Author's response to reviews

Title: Agreement of Left Ventricular Mass in Steady State Free Precession and Delayed Enhancement MR Images: Implications for Quantification of Fibrosis in Congenital and Ischemic Heart Disease

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Author's response to reviews:

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Dear editors of BMC

Thank you for the opportunity to revise our manuscript “Agreement of Left Ventricular Mass in Steady State Free Precession and Delayed Enhancement MR Images: Implications for Quantification of Fibrosis in Congenital and Ischemic Heart Disease”.

We have answered all the comments of the reviewers in a point-by-point basis and have revised the manuscript accordingly. We believe that the manuscript has improved after the input from the reviewers. We hope that our manuscript is now acceptable for publication but will make further changes if needed.

Yours sincerely,

Håkan Arheden
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Referee 1:

1) The mention of congenital heart in the second paragraph in the discussion section is not particularly relevant as this was not looked at in the study.
In this paragraph we discuss the significance and prognosis of infarcted and/or fibrotic myocardium in different patient populations, e.g. ischemic and congenital heart disease. Indeed, our study did include patients from both of these categories, patients with known ischemic heart disease and children with surgically repaired tetralogy of Fallot were included in the study population.

2) In the limitations. Line 3. Vendor-specific difference cannot be excluded. You probably mean the opposite of that.

We agree that this statement was unclear in the original manuscript. What we intended to say was that there are possible differences between vendors (GE, Philips and Siemens) due to differences in the sequences. Therefore our results from the Philips system could have been different if we had used a Siemens or GE scanner. We believe that this discussion is important to the CMR community and have expanded this section to clarify this (page 11, paragraph 2 and page 12 paragraph 2).

3) The conclusion: The difference between the two techniques in LV mass (SSFP and DE) is small and hence it is unreasonable to recommend that the contours for the LV mass should drawn twice, for such a small difference. The authors are quite right to state that the pulse sequence used for the LV volumes should be always stated and the same technique is always used for follow up. I believe all units use SSFP at present for LV volumes and hence suggesting using DE instead for calculating MI Percentage of LVM is unhelpful.

The difference between the two techniques in this study is 5.0#6.7%. This may be considered as a small difference and in a clinical setting it may be regarded as impractical to calculate the LVM twice for each patient with myocardial infarct. However, when using an automated quantification of infarct size, which is recommended for scientific purposes (1), using a full half width maximum (2) or standard deviation approach (3), delineation of the myocardium in the delayed enhancement images is necessary anyway. In that case we propose to use the LV mass from the delayed enhancement images based on the findings of our study. Furthermore, the differences may be even greater when comparing the results from different types of MRI scanners. For example when comparing our data from a Philips scanner, where DE was smaller than SSFP, with those from Grotheus et al on a GE scanner who found larger LVM when measured on DE than SSFP (2.4#3.5%) (4).

References:
Referee 2:

Major Compulsory Revision:
(a) The LV mass measured via the DE-MRI technique is strongly dependent on the myocardial-to-blood contrast-to-noise ratio. This myocardial-blood contrast in a DE-MRI varies a great deal based on the time of imaging after contrast administration (contrast wash-out), as well as on the choice of inversion time (TI) chosen for myocardial nulling. Some variation in the blood-myocardial contrast could account for the variation in LV mass computed using DE-MRI. Did the authors measure the blood-to-myocardial contrast on all the in-vivo animal images? If this data is not available, please add a few sentences in the discussion addressing this issue.

We agree that the time of imaging after contrast administration can be of significance. The DE images were acquired 10-20 minutes after the administration of the gadolinium and great care was taken to choose the right inversion time to null viable myocardium. Therefore the myocardial-blood contrast differences will be minimized. However, we did not measure the blood-to-myocardial contrast on all the in-vivo animal. We have added a section on this in the limitations as requested (page 12 paragraph 2).

Minor Essential revisions:
1) Table 2, may be removed, and the parameters can be integrated as a paragraph in the text.

Table 2 has been removed as suggested and the parameters are now a part of the text in the methods chapter (page 6 paragraph 1,2 and 3).

2) Include the animal study (in-vivo) results as an additional column in Table 3.

The animal in-vivo results are now a part of table 3 (revised table 2) as suggested.

3) Eliminate Figures 2, and 3, and provide the r2 value as a part of the Table.

In our opinion a scatter plot and Bland-Altman figure clarify the results for the
reader i.e. how the LVM on SSFP is generally higher than LVM on DE. However, to accommodate the reviewers’ suggestion of eliminating figures we have combined figures 2 and 3 and denoted infarct patients a different symbol from those without infarct.

4) The authors state that ex-vivo imaging was done on a quadrature head coil in the Methods section, but Table 2, shows that SENSE was used. This appears to be in error. Please verify.

We would like to thank the reviewer for noticing this typo error. SENSE was not used on ex-vivo imaging and this has been deleted from the manuscript.

Discretionary Revisions:
(a) It is somewhat surprising that the authors did not directly weigh the ex-vivo LV ventricle to estimate the mass (after pruning the explanted heart of unnecessary tissue). This would have provided an independent estimate of LV mass that was not based on imaging, and would have substantially strengthened the paper. If the authors do not have this data, it is probably worthwhile to add a couple of sentences in the discussion.

We agree that weighing the hearts would add independent information. Unfortunately this was not done and this is now addressed in the limitations (page 12, paragraph 2).

(b) For the ex-vivo imaging, it is curious that the authors did not use the same set of sequences used in-vivo in addition to the high-resolution T1-weighted images that they acquired, by soaking the specimen in a blood mimicking fluid. Doing so, would have permitted them to discretely assess the effect of the imaging technique (spatial resolution, as well as contrast resolution) in an ex-vivo setting.

This is a valid point that will be considered in future animal studies as well as the weighing of the heart itself after explantation.