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STATE OF THE ART REVIEW
Congenital heart disease

Three-dimensional printing, holograms, computational modelling, and artificial intelligence for adult congenital heart disease care: an exciting future

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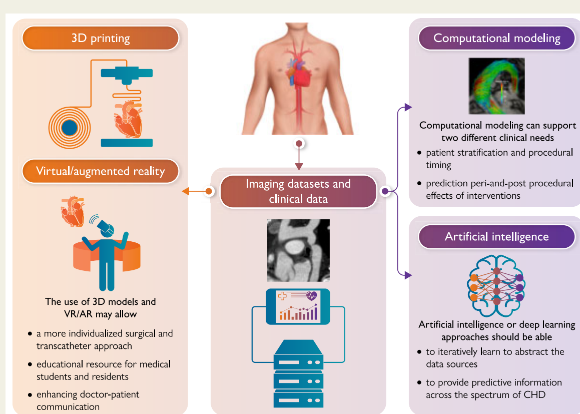
Graphical Abstract



An overview of these evolving technologies and approaches, helping physicians to better understand their real-world applications in adult congenital heart disease (ACHD) before a clinical workflow implementation. 3D, three-dimensional; CHD, congenital heart disease; VR/AR, virtual reality/augmented reality.

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Abstract

Congenital heart disease (CHD) is often comprised of complex three-dimensional (3D) anatomy that must be well understood to assess the pathophysiological consequences and guide therapy. Thus, detailed cardiac imaging for early detection and planning of interventional and/or surgical treatment is paramount. Advanced technologies have revolutionized diagnostic and therapeutic practice in CHD, thus playing an increasing role in its management. Traditional reliance on standard imaging modalities including echocardiography, cardiac computed tomography (CT) and magnetic resonance imaging (MRI) has been augmented by the use of recent technologies such as 3D printing, virtual reality, augmented reality, computational modelling, and artificial intelligence because of insufficient information available with these standard imaging techniques. This has created potential opportunities of incorporating these technologies into routine clinical practice to achieve the best outcomes through delivery of personalized medicine. In this review, we provide an overview of these evolving technologies and a new approach enabling physicians to better understand their real-world application in adult CHD as a prelude to clinical workflow implementation.

Keywords Computational modelling • 3D printing • Virtual reality • Augmented reality • Artificial intelligence • Adult with congenital heart defect

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Introduction

The treatment of congenital heart disease (CHD) represents a unique example of disruptive innovation. By applying various focused surgical and/or interventional haemodynamic procedures in early life to correct lesions, pioneers in the field have transformed the life of children born with CHD.[1] While this approach is central in addressing the immediate haemodynamic and structural issues of the young patients, long-term complications and sequelae remain, representing the new boundary for those dealing with CHD. In these patients blood fluid dynamics and pressure levels are often disarrayed, either due to the original anatomical defect or as a result of a previous surgical or transcatheter treatment.[2–5] Hence, a precise and profound understanding of their dynamic anatomy is a cornerstone in providing optimal management; the open-heart surgeon is used to interacting with the real three-dimensional (3D) anatomy whereas the clinical cardiologist and interventionalist have to build a mental concept of the anatomy usually derived from two-dimensional (2D) echocardiographic and fluoroscopic data displayed on a screen. In an attempt to bridge this gap, high-quality 3D volumetric data acquisition methods [e.g. 3D transthoracic and transesophageal echocardiography, 3D rotational angiography, computed tomography (CT), and magnetic resonance imaging (MRI)] have been developed.[6]

All these 3D datasets can be accessible within 3D view systems attempting to display true depth and can be available for simulating and planning procedures. Despite the widespread use of these imaging modalities along with their 2D and 3D reconstruction capabilities, current visualizations are still limited on 2D flat screens which do not convey realistic perception of the 3D relationship between anatomy and pathology. This is especially important for CHD due to its complexity with a range of abnormalities. This can be overcome by the rapidly evolving 3D printing and virtual reality (VR)/augmented reality (AR) technologies.[7–11] 3D printed personalized models offer advantages over current visualization tools by providing physical models with high accuracy of replicating anatomy and pathology,[8,9] while VR and AR tools provide real-life experience of understanding and simulating complex cardiovascular system.[10,11]

Nowadays, one may access large imaging datasets that can be merged with electronic health records (EHRs), electrocardiogram (ECG) information, remotely collected exercise data, genetic, laboratory and omics data that, over time, will enable us to predict, with the use of artificial intelligence (AI) and deep learning (DL) approaches the most likely future patient trajectory and move towards a truly personalized medicine approach.[12,13]

In this review, we provide an overview of these evolving technologies and approaches, helping physicians to better understand their real-world applications in adult CHD (ACHD) (*Graphical Abstract*).

Three-dimensional printing: where we are now and where we are going?

Transthoracic and transesophageal echocardiography in combination with detailed cross-sectional imaging obtained from cardiac CT (CCT) and cardiac magnetic resonance (CMR) imaging are used for diagnosis, monitoring and decision-making in patients with CHD.[6] 3D reconstructions on (flat screen) displays are nowadays commonplace providing improved spatial orientation. 3D printed cardiac models have the potential to further augment patient care as they are superior in providing true 3D perspective and tactile feel required for certain complex surgical and interventional procedures or to enhance education.

The workflow involved in model creation starts with acquisition of a 3D imaging dataset.[14] Segmentation is then performed to highlight the area of interest before transfer of the 3D file to a printer for model creation and printing. Image quality (high contrast between adjacent structures, low noise and high spatial resolution) governs the ease with which segmentation is performed as well as the quality of the final model. CCT or CMR are most commonly used as source datasets.[14] They offer good spatial resolution and whole heart coverage, but are limited in visualization of thin structures such as the atrial septum and valvular tissue. 3D echocardiography is superior in this respect but anatomic visualization is limited to a pyramidal window and the blood pool to myocardium contrast is not as sharp as in CCT or CMR.[15] Resources needed to solidify a workflow for cardiac 3D printing include the following (*Figure 1*):

(1) An imaging specialist or technologist familiar with congenital heart defects and cross-sectional images to perform the image post-processing.
(2) Post-processing software to segment the 3D image dataset.
(3) A 3D printer to translate the 3D digital file into a cardiac print.
(4) A specialist familiar with the 3D printer to perform post-printing optimization.

There is a wide array of 3D printers available which vary by technique, options for multimaterial and multicolor printing, build size, layer thickness, speed, and cost. A centre must identify their 3D printing needs in order to choose the ideal components for each step in their 3D cardiac printing workflow.

The use of 3D models may allow a more individualized surgical[16] and transcatheter approach[17] in CHD patients (*Figure 2*).[18] 3D printed models may be of value in complex redo surgeries in ACHD patients[19] (*Figure 3*) and played a pivotal role in the development of transcatheter occlusion of superior sinus venosus septal defects with partially abnormal pulmonary venous connection.[20] Utilizing patient-specific 3D printing for simulation of the complex or challenging cardiovascular procedures provides enough confidence that pulmonary veins would remain competent after the procedure (*Figure 4*).

