Rapid and Clinically Integrated Computer Simulations to Evaluate and Predict Outcome of Invasive Interventions in Patients with Fontan Circulation

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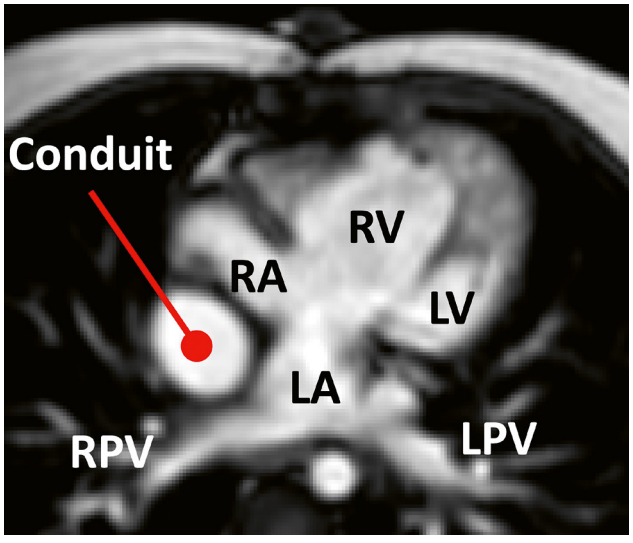
Introduction

Globally, approximately 1 in 100 children are born with some form of congenital heart defect, although this may vary in different geographical regions [1]. In cases of severe lesions where the heart cannot simultaneously sustain both the pulmonary and systemic circulation (Fig. 1), implementation of a univentricular heart is nowadays a well-established palliation.

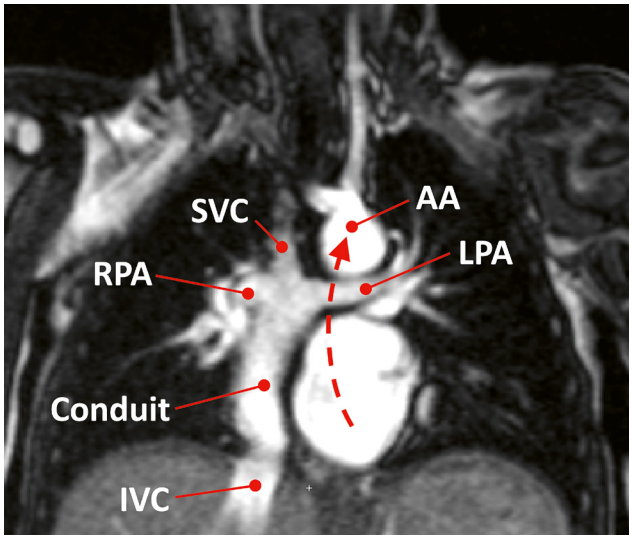
Patients with univentricular hearts typically undergo a three-stage surgical palliation and completion of Fontan circulation with a total cavopulmonary connection (TCPC). After Fontan completion, the systemic venous return flows passively to the pulmonary arteries, thereby completely bypassing the heart (Fig. 2).

Many complications follow, mainly related to increased loading of the univentricular heart, but also due to increased central venous pressure, which in turn may result in liver cirrhosis, pulmonary lesions, and a wide range of problems related to the lymphatic circulation. Additionally, these patients frequently develop various forms of systemic-to-pulmonary collaterals.

In this context, there has been great interest in the design of the TCPC itself. The shape and orientation of the



1 A 4-chamber view of a patient with hypoplastic left heart syndrome (HLHS). The hypoplastic left ventricle (LV) cannot sustain the systemic circulation. The right ventricle (RV) is instead surgically connected to the aorta and is provided with unrestricted inflow of oxygenated blood from the left and right pulmonary veins (LPV, RPV) via the left and right atrium (LA, RA). A surgically placed conduit bypasses the heart and routes deoxygenated blood from the inferior vena cava directly to the pulmonary arteries.



