**Department of Medical Radiation Science**

# Clinical Application of Three-dimensional Printing and Extended Reality in Congenital Heart Disease

**Ivan Wen Wen Lau**

**0000-0001-5925-1937**

**This thesis is presented for the Degree of**
**Doctor of Philosophy**
**of**
**Curtin University**

**February 2023**

## Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated 2018. The proposed research study received human research ethics approval from the Curtin University Human Research Ethics Committee (EC00262), Approval Number HRE2017-0138.

Date: February 2023

Dedicated to my husband, Dr Jonathan Ng, who has given me support,
encouragement, and motivation throughout my dissertation journey.

## Abstract

Conventional visualisation techniques of complex congenital heart disease (CHD), which include three-dimensional (3D) reconstructions of medical imaging datasets, are unable to provide comprehensive visualisation of the anomalous cardiac anatomy as the medical datasets can only be viewed from a flat, two-dimensional (2D) screen. This has posed challenges to doctors when attempting to assess the full picture of their patients' heart condition in extremely complex cases. The main theme of this project was to investigate the medical application of two emerging technologies in the domain of CHD: 3D printing and extended reality visualisation, which have garnered increasing interest in medicine to improve visualisation of human anatomy. In this study, two types of extended reality were explored: virtual reality (VR) and mixed reality (MR). This research project was conducted in four stages.

Stage 1 focused on the relative suitability of low-cost and high-cost 3D printing materials. The cost of 3D printed heart model (3DPHM) is commonly reported as the main factor that impedes the routine application of this technology in clinical practice. Therefore, during stage 1, a comparison was performed between low-cost and high-cost 3DPHM in terms of their dimensional accuracy, as well as their clinical value based on three cardiac specialists' opinion. In this study, the low-cost 3DPHM was printed in thermoplastic polyurethane (TPU) 95A (AUD $50), whereas the high-cost 3DPHM was printed in Tango Plus (AUD $300). Quantitative assessment of dimensional accuracy of the cardiac anatomy and pathology was compared between the 3DPHM and the original cardiac computed tomography (CT) images with excellent correlation ($r = 0.99$), suggesting that both the low-cost and high-cost 3DPHM can be generated at high accuracy. Qualitative evaluation showed no difference between the two types of 3DPHM in the clinical application.

In stage 2, the role of 3DPHM in improving immediate knowledge gain and long-term knowledge retention about CHD was investigated. In this prospective cohort study, fifty-three 2nd and 3rd year medical students were assigned into two groups to compare their immediate knowledge acquisition and knowledge retention after an education session on anatomy and pathophysiology of CHD. During the 1.5 hour-long education session, both the control ($n = 25$) and study groups ($n = 28$) had access to identical teaching materials: digital 3D heart models, 2D diagrams, and medical images, except for 3DPHM which were only used in the study group. The immediate knowledge gain was assessed via an online quiz, whereas the long-term knowledge retention was assessed using another quiz in 6-weeks' time post-intervention. A survey was also conducted to evaluate the participants' learning experience. The result showed no significant difference in the immediate knowledge acquisition and long-term knowledge retention between the groups (U = 272, p = 0.16 and r = –0.143, p = 0.15 respectively). Majority of the students (96% in control group and 85% in 3DPHM group) responded that the 3DPHM would have/had improved their learning experience.

Stage 3 was a cross-sectional study aimed at comparing the clinical value of VR and 3DPHM. Thirty-five medical practitioners were recruited to subjectively evaluate VR visualisation of four selected CHD cases in comparison with the corresponding 3DPHM. Twenty-nine completed questionnaires were included in the analysis. The results showed both VR and 3DPHM were comparable in terms of the degree of realism. VR was perceived as more useful in medical education and preoperative planning compared to 3D printed heart models, although there was no significant difference in the ratings (p = 0.54 and 0.35, respectively). Twenty-one participants (72%) indicated both the VR and 3DPHM provided additional benefits compared to the conventional visualisation technique.

During stage 4, the clinical value of both MR and 3D printing were compared concurrently with the medical imaging datasets in terms of their ability in assisting diagnosis, medical education, pre-operative planning, and intraoperative guidance of the CHD surgeries. Thirty-four cardiac specialists and physicians were recruited for evaluations of the MR models and 3DPHM. The analysis of the questionnaires showed that the MR models were ranked as the best modality amongst the three, and were significantly better than DICOM images in demonstrating complex CHD lesions (MD = 0.76, p = 0.01), in enhancing depth perception (MD = 1.09, p < 0.001), in portraying spatial relationship between cardiac structures (MD = 1.15, p < 0.001), as a learning tool of the pathology (MD = 0.91, p < 0.001), and in facilitating pre-operative planning (MD = 0.87, p = 0.02). The 3DPHM were ranked as the best modality and significantly better than DICOM images in facilitating communication with patients (MD = 0.99, p < 0.001).

In summary, both 3D printing and extended reality have their own strengths in different aspects and can be used as complementary tools to improve the current visualisation technique and management of CHD. In particular, MR was highly regarded by the cardiac specialists in demonstrating the cardiac anatomy, whereas the 3DPHM have a valuable role in facilitating communication. The result of this project also demonstrated that the 3DPHM can be replicated at high accuracy, and that the cost of the 3DPHM does not affect their clinical utility. This implies that if there is no specific requirement on the 3D printing material, a cheaper material can be opted to provide similar performance on the clinical application. 3DPHM did not appear to improve the students' immediate knowledge gain and long-term knowledge retention. However, it was shown that 3DPHM can enhance the students' learning experience.

## Acknowledgement

Throughout this doctorate degree, there are quite a few who I would like to express my sincere gratitude to. First of all, I would like to thank God for the gracious blessings He has bestowed upon me. I would also like to express my deepest appreciation to my supervisor, John Curtin Distinguished Prof. Zhonghua Sun for all the guidance and support he gave throughout these years. The professional research skills and knowledge that he has taught me has laid a firm foundation for my path as an early career researcher. I would not have made this far without his supervision. I would also like to thank Dr. Andrew Squelch as my co-supervisor for his unwavering support and insightful suggestions for my study.

Furthermore, I would like to thank Mr Wesley Lamont, Mrs Carley Tillett, Mr Bill Lau, Prof. Brad Zhang, and Mr Gil Stevenson for providing software and statistical support. I would also like to take this opportunity to thank Dr. Abdul Ihdayhid, Dr. Ashu Gupta, and Dr. Mauro Vaccarezza for assisting in participant recruitment. My sincere thanks also go to Prof. Chai Hong Yeong, Dr. Zack Wong, and Mr Werner Ducke for their assistance in printing 3D models. I also owe sincere gratitude to National Heart Foundation of Australia and Royal Perth Hospital Imaging Grant for the financial support of my PhD study. This research is also supported by an Australian Government Research Training Program (RTP) Scholarship.

To my church friends and work colleagues, I would like to thank you for your friendship and companion. To my family members, I cannot express enough thanks for your everlasting and unconditional love and encouragement all these years. Lastly, and above all, I would like to thank my beloved husband, Dr. Jonathan Ng, who has been a source of my motivation and inspiration for completing this thesis.

## Copyright Statement

I have obtained permission from the copyright owners to use any third-party copyright material reproduced in the thesis, or to use any of my own published work in which the copyright is held by another party.

## List of Publications included as part of this thesis

1. **Lau I**, Sun Z. Dimensional Accuracy and Clinical Value of 3D Printed Models in Congenital Heart Disease: Systematic Review and Meta-Analysis. *J Clin Med*. 2019; 8(9):1483. doi:10.3390/jcm8091483

2. **Lau I**, Wong YH, Yeong CH, Yang FAA, Nor Ashikin MS, Shahrul AH, et al. Quantitative and qualitative comparison of low- and high-cost 3D-printed heart models. *Quant Imaging Med Surg*. 2019; 9(1):107–114. doi:10.21037/qims.2019.01.02

3. **Lau I**, Z. Sun. The role of 3D printed heart models in immediate and long-term knowledge acquisition in medical education. *Rev Cardiovasc Med.* 2022; 23(1):22. doi:10.31083/j.rcm2301022

4. **Lau I**, Gupta A, Sun Z. Clinical Value of Virtual Reality versus 3D Printing in Congenital Heart Disease. *Biomolecules.* 2021; 11(6):884. doi:10.3390/biom11060884

5. **Lau I**, Gupta A, Ihdayhid A, Sun Z. Clinical Applications of Mixed Reality and 3D Printing in Congenital Heart Disease. *Biomolecules.* 2022; 12(11):1548. doi:10.3390/biom12111548

## List of additional publications relevant to the thesis but not forming part of it

1. **Lau I**, Squelch A, Sun Z. 3D printed models of congenital heart disease: How accurate and how useful are they? *Australas Med J*. 2019; 12(11):312-314. doi:10.35841/1836-1935.12.11.312-314

2. Sun Z, **Lau I**, Wong YH, Yeong CH. Personalized Three-Dimensional Printed Models in Congenital Heart Disease. *J Clin Med*. 2019; 8(4):522. doi: 10.3390/jcm8040522

These papers are attached to the thesis in the Appendices A and B respectively.

## List of conferences

1. **Lau I,** Liu D, Xu L, Fan Z, Sun Z. '*Clinical value of patient-specific three-dimensional printing of congenital heart disease: Quantitative and qualitative assessments*' at the 18th Asia-Oceania Congress on Medical Physics - South-East Asian Congress of Medical Physics, Biophysics, and Biomedical Engineering (AOCMP-SEACOMP), Kuala Lumpur, Malaysia (11 – 14th November 2018). Invited speaker presentation

2. **Lau I,** Gupta A, Ihdayhid A, Sun Z. '*Clinical Applications of Mixed Reality and 3D Printing in Congenital Heart Disease*' at the 2022 Curtin Medical School Research Symposium, Perth, Australia (7 – 8th July 2022). Oral presentation

**Content**

**Chapter 1: Introduction and literature review**

**Chapter 2: Dimensional accuracy and clinical value of 3D printed models in congenital heart disease: A systematic review and meta-analysis**

**Chapter 3: Quantitative and qualitative comparison of low- and high-cost 3D printed heart models**

**Chapter 7: Conclusions and future directions**

**Appendices**

# CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

## 1.1 Congenital heart disease

Congenital heart disease (CHD), or congenital heart defects, is one of the most common congenital anomalies among the newborns. In year 2010-2017, CHD affects up to 9 per 1000 newborns globally.[1] It is defined as structural malformations in the heart as well as surrounding great vessels which presented at birth, affecting the normal functioning of the heart.[1-3] Generally, CHD can be classified into cyanotic and acyanotic heart defects.[1,2,4,5] Cyanotic heart defects, as its name suggests, are caused by decreased oxygen saturation in the systemic arterial blood, and therefore the infants or babies will appear to have bluish skin.[2,6] These defects will disrupt the blood flow in the heart, causing a right-to-left blood shunting which allow deoxygenated blood to flow into the aorta.[2,3,6] If the cyanosis is severe, it is considered medical emergency and most often will require surgery immediately.[5] In contrary, acyanotic heart defects do not interfere with the amount of oxygen that reaches the body's tissues.[2] It can be further classified into obstructive lesions and left-to-right shunt lesions.[1,5] The obstructive lesions refer to stenosis or narrowing of the great vessels or valves, whereas the left-to-right shunt lesions increase the pulmonary arterial blood flow.[2,5]

**Figure 1.1:** Some examples of different types of congenital heart disease.

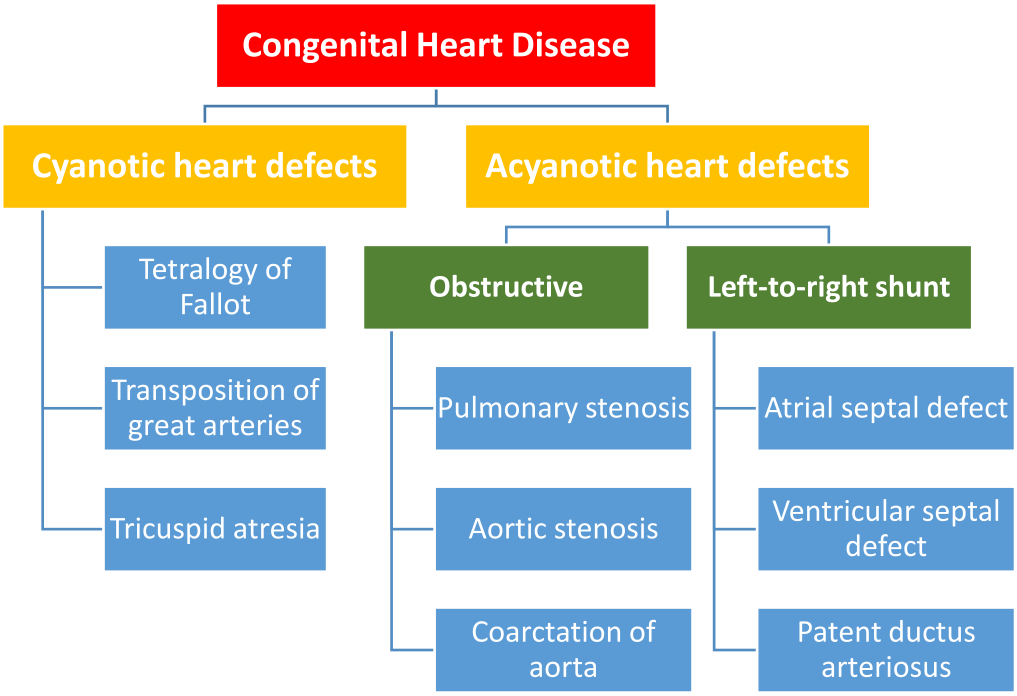


Figure 1.1 provides a few examples of different subtypes of CHD, however there are many other forms of CHD which are not listed. As the condition varies from individual to individual, individualised patient management is imperative for patients with CHD.[7] Some patients can

even suffer from multiple types of CHD, causing the management of these patients even more challenging than the already complex heart lesions.

There are many documented methods to assess complexity or severity of CHD. One of them is the Aristotle Basic Complexity Level (ABCL), which is derived to improve the quality of CHD surgeries by taking into account the mortality, morbidity, and technical difficulties of the surgical procedures.[8] The complexity of CHD is divided into 4 levels, with the ABCL increases as the complexity increases. A few examples of CHD with different ABCL will be discussed in the following in terms of their anatomy and pathophysiology.

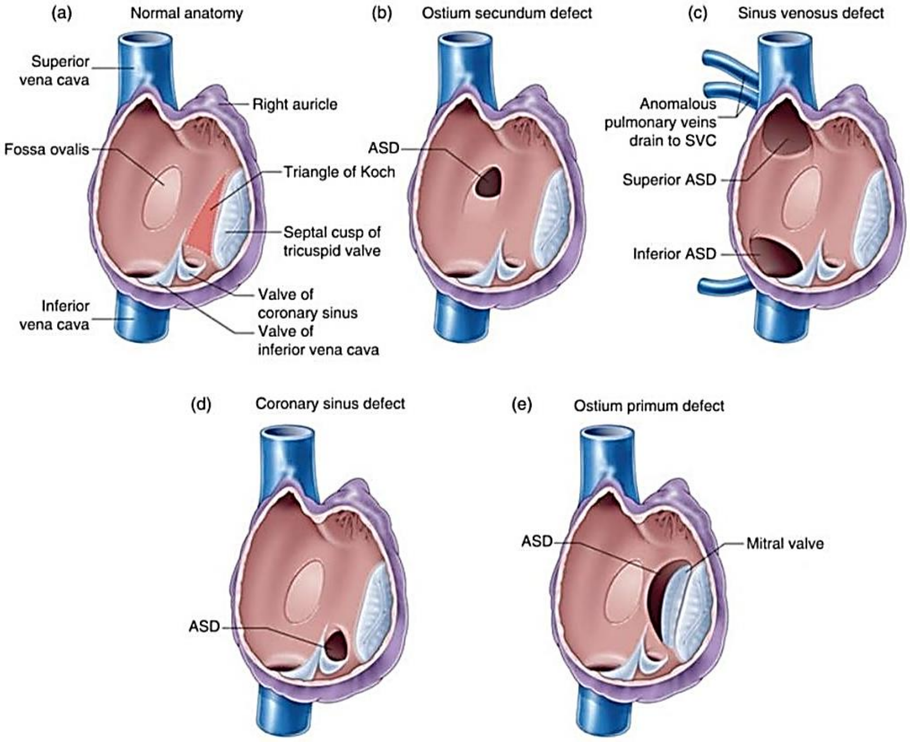
### 1.1.1 Atrial septal defect (ABCL = 1)

Atrial septal defect (ASD) is characterized by the presence of an opening in the septal wall separating the left and right atrium due to the failure of formation of the septal tissue, which permits the blood to mix around in the atria.[9,10] As the blood pressure in right atrium is lower than that of the left, the oxygenated blood will flow from the left atrium to the right atrium (left-to-right shunt).[3,10] This has caused extra workload for the right ventricle as it is now required to pump some of the oxygenated blood during systolic phase. Eventually this can cause hypertrophy of the right atrium and right ventricle as well as dilation of the pulmonary arteries.[9,10] The magnitude of the shunt is directly affected by the size of ASD, which will also influence the patients' clinical presentation and symptoms.

Isolated ASD is asymptomatic, hence it can go unnoticed for years. Patients can develop symptoms at the earliest of 3-4 years of age, and the latest during adulthood. If it is diagnosed in the neonatal period, most often it is incidental finding for other investigations.[4,10-12] ASD of size <5mm can close spontaneously, or diminish to an insignificant size in early childhood in most cases, whereas ASD >8mm usually requires interventional or surgical management.[4]

Generally, ASD can be classified into 4 different types according to their location: ostium secundum; ostium primum; sinus venosus; and coronary sinus (Figure 1.2).[2,3,9,10] Among these, only ostium secundum and ostium primum are true defects that occur in the interatrial septum.[9] Ostium secundum is the most common type of ASD.[3,12] It occurs when the septum secundum fails to overlap during its development and results in a defect in the septum secundum, usually located at the centre of interatrial septum.[3,13] Ostium primum occurs when the septum primum fails to attach to endocardial cushion and the embryonic ostium primum fails to close properly.[10,13] It can also be considered as atrio-ventricular septal defect as it is located at the inferior portion of the interatrial septum, close to the atrioventricular valves.[3,4,9,10,12] There are two common locations for sinus venosus ASD to occur: (1) posterior and superior portion of interatrial septum near the entry of superior vena cava (SVC) (more common), or (2) posterior and inferior portion of interatrial septum near the entry of inferior vena cava (IVC) (less common).[3,4,10] It is believed that this defect is a result of incomplete development of the wall that separates right pulmonary veins from SVC or IVC and right atrium.[9] Coronary sinus is the least common ASD. It is usually located at the roof of coronary sinus as a result of deficiency in the partition that separates coronary sinus from left atrium.[3,4,10,12] This allows a direct communication between left and right atrium.[9,11] It is also often associated with persistent left SVC.[9-11]

**Figure 1.2:** Normal anatomy (a) and different types of atrial septal defect (ASD) (b – e) looking from right atrium.



ASD, atrial septal defect; SVC, superior vena cava. Reprinted with permission from Hutchinson et al.[12]

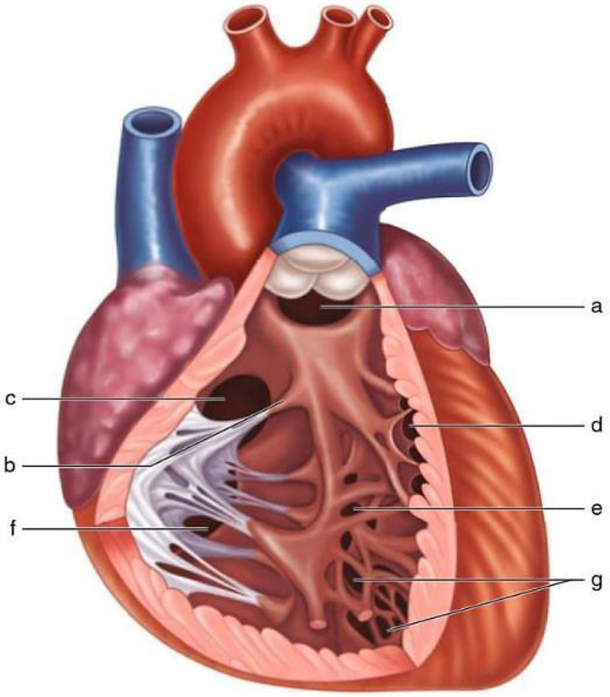
### 1.1.2 Ventricular septal defect (ABCL = 2)

Ventricular septal defect (VSD) is the most common type of CHD as it is often part of the more complex lesions, such as double outlet right ventricle (DORV) and Tetralogy of Fallot (TOF). Similar to ASD, VSD is also a deficiency in the septal tissues, however it is in the septal wall separating left and right ventricle (i.e. interventricular septum). As the left ventricle has higher blood pressure than the right ventricle, the blood will be shunted across from left-to-right.[3,5,12,14,15]

Depending on where the defect is located along the interventricular septum, VSD can generally be classified into four types: membranous (or perimembranous), muscular, outlet (or supracristal), and inlet (Figure 1.3).[14] Membranous VSD is the most common type of VSD. It is located at the membranous septum which is directly below the aortic valve, and at the superior part of the interventricular septum.[5,14-16] Muscular VSD occurs at the muscular septum, which is the apical part of the interventricular septum.[5,14,16] Occasionally, the patient can have multiple muscular VSDs, and this is described as 'swiss-cheese' VSD due to its appearance.[3,5] Outlet VSD, as its name suggests, is located in the right ventricular outflow tract (RVOT) at the septum beneath the aortic and pulmonary valves.[14-16] Inlet VSD is located at the posterior part of the interventricular septum below the tricuspid and mitral valves.

The clinical presentation of individuals with VSD is largely dependent on the size of the VSD, as it decides the magnitude of the left-to-right shunt.[3,5,16] For individuals with small isolated VSD, they can be asymptomatic, hence VSD are usually picked up during routine clinical examinations as they will create loud cardiac murmur unlike ASD.[5] As the shunting is small in small isolated VSD, the patients often do not have any serious complications. Moreover, it is very common for small VSD to close on its own without any intervention or treatment, especially for muscular VSD.[3,5,14,15] However, if larger VSD is left untreated, right ventricular hypertrophy can develop as the right ventricle is working harder to pump the blood out of the heart. Eventually, this can lead to pulmonary hypertension and congestive heart failure. If the pulmonary hypertension is too severe and the pulmonary resistance becomes higher than systemic resistance, the direction of shunt will be reversed, and the patient develops Eisenmenger syndrome, in which the blood is shunted from right-to-left.[3,15] This is when the patient becomes cyanotic.

**Figure 1.3:** Diagram showing the location of different types of ventricular septal defect (VSD).



(a) outlet or supracristal VSD, (b) septal papillary muscle of the tricuspid valve, (c) perimembranous VSD, (d) right ventricular muscle bundle, (e) muscular VSD, (f) inlet VSD, (g) muscular VSDs. Reprinted with permission from Driscoll.[16]

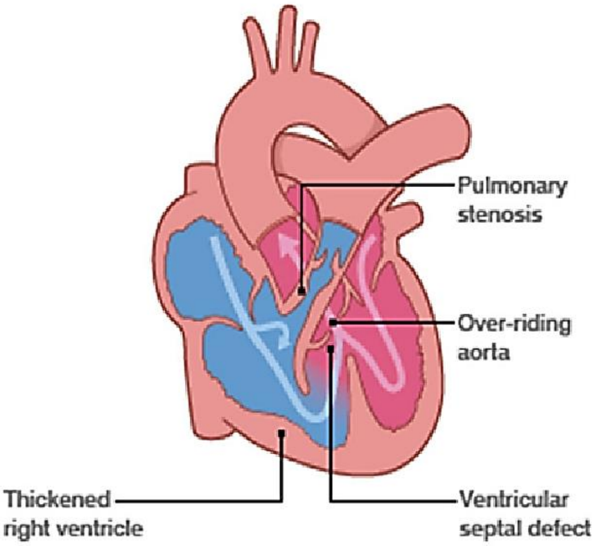
### 1.1.3 Tetralogy of Fallot (ABCL = 3)

TOF is the most common cyanotic heart defect among cyanotic patients beyond 1 year old.[15,17-19] It is a complex CHD which constitutes of 4 different types of heart lesions: VSD, pulmonary stenosis, overriding aorta, and right ventricular hypertrophy (Figure 1.4).[15,16,18,19] Morphologically, it is the anterior displacement and deficiency of the infundibular septum, which results in formation of perimembranous VSD, overriding aorta over the ventricles, and narrowing of the RVOT. Due to the RVOT obstruction, the pressure in the right ventricle becomes higher which results in hypertrophy of the right ventricular wall. This has forced the deoxygenated blood to flow into the aorta that overrides the ventricles though the VSD.[15,19,20]

TOF is most often cyanotic. However, in some mild cases, infants may be born acyanotic, the so-called “pink tetralogy”, and the condition progressively becomes cyanotic between 2 to 6 months of age due to the worsening of RVOT obstruction.[5,16] The severity of cyanosis is dependent on the degree of pulmonary stenosis, as it ultimately controls the amount of blood that enters pulmonary circulation. In severe TOF cases, the aorta are usually dilated as greater blood volume is entering the systemic circulation, and therefore aortic overriding are more conspicuous in these cases.[5,15,21]

Patients with TOF can sometimes experience marked and rapid reduction in pulmonary blood flow, developing symptoms of what is called 'tet spell' or 'hypoxic spell'. It is characterised by rapid and deep respiration, as well as increased cyanosis in the patients.[5,18] Tet spell can occur anytime during the day, however usually after sleep, crying, feeding, and defecation for infants, and during exercise for children.[5,18] This is considered a medical emergency and require immediate management, as it may cause serious complications to central nervous system and even death.[5,18]

**Figure 1.4:** Diagram showing Tetralogy of Fallot (TOF).



White arrows indicate the direction of blood flow through the ventricular septal defect (VSD). Adapted from Englert et al.[19]

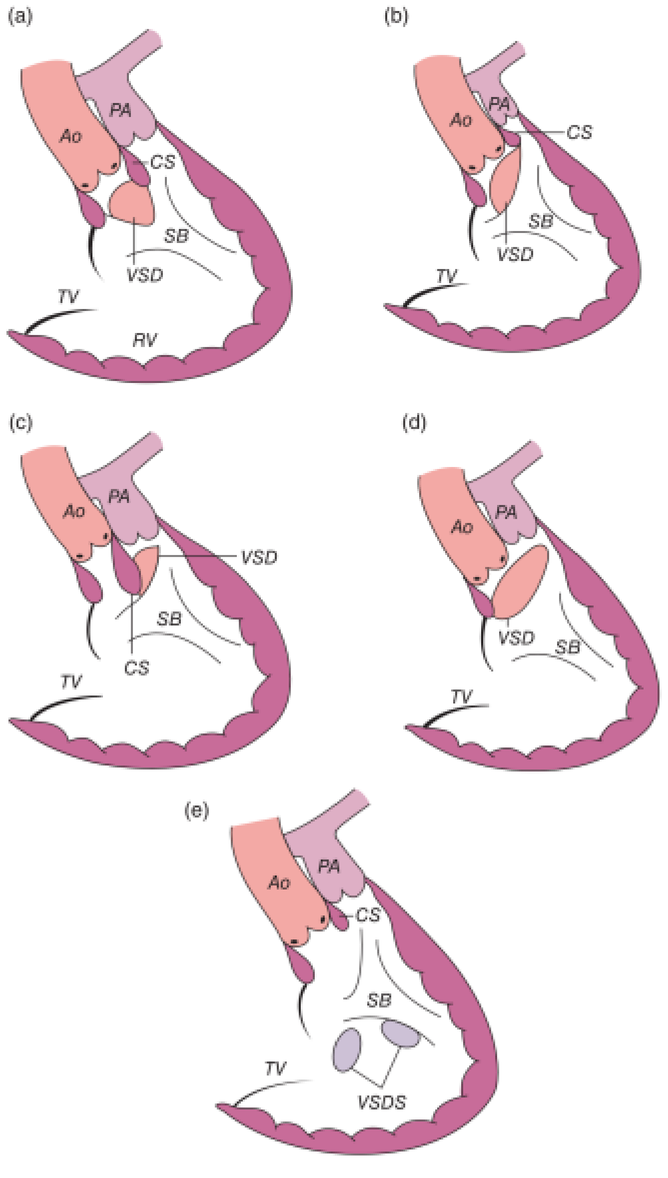
### 1.1.4 Double outlet right ventricle (ABCL = 4)

DORV, as its name suggests, is a condition when both of the great arteries arise completely or predominantly from the right ventricle.[4,9] It is associated with a VSD most of the time, but occasionally can also be associated with other types of anomalies.[3,9,17] Morphologically, it is the anterior transposition of the aorta.[21] Hence, in most of the DORV cases, the great arteries have a side-by-side orientation, with the aorta on the right side of the pulmonary artery.[9,18] This has made the VSD, if present, as the only outlet of left ventricle. In DORV, there is no fibrous continuity between the mitral valve and the aortic valve. Outlet septum, also known as conal septum, is exclusively a right ventricular structure which separates the aorta and the pulmonary trunk.[18]

Generally, DORV can be classified into 4 types based on the positon of VSD in relation to the great arteries: subaortic, subpulmonary, doubly committed, and remote (Figure 1.5).[3,18] DORV with subaortic VSD is the most common form of DORV.[18] The VSD is located closer to the aortic valve than the pulmonary valve and to the right of the outlet septum. This often causes anterior and leftward deviation of the outlet septum, resulting in obstruction of pulmonary trunk.[17,18] In subpulmonary VSD, the VSD is situated nearer to the pulmonary valve than the aortic valve and to the left of the outlet septum. This often causes posterior and rightward deviation of the outlet septum, resulting in subaortic stenosis. This type of DORV is also known as Taussig-Bing anomaly.[17,18] Doubly committed VSD is located close to both pulmonary and aortic valves and above the crista supraventricularis. Remote VSD is situated far apart from the pulmonary and aortic valves.[18]

During the evaluation of DORV, these following components are important in determining the pathophysiology, and thus altering the clinical managements: (a) the relationship of the VSD to the great arteries; (b) the presence or absence of RVOT or LVOT obstruction; (c) size of the VSD; (d) pulmonary vascular resistance; and (e) associated cardiovascular anomalies.[4,9,18] For example, the clinical manifestation of DORV with subaortic VSD and absence of RVOT obstruction (i.e. pulmonary stenosis) is no different than that of simple VSD. If RVOT obstruction is present, the pathophysiology of the DORV is similar to TOF.[4,9,17] This explains why DORV with RVOT obstruction is often confused with TOF, especially when the mitral-aortic fibrous continuity is not known. Hence, the surgeons prefer to use the 50% rule to differentiate DORV from TOF, that is, the aortic annulus has to overly the right ventricle for at least 50% for it to be considered DORV.[18]

**Figure 1.5:** Diagram showing different types of double outlet right ventricle (DORV)



(a) DORV with subaortic ventricular septal defect (VSD) without deviation of the conal septum (without pulmonary stenosis, (b) DORV with subaortic VSD and pulmonary stenosis, (c) DORV with subpulmonary VSD, (d) DORV with a doubly committed VSD and absent conal septum, (e) DORV with a remote VSD. Ao, aorta; CS, conal septum; PA, pulmonary artery; RV, right ventricle; SB, septal band; TV, tricuspid valve; VSD, ventricular septal defect. Reprinted with permission from Nasr et al.[9]

## 1.2 Diagnostic assessment techniques for CHD

Patients with CHD now are having much better prognosis and survival rates, thanks to the major advancements in the diagnosis and treatment of patients with CHD.[22,23] There are growing populations of patients with complex CHD who are reaching into adulthood.[23] Radiology plays a pivotal role in the diagnostic assessment for CHD, especially in assessing the anatomical and functional cardiac anomalies associated with CHD. There are a wide array of imaging modalities that can be used for the diagnostic assessment of CHD, this includes cardiac catheterization, echocardiography, cardiac MRI (CMR), and cardiac computed tomography angiography (CCTA). These tools are not only used to diagnose CHD, but also serve as fundamental tools for assessing their severity, intervention decision-making as well as routine follow-up.[24,25] The choice of diagnostic pathways of CHD and the frequency of imaging are based on the patients' age, the type of CHD, and the main intent of the assessment.[23,25] Most of the time, multiple imaging modalities are needed to fully address the clinical questions, especially for complex CHD.[26]

### 1.2.1 Echocardiography

Echocardiography is currently the first imaging modality of choice for initial assessment and routine check-up of both paediatric and adult patients with CHD.[22-26] With the development of new echocardiographic techniques, cardiac ultrasound is now able to offer much better and accurate evaluation of CHD anatomy and physiology.[22,23] One of the main advantages of cardiac ultrasound is that it is non-invasive and not associated with ionizing radiation, therefore it does not pose any procedure-related complications to the patients.[24,25] It also offers high temporal resolution and real-time imaging. It is also particularly superior in visualizing intra-cardiac anatomy. Furthermore, two-dimensional (2D) echocardiography with Doppler technique is capable for hemodynamic assessment and velocity measurement.[24] Three-dimensional (3D) echocardiography is a relatively new technique which is superior in assessing valvar structure and function, as well as in assessing the ventricular volumes.[24,25]

Nevertheless, there remains some limitations in echocardiography. It has small field of view, suboptimal penetration, and often limited by acoustic windows. While this does not necessarily affect imaging of paediatric patients as they usually have adequate acoustic windows, imaging of adults becomes a challenge due to larger chest walls and presence of post-operative scar tissues.[23,24,26] The anatomy that is more distal, or directly behind air and bone can also present poorly on the images. It is also incapable to delineate extra-cardiac structures distinctly.[22] Furthermore, cardiac ultrasound is highly operator-dependent, hence its accuracy depends on the operator's skills.[22,24] Due to these limitations, echocardiography is often coupled with other imaging modalities for complex CHD and post-surgical follow-up.[24]

### 1.2.2 Cardiac magnetic resonance imaging

CMR has gained increasing importance in non-invasive imaging of CHD over the past decades.[22,24] Unlike ultrasound, MRI has a large field of view, ability to reconstruct to infinite imaging planes for analysis, and it is non-operator-dependent.[22] Further, it does not use any ionizing radiation. Hence, CMR is suitable for imaging of patients from all age range with different body sizes, as long as they are not contraindicated.[23,26] CMR is particularly useful in demonstrating extra-cardiac structures with good temporal resolution. Moreover, contrast enhanced scans enable evaluation of the great arteries and blood vessels, which is critical in evaluating anomalous connection and obstruction.[24] It can also provide functional assessment of the heart, including blood flow assessment, analysis of aortic and pulmonary regurgitation, and evaluation of shunts.[23,24] Further, CMR with the steady-state free precession sequence is considered as the gold standard for left and right ventricular measurements, however it requires consistency in acquisition and measuring methods.[24-26]

CMR can pose some technical challenges to certain group of patients. This includes paediatric patients who are unable to remain still for long period of time, patients who are unable to follow breathing instructions, and patients who are claustrophobic. Hence, these patients might require sedation or general anaesthesia prior to the MRI scan, however this will need to be balanced against the risk imposed on the patients with prolonged sedation.[22-24] Furthermore, CMR is unsuitable for patients who have metallic implantable devices that are contraindicated for the scan. CMR is also susceptible to have image artefacts from metallic implants and irregular heartbeats which can degrade the image diagnostic quality.[24-26]

### 1.2.3 Cardiac Computed Tomography Angiography

CCTA is another non-invasive imaging which serves as invaluable tool in providing complementary and additional information of the heart anomalies.[23,27] With the technical advancement of multi-detector CT (MDCT), CCTA is now increasingly used in the diagnostic assessment of CHD. It is eminent in its superior spatial resolution, rapid acquisition, and the ability to reconstruct complex anatomy in 3D.[22,24-26] By having more rows of detectors along with the table motion to create spiralling effect, MDCT allows the scan of the cardiac anatomy to be acquired in a time shorter than a cardiac cycle, hence most patients including paediatrics are able to tolerate with the scan.[22,25] When it is used with ECG gating, the temporal resolution of the scan can be improved with less motion artefacts from the cardiac motion, enabling visualization of smaller anatomical structures such as coronary arteries and pulmonary veins.[25,27] ECG-gated CCTA can also be used to measure ventricular volumes and function, however its temporal resolution is lower than that of echocardiography and CMR.[23,26,27]

One shortcoming of CCTA is the inability to delineate tiny and fast-moving structures like heart valve leaflets.[28,29,30] Another downside of CCTA is that it requires the use of iodinated contrast agent to visualise the vessels, hence patients with renal failure are contraindicated.[25] It is also associated with ionizing radiation.[24-27] Even though the radiation dose from a single CCTA study might be low, cumulative radiation dose from multiple scans over a period of time can increase the risk of radiation-induced cancer.[25,26] Therefore, CT is often not the modality of choice for follow-up imaging for patients with CHD.[25] Regardless, it is definitely a useful alternative when the patients are contraindicated for MRI.[23-25] Other drawbacks of CCTA include its lack of ability in assessing valve regurgitation, suboptimal myocardial tissue characterization, and does not provide information on flow velocity.[25,27]

### 1.2.4 Cardiac Catheterization

Cardiac catheterization is an invasive study which used to be the primary imaging modality to assess the anatomy and physiology of CHD.[24] Now, with the development of non-invasive imaging modalities, cardiac catheterization is rarely used for CHD diagnosis, and it is mainly used for detailed hemodynamic assessment and percutaneous interventions.[23-26] For diagnostic assessment in CHD, this invasive option should only be chosen if all the other non-invasive options are inconclusive and additional information is required for intervention decision-making.[24]

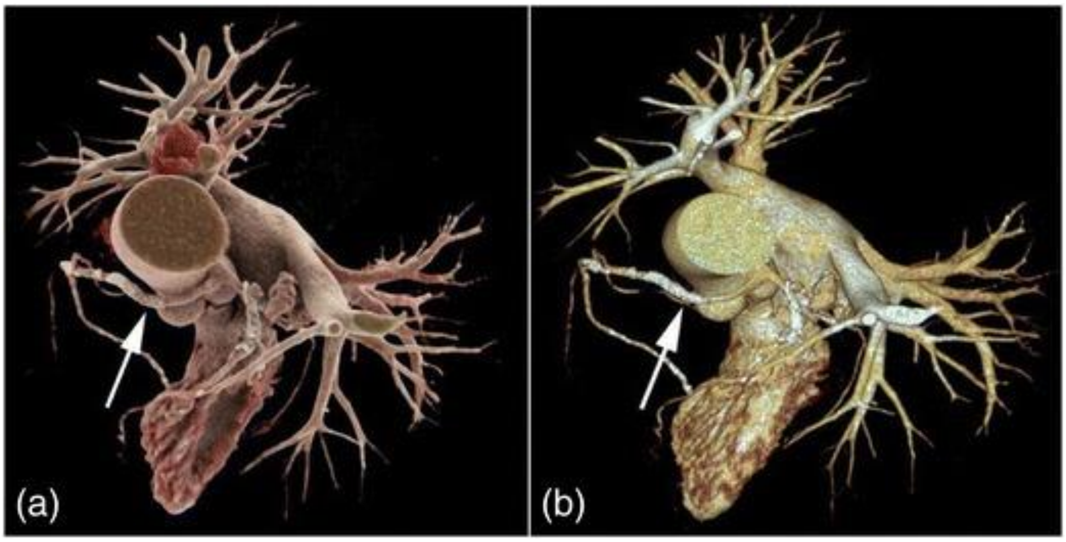
## 1.3 Visualization techniques of cardiac anatomy

As mentioned before, the diagnostic assessment tools play a significant role in helping the physicians to decide the optimal intervention or surgical approach for CHD. Hence, it is of paramount importance that the physicians are able to achieve full comprehension of the complex and dynamic 3D organ from the volumetric imaging datasets.[7,30,31] While this partially relies on the skills and expertise of the physicians, the visualization techniques play a significant part in enhancing and facilitating image interpretation.

The current visualization techniques for medical imaging datasets are mostly based on image post-processing tools such as multi-planar reformatting (MPR) and 3D volume rendering.[31-35] MPR allows the users to create images at orthogonal planes (sagittal and frontal) from the axial images and view them simultaneously. If required, the users can manipulate the three planes through the dataset, allowing them to view the anatomy in planes that are meaningful.[32] On the other hand, 3D volume rendering converts the 2D images of the selected anatomy into 3D representation, allowing the users to rotate, “cropping” or “cutting” the computerized 3D model to display the region of interest.[32,34] This also enables the users to understand the spatial relationships of the abnormal cardiac structures in a virtual 3D space.[35] Cinematic rendering

(CR) developed by Siemens Healthineers, has been increasingly used in medical imaging to enhance the verisimilitude of the medical data in 3D. Figure 1.6 demonstrates a comparison of the display effect of volume rendering and CR.[36] Despite so, there still exists some limitations with the current visualization methods. The MPR, 3D volume rendering, and CR require display of the datasets on 2D flat screen, causing variation in image interpretation between different observers.[7,37-42] Conceptual 3D understanding from 2D flat screen also heavily relies on the end-users' knowledge in 3D spatial orientation.[39,43] This can hamper full comprehension of the complex morphology of CHD, particularly for junior doctors and students.[30]

**Figure 1.6:** A comparison of cinematic rendering (a) and volume rendering (b).



Reprinted with permission under the open access from Dappa et al.[36]

An emerging technique that was reported to profoundly improve the visualization and interpretation of cardiac anatomy is 3D printing, which is also known as additive manufacturing. 3D printing fully exploits the 3D characteristics of the volumetric imaging and translates them into tangible and physical 3D models.[7,28,37] This technology does not require any digital display apart from the sole 3D model for visual inspection. The main merit of the 3D printed model is its characteristic of being tactile, improving the depth perception and allowing the users to do direct manipulations and devices fitting.[37,40] Certain flexible 3D printing materials can even act as surgical rehearsal tool which enables the surgeons to cut and suture.[7,37,42,45,46] The application of 3D printing in CHD is discussed more in Section 1.4.2.

Hitherto, with the advancement in visualization technologies, extended reality or advanced interactive visualization, which includes virtual reality (VR), augmented reality (AR), and mixed reality (MR) have been introduced in medical field to ameliorate the current visualization technique of medical imaging.[39,44] VR provides an immersive, virtual environment that allows the users to interact with the virtual objects; AR works by overlaying virtual objects on the real world settings; MR brings together the virtual and the real world objects to a greater extent, which allow the users to interact with the virtual and real world objects simultaneously.[44] Previously, the main drawback of VR and AR is the requirement of wearing cumbersome headsets, tracking devices, and the need of consoles.[39,44] However, with the emergence of standalone headsets (e.g. Oculus Quest 2 (Facebook Technologies, LLC, Irvine, California, United States), HoloLens 2 (Microsoft Crop., Redmond, DC, USA)), it has made the viewing more convenient without the need to connect to a separate computer. Holographic display system, Holoscope-i (RealView Imaging Ltd., Yokneam, Israel) creates holograms from interference of the light beams, which allows the users to view the holograms without the need of a headset.[39,44,47] The application of extended reality in CHD is discussed more in Section 1.5.2.

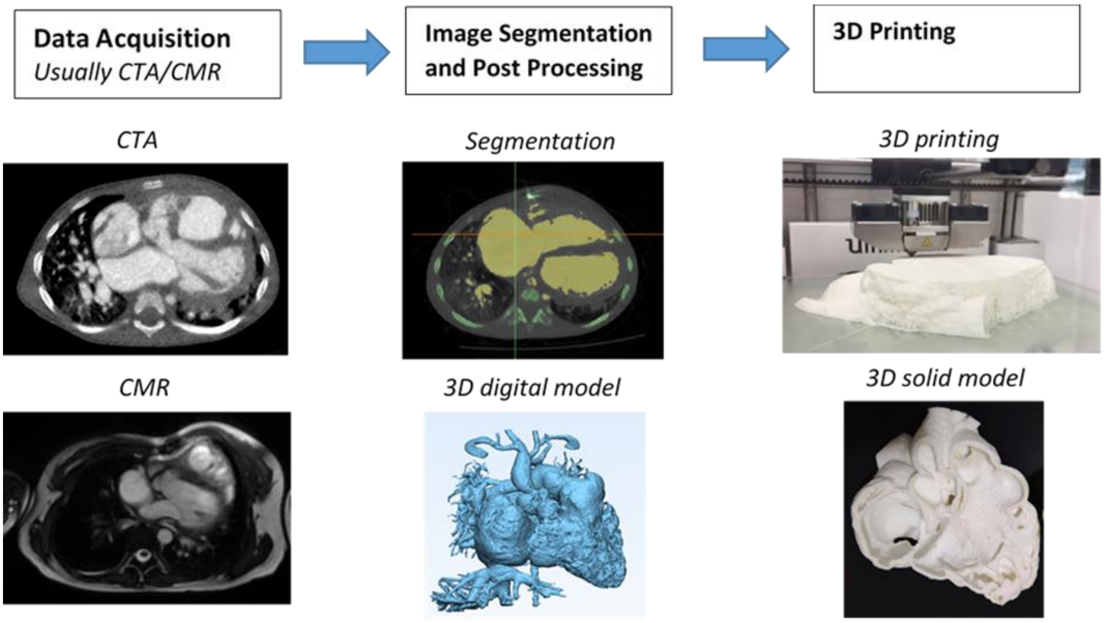
## 1.4 3D printing in CHD

3D printing technology has been around for at least three decades.[40,48] Its application in medicine is growing exponentially, which began from maxillofacial and dentistry specialty with the expansion into cardiovascular field since the early 21st century.[28,31] Its utilisation in healthcare settings, especially in the cardiovascular field is undoubtedly still under evolution.[30] This section will provide a brief overview of the steps involved in creating 3D printed heart models (3DPHM) and their current applications.

### 1.4.1 Process involved in creation of 3DPHM

The creation process of 3DPHM comprises of 3 consecutive steps: data acquisition, image segmentation and post-processing, and 3D printing (Figure 1.7).[28,40,41,44,49,50]

**Figure 1.7:** Flow chart showing the 3D printing process.



CTA, computed tomography angiogram; CMR, cardiac magnetic resonance. Reprinted with permission under the open access from Sun et al.[49]

### *1.4.1.1 Data acquisition*

There are a few requirements for a medical dataset to be eligible or suitable for 3D printing of heart models: (1) It has to be a volumetric scan (i.e. 3D scan) that is isotropic;[28,43,44,50] (2) It needs to be able to delineate the myocardium and vessel wall and separate them from the blood pool;[28] (3) It should have high spatial resolution and contrast to sufficiently differentiate the adjacent anatomical structures; (4) Slice thickness of the scan should be no more than the size of the smallest anatomy of interest; (5) Image artefacts should be minimized.[41,43,50] The quality of the input images will directly influence the time of image processing as well as the quality and the accuracy of the final 3D printed models.[42,44,51]

Due to these requirements, CCTA and CMR are the most preferred imaging modalities to generate 3DPHM due to their wide field of view, superior spatial resolution and good temporal resolution when they are gated.[28,41,50,52] In fact, according to a recent meta-analysis, the most reported imaging modality for 3D printing of CHD is CCTA, followed by CMR.[53] It was only until 2014 that it was shown feasible to derive 3DPHM from echocardiography datasets.[39,54] This also explains why echocardiography is the least reported imaging modality for 3D printing of CHD. This is expected to increase as 3D printing of CHD continues to expand. However, due to ultrasound's limited access windows and unavoidable artefacts from bones and air, 3D printing based on echocardiography can only be limited to certain part of the heart, such as the heart valves or the defect itself, instead of printing the heart in its entirety.[28,52,54]

Some research studies have reported the feasibility to fuse different imaging modalities in generating a single 3DPHM.[51,55] The advantage of this approach is that it is able to make use of the strengths of each imaging modality to cover the shortcomings of the others, and thus generating an accurate replica of the cardiac anatomy.[39,51] In the study by Gosnell et al., a hybrid 3DPHM was generated based on integration of CCTA and 3D transesophageal echocardiogram (TEE). The atrioventricular valves were derived from 3D TEE, whereas the other extra-cardiac structures were derived from CCTA.[51]

#### *1.4.1.2 Image segmentation and post-processing*

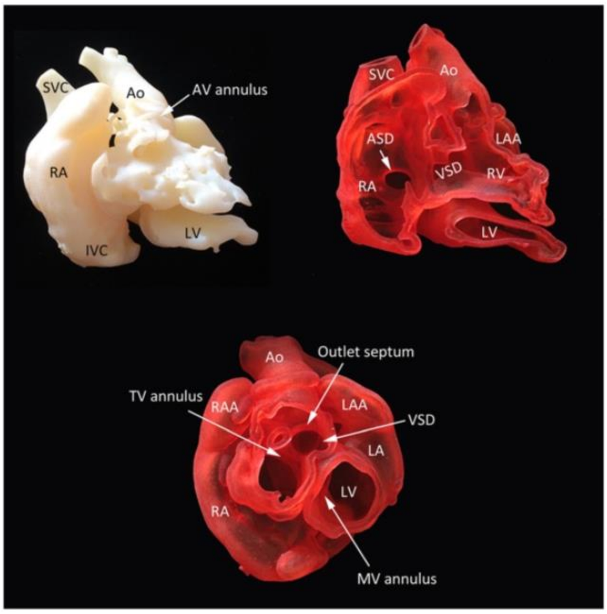
Image segmentation refers to the process of selecting the region of interest for 3D printing and separating them from irrelevant anatomies using a medical imaging processing software.[43,50] This process is very labour-intensive and time consuming, as it requires the operators' expertise in the processing software and knowledge in identifying the anatomy on cross-sectional imaging.[28,38,40,41,44,52]

A number of different medical imaging processing software were reported for heart segmentation, this includes commercially available software Mimics (Materialise HQ, Leuven, Belgium), as well as open source software such as 3D Slicer (Brigham and Women's Hospital, Boston, Mass), AYRA (Ikiria, Spain), and ITK Snap (http://www.itksnap.org/pmwiki/pmwiki.php).[41,49,53] Out of these software, Mimics is the most popular due to its extensiveness.[41,52,53] There is a detailed report on the steps involved in using Mimics for cardiac segmentation.[56]

The basic cardiac segmentation can be classified into two schemes, which are the blood pool segmentation (more common) and myocardium segmentation.[43] Each of them serve different purposes and should be selected according to the intent of 3D modelling. There are two types of heart models that can be generated through blood pool segmentation: cast model and wall model, which are invaluable for CHD assessment.[28] The cast model is basically a model of the blood pool, whereas the wall model is a shell of the cast model with graphically added thickness (Figure 1.8).[28] Generally, both of these models allow rapid localization of the blood-filled cavities such as the coronary arteries and the great vessels, as well as clearer delineation of the intra-cardiac structures.[28,43,57,58] However, these 3D heart models do not manifest true thickness of the myocardium.[28,58] On the other hand, the myocardium segmentation will produce models that reflect true myocardial thickness and demonstrate epicardial anatomy, hence they will be more useful in situations where these information are needed for surgical planning.[58] However, these models with full myocardial thickness require substantial amount of print materials, which can be costly to reproduce. They can also be quite rigid and heavy.[28]

There are a few different approaches in carrying out cardiac segmentation. The mostly reported method in the current literature is thresholding, region growing, and manual editing.[41,52] In thresholding method, the region of interest is identified based on their brightness intensity, so the anatomies that have brightness intensity beyond the set value will be excluded.[40,41] In region growing method, the operator is required to put a seed point on the region of interest, the software algorithm will then calculate if the neighbouring pixels are related to the seed point.[41] Manual editing is mainly utilised in correcting segmentation errors, which is to exclude the pixels that are incorrectly included as region of interest, or to fill in the gaps.[41] As these segmentation methods heavily rely on the spatial resolution of the source data to accurately identify the border of region of interest, it is therefore critical to have a high quality dataset to avoid the need of cumbersome manual editing and shorten the segmentation time.[44] It is also equally important to carry out the image segmentation meticulously to avoid introducing segmentation errors which can jeopardize the accuracy of the 3DPHM.

