Author's response to reviews

Title: Volume Tracking: A new method for quantitative assessment and visualization of intracardiac blood flow from three-dimensional, time-resolved, three-component magnetic resonance velocity mapping

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Author's response to reviews: see over
Dear Mr. Aldcroft,

Thank you for considering our manuscript “Volume Tracking: A New Method for Quantification and Visualization of Intracardiac Blood Flow from Three-Dimensional, Time-Resolved, Three-Component Magnetic Resonance Velocity Mapping”, manuscript ID 1752040677481393, for publication in BMC Medical Imaging.

We have carefully considered the reviewer's comments and updated the manuscript accordingly. Additionally, we have made efforts to conform to the journal style and specified the name of the ethics review board as requested. Specific changes and answers to the reviewers' comments are given below. Changes with respect to the previous version have been highlighted in the revised manuscript.

Sincerely,

Einar Heiberg
Response to review of the manuscript “Volume Tracking: A New Method for Quantification and Visualization of Intracardiac Blood Flow from Three-Dimensional, Time-Resolved, Three-Component Magnetic Resonance Velocity Mapping”

BMC Medical Imaging Manuscript ID 1752040677481393

Line numbers refer to the version of the manuscript with changes indicated. In addition to the changes below, we have made efforts to conform to the journal style as follows by removing unnecessary capitalization in headings, figure titles and the paper title, reformatting Table 1 and Table 2 and corrected the style of the references. We have also clarified the name of the ethics committee on page 4, lines 10-11, as requested by the editor.

Reviewer 1

Comment 1.1: As the reviewer understands, the authors of this paper are presenting a new visualization method for blood flow measured by 4D PC-CMR. The method allows to visualize how the surface of a specific blood flow volume is stretched and folded while this volume of blood evolves within cardiac chambers. The authors aim at validating this novel visualization method, which as a quantitative potential for blood flow from 4D PC-CMR, and investigate if Volume Tracking complements particle tracing, the most common visualization 4D method used today.

The authors apply the proposed method to eight healthy volunteers and one patient with a large apical left ventricular aneurysm. The authors claim that Volume Tracking complements and provides incremental information compared to particle tracing that may lead to a better understanding of blood flow and may improve diagnosis and prognosis of cardiovascular diseases.

The reviewer believes that the work undertaken in this paper is of interest to the scientific community and should be considered for publication in "BMC Medical Imaging", but needs major corrections before publication. Some of the issues that need to be clarified/addressed prior to publication are outlined below.

Response: No changes.

Major Compulsory Revisions

Comment 1.2: In the opinion of this Reviewer, the authors use the term “quantitative” in several statements and this is somewhat misleading. In fact, the Volume Tracking method does not give quantitative information as an output. The authors in fact use two independent observers to describe flow patterns in the left ventricle using Volume tracking visualization. I believe that this cannot be really considered a “quantitative approach”. For this reason, the authors should reconsider and mitigate some of their statements.

Response: The authors agree that “quantitative” may be a misleading description of the present approach. We have changed the title of the manuscript and wording in the text:

Page 7, line 17: Removed the word “quantitatively”.

Page 7, line 19: Changed “quantify” to “map”.

Page 10, 3rd line under “Discussion”: Removed the word “Quantitatively”.

Heading “Quantitative Analysis of LV Inflow Patterns” changed to “Analysis of LV Inflow Patterns” on pages 7, 9 and 11.

Comment 1.3: The Authors investigate if Volume Tracking complements particle tracing, i.e., the most common visualization 4D method used today. Did the authors perform a statistical analysis on the dimension of the dataset of the traced particles? Is the percentage number of injected traced particles within the tracked volume dependent on the number of traced particles? The authors should clarify this aspect, because the sensitivity to the number of tracked particles could influence the results of the comparison between particle tracing and volume tracking, in the opinion of this Reviewer.

Response: Thank you for bringing this point to our attention. We have investigated this in one of the volunteers, and concluded that the agreement changed only slightly, as long as at least 1000 particles were released. This is now clarified in the Methods section, page 7, lines 12-14, Results, page 9, lines 23-24 and in the discussion, page 11, lines 12-14.

Comment 1.4: The authors, in the Limitation section, state that “The evaluation of the visualization aspects of Volume Tracking was performed by visual comparison to particle tracing. An independent, quantitative evaluation for both methods would be desirable. However, currently available evaluation methods for flow
visualization do not treat time-resolved flow \cite{11, 12} and may not address the hypothesis-generating aspects of visualization". The authors raise here a still unanswered question, i.e., which is the right way to compare time-resolved flow visualizations?

**Response:** We agree that this is an important question. According to our knowledge, this remains an open problem in visualization research. This has been clarified in the Limitations section, page 12, lines 23-26.

**Comment 1.5:** In my opinion, the authors need to discuss the comparison of their results to recent studies that have used particle traces for both visualization (semi-quantitative) and for fully quantitative ranking of topological aspects of the flow measured with 4D time resolved PC MRI (Morbiducci et al., Annals of Biomedical Engineering, 2009; Morbiducci et al., Biomechanics and Modeling in Mechanobiology, 2011 in press). In those recent studies, a Lagrangian-based approach was applied and bulk flow metrics were applied to give fully quantitative description on topological features of the aortic flow. The authors should discuss the potency of their method with respect to state-of-the-art quantitative analysis on time resolved 4D PC MRI.

**Response:** Thank you for bringing these studies to our attention. Volume Tracking is now discussed in relation to these studies in the Discussion section, subsection “Evaluation and Validation of Volume Tracking” (page 10, lines 25-28).

