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Review

3D printing in cardiology: A review of applications and roles for advanced cardiac imaging

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ABSTRACT

With the rate of cardiovascular diseases in the U.S increasing throughout the years, there is a need for developing more advanced treatment plans that can be tailored to specific patients and scenarios. The development of 3D printing is rapidly gaining acceptance into clinical cardiology.

In this review, key technologies used in 3D printing are briefly summarized, particularly, the use of artificial intelligence (AI), open-source tools like MeshLab and MeshMixer, and 3D printing techniques such as fused deposition molding (FDM) and polyjet are reviewed. The combination of 3D printing, multiple image integration, and augmented reality may greatly enhance data visualization during diagnosis, treatment planning, and surgical procedures for cardiology.

1. Introduction

Three-dimensional (3D) printing, also known as additive manufacturing, involves the creation of 3D objects from a geometrically defined digital models. In clinical medicine, 3D digital models are obtained from medical imaging data. The development of 3D heart models have opened up a new door for cardiovascular interventions leading to a better understanding of cardiovascular diseases and provides a unique way to visualize patient specific anatomy. The fundamentals of 3D printing is a two-step process, the first step involves conversion of imaging data to printable models. As shown in Fig. 1, the first step involves medical imaging data acquisition, image segmentation, and mesh generation. The second step highlights the availability of 3D printing technologies.

The use of interactive 3D visualization (i3DV) and multi-modality image integration in cardiology can revolutionize physician's ability to diagnose and manage complex anomalies of the heart.

2. Medical imaging techniques

The most commonly used imaging techniques for 3D printing in cardiology are computed tomography (CT) and magnetic resonance (CMR), making up approximately 90% of the imaging-based 3D printed models for the cardiovascular system [1]. Ultrasound is another useful imaging modality. Particularly, 3D transesophageal echocardiography (TEE) is widely accessible, cost-effective, and has no ionizing radiation.

2.1. Computed tomography (CT)

CT provides high levels of spatial resolution, image quality, and ease of image segmentation for the cardiovascular system. Effective in increasing the signal-to-noise ratio of images, CT allows for easy separation of the region of interest from surrounding structures and is particularly useful in post-operative imaging and anatomical analysis [2]. However, CT-based image segmentation becomes difficult with inadequate opacification or blooming artifacts caused by implants, limiting its use in certain patients [3]. While not currently recommended for routine usage in pre-procedural coronary artery evaluation for patient populations with a prevalence of artery calcifications and cardiac arrhythmia, CT may still be considered on a case-by-case basis as the technology evolves [4]. Cases in which CT scan is utilized can be tailored for the patient's age and investigated condition, considering the ionizing radiation dosage, arterial phase, voltage implemented, and the appropriate current intensity [2]. It is of special value in structural and congenital imaging.

