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The Use of Three-Dimensional Printing in Complex Cardiovascular Disease: Our 5-year Experience in Greece

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Abstract

Introduction: 3D-printing is revolutionizing clinical medicine. We have pioneered the use of 3D-printed anatomic models for the management of complex congenital and acquired structural cardiac lesions. Herein, we report our relevant experience.

Methods: Since 2013, our team at Athens Heart Surgery Institute has created accurate 3D-printed cardiac anatomic models in selected complex cases, based on contrast–enhanced CT or MRI images, segmented to suitable STL files and fed to a highly accurate polyjet-technology 3D-printer. Each model was assessed with regard to its impact on improved diagnostic understanding, optimization of surgical planning, family education and for surgical teaching and simulation.

Results: 3D-printed models were created for 42 patients. In 40/42, the models proved extremely useful for pre-surgical diagnostic assessment and planning. In 2 cases, surgical inspection revealed inaccuracies of the models attributed to suboptimal preoperative imaging. All models were highly valued by parents/patients during preoperative counseling. Surgical pre-procedure simulation helped clarify aims and limitations of planned surgical interventions. Accordingly, our models were used in the successful first European Hands-On Surgical Simulation Workshop for teaching the Arterial Switch Operation (ASO). Our experience with this technology is available online at a unique and ever expanding anatomic "cloud library" (http://www.3dlife.gr/categories.php).

Conclusion: 3D-Printing of physical cardiac models is a powerful tool for improved diagnostic assessment and preoperative preparation for patients with complex congenital and other structural heart defects. This innovative technology promises to optimize personalized patient care for challenging cases, contributing to reduced mortality, morbidity, and costs.

Keywords: 3D printing; Congenital heart disease; Perioperative care; Surgical education

Abbreviations

3D: Three Dimensional; CT: Computed Tomography; DORV: Double Outlet Right Ventricle; PA: Pulmonary Artery; MRI: Magnetic Resonance Imaging

Introduction

Three-dimensional printing (3D printing) is a technology enabling creation of physical anatomic models from imaging data. It has been available for the last 30 years and has had several applications in various health care fields for several years. However, its application in Cardiovascular disease has emerged more recently [1,2]. A recent review found that, before the year 2000, only two papers (excluding case reports) were published about 3D printing in cardiovascular disease, but between 2011 and 2015, this number grew to 189 [3]. In the early 2000's, Binder et al., using echocardiographic data, published the first paper about cardiac 3D printing, following in 2001 by Pentacost et al., who produced the first 3D models replicating embryonic hearts based on photomicrographic data [4]. Today, this technology, with applications in Congenital Heart Disease (CHD) and now also in adult structural heart disease, is clearly disrupting the clinical practice of cardiovascular surgery and percutaneous interventions. The focus of this report is to review our growing experience with the use of 3D-printed cardiac models primarily in the management of complex congenital heart disease.

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Table A: Issues explored by 3D printing at Athens Heart Surgery Institute from 2013 (Total No of patients n=42).

Issues explored with 3D printing		No of cases
Feasibility of Biventricular Repair in complex DORV		2
Approach to coronary anomalies	Coronary fistula	2
	AAOCA (Figure 1,2)	3
Technical demands of Complex	Pulmonary Reoperations	7
	Aortic Reoperations	6
Technical demands of Complex	Aortic Operations	9
	Pulmonary operations	1
Multiple VSD's		1
Transposition of Great Arteries		1
Pulmonary Atresia-VSD-MAPCAS (Figure 3)		3
PAPVC		2
Truncus Arteriosus		1
Tetralogy of Falot		1
Management of Single Ventricle		1
Congenital Lung Malformations		1
Congenital mediastinal Tumors		1

Methods

Since 2013, our team of Athens Heart Surgery Institute has utilized the technology of cardiac 3D printing in the management of selected pediatric or adult patients with CHD, suffering from complex or extremely unusual lesions. Either contrast-enhanced CT or MRI imaging was obtained, as decided medically most appropriate. Specialized image segmentation software (Mimmiss®, Materialize) was used to isolate the anatomic areas of interest and extract appropriate STL files. These were then used to print the 3D models using a highly accurate, multicolored, polyjet 3D printer (Stratasys®). A specialized 3D-printing service was organized as 3D Life SA, where the entire process took place, with close collaboration of the medical and engineering team. The 3D-models were made available for hands-on preoperative evaluation and surgical simulation by the medical surgical team. In addition, the models were used for patient/family counseling.

