Author's response to reviews

Title: Computer-assisted determination of left ventricular endocardial borders reduces variability in the echocardiographic assessment of ejection fraction

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Version: 2 Date: 2 November 2008

Author's response to reviews: see over
Re MS: 1135504042228106
Computer-assisted determination of left ventricular endocardial borders reduces variability in the echocardiographic assessment of ejection fraction

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Thank you for reviewing our manuscript. Based on the valuable suggestions from the editor and from the reviewers, we have now prepared a new version of the manuscript (enclosed). We hope that the changes will be satisfactory and that the manuscript can be acceptable for publication.

Referee 1:
This is a well written manuscript addressing a long lasting methodological question such as the most objective way to assess EF by ultrasounds. There are a few issues that authors should address:
1. Please state if the proposed method is a proprietary software. This would make the method not particularly appealing for the echo community.

Response 1_1: AutoEF is a software sold by Siemens. We have used version 1.0 that analyses only Siemens DICOM. Revision 2.0, called “AutoLeftHeart”, analyses also non-proprietary DICOM. A sentence with this information was added on page 6.

2. Authors discuss at length the choice of MPI as the reference method for EF assessment. Nonetheless, the gold standard for volumes assessment is MRI and the use of MPI makes the results less reliable. They also acknowledge the limitations of 3D echocardiography, in which the quality of images have to be high to be reconstructed. However, 3D echo has demonstrated to have a very high correlation with MRI: Please comment.

Response 1_2: MPI is used as reference to show that our volumes and calculated ejection fraction results are plausible. MRI and 3D echo was not available at the time of the study. We have added a comment under “Limitations” about this.

3. The autoEF method needs to be corrected by manual definition in case of bad contour visualization. Again, the method suffers of the common limitation of echocardiography: when you cannot see you cannot measure.

Response 1_3: The idea of AutoEF is that by using learned pattern recognition, the database suggests the position of the cardiac wall even when it cannot be seen. The basis is of course that some points along the outline of the endocardium have been identified, such as the mitral valve plane and the apex. In this way, even images with restricted quality may be assessed. In fact, we had no difference in the result of AutoEF analysing images with either good or bad quality.

4. It would be very interesting to have the eyeballing assessment of EF by expert readers. We all agree that it is very important to be quantitative but, especially with patients with preserved LV function as is the present case, eyeballing exerts a very high diagnostic accuracy.
Response 1_4: We had performed visual assessment of LVEF but wanted to restrict the length of the manuscript. Now, the result of expert readers has been entered (also in a new Table 4). In the visual assessment LVEF was categorized into four levels as recommended by the guidelines from ESC/AHA (ref Lang) and compared with the corresponding categories based on AutoEF and manual planimetry. We have also added some text to the abstract (page 3-4), in the Protocol (pages 7 and 9), in the description on statistical methods (page 10), in the Results (page 11-13) and in the Discussion (page 15-16).

5. Authors study patients with preserved or mildly reduced LV function and as they state in the discussion section of the manuscript, it is a major limitation of the study. Please discuss if they believe that the presented method may be as reliable also in patients with altered LV geometry.

Response 1_5: About 25% of our patients had moderately or severely reduced LVEF (<45%). In these 15 patients, the difference between methods was not significant, neither for experts nor for the novices. In the normal/mildly depressed part, LVEF >45%, the novices had significantly lower LVEF and somewhat larger standard deviation using manual planimetry than using AutoEF. Due to the low number of patients with at least moderately reduced LVEF, we did not want to discuss this subgroup that could show erratic statistical behaviour. Basically, the performance of AutoEF depends on the reference database. Characteristics of that patient population is not known to us, as far as can be understood from a white paper published on the Siemens home-page http://www.medical.siemens.com/webapp/wcs/stores/servlet/PSGenericDisplay-q_catalogId-e -20-a_langId-e -20-a_pageld-e_79825-a_storeId-e_10001.htm

Referee 2:
http://www.cardiovascularultrasound.com/imedia/1755958513230051_comment.pdf
This is a well-written, accurate study, evaluating a computer-assisted determination of LVEF. It would have been interesting to perform the study by dividing the population into two groups: normal and abnormal EF (although there are a few patients with abnormal EF), as it is especially in patients with impaired LV geometry, that the assessment of EF poses technical challenge.

Response 2_1 (identical to that to reviewer 1): About 25% of our patients had moderately or severely reduced LVEF (<45%). In these 15 patients, the difference between methods was not significant, neither for experts nor for the novices. In the normal/mildly depressed part, LVEF >45%, the novices had significantly lower LVEF and somewhat larger standard deviation using manual planimetry than using AutoEF. Due to the low number of patients with at least moderately reduced LVEF, we did not want to discuss this subgroup that could show erratic statistical behaviour. Basically, the performance of AutoEF depends on the reference database. Characteristics of that patient population is not known to us, as far as can be understood from a white paper published on the Siemens home-page http://www.medical.siemens.com/webapp/wcs/stores/servlet/PSGenericDisplay-q_catalogId-e -20-a_langId-e -20-a_pageld-e_79825-a_storeId-e_10001.htm

It would be appropriate to improve the section about visual assessment, that remains one of the most accurate method for the evaluation of EF.
Response 2_2: We had performed visual assessment of LVEF but wanted to restrict the length of the manuscript. Now, the result of expert readers has been entered (also in Table 4 and a new figure). In the visual assessment LVEF was categorized into four levels as recommended by the guidelines from ESC/AHA (ref Lang) and compared with the corresponding categories based on AutoEF and manual planimetry. We have also added some text to the abstract (page 3-4), in the Protocol (pages 7 and 9), in the description on statistical methods (page 10), in the Results (page 11-13) and in the Discussion (page 15-16).

Sincerely,

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