Identification and further differentiation of subendocardial and transmural myocardial infarction by fast strain-encoded (SENC) magnetic resonance imaging at 3.0 Tesla

Noriko Oyama-Manabe, MD, PhD[1], Naoki Ishimori, MD, PhD [2], Hiroyuki Sugimori, RT[1], Marc Van Cauteren, PhD[3], Kohsuke Kudo, MD, PhD[4], Osamu Manabe, MD, PhD[5], Tomoyuki Okuaki, RT[3], Tamotsu Kamishima, MD, PhD[1], Yoichi M Ito, PhD[6], Hiroyuki Tsutsui, MD, PhD [2], Khin Khin Tha, MD, PhD[1], Satoshi Terae, MD, PhD [1], and Hiroki Shirato, MD, PhD [1]

[1]Department of Diagnostic and Interventional Radiology, Hokkaido University Hospital [2]Department of Cardiovascular Medicine, Hokkaido University Graduate School of Medicine, [3]Philips Healthcare MR Clinical Science, [4]Advanced Medical Research Center, Iwate Medical University, [5] Department of Nuclear Medicine, Hokkaido University Hospital and [6]Hokkaido Organization for Translational Research, Hokkaido University Graduate School of Medicine

Correspondence: Noriko Oyama-Manabe, MD, PhD

Department of Diagnostic and Interventional Radiology, Hokkaido University Hospital
Kita15, Nishi 7, kita-ku, Sapporo, JAPAN 060-8638
Office: +81-11-706-5977
Fax: +81-11-706-7876
e-mail: norikooyama@med.hokudai.ac.jp

Abstract

Objectives: To investigate whether subendocardial and transmural myocardial infarction can be identified and differentiated using the peak circumferential and longitudinal strains measured by fast strain-encoding (SENC).

Methods: Nineteen patients with ischemic heart diseases underwent imaging with fast SENC and late gadolinium enhancement (LGE) MRI at 3T. Fast SENC measurements were performed in three short-axis slices (basal, mid-ventricular and apical levels) and one long-axis view (four-chamber) to assess peak longitudinal and circumferential systolic strains.

Results: All patients showed myocardial infarction with an average of 7 positive LGE segments. A total of 304 segments for longitudinal strains (LS) and 114 segments for circumferential strains (CS) could be analysed. Positive LGE segments showed lower peak CS and LS compared with the no-LGE segments ($P<0.0001$ for both). Segments with subendocardial infarction showed reduced CS and LS compared with the no-LGE segments ($P<0.0001$ for both). There was a significant difference in CS between subendocardial and transmural infarct segments ($P=0.03$), but no significant difference in LS between them ($P=0.64$).

Conclusions: Fast SENC can identify old myocardial infarction and differentiate

subendocardial from transmural infarction.

Key words: magnetic resonance imaging, myocardial infarction, gadolinium, nephrogenic systemic fibrosis, diagnosis

Introduction:

Myocardium consists of several layers, inducing inner longitudinal muscle fibres and medial circumferential muscle fibres, which serve longitudinal and circumferential strains. The complex anatomical orientation of myocardial fibres, through their contribution to myocardial short-axis and long-axis functions [1-3], may give a clue as to the transmural extent of infarction. The identification of the transmural extent of myocardial infarction (TME) is clinically important because it has implications for both management and prognosis of patients. Transmural infarcts are associated with poor prognosis and more adverse cardiac events [4]. Kim et al. [5,6] have shown that subendocardial or non-transmural infarcts (TME < 50%) are associated with functional recovery after revascularisation.

Late gadolinium enhancement (LGE) with magnetic resonance imaging (MRI) is the gold standard for identifying myocardial infarction and differentiating subendocardial infarction from transmural infarction [7-9], but it has a limitation in that it increases the risk of nephrogenic systemic fibrosis (NSF) and is therefore unsuitable for patients with renal failure [10,11]. Tagging MRI of the heart as myocardial deformation imaging provides quantitative estimation of regional myocardial function. Myocardial tagging was shown to detect myocardial viability in patients with ischaemic heart disease [12].

However, the tagging method has some disadvantages, such as limited temporal resolution and the need for sophisticated and time-consuming methods of image processing [13].

Contrary to conventional tagging, strain-encoded magnetic resonance imaging (SENC) is a technique proposed by Osman et al. [14] that uses tag surfaces that are parallel, not orthogonal, to the image plane, combined with out-of-plane phase-encoding gradients in the perpendicular section-select direction. SENC provides the objective colour-coded evaluation of circumferential and longitudinal myocardial strain and has been validated in clinical settings [15,16]. Fast SENC using a spiral acquisition enables MR data acquisition times as short as a single heartbeat [15]. The advantages of fast SENC include short acquisition time, high temporal resolution and no need for breath-holding, time-consuming post-processing, and contrast agent injection.

The purpose of this study is to investigate whether the peak circumferential and longitudinal strains can identify and differentiate between subendocardial and transmural infarction with fast SENC at 3.0 Tesla (T).

Materials and methods

We performed gadolinium-enhanced cardiac MRI at 3.0 T in 19 patients with chronic

ischaemic heart disease（mean age 61, range 43-83 years old, 79% men）. The patients' characteristics are shown in **Table 1**. The study was conducted in accordance with the institutional review board, and all study patients provided written informed consent.

Imaging protocol

The experiments were performed on a clinical 3.0 T MR whole-body system (Achieva Tx; Philips Medical System, Best, The Netherlands) equipped with a gradient system capable of a gradient strength of 42 mT/m and a slew rate of 100 mT/m/ms. A six-element cardiac phased-array coil with three anterior and three posterior elements was used.

Fast SENC

Fast SENC uses interleaved tuning and a single spiral acquisition. The low- and high-tuning frequencies are applied in an interleaved manner through the cardiac cycle [14,15]. Through this combination of localised SENC, interleaved tuning and spiral imaging, a cine sequence of SENC images can be acquired in as short as one cardiac cycle. Typical parameters were: FOV 256x256mm^2, matrix size 64x64, slice thickness 10mm, flip angle 30°, TR/TE 13/0.81 ms. The temporal resolution was 25 ms, and the number of cardiac phases (typically 18–34) was adapted accordingly to cover the entire cardiac cycle. The average MR data acquisition time for this sequence of SENC images

was one heart beat (about 1 s).

Late gadolinium enhancement

Ten minutes after an intravenous injection of Gd-DTPA (0.1 mmol/kg, Magnevist; Berlex Laboratories, Wayne, NJ, USA), an inversion-recovery (IR)-prepared, fast field echo (FFE) pulse sequence was performed to obtain a delayed-enhancement image for localisation of the infarct region in the short axis (SA) and horizontal long axis (LA). The imaging parameters were: slice thickness 5 mm; FOV 380 mm; matrix size 256 x 256 (512 x 512 reconstructed matrix); TR/TE 3.0 ms/0.96 ms; flip angle 10°; NSA 1. For each subject, we adjusted the inversion time to null the signal from the normal myocardium; the typical inversion time was 250 to 290 msec.

Evaluation of images

Fast SENC MRI was acquired in all subjects for the assessment of longitudinal strains in three SA slices of the LV (basal, mid-ventricular and apical levels), and for circumferential strains in one LA view of the LV (four-chamber). Following American Heart Association segmentation, 6 segments (septum and lateral wall at basal, mid-ventricular and apical level) in LA for circumferential (Fig. 1a) and 16 segments (6 segments each at the basal and mid-ventricular levels, and 4 segments at the apical level) in SA for longitudinal (Fig. 1c) strains were evaluated with dedicated software

(Diagnosoft MAIN version 2, Diagnosoft, Palo Alto, CA, USA). The analysis was performed in the mid-layer of the myocardium. One click at each segment provided a time strain curve during one cardiac cycle (Fig. 1b and 1d), after which we could obtain the peak strain values for each longitudinal and circumferential strain.