**Figure 1.8:** Diagram depicting 3DPHM which feature transposition of the great arteries and a ventricular septal defect, generated from blood pool segmentation.



Top left: the cast model; top right: wall model after removal of the anterior free wall of the right atrium and right and left ventricles; bottom: wall model with the apical two thirds of the ventricles removed. Ao, aorta; ASD, atrial septal defect; AV, aortic valve; IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; MV, mitral valve; RA, right atrium; RV, right ventricle; SVC, superior vena cava; TV, tricuspid valve; VSD, ventricular septal defect. Adapted from Yoo et al. under a CC-BY 4.0 license.[28]

After segmentation of the heart, the 3D surface model will need to be exported to a computer-aided design (CAD) software for post-processing and refinement.[37,48,56,59] The segmented geometry usually has a rough surface, thus the use CAD software is required to smooth out the surface of the 3D object in order to remove any potential noise artefact from the source data.[28,48,56,59] However, the operator needs to be mindful that excessive smoothing can compromise the delicate detail on the surface of the segmented geometry.[28,50] Furthermore, the CAD software can also be used to add a user-defined thickness to the segmented blood pool for wall models production (Figure 1.4).[37,56] They are also capable to crop out the undesirable anatomy, add colours to the 3D surface model, and to graphically design devices or implants on the models, which can be meaningful to interventional or surgical planning.[41,48] A few commonly used CAD software for heart modelling are Meshlab (Italian National Research Council, Italy), Meshmixer (Autodesk Inc., San Rafael, CA, USA), and Blender (Blender Foundation, Amsterdam, the Netherlands).[41,59,60] Consequently, the desired 3D surface model will need to be exported in a file format that is readable by the 3D printers.[61] The most commonly used format is Standard Tessellation Language (STL).[48,50,61] STL is composed of a surface mesh of triangular faces, in which the amount of the triangles can affect the model's accuracy.[50,62]

#### *1.4.1.3 3D Printing*

There are various 3D printing technologies adopted in generation of 3DPHM. The choice of 3D printing technology should be made after considering the following parameters in relation to the main intent of 3D printing: time required for 3D printing, printer resolution, 3D printing cost, choice of printing materials (i.e. rigid/flexible, single/multi-materials), colour capabilities, and sterilization capabilities.[48,62] For instance, if the 3DPHM is generated only to demonstrate the cardiac anatomy, cheaper printing technology with rigid material is sufficient to fulfil the role.[28,48] If the 3DPHM is used for surgical simulation, then a more flexible material which can closely mimic the physical properties of human heart muscles should be opted.[28,48]

There are three commonly used 3D printing technologies in generation of 3DPHM: (1) fused deposition modelling (FDM, also known as material extrusion); (2) stereolithography (SLA, also known as vat photopolymerisation); and (3) PolyJet technology (also known as material jetting).[41,62,63] FDM printers extrudes very thin, melted thermoplastic filaments layer-by-layer in z-direction.[41,63] The filaments solidify and fuse with the adjacent layers as soon as they are cooled down.[41] SLA technology utilises photosensitive liquid resin and a high-intensity light source [usually ultraviolet (UV) light] to reproduce 3D printed models.[41,62,63] The light source traces the cross-section geometry of the 3D object in the liquid resin bath and sequentially cure and solidify the resin in successive layers.[41,62] The final model is then cured in a UV chamber.[62] Similar to SLA technology, PolyJet technology also utilises liquid photopolymers and UV light. However, instead of having a liquid resin bath, thin layers of photopolymers are jetted onto the build tray and are instantly cured by the UV light. These printers are capable of printing multi-colour and even multi-material on the same print and producing models of variable durometer by mixing the printing materials.[33,41,62] This is especially useful to produce 3D printed models of anatomies that have different physical properties (e.g. coronary arteries with calcified plaques).[48] As PolyJet printers are able to produce flexible, rubber-like models, this technology is usually opted when 3DPHM are required for interventional or surgical simulation.[28,63] Table 1.1 provides a summary of the print resolution and the relative price of the print materials associated with different 3D printing technologies.

**Table 1.1:** Properties of different 3D printing technologies

| | **FDM** | **SLA** | **PolyJet** |
|---|---|---|---|
| **Resolution (mm)** | 0.1 | 0.025 – 0.1 | 0.016 |
| **Print materials** | thermoplastic filaments | photopolymer | photopolymer |
| **Cost of print materials (relatively to each other)** | $ | $$ | $$$ |

FDM, fused deposition modelling; mm, millimetres; SLA, stereolithography

During the printing process, the 3D objects are often printed along with the supporting materials to prevent them from collapsing. These supporting materials hence need to be removed upon completion of 3D printing.[28,48] Depending on the types of the supporting materials, they can either be removed by using a waterjet, airjet, or chemicals. The time needed for the cleaning process is controlled by the size and complexity of the 3D geometry.[28]

### 1.4.2 Clinical applications of 3D printing in CHD

3DPHM have been reported invaluable for various applications due to its unparalleled ability in providing tactile perception of patient-specific cardiac replica. The reported applications can be classified into 5 main categories: (1) pre-operative planning; (2) pre-surgical simulation; (3) intra-operative orientation; (4) communication within clinical practice; and (5) medical education.[28,49,53,64]

#### 1.4.2.1 Pre-operative planning

Individualised pre-operative planning for complex CHD is extremely challenging due to the wide variations of cardiac morphologies and the limitations of current visualization techniques which were discussed in section 1.2. 3DPHM were shown to be useful in facilitating pre-operative planning in several studies, especially in complex cases which optimal surgical option could not be derived from conventional imaging data.[37,65,66] In fact, this is the mostly reported application of 3DPHM.[53] A recent prospective study by Valverde et al. included 40 complex CHD cases in which 3DPHM were used in pre-operative planning. In 19 cases, the use of 3DPHM have helped the surgeons to redefine the surgical approach, resulting in better patients' outcome. Ninety-six percent of the 22 surgeons indicated that the 3DPHM have allowed them to achieve better comprehension of the anatomy, and facilitated pre-operative planning.[37]

#### 1.4.2.2 Pre-surgical simulation

3DPHM have been utilised to rehearse various cardiac surgeries or interventions to increase the surgeons' or the cardiologists' confidence in carrying out the procedures.[31,45,46,67] They have also been used to test the fitting of medical devices, such as transcatheter aortic valve implantation or replacement (TAVI/ TAVR) procedures.[68,69] For this purpose, rubber-like and flexible 3D printing materials are preferred, as they possess the physical properties similar to the human heart tissues which allow surgeons to cut and suture.[28,48]

In the study conducted by Valverde et al., a rigid heart model was compared with another heart model that was printed in flexible material.[67] Surgical simulation was carried out on both models. It was found out that the flexible material is more suitable than the rigid material, as it allowed vessel wall expansion during balloon inflation for stent placement.[67] In another study carried out by Shiraishi et al., 12 rubber-like urethane models were made for simulative operation.[45] Although the flexible material allowed the surgeon to cut and suture the heart models, the authors claimed that the urethane material still falls short in imitating the texture of the real heart and blood vessels. It is necessary to improve or develop a material that can mimic the texture of realistic heart muscles for pre-operative simulation.[45]

#### 1.4.2.3 Intra-operative orientation

3D printed cardiac models are excellent in demonstrating CHD anatomy and were proved to be a useful reference tool intra-operatively to locate the anatomy. Until now, surgeons have been carrying out heart operations with their reminiscence of pre-operative images. However, in high-risk surgery like the case presented by Mottl-Link et al., even highly experienced surgeons can fail to recall the information from pre-operative images due to its complexity.[57]

In the study, the surgery was guided by direct comparison with the 3D printed models, therefore, the localisation of coronary arteries became a lot easier. The authors claimed that the surgery would not be successful without the intra-operative aid of the 3D printed heart replica.[57] Similarly, the use of 3D printed models has also been reported in other case reports for real-time comparison during the corrective surgical procedure.[31,70,71]

As the printed models are to be used intra-operatively, sterilization of the models becomes essential. The model used in the study by Bhatla et al. was not sterilized, hence the use of the model was limited.[31] Sterilized model is expected to improve real-time decision-making, as well as allows viewing of the heart at different angles that may not be able to be achieved intra-operatively. In contrast, sterilized 3D printed model was used in the study conducted by Sodian et al., indicating that it is feasible to sterilize the printed model for more effective intra-operative orientation.[71]

#### *1.4.2.4 Communication within clinical practice*

Effective patient-doctor communication is desirable to ensure the quality of patient care. The patients need to have adequate knowledge of their own condition in order to engage fully with the required health service. However, patient-doctor communication is challenging, not least because of the complexity of CHD. Furthermore, cardiology terminology can be too complicated for non-experts to understand.[72]

Even though ‘communication’ was ranked as least relevant application of 3D printed CHD models in a recent report,[73] studies have shown the usefulness of 3D printed models in enhancing patient-doctor communication during cardiology consultations. Biglino et al. created patient-specific 3DPHM from 20 adolescent patients and used as a communication tool during their consultation times.[72] Degree of how well the patients know about their condition was rated before and after the consultation. Generally, the self-reported knowledge of own condition has improved significantly post-consultation.[72]

In another study, 98 parents of children with CHD were involved in a questionnaire-based RCT to assess the potential of using 3D printed model as tool to facilitate communication during consultation with cardiologists. The participants were randomly assigned into 2 groups, 3D model group and control group.[74] Both the parents and cardiologists reported that the printed models were helpful in getting the parents engaged to discuss their children’s condition. Questions regarding CHD were also asked to assess any improvements in parental knowledge. Interestingly, even though the finding shows enhancement in parent-doctor communication with the use of 3D models, there is no significant improvement in parental knowledge after the consultation. The authors pointed out that this could be due to the design of the assessment questions, which could not fully assess the parental knowledge.[74]

#### *1.4.2.5 Medical education*

Currently, the medical education of heart anatomy and physiology heavily revolves around 2D resources such as textbooks and medical anatomy atlases, or cadaveric specimens. While 2D resources are the most readily available learning resource for the students, it demands the ability of the students to mentally reconstruct the spatial information into 3D. This can be challenging for novice who just learnt about CHD.[75-77] On the other hand, cadavers have its own shortcomings such as subjectivity to wear and tear, high maintenance cost, and inaccessibility.[28,75,77,78] Therefore, 3DPHM have been utilised as a novel teaching tool for paediatric residents, cardiac nurses, and students.[75,76,78-81]

From the currently available reports, there is paucity of evidence to indicate the users' knowledge improvements on CHD with the use of 3DPHM when compared to the traditional teaching methods. Su et al. carried out seminars on VSD which involved 63 medical students with 32 students in the 3D model group and 31 students in the control group. During the seminar, both groups have access to images and animations on VSD, whereas the experimental group has 3DPHM as an additional teaching tool. With no significant difference in academic performances between the two groups, the experimental groups improved significantly in structural conceptualization compared to the control group.[81] However, this finding is not supported in another study by Loke et al. Thirty-five paediatric residents were enrolled into a teaching session on TOF, with 18 of them in the 3D model group and 17 of them in the 2D image (control) group. The 3D model group only received 3DPHM as teaching tool, whereas the 2D image group only received 2D drawings of TOF as teaching tool. Upon completion of the education session, it was found out that both groups have similar mean post-test scores with no statistical difference.[76] Even though there is discrepancy in study findings, it is generally agreed that the 3DPHM can enhance the users' learning experience and satisfaction.[53]

Chapter 2 provides a detailed review and meta-analysis of clinical applications of 3D printing in these five areas.

## 1.5 Extended reality visualization in CHD

The very first application of VR with a head mounted display can be traced all the way back to 1990s in which it was used to simulate laporoscopic surgery as a medical teaching tool.[82,83] To date, the role of extended reality in medicine has grown rapidly into other specialities and application. However, its' reported application in the domain of CHD remains scarce. The extended reality headsets that were used for visualizing CHD is variable. It is expected to be ever-changing with the release of newer and better headsets. Table 1.2 presents the properties and specifications of a few extended reality headsets that were used to visualise CHD in the current literature.

The advancement and development in extended reality do not only enhance the users' viewing experience, but also brought the price down to a much more affordable range. For example, the introductory price of Oculus Quest which was released in 2018 was $399, however the Oculus Quest 2 costs $299 at release in 2020.[84] This is expected to reduce even more as the technology becomes more mainstream.

Apart from headsets or wearable computers, extended reality also exists in another form, which is called fish-tank display.[85,86] Kang et al. reported the use of Echopixel True 3D (Echopixel, Hewlett-Packard, Mountain View, CA), which is a MR software platform to interrogate stereoscopic heart models with DORV.[87] The users are required to wear a special glasses and interact with the stereogram with a stylus pen. The software also needs to be used in conjunction with a VR display monitor that has tracking sensors to track the users' head and hand movements.[87]

**Table 1.2:** Properties and specifications of extended reality headsets that were reported for the use in CHD

| **Extended Reality Headsets** | ***HTC Vive** [88-90] | **HTC Vive Pro** [91] | **Oculus Quest 2** [92] | **HP Windows MR Headset** [93] | ***HoloLens** [94,95] | **HoloLens 2** [96,97] |
|---|---|---|---|---|---|---|
| **Type** | VR | VR | VR | VR | MR | MR |
| **HMD/HUD** | HMD | HMD | HMD | HMD | HUD | HUD |
| **Resolution (pixels per eye)** | 1080 x 1200 | 1440 x 1600 | 1832 x 1920 | 1440 x 1440 | 1280 x 720 | 2048 x 1080 |
| **Refresh rate (Hz)** | 90 | 90 | 90 | 90 | 60 | 60 |
| **Need of separate console** | yes | yes | optional | yes | no | no |
| **Need of haptic devices** | yes | yes | optional | yes | no | no |
| **Weight (g)** | 470 | 550 | 503 | 524 | 579 | 566 |

* = discontinued

HMD, head mounted display; HUD, heads-up display; MR, mixed reality; VR virtual reality

HTC Vive / HTC Vive Pro (HTC, Taoyuan, Taiwan); Oculus Quest 2 (Facebook Technologies, LLC, Irvine, California, United States); HP Windows Mixed Reality Headset (HP, California, United States); HoloLens / HoloLens 2 (Microsoft Crop., Redmond, DC, USA)

### 1.5.1 Process involved in building extended reality application

Even though there are a range of different makes of extended reality headsets, the development of extended reality application follows the same general principle. The most commonly used environment for this is Unity (Unity Technologies, San Francisco, California, USA), integrated with Visualization Toolkit (VTK).[85,88,89] Currently, there are two main techniques to visualise models within Unity: surface rendering and volume rendering.[85] Surface rendering, which is to create a mesh surface models of the anatomy of interest, requires segmentation of the medical imaging datasets, as outlined in Section 1.4.1.2. Depending on the complexity and quality of the datasets, this method can be time-consuming. The main advantage of this technique however, is that it requires less processing power for the application to run. Volume rendering on the other hand, has higher requirement for the processing power of either the headset or the computer to run the application. However, it does not require segmentation, while offering more flexibility for the users to manipulate the datasets.[85]

Some segmentation software, such as 3D Slicer, have extension that supports direct viewing and manipulation of the surface models via the headsets.[93] This removes the step of creating an application on Unity, however only works with OpenVR-compatible headsets.[98]

### 1.5.2 Clinical applications of extended reality in CHD

While the clinical applications of extended reality are still in their infancy in the domain of CHD, there have been reports on the use of extended reality for pre-operative planning, simulation training, medical education, and intra-operative guidance.

#### *1.5.2.1 Pre-operative planning*

The main strength of advanced interactive visualization is the ability for the users to view the heart models intuitively at infinite amount of angles, which is otherwise difficult to be achieved on 3DPHM, the DICOM images, and intra-operatively.[91,99,100] Furthermore, the flexibility to allow users to hide certain structures as well as to scale the models up or down has facilitated the pre-operative planning.[100,101] In the study by Ye et al., 17 patients with DORV who had their surgeries planned under the guidance of MR holographic models, were compared with the control group. It was reported that MR visualization had significantly shortened the surgical planning time (51.65 ± 11.11 min) compared to the control group (65.71 ± 18.07 minutes, $p<0.05$). Furthermore, the MR models have helped the surgeons to decide the best surgical approach. This is reflected from the fact that none of the planned surgeries were changed intra-operatively in the MR-guided group; whereas the surgical procedures were changed in 3 cases in the control group.[101] Ghosh et al. had successfully carried out surgical procedure for a challenging case to repair multiple VSD, in which VR was incorporated in pre-operative planning. It was reported that the VR model had helped the surgeon to decide the precise incision location in RVOT.[90]

#### *1.5.2.2 Simulation training*

EchoCom (EchoCom GmbH, Leipzig, Germany) is a non-immersive VR training simulator for echocardiography developed by the research group Weidenbach et al.[102] In their study, they included 43 participants and stratified them based on their expertise. The simulator passed all three validity tests, which include face validity, content validity, and construct validity.[102] The simulator was used in another study by Dayton et al. to investigate its' effectiveness in diagnostic training of paediatric cardiology fellows.[103] It was reported that the participants' knowledge of CHD and the technical skills in performing transthoracic echocardiogram had improved after the simulation-based training session.[103] Although the presented VR simulator is non-immersive, it has already shown positive outcomes as a novel method in providing training to medical practitioners.

#### *1.5.2.3 Medical education*

Introduction of extended reality in medical education is changing the curriculum structure in health science and medicine.[104] With the use of consumer grade extended reality, students can learn anywhere outside the classroom.[104] Kim et al. compared the fully-immersive VR, non-immersive VR, and conventional 2D display in terms of their diagnostic accuracies and their popularities among a group of 22 medical trainees.[105] It was found that the group which used the fully-immersive VR in their CHD case discussion achieved the highest diagnostic accuracies compared to the other two. It was also ranked as the most preferred technology for facilitating CHD group discussions.[105]

The study by Patel et al. however, did not find evidence that VR improves CHD knowledge acquisition among the students.[87] Fifty-one students were randomly assigned to VR and control group, in which they had received identical lecture content on CHD. It was reported that no statistical significant difference in knowledge acquisition was found between the two groups. Despite so, the students in VR group reported enhanced learning experience with a better self-assessment of knowledge level.[87]

#### *1.5.2.4 Intra-operative guidance*

Bruckheimer et al. were the first to demonstrate the feasibility of generating real-time dynamic holograms based on intra-procedural 3D TEE and 3D rotational angiography scans using

Holoscope-I, or also known as RealView Holographic Display system. The coloured hologram was formed instantaneously as the medical imaging examination was taking place.[47] It was reported that the participants were able to correctly identify all the anatomical landmarks on the holograms, justifying the diagnostic accuracy of the holograms. As this is a feasibility study, the clinical impact of real-time holograms on intra-operative guidance could not be validated. Despite so, its' potential in this aspect is immense. This holds especially true for minimally invasive interventions where the interventionalists are not able to directly assess the patients' anatomy intra-operatively.[47] It is hence necessary for the interventionalists to know the patients' anatomy inside out.

In Soulami et al.'s study, AR had been successfully applied to guide valve-in-valve TAVI (ViV-TAVI) using minimal contrast injection.[106] The 3D virtual models of the aortic root was superimposed on the intra-interventional fluoroscopic images to spatially register the chosen landmarks. Dynamic tracking was then applied to maintain this superimposition.[106] In fact, accurate spatial registration in moving organs, such as heart, is very challenging due to extensive deformation of the heart during different cardiac cycle. To maintain the spatial registration with the motion, tracking devices are required.[43] The lack of accuracy in spatial registration and the need of ancillary tracking equipment are the two main factors that impede the application of AR or MR intra-operatively for CHD surgeries or interventions.[43,47]

## 1.6 Research question and objectives

The use of 3D printing and extended reality are still in their infancy in the domain of CHD. To the best of our knowledge, there are only very little research done to compare the use of extended reality and 3DPHM concurrently with the conventional visualization technique. Moreover, all of the existing studies focused on the effect of 3DPHM on short-term knowledge gain among the participants, while none of them investigated long-term knowledge retention. There is insufficient evidence to validate the impact of 3DPHM on users' knowledge acquisition on CHD. Therefore, the primary research question for this research is, in what ways do 3D printing and extended reality improve on the current patient management and medical education for CHD? This has been broken down into a few more specific research questions which were addressed in each chapter of this thesis. This will be discussed more in Section 1.7.

The intended outcomes of the project were:

1. To generate a range of lesion-specific 3DPHM, VR and MR applications which feature different types and complexity of CHD.
2. To compare the utility of low- and high-cost 3DPHM.

3. To incorporate the 3DPHM into medical teaching of CHD, and compare the test scores between the 3D models group and control group.
4. To provide more insights into the comparison of clinical application between 3DPHM, VR, and MR with the current visualization technique.

## 1.7 Thesis outline

This thesis consists of 5 papers which are presented from Chapter 2 to Chapter 6. This section presents a brief overview of each chapter. The overall aim of this thesis is to evaluate and compare the role of 3D printing and extended reality in improving the current visualization technique and medical education for CHD.

Paper 1

Dimensional Accuracy and Clinical Value of 3D Printed Models in Congenital Heart Disease: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine.* 2019;8(9):1843.

In order to find out the dimensional accuracy and review the existing application of 3DPHM, a systematic review and meta-analysis was carried out (Chapter 2). This paper was published in the Journal of Clinical Medicine.

Paper 2

Quantitative and qualitative comparison of low- and high-cost 3D-printed heart models. *Quantitative Imaging in Medicine and Surgery.* 2019;9(1):107-114.

As the cost of the 3DPHM is generally reported as one of the main factors that hinders the application of this technology,[75,107,108] Chapter 3 compared the dimensional accuracy and the clinical applications of low- and high-cost 3DPHM. This paper was published in Quantitative Imaging in Medicine and Surgery.

Paper 3

The role of 3D printed heart models in immediate and long-term knowledge acquisition in medical education. *Reviews in Cardiovascular Medicine.* 2022;23(1):022.

There had been no study that investigated the effect of 3DPHM on long-term knowledge retention in CHD education. Hence in Chapter 4, a prospective cohort study was presented to discuss the effect of incorporating 3DPHM in CHD education on the short-term and long-term knowledge acquisition among the second and third year medical students. This paper was published in Reviews in Cardiovascular Medicine.

Paper 4

Clinical Value of Virtual Reality versus 3D Printing in Congenital Heart Disease. *Biomolecules.* 2021;11(6):884.

Chapter 5 presented a cross-sectional study which involved 35 medical practitioners to qualitatively compare VR and 3D printing in terms of their medical applications. This paper was published in Biomolecules.

Paper 5

Clinical applications of Mixed Reality and 3D Printing in Congenital Heart Disease. *Biomolecules.* 2022;12(11):1548.

Chapter 6 presented a cross-sectional study which made a direct comparison of MR, 3D printing, and 2D medical datasets in terms of their diagnostic quality and medical applications. The study involved 34 cardiac specialists and physicians to assess each modality qualitatively. This paper was published in Biomolecules.

Finally, Chapter 7 of this thesis concluded the findings of this research and discussed some of the possible future work.

## 1.8 References

1. Liu Y, Chen S, Zuhlke L, Black GC, Choy M, Li N, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. *Int. J. Epidemiol.* 2019;48(2):455-463. doi: 10.1093/ije/dyz009
2. McCusker C, Casey F (Eds). *Congenital Heart Disease and Neurodevelopment: Understanding and Improving Outcomes*. San Diego: Academic Press; 2016.
3. Flocco SF, Lillo A, Dellafiore F, Goossens E (Eds). *Congenital Heart Disease: The Nursing Care Handbook*. Switzerland: Springer International Publishing; 2019. doi: 10.1007/978-3-319-78423-6
4. Satpathy M, Mishra BR (Eds). *Clinical Diagnosis of Congenital Heart Disease*. New Delhi: Jaypee Brothers Medical Publishers; 2015.
5. Rao PS. Congenital Heart Defects – A Review. In: Rao PS, editor. *Congenital Heart Disease – Selected Aspects*. UK: InTechOpen; 2012. doi: 10.5772/27002
6. Bruneau BG. The developmental genetics of congenital heart disease. *Nature*. 2008;451(7181):943-948. doi: 10.1038/nature06801
7. Lau I, Wong YH, Yeong CH, Abdul Aziz YF, Md Sari NA, Hashim SA, et al. Quantitative and qualitative comparison of low- and high-cost 3D-printed heart models. *Quant Imaging Med Surg*. 2019; 9(1):107–114.
8. Lacour-Gayet F, Clarke D, Jacobs J, Gaynor W, Hamilton L, Jacobs M, et al. The Aristotle score for congenital heart surgery. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2004;7(1):185-91.
9. Nasr VG, DiNardo JA. *The Pediatric Cardiac Anesthesia Handbook*. USA; John Wiley & Sons; 2017. doi: 10.1002/9781119095569
10. Rao PS. Atrial Septal Defect - A Review. In Rao PS, editor. *Atrial Septal Defect*. UK: IntechOpen. doi: 10.5772/38886
11. Barron DJ (Ed). *Core Topics in Congenital Cardiac Surgery*. UK: Cambridge University Press; 2018. doi: https://doi.org/10.1017/9781139524087
12. Hutchinson D, Hornberger L. Anomalies of Atrial Septation. In: Alboliras ET, Hijazi ZM, Lopez C, Hagler DJ, eds. *Visual Guide to Neonatal Cardiology*. UK: John Wiley & Sons; 2018:127-132. doi:10.1002/9781118635520
13. Heiden K. *Congenital Heart Defects, Simplified*. USA: Midwest Echosolutions; 2009.
14. Yeh DD, Bhatt A (Eds). *Adult Congenital Heart Disease in Clinical Practice*. Switzerland: Springer International Publishing; 2018. doi: 10.1007/978-3-319-67420-9
15. Mazur W, Siegel MJ, Miszalski-Jamka T, Pelberg R. *CT Atlas of Adult Congenital Heart Disease*. London: Springer; 2013.

16. Driscoll DJ. Clinical Presentation and Therapy of Ventricular Septal Defect. In: Rickert-Sperling S, Kelly RG, Driscoll DJ, eds. *Congenital Heart Diseases: The Broken Heart: Clinical Features, Human Genetics and Molecular Pathways*. Vienna (Austria): Springer-Verlag Wien; 2016:303-306. doi: https://doi.org/10.1007/978-3-7091-1883-2
17. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF (Eds). *Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia: Elsevier Saunders; 2019.
18. Park MK. *Pediatric Cardiology for Practitioners E-Book*. Philadelphia: Elsevier Saunders; 2014.
19. Englert JAR, Gupta T, Joury AU, Shah SB. Tetralogy of Fallot: Case-Based Update for the Treatment of Adult Congenital Patients. *Curr Probl Cardiol*. 2019;44(2):46-81. doi: https://doi.org/10.1016/j.cpcardiol.2018.03.002
20. Phibbs B. *The Human Heart: A Basic Guide to Heart Disease*. Philadelphia: Lippincott Williams & Wilkins; 2007.
21. Swischuk LE. *Imaging of the Newborn, Infant, and Young Child*. Philadelphia: Lippincott Williams & Wilkins; 2004.
22. Puranik R, Muthurangu V, Celermajer DS, Taylor AM. Congenital Heart Disease and Multi-modality Imaging. *Heart Lung Circ*. 2010;19(3):133-44.
23. Prakash JA, Powell JA, Geva JT. Multimodality Noninvasive Imaging for Assessment of Congenital Heart Disease. *Circ Cardiovasc Imaging*. 2010;3(1):112-25.
24. Orwat S, Diller G-P, Baumgartner H. Imaging of congenital heart disease in adults: choice of modalities. *Eur Heart J Cardiovasc Imaging*. 2014;15(1):6-17. doi:10.1093/ehjci/jet124
25. Burchill JL, Huang TJ, Tretter MJ, Khan MA, Crean RA, Veldtman SG, et al. Noninvasive Imaging in Adult Congenital Heart Disease. *Circ Res*. 2017;120(6):995-1014. doi: 10.1161/CIRCRESAHA.116.308983.
26. Kilner PJ. Imaging congenital heart disease in adults. *Brit J Radiol*. 2011;84:S258-S68. doi: 10.1259/bjr/74240815
27. Babu-Narayan SV, Giannakoulas G, Valente AM, Li W, Gatzoulis MA. Imaging of congenital heart disease in adults. *Eur Heart J*. 2016;37(15):1182-95. doi: 10.1093/eurheartj/ehv519
28. Yoo S-J, Thabit O, Kim E, Ide H, Yim D, Dragulescu A, et al. 3D printing in medicine of congenital heart diseases. *3D Print Med*. 2016;2(1):1-12. doi: 10.1186/s41205-016-0004-x

29. Zhao L, Zhou S, Fan T, Li B, Liang W, Dong H. Three-dimensional printing enhances preparation for repair of double outlet right ventricular surgery. *J Card Surg*. 2018;33(1):24-7. doi: 10.1111/jocs.13523
30. Kappanayil M, Koneti NR, Kannan RR, Kottayil BP, Kumar K. Three-dimensional-printed cardiac prototypes aid surgical decision-making and preoperative planning in selected cases of complex congenital heart diseases: Early experience and proof of concept in a resource-limited environment. *Ann Pediatr Cardiol*. 2017;10(2):117.
31. Bhatla P, Tretter JT, Ludomirsky A, Argilla M, Latson Jr. LA, Chakravarti S, 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. doi: 10.1007/s00246-016-1489-1
32. Bharucha T, Roman KS, Anderson RH, Vettukattil JJ. Impact of Multiplanar Review of Three-Dimensional Echocardiographic Data on Management of Congenital Heart Disease. *Ann Thorac Surg*. 2008;86(3):875-81.
33. Kim GB, Lee S, Kim H, Yang D, Kim Y, Kyung Y, et al. Three-Dimensional Printing: Basic Principles and Applications in Medicine and Radiology. *Korean J Radiol*. 2016;17(2):182-97.
34. Greil GF, Wolf I, Kuettner A, Fenchel M, Miller S, Martirosian P, et al. Stereolithographic reproduction of complex cardiac morphology based on high spatial resolution imaging. *Clin Res Cardiol*. 2007;96:176-85.
35. Farooqi K, Uppu S, Nguyen K, Srivastava S, Ko H, Choueiter N, et al. Application of Virtual Three-Dimensional Models for Simultaneous Visualization of Intracardiac Anatomic Relationships in Double Outlet Right Ventricle. *Pediatr Cardiol*. 2016;37(1):90-8.
36. Dappa E, Higashigaito K, Fornaro J, Leschka S, Wildermuth S, Alkadhi H. Cinematic rendering – an alternative to volume rendering for 3D computed tomography imaging. *Insights Imaging*. 2016;7:849-856. doi:10.1007/s13244-016-0518-1
37. Valverde I, Gomez-Ciriza G, Hussain T, Suarez-Mejias C, Velasco-Forte MN, Byrne N, et al. Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study. *Eur J Cardiothorac Surg*. 2017;52:1139-48.
38. Kim SM, Hansgen RA, Wink AO, Quaife DR, Carroll DJ. Rapid Prototyping: A New Tool in Understanding and Treating Structural Heart Disease. *Circulation*. 2008;117(18):2388-94.
39. Byl JL, Sholler R, Gosnell JM, Samuel BP, Vettukattil JJ. Moving beyond two-dimensional screens to interactive three-dimensional visualization in congenital heart

disease. *Int J Cardiovasc Imaging*. 2020;36:1567-1573. doi: https://doi.org/10.1007/s10554-020-01853-1

40. Abudayyeh I, Gordon B, Ansari MM, Jutzy K, Stoletniy L, Hilliard A. A practical guide to cardiovascular 3D printing in clinical practice: Overview and examples. *J Interv Cardiol*. 2018;31(3):375-383. doi:10.1111/joic.12446
41. Meier LM, Meineri M, Qua Hiansen J, Horlick EM. Structural and congenital heart disease interventions: the role of three-dimensional printing. *Neth Heart J*. 2017;25(2):65-75. doi: 10.1007/s12471-016-0942-3
42. Shi D, Liu K, Zhang X, Liao H, Chen X. Applications of three-dimensional printing technology in the cardiovascular field. *Intern Emerg Med*. 2015;10(7):769-80.
43. Valverde I. Three-dimensional Printed Cardiac Models: Applications in the Field of Medical Education, Cardiovascular Surgery, and Structural Heart Interventions. *Rev Esp Cardiol*. 2017;70(4):282-91.
44. Goo HW, Park SJ, Yoo SJ. Advanced Medical Use of Three-Dimensional Imaging in Congenital Heart Disease: Augmented Reality, Mixed Reality, Virtual Reality, and Three-Dimensional Printing. *Korean J Radiol*. 2020;21(2):133-45.
45. Shiraishi I, Yamagishi M, Hamaoka K, Fukuzawa M, Yagihara T. Simulative operation on congenital heart disease using rubber-like urethane stereolithographic biomodels based on 3D datasets of multislice computed tomography. *Eur J Cardiothorac Surg*. 2010;37:302-6.
46. Hoashi T, Ichikawa H, Nakata T, Shimada M, Ozawa H, Higashida A, et al. Utility of a super-flexible three-dimensional printed heart model in congenital heart surgery. *Interact Cardiovasc Thorac Surg*. 2018;27(5):749-55.
47. Bruckheimer E, Rotschild C, Dagan T, Amir G, Kaufman A, Gelman S, et al. Computer-generated real-time digital holography: first time use in clinical medical imaging. *Eur Heart J Cardiovasc Imaging*. 2016;17:845-849. doi:10.1093/ehjci/jew087
48. Giannopoulos AA, Mitsouras D, Yoo SJ, Liu PP, Chatzizisis YS, Rybicki FJ. Applications of 3D printing in cardiovascular diseases. *Nat Rev Cardiol*. 2016;13(12):701-718.
49. Sun Z, Lau I, Wong YH, Yeong CH. Personalized Three-Dimensional Printed Models in Congenital Heart Disease. *J Clin Med*. 2019;8(4):522.
50. Chepelev L, Wake N, Ryan J, Althobaity W, Gupta A, Arribas E, et al. Radiological Society of North America (RSNA) 3D printing Special Interest Group (SIG): guidelines for medical 3D printing and appropriateness for clinical scenarios. *3D Print Med*. 2018;4(1):1-38.

51. Gosnell J, Pietila T, Samuel BP, Kurup HK, Haw MP, Vettukattil JJ. Integration of Computed tomography and three-dimensional echocardiography for hybrid threedimensional printing in congenital heart disease. *J Digit Imaging*. 2016;29:665-9.
52. 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 Cardiovasc Dis*. 2016;5:1-9.
53. Lau I, Sun Z. Dimensional Accuracy and Clinical Value of 3D Printed Models in Congenital Heart Disease: A Systematic Review and Meta-Analysis. *J Clin Med*. 2019;8(9):1483.
54. Samuel B, Pinto C, Pietila T, Vettukattil J. Ultrasound-Derived Three-Dimensional Printing in Congenital Heart Disease. *The Journal of the Society for Computer Applications in Radiology*. 2015;28(4):459-61.
55. Moore T, Madriago EJ, Renteria ES, Fuss C, Sahn DJ, Shepard D, et al. Co-registration of 3D echo and MR data to create physical models of congenital heart malformations. *J Cardiovasc Magn Reson*. 2015;17(Suppl 1):198.
56. Giannopoulos A, Chepelev L, Sheikh A, Wang A, Dang W, Akyuz E, et al. 3D printed ventricular septal defect patch: a primer for the 2015 Radiological Society of North America (RSNA) hands-on course in 3D printing. *3D Print Med*. 2015;1(1):1-20.
57. Mottl-Link S, Hübler M, Kühne T, Rietdorf U, Krueger JJ, Schnackenburg B, et al. Physical Models Aiding in Complex Congenital Heart Surgery. *Ann Thorac Surg*. 2008;86:273-7.
58. Farooqi KM, Lengua CG, Weinberg AD, Nielsen JC, Sanz J. Blood Pool Segmentation Results in Superior Virtual Cardiac Models than Myocardial Segmentation for 3D Printing. *Pediatr Cardiol*. 2016;37:1028-36. doi: 10.1007/s00246-016-1385-8
59. Kurata A, Kiyama Y, Shirakawa T, Miyoshi T. Clinical Applications of Three-Dimensional Printing in Cardiovascular Disease. *Cardiovasc Imaging Asia*. 2018;2(4):153-165. doi: https://doi.org/10.22468/cvia.2018.00094
60. Mashari A, Montealegre-Gallegos M, Knio Z, Yeh L, Jeganathan J, Matyal R, et al. Making three-dimensional echocardiography more tangible: a workflow for three-dimensional printing with echocardiographic data. *Echo Res Pract*. 2016;3(4):R57-R64.
61. Garekar S, Bharati A, Chokhandre M, Mali S, Trivedi B, Changela VP, et al. Clinical Application and Multidisciplinary Assessment of Three Dimensional Printing in Double Outlet Right Ventricle With Remote Ventricular Septal Defect. *World J Pediatr Congenit Heart Surg*. 2016;7(3):344-50.

62. Mitsouras D, Liacouras P, Imanzadeh A, Giannopoulos AA, Cai T, Kumamaru KK, et al. Medical 3D Printing for the Radiologist. *Radiographics*. 2015;35(7):1965-1988. doi: 10.1148/rg.2015140320
63. Vukicevic M, Mosadegh B, Min JK, Little SH. Cardiac 3D Printing and its Future Directions. *JACC: Cardiovasc Imaging*. 2017;10(2):171-184.
64. Lau I, Sun Z. Three-dimensional printing in congenital heart disease: A systematic review. *J Med Radiat Sci*. 2018;65(3):226-236. doi:10.1002/jmrs.268
65. Vettukattil JJ, Mohammad Nijres B, Gosnell JM, Samuel BP, Haw MP. Three-dimensional printing for surgical planning in complex congenital heart disease. *J Card Surg*. 2019;34(11):1363-9.
66. Ngan EM, Rebeyka IM, Ross DB, Hirji M, Wolfaardt JF, Seelaus R, et al. The rapid prototyping of anatomic models in pulmonary atresia. *J Thorac Cardiovasc Surg*. 2006;132(2):264-9.
67. Valverde I, Gomez G, Coserria JF, Suarez-Mejias C, Uribe S, Sotelo J, et al. 3D printed models for planning endovascular stenting in transverse aortic arch hypoplasia. *Catheter Cardiovasc Interv*. 2015;85:1006-12.
68. Schmauss D, Schmitz C, Bigdeli AK, Weber S, Gerber N, Beiras-Fernandez A, et al. Three-Dimensional Printing of Models for Preoperative Planning and Simulation of Transcatheter Valve Replacement. *Ann Thorac Surg*. 2012;93(2):e31-e3.
69. Qian Z, Wang K, Liu S, Zhou X, Rajagopal V, Meduri C, et al. Quantitative Prediction of Paravalvular Leak in Transcatheter Aortic Valve Replacement Based on Tissue-Mimicking 3D Printing. JACC: *Cardiovasc Imaging*. 2017;10(7):719-31.
70. Ma XJ, Tao L, Chen X, Li W, Peng ZY, Chen Y, et al. Clinical application of three-dimensional reconstruction and rapid prototyping technology of multislice spiral computed tomography angiography for the repair of ventricular septal defect of tetralogy of Fallot. *Genet Mol Res*. 2015;14:1301-9.
71. Sodian R, Weber S, Markert M, Rassoulian D, Kaczmarek I, Lueth TC, et al. Stereolithographic models for surgical planning in congenital heart surgery. *Ann Thorac Surg*. 2007;83:1854-7.
72. Biglino G, Koniordou D, Gasparini M, Capelli C, Leaver L, Khambadkone S, et al. Piloting the use of patient-specifc cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr Cardiol*. 2017;38:813-8.
73. Biglino G, Capelli C, Leaver LK, Shievano S, Taylor AM, Wray J. Involving patients, families and medical staff in the evaluation of 3D printing models of congenital heart disease. *Commun Med*. 2015;12:157-69.

74. Biglino G, Capelli C, Wray J, Schievano S, Leaver L, Khambadkone S, et al. 3D-manufactured patient-specifc models of congenital heart defects for communication in clinical practice: feasibility and acceptability. *BMJ Open*. 2015;5:e007165.
75. Costello JP, Olivieri L, Krieger A, Thabit O, Marshall MB, Yoo SJ, et al. Utilizing Three-Dimensional Printing Technology to Assess the Feasibility of High-Fidelity Synthetic Ventricular Septal Defect Models for Simulation in Medical Education. *World J Pediatr Congenit Heart Surg*. 2014;5:421-6.
76. Loke YH, Harahsheh AS, Krieger A, Olivieri LJ. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. *BMC Med Educ*. 2017;17:54-61.
77. Smerling J, Marboe C, Lefkowitch J, Pavlicova M, Bacha E, Einstein A, et al. Utility of 3D Printed Cardiac Models for Medical Student Education in Congenital Heart Disease: Across a Spectrum of Disease Severity. *Pediatr Cardiol*. 2019;40(6):1258-65.
78. Lim KH, Loo ZY, Goldie S, Adams J, McMenamin P. Use of 3D printed models in medical education: A randomized control trial comparing 3D prints versus cadaveric materials for learning external cardiac anatomy. *Anat Sci Educ*. 2016;9:213–21.
79. Biglino G, Capelli C, Koniordou D, Robertshaw D, Leaver L, Schievano S, et al. Use of 3D models of congenital heart disease as an education tool for cardiac nurses. *Congenit Heart Dis*. 2017;12:113-8.
80. Costello JP, Olivieri LJ, Su L, Krieger A, Alfares F, Thabit O, 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.
81. Su W, Xiao Y, He S, Huang P, Deng X. Three-dimensional printing models in congenital heart disease education for medical students: a controlled comparative study. *BMC Med Educ*. 2018;18(1):178.
82. Satava RM. Virtual reality surgical simulator. *Surg Endosc*. 1993;7:203-205.
83. Coleman J, Nduka CC, Darzi A. Virtual reality and laparoscopicsurgery. *Br J Surg*. 1994;81:1709-1711.
84. Oculus Quest. Wikipedia. Accessed December 16, 2022. https://en.wikipedia.org/wiki/Oculus_Quest#:~:text=At%20launch%2C%20the%20device%
85. Wheeler G, Deng S, Toussaint N, Pushparajah K, Schnabel JA, Simpson JM, et al. Virtual interaction and visualisation of 3D medical imaging data with VTK and Unity. *Healthc Technol Lett*. 2018;5(5):148–153.

86. Ware C, Arthur K, Booth KS. Fish Tank Virtual Reality. Paper presented at: Conference on Human Factors in Computing Systems (CHI); April 24 - 29, 1993; New York, USA. Accessed December 20, 2022. doi:10.1145/169059.169066
87. Kang SK, Shkumat N, Dragulescu A, Guerra V, Padfield N, Krutikov K, et al. Mixed-reality view of cardiac specimens: a new approach to understanding complex intracardiac congenital lesions. *Pediatr Radiol*. 2020;50:1610–1616.
88. Pushparajah K. Chu KYK, Deng S, Wheeler G, Gomez A, Kabir S, et al. Virtual reality three-dimensional echocardiographic imaging for planning surgical atrioventricular valve repair. *JTCVS Tech*. 2021;7:269-277. doi:10.1016/j.xjtc.2021.02.044
89. Ayarbe VMC, Morales MLV, Rojas CJL, Cortés MLA. Visualization of 3D Models Through Virtual Reality in the Planning of Congenital Cardiothoracic Anomalies Correction: An Initial Experience. *World J Pediatr Congenit Heart Surg*. 2020;11(5):627-629. doi:10.1177/2150135120923618
90. Ghosh RM, Mascio CE, Rome JJ, Jolley MA, Whitehead KK. Use of Virtual Reality for Hybrid Closure of Multiple Ventricular Septal Defects. *J Am Coll Cardiol Case Rep*. 2021;3(14):1579–1583.
91. Patel N, Costa A, Sanders SP, Ezon D. Stereoscopic virtual reality does not improve knowledge acquisition of congenital heart disease. *Int J Cardiovasc Imaging*. 2021;37(7):2283-2290. doi:10.1007/s10554-021-02191-6
92. Lau I, Gupta A, Sun Z. Clinical Value of Virtual Reality versus 3D Printing in Congenital Heart Disease. *Biomolecules*. 2021;11(6):884.
93. Priya S, Nagpal P. Four-dimensional virtual reality cine cardiac models using free open-source software. *Pediatr Radiol*. 2020;50:1617–1623.
94. Gehrsitz P, Rompel O, Schöber M, Cesnjevar R, Purbojo A, Uder M, et al. Cinematic rendering in mixed-reality holograms: a new 3D preoperative planning tool in pediatric heart surgery. *Front Cardiovasc Med*. 2021;8:633611.
95. Butera G, Sturla F, Pluchinotta FR, Caimi A, Carminati M. Holographic Augmented Reality and 3D Printing for Advanced Planning of Sinus Venosus ASD/Partial Anomalous Pulmonary Venous Return Percutaneous Management. *JACC Cardiovasc Interv*. 2019;12(14):1389-1391.
96. Cen J, Liufu R, Wen S, Qiu H, Liu X, Chen X, et al. Three-Dimensional Printing, Virtual Reality and Mixed Reality for Pulmonary Atresia: Early Surgical Outcomes Evaluation. *Heart Lung and Circ*. 2021;30:296–302.
97. Lau I, Gupta A, Ihdayhid A, Sun Z. Clinical applications of Mixed Reality and 3D Printing in Congenital Heart Disease. *Biomolecules*. 2022;12(11):1548.

98. Pinter C, Lasso A, Choueib S, Asselin M, Fillion-Robin JC, Vimort JB, et al. SlicerVR for Medical Intervention Training and Planning in Immersive Virtual Reality. *IEEE Trans Med Robot Bionics*. 2020;2(2):108-117. doi: 10.1109/TMRB.2020.2983199
99. Brun H, Bugge RAB, Suther LKR, Birkeland S, Kumar R, Pelanis E, et al. Mixed reality holograms for heart surgery planning: First user experience in congenital heart disease. *Eur Heart J Cardiovasc Imaging*. 2019;20:883–888.
100. Ong CS, Krishnan A, Huang CY, Spevak P, Vricella L, Hibino N, et al. Role of virtual reality in congenital heart disease. *Congenit Heart Dis*. 2018;13:357–361.
101. Ye W, Zhang X, Li T, Luo C, Yang L. Mixed-reality hologram for diagnosis and surgical planning of double outlet of the right ventricle: a pilot study. *Clin Radiol*. 2021;76(3):237.e1-e237.e7. doi:10.1016/j.crad.2020.10.017
102. Weidenbach M, Rázek V, Wild F, Khambadkone S, Berlage T, Janoušek, et al. Simulation of congenital heart defects: a novel way of training in echocardiography. *Heart*. 2009;95:636–641. doi:10.1136/hrt.2008.156919
103. Dayton JD, Groves AM, Glickstein JS, Flynn PA. Effectiveness of echocardiography simulation training for paediatric cardiology fellows in CHD. *Cardiol Young*. 2018;28,611–615. doi:10.1017/S104795111700275X
104. Moro C, Phelps C, Redmond P, Stromberga Z. HoloLens and mobile augmented reality in medical and health science education: A randomised controlled trial. *Br J Educ Technol*. 2021;52:680–694.
105. Kim B, Loke YH, Mass P, Irwin MR, Capeland C, Olivieri L, et al. A Novel Virtual Reality Medical Image Display System for Group Discussions of Congenital Heart Disease: Development and Usability Testing. *JMIR Cardio*. 2020;4:e20633.
106. Soulami RB, Verhoye JP, Duc HN, Castro M, Auffret V, Anselmi A, et al. Computer-Assisted Transcatheter Heart Valve Implantation in Valve-in-Valve Procedures. *Innovations*. 2016;11(3):193-200.
107. Riesenkampff E, Rietdorf U, Wolf I, Schnackenburg B, Ewert P, Huebler M, Alexi-Meskishvili V, Anderson RH, Engel N, Meinzer H, Hetzer R, Berger F, Kuehne T. The practical clinical value of three-dimensional models of complex congenitally malformed hearts. *J Thorac Cardiovasc Surg*. 2009;138:571-580.
108. Olivieri LJ, Zurakowski D, Ramakrishnan K, Su L, Alfares FA, Irwin MR, Heichel J, Krieger A, Nath DS. Novel, 3D Display of Heart Models in the Postoperative Care Setting Improves CICU Caregiver Confidence. *World J Pediatr Congenit Heart Surg*. 2018;9:206-13.

Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged.

# CHAPTER 2: DIMENSIONAL ACCURACY AND CLINICAL VALUE OF 3D PRINTED MODELS IN CONGENITAL HEART DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

## 2.1 Introduction

Congenital heart disease (CHD) is one of the commonest birth defects among newborns. Its morphology varies greatly across individuals and each case is unique in its own way, hence the planning of the corrective surgery for complex CHD is often very challenging.[1,2] However, a comprehensive understanding of the patho-morphology of complex CHD is difficult to achieve due to the shortcomings of current visualization techniques which are mainly based on cardiac computed tomography (CT), magnetic resonance imaging (MRI), and echocardiography imaging displayed and being interpreted on two-dimensional (2D) flat screens.[3-9] In order to prevent unexpected findings during surgery, it is imperative to have a precise comprehension of the spatial relationships between the intra-cardiac structures as well as the geometric relationships between the great vessels and surrounding anatomies.[2,5,8-10]

Three-dimensional (3D) printing of anatomical models has shown to resolve the shortcomings of current visualization techniques.[2,4-30] It exploits the information from medical datasets and converts them into patient-specific 3D models that can be tangibly manipulated. As it manifests the cardiac structures in 3D views, observers can better interpret and gain a deeper understanding of the patho-morphology of complex CHD, thus helping surgeons to decide on the best surgical approach.[6,8,12,22] Despite the maturity of 3D printing technology in maxillofacial and orthopaedic fields, its application in the domain of CHD is still very limited.[2,3,31-33] Most of the published studies which investigated the application of 3D printed heart models (3DPHM; i.e., 3D printed anatomical models of the heart) are isolated case reports or case series that are largely anecdotal without strong statistical evidence, as shown in recent systematic reviews.[3,34] There are also no relevant meta-analyses to assess the dimensional accuracy as well as application of 3DPHM in the management of complex CHD. It remains unclear whether 3D printing can significantly improve on how the disease is managed in current clinical practice. Therefore, the aim of this systematic review and meta-analysis is to summarize and evaluate results from existing studies on accuracy and clinical value of 3DPHM.

Based on a previous systematic review, the current use of 3DPHM can be classified into five areas: pre-operative planning, pre-surgical simulation, intra-operative orientation, medical education, and communication in clinical practice.[34] These will be considered the indicators to assess whether 3D printing can improve current clinical practice.

## 2.2 Methods

The systematic review and meta-analysis were strictly performed in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines.[35,36] No ethics approval is required.

### 2.2.1 Search strategy

A comprehensive and systematic literature search was performed in different databases including Proquest, Google Scholar, Scopus, PubMed, and Medline until April 2019. No constraint was applied to the publication date as the authors aim to conduct a comprehensive search on the topic of interest. Keywords like ‘congenital heart disease/defect’, ‘3D printing’, ‘rapid prototyping’, ‘additive manufacturing’, and ‘stereolithography’ were used along with Boolean operators to yield relevant search results. The exact search expressions were ‘congenital heart d*’ AND ‘3D print*’ OR ‘additive manufactur*’ OR ‘rapid prototyp*’ OR ‘stereolithograph*’. In order to increase the relevancy of the search results, the databases were set to only include studies that contain these keywords in the abstract, and to exclude review articles and case reports.

### 2.2.2 Study selection and eligibility criteria

The title and abstract of the studies were screened for eligibility based on pre-designated inclusion and exclusion criteria. The inclusion criteria were as follows: (1) peer-reviewed articles, (2) published in English language, (3) used human data as subjects, (4) findings are based on patient-specific 3DPHM, and (5) studies contained at least one of the following indicators: Accuracy of the 3DPHM, evaluation of the usefulness of 3DPHM in planning surgeries or defining surgical approach, pre-surgical simulation, intra-operative orientation, medical education or training, and communication in clinical practice.

The exclusion criteria were as follows: (1) used non-human subjects, (2) studies about 3D bio-printing, (3) studies using virtual 3D heart models, and (4) case reports, reviews, commentary, or studies with only an abstract (or conference abstracts).

### 2.2.3 Data extraction

The full-text of the studies that meets the eligibility criteria were sought. Data extraction was performed manually by two independent reviewers (IL and ZS). There was no discrepancy between the reviewers. The following information was extracted from the chosen articles: Author, year of publication, study design, imaging modality, segmentation software, utility of 3DPHM, CHD types, and dimensional accuracy. Continuous variables were recorded in the form of arithmetic means and descriptive statistics if they were available in the study. The extracted data was tabulated in Microsoft Excel spreadsheet for analysis.

### 2.2.4 Quality assessment

The quality of the included articles was appraised using the risk of bias tools published on the National Institutes of Health (NIH) website by the same two independent reviewers according to their study design.[37] Each item on the risk of bias tools was scored with 'Yes' and 'No'. The number of 'Yes' was then tallied to decide if the article was of 'good', 'fair', or 'poor' quality. The author considered articles which scored 'Yes' in more than two-thirds of the questions as 'good' quality, more than one-third as 'fair' quality, and less than one-third as 'poor' quality.

### 2.2.5 Statistical analysis

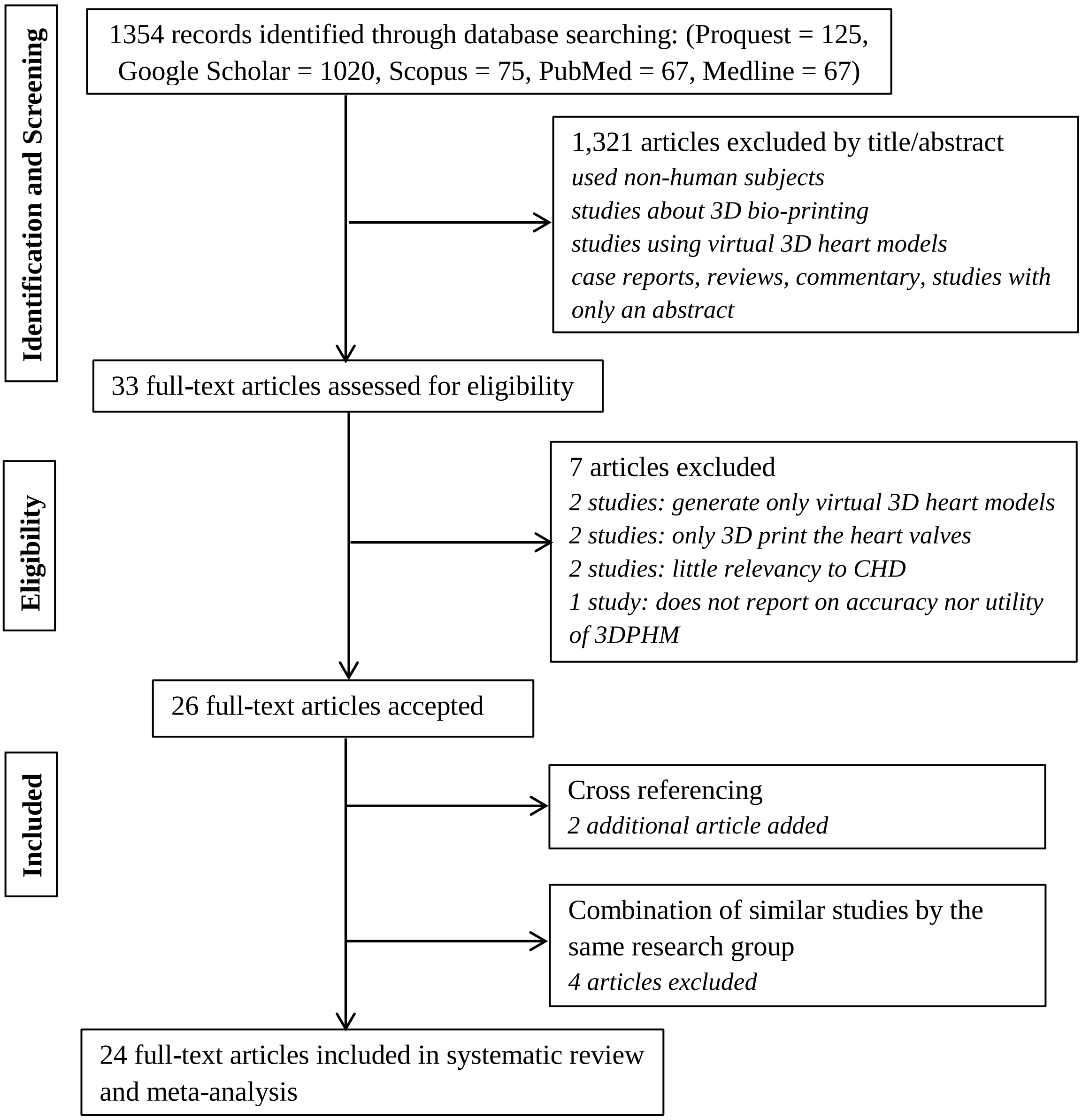
Statistical analyses were performed using R software, version 3.4.1 (http://www.r-project.org/), using the "metamean" and "metacont" functions in the R package meta, for single arm trials and two arms trials respectively. Single arm trials are studies which only consist of an experimental group, whereas two arms trials are studies consisting of both control and experimental groups. Cochran's Q test was used to determine the homogeneity of the study means. Homogeneity of the study variances was tested with Bartlett's test for the single arm trial. Null hypothesis (i.e., no statistical difference between the study data) is accepted only when p-values for both homogeneity tests are at least 0.05. Otherwise, the study data would not be pooled. The choice of 'random effects model' or 'fixed effect model' is determined by assessing whether there is any group structure present in the list of studies. If there is none, the fixed effect model is employed.

## 2.3 Results

### 2.3.1 Literature search

The literature search retrieved a total of 1354 search results (125 from Proquest, 1020 from Google Scholar, 75 from Scopus, 67 from PubMed, and 67 from Medline). Following screening of the titles and abstracts resulted in exclusion of 1321 articles, as they were either non-relevant to the scope of review or did not meet the selection criteria. Full manuscripts were sought for the remaining 33 studies. Seven of them were further excluded for the following reasons: generation of virtual 3D models and non-relevant to 3D printing (n = 2), fabrication of only the heart valves (n = 2), not directly relevant to CHD (n = 2), and neither reported accuracy nor the utility of the 3DPHM (n = 1). Two additional articles were obtained from cross-referencing, resulting in a total of 28 selected articles. Among these publications, some were conducted by the same research groups. In order to remove bias in the results of this review, data from studies by the same research groups that are highly similar were combined and treated as one study. The similarities between these studies were investigated based on their study characteristics. This results in a total of 24 studies included in this systematic review and meta-analysis. Figure 2.1 outlines the study selection process.

**Figure 2.1:** Flow chart of the study selection process.



3D, three-dimensional; 3DPHM, three-dimensional printed heart models; CHD, congenital heart disease.

### 2.3.2 Study characteristics

The characteristics of all included articles were summarized and are shown in Table 2.1 and Figure 2.2. Several publications that were conducted by the same research groups with similar characteristics (4 studies by Biglino et al. and 2 studies by Costello et al.) were combined and treated as one study, with only their most recent publication included in the systematic review. Table 2.1 highlights the 24 publications that are included in the review, whereas Figure 2.2 displays results with duplicates removed.

As demonstrated in Figure 2.2, the study design employed for this research topic has a broad spectrum, however is mainly dominated by case series. CT angiography (CTA) is the predominant imaging modality used for generation of 3DPHM, followed by cardiac magnetic resonance (CMR), and echocardiography. There are a range of segmentation software tools used for cardiac segmentation, either open-source or commercial packages. Some studies utilized a mixture of different software for segmentation, in this case all of the software used in the study were counted and included in the frequency histogram in Figure 2.2. Materialise Mimics (Materialise HQ, Leuven, Belgium) is the mostly used software, with 12 out of 24 studies reporting its' application for cardiac image segmentation.

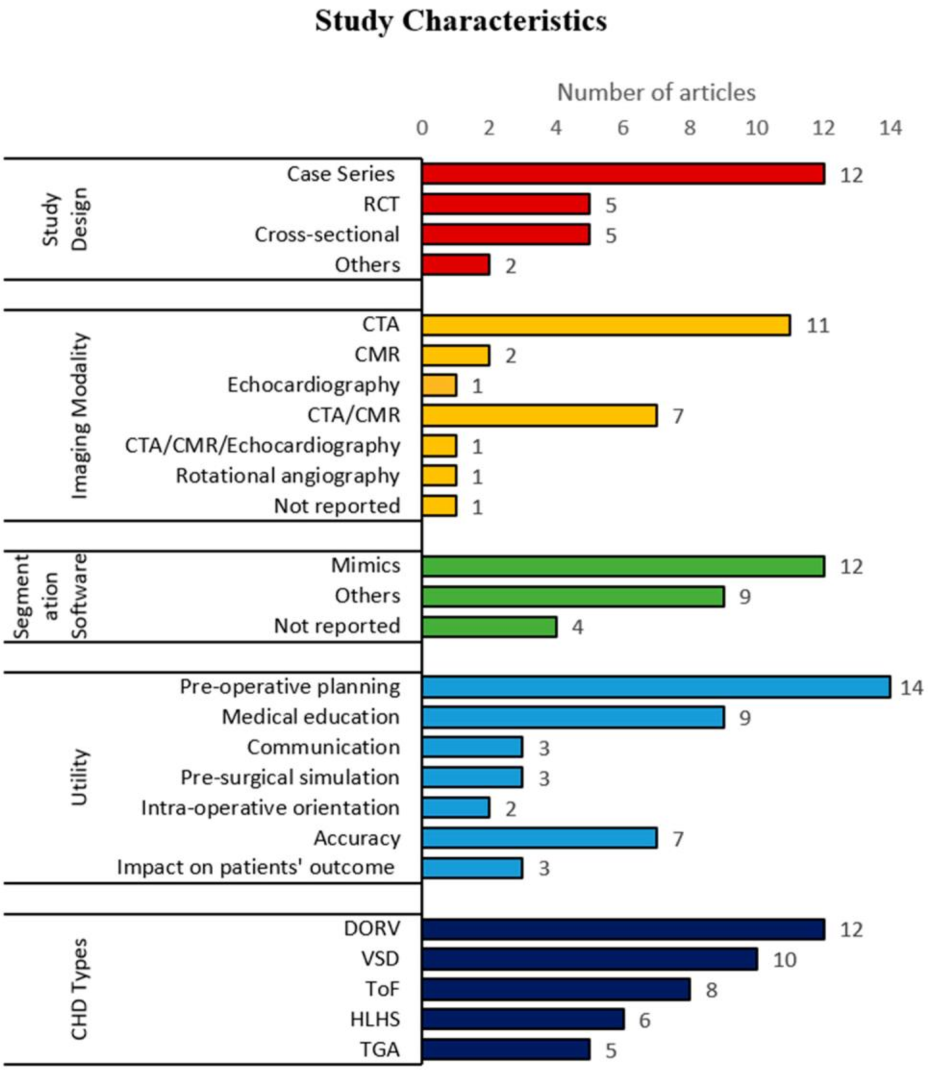
As mentioned before, 3DPHM have a range of applications. Some selected studies investigated more than one utility of the 3DPHM, in this case all of the utilities investigated are included in the count. Some studies reported important information on how the 3DPHM improve the patients' outcomes (e.g. the length of cardiopulmonary bypass time, aortic cross-clamp time, mechanical ventilation time, duration of the surgery, patients' readmission rate, length of hospitalization, and mortality rate), this type of information was classified under 'impact on patients' outcome'. It is found that pre-operative planning is reported as the primary utility of 3DPHM (Figure 2.2). The 3DPHM were generated for different types of CHD. Figure 2.2 lists the top five commonest types of CHD that were 3D printed. The most common type of CHD that has been 3D printed is the double outlet right ventricle (DORV). For the count for CHD types, the following rules apply:

1. In most of the cases, primary CHD is accompanied by secondary CHD. For example, DORV is usually accompanied by ventricular septal defect (VSD). In such cases, only the primary CHD is counted.

2. Each type of CHD is counted once per study, which means the number of cases per study does not contribute to the count.

3. CHD that have been repaired are also included in the count. For example, the study that produced 3DPHM of repaired TGA is counted.

**Figure 2.2:** Horizontal histogram of the characteristics of the included studies.



CHD, congenital heart disease; CMR, cardiac magnetic resonance; CTA, computed tomography angiography; DORV, double outlet right ventricle; HLHS, hypoplastic left heart syndrome; RCT, randomized controlled trial; TGA, transposition of great arteries; ToF, Tetralogy of Fallot; VSD, ventricular septal defect.

**Table 2.1:** Characteristics of the included studies.

| First Author/ Year | Study Design | CHD types | Imaging modality | Segmentation software | Utility |
|---|---|---|---|---|---|
| ***Lau et al. 2018** [2] | Cross-sectional | DORV with sub-aortic VSD | CTA | Mimics | Accuracy, pre-operative planning, communication, medical education |
| ***Ma et al. 2015** [5] | Case series | ToF, ToF with ASD, ToF with PDA | CTA | Philips EBW Comp-Cardiac post-processing software | Accuracy, intra-operative orientation, impact on patients' outcomes [a] |
| ***Riesenkampff et al. 2009** [6] | Case series | DORV, VSD, LVOTO, CoA, RVOTO, AVSD, pulmonary atresia, pulmonary stenosis, TGA, congenitally corrected TGA | CTA/CMR | Medical Imaging and Interaction Toolkit | Pre-operative planning |
| ***Schmauss et al. 2015** [7] | Case series | subpulmonary VSD, HLHS, pulmonary atresia and hypoplastic right ventricle, aortic stenosis | CTA/CMR | Amira, MeVisLab-Environment | Pre-operative planning, intra-operative orientation, pre-surgical simulation |
| ***Shiraishi et al. 2009** [8] | Case series | CoA, DORV, VSD, HLHS | CTA | NR | Pre-operative planning, pre-surgical simulation |
| ***Valverde et al. 2017** [9] | Prospective case-crossover | DORV, Complex TGA, univentricle, VSD, criss-cross heart, LVOTO, discordant AV and VA connections | CTA/CMR | ITK Snap | Accuracy, pre-operative planning, communication, medical education |

| | | | | | |
|---|---|---|---|---|---|
| ***Bhatla et al. 2017** [10] | Case series | Complex muscular VSD, DORV | CTA/CMR | Mimics | Pre-operative planning |
| ***Ejaz et al. 2013** [16] | RCT | NR | CTA | Advance Workstation (GE Health Systems), Mimics | Medical education, pre-operative planning |
| ***Garekar et al. 2016** [17] | Case series | DORV with remote VSD | CTA/CMR | NR | Pre-operative planning |
| ***Hoashi et al. 2018** [18] | Case series | DORV, TGA, congenitally corrected TGA, interrupted aortic arch Type B, ToF and MAPCA, HLHS, functional single ventricle, mitral stenosis, AVSD | CTA | NR | Pre-operative planning, pre-surgical simulation |
| ***Loke et al. 2017** [19] | RCT | unrepaired ToF, repaired ToF | CTA/CMR/ echocardiography | Mimics | Medical education |
| ***McGovern et al. 2017** [20] | Case series | univentricular heart, abnormal systemic or pulmonary venous drainage, dextrocardia, TGA, HLHS | CTA | Mimics | Pre-operative planning |
| ***Ngan et al. 2006** [21] | Case series | VSD, pulmonary atresia, MAPCA | CTA | Mimics | Pre-operative planning |
| ***Olejník et al. 2017** [22] | Case series | interrupted aortic arch type A with aortopulmonary window type 2, dextroversion, DORV with subaortic VSD, CoA, ToF | CTA | 3D Slicer | Accuracy, pre-operative planning |
| ***Olivieri et al. 2015** [23] | Case series | VSD | echocardiography | Mimics | Accuracy |

| | | | | | |
|---|---|---|---|---|---|
| ***Olivieri et al. 2016** [24] | Cross-sectional | HLHS, total anomalous pulmonary venous connection, supravalvar aortic stenosis, DORV with hypoplastic and stenotic aortic valve and hypoplastic aortic arch, aortic regurgitation, right partial anomalous pulmonary venous connection, left pulmonary artery sling, RVOTO, truncal valve regurgitation, double aortic arch, TGA with VSD and pulmonary atresia | CTA/CMR | Mimics | Medical education |
| ***Parimi et al. 2018** [25] | Case series | HLHS post Glenn shunt, CoA, ToF with MAPCAs, pulmonary atresia | Rotational angiography | Osirix | Accuracy |
| ***Ryan et al. 2018** [26] | Case control study | pulmonary atresia, ToF, DORV, truncus arteriosus, single ventricle | CTA/CMR | Mimics | Pre-operative planning, impact on patients' outcomes |
| ***Su et al. 2018** [27] | RCT | 3 different subtypes of VSD | CTA | NR | Medical education |
| ***Wang et al. 2017** [28] | RCT | VSD, pulmonary atresia, MAPCA | CTA | Mimics | Medical education |
| ***White et al. 2018** [29] | RCT | 3 different subtypes of VSD, ToF | NR | Philips IntelliSpace Portal | Medical education |
| ***Zhao et al. 2018** [30] | Cross-sectional | DORV | CTA | Mimics | Accuracy, pre-operative planning, impact on patients' outcomes |

| | | | | | |
|---|---|---|---|---|---|
| ***Biglino et al. 2017a** [4] | Pre-post study | ToF, TGA, CoA, pulmonary atresia, aortic stenosis with dilated ascending aorta, DORV, Ebstein's anomaly | CMR | Simpleware | Communication |
| **Biglino et al. 2015a** [11] | RCT | CoA, pulmonary atresia, ToF, TGA, aortic stenosis, bicuspid aortic valve, total anomalous pulmonary venous drainage, double-inlet left ventricle | CMR | Mimics | Communication |
| **Biglino et al. 2015b** [12] | Cross-sectional | TGA, ToF, pulmonary atresia, CoA, HLHS, TCPC | CMR | Mimics | Pre-operative planning, medical education, communication |
| **Biglino et al. 2017b** [13] | Cross-sectional | repaired TGA, CoA, ToF, pulmonary atresia with intact ventricular septum, palliated HLHS | CMR | NR | Medical education |
| ***Costello et al. 2015** [15] | Pre-post study | 5 different subtypes of VSD | CMR | Mimics | Medical education |
| **Costello et al. 2014** [14] | Pre-post study | 5 different subtypes of VSD | CMR | Mimics | Medical education |

* = articles that were included in the review. a patients' outcome includes length of cardiopulmonary bypass time, aortic cross-clamp time, mechanical ventilation time, duration of the surgery, patients' readmission rate, length of hospitalization, and mortality rate. 3DPHM, three-dimensional printed heart models; AV, atrio-ventricular; AVSD, atrio-ventricular septal defect; ASD, atrial septal defect; CHD, congenital heart disease; CMR, cardiac magnetic resonance; CoA, coarctation of aorta; CTA, computed tomography angiography; DORV, double outlet right ventricle; HLHS, hypoplastic left heart syndrome; LVOTO, left ventricular outflow tract obstruction; MAPCA, major aortopulmonary collateral arteries; NR, not reported; PDA, patent ductus arteriosus; RCT, randomized controlled trial; RVOTO, right ventricular outflow tract obstruction; SVC, superior vena cava; TCPC, total cavopulmonary connection; TGA, transposition of great arteries; ToF, Tetralogy of Fallot; VA, ventriculoarterial; VSD, ventricular septal defect.

### 2.3.3 Risk of bias of the included studies

Table 2.2 summarizes the quality of the 24 studies included in the review (good, fair, or poor). The scores of individual items in the assessment tool can be found in Appendices C1-C5.

**Table 2.2:** Quality of the included studies assessed by National Institute of Health assessment tools.

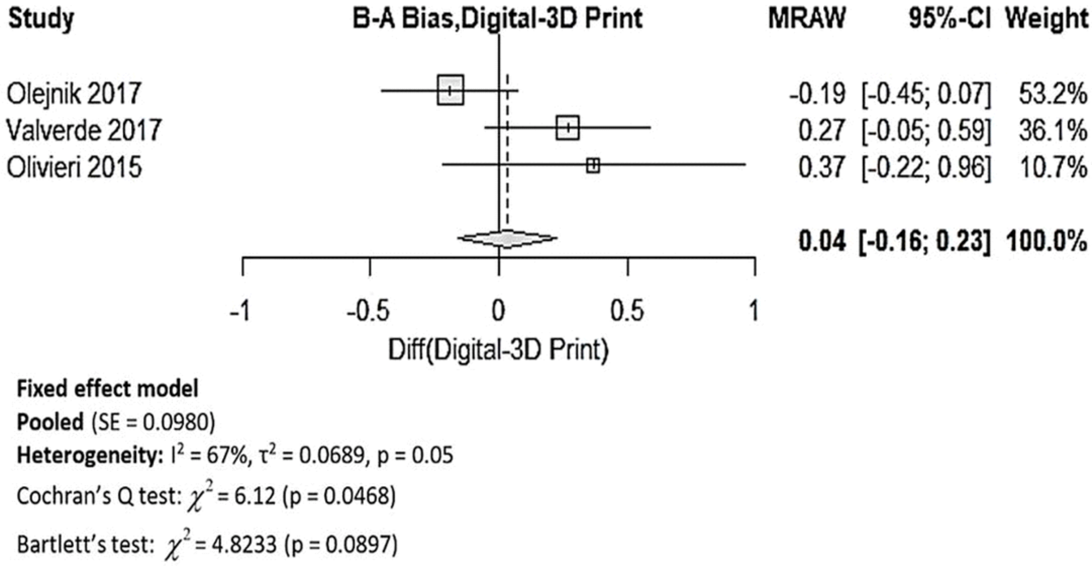
| **Studies** | **Quality Rating** |
|---|---|
| Lau et al. 2018 [2] | Fair |
| Biglino et al. 2017a [4] | Fair |
| Ma et al. 2015 [5] | Good |
| Riesenkampff et al. 2009 [6] | Fair |
| Schmauss et al. 2015 [7] | Good |
| Shiraishi et al. 2009 [8] | Fair |
| Valverde et al. 2017 [9] | Fair |
| Bhatla et al. 2017 [10] | Good |
| Costello et al. 2015 [15] | Fair |
| Ejaz et al. 2013 [16] | Fair |
| Garekar et al. 2016 [17] | Good |
| Hoashi et al. 2018 [18] | Good |
| Loke et al. 2017 [19] | Fair |
| McGovern et al. 2017 [20] | Good |
| Ngan et al. 2006 [21] | Good |
| Olejník et al. 2017 [22] | Good |
| Olivieri et al. 2015 [23] | Good |
| Olivieri et al. 2016 [24] | Fair |
| Parimi et al. 2018 [25] | Good |
| Ryan et al. 2018 [26] | Good |
| Su et al. 2018 [27] | Good |
| Wang et al. 2017 [28] | Fair |
| White et al. 2018 [29] | Good |
| Zhao et al. 2018 [30] | Fair |

### 2.3.4 Meta-analyses

#### *2.3.4.1 Dimensional accuracy of 3DPHM*

Upon data extraction, it was noticed that the data in the studies were presented very differently. Out of the 7 studies which reported the dimensional accuracy of 3DPHM,[2,5,9,22,23,25,30] 3 studies reported only the correlation coefficient between the 3DPHM and the measurements based on the medical images, which is unsuitable for meta-analysis.[2,25,30] The other 4 studies provided means and standard deviations of the measurements, in which inverse variance weight of the individual study is able to be calculated.[5,9,22,23] Out of these 4 studies, one study compared the 3DPHM with in vivo surgical measurements, which is different from the other 3 studies that compared 3DPHM with digital images measurements.[5] As a result, only 3 studies were included in the quantitative synthesis of accuracy of 3DPHM,[9,22,23] with mean bias and standard deviations (in millimeters) between the measurements of the 3DPHM and digital images as input data. Figure 2.3 demonstrates the forest plot generated for this meta-analysis. The pooled results demonstrated that the 3DPHM marginally underestimated the measurement, with a mean deviation of 0.04 mm, 95% CI (−0.16, 0.23) compared to the digital medical images. Cochran's Q test demonstrates that there is significant variation among the mean bias (p = 0.0468). There is no evidence against the assumption of variance homogeneity (p = 0.0897). Despite so, the studies should not be pooled, as the first homogeneity test fails.

**Figure 2.3:** Forest plot for mean bias of the 3DPHM measurement and the digital images measurement.



**Fixed effect model**

**Pooled** (SE = 0.0980)

**Heterogeneity:** $I^2 = 67\%$, $\tau^2 = 0.0689$, $p = 0.05$

Cochran's Q test: $\chi^2 = 6.12$ ($p = 0.0468$)

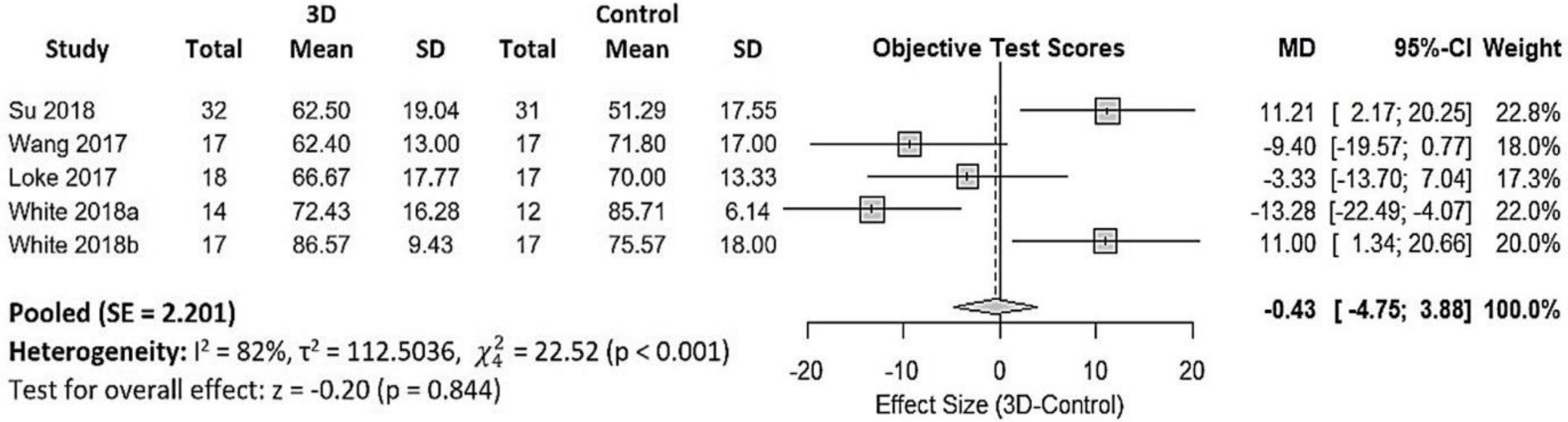
Bartlett's test: $\chi^2 = 4.8233$ ($p = 0.0897$)

3D, three-dimensional; B–A, Bland–Altman; MRAW, raw mean difference; CI, confidence interval; SE, standard error.

#### *2.3.4.2 3DPHM in medical education*

Twelve studies reported utility of 3DPHM in medical education.[2,9,12–16,19,24,27–29] However, 7 of them used a Likert-type questionnaire to assess the gain in knowledge among the participants subjectively,[2,9,12–15,24] and it is not known if the questionnaires used were tested for validity and reliability. Hence, this type of data is not suitable for quantitative synthesis. One study did not provide standard deviation of the data, hence was excluded from the meta-analysis.[16] This leads to 4 eligible studies for quantitative synthesis of 3DPHM in medical education.[19,27–29] These 4 studies are all two-arm trials which assessed the gain in knowledge among the participants by comparing test scores of the control group and 3DPHM group. The input data were converted to percentages as common unit for meta-analysis. Figure 2.4 is the forest plot generated for the meta-analysis. Please note that the study by White et al. had two independent groups of participants, in which one of the groups attended lecture on simple CHD, and the other group attended lecture for complex CHD. Therefore, these two separate observations were reflected in the forest plot as ‘White 2018a’ and ‘White 2018b’. The pooled results demonstrated that the test scores in the 3DPHM group is lower than the control group, however this did not reach statistical significance (−0.43, 95% CI (−4.75, 3.88), $p = 0.844$). Cochran’s Q test demonstrates that there are significant variations among the mean test scores and the variances of the studies ($p < 0.001$). Hence, the studies should not be pooled.

**Figure 2.4:** Forest plot for mean differences in test scores between the 3DPHM and the control groups.



| Study | 3D Total | 3D Mean | 3D SD | Control Total | Control Mean | Control SD | MD | 95%-CI | Weight |
|---|---|---|---|---|---|---|---|---|---|
| Su 2018 | 32 | 62.50 | 19.04 | 31 | 51.29 | 17.55 | 11.21 | [ 2.17; 20.25] | 22.8% |
| Wang 2017 | 17 | 62.40 | 13.00 | 17 | 71.80 | 17.00 | -9.40 | [-19.57; 0.77] | 18.0% |
| Loke 2017 | 18 | 66.67 | 17.77 | 17 | 70.00 | 13.33 | -3.33 | [-13.70; 7.04] | 17.3% |
| White 2018a | 14 | 72.43 | 16.28 | 12 | 85.71 | 6.14 | -13.28 | [-22.49; -4.07] | 22.0% |
| White 2018b | 17 | 86.57 | 9.43 | 17 | 75.57 | 18.00 | 11.00 | [ 1.34; 20.66] | 20.0% |
| **Pooled (SE = 2.201)** | | | | | | | **-0.43** | **[ -4.75; 3.88]** | **100.0%** |

**Heterogeneity:** $I^2 = 82\%$, $\tau^2 = 112.5036$, $\chi^2_4 = 22.52$ ($p < 0.001$)

Test for overall effect: $z = -0.20$ ($p = 0.844$)

3D, three-dimensional; CI, confidence interval; MD, mean difference; SD, standard deviation; SE, standard error.

## 2.4 Discussion

3D printing is an emerging new technology in the domain of cardiovascular surgeries. In spite of the increase in literature that suggested the benefits of this new technology, most of the studies remain as single-center experience with small sample size. There is also a lack of comprehensive systematic reviews and meta-analyses in the literature. A recent systematic review that was published in February 2019 provided an overview of the case studies available in the literature, mainly in the context of pre-operative planning.[38] However, there is neither inclusion nor exclusion criteria mentioned in the systematic review, nor are the steps conducted for the literature search. The comprehensiveness of this study remains questionable. This systematic review and meta-analysis fills in this research gap with a summary of six main utilities of 3DPHM in the context of CHD, which are pre-operative planning, pre-surgical simulation, medical education, intra-operative orientation, communication within clinical practice, and impact on patients' outcome. To the best of our knowledge, this is also the first meta-analysis performed to analyze the accuracy and application of 3DPHM of CHD.

### 2.4.1 Dimensional accuracy of 3DPHM

The image acquisition technique and the image resolution are two main factors that can directly impact the dimensional accuracy of 3DPHM. CT is found to be the most preferred imaging modality for 3DPHM fabrication, as shown in Figure 2.2.

The meta-analysis of the accuracy of 3DPHM demonstrates high heterogeneity amongst the three studies, hence the pooled mean deviation needs to be interpreted with care. The primary reason for this is likely due to the lack of eligible studies for analysis. It is also important to note that the analysis did not take into account the variability in segmentation methods, segmentation software and reconstruction protocol used, 3D printing methods, measuring methods, the imaging modality, image resolution, and the presence of artefacts in the source imaging data. All of the aforementioned factors can have notable influence on the dimensional accuracy of 3DPHM. Regardless of the heterogeneity, a mean deviation of 0.04 mm between the 3DPHM and medical images is considered negligible. This is because the 3D printing process works with tolerance ranges, and the model usually shrinks after curing of the polymer. Moreover, the image resolution for medical CT and MRI images will never be acquired in a resolution smaller than the range of deviation in daily clinical routine due to the high radiation dose from CT. Thus, mean deviation of 0.04 mm will not have any influence on the observation on the 3DPHM. Furthermore, all studies reported that the mean bias between the 3DPHM and the digital images are not significant, as indicated by the forest plot in Figure 2.3 (the confidence interval horizontal line for all three studies crosses over the vertical line).

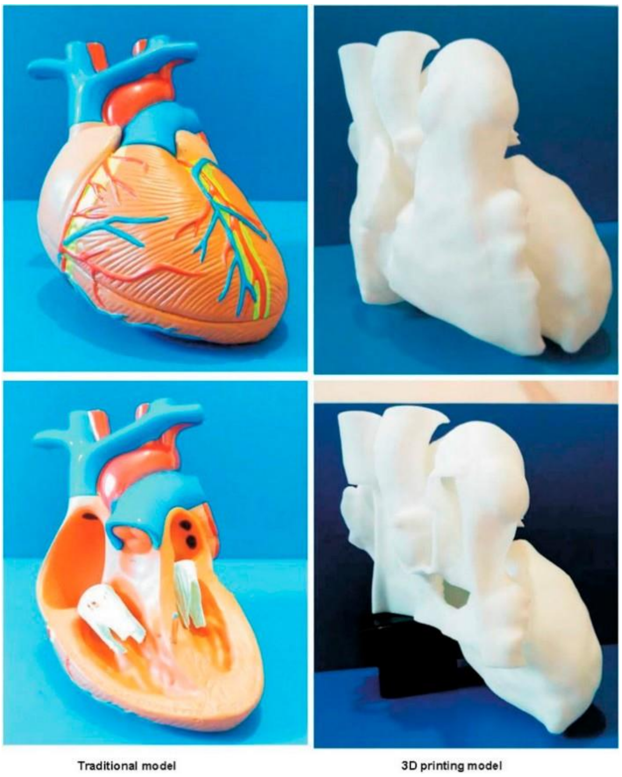
Additionally, all four studies that reported the correlation coefficient between the measurements of 3DPHM and the digital images indicated strong correlation ($r > 0.98$).[2,23,25,30] All the findings from the studies are directed towards a conclusion that the 3DPHM are highly accurate.

### 2.4.2 3DPHM in medical education

3DPHM were reported as a novel teaching approach when compared to the traditional way with 2D diagrams and sketches.[19,29] The forest plot may give the impression that 3D printing does not contribute to favorable outcomes in medical teaching. However, it is worth noting that White et al. studied the impact of 3DPHM in medical teaching for both simple and complex CHD, and they yielded very different results.[29] This is demonstrated in Figure 2.4 as ‘White 2018a’ and ‘White 2018b’. In the control group that attended VSD seminar (simple CHD), which only have access to images of the virtual models during the lecture, scored higher than the 3DPHM group in the post-lecture test. Interestingly, in the study group that attended ToF seminar (complex CHD), the 3DPHM group scored higher than the control group. In both of the VSD and ToF cohorts, there are no significant differences in their baseline knowledge on CHD.[29] This finding suggests that 3DPHM play a role in teaching and learning of complex CHD that cannot be overlooked, although it might not be as useful in medical teaching for simple CHD such as VSD.

In another study by Wang et al., the author compared the impact of utilizing 3DPHM versus the traditionally made cardiac model in medical teaching (Figure 2.5.[28] Their finding indicated that there is no significant improvement in the test scores among the 3DPHM group. However, the study did not have adequate bias control measures. First, the 3DPHM generated in the study features a simple VSD, whereas the traditional cardiac model demonstrates normal cardiac anatomy. Such difference in the teaching tools already made the two groups incomparable. Second, the medical questions asked in the test do not pertain to the pathology demonstrated on the 3DPHM. The lecture and the test questions in the study were designed for valvular heart diseases, thus in such case, a model with VSD was not the best teaching tool for the pathology of interest.

**Figure 2.5**: Traditional cardiac model (left) and 3D printed model (right) which are used in the study by Wang et al. for two different test groups to compare their role in facilitating medical education.



Reprinted with permission under the open access from Wang et al.[28]

Nevertheless, the findings from the selected studies indicate that 3DPHM can improve the learning experience and satisfaction. This is evidenced in all 12 studies that reported utility of 3DPHM in medical education, with the increased subjective evaluation scores and satisfactory level among the participants in the 3DPHM group.[2,9,12–16,19,24,27–29] In a study that involved 14 clinicians, medical education was ranked as the most relevant utility of 3DPHM. The 3DPHM were also described as more informative than the 2D diagrams.[12] However, due to the subjective nature of the evaluation, the results must be interpreted with care as they are more vulnerable to bias.

### 2.4.3 3DPHM in pre-operative planning

There are 15 studies that assessed the utility of 3DPHM in pre-operative planning. Out of these articles, 12 are observational and descriptive studies in which the surgeons utilized the 3DPHM to plan the surgical procedures before the surgery;[6–10,12,16–18,20–22,26,30] whereas the other 3 studies are quantitative studies that reported surgeons' opinion on 3DPHM in pre-operative planning.[2,12,16] In most of these studies, 3DPHM were only generated when the surgeons could not fully understand the patients' heart anatomy and needed further clarification.[6,7,9,10,17,22] It was reported that the tangible models have helped the surgeons to appreciate the complexity of the anomalous cardiac anatomy better, and even to help them visualize abnormalities that could not be clearly identified on the conventional cardiac images.[9,21] This has assisted the surgeons in defining the best surgical approach for the patients. It is important to note however, that the results from these studies only apply to complex CHD, as the fabrication of 3DPHM were mostly based on surgeons' requests to obtain additional information. This is also evidenced in the finding of this review, with DORV as the commonest type of CHD that have been 3D printed. DORV is considered as complex CHD, as it is most often accompanied by a broad spectrum of anomalies. Hence, the perceived clinical value of 3DPHM demonstrated in these studies may not be the same when it comes to simple CHD.[9]

In a multi-center study involving 10 international hospitals, it was reported that the 3DPHM acted as the deciding factor to alter the surgical decision in 19 out of 40 cases.[9] All 40 cases were assessed twice by the surgeons for operative planning, in which the first evaluation was based on conventional imaging data with virtual 3D reconstruction, and the second evaluation with the 3DPHM. The surgical plans derived from both of the evaluations were then compared. Three patients who were originally considered ineligible to undergo surgery based on conventional operative planning, were identified as surgical candidates based on 3DPHM planning and underwent successful surgical correction. The 3DPHM provide additional spatial information of the cardiac anatomy which is difficult to obtain from the 2D screen display, allowing the surgeons to appreciate potential surgical complications and modify the approach if necessary.[9]

In another study conducted by Ryan et al., 33 cases with 3DPHM generated were studied retrospectively with regards to their 30-days admission and mortality rate, as well as the duration of surgery.[26] These results were compared with another 113 cases with similar types of lesions which received routine operative planning. The findings demonstrated an overall reduction in mean operative time for the 3DPHM group. These results echo with the findings from another study by Zhao et al., who compared 8 cases in the 3DPHM group with 17 cases in the control group.[30] The 3DPHM group had a much shorter operative time, cardiopulmonary bypass time, aortic cross-clamping time, and mechanical ventilation time than the control group. The findings in both of these studies implicitly indicate that the 3DPHM play a critical role in enhancing pre-operative planning, with a possible added value to reduce the costs for surgery following the reduction in duration of surgery. However, it is important to note that both of these findings did not achieve statistical significance. Insufficient statistical powering is more likely to be due to small sample size, rather than non-favorable outcomes.[26]

### 2.4.4 3DPHM in communication within medical practice

All of the studies that reported the utility of 3DPHM in communication are questionnaire-based studies. The targeted population is variable, with 3 studies targeted at clinicians, radiologists, surgeons, and cardiologists,[2,9,12] whereas the other 2 targeted at patients and parents.[11,13] From the health professionals' perspective, both the studies by Valverde et al. and Lau et al. yielded very similar results where most of the participants agreed that the 3DPHM are useful in enhancing communication with other colleagues as well as patients and parents.[2,9] In a randomized controlled trial (RCT) in which 3DPHM were used during the consultation with parents, the cardiologists remarked that the use of 3DPHM resulted in a better interaction with the parents. This is evidenced by a 5-minutes-longer consultation duration on average in the 3DPHM group when compared to the control group ($21 \pm 10$ vs. $16 \pm 7$ min, $p = 0.02$), which implicitly indicated that the 3DPHM stimulated curiosity, resulting in a more detailed discussion among the doctors and parents.[11] Interestingly, in another study by the same research group which involved 14 clinicians, communication was ranked as the least relevant utility compared to medical teaching, pre-operative planning, and research. However, this should not be perceived as 3DPHM is unbeneficial in improving communication, as 5 clinicians still ranked communication as the most relevant utility of 3DPHM.[12]

From the non-professionals' (patients and parents) point of view, most of them are very satisfied with the 3DPHM used in their consultation.[11,13] Despite their satisfaction, there was no significant increase in short-term knowledge acquisition among the experimental group of 45 parents.[11] Surprisingly, there was even a decrease in the cardiologist-assessed parental knowledge compared to the control group of 53 parents ($7.0 \pm 1.9$ vs. $8.0 \pm 1.7$).[11] Another study carried out by the same group of researchers but with adolescent patients as the participants yielded result that is vastly different. There is a significant objective increase in knowledge acquisition in the 3DPHM group ($p < 0.001$) as well as a subjective increase in their confidence in explaining their heart condition to others.[13] Nevertheless, a minor group of patients in the 3DPHM group (30%) reported increase in anxiety level after their consultation.[11]

Instead of replacing the traditional approach that is to communicate based on medical images, 3DPHM seem to be acting as a complementary tool in the patient-doctor communication. In the study by Lau et al., the health professionals were asked if they prefer the 3DPHM or digital images to communicate with the patients or their colleagues. Sixty-seven percent of the participants indicated that they prefer to use both as a medium for communication.[2] This aligns with the finding in another study by Biglino et al., in which the teenage patients prefer to have digital simulations shown on the monitor in addition to the 3DPHM.[12]

The clinical value of 3DPHM in enhancing communication within clinical practice remains arguable. Further research based on larger sample size from different stakeholders is warranted to holistically study the impact of 3DPHM on communication improvement.

### 2.4.5 Limitations

The findings of this systematic review and meta-analysis are subjected to several limitations. First, even though there are 28 articles in total that met the inclusion criteria, only 24 were included in the final review, due to the similarities between studies by the same research groups. Out of the 24 studies, only 7 studies met the statistical requirements and are eligible for meta-analysis. One of the main reasons is because most of the studies are case series and did not provide quantitative data which is required for meta-analysis. However, this is due to case series being the dominant study design in the current literature, rather than a problem in the study selection process. Another reason is the lack of common outcomes assessment methods, which impede the authors from grouping the results for data synthesis. One solid example would be the measurement of the operative time to investigate if the use of 3DPHM in pre-operative planning can result in a reduction of surgery duration. Both the studies by Ryan et al. and Zhao et al. reported the operative time, however Zhao et al. did not define whether the operative time measured includes the time used to transport patients in and out of the operating theatre.[26,30] Second, the meta-analyses in this study demonstrated heterogeneity among the selected studies. This indicates that the study results should not be pooled. The pooled mean differences shown in the forest plot should be interpreted very carefully. This high heterogeneity is most likely due to the lack of studies eligible for meta-analysis.

## 2.5 Conclusion and implications of future work

Despite the limitations, this systematic review has analyzed the current literature with results that can be used to guide further research in this field. The results demonstrate that 3DPHM are dimensionally accurate. However, data from more studies are required to measure the mean deviation of the 3DPHM from the medical images measurement.

Even though 3DPHM might not increase the users' short-term knowledge on CHD, it was reported to improve the learning experience and satisfaction level among the users. Future studies should aim to investigate the long-term impact on the knowledge acquisition among different stakeholders, such as students, patients and parents, and junior doctors.

Meta-analysis of the utility of 3DPHM in pre-operative planning was not possible in this study, due to the nature of the data being difficult to quantify. Nevertheless, the finding of the review suggests that 3DPHM play an important role in facilitating pre-operative planning of complex

CHD cases, especially in helping surgeons to gain a deeper understanding in the complex patho-morphology of the diseased heart. Future studies are suggested to quantitatively measure whether the use of 3DPHM reduces the operative time, hospital admission duration, as well as morbidity and mortality rate. From there, a cost-benefit analysis can be carried out to evaluate if 3D printing of CHD is worthwhile in the healthcare industry.

The clinical value of 3DPHM in enhancing communication in clinical practice is arguable. Even though both health professionals and non-professionals are satisfied with the use of 3DPHM during the consultation, there is a lack of quantitative evidence to suggest the increase in parental knowledge with the use of 3DPHM, nor is there evidence to suggest the reduction in consultation time. However, with only 5 studies that investigated the utility of 3DPHM in this area, a solid conclusion could not be drawn. Future studies should aim to measure the impact of 3DPHM on the reduction in consultation time, as well as the knowledge acquisition among the patients and parents.

Last but not least, a comprehensive cost-benefit analysis for implementation of 3D printing technology in cardiovascular surgeries lacks in the current literature and this needs to be addressed by future studies.