Results

3D-printed cardiovascular models were produced for 42 patients for evaluation of anatomy and surgical planning as summarized in Table A. They proved extremely useful in enhancing the diagnostic understanding and management of Anomalous Aortic Origin of Coronary Arteries (AAOCA) and other congenital coronary pathologies, such as coronary fistulas (Figure 1, 2). In other complex cases, the model, helped us to choose if a biventricular repair was feasible (DORV, PA atresia) (Figures 3-6). Special mention is warranted for neonatal surgery applications. The very small size of the heart and its physiological vulnerability to extracorporeal circulation require extremely accurate and patient-specific preoperative planning. 3D models afforded exact knowledge of the cardiac anatomy and enabled us to simulate the planned operation, assessing its technical feasibility. For example, in a premature, low birth-weight neonate with hypoplastic aortic arch and coarctation it was possible, before surgery, to confirm that, *via* left thoracotomy, occlusion of the aortic arch just after the innominate artery was feasible with our instruments (neonatal aortic clamp), without compromise the

Figure 1: Anomalous Aortic Origin of Left Coronary Artery from Right Coronary sinus (single ostium), in a 12 years old boy. Left Coronary Artery (LCA) coursing between Aorta (Ao) and main Pulmonary Artery (PA). Repair of this lesion requires unroofing plus anterior and leftward PA translocation. (RCA: Right Coronary Artery)

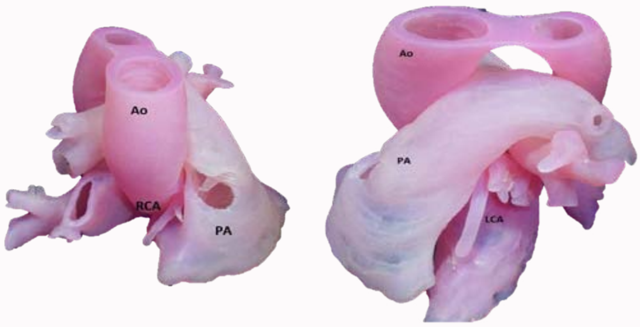

Figure 2: Anomalous Aortic Origin of Right Coronary Artery from Left Aortic Sinus. Right Coronary Artery (RCA), proximal section, crossing between Aorta (Ao) and main Pulmonary Artery (PA). Repair of this lesion requires unroofing of RCA. (LCA: Left Coronary Artery)

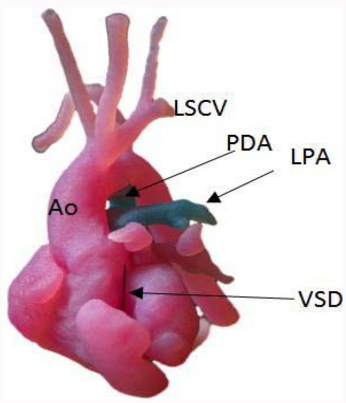

Figure 3: Neonate with Pulmonary Artery atresia, Ventricular Septal Defect (VSD), Right aortic arch, patent ductus arteriosus depended. Left Pulmonary Artery (LPA) anatomy suitable for placement of Left Subclavian artery (LSCV) shunt.

lumen of innominate artery. This provided the surgical team with the confidence that repair could be safety performed without use of cardiopulmonary bypass and circulatory arrest. Such was indeed successfully performed, sparing the neonate the significant morbidity and mortality risk associated with an open procedure (Figure 7).

A significant benefit, not to be underestimated, of using 3D-models is their use as an aid during preoperative the consultation with patients and their families. It proved easier for the family (and/or the patient) to see the pathology of his child in a 3D object and, of course, to understand the operation plan and the relevant possible

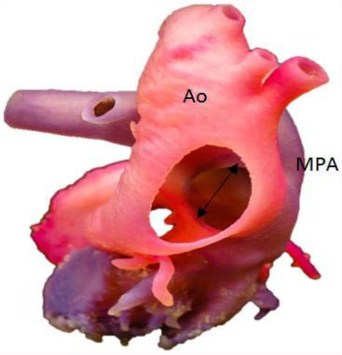

Figure 4: A large Aorto-Pulmonary Window (APW) (double arrow) in a 24-year-old male, remarkable without fixed Pulmonary Hypertension. A section of anterior aortic wall has been removed in order to visualize the APW. The defect had successfully repaired surgically. (Ao: Aorta; MPA: Main Pulmonary trunk)

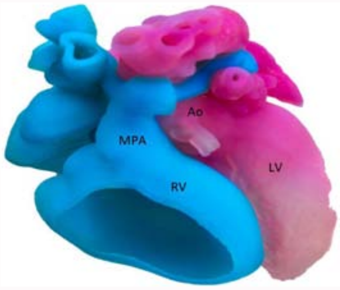

Figure 5: Branch (bifurcation) proximal Pulmonary Artery (MPA) Stenosis late after neonatal arterial switch operation for transposition of the great arteries. The neo-pulmonary artery is anterior of the posteriorly relocated neo Aorta (Ao) after the Le Compte maneuver. This defect is suitable for surgical correction by patched pulmonary artery plasty.

