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Applications of three-dimensional printing and advance visualization tools in congenital cardiology and cardiac surgery

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Sommario

L'utilizzo della stampa 3D applicato alla cardiologia e cardiochirurgia ha visto un rapido sviluppo nell'ultima decade. In presenza di complesse anatomie intra e extracardiche , creare una modello specifico per il paziente rapresenta una grande possibilità di migliorare la compresnione della patologia per le figure professionali convoilte nel percorso diagnostico-terapeutico del paziente (medici, infermieri, studenti) e anche per lo stesso paziente e per la sua famiglia. Tuttavia, ad oggi, non ci sono ancora forti evidenze che provino il reale benficio delll'utilizzo dei modelli 3D stampati nella pratica clinica e sono disponibili per lo più dati qualitativi e brevi case serieries o case reports. I modelli 3D possono essere stampati in molti diversi materiali, rigidi o flessibili, di diversi colori o trasparenti, e anche di dimensioni in scala superiore all'originale. La scelta di come realizzare il modelo dipende in aprticolare dalla sua applciazione clinica.

Le più comuni applicazioni sono la valutazione preoperatoria di anatomie complesse, l'uso a scopi educativi e nella comunicazione medico-paziente.

In questa tesi vengono esplorati alcuni degli usi di questa tecnica di visualizzazione tridimensioanle avanzata applicata allo studio delle cardiopatie congenite.

Abstract

Three-dimensional (3D) printing technology in congenital cardiology and cardiac surgery has experienced a rapid development over the last decade. In presence of complex cardiac and extra-cardiac anatomies, the creation of a physical, patient-specific model is attractive to most clinicians. However, at the present time, there is still a lack of strong scientific evidence of the benefit of 3D models in clinical practice and only qualitative evaluation of the models has been used to investigate their clinical use. 3D models can be printed in rigid or flexible materials, and the original size can be augmented depending on the application the models are needed for. The most common applications of 3D models at present include procedural planning of complex surgical or interventional cases, in vitro simulation for research purposes, training and communication with patients and families.

The aim of this work is to explore the applications of 3d printing as advance visualization tool in congenital cardiology and cardiac surgery.

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Chapter 1

Introduction

The possibility to create physical, patient-specific models by means of three-dimension (3D) printing is appealing when dealing with complex anatomies in paediatric and adult patients with congenital heart disease (CHD). Patients with CHD are regularly monitored with imaging, yet often a single imaging modality is not sufficient to fully appreciate the complexity of cardiac anatomy, physiology and extra-cardiac spatial relationships. Moreover, these patients frequently undergo multiple surgeries with implantation of devices, increasing their complexity and resulting in unique anatomical variations. For these reasons, 3D printing has proved useful in congenital cardiology and cardiac surgery[1,2].

Experts in non-invasive cardiovascular imaging have a great ability to understand cardiac anatomy from traditional cross-sectional images even in the presence of complex CHD. However, holding a physical 3D reconstruction of a patient's anatomy can augment the understanding of spatial relationships and of the real dimensions of both cardiac and extra-cardiac structures. Furthermore, 3D printing is likely to be even more helpful for physicians with less expertise in analysing and interpreting cardiovascular images, for instance cardiac surgeons and interventional cardiologists.

Generally, what can be imaged in 3D can be printed in 3D, so using 3D images from computed tomography (CT), magnetic resonance imaging (MRI) or 3D echocardiography as inputs, it is possible to produce 3D printed models of the entire heart or of a specific region of interest (Figure 1).

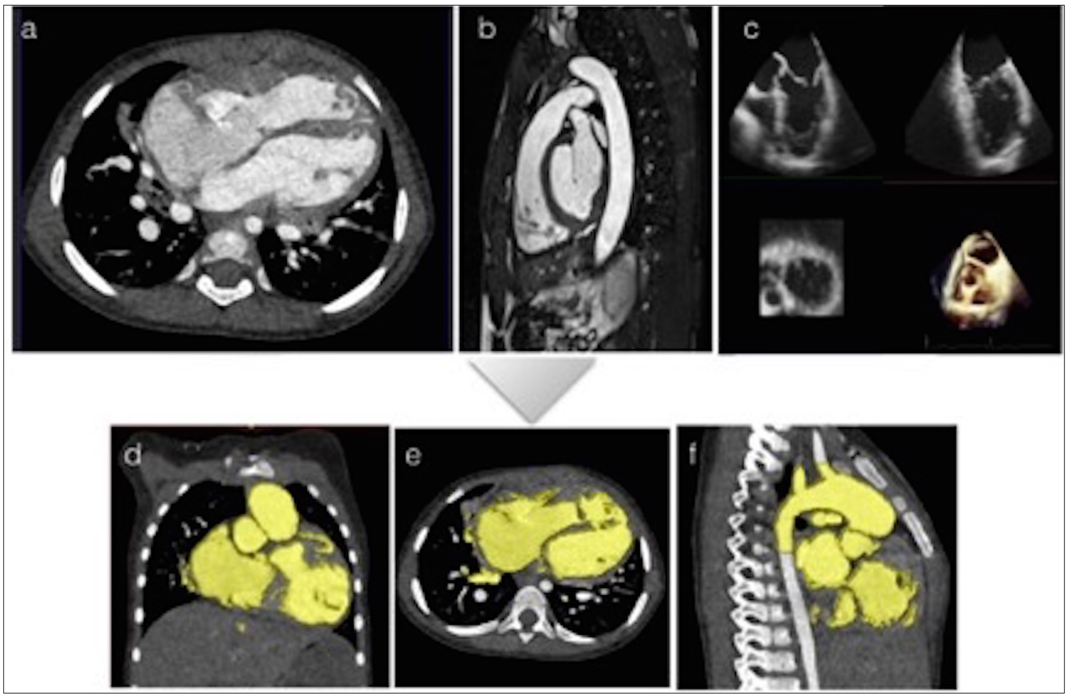

Figure 1 All imaging modalities can be used input images for the creation of 3D models. a) Non-gated cardiac CT of a patient with double outlet right ventricle and apical muscular VSD; b) Balance SSFP with ECG gating and respiratory navigation can be used to acquire 3D images of the heart in cardiac MRI. c) 3D echocardiography provides excellent visualization of the atrio-ventricular valves. Panels d), e) and f) are examples of the segmentation process with a commercially available software (ScanIP, Synopsis, US) using tresholding and manual editing from multiplanar non-gated CT images of a patient with DORV. This step allows the operator to identify and separate the different cardiac and extracardiac structures: the blood pool usually present a higher signal intensity comparing to the myocardiaum and vascular walls and this automated software identifies the endocardial contours creating a colour mask that need to be carefully checked for accuracy by the operator.

Most commonly, CT images or 3D MRI images (whole-heart MRI or contrast-enhance MR angiography) are used to produce 3D models. Through an accurate post-processing analysis, or "segmentation" process, the images are transformed into 3D surface files (.stl) and sent to the printer (Figure 2). The final result will depend greatly on the quality of the input images and on the operator performing the segmentation, who needs to be able to fully understand the cardiac anatomy. This suggests either the need to train a 3D printing operator for specific cardiac applications or the importance of close liaison between bioengineers and clinicians when creating a model.

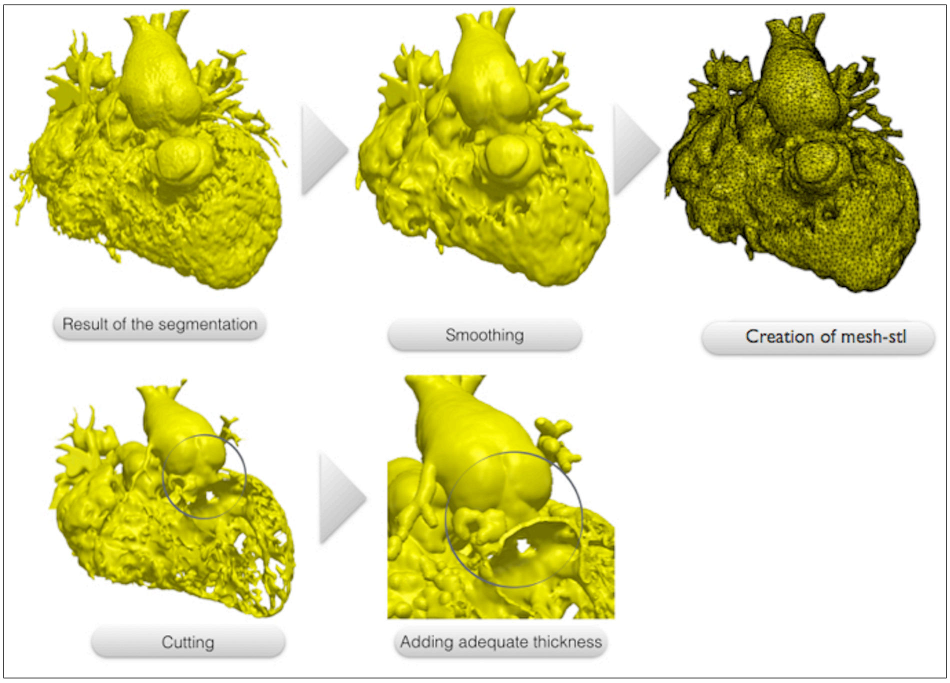

Figure 2 The 3D images resulting from the segmentation process usually present a dyshomogenous surface due to the presence of multiple trabeculations, mostly inside the right ventricle. This file is modified though a smoothing tool using a commercial available software (ScanIP, Synopsis, US) and converted to a surface mesh file called .stl. The surface can be cut exposing the region of interest for the surgeon. In our case, the right and left ventricle free walls have been removed to allow the visualization of the multiple apical VSD. Finally a 1.2 mm thickness is added to the surface to make it suitable for printing.

