



**SDI FINAL EVALUATION FORM 1.1**

**PART 1:**

Journal Name:	<a href="#">Annual Research &amp; Review in Biology</a>
Manuscript Number:	2013_ARRB_7229
Title of the Manuscript:	Initial insight to effect of exercise on maximum pressure in the aortic root using 2D fluid-structure interaction model

**PART 2:**

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
<p>Response to authors' major changes:</p> <ol style="list-style-type: none"><li>I thank the authors for their attempt to make their methods clearer. However, I still have troubles understanding<ul style="list-style-type: none"><li>what are the input measurements. For instance, in their response to my previous comment, the authors state that cardiac output is a measured input. This is never mentioned in Section "Material and Methods".</li><li>The authors should clearly list what is measured in the patient and how. Among the input measurements,</li><li>it should be distinguished between which are used for computations and which are used for validation (if any).</li><li>Also, I still have troubles understanding the output of the method.</li><li>If the goal is solely to compute MPLV, why is it necessary to use a detailed 2D aortic model?</li><li>An electrical model or a correlation study would probably require less hypotheses.</li></ul></li><li>The authors present a nearly perfect quadratic relation between cardiac output and heart rate. Any physiology textbook would tell that cardiac output depends on heart rate, preload, afterload and cardiac contractility. The observation that cardiac output only depends on heart rate is thus only valid at fixed preload, afterload and contractility. This probably prevents the method from being repeatable and should be mentioned in the discussion.</li><li>The authors cannot state that <math>r^2</math> values for Equations (8) and (9) are equal to 0.995, since these equations are obtained through correlations of Christie et al., which have their own <math>r^2</math> values as well.</li><li>I now agree with the author's derivation of Equations (6) and (7).</li><li>The thermodilution procedure is explained in the paper of Christie et al. It does not necessarily involve radiations, except sometimes for catheter positioning.</li><li>I thank the authors for the overall grammatical improvement of the paper. However, there remain some language issues.</li><li>I agree with the modifications.</li><li>I agree with the modifications.</li></ol> <p>Further major comments:</p> <ol style="list-style-type: none"><li>The authors should cite Wikipedia when copying-pasting from this website. (Sentence "Each aortic sinus can also be referred to as the sinus of Valsalva.")</li><li>The authors claim that their model "reliably predicted MPLV". For the reader to be convinced about that, a plot of (independently) measured vs. computed MPLV should be provided. Since it is not available, the authors cannot be so affirmative.</li><li>The "Discussion" section refers to "clinical reports", "clinical data" and "They", but all of these are not accompanied with proper references.</li><li>I do not understand why it is necessary to convert cardiac output to heart rate using the correlations.</li></ol>	<p>The authors thank the reviewer for their comments, and are pleased that the reviewers are satisfied with all the changes made to the manuscript following the original review.</p> <ol style="list-style-type: none"><li>First of all, note that this manuscript is the further findings of our research. The first one is published paper as ref [27] in which we describe elaborately FSI measurements of cardiac output, stroke volume and velocity integration. Ref 27 provides you, moreover, validation details. Current manuscript focuses on estimation of MPLV. This research is due to the fact that there is a difference between numerical and clinical cardiac output. The study question is that how much difference in MPLV gives rise to difference in cardiac output.<ul style="list-style-type: none"><li>Please see method and material section and Figure 1. (Workflow diagram). Inputs are aortic valve geometry (Echo-Doppler imaging), brachial pressures and heart rate [27].</li><li>Validation was done for cardiac output and stroke volume in ref 27 by comaring numerical and echo-Doppler measurements.</li><li>Outputs are VSPF, ADPF, VSPT and ADPT.</li><li>2D model allows us to calculate quickly, in comparison with 3D model. However, validation was done for that [27]. MPLV is the crucial contributor as the boundary condition in the aortic valve motions. To gain more exact result, clearly we must use the mechanism of aortic valve associated with the MPLV.</li><li>MPLV is the result of mechanical-based equation involved with the sophisticated aortic valve geometry. Thus, our mechanical model working on the mechanical relationship (FSI), are probable to result in more reasonable data. The rate of assumption is so high in the electrical model. Unlike electrical ones, our mechanical model can provide you mechanical parameters at each point of (x,y,z) that would be useful for further investigation. PLEASE SEE LINE 343 to 351.</li></ul></li><li>This was added in limitation section. Please see line 321</li><li>They were deleted</li><li></li><li>The amendment was done. Please see line 254</li><li>The manuscript again was revised by a native.</li><li></li><li></li><li>The sentence was restated.</li><li>They were omitted.</li><li>The amendment was done. Please see line 223</li><li>The question is not clear. If you mean equation (5), this is necessary for obtaining equations (8) and (9).</li><li>They are part of our measurements and methods.</li><li>Comsol "user's guide" was added in the ref, not the software. Matlab was omitted from the ref.</li><li>Figure 2 and its caption were amended and CDP was omitted.</li></ol>



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<p>13. Are Equations (3) and (4) part of the results as mentioned in the introduction? If so, they should be moved to the appropriate section.</p> <p>Other minor comments:</p> <p>14. Matlab or Comsol should not be included in the references list, but mentioned in the text.</p> <p>15. CDP is not included in the abbreviations table. I do not understand the difference between CDP and ADP or MPLV and VSP.</p>	
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