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STATE-OF-THE-ART REVIEW

3D Printing is a Transformative Technology in Congenital Heart Disease

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SUMMARY

Survival in congenital heart disease has steadily improved since 1938, when Dr. Robert Gross successfully ligated for the first time a patent ductus arteriosus in a 7-year-old child. To continue the gains made over the past 80 years, transformative changes with broad impact are needed in management of congenital heart disease. Three-dimensional printing is an emerging technology that is fundamentally affecting patient care, research, trainee education, and interactions among medical teams, patients, and caregivers. This paper first reviews key clinical cases where the technology has affected patient care. It then discusses 3-dimensional printing in trainee education. Thereafter, the role of this technology in communication with multidisciplinary teams, patients, and caregivers is described. Finally, the paper reviews translational technologies on the horizon that promise to take this nascent field even further.
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Three-dimensional (3D) printing is an additive manufacturing technique with increasing use in health care. As a fabrication technique 3D printing was recently listed by the McKinsey Global Institute as a "disruptive technology that will transform life, business and the global economy," with a potential economic impact of $200 billion to $600 billion between 2013 and 2025 (1). In health care, adoption of this technology has been a relatively recent phenomenon. A recent review found just 2 papers (excluding case studies and abstracts) in medical publications before 2000, and that number grew to 189 between 2011 and 2015 (2). Use within cardiology has followed a similar trend, with growth mainly in the past decade (3). Vukicevic et al. (4) recently published an excellent review of cardiac 3D printing focusing primarily on acquired structural heart disease. In this paper, we review the transformative role of 3D printing in congenital heart disease (CHD) (**Central Illustration**).

SCOPE OF CONGENITAL HEART DISEASE AND THE NEED FOR TRANSFORMATIVE CARE

The prevalence of CHD is approximately 9 in 1,000 live births (5,6). Survival rates vary by disease complexity, with long-term survival (>20 years) at approximately 95% for simple CHD, 90% for moderate complexity, and 80% for severe, complex CHD (7). Overall survival rates have steadily increased for even the most complex CHD (8–11), although survival alone

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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Basic to Translational Science* author instructions page.

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is not a sufficient outcome measure in the current era. Other important metrics include the following: long-term morbidity; reintervention rates; length of hospitalization; neurodevelopmental outcomes; cost to the health care system; and patient or caregiver satisfaction. Obtaining the best outcomes requires an impact at multiple levels, including patients and caregivers, individual clinicians, the medical team and the health care system. 3D printing is a disruptive technology that is affecting each of these key areas in CHD.

The earliest papers on cardiovascular 3D printing were published in the early 2000s. Binder et al. (12) showed feasibility from echocardiographic data in 2000, and Pentacost et al. (13) produced 3D models replicating cardiac embryology from photomicrographic data in 2001. Soon thereafter, datasets from computed tomography (CT) or magnetic resonance imaging (MRI) were used to produce 3D cardiac models of increasing complexity (14–16), with a steady rise in publications in the past decade (3). **Figure 1** shows the applications of 3D printing in medicine, broadly categorized as surgical planning, education, and manufacturing of custom parts (17). Given that a 3D model is a replica of a patient's anatomy, models may be used for precise pre-surgical planning and simulation (18–21). Patient-specific pre-surgical planning may potentially reduce time spent in the operating room (OR) and result in fewer complications. In turn, this may lead to shorter post-operative stays, decreased reintervention rates, and lower health care costs. Given the relatively recent use of 3D printing in CHD, there are currently no data supporting these presumed outcomes. Most of the evidence in published reports is qualitative, through case reports and series. Emerging reports from other surgical subspecialties appear promising. Recent data from craniofacial reports suggest that 3D printing can improve outcomes, including saving time in the OR and thus translating to direct cost savings (22,23).

3D PRINTING TECHNOLOGY AND OPTIONS FOR CARDIOVASCULAR PRINTING

Several recent publications have described the process of medical 3D printing (3,4,24–27), summarized as these key steps:

1. *Acquisition* of a high-resolution 3D imaging dataset
2. *Segmentation* of the anatomy using specialized post-processing software
3. *Computer-aided design* to refine the design, add cut-planes, or include elements required for model stability
4. *Creation of a 3D file* in a format recognized by the 3D printer, usually in the Surface Tessellation Language or stereolithography (STL) file format
5. *Printing* of the physical model

3D printing technologies may be categorized as *photopolymeric* (the use of light to harden a deposited photopolymer), *thermoplastic* (extruding melted thermoplastics in layers to build up a model), or *powder fusion* (a process that fuses ceramic or metal powder by using an adhesive or laser beam to create a 3D object) (4,24). Printer resolution for higher-end medical-grade printers is in the order of micrometers, well within the resolution needed to print cardiac structures. **Figure 2** shows these technologies in detail (28).

Principally, there are 2 main types of cardiac models: "blood-pool" and "hollow" models. Blood pool models are solid 3D representations of the blood pool within the cardiac chambers and vessels (**Figure 3**). They are created by segmenting the blood pool signal, usually from contrast-enhanced CT or MRI, after which the 3D object is printed. Non-cardiovascular structures such as airways or soft tissue may also be included for printing. These models provide excellent visualization of the great vessels, extracardiac vasculature, and surrounding structures such as airways or the esophagus. The drawback of these types of models is their limited views of intracardiac anatomy.

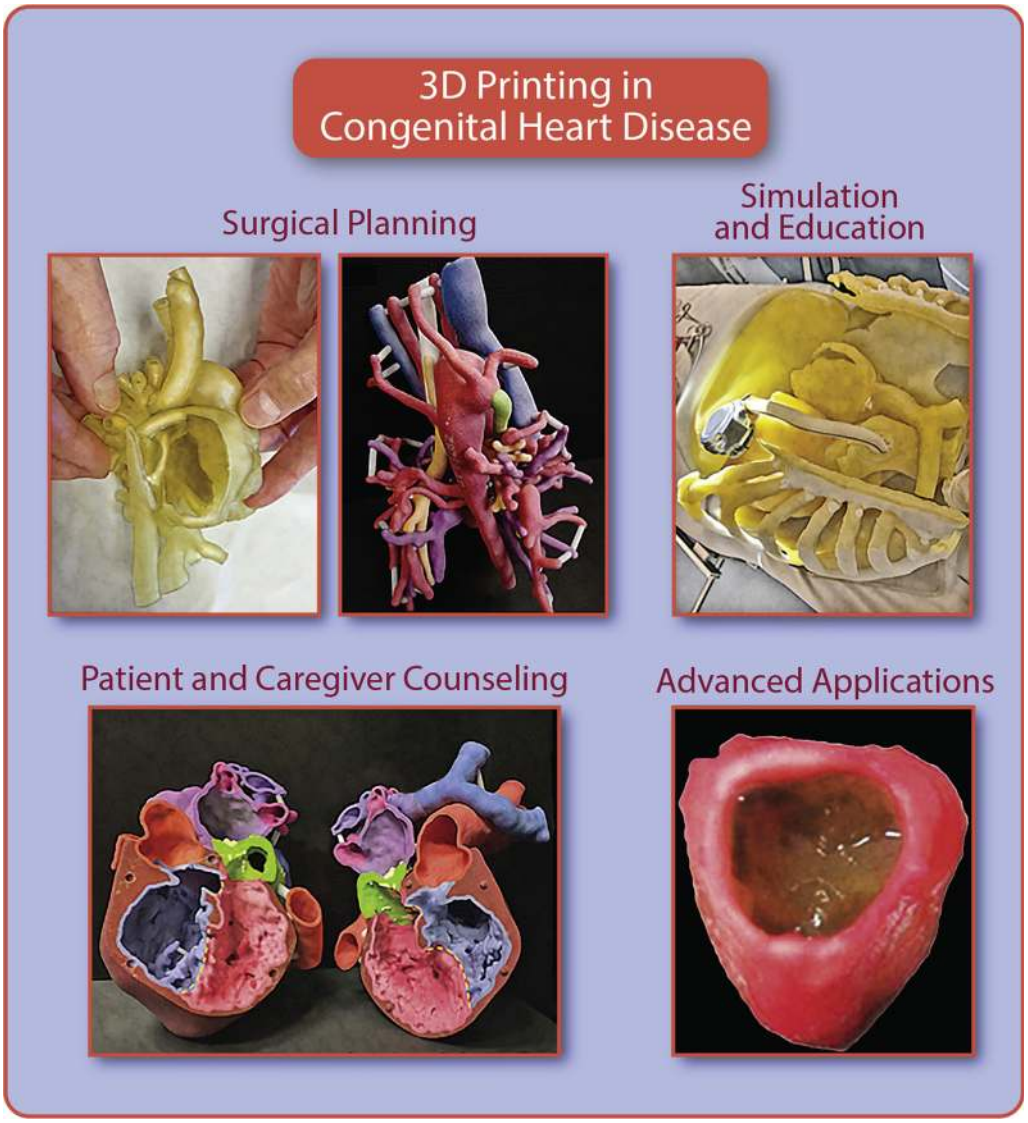
Hollow models are created by applying a mesh representing myocardium and vessel walls around the blood pool signal and then digitally removing the blood pool signal to show the intracardiac cavities. The end result is a hollow model showing the intracardiac anatomy in detail. These models are usually sectioned along a pre-determined cut-plane with 2 or more sections showing the intracardiac anatomy, as shown in **Figure 4**.

A subtype of the hollow models consists of intact hollow models. These models also show the intracardiac anatomy but are printed intact (i.e., without a cut-plane), thereby resulting in the most accurate representation of the heart as it sits in the chest. When printed in a flexible material, these models allow cardiothoracic surgeons to use standard surgical approaches and see the anatomy from a "surgeon's perspective," as they would for the actual case (**Figures 5A and 5B**). Thus, these models are ideal for surgical simulation, especially when they are printed in materials that can be cut, can hold suture,

ABBREVIATIONS AND ACRONYMS

3D = three-dimensional
ACHD = adults with congenital heart disease
APC = aortopulmonary collaterals
ASD = atrial septal defect
CHD = congenital heart disease
CT = computed tomography
DORV = double outlet right ventricle
MAPCAs = multiple aortopulmonary collaterals
MRI = magnetic resonance imaging
OR = operating room
VSD = ventricular septal defect

CENTRAL ILLUSTRATION **Applications of 3D Printing in Congenital Heart Disease**



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and can allow engraftment of foreign materials (e.g., patch, cannula).

APPLICATIONS OF 3D PRINTING IN CHD

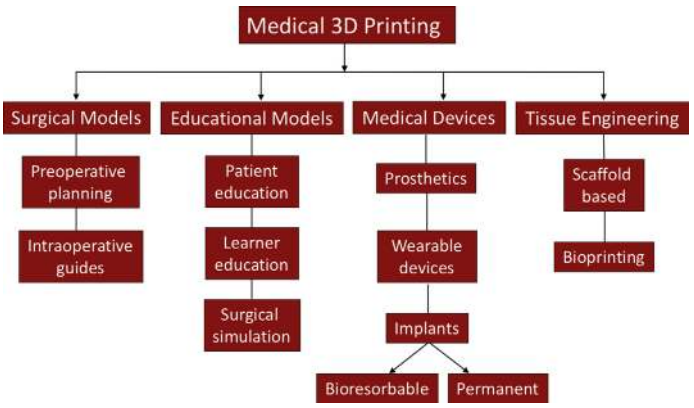
Several publications have described the use of 3D printing in CHD, spanning the spectrum from atrial or ventricular septal defects (ASDs, VSDs) (29,30) to the most complex cardiac lesions (18,21,25,31–36). Published reports have been summarized in a recent textbook on cardiac 3D printing (24).