Examples of time courses of circumferential and longitudinal strains in a cardiac cycle in cases with normal (Fig. 1) and myocardial infarction (Figs. 2 and 3) are shown.

Segments were grouped into three categories (trans-mural extent: TME 0% = no myocardial infarction; subendocardial infarction TME 1% to 50%; transmural infarction > 50% of wall thickness) on LGE images. This cut-off value of > 50% was previously shown to a have a negative predictive value for viability of up to 92% [6]. Fast SENC analysis and LGE were independently assessed by a reader (N.O-M., 13 years of experience with cardiac MR imaging) who was blinded to the patient data.

Statistical analysis

All data are expressed as mean values ± standard deviation. Differences in peak circumferential and longitudinal strains among different TME groups were assessed by analysis of variance with Bonferroni's post-hoc analysis using statistical software (JMP version 8, SAS Institute, Cary, NC, USA). The paired t-test was used to compare longitudinal and circumferential strains. Receiver operating characteristics (ROC) curve

analyses were performed to determine the cut-off points of longitudinal and circumferential strains as predictors of the presence of myocardial infarction and to calculate the area under the curve (AUC), sensitivity and specificity. A value of $P < 0.05$ was considered statistically significant.

Results

Feasibility of fast SENC and LGE MRI

For all patients, fast SENC sequences were done successfully within one heart beat without breath holding. We were able to analyse fast SENC in the entire of 304 segments for longitudinal strain and 114 segments for circumferential strain from all 19 patients. All 19 patients with suspected ischemic heart disease showed positive LGE segments. Seventy-seven segments had subendocardial infarcts with TME 1% to 50%, and 60 had transmural infarcts (TME >50%) in short-axis slices at three levels (basal, mid-ventricular and apical).

Myocardial strains in subendocardial and transmural infarcted segments

Positive LGE segments had lower peak circumferential strain than segments without LGE ($P<0.0001$) (Figs. 2, 4). Subendocardial infarct segments showed significantly lower peak strain than the no LGE segments ($P<0.0001$), while there was also a significant difference between subendocardial and transmural infarct segments ($P=0.03$) (Fig. 5).

Positive LGE segments also had lower peak longitudinal strain than the no LGE segments ($P<0.0001$) (Figs. 3, 4). Subendocardial infarct segments showed lower peak strain than the no LGE segments ($P< 0.0001$), while there was no significant difference

between subendocardial and transmural infarct segments (P=0.64) (Fig. 6). The peak longitudinal strain (-10.0%) was significantly reduced compared with relatively preserved circumferential strain (-13.4%) (P=0.003) in subendocardial infarcts, while there was no significant difference between them in the transmural and no-infarction segments.

According to our ROC analysis, a cut-off circumferential strain value of -14.8% has sensitivity of 81% and specificity of 74% for the detection of infarcted segments (AUC, 0.82), while a cut-off longitudinal strain value of -12.3% has sensitivity of 69% and specificity of 76% for the detection of infarcted segments (AUC, 0.76). Using an average of peak longitudinal and circumferential strains improved sensitivity to 88% and specificity to 72% (AUC, 0.88) for the detection of infarcted segments (Fig. 7).

Peak circumferential strain was better for differentiating subendocardial from transmural infarcted myocardium, with sensitivity of 95% and specificity of 47% (AUC, 0.71, P=0.01) at a cut-off value of -14.4%, while the peak longitudinal strain had lower sensitivity and specificity (80% and 33%, respectively) (AUC, 0.55, P=0.33) at a cut-off of -10.1%.

Discussion

The present study demonstrated that (1) fast SENC could provide objective and rapid assessment of myocardial function in patients with myocardial infarction and (2) it could distinguish non-infarcted, subendocardial and transmural infarcted tissues at 3.0 T.

The differential effects between subendocardial and transmural infarctions on longitudinal and circumferential strains in this study may be a consequence of the helical wrapping of cardiac fibres into three different anatomical layers [1-3]. The innermost subendocardial layer of fibres has an oblique orientation in the longitudinal direction, while the middle layer is wrapped circumferentially (Fig. 8). Myocardial infarction begins from the inner layer which provides longitudinal strain. Differentiation of subendocardial from transmural infarction is clinically important because it is associated with better prognosis and a greater likelihood of benefit from revascularisation [5,6]. Our results showed that, in subendocardial infarction, the peak circumferential strain was relatively preserved but longitudinal strain was reduced. On the other hand, in transmural infarction, both the peak longitudinal and circumferential strains were significantly reduced. These findings are consistent with previous studies using strain-rate imaging with 2D echocardiography [17] and MRI tagging [18].

Compared with the peak longitudinal strain, the peak circumferential strain had higher sensitivity and specificity with which to differentiate between subendocardial and transmural infarctions and had slightly higher sensitivity with which to detect any kinds of infarcted segments. The peak circumferential strain may allow the detection of old myocardial infarction and differentiation of its transmurality.

One advantage of the fast SENC technique is the simple observer-independent post-processing step to measure strains with the dedicated software. In addition, the data acquisition time is far shorter than for echocardiography and MRI tagging. Moreover, we analysed all data sets for both strains at 3.0 T (the unsuccessful ratio was 0%), while Neizel et al. reported an unsuccessful ratio of about 3.5% at 1.5 T [13]. This might be because 3.0 T provides significant improvement in the signal-to-noise ratio (SNR) and the longer T1 compared with 1.5 T provides reduced fading of the tags [16].

Late gadolinium enhancement with MRI is the gold standard for identifying myocardial infarction and for differentiating subendocardial from transmural infarction [7-9]. However, it must be used with caution in patients with renal failure because it increases the risk of NSF [10,11]. On the other hand, no contrast agent is required for SENC imaging. Therefore, fast SENC is more advantageous than LGE for an assessment of the extent of myocardial infarction, especially because the administration

of gadolinium contrast medium is not required in patients with advanced renal dysfunction and a high risk of NSF.

This study is an initial study using the fast SENC MRI technique and has been validated in only a limited number of patients at a single institution. However, these early results are promising and warrant the continuation and expansion of the current study. A multi-centre trial would be advisable for further clinical validation.

Conclusion

Fast SENC MRI is feasible for use in a clinical environment. The acquisition time and the post-processing time are short. This may be a promising technique for identifying old myocardial infarction and to further differentiate subendocardial from transmural infarction without the need for contrast agents.

References

1. Greenbaum RA, Ho SY, Gibson DG, Becker AE, Anderson R (1981) Left ventricular fibre architecture in man. Br Heart J 45:248-263.
2. Torrent-Guasp F, Buckberg GD, Clemente C, Cox JL, Coghlan HC, Gharib M (2001) The structure and function of the helical heart and its buttress wrapping. I. The normal macroscopic structure of the heart. Semin Thorac Cardiovasc Surg 13:301-319.
3. Waldman LK, Fung YC, Covell JW (1985) Transmural myocardial deformation in the canine left ventricle. Normal in vivo three-dimensional finite strains. Circ Res 57:152-163.
4. Thanavaro S, Krone RJ, Kleiger RE, Province MA, Miller JP, deMello VR, Oliver GC (1980) In-hospital prognosis of patients with first nontransmural and transmural infarctions. Circulation 61:29-33.
5. Kim RJ, Hillenbrand HB, Judd RM (2000) Evaluation of myocardial viability by MRI. Herz 25:417-430.
6. Kim RJ, Wu E, Rafael A, Chen EL, Parker MA, Simonetti O, Klocke FJ, Bonow RO, Judd RM (2000) The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 343:1445-1453.
7. Fieno DS, Kim RJ, Chen EL, Lomasney JW, Klocke FJ, Judd RM (2000) Contrast-enhanced magnetic resonance imaging of myocardium at risk: distinction between reversible and irreversible injury throughout infarct healing. J Am Coll Cardiol 36:1985-1991.
8. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM (1999) Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 100:1992-2002.
9. Shan K, Constantine G, Sivananthan M, Flamm SD (2004) Role of cardiac magnetic resonance imaging in the assessment of myocardial viability. Circulation 109:1328-1334.
10. Kuo PH (2008) Gadolinium-containing MRI contrast agents: important variations on a theme for NSF. J Am Coll Radiol 5:29-35.
11. Thomsen HS (2007) ESUR guideline: Gadolinium-based contrast media and nephrogenic systemic fibrosis. Eur Radiol 17:2692-2696
12. Garot J, Lima JA, Gerber BL, Sampath S, Wu KC, Bluemke DA, Prince JL, Osman NF (2004) Spatially resolved imaging of myocardial function with strain-encoded MR: comparison with delayed contrast-enhanced MR imaging after myocardial infarction. Radiology 233:596–602.