A variety of materials can be chosen for printing. Rubber-like material (e.g.TangoPlus and Agilus30) or silicone are likely preferable for surgical practice, enabling cutting into the model, but are typically more expensive (Figure 3).

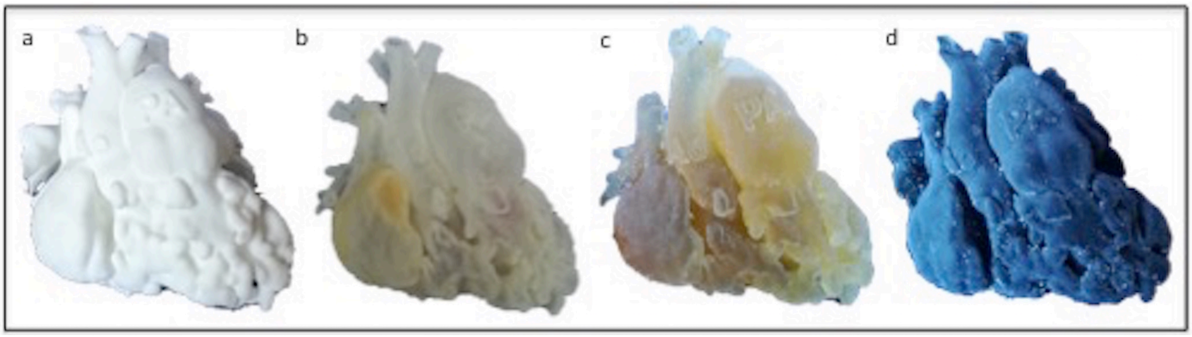

Figure 3 Depending on the application of the model, different materials can be used. In this figure, the same heart of a 1 year old patient with double outlet right ventricle was printed in a) Nylon; b) VeroClear c) TangoPlus and d) TangoBlackPlus

The cost of the model however depends also on its size, and small 3D models are cheaper because a smaller amount of material is used for printing. Rigid materials (e.g. SLA resins) can be used for educational or communication purposes. Indeed, 3D models have been used for different purposes in CHD, including procedural planning, research applications, training and doctor-patient communication (Figure 4).

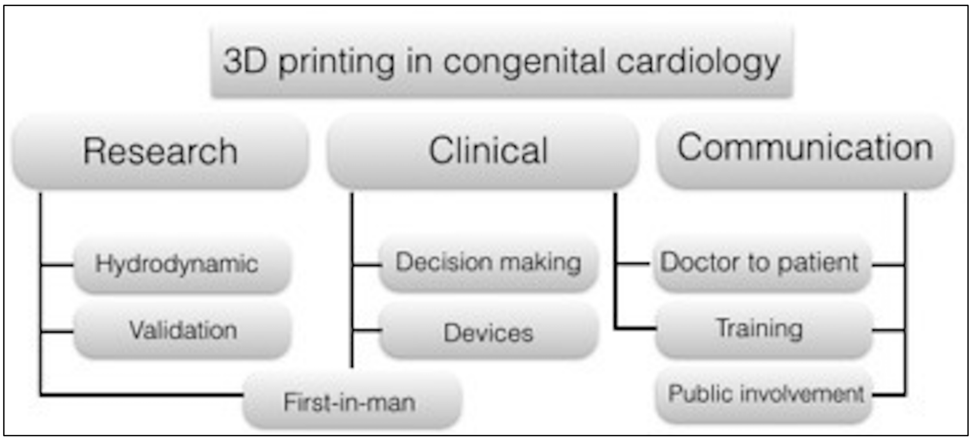

Figure 4 Application of 3D models in congenital cardiology and cardiac surgery. Biomedical engineers use the physical model to create experimental set ups and test hydrodynamic conditions in patient specific settings; these setups are used also to validate computation models. Physical models are used for clinical purposes in surgical planning and decision-making of complex procedures, as well as to test new application of devices to patient specific anatomy. Medical students and trainee can benefit from the use of three-dimensional models during cardiac morphology courses as well as cardiac surgeon from practicing complex procedures. Comparing to medical images, physical models are much easier to understand for patients and parents.

Procedural planning

Patient-specific 3D printed models can be used to plan surgical and percutaneous interventions (Figure 5). Case reports and small case series have suggested that 3D printed models facilitate the decision-making process in complex cases[3]. However, only qualitative analysis of the models by means of satisfaction questionnaires has so far been used to evaluate their benefit. A recent multicentre prospective study aimed to evaluate the impact of 3D printing models in planning 40 complex CHD surgeries, providing surgeons with a 3D printed model after a first multidisciplinary discussion and registering a change in surgical strategy in 19/40 cases[4].

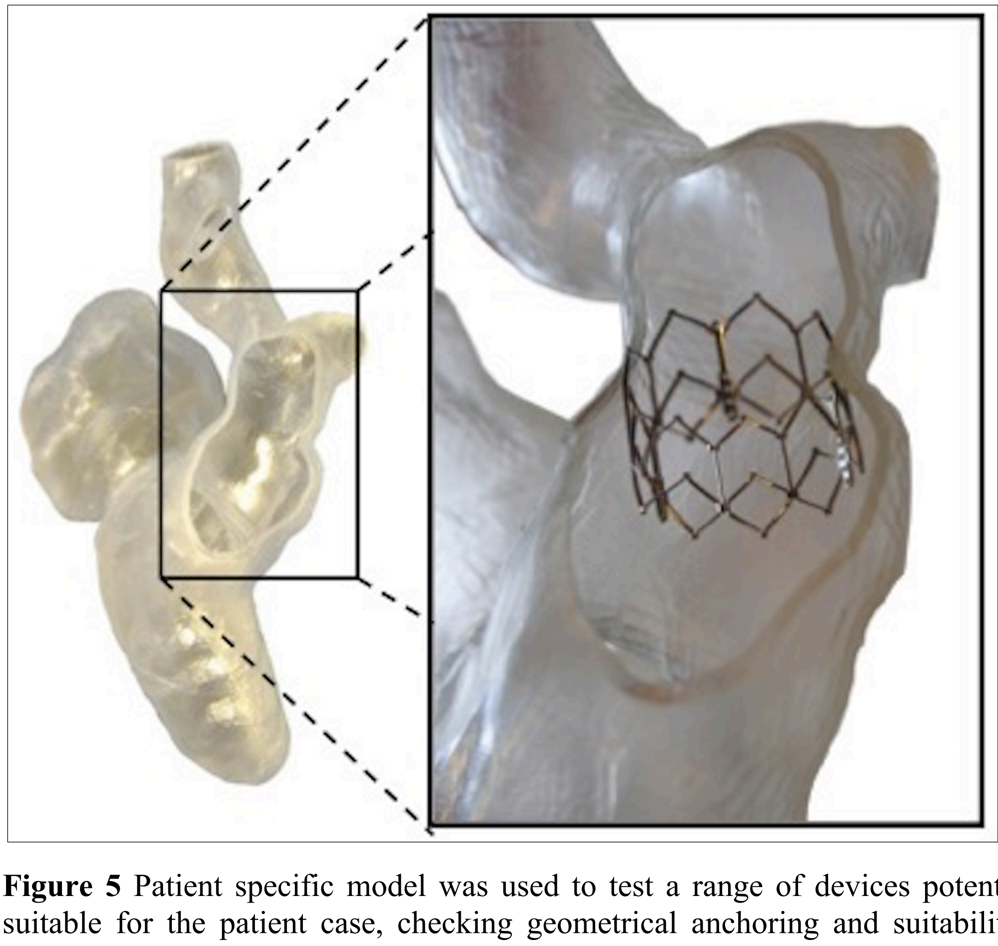

Figure 5 Patient specific model was used to test a range of devices potentially suitable for the patient case, checking geometrical anchoring and suitability to patient anatomy.

