Layer-specific analysis of myocardial deformation for assessment of infarct transmurality: comparison of strain-encoded cardiovascular magnetic resonance with 2D speckle tracking echocardiography

Ertunc Altiok1†, Mirja Neizel2†, Sonja Tiemann1, Vitali Krass2, Michael Becker1, Christian Zwicker1, Ralf Koos1, Malte Kelm2, Nils Kraemer3, Felix Schoth3, Nikolaus Marx1, and Rainer Hoffmann1*

1Department of Cardiology, Pneumology and Angiology, University Hospital RWTH Aachen, Aachen, Germany; 2Department of Cardiology, Pneumology and Angiology, University Hospital Düsseldorf, Düsseldorf, Germany; and 3Department of Diagnostic and Interventional Radiology, University Hospital RWTH Aachen, Aachen, Germany

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Aims
Separate analysis of endocardial and epicardial myocardial layer deformation has become possible using strain-encoded cardiovascular magnetic resonance (SENC) and 2D-dimensional speckle tracking echocardiography (Echo). This study evaluated and compared both modalities for the assessment of infarct transmurality as defined by late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR).

Methods and results
In 29 patients (age 62.4 ± 11.7 years, 23 male) with ischaemic cardiomyopathy, SENC using 1.5 T CMR and Echo were performed. Peak circumferential systolic strain of the endocardial and the epicardial layer of 304 myocardial segments was assessed by SENC and by Echo. The segmental transmurality of myocardial infarction was determined as relative amount of LGE (0%: no infarction; 1–50%: non-transmural infarction; 51–100%: transmural infarction). Endocardial and epicardial strain defined by SENC and by Echo differed significantly between segments of different infarct transmurality determined by CMR. Endocardial layer circumferential strain analysis by Echo and by SENC allowed distinction of segments with non-transmural infarction from non-infarcted segments with similar accuracy [area under the curve (AUC) 0.699 vs. 0.649, respectively, P = 0.239]. Epicardial layer circumferential strain analysis by Echo and by SENC allowed distinction of transmural from non-transmural myocardial infarction defined by LGE CMR with similar accuracy (AUC 0.721 vs. 0.664, respectively, P = 0.401). Endocardial strain by SENC correlated moderately with endocardial strain by Echo (r = 0.50; standard error of estimate = 5.2%).

Conclusion
Layer-specific analysis of myocardial deformation by Echo and by SENC allows discrimination between different transmurality categories of myocardial infarction with similar accuracy. However, accuracy of both methods is non-optimal, indicating that further tools for improvement should be evaluated in the future.

Keywords
Cardiovascular magnetic resonance • Echocardiography • Myocardial contraction

† Both authors contributed equally to this study.
* Corresponding author: Medical Clinic I, University RWTH Aachen, Pauwelsstraße 30, 52057 Aachen, Germany. Tel: +49 241 8088468; fax: +49 241 8082303, Email: rhoffmann@ukaachen.de

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Introduction

Accurate analysis of myocardial viability is crucial to the optimization of therapy in patients with ischaemic myocardial dysfunction and to the definition of their prognosis.\textsuperscript{1–3} Analysis of late gadolinium enhancement (LGE) using cardiovascular magnetic resonance (CMR) has become the reference technique for the assessment of myocardial viability.\textsuperscript{5–6} Myocardial deformation analysis based on 2D speckle tracking echocardiography (Echo) and strain-encoded CMR (SENC) have been described. SENC has been introduced as a novel CMR technique to measure myocardial deformation expressed as myocardial strain. It allows definition of regional function comparable with CMR tagging.\textsuperscript{7–11} Compared with CMR tagging, it has been shown to be superior in terms of temporal resolution, total scan duration, and required time for post-processing of the acquired data.\textsuperscript{12–14} Analysis of myocardial deformation parameters based on Echo as well as SENC considering the total myocardial wall thickness has been shown to allow assessment of myocardial viability.\textsuperscript{15,16} However, the distribution of myocardial infarction is commonly inhomogeneous within the total wall thickness.\textsuperscript{17,18} Non-transmural myocardial infarcts have been described to affect primarily the endocardial layer, with the epicardial myocardial layer being spared,\textsuperscript{18} whereas transmural infarcts affect all layers of the myocardium. Recently, layer-specific myocardial deformation analysis of an endocardial and an epicardial layer has been described for Echo as well as SENC.\textsuperscript{7,19,20} Separate analysis of endocardial as well as epicardial layer strain has been shown to be superior for the analysis of myocardial infarct transmurality.\textsuperscript{21}