13. Neizel M, Lossnitzer D, Korosoglou G, Schaufele T, Lewien A, Steen H, Katus HA, Osman NF, Giannitsis E (2009) Strain-encoded Magnetic Resonance Imaging to evaluate regional heterogeneity of myocardial strain in healthy volunteers: comparison with conventional tagging. J Magn Reson Imaging 29:99-105
14. Osman NF, Sampath S, Atalar E, Prince JL (2001) Imaging longitudinal cardiac strain on short-axis images using strain-encoded MRI. Magn Reson Med 46:324-334
15. Pan L, Stuber M, Kraitchman DL, Fritzges DL, Gilson WD, Osman NF (2006) Real-time imaging of regional myocardial function using fast-SENC. Magn Reson Med 55:386-395.
16. Korosoglou G, Youssef AA, Bilchick KC, Ibrahim ES, Lardo AC, Lai S, Osman NF (2008) Real-time fast strain-encoded magnetic resonance imaging to evaluate regional myocardial function at 3.0 Tesla: comparison to conventional tagging. J Magn Reson Imaging 27:1012-1018
17. Chan J, Hanekom L, Wong C, Leano R, Cho GY, Marwick TH (2006) Differentiation of subendocardial and transmural infarction using two-dimensional strain rate imaging to assess short-axis and long-axis myocardial function. J Am Coll Cardiol 48:2026-2033.
18. Moore CC, Lugo-Olivieri CH, McVeigh ER, Zerhouni EA (2000) Three-dimensional systolic strain patterns in the normal human left ventricle: characterization with tagged MR imaging. Radiology 214:453-466.

Patient characteristics (N=19)	
Age(yrs)	61±10
Male	15(79%)
MRI characteristics of Patients	
Number of segments with LGE per patient	7.3 segments
Endo-diastolic volume (ml)	179±74
Endo-diastolic volume indexed (ml/m^2)	106±45
Endo-systolic volume (ml)	112±78
Endo-systolic volume indexed (ml/m^2)	67±46
Ejection fraction (%)	43±21
Left ventricular mass (g)	134±49
Left ventricular mass index (g/m^2)	79±26

Table 1 Patient characteristics

LGE: late gadolinium enhancement

Fig.1 Demonstrable time course of longitudinal and circumferential strains during one cardiac cycle obtained from a patient with normal left ventricular function without late gadolinium enhancement.

Fig. 1a The left ventricular horizontal long-axis slice for the measurement of circumferential strain. Fig. 1b The time courses of circumferential strains showed homogeneous peak longitudinal strains in all segments. Fig. 1c The short-axis slice for the measurement of longitudinal strains at six points according to American Heart Association segmentation. Fig. 1d The time courses of longitudinal strains showed homogeneous peak longitudinal strains in all segments

Fig. 2 Demonstrable time course of circumferential strains during one cardiac cycle obtained from a 65-year-old male patient with old myocardial infarction.

Fig 2a: Left ventricular horizontal long-axis slice with late gadolinium enhancement

The basal lateral wall (red arrow) showed the transmural infarction while the apical wall showed no enhancement (blue arrow). Fig. 2b The time courses of circumferential strains at infarcted (in red) and remote segments (in blue)

The basal lateral wall (infarcted segment) showed reduced peak circumferential strain compared with the apex (remote segment) without late gadolinium enhancement.

Fig. 3 Demonstrable time course of longitudinal strains during one cardiac cycle obtained from a 60-year-old male patient with old myocardial infarction.

Fig. 3a Left ventricular short-axis slice at the basal level with late gadolinium enhancement

The lateral wall showed the transmural infarction.

Fig. 3b The time courses of longitudinal strains at infarcted (in red) and remote segments (in blue)

The lateral wall (infarcted segment) shows reduced peak longitudinal strain compared with the septum (remote segment).

Fig. 4 Comparisons of the peak circumferential and longitudinal strains between without and with LGE groups

Fig. 5 Peak longitudinal strains of three different groups with no LGE (n=167), subendocardial MI (n=77) and transmural MI (n=60) segments.

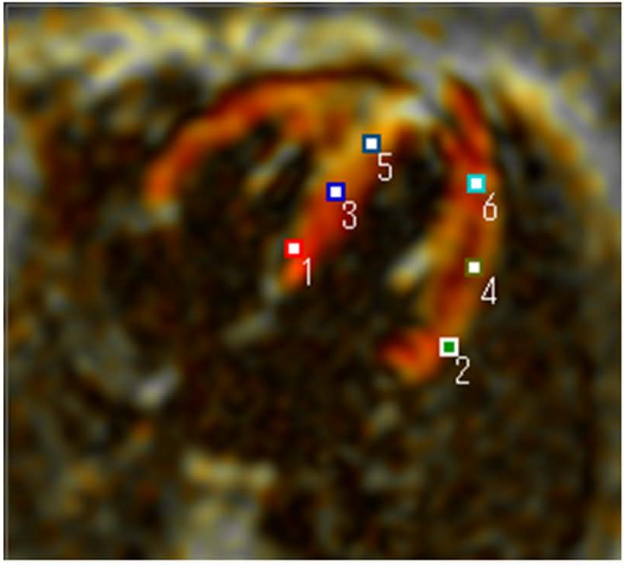
LGE: late gadolinium enhancement, MI: myocardial infarction

Fig. 6 Peak circumferential strains of three different groups

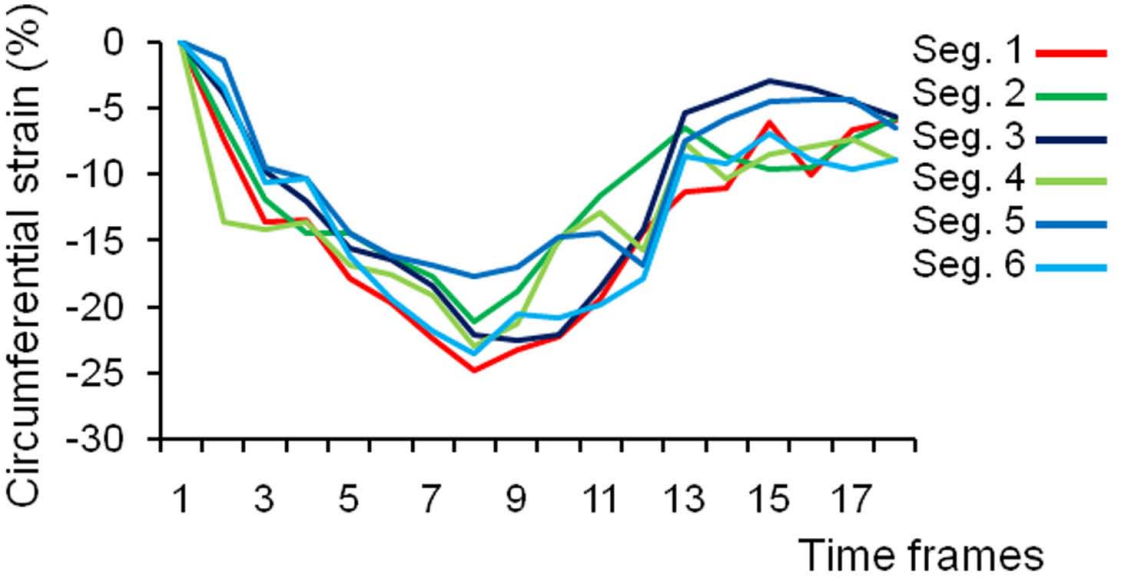
Fig. 7 Receiver operating characteristics curve to detect an infarcted segment using an average of the peak longitudinal and circumferential strains

