

## **Fluid–structure interaction simulations outperform computational fluid dynamics in the description of thoracic aorta haemodynamics and in the differentiation of progressive dilation in Marfan syndrome patients**

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### **Article citation details**

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### **Review timeline**

Original submission: 22 October 2019

Revised submission: 9 January 2020

Final acceptance: 9 January 2020

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

Note: This manuscript was transferred from another Royal Society journal with peer review.

## Review History

### RSOS-191752.R0 (Original submission)

#### Review form: Reviewer 1

**Is the manuscript scientifically sound in its present form?**

Yes

**Are the interpretations and conclusions justified by the results?**

Yes

**Is the language acceptable?**

Yes

**Do you have any ethical concerns with this paper?**

No

**Have you any concerns about statistical analyses in this paper?**

No

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**Recommendation?**

Accept with minor revision (please list in comments)

**Comments to the Author(s)**

The authors have tried to address all my concerns, the quality of the paper has been improved. I only have some minor comment as bellow,

(1) please explain 'f' in equation 1;

(2) the format of equations, some subscript is in normal font, some in Italic, which is little annoying when reading. It seems the authors used bold face for vector and matrix, but not consistent across the paper, for example equation 3.

(3) Thanks for providing details on obtaining patient-specific Young's modulus from PWV, while I am still not clear how E is optimized, the update of E seems not depending on the difference between PWV<sub>i</sub> and PWV<sub>MR</sub>. In theory, E<sub>0</sub> obtained from equation 5 should give a close value to PWV<sub>MR</sub>, no further steps are needed. Some explanations will be helpful.

## Review form: Reviewer 2

**Is the manuscript scientifically sound in its present form?**

Yes

**Are the interpretations and conclusions justified by the results?**

Yes

**Is the language acceptable?**

Yes

**Do you have any ethical concerns with this paper?**

No

**Have you any concerns about statistical analyses in this paper?**

No

**Recommendation?**

Accept as is

**Comments to the Author(s)**

The authors have addressed my comments. The manuscript can be accepted by Royal Society Open Science.

## Decision letter (RSOS-191752.R0)

20-Dec-2019

Dear Dr Pons

On behalf of the Editors, I am pleased to inform you that your Manuscript RSOS-191752 entitled "Fluid-structure simulations outperform computational fluid dynamics in the differentiation of progressive dilation in Marfan syndrome patients" has been accepted for publication in Royal

Society Open Science subject to minor revision in accordance with the referee suggestions. Please find the referees' comments at the end of this email.

The reviewers and handling editors have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the comments and revise your manuscript.

- Ethics statement

If your study uses humans or animals please include details of the ethical approval received, including the name of the committee that granted approval. For human studies please also detail whether informed consent was obtained. For field studies on animals please include details of all permissions, licences and/or approvals granted to carry out the fieldwork.

- Data accessibility

It is a condition of publication that all supporting data are made available either as supplementary information or preferably in a suitable permanent repository. The data accessibility section should state where the article's supporting data can be accessed. This section should also include details, where possible of where to access other relevant research materials such as statistical tools, protocols, software etc can be accessed. If the data has been deposited in an external repository this section should list the database, accession number and link to the DOI for all data from the article that has been made publicly available. Data sets that have been deposited in an external repository and have a DOI should also be appropriately cited in the manuscript and included in the reference list.

If you wish to submit your supporting data or code to Dryad (<http://datadryad.org/>), or modify your current submission to dryad, please use the following link:  
<http://datadryad.org/submit?journalID=RSOS&manu=RSOS-191752>

- Competing interests

Please declare any financial or non-financial competing interests, or state that you have no competing interests.

- Authors' contributions

All submissions, other than those with a single author, must include an Authors' Contributions section which individually lists the specific contribution of each author. The list of Authors should meet all of the following criteria; 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published.

All contributors who do not meet all of these criteria should be included in the acknowledgements.

We suggest the following format:

AB carried out the molecular lab work, participated in data analysis, carried out sequence alignments, participated in the design of the study and drafted the manuscript; CD carried out the statistical analyses; EF collected field data; GH conceived of the study, designed the study, coordinated the study and helped draft the manuscript. All authors gave final approval for publication.