3D printing may similarly provide confidence to implant mechanical circulatory support in ACHD, narrowing the gap between patients with and without CHD being offered these advanced heart failure therapies[21] (*Figure 5*).

In general, the usefulness of 3D printing lies in specific situations where a decision on the type and mode of intervention cannot be made confidently with 2D and 3D imaging alone (*Figure 6*).[22]

The wide heterogeneity of congenital heart lesions and interventions coupled with a scarcity in available pathologic specimens renders 3D printed models a valuable alternative educational resource. Several randomized controlled trials have shown the superiority of 3D printed models over traditional teaching methods in learning complex CHD for medical students and residents.[23–25]

Further, 3D printed models present clinical value in enhancing doctor–patient communication in daily practice by enhancing patients or parents of patients understanding of the cardiovascular disease, with reduced consultations in patients using the 3D printed models compared to those without using the models.[26,27]

In addition to improving visualization and communication about complex ACHD conditions and potentials repairs, a patient-specific 3D printed model can be used to predict the local deformation that an implanted device may create. By using highly selected print materials that mimic some biomechanical properties of cardiac tissue, the bidirection deformation of a transcathter procedure can be modelled. This two-way modelling refers to both the deformation of a cardiac device (e.g. valve stent frame compression) by cardiac tissue; as well as the deformation of the cardiac tissue by the device (e.g. annular enlargement or disruption). Models incorporating tissue-like mechanical properties were recently described for the deployment of transcatheter mitral valve replacement devices.[28]

The limitations of 3D printing may be summarized in several aspects including limited materials to represent realistic cardiac tissue properties, restricted resolution, manufacturing and turnaround time and high costs.[29] However, the main challenge is to standardize the 3D printing process itself. Tissue engineering is an emerging field which combines biology, medicine, engineering yielding the promise of 3D printing vascular scaffolds, valves, heart tissue patches, myocardium and ultimately beating hearts. Bioprinted cardiovascular tissue matching patient-specific geometry could be biodegradable and mechanically compatible with vascular tissues that will potentially allow regeneration, durability and growth.[30] Although promising, 3D bioprinting still faces many technological challenges before it is available to patients with ACHD in clinical practice.

Virtual reality and augmented reality: imaging or imagining?

VR and AR are innovative visualization tools for cardiovascular care.[31,32] VR and AR both simulate visual sensations in real-time and track the user's position and movements[33–35] but refer to two distinctly different aspects. More specifically, VR allows the user to completely immerse in a virtual 3D space, usually using a head-

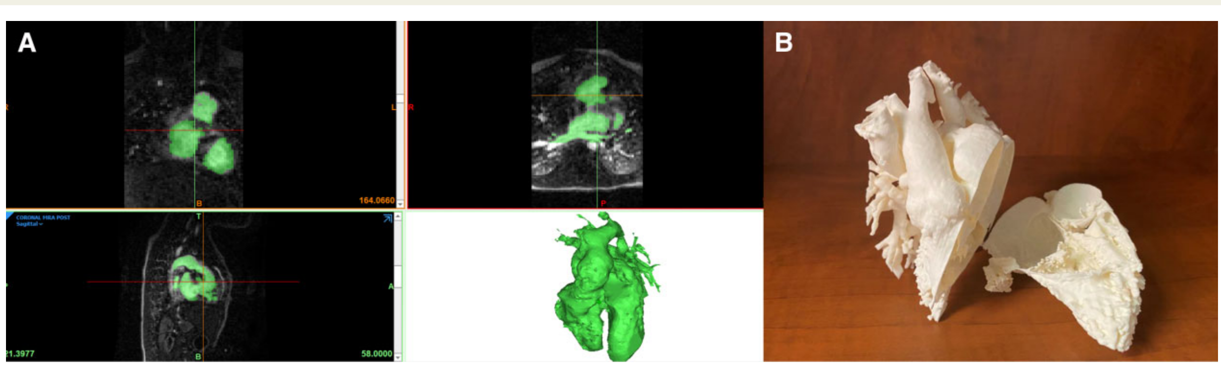

Figure 1 (*A*) An example of segmentation of a cardiac magnetic resonance imaging dataset in a patient with complex intracardiac anatomy including a ventricular septal defect and double outlet right ventricle. (*B*) Three-dimensional printed cardiac model cropped to demonstrate the intracardiac anatomy for presurgical planning.