As for other smaller series, the main limitation of the study is that measurable outcomes, e.g. cross-clamp time, bypass time, days of hospital admission or mid- and long-term follow-up information, were not included. 3D printing has also been used successfully for percutaneous procedures, for instance adopting 3D printed models of right ventricular outflow tract in patients with pulmonary valve regurgitation as a tool to aid clinicians in selecting patients eligible for percutaneous pulmonary valve implantation[5]. Meaningful clinical applications include:

a. Visualization of the size of the pathological structures in presence of rare congenital abnormalities (Figure 6)
b. Three-dimensional visualization of intra-cardiac structures (Figure 7)
c. Understanding of the spatial relationship of the great vessels in cases of complex CHD, particularly in post surgical anatomies (Figure 8)[6]

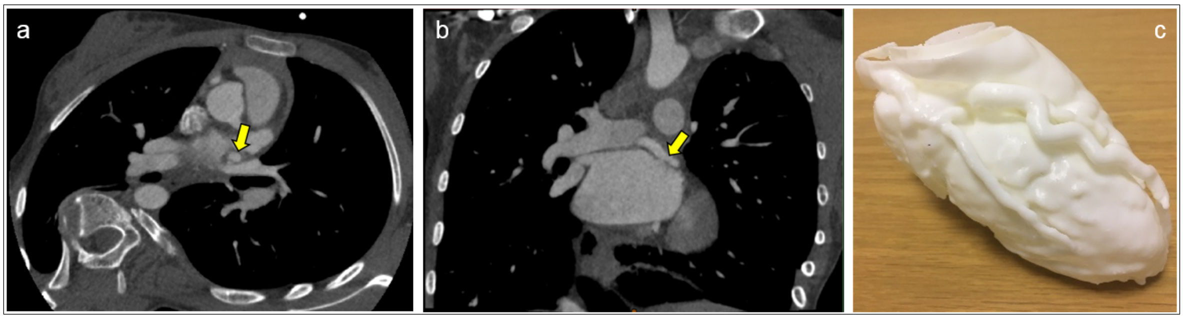

Figure 6 14-year-old female patient who was referred for cardiac CT after echocardiography showing prominent coronary artery flow, suggesting presence of fistula or anomalous artery connection. CT images confirmed the diagnosis of anomalous origin of the circumflex coronary artery from right pulmonary artery (a and b). 3D model was manufactured for better understanding of coronary anatomy and dimensions.

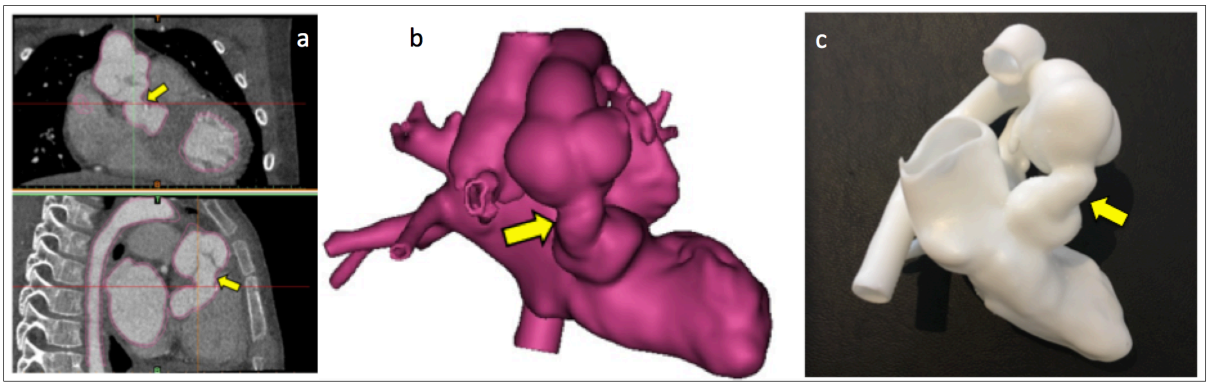

Figure 7 Complex congenital case: double outlet right ventricle with transposition of the great arteries and non committed VSD, repaired with LV to aorta baffle presenting with symptoms of left ventricular outflow tract (LVOT) obstruction. Model manufactured on clinical request for assessment of LVOT anatomy.

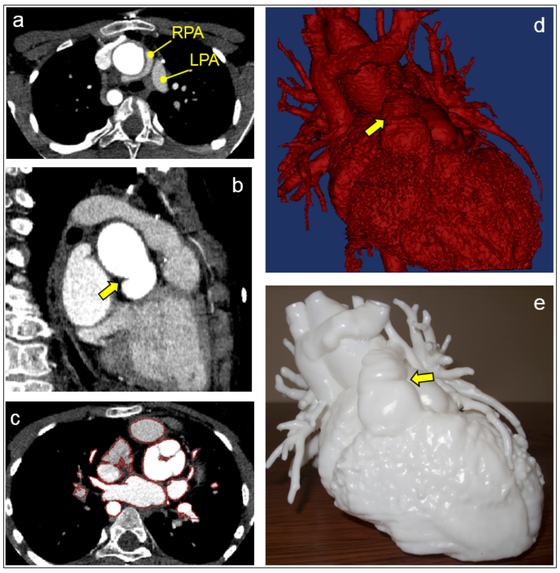

Figure 8 Complex congenital case: 11-year-old patient truncus arteriosus presenting with conduit and pulmonary stenosis. The model was used to assess the relationship between the aorta and the pulmonary arteries in order to plan the surgery.

Research applications

Patient-specific 3D models can be incorporated in the context of experimental set-ups for research applications (Figure 9). Models also represent useful tools to validate computational simulations, with several studies reporting good correlations between patient-specific model simulations *in vitro* and *in silico* when assessing cardiovascular hydrodynamics in CHD[(7)], also accounting for the presence of devices, such as percutaneous valves[(8)].

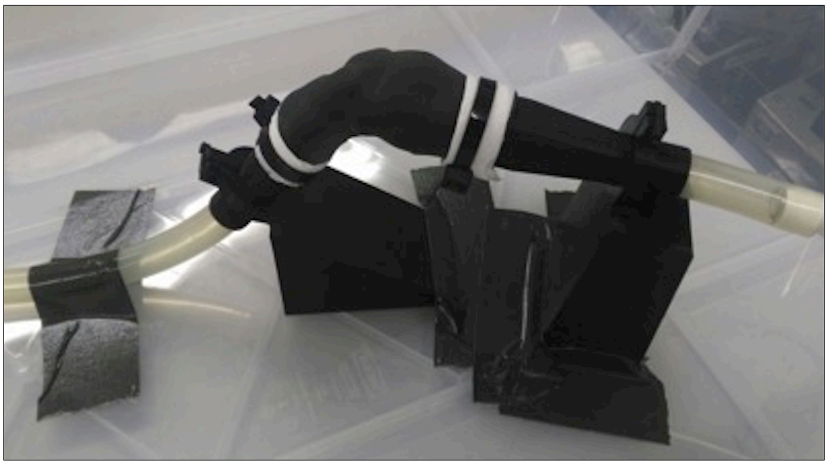

Figure 9 Patient-specific model of right ventricular outflow tract is connected to a hydrodynamic circuit to simulate realistic flow and pressure conditions to be assessed with MRI acquisitions. These in vitro setups are used to simulate hydrodynamic conditions and study the complex physiology of patients with CHD, typically performing parametric studies. Mock circulatory systems incorporating patient-specific models can also be designed to be MRI compatible and thus allow for the acquisition of detailed visual information, such as 4D MRI flow sequences.

Training

Congenital heart disease patients are particularly challenging for trainees and fellows in cardiac surgery, with limited opportunity to practice without endangering paediatric. 3D models printed with flexible materials have been proposed as a tool for practicing surgical procedures (Figure 10). Models were found useful although the elasticity of the material was reported as different from real myocardial tissue by the surgeons(9). Clinical staff can benefit from additional training with 3D models for increasing the appreciation of CHD anatomy after cardiac surgery, e.g. during training courses for cardiac nurses(10). Furthermore, 3D models present advantages over specimens in terms of their cost, ease of reproducibility and conservation/storage, or can be used in conjunction with specimens providing a richer training experience when studying congenital cardiac morphology.