- Acknowledgements

Please acknowledge anyone who contributed to the study but did not meet the authorship criteria.

- Funding statement

Please list the source of funding for each author.

Please ensure you have prepared your revision in accordance with the guidance at <https://royalsociety.org/journals/authors/author-guidelines/> -- please note that we cannot publish your manuscript without the end statements. We have included a screenshot example of the end statements for reference. If you feel that a given heading is not relevant to your paper, please nevertheless include the heading and explicitly state that it is not relevant to your work.

Because the schedule for publication is very tight, it is a condition of publication that you submit the revised version of your manuscript before 29-Dec-2019. Please note that the revision deadline will expire at 00.00am on this date. If you do not think you will be able to meet this date please let me know immediately.

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When submitting your revised manuscript, you will be able to respond to the comments made by the referees and upload a file "Response to Referees" in "Section 6 - File Upload". You can use this to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the referees. We strongly recommend uploading two versions of your revised manuscript:

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- 2) A 'clean' version of the new manuscript that incorporates the changes made, but does not highlight them.

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- 2) A separate electronic file of each figure (EPS or print-quality PDF preferred (either format should be produced directly from original creation package), or original software format);
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- 4) Included the raw data to support the claims made in your paper. You can either include your data as electronic supplementary material or upload to a repository and include the relevant doi within your manuscript. Make sure it is clear in your data accessibility statement how the data can be accessed;
- 5) All supplementary materials accompanying an accepted article will be treated as in their final form. Note that the Royal Society will neither edit nor typeset supplementary material and it will be hosted as provided. Please ensure that the supplementary material includes the paper details where possible (authors, article title, journal name).

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Once again, thank you for submitting your manuscript to Royal Society Open Science and I look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Kind regards,  
Andrew Dunn  
Royal Society Open Science Editorial Office  
Royal Society Open Science  
[openscience@royalsociety.org](mailto:openscience@royalsociety.org)

on behalf of Dr Francois Fages (Associate Editor) and Marta Kwiatkowska (Subject Editor)  
[openscience@royalsociety.org](mailto:openscience@royalsociety.org)

Associate Editor Comments to Author (Dr Francois Fages):

Dear Authors

It is my pleasure to accept your paper with just minor revision for the few points mentioned in the first review.

Thank you for your contribution

Best regards

Reviewer comments to Author:

Reviewer: 1

Comments to the Author(s)

The authors have tried to address all my concerns, the quality of the paper has been improved. I only have some minor comment as bellow,

(1) please explain 'f' in equation 1;

(2) the format of equations, some subscript is in normal font, some in Italic, which is little annoying when reading. It seems the authors used bold face for vector and matrix, but not consistent across the paper, for example equation 3.

(3) Thanks for providing details on obtaining patient-specific Young's modulus from PWV, while I am still not clear how E is optimized, the update of E seems not depending on the difference between PWV<sub>i</sub> and PWV<sub>MR</sub>. In theory, E<sub>0</sub> obtained from equation 5 should give a close value to PWV<sub>MR</sub>, no further steps are needed. Some explanations will be helpful.

Reviewer: 2

Comments to the Author(s)

The authors have addressed my comments. The manuscript can be accepted by Royal Society Open Science.

## Author's Response to Decision Letter for (RSOS-191752.R0)

See Appendix A.

## Decision letter (RSOS-191752.R1)

09-Jan-2020

Dear Dr Pons,

It is a pleasure to accept your manuscript entitled "Fluid-structure simulations outperform computational fluid dynamics in the differentiation of progressive dilation in Marfan syndrome patients" in its current form for publication in Royal Society Open Science.

You can expect to receive a proof of your article in the near future. Please contact the editorial office ([openscience\\_proofs@royalsociety.org](mailto:openscience_proofs@royalsociety.org)) and the production office ([openscience@royalsociety.org](mailto:openscience@royalsociety.org)) to let us know if you are likely to be away from e-mail contact -- if you are going to be away, please nominate a co-author (if available) to manage the proofing process, and ensure they are copied into your email to the journal.

