Analysis of Segmental Strain for the Detection of Chronic Ischemic Scars in Non-Contrast Cardiac MRI Cine Images: A Feasibility Study

Malgorzata Polacin  
University of Zurich

Mihaly Karolyi  
University of Zurich

Matthias Eberhard  
University of Zurich

Alexander Gotschy  
University of Zurich

Bettina Baessler  
University of Zurich

Hatem Alkadhi  
University of Zurich

Kozerke Sebastian  
University of Zurich

Robert Manka  
Robert.Manka@usz.ch  
University of Zurich

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Abstract

Aims Cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement (LGE) is considered the gold standard for scar detection after myocardial infarction. In times of increasing skepticism about gadolinium depositions in brain tissue and contraindications of gadolinium administration in some patient groups, tissue strain-based techniques for detecting ischemic scars should be further developed as part of clinical protocols. Therefore, the objective of the present work was to investigate the feasibility of scar detection in segmental strain calculations based on routinely acquired non-contrast cine images in patients with chronic infarcts.

Methods Forty-six patients with chronic infarcts and scar tissue in LGE images (5 female, mean age 52 ± 19 years) and 24 gender- and age- matched healthy controls (2 female, mean age 47 ± 13 years) were included. Global (global peak circumferential [GPCS], global peak longitudinal [GPLS], global peak radial strain [GPRS]) and segmental (segmental peak circumferential [SPCS], segmental peak longitudinal [SPLS], segmental peak radial strain [SPRS]) strain parameters were calculated from standard balanced SSFP cine sequences using commercially available software (Segment CMR, Medviso, Sweden). Two independent blinded readers localized potentially infarcted segments in segmental circumferential strain calculations (endo-/epicardially contoured short axis cine and resulting polar plot strain map) and by visual wall motion assessment of cine images.

Results Global strain values were reduced in patients compared to controls (GPCS p= 0.02; GPLS p= 0.04; GPRS p= 0.01). Patients with preserved ejection fraction showed also reduced GPCS compared to healthy individuals (p=0.04). In patients, mean SPCS was significantly impaired in subendocardially (-5.4% +/- 2) and in transmurally infarcted segments (-1.2% ± 3) compared to remote myocardium (-12.9% +/- 3, p=0.02 and 0.03, respectively). ROC analysis revealed an optimal cut-off value for SPCS for discriminating infarcted from remote myocardium of -7.2 % with a sensitivity of 89.4 % and specificity of 85.7%. Mean SPRS was impeded in transmurally infarcted segments (15.9 % +/- 6) compared to SPRS of remote myocardium (31.4% +/- 5; p= 0.02). The optimal cut-off value for SPRS for discriminating scar tissue from remote myocardium was 16.6% with a sensitivity of 83.3% and specificity of 76.5%. 80.3 % of all in LGE infarcted segments (118/147) were correctly localized in segmental circumferential strain calculations based on non-contrast cine images compared to 53.7% (79/147) of infarcted segments detected by visual wall motion assessment (p > 0.01).

Conclusion Global strain parameters are impaired in patients with chronic infarcts compared to healthy individuals. Mean SPCS and SPRS in scar tissue is impeded compared to remote myocardium in infarcts patients. Blinded to LGE images, two readers correctly localized 80% of infarcted segments in segmental circumferential strain calculations based on non-contrast cine images, in contrast to only 54% of infarcted segments detected by visual wall motion assessment. Analysis of segmental circumferential strain shows a promising alternative for scar detection based on routinely acquired, non-contrast cine images for patients who cannot receive or decline gadolinium.
**Introduction**