## 2.6 References

1. Valverde I, Gomez G, Gonzalez A, Suarez-Mejias C, Adsuar A, Coserria JF, et al. Three-dimensional patient-specific cardiac model for surgical planning in Nikaidoh procedure. *Cardiol Young*. 2015;25:698–704.
2. Lau I, Liu D, Xu L, Fan Z, Sun Z. Clinical value of patient-specific three-dimensional printing of congenital heart disease: Quantitative and qualitative assessments. *PLoS One*. 2018;13: e0194333.
3. Sun Z, Lau I, Wong YH, Yeong CH. Personalized Three-Dimensional Printed Models in Congenital Heart Disease. *J Clin Med*. 2019;8(4):522.
4. Biglino G, Koniordou D, Gasparini M, Capelli C, Leaver L, Khambadkone S, et al. Piloting the use of patient-specifc cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr Cardiol*. 2017;38:813-8.
5. Ma XJ, Tao L, Chen X, Li W, Peng ZY, Chen Y, et al. Clinical application of three-dimensional reconstruction and rapid prototyping technology of multislice spiral computed tomography angiography for the repair of ventricular septal defect of tetralogy of Fallot. *Genet Mol Res*. 2015;14:1301-9.
6. Riesenkampff E, Rietdorf U, Wolf I, Schnackenburg B, Ewert P, Huebler M, Alexi-Meskishvili V, Anderson RH, Engel N, Meinzer H, Hetzer R, Berger F, Kuehne T. The practical clinical value of three-dimensional models of complex congenitally malformed hearts. *J Thorac Cardiovasc Surg*. 2009;138:571-580.
7. 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;47:1044–1052.
8. Shiraishi I, Yamagishi M, Hamaoka K, Fukuzawa M, Yagihara T. Simulative operation on congenital heart disease using rubber-like urethane stereolithographic biomodels based on 3D datasets of multislice computed tomography. *Eur J Cardiothorac Surg*. 2010;37:302-6.
9. Valverde I, Gomez-Ciriza G, Hussain T, Suarez-Mejias C, Velasco-Forte MN, Byrne N, et al. Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study. *Eur J Cardiothorac Surg*. 2017;52:1139-48.
10. Bhatla P, Tretter JT, Ludomirsky A, Argilla M, Latson Jr. LA, Chakravarti S, 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. doi: 10.1007/s00246-016-1489-1

11. Biglino G, Capelli C, Wray J, Schievano S, Leaver L, Khambadkone S, et al. 3D-manufactured patient-specifc models of congenital heart defects for communication in clinical practice: feasibility and acceptability. *BMJ Open*. 2015;5:e007165.
12. Biglino G, Capelli C, Leaver LK, Shievano S, Taylor AM, Wray J. Involving patients, families and medical staff in the evaluation of 3D printing models of congenital heart disease. *Commun Med*. 2015;12:157-69.
13. Biglino G, Capelli C, Koniordou D, Robertshaw D, Leaver L, Schievano S, et al. Use of 3D models of congenital heart disease as an education tool for cardiac nurses. *Congenit Heart Dis*. 2017;12:113-8.
14. Costello JP, Olivieri L, Krieger A, Thabit O, Marshall MB, Yoo SJ, et al. Utilizing Three-Dimensional Printing Technology to Assess the Feasibility of High-Fidelity Synthetic Ventricular Septal Defect Models for Simulation in Medical Education. *World J Pediatr Congenit Heart Surg*. 2014;5:421-6.
15. Costello JP, Olivieri LJ, Su L, Krieger A, Alfares F, Thabit O, 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.
16. Ejaz F, Ryan J, Henriksen M, Stomski L, Feith M, Osborn M, et al. Color-coded patient-specific physical models of congenital heart disease. *Rapid Prototyp J*. 2014;20:336–343.
17. Garekar S, Bharati A, Chokhandre M, Mali S, Trivedi B, Changela VP, et al. Clinical Application and Multidisciplinary Assessment of Three Dimensional Printing in Double Outlet Right Ventricle With Remote Ventricular Septal Defect. *World J Pediatr Congenit Heart Surg*. 2016;7(3):344-50.
18. Hoashi T, Ichikawa H, Nakata T, Shimada M, Ozawa H, Higashida A, et al. Utility of a super-flexible three-dimensional printed heart model in congenital heart surgery. *Interact Cardiovasc Thorac Surg*. 2018;27(5):749-55.
19. Loke YH, Harahsheh AS, Krieger A, Olivieri LJ. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. *BMC Med Educ*. 2017;17:54-61.
20. McGovern E, Kelleher E, Snow A, Walsh K, Gadallah B, Kutty S, et al. Clinical application of three-dimensional printing to the management of complex univentricular hearts with abnormal systemic or pulmonary venous drainage. *Cardiol Young*. 2017;27:1248–1256.
21. Ngan EM, Rebeyka IM, Ross DB, Hirji M, Wolfaardt JF, Seelaus R, et al. The rapid prototyping of anatomic models in pulmonary atresia. *J Thorac Cardiovasc Surg*. 2006;132(2):264-9.

22. Olejník P, Nosal M, Havran T, Furdova A, Cizmar M, Slabej M, et al. Utilisation of three-dimensional printed heart models for operative planning of complex congenital heart defects. *Kardiol Pol*. 2017;75:495–501.
23. Olivieri LJ, Krieger A, Loke YH, 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;28:392–397.
24. Olivieri LJ, Su L, Hynes CF, Krieger A, Alfares FA, Ramakrishnan K, et al. “Just-In-Time” Simulation Training Using 3-D Printed Cardiac Models After Congenital Cardiac Surgery. *World J Pediatr Congenit Heart Surg*. 2016;7:164–168.
25. Parimi M, Buelter J, Thanugundla V, Condoor S, Parkar N, Danon S, et al. Feasibility and Validity of Printing 3D Heart Models from Rotational Angiography. *Pediatr Cardiol*. 2018;39:653–658.
26. Ryan J, Plasencia J, Richardson R, Velez D, Nigro J, Pophal S, et al. 3D printing for congenital heart disease: A single site’s initial three-year experience. *3D Print Med*. 2018;4:1–9.
27. Su W, Xiao Y, He S, Huang P, Deng X. Three-dimensional printing models in congenital heart disease education for medical students: a controlled comparative study. *BMC Med Educ*. 2018;18(1):178.
28. Wang Z, Liu Y, Luo H, Gao C, Zhang J, Dai Y. Is a Three-Dimensional Printing Model Better Than a Traditional Cardiac Model for Medical Education? A Pilot Randomized Controlled Study. *Acta Cardiol Sin*. 2017;33:664.
29. White SC, Sedler J, Jones TW, Seckeler M. Utility of three-dimensional models in resident education on simple and complex intracardiac congenital heart defects. *Congenit Heart Dis*. 2018;13:1045–1049.
30. Zhao L, Zhou S, Fan T, Li B, Liang W, Dong H. Three-dimensional printing enhances preparation for repair of double outlet right ventricular surgery. *J Card Surg*. 2018;33(1):24-7. doi: 10.1111/jocs.13523
31. Zuniga J, Katsavelis D, Peck J, Stollberg J, Petrykowski M, Carson A, et al. Cyborg beast: A low-cost 3d-printed prosthetic hand for children with upper-limb differences. *BMC Res Notes*. 2015;8:10–17.
32. Ebert J, Ozkol E, Zeichner A, Uibel K, Weiss O, Koops U, et al. Direct Inkjet Printing of dental Prostheses Made of Zirconia. *J Dent Res*. 2009;88:673–676.
33. Ploch CC, Mansi CSSA, Jayamohan J, Kuhl E. Using 3D Printing to Create Personalized Brain Models for Neurosurgical Training and Preoperative Planning. *World Neurosurg*. 2016;90:668–674.

34. Lau I, Sun Z. Three-dimensional printing in congenital heart disease: A systematic review. *J Med Radiat Sci*. 2018;65(3):226-236. doi:10.1002/jmrs.268
35. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4:1.
36. Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, Stewart G, et al. Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data: The PRISMA-IPD Statement. *JAMA*. 2015;313:1657–1665.
37. Study Quality Assessment Tools. National Heart, Lung, and Blood Institute. Accessed July 12, 2019. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools
38. Clément B, Moussa AH, Damien B. 3D-Printed Models for Surgical Planning in Complex Congenital Heart Diseases: A Systematic Review. *Front Pediatr*. 2019;7: 23.

Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged.

# CHAPTER 3: QUANTITATIVE AND QUALITATIVE COMPARISON OF LOW- AND HIGH-COST 3D PRINTED HEART MODELS

## 3.1 Introduction

Congenital heart disease (CHD) is a type of birth defect that involves structural anomalies in the heart and major blood vessels.[1] Depending on the severity of the condition, it can cause hemodynamic and functional consequences in patients, requiring corrective surgery to repair the heart.[2,3] Furthermore, the forms of CHD are very diverse, including, but not limited to, double outlet right ventricle (DORV), Tetralogy of Fallot (ToF), ventricular septal defect (VSD), atrial septal defect (ASD), truncus arteriosus, single ventricle, etc.[3,4] In most cases, these conditions co- exist and vary from individual to individual, and there is thus no one-treatment-fits-all surgical option.[5] It is imperative then for clinicians to achieve a comprehensive understanding of the patient's cardiac anatomy during pre- operative assessment to prevent unexpected findings during the surgery, and subsequently reduce surgical time and mortality.[6-20]

Despite this need, current visualization techniques lack the ability to provide a comprehensive viewing of the cardiac anatomy due to the medical images being interpreted from two-dimensional (2D) flat screens. Three-dimensional (3D) printing has consequently been introduced to produce models of exact replication of the heart that are both tangible and tactile.[7-25] Due to the excellent geometric information that 3D printed heart models (3DPHM) provide, this technology has been reported to facilitate the pre-operative planning of corrective surgery, improve patient-doctor communication, and enhance the learning experience of medical students.[5-13,26-35] A recent multicentre study holistically explored the clinical significance of 3DPHM by examining the practices of an international sample of surgeons and cardiologists from different hospitals. In 19 out of 40 cases, the 3DPHM were found to be the deciding factor in altering the surgical decision.[34]

Despite these advantages, the medical application of 3D printing in the domain of complex CHD is still under research and requires further validation. Several centres have adopted this technology and published case reports and series to share their experience in using 3DPHM.[5-12,22-24,27,33,36] The general consensus is that the cost of 3D printing remains one of the main hurdles impeding the wider application of this technology in medicine.[9,19,35,37] There have been a few studies which reported on the generation of 3D printed models using low-cost materials.[6,23,24,38] However, there is no indication of whether these low-cost models are as accurate or useful as the more costly models. This study aimed to provide insights into the reduction of costs in 3D printing through the optimization of 3D printing material selection. Thus, we compared the more expensive 3D printed model (Tango Plus) and the low-cost model [thermoplastic polyurethane (TPU)] in terms of dimensional accuracy and medical applications.

## 3.2 Materials and methods

Ten cases of de-identified cardiac computed tomography angiogram (CCTA) with CHD were retrospectively obtained from the radiology archives of two public hospitals. Of the 10 cases, 2 cases with good image quality and contrast enhancement were chosen for image segmentation. Case 1 features DORV and sub-aortic VSD, whereas case 2 demonstrates ASD. Both cases were imported to a separate workstation for segmentation using a commercially available software package, Mimics Innovation Suite software (Materialise HQ, Leuven, Belgium). Thresholding and region-growing tools were applied to isolate the regions of interest (i.e., the blood pool) from the unwanted structures (i.e., bones, soft tissues, lungs). The mask was also manually edited if the selected region did not correctly reflect the blood pool region. The digital model of the blood pool was then exported in standard tessellation language (STL) to 3-matic, a companion software in Mimics Innovation Suite software, in order to hollow out, smoothen, and split the digital model into two compartments. An arbitrary thickness of 2 mm was also added into the blood pool surface to prevent the model from collapsing during 3D printing.

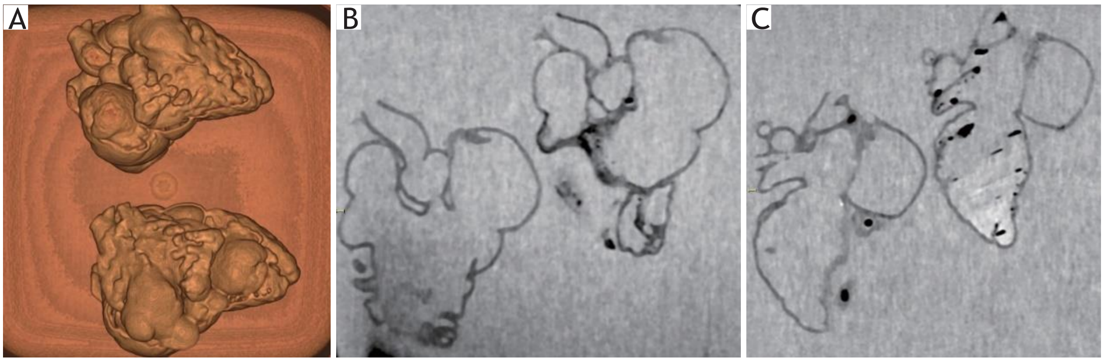
The digital models of both cases were sent for 3D printing using a low-cost material. Due to cost consideration, only the digital model of case 1 was printed using the more costly material. Tango Plus material was chosen as the “expensive” material, as it is able to reproduce models that are flexible and compressible, very much like human heart tissues. Case 1 was hence printed with a commercial Stratasys PolyJet printer (Objet Eden 260VS, Stratasys, United States), with a total printing and cleaning- up time of approximately 10 hours. The cost for 3D printing of the heart in Tango Plus was around AUD 300.

TPU 95A was chosen as the “low-cost” material. It is durable and semi-flexible, although not as flexible as Tango Plus. Both the STL files of these two cases were printed with Ultimaker 2 Extended+ 3D printer from Ultimaker BV (Geldermalsen, The Netherlands) using fused filament fabrication (FFF) technology, with an average total printing and cleaning-up time of approximately 100 hours. The average cost for 3D printing of the heart in TPU 95A was around AUD 50.

## 3.3 Results

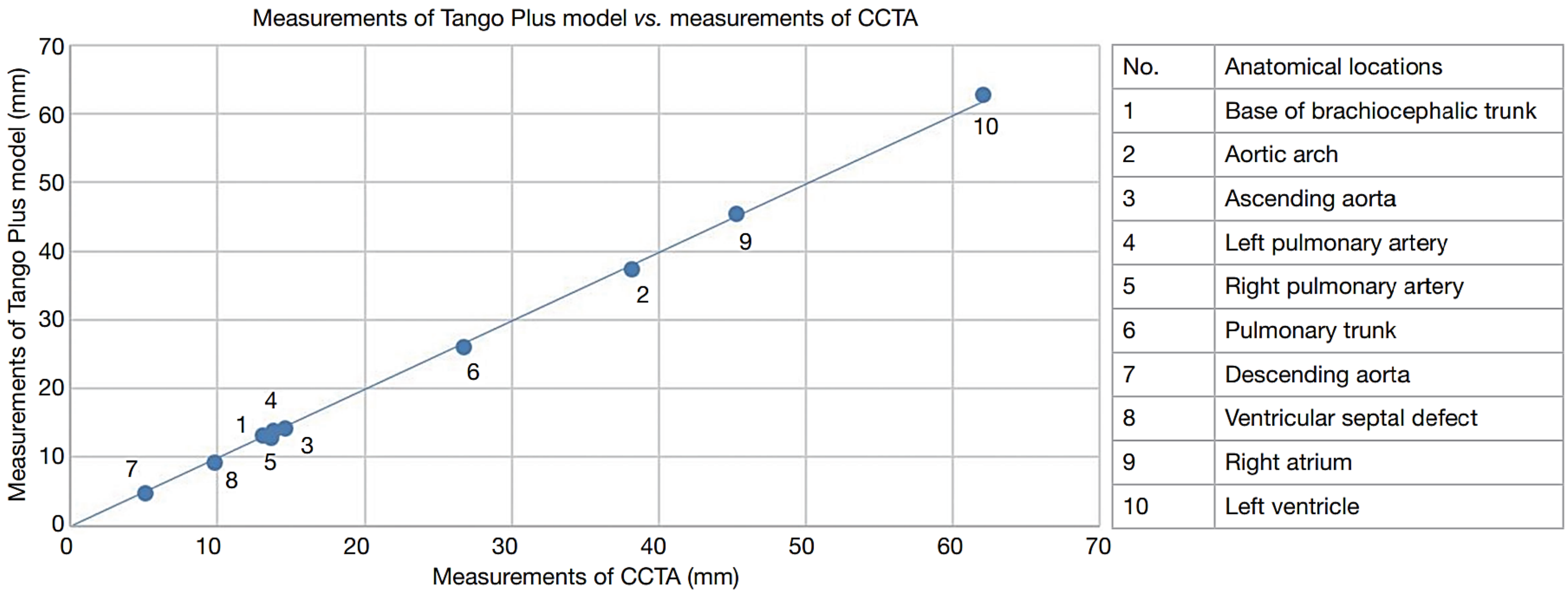
The dimensional accuracy of the 3DPHM was investigated. A contrast-enhanced CT scan was performed on both the Tango Plus and TPU models of case 1 using a contrast-enhanced CT chest protocol. Both models were immersed in a water-contrast mixture of 10% contrast and 90% water to obtain a CT attenuation of 200 Hounsfield units (HU) which is similar to routine CCTA (Figure 3.1). Measurements were taken at 10 different anatomical locations using the "ruler" feature in the Horos software (Horos Project, licensed under the GNU Lesser General Public License, version 3.0), which is an open-source Digital Imaging and Communications in Medicine (DICOM) viewer. The results were compared with the measurements obtained from the original CCTA. In order to reduce observer bias, each measurement was repeated 3 times by 2 independent observers. It was found that the Tango Plus heart model deviated from the measurements in the original data by a 0.23 mm average, whereas the TPU model deviated from the measurements in the original data by a 0.54 mm average. However, measurements from both models were strongly correlated with those of the original CCTA (r = 0.99), as demonstrated in Figures 3.2 and 3.3.

**Figure 3.1:** Cardiac CT scan of 3DPHM using different printing materials.



(A) 3D reconstruction showing the 3DPHM without contrast medium (top: Tango Plus material, bottom: TPU material). (B,C) Coronal reformatted contrast-enhanced CT images showing 3DPHM with Tango Plus (left) and TPU (right) materials. More air bubbles are seen in the model with TPU material. TPU, thermoplastic polyurethane.

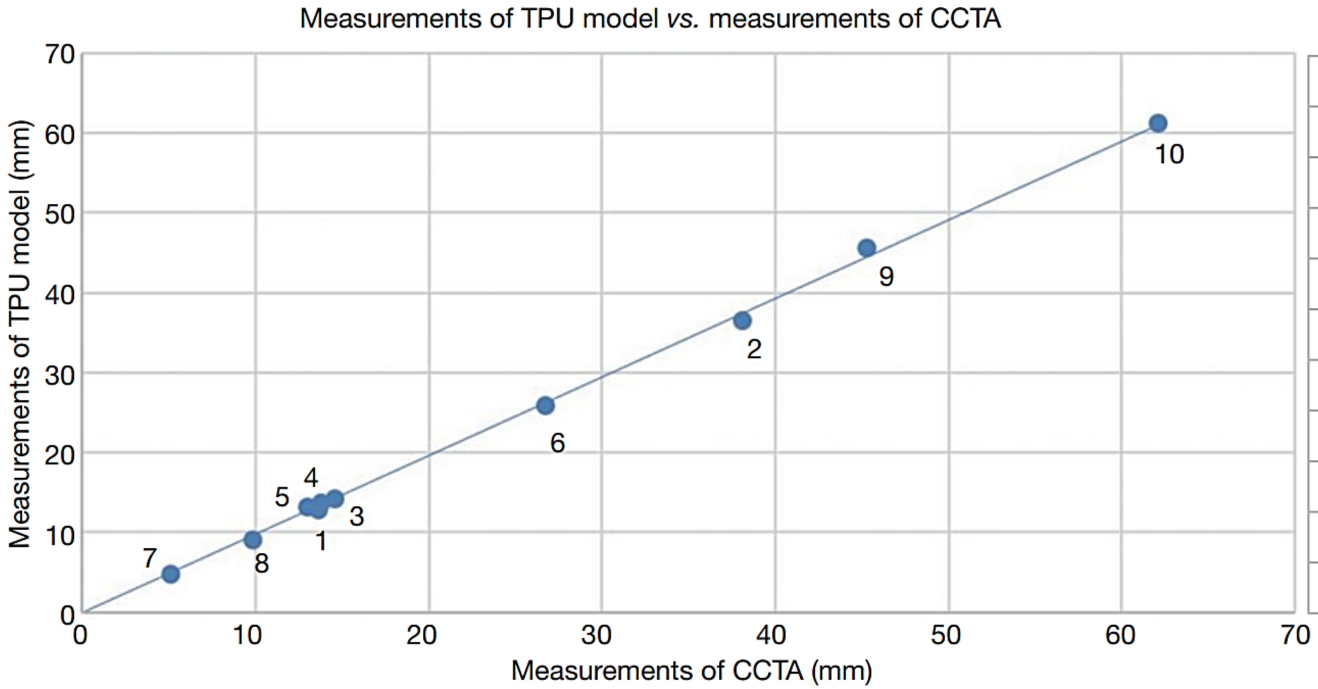
**Figure 3.2:** Scatter plot of measurements of the Tango Plus model against measurements of CCTA.



| No. | Anatomical locations |
|---|---|
| 1 | Base of brachiocephalic trunk |
| 2 | Aortic arch |
| 3 | Ascending aorta |
| 4 | Left pulmonary artery |
| 5 | Right pulmonary artery |
| 6 | Pulmonary trunk |
| 7 | Descending aorta |
| 8 | Ventricular septal defect |
| 9 | Right atrium |
| 10 | Left ventricle |

The data points were assigned with numbers to represent different anatomical locations. CCTA, cardiac computed tomography angiography.

**Figure 3.3:** Scatter plot of measurements of the TPU model against measurements of CCTA.



| No. | Anatomical locations |
|---|---|
| 1 | Base of brachiocephalic trunk |
| 2 | Aortic arch |
| 3 | Ascending aorta |
| 4 | Left pulmonary artery |
| 5 | Right pulmonary artery |
| 6 | Pulmonary trunk |
| 7 | Descending aorta |
| 8 | Ventricular septal defect |
| 9 | Right atrium |
| 10 | Left ventricle |

The data points were assigned with numbers to represent different anatomical locations. TPU, thermoplastic polyurethane; CCTA, cardiac computed tomography angiography.

In order to compare the clinical significance of the two models, surveys were conducted involving 3 medical professionals (1 cardiac surgeon, 1 cardiologist, and 1 cardiothoracic radiologist). During the meeting with them, they were asked to qualitatively assess the original CCTA of cases 1 and 2 prior to the evaluation of the 3DPHM, and allowed to discuss where the heart lesions were. Questionnaires were then distributed to the medical professionals to discover their opinions of both models. Each participant received 2 identical sets of questionnaires, 1 for the Tango Plus model, and 1 for the TPU model. They were requested to choose between responses of "yes", "maybe", and "no" with regards to the efficacy of the 3D heart models in the following areas: degree of reliability of the model, usefulness in pre-operative planning, usefulness in medical education, and usefulness in communication within clinical practice. All the participants found both the models useful in the above-mentioned areas, and they found no difference between the models in terms of their medical applications. On the 3-point scale questionnaires, each respondent rated the TPU model exactly the same as the Tango Plus model. Table 3.1 contains the responses from each respondent with regards to the medical application of the 3DPHM. It is worthwhile to note that no participant selected "no" in any of the questions, indicating that both 3DPHM were perceived positively in terms of their efficacy.

**Table 3.1:** Responses of the perceived efficacy of the 3DPHM

| **Questions** | **Cardiologist** | | **Radiologist** | | **Cardiac surgeon** | |
|---|---|---|---|---|---|---|
| | Cheap | Expensive | Cheap | Expensive | Cheap | Expensive |
| Does the model accurately display the cardiac structures? | Yes | Yes | Yes | Yes | Yes | Yes |
| Is the model helpful in planning interventions and pre-surgical simulation? | Yes | Yes | Yes | Yes | Yes | Yes |
| Is the model helpful for you to appreciate procedural difficulties and assess the likelihood of success/failure of the surgery? | N/A* | N/A | N/A | N/A | Yes | Yes |
| Is the model helpful in intra-operative orientation? | Yes | Yes | Yes | Yes | Yes | Yes |
| Can the model reduce operative time? | Maybe | Maybe | Yes | Yes | Yes | Yes |
| Is the model useful in enhancing your/patients understanding? | Yes | Yes | Yes | Yes | Yes | Yes |
| Can the model improve consultation experience? | N/A | N/A | N/A | N/A | Yes | Yes |
| Can the model shorten the consultation time? | N/A | N/A | N/A | N/A | Maybe | Maybe |
| Can you describe pathology better with the model? | Maybe | Maybe | Yes | Yes | Yes | Yes |
| Do you prefer using a 3D model or medical images to communicate with patients? | Both | Both | Both | Both | 3D model | 3D model |
| Satisfaction score (out of 10) | 7 | 7 | 10 | 10 | 9 | 9 |
| Would you recommend 3D printing to your colleagues? | Yes | Yes | Yes | Yes | Yes | Yes |

*, N/A means not applicable, therefore the question was not included in the questionnaire.

## 3.4 Discussion

The application of 3D printing has proliferated since its first introduction in the medical field, however mainly in the maxillofacial and orthopaedic specialties. In the past few years, 3D printing has increasingly gained attention within the cardiovascular domain, due to the potential ability of the technology to improve the patient management of cardiovascular disease.[6,8,29,32] In spite of the promising results that 3DPHM have shown in the current literature, the diffusion of this novel technology has been limited mainly due to its cost.[9,19,35] To the best of our knowledge, there is currently no study investigating the efficiency and accuracy of the low-cost 3DPHM and whether they are comparable with the more expensive models. This preliminary study demonstrated that the low- cost models can be as useful as the expensive models in medical applications. However, its accuracy in replicating cardiac structures is less than the expensive models, and its mean difference does not fall within the mean difference reported in the other relevant articles.[39] Further studies that include more cases are needed to validate this result. The low-cost model also requires a much longer duration for 3D printing—about 10 times longer than the high-cost model. Hence, it is probably not as practical when it comes to management of urgent cases.

In the free-text response questions, one of the participants made a suggestion about how the 3DPHM may be improved to bring more benefits in medical field:

“(Display of) thinner structures like valve leaflets and chordae tendineae, especially for adult valve reconstructive surgery.”

This points out one of the limitations of the 3DPHM generated purely based on CT scans: very fine structures cannot be well-defined, as they are best seen on echocardiographic images. A study by Gosnell et al. integrated CT and echocardiographic scans to produce a 3DPHM with an excellent replication of valve leaflets (Figure 3.4).[40] This method exploits the strengths of the two imaging modalities and combines them, producing a 3DPHM that can display more anatomical and pathological information.

**Figure 3.4:** 3DPHM with the cardiac contour derived from a CT scan, and atrioventricular valves (green and red) derived from an echocardiographic scan.

Reprinted with permission from Gosnell et al.[40]

The accuracy of the 3D printed models relies heavily on the quality of the original CT scan, especially on how well the entire blood pool is enhanced by the contrast medium. If the blood pool is not enhanced properly, manual editing is required to meticulously select the region of interest, making the process more prone to human error. One of the participants suggested it would be beneficial to develop CT imaging protocols to enhance the quality of the scans, thus reducing errors in the 3DPHM.

It is important to bring attention to several limitations in this study. First, the study lacks generalization as there were only 2 types of 3D printing materials being investigated. There are various types of 3D printing materials in the market with different properties and costs, and their cost- effectiveness as a material for 3DPHM has not yet been studied. It should not be assumed that the properties of TPU 95A and Tango Plus material can be generalized to all the other low- and high-cost 3D printed models. Second, the quantitative measurement of the 3D models' accuracy was only carried out in one dimension: the axial plane. It is yet to be determined whether 3D printing distorts the cardiac anatomy in coronal and sagittal planes, and whether the accuracy of the 3D models is consistent in all three dimensions. This being the case, the calculated mean difference of the 3DPHM is not completely indicative of the accuracy of the entire model. Third, detection bias may be present in the qualitative assessment due to the fact that all three participants were informed of the purpose of the study prior to the survey.

In conclusion, this technical report shows our preliminary experience in creating low-cost patient-specific 3DPHM of CHD with similar accuracy and clinical applications as costly 3DPHM. With further developments in 3D printing techniques and cost reductions in 3D printing materials, 3D printing will inevitably be incorporated into the diagnostic approach of daily clinical practice.

## 3.5 References:

1. Australian Institute of Health and Welfare. *How many Australians have cardiovascular disease?* Australian Institute of Health and Welfare; 2017. Accessed Dec 19, 2018. https://www.aihw.gov.au/reports-data/health-conditions-disability-deaths/heart-stroke-vascular- diseases/overview
2. Yoo S-J, Thabit O, Kim E, Ide H, Yim D, Dragulescu A, et al. 3D printing in medicine of congenital heart diseases. *3D Print Med*. 2016;2(1):1-12. doi: 10.1186/s41205-016-0004-x
3. Bruneau BG. The developmental genetics of congenital heart disease. *Nature*. 2008;451(7181):943-948. doi: 10.1038/nature06801
4. Ryan J, Plasencia J, Richardson R, Velez D, Nigro JJ, Pophal S, et al. 3D printing for congenital heart disease: a single site's initial three-year experience. *3D Print Med.* 2018;4:1-9.
5. Bhatla P, Tretter JT, Ludomirsky A, Argilla M, Latson Jr. LA, Chakravarti S, 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. doi: 10.1007/s00246-016-1489-1
6. Valverde I, Gomez G, Gonzalez A, Suarez-Mejias C, Adsuar A, Coserria JF, et al. Three-dimensional patient-specific cardiac model for surgical planning in Nikaidoh procedure. *Cardiol Young*. 2015;25:698–704.
7. 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;47:1044–1052.
8. Shiraishi I, Yamagishi M, Hamaoka K, Fukuzawa M, Yagihara T. Simulative operation on congenital heart disease using rubber-like urethane stereolithographic biomodels based on 3D datasets of multislice computed tomography. *Eur J Cardiothorac Surg*. 2010;37:302-6.
9. Riesenkampff E, Rietdorf U, Wolf I, Schnackenburg B, Ewert P, Huebler M, Alexi-Meskishvili V, Anderson RH, Engel N, Meinzer H, Hetzer R, Berger F, Kuehne T. The practical clinical value of three-dimensional models of complex congenitally malformed hearts. *J Thorac Cardiovasc Surg*. 2009;138:571-580.
10. Mottl-Link S, Hübler M, Kühne T, Rietdorf U, Krueger JJ, Schnackenburg B, et al. Physical Models Aiding in Complex Congenital Heart Surgery. *Ann Thorac Surg*. 2008;86:273-7.
11. Ma XJ, Tao L, Chen X, Li W, Peng ZY, Chen Y, et al. Clinical application of three-dimensional reconstruction and rapid prototyping technology of multislice spiral

computed tomography angiography for the repair of ventricular septal defect of tetralogy of Fallot. *Genet Mol Res*. 2015;14:1301-9.

12. Greil GF, Wolf I, Kuettner A, Fenchel M, Miller S, Martirosian P, et al. Stereolithographic reproduction of complex cardiac morphology based on high spatial resolution imaging. *Clin Res Cardiol*. 2007;96:176-85.
13. Biglino G, Koniordou D, Gasparini M, Capelli C, Leaver L, Khambadkone S, et al. Piloting the use of patient-specifc cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr Cardiol*. 2017;38:813-8.
14. Cantinotti M, Valverde I, Kutty S. Three-dimensional printed models in congenital heart disease. *Int J Cardiovasc Imaging*. 2017;33:137-44.
15. Bhatla P, Tretter JT, Chikkabyrappa S, Chakravarti S, Mosca RS. Surgical planning for a complex double-outlet right ventricle using 3D printing. *Echocardiography*. 2017;34:802-4.
16. Biglino G, Capelli C, Wray J, Schievano S, Leaver L, Khambadkone S, et al. 3D-manufactured patient-specifc models of congenital heart defects for communication in clinical practice: feasibility and acceptability. *BMJ Open*. 2015;5:e007165.
17. Biglino G, Capelli C, Leaver LK, Shievano S, Taylor AM, Wray J. Involving patients, families and medical staff in the evaluation of 3D printing models of congenital heart disease. *Commun Med*. 2015;12:157-69.
18. Biglino G, Capelli C, Koniordou D, Robertshaw D, Leaver L, Schievano S, et al. Use of 3D models of congenital heart disease as an education tool for cardiac nurses. *Congenit Heart Dis*. 2017;12:113-8.
19. Costello JP, Olivieri L, Krieger A, Thabit O, Marshall MB, Yoo SJ, et al. Utilizing Three-Dimensional Printing Technology to Assess the Feasibility of High-Fidelity Synthetic Ventricular Septal Defect Models for Simulation in Medical Education. *World J Pediatr Congenit Heart Surg*. 2014;5:421-6.
20. Costello JP, Olivieri LJ, Su L, Krieger A, Alfares F, Thabit O, 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.
21. Farooqi KM, Lengua CG, Weinberg AD, Nielsen JC, Sanz J. Blood Pool Segmentation Results in Superior Virtual Cardiac Models than Myocardial Segmentation for 3D Printing. *Pediatr Cardiol*. 2016;37:1028-36. doi: 10.1007/s00246-016-1385-8

22. Farooqi KM, Gonzalez-Lengua C, Shenoy R, Sanz J, Nguyen K. Use of a three dimensional printed cardiac model to assess suitability for biventricular repair. *World J Pediatr Congenit Heart Surg*. 2016;7:414-6.
23. Garekar S, Bharati A, Chokhandre M, Mali S, Trivedi B, Changela VP, et al. Clinical Application and Multidisciplinary Assessment of Three Dimensional Printing in Double Outlet Right Ventricle With Remote Ventricular Septal Defect. *World J Pediatr Congenit Heart Surg*. 2016;7(3):344-50.
24. Hadeed K, Dulac Y, Acar P. Three-dimensional printing of a complex CHD to plan surgical repair. *Cardiol Young*. 2016;26:1432-4.
25. Jones TW, Seckeler MD. Use of 3D models of vascular rings and slings to improve resident education. *Congenit Heart Dis*. 2017;12:578-82.
26. Kappanayil M, Koneti NR, Kannan RR, Kottayil BP, Kumar K. Three-dimensional-printed cardiac prototypes aid surgical decision-making and preoperative planning in selected cases of complex congenital heart diseases: Early experience and proof of concept in a resource-limited environment. *Ann Pediatr Cardiol*. 2017;10(2):117.
27. 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.
28. Loke YH, Harahsheh AS, Krieger A, Olivieri LJ. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. *BMC Med Educ*. 2017;17:54-61.
29. Olejník P, Nosal M, Havran T, Furdova A, Cizmar M, Slabej M, et al. Utilisation of three-dimensional printed heart models for operative planning of complex congenital heart defects. *Kardiol Pol*. 2017;75:495–501.
30. Olivieri LJ, Krieger A, Loke YH, 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;28:392–397.
31. Olivieri LJ, Su L, Hynes CF, Krieger A, Alfares FA, Ramakrishnan K, et al. “Just-In-Time” Simulation Training Using 3-D Printed Cardiac Models After Congenital Cardiac Surgery. *World J Pediatr Congenit Heart Surg*. 2016;7:164–168.
32. Sodian R, Weber S, Markert M, Rassoulian D, Kaczmarek I, Lueth TC, et al. Stereolithographic models for surgical planning in congenital heart surgery. *Ann Thorac Surg*. 2007;83:1854-7.

33. Valverde I, Gomez G, Coserria JF, Suarez-Mejias C, Uribe S, Sotelo J, et al. 3D printed models for planning endovascular stenting in transverse aortic arch hypoplasia. *Catheter Cardiovasc Interv*. 2015;85:1006-12.
34. Valverde I, Gomez-Ciriza G, Hussain T, Suarez-Mejias C, Velasco-Forte MN, Byrne N, et al. Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study. *Eur J Cardiothorac Surg*. 2017;52:1139-48.
35. Olivieri LJ, Zurakowski D, Ramakrishnan K, Su L, Alfares FA, Irwin MR, Heichel J, Krieger A, Nath DS. Novel, 3D Display of Heart Models in the Postoperative Care Setting Improves CICU Caregiver Confidence. *World J Pediatr Congenit Heart Surg*. 2018;9:206-13.
36. Lau I, Liu D, Xu L, Fan Z, Sun Z. Clinical value of patient-specific three-dimensional printing of congenital heart disease: Quantitative and qualitative assessments. *PLoS One*. 2018;13: e0194333.
37. Perica E, Sun Z. Patient-specific three-dimensional printing for pre-surgical planning in hepatocellular carcinoma treatment. *Quant Imaging Med Surg.* 2017;7:668-77.
38. Liu D, Sun Z, Chaichana T, Ducke W, Fan Z. Patient-specific 3D printed models of renal tumours using home-made 3D printer in comparison with commercial 3D printer. *J Med Imaging Health Inf*. 2018;8:303-8.
39. Lau I, Sun Z. Three-dimensional printing in congenital heart disease: A systematic review. *J Med Radiat Sci*. 2018;65(3):226-236. doi:10.1002/jmrs.268
40. Gosnell J, Pietila T, Samuel BP, Kurup HK, Haw MP, Vettukattil JJ. Integration of Computed tomography and three-dimensional echocardiography for hybrid threedimensional printing in congenital heart disease. *J Digit Imaging.* 2016;29:665-9.

Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged.

# CHAPTER 4: THE ROLE OF 3D PRINTED HEART MODELS IN IMMEDIATE AND LONG-TERM KNOWLEDGE ACQUISITION IN MEDICAL EDUCATION

## 4.1 Introduction

Congenital heart disease (CHD) is the most common birth defect among the newborn.[1-3] It has a broad spectrum of severity and morphology that is largely variable between individuals.[2] A strong foundation for education in CHD is therefore crucial among the medical students and young clinicians for the development and training of future cardiac specialists. Current teaching approach of heart anatomy and physiology relies heavily on two-dimensional (2D) medical images and cadaveric specimens, both of which have their own limitations and shortcomings. 2D medical images, or even three-dimensional (3D) digital reconstruction of heart presented on 2D plane requires the viewer to conceptually translate the information into 3D to understand the spatial relationship between the inter- and intra-cardiac structures. This is extremely challenging, especially for beginners who only just learn about CHD.[1-5] Cadaveric specimens are often inaccessible to students, expensive to maintain, and subjective to wear and tear overtime. Additionally, depending on the availability, the cadaveric specimens only demonstrate certain types of CHD (i.e., lesion-specific), and therefore cannot represent the whole spectrum of CHD.[1,3,6-8]

3D printed heart models (3DPHM) have shown to be a novel teaching approach that can improve students' and health providers' learning experience and satisfaction.[9] The 3DPHM were reported with the advantages of being easily accessible, affordable, and the ability to reproduce any type of lesions, including those which are rare and more complex.[1,3,7,8] Being tangible, the students can also assess the cardiac morphology up close at any viewing angle, achieving deeper understanding of the cardiac morphology without the need to master the knowledge of cardiac imaging.[8] A case-control study by Tan et al. which involved 132 nursing students, reported that the 3DPHM group scored significantly higher in both objective and subjective evaluations.[5] The study concluded that the 3DPHM were useful in improving the students' knowledge acquisition on atrial septal defect (ASD) as well as students' interest and satisfaction in their learning.[5] In a recently published randomized controlled trial which involved 5th year medical students, a significantly higher increase in test scores was observed in the 3DPHM group compared to the control group, regardless of the type of CHD being tested.[9] Similarly, in another study which involved 127 participants, Valverde et al. reported that the use of 3DPHM have significantly improved the anatomical knowledge of criss-cross cardiac anatomy, compared to the use of imaging datasets as a teaching tool.[10]

Despite these promising results, according to a recently published meta-analysis and systematic review, the use of 3D printed cardiac models do not necessarily increase the short-term knowledge gain among the students, even though their learning experience was enhanced.[11] To the best of our knowledge, none of the existing studies investigated the effect of 3D printed heart models on long-term knowledge gain among the students in the domain of CHD. This study aimed to investigate the immediate knowledge acquisition as well as long-term knowledge retention among the medical students with the use of 3DPHM incorporated in the teaching of CHD, compared to the conventional teaching approach.

## 4.2 Materials and methods

### 4.2.1 Study design

A prospective cohort study was conducted to compare the knowledge retention on the topic of CHD between the medical students who were exposed to conventional teaching approach versus those who were exposed to teaching approach with the use of 3DPHM. The study was approved by the Curtin University Human Research Ethics Committee. This research was advertised twice in first semester 2020 and first semester 2021 respectively in the Perth Campus, Curtin University. The participant recruitment was primarily limited to second and third year medical students in the year 2020, and only second year group in the year 2021, as these were the groups who were considered as novice in cardiac anatomy and pathology.

From both of the recruitments, a total of 53 medical students (5 in their 3rd year, and 48 in their 2nd year) voluntarily participated in the study. There were 5 education sessions on the topic of CHD carried out each year, with a duration of 1.5 hour for each of them. The participants were required to attend one of them based on their availability. A maximum of 9 students were allowed per session. To minimize potential bias, the participants were not informed if they were in the control or study group. There were 28 students who attended the education sessions with the use of 3D printed heart models (study group), and 25 students attended the education sessions without being presented with the 3D printed heart models (control group). All 53 medical students had previously been taught of CHD during their curriculum.

In order to assess the difference in knowledge gain and knowledge retention between the groups, the students completed two sets of quizzes which comprised of 20 questions relevant to CHD. The first set was completed immediately following the education session (immediate knowledge gain), while the second set was completed 6 weeks after the education session (knowledge retention). They also completed a survey to rate their learning experience. Appreciation gifts were given to the study participants at the completion of second quiz to prevent drop-outs.

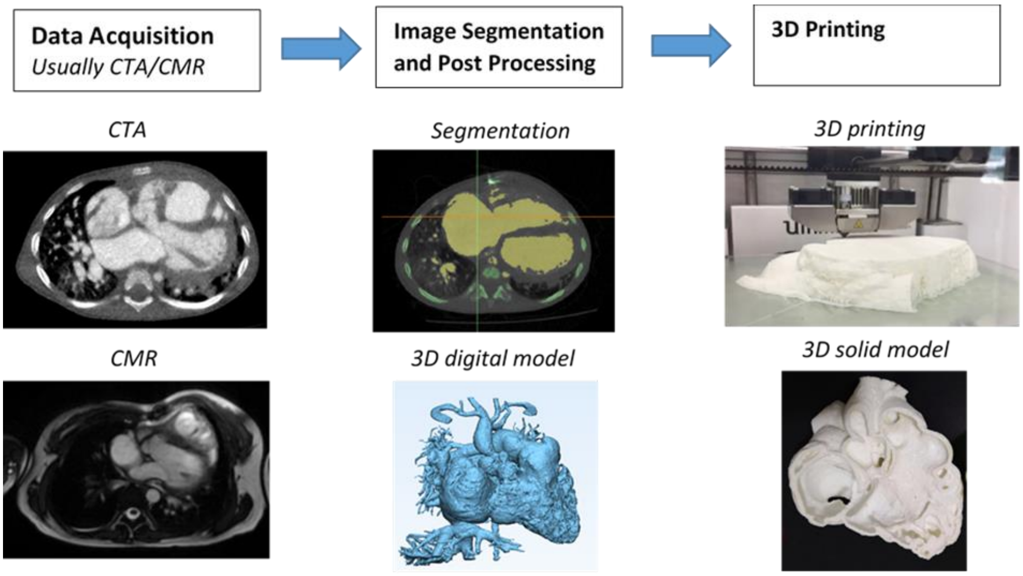
### 4.2.2 Generation of 3DPHM

In order for the participants to learn a range of CHD with different levels of complexity, four types of CHD were selected for generation of the 3D printed heart models based on their Aristotle Basic Complexity Level (ABCL). These include ASD (ABCL = 1), ventricular septal defect (VSD, ABCL = 2), Tetralogy of Fallot (ToF, ABCL = 3), and double outlet right ventricle (DORV, ABCL = 4). Anonymized cardiac computed tomography angiography (CCTA) images of four pediatric patients with the aforementioned CHD were used as the source data.

The first step to generate the 3DPHM was to convert the CCTA images into printable digital model in standard tessellation language (STL) format using Mimics Innovation Suite 22.0 (Materialise HQ, Leuven, Belgium) (Figure 4.1). The details of the conversion process were elucidated previously.[12,13] The required time for this conversion process was 45 minutes on average, however it was highly dependent on the image quality of the source data. Following that, the STL files were sent to the 3D printers for printing (Figure 4.1 [14]).

Two sets of four models were generated, each in a different printing material. One set was printed in Flexible V4 Resin from Formlabs (Somerville, MA, USA), while another was printed in TPU80A from Fabbxible Technology (Pulau Pinang, Malaysia) (Figure 4.2 [15]). Both printing materials are able to generate models that are flexible, which to some extent resemble the physical properties of heart muscles. Each cardiac model was divided into two components (transected at the right atrium-right ventricular plane) so that the structural defects of the heart can be clearly visualised. The average printing cost per model was approximately AUD 35.

**Figure 4.1:** Conversion of CCTA into printable STL files.



CTA, computed tomography angiography; CMR, cardiac magnetic resonance; 3D, three-dimensional. Reprint with permission under the open access from Sun et al.[14]

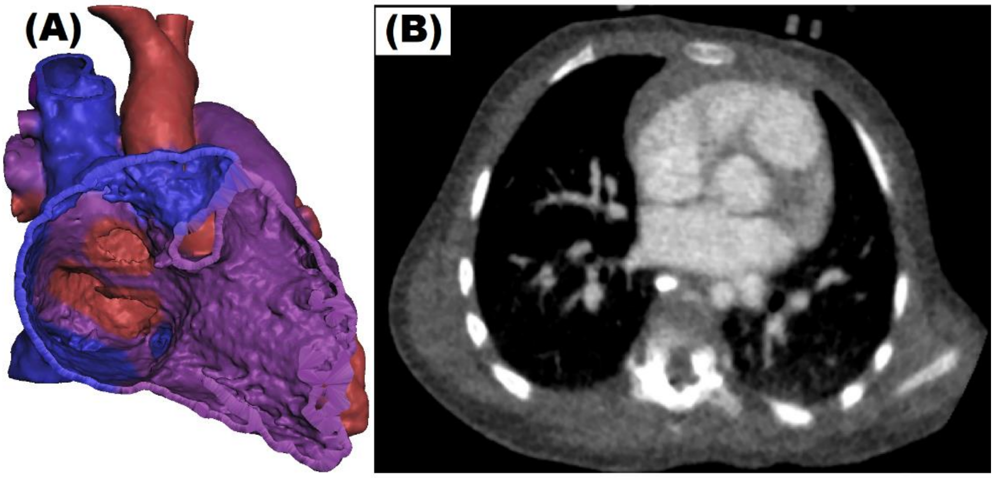
**Figure 4.2:** Two sets of heart models that feature different types of CHD (double outlet right ventricle is shown in this image) were printed in two different printing materials, Flexible V4 Resin from Formlabs (left), and TPU80A from Fabbxible Technology (right).

Reprint with permission under the open access from Lau et al.[15]

### 4.2.3 Education session on CHD

The education sessions were designed to mainly focus on anatomy and pathophysiology of ASD, VSD, ToF, and DORV. For this purpose, 3DPHM, digital 3D heart models, 2D diagrams, and digital imaging and communications in medicine (DICOM) images were utilized as the teaching tools (Figures 4.2, 4.3). The education sessions were carried out in PowerPoint lecture format, incorporating the aforementioned teaching tools with each type of CHD presented. The session was designed to mainly provide the students with a basic understanding of the morphology and hemodynamics of each type of CHD and their imaging appearances on CCTA. Each education session ran for 1.5 hour by the same investigator (IL) to avoid variations in teaching style between different tutors. In order to ensure the consistency between each education session, both the study and control groups received the identical learning content, apart from the 3DPHM that were only used in the education sessions for study group.

**Figure 4.3:** Different teaching tools were used during the CHD education session.



(A) Coloured digital 3D model on Meshmixer (Autodesk, San Rafael, CA, USA) in which students were able to rotate and zoom. (B) DICOM image.

