DEPARTMENT OF BIOMEDICAL ENGINEERING

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July 4, 2019

Dear Editor, Associate Editor, and Editorial Staff,

Enclosed is the revised manuscript, "Extraction of Peak Velocity Profiles from Doppler Echocardiography Using Image Processing". We would like to thank the reviewers for their helpful comments. We addressed all the reviewers comments. The reviewers comments as well as our answers are attached to this letter.

We thank you for your time and consideration.

Sincerely,

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Reviewer 1
 # Summary

Comment: *The authors propose an algorithm to extract velocity profiles from pulsed wave Doppler traces, using image processing. The algorithm is based in a thresholding operation that aims at finding the edge of the profile.*

I have two major concerns: 1. The work has not been put in context of similar methods in the literature, and 2. There is no comparison to ground truth traces (e.g. from experts) so there is no indication of how accurate the method is.
Answer: Thank you very much for your comments. We addressed both of these concerns in detail. Please see our answers to the following comments.

 # Major comments

Comment: *The authors justify the study based on the tediousness of manual delineation. However, there is no description of how much manual input (e.g. defining RoI, baseline, etc) is there in the proposed workflow, or whether the proposed workflow is less tedious than current clinical practice.*
Answer: The only manual inputs of the algorithm include the upper and lower borders of the ROI, i.e. n_{up} and n_{lo}. The algorithm is fed by the Doppler images and give the peak velocity profiles as output. The ROI and baseline are defined from the images by the algorithm. However, they can be adjusted by user.

Comment: *Moreover, the results are not compared to any reference, even when manual delineations could be made available sice they say that 2 specialists were involved in the study. How does the proposed method compare to the manual tracings of these specialists?*
Answer: To address this concern, we added the following to the manuscript. The E waves and A waves were manually calculated by the study specialists. These values were also calculated from the peak velocity profiles estimated using both thresholding methods for both raw and smoothed images. These results are listed in Table 2 and discussed in the results section.

Comment: *The methods and the results are mixed; there is quite a bit of methodology in the results/discussion section that should be re-organised.*
Answer: We re-organized the sections and moved the image smoothing methodology to the materials and methods sections.

Comment: *Last, there is a relevant body of literature on detection of the Doppler trace that outperform the Canny edge detector significantly, and should be included in this study. The proposed algorithm must be put in comparison to those. For example:*

Dhutia, Niti M., et al. "Open-source, vendor-independent, automated multi-beat tissue Doppler echocardiography analysis." The international journal of cardiovascular imaging 33.8 (2017): 1135-1148.

Biradar, Nagashettappa, M. L. Dewal, and Manoj Kumar Rohit. "Automated delineation of Doppler echocardiographic images using texture filters." 2015 2nd International Conference on Computing for Sustainable Global Development (INDIACom). IEEE, 2015.

Zolgharni, Massoud, et al. "Automated aortic Doppler flow tracing for reproducible research and clinical measurements." IEEE transactions on medical imaging 33.5 (2014): 1071-1082.

Wang, Zhe, et al. "Automatic tracing of blood flow velocity in pulsed Doppler images." 2008 IEEE International Conference on Automation Science and Engineering. IEEE, 2008.
Answer: We agree with the reviewer. To address this, we added a section, "Limitations and Future Work", and discussed this.

 # Minor comments

Comment: *Doppler ultrasound modes include: 1D continuous wave Doppler (CWD), 1D pulsed wave Doppler (PWD) and colour Doppler imaging (CDI). In this study, PWD is used and it should be mentioned.*
Answer: We used pulsed Doppler for this study. We added this information to Line 76.

(Materials and Methods)

Comment: *In section 2, the authors describe the Doppler formula as Af = ft-fr, and then discuss about the change in period. It would be informative to relate frequency and period here.*
Answer: We made this clear by relating the frequency and period as follows: "The motion of the structure toward the ultrasound transducer results in compression of the reflected waves, reducing its period (i.e., negative ΔP, where P is the period) and thus increasing their frequency (i.e., negative Δf)."

