective temporal resolution was 27 ± 5 ms. Each recruited control underwent quantitative CMR assessment from steady-state free-precession cine images in the horizontal long-axis (four-chamber) and short-axis planes using the protocol as above. The CMR measurements of end-diastolic and end-systolic volumes, mass at end-diastole, and ejection fractions for the LV and RV were obtained using commercial software (Q Mass MR 7.2; Medis, Leiden, The Netherlands). Ventricular end-diastolic volumes and mass were adjusted to body surface area.

2DE and CMR Feature Tracking:
Two-dimensional echocardiograms were analyzed offline by a single observer using 2D-CPA software (Image Arena VA Version 3.0; TomTec Imaging Systems, Unterschleissheim, Germany) for measurement of myocardial strains. Ventricular four-chamber and mid-ventricular short axis images were used for analyses, performed during the cardiac cycle by placing points along the endocardium in a single frame. Multiple manual corrections were performed to achieve adequate tracking for semiautomated processing by the 2DE-FT algorithm (Fig. 1). CMR studies were analyzed using FT software (2D Cardiac Performance Analysis MR 1.1.0; TomTec Imaging Systems). CMR images from horizontal long-axis (four-chamber) steady-state precession and mid-ventricular short-axis cine sequences were used for analysis as described previously. Similar to 2DE, multiple manual corrections were required to achieve acceptable tracking results. Segmental and global longitudinal strains (GLS) for the LV and RV were measured from 2DE and CMR four-chamber images; LV, global radial strain (GRS), and global circumferential strain (GCS) were measured from mid-ventricular short-axis images (Fig. 2). To determine the reproducibility of 2DE and CMR-FT, a blinded second observer repeated measurements in 10 randomly chosen TOF studies.

Statistical Analysis:
Paired Student’s t-tests were utilized to compare LV and RV strains in TOF between 2DE and CMR-FT. LV and RV strains from CMR-FT were compared between TOF patients and normal controls using nonpaired two-tailed Student’s t-tests. Bland–Altman limit of agreement analysis was used for interobserver reliability. Statistical analyses used SPSS version 17.0 (IBM, Armonk,
A P-value < 0.05 was considered statistically significant.

Results:
Forty subjects, including 20 patients with TOF (mean age 23.4 ± 7.5 years) and 20 healthy controls (mean age 37 ± 8.5 years) were studied. Demographics and standard CMR data for TOF patients are summarized in Table I. Peak global strains obtained by CMR-FT in TOF versus normal controls are shown in Table II. Derivation of FT data by 2DE and CMR for the LV and RV was feasible in all patients with TOF, and the strain results are summarized in Table III. Compared with normal controls, LV GCS, GRS, and RV GLS were significantly lower (P = 0.003, <0.001, 0.001, respectively), and LV GLS tended to be lower in TOF (–19.9 ± 5.1 vs. 17.8 ± 4.6, P = 0.191). In the TOF group, there was no significant difference between 2DE-FT- versus CMR-FT-derived LV GLS, LV GCS, and RV GLS (P = 0.196, 0.204, 0.959), whereas LV GRS showed statistically significant difference in values between modalities (P = 0.041). 2DE- and CMR-FT-derived segmental

Figure 1. Two-dimensional echocardiography and cardiac magnetic resonance feature tracking of the left ventricle (left panels) and right ventricle (right panels) in tetralogy of Fallot from four-chamber views.