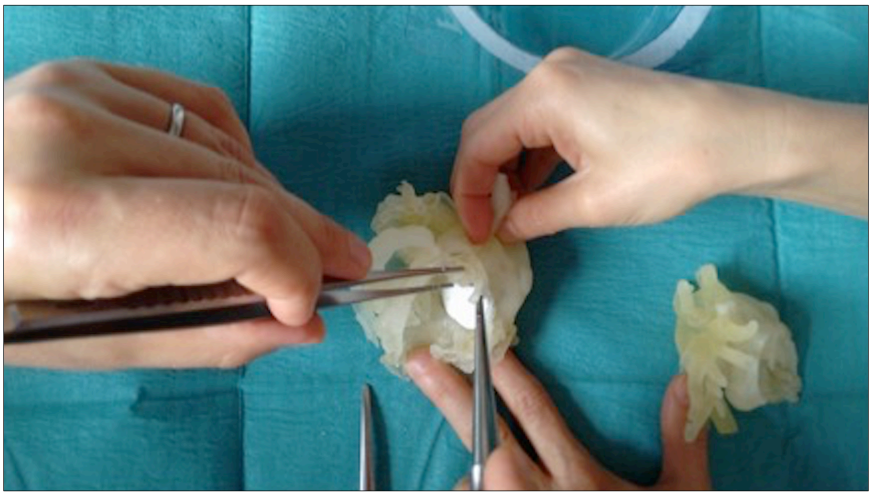

Figure 10 In this example, a cardiac surgery fellow is practicing on the creation of an intracardiac baffle from the VSD to the aorta in a patient with DORV using a 3D model printed in TangoPlus

From doctor-patient communication to public engagement

CHD's are chronic medical conditions that can affect the patient's lifestyle from childhood to adult age. The doctor-patient working alliance is a crucial component of patient adherence and satisfaction(11). Communication between cardiologists, cardiac surgeon and patients (and their families) is particularly challenging given the complexity of the defects and medical terminology, the need for multiple surgeries, the dynamics of a communication triad when considering clinician-patient-parent, as well as the delicate process of transition that CHD patients go through as adolescents and young adults. A study involving parents of CHD patients showed that the use of 3D models during medical consultations was enthusiastically appreciated, despite no objective evidence of substantially improved knowledge of their child's condition after viewing the models(12). Young people with CHD also responded positively when viewing their own 3D heart models during routine clinical consultations, reporting a better experience compared to previous visits(13). The benefit of 3D models in this context may derive from subtle changes in communication dynamics and overall engagement of patients with their health status, rather than measurable changes in knowledge.

Beyond the clinic, 3D models have also been used to bring together art and medicine to foster patients and public involvement and engagement and explore novel stimulating ways of portraying the complexity of cardiovascular anatomy in the presence of CHD.

Recommendations for use in clinical practice

There are no current recommendations or guidelines for standardised use of 3D models in congenital cardiology and cardiac surgery. Current use in clinical practice includes *ad hoc* application for planning or practicing complex procedures. The use of 3D models is currently limited to very complex cases with unique cardiac anatomy, e.g. patients with double outlet right ventricle with non-committed VSD. The outcomes of on-going research focused on scientific evidences of 3D models' usefulness will likely influence the development of clinical recommendations.

Chapter 2
Study design

The aim of this waork is to understand wether the use of 3D patient specific models can:

a) Improve decision-making process and procedural planning of complex congenital cardiac surgery procedures.
b) Improve di education and training for cardiologists and cardiac surgeons during educational teaching sessions

The study was therefor structured in different experiments.

<u>Experiment 1: Surgical planning</u>

Aim: Assess the role of patient specific 3D modelling techniques (3D pdf, printed models, and VR) compared to conventional cross-sectional imaging in order to determine which modality is most helpful in tailoring the surgical strategy in double outlet right ventricle repair.

This part of the study was conducted between Verona University Hospital, Great Ormond Street Hospital (London, United Kingdom) and Bristol Heart Institute (Bristol, United Kingdom).

<u>Experiment 2: Training</u>

Aim : determine wether having access to 3d printined models improves understanding of complex anatomies compared to traditional anatomical samples in the setting of anatomical teaching sessions for cardiologists nad cardiac surgeons.

The study was conducted at UCL Insitute of Cardiovascualr Science (London, United Kingdom).

Detailed methods of each experiment will be discussed in each dedicated chapter.

Chapter 3

3D printing and procedural planning in double outlet right ventricle biventricular repair

Double outlet right ventricle (DORV) represents a wide range of anatomical configurations that, together with associated abnormalities, often result in unique anatomies requiring individualised surgical repair. DORV is a form of ventriculao-arterial connection and, according to the International Society for Nomenclature of Pediatric and Congenital Heat disease, is defined by the presence of both arterial trunk supported entirely or predominately by the morphologically right ventricle (14). The anatomical variations within this spectrum including the presence of bilateral infundibula and ventricular septal defects are still highly debated criteria, A recent anatomical study by Do et al, reported that most DORV hearts examined presented a fibrous continuity between one of the arterial valves and an atrioventricular valve, with bilateral infundibula in 23%, and intact ventricular septum in 5% (15).

The interventricular communication (VSD) can be defined based on the location and the borders and VSD are usually classified into muscular, presenting mucular margins, perimembranous, with a fibrous floor, and juxa-arterial, with a fibrous roof. In the context of DORV, there is a large variability in the VSD location from sub-aortic or subpulmoanry, depending on the attachment of the outlet septum; juuxta-arterial, when the roof of the defect is made up of the leaflets of the arterial valves; and non-committed or remote with the most obvious examples being VSD of the muscular septum, or perimembranous with inlet opening. Sometimes it can be difficult to determine the non committed nature of a VSD and the decision may not be unanimous, in particular in presence of subarterial VSDS which are remote form the arteria trunks because of a long distance between the muscular septum and the arterial valve.

The presence of non-committed or remote interventricular communications (VSD) represents a particular surgical challenge and often drives the choice towards a univentricular repair, even in the setting of adequately sized left and right ventricles [16]. In addition, the atrio-ventricular valve anatomy, and the relationship with the VSD may also represent a surgical challenge in the planning of a biventricular repair.

The initial DORV sub-type influences patient outcomes: non-committed VSD are associated with early and late mortality [17] whilst an unfavourable intracardiac tunnel geometry may lead to left ventricular outflow tract obstruction [18]. Intracardiac tunnelling with arterial switch operation (ASO) carries the highest risk of early mortality [18].

Advanced visualisation techniques is currently available to appreciate the images of patients fully in 3D. Techniques now include visual patient-specific 3D modelling; 3D printing, augmented and virtual reality (VR) derived from conventional diagnostic image modalities such as cardiac magnetic resonance (CMR) and computed tomography (CT).

Over the last decade, the use of 3D printing in complex congenital heart disease, and particularly in DORV, has gained importance in surgical and interventional procedural planning [18-22], and anatomical evaluation [23-25]. However, access to this technology is still limited by the associated costs, timing, printer accessibility, thus leading to incompatibility with the workflow of clinical care.

3D model on screen, such as the 3d pdf file format, allows clinicians to visualise and to handle the 3D patient anatomy on any screen, computer, or mobile device, without the need for technical expertise in software navigation.

VR is an immersive technique offering the possibility of navigating and manipulating patient specific anatomies, thus potentially overcoming some of the limitations of 3D printing. Recent results of the use of VR in the field congenital heart disease [26-28] are promising. However, it has not been assessed yet whether there are any potential improvement in using VR to plan the surgical workup of patients with DORV.

We present a pilot study focused on a series of DORV patients operated at our Centre to assess the role of different 3D modelling techniques (3D pdf, printed models, and VR) and conventional cross-sectional imaging aiming to determine which modality is most helpful in tailoring the surgical strategy.

Methods

Patient population and image data

We retrospectively selected ten consecutive patients with complex DORV who underwent biventricular repair with intracardiac baffle, with or without arterial switch, between August 2015 and March 2018 at our Institution. All procedures were carried out by a senior surgeon who accessed a 3D patient-specific reconstruction before surgery. The relevant clinical information, including post-operative follow-up, and cross-sectional imaging data (CT or CMR) were collected for all patients.

CT images were acquired using dual source multidetector CT scan (Siemens Somatom Force, Siemens Healthineers, Erlangen, Germany), as contrast enhanced non ECG-gated datasets.

Cardiac MR imaging were acquired with contrast enhanced three-dimensional balance steady state free precession (3D whole heart) in mid-diastole with respiratory navigator at 1.5 Tesla (Siemens Avanto).

The study was approved by the local R&D office.

The intracardiac anatomy, in particular the location of the VSD, was defined according to the surgical inspection at the time of surgical correction. The VSD was defined non committed when was anatomically related to, or was close to, neither great vessel, being separated from both by considerable muscle.

Patient specific 3D anatomical model reconstructions

Volumetric images were post-processed by means of a commercially available software (ScanIP, Synopsis-N2018.03) to reconstruct the 3D anatomy of the heart including atria, ventricles, great vessels and, where possible, valvular structures. The segmentation process was performed by the same operator (CC) with over 10 years of experience. The resulting 3D anatomical reconstructions were imported as *.stl* file format into Meshmixer (2017 Autodesk, v3.5). For 3D printing, two planar cuts were performed, one across the RV free wall and one across the LV posterior wall, to expose the intracardiac anatomy and the VSD. A 1-mm homogenous thickness was added to each cardiac surface to allow for manufacturing.

<u>3D Visualisation tools</u>

Following the post processing, the 3D pdf file of each patient model was exported a built-in using ScanIP.

All models were printed at 1:1 scale, in rigid white nylon (EOS PA2200 Nylon 12) using selective laser technology (EOS P100).

The 3D reconstructions were imported into a novel VR environment developed in-house within the Unity engine. The target platform was the Oculus Rift system (comprised of a headset, two sensors and two hand controllers). The following specialised VR tools were specifically designed for this study: 1) Grabbing tool to hold and rotate the object; 2) Cutting tool for slicing and exposing the intracardiac anatomy in any plane; 3) Measuring tool to measure distance and diameters of the different cardiac structures; 4) Marking tool to place landmark on the virtual model; 5) Multiplanar reconstruction (MPR) tool to crosscut the model in three different perpendicular planes (axial, sagittal, coronal); and, 6) Virtual echo tool to scan the model with a virtual probe in any desirable plane. The user could freely interact, move and rotate each patient-specific model in virtual space and use any of the aforementioned tools (Supplemental video showing the interaction between the operator and 3D printed model on the left and the VR model on the right).