Myocardial infarction often results in irreversible scar formation of the myocardium. Cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement (LGE) is considered the gold standard method for detection and visualization of scar tissue after myocardial infarction (MI) [1, 2]. To this end, intravenous application of gadolinium-based contrast agents is required for visualizing scar tissue, as there are currently no alternatives in cardiac MRI for this task. LGE sequences are time consuming and typically use up more than 50% of the exam time due to the required 10–15 min time delay after contrast agent administration, which is important for contrast retention in scar tissue [3]. Moreover, the intravenous application of gadolinium-based contrast agents is restricted in patients with acute and chronic renal failure [4]. Additionally, intravenous contrast agent application may cause an allergic reaction in some circumstances, which can be life threatening [5]. Finally, recent studies suggest possible deposition of linear gadolinium chelates, e.g. in brain and bone [6, 7], which is nurturing uncertainty among both patients and treating physicians. Therefore, alternative scar detection methods based on routinely acquired cine images increasingly gain attention [8–10].

During cardiac contraction, myocardial deformation can be described by vectors in the radial, circumferential and longitudinal directions. In healthy myocardium, negative strain values are measured for circumferential and longitudinal direction during systole, while radial strain yields positive values due to thickening in the radial direction during ventricular contraction [11]. Scar tissue leads to regionally altered strain behavior of the myocardium due to reduced contractility of myofibroblasts, which replace myocytes after infarction [12].

Different techniques for measuring global and regional myocardial deformation have been developed in the past two decades, like myocardial tagging [13, 14], tissue displacement encoding with stimulated echoes [15] and strain encoded imaging [16]. All these techniques - with myocardial tagging being the reference modality for evaluating myocardial strain - have in common, that sequences need to be acquired additionally to an already long clinical protocol. Myocardial feature tracking (FT) was introduced for myocardial strain quantification using routinely acquired steady-state free precession (SSFP) cine sequences as input [9, 17–19]. Based on optical flow methods [20] or non-rigid algorithm for image registration and segmentation [21, 22], myocardial borders can be identified and displacement of myocardial segments can be tracked throughout the cardiac cycle.

Recent studies focused on the investigation of global strain parameters in patients with acute and chronic infarcts, revealing reduced global longitudinal and global circumferential strain in these patients [23, 24]. Until now, only few studies examined segmental strain in patients with infarction [25, 26], probably because reduced accuracy and reproducibility of segmental strain values was reported for optical flow-based FT methods [27]. FT software based on non-rigid algorithm for image registration and segmentation revealed higher accuracy and better reproducibility in segmental strain [21, 22] and therefore can be potentially used for scar detection in cine images with sufficient discrimination between remote and infarcted myocardium. The purpose of this study was to examine global and segmental
strain values in patients with chronic infarcts and healthy controls and to investigate the feasibility of using segmental strain for scar detection in non-contrast cine images.

**Methods**

**Study population**

From September 2018 to June 2019 46 patients (5 female, mean age 52 ± 19 years) with chronic ischemic scars as detected in standard LGE images were used for this retrospective study. Patients with recent myocardial infarction (within the last 4 weeks), unstable angina or previously diagnosed primary cardiomyopathies were excluded. A control group of 24 healthy age- and gender matched individuals (2 female, mean age 47 ± 13 years) were also enrolled during the same time period. This study was conducted in accordance to the Declaration of Helsinki and its later amendments and the institutional review board approved this retrospective study (Cantonal ethics commission Zurich, BASEC-Nr. 2019-00808). All participants gave written informed consent. Data including image material were handled anonymously.

**CMR data acquisition**

CMR was performed on a 1.5T MR system (Achieva, Philips Healthcare, Best, the Netherlands) using a dedicated 5-channel phased array coil. Cine balanced SSFP images in standard long-axis geometries (two-, three- and four-chamber view) as well as in short-axis orientation covering the entire left ventricle (LV) were acquired (field of view: 350 × 350 mm$^2$, matrix: 300 × 300, repetition time/echo time: 3.0/1.5 ms, in-plane resolution, 1.5 × 1.5 mm$^2$; number of cardiac phases: 25-50, section thickness: 8 mm). LGE images (inversion recovery gradient-echo sequence: field of view: 350 × 350 mm$^2$; matrix: 256 × 256; repetition time/echo time: 7.4/4.4; inversion time: 205–250 ms; flip angle: 20°; in-plane resolution: 1.5 × 1.5 mm$^2$; section thickness: 8 mm) covering the entire LV in short axis view as well as in 2-,3- and 4 chamber view were acquired 15 minutes after administration of a bolus of 0.2 mmol of gadobutrol (Gadovist; Bayer Schering Pharma, Zurich, Switzerland) per kilogram body weight.