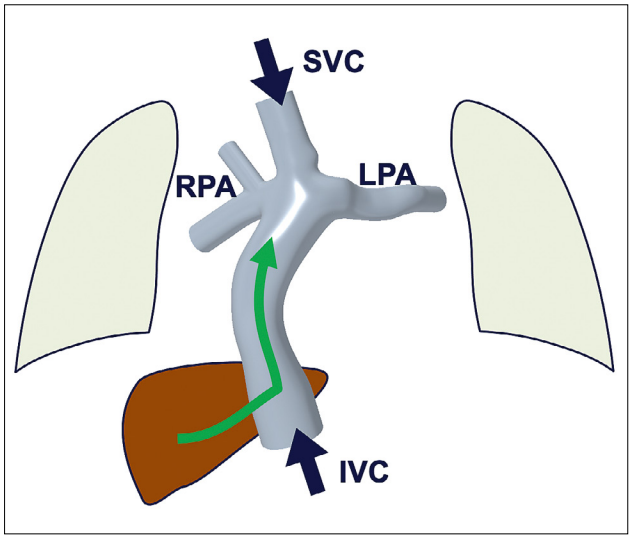
2 A coronal MR image of a total cavo-pulmonary connection (TCPC). The superior vena cava (SVC) is connected to the right pulmonary artery (RPA). The inferior vena cava (IVC) is extended with an extracardiac conduit and is connected to the pulmonary arteries (LPA, RPA). The heart only pumps to the ascending aorta (AA). Venous blood from the IVC and SVC flows passively to the lungs.

anastomosis affects the distribution of flow to the pulmonary arteries, as well as intravascular hemodynamics such as regional power loss and wall shear stress. Perhaps of greatest interest is the distribution of flow from the inferior conduit, which includes blood that drains from the hepatic veins. Inadequate distribution of hepatic flow to a lung is linked to formation of pulmonary arteriovenous malformations (PAVMs) and decreased blood oxygenation (Fig. 3).

Computational fluid dynamics (CFD) based on patient-specific anatomy and flow obtained from MRI has been used to provide an in silico assessment of the patient-specific hemodynamics of the TCPC. The aim is to improve outcomes and provide a clinically integrated framework that allows surgeons and interventionalists to evaluate invasive interventions prior to implementation [2–4].

While these efforts have to some degree been successful, significant challenges remain in translating this technology to everyday use at pediatric heart centers worldwide. The simulations are resource-intensive in terms of computational power, with run-times for solving the CFD simulations reported to be up to 45 hours on powerful servers [5]. Further advances in automation, hardware, and software may decrease the required lead time to support pre-interventional predictive simulations. In a summary of the state of progress in this field, Trusty et al. concluded that "A relatively short (one month) surgical planning timeline could be possible with these advances" [5].

Taking this aspirational goal one step further, we believe that for this technology to gain broad adoption, it is necessary to achieve clinically integrated simulations within just hours after MRI, with computational run-times of just minutes to solve the CFD simulations, such that iterations can be performed in real-time with the surgeons and interventionalists. We believe such aspirational goals are achievable with commercial off-the-shelf software. In a recent study, we aimed to validate this "lean" approach with a more "established" CFD approach [6].



3 A total cavo-pulmonary connection (TCPC). Hepatic blood (green) drains to the inferior vena cava (IVC) and reaches the lungs via the inferior conduit. A lung that receives too little hepatic blood via the pulmonary arteries (LPA, RPA) may develop pulmonary arteriovenous vascular malformations (PAVMs).

Methods

This published study included 15 patients with Fontan circulation (median age 6.7; six females) [6]. MRI was performed on a 1.5T scanner (MAGNETOM Aera, Siemens Healthineers, Erlangen, Germany). Cine images were acquired using a steady-state free precession (SSFP) sequence (typical parameters for TR/TE/flip angle: 2.9 ms/1.5 ms/60°; slice thickness: 5 mm; in-plane resolution: 1.2 ×1.2 mm). Two-dimensional phase contrast MRI (2D PC-MRI) flow measurements were acquired using a velocity encoded gradient echo sequence (typical parameters TR/TE/flip angle: 10 ms/6.5 ms/15°; in-plane resolution: 1.2 ×1.2 mm). Flow measurements of the SVC, the IVC/TCPC conduit, the pulmonary artery branches, and pulmonary veins were typically acquired using velocity encoding 80 cm·s–1 and for the aorta 200 cm·s–1.