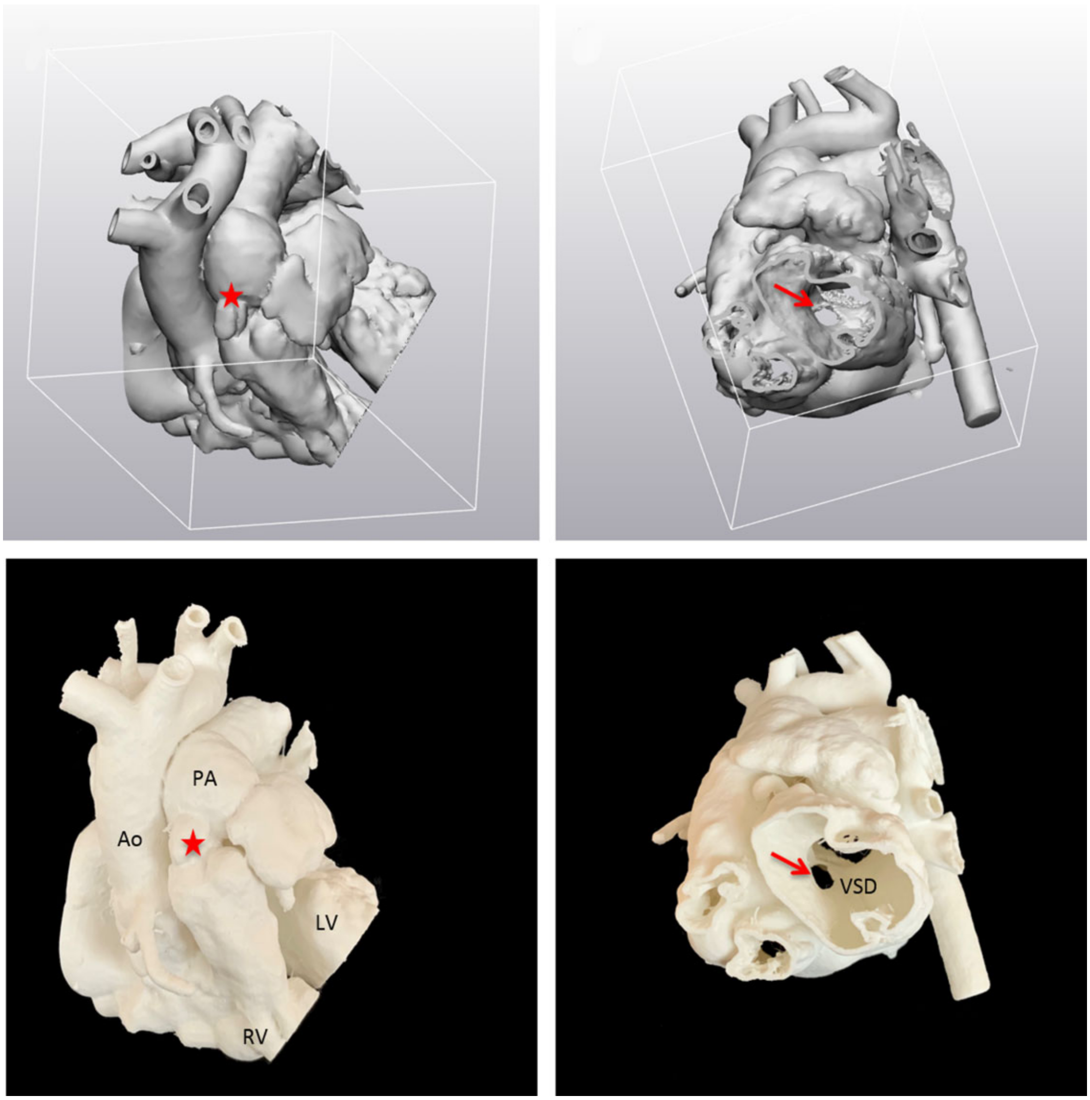

Figure 2 Double outlet right ventricle with side-by-side transposition of the great arteries and prior dilatable banding (asterisk) of the pulmonary artery. There is a non-committed ventricular septal defect (arrow). Based on the three-dimensional printed model, biventricular repair was deemed improbable and the child was referred for single ventricle palliation (total cavopulmonary connection). LV, left ventricle; RV, right ventricle; Ao, aorta; PA, pulmonary artery; VSD, ventricular septal defect.

mounted display covering the whole field of view[36] (*Figure 7A*). In contrast, AR illustrates virtual elements in a real-world environment, integrating selected imaging modalities into reality, improving management during complex cardiovascular procedures[37] applying translucent displays or head-mounted displays[21] (*Figure 7B*). The real-time fusion of different imaging modalities has already demonstrated a significant improvement in the quality and safety of cardiovascular care.[38]

Innovative strategies using VR and AR have also been successfully applied in CHD, in the field of education, (*Figure 7C*), as well as for training and planning of interventions. Especially VR has been evaluated in CHD: Kim *et al*. performed an observation study with medical trainees discussing different cases of CHD.[39] They demonstrated that the most preferred display system among medical trainees for visualizing CHD during group educational and diagnostic discussions is fully immersive VR. In a prospective, randomized controlled trial on students and healthcare professionals, two educational strategies have been compared. The intervention group used a VR headset to visualize a lecture with 3D heart models and the control group used a desktop computer interface with the same models; participants using the VR reported a better learning experience and self-assessment, suggesting VR may increase learner engagement in understanding CHD.[40] Lau *et al.*[41] compared 3D printing and VR in a cross-sectional study involving 35 medical practitioners in four selected CHD cases using six different questionnaires. Both VR and 3D printed heart models were comparable in terms of the degree of realism, but VR was perceived as more useful in medical education and preoperative planning. Of note, 72% of the participants indicated

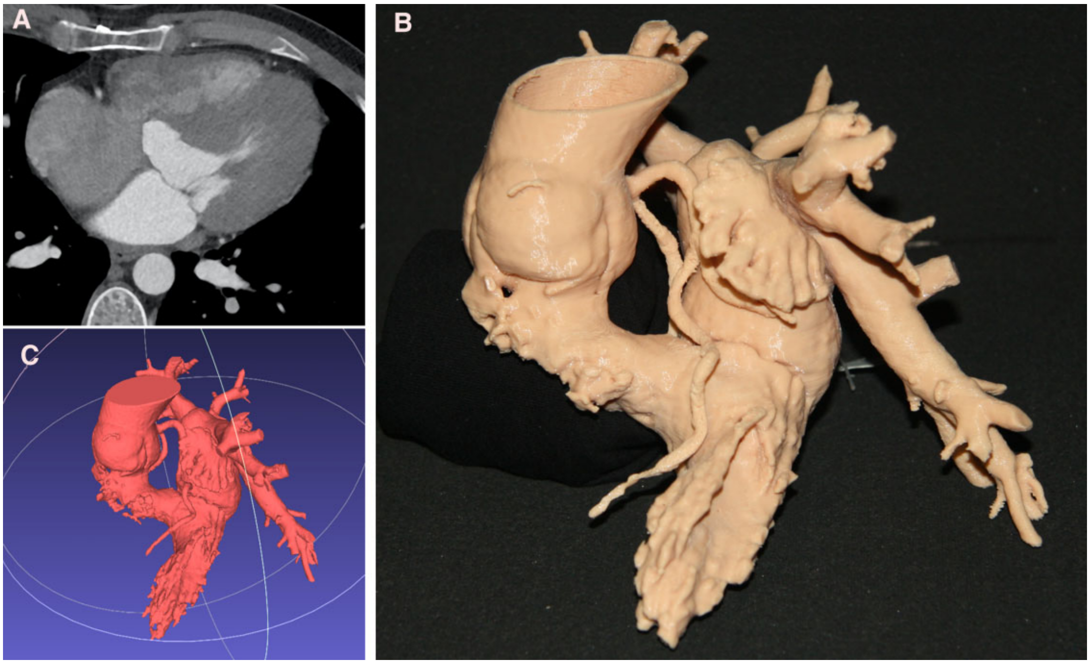

Figure 3 A 32-year-old patient with diagnosis of double outlet right ventricle and prior surgical repair of ventricular septal defect closure and residual subvalvular aortic stenosis. Pre-procedural surgical planning based on computed tomography images (*A*) was not conclusive regarding which approach would be better, either left ventricular outflow tract resection or Konno/Bentall. A three-dimensional virtual model was segmented (*B*) based on computed tomography images. The three-dimensional printed model (*C*) aided at convincing the clinical team of the seriousness of the surgery and to communicate with patient and relatives. Eventually, left ventricular outflow tract resection through the aortic valve was performed as with the three-dimensional printed model.

that VR provided additional benefits compared to conventional medical imaging visualizations. In- and outside CHD, evidence is growing that VR and AR can improve the education of medical students and trainees, especially in the context of the understanding of 3D relationships.[42,43]