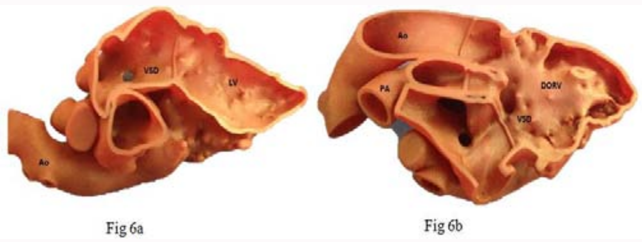

Figure 6: Double Outlet Right Ventricle (DORV), with highly restrictive Ventricular Septal Defect (VSD), and main Pulmonary Artery (PA) stenosis and hypoplasia. Section through Left Ventricle (LV). **6a:** shows LV outlet is only through tiny VSD. Section through Right Ventricle (RV). **6b:** shows VSD, both great arteries originate from RV and PA hypoplasia. Biventricular repair of this lesion would require extensive septal resection for VSD enlargement. Fontan circulation would be an alternative safer strategy.

surgical concerns. The consultation sessions were judged as extremely helpful by our patients.

Discussion

Historical perspective

The primary systematic method of learning human anatomy was human cadaveric dissection, introduced in Hellenistic Alexandria during the third century BC by the legendary Greek physicians Herophilus of Chalcedon and Erasistratus of Chios. This scientific tradition was abandoned after the destruction of the Hellenistic and Roman worlds only to be revived in 14th century Renaissance in Italy.

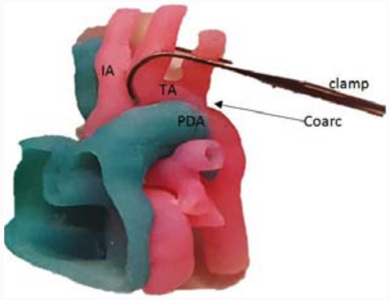

Figure 7: Neonate with aortic Coarctation (Coarc), Transverse Arch (TA) hypoplasia and prostaglandin depended Patent Ductus Arteriosus (PDA). Surgical clamp placement during surgical simulation demonstrates feasibility of repair *via* thoracotomy without circulatory arrest, as sufficient lumen for ejection into Innominate Artery (IA) remains.

Figure 8 a,b: Hands-on surgical workshop. Teaching the arterial switch operation for Transposition of Great Arteries (TGA), using 3D-printed models of neonate with TGA.

Andreas Vesalius's "De Humani Corporis Fabrica" [5] stands as a timeless atlas of detailed anatomical drawings of cadaveric dissections, and has served as a model for anatomical teaching until today. However, the next major step in studying the internal anatomy of a live patient had to wait for the discovery of the X-ray "röntgenogram" by Wilhelm Conrad Röntgen in 1895 [6]. Computerized Axial Tomographic imaging (CAT scanning), introduced commercially by Sir Godfrey Hounsfield in 1972 [7], has allowed physicians to view internal anatomy of the body in the form of multiple thin "tomographic" cuts, and Magnetic Resonance Imaging (MRI), invented by Paul Christian Lauterbur and Peter Mansfield, also in the 1970's, further provided the capability of viewing even the motion of internal organs, such as the heart, and to assess function. As a next step, volume rendering and three-dimensional reconstruction algorithms have allowed construction of virtual three-dimensional images of internal structures. These impressive images can be rotated on a computer screen, allowing the physician to visualize internal anatomy from different angles. Echocardiography has also progressed from the simple M-mode images to 2D-imaging and, over the last several years, with real-time 3D imaging, albeit with more noise and lesser image quality.

