Strain-Encoded MRI for Evaluation of Left Ventricular Function and Transmurality in Acute Myocardial Infarction

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Background—Strain-encoded imaging (SENC) is a new technique for myocardial deformation analysis in cardiac MRI. The aim of the study was, therefore, to evaluate whether myocardial deformation imaging performed by SENC allows for quantification of regional left ventricular function and is related to transmurality states of infarcted tissue in patients with acute myocardial infarction.

Methods and Results—Cardiac MRI was performed in 38 patients with acute myocardial infarction 3±1 days after successful reperfusion using a clinical 1.5-T MRI scanner. Ten healthy volunteers served as controls. SENC is a technique that directly measures peak circumferential strain from long-axis views and peak longitudinal strain from short-axis views. Measurements were obtained for each segment in a modified 17-segment model. Wall motion and infarcted tissue were evaluated semiquantitatively from steady-state free-precession cine sequences and contrast-enhanced MR images and were then related to myocardial strain. Comparison of peak circumferential strain assessed by SENC images was significantly different in regions defined as normokinetic, hypokinetic, or akinetic (P<0.001). A cutoff peak systolic circumferential strain value of 10% differentiated nontransmural from transmural infarcted myocardium, with a sensitivity of 97% and a specificity of 94%. Strain analysis of SENC and MR tagging correlated well (r=0.76) with narrow limits of agreement (−9.9% to 8.5%).

Conclusions—SENC provides rapid and objective quantification of regional myocardial function and allows discrimination between different transmurality states in patients with acute myocardial infarction. (Circ Cardiovasc Imaging. 2009;2:116-122.)

Key Words: myocardial infarction ■ myocardial strain ■ strain-encoded MRI ■ viability

Identification of the extent and degree of contractile dysfunction and infarcted tissue in patients after acute myocardial infarction (AMI) has important prognostic implications.1,2 Different imaging modalities can be used to analyze viability such as stress-echocardiography or nuclear imaging techniques.3,4 However, for improved evaluation of viability, a combination of assessment of objective regional myocardial function and the extent of infarcted tissue would be desirable.

Cardiac magnetic resonance (CMR) imaging has emerged as a technique that allows accurate assessment of myocardial function and myocardial scar.6–8 Although contrast-enhanced MR imaging can be used to distinguish between reversible and irreversible myocardial ischemic injury, myocardial deformation imaging allows for objective description of myocardial function.

The currently applied reference method for analysis of myocardial deformation in CMR is MR tagging.9,10 However, this method has some disadvantages, for example, long breath-hold acquisition times and time-consuming postprocessing.11 Thus, for a routine comprehensive evaluation of myocardial function and viability, other methods are needed.

Recently, strain-encoded imaging (SENC) has been introduced as a novel MR technique to measure myocardial deformation expressed as myocardial strain.11–14 SENC has proved to allow accurate quantification of myocardial function in healthy volunteers and in patients with myocardial infarction, however, in small patient samples.12 The advantages of SENC are the relatively short acquisition time, no need for time-consuming postprocessing, and high-temporal resolution. The aim of this study was to evaluate whether myocardial deformation parameters derived from SENC allow accurate...
and objective assessment of myocardial function and discrimination of transmurality states in patients with AMI.

Methods

Patients presenting with AMI were screened over a 10-month period (June 2007 to March 2008) at the University Hospital of Heidelberg. To be included, the patients had to have a first-time AMI with a clearly identified culprit coronary vessel. Moreover, patients with severe hemodynamic compromise or patients requiring inotropic support were excluded from the study. In addition, patients with contraindication to MRI or gadolinium-based contrast agent were excluded from the study.

All patients received successful reperfusion therapy by percutaneous coronary intervention. AMI was diagnosed by history, electrocardiographic changes, cardiac biomarker abnormalities, and coronary angiography in accordance with the consensus of the American College of Cardiology and the European Society of Cardiology.15

In 10 healthy volunteers, reference values for peak circumferential and longitudinal strain were established. These volunteers were screened by clinical history, physical examination, 12-lead ECG, blood testing, glucose intolerance testing, resting blood pressure measurement (<145/90 mm Hg), and MR stress testing.