This study evaluated and compared the diagnostic accuracy of Echo and SENC, using layer-specific analysis of myocardial deformation for the assessment of infarct transmurality in patients with chronic ischaemic left ventricular dysfunction. Results of both techniques were related to infarct transmurality defined by LGE CMR.

Methods

Study population

Twenty-nine consecutive patients (age 62.4 ± 11.7 years, 23 male) with chronic ischaemic left ventricular dysfunction underwent LGE for the assessment of myocardial viability. SENC was performed during the same CMR study, and Echo was performed within 24 h of the CMR study. Ischaemic origin of left ventricular cardiomyopathy was proved by coronary angiography within 7 days of SENC and Echo. The patient characteristics are given in Table 1. The study was validated by the ethical committee of the University Aachen, and all patients signed an informed consent form.

CMR protocol

The CMR studies were performed with a 1.5 T whole-body MR scanner (Achieva, Philips Medical Systems, Best, The Netherlands) using a 32-channel cardiac coil.

Contrast-enhanced imaging

After 15 min of intravenous injection of 0.2 mmol/kg body weight Gd-DTPA (Magnevist, Schering, Berlin, Germany), 8 mm short-axis slices were acquired with a prospective electrocardiogram-gated gradient echo sequence with inversion prepulse. Images were transferred to a workstation equipped with a dedicated cardiac software package (CAAS MRV, Pie Medical Imaging BV, Maastricht, The Netherlands) for further analysis. The endocardial and epicardial borders were traced manually to assess total myocardial area. Each myocardial segment was evaluated for the presence of LGE, defined as an area with signal enhancement ≥ 3 SD of the signal intensity of non-enhanced myocardium. The contrast-enhanced volume of each segment was calculated semi-automatically. The segmental extent of LGE was calculated as the percentage of contrast-enhanced volume of the total myocardial volume (VolumeLGE/Volume myocardium × 100). A 0% segmental amount of LGE was considered to reflect no infarction; 1–50% amount of LGE was considered to reflect non-transmural infarction, whereas 51–100% amount of LGE was considered to reflect transmural infarction (Figure 1).

Strain-encoded imaging protocol

SENC is a special modification of the CMR scanner software that enables the quantification of regional deformation of tissue. To calculate myocardial strain, SENC uses tag planes parallel and not orthogonal to the image plane. Therefore, two- and four-chamber views were generated to calculate circumferential strain (typical imaging parameters: voxel size of 4/4/10 mm\(^3\), repetition time/echo time of 25/0.9 ms, and a flip angle of 30°). The temporal resolution was set at 25 ms. The number of cardiac phases was adapted to 26 to 38 to cover ∼85 to 90% of the cardiac cycle. The total scan duration was 10 to 14 s.

Echocardiography

Echocardiographic studies were performed with a Vivid Seven System (GE Vingmed, Horton, Norway). Parasternal short-axis views were acquired with a frame rate of at least 50 frames per second at basal, midventricular, and apical levels.