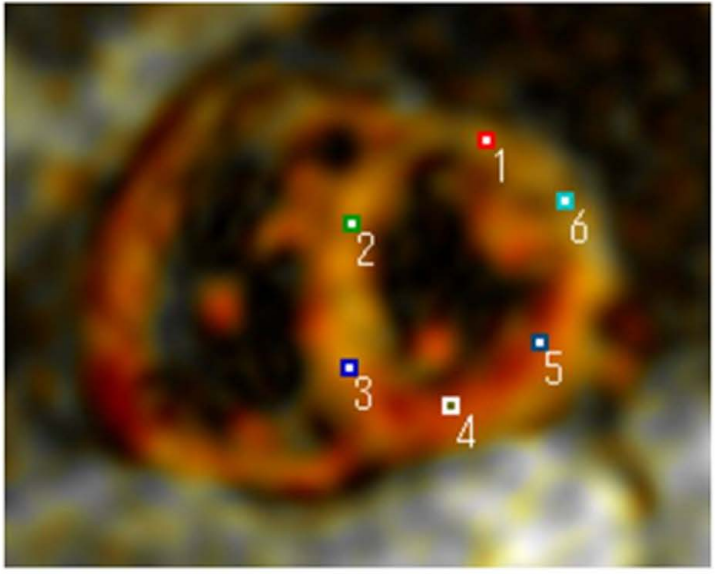
Fig. 8 Schema for myocardial fibers in different directions

Innermost subendocardial layer of fibres give longitudinal strains (black arrow), while the middle layer wrapped circumferentially give circumferential strains (white arrow).

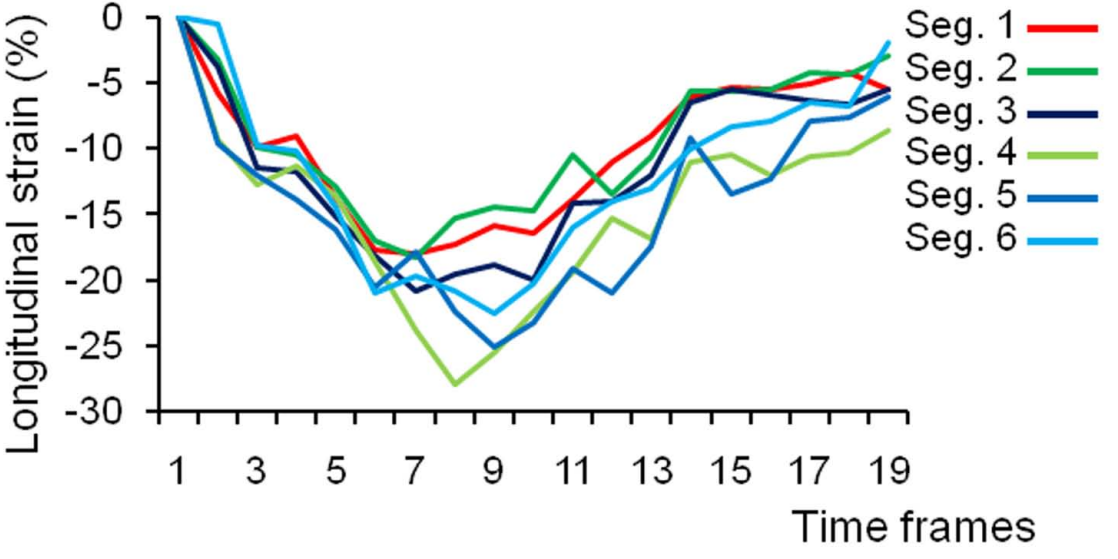


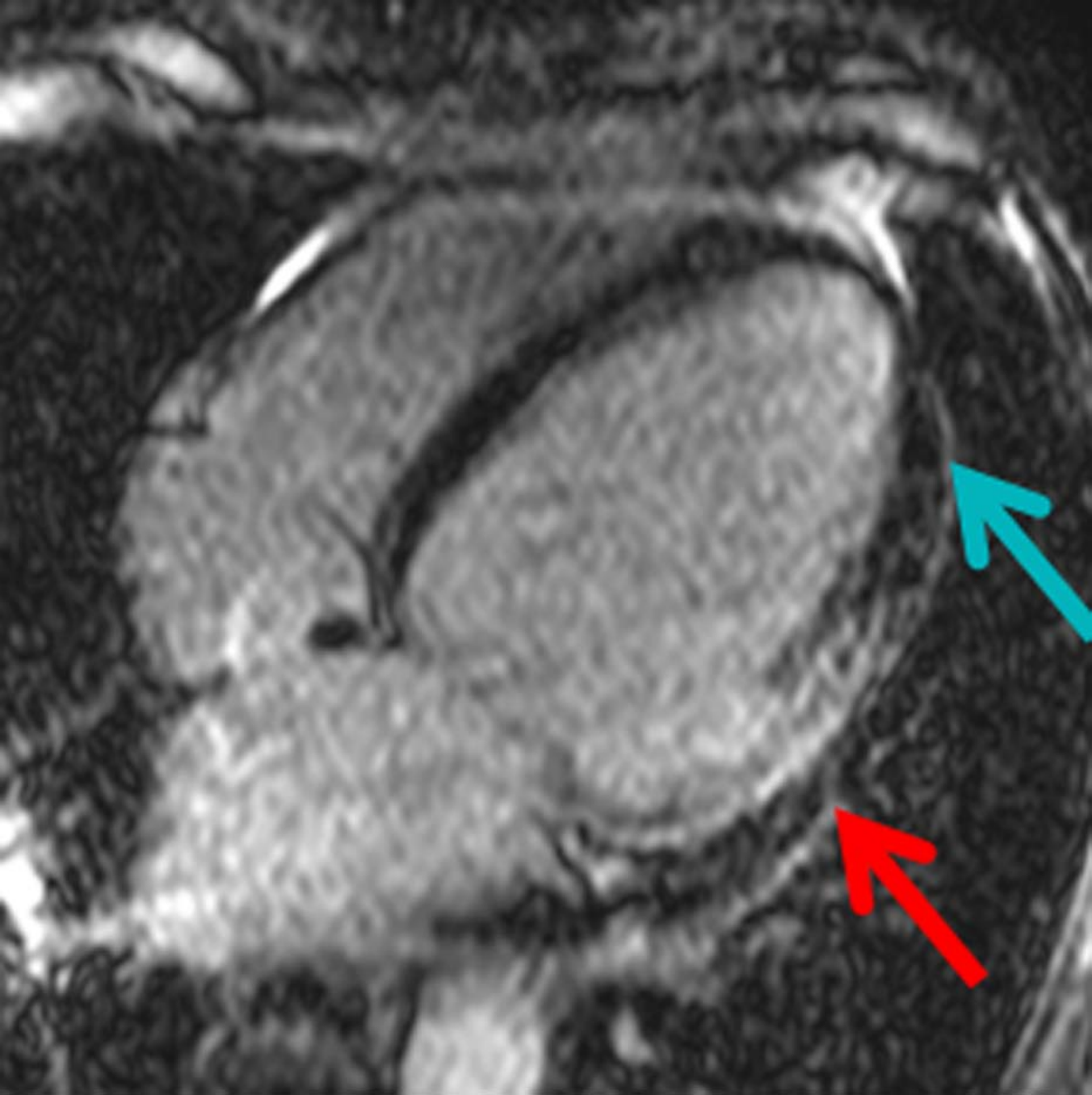
Seg. 1 Basal septum
Seg. 2 Basal lateral
Seg. 3 Mid septum
Seg. 4 Mid lateral
Seg. 5 Apical septum
Seg. 6 Apical lateral

