Author’s response to reviews

Title: Strain-encoded cardiac magnetic resonance imaging: a new approach for fast estimation of left ventricular function

Authors:

Tomas Lapinskas (lapinskas@dhzb.de)
Victoria Zieschang (zieschang@dhzb.de)
Jennifer Erley (jennifer.erley@charite.de)
Lukas Stoiber (stoiber@dhzb.de)
Christian Stehning (christian.stehning@philips.com)
Bernhard Schnackenburg (bernhard.schnackenburg@philips.com)
Rolf Gebker (gebker@dhzb.de)
Amit Patel (apatel2@medicine.bsd.uchicago.edu)
Keigo Kawaji (kkawaji@medicine.bsd.chicago.edu)
Henning Steen (henning.steen@gmx.de)
Remigijus Zaliunas (remigijus.zaliunas@kaunoklinikos.lt)
Sören Backhaus (soeren.backhaus@med.uni-goettingen.de)
Andreas Schuster (andreas.schuster@med.uni-goettingen.de)
Marcus Makowski (marcus.makowski@charite.de)
Sorin Giusca (soringiusca@gmail.com)
Grigorious Korosoglou (gkorosoglou@hotmail.com)
Burkert Pieske (pieske@dhzb.de)
Sebastian Kelle (kelle@DHZB.de)

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Author’s response to reviews:
Answers to Reviewer #1

1. The authors included 35 subjects in their study including 12 healthy volunteers. But, they did not mention about their baseline characteristics. It would be better to insert a baseline characteristics table in their manuscript.

We are very grateful to the reviewer for the comment. We do agree that baseline characteristics are important and may help readers to understand the study subjects better. To make the text more reader friendly we have provided this information in an additional table.

“Table 1. Study participants characteristics”. (page 19)

We also added additional text in the Results section:

Study participants with suspected or confirmed CAD were significantly older than healthy volunteers (61.37 ± 10.93 y vs. 28.67 ± 4.89 y, p < 0.001). In CAD group there were more male subjects (p < 0.001). Healthy volunteers had significantly lower body surface area (p = 0.026) and body mass index (p < 0.001). (page 9, line 3-7)

2. Is there any difference between control subjects and patients with known or suspected coronary artery disease (CAD) in the measurement of LV volumes? (Patients with known CAD may have possibilities of taking medications which can reduce heart rate.)?

We performed additional statistical analysis which demonstrated that there is no significant difference in LV volumes estimated at end-diastolic and end-systolic LV phases. We have added this to the table together with demographics of study participants.

“Table 1. Study participants’ characteristics” (page 19)
We have also added additional text in the Results section:

LVEDV and LVESV were similar in both, whereas LVSV and LVEF were significantly lower in CAD patients (LVSV: 80.48 ± 17.81 ml vs. 97.00 ± 18.96 ml, p = 0.021; LVEF: 52.09 ± 11.29 % vs. 59.75 ± 1.36 %, p = 0.034). Subjects with CAD had significantly higher LVEDM than healthy volunteers (143.96 ± 30.61 g vs. 82.00 ± 25.82 g, p < 0.001). Table 1 summarizes the demographic and functional parameters of the study population. (page 9, line 7-12).

Answers to Reviewer #2

We sincerely appreciate the interest in our work, as well as the very insightful review of our manuscript. We agree with the reviewer that several modifications are necessary to substantially improve our manuscript.

1. The authors describe a significant reduction in time for the analysis compared to cine imaging; a proper comparison of time for acquisition and image analysis should be added.

We agree with the reviewer that image acquisition and post-processing should be described in more detail; therefore we have included additional text in the Results section:

Data acquisition and analysis time

The total scan time spent to acquire CMR images using fast-SENC was 15 seconds as only six heart beats without any breath-hold are necessary to derive 3 long-axis and 3 short-axis slices. In contrast, conventional cine imaging using bSSFP sequence in a patient with heart rate of 75 beats per minute lasted approximately 45–60 seconds per slice (30 phases per cardiac cycle including breathing commands and recovery period before the next breath-hold and following slice acquisition could be started). To acquire 3 long-axis and 3 short-axis images the same process was repeated 6 times (for every slice) with a total scan duration of 270–360 seconds. (page 10, line 16-24; page 11, line 1-4)
The time spent for data post-processing using automated contour detection algorithm or machine learning software for fast-SENC (90 seconds) or bSSFP (120 seconds) was comparable. However, total time required for data acquisition and analysis was shorter for fast-SENC technique.

