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Author for correspondence:
Mari Nieves Velasco-Forte, School of Biomedical Engineering and Imaging Sciences, King's College London, F04 Lambeth Wing, St Thomas' Hospital, Westminster Bridge Rd, Lambeth, London SE1 7EH, UK.
Tel: +44 7849 912341;
E-mail: mnieves.velasco@kcl.ac.uk

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Living the heart in three dimensions: applications of 3D printing in CHD

Mari Nieves Velasco Forte[1,2,5], Tarique Hussain[4], Arno Roest[5], Gorka Gomez[2], Monique Jongbloed[5], John Simpson[1,3], Kuberan Pushparajah[1,3], Nick Byrne[1] and Israel Valverde[1,2,5]

[1]Division of Imaging Sciences and Biomedical Engineering, King's College, London, UK; [2]Cardiovascular Pathology Unit, Institute of Biomedicine of Seville, IBIS, Virgen del Rocio University Hospital/CSIC/University of Seville, Sevilla, Spain; [3]Department of Congenital Heart Disease, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK; [4]Department of Pediatrics, UT Southwestern Medical Center, 1935 Medical District Drive, Dallas, TX, USA and [5]Department of Pediatric Cardiology, Leiden University Medical Center, Leiden, The Netherlands

Abstract

Advances in biomedical engineering have led to three-dimensional (3D)-printed models being used for a broad range of different applications. Teaching medical personnel, communicating with patients and relatives, planning complex heart surgery, or designing new techniques for repair of CHD via cardiac catheterisation are now options available using patient-specific 3D-printed models. The management of CHD can be challenging owing to the wide spectrum of morphological conditions and the differences between patients. Direct visualisation and manipulation of the patients' individual anatomy has opened new horizons in personalised treatment, providing the possibility of performing the whole procedure in vitro beforehand, thus anticipating complications and possible outcomes. In this review, we discuss the workflow to implement 3D printing in clinical practice, the imaging modalities used for anatomical segmentation, the applications of this emerging technique in patients with structural heart disease, and its limitations and future directions.

Since 2014, the Association for European Paediatric and Congenital Cardiology has supported scientific projects in the field of paediatric and congenital cardiology in Europe led by junior members. The aim is to support junior members to develop an international and collaborative research study involving European centres.

In 2015, the Association for European Paediatric and Congenital Cardiology junior research grant was awarded for the evaluation of 3D-printed models in different scenarios of CHD, such as surgical planning, interventional planning, education of trainees, and communication with patients and parents. In this editorial, we will present the research output supported with this grant and introduce the readers to 3D printing technology, providing an overview of the imaging requirements for generating a 3D model. We will review current scientific evidence on the usefulness of 3D cardiovascular models in congenital and structural heart disease.

The increasing anatomical complexity of the patients undergoing congenital cardiac surgery over time has created the need for new techniques to assess cardiac morphology and structural defects, with multi-detector CT and cardiac MRI being currently part of their routine evaluation. Subsequently, 3D images have become available, with the limitation that although a 3D representation of the anatomy is provided, it is configured within the confines of a two-dimensional screen. The complexity of severe types of CHD precludes the understanding of the disease without the manipulation and direct visualisation of the patient's heart features.

The first medical 3D printing techniques were aimed to plan cranial,[1–4] maxillofacial,[3–6] and orthopaedic surgery.[7,8] Since then, a wide variety of different materials and printing techniques have developed, offering now the possibility of using them in different scenarios, including cardiovascular disease. In this review, we will discuss how to create a patient-specific 3D model and their applications for patients with CHD.

How to create a 3D-printed model

Image acquisition

Most 3D models are created from CT or MRI whole-heart datasets. Some minimum requirements are necessary. Each slice must be contiguous to the preceding one, the image should be isotropic, and any data element acquired must relate to every other image data point with a fixed relationship.

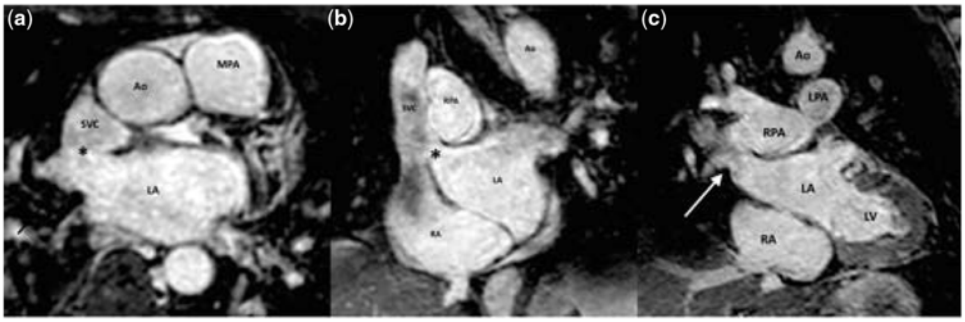

Figure 1. Adapted from Velasco Forte et al. 3D balance steady-state precession acquired with image-based navigation for a patient with partial anomalous pulmonary venous connection. Sinus venosus defect in axial (*a*) and coronal (*b*) reformats. Pathway of anomalous pulmonary veins into the LA (white arrow) in coronal view (*c*). Ao = aorta; LA = left atrium; LPA = left pulmonary artery; LV = left ventricle; MPA = main pulmonary artery; RA = right atrium; RPA = right pulmonary artery; SVC = superior caval vein.

The preference between one imaging technique and another is based on the experience of the centre, the main structure of interest, and the age of the patient, with a tendency to use MRI in younger population to avoid radiation.[9,10] Although being of significant relevance, the details for sequences acquisition are not always explained in clinical studies.[11–13] ECG-gated 3D balance steady-state precession and contrast-enhanced MRI angiography are the most common reported techniques when MRI is the selected imaging method.[9,10,14–17,18] Image-based navigation for motion correction in 3D balance steady-state precession acquisition has been used for creation of models in complex interventional planning.[10] The sharpness of the borders of the cardiac contours and vessels and the small voxel size achieved with this technique help the operator to perform a detailed segmentation of the patient's anatomy (Fig 1).