Evaluation of patient model and surgical strategy

Each case was retrospectively evaluated, separately, by two experienced paediatric cardiac surgeons, from different centres, each with more than 15 years of experience as first operator in paediatric cardiac surgery. They were neither involved in the original surgery nor with the clinical care of the patients and were completely blinded to the actual surgical repair and outcome. The two surgeons were asked to provide a surgical plan for each case retrospectively analysed. In particular, their opinion on the type of repair (biventricular vs univentricular) was recorded at the end of each stage of the analysis. The first assessment of patients was based on the clinical history, echocardiography and CT/CMR images alone. This review of the CT/CMR images was guided by a cardiologist with experience in cardiovascular imaging. Hence, the surgeons were presented sequentially with patient-specific models of each patient in form of: *i)* a 3D pdf; *ii)* a physical 3D printed model; and, *iii)* the VR setup (Figure 11).

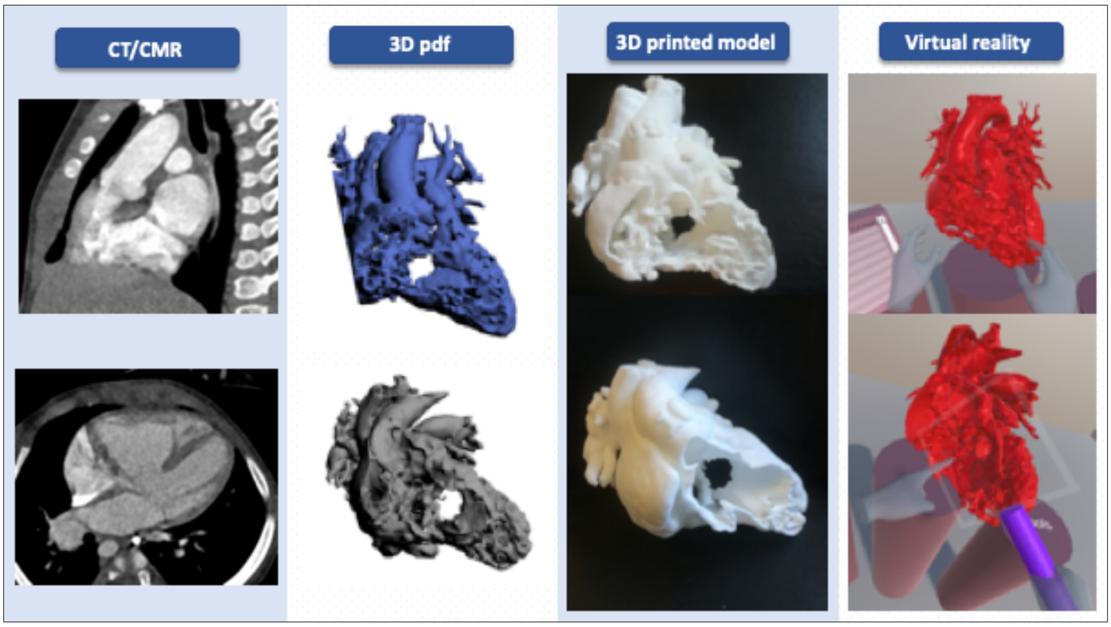

Figure 11. Two examples of 3D visualization tools used by Surgeon A and B to assess the cases.

At each step, the surgeons were asked to confirm or change their potential surgical approach. Each decision was compared to the actual strategy performed on each patient (i.e. the choice of reference) in order to evaluate the accuracy of each type of 3D modelling modality in planning complex surgical repairs.

Results

Patient population

Patient characteristics are summarized in Table 1. Nine patients had previous palliation at a median of 0.6 months (0.1-3) including pulmonary artery banding (PAB, n=6), arch repair and PAB (n=2) and bilateral PAB and PDA stent (n=1). All patients underwent biventricular repair with intracardiac tunnelling +/- VSD enlargement at a median of 8.4 months (2.6-13.8). Median cross-clamp and by-pass time were 110.5 (34-182) and 148.5 (46-308) minutes respectively. In three cases (case 1, case 6, case 7), ASO was performed. Details of each procedure and LVOT gradients at discharge are recorded in Table 2. VSD enlargement was performed in 2 cases.

The median follow-up was 31 months (10.2-44.6). There was no mortality during follow up. All patient presented good biventricular function at follow up and none of the patient presented significant AV regurgitation or neo-aortic regurgitation. Two patients underwent further surgical procedures. Patient #1 had surgical closure of residual apical VSDs due to the persistence of significant left to right shunt 24 months after initial repair with arterial switch, arch repair and intracardiac tunnel with limitation of pulmonary blood flow by creating a supravalvar PS (case 1). Patient #7 underwent two reoperations for recurrent LVOTO. A resection of a fibro-muscular shelf was performed at 8 months after repair and later replacement of VSD patch at second reoperation at 23 months. One more patient (i.e. Patient #5) is currently scheduled for reoperation with a LVOTO gradient of 4.1 m/sec 40 months after the biventricular repair. Follow up data such as LVOT gradients are summarised in Table 3.

Surgical planning

The choices of the two surgeons interviewed were evaluated if in agreement or not with the operation performed (Table 4 and 5). After review of the CT or CMR data, a biventricular repair strategy was in agreement with the actual procedure in 9/10 cases by *Surgeon A* and in 6 out of 10 cases by *Surgeon B*.

Following review of the 3D pdf models, *Surgeon A* did not change surgical strategy for any case (9/10 biventricular strategy), while *Surgeon B* modified the surgical plan for patient 6 (5/10 biventricular strategy).

Following the review of the 3D printed model, biventricular repair was suggested in 9 and 8 cases out of 10 by *Surgeon A* and *Surgeon B*, respectively.

Using the VR setup, the concordance of choices increased to 10 out of 10 (*Surgeon A*) and 9 out of 10 (*Surgeon B*).

The agreement between the two observers increased from 70% after cross-sectional imaging review, to 90% following 3D printed model and VR review.

When a univentricular repair strategy was suggested this was due to the distance between the aortic and pulmonary annulus and the VSD, the size of the VSD and presence of tricuspid valve tissue in the pathway to the creation of the LVOT baffle. The use of a 3D model has also highlighted to the surgeons other aspects of the surgical plan as for instance the possible substrates to RVOT and LVOT obstruction, as well as the need of excision of the conal septum or of a RV conduit.

Compared to traditional cross-sectional imaging, the 3D pdf did not increase the accordance on the feasibility of biventricular repair in any case. The agreement with the actual surgical plan improved in 4 cases with the use of the physical 3D printed model and in 5 cases using the VR setup, changing the surgical plan from univentricular to biventricular repair. The percentage of correct answers after reviewing all imaging modalities is summarized in Table 4.

The identification of ASO as part of the repair strategy was in accordance with the original surgical plan in 6/10 cases for *Surgeon A* and in 3/10 cases by *Surgeon B* after review of CT/CMR images. For both surgeons, there was no improvement after reviewing the 3D pdf.

The accuracy increased after the evaluation of the physical 3D printed model: *Surgeon A* and *Surgeon B* correctly suggested the adoption of ASO in 7/10 and 4/10 patients respectively. This did not change after VR assessment for *Surgeon A* but improved for *Surgeon B* from 4/10 to 5/10.

Discussion

Three-dimensional modalities to visualize cardiac anatomy and plan surgical approaches are increasingly used in clinical practice. Over the last decade, 3D models including computer and 3D printed replica have shown both benefits and limitations. More recently, novel and more immersive ways to explore and interact with cardiac anatomy such as virtual reality have been proposed. With the increasing use of these technologies, the aim of this study was to compare such 3D modalities in the context of repair of a complex of double outlet right ventricle. To the best of our knowledge, this is the first pilot study aiming to compare all the 3D modelling techniques available for presurgical planning of complex congenital heart disease.

The main findings of our study on the use of 3d models in the planning of DORV are the following:

1. The use of a 3D model on screen (i.e. 3D pdf) did not provide additional support in the selection and planning for patients suitable for biventricular repair procedure, compared to traditional cross-sectional imaging.
2. Three-dimensional printed models increased the accuracy in identifying the patients suitable for biventricular repair and in deciding about whether to perform arterial switch operation in the context of biventricular repair, compared to traditional cross-sectional imaging and also to 3D pdf.

3. VR assessment represents the best 3D modelling modality in the planning of DORV repair, increasing the accuracy of the selection of ideal candidates for biventricular repair to 95% (19/20 cases), compared to 75% (15/20 cases) of the traditional cross-sectional imaging techniques.

