Review

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Emerging 3D technologies and applications within congenital heart disease: teach, predict, plan and guide

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3D visualization technologies have evolved to become a mainstay in the management of congenital heart disease (CHD) with a growing presence within multiple facets. Printed and virtual 3D models allow for a more comprehensive approach to educating trainees and care team members. Computational fluid dynamics can take 3D modeling to the next level, by predicting post-procedural outcomes and helping to determine surgical approach. 3D printing and extended reality are developing resources for pre-procedural planning and intra-procedural guidance with the potential to revolutionize decision-making and procedural success. Challenges still remain within existing technologies and their applications to the CHD field. Addressing these gaps, both by those within and outside of CHD, will transform education and patient care within our field.

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Congenital heart disease (CHD) is a field in which 3D relationships must be understood in order to conceptualize complex lesions and to make educated decisions on interventional strategies. However, previous generations have been limited by inferring 3D anatomy and relationships almost exclusively from 2D information. This approach often suffices because of the experience and knowledge gained with time by both individuals and the field at large, as well as the inherent interest in and appreciation of those 3D relationships by care leaders. The development of 3D visualization technologies has brought with it a recognition that there are aspects of a patient's unique anatomy, such as the relationship between vascular structures and surrounding noncardiac structures, which are much more difficult to infer. Further, developing prediction tools that rely on 3D technologies may one day be the standard of care in the field of CHD. This review outlines certain emerging 3D technologies and their applications throughout the continuum of CHD care, from education to predictive models to procedural preparation and guidance, as we "Teach, Predict, Plan and Guide".

Teach: 3D technologies in CHD education

Advances in 3D printing and visualization are evolving as unique and promising tools in medical education. In order to truly understand CHD, trainees need to master a fundamental 3D conceptualization of the various heart structures. Traditionally, educators use 2D drawings and diagrams and ask students to reconstruct a mental 3D image. This can be an extremely challenging process. Emerging technology in the areas of 3D printing and extended reality (XR) lends itself nicely to allowing medical educators to overcome this obstacle.

3D printing technology can be used to create high-fidelity synthetic heart models which have been effectively incorporated into simulation-based curricula to educate premedical and medical students about CHD [1,2]. A curriculum using 3D printed models for pediatric resident education showed improvement of qualitative assessment of knowledge reporting, knowledge acquisition, and structural conceptualization [3]. 3D models have also been

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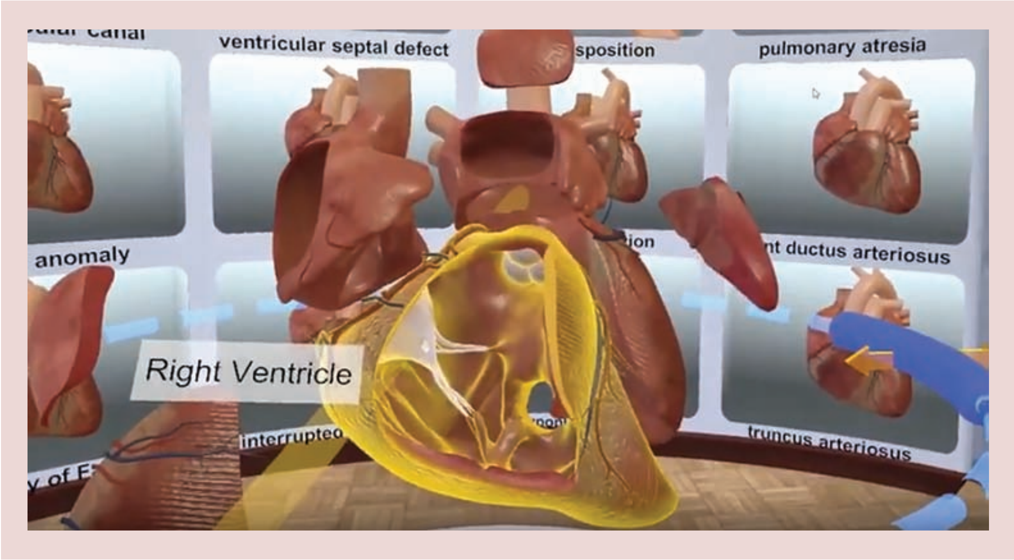

Figure 1. Example of a virtual reality display showing heart models of multiple common congenital heart lesions. Reproduced with permission from a video posted on www.lighthaus.us [13].

used to teach the morphologic characteristics of specific heart lesions and showed higher learner satisfaction scores and retention rates in groups that used the 3D models [4].

In addition to educating trainees about the anatomy and physiology of various defects, 3D models have also been used to teach concepts through simulation with various other groups, including advanced trainees, nurses and patients. Simulations involving 3D cardiac models have given advanced trainees (such as interventional cardiology fellows) the opportunity to practice procedures and utilize iterative learning without putting patients at risk [5]. It has also been shown that 3D patient-specific models can be useful tools for training cardiac nurses, particularly for a better understanding of CHD following repair [6]. Patient and parent input have been incorporated into modifications of 3D model presentations meant for clinical communication through focus groups and feedback mechanisms [7]. These models have been useful for explaining procedures to patients during consultations, demonstrating improved patient satisfaction with their use [8]. Adolescent patients have also reported significant improvements in confidence in explaining their condition to others when 3D models of their heart were presented to them during consultations [9].

Additional exciting and growing technologies that will have a role in how we teach CHD in the future are augmented and virtual reality, collectively called XR or mixed reality. Both technologies involve computer-generated simulation models of a 3D image or environment. In an augmented reality (AR) application, a modeled image is projected onto the user's real-world environment. In contrast, a virtual reality (VR) application is a simulated experience in a completely new, digital environment. These applications can often run on common and commercially available gaming consoles and wearable headsets. Learners are immersed and interact in this virtual environment in a seemingly real or physical way, often by using hand-held electronic equipment. AR applications have been used in medical education to train specialists in various areas for specific procedures, including laparoscopic surgery, neurosurgical procedures, and echocardiography [10], as well as middle and high school students for cardiopulmonary resuscitation [11]. The potential of this technology has not yet been fully realized as a tool to teach fundamentals of the anatomy and pathophysiology of CHD.

VR provides a particular opportunity for teaching the visuospatial aspects of congenital heart defects. Recent projects have tried to merge the worlds of XR and CHD and are currently investigating both the feasibility and effectiveness in teaching trainees about common congenital heart defects using this technology [12]. A VR application allows learners to experience an immersive and interactive educational platform, which can be designed specifically to learn about CHD and can allow for an appreciation of defects that often require 3D (and even 4D) understanding. In this VR environment, learners can select various heart models representing a variety of anatomic defects to explore in detail (Figure 1). These computer-generated hearts can be manipulated by the learner in multiple ways to obtain a true 3D understanding of the anatomy. In addition, learners have the ability to teleport

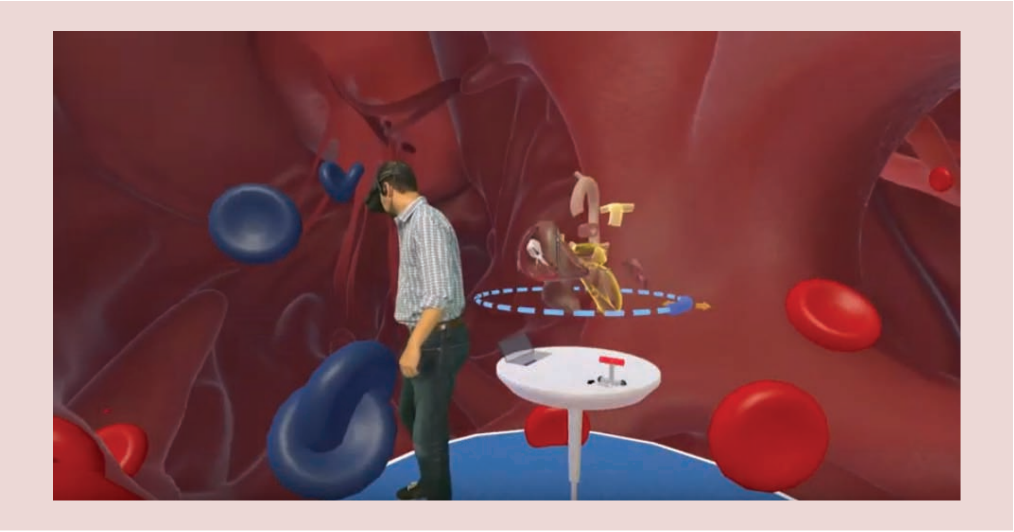

Figure 2. Example of an integrative environment within a beating heart in a virtual reality platform. Reproduced with permission from a video posted on www.lighthaus.us [13].

inside a beating heart (Figure 2), see lesion-specific blood flows, explore the anatomy and physiology for specific lesions, and even perform simplified surgical repairs of the defects. Further work is certainly needed and currently being performed on this topic through an ongoing prospective, multicenter educational trial with pediatric residents assessing both the feasibility and effectiveness of an educational VR curriculum for CHD using a multiple-item, multimedia, knowledge-based assessment tool for common congenital heart lesions.