<table>
<thead>
<tr>
<th>Table 1 Patient characteristics</th>
<th>n = 29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.4 ± 11.7</td>
</tr>
<tr>
<td>Male/female</td>
<td>23/6</td>
</tr>
<tr>
<td>End-diastolic volume (mL)</td>
<td>177.0 ± 66.6</td>
</tr>
<tr>
<td>End-systolic volume (mL)</td>
<td>103.7 ± 68.0</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>46.0 ± 15.2</td>
</tr>
<tr>
<td>Myocardial infarct mass (g)</td>
<td>27.2 ± 28.8</td>
</tr>
<tr>
<td>Total myocardial mass (g)</td>
<td>163.8 ± 56.3</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td></td>
</tr>
<tr>
<td>One-vessel</td>
<td>3 (10.3%)</td>
</tr>
<tr>
<td>Two-vessel</td>
<td>15 (51.7%)</td>
</tr>
<tr>
<td>Three-vessel</td>
<td>11 (37.9%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (75.9%)</td>
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<tr>
<td>Smoking</td>
<td>19 (65.5%)</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>17 (58.6%)</td>
</tr>
<tr>
<td>Obesity (BMI ≥ 30kg/m(^2))</td>
<td>5 (17.2%)</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>12 (41.4%)</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>28 (96.6%)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>26 (89.7%)</td>
</tr>
<tr>
<td>Statins</td>
<td>29 (100%)</td>
</tr>
<tr>
<td>ACE-inhibitors/ARBs</td>
<td>28 (96.6%)</td>
</tr>
</tbody>
</table>

Figure 1
Quantitative analysis of myocardial deformation
Quantitative layer-specific analysis of segmental left ventricular function was performed based on the definition of peak systolic circumferential strain of an endocardial and an epicardial myocardial layer by SENC and by Echo. Analysis was performed on 12 of 16 segments, considering the 16-segment model of the American Society of Echocardiography. These 12 segments included the septal basal, midventricular and apical, anterior basal, midventricular and apical, lateral basal, midventricular and apical and inferior basal, midventricular and apical left ventricular wall in all 29 patients. The four segments of the apical long-axis view were not evaluated with both modalities.

Strain-encoded imaging
All strain measurements were performed based on SENC-images using dedicated software (Diagnosoft MAIN version 1.06, Diagnosoft, Inc., Palo Alto, CA, USA). Circumferential strain was calculated at a specific point set in the middle of the endocardial as well as the epicardial layer of each segment (Figure 2).

Speckle tracking echocardiography
Circumferential strain was calculated using 2D parasternal short-axis views. Analysis of the three acquired parasternal short-axis views was performed off-line with the aid of a dedicated customized software package (EchoPAC, GE Vingmed, Haifa, Israel). The system allows analysis of endocardial and epicardial peak systolic circumferential strain for six segments within one short-axis cut-plane based on the detection of acoustic speckles as described previously. It averages the circumferential strain values of the whole segments’ endocardial as well as epicardial layer. The system automatically determines tracking quality for each analysed segment. In this analysis, only segments with optimal tracking quality were included (Figure 3).

Observer agreement
In 10 randomly selected studies, strain analysis by SENC and by Echo was repeated by other experienced observers to determine interobserver agreement.

Statistics
Statistical analysis was performed with a special statistical analysis program (MedCalc Software, Version 9.5.1.0, Mariakerke, Belgium). Continuous data were presented as mean ± SD and compared using Student’s t-test or ANOVA as adequate with post hoc analysis and using Student–Newman–Keuls test for all pairwise comparisons. Pearson’s correlation coefficient (r) with 95% confidence interval was calculated to express agreement between strain defined by SENC and by Echo. Endocardial and epicardial strain values as determined by SENC were compared with those by Echo, using linear regression analysis with the presentation of the standard error of estimate (SEE) and using the Bland–Altman analysis. Receiver operating curves (ROCs) of peak systolic circumferential strain of the endocardial and the epicardial layer determined by SENC and by Echo were calculated for the distinction of myocardial segments with non-transmural infarction from non-infarcted segments and for the distinction of segments with transmural infarction and those with non-transmural infarction. ROC analysis as well as comparison of areas under the curve was done by the method of DeLong et al. Pearson’s correlation coefficient and the Bland–Altman analysis were used to express interobserver variability of SENC and of Echo. P < 0.05 was considered significant.