**Comment 1.6:** The authors should give proof of the ability of the volume tracking method in catching peculiar flow features such as vortex identification, because vortex development and evolution within cardiac chambers is considered a relevant issue. This reviewer believes that a discussion, at least, is needed on this topic.

**Response:** The authors agree that vortices are important in blood flow. Vortex identification, however, may be better handled by dedicated vortex identification methods, complementing Volume Tracking. This is now clarified in the discussion, page 10, lines 25-28.

**Comment 1.7:** The Authors use a 50 ms temporal resolution. However, particle traces are released every 20 ms. Did the author apply an interpolation strategy to the PC-MRI measured data? Please clarify. If so, did the author check for the sensitivity of the results to the level of interpolation? I believe that more details should be furnished, in order to assess the real quality of the paper (maybe in Appendix).

**Response:** According to our communications with CEI support technicians, the particle tracing algorithm in Ensight employs linear interpolation between timesteps. This is now clarified in the Methods section, page 6, line 22-23. A discussion of the errors introduced with the interpolation has been added to the Limitations section, page 12, lines 17-21.

**Comment 1.8:** The Authors state that “the volume tracking surface shows the boundary between inflowing blood and blood already in the ventricle from the previous heartbeat”. In the opinion of this Reviewer, the Volume tracking method, when applied to cardiac chambers, accounts only indirectly for important features developing in the flow field, because blood already in the ventricle is significantly modified from the streaming blood in the filling phase. On the contrary, the volume tracking method could furnish a more complete information when applied to vascular districts such as the thoracic aorta. The authors should comment on this, in the opinion of this Reviewer.

**Response:** The authors agree that Volume Tracking only shows one part of intracardiac blood flow dynamics. This is now included in the Limitations section, page 12, line 14-16. The application of Volume Tracking to aortic flow is now discussed in the Discussion section, page 10, lines 15-18.

**Minor Compulsory Revisions**

**Comment 1.9:** Abstract – please indicate the site on investigation not at the end, but at the beginning of the Methods section.

**Response:** This has now been clarified in the first sentence of the methods part of the abstract.

**Comment 1.10:** Background – the Authors should mention quantitative methods (i.e., not only visualization) currently applied to 3D and 4D PC MRI data, with particular attention to wall shear stress estimation and topological features quantification.

**Response:** The background has now been extended to include quantitative methods (page 3, lines 13-20).
**Comment 1.11:** Results, Volume tracking subsection – Please consider to move the second part of the subsection (starting from “By implementing a pre-computation step...”) to the Methods section.

**Response:** The description of the Volume Tracking method has been moved to the Methods section (bottom of page 4, heading “Volume Tracking”).

**Comment 1.12:** Results, Evaluation and Validation of Volume tracking subsection – maybe the sentence in the caption of figure 1 should be included in the text, being very appropriate for a clear understanding of the volume tracking method’s output (“...the volume tracking surface shows the boundary between inflowing blood and blood already in the ventricle from the previous heartbeat...”).

**Response:** Thank you for this excellent suggestion. This has been added in the Methods section (page 7, lines 1-3) and in the Results section (page 8, lines 8-9).

**Comment 1.13:** Results, Evaluation and Validation of Volume tracking subsection – The sentence “Volume Tracking, compared to particle tracing, shows the spatial distribution and location of the tracked blood with greater clarity” is misleading. What do the authors mean with “greater clarity”? Please reconsider this sentence.

**Response:** This sentence has been rewritten (page 8, line 28 – page 9, line 1).

**Comment 1.14:** Discussion, Evaluation and Validation of Volume tracking subsection – The sentence “Volume Tracking shows the distribution of LV inow blood clearer than particle tracing” is misleading. What do the authors mean with “clearer”? Please reconsider this sentence.

**Response:** This sentence has been rewritten (page 10, lines 14-15).

**Reviewer 2**

**Comment 2.1:** The authors present Volume Tracking as a new approach for visualization of time-resolved PC-MR velocity imaging applied to intracardiac blood flow. They argue that this approach gives more and complementary information about blood flow compared to commonly used particle tracing. Furthermore they propose its application to quantitatively describe flow patterns. They evaluated their method with data from eight healthy volunteers and one patient with apical LV aneurysm.

Overall the article is well designed and understandably written. Data are sound. State-of-the-Art, methods, and results are clearly presented. Figures and animations impressively illustrate the results. Discussion and conclusion are appropriate and clearly state potential as well as limitations of the approach. Some minor revisions would further improve the article.

The proposed approach is an appreciable contribution to the analysis of blood flow patterns. It will be interesting to see it applied to more pathological cases including those where more than one cavity is affected such as mitral valve insufficiency or ventricular septal defect.

**Response:** No changes.

**Discretionary Revisions**

**Comment 2.2:** The technical details of Volume Tracking are described in an appendix which is a good decision. However, it would be very helpful to include some more information in the main article.

**Response:** The authors agree that an overview of the Volume Tracking algorithm may be of interest in the main text. The Methods section has now been extended to cover some details about Volume Tracking (page 4, heading “Volume Tracking”, page 5, page 6, lines 1-12).

**Comment 2.3:** It remains unclear, what processing is performed by the Segment plugin and Ensight respectively.

**Response:** This has now been clarified (page 6, lines 17-21).

**Comment 2.4:** Also, more explication is needed to help interpret the Volume Tracking surfaces shown in the figures.

**Response:** We have now rewritten the captions for the flow visualization figures 1, 2, 4 and 5, and improved the labels in the images.