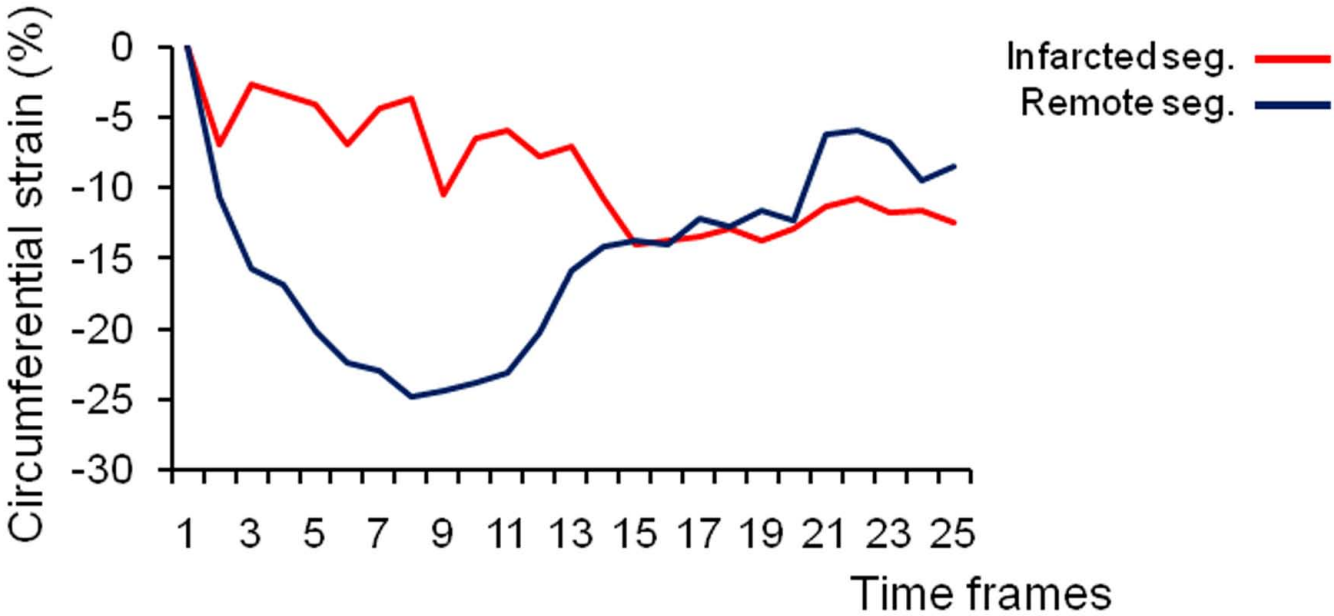

Circumferential strain (%)
0
-5
-10
-15
-20
-25
-30
1
3
5
7
9
11
13
15
17
Time frames
Seg. 1
Seg. 2
Seg. 3
Seg. 4
Seg. 5
Seg. 6