**CMR Data analysis**

*Assessment of infarcted segments in LGE images* – After calculation of ventricular volumes and function (IntelliSpace Portal, Philips, Version 8.0.3) (Tab. 1), infarcted segments were identified on LGE images and double checked with the existing corresponding report (revised by a cardiologist with over 15 years of experience in cardiac MRI). Infarcted segments were considered transmural if >50% of the wall thickness was involved. Scars with less than 50% of the wall thickness were classified as subendocardial.

*Feature tracking strain analysis* – Global (global peak circumferential [GPCS], global peak longitudinal [GPLS] and global peak radial strain [GPRS]) and segmental (segmental peak circumferential [SPCS],
segmental peak longitudinal [SPLS], segmental peak radial strain [SPRS]) strain parameters were calculated from standard balanced SSFP cine sequences using commercially available software (Segment CMR, Medviso, Lund, Sweden) in accordance with the American Heart Association’s 16 segment model. After image registration by the software, endocardium and epicardium of short axis cine images were manually contoured in end-diastole and in end-systole and results were automatically calculated by the software. Contours could be manually corrected throughout the cardiac cycle, if necessary. All FT strain analysis were performed blinded to patient information and LGE images. Twenty-four cases were chosen for performing interobserver agreement.

*Localization of potentially infarcted segments in circumferential strain calculations and in cine images* – Two independent blinded readers were advised to localize potentially infarcted segments in segmental circumferential strain calculations (endo-/epicardially contoured short axis cine images and resulting polar plot strain map, *Fig. 1*) as well in the corresponding cine short axis images by visual wall motion assessment.

**Statistical analyses**

Statistical analyses were performed using commercially available software (SPSS, release 20.0; SPSS, Chicago, IL, USA). Quantitative data are expressed as means ± standard deviations and categoric data are expressed as numbers or percentages. The Kolmogorov–Smirnov Test was used to evaluate normal distribution. Depending on distribution of normality, two-tailed paired *t*-tests and Wilcoxon signed rank were used to compare global and segmental strain values as well as to compare infarcted segments found in LGE, circumferential strain calculations and by visual wall motion assessment. The Intraclass Correlation Coefficient (ICC) was used to determine interobserver agreement in strain calculations and to determine interobserver agreement in identified infarcted segments in circumferential strain calculations and in visual wall motion assessment. ICC = 0.60-0.74 was considered good and ICC > 0.74 was considered excellent agreement [28]. Receiver operating characteristics (ROC) curve analysis was performed to determine the cut-offs of segmental strain values and area under the curve (AUC) for circumferential and radial strain in order to differentiate infarcted from remote myocardium. ROC curve analysis was not performed for segmental longitudinal strain due to lacking significance between strain values in infarcted and remote myocardium. Statistical significance was assumed at a p-value below 0.05.

