Author's response to reviews

Title: Automated quantification of left atrial size using three-beat averaging real-time three dimensional echocardiography in patients with atrial fibrillation

Authors:

Ran Heo (cardiohr@yuhs.ac)  
Geu-Ru Hong (grhong@yuhs.ac)  
Young-Jin Kim (dryj@yuhs.ac)  
Joel Mancina (joel.mancina@siemens.com)  
In-Jeong Cho (INJEONGCHO@yuhs.ac)  
Chi Young Shim (CYPERS@yuhs.ac)  
Hyuk-Jae Chang (hjchang@yuhs.ac)  
Jong-Won Ha (JWHA@yuhs.ac)  
Namsik Chung (NAMSIKC@yuhs.ac)  

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Author's response to reviews: see over
**Regarding Referee 1’s report**

**Version:** 1  **Date:** 4 July 2015  
**Reviewer:** Jaroslaw Kasprzak

**Reviewer’s report:** This is an original report comparing a novel automated method for 3DE based left atrial volume (LAV) quantification (Siemens SC2000 implemented) with standard 2D methods. The study concerns, interestingly, patients with atrial fibrillation (AF) group of rather limited count (31 subjects). The main finding of the study is that novel 3D LAV quantification showed significant correlations with but demonstrated a significant degree of underestimation of LA volume compared to 2DEbased measurements. Good-quality of 3D images contributed to better correlation which is rather expected. Unfortunately there are critical methodological aspects which reduce the validity of findings.

Heart rate differences between 2D, 3D and CT play an important role - how were heart rates calculated? Over a minute or by cycle durations from 3 beats selected for study? (then this is NOT beats per minute count in AF). No info is given for 2D and 3D echo study heart rate and even though 10 bpm difference echo/CT is formally statistically nonsignificant (small study group!), it carries a physiological meaning. HOW were the specific three beats for echo selected from irregular rhythm (with regard to RR selection?)?

- Thank you for your thoughtful comments. For heart rate, as 3D images were acquired at the same time with 2D images, there was no significant difference in heart rate between the two modalities. We stated this on page 6. Also, the heart rate was based on the acquired images and ECG at the timing of image acquisition. There was no significant difference between image based heart rate and that from ECG. (76.9 ± 20.1 vs. 71.5 ± 17.2, p=0.09)

Moreover, CT protocol included beta-blockade - what dose? How often? This is not irrelevant for LAV!

- Thank you for your comment. There were 10 patients (32.3%) who were already taking beta blockers. Apart from those patients, 9 other patients took beta blocker
once (Metoprolol 50mg, p.o.) before CT acquisition. As we have demonstrated in the results part, there was no significant difference in heart rate between TTE and CT group.

Second, the dataset quality and effective temporal resolution play a pivotal role for volume quantification of highly dynamic structure such as LA. No info is provided with this regard and this clearly constitutes a source of variability.

- Thank you for this important technical comment. The mean volume rate was 18.1 ± 2.8 volume per second. We added this in the results section (page 8).

Finally, 3DE quality. I do not know if the figure represents echo quality judged as fair or good, but by general standards it is mediocre. Moreover, the graphics shows an acquisition clearly not optimized for 3DE. An easy structure such as LA should be centered in the narrowest possible dataset, thus optimizing dataset resolution which is not the case in the example shown, with severely pixelized far field data which must impact on the quality. No details of tracking convention for specific modalities, or rate of use of manual correction vs fully automated tracking are provided.

- Thank you for this very important comment. For the division into two groups according to image quality, we referred to a previous study (Tighe DA, et al; Influence of image quality on the accuracy of real time three-dimensional echocardiography to measure left ventricular volumes in unselected patients: a comparison with gated-SPECT imaging. Echocardiography 2007,24(10):1073-1080.). Dropped out area might affect the accuracy and feasibility of the volume measurement, so we thought it could be a practical way in clinical setting. The image quality of LA was much better than that of the figure when it was visualized and measured at the work station; its quality inevitably decreased while making it into a figure. For the rate of manual correction, we corrected images from the fair image quality group.

References are too many.

- We reviewed reference section and reduced it from 42 to 37 references.
Reviewer's report: General comments The study is interesting and potentially clinical useful. I have some remarks that should be considered in any revision, regarding particularly the patients selection and the interpretation of the results.

Major Specific Comments About the patients selection: the exclusion criteria included decompensated heart failure, tachycardia (heart rate over 100 beats per minute). The heart rate >100 b/min is a main limitation for the use of such method. It might be useful to know what is the accuracy of LA sizing for HR >100 b/min, if the authors tested this method in a small subset of this population and how many patients were excluded for HR >100 b/min.

- Thank you for your important and practical comments. It would have been great if we had data from patients with tachycardia. Unfortunately, we initially aimed to examine the feasibility and accuracy of the new technique in general atrial fibrillation population. We added this in the methods section, page 4. Moreover, as patients with tachycardia who were critically ill enough to be excluded from the study were usually in the intensive care unit.

For practical reasons, it might be useful to know the mean time employed for the dataset acquisition and analysis.

- Mean operation time including image acquisition and analysis was 5 minutes.

The CT scan was used as reference standard, I personally believe that contrary to what one believes the CT is in fact overvalued and some doubts remain about the use of a reference standard. In fact, as reported by the authors in the discussion, CT overestimated LA volume compared to MRI in patients with permanent AF. However, this aspect should be most stressed by the authors to emphasize the results of the study. On the other hand the results are suboptimal in fact an underestimation of 30.5 mL is not negligible and potentially clinically important. Therefore, in my opinion it is important to discuss very well the comparison between the values obtained with 3D and CT.
Thank you for this great comment. We agree that CT is not a gold standard for LA volume measurement in AF patients. So we mentioned it in the discussion and limitation part previously. However, defining CT as a reference method could be confusing, so we changed the term to ‘comparison modality’ in page 10. However, there have been many studies assessing LA volume in AF patients using CT, and LA volume by CT predicted successful outcome [1] and recurrence [2] after catheter ablation. Therefore, we thought it could be a comparison modality to novel 3DE technique even though it has many limitations.