The role of three-dimensional printing technology has become increasingly recognised in the evaluation of complex congenital anatomy [(30)]. From the initial experience with the use of rapid prototyping in the evaluation of the right ventricular outflow tract in candidates for percutaneous pulmonary valve implantation [(23)], novel 3D visualization have been developed to aid planning, such as VR and augmented reality [(29)].

According to our results, the use of a simple 3D reconstruction such as the 3D pdf does not result in any additional benefit in identifying patients suitable for biventricular repair. This may be explained by the fact that the 3d pdf format allows a limited manipulation of the model and may result in difficult interpretation by the cardiac surgeon. Nevertheless, this format is easily portable on any device and sharable within the clinical team.

Physical 3D printed models in 1:1 scale allow a better appreciation of the spatial relationship between the interventricular communication and the great arteries, of the volume of the two outflows and of the orientation and extent of the outlet septum. However, once printed, they are not easy to modify by the user. In our study, we used rigid white nylon 3D models prepared with two cuts on the right ventricle free wall and on the and left ventricle posterior wall to expose the intracardiac anatomy. This type of model is easier and less expensive to manufacture if compared with the flexible full models (rubber-like polyurethane filament) used in previous studies [(20, 32)], yet, in this format the models were still effective in identifying the performed procedures and superior to 3D pdf and CT/CMR alone.

VR proved to be the best tool for our two evaluating surgeons to identify correctly the feasibility of biventricular repair and the need for arterial switch operation.

The immersive nature of the VR experience confirmed to be an advantage for the study of complex anatomies in line with recent developments [33]. The in-house VR setup was designed to provide the surgeons with the evaluation of the patient-specific model from conventional and non-conventional surgical views, to simulate the best surgical approach to the defect and to explore the intracardiac anatomy in a more comprehensive way than what is possible in the operating theatre where intracardiac anatomical assessment is limited by the surgical approach, usually from the right cardiac chambers.

Although small, our cohort represents a carefully selected and homogenous population of DORV with complex interventricular communications, a rather rare cardiac anomaly where the application of 3D technologies could meaningfully contribute to surgical planning. The results of this preliminary experience will be verified in future studies on larger and heterogeneous cohort of patients and conditions.

An inherent limitation of all the 3D modelling techniques used in this study is the assessment of the atrioventricular valves. This depends on the source imaging modality (either CT or CMR), which cannot display valve structures with sufficient resolution for 3D reconstruction. Since the insertion of the tricuspid valve represents a crucial part of the surgical correction of DORV, it is recommended that 3D models fuse information from multimodality imaging information such as conventional and 3D echocardiography. In this context, 3D visualization, in particular VR, should be considered as a very valuable addition to non-invasive imaging modality (Figure 12).

The choices of the two evaluating surgeons were compared to actual operation successfully performed. This assumption is confirmed by the demonstrated feasibility of the repair and the excellent short-term results, as summarised in Tables 2 and 3. In presence of complex cardiac anatomies, the surgical strategy may not univocal and in some cases more than one option may be anatomically feasible. The surgical strategy often depends on the surgeon’s and centre experience and this is likely a reason why in some cases the surgeons A and B do not agree on the proposed strategy. Being aware of these the differences that may be present between surgeons, rather than comparing surgeon A and surgeon B among themselves, we found interesting how the use of the different modalities could add information and modify the surgical plan for each individual surgeon on each specific case.

Ultimately, it is the long-term re-intervention free survival that determines the best approach to this challenging group of patients, and this can be achieved using different surgical strategies. In addition, even a VR model will not inform about the details of surgical repair such as choice of material and patch geometry, which together with the underlying anatomy will influence freedom from re-intervention in long term.

A limitation of this study is the fact that testing of our hypothesis was done by two senior evaluators only. We felt, however, that given the complexity of the assessed conditions, additional testing by less expert evaluators may not offer conclusive results.

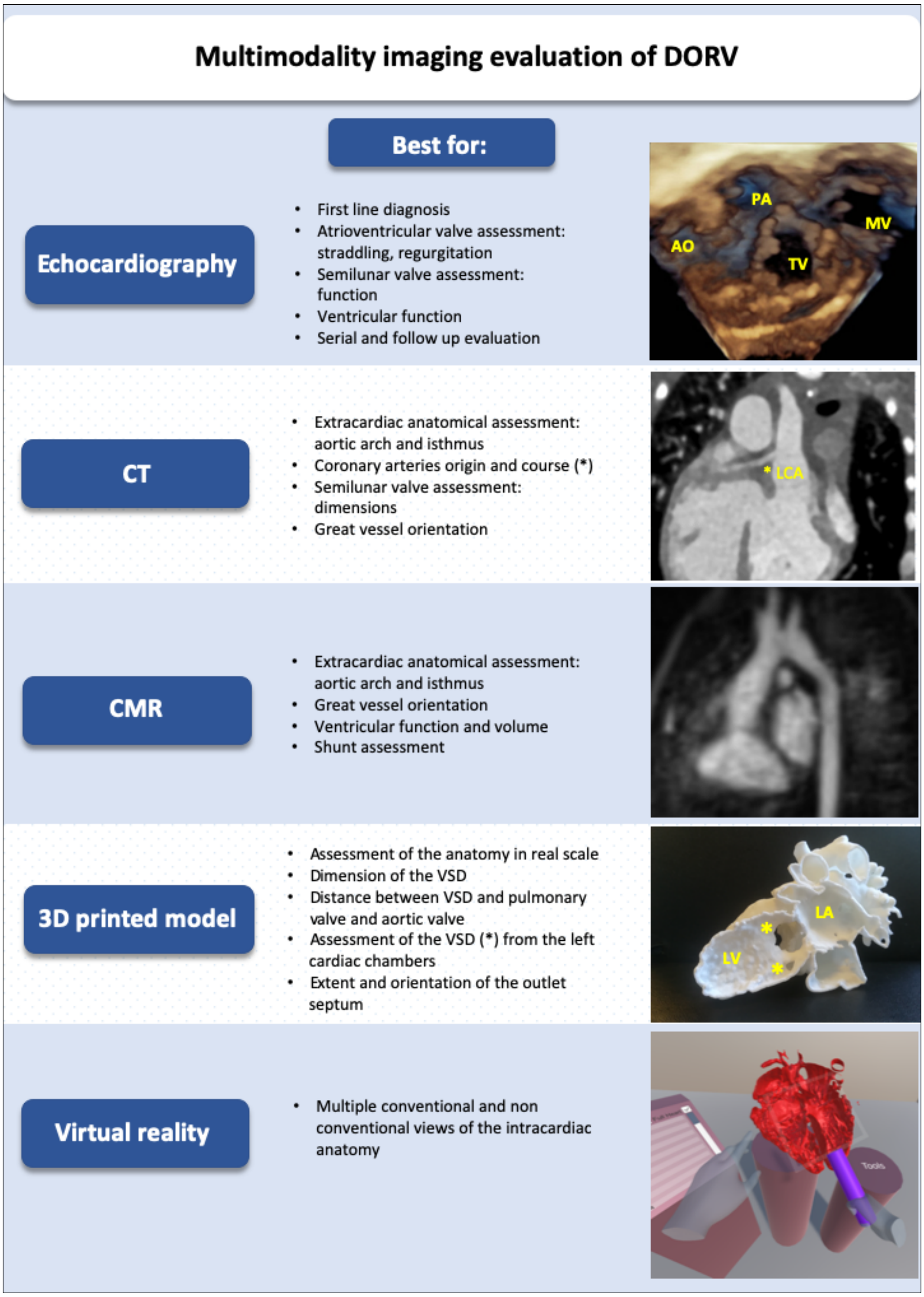

Figure 12 Non-invasive multimodality imaging assessment of double outlet right ventricle (DORV): 3D modelling techniques like 3D printing and virtual reality represent additional non-invasive imaging tools for the assessment of complex congenital cases, such as DORV.

Chapter 4

3D printing and education

Alongside such growing interest in the clinical community and increasing recognition of the possibilities offered by 3D printing technology, methodological advances are rendering image-processing faster and, especially, the technology itself more accessible, with affordable desktop 3D printers able to produce models of very good quality for the applications outlined above. As a result of the growing interest in the CHD community and the increasing availability of the technology, new questions arise, including around standardisation of methodologies, training provision and possible configuration of 3D printing services.

In or study we aimed to evaluate the use of 3D printed models in the context of cardiac morphology courses delivered to health care professionals in particular cardiologists and cardiac surgeons.

Methods

Over a period of one year (from September 2018 to October 2019), participants to cardiac morphology courses held at UCL Institute of Cardiovascular Science were enrolled in the present study.

Course delivery

A one hour teaching session was delivered by an expert in cardiovascular anatomy prior to the use of the 3D models. The session covered the main characteristics of the double outlet right ventricle anatomy spectrum and the main associated cardiac abnormalities. It was supported by the use of videos showing anatomical samples and power point presentation.