**Results**

**Left ventricular ejection fraction (LVEF) and global strain:**

Overall LVEF was 46.9 ± 10 % in the patient group and 58.6 ± 4 % in the control group (*p*=0.8, *Tab. 1*). Global strain values were reduced in patients compared to healthy controls (GPCS -10.5% ± 3 vs. 20.6% ± 2, *p*= 0.02; GPLS -11.8% ± 3 vs. 18.2% ± 2, *p*=0.04; GPRS 27.5% ± 6 vs. 39.6% ± 4; *p*=0.01, *Tab. 1*), interobserver agreement was excellent (*Tab. 2*). Also patients with preserved LVEF (LVEF > 50%, 19
patients) [29] had markedly reduced GPCS compared to healthy individuals (-12,3% ± 2 vs. 20,6% ± 2, p=0,04), while GPLS and GPRS was not significantly impaired (GPLS -13,6% ± 4 vs. 18,2% ± 2, p=0,2; GPRS 33,4% ± 6 vs. 39,6% ± 5, p=0,3) (Fig. 2). Remote myocardium in infarct patients showed reduced peak circumferential strain compared to controls (12,9% ± 3 vs. 20,6% ± 2, p=0,04), peak longitudinal strain (-12,8% ± 3 vs. 18,2% ± 2, p=0,2) and peak radial strain (31,4% ± 5 vs. 39,6% ± 5, p=0,3) on the other hand was only mildly impaired in remote myocardium of infarct patients compared to healthy individuals.

**Segmental strain:**

From 736 segments 147 segments were diagnosed with scars on LGE images (20%), of which 102 were considered transmurally infarcted and 45 were subendocardially infarcted. The average amount of infarcted segments per patient was 3.4 (range: 2-7). The most frequently infarcted segments were segment 4, 7 and 10, in descending order.

**Segmental circumferential strain:**

Among the patient population mean segmental peak circumferential strain (SPCS) was significantly impaired in subendocardial infarcts (-5,4% ± 2) and even more in transmurally infarcted segments (-1,2% ± 3) compared to mean SPCS of remote myocardium (-12,9% ± 3, p= 0,02 and 0,03) (Fig. 3) with excellent interobserver agreement (Tab. 2). In ROC analysis the optimal cut-off value for SPCS for discriminating scar tissue from remote myocardium was -7,2 % with a sensitivity of 89,4 % and specificity of 85,7%, AUC 0,94 [0,912 – 0,962] (Fig. 4, left image).

**Segmental longitudinal strain:**

Among the patient population mean segmental peak longitudinal strain (SPLS) was mildly impaired in subendocardially (-7,5% ± 8) and transmurally (-5,9 % ± 7) infarcted segments compared to mean SPLS of remote myocardium (-12,8% ± 3, p= 0,3 and 0,4) (Fig.3). Interobserver agreement was good (Tab. 2).

**Segmental radial strain:**

Mean segmental peak radial strain (SPRS) was mildly impaired in subendocardially infarcted segments in the patient cohort (18,9% ± 10), but significantly impeded in transmurally infarcted segments (15,9 % ± 6) compared to SPRS of remote myocardium (31,4% ± 5; p=0.3 and 0.02) (Fig.3), interobserver agreement was excellent (Tab. 2). The optimal cut-off value for SPRS for discriminating scar tissue from remote myocardium was 16,6% with a sensitivity of 83,3% and specificity of 76,5%, AUC 0,86 [0,827 – 0,902] (Fig. 4, right image).

**Localization of infarcted segments in circumferential strain calculations and by visual wall motion assessment**
Localization of potentially infarcted segments based on segmental circumferential strain calculations (endo-/epicardially contoured short axis cine images and resulting polar plot strain map, Fig. 1) revealed 118 infarcted segments from 147 infarcted segments (80.3%, 88 transmural, 30 subendocardial; Fig. 5) with excellent interobserver agreement (ICC 0.904, 95%CI: 0.845-0.933). 29 infarcted segments were not detected (24 subendocardial and 5 transmural), among them one patient with only a small transmural scar in segment 15. All other patients diagnosed with scars in LGE images had at least one impaired segment in circumferential strain calculations and the missed infarcted segments were localized adjacent to already diagnosed infarcts.