In other studies, CT is the imaging technique of choice, and it has been described as being one of the easiest modalities with which to create a model for 3D printing in a recent review.[19] 3D echocardiography has also been utilised when cardiac valves are the target of the segmentation. Promising results have been achieved both in combining 3D echo with CT or as isolated datasets.[20–22] However, a recent study states that CT may be better than echocardiography when the left atrial appendage is the region of interest, to plan device closure in patients with atrial fibrillation.[23]

As this field is still developing, new imaging modalities are emerging as possible options for 3D printing. This is the case of rotational angiography, which allows tomographic slices to be routinely reconstructed with high spatial resolution. A short case series has been recently published, suggesting that this option may spread the opportunity to create 3D models to a larger number of centres.[24]

Image segmentation

Once the image is acquired, the data are imported into a segmentation software, where the anatomy of interest is delineated and separated from the surrounding tissues. Several software packages have been reported for this purpose. It is, however, quite common that the name of the software or program used is not mentioned in the study. Our group performed a systematic review on the image segmentation methodology,[18] showing that only 34% of journal publications provided sufficient detail for their methodology to be reproduced. A further 38% mentioned the methods that they had used but did not explain how these had been applied, and the remaining 29% of publications did not provide any description of their method whatsoever.

There are several software packages available either commercially or as open source access platforms.[18,25–29] The segmentation process is carried out by the use of manual and semi-automatic methods. Brightness thresholding, region growing, and manual editing are the three most frequently used methods.[18,25,30]

Once the segmentation is finished, the stereolithography file (.stl) created is sent to computer-aided design software, where refinement of the anatomy is performed. This process allows the creation of hollow models with smooth surfaces, as well as trimming the end of the vessels or cutting the model to show its inside. The segmentation process using a free-access segmentation tool and computer-aided design methodology are represented in Figure 2.

3D printing technologies and materials

Rapid prototyping technology can be subtractive or additive depending on the printing method used. Regarding subtractive techniques, only milling is applied in the medical field. Fused deposition modelling, polyjet printing, stereolithography, and selective laser sintering are the most common additive techniques utilised in medicine.[29,31,32]

In fused deposition modelling, a thermoplastic filament is forced through a heated extrusion nozzle. The filament is melted while moving in vertical and horizontal directions. The layer of material hardens immediately after extrusion; the process is repeated layer by layer until the model is finished. A support material that is later dissolved is printed within the actual model.

Polyjet modelling works in a similar way to an ink-jet printer. During the process, layers of liquid photopolymers are jetted in the predefined shape using computer-aided files. Each layer hardens quickly under ultraviolet light. Multiple layers are incorporated until the model is complete.

Stereolithography builds the models through the polymerisation of a photopolymeric resin. A digitally controlled ultraviolet beam hardens the surface of the resin layer by layer.

Selective laser sintering uses a high-power laser to fuse metal or ceramic powder. It offers highly accurate 3D models, used for functional prototypes or medical implants, but it is also generally higher in cost when compared to other additive manufacturing techniques.

Several materials with different properties have been used to print cardiovascular structures. Initially, hard materials were utilised to show cardiac anatomy and great vessels.[13,33] However, rubber-like models printed in a hollow fashion have become more common for the routine planning of interventions as they provide a more realistic representation of the patient's cardiac anatomy, which is essential to plan any surgical or interventional procedure.[34] Other interesting features of new materials are the spectrum of opacity and transparency and softness.

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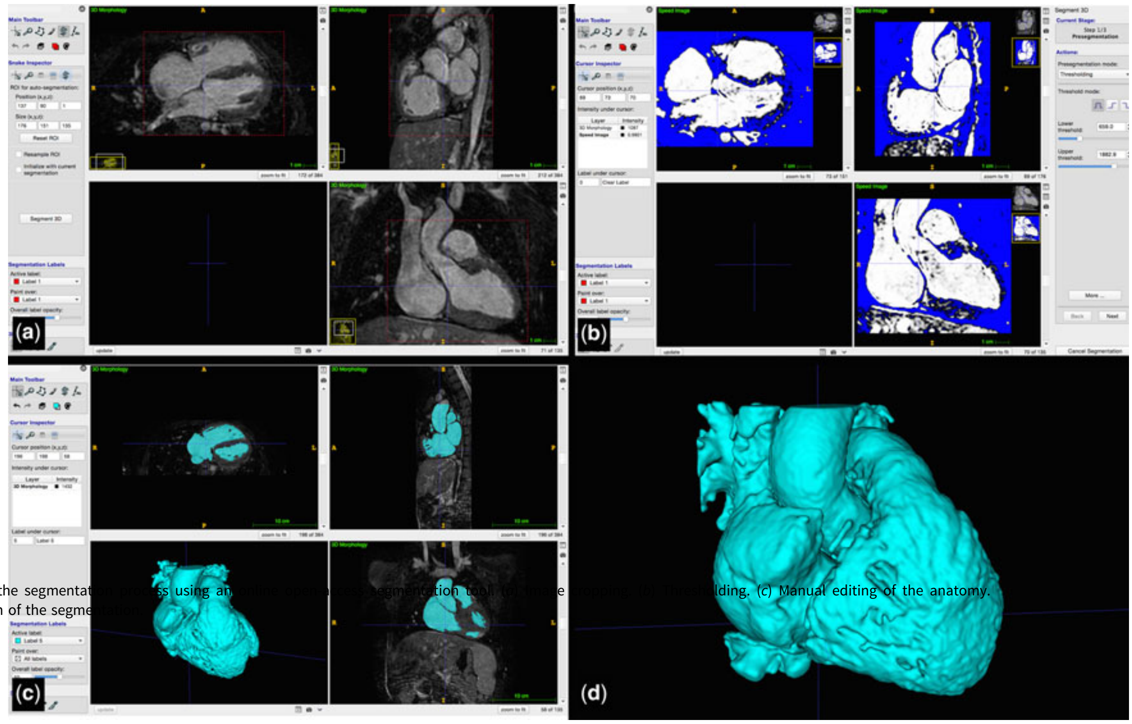

Figure 2. Steps of the segmentation process using an online open-access segmentation tool. (*a*) Image cropping. (*b*) Thresholding. (*c*) Manual editing of the anatomy. (*d*) 3D representation of the segmentation.