Several studies investigated the value of VR and AR in surgical or interventional therapy planning.[44,45] Ong *et al.*[46] reported that use of VR presurgical planning in complex CHD allowed interaction with intra- and extracardiac anatomy. The authors concluded that VR served as a valuable complement to traditional preoperative planning methods. This has been confirmed in a study investigating the planning of surgical atrioventricular valve repair in children. Compared with standard imaging, in 67% of cases, VR improved the surgeon's understanding of each patient's pathology and the most appropriate surgical approach. Furthermore, the study reported that after viewing patient cases on VR, surgeons reported that they would have made minor modifications to the surgical approach in more than half of the cases.[47] In pre-surgical planning, AR can help to illustrate holograms in 3D. In a study on 26 patients scheduled for CHD surgery, AR-supported preparation surpassed 2D-monitor imaging in all categories, especially the depth perception and the representation of the pathology. Interestingly, it also significantly decreased the preparation time.[48] VR models can also help plan and decide on hybrid surgical and transcatheter strategies in CHD.[49] The best evidence for the role of VR exists in imaging in the interventional closure of shunts. The increasing role of VR in determining individual threshold or need for intervention as well as assessing suitability for intervention has been recently reviewed.[50] Another approach is the simulation of transcatheter CHD interventions in VR. Nam *et al.*[51] developed a method allowing virtual 'testing' of device placements in multiple cardiac phases rather than inferring adequate fit from 2D measurements. The authors conclude that VR might allow facilitating the estimation of the force of the device on the tissue with relevance for predicting embolization and erosion. This also applies to catheter ablation to treat arrhythmias in adults with CHD. Knecht *et al.*[52] described the advantage of integrating the electro-anatomical map into the 3D surrounding structures as well as the possibility to follow the access path of the catheter to guide catheter manipulation. VR has also been used directly after surgical correction of ventricular septal defects; intraoperative echocardiographic visualization in VR improved assessment of the tricuspid valve leaflet mobility analysis after surgery.[53]

Besides these applications, VR can help explaining CHD to patients and relatives to increasing understanding, including potential treatment strategies.[54] However, technical aspects need further improvements, especially concerning real-time VR/AR visualization of 3D data with sufficient resolution. More data, user-friendliness, flexibility, portability, and cost-benefit analyses will determine the future use of VR and AR in diagnostic and therapeutic strategies in CHD.[55] Cost efficiency seems promising since VR devices currently cost several hundred Euro and AR devices around 5000 Euro and they can be re-used in each individual case contrasting 3D printing. Nevertheless, software availability is currently limited but distribution growing and must come beyond academic single developments. Therefore, the

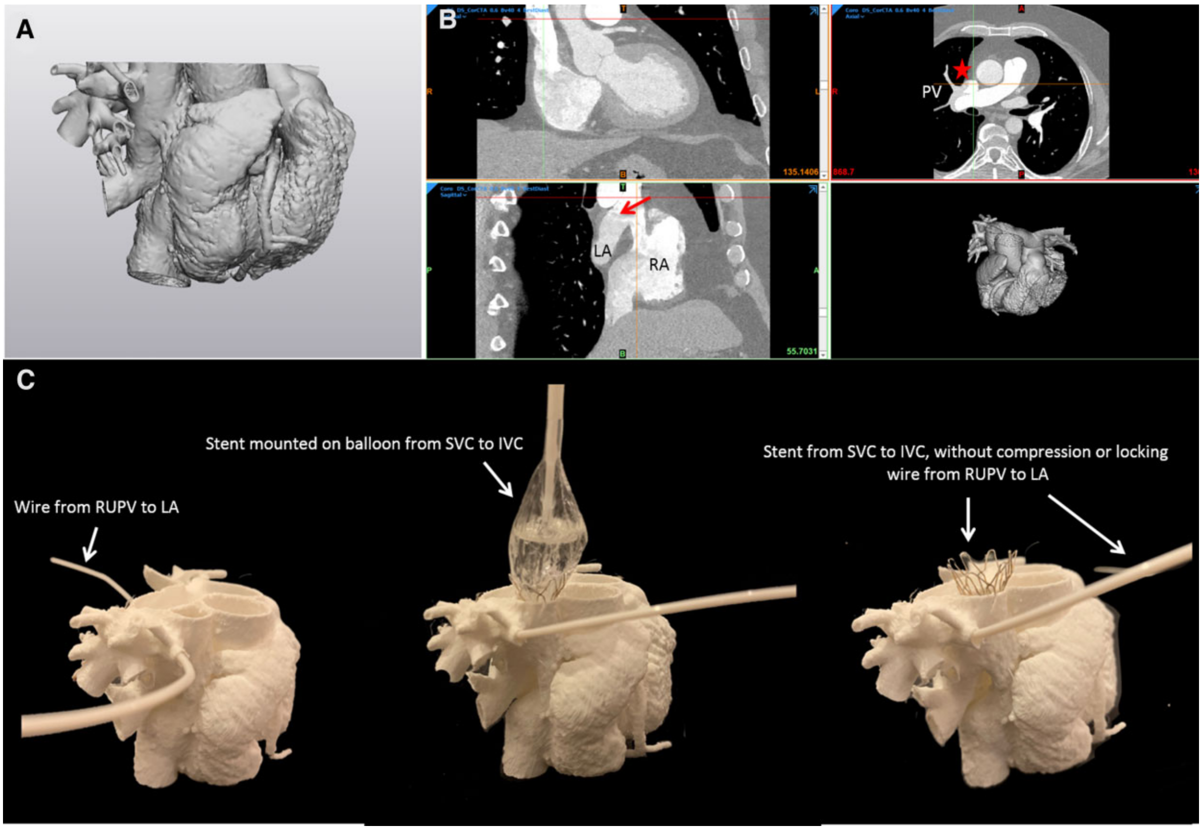

Figure 4 Three-dimensional segmentation (*A*), computed tomography (*B*) and three-dimensional printed model (*C*) of a patient with a superior sinus venosus septal defect with partially abnormal pulmonary venous connection from the right upper pulmonary vein to the superior vena cava. The three-dimensional printed model allows to check whether pulmonary veins remain competent after stent implantation in the superior vena cava. IVC, inferior vena cava; LA, left atrium; RA, right atrium; RUPV, right upper pulmonary vein.

software is the central demand for individual use. However, these virtual techniques are already finding their role in real care of CHD.

Computational modelling

The impact of biomechanical disarray on disease progression and post-surgical late complications can be reliably quantified via patient-specific computational modelling that can support two different clinical needs: (i) patient stratification and procedural timing and (ii) prediction of peri- and post-procedural effects of interventions.

Support to patient stratification and procedural timing

criteria for monitoring disease progression and defining the timing for intervention currently rely mostly on morphologic and macroscopic functional markers (e.g. volumes, ejection fraction, and global longitudinal strain for ventricles; diameter and diameter growth rate for the aorta), which are limited by measuring the late and irreversible expression of the underlying pathophysiological changes. Sharper and more sensitive markers able to capture disease progression even in the absence of macroscopic anomalies and are highly desirable and can consist of biomechanical quantities, which can be quantified through two approaches, each one with its own pros and cons:

- *Via advanced processing of medical imaging* that does not require major assumptions, however, they are affected by the uncertainty inherent to the imaging data. An example is the quantification of blood fluid dynamics based on time-resolved phase-contrast CMR imaging (4DFlow). This imaging modality yields the voxel-wise quantification of blood velocity in the 3D space over a region of interest, at multiple time points during the cardiac cycle. Upon suitable filtering, velocity data can be post-processed to compute a broad variety of hemodynamic parameters providing insight into CHD-related alterations (*Figure 8*).