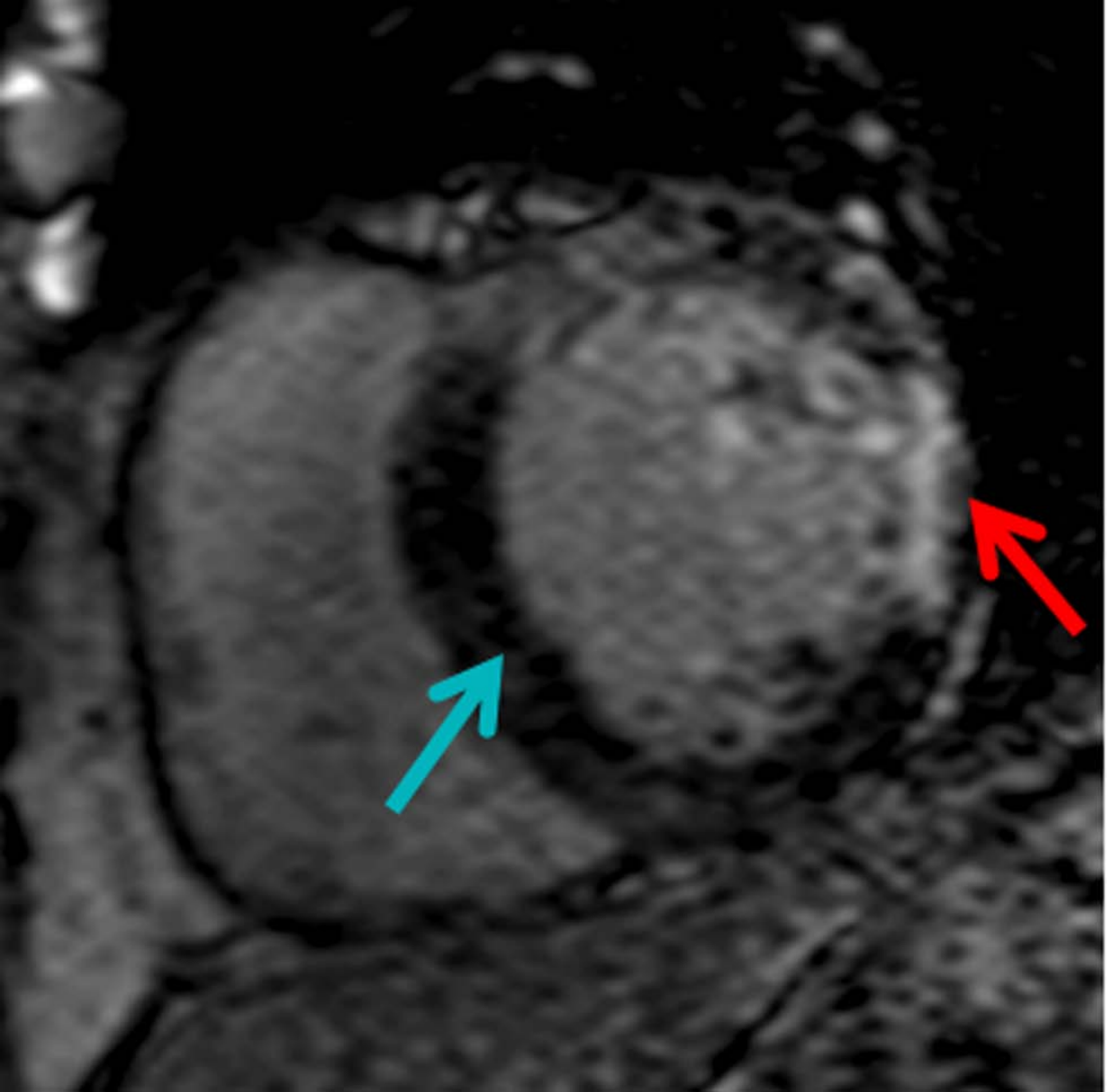


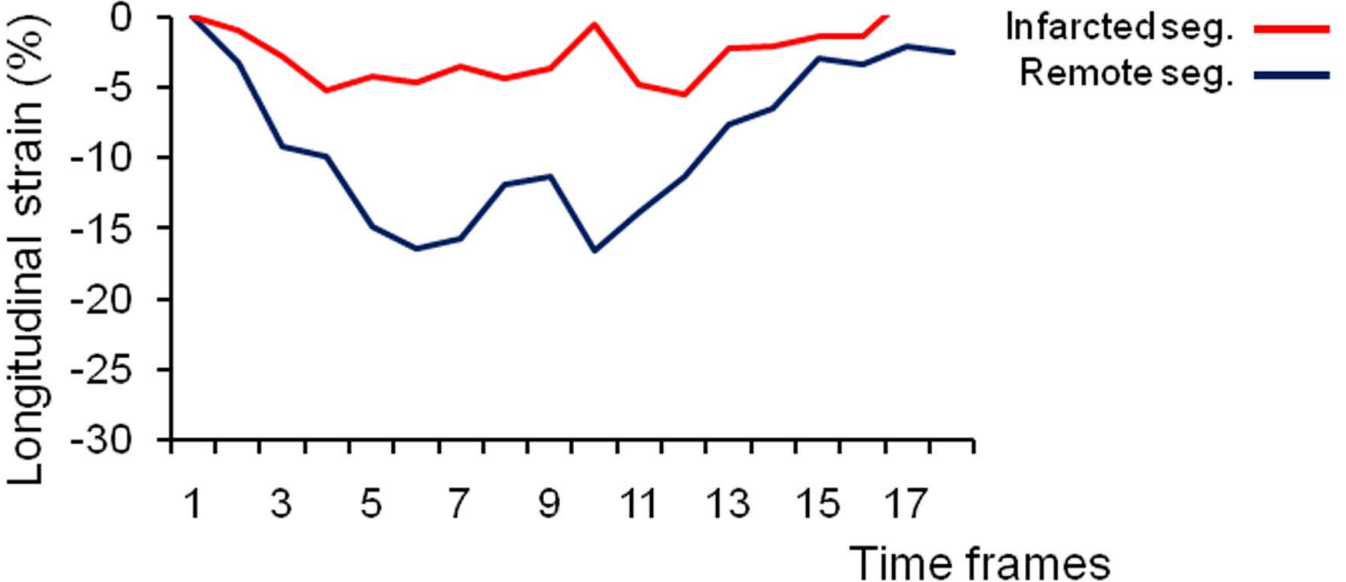
Seg. 1 anterior
Seg. 2 antero-septum
Seg. 3 infero-septum
Seg. 4 inferior
Seg. 5 infero-lateral
Seg. 6 antero-lateral

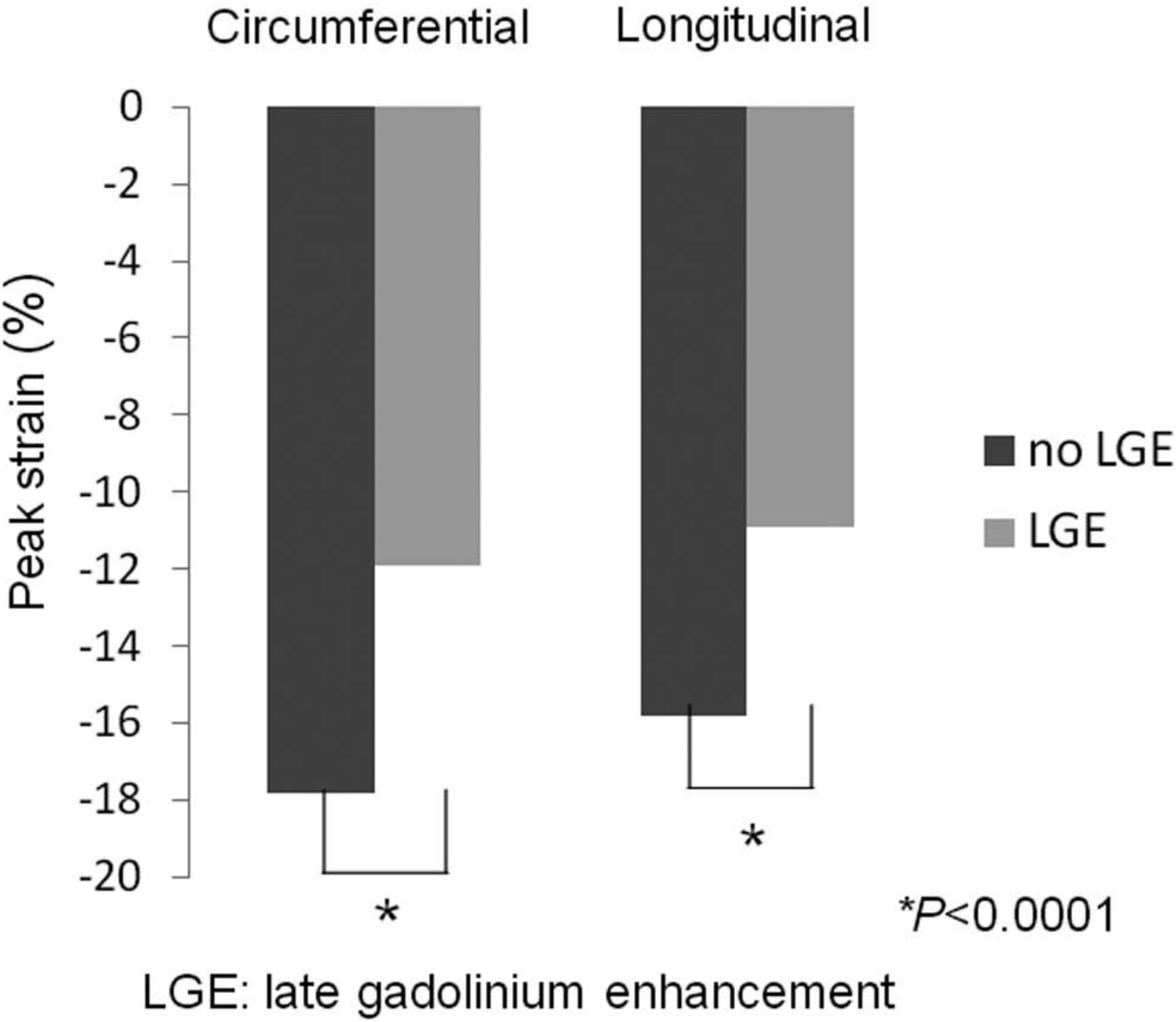

Longitudinal strain (%)
0
-5
-10
-15
-20
-25
-30
1
3
5
7
9
11
13
15
17
19
Time frames
Seg. 1
Seg. 2
Seg. 3
Seg. 4
Seg. 5
Seg. 6