A selection of cases is now reviewed to show the main applications of 3D printing in CHD. These cases were selected from a cohort of pediatric and adult patients with CHD at our institution who underwent 3D printing. For the complete list of cases, please refer to Supplemental Table 1. Most of these cases were printed for surgical planning and simulation; others with unique or rare anatomy were printed for trainee education. The majority of cases had complex CHD, with a median complexity score of 3 (simple = 1, moderate = 2, great = 3) (37). Most of the cases printed for surgical planning were high-risk surgical candidates, and the median Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery mortality category (1 to 5) was 4.

PLANNING COMPLEX INTRACARDIAC REPAIR. Three of 1,000 patients born with CHD require catheter-based or surgical intervention early in life (38). Outcomes are significantly affected by the complexity of the underlying anatomy and perioperative factors, including cardiopulmonary bypass time, ischemic time, or circulatory arrest time (39-43). 3D models allow the visualization and understanding of complex spatial relationships and enable precise pre-surgical planning. A common application in CHD is planning repair of a double-outlet right ventricle (DORV) requiring a complex intracardiac baffle. This is typically a high-risk operation, Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery category 4 (44). **Figure 6** shows this application in an 8-month-old (8 kg) patient with a complex DORV, previously reported by our group (18). The patient had visceroatrial situs inversus, dextrocardia, and a DORV with levomalposed great arteries. The model in **Figure 6** demonstrates the key anatomy to plan a 2-ventricle repair. The patient had a successful 2-ventricle repair consistent with the model-guided pre-surgical plan. Several other groups have reported the use of 3D printing to plan complex intracardiac repairs in patients with multiple VSDs or DORV (30-32,36).

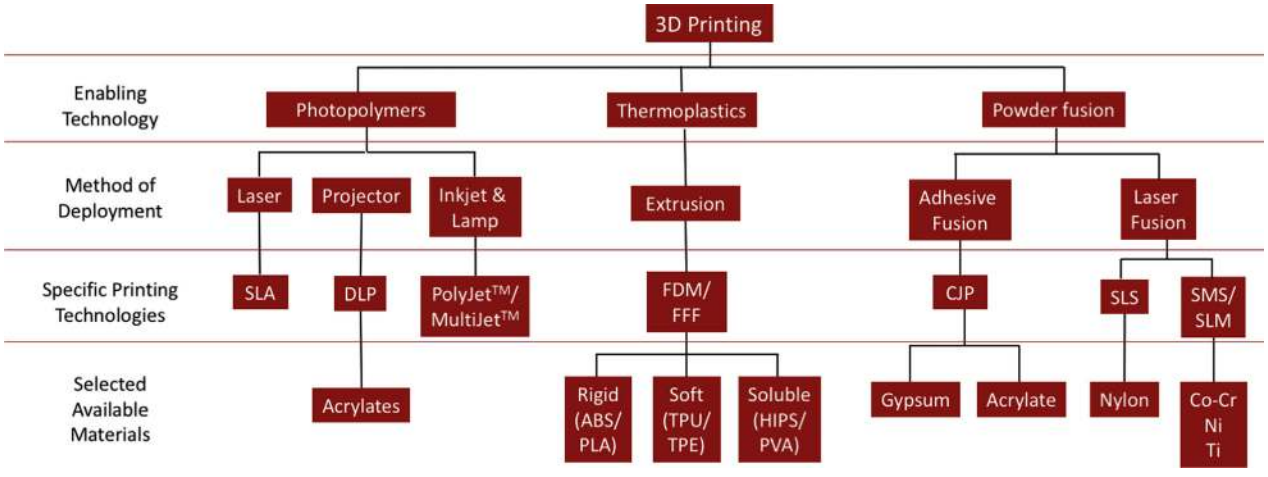
SURGICAL SIMULATION. The ultimate in pre-surgical planning using 3D models is one in which a "simulated surgery" is performed, as illustrated by the next case. The patient was a 3 1/2-year-old male child with heterotaxy, asplenia syndrome with complex single ventricle anatomy, and abnormal systemic and pulmonary venous connections (**Figure 7**). He had previously undergone bilateral bidirectional superior cavopulmonary connections (bilateral Glenn procedure) as part of single ventricle palliation. 3D printing was performed to plan his next surgery, a total cavopulmonary connection (aka Fontan). Two 3D models were printed; 1 multicolor with an axial cut-plane and

FIGURE 1 Application of 3D Printing in Medicine



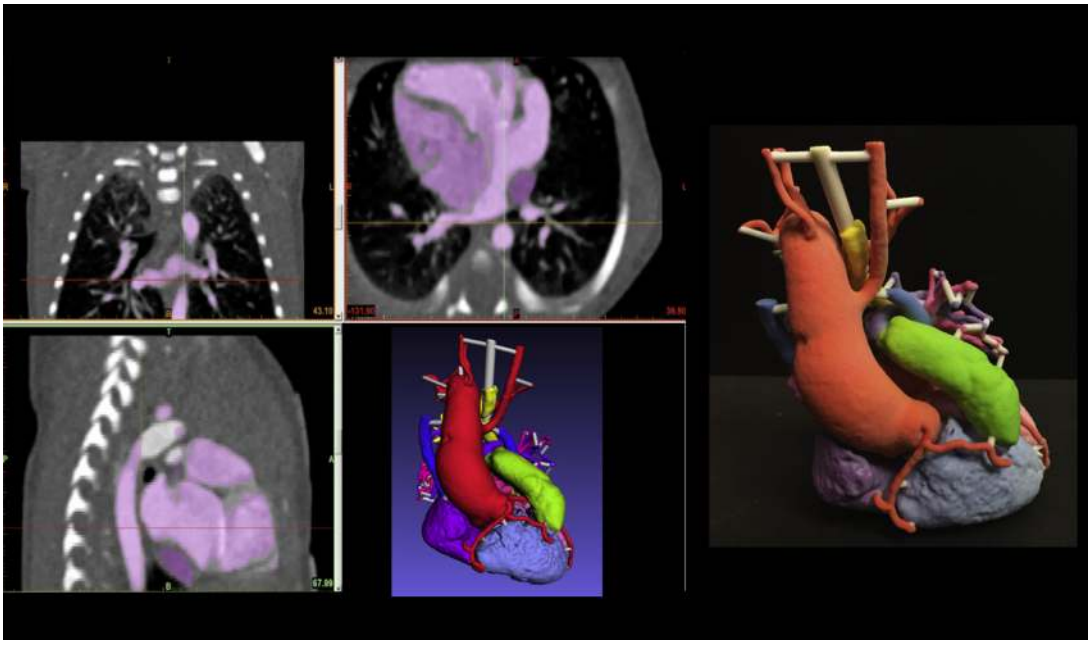
Most of these applications pertain to cardiology, except for wearable devices, for which the authors did not find any cardiac-specific published reports. Adapted with permission from VanKoevering et al. (17).

FIGURE 2 3D Printing Technologies



ABS = acrylonitrile butadiene styrene; CJP = color jet printing; Co = cobalt; Cr = chromium; DLP = direct light processing; FDM = fused deposition modeling; FFF = fused filament fabrication; HIPS = high impact polystyrene; Ni = nickel; PLA = polylactic acid; PVA = polyvinyl alcohol; SLA = stereolithography apparatus; SLM = selective laser melting; SLS = selective laser sintering; Ti = titanium; TPE = thermoplastic elastomer; TPU = thermoplastic urethane. Reproduced with permission from Borrello et al. (28).

FIGURE 3 Blood Pool Cardiac 3D Model



Source images on the **left** show the segmented blood pool signal. The model is shown on the **right.**

a second flexible intact-heart model (no cut-plane) for surgical simulation. The internal anatomy of both models was identical. By using the models, detailed pre-surgical planning was performed. Specifically, the models were used to plan placement of the Fontan conduit (intracardiac or extracardiac) and to evaluate its relationship with systemic veins and impact on pulmonary veins. The model was also used to simulate "plan A," "plan B," or "bailout" scenarios, each with a unique surgical plan. This level of detailed surgical simulation is not feasible with current standard of care (e.g., 3D volumetric rendering), and it shows the added value of 3D printed models. Supplemental Video 1 (**Figure 7**) shows the pre-surgical planning session for this case with the cardiothoracic surgeon and cardiologists.

FIGURE 4 Hollow Cardiac 3D Model Showing Intracardiac Anatomy

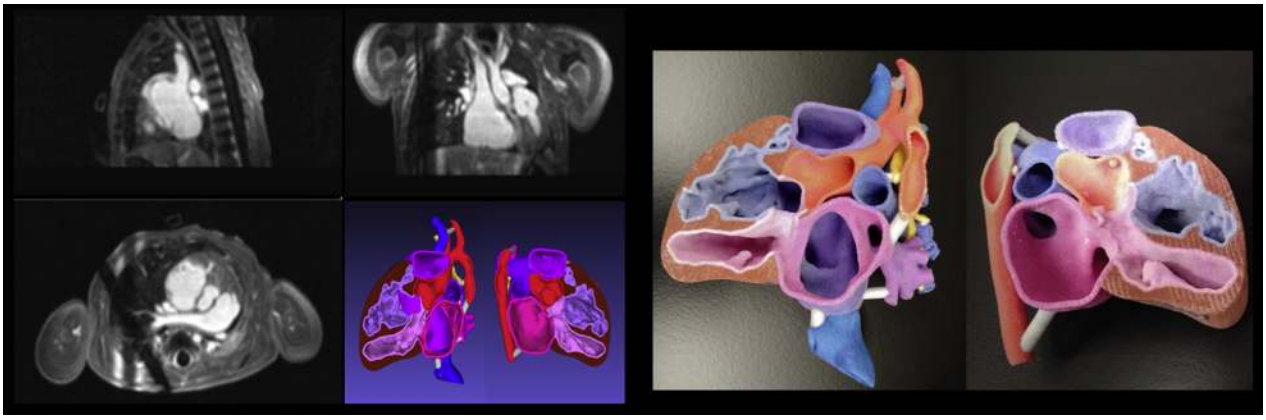
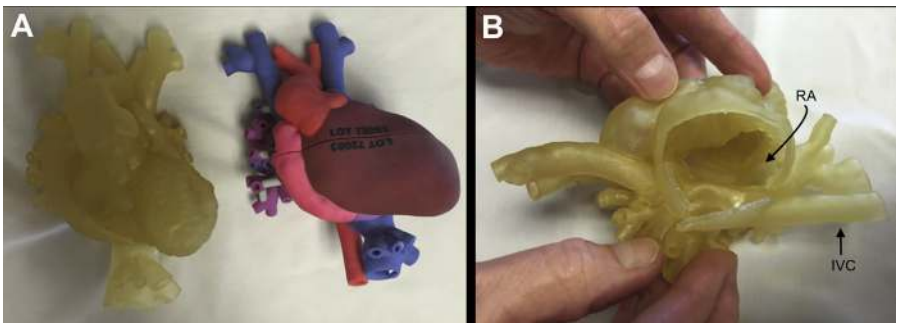


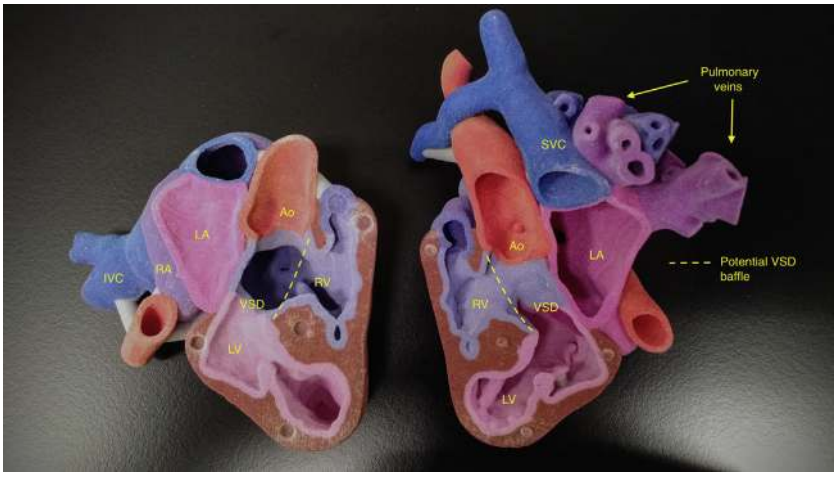
FIGURE 5 Models for Surgical Planning



(A) Flexible hollow model printed intact with corresponding rigid multicolor model. **(B)** The "surgeon's view" through a right atriotomy. IVC = inferior vena cava; RA = right atrium.