In the ascending aorta of patients with the bicuspid aortic valve (BAV), wall shear stresses (WSS) anomalies associated with the skewed high-velocity jet impinging on the wall can be computed and evident anomalies in their peak value, direction and time-course can be detected even in absence of vessel dilation, suggesting that WSS-related anomalies may precede aortic dilation.[56]

In coarcted aortas, it is possible to quantify the trans-coarctation pressure drop.[57,58] In patients with pulmonary regurgitation after

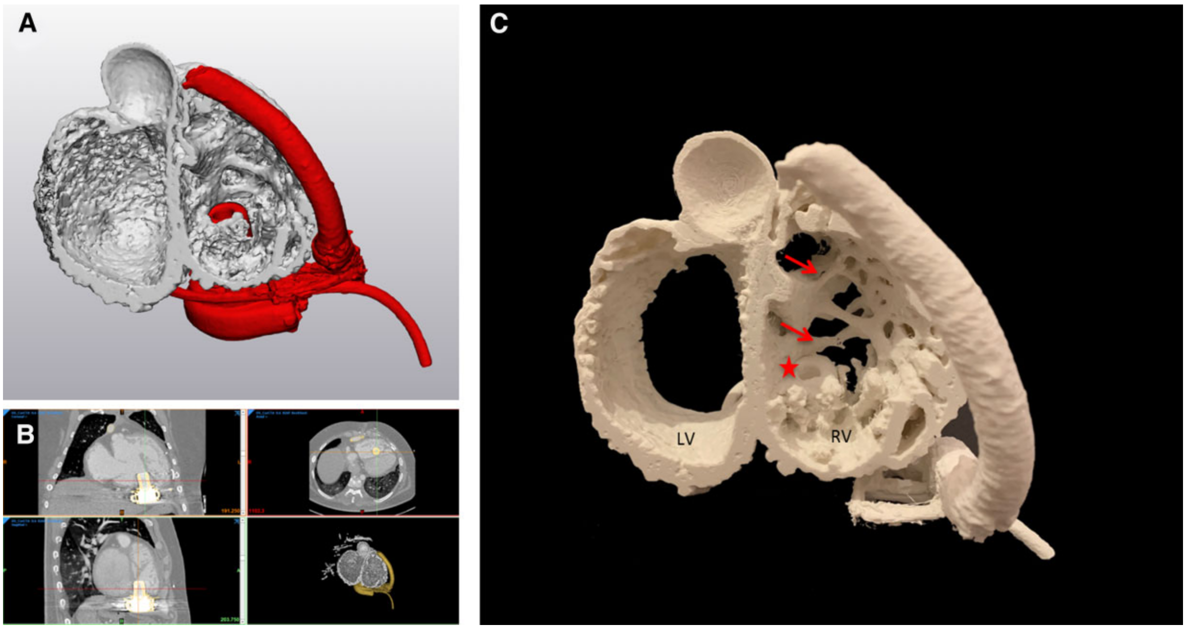

Figure 5 Three-dimensional segmentation (*A*), computed tomography (*B*) and three-dimensional printed model (*C*) of a HeartWare (Medtronic, MI) device (asterisk) placed on the diaphragmatic side of the systemic right ventricle in a patient with transposition of the great arteries after Senning repair with end-stage heart failure. Note that apical implantation was not feasible as it would cause inflow limitation caused by the hypertrophic moderator band and trabeculae (arrows). LV, left ventricle.

surgical repair of tetralogy of Fallot, derangements in intracavitary kinetic energy (KE)[59] and in turbulent kinetic energy (TKE)[60] were observed in the right ventricle (RV), with the highest TKE values localized in RV outflow tract.[60] Also, in both RV and left ventricle (LV), the pattern of the resultant load exerted by blood on the myocardial wall, i.e. the haemodynamic force, is altered with respect to healthy subjects and these alterations may remain after pulmonary valve replacement, suggesting that biventricular pumping does not normalize after surgery.[61] Despite the potential highlighted, 4DFlow imaging has limitations to bear in mind when exploiting it: in a nutshell, 4DFlow-derived velocity data are reasonably accurate in the bulk flow, characterized by mid-to-high velocities, but not in the near-wall regions, characterized by low-velocities. Consequently, quantities such as peak velocities and KE can be reliably quantified, whereas the computation of quantities such as WSSs is affected by major uncertainty.[62]

- *Via computational simulations*, where the relevant biomechanical indices are not quantified based on measurements but computed by solving the equations that describe the physics of the analyzed tissues and organs. For instance, blood fluid dynamics can be quantified with extreme space- and time-resolution via computational fluid dynamics (CFD) models, where blood flow patterns within the cardiovascular system are computed by solving in a well approximated way the physical laws governing fluid motion.[63] These data are still affected by uncertainty due to simplifying assumptions and model settings. However, this uncertainty can be quantified, and confidence intervals can be extracted for the computed indices[64] (*Figure 8*).

Simulation-based predictive analysis

CFD can also be used to predict post-operative haemodynamic changes and may contribute to the design of the optimal surgical reconstruction, e.g. in case of patients with aortic coarctation treated by resection with end-to-end anastomosis.[65] The Fontan circulation, in patients with palliated single ventricle heart defects, has been largely simulated through CFD to identify the configuration that minimizes energy loss and power loss associated with the Fontan connection, which can impact the clinical outcome.[66,67]

Along with CFD, other simulation techniques can be used to quantify different aspects: lumped-parameter models (LPMs) to quantify flow rate and pressure in vast and complex portions of the cardiovascular tree, finite element models (FEMs) to quantify stresses and strains in cardiovascular solid tissues,[68,69] fluid–structure interaction (FSI) models to study the interplay between blood flow and the surrounding solid tissues.[70,71] FEMs and FSI models fall in the same general framework outlined with reference to CFD, thus requiring simplifying assumptions and fine-tuning of model parameters. Instead, LPMs use a more simplified approach: the relevant part of the cardiovascular system is described as a network of compartments; each compartment represents, e.g. a vessel or a heart chamber and describes the corresponding pressure-flow rate response through a combination of hydraulic resistances, compliances, and blood inertances. The geometrical and physical properties of blood and of wall tissue are not described in detail but are condensed in these parameters, leading to the fast computation of pressures and flow rates in the different compartments. However, the detailed distribution of blood velocity and of WSSs cannot be obtained; also, the tuning of a relevant number of parameters is typically required to personalize these models.