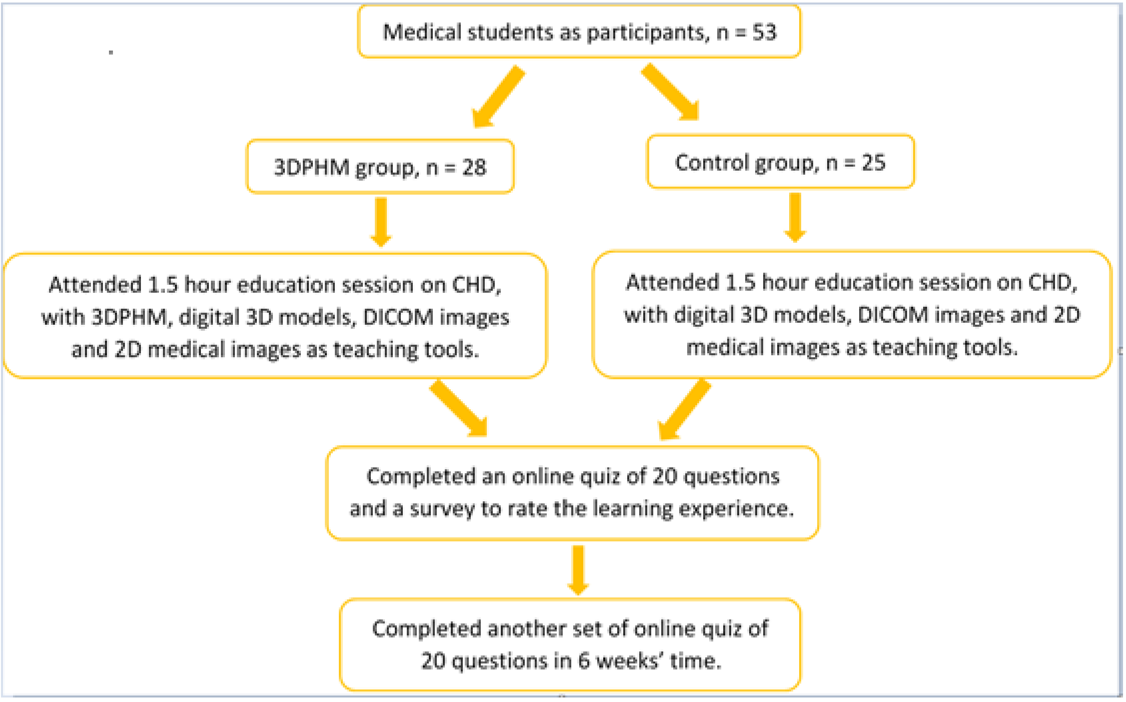
The education sessions took place in a computer laboratory. At the start of the session, the students were asked to download the digital teaching materials (i.e., DICOM dataset and digital 3D heart models), so that all of the participants would be able to access them on their own computer while listening to the tutor's explanation. After giving the students a quick revision of normal heart anatomy and general overview of acyanotic and cyanotic CHD, the session was followed by explanation of each type of chosen CHD in the following format and progression: (i) explanation of hemodynamic change using a 2D diagrams, (ii) subtypes of each CHD, (iii) possible complications if the CHD is left untreated, (iv) case study using DICOM images, digital 3D heart models, and 3DPHM. While the tutor was demonstrating the digital 3D heart models and the DICOM images on the projected screen, the participants were also encouraged to view and manipulate the digital 3D heart models and the DICOM images on their own computer using open-source software, Meshmixer (Autodesk, San Rafael, CA, USA) and RadiAnt (Medixant, Poznan, Poland). The digital 3D heart models were coloured according to the type of blood (oxygenated, deoxygenated or mixed) that the heart chamber is carrying to enable the students in achieving better understanding of the hemodynamic changes due to the CHD (Figure 4.3). Using Meshmixer, the participants were allowed to rotate and zoom in the 3D models virtually. For the education sessions in which 3DPHM were used, each set of 3DPHM was shared among 3–5 students, and they were encouraged to refer to the 3DPHM freely throughout the session. 3DPHM were used to pinpoint the location of heart defects, to explain the hemodynamic changes, to highlight the malpositioning of the great arteries (if present), and to emphasize the difference in size between the major blood vessels, especially when a stenosis is present.

### 4.2.4 Assessment of participants' knowledge acquisition and learning experience

Immediately after the education session, the participants were asked to complete a set of online quiz (Quiz 1) which comprised of 20 multiple choice and short-answer questions on CHD, with a time limit of 15 minutes. The participants were also asked to complete a survey to rate their learning experience based on a 5-point Likert scale. In 6 weeks' time after the education session, the participants completed another online quiz (Quiz 2) of 20 questions, again with a time limit of 15 minutes. The score (out of 20) and the time taken for the participants to complete both of the quizzes were recorded. The process of the study is summarized in Figure 4.4.

Both the online quizzes were designed to ensure that the students were tested on the content covered in the education session, whereas the survey was designed to address the students' learning experience with the teaching tools used and their self-rated knowledge acquisition. The questions for Quiz 1, Quiz 2, and the survey can be found in Appendices D1-D3 respectively.

**Figure 4.4:** A flow chart of the study process.



2D, two-dimensional; 3DPHM, three-dimensional printed heart model; CHD, congenital heart disease; DICOM, digital imaging and communications in medicine.

### 4.2.5 Statistical analysis

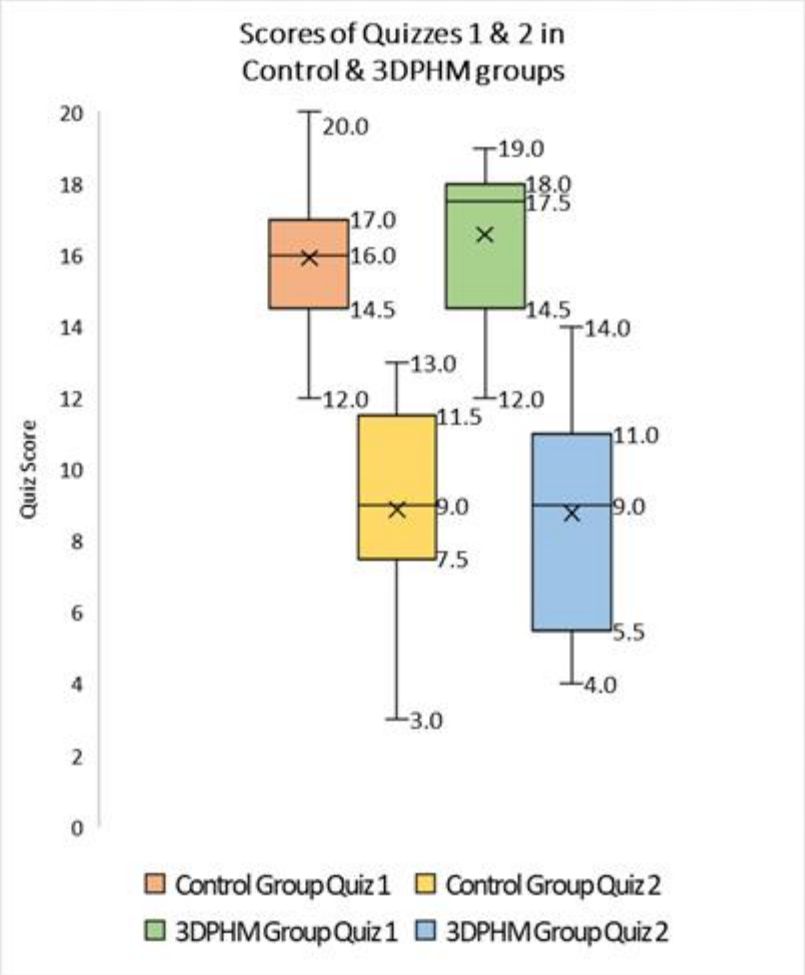
Data analyses were performed using IBM SPSS statistical package, version 26 (IBM Corp, Armonk, NY, USA), whereas the plots were generated using Microsoft Excel 2016 (Microsoft Corporation, Redmond, Washington, USA). Shapiro-Wilk's and Levene's test were used to analyze the normality and homogeneity of the variance. Student t-test was used to analyze the score of anatomy unit that the students achieved in Year 1 between two groups to compare their baseline knowledge on anatomy. The following data were being analyzed using Mann-Whitney U test: score of Quiz 1 between two groups to compare the immediate knowledge acquisition of the participants, and survey responses for the students' learning experience. Linear regression was conducted to analyze score difference between Quiz 1 and Quiz 2 of each participant to measure the knowledge retention among the medical students, using the type of group (control or study) and year of recruitment as predictors. It is hypothesized that the 3DPHM group will experience smaller score difference between the two quizzes when compared to the control group. Pearson's correlation was also used to measure the strength of correlation between the predictors and the outcome variable. P-value of $<0.05$ (two-tailed) is considered statistically significant.

## 4.3 Results

Normality of test scores were met by Shapiro-Wilk's test for Quiz 2 score ($p = 0.25$ and $p = 0.08$, respectively), but not for Quiz 1 score ($p = 0.014$). Both quiz scores met the assumption of homogeneity of variance by Levene's test ($p > 0.05$).

The Quiz 1 score was marginally higher in the 3DPHM group, with a median score of 17.5 and compared to median score of 16 in the control group, however Mann-Whitney U test demonstrates no statistical significance ($U = 272$, $p = 0.16$). Figure 4.5 presents a boxplot of the scores achieved by both student groups in Quizzes 1 and 2.

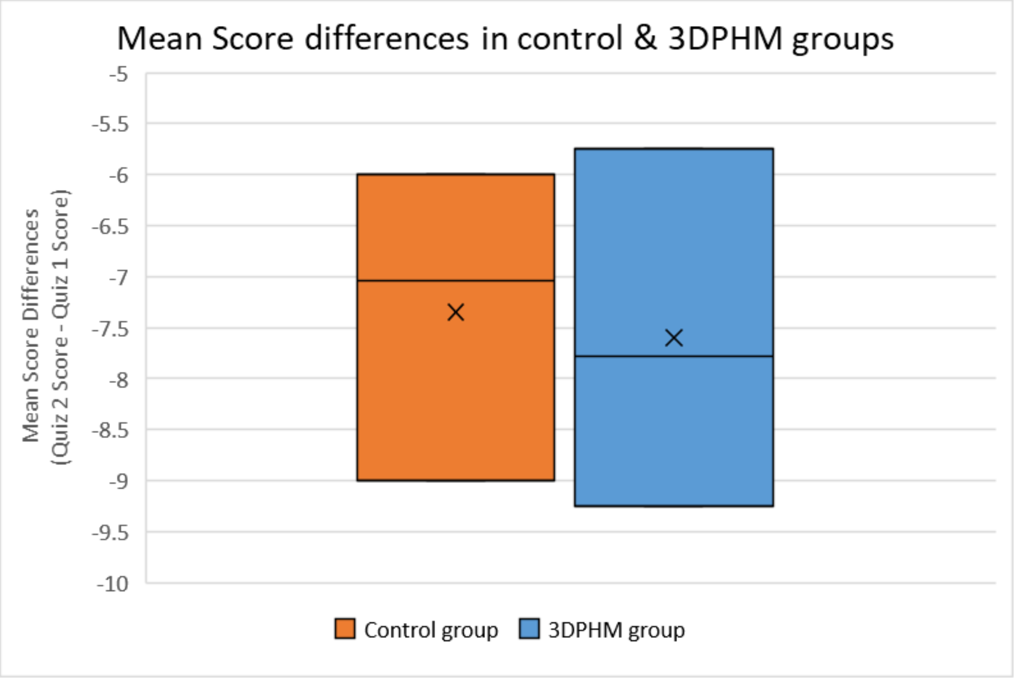
**Figure 4.5:** Boxplot of the scores (out of 20) achieved by control and 3DPHM groups in Quiz 1 and Quiz 2.



3DPHM, three-dimensional printed heart model.

The 3DPHM group experienced slightly higher score difference between Quiz 1 and Quiz 2, with a mean score difference of 7.79 (±2.63), compared to the control group, 7.04 (±2.64). Figure 4.6 illustrates the mean score differences between Quizzes 1 and 2 of both control and 3DPHM groups. The biserial correlation between the score difference and type of group and year of recruitment was very weak and not statistically significant, r = –0.143 (p = 0.308) and r = 0.043 (p = 0.757), respectively. The fitted regression equation for predicting the score difference of the two quizzes from the predictors was $\hat{y} = -7.137 + 0.220x - 0.743z$, where $\hat{y}$ is the score difference of Quiz 1 and Quiz 2, $x$ is the year of recruitment (coded as 0 = year 2020, 1 = year 2021), and z is the type of group (coded as 0 = control group, 1 = 3DPHM group). The r2 for the fitted regression was 0.022; that is, only 2% of the variance in score difference was predictable from the predictors. In other words, the result does not suggest improvement in long-term knowledge acquisition within the 3DPHM group when compared to the control group.

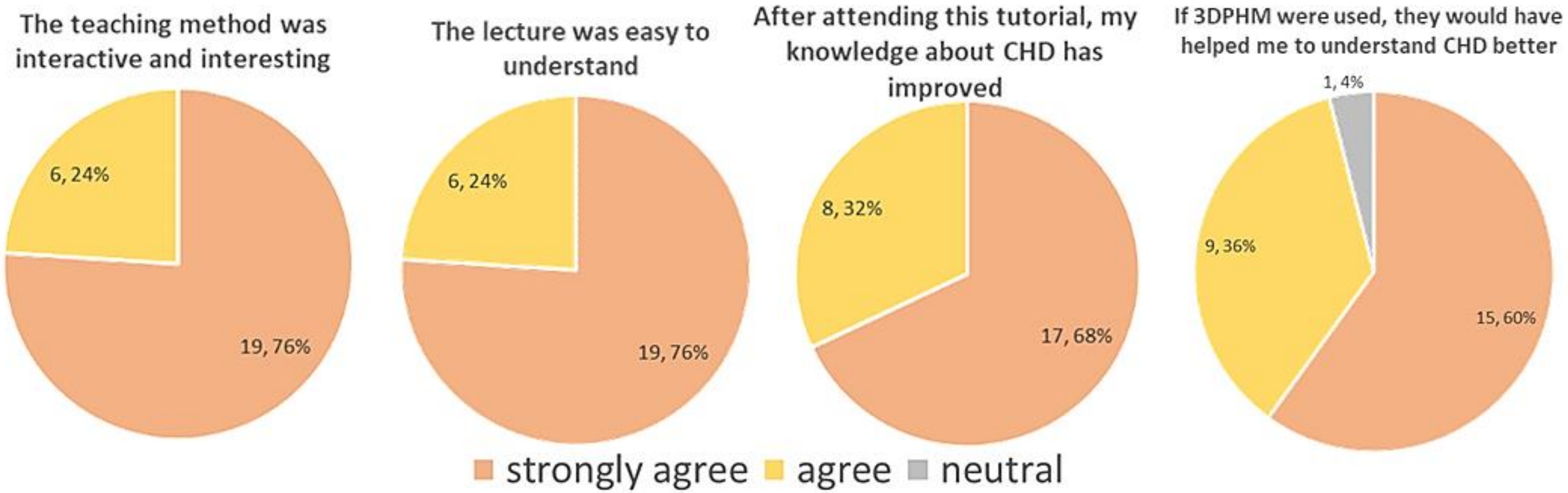
**Figure 4.6:** Mean changes in score between Quizzes 1 and 2 (Quiz 2 score – Quiz 1 score) for both control and 3DPHM groups.



3DPHM, three-dimensional printed heart model.

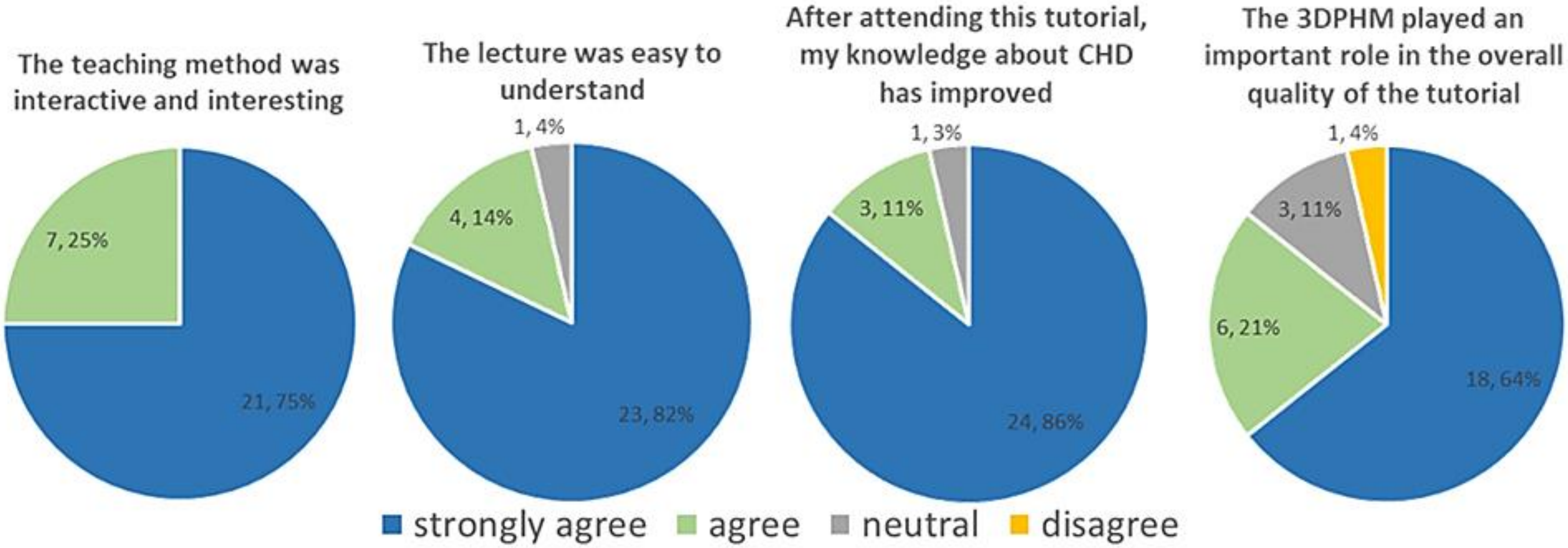
In comparing survey responses between the control and 3DPHM groups, the Mann-Whitney U test showed no significant difference in all of the questions. Figures 4.7 and 4.8 illustrate the survey responses in percentage for the control group and 3DPHM group, respectively. Both groups of students indicated either ‘strongly agree’ or ‘agree’ that the teaching method was interactive and interesting (U = 346.5, p = 0.93). Slightly more students in 3DPHM group indicated ‘strongly agree’ that the education was easy to understand (82%) compared to the control group (76%), although this is not statistically significant (U = 331.5, p = 0.64). More students in 3DPHM indicated ‘strongly agree’ that their knowledge about CHD has improved (86%) compared to the control group (68%), and again this is not statistically significant (U = 292, p = 0.16). About 64% of the students in 3DPHM group indicated ‘strongly agree’ that the 3DPHM played an important role in helping them understand CHD. This is similar to the control group where 60% indicated ‘strongly agree’ that the 3DPHM would help them to understand CHD (U = 349.5, p = 0.99). However, one student in the 3DPHM group disagreed that the 3DPHM helped in his/her learning of CHD.

**Figure 4.7:** Survey responses (number of students, percentage) of the control group with regards to the education session.



3DPHM, three-dimensional printed heart model; CHD, congenital heart disease.

**Figure 4.8:** Survey responses (number of students, percentage) of the 3DPHM group with regards to the education session.



3DPHM, three-dimensional printed heart model; CHD, congenital heart disease.

## 4.4 Discussion

This cohort study has evaluated the value of 3DPHM in both immediate and long-term knowledge acquisition among the medical students on the topic of CHD when compared to the conventional teaching tools. Even though there are published articles which assessed the role of 3DPHM in immediate knowledge gain on the topic of CHD, the present study is the first to investigate the effect of 3DPHM in long-term knowledge retention in the domain of CHD.

The results showed that the 3DPHM group scored slightly higher in Quiz 1, which indicated improvement in immediate knowledge acquisition compared to the control group. This difference however, did not achieve statistical significance. This finding echoes the finding in Jones et al.'s study, in which 36 residents were divided into 3D printed model group and control group with their pre-test and post-test scores analyzed.[16] In their study, the 3D printed model group experienced slightly greater improvement in the post-test compared to the control group, however the difference was not statistically significant.[16] In another study conducted by Loke et al., the 3DPHM group did not show improvement in the immediate knowledge gain among the pediatric residents.[2] Despite these positive reports, there are other studies documenting contrasting findings. In a study which involved 63 medical students, the 3DPHM group was reported to have a significant improvement in the test results when compared to the control group.[17] In another study by Lim et al., 53 first year medical students were randomly assigned into three groups (cadaveric materials, 3DPHM, and combined materials) and were objectively tested in pre- and post-test for their knowledge acquisition on external cardiac anatomy.[7] It was reported that the 3DPHM group had significant improvement in test scores ($p = 0.003$).[7] This is not a surprising finding. In a meta-analysis conducted by Yammine et al., physical models were reported to significantly improve the overall knowledge outcome and the spatial knowledge acquisition, but not the factual knowledge acquisition.[18] In the present study, we focused on the topic of CHD using 3DPHM which feature 4 different types of CHD. Even though the result did not reach statistical significance, which likely was due to the small sample size, the role of 3DPHM in improving short-term knowledge gain on CHD should not be overlooked, as the effect of 3DPHM on immediate knowledge acquisition appears to vary with the complexity of the CHD. In the study by White et al., residents were objectively tested on two types of CHD of different complexities to explore the usefulness of 3DPHM in improving residents' knowledge on VSD and ToF.[19] They were divided into 3DPHM and control groups for both VSD and ToF lecture. It was reported that the 3DPHM group scored higher in the ToF post-test ($p = 0.037$), but lower in the VSD post-test ($p = 0.02$).[19] Similarly, in another study by Smerling et al., first year medical students were subjectively tested to assess their perceived knowledge acquisition using 3DPHM of different lesion complexity.[3] It was reported that with the use of 3DPHM, as the complexity of CHD increases, the mean knowledge also increases.[3] This however, was not validated in our study, which could contribute to the findings of no significant difference. This limitation could be addressed in future studies.

Surprisingly, the 3DPHM group performed slightly inferior to the control group for long-term knowledge retention, even though this was not statistically significant. This is in contrast to another study by Lombardi et al., in which plastic heart models were compared to organ dissection of a sheep heart and virtual dissection using physiology software program, to assess the students' immediate knowledge acquisition and long-term knowledge retention on normal heart anatomy and physiology. It was found that the plastic model group performed significantly better during the initial exam and the 2-month follow-up exam.[20] This difference in findings might be due to the difference in methods of lecture being carried out in both studies. In Lombardi et al.'s study, the students in plastic model group were allowed 45-minute of hands-on activity with the models as well as within-group discussions after 15-minute of PowerPoint lecture;[20] whereas in our study, the students in the 3DPHM group learned individually and had full 1.5 hour of PowerPoint lecture with different teaching tools incorporated throughout the sessions. The amount of time that they spent on the models might not be enough. On the other hand, the study by Lombardi et al. only focused on normal heart anatomy and physiology,[20] whereas our study focused on CHD, which could justify the difference in findings.

As for the survey responses, although not statistically significant, greater percentage of students in 3DPHM group responded that the lecture was easy to understand, and that their knowledge on the topic of CHD has improved. In Loke et al.'s study, the 3DPHM group rated significantly higher satisfaction score towards the teaching session, when compared to the control group.[2] On the other hand, a meta-analysis found that the 3DPHM is associated with higher subjective evaluation scores and satisfactory level among the study participants.[9] This is also reflected in our study in which majority of the students responded (96% in the control group and 85% in the 3DPHM group) 'agree' or 'strongly agree' that the 3DPHM had helped them to gain a deeper understanding of CHD. Hence, the 3DPHM has contributed to improving students' learning experience.

It is worthwhile to report that in the survey when the students were asked to provide additional comments, some of them mentioned that the coloured digital 3D models were helpful for them to understand CHD compared to the CT images (total of 9 from the control group and 4 from the 3DPHM group). This is not surprising. As a novice, the students may not have the ability yet to mentally reconstruct the heart anatomy in 3D views based on the 2D images, not to mention when it comes to CHD when the heart morphology is more complex than the normal anatomy.[2, 4, 21] Hence, the digital 3D models were helpful for the students to visualise the heart defects in 3D, and the colour on the digital 3D models were helpful for them to understand the hemodynamic changes in the heart for each type of CHD. In fact, a recently published study by Liddle et al. found that the use of digital 3D heart models over tele-consultation had significantly improved the CHD patients' knowledge about their disease as well as their cardiac surgical history.[22] This has demonstrated the value of digital 3D heart models as an alternative or complementary teaching tool in medical education, especially when physical meeting is not possible during COVID-19 pandemic. In light of the pandemic, virtual education had formed an integral part of medical education.[23] While there are limited publications on virtual teaching of CHD, our group had compared the value of 3DPHM and virtual reality (VR) in medical teaching of CHD based on the opinions from radiologists, sonographers, and radiographers. It was found out that the VR heart models had comparable benefits with 3DPHM in medical teaching of CHD.[15] This is another area that can be explored further in future studies to investigate the use of virtual models in medical education.

This study has some limitations. Firstly, there were no pre-test done to test the students' actual baseline knowledge on CHD, hence it remains unknown that if both groups are comparable. Secondly, the selection criteria for the study participants could not exclude those who had pre-existing tertiary education, which could affect the results to some extent. Thirdly, the amount of time that each student in the 3DPHM group spent on assessing 3DPHM was not controlled. Even though they were encouraged to share the 3DPHM among themselves, some students may not spend as much time on the models as others, therefore reducing the level of benefits they could gain from the 3DPHM. Fourthly, both Quizzes 1 and 2 are a mixture of questions on factual and spatial knowledge on CHD, which might be too generalized to evaluate the actual effect of 3DPHM on CHD knowledge acquisition. It is suggested that future studies should group the questions into different educational components, for example, knowledge acquisition and structural conceptualization,[17] to investigate the effect of 3DPHM on these two components separately. Additionally, in the last question of the survey, the control group was being asked speculatively about their opinion on 3DPHM. This could have led to bias in the results, hence should be interpreted with caution. Lastly, it is unknown if the students had done any extra studies or revision on CHD during the 6-week's duration between Quizzes 1 and 2, which could have affected their score in Quiz 2. Future similar studies should take this confounding variable into account.

## 4.5 Conclusion

The results of this study suggested no significant improvement in CHD knowledge acquisition and knowledge retention with the use of 3DPHM compared to the conventional teaching methods. The 3DPHM did not significantly enhance the self-perceived knowledge improvement either among the students when compared to the conventional teaching methods. However, the positive benefit that the 3DPHM could bring to enhance the students' learning experience should not be overlooked. Future research should include larger number of sample size, and categorize the quiz questions into different educational components, allowing measurement of the true effect of 3DPHM on knowledge acquisition of different aspects of CHD.

## 4.6 References

1. Costello JP, Olivieri L, Krieger A, Thabit O, Marshall MB, Yoo SJ, et al. Utilizing Three-Dimensional Printing Technology to Assess the Feasibility of High-Fidelity Synthetic Ventricular Septal Defect Models for Simulation in Medical Education. *World J Pediatr Congenit Heart Surg*. 2014;5:421-6.
2. Loke YH, Harahsheh AS, Krieger A, Olivieri LJ. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. *BMC Med Educ*. 2017;17:54-61.
3. Smerling J, Marboe C, Lefkowitch J, Pavlicova M, Bacha E, Einstein A, et al. Utility of 3D Printed Cardiac Models for Medical Student Education in Congenital Heart Disease: Across a Spectrum of Disease Severity. *Pediatr Cardiol*. 2019;40(6):1258-65.
4. Costello JP, Olivieri LJ, Su L, Krieger A, Alfares F, Thabit O, 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.
5. Tan H, Huang E, Deng X, Ouyang S. Application of 3D printing technology combined with PBL teaching model in teaching clinical nursing in congenital heart surgery. *Medicine*. 2021;100:e25918.
6. Yoo S-J, Thabit O, Kim E, Ide H, Yim D, Dragulescu A, et al. 3D printing in medicine of congenital heart diseases. 3D Print Med. 2016;2(1):1-12. doi: 10.1186/s41205-016-0004-x
7. Lim KH, Loo ZY, Goldie S, Adams J, McMenamin P. Use of 3D printed models in medical education: A randomized control trial comparing 3D prints versus cadaveric materials for learning external cardiac anatomy. *Anat Sci Educ*. 2016;9:213–21.
8. Krishnasamy S, Mokhtar RAR, Singh R, Sivallingam S, Aziz YFA, Mathaneswaran V. 3D Rapid Prototyping Heart Model Validation for Teaching and Training - A Pilot Project in a Teaching Institution. *Braz J Cardiovasc Surg*. 2021;36(5):707-716. doi: 10.21470/1678-9741-2020-0433
9. Karsenty C, Guitarte A, Dulac Y, Briot J, Hascoet S, Vincent R, et al. The usefulness of 3D printed heart models for medical student education in congenital heart disease. *BMC Med Educ*. 2021;21:1–8.
10. Valverde I, Gomez G, Byrne N, Anwar S, Cerpa MAS, Talavera MM, et al. Criss-cross heart three-dimensional printed models in medical education: A

multicenter study on their value as a supporting tool to conventional imaging. Anat Sci Educ. 2022;15(4):1–12.

11. Lau I, Sun Z. Dimensional Accuracy and Clinical Value of 3D Printed Models in Congenital Heart Disease: A Systematic Review and Meta-Analysis. *J Clin Med*. 2019;8(9):1483.
12. Lau I, Liu D, Xu L, Fan Z, Sun Z. Clinical value of patient-specific three-dimensional printing of congenital heart disease: Quantitative and qualitative assessments. *PLoS One*. 2018;13: e0194333.
13. Giannopoulos A, Chepelev L, Sheikh A, Wang A, Dang W, Akyuz E, et al. 3D printed ventricular septal defect patch: a primer for the 2015 Radiological Society of North America (RSNA) hands-on course in 3D printing. *3D Print Med*. 2015;1(1):1-20.
14. Sun Z, Lau I, Wong YH, Yeong CH. Personalized Three-Dimensional Printed Models in Congenital Heart Disease. *J Clin Med*. 2019;8(4):522.
15. Lau I, Gupta A, Sun Z. Clinical value of virtual reality versus 3D printing in congenital heart disease. *Biomolecules*. 2021;11:884.
16. Jones TW, Seckeler MD. Use of 3D models of vascular rings and slings to improve resident education. *Congenit Heart Dis*. 2017;12:578–582.
17. Su W, Xiao Y, He S, Huang P, Deng X. Three-dimensional printing models in congenital heart disease education for medical students: a controlled comparative study. *BMC Med Educ*. 2018;18(1):178.
18. Yammine K, Violato C. The effectiveness of physical models in teaching anatomy: a meta-analysis of comparative studies. *Adv Health Sci Educ*. 2016;21:883–895.
19. White SC, Sedler J, Jones TW, Seckeler M. Utility of three-dimensional models in resident education on simple and complex intracardiac congenital heart defects. *Congenit Heart Dis*. 2018;13:1045–1049.
20. Lombardi SA, Hicks RE, Thompson KV, Marbach-Ad G. Are all hands-on activities equally effective? Effect of using plastic models, organ dissections, and virtual dissections on student learning and perceptions. *Adv Physiol Educ*. 2014;38:80–86.
21. Lion RP, Oei G, Collado NA, Singh S, Martens T. Integration of 3-dimensional Imaging into a Congenital Heart Disease Curriculum for the Cardiac Intensive Care Unit. *J Cardiovasc Dis Res*. 2020;11:12–15.

22. Liddle D, Balsara S, Hamann K, Christopher A, Olivieri L, Loke Y. Combining patient-specific, digital 3D models with tele-education for adolescents with CHD. *Cardiol Young*. 2022;32(6):912-917. doi: 10.1017/S1047951121003243
23. Tabatabai S. COVID-19 impact and virtual medical education. *J adv med educ prof*. 2020;8:140–143.

Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged.

# CHAPTER 5: CLINICAL VALUE OF VIRTUAL REALITY VERSUS 3D PRINTING IN CONGENITAL HEART DISEASE

## 5.1 Introduction

Due to the complex cardiac anatomy and the spectrum of pathologies associated with different types of CHD, a complete and scrupulous understanding of the morphology of CHD and the patient's management is often deemed challenging.[1–4] Although 2D and 3D rendering of the medical imaging datasets allow presentation of extra- and intra-cardiac structures, they are still limited to be viewed on 2D screens which do not depict the depth of the objects, and hence do not realistically convey the 3D views of anomalies. The interpretation of the heart patho-morphology still relies on operators' imagination to some extent.[2,4–13] The limitations of current visualization techniques have driven clinicians and researchers to continually search for solutions to enhance the visualization of complex CHD morphologies. VR provides simulation of the real world and allows users to interact directly with the virtual space.[14] The ability of VR to provide the end users free-form 3D visualization in a fully immersive environment has earned it an increasing role in facilitating group diagnostic discussions, complementing conventional surgical planning methods for cardiac surgeries, as well as improving the learning experience among clinicians and trainees.[12–14] A study by Ong et al. has demonstrated the value of VR in facilitating group based collaborative discussion, aiding the pre-operative planning process for CHD surgeries.[14] Kim et al. further validated this by evaluating the usefulness of full-immersive VR in facilitating group diagnostic discussions compared to that of non-immersive VR and a conventional 2D display. The result suggests that full-immersive VR is not only the most preferred display system among the participants, it also significantly improves the diagnostic accuracy of group discussions.[12]

3D printing technology is another option that has attracted increasing interest in cardiovascular medicine by providing more comprehensive visualization of the anomalous heart.[1–10,15,16] The main reason for using 3D printed models is to overcome the limitations of 2D medical images which fail to fully demonstrate the spatial relationships between intracardiac structures as well as the geometric relationship between the great vessels and surrounding anatomies.[17–19] With the tangible 3D printed model in hand, physicians can manipulate and assess the diseased heart to their liking. A multicenter study involving 40 patients with complex CHD reported the usefulness of 3DPHM in the pre-operative planning of their surgeries. In 19 of the 40 cases, the

3DPHM helped the surgeons to redefine a more suitable surgical approach through improving their perception of the size and spatial relationship of cardiac structures.[15]

However, both the use of VR in medicine and application of 3DPHM in CHD surgeries are still in their infancy. To the best of our knowledge, there is no published article to compare the value of VR against 3DPHM in providing a more comprehensive visualization for educating young physicians or medical practitioners about CHD and even aiding cardiac specialists in pre-operative planning of CHD. Thus, the aim of this study was to compare the clinical value of both VR and 3D printing in diagnostic assessment, medical education, and pre-operative planning of CHD through subjective evaluations from medical practitioners.

## 5.2 Materials and methods

### 5.2.1 Study design

A cross-sectional study was conducted to compare the clinical value of both VR and 3DPHM. The study was approved by the Curtin University Human Research Ethics Committee. To recruit the study participants, the study was advertised in the radiology department of a major public hospital in Perth, Western Australia. Thirty-five participants comprising radiologists, sonographers, and radiographers voluntarily participated in the study. Due to the limited number of VR headsets, the participants were divided into groups of 3 or 4 to ensure each of them had sufficient time for VR and 3DPHM assessment. Each group attended a 15-min VR and 3DPHM demonstration session. At the start of the session, they were briefed with the process of conversion from medical imaging datasets to VR and 3DPHM (an average of 3 min). Following that, they were given basic training of how to interact with the VR models using hand-held controllers. For the rest of the session (an average of 10 min), all the participants were encouraged to assess both VR and 3DPHM closely (Figure 5.1). There was no restriction in terms of the model assessment. The participants were allowed to assess the VR and 3DPHM in the order that they preferred, and were allowed discussion. At the end of the demonstration, they were asked to fill out a questionnaire, which was designed primarily to address the following aspects: (i) degree of realism of the heart models for each technology; (ii) the ability of each technology in displaying pathology and anatomy; (iii) the utility of each technology in educating medical students or young physicians about complex CHD; (iv) the usefulness of each technology in pre-operative planning for CHD. The questionnaire can be found in Appendix E1. All responses were recorded anonymously.

**Figure 5.1:** One of the participants assessed the VR heart models using Oculus Quest 2 (Facebook Technologies, LLC, Irvine, California, United States).

He was able to interact with the VR heart models using hand-held controllers.

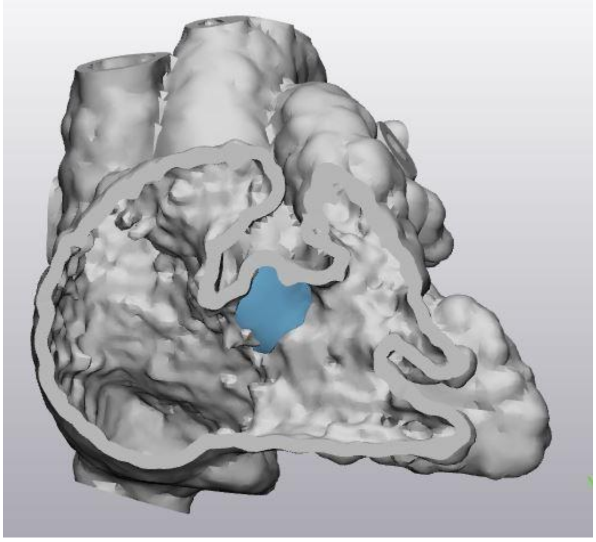
### 5.2.2 Generation of the heart models

The computed tomography angiography (CTA) imaging datasets of four different CHD cases were collected and used as the source data for this project. These four cases featured a range of CHD with different levels of complexity, defined by the Aristotle Basic Complexity Level (ABCL): atrial septal defect (ASD, ABCL = 1), ventricular septal defect (VSD, ABCL = 2), Tetralogy of Fallot (ToF, ABCL = 3), and double outlet right ventricle (DORV, ABCL = 4).

In order to convert the imaging dataset into printable and VR-viewable files, the heart was segmented to separate it from the surrounding bones, organs, and tissues. This process was performed using Mimics Innovation Suite 23.0 (Materialise HQ, Leuven, Belgium). An arbitrary thickness of a 1mm-thick shell was added onto the digital model before it was hollowed out to prevent the 3D printed model from collapsing during the 3D printing process. Following that, the digital model was smoothed out to remove any tiny spikes on the heart surface using 3-Matic, which is 3D modelling software accompanied by the Mimics Innovation Suite. A cutting plane transecting the right atrium and right ventricle was also created to separate the models in halves in order to demonstrate the critical anatomy (Figure 5.2). This cutting plane was kept consistent for both VR and 3DPHM.

For each case, a virtual patch was designed using 3-Matic to provide an option for the users to view the heart when the defect was closed (Figure 5.2).

**Figure 5.2:** A transected digital heart model demonstrating a ventricular septal defect with a virtual patch (in blue) over the defect.



### 5.2.3 3D printing of the heart

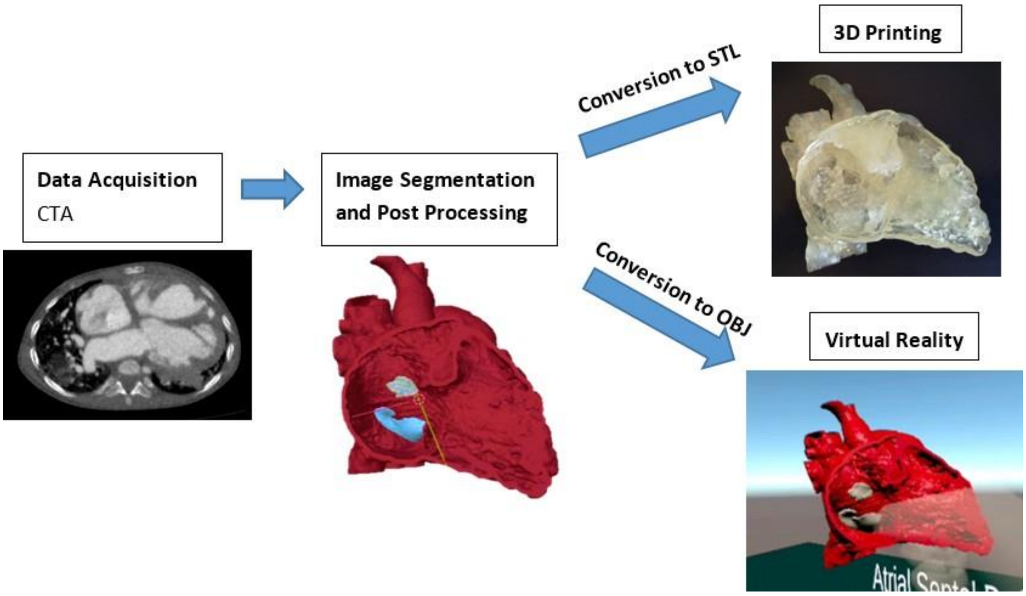
For 3D printing purposes, the digital heart models were converted into a standard tessellation language (STL) format. The models were printed in polyurethane (TPU80A, Fabbxible Technology Sdn Bhd, Pulau Pinang, Malaysia) and flexible resin (Flexible V4 Resin, Formlabs, Somerville, Massachusetts, United States), both with shore hardness of 80A.

### 5.2.4 Creation of the VR project

Unity 3D (Unity Technologies, San Francisco, California, USA) was used with C# coding to build a VR project to allow users to grab the heart models, rotate, and to view them up close within an immersive, virtual environment. The digital heart models were loaded into Unity 3D in object file (OBJ) format. Four tables were designed and placed in the virtual scene in Unity 3D, with the heart models of four different cases placed on the table respectively. Heart models with the virtual patch were also loaded into the virtual scene so that the users could visualize how the heart appeared when the defect was closed. The VR build was then exported in an android (APK) file format and loaded into Oculus Quest 2 (Facebook Technologies, LLC, Irvine, California, United States). Within the VR project, the users could turn around and use the hand-held controllers to grab different heart models, rotate them “in hand”, and view them up close (Figure 5.1).

Figure 5.3 illustrates the steps involved in creating the 3DPHM and the VR project. The video and images of VR and 3DPHM can be found in Appendices E2 and E3.

**Figure 5.3:** Steps involved in the creation of 3DPHM and the VR project.



3D, three-dimensional; CTA, computed tomography angiography; OBJ, object files; STL, standard tessellation language.

### 5.2.5 Statistical analysis

The data from the questionnaire were analyzed using SPSS 26.0 (IBM SPSS statistics). Quantitative data and categorical variables were analyzed using descriptive statistics (frequencies and median). Kendall’s W (coefficient of concordance) test was used to assess the agreement among participants with regard to the ability of VR and 3DPHM in demonstrating anatomy and pathology. The Mann-Whitney U test was used to compare the ratings given for both VR and 3DPHM, and also for subgroup (doctors and non-doctors) analysis. A p-value below 0.05 was considered statistically significant. Free-text in open-ended questions was analyzed using thematic analysis.

## 5.3 Results

Out of the 35 participants, 6 participants did not fully complete the questionnaire, therefore their responses were excluded from the data analysis. As a result, a total of 29 responses were included in the data analysis (1 cardiac radiologist, 1 interventional radiologist, 3 general radiologists, 4 radiology registrars, 3 sonographers, 16 radiographers, and 1 student radiographer).

Tables 5.1–5.4 are the frequency tables of the individual questions on the questionnaire with regard to the four aspects. Generally, both VR and 3DPHM were comparable with each other in terms of the degree of realism (Table 5.1); the 3DPHM was better in displaying the CHD pathology and anatomy (Table 5.2); VR was perceived as more useful for educating medical students and young physicians about CHD (Table 5.3), as well as pre-operative planning (Table 5.4). The Kendall's W test shows no significant difference in the frequencies between VR and 3DPHM according to the results shown in Table 5.2 ($p = 0.32$), but there was a significant difference between other comparisons (VR vs. Both and Unsure, 3DPHM vs. Both and Unsure, $p = 0.04$).

The Mann–Whitney U test shows no significant difference between VR and 3DPHM in terms of the ratings for their usefulness in medical education and pre-operative planning, with the mean rank of 3DPHM slightly higher than the VR models in both aspects ($p = 0.35$ and $p = 0.54$, respectively) (Table 5.5). Subgroup analysis was also performed to determine if there was any difference in the responses depending on the participants' clinical background. The clinicians were grouped into doctors' and non-doctors' groups for the subgroup analysis. The non-doctors' group consisted of sonographers, radiographers, and a student radiographer ($n = 20$), while the others were grouped as the doctors' group ($n = 9$). The Mann–Whitney U test demonstrates no significant difference in responses between the doctors' and non-doctors' groups (Table 5.6).

**Table 5.1:** Participants' responses on the degree of realism of the VR and 3DPHM.

| **Question** **Option** | **VR Models** | | **3DPHM** | | **Both are the same** | | **Unsure** | |
|---|---|---|---|---|---|---|---|---|
| | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** |
| Better depth perception? | 8 | 27.6 | 16 | 55.2 | 5 | 17.2 | 0 | 0 |
| Better and more comprehensive viewing experience? | 19 | 65.5 | 8 | 27.6 | 1 | 3.4 | 1 | 3.4 |
| More realistic visualization? | 9 | 31.0 | 12 | 41.4 | 5 | 17.2 | 3 | 10.3 |
| Total | 36 | 41.38 | 36 | 41.38 | 11 | 12.64 | 4 | 4.60 |

3DPHM, 3D printed heart models; Freq., frequency; VR, virtual reality.

**Table 5.2:** Participants' responses on the ability of VR and 3DPHM in displaying pathology and anatomy.

| **Question** **Option** | **VR Models** | | **3DPHM** | | **Both are the same** | | **Unsure** | |
|---|---|---|---|---|---|---|---|---|
| | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** |
| Better appreciation of heart defects? | 14 | 48.3 | 11 | 37.9 | 3 | 10.3 | 1 | 3.4 |
| Better understanding of the spatial relationship between cardiac structures? | 7 | 24.1 | 17 | 58.6 | 5 | 17.2 | 0 | 0 |
| Better visualization of external cardiac structures? | 5 | 17.2 | 19 | 65.5 | 4 | 13.8 | 1 | 3.4 |
| Better visualization of internal cardiac structures? | 15 | 51.7 | 13 | 44.8 | 1 | 3.4 | 0 | 0 |
| Total | 41 | 35.35 | 60 | 51.72 | 13 | 11.21 | 2 | 1.72 |

3DPHM, 3D printed heart models; Freq., frequency; VR, virtual reality.

**Table 5.3:** Participants’ responses on the utility of VR and 3DPHM in educating medical students or young physicians about complex CHD.

| **Question**<br>**Option** | **VR Models** | | **3DPHM** | | **Both are the same** | | **Unsure** | |
|---|---|---|---|---|---|---|---|---|
| | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** |
| More useful in educating medical students or young physicians about CHD? | 12 | 41.4 | 4 | 13.8 | 12 | 41.4 | 1 | 3.4 |

3DPHM, 3D printed heart models; Freq., frequency; VR, virtual reality.

**Table 5.4:** Participants’ responses on the usefulness of VR and 3DPHM in pre-operative planning for CHD.

| **Question**<br>**Option** | **VR Models** | | **3DPHM** | | **Both are the same** | | **Unsure** | |
|---|---|---|---|---|---|---|---|---|
| | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** | **Freq.** | **%** |
| More useful in pre-operative planning for CHD? | 10 | 34.5 | 9 | 31.0 | 4 | 13.8 | 6 | 20.7 |

3DPHM, 3D printed heart models; Freq., frequency; VR, virtual reality.

**Table 5.5:** Participants' responses on the ratings for VR and 3DPHM, out of score of 5 [a].

| Question / Option | VR Models, n = 29 clinicians | 3DPHM, n = 29 clinicians | Mann Whitney U-value | p-value |
|---|---|---|---|---|
| Rate the usefulness of the models in medical education | 4 (27.60) | 4 (31.40) | 365.50 | 0.35 |
| Rate the usefulness of the models in pre-operative planning | 4 (28.26) | 4 (30.74) | 384.50 | 0.54 |

3DPHM, 3D printed heart models; VR, virtual reality. [a] Data are median score (mean rank).

**Table 5.6:** Subgroup analysis for participants' responses on the ratings for VR and 3DPHM, out of score of 5 [a].

| Question / Option | Doctors' Group, n = 9 | Non-doctors' Group, n = 20 | Mann Whitney U-value | p-value |
|---|---|---|---|---|
| Rate the usefulness of VR models in medical education | 4 (11.22) | 4 (16.70) | 56.00 | 0.07 |
| Rate the usefulness of 3DPHM in medical education | 4 (11.11) | 5 (16.75) | 55.00 | 0.07 |
| Rate the usefulness of VR models in pre-operative planning | 4 (11.06) | 4 (16.77) | 54.50 | 0.07 |
| Rate the usefulness of 3DPHM in pre-operative planning | 4 (12.39) | 4.5 (16.18) | 66.50 | 0.23 |

3DPHM, 3D printed heart models; VR, virtual reality. [a] Data are median score (mean rank).

Out of the 29 participants, 22 (76%) indicated both the VR and 3DPHM were helpful to increase surgeons' confidence for CHD surgeries (Figure 5.4). No one indicated 'No' for this question, suggesting the participants' positivity towards this aspect.

Twenty-one participants (72%) indicated both the VR and 3DPHM provided additional benefits compared to the conventional medical imaging visualizations. Eight of them commented on the 3D visualization helping them to better appreciate the spatial information; six of them indicated the tactile models (3DPHM) as being beneficial for the learning of CHD; three of them pointed out both of the technologies as being helpful in visualizing and conceptualizing the cardiac structures; and four of them mentioned the added benefits of the models to convey anatomy or pathology to patients.

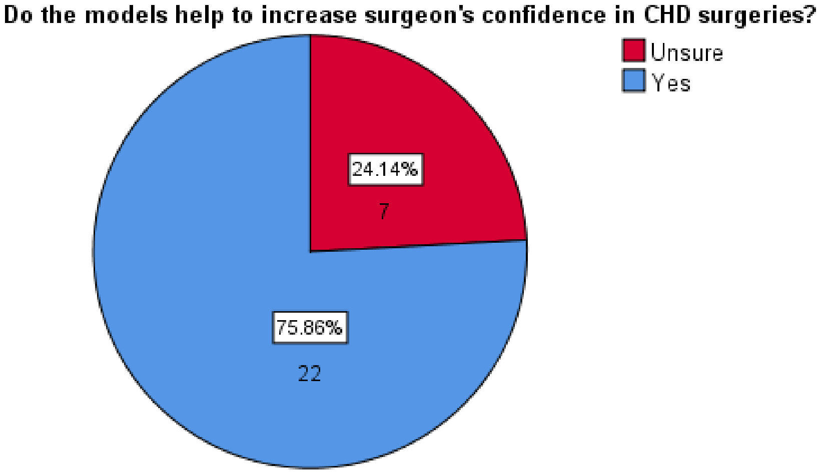


**Figure 5.4:** Responses from the participants with regard to their opinion on whether VR and 3DPHM help to increase surgeons' confidence in CHD surgeries.