Predict: the role & challenges of computational fluid dynamics

Computational fluid dynamics (CFD) is a well-established technique that has been developed to study fluid flows in a variety of applications spanning from traditional engineering fields such as aerospace and automotive to, more recently, biomedical engineering [14]. CFD methods, combined with advanced cross-sectional imaging, provide high spatial and temporal resolution on hemodynamic quantities (primarily blood velocity and pressure) which cannot be achieved with any other technique in complex, patient-specific 3D models. Driven by the mounting evidence linking abnormal biomechanical stimuli and the development of cardiovascular disease [15], CFD methods have been used extensively to study hemodynamics in hypertension [16], aneurysmal vessel disease [17,18], coronary artery disease [19], aortic dissection [20] and carotid artery disease [21]. CFD has also seen significant applications to the areas of noninvasive diagnostics [22,23], medical device evaluation [24–26] and clinical decision-making through prediction of changes in blood flow following interventions in CHD [27–30].

In addition to these research applications, faster computer hardware and user-friendly commercial CFD packages have made patient-specific simulation of hemodynamics more accessible to clinical settings. However, obtaining trustworthy estimates of flow and pressure fields requires understanding of key aspects of numerical simulation, which are often overlooked. Specifically, one must understand how the availability of hemodynamic data affects the specification of the boundary conditions and the importance of achieving mesh-independent results. As this understanding becomes more widespread, CFD could play a routine role in CHD management.

The methodology of CFD hinges on solving Navier–Stokes Equations, which are differential equations describing balance of mass (e.g., flow in must equal flow out) and momentum (e.g., blood moves as result of different forces, including pressure gradients and viscous forces). Solving these equations renders 3D, time-resolved maps of velocity ($\vec{V}$) and pressure (p). Figure 3A illustrates several key differences in boundary condition specification between traditional CFD methods and those applied to CHD. 'Boundary conditions' are information on velocity, flow, or pressure, which must be specified at each inflow or outflow branch of the model. This step is critical, as different boundary conditions will lead to entirely different solutions for velocity and pressure. In traditional CFD applications, there are typically enough measurements to directly specify boundary conditions on either velocity or pressure on all boundaries of the model.

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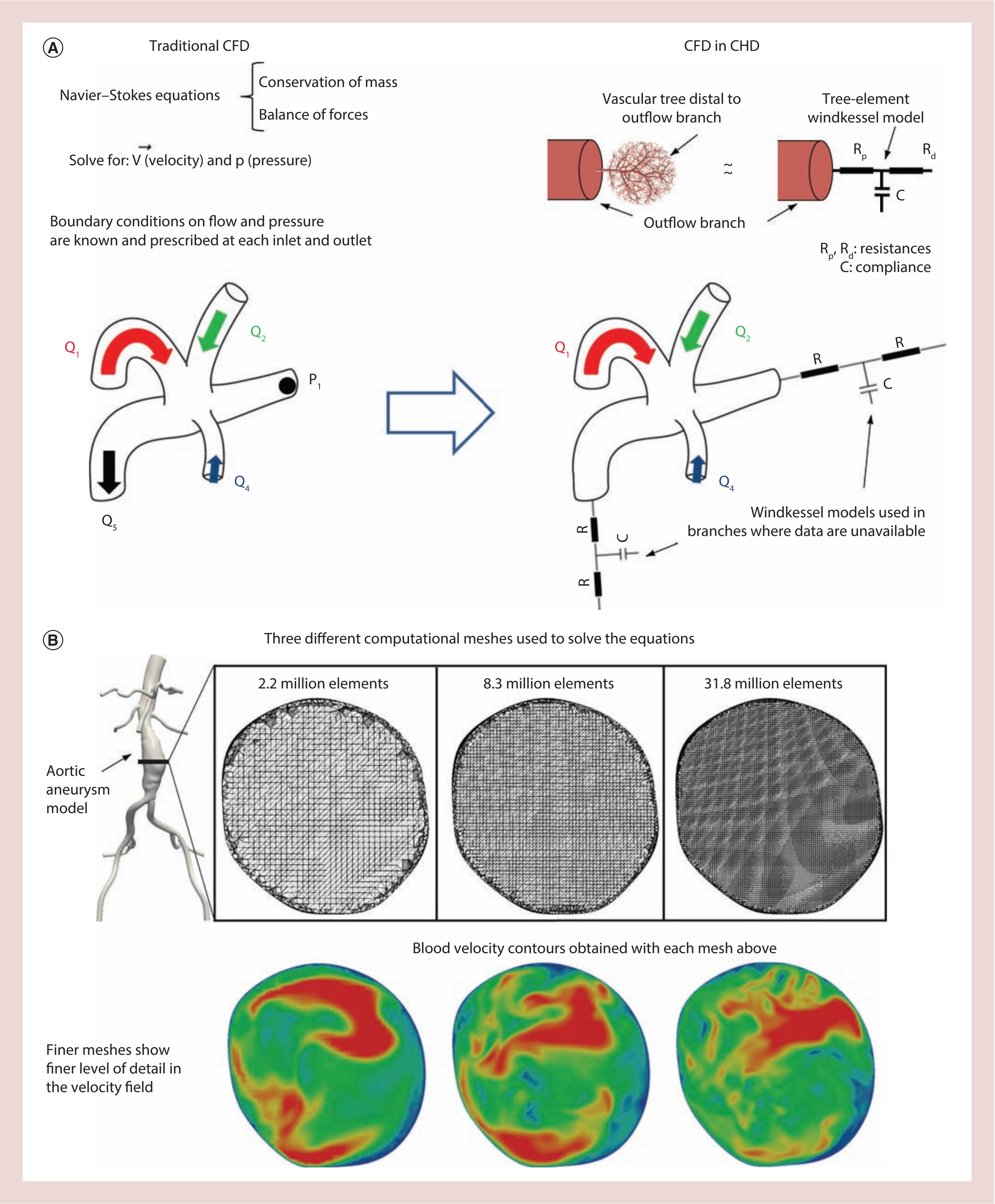