Comment: *Authors state that images were acquired at 30fps. However, Doppler waves like the one in Fig. 1.b, have a temporal axis which may be different from the BMode image acquisition frame rate. In this case, it is more appropriate to talk about temporal resolution of the Doppler wave (which may have implications in validity of derived quantities, such aa velocity gradients).*
Answer: Thank you for raising this issue. The pulsed Doppler was acquired at sweep speed of 75 mm/s. We added this information to Line 78.

Comment: *In Step 2, authors describe the Doppler wave as "the Doppler shift". What the PWD trace shows is the distribution (in frequency) of the Doppler shift, due to variation in insonation angle within the resolution cell and to particles moving at different velocities and different directions. Each will show a different Doppler shift hence the imag shows the overall distribution, for each time instant, as a gray-level column. Please rephrase appropriately.*
Answer: We rephrased this sentence as follows: "Step 2 - Define a region of interest (ROI) that encompasses the gray pixels containing the blood velocity information …"

Comment: *Step 3 is not a processing step: retrieving the intensities does not need any calculation, just querying the image. If interpolation was done, please state so.*
Answer: In the revised version Steps 2 and 3 are combined to address this concern.
Comment: *Fig. 1: It is unclear why the histogram there is relevant and what the red arrows are pointing at. This should be indicated in the Figure's caption.*
Answer: We now added the following description to the figure caption: "The red arrows show the main peaks of the histogram which were used to determine the threshold values."

Comment: *Step 5 is an edge detection algorithm. As such, an algorithmic description (e.g. using pseudocode) would be a more appropriate way of describing it. Also, The reader is directed to figure 2 to follow the algorithm: this figure should be labelled consistently with the description, i.e. the horizontal axis should be Y (instead of vertical pixel) and so on.*
Answer: Thanks. We added a pseudo-code that describes the proposed algorithm. We also fixed the figure accordingly.

Comment: *Fig. 2: Label the baseline (dashed grey line)*
Answer: The following description is added to the figure caption: "The dashed gray and red lines show the baseline and threshold, respectively. For each method, the edge search direction is shown with gray arrows."

Comment: *How is the baseline detected from raw images?*
Answer: It is a manual input in the current version. It will be automatically detected in future work.

Comment: *Fig. 3 should be put first, as an overview, then followed byu the details of each block. Also, there are many ways of carrying out image smoothing. Also, it is not clear why the smoothing block is dashed. Figure 3 should be described in its caption.*
Answer: The following description is added to the figure caption: "These steps are described in detail in the Section 2 of this paper. Dashed lines show the arbitrary steps." We also moved this figure to the beginning of section 2 per reviewer's suggestion. Therefore, this figure is now Figure 1, and old Figure 1 and 2 are now numbered as Figure 2 and 3, respectively.

(Results)

Comment: *Smoothing is described in the results section, but this is clearly a methods step. Re-organise the paper to include this in the methods section. Why was a moving average used (i.e. convolution with a square step kernel), instead of other, more common smoothing methods such as convolution with a Gaussian kernel?*

Answer: We moved the smoothing details to the end of section 2 and added the following description: "These steps are also used to detect the peak velocity profiles from the images after they are smoothed by convolving with a square step kernel. The pixels' intensity is smoothed by a moving average process. Here, the smoothed image intensity, μ_{smooth}, at (X, Y) is calculated as the mean intensity of a $(2p + 1) \times (2q + 1)$ rectangle centered at (X, Y):

$$\mu_{smooth}(X,Y) = \sum_{j=Y-q}^{Y+q} \sum_{i=X-p}^{X+p} \mu(i,j) / ((2p + 1)(2q + 1)), \tag{1}$$

where μ is the image intensity before smoothing. The peak velocity profiles detected from the original and smoothed images are then compared."

Comment: The results in Fig. 5 show agreement between the two methods, but they could be both wrong-can authors provide any validation with a ground truth, e.g. manual delineations from the 2 specialists involved in the study?
Answer: To address this concern, we added the following to the manuscript. The E waves and A waves were manually calculated by the study specialists. These values were also calculated from the peak velocity profiles estimated using both thresholding methods for both raw and smoothed images. These results are listed in Table 2 and discussed in the results section.