Patient-specific 3D models of the proximal Glenn/TCPC anastomosis were constructed in the computer-aided design (CAD) software Creo Parametric (v8, PTC, Boston, MA, USA). The geometry was created by importing MRI segmentation curves created with a user-provided plugin for the freely available software Segment R4.0 (Medviso, Lund, Sweden, segment.heiberg.se) [7] into Creo Parametric, where geometry was created on the curve boundaries.

For the "lean" approach, we used Siemens Simcenter FLOEFD for Creo (v2205, Siemens EDA, Wilsonville, OR, USA), which can be integrated in various CAD systems. With the integration of FLOEFD and Creo, there is no need to manually transfer or import the anatomy to a separate CFD software. If the anatomy is modified, the user simply re-computes the CFD solution within the same user interface.

For the "established" CFD approach, we used STAR-CCM+ (v2019.1, Siemens PLM Software, Plano, TX, USA). STAR-CCM+ has been experimentally validated by Rasooli et al., with excellent agreement between in vitro measurements of tracer ink representing the distribution of hepatic blood in a TCPC and corresponding in silico simulations [8].

Both time-averaged inflows from MRI and time-dependent inflows were used as inlet flows in CFD. Computation time, as well as various hemodynamic measurements such as the hepatic flow distribution, wall shear stress, and power loss were compared.

Results

Results for the hepatic flow distribution, wall shear stress, and power loss showed excellent agreement between the hypothetically more accurate "established" solutions (time-dependent inflows in StarCCM+), and the hypothetically less accurate "lean" solution (steady-state inflows in FLOEFD). Of particular clinical interest, as previously mentioned, is the distribution of hepatic blood. Figure 4 shows regression and Bland-Altman plots of the hepatic flow distribution calculated using the hypothetically least- and most-accurate CFD approach.

The main difference between the "lean" and "established" approach was in the user time needed to prepare the simulations, and in the computation time. Based on pre-prepared templates, the user time to apply boundary conditions and mesh was 15 ± 3 minutes for the lean approach, and 54 ± 9 minutes for the established approach. In even greater contrast, the simulation time for TCPC patients using the lean approach was 2.7 (8.7 – 2.5) (median, range) minutes, whereas for the established approach the computation time was 9.7 (12.8 – 6.5) hours. Lean simulations ran on a standard 8-core workstation, while the established simulations ran on a high-performance 32-core server.