2. As the LV ejection fraction and mass computations require a manual contouring of LV, inter- and intra-observer variability should be assessed.

We recently demonstrated that fast-SENC is a highly reproducible technique to assess LV strain and have added this with a reference to the Discussion section:

Recently we demonstrated that fast-SENC is highly reproducible method for assessing LV strain [8]. (page 12, line 17-18).

We performed intraobserver and interobserver reproducibility analysis for LVEF and LVEDM and the following text is now included in the manuscript:

In Methods section:

Intraobserver and interobserver reproducibility for LVEF and LVEDM was quantified using intraclass correlation coefficient (ICC) and Bland-Altman analysis. Agreement was considered excellent for ICC <0.74, good for ICC 0.60–0.74, fair for ICC 0.40–0.59, and poor for ICC <0.40. (page 7, line 23-24 and page 8, line 1-2).
In Results section:

Intraobserver and interobserver reproducibility

There was excellent intraobserver agreement for LVEF: ICC 0.976 (0.918–0.992) and LVEDM: ICC 0.983 (0.949–0.994) derived using fast-SENC technique. The analysis of in-terobserver reproducibility also demonstrated excellent agreement, with slightly larger limits of agreement: ICC 0.895 (0.654–0.966) for LVEF and ICC 0.846 (0.157–0.958) for LVEDM. Figure 4 demonstrates Bland-Altman analysis of intraobserver and interobserver agreement for LVEF and LVEDM. (page 10, line 10-15).

In Discussion section:

In this study we found that intraobserver and interobserver agreement for LVEF and LVEDM measurements derived using fast-SENC technique is also excellent. (page 12, line 18-20).

In Conclusion section:

LVEF and LVEDM measurements derived using fast-SENC technique are highly re-producible. (page 13, line 5-6).

Moreover, we have created an additional Figure to demonstrate Bland-Altman analysis for intraobserver and interobserver reproducibility for LVEF and LVEDM.

Figure 4. Bland-Altman analysis demonstrates the intraobserver (A and B) and in-terobserver (C and D) reproducibility of fast-SENC technique for LVEF (A and C) and LVEDM (B and D). The middle dashed line is the mean of difference of measures. The upper and lower dotted lines are 1.96 standard deviation. LVEF = LV ejection fraction; LVEDM = LV end-diastolic mass. (page 17, line 21-24).

3. 23 of the patients enrolled are described as "with known or suspected coronary artery disease": is that diagnosis confirmed? Is there any kind of segmental kinesis analysis?
All patients with suspected or known coronary artery disease underwent conventional coronary angiography. To make it more evident for reader we added additional sentence in the Methods section:

The coronary artery disease (CAD) was confirmed by previous quantitative coronary angiography. (page 6, line 4-5).

We also performed additional analysis of regional myocardial deformation and have added additional text in the following sections:

In Methods:

The LV longitudinal and circumferential strain was extracted from three LV short-axis and three LV long-axis fast-SENC images respectively. The global strain values were calculated by averaging measurements obtained from 16 segments for global longitudinal strain (GLS) and 18 segments for global circumferential strain (GCS). (page 7, line 13-16).

In Results:

Myocardial deformation analysis

As described in the methods, analysis of regional myocardial deformation was performed using three long-axis fast-SENC images (for GCS) and three short-axis fast-SENC images (for GLS). LV GLS and GCS were significantly lower in CAD patients compared with healthy volunteers (GLS: \(-17.29 \pm 3.17\) % vs. \(-19.34 \pm 1.28\), p = 0.034; GCS: \(-17.67 \pm 2.63 \pm -20.21 \pm 1.48\) %, p = 0.001) (Table 1). (page 9, line 13-18).