Figure 2. Two-dimensional echocardiography feature tracking (top panel) and cardiac magnetic resonance feature tracking (bottom panel) from short-axis images of the left ventricle in tetralogy of Fallot.
### TABLE I
Demographics and Cardiac Magnetic Resonance Data in Tetralogy of Fallot Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.4 ± 7.5</td>
<td>13.2–40.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.8 ± 15.2</td>
<td>48–106</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>171.7 ± 10.6</td>
<td>155–189</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.8 ± 0.2</td>
<td>1.5–2.3</td>
</tr>
<tr>
<td>Age at operation (years)</td>
<td>2.7 ± 3.5</td>
<td>0.01–14.6</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>76.1 ± 13.5</td>
<td>53–110</td>
</tr>
<tr>
<td>LV indexed EDV (mL/m²)</td>
<td>89.8 ± 14.9</td>
<td>68.3–116.9</td>
</tr>
<tr>
<td>LV indexed ESV (mL/m²)</td>
<td>40.9 ± 8.4</td>
<td>29.4–52.5</td>
</tr>
<tr>
<td>LV indexed mass (g/m²)</td>
<td>54.7 ± 10.6</td>
<td>35.5–70.2</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>55.3 ± 4.7</td>
<td>44–62.1</td>
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<tr>
<td>RV indexed EDV (mL/m²)</td>
<td>123.6 ± 29.2</td>
<td>85.7–191.7</td>
</tr>
<tr>
<td>RV indexed ESV (mL/m²)</td>
<td>68.4 ± 24.6</td>
<td>40.6–136.1</td>
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<tr>
<td>RV indexed mass (g/m²)</td>
<td>30 ± 9.5</td>
<td>12.3–46.9</td>
</tr>
<tr>
<td>RV EF (%)</td>
<td>45.3 ± 6.9</td>
<td>22–56</td>
</tr>
</tbody>
</table>

LV = left ventricle; RV = right ventricle; EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction.

### TABLE II
Peak Global Strains by CMR-FT in Tetralogy of Fallot (TOF) Versus Normal Controls

<table>
<thead>
<tr>
<th></th>
<th>TOF</th>
<th>Normal</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV GLS</td>
<td>−17.8 ± 4.6</td>
<td>−19.9 ± 5.1</td>
<td>0.191</td>
</tr>
<tr>
<td>LV GCS</td>
<td>−21.5 ± 3.6</td>
<td>−24.6 ± 2.5</td>
<td>0.003</td>
</tr>
<tr>
<td>LV GRS</td>
<td>26.3 ± 9.4</td>
<td>50.9 ± 12.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV GLS</td>
<td>−14.9 ± 4.1</td>
<td>−19.9 ± 4.0</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CMR = cardiac magnetic resonance; FT = feature tracking; LV = left ventricle; RV = right ventricle; GLS = global longitudinal strain; GCS = global circumferential strain; GRS = global radial strain.

### TABLE III
2DE-FT versus CMR-FT Derived Peak Global Strains in Tetralogy of Fallot (TOF)

<table>
<thead>
<tr>
<th></th>
<th>2DE</th>
<th>CMR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV GLS</td>
<td>−16.5 ± 5.1</td>
<td>−17.8 ± 4.6</td>
<td>0.196</td>
</tr>
<tr>
<td>LV GCS</td>
<td>−22.3 ± 2.4</td>
<td>−21.5 ± 3.6</td>
<td>0.204</td>
</tr>
<tr>
<td>LV GRS</td>
<td>37.2 ± 1.8</td>
<td>26.3 ± 9.4</td>
<td>0.041</td>
</tr>
<tr>
<td>RV GLS</td>
<td>−15.2 ± 4.2</td>
<td>−14.9 ± 4.1</td>
<td>0.959</td>
</tr>
</tbody>
</table>

CMR = cardiac magnetic resonance; FT = feature tracking; LV = left ventricle; RV = right ventricle; GLS = global longitudinal strain; GCS = global circumferential strain; GRS = global radial strain.

Strains in TOF, and segmental CMR-FT strain in normal controls are shown in Table IV. Figure 3 demonstrates the Bland–Altman plots comparing intermodality agreements for GCS, GLS, and GRS in TOF. For the LV, GCS showed the narrowest intermodality limits of agreement (mean percentage error 9.5%), followed by GLS measurements (mean error 16.4%). RV GLS had a mean intermodality difference of 25.7%. Bland–Altman analyses of interobserver agreement of measurements (Fig. 4) showed no evidence of a systematic over or underestimation between observers. GRS had the highest interobserver and intermodality variability.