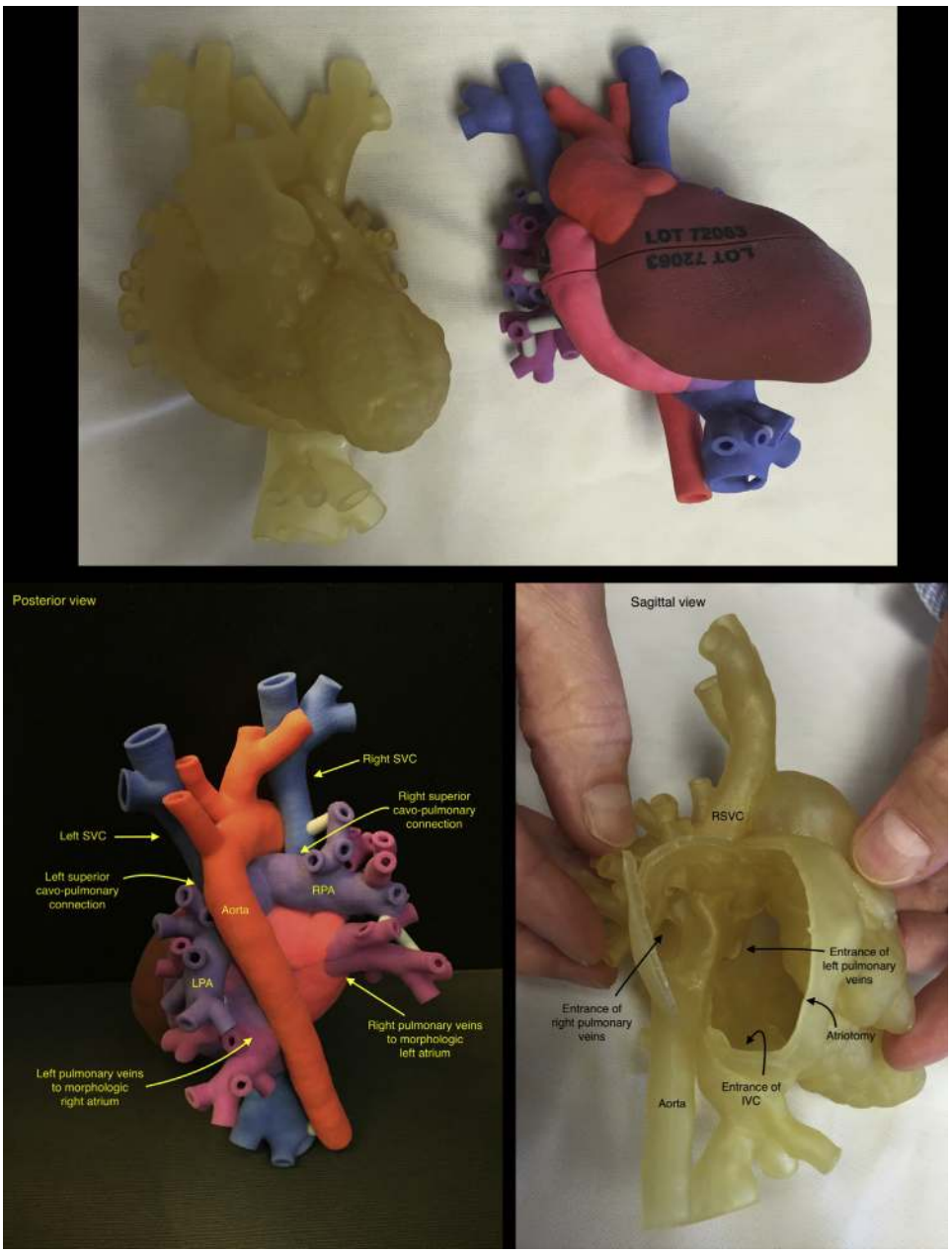
EXTRACARDIAC AND VASCULAR SURGERY. 3D printing can be a valuable tool to plan extracardiac and vascular surgery in patients with CHD. 3D models are helpful for planning high-risk unifocalization surgery, as illustrated by the following case. **Figures 8A to 8E** show a case of tetralogy of Fallot, pulmonary atresia, and MAPCAs in a patient with 22q11 deletion (DiGeorge syndrome), with repair undertaken in 3 stages because of high pre-surgical morbidity in this patient. We previously reported the first stage of this operation done at 10 months of age (18). **Figure 8** shows all 3 stages. The 3D models show spatial relationships among the aorta, aortopulmonary collaterals (APCs), pulmonary veins, and airways that enabled detailed pre-surgical planning. Precise visualization of the complex relationships between APCs and surrounding structures enables easier identification and surgical manipulation during the case, thereby reducing operative time and potentially improving the surgical outcome. This patient underwent a right modified Blalock-Taussig-Thomas shunt to the right-sided APCs (**Figure 8B**), followed by a left modified Blalock-Taussig-Thomas shunt (**Figure 8D**) and, ultimately, successful unifocalization (**Figure 8E**). 3D printing for pulmonary atresia and MAPCAs offers significant benefits over

FIGURE 6 3D Model of Double-Outlet RV Showing Relationships Among Ventricles, VSD, and Outflows



The **dashed line** indicates the potential ventricular septal defect (VSD) baffle pathway to achieve a 2-ventricle repair. Ao = aorta; LA = left atrium; LV = left ventricle; RV = right ventricle; SVC = superior vena cava; other abbreviations as in **Figure 5**.

FIGURE 7 Simulated Surgery for Complex Total Cavopulmonary Connection Planning Using Flexible, Intact-Heart Model

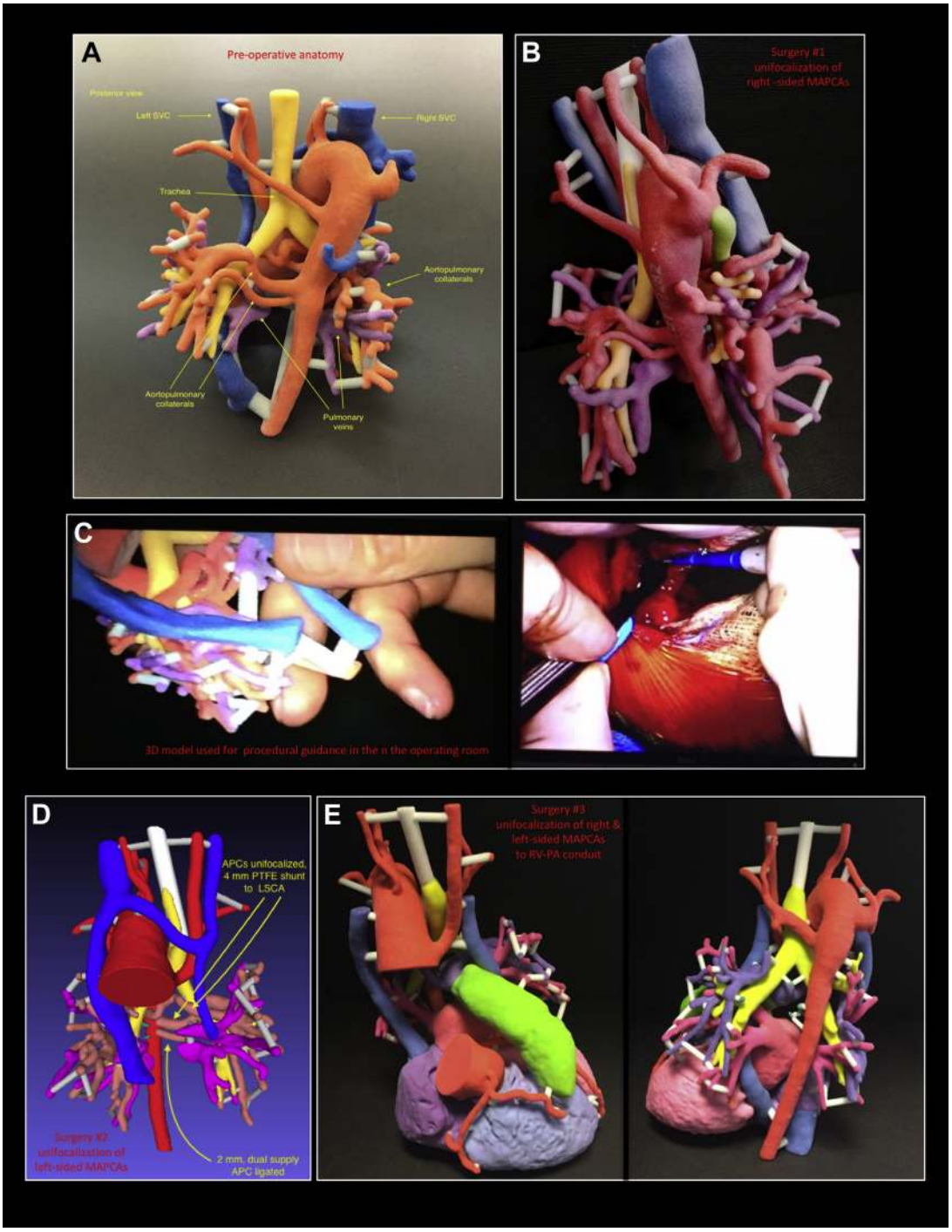


See Supplemental Video 1. LPA = left pulmonary artery; RPA = right pulmonary artery; RSVC = right superior vena cava; other abbreviations as in **Figures 5 and 6**.

current standard of care, also described in prior publications (14,21).