Applications in CHD

Clinical practice

Recent reviews have extensively described the use of 3D printing for procedural planning in a wide range of patients with congenital and structural heart disease.[19,25,29,30,34]

- Surgical planning

3D models have proven to be useful when complex anatomy precludes anatomical understanding using 2D images provided by conventional imaging such as echocardiography, CT, and MRI. We recently published a multicentre study involving 10 international centres showing high accuracy of the models, with no significant difference between the model itself and the CT or MRI images used to perform the segmentation, the design methodology is illustrated in Figure 3.[34] In the same study, in 19 of 40 cases, the 3D model changed the management or surgical approach initially concluded by multidisciplinary discussion before having access to the model.

Patients with double-outlet right ventricle, tetralogy of Fallot, pulmonary atresia, and hypoplastic left heart syndrome seem to be the groups that have benefit the most from this emerging technique.[17,33,35–39] In a single-centre study including five patients with double-outlet right ventricle and non-committed ventricular septal defect, the 3D model showed better scoring than conventional imaging, and in three cases, a biventricular repair was successfully carried out.[38] A case report also illustrated the importance of 3D printing in a patient with double-outlet right ventricle, dextrocardia, and supra-tricuspid ring.[39]

Other studies have also demonstrated the relevance of this technique in patients with other cardiac disease, such as complex atrioventricular septal defect, congenitally corrected transposition of the great arteries, complex total anomalous pulmonary venous connection, multiple ventricular septal defects, crisscross heart, or isomerism.[34,37]

In addition to CHD, rapid prototyping has been utilised for patients with different types of structural heart disease. Simulation of cardiac myomectomy has been performed in patients with severe forms of hypertrophic obstructive cardiomyopathy.[40,41] Cardiac tumours have also been benefitted from this technique and have been utilised to identify structures at risk and to determine appropriate therapeutic option and surgical approaches.[26,42–44]

A new procedure has emerged for the treatment of aortic root aneurysm in patients with Marfan syndrome, using 3D-printed models of the aortic root. These are made in thermoplastic by rapid prototyping, manufacturing a personalised support of a macroporous polymer mesh. The support is positioned around the aorta, closely applied from the aortoventricular junction to the proximal aortic arch, allowing preservation of the aortic valve and the patient's coronary arteries.[45–47]

- Cardiac catheterisation: interventional planning

Visualisation of patients' anatomy in three dimensions and the opportunity to manipulate it in our own hands have allowed us to understand better the relationships between cardiac structures and have opened new horizons in treatment for patients with CHD. This is the case of patients with aortic arch anomalies[16] or mitral valve disease. High-risk patients in whom open-heart surgery is not a therapeutic option can now benefit from palliative procedures. This is the case of patients receiving a Mitraclip via cardiac catheterisation. Although mimicking the properties of the tissue of the cardiac leaflets appears challenging, some groups have developed models with deformable leaflets. During simulations, patient-specific models helped to plan the best landing

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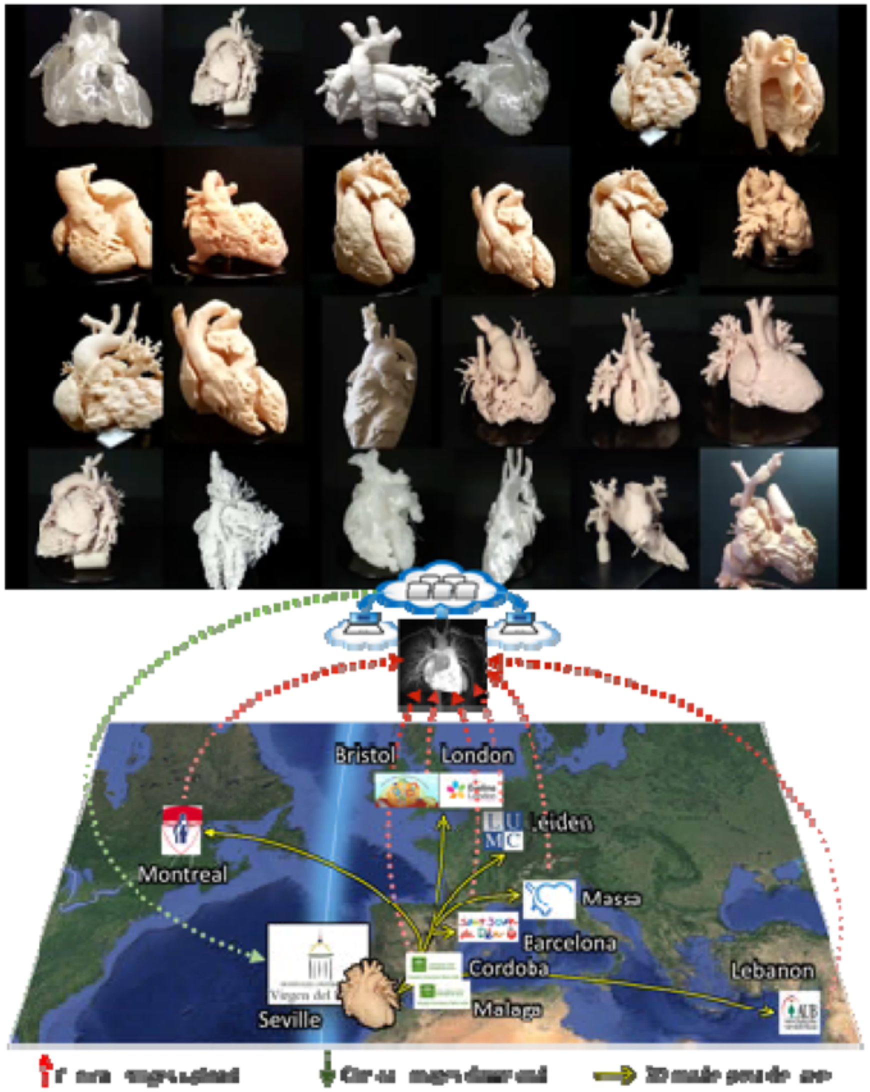

Figure 3. International study involving ten participating centers. Demographic, clinical and imaging data (CT and MRI) were collected by participating centres, de-identified and uploaded to a dedicated cloud server. Data was downloaded by a single centre (VRH) for consolidation, 3D printing and evaluation of 3D printing measurement accuracy. 3D printed models were sent by urgent delivery post to the referral centre for examination, communication with the medical team and parents of the patients and hands-on simulation of the surgery. Participating centres: Hospital Virgen del Rocio (Seville, Spain), Evelina Children's Hospital (London, United Kingdom), Bristol Royal Hospital for Children (Bristol, United Kingdom), Leiden University Medical Centre (Leiden, The Netherlands), Montreal Children's Hospital (Montreal, Canada), Fondazione Toscana Gabriele Monasterio (Massa, Italy), Hospital Sant Joan de Deu (Barcelona, Spain), Hospital de Cordoba (Cordoba, Spain), Hospital Regional de Malaga (Malaga, Spain), American University of Beirut (Beirut, Lebanon). Adapted from Valverde et al.[34]