### Discussion
Feature tracking is an important extension to conventional 2DE that provides quantitative assessment of myocardial function. A major advantage of 2DE-FT is that strain and strain rate data can be obtained in real time with high temporal and spatial accuracy. However, 2DE-FT assessment is prone to image and signal quality limitations. The recently introduced CMR-FT allows global and regional strain and strain rate measurements using a semiautomatic tracking algorithm analogous to 2DE-FT. CMR-FT with its greater signal-to-noise ratio may...
provide improved border tracking. The tool has been validated against myocardial tagging, and has also shown promise in preliminary applications for congenital heart disease. CMR-FT has also been applied for strain quantification during dobutamine stress and as part of viability assessment in ischemic cardiomyopathy. Cardiac magnetic resonance-FT assumes particular relevance because of the limitations of the alternative CMR-based strain analysis technique—myocardial tagging. This results from the inherent dependency of tagging analysis on the contrast between the tag lines and the myocardium, and the significant amount of postprocessing that may be involved. Although the newer spatially modulated magnetization (CSPAMM) tagging has improved the overall results, the issue of rapid decay/fading of tags continues to be a problem and makes automated quantification cumbersome.

Feasibility of FT and Findings in TOF:
In patients with surgically modified TOF, RV and LV dysfunction may coexist. Analysis of RV and LV function is important in determining risk of late morbidity and mortality after TOF repair. Load stresses to the RV in this setting may negatively impact RV and LV performance, even in the absence of clinical symptoms. Several studies have pointed out the limitations of using volumetric ventricular function assessments alone in TOF, and the potential benefit of global and regional myocardial strain assessment. RV peak systolic GLS has been reported as a sensitive marker for deterioration of RV function in adults with repaired TOF. Others have shown that RV dilation negatively impacts LV mechanics and LV GCS decreases with increasing RV dilation. Most of the previous work in TOF utilized Doppler tissue or 2DE-FT-based strain measurements. In the present study, both 2DE-FT and CMR-FT were used nearly simultaneously in the same patient. Strain measurements were feasible, and relatively simple to obtain by either technique.

The LV GCS and GRS in TOF by CMR-FT were decreased compared with normal controls, and this is in agreement with previous 2DE-based strain data in TOF. The anterior and inferior septal wall segments of the LV form a component of interventricular septum with the RV, and the circumferential and radial strains from these segments are likely to be decreased from RV load stresses and ventricular–ventricular interactions. The decrease in LV GLS in our study did not reach statistical significance, which also

Figure 3. Bland–Altman plots showing intermodality (cardiac magnetic resonance-feature tracking vs. two-dimensional echocardiography-feature tracking) agreement of global LV and RV strains in tetralogy of Fallot. LV = left ventricle; RV = right ventricle.
agrees with previously published results on 2DE strain imaging.\textsuperscript{11,18}

Comparison of 2DE-ST and CMR-FT: Our results show that both 2DE-FT and CMR-FT provide quantitative information on displacement, velocity, and strain. In 2DE-FT, “features” or “speckles” (natural acoustic markers) are tracked in the ultrasound image from frame to frame in 2D, and local tissue movement is determined from the geometric shift of the those features. This is similar in physical principle to CMR-FT, wherein 2D border tracking is combined with a pattern-tracking algorithm utilizing the inhomogeneity of tissue brightness, anatomic characteristics, and cavity–myocardial border.\textsuperscript{24} The accuracy of 2DE-FT is dependent on image quality. 2DE has a resolution advantage over CMR; however, the latter has greater signal-to-noise ratio and thereby improved endocardial border tracking. Exploring the factors potentially responsible for the intermodality differences observed in the present investigation are instructive.

Slice Thickness and Position: Although the 2DE and CMR images analyzed were obtained at the level of mid-ventricular short-axis and in four-chamber views, the slice position and thickness were not exactly the same resulting in changes in the slice and its spatial resolution. Therefore, visualization of the endocardial boundary that determined tracking varied slightly between 2DE and CMR acquisitions. For this reason, simultaneous analysis of exactly the same slice in both modalities was not feasible.

Frame Rate: For this study, we attempted to keep the differences in the frame rate between 2DE and CMR acquisitions low (the average frame-rate difference was 30–40 Hz). As the frame rates of acquired images are typically higher for 2DE as compared to CMR, we compared the relatively frame-rate independent parameters. Accordingly, the relatively frame-rate sensitive parameters (velocity and strain rate) were not compared. Lower frame rates are known to result in under-sampling, whereby isovolumic phases may be affected and peak strain rate and velocity values may be reduced depending on temporal resolution of the acquired image.\textsuperscript{5} Strain and displacement measurements are likely to be less affected at this frame-rate difference between the modalities. However, it is possible that the lower
temporal resolution of CMR images may give rise to more relative motion of a given feature in between frames, affecting the tracking results.