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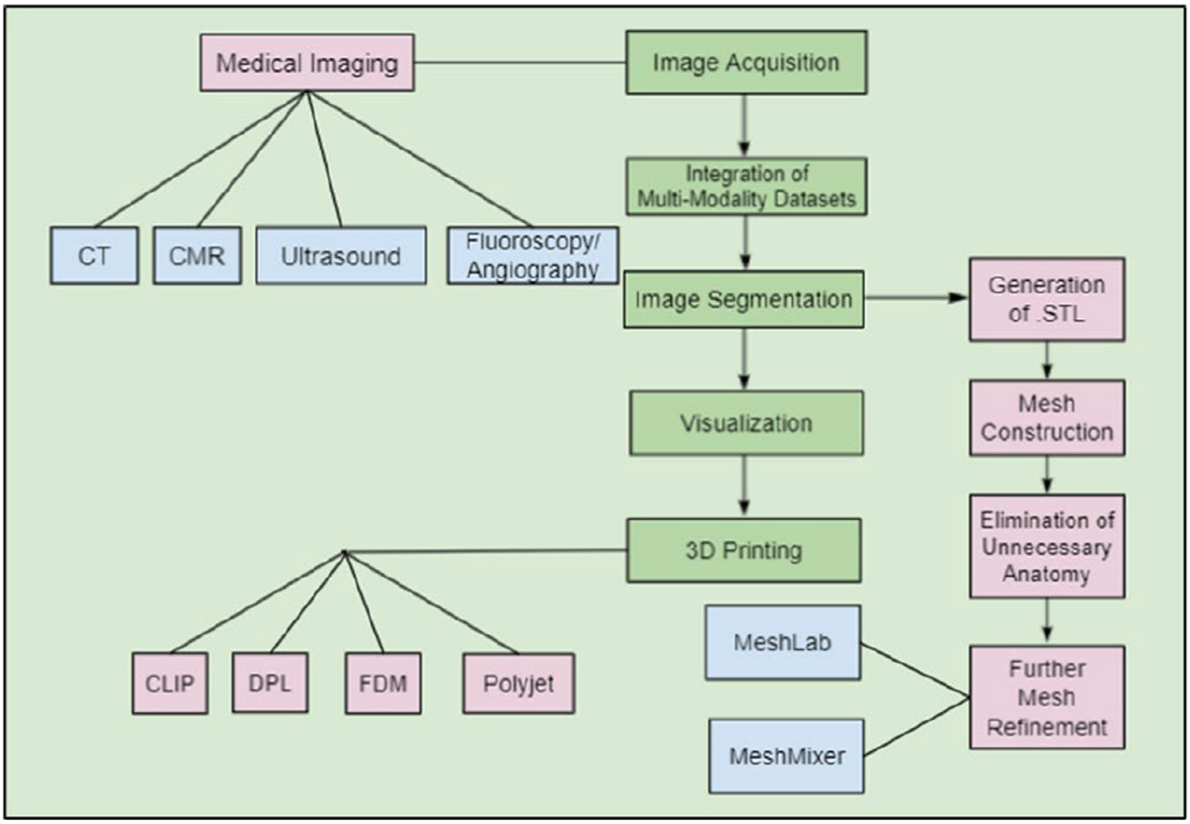

Fig. 1. Flowchart outlining the process of 3D printing in cardiology, from image acquisition to 3D printing. The chart also includes the software available for use.

2.2. Cardiac magnetic resonance (CMR) and magnetic resonance imaging (MRI)

CMR has considerable limitations in applications of 3D printing when compared with CT. Due to the prolonged acquisition time, need for patients to lay still, and frequent need for sedation of children for CMR scans, this approach has its drawbacks. MRI has a minimal slice thickness of 3 mm, falling short when it comes to providing the detail needed to recreate smaller vasculature. Instead, MRI tends to provide greater benefit for differentiation between the white and the gray matter of the brain due to its excellent soft-tissue contrast [5]. MRI also allows for a better opportunity for homogenous opacification if there are concerns about inadequate contrast opacification of anatomic regions of interest. Despite the above concerns, MRI is used more often for the reconstruction of larger cardiac masses and studying congenital heart defects and disorders [3]. MRI is often necessary for use in patients with most congenital defects including Tetralogy of Fallot, a birth defect due to incorrect formation of the heart during fetal development, to identify the timing of pulmonary regurgitation and revalvulation palliation [2].

2.3. Echocardiography

Echocardiography using ultrasound (US) is a non-invasive imaging modality for the physical examination of patients. This provides portable means to diagnose diseases through pattern recognition [6]. A combination of advances in 3D and 4D echocardiography has resulted in the creation of 3D printed models for fetal hearts and valvular and septal CHD. This imaging technique is cost-effective without requiring the use of anesthesia, contrast medium, or ionizing radiation, making this imaging modality safer for younger patients [7]. However, the use of ultrasound for 3D printing is limited due to spatial resolution, adequacy of acoustic imaging windows andartifacts, and 3D volume capacity restrict the utility of creating 3D models from this modality. Specifically, for cardiac applications, transesophageal echocardiography bypasses some of the above limitations but does require the use of anesthesia. Continued advances in 3D and 4D ultrasound hold promise in improving the management and planning in CHD, along with the outcomes of the patients overall [1].