Comment: Smoothing is a low-pass filtering operation, so the fact that there are fewer high-frequency components is only trivial. This should not be part of the results/conclussion.
Answer: Thank you for raising this issue. We kept the figure since we thought that making this point is good. However, to address the issue raised by the reviewer, we mentioned in the revised manuscript that this results were expected. See Line 203.

Comment: Authors also say (in the results) that edge detectors were used for comparison (Fig. 7) but no quantitative analysis was made. Canny edge detector is usually applied on smoothed images (even more so here, where authors are smoothing the datafor their own method). I believe that results in Fig 8 where obtained from the original images, without smoothing. Please, re-compute those images after smoothing.
Answer: Thanks. The reviewer is completely right. However, the results shown in Figure 8 are indeed obtained from the smoothed image. We added this information in the figure caption as well as in the body of the paper (Line 210) in order to avoid future confusions.

 # Phrasing/typos

Comment: p2 - "In a Doppler echocardiography" -> In Doppler echocardiography or In a Doppler echocardiography examination
Answer: Thanks. We changed "In a Doppler echocardiography" to "In Doppler echocardiography"

Comment: p2 - "using Doppler effect" -> using the Doppler effect
Answer: Thanks. We fixed this.

Comment: p2 - "In doppler cardiography," -> In Doppler cardiography,
Answer: Thanks. We fixed this.

Reviewer 2

Comment: *In this paper the authors propose a method to extract positive and negative peak velocity profiles from Doppler echocardiographic images.*

The proposed approach is based on intensity calculations and two different thresholding methods have been proposed and tested.

In general, the paper is well written and clear. However, there are some minor points to address.

Comment: *1. A minor mistake is in raw 81: the range is [0,255] and not [0, 256].*

Answer: Thanks. This is now fixed in the revised manuscript.

Comment: *2. The authors should explain and motivate the meaning of "consistent" in raw 225.*

Answer: We meant that the general trend (e.g. overestimating the profiles by one method and underestimating by another one) was seen in the results for other images as well.

Comment: *3. Information about the hardware and software resources used to implement the system*

Answer: Thanks. These information are provided in the second paragraph of the Materials and Methods section.

Comment: *4. And finally, but more important, the paper presents only some examples without any groundtruth and any quantitative measure useful to better evaluate the performance of the proposed method. A visual analysis of the results is not enough to confirm the goodness of the algorithm. At least the authors should add a visual and numerical comparison with a possible groundtruth proposed by experts.*
In my opinion the paper is suitable for publication in the Journal after just the suggested minor corrections.
Answer: To address this concern, we added the following to the manuscript. The E waves and A waves were manually calculated by the study specialists. These values were also calculated from the peak velocity profiles estimated using both thresholding methods for both raw and smoothed images. These results are listed in Table 2 and discussed in the results section.

Reviewer 3
Comment: Only one echo machine, one subject and 13 images were considered in this study. Perhaps discussing the current/usual methods of peak velocity detection in several examples of echocardiography machines would improve the understanding of the generalisability of the results.

Answer: We agree with the reviewer. To address this, we added a section, "Limitations and Future Work", and discussed this.
"The proposed algorithm in this study was employed to detect peak velocity profiles from the images recorded by only one echo machine. In future studies, this algorithm should be tested on more subjects and different echocardiography machines. In addition, the performance of this algorithm was compared with the manual calculations of the study clinicians. The results were also qualitatively compared with a standard edge detection method. However, there are other algorithms for Doppler trace detection in literature [19–21] that outperform the Canny edge detector. The proposed algorithm should be compared against these algorithms."

Comment: A clearer separation of the proposed method versus usual methods could improve the understanding of the novelty of the study for the reader.

Answer: Thanks. We explained this in Line 240 as follows
"The proposed algorithm in this study, on the other hand, always estimates a lower and an upper edge in each vertical line. The proposed algorithm also resulted in continuous velocity profiles and less artifacts compared to the Canny method. In addition, it was simpler and less computationally expensive since it was only based on two simple thresholding operations."