3D models assessment

After the teaching sessions, the participants received one 3D printed heart in 1:1 scale representing a complex cardiac anatomy to examine in approximately 15 minutes. The 3 D model was printed in white ABS and available as a whole heart and with two cuts to show the intracardiac anatomy on the RC free wall and LV lateral wall. Aortic and pulmonary valve were not included in the 3D printed models and the participants were made aware of this.

Survey assessment

A short questionnaire including eight questions and a box for free text comments was administered to the participants at the end of the 3D model assessment session.

They were asked to identify as many cardiac abnormalities as possible in the model (up to 9), the location of the VSD (answer options: subaortic/subpulmonary/uncommitted), the type of atrioventricular (answer options: normal: yes/no) and ventricular-arterial connections (answer options: normal: yes/no), to propose a surgical plan (answer options: univentricualr repair/ biventricular repair with or without arterial switch operation).

In addition to these information, the survey asked their professional background and prior experience with 3D printing models, the clarity of the 3d printed models comparing to the traditional anatomical samples (used during the cardiac morphology course in different sessions) using a 10 point Likert scal from 1 extremely less clear than anatomical samples to 10 extremely more clear than anatomical samples.

The first question was scored as x/9. Survey results are presented as counts and proportions.

Following the questionnaire the participants were given the correct answers and a brief clinical case was discussed.

Results

Overall, 64 participants were enrolled in the study and all of them completed the questionnaire provided.

The participants had mixed professional background as shown in Figure 14, with 36% being paediatricians, 24% being cardiologist, 9 % being cardiac surgeons, and 32% with other professional backgrounds including pathologists (n=2), anesthesists (n=4), cardiac sonographers (n=2), radiologist (n=1), medical illustrator student (n=1), clinical genetist (n=1), biologist (n=1), veterinary doctors (n=2), and medical background (n=5), not speicified (n=5).

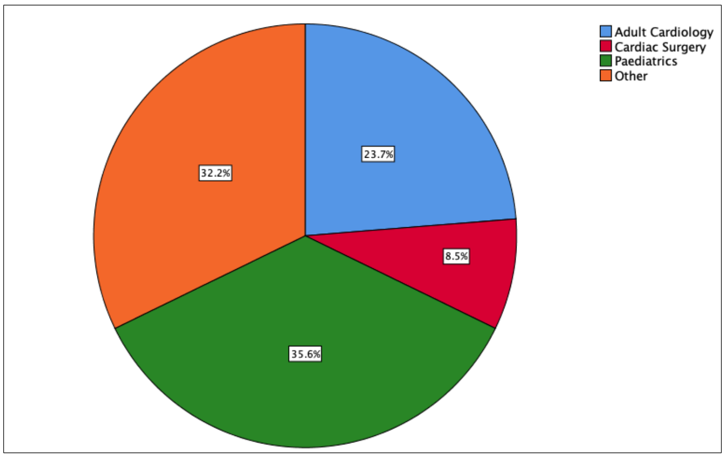

Figure 14 Professional background of the attendees.

The average score in question 1 was 3.8 out of 9 (1-7 out of 9), with no significant differences among the 4 groups. The average score for question 1 of first time user was 3.85 out of 9 with no significant difference compared to the score of non first time users (3.95 out of 9).

Among the participants, 90% were able to identified the main diagnosis (DORV) and the large VSD (85%) and the patent ductus arteriosus (40%). Only 18% of the partiecipants were able to identify the small apical VSD (Figue 15).

Seventy five per cent of the participants correctly identify the normal atrio-ventricular connections and 39% the presence of discordant ventricular arterial connections.

When asked about the surgical plan for the specific anatomy, 19% did not answer the question, among the remnaing partecipants, 60% correctly chose biventricular repair.

On avarage, the particpants found the 3d printed models more clear than the anatomical samples, with an avarange score of 7.2 out of 10 on Likert scale.

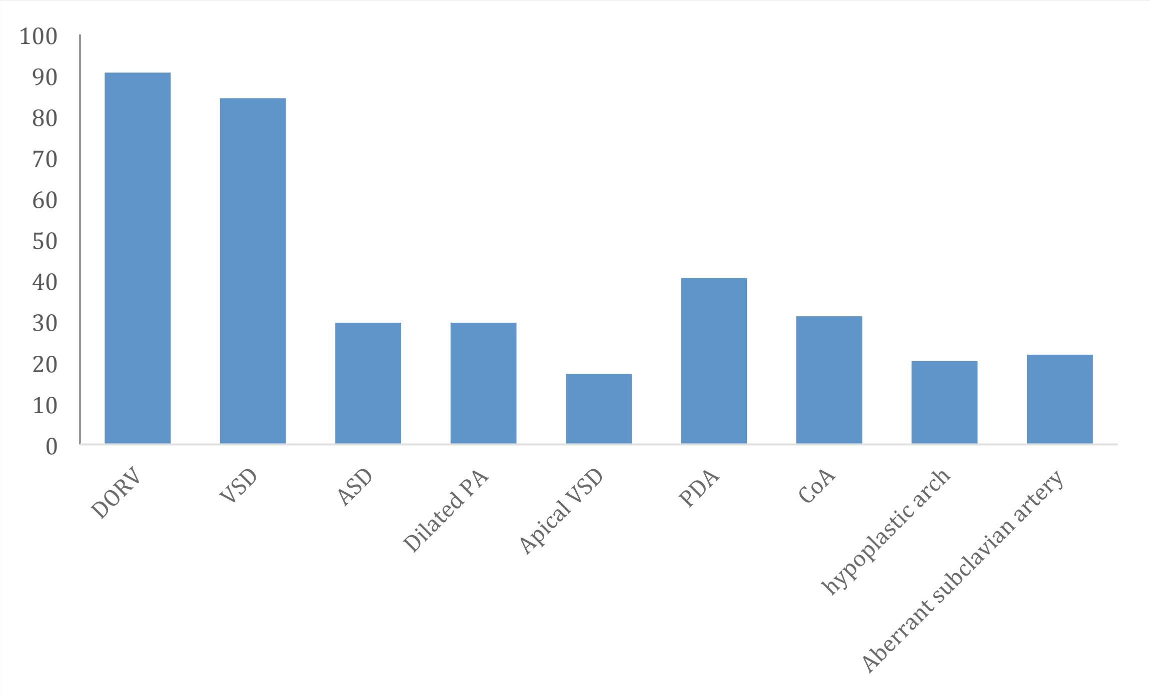

Figure 15 Cardiac defects identified by the attendees (percentage)

Some participants reported that it was difficult to understand what was artefactual and what real on the 3d printed model.

Discussion

In our study we tested the use of three-dimensional models in the context of teaching congenital heart disease to an audience with mixed scientific professional backgrounds.

Overall participants did appreciate the use of the 3d printed models, compared to traditional anatomical samples and this was likely because of the clarity of the 3d printed model and also because of the growing interest and use among clinicians of this 3d visualization modality. The use of 3D printed models allows the simultaneous analysis of the same cardiac anatomy by all attendees; this cannot happen with traditional anatomical samples, which are by definition unique.

The session was focused on a complex cardiac anatomy and the vast majority of the participants were able to identify the main diagnosis, regardless their previous experience with 3d printed models. Comparing to other imaging modalities the 3d printed models appear to be easily accessible without any specific training, whereas crossectional imaging data such as CT and CMR required advance expertise and training to be able to adequate assess the cardiac anatomy and make a diagnosis.

Our survey revealed moreover that some cardiac defects are easier to be identified by attendees and others are less obvious. For instance small apical VSD and ASD were not often identified by participants. This can be explained by the fact the small and thin cardiac structures may not be clearly visible on the 3 d printed models, in particular if mobile like atrioventricular valve and inter atrial septum. This information could be useful in planning cardiac morphology teaching since there appear to be some congenital defects which are more easily studied by attendees on printed models rather than others.

Previous experience with 3d printed models indicate similar results to our, with participants showing growing interest in this visualization modality [(34)] and surgeons being able to practice complex procedures on the models [(35)].

The limitations of this study include a small sample, limiting the generalizability of the findings and the ability to undertake any sub-group analyses. Moreover, it was not possible to perform a direct comparison between 3d models and anatomical samples since each anatomical sample present specific an unique anatomical features , associated defects and size that do not allow 1:1 comparison.

Chapter 7
Conclusions and future perspectives

All imaging modalities (CT, MRI and echocardiography) have developed towards 3D reconstruction techniques, implicitly suggesting the clinical need of going beyond the traditional 2D evaluation of cardiac structures and better appreciating CHD anatomy. Despite its attractiveness, scientific evidence of the usefulness of 3D printing in CHD there is still lacking, and several factors still prevent its becoming widely available or embedded in clinical centres. Firstly, initial costs related to equipment capital investments are high (although smaller, more affordable 3D printers are becoming increasingly refined). Secondly, a relatively long time is required to produce a model from start to finish, with the time of segmentation depending on image quality and printing time on the technology being used, but in certain cases taking >24 hours. And finally, the need for expertise in both cardiovascular imaging and engineering to create a model.
Up to now, 3D models have been proposed for complex cases where surgical planning is controversial, with subjective benefit of the use of the models. It may also be the case that practicing a surgery on a patient-specific model also in simple cases might also be beneficial, leading to reduced surgical time in the theatre. Further prospective studies quantifying the impact of 3D printing technology on peri-operative and long-term outcomes as well as a cost-benefit analysis are urgently needed to prove the real impact of this technology in the management of patients with CHD.

