Author's response to reviews

Title: Noninvasive monitoring of cardiac function in a chronic ischemic heart failure model in the rat: Assessment with tissue Doppler and non-Doppler 2D strain echocardiography

Authors:

sebastian holinski (sebastian.holinski@charite.de)
fabian knebel (fabian.knebel@charite.de)
georg heinze (georg.heinze@charite.de)
wolfgang konertz (wolfgang.konertz@charite.de)
gert baumann (gert.baumann@charite.de)
adrian c borges (adrian.borges@charite.de)

Version: 2 Date: 14 April 2011

Author's response to reviews: see over
Dear editor and reviewers,

thank you for the reading my manuscript and your help to improve it.
In addition to the revised manuscript with red coloured changes in the following I provide you with a point-by-point response to the reviewers questions.

Concerning referee 1:

1. As it was mentioned in the manuscript (e.g. 1st sentence of abstract) it is a feasibility study. It was also mentioned in the 1st sentence of the results section that successful analysis was performed in all animals.
2. The aim (objective) is clearly defined as evaluation of feasibility of noninvasive monitoring of cardiac function after surgically induced ischemic cardiomyopathy with tissue Doppler and non-Doppler 2 D strain echocardiography in rats (see objective section in abstract and last sentence of the background chapter of the manuscript). The study design (prospective, paired samples, blinded) was added to the method Section.
3. It is true that in high heart rates (as in rats), the diagnostic accuracy of strain and strain rate are inaccurate. In a previous study of our group, we have analysed 2D Strain in small animals. As the heart rate in these animals is as high as 300/min, the frame rate had to be set between 180 and 230 for tissue Doppler measurements and between 60 and 80 for non-Doppler 2D strain, in order to obtain optimal temporal and spatial resolution.
4. Left ventricular ejection fraction describes global left ventricular function. However, tissue Doppler and non-doppler 2D echocardiography provide precise information of regional myocardial function. This is particularly useful to evaluate cardiac diseases like myocardial infarction that have regional causes e.g. the occlusion of the LAD. Moreover the functional efficiency of regional therapeutic intervention like intramyocardial stem cell injection can be exactly monitored. These values of the new applied echocardiographic techniques compared to the common analysis of EF are explained in the discussion section of the revised manuscript. Furthermore, an EF calculation from an apical view in the rats (especially after the operation) is technically rewarding and not possible in most animals. We have chosen the best acoustic window, i.e. the parasternal view. In this view, in the long axis we performed m-mode and an EF calculation. As the rats had anteroseptal myocardial infarctions, the EF calculation by Teichholz is problematic. Therefore, we used the short axis for the assessment of radial contractility (radial 2D strain) in six segments as marker of myocardial function, rather than Teichholz LVEF.
5. 95 % CI were provided for all box and whiskers figures. Therefore figures 4, 5, and 6 have been revised.
6. It was mentioned in the revised manuscript that an impairment of regional function was detected not only strictly in the infarct related artery territory before (e.g. Thomas D et al. MAGMA (2004) 17:179-187.
7. The wording of “contemporary” echocardiography will be improved. We mean “echocardiography according to current standards and the use of newer methods such as Tissue Doppler and 2D Strain.
8. the expression “desperately” in the background section was deleted as suggested.
9. as wished the manuscript was proofread concerning typos.
Concerning referee 2:

Mayor Revisions

I do not agree that the mean of many parameters is comparable to the SD. In fact, this is only true for only 3 of 32 measured parameters listed in table 1. However, the interobserver variability and intraobserver variability in our echo lab for 2D strain analysis was 7.9% and 12.5%, respectively.

Specific Revisions
1. Mean values of IVSs are not identical and are corrected in the table.
2. Table 1 was changed as suggested.
3. Figures are linked to the text in the revised manuscript.
4. We avoided showing individual data points before and after MI because of the rather high number of 20 individuals. To our mind this would rather confuse the reader. Moreover box plots provide instant statistic informations like median or quartils.

Discretionary Revisions
1. A sham operated group would have been a nice extra. However, due to our experience neither anesthesia nor chest opening leads to such significant myocardial dysfunctons as LAD ligation.
2. It was mentioned in the revised manuscript that an impairment of regional function was detected not only strictly in the infarct related artery territory before (e.g. Thomas D et al. MAGMA (2004) 17:179-187. MRI studies were not available in our study.
3. Left ventricular ejection fraction describes global left ventricular function. However, tissue Doppler and non-doppler 2D echocardiography provide precise information of regional myocardial function. This is particularly useful to evaluate cardiac diseases like myocardial infarction that have regional causes e.g. the occlusion of the LAD. Moreover the functional efficiency of regional therapeutic intervention like intramyocardial stem cell injection can be exactly monitored. These values of the new applied echocardiographic techniques compared to the common analysis of EF are explained in the discussion section of the revised manuscript. Furthermore, an EF calculation from an apical view in the rats (especially after the operation) is technically rewarding and not possible in most animals. We have chosen the best acoustic window, i.e. the parasternal view. In this view, in the long axis we performed m-mode and an EF calculation. As the rats had anteroseptal myocardial infarctions, the EF calculation by Teichholz is problematic. Therefore, we used the short axis for the assessment of radial contractility (radial 2D strain) in six segments as marker of myocardial function, rather than Teichholz LVEF.
4. A limitation section was created within the discussion.