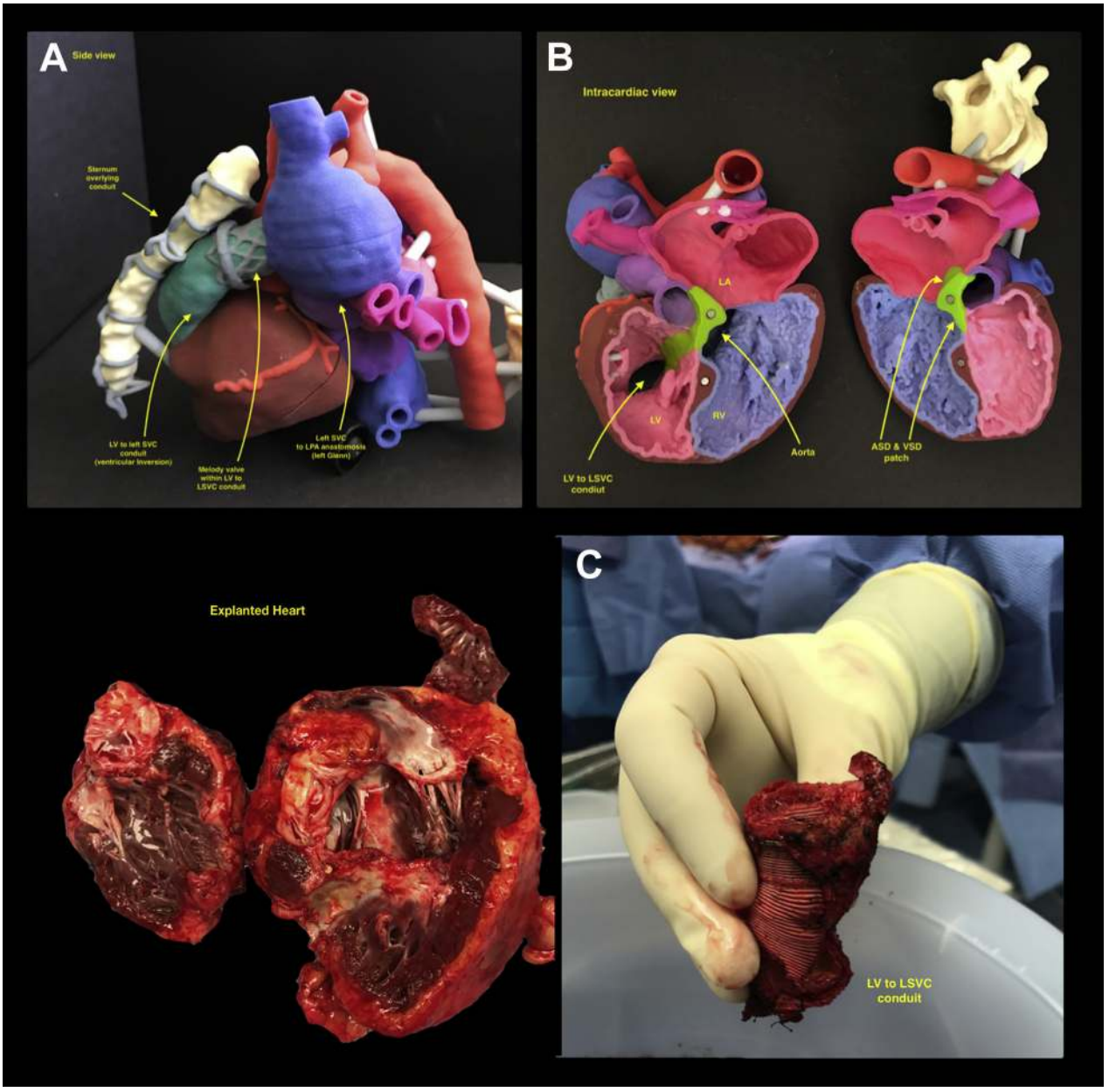
VENTRICULAR ASSIST DEVICE AND HEART TRANSPLANT. An endpoint of many patients with CHD is heart failure requiring a ventricular assist device or heart transplant. 3D printing can aid in ventricular assist device placement and optimizing function in complex CHD, as recently described by Farooqi et al (20) and Saeed et al. (45). 3D printing can also assist with transplant planning for recipients with complex CHD, as in the following case. **Figures 9A to 9C** show a 22-year-old male patient with heterotaxy syndrome, unbalanced atrioventricular canal, L-looped

FIGURE 8 Staged Repair of Tetralogy of Fallot, Pulmonary Atresia, and MAPCAs



(A) Pre-operative anatomy. **(B)** Unifocalization of right-sided major aortopulmonary collateral arteries (MAPCAs) and small right pulmonary artery (PA)-to-right modified Blalock-Taussig-Thomas shunt. **(C)** Use of 3D model in the operating room for procedural guidance. **(D)** Unifocalization of left-sided major aortopulmonary collateral arteries-to-left modified Blalock-Taussig-Thomas shunt. **(E)** Right ventricular (RV)-to-pulmonary artery conduit placement **(green)** to unifocalized major aortopulmonary collateral arteries and takedown of bilateral modified Blalock-Taussig-Thomas shunts. APC = aortopulmonary collateral; LSCA = left subclavian artery; PTFE = polytetrafluoroethylene; SVC = superior vena cava.

FIGURE 9 Heterotaxy, Unbalanced Atrioventricular Canal, Ventricular Inversion, Modified Fontan



(A) 3D model showing a left ventricle (LV)–to–left superior vena cava (LSVC) conduit and left-sided Glenn procedure that complicates transplantation of a normal donor heart. **(B)** Intracardiac anatomy. **(C)** Intraoperative findings: explanted heart and a left ventricle–to–left superior vena cava conduit, showing accuracy of the 3D model. ASD = atrial septal defect; other abbreviations as in Figures 6 and 7.

ventricles (ventricular inversion), and pulmonary atresia. He had undergone 6 prior sternotomies including ASD and VSD closure, culminating in a unique modified Fontan procedure with a left ventricular (pulmonic ventricle)-to-left superior vena cava conduit after thrombosis of his right-sided Glenn procedure. More recently, a Melody valve was placed in a left ventricular-to-left superior vena cava conduit for conduit stenosis. He presented with severe protein-losing enteropathy and heart failure. Given the patient's debilitated state and multiple prior sternotomies, he was deemed a very high

surgical risk for cardiac transplantation. 3D printing was performed to plan key components of the transplant, including thoracic entry, cannulation options, conduct of bypass, and graft-donor connections. 3D printing for transplant planning has been previously described for patients with complex pre-transplant anatomy (46,47).

AIRWAY ABNORMALITIES. In CHD cases, the airways may be involved in the pathophysiology or need to be accounted for in surgical planning, as demonstrated earlier in the case with tetralogy of Fallot with pulmonary atresia and MAPCAs. In some CHD lesions, airways may be directly affected by the cardiovascular disease. Examples include vascular rings (**Figure 10A**), where aberrant vessels cause airway compression, or compression from dilated pulmonary arteries in tetralogy of Fallot with absent pulmonary valve (**Figure 10B**).

Airway compression or tracheobronchomalacia can significantly add to morbidity of patients with CHD from prolonged ventilator dependence. 3D printing recently led to a momentous breakthrough in the management of these patients with the use of 3D printed bioresorbable airway splints (48,49). Pilot data from 4 patients are shown in **Figure 11**. In this series 3D printed splints were implanted without complications and resulted in patency of the airway. If successful in larger cohorts, this application of 3D printing will dramatically change the management and outcomes for these challenging patients. Other applications of 3D printing in otolaryngology and airway abnormalities were recently reviewed by VanKoevering et al. (17).

CATHETER-BASED INTERVENTIONS. 3D printing has been used for catheter-based interventions in CHD, although to a lesser degree compared with cardiothoracic surgery. Some noteworthy applications include the following: percutaneous pulmonary valve implantation, reported as early as 2007 (50); coarctation procedures (51); and stenting for aortic arch hypoplasia (52). Other reported applications include transcatheter ASD closure (29), double-lobed left atrial appendage closure (53), caval valve implantation (54), and stenting of Mustard baffle obstruction (55). 3D printing is of particular interest in noncongenital structural heart disease, including transcatheter mitral and aortic valve interventions (56–58). Potential benefits in interventional cardiology include visualization of complex anatomy that leads to decreased radiation and contrast from fluoroscopy and angiography and improved procedural outcome. Other benefits may include device development and testing in models that replicate abnormal anatomy (59). Finally, a key benefit may be feasibility testing for complex or borderline cases, as in the case of this 15-year-old male patient from our institution with repaired tetralogy of Fallot who met the criteria for pulmonary valve replacement (**Figure 12**). MRI measurements indicated that his right ventricular outflow tract dimensions were borderline large for transcatheter pulmonary valve replacement; thus, a 3D model was made in flexible material to trial pre-stenting as a precursor to transcatheter pulmonary valve replacement. The 3D model showed feasibility of the catheter-based strategy, and the procedure was carried out, with subsequent successful implantation of a transcatheter pulmonary valve, thereby avoiding surgery.

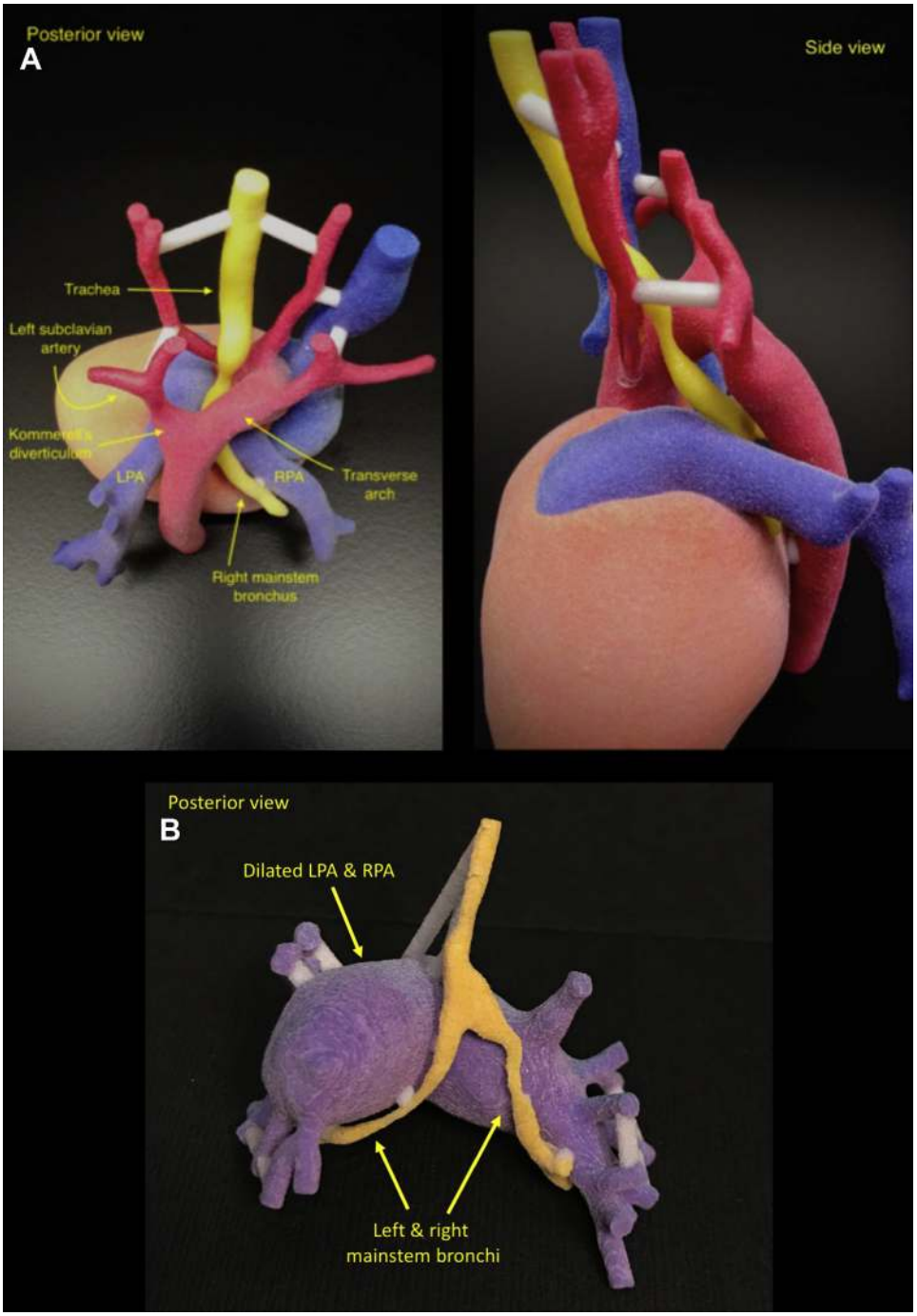
Impediments to greater use of 3D models in catheter-based procedures include tissue characteristics of the models that do not respond to balloons and stents in the same way as native tissue. Moreover, current models do not reflect the physiological environment encountered during catheterization, with nonpulsatility a major limitation of static models. Both these limitations may be overcome with future iterations of 3D models, as discussed later in this article.