Figure 3. Computational fluid dynamic methodology. (A) Key differences in boundary condition specifications between traditional CFD methods and those applied to CHD. **(B)** Examples of three difference sizes of meshes for velocity contours within a plane located in the mid-section of an abdominal aortic aneurysm.
CFD: Computational fluid dynamics; CHD: Congenital heart disease; C: Compliance of vascular bed distal to the outlet of the model; R_p: Proximal resistance; R_d: Distal resistance; Q: Flow in and out of the model; P: Prescribed pressure waveform.
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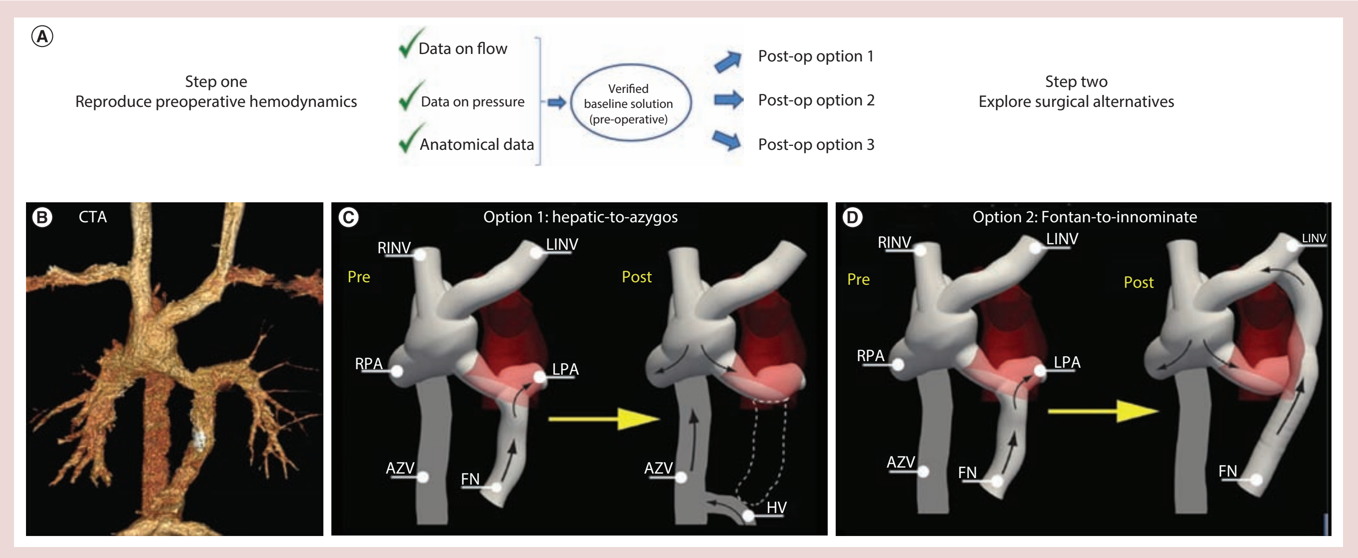

Figure 4. Computational fluid dynamics used in an example of surgical planning. (A) Steps required to build a computational model in order to simulate surgical alternatives. **(B)** A 3D reconstruction of a CTA for a patient with complex, palliated single-ventricle congenital heart disease, followed by two surgical options **(C and D)**.
AZV: Azygous vein; CTA: Computed tomography angiogram; FN: Fontan connection; HV: Hepatic veins; LINV: Left innominate vein; LPA: Left pulmonary artery; RINV: Right innominate vein; RPA: Right pulmonary artery.
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As is the nature of the complexity of CHD applications within most diagnostic techniques, it is challenging to have enough data to specify boundary conditions for all the inflow and outflow branches of the model. To circumvent this limitation, 'reduced-order' (e.g., simpler) models of the distal circulation are coupled as boundary conditions to the outlet faces of the model. These models represent the characteristics of the vascular bed distal to the outflow branch. A widely popular reduced-order model is the so-called three-element Windkessel, which requires specifying three parameters: R_p (proximal resistance), R_d (distal resistance), and C (compliance of the vascular bed distal to the outlet of the model) (Figure 3A) [31]. These parameters can be estimated even if no direct measurements are available on a given branch, using population or morphometric data on mean pressure, pulse pressure, and mean flow. The use of reduced-order models has an additional important advantage for surgical planning applications in CHD, as it enables specifying boundary conditions for vessels or grafts which are part of the *proposed* surgical solution and therefore cannot be imaged pre-operatively. While the 4D flow-derived boundary conditions that are commonly used in clinical settings provide rapid visualization of possible flow patterns, the data is usually 'noisy' and it does not satisfy basic conditions such as balance of mass.

A second key concept in CFD is 'mesh independence'. A computational mesh is produced by breaking up the vascular model into millions of small pieces known as 'elements'. The quality of the mesh is key to obtaining an accurate solution. In general, the larger the number of elements of the computational mesh, the more accurate the solution for velocity and pressure. Figure 3B shows velocity contours for a plane located in the midsection of an abdominal aortic aneurysm, for meshes of three different sizes: 2, 8, and 32 million elements, respectively [17]. The differences between the velocity contours are apparent: the 32 million element mesh offers higher level of detail and reveals flow structures absent from the results obtained with the coarser meshes. Simulations should always be run with computational meshes of different sizes until the obtained solution does not change (e.g., until mesh independence is achieved).

A specific case of CFD-supported surgical planning in CHD was reported by our group [29] and motivates several challenges and opportunities in the field. Conceptually, the computational surgical planning paradigm consists of two steps: in Step 1, the available pre-operative data on anatomy, flow and pressure are used to produce a calibrated model that matches the hemodynamic state of the patient. Once calibrated, Step 2 involves using this virtual pre-operative model in order to explore the different surgical alternatives for the problem (Figure 4A).

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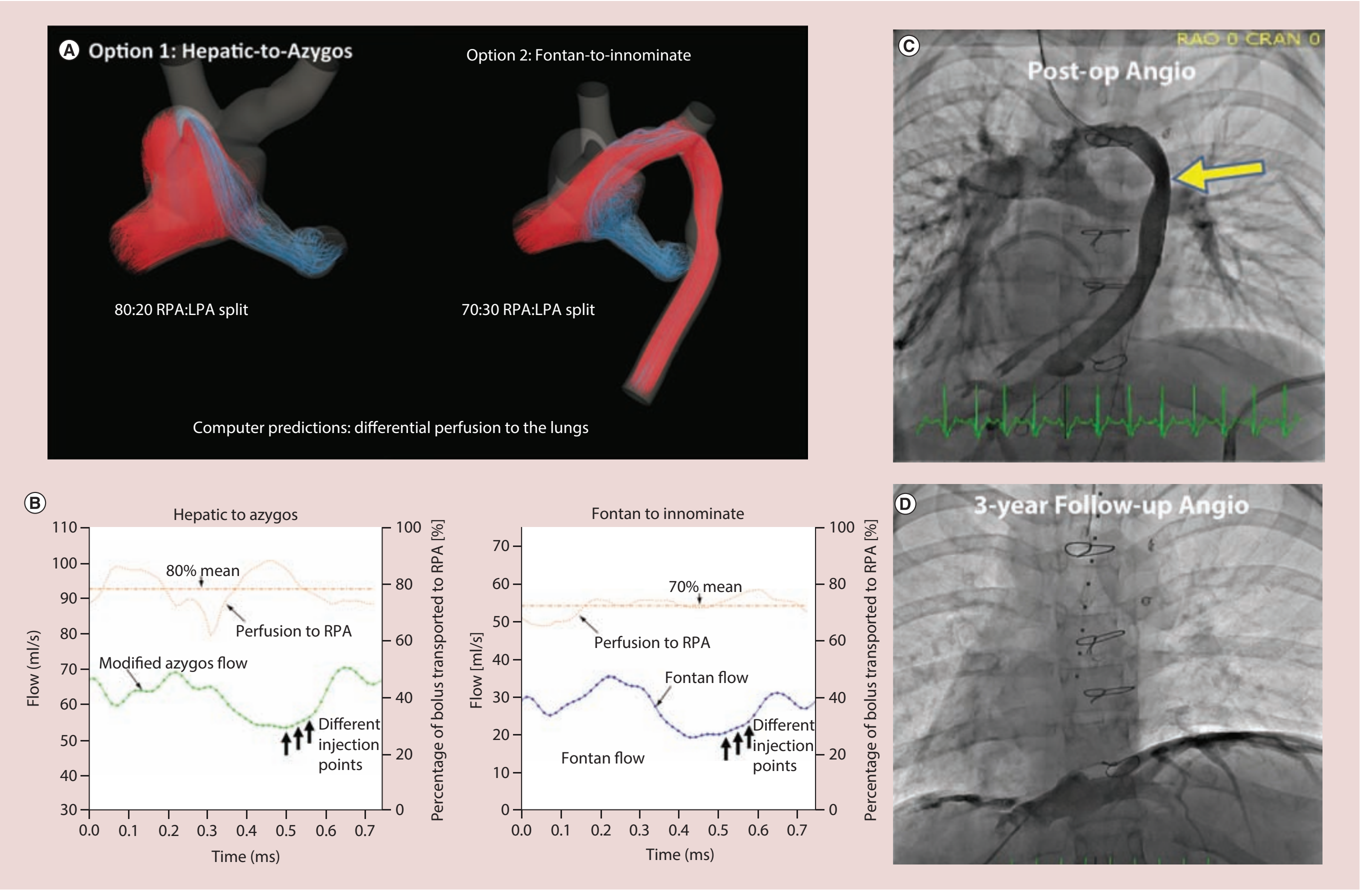