3D-Printing technology in medicine

Impressive as these achievements are, they still require of the physician to create an internal understanding, a mental 3D image of the structures involved and their interrelationships. This falls short of having an actual physical three-dimensional replica of the anatomy, which is exactly what 3D printing achieves. Three dimensional printing is described as "additive manufacturing", in contrast to the traditional types of "subtractive manufacturing", in which an object is created by stepwise removal of material from a larger block, as occurs in sculpture or in milling. In 3D printing, successive layers of material are layered on top of each other, each layer forming the foundation for the next. A variety of materials and techniques to stabilize the layers have been used, including the most currently popular technology of inkjet printers layering photopolymerizable materials, but even metal objects are possible to create by various printing techniques [8]. The technology, invented by Charles Hull in 1986 and first termed "stereolithography", has found many applications in architecture, engineering, and industry, where it has been used in "rapid prototyping" mode, and, increasingly, in producing actual components of industrial products [9].

As the printers create the objects based on special digital files containing digital volumetric (voxel) imaging data (stereolithographic or STL files), accurate primary imaging data are necessary for medical applications. These are obtained usually from CT or MRI scans [10,11]. Such images of bony structures are readily obtained, and this has enabled the first applications of 3D printing in maxillofacial surgery, dentistry, and orthopedics. Cardiac applications have lagged behind partly due to the additional challenges of cardiac imaging involving the similarity of image density of the heart with that of surrounding tissues, the resulting need of administration of suitable contrast material, the relevant timing of such administration, the development of techniques to counteract the motion of the heart (ECG gating) or of the thoracic cage (respiratory gating in MRI scans), and the development of suitable imaging protocols [12].

Clinical benefits of cardiac 3D-printed models

From the clinical point of view, the driving force for development of cardiac 3D printing has been the great need of the surgeon to fully understand complex three-dimensional anatomy, based on multiple images, images which the surgeon himself is called to combine in his head in order to reconstruct the three-dimensional anatomy which will be encountered in the operating room. Ambiguities or deficiencies in this understanding are necessarily either unexpectedly discovered or even missed in the operating room, especially since the surgeon is not at liberty to inspect all the internal structures of the heart, but only those in the surgically accessible field of view. As a result, it is not rare for an operative strategy to have to be modified or formulated ad hoc during the actual operation, or the operation may miss important anatomy and be imperfect. All these factors may result in longer operative times, less precise or effective operations, increased complications and risk for the patient, and unavoidably, greater health care cost.

Furthermore, a 3D patient-specific model provides visual engagement of the patient/family with the specific anatomy, which allows the physician to explain the goal of the procedure, the associated risk, and, finally, to achieve more fully informed understanding and consent.

In addition, the potential role of 3D-models in education of medical students and junior surgeons must be emphasized. Digital anatomic Libraries with 3D models can provide the opportunity to easily study cases with rare cardiovascular variations. Such libraries will supplement the existing few true anatomical libraries, (which are collection of actual cadaveric specimens, and are not easily accessible). 3D model libraries may finally supplant cadaveric organ libraries for many of their functions [13]. Moreover, surgeons, particularly more junior ones, can use 3D printed models in simulation difficult and uncommon operations, enabling them to acquire sufficient knowledge, skill and confidence to learn, and to ultimately perform, high-risk procedures while still in training [14,15].

As all the above issues, clearly applicable to many medical subspecialties, are much more severe in pediatric and congenital heart surgery, where the underlying pathologic anatomy can have practically infinite variety and the operative procedures involved can be extremely complex with attendant high mortality and morbidity. For these reasons, we have been seeking some disruptively new way to enhance our preoperative understanding and improve the safety and effectiveness of complex planned operations. Accordingly, a few years ago, along with a few colleagues around the world, we have also began exploring the possible utility of 3D printing technology initially in complex congenital cardiac lesions, motivated by the specific needs of some of our patients. After some very encouraging early experiences, which we had by building 3D models in collaboration with the team at Toronto Children's Hospital led by Dr. Shi Joon Yoo, we established our own 3D printing team in Athens organized in a small start-up company, 3D Life (www.3dlife.gr).

Education

Our experience has also led to the realization that 3D printed models can revolutionize surgical education in the context of hands-on surgical simulation. Accordingly, we have created a unique "cloud" anatomic library of 3D models created from great variety of complex anatomic problems of real patients, with the intent that it will grow ad infinitum and serve as a unique educational resource [16]. We have also launched a series of hands-on surgical simulation workshops, the first one held very successfully in the context of the Athens Crossroads Congress on Cardiovascular Surgery held in Athens, Greece in November 2018, teaching the arterial switch operation for TGA. In that workshop, the supervisors demonstrated technical skills of the procedure without any time-limits, and the trainees were able to perform the operation on their own 3D model, under teaching supervision, but without the anxiety of a real operation (Figure 8). Yoo et al. [17] who had organized in Toronto such courses, said that one of his senior surgeons commented that it usually takes a few years for surgeons to learn how to do the Norwood operation in hypoplastic left heart syndrome and that he should have been able to learn the procedure overnight if 3D print models of a few cases with different pathologic variations would have been available for practice. He strongly advised surgeons and trainees to practice their surgical skills on 3D print models, before performing the specific operation on the patients.