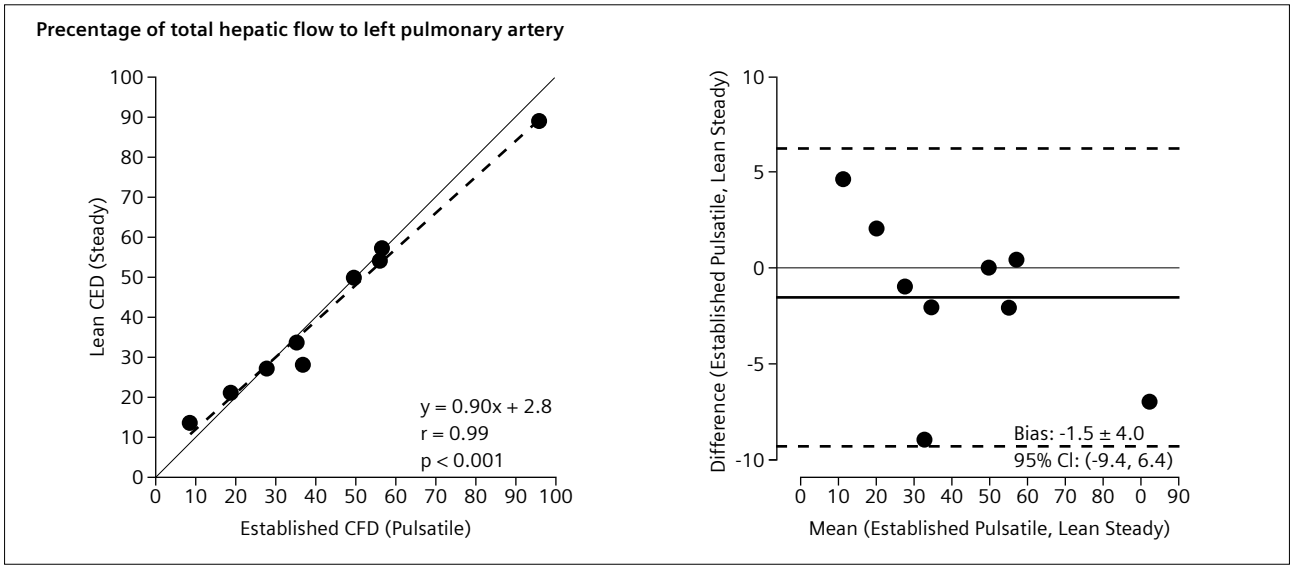
Discussion and patient cases

These results suggest that predictive simulations of Fontan hemodynamics can be prepared and accurately simulated in a matter of minutes, in contrast to the days and weeks previously reported. Moreover, the results from the rapid "lean" approach agree well with results obtained with more "established", albeit more resource-intensive methods, which have been validated in highly controlled in vitro experiments [8].

It is important to note that the total time to achieve such simulations also requires a prior MRI examination, interpretation of MRI anatomy and flows, and 3D segmentation of the anatomy. In our experience, with planning, these preceding steps can be performed in approximately four hours. This means that all such pre-surgical diagnostics and predictions can be prepared on the same day, as integrated elements of routine pre-surgical preparations.

With increased regionalization and centralization, reducing the number of outpatient visits is important. With lean CFD, there is time to perform predictive simulations even when the pre-interventional MRI is performed after the patient has arrived for elective surgery. This may be a time-efficient way to obtain updated information prior to the surgical intervention and can save time and travel costs for the family. Additionally, in catheter-based interventions between and after the major Fontan surgical stages, the short simulation times of lean CFD may aid in interventional decision-making based on acute findings from these procedures.

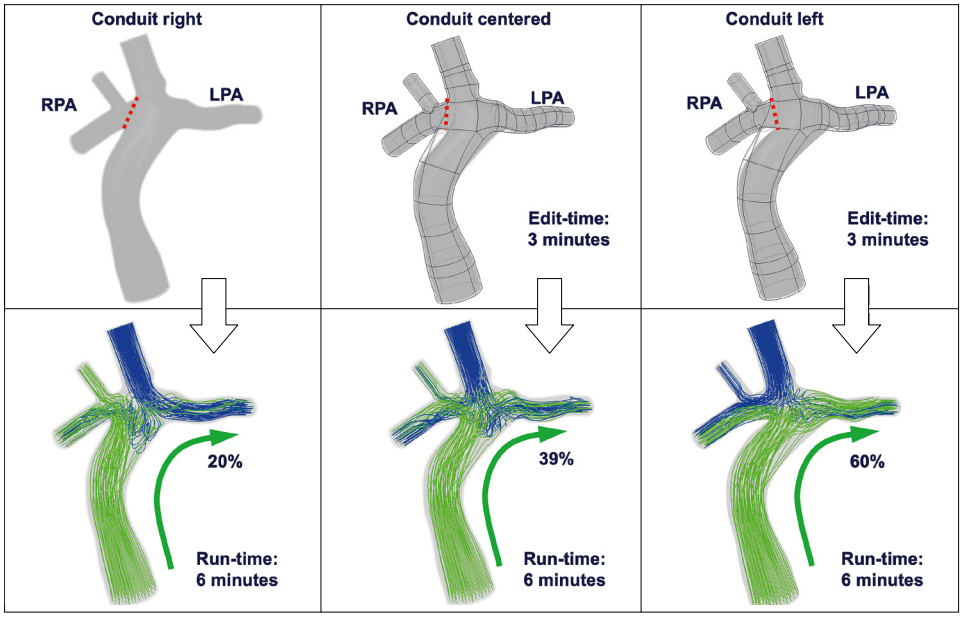
We can illustrate this with a case in which surgeons wish to explore the effect of various placements of the inferior conduit prior to TCPC surgery (Fig. 5). Given that MRI was previously performed, the model was segmented and prepared in CFD with boundary conditions of flow obtained from MRI. The CFD user can then sit with the surgeons and interactively change the model with suggest-