Results
The analysis included 348 myocardial segments; 44 (12.6%) segments had to be excluded due to suboptimal echocardiographic tracking quality. No segment had to be excluded due to insufficient image quality of SENC.

LGE by CMR
A total of 172 of 304 myocardial segments (56.6%) were classified as non-infarcted; 88 segments (28.9%) were classified as non-transmural infarcted and 44 segments (14.5%) as transmural infarcted.

Myocardial deformation related to the amount of LGE
Endocardial as well as epicardial peak systolic circumferential strain by SENC and by Echo was significantly different between non-infarcted, non-transmural infarcted, and transmural infarcted segments as defined by LGE (Table 2).

Considering the non-infarcted segments, peak circumferential strain was more negative by Echo compared with SENC in the endocardial layer (bias between Echo and SENC = 7.3% to 24.7%; P < 0.0001), although there was no significant difference in the epicardial layer (bias = 0.5% to 13.5 to 14.4%; P = 0.4019). In non-transmural infarcted segments, strain values determined by Echo were more negative than strain values determined by SENC in the endocardial layer (bias = 3.5% to 14.1 to 21.1%; P = 0.0004), but less negative in the epicardial layer (bias = -2.3% to -17.7 to 13.1%; P = 0.0071). In transmural infarcted segments, circumferential strain by Echo was less negative compared with SENC in the endocardial layer (bias = -1.9% to 16.5 to 12.6%;
\( P = 0.0925 \) and in the epicardial layer (bias = \(-4.2\%\), \(-16.9\%\) to \(8.5\%\); \( P = 0.0001 \)).

### Distinction of non-transmural infarction vs. no infarction

Considering findings by LGE, segments with non-transmural infarction could be distinguished from segments without infarction, using layer-specific circumferential strain analysis by SENC and by Echo (Table 3).

Performing ROC analysis for the detection of non-transmural infarction vs. no infarction, the area under the curve (AUC) was 0.699 (95% CI 0.639–0.754), considering endocardial layer circumferential strain analysis by Echo. The AUC was not significantly different for epicardial layer-specific strain analysis by Echo (0.673, 95% CI 0.612–0.730; \( P = 0.2073 \)). Considering endocardial circumferential strain analysis by SENC, the AUC for the detection of non-transmural infarction vs. no infarction was not significantly lower than using Echo (0.649, 95% CI 0.588–0.707; \( P = 0.2387 \)). The AUC using SENC was significantly lower for epicardial layer strain analysis than for the endocardial layer analysis (0.574, 95% CI 0.512–0.635; \( P = 0.0034 \)) (Figure 4, left panel).

### Distinction of transmural vs. non-transmural infarction

Segments with transmural infarction could be distinguished from segments with non-transmural infarction, considering layer-specific circumferential strain analysis by Echo and by SENC (Table 4). ROC analysis for the distinction of transmural vs. non-transmural infarction demonstrated an AUC of 0.721 (95% CI 0.688–0.838), considering epicardial strain analysis by Echo. Considering epicardial strain analysis by SENC for the distinction of transmural vs. non-transmural infarction, the AUC was 0.664 (95% CI 0.577–0.744; \( P = 0.4005 \)). The AUC of endocardial layer circumferential strain analysis was higher than the epicardial layer strain analysis using Echo but not significantly different using SENC (\( P = 0.0388 \) and \( P = 0.9109 \), respectively) (Figure 4, right panel).