The study protocol complies with the Declaration of Helsinki and was approved by the local institutional ethical committee. Written informed consent was obtained from each patient. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Imaging Protocol

Patients were investigated in a clinical 1.5-T whole-body MR scanner (Achieva, Philips, Best, The Netherlands) 3±1 days after successful mechanical reperfusion of the infarct-related vessel using a 5-element phased array cardiac synergy coil. The overall CMR imaging time of the entire study was 45±10 minutes.

Cine Imaging

Assessment of resting left ventricular (LV) function was determined by cine images using a steady-state free-precession (SSFP) sequence in 10 to 12, 8-mm-thick slices covering the whole left ventricle from base to apex as well as long axis 2- and 4-chamber views (echo time, 1.39 ms; repetition time, 2.8 ms; flip angle, 60°; spatial resolution, 2.5×2.5×8 mm3; 35 phases per cardiac cycle) with a breath-hold time of 7 to 10 seconds per image. The pulse sequence was prospectively gated.

Myocardial Deformation Imaging

Strain-encoded images as well as tagged MR images, as reference standard for measurement of myocardial strain, were acquired sequentially in all subjects to calculate myocardial strain. Strain is expressed as the percentage of shortening or lengthening of myocar-dium in relation to its original length.

Strain-Encoded MR Imaging

SENC is a special modification to the MRI scanner software that enables the quantification of regional deformation of tissue as a result of cardiac motion. This technique produces images whose intensity depends on the degree of tissue deformation, as measured by the strain, which is the change in length per unit length of tissue. Therefore, the resulting anatomic images of the scanner are encoded with the strain values of the deformations. To calculate myocardial strain, SENC uses tag planes parallel and not orthogonal to the image plane. Thus, 2- and 4-chamber views in the same plane orientation as the CINE images are generated to calculate circumferential strain, and 3 short-axis views (basal, midventricular, and apical) are acquired to measure longitudinal strain.14

Typical imaging parameters of the prospectively triggered pulse sequence were a 380-mm field of view, a voxel size of 2.5/2.5 mm2, a repetition time/echo time 2.5/0.9 ms, and a flip angle 30°. Spiral acquisition was used to perform faster image acquisition without sacrificing the signal-to-noise ratio. SENC as a pulse sequence has relatively lower signal-to-noise ratio than conventional CINE acquisition, and to supplement the loss, thicker slices (10 mm) were used. The temporal resolution was 25 ms, and the number of phases (typically 27 to 35) was adapted to the current heart rate to cover approximately 100% of the cardiac cycle with a breath-hold time of 8 to 10 seconds per image.

2D Tagged MR Imaging

Tagged images were acquired at the same location as the SSFP and SENC images, with an 8-mm slice thickness. An electrocardiographically triggered segmented k-space version of the spatial modulation of magnetization tagging sequence was used to create a tag grid on the images with a tag separation of 7 mm using an FFE multishot sequence (repetition time/echo time, 3.9/1.7 ms; voxel size, 2/2 mm2; flip angle, 5°; spacing, 6.3; tag grid angle, 45°) with 10 to 14 phases per cardiac cycle. Three short-axis images from base to apex were acquired. The breath-hold time was 14 to 18 seconds per image.

Contrast-Enhanced Imaging

Ten minutes after gadolinium contrast injection (0.2 mmol/kg body weight of gadolinium-DTPA; Magnevist, Bayer, Germany), late-enhancement imaging was performed using a 3D-gradient spoiled turbo-fast field-echo sequence with a selective 180° inversion-recovery prepulse triggered to end-diastole acquired in the short axis covering the whole ventricle (repetition time/echo time, 3.2/1.16 ms; flip angle, 15°; spatial resolution, 1.5×1.7 mm2). The acquired 10-mm-thick slices were interpolated to 5-mm slices. The inversion time was adapted individually to suppress signal of normal myocardial tissue (typically 200 to 300 ms).