Simultaneously performed visual wall motion assessment of cine short axis images revealed 79 from 147 infarcted segments (53.7%, 70 transmural, 9 subendocardial; ICC 0.811, 95%CI: 0.782-0.859), especially infarcts in the posterior wall (segments 4, 10, 15) were missed (41 from 68 missed infarcts, 60.3%).

**Discussion**

This study examined global and segmental myocardial deformation indices in patients with chronic ischemic scars and the feasibility of using segmental strain for scar detection in non-contrast cine images.

Main findings of this study are: a) global strain values are markedly impaired in patients with infarcts, also in patients with preserved EF compared to controls b) both transmurally and subendocardially infarcted segments show significantly reduced segmental circumferential strain compared to remote myocardium in infarct patients c) 80% of infarcted segments could be correctly localized from segmental circumferential strain calculations based on non-contrast cine images, while only 54% of infarcted segments could be detected by visual wall motion assessment of cine images.

Scar tissue leads to altered strain behavior of the myocardium due to reduced contractility of myofibroblasts, which replace myocytes after infarction. Recent studies focused on the investigation of global strain parameters in patients with acute and chronic infarcts, revealing reduced global longitudinal and global circumferential strain in these patients [23, 24]. Until now, only few studies examined segmental strain in patients with infarction [25, 26], possibly because reduced accuracy and reproducibility of segmental strain values was reported for optical flow-based FT methods in the past [27]. The FT software used in this study is based on a non-rigid algorithm for image registration and segmentation and showed higher reliability and interobserver agreement in segmental strain than software based on optical flow methods [21, 22]. In line with current study results, GPLS, GPCS and GPRS was reduced in our patient cohort compared to healthy controls [30]. Strain parameters were able to detect subclinical impairment of cardiac function in infarct patients with normal ejection fraction, concluding that strain is a more sensitive parameter for cardiac function compared to LVEF [31]. Moreover, we discovered that remote myocardium in infarct patients has lower mean strain values.
compared to healthy controls, suggesting subclinical changes in strain behavior of remote myocardium of patients after ischemia and scar formation [32] [33].

Both transmural and subendocardial scars showed significantly impaired mean SPCS compared to remote myocardium as well as impeded mean SPRS in transmurally infarcted segments. There are no definite cut-off values published for discriminating infarcts from remote myocardium. In our patient cohort the derived cut-off value was −7.2% for segmental circumferential strain (below which segments are considered remote) and 16.6% for radial strain (above which segments are considered remote). Cut-off values for circumferential strain were comparable with those from other research groups [34][26], but the cut-off value for radial strain was higher than in other studies, mostly due to already higher normal value for radial strain in our patient group. In our patient group, mean segmental longitudinal strain was not significantly impaired in scar tissue compared to remote myocardium.

Based on the observation of markedly impaired mean SPCS in scars, we examined infarct localization in segmental circumferential strain calculations (endo-/epicardially contoured short axis cine images and resulting polar plot strain map) in all 46 patients by two readers, blinded to LGE images. While visual wall motion assessment based on non-contrast cine short axis images detected about half of all infarcted segments (53.7%), 80% of infarcted segments could be localized correctly in circumferential strain calculations. One patient with a small transmural scar in the posterior wall was not detected in segmental circumferential strain calculation. Further analysis of the other 28 missed infarcted segments showed that those segments were localized adjacent to already as “infarcted” classified segments and were mostly subendocardial.

Our study shows that strain calculations are of substantial benefit for scar detection in non-contrast cine images compared to scar detection based on visual wall motion assessment. This method shows a promising alternative for scar detection in patients who cannot receive or refuse gadolinium. Since FT is already in clinical use, this method can be easily incorporated in the clinical routine in contrast to elaborate postprocessing methods like machine learning techniques, that are often time consuming. Combined use of strain calculations and T1 mapping could probably enhance the diagnostic accuracy of scar localization in non-contrast MRI protocols even more [35].