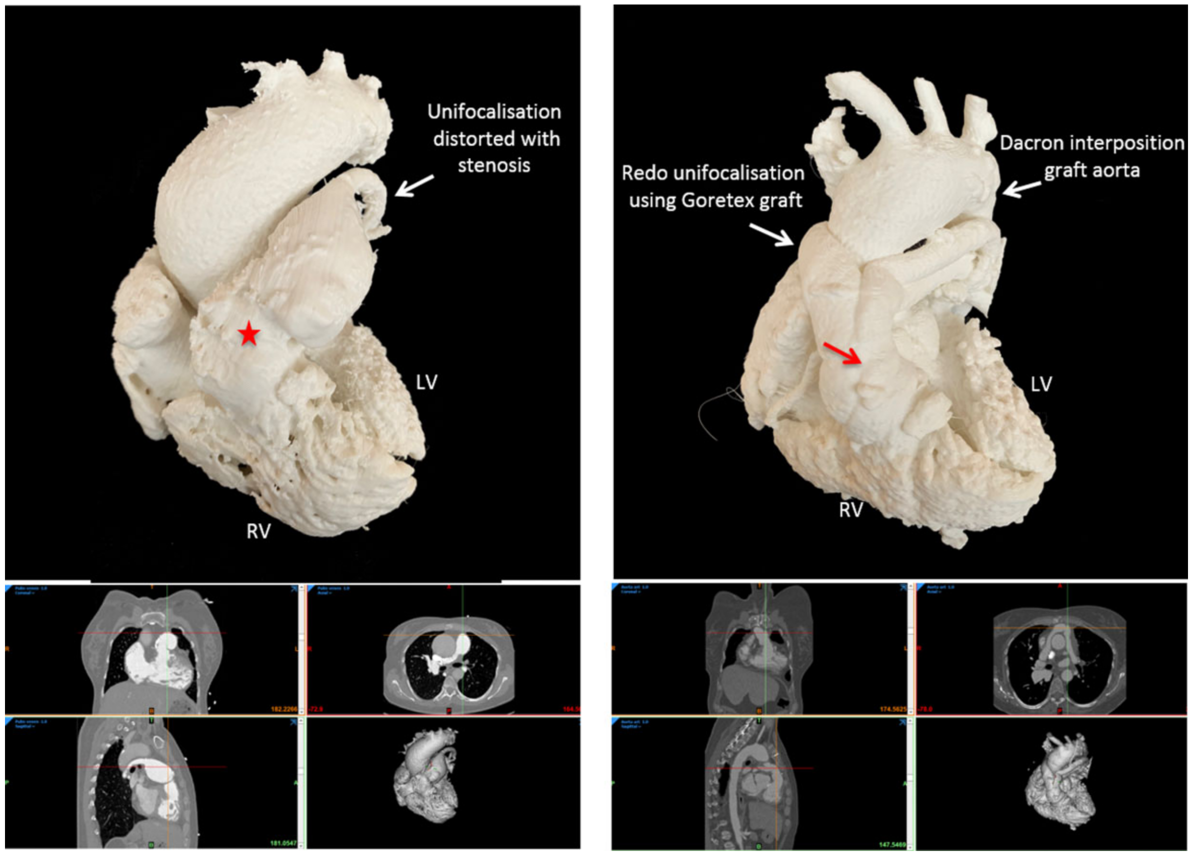

Figure 6 Three-dimensional segmentation and three-dimensional printed model of a patient with tetralogy of Fallot (pulmonary atresia) and multiple major aortopulmonary collateral arteries following bilateral unifocalization and Fallot repair with a 24 mm homograft (asterisk). Referral because of right ventricular pressure load of the right ventricle. Based on the three-dimensional printed model the surgeon opted for redo unifocalization with Goretex grafts (2 left, 2 right) placed anterior of the aorta and a new pulmonary homograft (arrow). The aneurysmatic aorta was replaced with a Dacron graft.[7] LV, left ventricle; RV, right ventricle.

FEMs have been used to simulate stent deployment in complex CHD cases to aid preprocedural planning. In candidates for transcatheter pulmonary valve replacement, FEMs can help assess procedure feasibility and clinically relevant peri-procedural risks, e.g. coronary artery compression, stent fracture, RV outflow tract injury or arterial distortion.[72,73]

In patients affected by aortic coarctation, percutaneous stenting of the coarcted region was simulated to test different treatment scenarios in terms of stresses induced by stent expansion on the aortic wall.[74–76]

FSI models have been used to reproduce the native BAV haemodynamics and biomechanical response to deepen the biomechanical implications associated with flow-induced WSSs acting on BAV leaflets and progressive valve calcification.[77–79] Of note, this is the only approach allowing for the analysis of WSS on heart valves, which are thin and highly deformable and undergo fast transient motions, so that they cannot be captured by 4DFlow imaging nor analyzed by CFD.

An FSI approach, able to take the compliance of vessels into account, has been employed to investigate blood flow haemodynamics in a patient-specific total cavopulmonary connection and numerically test novel approaches for increasing both pulsatility and pressure of blood flow in pulmonary arteries.[80]

The use of these modelling strategies in a real clinical setting has been and still is hampered by their requirement in terms of engineering background, computational resources, and time expense of the pipeline that starts with image processing and ends with the analysis of the model results. However, clinically oriented modelling solutions were recently proposed in the attempt to fill this gap. For instance, Hsia and colleagues proposed a LPM for the fast patient-specific prediction of the haemodynamics following the different stages of Fontan procedure, including the possibility to account for different surgical options. This model showed good clinical accuracy and was embedded in a user-friendly app for the iOS platform, a mobile operating system.[81] Frieberg *et al.*[82] instead proposed a 'lean' CFD pipeline to simulate post-Fontan blood flow; the entire pipeline was integrated in a single software package, thus avoiding tedious data transfer operations, it proved accurate when compared with a gold standard, and yielded detailed results in minutes when using a standard workstation.