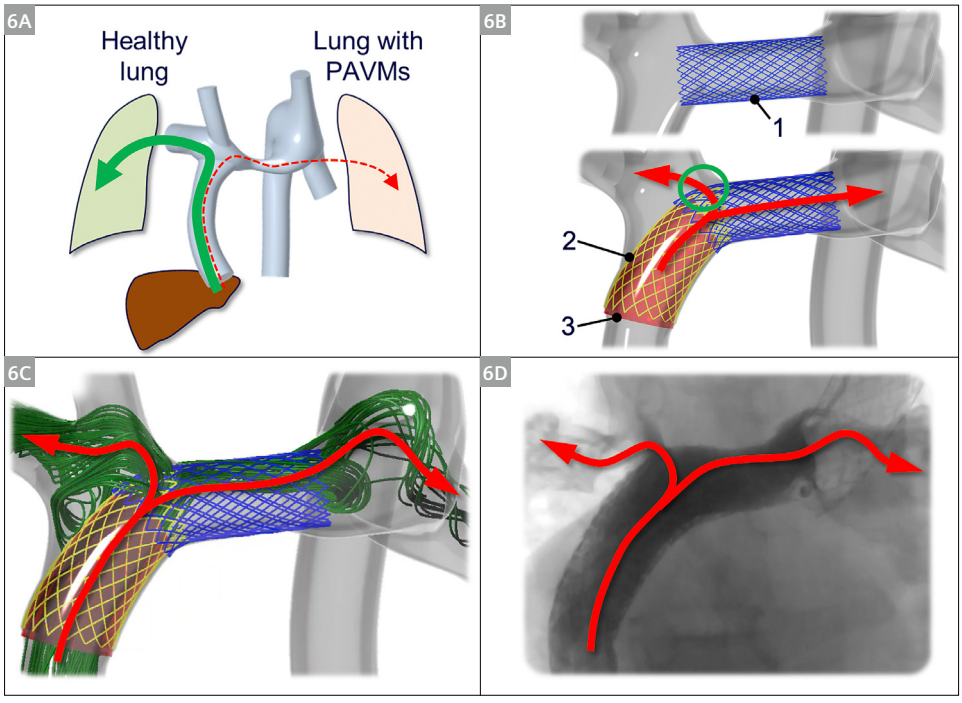
4 Linear regression (left) and Bland-Altman analysis (right) of hepatic flow distribution to the left pulmonary artery, comparing steady-state lean CFD with pulsatile established CFD. In the left graph, computation time for the x-axis results was 9.7 (12.8 – 6.5) (median, range) hours, whereas computation time for the y-axis results was 2.7 (8.7 – 2.5) minutes. Figure adapted from Frieberg et al., Springer Nature, through a CC BY license.

ed conduit placements, well within half an hour. Thus, surgeons can explore surgical options very close to the start of procedures, and even during ongoing surgery if unexpected situations arise.

Beyond these benefits of rapid and clinically integrated computer simulations, modern CAD systems offer tools for designing complex geometries such as endovascular devices and deformed stents. With integrated CAD and CFD software, these devices can be included in the 3D model for visualization and simulation purposes. Figure 6 illustrates a case where a minimally invasive endovascular intervention with a complex stent implantation was designed with support from CFD [9]. Only 8% of the hepatic blood reached the left lung, which resulted in formation of pathological pulmonary arterio-venous malformations (PAVMs) [10]. CFD simulations of the proposed stent design showed that hepatic flow to the left lung would increase to 20%. Post-interventional MRI confirmed that the hepatic flow to the left lung had increased to 20%, and the patient's oxygen saturation at rest improved, as did her general well-being (Fig. 6).