3. Image segmentation

After gathering the necessary medical images, specific structures of interest from the heart are selected from a specific phase of the cardiac cycle that defines the structure of interest and segment it in order to be converted into digital models. This process follows the general steps of 1) segmentation to obtain a STL file, often using edge-based algorithms used to identify and isolate key features, 2) digital mesh construction, 3) processing for the elimination of unnecessary anatomy, and 4) surface conditioning and refinement for the final model generation [8]. More specifically, image segmentation involves the automated or semi-automated subdivision of images into regions sharing similar properties such as brightness, gray level, and texture [5]. Because basic segmentation techniques are reliant on the principle that different tissue types have their own specific range of properties such as these, it is possible to distinguish the different tissues and boundaries in a medical image to identify regions of interest, measure tissue volumes, and study anatomical structures. The contours from the regions of interest can then be identified from the medical images on several 2D image planes and converted into respective digital models comprised of 3D surface mesh-work [3].

Commercially available software packages such as Amira (ThermoFisher Scientific Inc., MA, USA) or Mimics (materialise Inc., Leuven, Belgium) can first load/import DICOM images and then perform intensity-based image segmentation. As shown in Fig. 2, because CT/

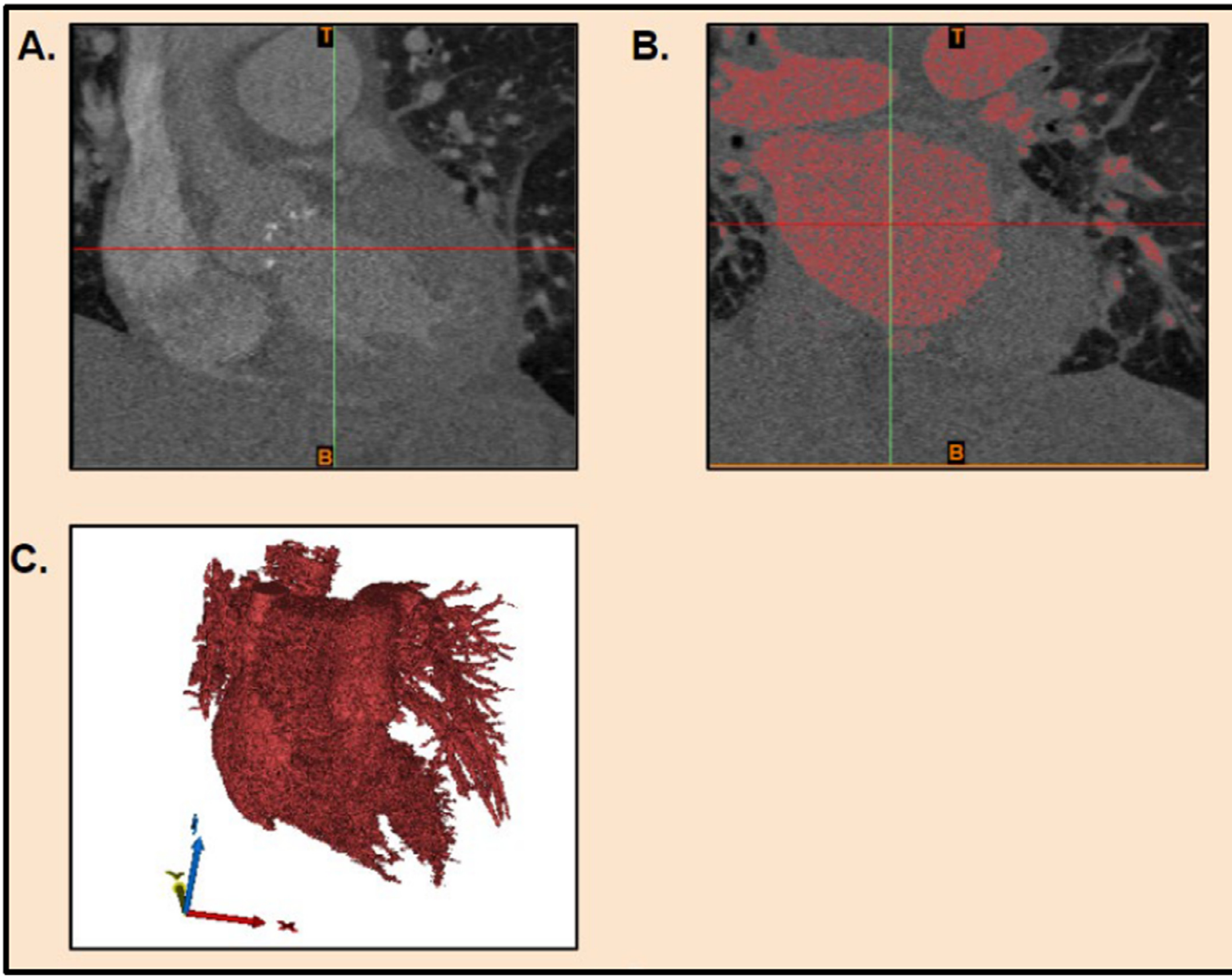

Fig. 2. Rough depiction of the process of image segmentation. A) Displays the original DICOM image of the cross-section of the heart, supplied by Mimics Materialize. Student Edition. B) Displays the mask made from a selection of target regions. C) Displays the calculated 3D geometry to be meshed.

MR/US images all contain considerable noise, intensity-based image segmentation (through a threshold or a window) often results in a noisy definition of the anatomy of interest (see Fig. 2c). As a result, manual editing uses a paintbrush to either remove unwanted objects or fill in voids from one image slice to the next. This process may be labor-intensive and can be a bottleneck for clinical adoption of the 3D printing technology.