ADULTS WITH CONGENITAL HEART DISEASE. Approximately 85% of children with CHD now survive into adulthood (60), and adults with CHD (ACHD) now outnumber children (61). There are an estimated 5 million adult survivors in the United States alone (62,63). Over the past few decades the proportion of all deaths in patients with CHD has shifted from infants to the ACHD population (64). Similar to their pediatric counterparts, risk factors that worsen ACHD outcomes include complex anatomy, prior surgeries, and length of time spent on cardiopulmonary bypass (65–67). Although the challenges involving complex ACHD are considerable, 3D printing may help in their management by applications described in prior sections and in recent publications (20,25,26,68,69). Representative cases are shown in **Figures 13A to 13D**, as previously described (68).

ACCURACY AND QUALITY ASSURANCE IN CARDIAC 3D PRINTING

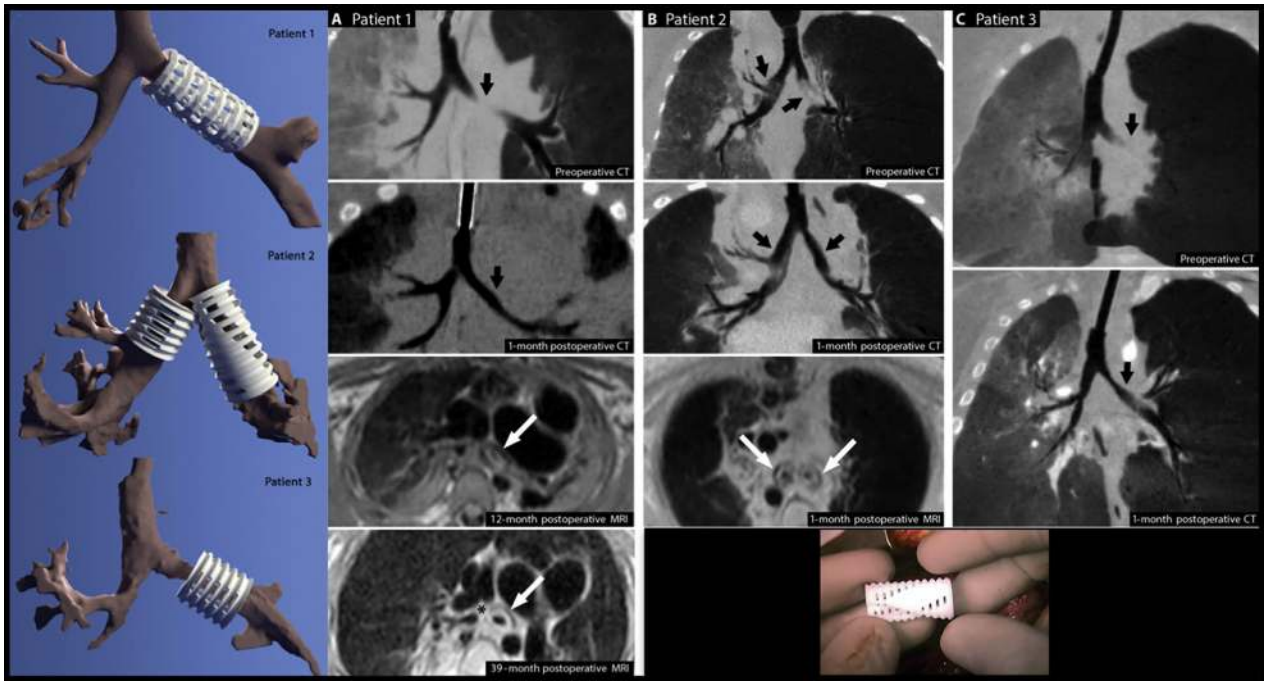
Accuracy in medical 3D printing is of paramount importance, although published reports on this topic are limited. Accuracy is defined by comparison with a gold standard, and in the case of 3D printed models, 1 metric of accuracy is comparison with operative findings. At our institution, the quality assurance process is driven by feedback from our surgical

FIGURE 10 Airway Abnormalities in Congenital Heart Disease



(A) Vascular ring with posterior compression of trachea by a circumflex transverse arch coursing behind the aorta. **(B)** Severe branch pulmonary artery dilation in tetralogy of Fallot with absent pulmonary valve with compression and malacia of bilateral mainstem bronchi. Abbreviations as in Figure 7.

FIGURE 11 **Bioresorbable Airway Splint Manufactured From Polycaprolactone With a Bellowed Design to Promote Expansion and Growth Over Time**



Reproduced with permission from Morrison et al. (48).

FIGURE 12 **3D Printed Model in a Case of TOF With Borderline Large PA Measurements**

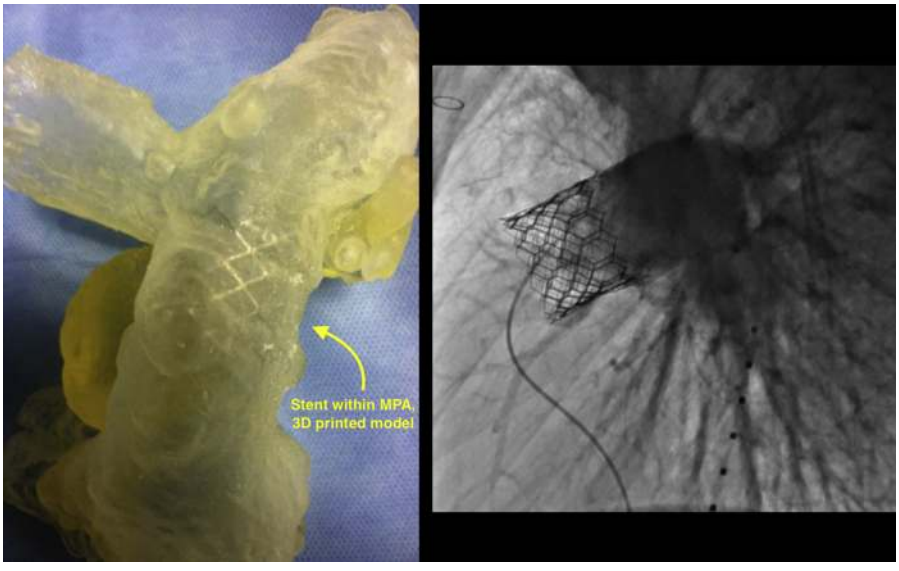
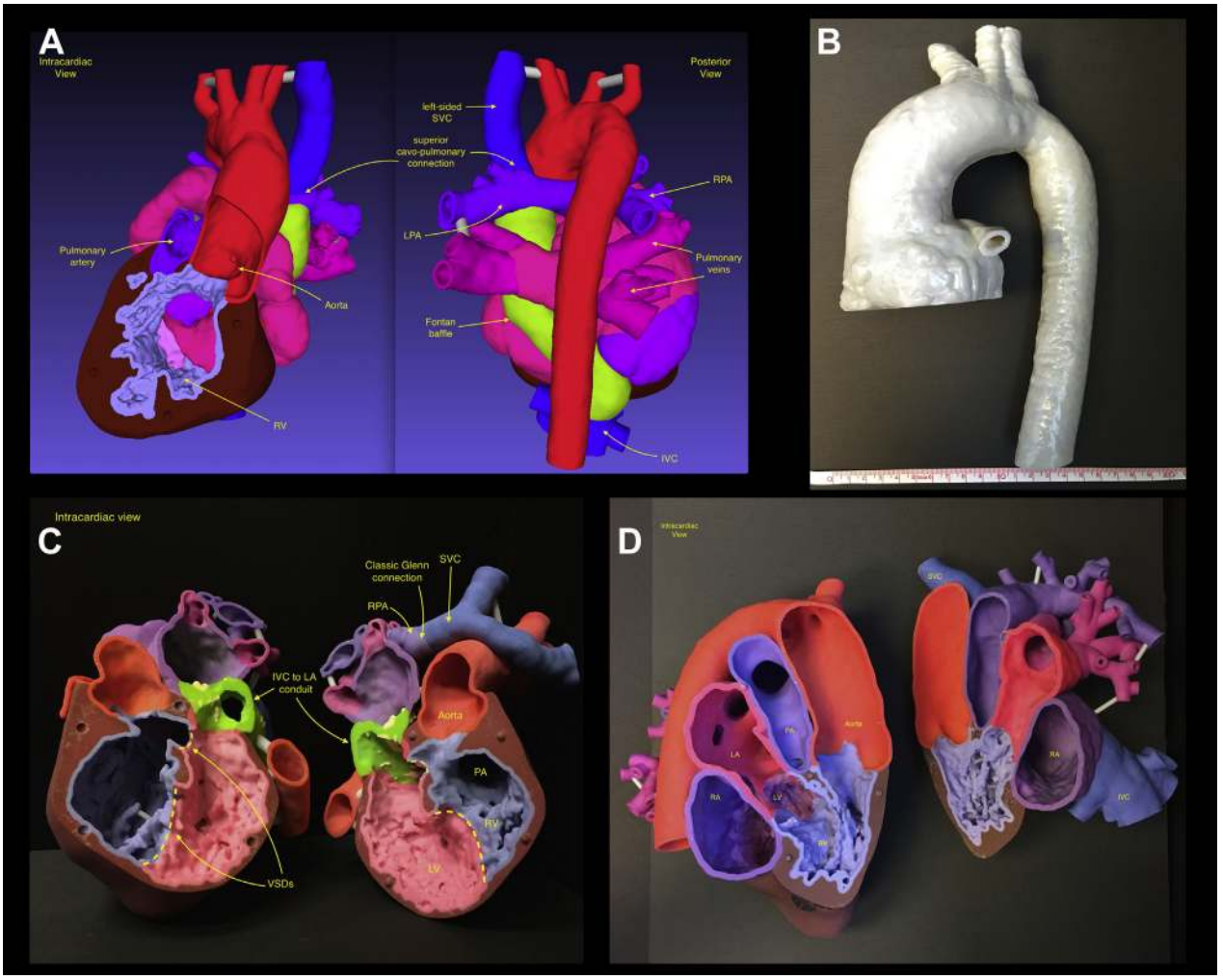


Image on the **left** shows a stent within main pulmonary artery (MPA). Image on the **right** is an angiogram taken after successful transcatheter implantation of pulmonary valve. PA = pulmonary artery; TOF = tetralogy of Fallot.