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Thank you for your fine contribution. On behalf of the Editors of Royal Society Open Science, we look forward to your continued contributions to the Journal.

Kind regards,  
Lianne Parkhouse  
Editorial Coordinator  
Royal Society Open Science  
[openscience@royalsociety.org](mailto:openscience@royalsociety.org)

on behalf of Dr Francois Fages (Associate Editor) and Professor Marta Kwiatkowska (Subject Editor)  
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# Appendix A

## Response to Reviewers

Reviewer: 1

Comments to the Author(s)

The authors have tried to address all my concerns, the quality of the paper has been improved. I only have some minor comment as bellow,

(1) please explain 'f' in equation 1;

We thank the reviewer for their comment and understand the potential confusion. There are two 'f' in equation 1, the subindex (a) and the one at the end of the equation (b).

(a) The subindex 'f' means that the property described is from the fluid. For example,  $\rho_f$  is the density of the fluid. This is important as the subindex 'm' is used for the mesh (or domain) velocity ( $\mathbf{u}_m$ ).

(b) The vector '**f**' represents external forces that may be acting on the fluid, such as gravity or fictitious forces (Coriolis or centrifugal forces).

We have incorporated such explanations in the text, which now reads:

*"where  $\rho_f$  is the fluid density,  $\mu_f$  is the fluid viscosity,  $p$  is the pressure,  $\mathbf{u}_f$  is the fluid viscosity,  $\mathbf{u}_m$  represents the domain velocity,  $\epsilon$  is the velocity strain rate  $\epsilon = \frac{1}{2}(\nabla\mathbf{u}_f + \nabla\mathbf{u}_f^t)$ ,  $t$  is time and the vector **f** represents external forces that may be acting on the fluid, such as gravity or fictitious forces (Coriolis or centrifugal forces)."*

(2) the format of equations, some subscript is in normal font, some in Italic, which is little annoying when reading. It seems the authors used bold face for vector and matrix, but not consistent across the paper, for example equation 3.

We agree with the reviewer. The number of internal iterations in the manuscript has led to some inconsistencies throughout the text. We have corrected the format of the equations and standardized to bold face for vector and matrix. Italic characters have been eliminated from all the equations.

(3) Thanks for providing details on obtaining patient-specific Young's modulus from PWV, while I am still not clear how E is optimized, the update of E seems not depending on the difference between PWV\_i and PWV\_MR. In theory, E\_0 obtained from equation 5 should give a close value to PWV\_MR, no further steps are needed. Some explanations will be helpful.

As the reviewer says, in theory, the value for  $E_0$  obtained from equation 5 should give a close value to  $PWV_{MR}$ . However, due to the intrinsic (and explained) limitations of the simulations, sometimes the error of  $PWV_0$  was above 5%. Some of these limitations include segmentation model imperfections or using anisotropic model for the solid. The iterative process was used to reduce the difference between PWV from clinical data and simulations

Reviewer: 2

Comments to the Author(s)

The authors have addressed my comments. The manuscript can be accepted by Royal Society Open Science.

We thank the reviewer for their endorsement.

Tracking of changes to the manuscript

- (1) Added the 'f' definition under equation 1.
- (2) Bold face for vector and matrix in equation 3.
- (3) We have changed the text:

"Recently, multiple studies (8,18) have used 4D flow MRI for the assessment of hemodynamics of the aorta evaluating aortic flow patterns, wall shear stress and regional aortic stiffness (via pulse wave velocity) in the thoracic aorta of bicuspid aortic valve patients"

The final form in order to add references (19,20,21) is:

"Recently, multiple studies have used 4D flow MRI for the assessment of hemodynamics of the aorta evaluating aortic flow patterns, wall shear stress and regional aortic stiffness (via pulse wave velocity) in the thoracic aorta of bicuspid aortic valve [8,18–20] and Marfan [21,22] patients."

- (4) Author order list in the web has been matched with the one in the paper.