This time-consuming image segmentation task could benefit from the automation that deep-learning artificial intelligence (AI) could bring, greatly decreasing the time to perform image segmentation. Consequently, automated image segmentation is appealing [3].

3.1. AI terminology

While AI is referring to the broader idea of machines with human intelligence applied to perform tasks, machine learning (ML) is one of the specific applications to solve actual problems through the formation of a family of pattern-elucidating algorithms [9]. As shown in Fig. 3, there are different categories of ML, supervised, unsupervised, and reinforcement types [10]. Supervised ML, a vital aspect in the formation of biological and artificial neural networks, involves models that are trained using data that has already been labeled by humans [10]. These models then make predictions on the new, input data based off the already-labeled data [9]. Approaches for supervised ML include regression and classification. Unsupervised ML makes inferences on structural relationships and their dependencies from input data without the human input that supervised ML uses [9]. The algorithms that are included in unsupervised ML are clustering and association. Reinforcement learning is a combination of the supervised and unsupervised learning techniques, maximizing the accuracy of algorithms through a series of trial and error, given only the input data and the outcome to be optimized [11].

Deep learning (DL) is an important branch of ML and has been applied in both supervised and unsupervised setting. Utilizing multiple layers of artificial neural networks, also called deep neural networks (DNN), DLs generate automated predictions from input data by mimicking the operation of the human brain [12]. The most commonly known applications of DL are Facebook's facial recognition algorithm and Google's image search abilities, with enhanced abilities in speech and visual object detection and drug invention [10]. DL also holds potential in cardiovascular imaging in terms of use with echocardiograms and MRI. A very powerful tool, DL works well with noisy data and can also facilitate real-time, artificial cardiovascular imaging with improved resolution and reduced costs [11].

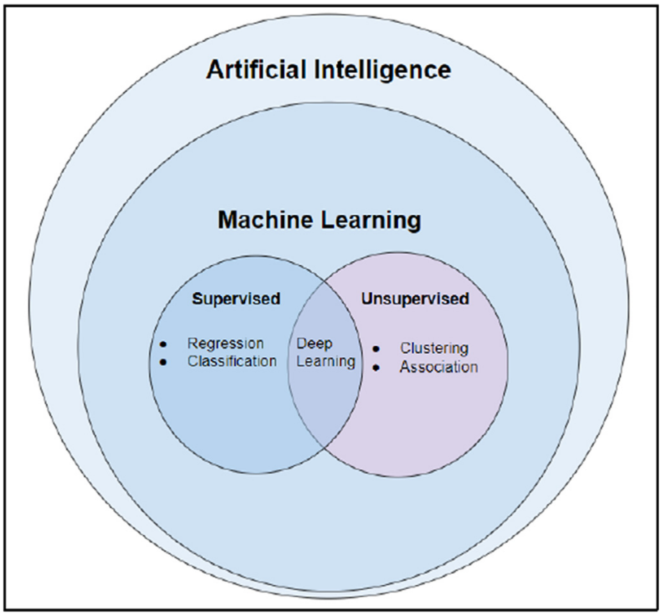

Fig. 3. Venn diagram of the different approaches falling under the category of artificial intelligence. The main AI approach shown is machine learning (ML), with subsequent supervised and unsupervised approaches.