Figure 5. Results of computational fluid dynamics modeling and transcatheter angiographic evaluation. (A) Comparison of differential perfusion of the right and left pulmonary arteries between Options 1 and 2. **(B)** Graphic representations of flow within the modified azygous vein in Option 1 and Fontan flow in Option 2 during simulated bolus injections, as well as the differential branch pulmonary artery flow in the time following those injections. **(C)** Transcatheter angiogram performed shortly after completion of Option 2 showing a patent connection of the new Fontan conduit to the left innominate vein with a mild stenosis (yellow arrow). **(D)** Transcatheter angiogram performed 3 years following surgery, showing complete occlusion of the Fontan connection to the left innominate vein. Reproduced with permission from [29] © Springer Nature (2017).

The case reported an 18-year-old patient with complex single ventricle CHD (heterotaxy syndrome with dextrocardia and an interrupted inferior vena cava with azygous continuation to the superior vena cava, with an unbalanced atrioventricular septal defect). The patient previously completed staged surgical palliation, consisting of connecting the superior vena cava to the pulmonary arteries (bidirectional Glenn anastomosis) and connection of the hepatic veins to the pulmonary arteries (extracardiac Fontan pathway) (Figure 4B). She was found to have significant right-sided pulmonary arteriovenous malformations. These arteriovenous malformations cause significant cyanosis and hypoxia and are related to insufficient flow of hepatic venous blood to one (or both) of the branch pulmonary arteries, although the mechanism for this is not fully known. A computer model of the patient's Fontan circulation, including the distribution of the hepatic venous blood, was built from the CT data. The cardiac surgeon considered two different alternatives for surgical revision of the Fontan pathway with the goal of achieving a more balanced distribution of hepatic venous blood flow between both lungs. As shown in the Figure 4C, Option 1 consisted of an anastomosis between the hepatic veins and the azygos vein with removal of the Fontan conduit and Option 2 (Figure 4D) consisted of removal of the Fontan connection with the left pulmonary artery and creation of an anastomosis between the Fontan conduit and the left innominate vein. When comparing the hemodynamic performance of the two options, Option 1 resulted in an 80:20 split of hepatic flow between the right and left pulmonary arteries, whereas Option 2 rendered a more even 70:30 split between the right and left pulmonary arteries (Figure 5A). Computations also revealed a higher degree of pulsatility in distribution of hepatic venous flow between branch pulmonary arteries for Option 1 (Figure 5B), however, with unclear significance. After reviewing the data, the patient successfully underwent surgical revision using Option 2 (Fontan-to-left innominate vein anastomosis) and this resulted in a drastic improvement in the patient's symptoms with systemic oxygen saturation increasing from 82% pre-operatively to 85% postoperatively. The postoperative angiograms were consistent with the simulation results (Figure 5C). Over the next 3 years, the oxygen saturations continued to improve to an average of 95% and the patient remained asymptomatic with improved exercise tolerance. Routine abdominal ultrasound showed stable liver nodules consistent with Fontan associated liver fibrosis with preserved liver function. This was considered a short-term success for this patient. However, a routine follow-up MRI performed 36 months postoperatively as a surveillance study revealed that the Fontan pathway had occluded, which was further confirmed by transcatheter angiography (Figure 5D).

Understanding an unexpected long-term outcome such as this remains one of the greatest challenges in surgical planning for CHD. Anatomical deviations between planned and actual reconstruction, such as the mild narrowing in the reconstructed Fontan pathway (Figure 5C), must be fed back to the computational model to recalculate the hemodynamic conditions under the actual reconstruction. Furthermore and as indicated previously, a better understanding of the meaning of time-dependent hemodynamic indices is needed to avoid graft occlusions such as that reported in this example. Nonetheless, as we learn more about and refine CFD applications in CHD, this combination of advanced 3D imaging and computational modeling could revolutionize how complex lesions are approached.

Plan: 3D visualization technologies in pre-procedural planning

Due to limited intra-operative visibility, pre-operative delineation of anatomy is critical to optimizing patient outcomes in congenital cardiac surgery. Specific lesions, such as ventricular septal defects, double outlet right ventricle, and complex atrioventricular valve anatomy can be better understood using 3D imaging modalities [32]. Computed tomography (CT) and MRI allow for high-resolution imaging with a larger field of view than echocardiography ('whole-heart representation'), which can be particularly useful in repair of complex congenital cardiac operations, such as intracardiac baffles and biventricular repairs in patients with double outlet right ventricle anatomy. The use of 3D printing for surgical planning in CHD has been well-established [33–36]. Printed 3D models represent intracardiac anatomy with high fidelity [33–35] and can influence surgeons' understanding of cardiac anatomy and change surgical approach [34,36]. However, printing models requires significant post-processing, infrastructure, and investment of both time and money to produce models adequate for clinical use, which can limit application and widespread utilization. In addition, prints are limited by a fixed cut plane and a single scale.

As mentioned, stereoscopic presentation of 3D datasets allows for true 3D representation, rather than projection onto a 2D screen and allows for dynamic manipulation of datasets, such as changing perspective, zooming and changing the cut plane. Manipulation may be more intuitive and user friendly than traditional 3D viewing platforms, which can greatly improve orientation and facilitate interpretation of complicated datasets. For example, a commercially available platform (True3D, EchoPixel, CA, USA) can facilitate interpretation of cardiac anatomy in thoracopagus conjoined twins (Figure 6A). A chest CT was obtained on these patients, imported into the system and with minimal segmentation and labeling, the dataset could be manipulated to facilitate real-time, 3D interpretation of the study. Twin A had pulmonary atresia with confluent branch pulmonary arteries supplied from a patent ductus arteriosus. Twin B had bilateral superior vena cavae and a small main pulmonary artery segment. The majority of the cardiac mass was committed to Twin A, with the infants sharing a common atrial chamber and a common left ventricle. Using this stereoscopic platform allowed for labeling of the twins to easily identify which infant was being evaluated, as well as for rapid re-orientation (Figure 6B & C). Due to the orientation of the infants, a 180° rotation could be quickly performed to keep the images oriented to the twin in question, whether in an axial or coronal orientation. This modeling proved that these infants were unable to be separated safely within this complex orientation, informing an important management decision. Similar use of VR has also been reported in planning for division of a more straightforward interatrial communication during successful separation of thoracopagus conjoined twins [37].

Stereoscopic images can also provide unique opportunities to augment the information provided by advanced non-invasive cardiac imaging as part of preprocedural planning. From cardiac MRI data, stereoscopic vision has been shown to be additive in evaluating shunts and regurgitation [38]. Although limited validation data are available, mitral valve measurements of 3D echocardiographic datasets using the True3D platform were shown to be similar to measurements using the traditional QLAB platform (Philips, Best, The Netherlands), with low intra- and interobserver variability [39]. Proof of concept of VR for surgical planning has been demonstrated using CT datasets