Data Analysis

For measurement of circumferential and longitudinal strain, the ventricle was divided into 12 segments (septal basal, midventricular, and apical; lateral basal, midventricular, and apical; anterior basal, midventricular, and apical; inferior basal, midventricular, and apical), resulting in 456 segments. For comparison of circumferential strain values obtained by MR tagging and SENC, the SENC long-axis views were compared with short-axis MR tagging images according to differences in strain quantification between the 2 techniques. To obtain optimal geometric matching, the LV outflow tract and the papillary muscles were used as landmarks. All strain measurements were performed using a dedicated software (Diagnosoft MAIN version 1.06, Diagnosoft Inc, Palo Alto, Calif), including HARP for data analysis of tagged images and a special tool for analysis of SENC images. The analysis was performed in the subendocardium.

To compare SENC values to visual assessment of LV function, 2 experienced observers, blinded to the strain values, evaluated regional myocardial function by consensus reading considering a 12 segment model of the LV. For each segment, myocardial function was described as normokinetic, hypokinetic, and adyskinetic.

For comparison of strain values and delayed enhancement imaging, segments were categorized in a 5-point scale proposed by Kim et al.,2 in which a score of 0 indicated no hyperenhancement, a score of 1 indicated 1% to 25% hyperenhancement, a score of 2 26% to 50% indicated hyperenhancement, a score of 3 51% to 75% indicated hyperenhancement, and a score of 4 76% to 100% indicated hyperenhancement. Transmural was defined as hyperenhancement extending >75% of the myocardium.

Reproducibility

Interobserver variability of the measurements of myocardial strain assessed with SENC and MR tagging was evaluated in 15 randomized patients with AMI (180 segments) by 2 independent observers who were blinded to the strain results from either SENC or MR tagging.

Statistical Analysis

Data are expressed as mean±SD. Continuous variables were compared by Student t test; otherwise, comparisons were analyzed by Mann–Whitney U test. For method comparison, rank correlation and
Table. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (n=38)</th>
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>56±11</td>
</tr>
<tr>
<td>Male/female n (%)</td>
<td>31 (82)/7 (18)</td>
</tr>
<tr>
<td>STEM/NISTEMI</td>
<td>32 (84)/6 (16)</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>54±14</td>
</tr>
<tr>
<td>Infarct size, g</td>
<td>38±31</td>
</tr>
<tr>
<td>Infarct location</td>
<td></td>
</tr>
<tr>
<td>LAD n (%)</td>
<td>18 (48)</td>
</tr>
<tr>
<td>RCA n (%)</td>
<td>13 (34)</td>
</tr>
<tr>
<td>LCX n (%)</td>
<td>7 (18)</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or n (%).

STEMI indicates ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery.

Bland-Altman analysis were performed. Furthermore, concordance correlation coefficient was calculated. For comparison of strain values across different categories of transmurality and wall motion abnormalities, a linear mixed model was applied to address the issue of multiple observations per patient.

Taking into account that there were 12 segments per patient to be analyzed, a generalized estimating equation approach with a binomial distribution, a logit link, and a working correlation matrix with exchangeable correlation was used to explore the ability of strain parameters to differentiate between normokinetic, hypokinetic, and a/dyskinetic segments as well as hyperenhancement >75% and <75%. The output from this analysis allowed the derivation of receiver operating characteristics curves, which were used to designate cutoffs and calculate the area under the curve (AUC), sensitivities and specificities.

Interobserver variability was calculated by intraclass correlation coefficient (ICC) and Bland-Altman analysis. A probability value <0.05 was regarded as statistically significant. Statistical analysis was performed using MedCalc version 9.6.3 (Mariakerke, Belgium) and SAS version 9.13 (SAS Institute Inc, Cary, NC).

Results

In total, 118 patients presenting with AMI were screened over a 10-month period. Of these patients, 70 were eligible for participation in the study.

The reason for the exclusion of the remaining 32 patients was severe hemodynamic compromise (n=16) and contraindication to MRI (n=10). Two patients refused to participate and four patients suffered from claustrophobia. Thus, in total, 38 patients (mean age, 56±11 years) were enrolled in this study. The patient characteristics are displayed in Table 1.

Strain Analysis of SENC and Tagging

In total, 38 patients were analyzed resulting in 456 segments. For strain-analysis of SENC images, 7 (1.5%) segments for circumferential strain-analysis and 12 (2.6%) segments for longitudinal strain-analysis had to be excluded because of insufficient image quality. In MR tagging, comparably 28 segments (6%) were excluded.