3.2. AI-based image segmentation

Image segmentation involves the process of splitting images into regions and isolating the features of interest. In cardiology, AI is most often used in tandem with MRI and CT images for segmentation. The use of AI in image segmentation allows for a more efficient and optimized segmentation process, improving the effect of segmentation algorithms [13]. Deep learning is a widely adopted form of AI in processing medical images with many frameworks to choose from such as the Convolution Neural Network (CNN), Recurrent Neural Network (RNN), Stacked Auto-Encoder (SAE), and Deep Belief Nets (DBN) [14]. DL differs from traditional ML methods for image segmentation in that DL is capable of extracting high-level abstraction from training data. This is due to the multiple processing layers of complex structures that make up DL, resulting in higher accuracy-provided that there is enough data available during the training of the algorithm [14].

Neural network models mentioned above have been applied to image segmentation of tumors in various parts of the body with great success, showing a superior performance when compared to traditional methods such as region growing and level set [15]. Typically, neural network models include multiple layers and, loosely speaking, a training process allows neural network models to automatically learn features/representations from image data. Those learned features or knowledge representations can be combined to classify the original image data into two or more regions. utilizing the convolutional kernels' local connections and shared weights. These are followed by pooling operators, resulting in the translation of features. The fully connected layers are responsible for image classification, using high-level features from the image that are extracted from the previous, convolutional layers. These features are used as the input for learning the mapping between image features [15].

4. Mesh generation

Collectively, 3D masks obtained through the image segmentation process described above determine the anatomy and pathology. Then, high-quality triangulated surface meshes will be generated to define an enclosed volume. This process is known as mesh generation or tessellation. Triangular surface mesh generation is the industry standard because of its simplicity and flexibility.

It is important to note that medical imaging data contain noise (see Fig. 2). Thus, further processing or refinement of initial meshes is often needed. The availability of free software tools that can be used to refine initial meshes has greatly attributed to the rapid development of the 3D printing field. Those open-source tools provide a wide variety of cost-effective ways to help modify and clean up the created models for better model accuracy. Two well-known free software packages, namely MeshLab and MeshMixer, and their use in cardiology (see **Table 1**) are briefly introduced below for the sake of completeness.

4.1. MeshLab

MeshLab (www.meshlab.net) is known as a comprehensive software package that can be used for mesh editing, repair, inspection, and rendering, among several other attributes. There has been some success in using MeshLab in the 3D printing process within the cardiovascular field clinically. For instance, an experiment conducted by Muraru et al. explored the feasibility of using a combination of transthoracic 3D echocardiography (3DTTE) data and MeshLab to develop patient-specific models of the tricuspid valve. By importing coordinates representing different parts of the tricuspid valve of a patient into MeshLab, a solid model was obtained and converted into an STL file for 3D printing [16]. The experiment saw great success in creating an accurate 3D model of the patient-specific tricuspid valve, resulting in similar measurements between the echo-set data and the 3D printed model. This experiment showed much potential in the integration of the methodology into clinical practice [16].

Another example of successful MeshLab usage in cardiology lies in the study performed by Laing et al. in 2018. Lainge et al. constructed geometric models of a patient-specific heart using image segmentation of the gathered CT images. The resulting STL files of the geometries were imported and corrected, reducing the overall number of triangles in the mesh to reduce the model size and smoothing the model to remove artifacts [17]. This refined model was used as a phantom model and validated against the original CT scanned heart by comparing the molded point cloud data set to the original patient data set. The study found that the maximum Euclidean distance error between points was 7.7 mm, the average error was 0.98 mm, and the standard deviation was 0.91 mm [17]. The methodology used in this study pointed towards the accounting of surgical complications during preoperative planning and potentially shorter procedural times [17].