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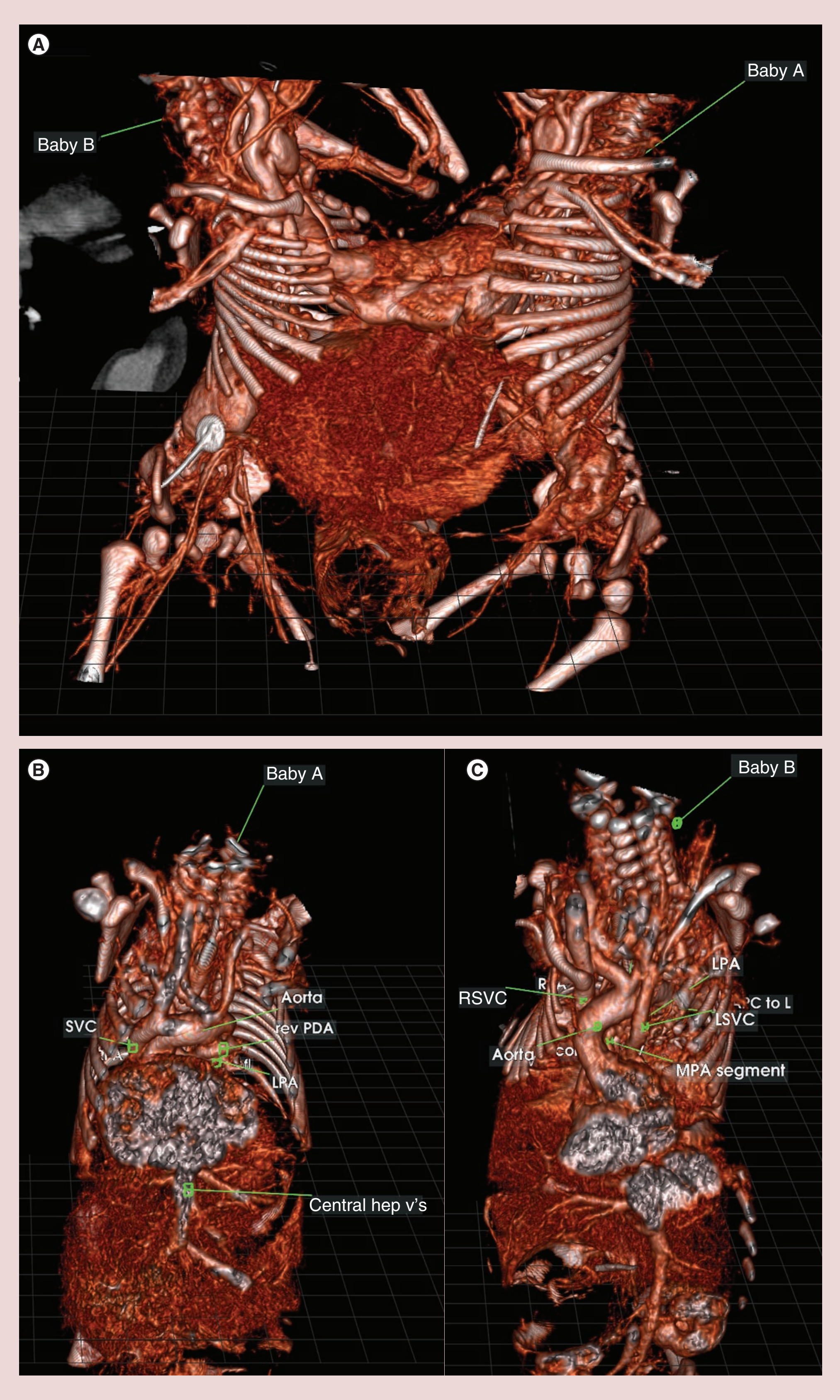

Figure 6. 3Dreconstruction of computed tomography of thoracopagus conjoined twins, viewed on a stereoscopic viewing platform. (A) Although represented here in 2D form, this image can be viewed as a 3D image. **(B)** Oriented coronal oblique view of Twin A. **(C)** Oriented coronal oblique view of Twin B.

in neonates with ventricular septal defects [40]. Our center has used the True3D platform with cardiac MRI and an endoluminal windowing preset as a replacement for 3D printing in complex double outlet right ventricle. For example, we achieved an excellent biventricular surgical outcome for an infant with complex intracardiac anatomy (double outlet right ventricle, D-malposed great arteries, subpulmonary ventricular septal defect (VSD) with valvar and subvalvar pulmonary stenosis, straddling mitral valve and a RV muscle band from the subpulmonary region to the RV side of the septum) after this unique 3D platform provided the well-visualized location of the straddling attachments (Supplementary Video 1), such that the VSD patch could be deviated around the attachments with VSD flow directed to the pulmonary valve. This was performed with an arterial switch operation and subpulmonary resection. While this platform requires less segmentation and processing than some platforms, an important consideration for pre-procedural planning would include advances to streamline workflow, such as more automated tools (e.g., integration of artificial intelligence) and better integration with existing systems. Currently, significant additional effort for postprocessing on most platforms limits accessibility and routine utilization.

Stereoscopic visualization and VR are also limited by the need for eyewear or headgear, potentially limiting the number of viewers and posing obstacles to intra-procedural usage. AR and other forms of holography have the potential to overcome some of these barriers, although some current iterations still require lenses or headgear. In a feasibility study, CT images of a patient with double outlet right ventricle with transposed great arteries were segmented and displayed on the commercially available, wearable holographic platform, HoloLens (Microsoft, WA, USA) [41]. The anatomy could be well appreciated and the platform was rated highly, particularly by younger professionals. Holographic representation of atrial septal defects, using the RealView Holographic Display (Realview Imaging Inc, Yokneam, Israel), was also shown to be feasible in a series of eight patents, with all relevant landmarks identifiable [42]. The next question will be whether these modalities enhance the planning required to correct these defects or to make important management decisions.

Digital presentation rather than printed models also allows for virtual testing of potential interventions. Given the previously noted data on atrial septal defects, it would be straightforward to envision virtual testing of transcatheter devices, with potential to evaluate for aortic impingement or obstruction of venous inflow. In a series of 28 patients with sinus venosus defects, virtual placement of covered stents allowed prediction of which patients would be suitable for this unique transcatheter approach [43]. Future innovations, such as estimating deformability of tissue with expansion of devices, could allow for more realistic simulation of device implantation.

Existing data largely consists of case reports or small case series. Further evaluation will likely require multicenter collaboration, which may be difficult due to variation in technology and platforms in current use at various institutions. There is preliminary data showing some evidence that surgical decision-making may be altered based on improved understanding of cardiac anatomy through virtual 3D imaging [44]. Prospective data, with evaluation for fidelity to intra-operative findings and potential changes in surgical plan, are clearly needed.

Guide: 3D intraprocedural guidance

3D intraprocedural guidance has been a popular concept and evolving presence within CHD, particularly with the advancements in fluoroscopy platforms within the cardiac catheterization laboratory. CT and MRI have been the optimal advanced imaging modalities for 3D visualization [45,46]. These modalities allow for both visualization of 3D structures, as well as vessel-airway interactions, but have classically lacked the ability to guide most cardiac procedures. More recently, MRI has been utilized by the interventional cardiologist to guide cardiac catheterizations in select centers [47–49] and even as a model to guide complex interventions [50]. These new techniques provide a radiation-free environment while elucidating unique spatial information. This is an exciting new venture that is still being optimized for the congenital laboratory, but has already allowed for pre-clinical and clinical cardiac interventions to be performed [51]. The ability to perform MRI-guided catheterizations requires significant resources and space to appropriately accommodate its use. The natural progression for most centers without the set-up for this approach has been to include retrospective CT and MRI data into catheterization procedures using 3D overlay onto 2D fluoroscopy. 3D overlay, or 'roadmapping', of CT and MRI images has been shown to be effective for interventions on branch pulmonary arteries, patent ductus arteriosus, intracardiac baffles, coarctation of the aorta, and for pulmonary valve implantations [52–56]. 3D MRI overlay has even been reported to guide percutaneous transhepatic access in a patient with a liver mass and no other avenues for vascular access [57]. These well-described overlay techniques have been shown to reduce radiation exposure, contrast volume, and procedural time for certain interventions [52,53,55], while providing a 3D representation of the patient's anatomy.

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Figure 7. 3D rotational angiogram of a patient with complex stenosis of the right ventricle-to-pulmonary artery conduit and branch pulmonary arteries. (A) Extreme right anterior-oblique view with steep cranial angulation. **(B)** Posterior view with steep caudal angulation.