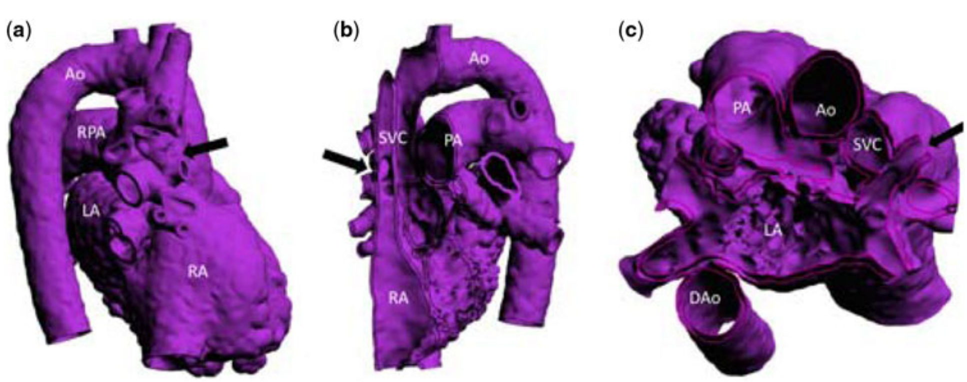

Figure 4. 3D segmentation of the heart of a patient with partial anomalous pulmonary venous connection. The model was printed 1:1 scale, and 2 mm thickness was added using computer-aided design techniques. (*a*) Lateral view of the heart showing right upper pulmonary vein (RUPV, black arrow) draining into the superior caval vein (SVC). (*b*) Sagittal cut showing orifice of the drainage of the RUPV into the SVC (black arrow). (*c*) Axial reformat showing pathway of the RUPV (black arrow), draining into the SVC and continuing towards the left atrium (LA).

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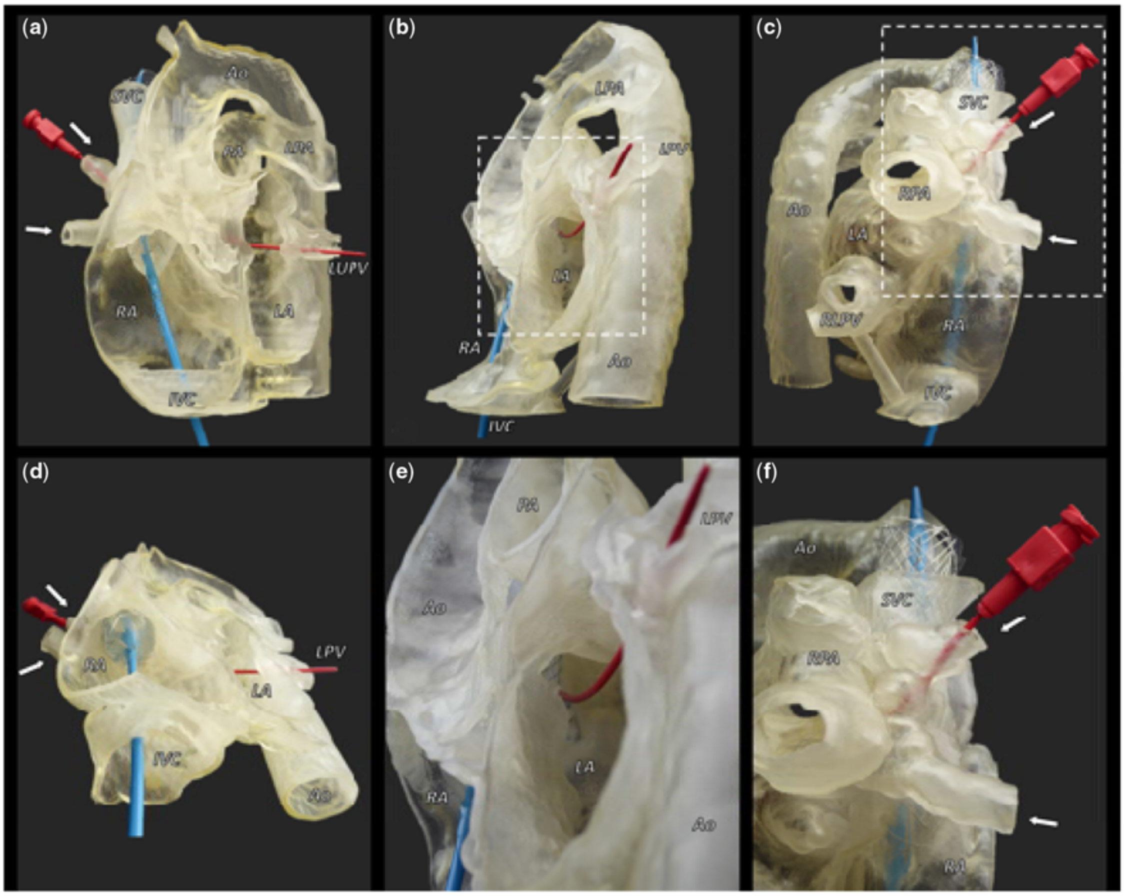

Figure 5. The flexible, translucent models were examined to confirm the expected relationship of the anomalous pulmonary veins (PVs) (arrows) to the superior caval vein (SVC) and left atrium (LA). Within the model, a balloon-mounted stent catheter was placed in the SVC to right atrium (RA) junction (blue catheter), while a dilator (red) was passed from the anomalous right upper PV to the left upper pulmonary vein (LUPV). The distance from the anomalous PV to the SVC–RA junction was measured using the three-dimensional (3D) model and the cross-sectional images described in the preceding text. This allowed calculation of the length of the stent to close the defect and redirect the flow of the partial anomalous pulmonary venous drainage towards the LA.

point and provided direct visualisation of the morphological result.[20,48]