4.2. MeshMixer

MeshMixer (www.meshmixer.com) is similar to MeshLab in that it also works with triangular meshes, holding the advantage of not needing to worry about the 3D topology as you modify the model itself. Much like MeshLab, MeshMixer has also been used successfully in the field of cardiology. Its usage can be seen in optimization studies, such as one performed by Sommer et al., and pre-procedural planning, as studied by Izzo *et al.* Sommer et al. utilized MeshMixer in their creation of different flow models of six patient-specific coronary trees to investigate and optimize the design of accurate flow simulations. Their study displayed physiological relevant waves with blood pressure and flow rates that correlated with previously reported values from literature [18]. The pressure waves within the modeled trees were similar to those seen in the patients, demonstrating the ability of the 3D printed models from MeshMixer-refined coronary tree geometries to accurately reproduce patient-specific anatomy for testing and image-guided interventions [18].

Izzo et al. additionally used MeshMixer to refine the 3D model of a functional flow loop phantom within a patient's cardiac vasculature

Table 1.
Display of the specific studies assessed during discussion of open-source meshing tools and 3D printing techniques.

Title	Author/Publication Year	no. Patients	Patient Characteristics	Technology/ Technique	Results
3D Printed Cardiac Phantom for Procedural Planning of a Transcatheter Native Mitral Valve Replacement	Izzo et al., 2016	1	Age, gender, medical history, presence of severe mitral stenosis	Mesh: MeshMixer	Mitral valve stenosis and calcification clearly visible in model,cardiologists optimized surgical approach
Patient-specific cardiac phantom for clinical training and preprocedure surgical planning	Laige et al., 2018	n/a	n/a	Mesh: MeshLab	Euclidean distance error= 7.7 mm Average error = 0.98 mm Standard deviation=0.91 mm
Fused deposition modeling for the development of drug loaded cardiovascular prosthesis	Martin et al., 2021	n/a	n/a	3D Printing: FDM	Antimicrobial properties shown within graft past 30 days
3D printing of normal and pathologic tricuspid valves from transthoracic 3D echocardiography data sets	Muraru et al., 2017	5	TV morphology	Mesh: MeshLab	High correlation: $r = 0.96$ between model and patient data
Use of 3D Models in the Surgical Decision-Making Process in a Case of Double-Outlet Right Ventricle With Multiple Ventricular Septal Defects	Shear et al., 2019	1	Age, presence of double-outlet right ventricle + two ventricular septal defects	3D Printing:Polyjet	Soft myocardium model allowed assessment of VSD anatomy; Models benefitted surgical plan development
Design Optimization for Accurate Flow Simulations in 3D Printed Vascular Phantoms Derived from Computed Tomography Angiography	Sommer et al., 2017	3	n/a	Mesh: MeshMixer	Phantom showed physiologically relevant waves: oscillated 80-120 mmHg within literrature values Flow rate: ~125 ml/min
Three-dimensional printed models for surgical planning of complex congenital heart defects: an international multicentre study	Valverde et al., 2017	40	Presence of CHO	3D Printing:FDM	30 model mean bias of -0.27 ± 0.73 mm; 96% surgeons agreed 3D models bettered their understanding of CHD morphology; Surgical decision in 19 of the 40 cases changes; Improved surgical correction in 8 cases

for assistance in the surgical planning of a novel transcatheter mitral valve replacement (TMVR) procedure. After acquiring CT angiography (CTA) scans of a patient before they underwent the TMVR procedure, the 3D geometry of their cardiac chamber and the severely stenosed mitral valve was segmented. This geometry was later imported to MeshMixer, where the vascular surface was transformed into a functioning closed flow loop [19]. Cardiologists were then able to use the 3D printed phantom model to perform a mock surgery and optimize their approach to the novel procedure because the sizing of the valve to be replaced was readily apparent [19]. The methods discussed in the study showed great potential in the usage of 3D printing as a more informative approach towards procedural planning.

In short, those studies referenced above show how MeshLab and MeshMixer are both very useful tools that help to make the process of 3D printing both cost-effective and time-effective. Considering the importance of the meshing step in 3D printing and their overall success, the aforementioned studies further display the field of cardiology's potential for future advancement using freeware and 3D printing.

5. Currently available 3D printing technologies

3D printing technologies (fused deposition modeling [FDM] and polyjet) have been commonly used to print models in cardiology. Some selected applications are summarized in Table 1.