The technology gap remains with the application of real-time acquisition and intraprocedural guidance using patient-specific 3D images. 3D rotational angiography (3DRA) has allowed for acquisition of 3D imaging within a congenital cardiac catheterization laboratory (Figure 7). The ability to overlay those images onto the live fluoroscopy screen with synchronized image movement with gantry angles has been well described [55,58,59]. The overlay of these images has become particularly useful for procedural guidance in cases involving complex interventions on the aortic arch and branch pulmonary arteries and is beginning to become standard of care within the congenital catheterization laboratory. A recent case series reported the first use of cardiac 3D rotational angiography for CFD in three patients undergoing stent implantation in aortic coarctation, without the need for pre-operative imaging [60]. The analysis showed that patient-specific predictive modeling can be performed as an intra-procedural analysis in the cardiac catheterization laboratory. Certain platforms have also developed the capability to overlay intra-procedural 3D transesophageal echocardiographic imaging onto fluoroscopy, bridging a need for 3D imaging of complex atrial and ventricular septal defects [61], as well as valvular defects that lack detail within other forms of imaging.

The common limitation of these various modalities is that 3D images are being represented on 2D screens. This becomes especially important with hopes of integrating it into the operating room setting, where some of the most complex interventions occur for the CHD population. There have been reports of noncardiac surgeries using augmented reality for this purpose. Overlay of axial MRI images onto the patient has been reported as a guide during vertebroplasty [62] and studies have demonstrated utility of AR in guiding neurosurgical operations on cerebral aneurysms, cerebral arteriovenous malformation, a skull base procedure, and degenerative spine surgery using image projection through the eyepiece of the microscope used for those operations [63–66]. Results from these studies included minimal additional time added to the operations due to the use of AR and subsets of operations in which there were reported clinical benefits from the use of AR guidance. As with all overlay modalities, whether onto fluoroscopy or a live patient, accuracy of coregistration of images requires particular attention and scrutiny, as well as planning prior to initial imaging acquisition and patient positioning during the procedure. Preliminary attempts have been made to utilize CT data for AR display within the cardiac catheterization laboratory to guide percutaneous branch pulmonary artery interventions [67] as well as transcatheter pacemaker implantation in complex CHD [68]. There are true barriers to potential routine integration of this technology into the congenital cardiac catheterization laboratory. This would likely require a step-wise training process for providers, a feedback mechanism during initial stages of use, and a simple way to revert to traditional imaging modalities if needed to assure that the 'standard of care' is not disrupted. Nonetheless, these aspirations may revolutionize the intraprocedural appreciation of patient anatomy.

The ultimate goal with this technology is to discover ways of obtaining 3D information during a procedure with the ability to display it nearly simultaneously in a true 3D format that can be manipulated and used for intra-procedural guidance. There is a lack of data with this process in the field of CHD. An animal model using a stereoscopic vision display of real-time 3D echocardiography images to guide atrial septal defect closures on beating hearts was described by Vasilyev and colleagues [69]. This study compared the results of visualization of 3D echocardiography utilizing a stereoscopic display to 3D echocardiography displayed on a traditional 2D screen and found that stereoscopic visualization improved the time to task completion, as well as precision of navigation of surgical instruments. Further work is surely needed to advance the workflow of obtaining and utilizing this type of 3D information in real-time for intra-procedural guidance.

Future perspective

The challenge within the field of CHD remains its vast complexity and range of lesions. To the educator, this presents an obstacle to enhancing the understanding of basic cardiac anatomy for the novice learner. To the clinician, this poses a unique challenge to the personalization of decision making and treatment. The optimization of 3D visualization technologies will rely on an appreciation for the spectrum of its applications within multiple realms. To understand clinical application, there must be educational utility for its users. To be truly educational, there must be clinical value in its content. To bridge the gap between knowledge and technology, partnership between medicine and industry is paramount.

As extended reality continues to become more widespread within the learning environment, full educational programs may become embedded within VR, including instruction and assessment. Future learners may work through an online learning management system through a VR profile and the classroom setting may include a multi-user VR environment so that a group of students can interact with a model and its associated didactics. This will require a breakthrough in sufficient rigorous VR educational content, particularly within CHD. This also requires the support of academic institutions, both financially and with the time dedicated for faculty to develop such content.

CFD could be the future of our field, as our biggest challenge is not simply properly representing images, but in predicting the outcomes of various options. As the sophistication and fidelity of CFD and flow simulations

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build, representations of physiology through XR may support true pre-surgical planning in the future. For example, the assessment of the borderline left ventricle will be simulated with flow data modeled from cardiac MRI, then represented in XR where a surgeon may perform a virtual biventricular repair (e.g., Rastelli baffle). Intracardiac flow, adequacy of surgical technique, and cardiac performance over time may be assessed in a fully immersive virtual representation. While immediate post-operative outcomes are important, long-term results are paramount for the pediatric population. The future of simulation should strive for modeling the lifetime of that complex operation through 3 billion heart beats and 10,000 h of exercise to see what the natural history of a repair is to the point of guiding initial approach. This could one day be the way data is presented at regular management conferences held within institutions throughout the country. This immersion of image and data acquisition, predictive modeling, and extended reality representation of that data for pre-procedural planning and intra-procedural guidance will require a commitment to tailoring the 3D visualization technology to the CHD population, forming a '3D team' that can sustainably support the infrastructure needed, and training the proceduralist to perform complex tasks with the assistance of real-time 3D data. This challenging task likely needs to start with animal models and simpler interventions as this will be outside the realm of the current proceduralist's routine practices.

With time, headsets will get faster, lighter, and more powerful. Interventional cardiologists and surgeons can wear them as part of their regular equipment and can image the defect that is about to be closed, look at the device they are about to choose or patch they are about to cut, simulate the procedure, observe the post-intervention imaging, or watch the virtual heart come back off cardiopulmonary bypass. With time, residual lesions can be predicted and postoperative complications can be anticipated. At last, ideal future generations of this XR technology could be viewed by the naked eye with equal quality, resolution, and ability to manipulate the images, rather than using additional eyewear, headgear, or need for handheld controllers, with real-time feedback on anatomy and patient data.

Executive summary

- The possibilities for the future of 3D visualization technologies in congenital heart disease are exciting and endless.

Teach

- Three-dimensional visualization provides a unique perspective for the novice and advanced learners. Extended reality modalities allow for an immersive experience that may be the future of the standard congenital heart disease (CHD) curriculum.

Predict

- Computational fluid dynamics involve an intricate set of measured and estimated parameters to model a patient's current hemodynamics and the potential outcomes of interventional outcomes. Understanding these outcomes is one of the greatest challenges for the field of CHD and refining the accuracy of this prediction tool with existing and developing 3D technologies will require a commitment to tailoring this technology to the CHD population.

Plan

- Printed and virtual 3D models have been shown to be accurate and valuable in surgical and transcatheter interventional planning. Stereoscopic visualization can augment the information provided by traditional advanced non-invasive imaging modalities and has the potential to alter interventional approaches.

Guide

- 3D intraprocedural guidance has evolved with advances in MRI-guided cardiac catheterizations and 3D fluoroscopic overlay, providing unique spatial information that must otherwise be inferred. Real-time acquisition and intraprocedural guidance using patient-specific 3D imaging has been described in other fields and could be an invaluable addition to the complexity of CHD interventions.
- As we teach our trainees and team members, attempt to predict optimal outcomes, plan our interventions and strive to guide our procedures, we must continue to innovate and combine expertise to span the continuum of care for these patients using these emerging technologies.

Financial & competing interests disclosure

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Supplementary Data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/fca-2020-0004

References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

1. Costello JP, Olivieri LJ, Krieger A, *et al.* Utilizing three-dimensional printing technology to assess the feasibility of high-fidelity synthetic ventricular septal defect models for simulation in medical education. *World J. Pediatr. Congenit. Heart Surg.* 5(3), 421–426 (2014).