**Image Resolution:**
2DE has significantly higher resolution compared with CMR, so the difference in image resolution between modalities is important. The pixel size in a typical CMR image is 3 or 4 times larger than in 2DE, so differences between endocardium and epicardium (essentially the radial strain measurements) are difficult to compare between the modalities. The slice thickness in the CMR image is composed of fewer pixels, and a small error of even 1 pixel may change the calculated radial strain value significantly. Any mathematical calculation, that forms the basis of a tracking algorithm from which a strain parameter is derived, has an “intrinsic uncertainty” due to the impossibility to look inside the pixels. The graphical display for the three strains—longitudinal, circumferential, and radial—look visually very similar because the difference of 1 or a few pixels cannot be visually appreciated. However, the numeric value for radial strain may change substantially when the traces differ by a few, or even a single pixel. The radial strain value could also change because the errors of two borders can sum up. For example, myocardium that is 25-pixels wide at end-diastole and with a radial strain of 32% becomes 33 pixels at end-systole. If there is a small error of 1 pixel on both borders from diastole to systole, the end-systole can change from 31 to 35 pixels resulting in a range of radial strain values from 24% or 40%. These factors are likely responsible for the high variability of radial strain (intermodality and interobserver) noted in this study.

**Tracking Algorithm Differences:**
A fourth possible factor is the variability in the 2 modalities with regard to refinement and optimization of the tracking algorithm. 2DE-FT has undergone more extensive reliability testing of its tracking algorithm. In our experience, qualitative results of CMR-FT were comparable to 2DE-FT for tracking from short-axis slices. For apical four-chamber images, the visual tracking results with CMR-FT were qualitatively suboptimal in several instances compared with 2DE-FT, especially the annulus tracking; and required multiple contour revisions in each study.

**Interobserver Variability:**
Our results confirm that longitudinal and circumferential strains are better reproducible in a FT algorithm. Longitudinal strain had superior interobserver agreement among the 3 strains for the LV, whereas circumferential strain had the best agreement between 2DE-FT and CMR-FT. The interobserver reproducibilities of LV GCS, LV GLS, and RV GLS were acceptable for both 2DE-FT and CMR-FT; both intermodality and interobserver agreements for LV GRs were poor. Similar to our results, others have found wide interobserver variability with 2DE measurements of radial strain.25

**Limitations:**
Several limitations of this study should be mentioned. First, the sample size was small. The controls were not age and gender matched, and older than the TOF patients. FT is an evolving technique. FT software is currently only capable of deriving in-plane strains from the apparent in-plane movements. Further technical developments and refinements may someday address its insensitivity to, and misinterpretation of through-plane displacements of oblique or tapering structures. CMR image data are acquired over >1 cardiac cycle and not “real time.” In theory, changing the parameters of CMR acquisition, whereby resolutions in both time and space are increased would bring CMR-derived parameters closer to those derived by 2DE; this needs further study. Finally, we did not explore correlations of CMR or 2DE strains with standard measures of volumetric RV function as part of this study. Investigation of the utility of feature tracking strains to predict clinical outcomes in repaired TOF also warrants further work.

**Conclusions:**
In summary, 2DE-FT has higher resolution and frame rate, but tracking results are degraded by noise from lower image quality. CMR-FT in comparison is probably less precise due to its lower resolution, but more reliable due to the inherently high image quality. RV and LV strains derived from currently available 2DE-FT and CMR-FT software are subject to considerable intermodality variability. Circumferential strain has the best intermodality agreement, while both intermodality and interobserver agreements were poor for radial strain. Based on interobserver testing for both modalities, LV GCS, LV GLS, and RV GLS are reproducible enough to warrant further investigation of incremental clinical merit. Continued clinically supported refinements of the CMR-FT algorithms are necessary to ensure accurate and reproducible tracking.

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References