FIGURE 13 **3D Models of Adults With Congenital Heart Disease**

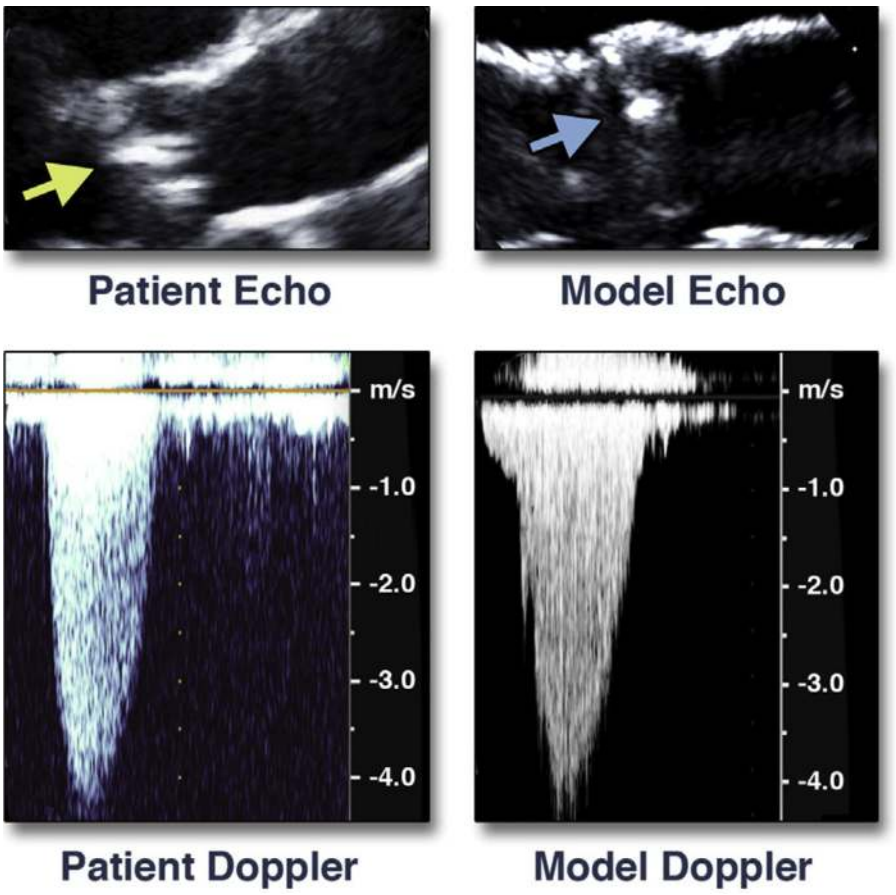


(A) A 31-year-old patient with dextrocardia, a double-outlet right ventricle (DORV), and a Fontan procedure. **(B)** A 19-year-old patient with a bicuspid aortic valve (not shown) and a severely dilated aortic root and ascending aorta. **(C)** A 40-year-old patient with a double-outlet right ventricle, 2 VSDs, and classic Glenn and modified Mustard procedures (conduit from inferior vena cava [IVC] to left atrium [LA], in **green**). **(D)** A 45-year-old patient with a left dominant unbalanced atrioventricular canal, a double-outlet right ventricle, and right ventricular outflow tract obstruction. Abbreviations as in **Figures 5 to 8**. Reproduced with permission from Anwar et al. (68).

colleagues and findings in the OR. Between February 2015 and May 2017, the average accuracy score for 21 3D printed models at our institution was 4 of a possible 5 points when the surgeon compared model anatomy with findings in the OR. A similar quality assurance process was described by Hermsen et al. (70) for surgical models of hypertrophic obstructive cardiomyopathy. We have found that direct and ongoing communication among the imaging, modeling, and surgical teams is essential for maintaining high levels of accuracy. In addition, model accuracy may be diminished if there is a significant delay between acquisition of source images and time of surgery. In infants and young children somatic growth and evolution of the pathophysiology can produce relatively large changes to the anatomy as time passes; thus, the pre-operative imaging and 3D modeling should be performed close to the time of anticipated surgery.

Besides direct comparison with OR findings, other metrics of accuracy include comparison with source images and user feedback. Olivieri et al. (71) reported that 3D printed models from echocardiographic data were comparable in measurements of VSDs when compared with source images. Yoo et al. (72) reported data from 50 surgeons after undergoing a Hands-on

FIGURE 14 Patient and Model Doppler Comparisons



Doppler profile of a patient's echocardiogram on the **left,** compared with the Doppler image from the 3D printed model on the **right**. **Arrows** point towards the aortic valve from the patient's echocardiogram **(left)** and model **(right)**. Adapted with permission from Vukicevic et al. (4).

Surgical Training course using 3D models. The majority of cardiothoracic surgeons reported that the 3D models were of "excellent" or "good" quality for surgical simulation (72). Finally, accuracy of 3D models may be judged in terms of their ability to recreate native physiology, not just anatomy. The innovative work of Vukicevic et al. (4) has shown the ability to recreate "hemodynamics" of abnormal aortic valves in 3D models, with Doppler characteristics nearly identical to those of the patient's own diseased valve (**Figure 14**).

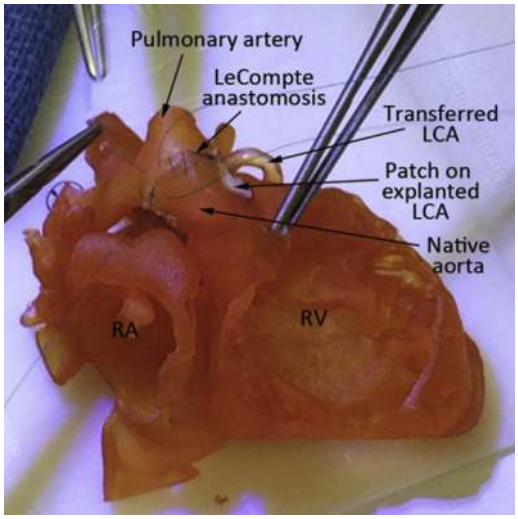
3D PRINTING FOR TRAINEE EDUCATION AND SURGICAL SIMULATION

Another arena where 3D printing can bring about transformative change is in the education and training of the next generation of physicians. This is an established practice in neurosurgery (73,74) and otolaryngology (17), with more recent application in cardiology (75–78). Although medical training has long followed the practice of "see 1, do 1, teach 1," use of 3D models in education represents a paradigm shift from an apprenticeship model to a simulator-based learning method that complements traditional mentored training (79,80). 3D models in CHD can reduce the learning curve for cardiac trainees in 3 key areas:

1. Understanding complex 3D anatomy
2. High-fidelity simulation experiences
3. Exposure to rare cases

As a tool for surgical simulation, 3D printing has been applied toward septal myectomy for hypertrophic obstructive cardiomyopathy (70), vascular procedures (76,77,81), and complex congenital procedures, as described by Yoo et al. (72) (**Figure 15**).

FIGURE 15 Simulated Arterial Switch Operation From a Hands-on Surgical Training Course for Cardiothoracic Surgeons



Reproduced with permission from Yoo et al. (72). See Supplemental Video 2. LCA = left coronary artery; other abbreviations as in **Figures 5 and 6**.

In addition to allowing practice on highly accurate simulators, the 3D models expose trainees to pathological features they may rarely encounter. This shifts the practice of surgery from an "opportunity-based" (26) to a "curriculum-based" experience. For experienced practitioners, models may be used for lifelong learning, for maintenance of certification, or for practice before challenging cases. Thus, a repository of 3D printed cardiovascular models with the spectrum of CHD would be an ideal educational resource (82,83). The 3D print Heart Library at the National Institutes of Health (84) is a good example of this concept. Electronic 3D models may supplement traditional learning methods, and an example is shown in Supplemental Video 2 (**Figure 15**). Finally, virtual reality displays may be used as complementary platforms to interact with electronic 3D models, with several robust options currently available (25,85).

3D PRINTING TO FACILITATE COMMUNICATION WITHIN THE MEDICAL TEAM AND FOR COUNSELING PATIENTS AND FAMILIES

Cardiac surgery and perioperative care are conducted in a multidisciplinary setting requiring highly skilled and specialized teams. Communication among specialists is essential for avoiding errors and optimizing patient outcomes (86–88). 3D models provide clarity, and they are cornerstones around which multiple subspecialists can gather to discuss the pathological condition, surgical plan, anticipated outcomes, and perioperative care. In so doing, they may reduce medical errors, a postulate that deserves further investigation.

In addition to facilitating communication among medical team members, 3D models enable better communication between the medical team and patients or their caregivers (51,89,90). The models can help the patient or caregiver better understand the disease process, risks, benefits, and alternatives. Anecdotally, our institutional practice is to counsel patients and families by using 3D models if a model has been printed for a case. Eleven caregivers who completed a questionnaire for cardiac models between 2014 and 2017 reported that the models were "very helpful" (score 5 of 5) to improve understanding of the anatomy. Similarly, Biglino et al. (75) reported that 3D models could help improve the family's experience with medical care when models were used for counseling. More data are needed on the potentially powerful impact of 3D printing in patient and family education and shared decision making.

ADVANCED APPLICATIONS AND FUTURE DIRECTIONS

3D printing is rapidly evolving in medicine, with technical improvements in printers and software fueling new and exciting applications in patient care, innovation, and research. In cardiovascular medicine, a major limitation is high-resolution printing of structures currently not well resolved by CT or MRI, such as atrioventricular valves (91) or the atrial septum. 3D printing from 3D echocardiography could potentially overcome these limitations, with some promising early results (92–96). 3D printing from angiographic imaging could expand options, currently largely unexplored (97). The next evolution in 3D printing would be "multimodality" printing, with a model created by combining key elements of the anatomy from different imaging modalities. True co-registration of a highly accurate dataset is a technical challenge, and there are some early feasibility data (98,99).

In addition to advances in 3D dataset acquisition and post-processing, the next major step forward in 3D printing will likely be driven by improvements in printer technology and print materials. "Tissue mimicking" materials currently under development (100,101) would enable the creation of more life-like models that replicate the patient's unique anatomy

and physiology. Currently there are highly accurate noninvasive methods to assess cardiac function and blood flow (102), including methods to assess 3D information over the cardiac cycle, thereby providing "4D" function and flow. These multivariate datasets could be integrated into 3D models to build holistic models to advance our understanding of cardiac disease. As 3D models achieve more realistic states, they may be used to study pathophysiology, predict long-term outcomes, and choose optimal treatment plans or surgical repairs (58,103–107). Recent studies have analyzed blood flow in deformable models (108,109), including flow characteristics in patients with hypoplastic left heart syndrome following Norwood arch reconstruction (75,110).

Finally, bioprinting offers the potential to make the leap from printing "life-like" to living tissue itself. This revolutionary technology is in its infancy; however, several techniques now exist that can deposit bioinks in precise locations to build up complex tissue constructs (111). Bioprinting has been applied to print anatomically shaped cartilage structures (112), skin (113,114), implants for bone growth (115), and even a 3D printed "bionic ear" (116). Within cardiology, researchers have reported techniques to print vasculature, myocardium, and valves (117–121). These applications and bioprinting techniques were recently reviewed by Duan. (111).

Although current and future applications of 3D printing are exciting and potentially game-changing, broad adoption is currently hampered by the costs of modeling and printing. The cost of a 3D printing center to a medical program is considerable, and at minimum it includes the cost of segmentation software, a medical-grade 3D printer, material costs, and personnel with 3D printing expertise. Some of the costs may be lowered by printing off-site through commercial vendors, although with inherent trade-offs in long-term costs and turn-around time. These are evolving issues, and the ultimate viability of medical 3D printing will in large part depend on the impact it has on improving patient care.

CONCLUSIONS

3D printing is a transformative technology that is affecting key aspects of CHD care. As a planning and simulation tool, if offers the promise of more precise surgery with fewer complications. For training, 3D models can reduce the learning curve and increase opportunities for procedural practice. The models can facilitate communication among multidisciplinary teams, thus potentially reducing medical errors. They can increase engagement of patients and families, thereby enhancing shared decision making. Finally, 3D models can lead to medical breakthroughs by enabling basic science, translational, and clinical investigations. More data are needed to quantify these potential benefits from 3D printing, and the early experience is promising.

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REFERENCES

1. Manyika J, Chui M, Bughin J, Dobbs R, Bisson P. Disruptive Technologies: Advances That Will Transform Life, Business, and the Global Economy. McKinsey Global Institute, 2013. Available at: https://www.mckinsey.com/business-functions/digital-mckinsey/our-insights/disruptive-technologies. Accessed November 2, 2017.