Myocardial Strain Related to Segmental Left Ventricular Function

For visual analysis of wall motion abnormalities, 302 of 456 analyzed segments were defined as normokinetic, 82 as hypokinetic, and 72 as a/dyskinetic.

Peak circumferential strain assessed by SENC was significantly decreased in regions defined as hypokinetic or a/dyskinetic by cine MRI compared with normokinetic regions. Furthermore, hypokinetic segments could be distinguished from a/dyskinetic regions by circumferential strain and had significantly different peak circumferential strain values as demonstrated in Figures 1 and 2 (P<0.001 for all).

For peak longitudinal strain assessed by SENC, the strain-values were also significantly different in normo-, hypo- and a/dyskinetic regions of the heart (−20±4%, −14±5%, −10±5%; P<0.001 for all).

Performing receiver operating characteristics analysis, a peak systolic circumferential strain value of <−17% was related to hypokinesia with a sensitivity of 85% and a specificity of 86% (AUC, 0.91; 95% CI, 0.88 to 0.93; P<0.001) and a peak systolic circumferential strain value <−10% corresponded to a/dyskinesia with a sensitivity of 95% and a specificity of 92% (AUC, 0.96; 95% CI, 0.94 to 0.98; P<0.0001). Longitudinal strain showed slightly inferior results in receiver operating characteristics analysis. A peak systolic longitudinal strain value of <−18% was related to hypokinesia with a sensitivity of 85% and a specificity of 80% (AUC, 0.86; 95% CI, 0.79 to 0.91), whereas a cutoff value <−14% corresponded to a/dyskinesia with a sensitivity of 74% and a specificity of 88% (AUC, 0.887; 95% CI, 0.83 to 0.93).

Circumferential strain was shown to be significantly more precise in detecting hypokinesia (P=0.05). No significant difference was observed in detecting akinsesia (P=0.4).

Circumferential Strain of Remote Regions Versus Circumferential Strain in the Normal Left Ventricle

A total of 301 segments of remote myocardium of AMI patients were compared with segments in the left ventricle of healthy volunteers. Remote myocardium was defined as segments without hyperenhancement in the contrast-enhanced images and no wall motion abnormalities in the cine-images. Strain values of healthy volunteers (mean age 55±9) were slightly heterogeneous in different segments with highest subendocardial strain values anterior and lowest strain values inferior (−22.8±3.4 septal, −23.4±3.1 lateral, −25.3±2.4 anterior, −22.3±3.9 inferior). We found reduced strain parameters in the remote region compared with segments in the normal left ventricle (−21±4.9 versus −23.4±3.6, P<0.001).

Circumferential and Longitudinal Strain Related to Ejection Fraction

Mean myocardial strain values inversely correlated with the ejection fraction. The inverse correlation of mean peak circumferential strain was superior to mean peak longitudinal strain (correlation coefficient, r = −0.68 versus r = −0.45).

Myocardial Strain Related to Infarcted Tissue

Among 456 segments, segmental analysis of contrast-enhanced MR imaging indicated noninfarcted tissue in 322 segments, 1% to 25% hyperenhancement in 17 segments, 26% to 50% hyperenhancement in 29 segments, 51% to 75% hyperenhancement in 13 segments and 76% to 100% hyperenhancement in 75 segments. Transmural infarcted tissue was
defined as hyperenhancement $>$75%, resulting in 59 segments with nontransmural infarcted myocardial tissue and 75 segments with transmural infarcted myocardial tissue.

Regarding the nontransmural infarcted segments, in wall motion analysis 70% (32) were classified as hypokinetic, 22% (10) were normokinetic, and 9% (4) were akinetic. Regarding the transmural-infarcted segments, 73% (64) were defined as akinetic, 20% (18) as hypokinetic, and 7% (6) as normokinetic.

Significant differences in peak circumferential strain in noninfarcted, nontransmural infracted, and transmural infarcted segments were observed ($-20 \pm 6\%, -12 \pm 7\%, -6 \pm 7\%; P<0.0001$).