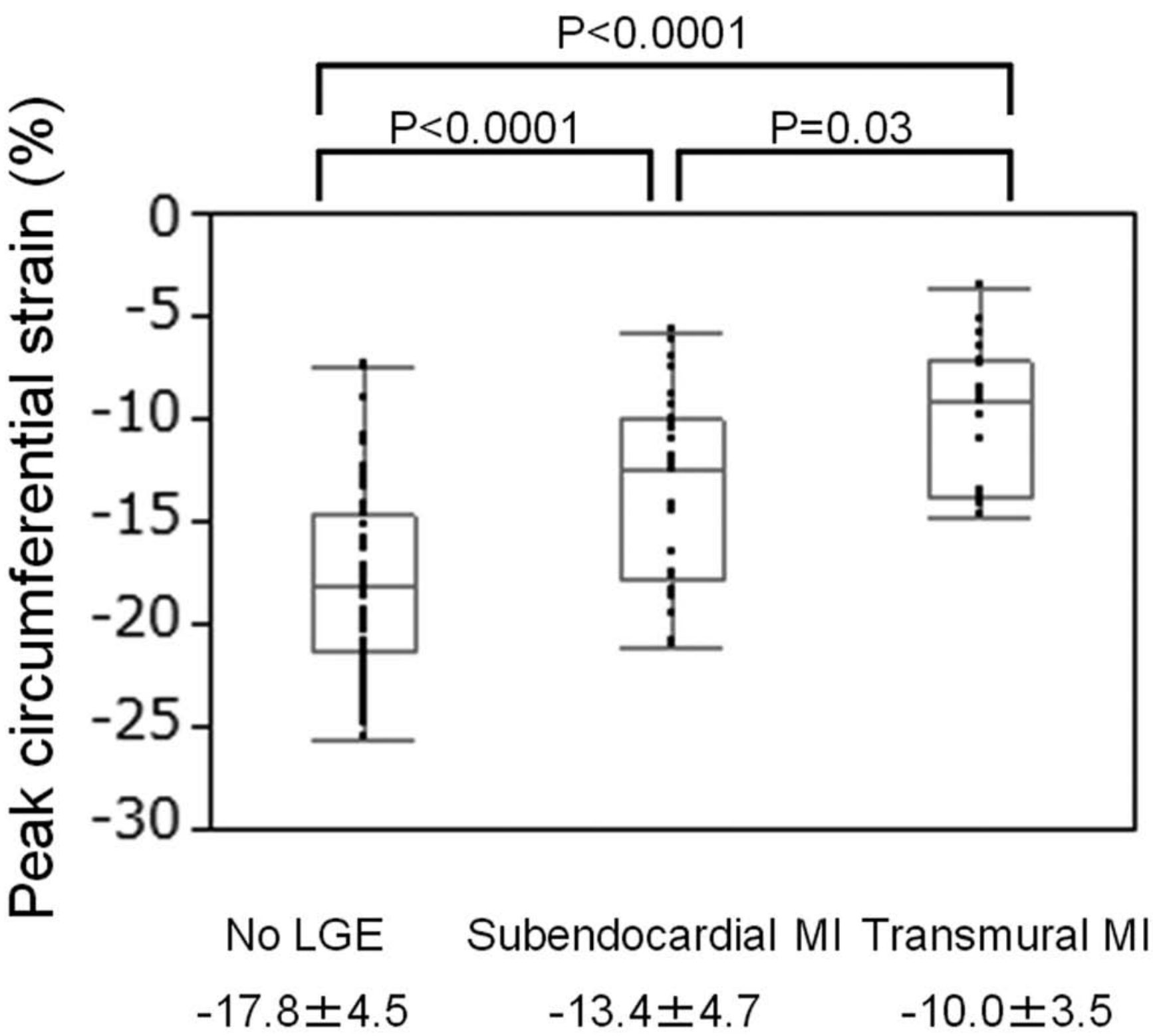

Circumferential strain (%)
0
-5
-10
-15
-20
-25
-30
1
3
5
7
9
11
13
15
17
19
21
23
25
Time frames
Infarcted seg.
Remote seg.

