Author's response to reviews

**Title:** Functional measurements based on feature tracking of cine magnetic resonance images identify left ventricular segments with myocardial scar

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**Author's response to reviews:** see over
**Title:** Functional measurements based on feature tracking of cine magnetic resonance images identify left ventricular segments with myocardial scar

**Reviewer:** Rosa Sicari

This is an interesting and well conducted study, the methodology is appropriate and the methodology is sound. There are only minor issues that authors should address:

1. They state, and address in the discussion section of the manuscript that, restenosis was excluded only on clinical grounds. This may be a drawback of the study, since asymptomatic patients may have restenosis. Please address.

   -A sentence was added in the section on Limitations of the study

2. It would be interesting to have a diagnostic algorithm proposed by authors on the use of different techniques to assess the extent of necrotic tissue after an AMI. Should Doppler techniques be discarded?

   -A paragraph discussing this issue was inserted on page 15, line 10.

3. The clinical implications of the present results should be clearly stated.

   -A sentence was added on page 13, line 10

4. A statement on cost-effectiveness analysis in the use of CMR should be made.

   -A sentence added page 15, line 16

**Reviewer 2:** Pier Giorgio Masci

This paper by Maret E at Al evaluates the utility of a relative new tool (feature tracking) in analyzing left ventricular regional function in patients with anterior myocardial infarction. The authors investigate a interesting approach to derive myocardial deformation and velocity parameters in radial and longitudinal directions using the cine MR images and echo derived software. The authors found that the so obtained parameters have good accuracy in detecting the infarcted myocardium as compared to the in-vivo reference standard, i.e. the delayed enhancement MR imaging. This approach also yields good inter-and inter-observer reproducibility, and seems to be promising representing an alternative to the time consuming tagged MR imaging by HARP. However, several considerations should be addressed by the authors:

**Major Compulsory Revision:**

1)Page 6, Methods section, Study population paragraph: inclusion criteria are confusing, please redefine this section. For example the authors stated that the inclusion in the study was based upon the presence or absence of extensive myocardial scar in myocardium in LAD perfusion territory. However, in the non scar group 7 patients had the culprit lesion in LAD/diagonal system.
-New wording: page 6 line 12: i.e. some patients did not develop chronic scar despite presenting with unequivocal signs of STEMI and line 17: “… the lesion treated with PCI was within the LAD/diagonal system in 7”

2) Page 7-8, Methods section, paragraph Left ventricular size and function: in a separate paragraph, please provide detailed information of the software used for the analysis and pertinent references

- The following information has been added to the text: Philips ViewForum R6.3 Dicom conformance statement, http://www.medical.philips.com/connectivity. For Diogenes MRI, related information regarding the echocardiographic version of the software can be found at http://www.tomtec.de/end_users/2d_echo/cardiac_performance_analysisc.html.

3) Page 8, Methods section, Infarct size paragraph: why infarct area was determined using only 3 long views?

- The infarct area and volume was determined in short axis views, page 8 line 9.

The extent of necrosis/fibrosis could not have been comprised in the 3 long-axis views used for the analysis. It is not clear whether infarct transmurality was measured using long-axis or short-axis images.

- The transmurality was determined on apical views to avoid misregistration. They were acquired from cut planes identical to the cine images which were used for performing deformation measurements. To clarify, “segmental” was added on page 8 line 10: Infarct segmental scar area was determined in 3 apical views.

The, infarct transmurality should have been determined in short axis orientation.

- We maintain that it is not obvious that transmurality is better determined in shortaxis slices when a direct comparison with functional measures is planned. The scar in the shortaxis may not correspond to where motion is determined in the apical cine image. Then it is better to determine scar transmurality in views that are going to be used for the functional measurements, i.e. the apical views. We prefer transmurality from apical sections even if the infarct size has been determined from a stack of shortaxis cut planes.

Please specify better how the authors define the adjacent and remote regions.

- Adjacent segments are those of the LAD-perfusion area as defined from the AHA statement (Cerqueira 2002) that are not affected by scar. Remote segments are those belonging to the other coronary territories, see page 8, line 16

Which was the threshold used for the determination of infarct size? This is crucial. Usually it is recommended a signal intensity threshold of at least 5 SD more than that of the remote myocardium. This could not be the case since the authors found scar also in the remote non infarcted myocardium. Did these scars show an ischemic pattern? Were they really scars of just noise? This is closely related to the threshold used to measure the late gadolinium enhancement.