A cutoff peak systolic circumferential strain value of $-10\%$ differentiated nontransmural infarcted myocardium from transmural infarcted myocardium with a sensitivity of 97% and a specificity of 94% (AUC, 0.96; 95% CI, 0.94 to 0.98). Peak systolic longitudinal strain achieved a sensitivity of 64% and a specificity of 85% (AUC, 0.76; 95% CI, 0.69 to 0.83) to differentiate between nontransmural infarcted and transmural infarcted myocardium at a cutoff of $-17\%$ (Figure 3). Circumferential strain was slightly better to differentiate between transmural and nontransmural infarcted myocardium, however, not statistically significant ($P=0.7$).

**Comparison of SENC Versus MR Tagging**

Strain parameters measured by SENC and MR tagging correlated well ($r=0.76$, $P<0.0001$). The 95% limits of agreement in Bland-Altman plot were $-9.9\%$ to 8.5% with a concordance correlation coefficient of 0.80 (Figure 4).

**Reproducibility**

A total of 180 segments were evaluated for interobserver variability of SENC and MR tagging. The interobserver variability for SENC was excellent and superior to that of MR tagging (ICC for SENC=0.92, ICC for tagging=0.80). In Bland-Altman plot, the limits of agreements were $-7.6\%$ to 7.4% for SENC and $-6.5\%$ to 8.1% for MR tagging.
Scan Time
The total scan duration for SSFP and SENC imaging was 30 to 40 seconds per patient (2- and 4-chamber view with SSFP and SENC). For a SSFP and MR tagging study the total scan time was 56 to 74 seconds (2- and 4-chamber view with SSFP, 3 short-axis views with MR tagging).

Time Spent for Data Analysis
The time spent for strain analysis per patient was significantly lower for SENC compared with tagging (4.1±0.6 minutes versus 9.2±1.2 minutes, P<0.001).

Discussion
The present study demonstrates that (1) SENC allows objective and rapid assessment of myocardial function in patients with AMI, (2) SENC allows discrimination between different degrees of myocardial hyperenhancement and can therefore distinguish transmural from nontransmural infarcted tissue in patients with AMI, and (3) strain parameter obtained by SENC closely correlate with MR tagging.

Objective Quantification of Regional Myocardial Function and Infarct Transmurality
We have shown that SENC provides accurate regional description of LV function and transmurality of infarcted myocardium. The results of this study extend data of a previously published study introducing SENC as a novel MR technique for myocardial function imaging in AMI.12 In that study by Garot et al, longitudinal strain was assessed in 9 patients after AMI and was compared with infarcted myocardial tissue. In our study, we measured circumferential as well as longitudinal strain in 38 patients and found that circumferential strain was more precise in detecting hypokinesia and was also slightly more precise, however, not significantly, to distinguish between nontransmural and transmural infarcted tissue in patients after AMI.

Previous studies have shown that contrast-enhanced MR imaging cannot only accurately detect myocardial scar with higher spatial resolution than nuclear imaging techniques,16 but also predict functional recovery in patients with ischemic heart disease.7 In patients with chronic ischemic heart disease

Figure 3. SENC for distinction between nontransmural and transmural infarcted myocardial tissue. Receiver operating characteristics curve demonstrating that a cutoff peak systolic circumferential strain value of −10% obtained by SENC is able to differentiate nontransmural infarcted myocardium from transmural infarcted myocardium, with a sensitivity of 97% and a specificity of 94%. Longitudinal strain was less sensitive and specific for distinction between nontransmural and transmural infarcted myocardial tissue (sensitivity, 64%; specificity, 85%).

Figure 4. Comparison of SENC and MR tagging. A, Linear regression analysis of the comparison of SENC and MR tagging. B, Bland-Altman plot shows narrow limits of agreement between SENC and MR tagging (−9.9% to 8.5%).
the threshold to regain functional recovery is hyperenhancement <50%.7,8 Choi et al,17 Kramer et al,18 and Rogers et al19 have demonstrated that in patients with AMI even segments with an extent of 51% to 75% hyperenhancement exhibit some improvement in contractile function.

Therefore, in the present study segments with hyperenhancement <75% were classified as having potential to regain functional recovery whereas segments with hyperenhancement >75% were considered to have low probability for functional recovery.

Circumferential strain values achieved an excellent sensitivity and specificity to differentiate segments which have potential to regain functional recovery and those which have less.