## 5.4 Discussion

This study presents a side-by-side comparison of both 3D printing and VR technologies from subjective evaluations of a group of medical practitioners. The results show both of them being on a similar level with each other in providing a better visualization experience compared to the conventional visualization technique. In fact, the advent of 3D printing and VR are currently transforming and improving visualization techniques for medical imaging.[12,20,21] The benefits of 3D printing in pre-operative planning for CHD can be seen from the increasing reports over the years.[1–10,15–19,22] Yoo et al. reported the use of 3DPHM in planning and simulation of an extremely complex heart surgery for dextrocardia which involved heart transplantation.[22] In another cross-sectional study which involved 71 pediatric cardiologists from different countries, it was found that 85% of the participants agreed or strongly agreed, that 3DPHM are beneficial in the treatment of CHD, with surgical planning as the primary utility of 3DPHM.[23] This echoes the finding from a recent meta-analysis, which found pre-operative planning being the most relevant application of 3DPHM.[24] VR has also been reported in the current literature for its ability to provide an immersive, interactive, and free-form visualization experience, despite it not being tactile like 3DPHM.[12,14,25–27] Unlike 3DPHM, being static and unable to show cardiac functional information, the VR project can be "programmed" to show dynamic cardiac models,[28,29] to allow users to scale, rotate, crop the cardiac models, and change the viewing planes according to their needs.[12]

However, both of these technologies do not come without limitations. The main barrier that impedes the wide application of 3D printing in CHD is the associated start-up cost. This includes the costs of 3D printers, their operation and maintenance, 3D printing materials, segmentation software, and the hiring of expertise.[23,30] With the advancement of this technology, this cost is expected to be reduced.[20] A recent study reported that the low-cost 3DPHM is just as accurate as the high-cost 3DPHM in delineating cardiac anatomy.[31] Therefore, depending on the medical application, a low-cost 3DPHM can be used to reduce the cost of 3D printing. Secondly, the segmentation process is laborious and time-consuming. It requires skilled personnel or most often, a multi-disciplinary team to have the knowledge of anatomy, imaging physics, and engineering knowledge pertaining to 3D printing.[23,30] As for VR, the main limitation is the need to wear bulky headsets.[32] Additionally, the users may also have motion sickness, which could pose risks to patients' safety during procedures.[21,32]

In the present study, the results demonstrated that 3DPHM are perceived to be better in displaying CHD pathology and anatomy. This contradicts the finding of another study. Raimondi et al. compared 3DPHM and VR models of three cases of complex CHD, and their result suggested that the VR models were superior to the 3DPHM in conveying ventricular-arterial connections and the aortic arch.[25] This could be related to the difference in the development of VR models. Raimondi et al. used DIVA software to convert the DICOM dataset into VR models in a matter of minutes, skipping the image segmentation step completely. This software exploits the potential of volumetric rendering, which is able to generate 3D models without the need of image segmentation.[33] The software also allowed the end users to change the viewing plane and navigate within the heart.[25] This is different to the VR project that is presented in our study. Our VR project is relatively simple to create and easy to use, which allows users to get the hang of it really quickly (Appendix E2). The users were allowed to grab, rotate and view the VR models up close by simply bringing the hand controller closer to them. It also supports multiple cardiac models to be loaded within the VR project. However, the users were not able to change the viewing planes or crop the cardiac models, which is one of the limitations of the presented VR project. The simplicity of this VR project makes it quite different from other studies in which the users are able to change the clipping plane,[12,14,25,26] or view the models intraluminally.[27] In fact, there is no standardized way for creating a VR project.[25] The users can design it according to their needs. Even though this VR project does not feature as many interactive elements as other studies reported, its ability to provide a fully immersive and enhanced viewing experience should not be overlooked. During the evaluation, one of the participants dropped the hand controller as she was putting the cardiac model back onto the virtual table, thinking that there was a ‘real’ table in front of her. This implicitly highlights the immersiveness of the VR tool.

There is one contradictory finding from the results, which could be related to the insufficiency of the design of the questionnaire. While the majority of the participants indicated VR is more useful in medical education and pre-operative planning, 3DPHM has a higher mean rank compared to VR according to the ratings given by the participants, although the difference in mean ranks does not reach statistical significance. This can be explained by the limitation of the use of a 5-point rating scale in this instance, and it might be inadequate to measure the difference in responses. Many of the participants have given both VR and 3DPHM the same ratings even though they indicated otherwise for questions in Tables 5.3 and 5.4.

There are a few limitations in this study which need to be acknowledged. Firstly, this study only involves radiologists and radiographers; therefore, the application of 3D printing and VR in CHD may not be as relevant for them as opposed to cardiac specialists. Secondly, there were only 15 min for the evaluations of both VR and 3DPHM, which may not be sufficient for some participants should they need a longer time to get a better understanding of these two new visualization tools. Thirdly, as the participants were allowed to assess the models freely in any order with group discussions permitted, their responses could have been affected by the order effect and conformity bias. Lastly, we only included four categories of CHD in this study, which limits it to CHD cases only. Further studies should look at the application of VR and 3DPHM in other cardiovascular disease, such as complex aortic aneurysm or aortic dissection.

## 5.5 Conclusion

This study compared the clinical value of both VR and 3D printing in diagnostic assessment, medical education, and pre-operative planning of CHD through subjective evaluations from medical practitioners. The results show no significant difference between both technologies in the aforementioned areas. However, we should not overlook the benefits of both technologies in providing advanced visualization in medicine. Future studies should involve cardiac specialists to provide more pertinent opinions and evaluations of these two visualization tools in CHD and other cardiovascular diseases. Additionally, it could be useful for future studies to investigate the difference in the level of clinical benefits gained from VR and 3DPHM for CHD of different complexities.

## 5.6 References

1. Bhatla P, Tretter JT, Ludomirsky A, Argilla M, Latson Jr. LA, Chakravarti S, 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. doi: 10.1007/s00246-016-1489-1
2. Schmauss D, Haeberle S, Hagl C, Sodian R. Three-dimensional printing in cardiac surgery and interventional cardiology: A single-centre experience. *Eur J Cardio Thorac Surg*. 2015;47:1044–1052.
3. Valverde I, Gomez G, Gonzalez A, Suarez-Mejias C, Adsuar A, Coserria JF, et al. Three-dimensional patient-specific cardiac model for surgical planning in Nikaidoh procedure. *Cardiol Young*. 2015;25:698–704.
4. Riesenkampff E, Rietdorf U, Wolf I, Schnackenburg B, Ewert P, Huebler M, Alexi-Meskishvili V, Anderson RH, Engel N, Meinzer H, Hetzer R, Berger F, Kuehne T. The practical clinical value of three-dimensional models of complex congenitally malformed hearts. *J Thorac Cardiovasc Surg*. 2009;138:571-580.
5. Shiraishi I, Yamagishi M, Hamaoka K, Fukuzawa M, Yagihara T. Simulative operation on congenital heart disease using rubber-like urethane stereolithographic biomodels based on 3D datasets of multislice computed tomography. *Eur J Cardiothorac Surg*. 2010;37:302-6.
6. Greil GF, Wolf I, Kuettner A, Fenchel M, Miller S, Martirosian P, et al. Stereolithographic reproduction of complex cardiac morphology based on high spatial resolution imaging. *Clin Res Cardiol*. 2007;96:176-85.
7. Biglino G, Koniordou D, Gasparini M, Capelli C, Leaver L, Khambadkone S, et al. Piloting the use of patient-specifc cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr Cardiol*. 2017;38:813-8.
8. Mottl-Link S, Hübler M, Kühne T, Rietdorf U, Krueger JJ, Schnackenburg B, et al. Physical Models Aiding in Complex Congenital Heart Surgery. *Ann Thorac Surg*. 2008;86:273-7.
9. Cantinotti M, Valverde I, Kutty S. Three-dimensional printed models in congenital heart disease. *Int J Cardiovasc Imaging*. 2017;33:137-44.
10. Gosnell J, Pietila T, Samuel BP, Kurup HK, Haw MP, Vettukattil JJ. Integration of Computed tomography and three-dimensional echocardiography for hybrid threedimensional printing in congenital heart disease. *J Digit Imaging.* 2016;29:665-9.

11. Brun H, Bugge RAB, Suther LKR, Birkeland S, Kumar R, Pelanis E, et al. Mixed reality holograms for heart surgery planning: First user experience in congenital heart disease. *Eur Heart J Cardiovasc Imaging*. 2019;20:883–888.
12. Kim B, Loke YH, Mass P, Irwin MR, Capeland C, Olivieri L, et al. A Novel Virtual Reality Medical Image Display System for Group Discussions of Congenital Heart Disease: Development and Usability Testing. *JMIR Cardio*. 2020;4:e20633.
13. Kumar RP, Pelanis E, Bugge R, Brun H, Palomar R, Aghayan DL, et al. Use of mixed reality for surgery planning: Assessment and development workflow. *J Biomed Inform*. 2020;8:100077.
14. Ong CS, Krishnan A, Huang CY, Spevak P, Vricella L, Hibino N, et al. Role of virtual reality in congenital heart disease. *Congenit Heart Dis*. 2018;13:357–361.
15. Valverde I, Gomez-Ciriza G, Hussain T, Suarez-Mejias C, Velasco-Forte MN, Byrne N, et al. Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study. *Eur J Cardiothorac Surg*. 2017;52:1139-48.
16. Anwar S, Singh GK, Miller J, Sharma M, Manning P, Billadello JJ, et al. 3D Printing is a transformative technology in congenital heart disease. *JACC Basic Transl Sci*. 2018;3:294–312.
17. Hoashi T, Ichikawa H, Nakata T, Shimada M, Ozawa H, Higashida A, et al. Utility of a super-flexible three-dimensional printed heart model in congenital heart surgery. *Interact Cardiovasc Thorac Surg*. 2018;27(5):749-55.
18. Olivieri LJ, Zurakowski D, Ramakrishnan K, Su L, Alfares FA, Irwin MR, Heichel J, Krieger A, Nath DS. Novel, 3D Display of Heart Models in the Postoperative Care Setting Improves CICU Caregiver Confidence. *World J Pediatr Congenit Heart Surg*. 2018;9:206-13.
19. Smith M, McGuinness J, O'Reilly M, Nolke L, Murray J, Jones J. The role of 3D printing in preoperative planning for heart transplantation in complex congenital heart disease. *Ir J Med Sci*. 2017;186:753–756.
20. Sun Z, Lau I, Wong YH, Yeong CH. Personalized Three-Dimensional Printed Models in Congenital Heart Disease. *J Clin Med*. 2019;8(4):522.
21. Goo HW, Park SJ, Yoo SJ. Advanced Medical Use of Three-Dimensional Imaging in Congenital Heart Disease: Augmented Reality, Mixed Reality, Virtual Reality, and Three-Dimensional Printing. *Korean J Radiol*. 2020;21(2):133-45.

22. Yoo JS, Reddy YNV, Kim KH. Heart transplantation for dextrocardia: Preoperative planning using 3D printing. *Eur Heart J Cardiovasc Imaging*. 2020;21:346.
23. Illmann CF, Hosking M, Harris KC. Utility and Access to 3-Dimensional Printing in the Context of Congenital Heart Disease: An International Physician Survey Study. *CJC Open*. 2020;2:207–213.
24. Lau I, Sun Z. Dimensional Accuracy and Clinical Value of 3D Printed Models in Congenital Heart Disease: A Systematic Review and Meta-Analysis. *J Clin Med*. 2019;8(9):1483.
25. Raimondi F, Vida V, Godard C, Bertelli F, Reffo E, Boddaert N, et al. Fast-track virtual reality for cardiac imaging in congenital heart disease. *J Card Surg*. 2021;1–5.
26. Milano EG, Pajaziti E, Sauvage E, Cook A, Schievano S, Mortensen KH. Taking Surgery Out of Reality: A Virtual Journey Into Double Outlet Right Ventricle. *Circ Cardiovasc Imaging*. 2019;12:e009297.
27. Mendez A, Hussain T, Hosseinpour AR, Valverde I. Virtual reality for preoperative planning in large ventricular septal defects. *Eur Heart J*. 2019;40: 1092.
28. Wierzbicki M, Drangova M, Guiraudon G, Peters T. Validation of dynamic heart models obtained using non-linear registration for virtual reality training, planning, and guidance of minimally invasive cardiac surgeries. *Med Image Anal*. 2004;8:387–401.
29. Pushparajah K. Chu KYK, Deng S, Wheeler G, Gomez A, Kabir S, et al. Virtual reality three-dimensional echocardiographic imaging for planning surgical atrioventricular valve repair. *JTCVS Tech*. 2021;7:269-277. doi:10.1016/j.xjtc.2021.02.044
30. Bramlet M, Olivieri L, Farooqi K, Ripley B, Coakley M. Impact of Three-Dimensional Printing on the Study and Treatment of Congenital Heart Disease. *Circ Res*. 2017;120:904–907.
31. Lau I, Wong YH, Yeong CH, Abdul Aziz YF, Md Sari NA, Hashim SA, et al. Quantitative and qualitative comparison of low- and high-cost 3D-printed heart models. *Quant Imaging Med Surg*. 2019; 9(1):107–114.
32. Byl JL, Sholler R, Gosnell JM, Samuel BP, Vettukattil JJ. Moving beyond two-dimensional screens to interactive three-dimensional visualization in congenital heart disease. *Int J Cardiovasc Imaging*. 2020;36:1567-1573. doi: https://doi.org/10.1007/s10554-020-01853-1

33. Wheeler G, Deng S, Toussaint N, Pushparajah K, Schnabel JA, Simpson JM, et al. Virtual interaction and visualisation of 3D medical imaging data with VTK and Unity. *Healthc Technol Lett*. 2018;5(5):148–153.

Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged.

# CHAPTER 6: CLINICAL APPLICATIONS OF MIXED REALITY AND 3D PRINTING IN CONGENITAL HEART DISEASE

## 6.1 Introduction

Congenital heart disease (CHD) is considered as one of the most challenging pathologies to manage in clinical practice due to its broad spectrum of morphologies that vary from individuals to individuals.[1-3] If surgery or intervention is required to repair the heart lesion, a full understanding of the anomalous cardiac structure plays a fundamental role in a successful surgery.[3,4] However, current visualization techniques based on cardiac computed tomography (CT) or magnetic resonance imaging with volume rendering lacks realism as they do not depict the actual depth of the object.[1,2]

Three-dimensional (3D) printing is a technique that has been adopted in cardiovascular medicine in the last two decades to demonstrate the geometric relationships between the intra- and extra-cardiac structures. [5-14] One recent study presented the use of 3D printed heart models (3DPHM) in 40 cases where types of surgical strategy could not be determined from the conventional imaging. 3DPHM had helped the surgical team to decide and modify the best treatment plan for 31 cases, while the remaining 9 cases remain equivocal.[15] Other studies have also demonstrated the usefulness of 3DPHM in surgical simulation, hands-on training, and medical education.[3,5-18] Despite these benefits from using 3DPHM, the time and cost in producing them are the two main factors that impede its widespread application in medical field.[3] Furthermore, as it is a relatively novel technology for medical application, its application still require long process of standardization and quality control.[3]

Mixed reality (MR), which is an advancement of augmented reality (AR), has only very recently been introduced to the realm of medicine.[19] MR works by overlaying virtual objects on the real world settings via head-mounted displays or hand-held mobile devices, allowing the users to manipulate or interact with the virtual objects within an immersive environment.[20] A recent study by Gehrsitz et al. has demonstrated the usefulness of MR in the preoperative planning of paediatric heart surgeries. The use of MR was found to significantly improve the depth perception and portrayal of the pathology when compared to the two-dimensional (2D) medical images and 3DPHM.[21] Use of AR has also been shown constructive in Valve-in-Valve Transcatheter Heart Valve Implantation and percutaneous coronary intervention procedures.[22,23] The superimposition of the computed tomography angiography (CTA) reconstructions with the real-time fluoroscopic images had allowed the cardiologist to accurately deploy the transcatheter heart valve with minimal contrast administration.[22] However, both the use of MR in medicine and application of 3DPHM in complex cardiac surgeries are still in their infancy. Especially for MR, its superiority over the current visualization technique requires further validation. The published article to compare 3D printing and MR in paediatric heart surgeries is limited to one surgeon's assessment based on a single centre experience.[21]

Hence, the aim of this study is to investigate the clinical value of both MR and 3D printing in CHD by comparing these innovative technologies concurrently with the conventional visualization technique in terms of assisting clinical diagnosis, medical education, pre-operative planning and intra-operative guidance of the CHD surgeries through evaluations from cardiac specialists and physicians.

## 6.2 Materials and methods

This is a cross-sectional study performed to assess the cardiac specialists' and physicians' opinion on the two rapidly evolving 3D visualization techniques: 3D printing and MR, comparing to the conventional method using Digital Imaging and Communications in Medicine (DICOM) images. This study was conducted following the clinical practice guidelines with ethics approval sought from Curtin University Human Research Ethics Committee.

### 6.2.1 Generation of the digital heart models

Two cases of anonymized cardiac CT angiography scans featuring CHD were retrospectively chosen as the source data. In order to find out if the study result is dependent on the complexity of the disease, we have included cases with Aristotle Basic Complexity Level (ABCL) of 1 and 4: atrial septal defect (ASD) and Double Outlet Right Ventricle (DORV), respectively. The CT datasets were transferred to a workstation for image post-processing using Mimics Innovation Suite 22.0 (Materialise HQ, Leuven, Belgium). The segmentation process was semi-automated using thresholding technique by selecting the blood pool as area of interest. After removing all the unwanted structures, a 1-mm thick shell was added onto the models using 3-Matic (Materialise HQ, Leuven, Belgium). Then, the digital model were hollowed out and smoothed. The digital heart models took approximately 30 minutes each to be generated.

### 6.2.2 3D printing

The digital models were exported in standard tessellation language (STL) format for 3D printing. In order to view the intra-cardiac structures, the STL files were imported to Meshmixer (Autodesk, San Rafael, CA, USA) for separation of the heart models into two compartments. A suitable cutting plane transecting the right atrium and right ventricle was created on both models. They were then exported as separate STL files for 3D printing. They were printed commercially in clear Agilus 30 (Objective 3D, Stratasys,, Melbourne, Victoria, Australia), which has a shore hardness of 30A and therefore are able to provide a flexible touch (Figure 6.1). The ASD model costs AUD350, whereas the DORV costs AUD270 to print.

**Figure 6.1:** Flexible heart models printed in Agilus 30 featuring atrial septal defect (left) and double outlet right ventricle (right).

### 6.2.3 Development of mixed reality application

Figure 6.2 illustrates the process of the development of MR application. The digital models were exported in object file (OBJ) format and loaded into Blender (V2.91.0, Blender Foundation, Amsterdam, The Netherlands) for optimization for holographic viewing. Due to the highly complex polygon mesh of the heart models, the models were required to undergo primitive UV sphere in Blender to optimize the performance of the application on HoloLens 2 (Microsoft Crop., Redmond, DC, USA). For the development of the MR application, Unity engine (V2020.3.13f1, Unity Technologies ApS., San Francisco, CA), Microsoft OpenXR Plugin, Mixed Reality Toolkit (MRTK) (V2.7.0), and Microsoft Visual Studio 2019 (Version 16.11.9, Microsoft Corp., Redmond, DC, USA) were utilized. The initial steps to set up the application were referenced from the Microsoft HoloLens 2 tutorial webpage.[24]

Within Unity, both optimized models were loaded into the scene. Red colour was added as the models' material to give the heart models a more realistic look. A sphere was added into the scene with a custom shader script written in High-Level Shading Language (HLSL), allowing the sphere to serve as a clipping tool (Figure 6.3). A C# script was also written to allow the clipping range to change according to the size of the sphere, which is determined by the users. This allows the users to manipulate the cutting plane of the MR heart models by changing the size of the sphere using different hand gestures (Figure 6.4). A video of the MR application can be viewed in Appendix F1.

**Figure 6.2:** A flow diagram illustrating the process of mixed reality application development.

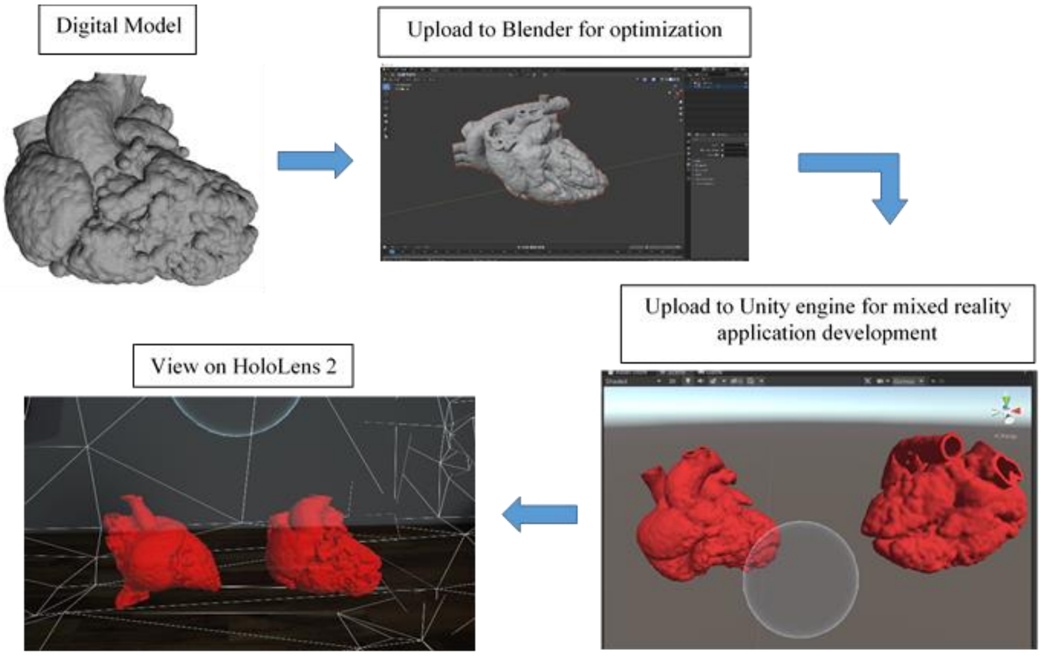


**Figure 6.3:** A screenshot of the Unity scene with 2 heart models and a sphere to serve as the clipping tool.

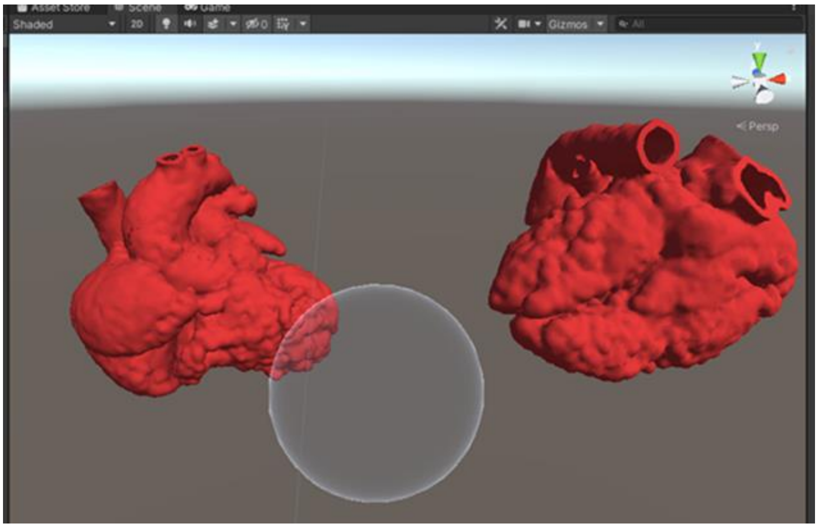
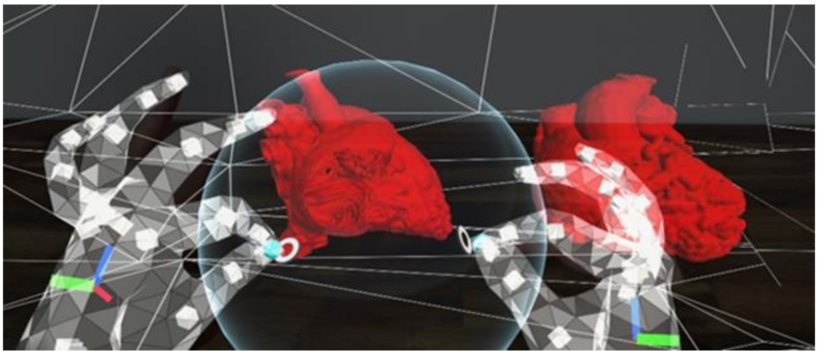


**Figure 6.4:** A screenshot using the HoloLens 2.



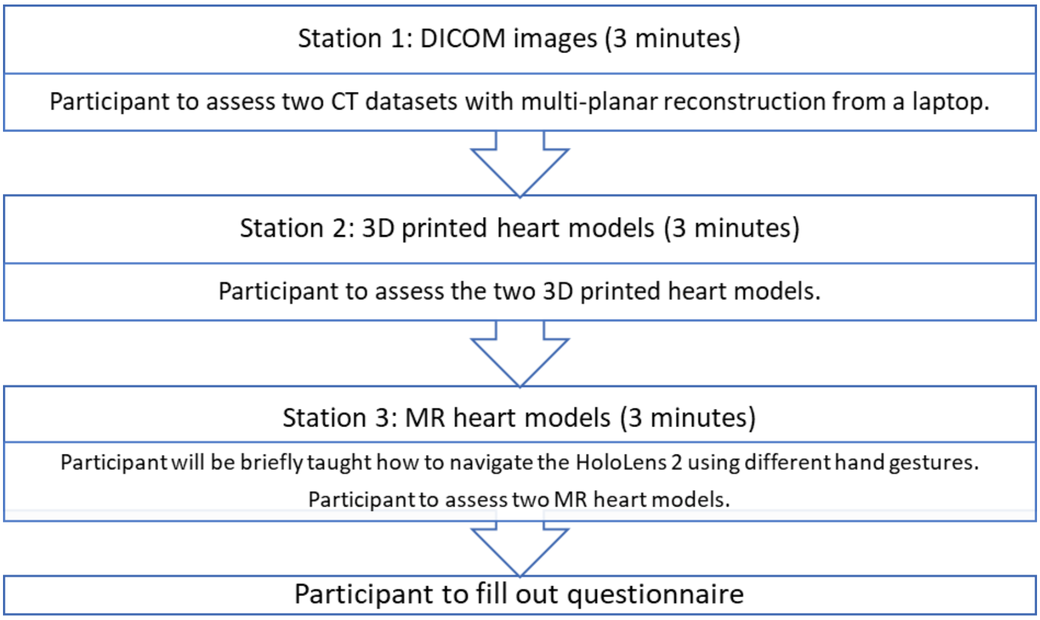
The user is using the sphere to cut through the heart models in order to view the intra-cardiac structures. The sphere can be enlarged or sized down to change the amount of anatomy to be cut out.

### 6.2.4 Participant recruitment and data collection

Thirty-four cardiac specialists and physicians were recruited from public and private hospitals in Western Australia. Each participant attended a one-to-one session with one of the authors (IL), therefore their responses were independent to each other. Each participant went through 3 different stations for assessment of heart models in different forms. In order to mimic the real clinical situation, the participants were not informed of the diagnosis during the assessment, and were asked to make their own diagnosis. The answers were only revealed at the end of third station. In order to keep consistent the amount of time each participant spend on assessing the models, each participant were given a time limit of 3 minutes per station.

At station 1, the participants were presented with the CT images of ASD and DORV cases on a laptop using an open-source DICOM viewer, RadiAnt (Medixant, Poznan, Poland). Without being told the diagnosis of the cases, they were asked to examine the anatomy and pathology based on the DICOM datasets. As this is the routine approach to examine the pathologies, this station acted as a control for the study. At station 2, the participants were presented with the 3DPHM. At station 3, the participants were presented with HoloLens 2. They were first given brief instructions on how to manipulate the MR heart models using different hand gestures (zooming in and out, changing the clipping plane, rotating the models) prior to assessment of the models. The time taken for each participant to learn manipulating the MR models was excluded from the 3-minutes time limit. After that, the participants filled out a questionnaire to rank each modality from 1 to 3 for each of the question. The questionnaire was designed particularly to focus on (i) the ability of each modality in displaying normal/abnormal cardiac and vascular structures and pathologies; (ii) the utility of each modality in educating young doctors or physicians about CHD; (iii) the usefulness of each modality in pre-operative planning and intraoperative guidance of CHD surgeries. For participants who are non-surgical nor interventional, their questionnaire only focused on (i) and (ii). The questionnaire can be found in Appendix F2. Figure 6.5 illustrates this process.

**Figure 6.5:** The process each participant undertook.



Station 1: DICOM images (3 minutes)

Participant to assess two CT datasets with multi-planar reconstruction from a laptop.

Station 2: 3D printed heart models (3 minutes)

Participant to assess the two 3D printed heart models.

Station 3: MR heart models (3 minutes)

Participant will be briefly taught how to navigate the HoloLens 2 using different hand gestures.

Participant to assess two MR heart models.

Participant to fill out questionnaire

### 6.2.5 Statistical analysis

The quantitative data from the questionnaire was analysed using IBM SPSS statistical package, version 26 (IBM Corp, Armonk, NY, USA). Normality of the data was assessed by normal probability plot and skewness and kurtosis of the distribution were reported. To assess the statistical differences of the mean scores between DICOM images, 3DPHM, and the MR models, general linear model was applied with gender, age, occupation, AR experience and 3D printing experience as confounding factors. Independent samples t-test was used to compare the responses between interventionists and non-interventionists. A p-value of <0.05 is considered statistically significant. The qualitative data from the free-text section on the questionnaire was analyzed using thematic analysis.

## 6.3 Results

Out of the 34 participants, there were 27 males, and 16 below the age of 40. There were 8 cardiac surgeons, 16 interventional cardiologists and cardiology registrars, 6 cardiologists and cardiac imaging fellow, and 4 radiologists and general physicians (Table 6.1). About 58.8% and 52.9% of the participants indicated they have never used AR and 3D printing in their medical practice, respectively.

The responses for each question on the questionnaire follow approximately a normal distribution, except for Question 7 with the modality of 3D printing (skewness = 2.986 for ASD, 2.728 for DORV). The results of the normality of the data can be found in Appendix F3. Table 6.2 presents the mean rank of each modality for each question. The participants were asked to rank the modality from 1 to 3 (1 being the best modality). Therefore, the closer the mean rank gets to 1, the better the modality is perceived by the participants. Table 6.3 presents the mean rank differences between modalities and their respective p-values. Table 6.4 presents the mean differences in the responses between the two occupation groups, interventionalists or non-interventionalists. The result shows that there is no significant differences in their responses.

**Table 6.1:** Characteristics of study participants.

| **Variables** | **No. of participants (%)** |
|---|---|
| *Gender* | |
| Male | 27 (79.4) |
| Female | 7 (20.6) |
| *Age* | |
| Below 40 | 16 (47.1) |
| Above 40 | 15 (44.1) |
| Missed responses | 3 (8.8) |
| *Occupation* | |
| *Surgical / interventional* | |
| Cardiac surgeon | 8 (23.5) |
| Interventional cardiologist, cardiology registrar | 16 (47.0) |
| *Non-surgical / non-interventional* | |
| Cardiologist, cardiac imaging fellow | 6 (17.6) |
| Radiologist, general physicians | 4 (11.8) |
| *AR experience* | |
| Yes | 12 (35.3) |
| No | 20 (58.8) |
| Missed responses | 2 (5.9) |
| *3D printing experience* | |
| Yes | 14 (41.2) |
| No | 18 (52.9) |
| Missed responses | 2 (5.9) |

3D, three-dimensional; AR, augmented reality

**Table 6.2:** The mean rank of different modalities for each question.

| Questions | Modality | ASD | | | DORV | | |
|---|---|---|---|---|---|---|---|
| | | **Mean** | **SD** | **p-value** | **Mean** | **SD** | **p-value** |
| 1. Assessment of major vessels | DICOM | 1.85 | 0.86 | 0.28 | 2.09 | 0.90 | 0.85 |
| | 3DP | 2.03 | 0.67 | | 2.06 | 0.69 | |
| | MR | 2.12 | 0.91 | | 1.85 | 0.86 | |
| 2. Appreciation of heart defects | DICOM | 2.47 | 0.83 | 0.05 | 2.50 | 0.75 | 0.05 |
| | 3DP | 1.62 | 0.74 | | 1.76 | 0.74 | |
| | MR | 1.91 | 0.67 | | 1.74 | 0.75 | |
| 3. Spatial relationship between the cardiac structures | DICOM | 2.56 | 0.75 | 0.02 | 2.65 | 0.69 | 0.00 |
| | 3DP | 1.74 | 0.71 | | 1.85 | 0.74 | |
| | MR | 1.71 | 0.72 | | 1.50 | 0.56 | |
| 4. Depth perception | DICOM | 2.68 | 0.68 | 0.00 | 2.62 | 0.70 | 0.00 |
| | 3DP | 1.74 | 0.67 | | 1.85 | 0.70 | |
| | MR | 1.59 | 0.66 | | 1.53 | 0.66 | |
| 5. Pathology learning | DICOM | 2.59 | 0.74 | 0.00 | 2.50 | 0.79 | 0.01 |
| | 3DP | 1.74 | 0.50 | | 1.88 | 0.73 | |
| | MR | 1.65 | 0.65 | | 1.59 | 0.66 | |
| 6. Communication tool with another health professional | DICOM | 2.00 | 0.89 | 0.09 | 2.15 | 0.86 | 0.33 |
| | 3DP | 1.79 | 0.73 | | 1.76 | 0.78 | |
| | MR | 2.21 | 0.81 | | 2.09 | 0.79 | |
| 7. Communication tool with patients | DICOM | 2.59 | 0.61 | 0.00 | 2.65 | 0.54 | 0.00 |
| | 3DP | 1.18 | 0.52 | | 1.21 | 0.59 | |
| | MR | 2.24 | 0.55 | | 2.15 | 0.56 | |
| 8. Prepares me for surgery / intervention | DICOM | 2.23 | 0.87 | 0.18 | 2.27 | 0.83 | 0.09 |
| | 3DP | 2.00 | 0.69 | | 2.14 | 0.77 | |
| | MR | 1.77 | 0.87 | | 1.59 | 0.73 | |
| 9. Helps to understand possible complications | DICOM | 2.22 | 0.85 | 0.92 | 2.39 | 0.78 | 0.05 |
| | 3DP | 1.91 | 0.73 | | 2.00 | 0.80 | |
| | MR | 1.87 | 0.87 | | 1.61 | 0.72 | |
| 10. Pre-operative planning | DICOM | 2.43 | 0.79 | 0.03 | 2.39 | 0.78 | 0.03 |
| | 3DP | 1.87 | 0.76 | | 1.77 | 0.73 | |
| | MR | 1.70 | 0.77 | | 1.52 | 0.73 | |
| 11. Intra-operative guidance | DICOM | 2.39 | 0.78 | 0.39 | 2.39 | 0.78 | 0.06 |
| | 3DP | 1.91 | 0.73 | | 2.04 | 0.77 | |
| | MR | 1.70 | 0.82 | | 1.57 | 0.73 | |

3DP, three-dimensional printing; ASD, atrial septal defect; DICOM, Digital Imaging and Communications in Medicine; DORV, double outlet right ventricle; MR, mixed reality; SD, standard deviation

**Table 6.3:** Mean differences between modalities and significance values of pairwise comparisons.

| Questions | | ASD | | | DORV | | |
|---|---|---|---|---|---|---|---|
| | | **Mean diff.** | **SD** | **p-value[a]** | **Mean diff.** | **SD** | **p-value[a]** |
| 1. Assessment of major vessels | DICOM-3DP | -0.18 | 1.24 | 0.41 | 0.03 | 1.36 | 1.00 |
| | DICOM-MR | -0.26 | 1.64 | 0.15 | 0.24 | 1.62 | 1.00 |
| | 3DP-MR | -0.09 | 1.36 | 1.00 | 0.21 | 1.27 | 1.00 |
| 2. Appreciation of heart defects | DICOM-3DP | 0.85 | 1.42 | 0.06 | 0.74 | 1.29 | 0.18 |
| | DICOM-MR | 0.56 | 1.31 | 0.16 | 0.76 | 1.30 | 0.01 |
| | 3DP-MR | -0.29 | 1.14 | 1.00 | 0.03 | 1.29 | 0.18 |
| 3. Spatial relationship between the cardiac structures | DICOM-3DP | 0.82 | 1.27 | 0.06 | 0.79 | 1.32 | 0.07 |
| | DICOM-MR | 0.85 | 1.28 | 0.10 | 1.15 | 1.02 | 0.00 |
| | 3DP-MR | 0.03 | 1.22 | 1.00 | 0.35 | 1.12 | 1.00 |
| 4. Depth perception | DICOM-3DP | 0.94 | 1.18 | 0.02 | 0.76 | 1.23 | 0.06 |
| | DICOM-MR | 1.09 | 1.16 | 0.00 | 1.09 | 1.16 | 0.00 |
| | 3DP-MR | 0.15 | 1.13 | 0.66 | 0.32 | 1.17 | 0.40 |
| 5. Pathology learning | DICOM-3DP | 0.85 | 1.28 | 0.02 | 0.62 | 1.35 | 0.26 |
| | DICOM-MR | 0.94 | 1.20 | 0.00 | 0.91 | 1.26 | 0.00 |
| | 3DP-MR | 0.09 | 1.14 | 1.00 | 0.29 | 1.14 | 0.33 |
| 6. Communication tool with another health professional | DICOM-3DP | 0.21 | 1.41 | 1.00 | 0.38 | 1.44 | 1.00 |
| | DICOM-MR | -0.21 | 1.53 | 0.29 | 0.06 | 1.46 | 1.00 |
| | 3DP-MR | -0.41 | 1.26 | 0.29 | -0.32 | 1.32 | 0.57 |
| 7. Communication tool with patients | DICOM-3DP | 1.41 | 0.99 | 0.00 | 1.44 | 0.99 | 0.00 |
| | DICOM-MR | 0.35 | 1.04 | 0.29 | 0.50 | 0.93 | 0.12 |
| | 3DP-MR | -1.06 | 0.89 | 0.00 | -0.94 | 1.01 | 0.01 |
| 8. Prepares me for surgery / intervention | DICOM-3DP | 0.23 | 1.31 | 1.00 | 0.14 | 1.42 | 1.00 |
| | DICOM-MR | 0.45 | 1.60 | 0.57 | 0.68 | 1.36 | 0.23 |
| | 3DP-MR | 0.23 | 1.31 | 1.00 | 0.55 | 1.26 | 0.34 |
| 9. Helps to understand possible complications | DICOM-3DP | 0.30 | 1.33 | 1.00 | 0.39 | 1.41 | 1.00 |
| | DICOM-MR | 0.35 | 1.56 | 1.00 | 0.78 | 1.28 | 0.05 |
| | 3DP-MR | 0.44 | 1.36 | 1.00 | 0.39 | 1.31 | 0.22 |
| 10. Pre-operative planning | DICOM-3DP | 0.57 | 1.34 | 0.30 | 0.30 | 1.33 | 1.00 |
| | DICOM-MR | 0.74 | 1.36 | 0.00 | 0.87 | 1.32 | 0.02 |
| | 3DP-MR | 0.17 | 1.30 | 1.00 | 0.57 | 1.24 | 0.22 |
| 11. Intra-operative guidance | DICOM-3DP | 0.48 | 1.27 | 0.88 | 0.35 | 1.37 | 1.00 |
| | DICOM-MR | 0.70 | 1.43 | 0.36 | 0.83 | 1.30 | 0.14 |
| | 3DP-MR | 0.22 | 1.35 | 1.00 | 0.18 | 1.27 | 0.08 |

[a] after Bonferroni correction. 3DP, three-dimensional printing; ASD, atrial septal defect; DICOM, Digital Imaging and Communications in Medicine; DORV, double outlet right ventricle; mean diff., mean difference; MR, mixed reality; SD, standard deviation

**Table 6.4:** Mean differences in responses between interventionalists and non-interventionalists

| Questions[a] | Mean difference | p-value |
|---|---|---|
| 1. Assessment of major vessels | 0.02 | 0.41 |
| 2. Appreciation of heart defects | -0.06 | 0.74 |
| 3. Spatial relationship between the cardiac structures | -0.01 | 0.50 |
| 4. Depth perception | 0.26 | 0.66 |
| 5. Pathology learning | -0.15 | 0.85 |
| 6. Communication tool with another health professional | 0.22 | 0.59 |
| 7. Communication tool with patients | 0.14 | 0.86 |

[a] only Question 1 to 7 were applicable for the analysis

The 3DPHM were ranked as the best modality to visualise the heart defect for ASD, and MR model as the best for DORV. However, significant difference is only found between the mean rank of DICOM and MR for DORV ($p = 0.01$). In other words, the participants found that for a more complex type of CHD, the MR models allowed them to appreciate the heart defects better.

MR models were ranked the best in demonstrating the spatial relationship between the cardiac structures for both types of CHD. It was found significantly better compared to DICOM for DORV ($p = 0.00$). Similarly, MR models were ranked the best for depth perception for both CHD. It is significantly different to DICOM ($p = 0.00$ for both ASD and DORV). The 3DPHM which was ranked second for depth perception is also significantly different to DICOM ($p = 0.02$ for ASD).

As for the learning of the CHD pathology, MR models were ranked the best, and it is found to be significantly better than the DICOM images ($p = 0.00$ for both ASD and DORV). 3DPHM which were ranked the second in this category, has also achieved statistical significance compared to DICOM ($p = 0.02$ for ASD).

When it comes to communication with patients, 3DPHM were ranked as the best modality for both CHD. The pairwise comparisons indicate that 3DPHM were significantly different from both DICOM and MR models ($p = 0.00$ for both ASD and DORV). In fact, nearly 90% (30 out of 34) participants indicated their preference of using 3DPHM as a communication tool with patients. This explains why the response for this particular question is greatly skewed.

MR models were also ranked the most superior in helping the participants to foresee possible complications associated with the surgeries or interventions, especially for complex CHD like DORV ($p = 0.05$) (Table 6.3). For both types of CHD, MR models were ranked as the best tool for pre-operative planning. Its' mean rank is significantly different than DICOM ($p = 0.00$ for ASD, $p = 0.02$ for DORV). Generally speaking, the complexity of the CHD does not cause significant difference in the results (Appendix F4).

For the free-text section of the questionnaires, the participants' feedbacks can be categorized into 5 themes: (i) intuitiveness of the clipping tool in the MR application; (ii) requirement of training for MR application; (iii) advantages of MR application; (iv) limitations of MR application; and (v) suggestions for MR application (Table 6.5). There were more participants who found that the MR application was easy to use ($n = 10$), compared to those who indicated that it was not fully intuitive ($n = 4$) and steep learning curve for them ($n = 2$). Nine participants commented that more training is required for them to get used to the MR application. Seven participants mentioned about the usefulness of the clipping tool in visualising the internal cardiac structures at different angles that is difficult to achieve on DICOM. Despite so, the clipping tool does have a limitation of creating artificial defects on the MR models due to its shape of a 3D sphere ($n = 2$). Thus, one of the participants had suggested to replace the clipping tool to a flat 2D plane. More feedbacks from participants are detailed in Table 6.5.

**Table 6.5:** Thematic analysis of qualitative data.

| Themes | Feedbacks | Total |
|---|---|---|
| Intuitiveness of the clipping tool in the MR application | Relatively easy to use (n=10)<br>Not fully intuitive (n=4)<br>Steep learning curve (n=2) | n=16 |
| Requirement of training for MR application | Training required to get the greatest benefit (n=5)<br>Training is needed (n=4) | n=9 |
| Advantages of MR application | Clipping tool is very helpful to visualise internal structures at different angles (n=7)<br>Help to plan surgeries (n=2)<br>Excellent 3D visualization (n=3)<br>Exciting possibilities to improve our practice (n=1) | n=13 |
| Limitations of MR application | Creation of artificial defects from the clipping tool (n=2)<br>Difficult to look at structural connections (n=1)<br>Visual field of MR is too small (n=1) | n=4 |
| Suggestions for MR application | A preset button to auto-crop the MR models (n=2)<br>Flat 2D ‘clipping plane’ is better (n=1)<br>Coloured models (n=1)<br>Measuring tool (n=1)<br>Ability to offer ‘tunnel view’ (n=1)<br>Image definition needs improvement (n=1)<br>Ability to isolate the heart vessels or chambers (n=1) | n=8 |

2D, two-dimensional; 3D, three-dimensional; MR, mixed reality.

## 6.4 Discussion

Visualization of the anatomical features of the diseased heart plays a vital role in the success of the CHD surgeries. By improving the degree of verisimilitude of the visualization technique, the cognitive gap between the 2D medical images and the real heart in 3D can be closed, hence allowing the surgeons to decide the best surgical approach.[25] To date, there have been increasing reports on the usefulness of 3DPHM in redefining the best surgical strategies for complex CHD, in facilitating communication with patients, and in medical education for healthcare workers and students.[1,2,4-18] With the advancement in high-quality holographic visualization, application of MR in the medical field has also been explored in recent years for its use in pre-operative planning.[19-23,25-27]

To the best of our knowledge, this cross-sectional study is the first in the literature to concurrently compare the usefulness of these two emerging technologies to the conventional visualization method in the clinical management of CHD. The evaluations from the cardiac specialists and the physicians based on the two provided CHD cases had suggested promising results for both of these technologies. This is especially apparent for MR, which was ranked as the best modality for most of the questions. In real clinical application, the potential benefits of MR heart models in improving the visualization of the pathology, medical education, and pre-operative planning should not be overlooked. In terms of communication facilitation, 3DPHM is the best approach according to the results, as it is tangible and is able to effectively demonstrate the spatial relationship between the cardiac structures in 3D.

Even though the participants did not find the MR models as useful as 3DPHM in facilitating communication among the health professionals in the present study, its usefulness in this aspect should not be underestimated. The study by Kumar et al. reported that MR is extremely useful for multidisciplinary team meetings. All the surgeons wore the HoloLens headset, and were able to view and interact with the heart and liver models in the same 3D space. This had facilitated the discussion among the surgeons to decide the best surgical approach.[26] We believe the main reason behind this difference in study findings is that there was only one HoloLens 2 headset for use in our study. Therefore, the evaluations were strictly limited to singer-user experience instead of multi-users experience.

Nonetheless, the other findings about MR from our study are similar to other studies.[25,27] Ye et al. had reported the value of using HoloLens in shortening the time taken for pre-operative planning of DORV surgeries and improving the accuracy of the selection of surgical approach.[25] The results of our study also suggested MR is the best modality to aid in pre-operative planning. In another study by Brun et al., the paediatric heart team members had rated highly positively of the MR models in terms of the depth perception, morphology understanding, and the ability of it to share the view of the heart holograms.[27] In our study, we have provided more insights by comparing MR with 3DPHM and DICOM, and the results show that MR is much better than the others in demonstrating the heart defects, depth information and spatial relationship.

Compared to 3D printing, one of the advantages of MR is the avoidance of 3D printing turnaround time which is usually long.[25,27] Therefore, for emergency complex cases when urgent surgical approach decision is required, MR is a better option. On the other hand, unlike 3DPHM which can only demonstrate single cutting plane,[25] the MR models can demonstrate unlimited numbers of cutting plane at a user-defined angle or perspective, and therefore greatly improve the perception of the anatomy.[27] Further, there will be additional cost associated with 3D printing each time a model is printed. In this aspect, MR could be more cost-effective depending on the departments' need.

Despite these advantages, MR does come with its own limitation. In order to exploit the full benefits of MR, the users will have to spend some time for training to get used to manipulating the MR models. This is the main concern that the participants indicated in the questionnaire (Table 6.5). In fact, during the face-to-face session, the author had noticed that the learning curve for each participant to master skill varied differently. Participants with younger age (in their 30s) tend to learn the gesturing techniques quicker and therefore able to manipulate the MR models better compared to the others, despite absence of previous experience with AR. Another potential issue associated with MR or extended reality headset is motion sickness. By default, the MRTK on Unity which was used to build the application, has spatial awareness system enabled. It creates meshes of triangles of the real world surfaces (Figure 6.3) to allow interactions of the holograms with the real environment.[28] Due to this, a number of participants complained about motion sickness after taking the headset off, as the meshes of triangles constantly change with the users' head movement. For the subsequent meetings with other participants, the setting was changed so that the triangle meshes would be hidden, and no more complaints were made about motion sickness. Future studies should take note of this as it is related to work health and safety issues if it were to be used intra-operatively/during interventions. Another limitation of HoloLens 2 is that the image contrast and the sensitivity of the hand tracking are very much dependent on the room lighting. If the room is too dark or bright, the quality of both of the aforementioned elements will be degraded, hence affecting the users' experience.

This study does have a few limitations. First, as the participants were asked to assess the same two CHD cases in different modalities, by the time they get to station 3, they already more or less knew the patho-morphology of the CHD, and hence the results might be subjected to bias from repeated measures. In order to prevent this, future study could randomize the sequence of the modalities to different participants. Second, the time limit of 3 minutes per station might not be enough for some to evaluate the modality in a comprehensive manner. This might have introduced some bias to the participants' responses. Third, even though a brief tutorial was already given to the participants in manoeuvring the MR models, some of them still struggled to do so. This might have affected their experience during the assessment of the MR models, impeding them to evaluate the models properly. Future studies could address this limitation by running a simulation tutorial within the MR headset, very much like a mini game, to serve as a guidance for the participants. Fourth, we only chose two CHD cases in this study. Although they represented simple and complex CHD situations, more cases with different pathologies would be desirable to allow robust conclusions to be drawn. In spite of this limitation, our models were printed with the Agilus A30 material simulating normal cardiac tissue properties. Recent studies have shown the value of using Agilus A30 to print aortic dissection model for investigation of optimal CT angiography protocols.[29,30] Current literature shows a wide range of materials (from plastic to polylactic acid and thermoplastic polyurethane to rigid materials such as resin) and printers being used for 3D printing CHD models as indicated by a recent review article.[31] These 3D printed CHD models are acceptable for education purpose due to its high accuracy of replicating both normal anatomy and pathology (mean dimensional difference between 3D printed models and original source images is <0.5mm).[2,12,14,32-34] However, when used for pre-surgical planning and simulation purpose, a more realistic model (soft and elastic) is preferred by clinicians as it allows the user to acquire tactile experience when performing cardiac or interventional procedures.[35,36] This was not assessed in this study as we did not focus on the user's experience of using 3DPHM for simulations. Identification of the ideal 3D printed heart models by clinicians with regard to model's resilience, toughness and hardness deserves to be investigated. Further, use of 3DPHM or MR to contribute to patient treatment and outcomes will need to be investigated in further studies to determine how these technologies advance clinical practice.