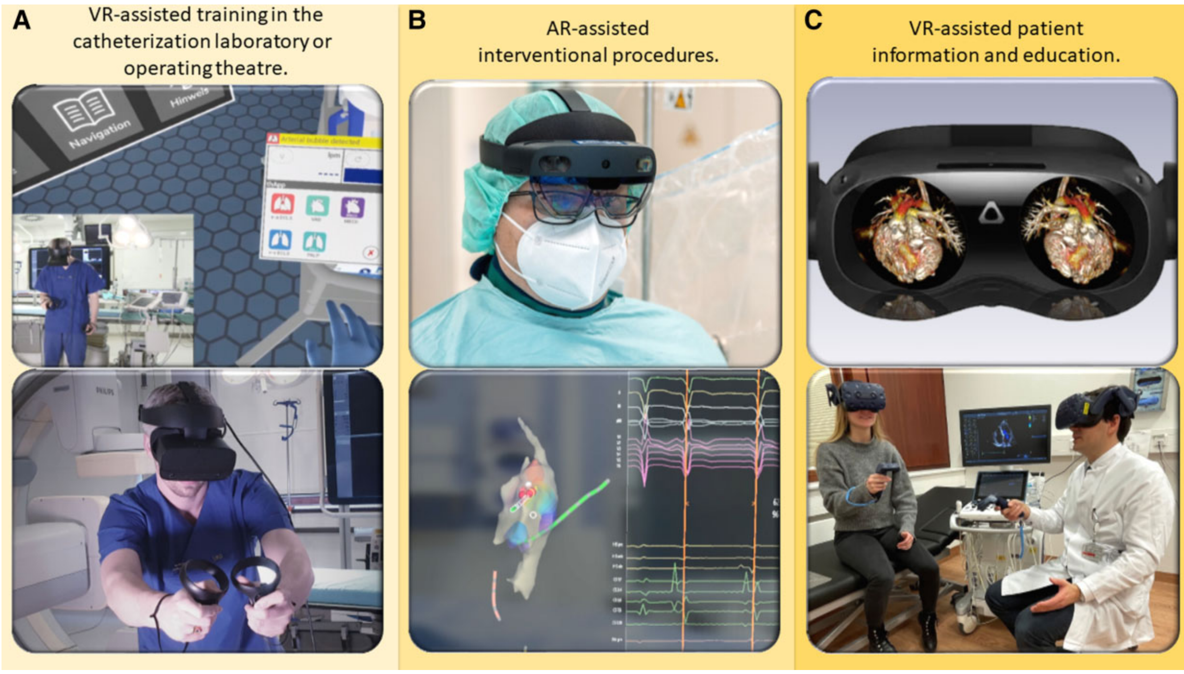

Figure 7 (*A*) Virtual reality-assisted training the catheterization laboratory or operating theatre. (*B*) Augmented reality-assisted interventional procedures; (*C*) virtual reality-assisted patient information and education.

Artificial intelligence

All the new technological tools described above give us the hope that a more appropriate and better evaluation of the specific problem will be not only possible but available in the clinical routine; however, we also need a better understanding of the life span trajectories of our ACHD patients, determined by a multitude of variables, such as genetic and epigenetic factors, socioeconomic environment, and lifestyle, previously performed and omitted medical procedures as well as stochastically determined complications affecting the phenotypic expression and expression of risk throughout life.[1]

Over the last decade, innovation in computer science has transformed the area of machine learning and neuronal networks. While neuronal networks have—in principle—been around for more than 40 years, they had previously failed to have a relevant impact on medical decision-making. This changed dramatically with the introduction of DL architectures, convolutional deep networks and backpropagation in the early 2010 s.[83]

Provided sufficient raw data are available, AI or DL approaches should be able to iteratively learn to abstract the data sources and provide predictive information across the spectrum of CHD. These algorithms being non-parametric and non-linear in nature have, however, the tendency to overinterpret/overfit data thus potentially placing too much emphasis on idiosyncrasies of the underlying dataset. The inherent danger is therefore that the results of algorithms trained on one isolated dataset maybe poorly extrapolated to other datasets.[84] This problem is aggravated by the black-box character of many AI approaches hampering efforts to clearly explain the factors that contributed to a given result of the AI algorithm.[85] These problems can be overcome with appropriate study designs, external validation, and careful evaluation of the final models but clinicians should be vigilant that the mere application of AI methods to routine datasets might not necessarily improve the predictive ability of models compared to conventional statistical methods.[86]

Examples of successful application of DL approaches to CHD data include both harvesting useful clinical information from unstructured medical reports in natural language as well as DL applications to the vast amounts of available imaging data. Diller *et al.*[87] have previously applied machine learning algorithms to estimate prognosis and guide therapy in ACHD using data from a single tertiary centre including over 10 000 patients. To this end, clinical and demographic data, ECG parameters, cardiopulmonary exercise testing, and laboratory values were accumulated and included in appropriate recurrent DL algorithms. Specific models were built based on raw data to categorize diagnostic group, disease complexity, and functional class. In addition, models were developed to estimate need for discussion at multidisciplinary team meetings and to estimate prognosis of individual patients. Overall, the DL algorithms successfully categorized diagnosis, disease complexity, functional class, and presentation at multidisciplinary meeting with an accuracy of over 90%. The DL-based automatic disease severity score was also shown to predict survival independently of other demographic, clinical and laboratory parameters on multivariable analysis. The Montreal group has recently demonstrated the ability of recurrent neural networks to model longitudinal medical data. Based on a large administrative database the model was able to predict future heart failure events at various time points based on various patient characteristics and previous events.[88]

Using multi-centre MRI raw data from the German National Register for CHD, it could be demonstrated that fully automated