In contrary to the theory of increased function in remote myocardium early after AMI20 we found impaired strain parameters in all segments, including the remote region, compared with strain values of the same segments of the left ventricle of healthy volunteers. MR tagging studies showed the same findings using circumferential strain.12,21,22 Different loading conditions of the infarct-related myocardium may reduce function in the remote myocardium. Reduced function in the noninfarcted myocardium may lead to redistribution of regional wall stress and smaller compliance mismatch between functioning and nonfunctioning myocardium.23

The inverse correlation between global ventricular function and regional myocardial function quantified by strain analysis was higher using circumferential strain compared with longitudinal strain parameters \( r = -0.68 \) versus \( r = -0.45 \). Thus, it is suggested that the level of contribution of circumferential fibers to the LV-function is greater than that of the longitudinal fibers. This may be explained by the fiber architecture and the contraction pattern of the left ventricle.24

Advantages of SENC
The extent and degree of contractile dysfunction and infarcted tissue are both important factors in determining long-term prognosis after AMI. For assessment of regional dysfunction in clinical routine, wall motion analysis and wall thickening are often used parameters.25 These parameters are often subjective and have a limited reproducibility. However, objective reproducible methods for quantification of myocardial function are of critical importance for patient management, therapy monitoring and outcome studies.

Myocardial strain imaging in CMR offers a reproducible measure of strain and therefore provides objective assessment of regional myocardial deformation. The current reference standard of myocardial deformation imaging in CMR is tagging. However, MR tagging still has some disadvantages, for example time-consuming postprocessing, despite the use of HARP concepts.26,27 We demonstrated that strain-analysis of SENC data are significantly faster than analysis of tagging data, which is in agreement with previous studies.11 Furthermore, the reproducibility of MR tagging was also slightly inferior to that of SENC imaging (ICC = 0.80 versus ICC = 0.92), even though it was in the reported ranges.28,29 Moreover, SENC provides a shorter breathhold time and therefore also a shorter overall image time, which may be an advantage, especially when examining acutely ill patients like patients presenting with AMI.

SENC provides spatially resolved imaging and assessment of myocardial strain without the need for complex image postprocessing as this technique offers direct pixel-related imaging and therefore direct assessment of longitudinal and circumferential strain. Our data show that SENC provides reduced breathhold times with improved spatial and temporal resolution as SENC provides pixel-related quantification of myocardial strain, obviating the measure of myocardial strain derived from tags with relevant separation of \( \approx 7 \) mm.

Limitations
First, as we did not investigate the patients at follow-up it remains to be investigated whether strain parameters obtained by SENC allow improved prediction of functional recovery at follow-up. However, we have shown for the first time in a large patient population that SENC provides accurate assessment of circumferential and longitudinal strain in infarcted, adjacent and remote myocardium and allows distinction between nontransmural and transmural infarcted myocardial tissue. Second, because of the nature of this method we compared SENC long-axis views with MR tagging short-axis views. By using anatomic landmarks we intended to find the same image plane. However, we cannot exclude that the image plane was not always exactly the same. Third, longitudinal strain parameters assessed by SENC were not compared with MR tagging. A close correlation of these 2 methods has been demonstrated before, however, in a small patient population.

Conclusion
The present study demonstrates that strain parameters obtained from SENC MR imaging can be used to assess regional contractile function as well as transmurality states of infarcted myocardial tissue in patients with AMI.

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Disclosures
Dr Osman is a founder and shareholder in Diagnoisoft Inc. This is approved by the Conflict of Interest committee at Johns Hopkins University. The other authors have no conflicts of interests to disclose.

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References
Identification of the extent and degree of contractile dysfunction and myocardial scar in patients after acute myocardial infarction has important prognostic implications. In this study, we introduced strain-encoded imaging as a novel MR technique for myocardial deformation imaging that enables the quantification of regional deformation of tissue as a result of cardiac motion. We demonstrated that strain parameters obtained from strain-encoded MR imaging can be used to analyze regional contractile function and transmural states in patients with acute myocardial infarction. As quantification of regional myocardial function becomes more and more important in clinical routine, strain-encoded imaging provides rapid and objective strain analysis, without the need for time-consuming postprocessing.
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