- The method has been described in detail in Heiberg E, Ugander M, Engblom H, Götberg M, Olivecrona GK, Erlinge D, Arheden H. Radiology. 2008 Feb;246(2):581-8 and in Heiberg E, Engblom H, Engvall J, Hedström E, Ugander M, Arheden H. Scand Cardiovasc J. 2005 Oct;39(5):267-75. It is basically a +2SD method but needs manual visual correction especially of the segmentation of the endo- and epicardium. There is a fine balance between excluding myocardium and including blood pool. For this reason, manual correction of what is basically noise is necessary – maybe it should have been expressed as “noise” and not as “infarct less than 1%”. On line 22, page 10, the sentence explains the reason for small scar areas, namely the inclusion of blood pool in the segmentation (no ischemic pattern and avoidable by better definition of the border) or the extension of infarct
into segments traditionally referred to belonging to the RCA or LCX circulations. We believe that this latter effect is related to a variable vascular supply that does not always follow the standard distribution of the AHA definition.

4) Page 10, Result section, Left ventricular volume and LVEF: the difference between LVEF measured by shortaxis cine MR imaging and that from biplane tracking is massive in the scar group but not in the non-scar group. How can the authors explain this divergence? Comments on this finding are needed

- The geometry of infarcted ventricles cannot be simplified to be represented by a stack of oval discs. This has been commented upon in the discussion, page 15, line 13.

5) Page 13, Discussion section, scar size and segmental scar area: this paragraph is not clear. The findings should be explained better and in more consistent way.

- Page 13, line 5 has been re-phrased to: Here, we defined transmurality as infarct area per segment from scar recordings in cut planes identical to the ones where the cine-loops were recorded

6) Page 13, Discussion section, functional measurements paragraph: the authors referred to differences in tissue contrast between MRI-HARP and VVI to explain the incongruence between the two methods (reference 21). This statement is not correct since HARP-MRI is based on the generation of non-magnetized lines which are able to tag the myocardium during the cardiac cycle.

- Our statement related more to echo displaying low contrast between the epicardium of the heart and the surrounding tissue. Low contrast of the epicardial border complicates analysis of echo radial strain using VVI since epicardial segmentation is necessary

It is necessary to better substantiate the finding of higher remote deformation-velocity parameters as compared to those of anteroseptal regions in non scar patients.

- This statement refers to Table 2. All measures for remote regions (=RCA and LCX) are higher in the non-scar group than in the scar group – see Table 2!

7) The discussion is not focused in explaining and commenting the manuscript results but rather in explaining why remote region deformation was less in scar patients compared to that of the corresponding region in non scar patients. Please the discussion should comment the manuscript results.

- An initial paragraph – “Main findings of the study” – has been added in the first part of the discussion, page 13, line 2-14.

Minor essential revisions:

1) Please use consistent abbreviations in both the abstract and text.

- Done

2) There are several orthographic and copy editing mistakes. Language revision by an English mother-tongue investigator is needed.

- Done
3) Page 6, Methods section, Study population paragraph: if needed, consider to use body surface area instead of height and weight.

- Considering the uncertainty in the calculation of body surface area, we preferred to retain height and weight.

4) Page 7, Methods section, MR imaging paragraph, please report the range of inversion time used in post-contrast MR imaging to null the normal remote myocardium

- A sentence inserted on page 7, line 21

5) Figure 4. Please use the same scale on the ordinate axis in the graphs displaying the radial and longitudinal displacement and also for the radial and longitudinal velocity. Please also choose a more appropriate ordinate axis scale. Strain graphs have also different scale increment (i.e. 10% increment for radial strain and 5% increment for longitudinal strain).

- Scaling has been changed and a redrawn figure 4 is enclosed

6) Page 14, Discussion section, functional measurements paragraph: the authors claimed that the deformation of the remote region is less in patients with infarcted and dysfunctional left ventricles as compared to the same region in non scarred patients. This statement is correct but needs to be substantiated by pertinent references (ex. Bogaert and Rademakers J Am Coll Cardiol)

- The suggested reference was added to the text.