**Limitations**

Some study limitations must be acknowledged. This is a retrospective analysis of data from 46 patients and 24 age- and gender matched controls and most patients and controls are male. Equal amount of both genders should be investigated, since it has been shown, that global strain values differ between men and women [36, 37]. Further studies with more patients are needed to establish reliable cut-off segmental strain values for remote and scarred myocardium. The benefit of segmental circumferential strain calculations over visual wall motion evaluation based on cine images should be investigated in a prospective setting. Finally, since strain parameters are based on myocardial deformation, akinetic but
not infarcted myocardium (“stunned myocardium”) may provide false positive results in strain calculations.

**Conclusion**

Global strain parameters are impaired in patients with chronic infarcts compared to healthy individuals. 80% of infarcted segments could be detected in segmental circumferential strain calculations based on non-contrast cine images, while visual wall motion assessment of cine images revealed only about 54% of all infarcted segments. Analysis of segmental circumferential strain shows a promising alternative for scar detection in patients who cannot receive or decline gadolinium. This technique may be a further step in reducing gadolinium in cardiac MRI protocols in the future.

**Abbreviations**

AUC area under the curve

FT feature tracking

GPCS global peak circumferential strain

GPLS global peak longitudinal strain

GPRS global peak radial strain

ICC Intraclass Correlation Coefficient

i.v. intravenous

*LGE late gadolinium enhancement*

*LV left ventricle/left-ventricular*

LVEDV left ventricular end-diastolic volume

LVEF left ventricular ejection fraction

LVESV left ventricular end-systolic volume

LVSV left ventricular stroke volume

MRI magnetic resonance imaging

MI myocardial infarction

ms milliseconds
Declarations

Author contribution

M.P., M.K., A.G., R.M. wrote the manuscript. M.P., R.M., S.K. designed the study. M.P., M.K., M.E. provided patient data and images. M.P., M.K. performed data analysis. B.B., H.A., S.K. proofread the manuscript.

Competing interest

The authors declare no competing interests.

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### Tables

Due to technical limitations, table 1,2 is only available as a download in the Supplemental Files section.

### Figures
Figure 1

Basal, midventricular and apical cine (upper row) and LGE (middle row) in a patient with RIVA infarction (segment 2,8,9,15) and correlating segmental circumferential (upper row) and radial (middle row) strain values. Subendocardial infarction in segment 2 shows no segmental radial strain impairment. Basal, midventricular and apical LGE sections and circumferential strain values of a healthy control (lower row).
Figure 2

Global strain values in all patients, patients with preserved EF (LVEF > 50%) and healthy controls. Brackets signalize significantly different strain values between groups. (LV)EF= (left ventricular) ejection fraction, GPCS = global peak circumferential strain, GPLS = global peak longitudinal strain, GPRS = global peak radial strain.
Figure 3

Segmental strain values in patients and healthy controls. Brackets signalize significantly different strain values between groups. Significance between infarcted segments and controls are presumed and thus not marked. SPCS = segmental peak circumferential strain, SPLS = segmental peak longitudinal strain, SPRS = segmental peak radial strain.
Figure 4

ROC curves for distinguishing infarcted and remote myocardium based on strain parameters. In SPCS the optimal cut-off is -7.2% (sensitivity of 89.4% and specificity of 85.7%) and in SPRS the optimal cut-off is 16.6% (sensitivity of 83.3% sensitivity and specificity of 76.5%). ROC= Receiver operating characteristic, SPCS= segmental peak circumferential strain, SPRS= segmental peak radial strain
Localization of infarcted segments in segmental circumferential strain calculations (SPCS) showed significantly more infarcted segments (80.3%) than visual assessment of wall motion abnormalities in cine images (53.7%); infarcted segments in LGE images served as gold standard. Brackets signalize significantly different strain values between groups. LGE = late gadolinium enhancement, SPCS = segmental peak circumferential strain, VWMA = visual wall motion assessment.

**Figure 5**

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.JPG
- Table2.JPG