5 The left column shows anatomy and CFD results of a TCPC investigation where the conduit was initially oriented toward the RPA. The center column shows anatomy and results where the conduit placement was moved slightly to the left. The right column shows anatomy and CFD results of a further left placement of the conduit. Results show increased hepatic flow toward the LPA as the conduit is shifted left. All simulations took 6 minutes on a standard DELL XPS 15 laptop with an i7 processor and 16 GB RAM.



6 **(6A)** Patient with hepatic blood flowing mainly to the left right lung and PAVMs in the left lung. **(6B)** Proposed staged endovascular intervention to improve hepatic flow to the left lung. 1: Open cell stent in central pulmonary artery. 2, 3: Open cell stent into conduit with internal covered stent, leaving a fenestration (green circle) for hepatic blood to flow to the right lung. **(6C)** MRI-based pre-interventional simulation of proposed stenting. **(6D)** Post-interventional fluoroscopic angiogram showed good agreement between contrast flow and the pre-interventional simulation. Figure adapted from Frieberg et al., Springer Nature, through a CC BY license.

Conclusion

We conclude that rapid and clinically integrated MRI-based computer simulations to evaluate and predict the outcome of invasive interventions are feasible and cost-effective in terms of technical and medical resources. We hope that these advances, based entirely on off-the-shelf commercial software, will be adopted by more centers worldwide.

References

1 Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, et al. Global birth prevalence of congenital heart defects 1970-2017: Updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019;48(2):455–463.

2 Restrepo M, Colleen Crouch A, Haggerty CM, Rossignac J, Slesnick TC, Kanter KR, et al. Hemodynamic Impact of Superior Vena Cava Placement in the Y-Graft Fontan Connection. Ann Thorac Surg. 2016;101(1):183–9.

3 Haggerty CM, Restrepo M, Tang E, de Zélicourt D a, Sundareswaran KS, Mirabella L, et al. Fontan hemodynamics from 100 patient-specific cardiac magnetic resonance studies: A computational fluid dynamics analysis. J Thorac Cardiovasc Surg. 2014;148(4):1–10.

4 Ahmed Y, Tossas-Betancourt C, van Bakel PAJ, Primeaux JM, Weadock WJ, Lu JC, et al. Interventional Planning for Endovascular Revision of a Lateral Tunnel Fontan: A Patient-Specific Computational Analysis. Front Physiol. 2021;12:718254.

5 Trusty PM, Slesnick TC, Wei ZA, Rossignac J, Kanter KR, Fogel MA, et al. Fontan surgical planning: Previous accomplishments, current challenges, and future directions. J Cardiovasc Transl Res. 2018;11(2):133–144.

6 Frieberg P, Aristokleous N, Sjöberg P, Töger J, Liuba P, Carlsson M. Computational Fluid Dynamics Support for Fontan Planning in Minutes, Not Hours: The Next Step in Clinical Pre-Interventional Simulations. J Cardiovasc Transl Res. 2022;15(4):708–720.

7 Heiberg E, Sjögren J, Ugander M, Carlsson M, Engblom H, Arheden H. Design and validation of Segment - freely available software for cardiovascular image analysis. BMC Med Imaging. 2010;10:1.

8 Rasooli R, Kose B, Samaneh Lashkarinia S, Sasmazel A, Pekkan K. In vitro measurement of hepatic flow distribution in Fontan vascular conduits: Towards rapid validation techniques. J Biomech. 2022;137:111092.

9 Frieberg P, Sjöberg P, Hedström E, Carlsson M, Liuba P. In vivo hepatic flow distribution by computational fluid dynamics can predict pulmonary flow distribution in patients with Fontan circulation. Sci Rep. 2023;13(1):18206.

10 Duncan BW, Desai S. Pulmonary arteriovenous malformations after cavopulmonary anastomosis. Ann Thorac Surg. 2003;76(5):1759–66.

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