3D printing has also facilitated the implementation of transcatheter approach in the treatment of the aortic valve.[49] Aortic root 3D models have proven to accurately reproduce the anatomy of patients and aid prediction of paravalvular aortic regurgitation in transcatheter aortic valve replacement.[50]

Our group recently described a novel procedure to treat partial anomalous pulmonary venous connection and sinus venosus defect based on patient-specific models. 3D models helped to demonstrate that stenting the superior caval vein towards the right atrium, occluding the sinus venosus defect, and redirecting the pulmonary venous flow into the left atrium to correct this common defect diagnosed in adulthood are feasible (Figs 4 and 5). This new technique avoids cardiac bypass and allows the patient to be discharged home within 24 hours.[10]

Coronary fistulae have a tendency to show tortuous course and unpredictable places of drainage. We demonstrated that in patients with this condition, 3D models have an impact in decision making within professionals in the medical field and on how to proceed with patients' management, they assist to plan the procedure and to explain patients and relatives the anatomy of their heart (Fig 6).[9]

Patients with tetralogy of Fallot and other forms of right ventricular outflow tract abnormalities tend to need repeated surgical procedures in life to treat pulmonary stenosis at different levels or valvar regurgitation. The use of transcatheter pulmonary valve replacement has slowly gained popularity in this context. However, the density of trabeculations and irregularities, combined with dilatation of the right ventricle of these patients, often make it difficult to perform the percutaneous implantation of the valve, leading to prolonged procedure and radiation times. Several studies have aimed to plan the valve implantation using patient-specific models,[51] based on segmentations from MRI[52] and CT.[53] In these studies, 3D models helped the whole multidisciplinary team to visualise the intervention, try out different strategies, and design individualised solutions for a population with widely differing cardiac anatomies[53] and more accurate selection of patients for percutaneous pulmonary valve implantation than using MRI images alone,[52] as well as better planning of the procedure in the context of complications like right ventricular outflow tract aneurysms.[54]

Education and training

3D printing models have the potential to serve as unique educational tools for healthcare professionals. They have been used across a different range of medical personnel for training purposes.

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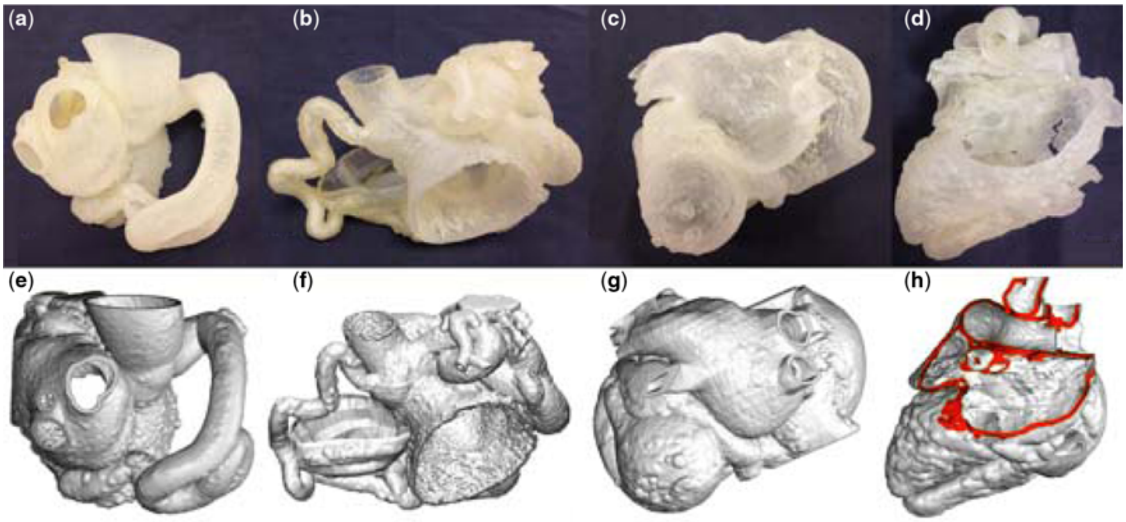

Figure 6. Adapted from Velasco et al. Patient-specific surface-rendered image (upper row) and respective 3D models (lower row) for the four patients included in the study.

Biglino et al discussed the utility of using 3D models to teach nurses through a wide spectrum of CHD.[55] In their study, 100 paediatric and adult cardiac nurses were offered the possibility of handling 3D models of a healthy heart, repaired transposition of the great arteries (arterial switch operation), aortic coarctation, tetralogy of Fallot, pulmonary atresia with intact ventricular septum, and the three stages of palliated hypoplastic left heart syndrome. They concluded that 3D models helped in the appreciation of anatomy; however, implementation of the models by using labels and colours to highlight the lesion of interest may help optimising the 3D models for teaching and training purposes.

Other studies have offered expert input with a more orientated pattern of teaching on topics such as tetralogy of Fallot.[56] Surgical trainees have also benefitted from 3D printing on rubberlike materials. In a study by Yoo et al,[57] 81 surgeons or trainees performed simulated surgical procedures during different hands-on courses. In a similar way, simulations are encouraged for interventional procedures.[58,59] Hands-on seminars have also been proposed as an educational tool using 3D models for paediatric registrars learning on ventricular septal defects.[60] Another study has shown the benefits of its use for vascular rings in this population of trainees.[61]

As illustrated by the above examples, the methodology of the teaching varies among studies. The lack of consistency makes the possibility of comparisons between outcomes between studies challenging. Although results on improvements in knowledge acquisition when comparing 3D models against images alone remain controversial,[55–57,60,61] there is a generally positive and enthusiastic feedback from participants with a higher score in satisfaction when 3D printing is involved.[56]

The limited amount of original pathological specimens available for teaching purposes and the increasing number of clinical applications of these models as well the current facility to share digital files make 3D models a desirable alternative to offer direct visualisation of the anatomy to students and medical personnel in training. The creation of a library has previously been suggested in this context. As part of the Junior Association for European Paediatric and Congenital Cardiology grant, an open-source library to share stereolithography files ready to print across all the Association for European Paediatric and Congenital Cardiology members has been created. Making 3D images available through online collections can provide hospitals and research centres with free access to a broad spectrum of heart conditions. A wide range of anatomical variants for different spectrums of CHD has been gathered with this purpose, including hypoplastic left heart syndrome and its surgical stages, double-outlet right ventricle, tetralogy of Fallot, and truncus arteriosus (Figs 7–9).[62]