2. Tack P, Victor J, Gemmel P, Annemans L. 3D-printing techniques in a medical setting: a systematic literature review. Biomed Eng Online 2016;15:115.

3. Byrne N, Velasco Forte M, Tandon A, Valverde I, Hussain T. A systematic review of image segmentation methodology, used in the additive manufacture of patient-specific 3D printed models of the cardiovascular system. JRSM Cardiovascular Disease 2016;5:2048004016645467.

4. Vukicevic M, Mosadegh B, Min JK, Little SH. Cardiac 3D printing and its future directions. J Am Coll Cardiol Img 2017;10:171–84.

5. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009;119:e21–181.

6. Botto LD, Correa A, Erickson JD. Racial and temporal variations in the prevalence of heart defects. Pediatrics 2001;107:e32–2.

7. Warnes CA, Liberthson R, Danielson GK, et al. Task force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol 2001;37:1170–5.

8. Mahle WT, Spray TL, Wernovsky G, Gaynor JW, Clark BJ. Survival after reconstructive surgery for hypoplastic left heart syndrome. Circulation 2000;102 Suppl 3:III136–41.

9. Erikssen G, Liestøl K, Seem E, et al. Achievements in congenital heart defect surgery: a prospective, 40-year study of 7038 patients. Circulation 2015;131:337–46.

10. Boneva RS, Botto LD, Moore CA, Yang Q, Correa A, Erickson JD. Mortality associated with congenital heart defects in the United States. Circulation 2001;103:2376–81.

11. Moons P, Bovijn L, Budts W, Belmans A, Gewillig M. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. Circulation 2010;122:2264–72.

12. Binder TM, Moertl D, Mundigler G, et al. Stereolithographic biomodeling to create tangible

hard copies of cardiac structures from echocardiographic data: in vitro and in vivo validation. J Am Coll Cardiol 2000;35:230–7.

13. Pentecost JO, Sahn DJ, Thornburg BL, Gharib M, Baptista A, Thornburg KL. Graphical and stereolithographic models of the developing human heart lumen. Comput Med Imaging Graph 2001;25:459–63.

14. Ngan EM, Rebeyka IM, Ross DB, et al. The rapid prototyping of anatomic models in pulmonary atresia. J Thorac Cardiovasc Surg 2006;132:264–9.

15. Noecker AM, Chen J-F, Zhou Q, et al. Development of patient-specific three-dimensional pediatric cardiac models. ASAIO J 2006;52:349–53.

16. Markert M, Weber S, Lueth TC. A beating heart model 3D printed from specific patient data. Conf Proc IEEE Eng Med Biol Soc 2007;2007:4472–5.

17. VanKoevering KK, Hollister SJ, Green GE. Advances in 3-dimensional printing in otolaryngology: a review. JAMA Otolaryngol Head Neck Surg 2017;143:178–83.

18. Anwar S, Singh GK, Varughese J, et al. 3D printing in complex congenital heart disease: across a spectrum of age, pathology, and imaging techniques. J Am Coll Cardiol Img 2017;10:953–6.

19. Farooqi KM, Uppu SC, Nguyen K, et al. Application of virtual three-dimensional models for simultaneous visualization of intracardiac anatomic relationships in double outlet right ventricle. Pediatr Cardiol 2015;37:90–8.

20. Farooqi KM, Saeed O, Zaidi A, et al. 3D printing to guide ventricular assist device placement in adults with congenital heart disease and heart failure. J Am Coll Cardiol HF 2016;4:301–11.

21. Ryan JR, Moe TG, Richardson R, Frakes DH, Nigro JJ, Pophal S. A novel approach to neonatal management of tetralogy of Fallot, with pulmonary atresia, and multiple aortopulmonary collaterals. J Am Coll Cardiol Img 2015;8:103–4.

22. Jacobs CA, Lin AY. A new classification of three-dimensional printing technologies: systematic review of three-dimensional printing for patient-specific craniomaxillofacial surgery. Plast Reconstr Surg 2017;139:1211–20.

23. Zweifel DF, Simon C, Hoarau R, Pasche P, Broome M. Are virtual planning and guided surgery for head and neck reconstruction economically viable? J Oral Maxillofac Surg 2015;73:170–5.

24. Farooqi KM, editor. Rapid Prototyping in Cardiac Disease. Cham, Switzerland: Springer International Publishing, 2017.

25. Meier LM, Meineri M, Hiansen JQ, Horlick EM. Structural and congenital heart disease interventions: the role of three-dimensional printing. Neth Heart J 2017;25:65–75.

26. Giannopoulos AA, Mitsouras D, Yoo S-J, Liu PP, Chatzizisis YS, Rybicki FJ. Applications of 3D printing in cardiovascular diseases. Nat Rev Cardiol 2016;13:701–18.

27. Mitsouras D, Liacouras PC. 3D Printing Technologies, Vol. 3. Cham, Switzerland: Springer International Publishing, 2017.

28. Borrello J, Backeris P. Rapid prototyping technologies. In: Farooqi KM, editor. Rapid Prototyping in Cardiac Disease. Cham, Switzerland: Springer International Publishing, 2017:41–9.

29. Chaowu Y, Hua L, Xin S. Three-dimensional printing as an aid in transcatheter closure of secundum atrial septal defect with rim deficiency: in vitro trial occlusion based on a personalized heart model. Circulation 2016;133:e608–10.

30. 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 2017;38:103–14.

31. Garekar S, Bharati A, Chokhandre M. 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 2016;7:344–50.

32. Farooqi KM, Nielsen JC, Uppu SC, et al. Use of 3-dimensional printing to demonstrate complex intracardiac relationships in double-outlet right ventricle for surgical planning. Circ Cardiovasc Imaging 2015;8. e003043–3.

33. Deferm S, Meyns B, Vlasselaers D, Budts W. 3D-printing in congenital cardiology: from flatland to spaceland. J Clin Imaging Sci 2016;6:8–5.

34. Hadeed K, Dulac Y, Acar P. Three-dimensional printing of a complex CHD to plan surgical repair. Cardiol Young 2016;26:1432–4.

35. Schmauss D, Haeberle S, Hagl C, Sodian R. Three-dimensional printing in cardiac surgery and interventional cardiology: a single-centre experience. Eur J Cardiothorac Surg 2015;47:1044–52.

36. Yoo S-J, Thabit O, Kim EK, et al. 3D printing in medicine of congenital heart diseases. 3D Printing Med 2016;2:1–12.

37. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). J Am Coll Cardiol 2008;52:e143–263.

38. Hoffman J, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002;39:1890–900.

39. Kirklin JW, Blackstone EH, Tchervenkov CI, Castaneda AR. Clinical outcomes after the arterial switch operation for transposition: patient, support, procedural, and institutional risk factors. Congenital Heart Surgeons Society. Circulation 1992;86:1501–15.

40. Brown KL, Ridout DA, Goldman AP, Hoskote A, Penny DJ. Risk factors for long intensive care unit stay after cardiopulmonary bypass in children. Crit Care Med 2003;31:28–33.

41. Gentles TL, Mayer JE Jr., Gauvreau K. Fontan operation in five hundred consecutive patients: factors influencing early and late outcome. J Thorac Cardiovasc Surg 1997;114:376–91.

42. Gaynor JW, Mahle WT, Cohen MI. Risk factors for mortality after the Norwood procedure. Eur J Cardiothorac Surg 2002;22:82–9.

43. Barach P, Johnson JK, Ahmad A, et al. A prospective observational study of human factors, adverse events, and patient outcomes in surgery for pediatric cardiac disease. J Thorac Cardiovasc Surg 2008;136:1422–8.

44. O'Brien SM, Clarke DR, Jacobs JP, Jacobs ML. An empirically based tool for analyzing mortality associated with congenital heart surgery. J Thorac Cardiovasc Surg 2009;138:1139–53.

45. Saeed O, Farooqi KM, Jorde UP. Assessment of ventricular assist device placement and function. In: Farooqi KM, editor. Rapid Prototyping in Cardiac Disease. Cham, Switzerland: Springer International Publishing, 2017:133–41.

46. Sodian R, Weber S, Markert M, et al. Pediatric cardiac transplantation: three-dimensional printing of anatomic models for surgical planning of heart transplantation in patients with univentricular heart. J Thorac Cardiovasc Surg 2008;136:1098–9.

47. Smith ML, McGuinness J, O'Reilly MK, Nolke L, Murray JG, Jones JFX. The role of 3D printing in preoperative planning for heart transplantation in complex congenital heart disease. Ir J Med Sci 2017;186:753–6.

48. Morrison RJ, Hollister SJ, Niedner MF, et al. Mitigation of tracheobronchomalacia with 3D-printed personalized medical devices in pediatric patients. Sci Transl Med 2015;7:285ra64–4.

49. Zopf DA, Hollister SJ, Nelson ME, Ohye RG, Green GE. Bioresorbable airway splint created with a three-dimensional printer. N Engl J Med 2013;368:2043–5.

50. Schievano S, Migliavacca F, Coats L, et al. Percutaneous pulmonary valve implantation based on rapid prototyping of right ventricular outflow tract and pulmonary trunk from MR data. Radiology 2007;242:490–7.

51. Biglino G, Capelli C, Taylor AM, Schievano S. 3D printing cardiovascular anatomy: a single-centre experience. In: Shishkovsky IV, editor. New Trends in 3D Printing. London, United Kingdom: InTechOpen, 2016:1–20.

52. Valverde I, Gomez G, Coserria JF, et al. 3D printed models for planning endovascular stenting in transverse aortic arch hypoplasia. Catheter Cardiovasc Interv 2015;85:1006–12.

53. Fan Y, Kwok KW, Zhang Y, Cheung G. Three-dimensional printing for planning occlusion procedure for a double-lobed left atrial appendage. Circ Cardiovasc Interv 2016;9:e003561.

54. O'Neill B, Wang DD, Pantelic M, et al. Transcatheter caval valve implantation using multimodality imaging. J Am Coll Cardiol Img 2015;8:221–5.

55. Olivieri L, Krieger A, Chen MY, Kim P, Kanter JP. 3D heart model guides complex stent angioplasty of pulmonary venous baffle obstruction in a Mustard repair of D-TGA. Int J Cardiol 2014;172:e297–8.

56. Vukicevic M, Puperi DS, Jane Grande-Allen K, Little SH. 3D printed modeling of the mitral valve for catheter-based structural interventions. Ann Biomed Eng 2017;45:508–19.

57. Little SH, Vukicevic M, Avenatti E, Ramchandani M, Barker CM. 3D printed modeling

for patient-specific mitral valve intervention: repair with a clip and a plug. J Am Coll Cardiol Intv 2016;9:973–5.

58. Maragiannis D, Jackson MS, Igo SR, et al. Replicating patient-specific severe aortic valve stenosis with functional 3D modeling. Circ Cardiovasc Imaging 2015;8:e003626.

59. Grant EK, Olivieri LJ. The role of 3-D heart models in planning and executing interventional procedures. Can J Cardiol 2017;33:1074–81.

60. Green A. Outcomes of congenital heart disease: a review. Pediatr Nurs 2004;30:280–4.

61. Dearani JA, Connolly HM, Martinez R, Fontanet H, Webb GD. Caring for adults with congenital cardiac disease: successes and challenges for 2007 and beyond. Cardiol Young 2007; 17 Suppl 2:87–96.

62. Warnes CA, Bhatt AB, Daniels CJ, Gillam LD, Stout KK. COCATS 4 Task Force 14: training in the care of adult patients with congenital heart disease. J Am Coll Cardiol 2015;65:1887–98.