Finally, the locally developed MR application in this study is very basic, without the menu bar on the interface. Despite so, the participants already had very positive comments about this tool. In the future, we would like to further develop this application by adding some interactive buttons that would allow the users to show or hide certain structures, to measure, and to auto-crop the models in different axes. Another 3D visualization tool is generation of 3D Portable Document Format (PDF) with embedded 3D objects (segmented volume data) which offers free rotatability and slicing features, thus allowing interactive visualization of anatomical structures.[37,38] Comparison of 3D

PDF with MR in CHD could reveal the real benefits of virtual reality in clinical practice and this could be considered in future studies.

### 6.5 Conclusion

This study has shown the key findings that the MR models were ranked as the preferred tool in demonstrating complex CHD lesions, in enhancing depth perception, in portraying spatial relationship between cardiac structures, as a learning tool of the pathology, and in facilitating pre-operative planning. The 3DPHM were ranked the preferred tool in facilitating communication with patients, in enhancing depth perception, and as a learning tool of the pathology. Both MR and 3DPHM serve as complementary tools to the current image visualization method by providing more valuable information beneficial to diagnostic assessment of patients with CHD.

## 6.6 References:

1. Biglino G, Koniordou D, Gasparini M, Capelli C, Leaver L, Khambadkone S, et al. Piloting the use of patient-specifc cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr Cardiol*. 2017;38:813-8.
2. Valverde I, Gomez-Ciriza G, Hussain T, Suarez-Mejias C, Velasco-Forte MN, Byrne N, et al. Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study. *Eur J Cardiothorac Surg*. 2017;52:1139-48.
3. Yoo SJ, Hussien N, Peel B, Coles J, van Arsdell GS, Honjo O, et al. 3D Modeling and Printing in Congenital Heart Surgery: Entering the Stage of Maturation. *Front Pediatr*. 2021;9:621672.
4. Liang J, Zhao X, Pan G, Zhang G, Zhao D, Xu J, et al. Comparison of blood pool and myocardial 3D printing in the diagnosis of types of congenital heart disease. *Sci Rep*. 2022;12:7136.
5. Hoashi T, Ichikawa H, Nakata T, Shimada M, Ozawa H, Higashida A, et al. Utility of a super-flexible three-dimensional printed heart model in congenital heart surgery. *Interact Cardiovasc Thorac Surg*. 2018;27(5):749-55.
6. Olivieri LJ, Zurakowski D, Ramakrishnan K, Su L, Alfares FA, Irwin MR, Heichel J, Krieger A, Nath DS. Novel, 3D Display of Heart Models in the Postoperative Care Setting Improves CICU Caregiver Confidence. *World J Pediatr Congenit Heart Surg*. 2018;9:206-13.
7. Smith M, McGuinness J, O'Reilly M, Nolke L, Murray J, Jones J. The role of 3D printing in preoperative planning for heart transplantation in complex congenital heart disease. *Ir J Med Sci*. 2017;186:753–756.
8. Yang DH, Park SH, Kim N, Choi ES, Kwon BS, Park CS, et al. Incremental Value of 3D Printing in the Preoperative Planning of Complex Congenital Heart Disease Surgery. *JACC Cardiovasc Imaging*. 2021;14:1265-1270.
9. Loke YH, Harahsheh AS, Krieger A, Olivieri LJ. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. *BMC Med Educ*. 2017;17:54-61.
10. Hermsen JL, Burke TM, Seslar SP, Owens DS, Ripley BA, Mokadam NA, 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*. 2016;153:132-140.

11. Sun Z, Lau I, Wong YH, Yeong CH. Personalized Three-Dimensional Printed Models in Congenital Heart Disease. *J Clin Med*. 2019;8(4):522.
12. Lau I, Sun Z. Three-dimensional printing in congenital heart disease: A systematic review. *J Med Radiat Sci*. 2018;65(3):226-236. doi:10.1002/jmrs.268
13. Lau I, Gupta A, Sun Z. Clinical value of virtual reality versus 3D printing in congenital heart disease. *Biomolecules*. 2021;11:884.
14. Sun, Z. Clinical applications of patient-specific 3D printed models in cardiovascular disease: Current status and clinical applications. *Biomolecules*. 2020;10:1577.
15. Valverde I, Gomez G, Coserria JF, Suarez-Mejias C, Uribe S, Sotelo J, et al. 3D printed models for planning endovascular stenting in transverse aortic arch hypoplasia. *Catheter Cardiovasc Interv*. 2015;85:1006-12.
16. Valverde I, Gomez G, Byrne N, Anwar S, Silva Cerpa MA, Talavera MM, et al. Criss-cross heart three-dimensional printed models in medical education: A multicentre study on their value as a supporting tool to conventional imaging. *Anat Sci Educ*. 2022;15:719-730.
17. Lau I, Sun Z. The role of 3D printed heart models in immediate and long-term knowledge retention in medical education. *Rev Cardiovasc Med*. 2022;23:022.
18. Karkkainen JM, Sandri G, Tenorio ER, Alexander A, Bjellum K, Matsumoto J, et al. Simulation of endovascular aortic repair using 3D printed abdominal aortic aneurysm model and fluid pump. *Cardiovasc Intervent Radiol*. 2019;42: 1627-1634.
19. Mitsuno D, Ueda K, Hirota Y, Ogino M. Effective Application of Mixed Reality Device HoloLens: Simple Manual Alignment of Surgical Field and Holograms. *Plast Reconstr Surg*. 2019;143:647-651.
20. Moro C, Phelps C, Redmond P, Stromberga Z. HoloLens and mobile augmented reality in medical and health science education: A randomised controlled trial. *Br J Educ Technol*. 2021;52:680–694.
21. Gehrsitz P, Rompel O, Schöber M, Cesnjevar R, Purbojo A, Uder M, et al. Cinematic rendering in mixed-reality holograms: a new 3D preoperative planning tool in pediatric heart surgery. Front Cardiovasc Med. 2021;8:633611.
22. Soulami RB, Verhoye JP, Duc HN, Castro M, Auffret V, Anselmi A, et al. Computer-Assisted Transcatheter Heart Valve Implantation in Valve-in-Valve Procedures. *Innovations*. 2016;11(3):193-200.

23. Opolski MP, Artur D, Bartosz B, Staruch AD, Kepka C, Rokicki JK, et al. Feasibility and safety of augmented-reality glass for computed tomography-assisted percutaneous revascularization of coronary chronic total occlusion: A single center prospective pilot study. *J Cardiovasc Comput Tomogr*. 2017;11:489-496. doi:10.1016/j.jcct.2017.09.013
24. Microsoft. HoloLens 2 fundamentals: develop mixed reality applications. Accessed October 3, 2021. https://docs.microsoft.com/en-us/learn/paths/beginner-hololens-2-tutorials/.
25. Ye W, Zhang X, Li T, Luo C, Yang L. Mixed-reality hologram for diagnosis and surgical planning of double outlet of the right ventricle: a pilot study. *Clin Radiol*. 2021;76(3):237.e1-e237.e7. doi:10.1016/j.crad.2020.10.017
26. Kumar RP, Pelanis E, Bugge R, Brun H, Palomar R, Aghayan DL, et al. Use of mixed reality for surgery planning: Assessment and development workflow. *J Biomed Inform*. 2020;8:100077
27. Brun H, Bugge RAB, Suther LKR, Birkeland S, Kumar R, Pelanis E, et al. Mixed reality holograms for heart surgery planning: First user experience in congenital heart disease. *Eur Heart J Cardiovasc Imaging*. 2019;20:883–888.
28. Microsoft. Spatial awareness getting started — MRTK2. March 8, 2022. Accessed August 19, 2022. https://docs.microsoft.com/en-us/windows/mixed-reality/mrtk-unity/mrtk2/features/spatial-awareness/spatial-awareness-getting-started?view=mrtkunity-2022-05.
29. Wu CA, Squelch A, Sun Z. Investigation of three-dimensional printing materials for printing aorta model replicating type B aortic dissection. *Curr Med Imaging*. 2021;17:843-849.
30. Wu CA, Squelch A, Jansen S, Sun Z. Optimization of computed tomography angiography protocols for follow-up type B aortic dissection patients by using 3D printed model. *Appl Sci*. 2021;11:6844.
31. Sun Z, Wee C. 3D printed models in cardiovascular disease: An exciting future to deliver personalized medicine. *Micromachines*. 2022;13:1575.
32. Kaufmann R, Zech CJ, Takes M, Brantner P, Thieringer F, Dentschmann M, et al. Vascular 3D printing with a novel biological tissue mimicking resin for patient-specific procedure simulations in interventional radiology: A feasibility study. *J Digit Imaging*. 2022;35:9–20.
33. Lee S, Squelch A, Sun Z. Quantitative assessment of 3D printed model accuracy in delineating congenital heart disease. *Biomolecules*. 2021;11:270.

34. Lau I, Liu D, Xu L, Fan Z, Sun Z. Clinical value of patient-specific three-dimensional printing of congenital heart disease: Quantitative and qualitative assessments. *PLoS One*. 2018;13: e0194333.
35. Yoo SJ, Spray T, Austin EH, Yun TJ, van Arsdell GS. Hands-on surgical training of congenital heart surgery suing 3-dimensional print models. *J Thorac Cardiovasc Surg*. 2017;153:15301–15540.
36. Brunner BS, Thierij A, Jakob A, Tengler A, Grab M, Thierfelder N, Leuner CJ, Haas NA, Hopfner C. 3D-printed heart models for hands-on training in pediatric cardiology-the future of modern learning and teaching? *GMS J Med Educ*. 2022;39:Doc23.
37. Newe A, Becker L. Three-dimensional portable document format (3D PDF) in clinical communication and biomedical sciences: systematic review of applications, tools and protocols. *JMIR Med Inform*. 2018;6:e10295.
38. Newe A, Becker L, Schenk A. Application and evaluation of interactive 3D PDF for presenting and sharing planning results for liver surgery in clinical routine. *PLoS One*. 2014;9:e115697.

Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged.

# CHAPTER 7: CONCLUSIONS AND FUTURE DIRECTIONS

## 7.1 Conclusions

This thesis investigated and compared the two emerging technologies in the medical field, 3D printing and extended reality, for their clinical roles in the domain of CHD. In particular, their clinical value in improving the visualization, medical education, pre-operative planning, and communication was investigated.

Overall, this study has achieved the outcomes of developing personalized 3DPHM of accurately replicating cardiac anatomy and congenital defects, applying these 3DPHM in both medical education and clinical value assessments. The research outcomes are summarized as follows:

- The low- and high-cost 3DPHM are comparable in their dimensional accuracy and clinical value. This has demonstrated the potentiality to opt for cheaper 3D printing materials when there is no prerequisite for 3D printing time and the material properties of the 3DPHM.
- No significant improvement was found in immediate knowledge acquisition or long-term knowledge retention among the medical students with the use of 3DPHM versus the conventional learning tools in the learning of CHD. The role of 3DPHM in improving medical education remains to be determined.
- The qualitative assessments of 3DPHM, VR, and MR have demonstrated positive perception of these emerging technologies among the health professionals, reflected in the high ratings in scores given by the participants.
- Both 3D printing and extended reality have their own strengths in different aspects. In particular, MR was highly regarded by the cardiac specialists in demonstrating the cardiac anatomy, in facilitating pre-operative planning and medical education; whereas the 3DPHM have a valuable role in enhancing communication with patients.
- Both 3D printing and MR were ranked better than original DICOM images in visualization, communication, medical education, pre-operative planning, and intra-operative guidance. This shows that both of these technologies serve as complementary tools to the current visualization technique in improving the

diagnostic assessment and patient management of CHD.

## 7.2 Future directions

This thesis provides additional insights into the clinical applications of 3D printing and extended reality in comparison with the current visualization technique. The positive perception of these technologies warrants further research before their wide acceptance and clinical implementation. There are a few areas that require further investigation as listed below:

- A detailed cost-benefit analysis of incorporating 3DPHM or extended reality into pre-operative planning of CHD surgeries is needed to justify the associated extra departmental expenditure;

- Research that incorporates extended reality into actual CHD surgeries based on a wide range of CHD types is required to verify the usefulness of extended reality in pre-operative planning and intra-operative guidance;

- A comparison of non-immersive visualization tool (e.g. 3D PDF) with immersive extended reality application is deserved to reveal the benefits of immersive visualization in clinical practice;

- Randomized controlled trials or large experimental studies are warranted to investigate the clinical benefits of 3DPHM in real clinical practice, as there are still lacking studies based on large sample size in the current literature;

- There is a need to investigate the role of 3DPHM in medical education based on larger sample size, and particularly studying the difference in educational benefits of 3DPHM between CHD of differing complexities;

- Simulation of haemodynamic physiology in the 3D printed CHD models could further advance the applications of 3D printing technology in cardiac surgery, and this can be achieved through connecting the 3DPHM with a cardiac pump.

# Appendix A

AMJ Australasian Medical Journal

[AMJ 2019;12(11):312-314]

## 3D printed models of congenital heart disease: How accurate and how useful are they?

Ivan Lau,[1] Andrew Squelch,[2,3] and Zhonghua Sun[1]

1. Discipline of Medical Radiation Sciences, School of Molecular and Life Sciences, Curtin University, Perth, Western Australia, Australia
2. Discipline of Exploration Geophysics, Western Australian School of Mines, Minerals: Energy and Chemical Engineering, Curtin University, Perth, Western Australia, Australia
3. Computational Image Analysis Group, Curtin Institute for Computation, Curtin University, Perth, Western Australia, Australia

### Editorial

Please cite this paper as: Lau I, Squelch A and Sun Z. 3D printed models of congenital heart disease: How accurate and how useful are they? AMJ 2019;12(11):312–314.
https://doi.org/10.35841/1836-1935.12.11.312-314

Corresponding Author:
Prof Zhonghua Sun
Discipline of Medical Radiation Sciences, School of Molecular and Life Sciences, Curtin University, Perth, WA, 6845, Australia
Email: z.sun@curtin.edu.au

### ABSTRACT

Three-dimensional (3D) printing in the domain of congenital heart disease (CHD) is still in its infancy. The aim of this editorial is to highlight the key findings of a recently published systematic review and meta-analysis on the accuracy and clinical value of 3D printed heart models (3DPHM). The analysis found that 3DPHM can be generated with high accuracy and the most reported application of 3DPHM is to facilitate pre-operative planning.

Key Words
3D printing, additive manufacturing, stereolithography, 3D model, congenital heart disease, congenital heart defect

### Introduction

Three-dimensional (3D) printing has been widely utilized in different specialties within the medical field for decades.[1-3] However, in the domain of cardiovascular specialties, this technology is still considered fairly new.[4] The conventional way to interpret the medical images from two-dimensional (2D) flat screen lacks comprehensiveness, hence tangible 3D printed heart models (3DPHM) were created to improve the users' perception on the depth information of the cardiac anatomies.[3-6] Although there are increasing reports on the use of 3DPHM, most of them remain anecdotal, and very few of them perform quantitative measurements of the accuracy and clinical value of the 3DPHM.[4,7] The relevant questions are: if the 3DPHM are accurate, to what extent are they accurate; if the 3DPHM are useful, in what areas are they useful; and do all the studies share the same findings? This editorial aims to provide a succinct summary of a recently published systematic review and meta-analysis on the accuracy and clinical value of 3DPHM.[4]

### How accurate and useful are the 3D printed heart models?

A total of 24 articles were included in the systematic review and 7 of them were used in the meta-analysis.[4] Based on the findings of this review, there are 4 different imaging modalities that can be used to generate 3DPHM, with computed tomography angiography (CTA) being the dominant, followed by cardiac magnetic resonance (CMR), echocardiography, and rotational angiography. Materialise Mimics is the most popular software for cardiac image segmentation, with 12 out of 24 studies (50 per cent) reporting its application.[4]

It was found that the accuracy of the 3DPHM is reported in relatively few studies since only 7 out of 24 provided the statistical measurements of the 3DPHM. Nevertheless, all of these studies shared the same findings: 3DPHM is highly accurate. Based on the meta-analysis of 3 eligible studies, the pooled mean deviation of 3DPHM measurement and original medical images measurement is 0.04mm, 95 per cent CI (-0.16, 0.23) (Figure 1), which is considered negligible as it is below the image resolution of routine medical CTA and CMR images. This however, needs to be interpreted with care as the Cochran's Q test demonstrates high heterogeneity among the studies (p=0.0468).[4] It is also important to note that the quantitative synthesis of 3DPHM accuracy did not take into account the 3D printing technique and segmentation software used in the individual studies, which could also explain the significant heterogeneity among the studies.

In terms of the uses of 3DPHM, the most reported use of 3DPHM is its role in facilitating pre-operative planning, followed by medical education, communication, pre-surgical simulation, and intra-operative orientation.[4] Meta-analysis is only possible for 4 out of 12 studies which reported the use of 3DPHM in medical education. It was found that the 3DPHM group scored less in the test group compared to the control group, although it did not reach statistical significance (-0.43, 95 per cent CI (-4.75, 3.88), p=0.844) (Figure 2). This finding also needs to be interpreted carefully as the Cochran's Q test demonstrates high variations among the studies (*p*<0.001).[4] Although the use of 3DPHM might not improve the students' short-term knowledge on CHD (measured by the test scores), the students' learning experience and satisfaction were reported to be improved in all 12 studies.[4]

The 3DPHM were also found to be valuable in helping surgeons to decide and define the best surgical approach, particularly for complex CHD. 3DPHM also have the potential to reduce the operational cost of the surgery due to the reduction in surgical duration, however this needs to be investigated further with a comprehensive cost-benefit analysis.[4] The role of 3DPHM in improving communication within clinical practice is uncertain. Some studies reported that the use of 3DPHM can enhance patient-doctor interaction, however it does not seem to shorten the consultation duration, nor does it increase the short-term parental knowledge on CHD. Despite the contradicting results, 3DPHM is perceived as a complementary tool in patient-doctor communication, in addition to the original medical images.[4]

## Conclusion

Based on the results from this systematic review and meta-analysis, it can be concluded that there is a paucity of comprehensive and systematic studies about 3D printing of CHD in the current literature. Although 3D printing of CHD is still considered at its early development stage, the results from current studies are promising. 3DPHM can be fabricated with high accuracy, and multiple groups of stakeholders can benefit from the application of this technology in the diagnosis and treatment of CHD. However, more studies based on larger sample sizes are required to validate these positive findings. Future studies should also focus on investigating the cost-benefit of implementing 3D printing technology in the domain of CHD before it is incorporated into a routine diagnostic approach.

---

## References

1. Kim GB, Lee S, Kim H, et al. Three-Dimensional Printing: Basic Principles and Applications in Medicine and Radiology. Korean J Radiol. 2016;17(2):182–197.
2. Batteux C, Haidar MA, Bonnet D. 3D-Printed Models for Surgical Planning in Complex Congenital Heart Diseases: A Systematic Review. Front Pediatr. 2019;7.
3. Shi D, Kai L, Zhang X, et al. Applications of three-dimensional printing technology in the cardiovascular field. Intern Emerg Med. 2015;10:769–780.
4. Lau I, Sun Z. Dimensional Accuracy and Clinical Value of 3D Printed Models in Congenital Heart Disease: A Systematic Review and Meta-Analysis. J Clin Med. 2019;8:1483.
5. Biglino G, Koniordou D, Gasparini M, et al. Piloting the Use of Patient-Specific Cardiac Models as a Novel Tool to Facilitate Communication During Clinical Consultations. Pediatr Cardiol. 2017;38:813–818.
6. Valverde I, Gomez-Ciriza G, Hussain T, et al. Three-dimensional printed models for surgical planning of complex congenital heart defects: An international multicentre study. Eur J Cardiothorac Surg. 2017;52:1139–1148.
7. Sun Z, Lau I, Wong YH, et al. Personalized three-dimensional printed models in congenital heart disease. J Clin Med. 2019;8:522.

## PEER REVIEW

Peer reviewed.

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

## FUNDING

None

## Appendix B

Journal of
*Clinical Medicine*

*Review*

# Personalized Three-Dimensional Printed Models in Congenital Heart Disease

**Zhonghua Sun [1,*], Ivan Lau [1], Yin How Wong [2] and Chai Hong Yeong [2,*]**

[1] Discipline of Medical Radiation Sciences, School of Molecular and Life Sciences, Curtin University, Perth 6102, Australia; ivan.w.lau@curtin.edu.au
[2] School of Medicine, Faculty of Health and Medical Sciences, Taylor's University, Subang Jaya 47500, Malaysia; YinHow.Wong@taylors.edu.my
* Correspondence: z.sun@curtin.edu.au (Z.S.); chaihong.yeong@taylors.edu.my (C.H.Y.); Tel.: +61-8-9266-7509 (Z.S.); +60-16-701-6875 (C.H.Y.)

Received: 27 March 2019; Accepted: 16 April 2019; Published: 16 April 2019

**Abstract:** Patient-specific three-dimensional (3D) printed models have been increasingly used in cardiology and cardiac surgery, in particular, showing great value in the domain of congenital heart disease (CHD). CHD is characterized by complex cardiac anomalies with disease variations between individuals; thus, it is difficult to obtain comprehensive spatial conceptualization of the cardiac structures based on the current imaging visualizations. 3D printed models derived from patient's cardiac imaging data overcome this limitation by creating personalized 3D heart models, which not only improve spatial visualization, but also assist preoperative planning and simulation of cardiac procedures, serve as a useful tool in medical education and training, and improve doctor–patient communication. This review article provides an overall view of the clinical applications and usefulness of 3D printed models in CHD. Current limitations and future research directions of 3D printed heart models are highlighted.

**Keywords:** three-dimensional printing; congenital heart disease; medical education; heart models; pre-operative planning; simulation

## 1. Introduction

Computed tomography (CT), magnetic resonance imaging (MRI), and echocardiography represent commonly used imaging modalities in the diagnostic assessment of congenital heart disease (CHD). These imaging techniques allow for generation of two-dimensional (2D) and three-dimensional (3D) visualizations, which play an important role in understanding the complexity of CHD and assisting pre-procedural planning of cardiac procedures. Despite useful information provided by these imaging modalities, the images are still limited to be viewed on 2D screens which is very different from the physical models that offer realistic visualization of 3D spatial relationship between normal and anomalous anatomy. 3D printing overcomes this limitation by creating patient-specific or personalized medical models [1–3]. The tactile experience offered by 3D printed models is another advantage over traditional image visualizations as the physical models enable comprehensive evaluation of anatomical and pathological structures which cannot be obtained by other methods [4].

*J. Clin. Med.* 2019, *8*, 522; doi:10.3390/jcm8040522

3D printing has been increasingly utilized in the medical field with studies confirming its clinical value and usefulness in many areas, ranging from medical education to pre-surgical planning and simulation of complex surgeries, and to patient–doctor communication [5–10]. In particular, personalized 3D printed models have been shown to offer valuable information for treating patients with CHD due to complexity and anatomic variation associated with this disease. Most of the current reports on 3D printing in CHD are dominated by isolated case reports or case series, with only a few single or multi-center studies and randomized controlled trials (RCT) available in the literature. This review aims to provide an in-depth overview of the current applications of 3D printed models in CHD, with limitations and future directions briefly highlighted.

## 2. Image Post-Processing and Segmentation Process for Three-Dimensional (3D) Printing in Congenital Heart Disease (CHD)

The first step to generate a 3D printed heart model is to undergo a series of image post-processing and segmentation of volumetric data, which are commonly acquired with cardiac CT or MRI imaging. While high-resolution original datasets are important for accurately isolating the desired anatomy of interest and pathology from surrounding structures, segmentation of cardiac structures remains challenging due to complexity of cardiac features, especially in the CHD cases. Different software is used for segmentation, with Mimics (Materialise HQ, Leuven, Belgium) being the most commonly used commercial software and 3D Slicer (Brigham and Women's Hospital, Boston, Mass) as the most common open-source tool. Several review articles have provided excellent description of details about the steps required from data acquisition to image post-processing and segmentation [11–14]. Figure 1 shows the steps to create 3D printed models from data acquisition to image post-processing and segmentation.

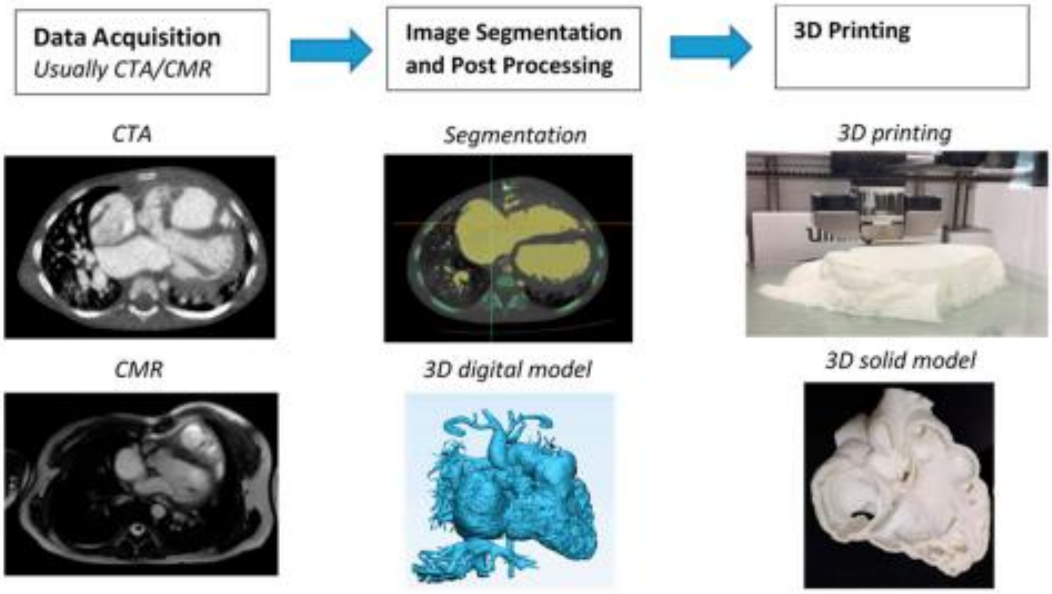


**Figure 1.** Steps involved in fabrication of 3D printed heart models. CTA—computed tomography angiography; CMR—cardiac magnetic resonance; 3D—three-dimensional.

## 3. Accuracy of 3D Printed Heart Models

The most important part of creating 3D printed models is to ensure that 3D models accurately delineate anatomical structures and pathologies since the model accuracy is essential for treatment planning [15]. Current research evidence indicates that 3D printed heart models are generally accurate [16], and this has been validated by other studies, either based on case reports/series or single- or multi-center studies [17–23]. In most of the studies, model accuracy is determined by the degree of agreement between the measured dimensions of the 3D printed model and the dimensions of original source images, usually using cardiac CT, MRI, and sometimes using rotational angiography or echocardiography [16–18,22], or intraoperative findings [19]. Currently, there is no standardized method to measure the dimensions of the 3D printed heart models. Most of the studies carried out measurement using calipers on the physical 3D printed models [17,20,21]. Only a few studies conducted measurement on the standard tessellation language (STL) file [18] and conducted CT scan on the 3D printed model for measurement [16]. The authors claimed it is easier to replicate the exact plane for measurement comparison, hence improving the accuracy of the results [16,18].

Despite limited studies available in the literature regarding quantitative assessment of 3D printed heart models, the accuracy of 3D printed heart models is within 1 mm in terms of dimensional differences when compared to the original images. Lau et al. compared model accuracy between contrast-enhanced CT images of the 3D printed heart model (Figures 2 and 3) and original cardiac CT images in 10 anatomical locations including ventricular septal defect (VSD) [16]. High accuracy was achieved between these measurements by only 0.23 mm difference in average. Ma et al. in their study comprising 35 patients of Tetralogy of Fallot (ToF), compared measurements of VSD sizes between 3D printed models and intraoperative findings with no significant differences found (mean value ± standard deviation: 14.98 ± 1.91 vs. 15.11 ± 2.06 mm, $p > 0.05$) [19]. This is further confirmed by a multi-center study showing the model accuracy. Valverde et al. recruited 40 patients diagnosed with complex CHD from 10 international centers in their prospective study [21]. 3D printed models were created from CT or MRI images, and they were found to be highly accurate with mean differences of 0.27 ± 0.73 mm between measurements performed on the 3D printed models and CT/MRI images.

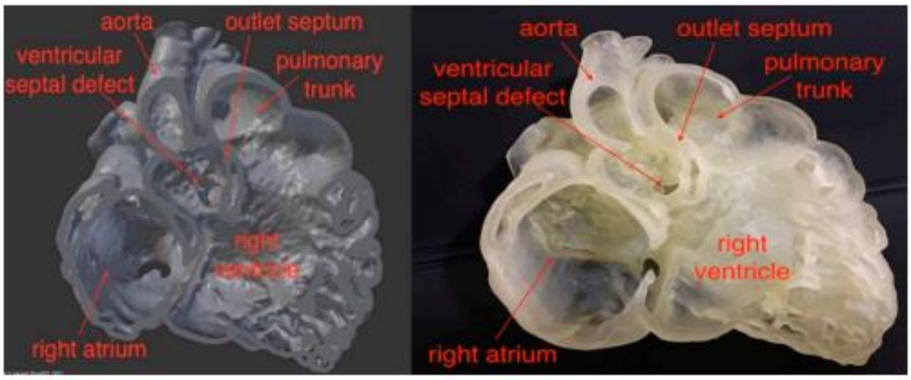


**Figure 2.** Comparison of virtual 3D reconstruction model (left) and 3D printed heart model (right). Reprinted with permission under the open access from Lau et al. [16].

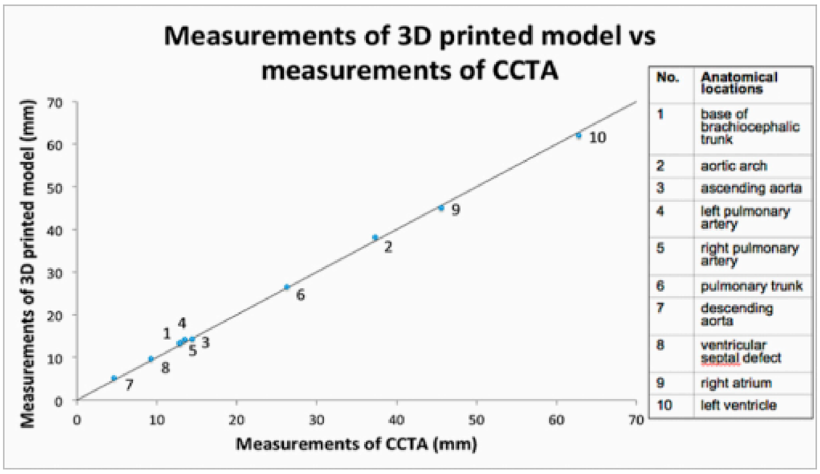


**Figure 3.** Scatterplot showing measurements of 3D printed model in comparison with those from cardiac computed tomography (CT) images at 10 anatomical locations. CCTA—cardiac computed tomography angiography. Reprinted with permission under the open access from Lau et al. [16].

Currently, there is a lack of measurement comparison between 3D printed heart models and STL file, hence, it is unknown whether there is any dimensional error introduced during 3D printing process. This needs to be addressed by future studies.

## 4. 3D Printed Models in Medical Education and Training

3D printed heart models have been shown to serve as a novel teaching tool in medical education and training and this is confirmed by RCT available in the literature [22–25]. Three of them reported the usefulness of 3D printed models of different types of CHD in medical education [22–24]. Table 1 shows details of these three studies and other single- and multi-center reports.

Studies by Loke et al. and White et al. investigated how 3D printed models improved pediatric residents' knowledge and understanding of CHD, while the study by Su et al. focused on how 3D printed models improved medical students' knowledge in CHD. In these studies, 3D printed models of VSD and ToF representing simple and complex CHD were created and used for teaching in the test groups (Figure 4), while the control groups were only given the usual lectures with 2D images. Overall results showed significant improvements of residents and medical students' learning and confidence in managing CHD, especially in dealing with complex CHD situations such as ToF as confirmed by White et al. [24]. Furthermore, 3D printed models significantly improved residents' satisfaction and self-efficiency scores when compared to learning from 2D images [22] (Figure 5).

**Table 1.** Study characteristics of randomized controlled trials and multi- and single-center studies.

| Authors | Study Design | Sample Size and Participants | Types of CHD | Key Findings |
|---|---|---|---|---|
| Loke et al., 2017 [22] | RCT: study group was presented with 3D printed models, while control group with 2D images | 35 pediatric residents:18 in study group and 17 in control group | Tetralogy of Fallot (ToF) | 3D printed models resulted in significantly higher satisfaction scores than 2D images ($p = 0.03$). 3D printed models improved residents' self-efficacy scores in managing ToF, although this did not reach significant difference when compared to 2D images ($p = 0.39$). |
| Su et al., 2018 [23] | RCT: study group participated in teaching seminar including 3D printed models, while control group only attended teaching seminar without having 3D models | 63 medical students: 32 in study group and 31 in control group | Ventricular septal defect (VSD) | Significant improvement in VSD learning and structure conceptualization in the study group compared to the control group ($p < 0.05$). |
| White et al., 2018 [24] | RCT: study group was given 3D printed models in addition to lectures, while control group received only the lectures | 60 pediatric residents:31 in study group and 29 in control group | VSD and ToF | 3D printed models of CHD improved residents' knowledge and confidence in managing complex CHD such as ToF but did not seem to improve simple CHD such as VSD. |
| Olivieri et al., 2016 [26] | Single-center report of 3D printed models for training and simulation | 10 3D printed models, 70 clinicians participated in the training sessions | Cardiac and vascular anomalies | 3D printed models can be used as a simulation training tool for multidisciplinary intensive care providers by enhancing their anatomic knowledge and clinical management of CHD patients. |
| Hoashi et al., 2018 [27] | Single-center experience | 20 cases | DORV and other cardiac anomalies | 3D printed heart models improved understanding of the relationship between intraventricular communications and great vessels. Further, 3D printed models allowed simulation of cardiac surgeries by creating intracardiac pathways, thus providing benefits to inexperienced cardiac surgeons. |
| Valverde et al., 2017 [21] | Multi-center study consisting of 10 international centers | 40 patients with complex CHD | DORV (50%) and other cardiac anomalies | 3D models were accurate in replicating anatomy. 3D models refined the surgical approach in nearly 50% cases. 3D models resulted in significant change in the surgical plan in 24% of cases. |
| Zhao et al., 2018 [28] | Single-center experience | 25 patients with 8 in 3D printing group and 17 in control group | DORV | 3D printed models showed high accuracy in measurements of aortic diameters and the size of VSD when compared to original CT data. 3D printed models significantly reduced ICU time and mechanical ventilation time ($p < 0.05$). |
| Ryan et al., 2018 [29] | Single-center experience | Of 928 cardiothoracic surgeries, 164 3D models were printed for various purposes | DORV, ToF and other cardiac anomalies | 3D printed models reduced mean time in the operating room and 30-day readmission and mortality rates when compared to the standard of care. |

CHD—congenital heart disease, DORV—double outlet right ventricle, ICU—intensive care unit, RCT—randomized controlled trial.

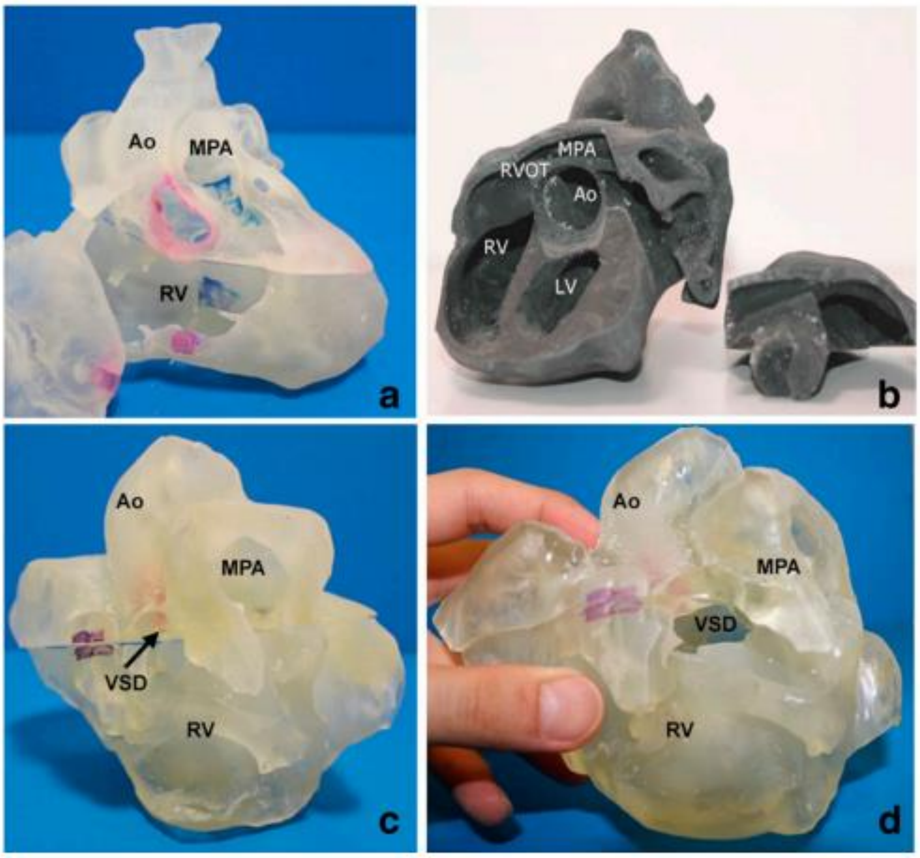


**Figure 4.** 3D printed heart models showing normal anatomy and pathology. (**a**) Normal heart model created from cardiac CT and is partitioned into three pieces allowing visualization of interventricular septum. (**b**) Repaired Tetralogy of Fallot (ToF) from an adult patient. The model was created from cardiac magnetic resonance imaging (MRI) and separated into two pieces allowing for clear visualization of overriding aorta and pulmonary infundibular stenosis. (**c**) Unrepaired ToF heart model from an infant. The model was created from 3D echocardiographic images and partitioned into two pieces showing the ventricular septal defect (VSD). (**d**) Unrepaired ToF heart model from an infant with superior and inferior portions showing VSD and the aortic overriding in relation to the VSD. Reprinted with permission under the open access from Loke et al. [22]. Ao—Aorta; MPA—Main Pulmonary Artery; LV—Left Ventricle; RV—Right Ventricle; RVOT—Right Ventricular Outflow Tract; VSD—Ventricular Septal Defect; ToF—Tetralogy of Fallot.

Results from cross-sectional studies are consistent with these findings from RCT [5,6,30–32]. To date, there is sufficient evidence to prove that 3D printed models of CHD play a valuable role in education and training of medical students, pediatric residents, and healthcare professionals in improving their understanding of complex cardiac pathology and increasing their confidence in managing CHD patients.

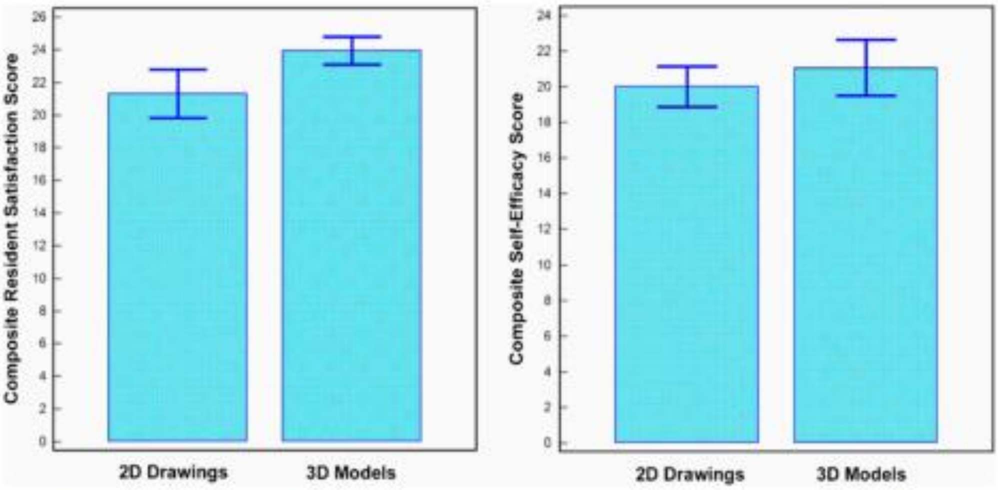


**Figure 5.** Impact of 3D printed heart models on medical education. Improvement was found in residents' knowledge on congenital heart disease with use of 3D printed models when compared to 2D images. A statistically significant difference was noticed in satisfaction ratings in the group having 3D printed heart models when compared to the control group ($p = 0.03$). While residents in the 3D printed model group had higher self-efficacy scores, this did not reach significant difference compared to the control group using 2D images/drawings ($p = 0.39$). Reprinted with permission under the open access from Loke et al. [22].

## 5. 3D Printed Models in Pre-Surgical Planning and Simulation

Due to complexity of the cardiac conditions with wide variations between individuals with CHD, 3D printed models demonstrate great advantages over traditional image visualizations in pre-surgical planning and simulation of cardiac surgeries. A recent systematic review has summarized findings from a number of case reports and series with regard to the use of 3D printed models in facilitating preoperative planning and surgical decision-making in CHD cases [33]. Table 1 shows some results from single- and multi-center studies which involved more than 20 cases or participants about the value of 3D printed heart models in this aspect [20,26–29]. These studies reported the usefulness of 3D printed heart models from different perspectives. Among all types of CHD, double outlet right ventricle (DORV) and ToF represent the most common types of CHD for fabrication of 3D printed models. This is reported in four out of the five studies mentioned above [21,27–29].

Olivieri et al. created 3D printed models from 10 patients who underwent congenital cardiac surgery due to various cardiac and vascular anomalies [26]. They presented the 3D models to 70 clinicians including 22 physicians, 38 critical care nurses, and 10 ancillary providers. At completion of the cardiac surgeries, all participants underwent a training session of simulating intra- and post-operative care using 3D printed heart models. The use of 3D printed models was found to be more effective than standard verbal hand off with average score of 8.4 out of 10. In total, 90% of participants scored it very highly with regard to the efficacy of 3D printed models in improving cardiac anatomy understanding, surgical understanding, and ability to manage CHD clinically.

Two other studies reported utilizing 3D printed heart models in the diagnostic management of patients with CHD [21,27]. Hoashi et al. created 20 3D printed heart models for the purpose of preoperative simulations of cardiac surgeries [27]. Despite realistic and expensive models being produced (each model costs between $2000 and $3000), this study mainly focused on findings related to patient's cardiac surgery outcomes, while the value of 3D printed models was briefly mentioned in some sample cases. Specifically, authors concluded that 3D printed heart models did not reduce cardiopulmonary bypass time. In contrast, Valverde et al. conducted a multi-center study and performed both quantitative and qualitative assessments of the role of 3D printed models in clinical decision-making in patients with complex CHD [21]. Forty patients recruited from 10 international centers were included in this prospective study with 3D models fabricated using CT or MRI images. 3D printed models were assessed as to whether they changed the surgical decision (from conservative management to surgical intervention) and whether the surgical plan was modified. In more than half of the cases (52.5%), 3D printed models did not result in any change to the surgical decision. However, 3D printed models showed significant clinical impact on redefining the surgical approach in 47.5% cases. In 25% of cases, after inspection of 3D printed models, the surgical plan was modified with conservative management changed to surgery. As the only multi-center study available in the literature, this study shows the impact of 3D printed models on deciding the best surgical approach. However, more similar studies are desirable to validate this.

The other two studies are based on single-center experience reporting the clinical impact of 3D printed models in CHD treatment outcomes [28,29]. Zhao et al. divided 25 patients with complex DORV into two groups, 8 in the 3D printing group and 17 in the control group, with all patients undergoing cardiac surgery [28]. The intensive care unit stay time and mechanical ventilation time in the 3D printing group was significantly shorter than in the control group ($p < 0.05$). Although the operative duration, cardiopulmonary bypass time, and aortic cross-clamping time in the 3D printing group was shorter than the control group, this did not reach statistical significance ($p > 0.05$). Similar findings are reported by Ryan and colleagues [29]. The authors presented their single-site three-year experience of using 3D printed models for managing CHD cases. Of 164 models fabricated for different purposes, 79 models covering a range of CHD complexities were selected for surgical planning. When compared to the standard care (without anatomical models) group, the 3D printed heart model group was found to have shorter mean duration in the operative room and lower 30-day readmission and mortality rates. However, it is worthwhile to note that it did not reach statistical significance, and it is likely due to limited study sizes for each CHD types. These reductions in durations could contribute to lower morbidity and mortality associated with management of CHD, although this needs to be validated by further studies. One example would be by investigating the impact of 3D printed models on 30-day post-operative outcome.

## 6. 3D Printed Models in Doctor–Patient Communication

Physician–patient relationship and working alliance plays a crucial role in improving patient adherence, level of satisfaction, and treatment outcomes [34]. Due to complexity and variations of cardiac anatomy in CHD, it is especially challenging in achieving good physician–patient communication (physicians specifically refer to cardiologists and cardiac surgeons in the situation of managing patients with CHD) [35]. Traditional approaches of using diagrams or image visualizations for explanation of complicated cardiac pathologies do not allow doctors to effectively communicate to patients or parents because of difficulty in interpreting 3D conceptualization of spatial relationship between cardiac structures. 3D printed models are able to eliminate this limitation as observers have no restriction in appreciating the spatial relationship between cardiac structures in all dimensions, thus improving doctor–patient communication.

A study by Biglino et al. first attempted to quantify the benefit of 3D printed models in doctor–patient communication [36]. Ninety-two parents of patients with CHD were randomly allocated to two groups with 45 assigned to the model group using 3D printed heart models during their visit, and 52 to the control group with no models during consultation. Parents were asked to complete two questionnaires: A first brief questionnaire before their child's consultation and a second brief questionnaire after the consultation with regard to understanding of their child's heart condition, identification of cardiac defects, and clarity of planned intervention or procedure. Both cardiologists and parents rated the 3D printed models as very useful. Despite the improvement in doctor–parent communication, 3D printed models did not lead to improving parents' knowledge and understanding of their child's heart condition. Furthermore, consultations using the 3D printed models were found to be longer than those without the models (21 ± 10 vs. 16 ± 7 min, $p = 0.02$), although this did not show significant impact on overall duration of the visits.

The same group conducted another study determining the impact of using 3D printed heart models on facilitating consultations between doctor and young people with CHD [37]. Twenty adolescent patients with CHD (age range 15–18 years) were included in this study with use of the same approach as stated in the previous study involving completion of two questionnaires, pre and post-consultations with their doctors. Positive responses were found in the study with use of 3D printed models with significant improvements in their knowledge of CHD ($p < 0.05$), confidence in explaining conditions to others ($p < 0.001$), and overall satisfaction ($p < 0.05$) (Figure 6). The majority of participants indicated that the 3D printed models improved their clinical visits, however, 30% of them expressed their concern of feeling more anxious about their heart condition with use of the 3D models (Figure 7).

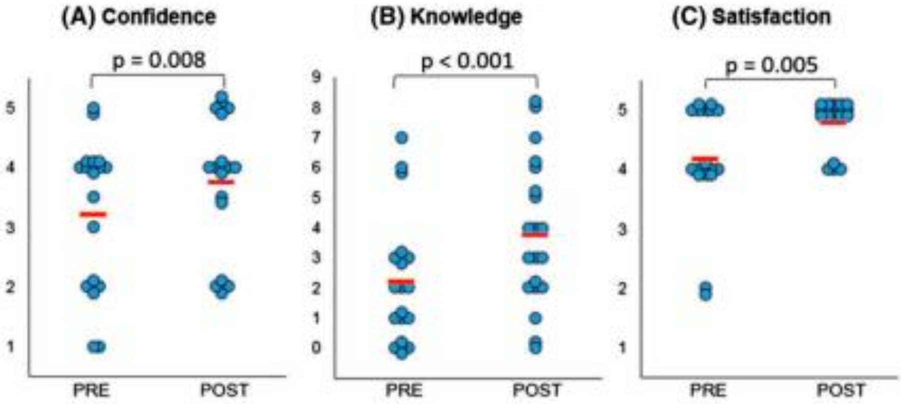


**Figure 6.** Statistically significant differences were noted in confidence (**A**), knowledge (**B**), and satisfaction (**C**) amongst participants comparing responses before ("Pre") and after ("Post") their medical consultation. (**A**) 1 refers to not at all confident and 5 very confident. (**B**) Each point represents a point in knowledge, as marked based on the correct name of primary diagnosis, correctly identified keywords, and correct use of diagrams. (**C**) 1 indicates very dissatisfied and 5 very satisfied. The red lines indicate average score. Reprinted with permission under the open access from Biglino et al. [36].

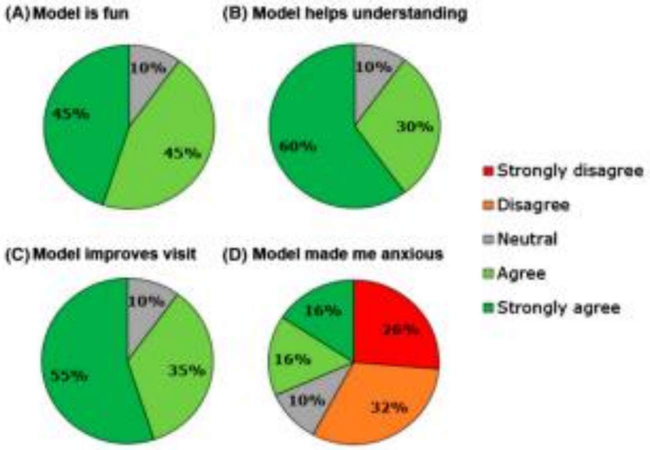


**Figure 7.** Participants' response to different statements on the usefulness of 3D printed models. Reprinted with permission under the open access from Biglino et al. [36].

