Computational modelling in congenital heart disease: challenges and opportunities

Computational Modelling in Congenital Heart Disease: Challenges and Opportunities

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In the last 70 years, the natural history of patients born with congenital heart disease (CHD) has been dramatically modified by the introduction and evolution of surgical repair, and more recently, percutaneous intervention. Nowadays many imaging modalities, including echocardiography, computed tomography and cardiac magnetic resonance (CMR) assist the surgeon to plan operations. In parallel, the integration of these imaging modalities with computational sciences has led to the development of patient-specific computational modelling, which is driving a paradigm shift towards predictive personalized medicine. As discussed in this editorial, robust applications of computational modelling to many CHD clinical problems will make their way into clinical practice. Recently, Yu et al. [1] applied computational modelling to tetralogy of Fallot (TOF), a cyanotic congenital heart defect occurring in approximately 1 in 3,500 births and accounting for 7% to 10% of all congenital cardiac malformations [2]. The spectrum of TOF ranges from a mild form of antero-cephalic displacement of the anterior limb of the trabecula septo-marginalis to a severe form characterised by pulmonary atresia. Complete intracardiac repair of TOF can be particularly challenging in the presence of pulmonary atresia, double outlet right ventricle, large ventricular septal defect or anomalous coronary artery pattern. Combining CMR imaging with computational mechanics, Yu et al. [1] characterised the material properties of the ventricle, suggesting that they could discriminate normal subject from those with TOF. Additionally, the proposed computational approach holds the potential to (1) predict the outcome after pulmonary valve replacement (PVR) in TOF patients, and (2) guide novel surgical procedures.

The study by Yu et al. [1] represents an interesting example of how computational modelling can improve the understanding of clinical problems with the estimation of clinically-relevant parameters and the identification of potential risks. Personalized computational modelling requires imaging data and definition of boundary conditions for the virtual construction and analysis of anatomical models. It uses mathematical models based on a set of complex equations to simulate, e.g., vessel wall mechanics, blood flow and transport phenomena in different conditions. Simulation results ideally provide clinically-relevant and insightful information to clinicians (Figure 1) [3]. Sources of uncertainty unavoidably accumulate during the modelling process, from artefacts, noise and inherent limitations of the image acquisition, to modelling assumptions and simplifications.

Stimulated by unexplored issues, and facilitated by the increasing availability in computing power, the efficiency of methods, and the ability to tackle complex problems, the ability of computational modelling to advance personalized predictive medicine in a broad range of applications is now widely recognized. By testing hypothesis in controlled conditions, recent advances in computation modelling have increased our understanding of the origin and progression of disease, providing mechanistic explanation for clinical observations. For example, computational models have contributed to the understanding if the interaction between pulmonary artery compliance, pulmonary regurgitation and right ventricle dilatation and dysfunction in TOF [4].

Furthermore, observations based on computational models can lead to the anticipation of future events. In this context, the increasing sophistication of therapeutic solutions has stimulated the development of computational tools for the virtual exploration of post-operative scenarios and patient-specific outcomes prediction [5]. Such prediction aids therapeutic planning and procedural decision-making through an optimal device selection and assessment of the effects on physiologic functions, as demonstrated by numerous examples applied to PVR, pulmonary artery stenting in TOF patients and stenting of coarctation of the aorta [6,7].

In addition, computational modelling has a fundamental role in the design, and optimization of new devices, as their performance can be predicted in conditions likely to be encountered in human trials in a cost and time effective way. [7].

Patient-specific computational modelling is receiving considerable attention from regulatory agencies and policy makers, for example the European Commission and the Food and Drug Administration (FDA). In this regard, the use of computational modelling has been advocated in the development and regulatory evaluation of new devices and interventions. To advance this, the EU-sponsored initiative “Avicenna Alliance” developed a roadmap for clinical trials based on computational models, and very recently, has recognised the urgency of having mutual standard operating procedures, identifying regulatory opportunities to position computational modelling in legislative frameworks [8]. Similar initiatives have being carried out by the FDA’s “Medical Device Innovation Consortium”.

In the near future, challenges and potential rewards of the clinical translation of computational modelling will be related to rigorous testing against clinical data, the standardization and certification of modelling techniques, and the need to obtain results within clinically relevant time scales. Large-scale studies to demonstrate the reliability of computational models and their clinical utility in terms of the impact on patients' outcome are warranted. Moreover, there is a need to carefully assess model fidelity by considering the uncertainties arising from the assumptions and the input data that underpin a model [9]. Equally, the level of uncertainty that might be acceptable in the model results must be evaluated [4]. This issue is gaining increasing recognition, with recent studies proposing uncertainty quantification strategies providing confidence levels of model predictions [10].

Another challenge will be to increase the relevance of computational models by incorporating biological and physiological processes spanning many scales and many levels of detail: such processes include vascular growth, tissue remodelling and thrombus formation. Furthermore, it is worth noting that advances in computational modelling go hand in hand with advances in imaging technologies, by incorporating increasingly high-quality functional and anatomical data, and verification of results.

In conclusion, computational modelling promises to be widely applied in the clinical practice of CHD by enriching the information from clinical imaging, improving diagnostics, surgical planning, as well as device placement. The application of computational modelling is poised to yield increasingly realistic results, to gain increasingly large clinical acceptance, and, ultimately, to improve the outcome for patients.

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Figure 1.

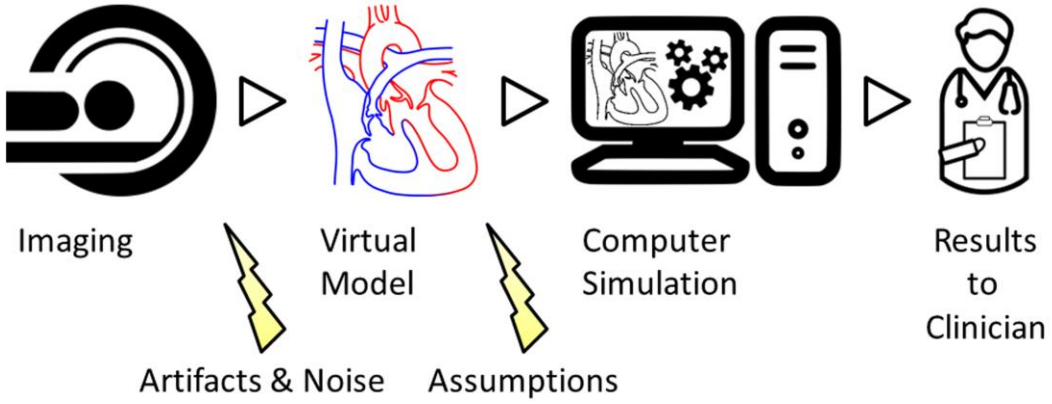

Figure 1. An example of workflow for the development of personalized computational models. The model starts from imaging data to virtually reconstruct the anatomical geometry of interest (e.g. TOF). Mathematical equations describing the physics are then solved in the virtual model via computer simulation. Simulation results ideally provide clinically-relevant information to clinicians. Final results are affected by sources of uncertainty propagating and accumulating from image acquisition to computer simulation.