63. Williams RG, Pearson GD, Barst RJ, et al. Report of the National Heart, Lung, and Blood Institute Working Group on research in adult congenital heart disease. J Am Coll Cardiol 2006; 47:701–7.

64. Khairy P, Ionescu-Ittu R, Mackie AS, Abrahamowicz M, Pilote L, Marelli AJ. Changing mortality in congenital heart disease. J Am Coll Cardiol 2010;56:1149–57.

65. Giamberti A, Chessa M, Abella R, et al. Morbidity and mortality risk factors in adults with congenital heart disease undergoing cardiac reoperations. Ann Thorac Surg 2009;88:1284–9.

66. Holst KA, Dearani JA, Burkhart HM, et al. Risk factors and early outcomes of multiple reoperations in adults with congenital heart disease. Ann Thorac Surg 2011;92:122–30.

67. Holst KA, Dearani JA, Burkhart HM, et al. Reoperative multivalve surgery in adult congenital heart disease. Ann Thorac Surg 2013;95:1383–9.

68. Anwar S, Singh GK, Petrucci O, Eghtesady P, Woodard PK, Billadello JJ. Adult congenital heart disease. In: Farooqi KM, editor. Rapid Prototyping in Cardiac Disease. Cham, Switzerland: Springer International Publishing, 2017:99–109.

69. Riesenkampff E, Rietdorf U, Wolf I, et al. The practical clinical value of three-dimensional models of complex congenitally malformed hearts. J Thorac Cardiovasc Surg 2009;138: 571–80.

70. Hermsen JL, Burke TM, Seslar SP, et al. Scan, plan, print, practice, perform: Development and use of a patient-specific 3-dimensional printed model in adult cardiac surgery. J Thorac Cardiovasc Surg 2017;153:132–40.

71. Olivieri LJ, Krieger A, Loke Y-H, Nath DS, Kim PCW, Sable CA. Three-dimensional printing of intracardiac defects from three-dimensional echocardiographic images: feasibility and relative accuracy. J Am Soc Echocardiogr 2015;28:392–7.

72. Yoo S-J, Spray T, Austin EH, Yun T-J, Van Arsdell GS. Hands-on surgical training of congenital heart surgery using 3-dimensional print models. J Thorac Cardiovasc Surg 2017;153: 1530–40.

73. Rehder R, Abd-El-Barr M, Hooten K, Weinstock P, Madsen JR, Cohen AR. The role of simulation in neurosurgery. Childs Nerv Syst 2016; 32:43–54.

74. Randazzo M, Pisapia JM, Singh N, Thawani JP. 3D printing in neurosurgery: a systematic review. Surg Neurol Int 2016;7 Suppl 33:S801–9.

75. 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 2015;5:e007165–5.

76. Javan R, Herrin D, Tangestanipoor A. Understanding spatially complex segmental and branch anatomy using 3D printing: liver, lung, prostate, coronary arteries, and circle of Willis. Acad Radiol 2016;23:1183–9.

77. Conti A, Pontoriero A, Iatì G, et al. 3D-printing of arteriovenous malformations for radiosurgical treatment: pushing anatomy understanding to real boundaries. Cureus 2016;8:e594.

78. 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 2015;10:185–90.

79. Rodriguez-Paz JM, Kennedy M, Salas E, et al. Beyond "see one, do one, teach one": toward a different training paradigm. Postgrad Med J 2009; 85:244–9.

80. Kotsis SV, Chung KC. Application of the "see one, do one, teach one" concept in surgical training. Plast Reconstr Surg 2013;131:1194–201.

81. Wilasrusmee C, Suvikrom J, Suthakorn J, et al. Three-dimensional aortic aneurysm model and endovascular repair: an educational tool for surgical trainees. Int J Angiol 2008;17:129–33.

82. Giroud JM, Jacobs JP, Fricker FJ, Spicer D. Web based "global virtual museum of congenital cardiac pathology." Prog Pediatr Cardiol 2012;33: 91–7.

83. Jonas RA. Training fellows in paediatric cardiac surgery. Cardiol Young 2016;26:1474–83.

84. Bramlet M, Dori Y, Olivieri LJ. NIH 3D Print Exchange. Bethesda, MD: National Institutes of Health. Available at: https://3dprint.nih.gov/collections/heart-library. Accessed June 28, 2017.

85. Bucher K. New frontiers of medical illustration. JAMA 2016;316:2340–1.

86. Fleming M, Smith S, Slaunwhite J. Investigating interpersonal competencies of cardiac surgery teams. Can J Surg 2006;49:22–30.

87. Sutcliffe KM, Lewton E, Rosenthal MM. Communication failures: an insidious contributor to medical mishaps. Acad Med 2004;79:186–94.

88. Kappetein AP, Windecker S. The heart team in acute cardiac care. In: Tubaro M, Vranckx P, editors. The ESC Textbook of Intensive and Acute Cardiovascular Care. 2nd ed. Oxford, United Kingdom: Oxford University Press, 2015:87–90.

89. Hu A, Wilson T, Ladak H, Haase P, Fung K. Three-dimensional educational computer model of the larynx: voicing a new direction. Arch Otolaryngol Head Neck Surg 2009;135:677–81.

90. Bernhard J-C, Isotani S, Matsugasumi T, et al. Personalized 3D printed model of kidney and tumor anatomy: a useful tool for patient education. World J Urol 2016;34:337–45.

91. Mashari A, Montealegre-Gallegos M, Knio Z, et al. Making three-dimensional echocardiography more tangible: a workflow for three-dimensional printing with echocardiographic data. Echo Res Pract 2017;3:R57–64.

92. Kapur KK, Garg N. Echocardiography derived three- dimensional printing of normal and abnormal mitral annuli. Ann Card Anaesth 2014;17:283–4.

93. Mahmood F, Owais K, Taylor C, et al. Three-dimensional printing of mitral valve using echocardiographic data. J Am Coll Cardiol Img 2015;8: 227–9.

94. Witschey WRT, Pouch AM, McGarvey JR, et al. Three-dimensional ultrasound-derived physical mitral valve modeling. Ann Thorac Surg 2014;98: 691–4.

95. Muraru D, Veronesi F, Maddalozzo A, et al. 3D printing of normal and pathologic tricuspid valves from transthoracic 3D echocardiography data sets. Eur Heart J Cardiovasc Imaging 2017;18:802–8.

96. Samuel BP, Pinto C, Pietila T, Vettukattil JJ. Ultrasound-derived three-dimensional printing in congenital heart disease. J Digit Imaging 2014;28: 459–61.

97. Poterucha JT, Foley TA, Taggart NW. Percutaneous pulmonary valve implantation in a native outflow tract. J Am Coll Cardiol Intv 2014;7: e151–2.

98. Gosnell J, Pietila T, Samuel BP, Kurup HKN, Haw MP, Vettukattil JJ. Integration of computed tomography and three-dimensional echocardiography for hybrid three-dimensional printing in congenital heart disease. J Digit Imaging 2016;29: 665–9.

99. Moore T, Madriago EJ, Renteria ES, et al. Co-registration of 3D echo and MR data to create physical models of congenital heart malformations. J Cardiovasc Magn Resonan 2015;17:P198.

100. Wang K, Wu C, Qian Z, Zhang C, Ben Wang, Vannan MA. Dual-material 3D printed metamaterials with tunable mechanical properties for patient-specific tissue-mimicking phantoms. Additive Manufacturing 2016;12:31–7.

101. Wang K, Zhao Y, Chang Y-H, et al. Controlling the mechanical behavior of dual-material 3D printed meta-materials for patient-specific tissue-mimicking phantoms. Mater Des 2016;90:704–12.

102. Whitlock MC, Hundley WG. Noninvasive imaging of flow and vascular function in disease of the aorta. J Am Coll Cardiol Img 2015;8:1094–106.

103. Taylor CA, Figueroa CA. Patient-specific modeling of cardiovascular mechanics. Annu Rev Biomed Eng 2009;11:109–34.

104. Santos dos J, Werner H, de Azevedo BA, Lanziotti L. 3D-printed models applied in medical research studies. In: Shishkovsky IV, editor. New Trends in 3D Printing. London, United Kingdom: InTechOpen, 2016.

105. Sodian R, Schmauss D, Schmitz C, et al. 3-dimensional printing of models to create custom-made devices for coil embolization of an

anastomotic leak after aortic arch replacement. Ann Thorac Surg 2009;88:974–8.

106. Ripley B, Kelil T, Cheezum MK, et al. 3D printing based on cardiac CT assists anatomic visualization prior to transcatheter aortic valve replacement. J Cardiovasc Comput Tomogr 2016; 10:28–36.

107. Vukicevic M, Maragiannis D, Jackson M, Little SH. Functional evaluation of a patient-specific 3D printed model of aortic regurgitation (abstr). Circulation 2015;132 Suppl 3:A18647.

108. Kung EO, Les AS, Figueroa CA, et al. In vitro validation of finite element analysis of blood flow in deformable models. Ann Biomed Eng 2011;39: 1947–60.

109. Kolli KK, Min JK, Ha S, Soohoo H, Xiong G. Effect of varying hemodynamic and vascular conditions on fractional flow reserve: an in vitro study. J Am Heart Assoc 2016;5: e003634–14.

110. Kiraly L, Tofeig M, Jha NK, Talo H. Three-dimensional printed prototypes refine the anatomy of post-modified Norwood-1 complex aortic arch obstruction and allow presurgical simulation of the repair. Interact Cardiovasc Thorac Surg 2016;22:238–40.

111. Duan B. State-of-the-art review of 3D bioprinting for cardiovascular tissue engineering. Ann Biomed Eng 2017;45:195–209.

112. Markstedt K, Mantas A, Tournier I, Martínez Ávila H, Hägg D, Gatenholm P. 3D bioprinting human chondrocytes with nanocellulose-alginate bioink for cartilage tissue engineering applications. Biomacromolecules 2015;16:1489–96.

113. Lee W, Debasitis JC, Lee VK, et al. Multi-layered culture of human skin fibroblasts and keratinocytes through three-dimensional freeform fabrication. Biomaterials 2009;30:1587–95.

114. Michael S, Sorg H, Peck C-T, et al. Tissue engineered skin substitutes created by laser-assisted bioprinting form skin-like structures in the dorsal skin fold chamber in mice. PLoS One 2013;8:e57741.

115. Shah FA, Snis A, Matic A, Thomsen P, Palmquist A. 3D printed Ti6Al4V implant surface promotes bone maturation and retains a higher density of less aged osteocytes at the bone-implant interface. Acta Biomater 2016;30:357–67.

116. Mannoor MS, Jiang Z, James T, Kong YL. 3D printed bionic ears. Nano Lett 2013;13:2634–9.

117. Duan B, Hockaday LA, Kang KH, Butcher JT. 3D bioprinting of heterogeneous aortic valve conduits with alginate/gelatin hydrogels. J Biomed Mater Res A 2013;101:1255–64.

118. Fukunishi T, Best CA, Sugiura T, et al. Preclinical study of patient-specific cell-free nanofiber tissue-engineered vascular grafts using 3-dimensional printing in a sheep model. J Thorac Cardiovasc Surg 2017;153:924–32.

119. Jana S, Lerman A. Bioprinting a cardiac valve. Biotechnol Adv 2015;33:1503–21.

120. Lee JM, Sing SL, Tan E, Yeong WY. Bioprinting in cardiovascular tissue engineering: a review. Int J Bioprinting 2016;2:27–36.

121. Tabriz AG, Hermida MA, Leslie NR, Shu W. Three-dimensional bioprinting of complex cell laden alginate hydrogel structures. Biofabrication 2015;7:045012.

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APPENDIX For a supplemental table and videos, please see the online version of this article.