### Comparison of SENC with Echo

Endocardial strain by SENC correlated moderately with endocardial strain by Echo (\( r = 0.50 \); SEE = 5.2%). Correlation of epicardial strain between both methods was weak (\( r = 0.19 \); SEE = 4.5%). Endocardial strain by SENC was less negative than endocardial strain by Echo (bias = 4.9%, 95% CI \(-13.3\) to \(23.1\%\); \( P < 0.001 \)). Epicardial strain analysed by the two methods was less different.
The bias between Echo and SENC was strain amplitude-dependent, with greater bias at greater strain values (Figure 5). The bias between endocardial strain by SENC and Echo was strain amplitude-dependent, with greater bias at greater strain values (Figure 5).

Observer agreement
There was a sufficient interobserver agreement on the circumferential strain analysis of the endocardial and the epicardial layer by SENC ($r = 0.824$, bias = 0.8%, $-6.2$ to $7.8$%; $r = 0.893$, bias = 0.9%, $-3.4$ to $5.3$%, respectively) as well as by Echo ($r = 0.939$, bias = 1.0%, $-7.4$ to $9.5$%; $r = 0.848$, bias = 0.9%, $-7.4$ to $9.2$%, respectively).

Discussion
The major findings of this study are (i) SENC as well as 2D Echo demonstrates an incremental decrease of the endocardial and the epicardial layer myocardial deformation with increasing degree of myocardial infarction; (ii) SENC and Echo showed no significant difference in the distinction of non-transmural infarcted segments vs. myocardial segments without infarction; however, a slightly higher accuracy using endocardial layer analysis compared with epicardial layer analysis was noted in this setting; (iii) there was a higher accuracy in the distinction between transmural vs. non-transmural infarcted myocardial segments, using endocardial strain analysis by Echo compared with analysis by SENC, although...
there was no significant difference between epicardial strain analysis using SENC or Echo.

**Strain analysis by SENC vs. Echo**

We found a moderate correlation between SENC and Echo for the deformation analysis of the endocardial layer, and only a weak correlation for the epicardial layer. Cho et al.\textsuperscript{26} compared 2D Echo with CMR tagging, considering the total wall thickness. They reported a correlation of $r = 0.51$. This is on a level similar to the one found by us for the endocardial layer. It should be kept in mind that any comparison of imaging techniques may be hampered by possible misalignment in segmental analysis. This issue may be even more complex for the correlation of SENC and Echo deformation data, as SENC uses long-axis views for circumferential function analysis, whereas Echo uses short axis views. However, strict application of the 16-segment LV model was taken care of in the analysis of both imaging techniques. Furthermore, in the comparison of SENC and Echo deformation analysis with LGE, SENC should have been at an advantage if misalignment would have been a major issue.

**Endocardial and epicardial layer strain**

Peak systolic circumferential strain of the endocardial layer of myocardial segments without infarction was found to be more negative in the Echo analysis compared with the SENC analysis. In contrast,
peak systolic circumferential strain of the epicardial layer of myocardial segments with transmural infarction was found to be less negative in the Echo analysis compared with the SENC analysis. In these segments, strain values close to zero are expected. These differences between Echo and SENC may be due to the better temporal and spatial resolution of Echo. Better temporal resolution of an imaging technique allows improved definition of the peak of the cyclic strain curve compared with an imaging modality with lower frame rate. Similarly, improved spatial resolution obtained by Echo may allow better distinction between the epicardial and endocardial layers with those obtained by SENC.

Although SENC and Echo have been described to provide strain values of different layers within a segment, it should be recognized that deformation parameters within the layers are not independent. Because of constancy of mass and volume, any deformation of the epicardial layer resulting in circumferential shortening of that segment will result in a deformation of the endocardial layer even if the endocardial layer is completely non-functional. This passive deformation results in persistent deformation of the endocardial layer even in case of non-transmural infarction affecting the complete endocardial layer. Thus, myocardial deformation of each layer is the result of active function within the layer and passive motion from adjacent tissue.