More research is needed to investigate the clinical translation of 3D printed heart models for doctor–patient/parent communication with involvement of different stakeholders including patients, parents, families, clinicians, and other healthcare professionals such as nurses and ancillary providers [28]. Further studies are also required to address the limitations of lack of evidence of clinical follow-up with regard to the impact of 3D printed models on patient's lifestyle and eventually patient outcomes.

## 7. Summary and Future Research Directions

Personalized 3D printed models of CHD are changing the current practice in the diagnostic management of patients with CHD. 3D printed models have demonstrated advantages over traditional image visualizations in the assessment of complex cardiac structures as observers are able to appreciate various CHD conditions with more confidence. Three main applications of 3D printed heart models have been discussed in this review, including medical education and training, pre-surgical planning and simulation, and doctor–patient communication. Despite attractiveness of 3D printed realistic models and promising results associated with their applications, more scientific evidence with high statistical power is needed before 3D printing is widely used in clinical practice. In addition to the lack of large-scaled studies (prospective and multi-center studies), some limitations should be addressed with future technical developments so that 3D printing will be more practicable in medical applications.

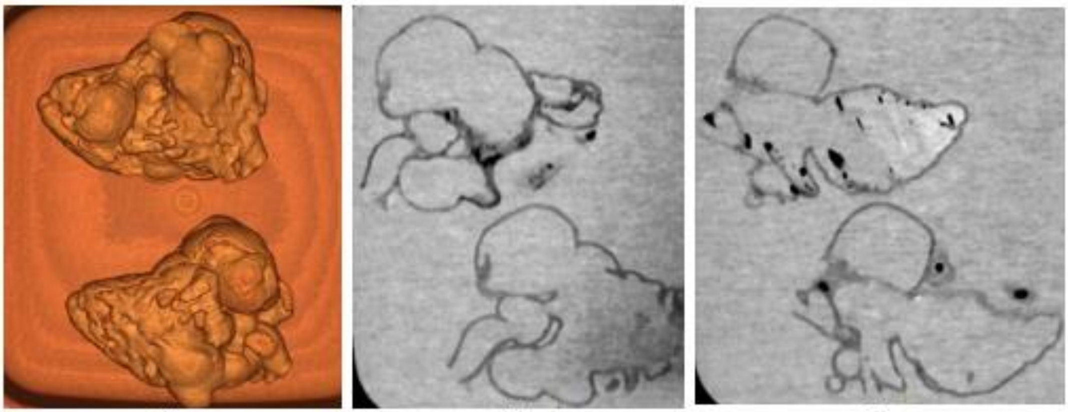
One of the main limitations in generating 3D printed heart models lies in image post-processing and segmentation of cardiac imaging data, which is exceptionally time-consuming and requires expertise in image analysis. The duration needed to complete the segmentation and image post-processing is highly dependent on segmentation software tools (whether it is powerful enough for automatic segmentation), and researcher's familiarity with the software, as highlighted by two systematic reviews and other review articles (Table 2) [29,35,38–40]. This operator-dependent process is inevitably associated with interobserver and intraobserver variability. This limitation could be resolved with the use of artificial intelligence or machine learning algorithms which are increasingly used in the domain of cardiovascular disease by providing automated image segmentation of coronary plaque lesions or coronary lumen [41–44], thus improving the workflow efficiency from image acquisition to 3D printing.

**Table 2.** Summary of systematic reviews of 3D printed models in congenital heart disease.

| Authors | Number of Studies Analyzed | Review Purpose | Key Findings |
|---|---|---|---|
| Batteux et al., 2019 [38] | NR | Accuracy and reliability of 3D printed models in surgical planning in complex CHD | 3D printed models improve understanding of complex cardiac anatomy and disease and can be used to guide surgical planning. |
| Lau and Sun 2018 [29] | 28 | Clinical value of 3D printed models in CHD | 3D printed models accurately replicate cardiac anatomy and pathology and are shown to be valuable in preoperative planning and simulation of cardiac procedures. |

NR—Not reported.

High 3D-printing costs represent another obstacle, however this is being resolved with the use of low-cost 3D printing materials, provided that the accuracy of the 3D printed models is not affected. A recent study has demonstrated the feasibility of creating accurate 3D printed models using low-cost as opposed to high-cost material ($50 vs. $300) for delineation of cardiac anatomy and defects (Figures 8 and 9) [45]. With further cost reductions in 3D printers and printing materials in the near future, personalized 3D printed heart models will become more affordable to patients with CHD. Table 3 shows different types of 3D printers and printing materials that are available in the 3D printing of cardiac models and strengths and weaknesses of these models corresponding to each type of 3D printers [36,46–49].



(**A**) (**B**) (**C**)

**Figure 8.** CT scan of 3D printed heart models created using different printing materials. (**A**) 3D volume rendering showing the 3D printed models without contrast medium (top: Tango Plus material, bottom: TPU material). (**B**,**C**) Coronal multiplanar reformatted contrast-enhanced CT images showing 3D printed models with Tango Plus (left) and TPU (right) materials. Air bubbles are noticed in the model with TPU material. TPU—thermoplastic polyurethane. Reprinted with permission under the open access from Lau et al. [45].

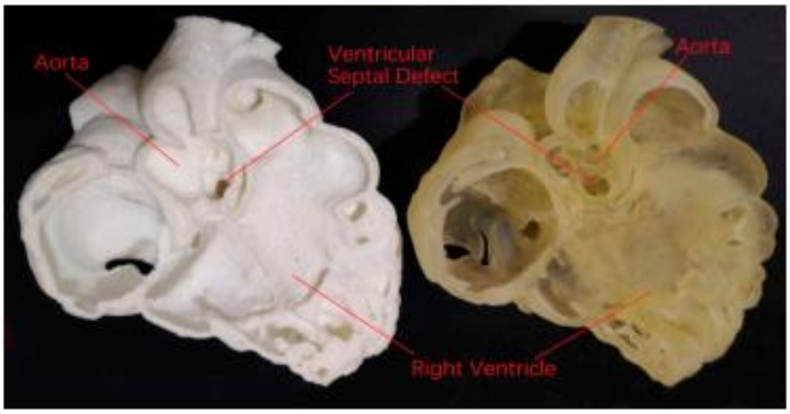


**Figure 9.** Comparison of low-cost (left image) with high-cost (right image) 3D printed heart model with similar accuracy in delineating cardiac anatomy and ventricular septal defect.

Very few materials that are currently used for creating 3D printed heart models represent elastic properties similar to human tissue which allow for performance of realistic surgical simulation such as cutting and suturing of cardiac structures. Despite softness of the Tango Plus material as shown in Figure 9, the mechanical properties of these materials are still different from biologic heart tissues. Furthermore, current 3D printers generate a static heart model instead of a dynamic organ, therefore, allowing for assessment of morphological cardiac features rather than hemodynamics of the cardiovascular system. Future developments in printing technologies should aim to produce 3D printed dynamic heart models which enable detection of both anatomic and physiological changes during the cardiac cycle [11,39,50]. 3D bioprinting represents another major advancement with the capability of printing biomaterials, 3D printed tissue scaffolds, and 3D printed functional vascular networks [51–53]. Bioprinting of patient-specific heart tissues will broaden applications of 3D printing in CHD, although many challenges need to be overcome before it can be translated to clinical applications [54,55].

**Table 3.** Summary of different types of 3D printing technologies and corresponding 3D printed heart models. Adapted from References [36,46–49].

| **3D Printing Technologies** | **Printing Materials** | **Advantages** | **Disadvantages** | **3D Printed Heart Models** | |
|---|---|---|---|---|---|
| | | | | **Strengths** | **Weaknesses** |
| Stereolithography (SLA) | Photopolymers | Large part size | High cost, moderate strength | High detail and accuracy, smooth surfaces | Low tensile strength |
| Polyjet (PJ) | Photopolymers | Variety of materials including multi-colored materials | Slow speed, high cost | High accuracy with flexibility, durability, and translucency | Low tensile strength |
| Selective Laser Sintering (SLS) | Powder materials | Large part size, variety of materials and good strength | High cost, low resolution | Moderate accuracy | Inferior anatomical details |
| Binder Jetting (BJ) | Powder materials | Very low cost, variety of materials, relatively fast, does not use heat | Slow speed, fragile parts with limited mechanical properties | NR | Low accuracy |
| Fused Deposition Modeling (FDM) | Thermoplastic materials | Low cost, variety of materials, good strength | Slow speed and a scaffold is needed to support the object during printing | Moderate accuracy, more suitable for medical devices | Limited values in surgical and anatomical models |

Currently, no guidelines or recommendations are available regarding the standardized use of 3D printed models in CHD patients. Use of 3D printed models is limited to complex CHD such as DORV (Figure 10) and ToF as evidenced by anecdotal reports and case series [16,21–23,31–33,56,57]. Other clinical benefits of using 3D printed heart models such as its impact on procedural safety and long-term outcomes are still yet to be investigated. Future research should focus on these areas as they will contribute to the development of clinical recommendations of using 3D printed models routinely in medical practice, therefore having great impact on the treatment of congenital heart disease. Figure 11 presents a summary of the current applications and future directions of 3D printing in CHD.

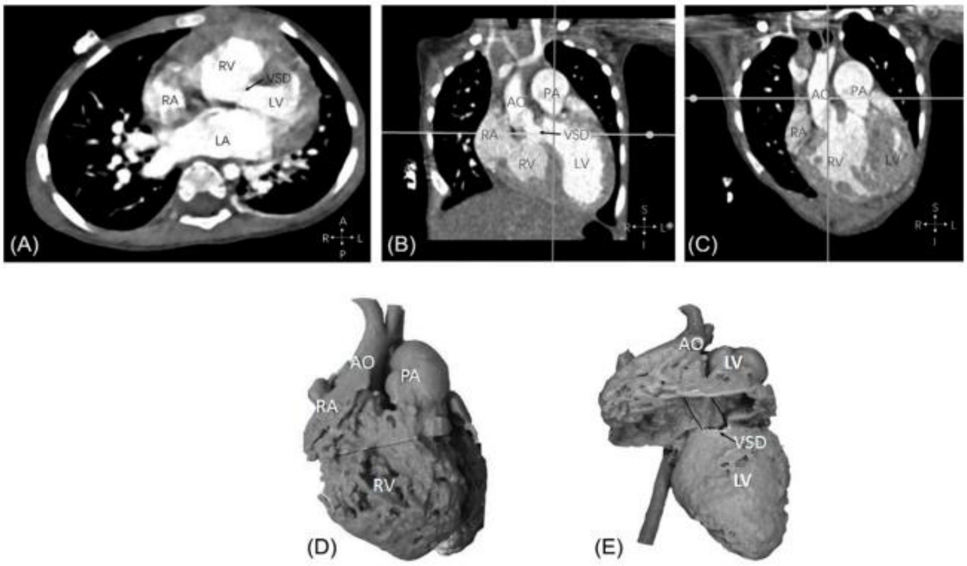
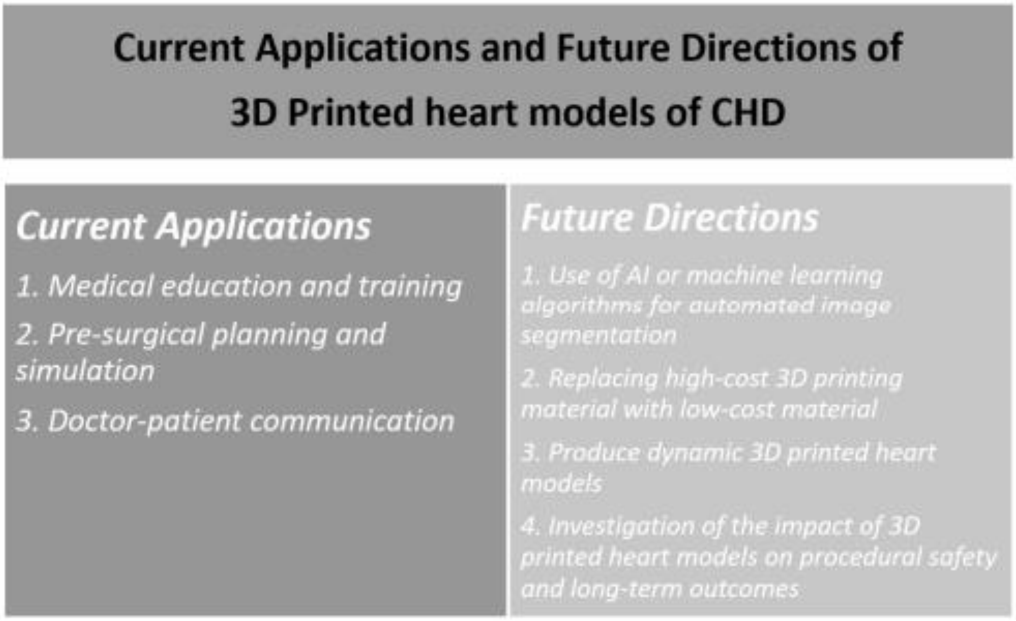


**Figure 10.** Example of double outlet right ventricle with aorta and pulmonary artery arising from the right ventricle and perimembranous ventricular septal defect from computed tomography images (**A–C**). Anterior view of the 3D printed heart model, aorta, and pulmonary artery are side-by-side with both arising from the right ventricle (**D**). Perimembranous VSD remoted from the arteries. Position of potential intracardiac tunnel from the left ventricle to the aorta is shown as the solid lines (**E**). AO—ascending aorta; LA—left atrium; LV—left ventricle; PA—pulmonary artery; RA—right atrium; RV—right ventricle; VSD—ventricular septal defect. Reprinted with permission from Zhao et al. [32].



Current Applications and Future Directions of 3D Printed heart models of CHD

*Current Applications*

*1. Medical education and training*
*2. Pre-surgical planning and simulation*
*3. Doctor-patient communication*

*Future Directions*

*1. Use of AI or machine learning algorithms for automated image segmentation*
*2. Replacing high-cost 3D printing material with low-cost material*
*3. Produce dynamic 3D printed heart models*
*4. Investigation of the impact of 3D printed heart models on procedural safety and long-term outcomes*

**Figure 11.** Summary of current applications and future research directions of 3D printing in congenital heart disease. 3D—three-dimensional; CHD—congenital heart disease; AI—artificial intelligence.

**Author Contributions:** Conceptualization: Z.S.; writing—original draft preparation, Z.S.; writing—review and editing, Z.S., I.L., Y.H.W., and C.H.Y.

**Funding:** This work was supported by the National Heart Foundation of Australia (101843).

**Conflicts of Interest:** Authors declare no conflict of interest.

## References

1. Yao, R.; Xu, G.; Mao, S.S.; Yang, H.Y.; Sang, X.T.; Sun, W.; Mao, Y.L. Three-dimensional printing: Review of application in medicine and hepatic surgery. *Cancer. Biol. Med.* **2016**, *13*, 443–451.
2. Chepelev, L.; Souza, C.; Althobaity, W.; Miguel, O.; Krishna, S.; Akyuz, E.; Hodgdon, T.; Torres, C.; Wake, N.; Alexander, A.; et al. Preoperative planning and tracheal stent design in thoracic surgery: A primer for the 2017 Radiological Society of North America (RSNA) hands-on course in 3D printing. *3D Print Med.* **2017**, *3*, 14. [CrossRef]
3. Matsumoto, J.S.; Morris, J.M.; Foley, T.A.; Williamson, E.E.; Leng, S.; McGee, K.P.; Kuhlmann, J.L.; Nesberg, L.E.; Vrtiska, T.J. Three-dimensional physical modeling: applications and experience at Mayo Clinic. *Radiographics* **2015**, *35*, 1989–2006. [CrossRef] [PubMed]
4. Mitsouras, D.; Liacouras, P.; Imanzadeh, A.; Giannopolous, A.A.; Cai, T.; Kumamaru, K.K.; George, E.; Wake, N.; Caterson, E.J.; Pomahac, B.; et al. Medical 3D printing for the radiologist. *Radiographics* **2015**, *35*, 1965–1988. [CrossRef] [PubMed]
5. Costello, J.; Olivieri, L.; Krieger, A.; Thabit, O.; Marshall, M.B.; Yoo, S.J.; Kim, P.C.; Jonas, R.A.; Nath, D.S. Utilizing three-dimensional printing technology to assess the feasibility of high-fidelity synthetic ventricular septal defect models for simulation in medical education. *World J. Pediatr. Congenit. Heart Surg.* **2014**, *5*, 421–426. [CrossRef]
6. Costello, J.P.; Olivieri, L.J.; Su, L.; Krieger, A.; Alfares, F.; Thabit, O.; Marshall, M.B.; Yoo, S.J.; Kim, P.C.; Jonas, R.A.; Nath, D.S. Incorporating three-dimensional printing into a simulation-based congenital heart disease and critical care training curriculum for resident physicians. *Congenit. Heart Dis.* **2015**, *10*, 185–190. [CrossRef]

7. Valverde, I.; Gomez, G.; Gonzales, A.; Suraz-Mejias, C.; Absuar, A.; Coserria, J.F.; Uribe, S.; Gomez-Cia, T.; Hosseinpour, A.R. Three-dimensional patient-specific cardiac model for surgical planning in Nikaidoh procedure. *Cardiol. Young* **2015**, *25*, 698–704. [CrossRef] [PubMed]
8. Hossien, A.; Gesomino, S.; Maessen, J.; Autschbach, R. The interactive use of multi-dimensional modeling and 3D printing in preplanning of type A aortic dissection. *J. Card. Surg.* **2016**, *31*, 441–445. [CrossRef] [PubMed]
9. Wang, H.; Liu, J.; Zheng, X.; Rong, X.; Zheng, X.; Peng, H.; Silber-Li, Z.; Li, M.; Liu, L. Three-dimensional virtual surgery models for percutaneous coronary intervention (PCI) optimization strategies. *Sci. Rep.* **2015**, *5*, 10945. [CrossRef]
10. Sun, Z.; Squelch, A. Patient-specific 3D printed models of aortic aneurysm and aortic dissection. *J. Med. Imaging Health Inf.* **2017**, *7*, 886–889. [CrossRef]
11. Sun, Z.; Lee, S. A systematic review of 3D printing in cardiovascular and cerebrovascular diseases. *Anatol. J. Cardiol.* **2017**, *17*, 423–435.
12. Perica, E.; Sun, Z. A systematic review of three-dimensional printing in liver disease. *J. Digit. Imaging* **2018**, *31*, 692–701. [CrossRef] [PubMed]
13. Vukicevic, M.; Mosadegh, B.; Min, J.K.; Little, S.H. Cardiac 3D printing and its future directions. *JACC. Cardiovasc. Imaging* **2017**, *10*, 171–184. [CrossRef] [PubMed]
14. Giannopoulos, A.A.; Steigner, M.L.; George, E.; Barile, M.; Hunsaker, A.R.; Rybicki, F.J.; Mitsouras, D. Cardiothoracic applications of 3-dimensional printing. *J. Thorac. Imaging* **2016**, *31*, 253–272. [CrossRef]
15. George, E.; Liacouras, P.; Rybicki, F.J.; Mitsouras, D. Measuring and establishing the accuracy and reproducibility of 3D printed medical models. *Radiographics* **2017**, *37*, 1424–1450. [CrossRef] [PubMed]
16. Lau, I.; Liu, D.; Xu, L.; Fan, Z.; Sun, Z. Clinical value of patient-specific three-dimensional printing of congenital heart disease: Quantitative and qualitative Assessments. *PLoS ONE* **2018**, *13*, e0194333. [CrossRef] [PubMed]
17. Parimi, M.; Buelter, J.; Thanugundla, V.; Condoor, S.; Parkar, N.; Danon, S.; King, W. Feasibility and validity of printing 3D heart models from rotational angiography. *Pediatr. Cardiol.* **2018**, *39*, 653–658. [CrossRef] [PubMed]
18. Olivieri, L.J.; Krieger, A.; Loke, Y.H.; Nath, D.S.; Kim, P.C.; Sable, C.A. Three-dimensional printing of intracardiac defects from three dimensional echocardiographic images: feasibility and relative accuracy. *J. Am. Soc. Echocardiogr.* **2015**, *28*, 392–397. [CrossRef]
19. Ma, X.J.; Tao, L.; Chen, X.; Li, W.; Peng, Z.Y.; Jin, J.; Zhang, X.L.; Xiong, Q.F.; Zhong, Z.L.; Chen, X.F. Clinical application of three-dimensional reconstruction and rapid prototyping technology of multislice spiral computed tomography angiography for the repair of ventricular septal defect of tetralogy of fallot. *Genet. Mol. Res.* **2015**, *14*, 1301–1309. [CrossRef]
20. Ngan, E.M.; Rebeyka, I.M.; Ross, D.B.; Hirji, M.; Wolfaardt, J.F.; Seelaus, R.; Grosvenor, A.; Noga, M.L. The rapid prototyping of anatomic models in pulmonary atresia. *J. Thorac. Cardiovasc. Surg.* **2006**, *132*, 264–269. [CrossRef]
21. Valverde, I.; Gomez-Ciriza, G.; Hussain, T.; Suarez-Mejias, C.; Velasco-Forte, M.N.; Byrne, N.; Ordoñez, A.; Gonzalez-Calle, A.; Anderson, D.; Hazekamp, M.G.; et al. Three dimensional printed models for surgical planning of complex congenital heart defects: an international multicenter study. *Eur. J. Cardiothorac. Surg.* **2017**, *52*, 1139–1148. [CrossRef] [PubMed]
22. Loke, Y.H.; Harahsheh, A.S.; Krieger, A.; Olivieri, L.J. Usage of 3D models of tetralogy of Fallot for medical education: impact on learning congenital heart disease. *BMC Med. Educ.* **2017**, *17*, 54. [CrossRef]
23. Su, W.; Xiao, Y.; He, S.; Huang, P.; Deng, X. Three-dimensional printing models in congenital heart disease education for medical students: a controlled comparative study. *BMC Med. Educ.* **2018**, *18*, 178. [CrossRef] [PubMed]
24. White, S.C.; Sedler, J.; Jones, T.W.; Seckeler, M. Utility of three-dimensional models in resident education on simple and complex intracardiac congenital heart defects. *Congenit. Heart Dis.* **2018**. [CrossRef] [PubMed]
25. Lim, K.H.A.; Loo, Z.Y.; Goldie, S.J.; Adams, J.W.; McMenamin, P.G. Use of 3D printed models in medical education: A randomized control trial comparing 3D prints versus cadaveric materials for learning external cardiac anatomy. *Anat. Sci. Educ.* **2016**, *9*, 213–221. [CrossRef]

26. Olivieri, L.J.; Su, L.; Hynes, C.F.; Krieger, A.; Alfares, F.A.; Ramakrishnan, K.; Zurakowski, D.; Marshall, M.B.; Kim, P.C.; Jonas, R.A.; et al. "Just-In-Time" simulation training using 3-D printed cardiac models after congenital cardiac surgery. *World J. Pediatr. Congenit. Heart Surg.* **2016**, *7*, 164–168. [CrossRef]
27. Lau, I.; Sun, Z. Three-dimensional printing in congenital heart disease: A systematic review. *J. Med. Radiat. Sci.* **2018**, *65*, 226–236. [CrossRef]
28. Jones, T.W.; Seckeler, M.D. Use of 3D models of vascular rings and slings to improve resident education. *Congenit. Heart Dis.* **2017**, *12*, 578–582. [CrossRef]
29. Biglino, G.; Capelli, C.; Leaver, L.K.; Shievano, S.; Taylor, A.M.; Wray, J. Involving patients, families and medical staff in the evaluation of 3D printing models of congenital heart disease. *Commun. Med.* **2015**, *12*, 157–169. [CrossRef]
30. Biglino, G.; Capelli, C.; Koniordou, D.; Robertshaw, D.; Leaver, L.K.; Schievano, S.; Taylor, A.M.; Wray, J. Use of 3D models of congenital heart disease as an education tool for cardiac nurses. *Congenit. Heart Dis.* **2017**, *12*, 113–118. [CrossRef]
31. Hoashi, T.; Ichikawa, H.; Nakata, T.; Shimada, M.; Ozawa, H.; Higashida, A.; Kurosaki, K.; Kanzaki, S.; Shiraishi, I. Utility of a super-flexible three-dimensional printed heart model in congenital heart surgery. *Interact. Cardiovasc. Thorac. Surg.* **2018**, *27*, 749–755. [CrossRef]
32. Zhao, L.; Zhou, S.; Fan, T.; Li, B.; Liang, W.; Dong, H. Three-dimensional printing enhances preparation for repair of double outlet right ventricular surgery. *J. Card. Surg.* **2018**, *33*, 24–27. [CrossRef] [PubMed]
33. Ryan, J.; Plasencia, J.; Richardson, R.; Velez, D.; Nigro, J.J.; Pophal, S.; Frakes, D. 3D printing for congenital heart disease: A single site's initial three-year experience. *3D Print. Med.* **2018**, *4*, 10. [CrossRef] [PubMed]
34. Fuertes, J.N.; Toporovsky, A.; Reyes, M.; Osborne, J.B. The physician-patient working alliance: Theory, research, and future possibilities. *Patient Educ. Couns.* **2017**, *100*, 610–615. [CrossRef]
35. Milano, E.G.; Capelli, C.; Wray, J.; Biffi, B.; Layton, S.; Lee, M.; Caputo, M.; Taylor, A.M.; Schievano, S.; Biglino, G. Current and future applications of 3D printing in congenital cardiology and cardiac surgery. *Br. J. Radiol.* **2019**, *91*, 20180389. [CrossRef] [PubMed]
36. Biglino, G.; Capelli, C.; Wray, J.; Schievano, S.; Leaver, L.K.; Khambadkone, S.; Giardini, A.; Derrick, G.; Jones, A.; Taylor, A.M. 3D-manufactured patient-specific models of congenital heart defects for communication in clinical practice: Feasibility and acceptability. *BMJ Open* **2015**, *5*, e007165. [CrossRef]
37. Biglino, G.; Koniordou, D.; Gasparini, M.; Capelli, C.; Leaver, L.K.; Khambadkone, S.; Taylor, A.M.; Wray, J. Piloting the use of patient-specific cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatr. Cardiol.* **2017**, *38*, 813–818. [CrossRef] [PubMed]
38. Batteux, C.; Haidar, M.A.; Bonnet, D. 3D-printed models for surgical planning in complex congenital heart diseases: A systematic review. *Front. Pediatr.* **2019**, *7*, 23. [CrossRef]
39. Bartel, T.; Rivard, A.; Jimenez, A.; Mestres, C.A.; Muller, S. Medical three-dimensional printing opens up new opportunities in cardiology and cardiac surgery. *Eur. Heart J.* **2018**, *39*, 1246–1254. [CrossRef] [PubMed]
40. 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 Cardiovasc. Dis.* **2016**, *5*, 2048004016645467. [CrossRef]
41. Motwani, M.; Dey, D.; Berman, D.S.; Germano, G.; Achenbach, S.; Al-Mallah, M.H.; Andreini, D.; Budoff, M.J.; Cademartiri, F.; Callister, T.Q.; et al. Machine learning for prediction of all-cause mortality in patients with suspected coronary artery disease: A 5-year multicentre prospective registry analysis. *Eur. Heart J.* **2017**, *38*, 500–507. [CrossRef]
42. Van Rosendael, A.R.; Maliakal, G.; Kolli, K.K.; Beecy, A.; Al'Aref, S.J.; Dwivedi, A.; Singh, G.; Panday, M.; Kumar, A.; Ma, X.; et al. Maximization of the usage of coronary CTA derived plaque information using a machine learning based on algorithm to improve risk stratification: insights from the CONFIRM registry. *J. Cardiovasc. Comput. Tomogr.* **2018**, *12*, 204–209. [CrossRef]
43. Nakanishi, R.; Sankaran, S.; Grady, L.; Malpeso, J.; Yousfi, R.; Osawa, K.; Ceponiene, I.; Nazarat, N.; Rahmani, S.; Kissel, K.; et al. Automated estimation of image quality for coronary computed tomographic angiography using machine learning. *Eur. Radiol.* **2018**, *28*, 4018–4026. [CrossRef] [PubMed]
44. Freiman, M.; Nickisch, H.; Prevrhal, S.; Schmitt, H.; Vembar, M.; Maurovich-Horvat, P.; Donnelly, P.; Goshen, L. Improving CCTA-based lesions' hemodynamic significance assessment by accounting for partial volume modeling in automatic coronary lumen segmentation. *Med. Phys.* **2017**, *44*, 1040–1049. [CrossRef] [PubMed]

45. Lau, I.; Wong, Y.H.; Yeong, C.H.; Abdul Aziz, Y.F.; Md Sari, N.A.; Hashim, S.A.; Sun, Z. Quantitative and qualitative comparison of low- and high-cost 3D-printed heart models. *Quant. Imaging Med. Surg.* **2019**, *9*, 107–114. [CrossRef]
46. Rengier, F.; Mehndiratta, A.; von Tengg-Kobligk, H.; Zechmann, C.M.; Unterhinninghofen, R.; Kauczor, H.U.; Giesel, F.L. 3D printing based on imaging data: Review of medical applications. *Int. J. Comput. Assist. Radiol. Surg.* **2010**, *5*, 335–341. [CrossRef]
47. Garcia, J.; Yang, Z.; Mongrain, R.; Leask, R.L.; Lachapelle, K. 3D printing materials and their use in medical education: A review of current technology and trends for the future. *BMJ Simul. Technol. Enhanc. Learn.* **2017**, *4*, 27–40. [CrossRef] [PubMed]
48. Sun, Z.; Squelch, A. 3D printed models of complex anatomy in cardiovascular disease. *Heart Res. Open. J.* **2015**, *2*, 103–108. [CrossRef]
49. Ratinam, R.; Quayle, M.; Crock, J.; Lazarus, M.; Fogg, Q.; McMenamin, P. Challenges in creating dissectible anatomical 3D prints for surgical teaching. *J. Anat.* **2019**, *234*, 419–437. [CrossRef] [PubMed]
50. Anderson, J.R.; Diaz, O.; Klucznik, R.; Zhang, Y.J.; Britz, G.W.; Grossman, R.G.; Lv, N.; Huang, Q.; Karmonik, C. Validation of computational fluid dynamics methods with anatomically exact, 3-D printed MRI phantoms and 4D pcMRI. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* **2014**, *2014*, 6699–6701. [PubMed]
51. Jan, J.; Park, H.J.; Kim, S.W.; Kim, H.; Park, J.Y.; Na, S.J.; Kim, H.J.; Park, M.N.; Choi, S.H.; Park, S.H.; Kim, S.W.; Kim, P.J.; et al. 3D printing complex tissue construct using stem cell-laden decellularized extracellular matrix bioinks for cardiac repair. *Biomaterials* **2017**, *112*, 264–274.
52. Özbolat, I.T.; Hospodiuk, M. Current advances and future perspectives in extrusion-based bioprinting. *Biomaterials* **2016**, *76*, 321–343. [CrossRef]
53. Tricomi, B.J.; Dias, A.D.; Corr, D.T. Stem cell bioprinting for applications in regenerative medicine. *Ann. N. Y. Acad. Sci.* **2016**, *1383*, 115–124. [CrossRef] [PubMed]
54. Duan, B. State of the art review of 3D bioprinting for cardiovascular tissue engineering. *Ann. Biomed. Eng.* **2017**, *45*, 195–209. [CrossRef]
55. Cui, H.; Miao, S.; Esworthy, T.; Zhou, X.; Lee, S.J.; Liu, C.; Yu, Z.X.; Fisher, J.P.; Mohiuddin, M.; Zhang, L.G. 3D bioprinting for cardiovascular regeneration and pharmacology. *Adv. Drug. Deliv. Rev.* **2018**, *132*, 252–269. [CrossRef] [PubMed]
56. Kiraly, L. Three-dimensional modelling and three-dimensional printing in pediatric and congenital cardiac surgery. *Transl. Pediatr.* **2018**, *7*, 129–138. [CrossRef] [PubMed]
57. Xu, J.J.; Luo, Y.J.; Wang, J.H.; Xu, W.Z.; Shi, Z.; Fu, J.Z.; Shu, Q. Patient-specific three-dimensional printed heart models benefit preoperative planning for complex congenital heart disease. *World J. Pediatr.* **2019**. [CrossRef] [PubMed]

## Appendix C1: Quality assessment of RCTs

| **Items** | **Ejaz 2013** | **Loke 2017** | **Su 2018** | **Wang 2017** | **White 2018** |
|---|---|---|---|---|---|
| Described as RCT | Yes | Yes | Yes | Yes | Yes |
| Adequate randomization | No | No | Yes | No | Yes |
| Treatment allocation concealed | No | No | Yes | No | Yes |
| Participants and providers blinded | Yes | No | Yes | Yes | Yes |
| Outcomes assessors blinded | No | No | No | No | Yes |
| Similarity of groups at baseline | No | Yes | Yes | No | Yes |
| Drop-out rate < 20% | Yes | Yes | Yes | Yes | Yes |
| Differential drop-out rate < 15% | Yes | Yes | Yes | Yes | Yes |
| Adherence to intervention protocols | Yes | Yes | Yes | Yes | Yes |
| Avoid other interventions | N/A | N/A | N/A | N/A | Yes |
| Outcomes measures assessment | Yes | Yes | Yes | No | Yes |
| Power calculation | No | No | No | No | No |
| Prespecified outcomes | Yes | Yes | Yes | Yes | Yes |
| Intent-to-treat analysis | Yes | Yes | Yes | Yes | Yes |
| Total of ‘Yes’ | 8 | 8 | 11 | 7 | 13 |
| Quality rating | Fair | Fair | Good | Fair | Good |

RCT, randomised controlled trial; N/A, not available

## Appendix C2: Quality assessment of observational cohort and cross-sectional studies

| **Items** | **Biglino 2017a** | **Lau 2018** | **Olivieri 2016** | **Valverde 2017** | **Zhao 2018** |
|---|---|---|---|---|---|
| Research question | Yes | Yes | Yes | Yes | Yes |
| Study population specified | Yes | Yes | Yes | Yes | Yes |
| Participation rate >50% | Yes | Yes | Yes | Yes | Yes |
| Groups recruited from the same population/ uniform eligibility criteria | Yes | Yes | Yes | Yes | Yes |
| Sample size justification | No | Yes | No | No | No |
| Exposure assessed before outcome measurement | Yes | Yes | Yes | Yes | Yes |
| Sufficient timeframe to see an effect | No | No | No | Yes | No |
| Different levels of exposure examined | No | No | No | Yes | No |
| Exposure measures and assessment | Yes | Yes | Yes | Yes | Yes |
| Repeated exposure assessment | No | No | Yes | No | No |
| Outcomes measures | Yes | Yes | Yes | Yes | Yes |
| Outcomes assessors blinded | No | No | No | No | No |
| Follow-up rate | Yes | Yes | Yes | Yes | Yes |
| Statistical analyses | No | No | No | No | No |
| Total of ‘Yes’ | 8 | 9 | 9 | 10 | 8 |
| Quality rating | Fair | Fair | Fair | Good | Fair |

## Appendix C3: Quality assessment of pre-post studies with no control group

| **Items** | **Costello 2015** |
|---|---|
| Research question | Yes |
| Eligibility criteria and study population | No |
| Study participants representative of clinical populations of interest | Yes |
| All eligible participants enrolled | No |
| Sample size | No |
| Intervention clearly described | Yes |
| Outcome measures clearly described, valid, and reliable | Yes |
| Outcomes assessors blinded | No |
| Follow-up rate | Yes |
| Statistical analyses | Yes |
| Multiple outcomes measures | No |
| Group-level interventions and individual- level outcome efforts | Yes |
| Total of ‘Yes’ | 7 |
| Quality rating | Fair |

## Appendix C4: Quality assessment of case-control study

| **Items** | **Ryan 2018** |
|---|---|
| Research question | Yes |
| Study population | Yes |
| Target population and case representation | No |
| Sample size justification | Yes |
| Groups recruited from the same population | Yes |
| Inclusion/exclusion criteria | Yes |
| Case and control definitions | No |
| Random selection of study participants | No |
| Concurrent controls | Yes |
| Exposure assessed before outcome measurement | Yes |
| Exposure assessors blinded | No |
| Statistical analyses | No |
| Total of ‘Yes’ | 9 |
| Quality rating | Good |

## Appendix C5: Quality assessment of case series studies

| **Items** | **Bhatla 2017** | **Gare-kar 2016** | **Hoashi 2018** | **Ma 2015** | **McG-overn 2017** | **Ngan 2006** | **Olejn-ik 2017** | **Olivie-ri 2015** | **Parimi 2018** | **Riesen kamp-ff 2009** | **Schm-auss 2015** | **Shirai-shi 2009** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Research question | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Study population clearly described | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Case consecutive | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No |
| Comparable subjects | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Intervention clearly described | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Outcome measures clearly described, valid, and reliable | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Follow-up rate | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes | No |
| Statistical methods described | No | No | No | Yes | No | No | Yes | Yes | Yes | No | No | No |
| Results well described | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No |
| Total of ‘Yes’ | 8 | 8 | 8 | 9 | 8 | 8 | 9 | 8 | 8 | 6 | 8 | 4 |
| Quality rating | Good | Good | Good | Good | Good | Good | Good | Good | Good | Fair | Good | Fair |

## Appendix D1: Quiz 1

https://docs.google.com/forms/d/e/1FAIpQLScsWfUR6fEhUWFRn8A2oOv50HrNq2QONOScyEAsn_iWAp7tTQ/viewform

## Appendix D2: Quiz 2

https://docs.google.com/forms/d/e/1FAIpQLSfgxIPWa9Quy78p6fX9GfabcSDWl95TsMGvKvq15FjhkyjNoQ/viewform

## Appendix D3: Survey for control and 3DPHM groups respectively

### Survey (Please tick the appropriate boxes)

| | **Strongly agree** | **Agree** | **Neutral** | **Disagree** | **Strongly disagree** |
|---|---|---|---|---|---|
| 1. The teaching method was interactive and interesting. | | | | | |
| 2. The lecture was easy to understand. | | | | | |
| 3. After attending this tutorial, my knowledge about congenital heart disease has improved. | | | | | |
| 4. If 3D printed heart models were used, they would have helped me to understand congenital heart disease better. | | | | | |

5. Do you have any additional comments?

### Survey (Please tick the appropriate boxes)

| | **Strongly agree** | **Agree** | **Neutral** | **Disagree** | **Strongly disagree** |
|---|---|---|---|---|---|
| 1. The teaching method was interactive and interesting. | | | | | |
| 2. The lecture was easy to understand. | | | | | |
| 3. After attending this tutorial, my knowledge about congenital heart disease has improved. | | | | | |
| 4. The 3D printed heart models played an important role in the overall quality of the tutorial. | | | | | |

5. Do you have any additional comments?

## Appendix E1: 3DPHM versus VR questionnaire

### General information

**Are you a…**

☐ Cardiologist ☐ Interventional Cardiologist ☐ Cardiac Radiologist ☐ General Radiologist ☐ Radiology Registrar

☐ Radiographer ☐ Others: ____________

**Please place a tick (✓) in the box of your chosen option.**

| **No** | **Questions** | **VR models** | **3D printed heart models** | **Both are the same** | **Unsure** | **None** |
|---|---|---|---|---|---|---|
| 1 | Which allows a better depth perception for the heart structures? | | | | | |
| 2 | Which allows a better and more comprehensive viewing experience for yourself? | | | | | |
| 3 | Which has a more realistic visualization compared to 3D rendered DICOM images*? | | | | | |
| 4 | Which helps you to appreciate the heart defects better? | | | | | |
| 5 | Which helps you to understand the spatial relationship between the cardiac structures better? | | | | | |
| 6 | Which allows you to visualise the external cardiac structures better? | | | | | |
| 7 | Which allows you to visualise the internal cardiac structures better? | | | | | |
| 8 | In your opinion, which is more useful in the aspect of educating medical students or young physicians about congenital heart disease? | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 9 | In your opinion, which is more useful in the aspect of pre-operative planning for congenital heart disease surgeries? | | | | | |

10. In your opinion, please rate the usefulness of both the VR and 3D printed heart models in educating medical students or young physicians about congenital heart disease. (1-5, 1 = not useful, 5 = extremely useful)

| | | | | | |
|---|---|---|---|---|---|
| VR models | 1 | 2 | 3 | 4 | 5 |
| 3D printed heart models | 1 | 2 | 3 | 4 | 5 |

11. In your opinion, please rate the usefulness of both the VR and 3D printed heart models in preoperative planning. (1-5, 1 = not useful, 5 = extremely useful)

| | | | | | |
|---|---|---|---|---|---|
| VR models | 1 | 2 | 3 | 4 | 5 |
| 3D printed heart models | 1 | 2 | 3 | 4 | 5 |

12. Do you think patient-specific 3D models (regardless of VR or 3D printed) can help to increase the surgeon’s confidence in congenital heart disease surgeries?

☐ Yes ☐ No ☐ Unsure

13. Do you think patient-specific 3D models (regardless of VR or 3D printed) have provided additional benefits compared to the conventional medical imaging visualizations (e.g. 3D CT or MRI image visualization)? If so, briefly explain the reasons.

14. Can you identify any other areas that VR or 3D printed heart models could be useful in clinical practice?

## Appendix E2: Video of VR application

https://youtu.be/AhamB44aEZY

## Appendix E3: Images of 3DPHM

**Figure 1:** 3D printed heart models in two different materials, Flexible V4 Resin (gray) and TPU 80A (translucent).

**Figure 2:** 3D printed heart models of 4 different types of congenital heart disease.

Starting from left: atrial septal defect, ventricular septal defect, Tetralogy of Fallot, double outlet right ventricle.

## Appendix F1: Video of MR application

https://youtu.be/WMVn6I-DKf0

## Appendix F2: Questionnaires for Mixed Reality, 3D printing, and current visualization techniques

SURVEY: Radiologists, doctors, junior doctors

| | |
|---|---|
| Age | |
| Gender | |
| Medical Specialty & Year of Experience | |
| Have you ever used AR before? | ☐ Yes ☐ No |
| Have you ever used 3D printing technology in your specialty? | ☐ Yes ☐ No |

**Please rank the following with 1 being the highest/ best, and 3 being the lowest/ worst.**

| | **ATRIAL SEPTAL DEFECT** | | | **DOUBLE OUTLET RT VENTRICLE** | | |
|---|---|---|---|---|---|---|
| **Questions** | DICOM images | 3D printed models | HoloLens 2 | DICOM images | 3D printed models | HoloLens 2 |
| 1. The major vessels of the heart can be well assessed. | | | | | | |
| 2. The heart defects can be easily appreciated. | | | | | | |
| 3. The spatial relationship between the cardiac structures can be easily understood. | | | | | | |
| 4. The model offers a good depth perception for the heart structures. | | | | | | |
| 5. I prefer the use of this method to learn about the pathology. | | | | | | |
| 6. I prefer the use of this method to communicate with another health professional during discussion. | | | | | | |
| 7. I prefer the use of this method to communicate with patients about the pathology. | | | | | | |

8. How do you feel about the ability to change the clipping plane on the AR models?

9. Additional comments:

SURVEY: Cardiac surgeons, Interventional cardiologists

| | |
|---|---|
| Age | |
| Gender | |
| Medical Specialty | ☐ Cardiac surgeon ☐ Interventional cardiologist |
| Have you ever used AR before? | ☐ Yes ☐ No |
| Have you ever used 3D printing technology in your specialty? | ☐ Yes ☐ No |

**Please rank the following with 1 being the highest/ best, and 3 being the lowest/ worst.**

| | **ATRIAL SEPTAL DEFECT** | | | **DOUBLE OUTLET RT VENTRICLE** | | |
|---|---|---|---|---|---|---|
| **Questions** | DICOM images | 3D printed models | HoloLens 2 | DICOM images | 3D printed models | HoloLens 2 |
| 1. The major vessels of the heart can be well assessed. | | | | | | |
| 2. The heart defects can be easily appreciated. | | | | | | |
| 3. The spatial relationship between the cardiac structures can be easily understood. | | | | | | |
| 4. The model offers a good depth perception for the heart structures. | | | | | | |
| 5. I prefer the use of this method to learn about the pathology. | | | | | | |
| 6. I prefer the use of this method to communicate with another health professional during discussion. | | | | | | |
| 7. I prefer the use of this method to communicate with patients about the pathology. | | | | | | |
| 8. This model prepares me for surgery. | | | | | | |
| 9. This model helps me to understand the possible complications related to the procedure/ surgery. | | | | | | |
| 10. I am likely to consult this model for preoperative planning. | | | | | | |
| 11. This model can be helpful for intraoperative guidance. | | | | | | |

12. How do you feel about the ability to change the clipping plane on the AR models?

13. Additional comments:

## Appendix F3: Skewness and kurtosis for each question

| Question | Modality | ASD | | DORV | |
|---|---|---|---|---|---|
| | | **Skewness** | **Kurtosis** | **Skewness** | **Kurtosis** |
| 1. Assessment of major vessels | DICOM | 0.297 | -1.595 | -0.181 | -1.787 |
| | 3DP | -0.034 | -0.651 | -0.078 | -0.804 |
| | MR | -0.244 | -1.809 | 0.297 | -1.595 |
| 2. Appreciation of heart defects | DICOM | -1.104 | -0.570 | -1.151 | -0.156 |
| | 3DP | 0.764 | -0.722 | 0.414 | -1.026 |
| | MR | 0.100 | -0.625 | 0.487 | -1.032 |
| 3. Spatial relationship between the cardiac structures | DICOM | -1.375 | 0.329 | -1.737 | 1.572 |
| | 3DP | 0.435 | -0.862 | 0.248 | -1.101 |
| | MR | 0.513 | -0.865 | 0.538 | -0.735 |
| 4. Depth perception | DICOM | -1.897 | 2.106 | -1.589 | 1.121 |
| | 3DP | 0.354 | -0.678 | 0.213 | -0.867 |
| | MR | 0.677 | -0.489 | 0.884 | -0.247 |
| 5. Pathology learning | DICOM | -1.497 | 0.637 | -1.184 | -0.267 |
| | 3DP | 0.435 | -0.862 | 0.186 | -1.027 |
| | MR | 0.486 | -0.592 | 0.677 | -0.489 |
| 6. Communication tool with another health professional | DICOM | 0.000 | -1.771 | -0.297 | -1.595 |
| | 3DP | 0.344 | -0.997 | 0.449 | -1.194 |
| | MR | -0.403 | -1.343 | -0.162 | -1.368 |
| 7. Communication tool with patients | DICOM | -1.214 | 0.556 | -1.233 | 0.638 |
| | 3DP | 2.986 | 8.127 | 2.728 | 6.050 |
| | MR | 0.079 | -0.144 | 0.067 | 0.253 |
| 8. Prepares me for surgery / intervention | DICOM | -0.485 | -1.532 | -0.574 | -1.282 |
| | 3DP | 0.000 | -0.685 | -0.249 | -1.225 |
| | MR | 0.485 | -1.532 | 0.847 | -0.538 |
| 9. Helps to understand possible complications | DICOM | -0.454 | -1.480 | -0.851 | -0.765 |
| | 3DP | 0.139 | -1.008 | 0.000 | -1.392 |
| | MR | 0.269 | -1.659 | 0.773 | -0.587 |
| 10. Pre-operative planning | DICOM | -0.988 | -0.578 | -0.851 | -0.765 |
| | 3DP | 0.228 | -1.140 | -0.139 | -1.008 |
| | MR | 0.601 | -0.974 | 1.068 | -0.168 |
| 11. Intra-operative guidance | DICOM | -0.851 | -0.765 | -0.851 | -0.765 |
| | 3DP | 0.139 | -1.008 | -0.076 | -1.223 |
| | MR | 0.647 | -1.190 | 0.916 | -0.414 |

3DP, three-dimensional printing; DICOM, Digital Imaging and Communications in Medicine; MR, mixed reality

## Appendix F4: Comparison of the mean ranks difference of both CHD

| Question | Modality | Mean diff. (ASD-DORV) | p-value[a] |
|---|---|---|---|
| 1. Assessment of major vessels | DICOM | -0.24 | 0.26 |
| | 3DP | -0.03 | 0.44 |
| | MR | 0.27 | 0.16 |
| 2. Appreciation of heart defects | DICOM | -0.03 | 0.72 |
| | 3DP | -0.14 | 0.65 |
| | MR | 0.17 | 0.43 |
| 3. Spatial relationship between the cardiac structures | DICOM | -0.09 | 0.50 |
| | 3DP | -0.11 | 0.55 |
| | MR | 0.21 | 0.39 |
| 4. Depth perception | DICOM | 0.06 | 0.68 |
| | 3DP | -0.11 | 0.42 |
| | MR | 0.06 | 0.35 |
| 5. Pathology learning | DICOM | 0.09 | 0.82 |
| | 3DP | -0.14 | 0.25 |
| | MR | 0.06 | 0.32 |
| 6. Communication tool with another health professional | DICOM | -0.15 | 0.01 |
| | 3DP | 0.03 | 0.44 |
| | MR | 0.12 | 0.11 |
| 7. Communication tool with patients | DICOM | -0.06 | 0.09 |
| | 3DP | -0.03 | 0.77 |
| | MR | 0.09 | 0.22 |
| 8. Prepares me for surgery / intervention | DICOM | -0.04 | 0.88 |
| | 3DP | -0.14 | 0.78 |
| | MR | 0.18 | 0.80 |
| 9. Helps to understand possible complications | DICOM | -0.17 | 0.02 |
| | 3DP | -0.09 | 0.79 |
| | MR | 0.26 | 0.09 |
| 10. Pre-operative planning | DICOM | 0.04 | 0.74 |
| | 3DP | 0.10 | 0.09 |
| | MR | 0.18 | 0.42 |
| 11. Intra-operative guidance | DICOM | 0.00 | 0.45 |
| | 3DP | -0.13 | 0.23 |
| | MR | 0.13 | 0.17 |

[a] after Bonferroni correction

3DP, three-dimensional printing; DICOM, Digital Imaging and Communications in Medicine; MR, mixed reality