Communication with patients and relatives

Although the main areas of research in rapid prototyping have been focused on pre-surgical planning and cardiac catheterisation, there is an increasing awareness of their importance in communication with patients. Biglino et al[63] demonstrated that parents find the model useful to understand their child's disease. It was described in their feedback as more user friendly than medical images. Their employment did not significantly increase the duration of the consultation. Interestingly, the blind assessment performed to assess parent's knowledge on the CHD did not improve significantly after the consultation regardless the use of the 3D model; however, their perceived understanding of the disease was rated as higher. A study aiming to assess their impact on patients with hypertrophic obstructive cardiomyopathy also showed high satisfaction rates.[64]

Evaluation of their impact in transition clinic has also been carried out.[65] This study involved 20 adolescents aged 14–18 years with tetralogy of Fallot, transposition of the great arteries, aortic coarctation, pulmonary atresia, aortic valve stenosis, double-outlet right ventricle, and Ebstein's anomaly. Teenagers reported to be impressed by seeing their own heart and the level of detail the models were constructed with. They described the models as interesting, useful, and helpful in understanding their disease, and 30% of the patients referred that the models made them more anxious. An increase in their awareness of the impact of the disease in their life style was also disclosed after the consultation.

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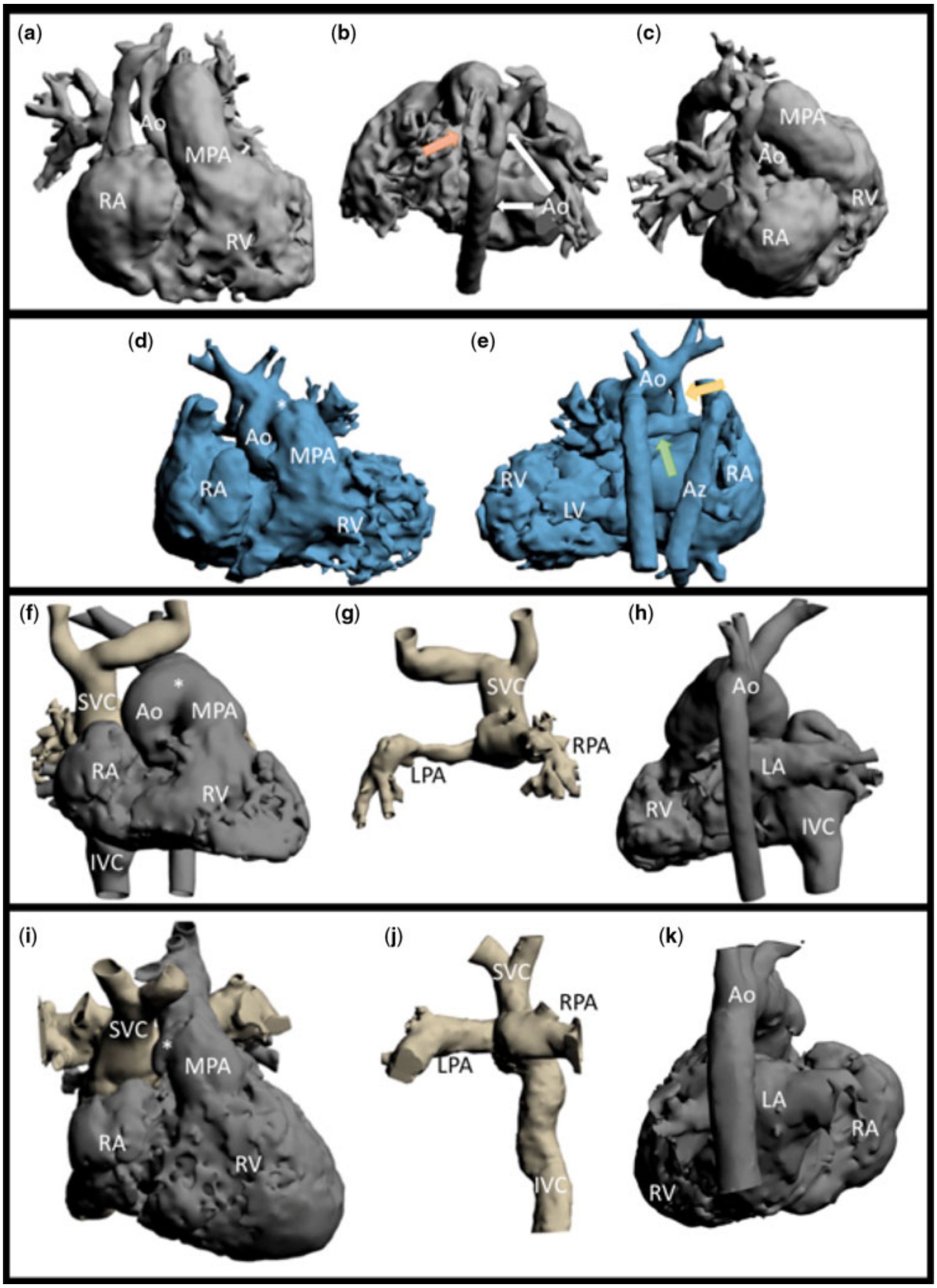

Figure 7. Hypoplastic left heart syndrome (HLHS), spectrum of post-operative anatomies. (*a, b, c*) HLHS s/p hybrid procedure view: anterior, posterior, and lateral view, respectively. Note patent ductus arteriosus (PDA) with stent in situ (pink arrow). (*d and e*) S/p Norwood stage I, anterior and posterior view, respectively. Note Blalock–Taussig (BT) shunt (orange arrow) connecting to pulmonary branches (green arrow). (*f, g, h*) S/p Glenn procedure. (*f*) Anterior view, showing full anatomy. (*g*) Posterior view of Glenn configuration (superior caval vein (SVC) connected to right pulmonary artery (RPA)). (*h*) Posterior view of cardiac anatomy when removing Glenn connection. (*i, j, k*) S/p Fontan completion. (*i*) Anterior view of the cardiac anatomy. (*j*) Posterior view of the Fontan connection (SVC and inferior caval vein (IVC) to RPA). (*k*) Posterior view of cardiac anatomy when removing Fontan connection.