• **Provides detailed information about implementation of a 3D printing program within an educational curriculum for premedical and medical students**

2. Smerling J, Marboe CC, Lefkowitch JH *et al.* Utility of 3D printed cardiac models for medical student education in congenital heart disease: across a spectrum of disease severity. *Pediatr. Cardiol.* 40(6), 1258–1265 (2019).
3. Costello JP, Olivieri LJ, Su L, *et al.* Incorporating three-dimensional printing into a simulation-based congenital heart disease and critical care training curriculum for resident physicians. *Congenit. Heart Dis.* 10(2), 185–190 (2015).
4. Loke T, Krieger A, Sable C, Olivieri L. Novel uses for three-dimensional printing in congenital heart disease. *Curr. Pediatr. Rep.* 4(2), 28–34 (2016).
5. Valverde I, Gomez G, Coserria JF *et al.* 3D printed models for planning endovascular stenting in transverse aortic arch hypoplasia. *Catheter. Cardiovasc. Interv.* 85(6), 1006–1012 (2015).
6. Biglino G, Capelli C, Koniordou D *et al.* Use of 3D models of congenital heart disease as an education tool for cardiac nurses. *Congenit. Heart Dis.* 12(1), 113–118 (2017).
7. Biglino G, Capelli C, Leaver LK, Schievano S, Taylor AM, Wray J. Involving patients, families and medical staff in the evaluation of 3D printing models of congenital heart disease. *Commun. Med.* 12(2–3), 157–169 (2015).
8. Biglino G, Capelli C, Wray J *et al.* 3D-manufactured patient-specific models of congenital heart defects for communication in clinical practice: feasibility and acceptability. *BMJ Open* 5(4), e007165 (2015).
9. Biglino G, Koniordou D, Gasparini *et al.* Piloting the use of patient-specific cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr. Cardiol.* 38(4), 813–818 (2017).
10. Barsom EZ, Graafland M, Schijven MP. Systematic review on the effectiveness of augmented reality applications in medical training. *Surg. Endosc.* 30(10), 4174–4183 (2016).
11. Sarno DA, Gent L, Coppock K, Axelrod DM. Successful virtual-reality cardiopulmonary resuscitation training in schools: digitally linking a physical manikin to a virtual lifesaving scenario. Presented at: *American Heart Association Scientific Sessions 2019.* Philadelphia, PA, USA (2019).
12. Seeker. Revolutionizing heart surgery with virtual reality (2017). https://www.seeker.com/videos/revolutionizing-heart-surgery-with-virtual-reality
13. Lighthaus Inc. www.lighthaus.us
14. Taylor CA, Figueroa CA. Patient-specific modeling of cardiovascular mechanics. *Annu. Rev. Biomed. Eng.* 11, 109–134 (2009).

• **Thorough review of methods to create customized 3D models and perform computational fluid dynamics**

15. Cecchi E, Giglioli C, Valente S *et al.* Role of hemodynamic shear stress in cardiovascular disease. *Atherosclerosis* 214, 249–256 (2011).
16. Cuomo F, Roccabianca S, Dillon-Murphy D, Xiao N, Humphrey JD, Figueroa CA. Effects of age-associated regional changes in aortic stiffness on human hemodynamics revealed by computational modeling. *PLoS ONE* 12(3), e0173177 (2017).
17. Les AS, Shadden SC, Figueroa CA *et al.* Quantification of hemodynamics in abdominal aortic aneurysms during rest and during exercise using magnetic resonance imaging and computational fluid dynamics. *Ann. Biomed. Eng.* 38(4), 1288–1313 (2010).
18. Cebral JR, Lohner R. Efficient simulation of blood flow past complex endovascular devices using an adaptive embedding technique. *IEEE Trans. Med. Imaging* 24, 468–476 (2005).
19. Kim HJ, Vignon-Clementel IE, Coogan JS, Figueroa CA, Jansen KE, Taylor CA. Patient-specific modeling of blood flow and pressure in human coronary arteries. *Ann. Biomed. Eng.* 38(10), 3195–3209 (2010).
20. Dillon-Murphy D, Noorani A, Nordsletten DA, Figueroa CA. Multi-modality image-based analysis of hemodynamics of aortic dissection. *Biomech. Model. Mechanobiol.* 15, 857–876 (2016).
21. Stuhne GR, Steinman DA. Finite-element modeling of the hemodynamics of stented aneurysms. *J. Biomech. Eng.* 126, 382–387 (2004).
22. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve. *J. Am. Coll. Cardiol.* 61, 2233–2241 (2013).
23. Saitta S, Pirola S, Piatti F *et al.* Evaluation of 4D flow MRI-based non-invasive pressure assessment in aortic coarctations. *J. Biomech.* 94, 13–21 (2019).

24. Figueroa CA, Yeh V, Taylor CA, Gorrepati ML, Zarins CK. *In vivo* displacement force (DF) is higher in patients who experience aortic endograft migration: a 3D computational analysis. *J. Vasc. Surg.* 51, S93 (2010).

25. Cuomo F, Ferruzzi J, Humphrey JD, Figueroa CA. An experimental-computational study of catheter induced alterations in pulse wave velocity in anesthetized mice. *Ann. Biomed. Eng.* 43(7), 1555–1570 (2015).

26. Van Bakel TMJ, Arthurs CJ, Herwaarden JA *et al.* A computational analysis of different endograft designs for zone 0 aortic arch repair. *Eur. J. Cardiothorac. Surg.* 54(2), 389–396 (2018).

27. Nauta FJ, Lau KD, Arthurs CJ *et al.* Computational fluid dynamics and aortic thrombus formation following thoracic endovascular aortic repair. *Ann. Thorac. Surg.* 103(6), 1914–1921 (2017).

28. De Zélicourt DA, Haggerty CM, Sundareswaran KS *et al.* Individualized computer-based surgical planning to address pulmonary arteriovenous malformations in patients with a single ventricle with an interrupted inferior vena cava and azygous continuation. *J. Thorac. Cardiovasc. Surg.* 141(5), 1170–1177 (2011).

29. Van Bakel TMJ, Lau KD, Hirsch-Romano J, Trimarchi S, Dorfman AL, Figueroa CA. Patient-specific modeling of hemodynamics: supporting surgical planning in a fontan circulation correction. *J. Cardiovasc. Transl. Res.* 11(2), 145–155 (2017).

30. Arthurs CJ, Agarwal P, John A, Dorfman A, Grifka R, Figueroa CA. Reproducing patient-specific hemodynamics in the Blalock-Taussig circulation using a flexible multi-domain simulation framework: applications for optimal shunt design. *Front. Pediatr.* 5, 78 (2017).

31. Vignon-Clementel IE, Figueroa CA, Jansen KE, Taylor CA. Outflow boundary conditions for three-dimensional simulations of non-periodic blood flow and pressure fields in deformable arteries. *Comp. Meth. Biomech. Biomed. Eng.* 13(5), 625–640 (2010).

32. Simpson J, Lopez L, Acar P *et al.* Three-dimensional echocardiography in congenital heart disease: an expert consensus document from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J. Am. Soc. Echocardiogr.* 30(1), 1–27 (2017).

33. Olivieri LJ, Krieger A, Loke YH, Nath DS, Kim PC, Sable CA. Three-dimensional printing of intracardiac defects from three-dimensional echocardiographic images: feasibility and relative accuracy. *J. Am. Soc. Echocardiogr.* 28(4), 392–397 (2015).

34. Valverde I, Gomez-Ciriza G, Hussain T *et al.* Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study. *Eur. J. Cardiothorac. Surg.* 52(6), 1139–1148 (2017).

•• **Prospective, multicenter study evaluating understanding of complex congenital heart disease and consequent surgical approach**

35. Garekar S, Bharati A, Chokhandre M *et al.* Clinical application and multidisciplinary assessment of three dimensional printing in double outlet right ventricle with remote ventricular septal defect. *World J. Pediatr. Congenit. Heart Surg.* 7(3), 344–350 (2016).

36. Bhatla P, Tretter JT, Ludomirsky A *et al.* Utility and scope of rapid prototyping in patients with complex muscular ventricular septal defects or double-outlet right ventricle: does it alter management decisions? *Pediatr. Cardiol.* 38(1), 103–114 (2017).

37. Juhnke B, Mattson AR, Saltzman D *et al.* Use of virtual reality for pre-surgical planning in separation of conjoined twins: a case report. *Proc. Inst. Mech. Eng. H* 233(12), 1327–1332 (2019).