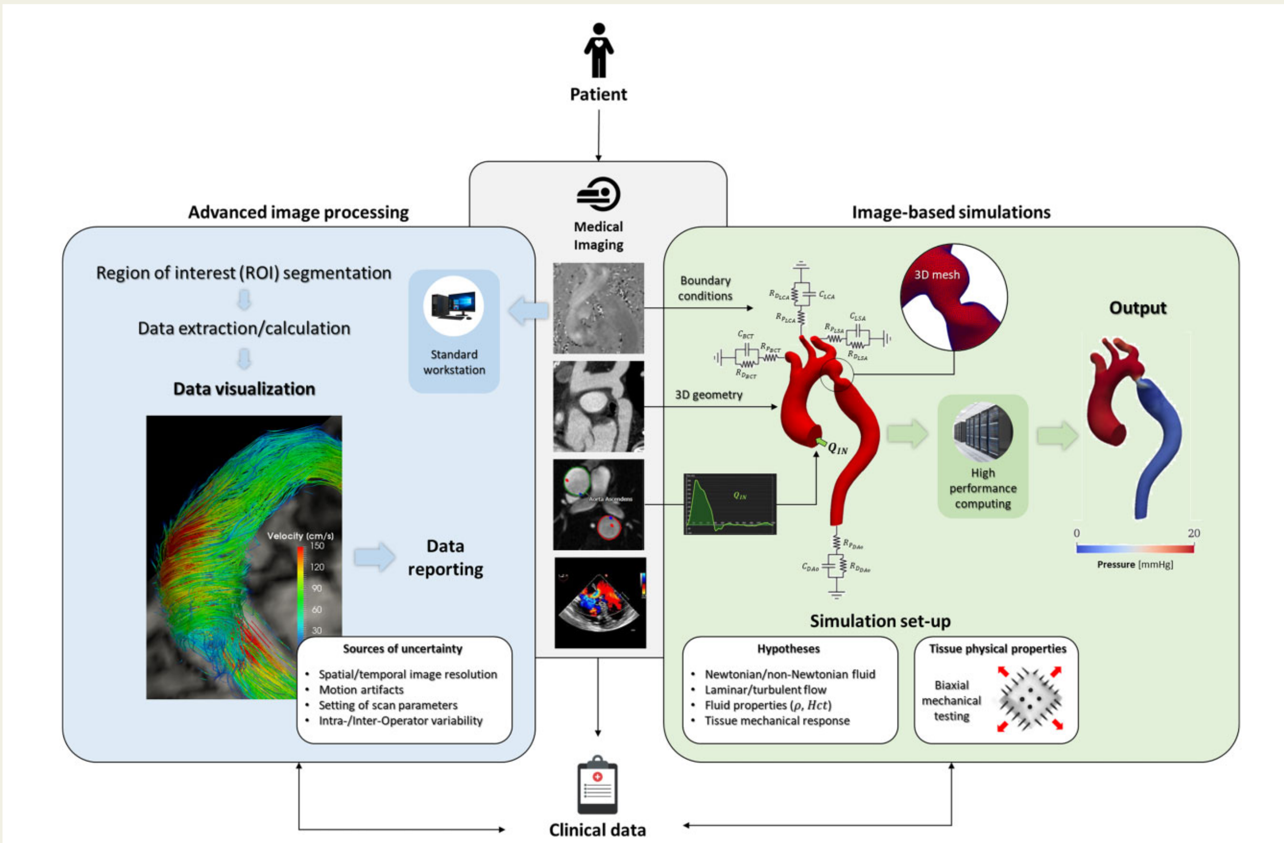

Figure 8 With reference to aortic flow fluid-dynamic analysis, two different approaches to image-based computational modelling are represented. Left: advanced post-processing medical imaging; by post-processing four-dimensional Flow magnetic resonance imaging, blood velocity field is reconstructed and visualized by means of standard computational resources; clinically relevant biomechanical indices can be quantified without major assumptions, but computations are affected by the sources of uncertainty inherent to the raw clinical images. Right: computer simulations, exemplified by a fluid-structure interaction model. Different imaging modalities can be used to define the three-dimensional anatomy of the region of interest, the boundary conditions of the model (e.g. the inlet blood flow rate), and the outflow boundary conditions (here provided by Windkessel models coupled to the three-dimensional model). Data (e.g., from ex vivo tissue testing) and hypotheses are needed to set simulations, which typically run on high end supercomputing facilities. In turn, highly resolved and noise-free data on blood fluid-dynamics are obtained.

DL-based risk prediction is possible in patients with tetralogy of Fallot. In this study convolutional DL networks were trained to prepare the raw images for segmentation and dedicated networks were used to measure ventricular dimensions and function. Over a median follow-up of 10 years, their results showed that DL parameters served as significant predictors of adverse outcomes independently of LV and RV ejection fraction and peak oxygen uptake.[89]

Future approaches capitalizing on the inherent ability of machine learning algorithms to accept heterogeneous raw data and integrate various high-volume data streams will allow tackling the complex lifelong management of CHD patients.

Conclusions and future perspectives

Advanced technologies have revolutionized our practice in diagnosing and treatment patients with cardiovascular disease, and they are playing an important role in dealing with CHD due to its complexity inherent in the various congenital anomalies. Traditional reliance on the standard imaging modalities including echocardiography, cardiac CT and MRI has been challenged by the use of recent technologies such as 3D printing, VR, AR, computational modelling, and AI because of insufficient information available with these standard imaging techniques. This has created potential opportunities of incorporating these technologies into routine clinical practice to achieve the best outcomes through delivery of personalized medicine. Despite promising results as indicated in this review, there are some unresolved issues.

Guidelines for appropriate criteria need to be developed with regard to the use of 3D printing in CHD since appropriate use criteria for abdominal, hepatobiliary, and gastrointestinal 3D printing applications are available in the literature.[90] Medical reimbursement is another issue for consideration if the 3D printed heart models are used in routine practice. The cost of printing a heart model ranges from 50 Euro to several hundred Euro depends on the printing material (whether to print a flexible or multi-colour heart model) and type of printer used (from a desktop printer of several thousand dollars to over a hundred thousand dollars of a large industrial size printer).[21,91] Further, other factors should be considered as well, such as access to post-processing software and skillful personnel needed to perform image segmentation. When access to a 3D printing facility is not available, use of VR could be an alternative tool as it offers the same advantages of 3D visualization and 3D printed models for comprehension of CHD, but in a faster approach (5 min for VR and 8 h for 3D printed model) according to a recent report.[92]

Currently, 3D printed heart models are highly accurate in replicating anatomy and pathology with materials available to simulate cardiac tissue properties, such as Agilus A30 (Stratasys).[93] However, most models are printed in static nature lacking haemodynamic features to represent realistic cardiovascular circulatory condition. This could be addressed by printing the models with flexible materials coupled with computational modelling technique to simulate cardiovascular haemodynamics of CHD. With further reductions of 3D printers and printing costs, use of 3D printing in patients with CHD needs to be determined in terms of cost-effectiveness and long-term clinical outcomes.

Use of VR and AR in medical domain, in particular its application in the CHD, is still limited. Further research should aim to explore its educational value for medical students and graduates, and investigate clinical usefulness of using these innovative technologies on pre-surgical planning and simulation, in addition to cardiac surgeon's skill development. Randomized controlled trials and multi-centre studies are desirable to address this limitation by providing robust findings. Further, since both 3D printed models and VR/AR may improve doctor–patient–parents communication in daily practice by enhancing their understanding of the defect and the proposed surgical/interventional therapy, this could be another research area that deserves investigation.

Finally, computational modelling and AI have seen its clinical value in many areas serving as a complementary tool to current imaging modalities. The main application of using CFD in CHD lies in preoperative planning and optimization of surgical outcomes.[94] Despite availability of powerful computers nowadays, studies of modelling complex CHD problems are still limited by computer power. Another challenge of incorporating CHD into clinical practice is that clinicians are not familiar with CFD techniques. Use of AI in adult CHD requires further investigation with inclusion of different types of CHD categories. Given the widespread use of AI in the medical domain, implementation of AI into medical education curriculum is highly recommended to enrich the undergraduate's knowledge and understanding of various cardiovascular conditions.[84,95] This aims to increase medical graduates/future physicians' skills and confidence in managing AI applications that involve aggregation of large imaging and clinical data for diagnostic and treatment recommendations. Ethical and legal challenges should also be included in the medical curriculum. A multi-disciplinary team collaboration is essential to achieve the goal as these innovative technologies require the knowledge and skills of researchers from different disciplines. This involves the process ranging from acquisition of high-resolution data for image processing and segmentation to printing 3D physical models with selection of appropriate printers and materials to meet clinical requirements, and VR and AR demonstration and simulation of complex cardiovascular structures and pathologies, computational modelling of the volume data for haemodynamic analysis as well as use of AI or DL for analysis of various parameters for diagnosis and prediction of CHD.[96,97] This phenomenon would be expected soon in clinical practice, with the incorporation of these technologies into routine diagnostic strategy and clinical decision-making in CHD.

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Corrigendum

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In the originally published version of this manuscript, full attribution for the Figure was not included and three references were missing. This has now been corrected online.