Limitations and future directions

Patient-specific 3D-printed models have extensively proven to have a significant effect in clinical decision making and procedure planning in open-heart surgery or cardiac catheterisation, allowing for development of new techniques and approaches in patients with CHD.[33–35,37–39,41,47,9,10,16,20,48–52] Special efforts are currently being made in order to improve the materials that the models are built with in order to mimic the behaviour of the myocardium, the valve leaflets, and the great vessels' wall as much as possible. Differences in healthy and pathologic cardiac tissue are also to be taken into account. The segmentation process in rapid prototyping is based on their visual characteristics; therefore, advances in imaging methods such as 3D echo are necessary before a more detailed characterisation is achievable. This fact also brings on

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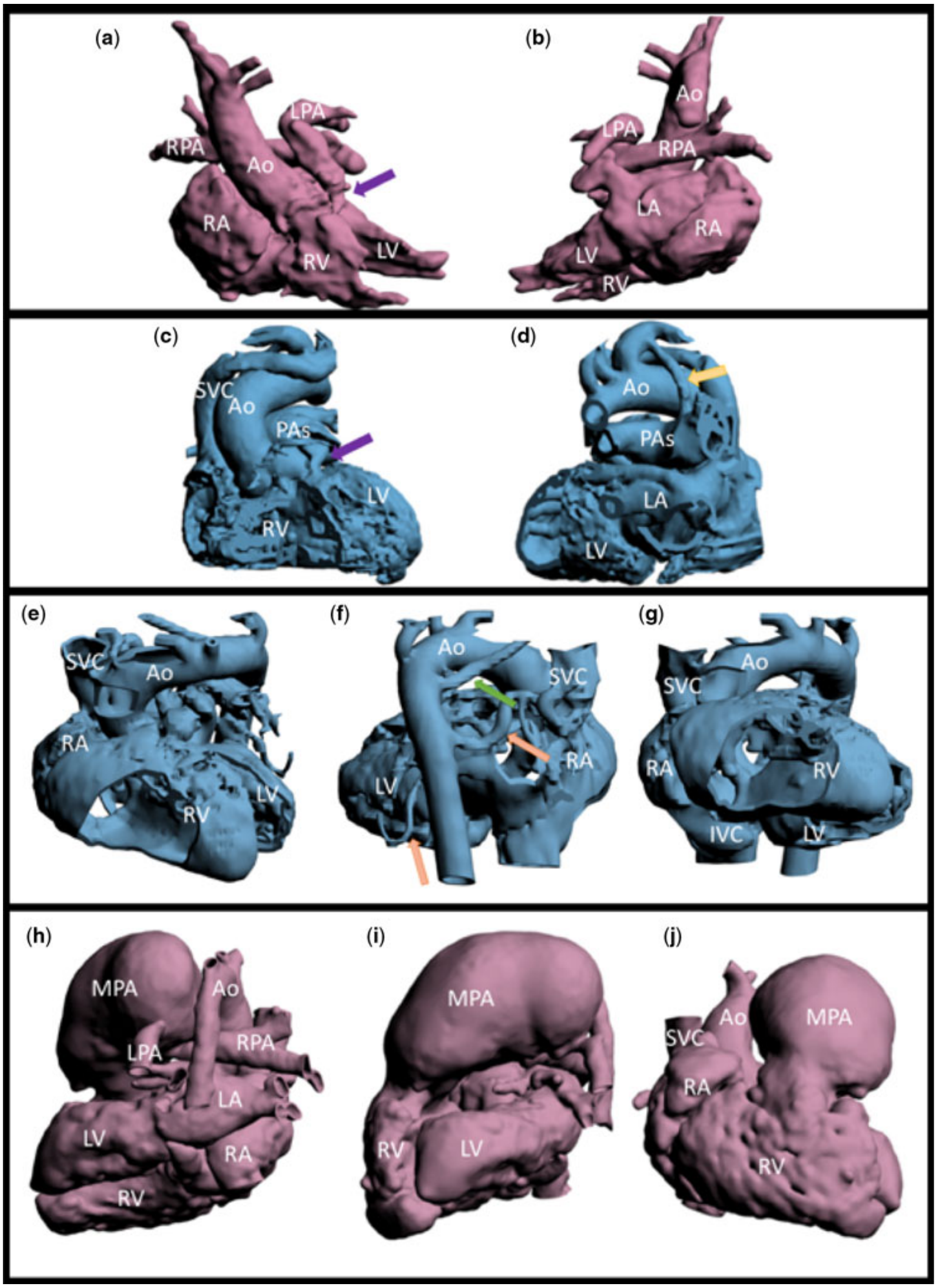

Figure 8. Tetralogy of Fallot (TOF). (*a* and *b*) Unrepaired TOF. Anterior and posterior view, respectively. Note severe RVOTO (right ventricular outflow tract obstruction, purple arrow). (*c* and *d*) TOF – absent pulmonary valve. Anterior and posterior view, respectively. Note dilatation of pulmonary branches and Blalock–Taussig (BT) shunt (yellow arrow) because of the severely narrow RVOT (purple arrow). (*e*, *g*, *f*) TOF – severe RVOTO. (*e*) Anterior view. (*f*) Posterior view. Note aberrant right subclavian artery (green arrow) and Major aortopulmonary collateral arteries (MAPCAs) (pink arrows). (*g*) Lateral view showing ventricular septal defect (VSD). (*h*, *i*, *j*) TOF – severe MPA dilatation post-repair with trans-annular patch. Posterior, lateral, and anterior view, respectively. Ao = aorta; IVC = inferior caval vein; LA = left atrium; LPA = left pulmonary artery; LV = left ventricle; MPA = main pulmonary artery; RA = right atrium; RPA = right pulmonary artery; RV = right ventricle; SVC = superior caval vein

board another limitation: the segmentation process is time consuming and requires familiarity with the software, the use of cross-sectional imaging, and a broad understanding on cardiac morphology. The manual editing of the segmentation process allows free creation and deletion of anatomical features, and consequently, expert's notion on the methodology is paramount to complete a reliable model.

The limited number of available pathological specimens makes 3D models an attractive option for teaching purposes. However, we believe that providing expert's input during the teaching session is essential, in the same way that imaging modalities in which MRI or echocardiography are explained during training. The involvement of the lecturer may improve the interaction of the students with the model and the understanding of the anatomy as reported in hands-on seminars.[56,57,60]

In future, automatic segmentation with minimal manual editing may reduce the amount of time invested in the process, therefore decreasing its costs and spreading its use across the world.