38. Hsiao A, Lustig M, Alley MT, Murphy MJ, Vasanawala SS. Evaluation of valvular insufficiency and shunts with parallel-imaging compressed-sensing 4D phase-contrast MR imaging with stereoscopic 3D velocity-fusion volume-rendered visualization. *Radiology* 265(1), 87–95 (2012).

39. Ballocca F, Meier LM, Ladha K, Qua Hiansen J, Horlick EM, Meineri M. Validation of quantitative 3-dimensional transesophageal echocardiography mitral valve analysis using stereoscopic display. *J. Cardiothorac. Vasc. Anesth.* 33(3), 732–741 (2019).

40. Ong CS, Krishnan A, Huang CY *et al.* Role of virtual reality in congenital heart disease. *Congenit. Heart Dis.* 13(3), 357–361 (2018).

41. Brun H, Bugge RAB, Suther LKR *et al.* Mixed reality holograms for heart surgery planning: first user experience in congenital heart disease. *Eur. Heart J. Cardiovasc. Imaging* 20(8), 883–888 (2019).

• **Proof-of-concept study on preoperative use of mixed reality holograms on patient-specific 3D heart models, showing highly rated diagnostic value.**

42. Bruckheimer E, Rotschild C, Dagan T *et al.* Computer-generated real-time digital holography: first time use in clinical medical imaging. *Eur. Heart J. Cardiovasc. Imaging* 17(8), 845–849 (2016).

43. Tandon A, Burkhardt BEU, Batsis M *et al.* Sinus venosus defects: anatomic variants and transcatheter closure feasibility using virtual reality planning. *JACC Cardiovasc. Imaging* 12(5), 921–924 (2019).

44. Lu JC, Ensing GJ, Ohye RG, *et al.* Virtual reality three-dimensional modeling for congenital heart surgery planning. *J. Am. Soc. Echocardiogr.* 32(6), B1–B137 (2019).

45. Bonnichsen C, Ammash N. Choosing between MRI and CT imaging in the adult with congenital heart disease. *Curr. Cardiol. Rep.* 18(5), 45 (2016).

46. Sahu A, Slesnick TC. Imaging adults with congenital heart disease part II: advanced CMR techniques. *J. Thorac. Imaging* 32, 245–247 (2017).

47. Kakareka JW, Faranesh AZ, Pursley RH *et al.* Physiological recording in the MRI environment (PRiME): MRI-compatible hemodynamic recording system. *IEEE J. Transl. Eng. Health Med.* 6, 4100112 (2018).

48. Ratnayaka R, Kanter JP, Faranesh AZ *et al.* Radiation-free CMR diagnostic heart catheterization in children. *J. Cardiovasc. Magn. Reson.* 19(1), 65 (2017).

49. Rogers T, Ratnayaka K, Khan JM *et al.* CMR fluoroscopy right heart catheterization for cardiac output and pulmonary vascular resistance: results in 102 patients. *J. Cardiovasc. Magn. Reson.* 19(1), 54 (2017).

50. Ratnayaka K, Rogers T, Schenke WH *et al.* Magnetic resonance imaging-guided transcatheter cavopulmonary shunt. *JACC Cardiovasc. Interv.* 9(9), 959–970 (2016).

51. Campbell-Washburn AE, Tavallaei MA, Pop M *et al.* Real-time MRI guidance of cardiac interventions. *J. Magn. Reson. Imaging* 46(4), 935–950 (2017).

52. Glockler M, Halbfab J, Koch A *et al.* Multimodality 3D-roadmap for cardiovascular interventions in congenital heart disease-A single-center, retrospective analysis of 78 cases. *Catheter. Cardiovasc. Interv.* 82, 436–442 (2013).

53. Goreczny S, Dryzek P, Moszura T *et al.* Magnetic resonance and computed tomography imaging fusion for live guidance of percutaneous pulmonary valve implantation. *Adv. Interv. Cardiol.* 14(4), 413–421 (2018).

54. Goreczny S, Dryzek P, Morgan GJ *et al.* Novel three-dimensional image fusion software to facilitate guidance of complex cardiac catheterization: 3D image fusion for interventions in CHD. *Pediatr. Cardiol.* 38, 1133–1142 (2017).

55. Goreczny S, Moszura T, Dryzek P *et al.* Three-dimensional image fusion guidance of percutaneous valve implantation to reduce radiation exposure and contrast dose: a comparison with traditional two-dimensional and three-dimensional rotation angiographic guidance. *Neth. Heart J.* 25, 91–99 (2017).

56. Krishnaswamy A, Tuzcu EM, Kapadia SR. Integration of MDCT and fluoroscopy using C-arm computed tomography to guide structural cardiac interventions in the cardiac catheterization laboratory. *Catheter. Cardiovasc. Interv.* 85, 139–147 (2015).

• **Evaluation of fluoroscopic 3D overlay of computed tomographic images to guide structural heart interventions**

57. Whiteside W, Christensen J, Zampi JD. Three-dimensional magnetic resonance imaging overlay to assist with percutaneous transhepatic access at the time of cardiac catheterization. *Ann. Pediatr. Cardiol.* 8(2), 150–152 (2015).

58. Fagan T, Kay J, Carroll J, Neubauer A. 3-D guidance of complex pulmonary artery stent placement using reconstructed rotational angiography with live overlay. *Catheter. Cardiovasc. Interv.* 79, 414–421 (2012).

59. Goreczny S, Morgan GJ, Dryzek P. Live 3D image overlay for arterial duct closure with Amplatzer Duct Occluder II additional size. *Cardiol. Young* 26, 605–608 (2016).

60. Armstrong AK, Zampi JD, Itu LM, Benson LN. Use of 3D rotational angiography to perform computational fluid dynamics and virtual interventions in aortic coarctation. *Catheter. Cardiovasc. Interv.* DOI: 10.1002/ccd.28507 (2019) (Epub ahead of print).

•• **Report of the first use of cardiac 3D rotational angiography for computational fluid dynamics, showing validity of hemodynamic computations**

61. Fagan TE, Truong UT, Jone P *et al.* Multimodality 3-dimensional image integration for congenital cardiac catheterization. *Methodist Debakey Cardiovasc. J.* 10(2), 68–76 (2014).

62. Fritz J, U-Thainual P, Ungi T *et al.* MR-guided vertebroplasty with augmented reality image overlay navigation. *Cardiovasc. Intervent. Radiol.* 37, 1589–1596 (2014).

63. Cabrilo I, Bijlenga P, Schaller K. Augmented reality in the surgery of cerebral aneurysms: a technical report. *Neurosurgery* 10(2), 252–260 (2014).

64. Cabrilo I, Bijlenga P, Schaller K. Augmented reality in the surgery of cerebral arteriovenous malformations: technique assessment and considerations. *Acta Neurochir.* 156, 1769–1774 (2014).

65. Cabrilo I, Sarrafzadeh A, Bijlenga P, Landis BN, Schaller K. Augmented reality-assisted skull base surgery. *Neurochirurgie* 60, 304–306 (2014).

66. Carl B, Bopp M, Sab B, Nimsky C. Microscope-based augmented reality in degenerative spine surgery: initial experience. *World Neurosurg.* 128, e541–551 (2019).

67. Witowski J, Darocha S, Kownacki L *et al.* Augmented reality and three-dimensional printing in percutaneous interventions on pulmonary arteries. *Quant Imaging Med. Surg.* 9(1), 23–29 (2019).

68. Opolski MP, Michalowska LM, Borucki BA, Nicinska B, Szumowski L, Sterlinski M. "Augmented-reality computed tomography-guided transcatheter pacemaker implantation in dextrocardia and congenitally corrected transposition of great arteries". *Cardiol. J.* 25(3), 412–413 (2018).

69. Vasilyev NV, Novotny PM, Martinez JF *et al.* Stereoscopic vision display technology in real-time three-dimensional echocardiography-guided intracardiac beating-heart surgery. *J. Thorac. Cardiovasc. Surg.* 135, 1334–1341 (2008).

10.2217/fca-2020-0004