### Extent of myocardial infarction

Although LGE has evolved into the commonly used imaging modality in clinical practice to define myocardial viability based on a direct visualization of scar tissue, quantitative analysis of myocardial function has also been shown to allow assessment of myocardial viability. The concept of myocardial viability assessment based on analysis of function has been proved in experimental as well as clinical studies to allow reliable evaluation of the extent of myocardial infarction in ischaemic cardiomyopathy.15,16,27–30 More recently, this concept has even evolved with the availability of layer-specific analysis of function.21,31 The findings of layer-specific strain analysis based on SENC as well as Echo have been shown to relate to LGE and also allow prediction of reversible ischaemic dysfunction in patients undergoing revascularization procedures.7,21,32 The current study is the first to compare strain analysis based on SENC with strain analysis based on 2D Echo for the prediction of myocardial viability by LGE. This study confirms the validity of viability assessment based on myocardial function. Echo and SENC had similar accuracies in the distinction between segments with non-transmural infarction vs. those with no infarction by LGE. Similarly, both techniques allowed distinction of segments with transmural and those with non-transmural infarction as defined by LGE. Endocardial strain analysis using Echo was more accurate than endocardial analysis using SENC, although there was no difference of accuracy of epicardial strain analysis between both techniques. The AUC for endocardial peak systolic circumferential strain determined by SENC to distinguish transmural from non-transmural infarction was lower in this study as has been previously reported for the total myocardial wall thickness analysis by SENC.16 This may be due to the different cut-off values used to define infarct transmurality. We used a cut-off value of >50% and not >75% of segmental LGE. This definition of transmural infarction relates to a definition applied by Derumeaux et al.33 and considers the potential for functional recovery after revascularization procedures as described by Kim et al.5

### Limitations

Analysis of LGE was used as reference to evaluate the accuracy of quantitative deformation parameters determined by SENC and by Echo for the distinction of different infarct transmurals. Although this analysis nicely demonstrated the correlation between the extent of infarcted myocardium and the impairment of functional capacity, SENC as well as Echo could not be validated against a reference method to determine layer-specific myocardial deformation. This is due to the lack of validated references to define layer-specific myocardial deformation. Sonomicrometry has been used for the validation of deformation parameters obtained by imaging methods, considering the total myocardial wall thickness.34 However, the use of sonomicrometry has failed for layer-specific analysis. In patients with thin left ventricular walls, the voxel size of the SENC analysis may be too large for accurate determination of transmural differences. However, this potential limitation should not have any impact in patients with normal wall thickness.

In 12.6% of the segments, myocardial deformation analysis could not be performed by automatic analysis of Echo due to insufficient image quality. This is on a comparable level with previously
reported studies. In contrast, all segments could be analysed by SENC, whereas in a previous study ~1.5% of the segments had to be excluded. It should be acknowledged that the method to obtain strain data by SENC and by Echo differs. Although SENC determined strain for a specific myocardial point in space which can be selected manually, Echo calculates mean strain values for whole left ventricular segments. This may result in differences in strain values if abnormalities are confined to small areas. We confined this analysis to 12 segments as there were technical limitations in some patients in the analysis of apical long-axis views with SENC.

The ROC analysis, which yields a maximized AUC, resulted for the SENC analysis in an asymmetric level of sensitivity and specificity. This was associated with a rather high cut-off strain value to differentiate non-transmural from transmural infarction and a rather low cut-off strain value to differentiate non-transmural infarction from non-infarction. This should be kept in mind when applying the cut-off values.

Conclusions

Layer-specific analysis of myocardial deformation by Echo and by SENC allows discrimination between different transmurality categories of myocardial infarction with similar accuracy. Considering both imaging methods, analysis of endocardial layer deformation tended to be more accurate than analysis of the epicardial layer to distinguish between non-transmural infarction vs. non-infarction. Accuracy of both methods is non-optimal, indicating that further tools for improvement should be evaluated in the future. However, analysis of myocardial viability based on Echo or SENC may be considered in clinical practice if other imaging modalities like LGE are not available or application of a CMR contrast agent is prohibited due to severe renal failure.

Conflict of interest: none declared.

References


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