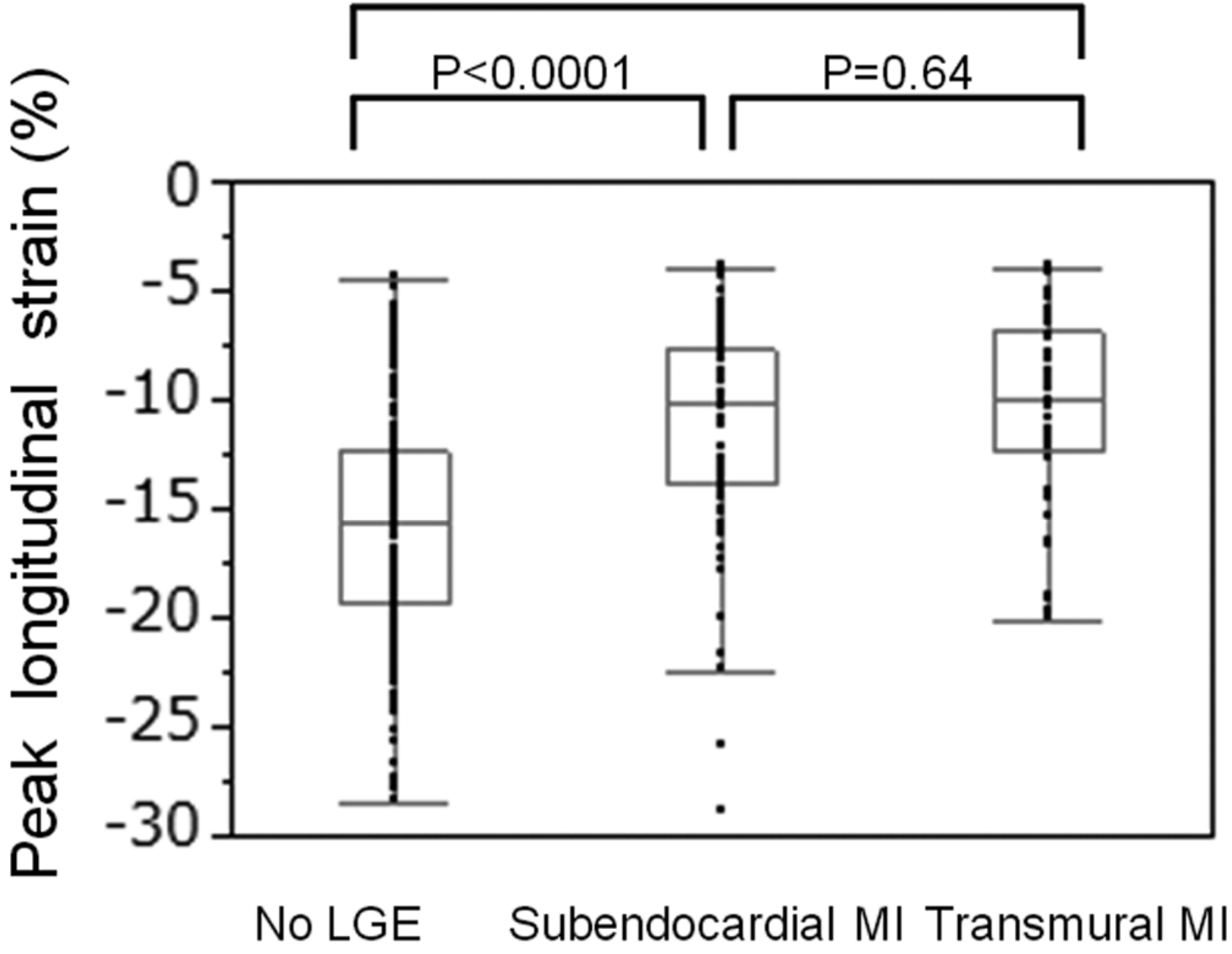


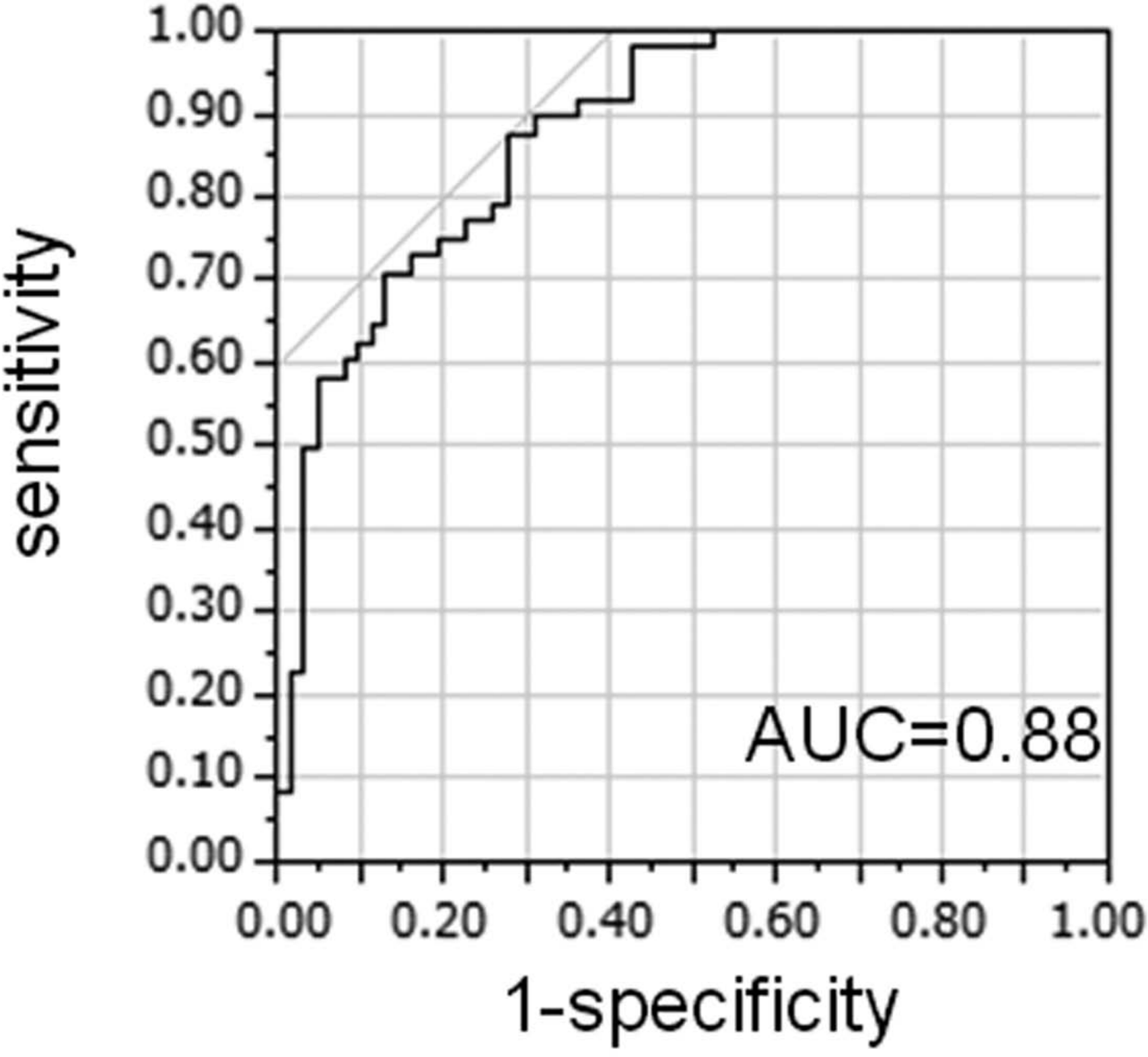

Infarcted seg.
Remote seg.
Longitudinal strain (%)
0
-5
-10
-15
-20
-25
-30
1
3
5
7
9
11
13
15
17
Time frames

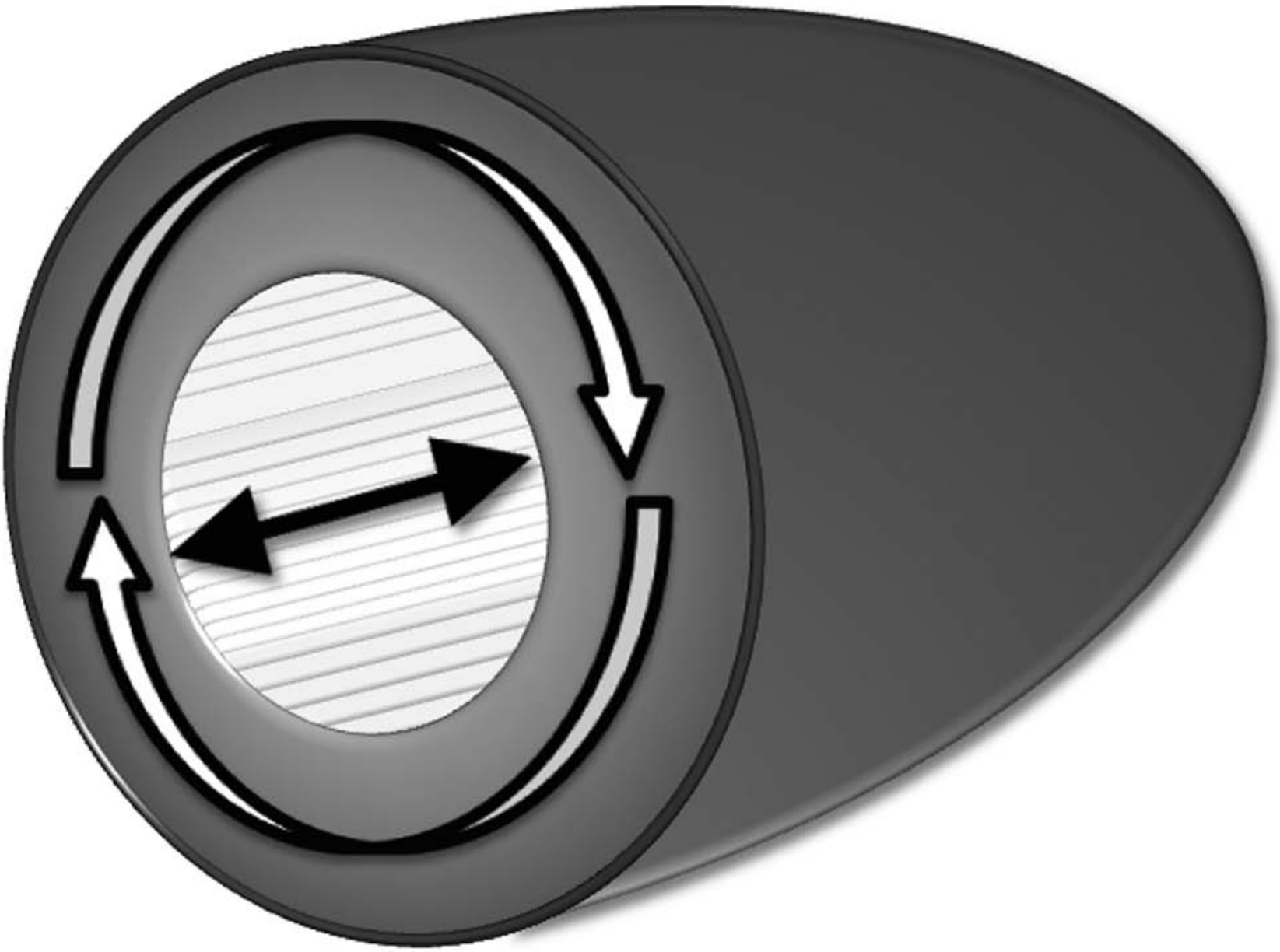


LGE: late gadolinium enhancement


P<0.0001
P<0.0001
P=0.03
Peak circumferential strain (%)
0
-5
-10
-15
-20
-25
-30
No LGE
Subendocardial MI
Transmural MI
-17.8±4.5
-13.4±4.7
-10.0±3.5


P<0.0001
P=0.64
Peak longitudinal strain (%)
0
-5
-10
-15
-20
-25
-30
No LGE
Subendocardial MI
Transmural MI


1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
sensitivity
0.00
0.20
0.40
0.60
0.80
1.00
1-specificity
AUC=0.88



Patient characteristics (N=19)	
Age(yrs)	61±10
Male	15(79%)

MRI characteristics of Patients	
Number of segments with LGE per patient	7.3 segments
Endo-diastolic volume (ml)	179±74
Endo-diastolic volume indexed (ml/m^2)	106±45
Endo-systolic volume (ml)	112±78
Endo-systolic volume indexed (ml/m^2)	67±46
Ejection fraction (%)	43±21
Left ventricular mass (g)	134±49
Left ventricular mass index (g/m^2)	79±26