Author's response to reviews

Title: A novel software program for detection of potential air emboli during cardiac surgery

Authors:

Frank Secretain (secret@me.queensu.ca)
Andrew Pollard (andrew.pollard@queensu.ca)
Mesbah Uddin (muddin@uncc.edu)
Christopher G Ball (cball@toh.on.ca)
Andrew Hamilton (hamiltoa@kgh.kari.net)
Robert C Tanzola (tanzolar@kgh.kari.net)
Joelle B Thorpe (jt59@queensu.ca)
Brian Milne (milneb@queensu.ca)

Version: 2
Date: 19 December 2014

Author's response to reviews:

Response to Reviewers

Reviewer #1 (Mark Jermy): We thank the reviewer for the effort to review our paper and to provide comments. We have made the two changes suggested in the revised manuscript (we have deleted the word “the” on page 8, line 21, and we have replaced the word “calculations” with “estimates” on page 9, line 10).

Reviewer #2 (Francesco Faita): We thank the reviewer for his thorough review and insightful questions. Our changes are included in the revised manuscript, and our responses to each comment/question are included below.

Major Compulsory Revisions:

1. Only qualitative results are presented in in-vivo section. Moreover, data are coming from only 5 patients, which are claimed to be subjected to cardiac surgery, but without details on applied procedures. This section should be removed and should be presented in a next paper when more data will be available.

   We agree that more data would be ideal for our analysis; we have removed this section from the paper. However, we feel that the figure (former Figure 6) and video assist the reader to visualize the output of our software program. Therefore, we have kept this figure (now Figure 3) and video in the paper, but have removed the emphasis of the in vivo section by including this information in the “DETECTS™ software algorithm and interface” section.

2. The software do not reconstruct a full real 3D volume and it is only presenting a potential bubble path, taking in consideration only the starting position of the recognized bubble. Authors are encouraged to better explain how they obtained...
the 3D reconstruction and what it represent, in order to not mislead readers which could believe that DETECTS™ implement a true 3D imaging system.

We have added a sentence clarifying that DETECTS™ does not show the full bubble path, but instead it does provide an estimate of the volume of air that passes through the plane of the TEE probe placed on the ascending aorta (page 6, line 23 to page 7, line 2). We have also added an explanation of how the 3D reconstruction was obtained (page 6, lines 10-23).

3. In vitro section is too long and it should be shortened.

This section has now been shortened to improve readability.

4. When dealing with ultrasound image processing algorithms characterized by use of thresholds, the relationships between ultrasound machine adjustments should be dealt with great attention because it could have a great impact on reliability and reproducibility of the results. Authors only investigate (qualitatively) the sensitivity of the bubble threshold respect the MI and the gain of the ultrasound machine. However, the interaction with other ultrasound machine adjustment should be also tested and reported with numerical results.

There are many adjustments that can be made on an ultrasound machine to enable the user to create a suitable image. Practically speaking, physicians at our centre rarely make adjustments beyond mechanical index (MI) and gain, which are the two most common adjustments on ultrasound machines. We have included some data (in the attached cover letter), regarding how DETECTS™ deals with different MI and gain levels. However, we have chosen not to include this in the current submission, since it may not be either appropriate for or of interest to the readership.

DETECTS™ was designed to extract a circular region (within given bounds of eccentricity) and the features of the image within that region. In the case of TEE images of the ascending aorta, the circular region (region of interest, or ROI) should be the aorta, and the features are the passing air bubbles. DETECTS™ extracts the ROI using a grey scale thresholding and an ellipse fitting technique. The air bubbles are extracted using grey scale thresholding, a blob detection technique, and aspect ratio filters. Users are able to adjust the thresholds of the ROI and air bubbles to fine tune the accuracy of the software. Default threshold values are calculated by DETECTS™; however, the input image must have a visible circular region and some features within it. The default threshold calculated by DETECTS™ for ROI was tested against the MI and gain parameters (see figure in attached cover letter). The default thresholds were most affected by the MI parameter and less so by gain. Nevertheless, the software was able to adjust for the input image and still calculated the appropriate threshold for the ROI.

Minor Essential Revisions and Discretionary Revisions:

1. The last two sentences of “DETECTS™ software algorithm and interface” section (page 6, lines 9-12) are comments and they should be (re)moved.
We have now moved these sentences to the Conclusion/Future Directions section of the revised manuscript.

2. Few details are reported about the software used to elaborate optical images. Did the authors develop it? If it is the case, did the authors validate it?

DETECTS™ was validated to correlate bubbles measured by ultrasound to optical images of these bubbles. Air bubbles in a liquid subject to imaging ultrasound respond by reflecting the input acoustic wave (99.9% reflectance). The air bubble size and intensity displayed on the ultrasound screen was correlated to the optical method. Matlab (2009) was used to extract the air bubbles as seen by the camera and DETECTS™ was used for the ultrasound. We have now added a description of this into the revised manuscript (page 8, lines 8-13).

3. Some sentences of “In vitro validation of DETECTS™” section are comments and they should be (re)moved, in particular (page 8, lines 7-10), (page 8, lines 18-20) and (page 8, lines 21-22).

We have now moved these sentences to the Conclusion section of the revised manuscript (page 9, line 19 to page 10, lines 1-20).

4. The phenomenon of phantom bubbles presented in figure 3 and described in “In vitro validation of DETECTS™” section is not so unexpected, because the experimental setup composed by a Plexiglas box filled with water and air bubble is prone to this type of ultrasound artifact caused by multiple echos. This could suggest that this experimental setup is not the optimal one for testing the algorithm and that different (larger) chamber and fluid (blood mimicking) should be considered.

We agree that performing these experiments in blood would yield interesting and informative results. However, we believe this experimental setup was optimal at this phase of the validation process. We chose to use water for this initial study in order to compare optical and ultrasound images to validate DETECTS™ against true (optical) measurements. This would not be possible in blood. We have added a Future Directions section to the revised manuscript (page 11 lines 1-9), in which we suggest that future studies replicating this work in blood (or blood equivalent) would be fruitful.

It is correct that there were echoes as a result of the experimental setup. The Plexiglas does show multiple wave reflectance on the bounds of the chamber, but this would not explain the multiple points seen in front of the bubbles. The multiple points observed in front of the bubbles and on the bounds of the chamber come from the high-reflectance of the air-water interface.