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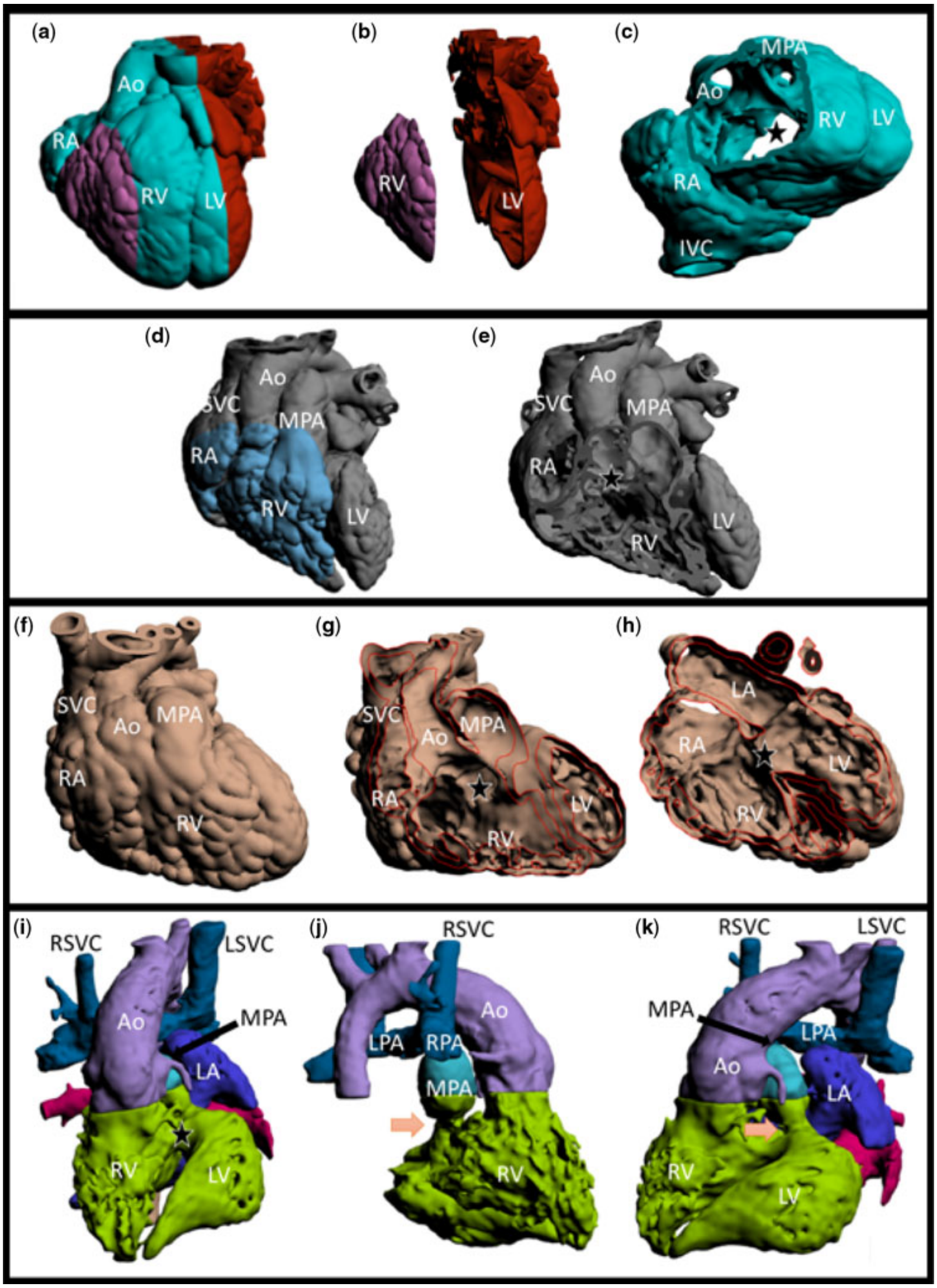

Figure 9. Double-outlet right ventricle (DORV). (*a*, *b*, *c*) Atrioventricular septal defect (AVSD) and DORV. (*a*) Whole-heart anatomy. (*b*) Cuts performed in both ventricles to show internal morphology. (*c*) Lateral view after removal of ventricular cuts. Note AVSD (star) and aorta and main pulmonary artery (MPA) arising from the right ventricle (RV). (*d* and *e*) DORV – perimembranous ventricular septal defect (VSD). (*d*) Anterior view of whole-heart anatomy. Note cut performed in 3D model to show the internal structures and its relationships. (*e*) Anterior view after removing previous cut structures, showing aorta and MPA arising from the RV and VSD (star). (*f*, *g*, *h*) DORV – non-committed VSD. (*f*) Whole-heart anatomy. (*g*) Model has been cut in a coronal fashion to allow visualisation of internal structures, note aorta and MPA arising from RV and non-committed VSD (star). (*h*) Axial cut of the model showing VSD (star) at the level of the atrioventricular valves. (*i*, *j*, *k*) DORV – severe subpulmonary stenosis s/p bilateral Glenn. Each cardiac structure has been segmented in a different colour (light blue: MPA, navy blue: LA, pink: RA, green: ventricles, purple: aorta, turquoise: pulmonary arteries post bilateral Glenn). (*i*) Anterior view showing all cardiac structures, note VSD (star) and MPA (black arrow) posterior to aorta. (*j*) Right lateral view showing relationship of the great vessels and the severe subpulmonary stenosis (orange arrow). Note LA and RA have been removed. (*k*) Left lateral view showing all cardiac structures. Note severe RVOTO (orange arrow). Ao = aorta; IVC = inferior caval vein; LA = left atrium; LPA = left pulmonary artery; LV = left ventricle; RA = right atrium; RPA = right pulmonary artery; SVC = superior caval vein.

Visualisation of the anatomy in 3D will become routine practice before cardiac surgery, allowing for better planning of the procedure and selection of candidates for novel, less invasive techniques.

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Author ORCIDs. Israel Valverde 0000-0001-5661-9900

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Conflicts of Interest. The authors declare no conflicts of interest.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the Health Research Authority (REC reference: 16/LO/1483).

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