Application in other structural heart disease

During this time period, it became clear to us that this technology was not only immensely useful as a unique tool to deliver highest quality personalized surgery to patients with complex congenital disease, including neonates, infants, children, and adults, but also to many patients with acquired structural heart disease, being considered for either complex surgical operations or interventional catheter procedures. Accordingly, the technology has proved invaluable in the management of ventricular and complex aortic aneurysms. Interventional cardiologists have also reported great success using 3D printed models in planning TAVI procedures [18-23]. More recently, interventional cardiologists with whom our team has cooperated in producing 3D models have reported impressively successful applications not only in TAVI but also in electrophysiology procedures [24].

Previous reports

Our growing experience has been reported at several international meetings. At first, our efforts have gained first place in the crowd voting competition of the American Medical Association's Innovation Challenge in 2016. Appropriate abstract reports were presented at 2016 Annual Meeting of Association for European Pediatric and Congenital Cardiology (AEPC) in Rome, and at the 2017 Spring Meeting of European Congenital Heart Surgery Association (ECHSA) in Leicester, UK. A multi-institutional study, to evaluate the utility of 3D printing in the management of complex congenital heart disease, as perceived by the clinicians, is underway, with a preliminary very positive approval reported at the 2018 AEPC Annual conference in Athens.

Limitations

3D-printing cardiac technology is still limited by imaging imperfection (iv contrast density, timing, etc). Computing tomography or magnetic resonance imaging are not very successful in imaging valves. Three-dimensional echo is better suited for valve imaging, but it is still affected by noise, lacking sufficient detail. Finally, a great disadvantage of this technology is the still high cost, which hopefully will be diminished, as the technology is used more widely.

Future Direction

The role of 3D printing models in day-to-day clinical practice is in evolution. Future efforts are directed in several areas. Enhancing preoperative understanding, augmenting family education, and optimizing planning of intraoperative and perioperative care, are intuitively obvious. Still there is no prospective randomized comparison of the usefulness of 3D printing compared with conventional imaging. Furthermore, no data exists proving the cost-effectiveness of this technology, or that its use, improves clinical outcomes or surgical training. There are studies in evolution exploring these aspects.

Hands-on surgical training on 3D models will gradually become an essential component in the surgical training programs, especially in the field of congenital heart disease. Currently the print materials are both expensive and suboptimal in simulating real tissue properties [25]. It is hoped that more ideal materials will be developed. Although CT and MRI can provide excellent imaging data of the blood pool, they cannot provide satisfactory imaging of cardiac valves. Since 3D printing of cardiac valves is still largely unsatisfactory, a new mathematical algorithm, which could provide image fusion of CT, MRI and 3D echo data could enable production of accurate 3D models of valves [26].

Finally, 3D printing can be in used in combination with molecular biology techniques (tissue engineering) for creating personalized implants such as conduits, stents, artificial valves, etc [27]. 3D printing has also experimentally used for tissue engineering (cardiac valves), by creating a printed scaffold, where progenitor cardiac cells are laid down [28,29]. Of course, till now, tissue printing has not fabricated any viable product but the future of bioprinting and tissue engineering will be the new era in personalized medicine.

Summary

3D Printing of cardiac models is a powerful tool with proven utility for the management of complex cardiovascular disease (acquired and congenital), because it overcomes some of the limitations of conventional 2D/3D imaging methods. The opportunity to handle accurate physical models of the anatomy in ways impossible even at operation enables the care team to appreciate potential procedural difficulties, avoid surprises during operation, and clarify aims and limitations of planned surgical interventions. This new technology clearly empowers the entire heart team, along with patients/families to greater understanding of congenital/structural heart disease with the ultimate result of improvement the quality of care.

Our team, is the first team, in Greece, which has introduced and adapted this technology in its standard clinical practice in the field of congenital heart disease, in all of its aspects (preoperative, postoperative, educative and consulting). Our future efforts are in two directions: The combination of 3D printing and virtual reality or augmented reality to enhance preoperative understanding and surgical planning, and the development of bioprintable tissues and, ultimately, organs, which can be patient specific both anatomically and biologically.

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