Alongside 3d printing, other advance 3d visualization techniques are rapidly emerging such as virtual reality and augmented reality.

According to our results, VR assessment of patient-specific models for procedural planning can offer superior information helping to select patients suitable for biventricular repair if compared to other 3D visualizations. It complements surgical strategy planning and should be included in the diagnostic work-up of complex DORV, alongside traditional imaging modalities (echocardiography, CT, CMR) to reach the most comprehensive evaluation possible.

Further studies are required to determine the role of VR experiences in other conditions, establish which other clinical settings may benefit from such technologies and to evaluate their additional value in training of junior surgeons.

Furthermore, the use of patients specific 3d models by the cardiologists during clinical consultation also represent a field of interest for this new technology and may improve significantly patient experience and their compliance to therapy and medical appointments as well as improve the understanding of their own cardiac conditions when transitioning from paediatric to adult care. Future studies on this topic may represent and important milestone the way we perform our clinical consultations with adolescent patients.

The patient-specific approach that is very often necessary in the management of patients with CHD may also be applied also in challenging cases of patients with acquired conditions. The use of the patients specific models may facilitate the development of new devices and new surgical techniques, also beyond CHD, whilst the combination of 3D models with tissue engineering could lead to bioprinting patient-specific grafts and heart valves[34, 35].

Tables

Table 1. Patients baseline characteristics

Patient Case	Imaging	Visceral / atrial situs	AV connections	VA connections	Tricuspid valve straddling	Location of interventricular communication	Arrangement of great arteries	Additional findings
1	CT	Solitus	Concordant	DORV	No – some chordal attachment to the septum	Multiple (non committed+apical)	Parallel, aorta anterior and to right	Atrial septal defect, Aortic arch hypoplasia, Aortic coarctation
2	CMR	Solitus	Concordant	DORV	No	Subpulmonary	Parallel, Side by side, aorta to right	Patent foramen ovale, Aortic coarctation, RCA from left facing sinus
3	CT	Solitus	Concordant	DORV	No	Non committed	Parallel, Side by side, aorta to right	-
4	CT	Solitus	Concordant	DORV	No – thickened tricuspid valve leaflets	Non committed	Parallel, Side by side, aorta to right	Large VSD split in two by large muscular bridge
5	CT	Solitus	Concordant	DORV	No	Double committed with inlet extension	Parallel, Side by side, aorta to right	Sub aortic narrowing, anomalous left anterior descending from right coronary artery
6	CT	Solitus	Concordant	DORV	No – tricuspid valve attachment to the VSD margin not crossing the VSD	Non committed	Parallel, Side by side, aorta to right	Large conal branch running on the anterior wall of RV
7	CT	Solitus	Concordant	DORV	Yes – mild TV valve override	Multiple (non committed + small muscular)	Parallel, aorta anterior and to right	-
8	CT	Solitus	Concordant	DORV	No	Non committed	Parallel, Side by side, aorta to right	Subpulmonary and main pulmonary artery stenosis
9	CT	Solitus	Concordant	DORV	No	Non committed	Parallel, aorta anterior and to right	Atrial septal defect, papillary muscle to the anterior tricuspid valve leaflet in the pathway to LVOT
10	CT	Solitus	Concordant	DORV	No - some chordal attachment to the septum	Non committed	Parallel, aorta anterior and to right	Aortic arch hypoplasia, Aortic coarctation

Table 2 Procedural data

Patient Case	Type of Repair	Previous palliation	Age at palliation [months]	Age at repair [months]	Weight at repair [kg]	Cross-clamp time [minutes]	CPB time [minutes]	Discharge LVOT [m/sec]
1	Bi-v+ ASO, intraventricular tunnel and arch repair	Bilateral PAB and PDA stent	0.7	6	5.5	149	244	1.2
2	Intraventricular tunnel	arch repair, PAB	0.1	11	9.4	114	196	1.1
3	Intraventricular tunnel	PAB	1.4	7	6.4	63	94	1.4
4	Intraventricular tunnel	PAB	0.5	5	6.4	114	151	2.2
5	Intraventricular tunnel	PAB	2.0	3	4.7	107	146	1.2
6	ASO and intraventricular tunnel	PAB	2.6	10	8.6	126	178	1.4
7	ASO and intraventricular tunnel	PAB	0.4	13	8.0	182	308	2.5
8	Intraventricular tunnel	n/a	n/a	5	7.5	90	116	1.3
9	Intraventricular tunnel	PAB	3.0	11	7.9	53	96	1.2
10	Intraventricular tunnel	Arch repair, PAB	0.1	10	9.1	34	46	1.1

CPB – Cardio-pulmonary bypass; LVOT - left ventricular outflow tract; Bi-v – Biventricular; ASO – arterial switch operation; PAB – pulmonary artery banding; PDA – patent duct arteriosus.

Table 3 Follow up (FU) data
LVOT – left ventricular outflow tract, RVOT righ ventricular outflow tract, VSD – ventriculat septal defect

Patient case	Time of FU (months)	Reoperations during FU	LVOT V_{max} (m/s)	RVOT V_{max} (m/s)
1	44.6	Closure of apical VSDs	1.5	1.7
2	33.6	No	1.5	1.5
3	40.5	No	3.3	2.1
4	28.6	No	2.2	2.4
5	39.9	No	4.1	1.9
6	43.8	No	1.5	1.5
7	23.0	LVOTO relief (x2)	1.5	1.3
8	10.2	No	1.3	2
9	24.2	No	1.3	1.7
10	16.0	No	1.3	1.5

Table 4 Agreement with original surgical strategy (biventricular repair) according to different 3D tools: : the tick (✔) shows the cases in agreement with the original surgical strategy (where the surgeon correctly identified the possibility of biventricular repair); the cross (x) shows the cases in disagreement with the original surgical strategy (where the surgeon did not correctly identified the possibility of biventricular repair, proposing a univentricular repair instead).

	Surgeon	CT/CMR	3D PDF	3D print	VR
1	*surgA*	✔	✔	x	✔
	surgB	x	x	x	✔
2	*surgA*	✔	✔	✔	✔
	surgB	✔	✔	✔	✔
3	*surgA*	✔	✔	✔	✔
	surgB	✔	✔	✔	✔
4	*surgA*	✔	✔	✔	✔
	surgB	✔	✔	✔	✔
5	*surgA*	✔	✔	✔	✔
	surgB	✔	✔	✔	✔
6	*surgA*	✔	✔	✔	✔
	surgB	✔	Not sure	x	x
7	*surgA*	✔	✔	✔	✔
	surgB	Not sure	Not sure	✔	✔
8	*surgA*	✔	✔	✔	✔
	surgB	✔	✔	✔	✔
9	*surgA*	x	x	✔	✔
	surgB	x	x	✔	✔
10	*surgA*	✔	✔	✔	✔
	surgB	Not sure	Not sure	✔	✔
TOT	-	15/20 (75%)	14/20 (70%)	17/20 (85%)	19/20 (95%)

Table 5 Agreement with original surgical strategy (Arterial Switch Operation: *Yes* vs *No*) according to different 3D tools: the tick (✔) shows the cases when the surgeon correctly identified the need for ASO; the cross (x) shows the cases when the surgeon did not correctly identified the need for ASO.

	ASO		CT/CMR	3D PDF	3D print	VR
1	*Yes*	*surgA*	✔	✔	*Uni-V repair*	✔
		surgB	*Uni-V repair*	*Uni-V repair*	*Uni-V repair*	x
2	*No*	*surgA*	x	x	x	x
		surgB	x	x	x	x
3	*No*	*surgA*	x	x	✔	✔
		surgB	✔	✔	x	✔
4	*No*	*surgA*	✔	x	x	x
		surgB	x	x	✔	x
5	*No*	*surgA*	x	✔	✔	✔
		surgB	x	x	x	x
6	*Yes*	*surgA*	✔	✔	✔	✔
		surgB	✔	✔ *possible*	*Uni-V repair*	*Uni-V repair*
7	*Yes*	*surgA*	✔	✔	✔	✔
		surgB	*Not sure*	*Not sure*	✔	✔
8	*No*	*surgA*	✔	✔	✔	✔
		surgB	✔	✔	✔	✔
9	*No*	*surgA*	*Uni-V repair*	*Uni-V repair*	✔	✔
		surgB	*Uni-V repair*	*Uni-V repair*	*Not sure*	✔
10	*No*	*surgA*	✔	✔	✔	x
		surgB	*Not sure*	*Not sure*	✔	✔
TOT		-	9/20 (45%)	9/20 (45%)	11/20 (55%)	12/20 (60%)

ASO, Arterial switch operation; Uni-V, univentricular.

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