5.1. FDM

FDM is a widely used processes for 3D printing that typically involves the use of thermoplastic filaments. The filament is heated to the melting point and is extruded from the printer nozzle in layers to create the 3D model. FDM can output highly detailed models and prototypes, proving itself to be very useful in the field of cardiology. For example, Valverde et al's study on the impact of 3D printed models on surgical planning for complex CHD surgery utilized FDM with a polyurethane filament. When comparing the dimensions of the model with those from the medical images, it was found that the FDM models accurately represented the anatomy, with 96% of surgeons agreeing that the models provided a better understanding of the CHD and the 3D models changing the surgical decision in almost half of the 40 cases and refining the originally planned biventricular repair [20]. This resulted in an improved surgical correction for 8 cases [20].

FDM's cardiovascular usefulness can be applied to more than just the area of surgical planning, as seen in Martin et al's study. This study described how a vascular prosthesis was developed using FDM in order to investigate and overcome previous limitations and risks of cardiovascular prostheses such as infection and blood clots [21]. A combination of thermoplastic polyurethane (TPU) and rifampicin (RIF) were combined using hot-melt extrusion (HME) to create a material capable of extended RIF release and Staphylococcus aureus inhibition [21]. The results showed that even after 30 days of RIF release, the printed TPU model still displayed anti-microbial properties [21]. These results displayed the success and versatility of FDM in its ability to produce drug-loaded vascular grafts, with great potential in clinical applications in the future.

5.2. Polyjet

Polyjet is similar to FDM in that the 3D printed model is built up layer by layer. However, each layer of liquid polymer printed via polyjet is solidified and cured via ultraviolet (UV) light whereas each layer of semi-molten material printed via FDM cools and solidifies on its own. Polyjet can create truly smooth and accurate 3D models out of a huge array of materials for use as prototypes and parts, holding the capability to produce complex, multi-colored, and multi-material models with smoother and thinner walls. Because of the flexibility and complexity of the resulting models, polyjet is an ideal 3D printing approach for creating patient-specific cardiovascular models (Fig. 4) [22]. A study conducted by Shearn et al. illustrates the usefulness of polyjet in their creation of a white rigid model and multi-color model from the CT data of a 1-year-old child with double-outlet right

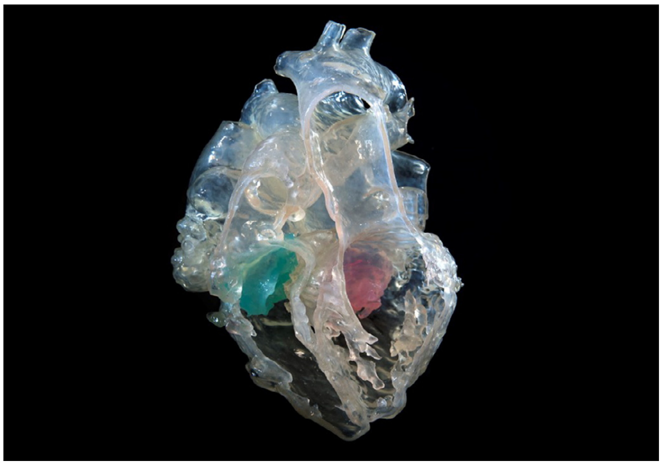

Fig. 4. Model of the heart and major arteries using a polyjet 3D printer.

ventricle and two ventricular septal defects (VFD) [23]. These models helped clinicians in their determination of the unlikely feasibility of an arterial switch procedure and their assessment of the anatomy and relationship between the VFD's anatomy and the aorta. These results ultimately showed how the polyjet models were of benefit in developing a plan for surgery [23].

While FDM and polyjet are both popular for 3D printing in cardiology, there are additional approaches such as digital light processing (DLP) and continuous liquid interface production (CLIP). DLP projects the cross-sectional image of the target object into a photosensitive liquid resin via the use of a projector. The optical semiconductor (DLP chip) that at the core of the DLP technology that makes up DLP printing is likely the most advanced optical switching device to date [24]. CLIP printing is similar to polyjet printing in that it also uses UV light to cure the resin used in printing the model. The UV light, in the case of CLIP printing, is located at the bottom of the printing bed, solidifying photosensitive resin while oxygen inhibition at the bottom of the bed maintains a liquid area [24]. Additionally, CLIP can be a continuous process, rather than the traditional layer-by-layer process. This is because of the sheer speed of the technology used in CLIP, which can go up to 1000 times faster than DLP, resulting in infinitely fine stratification [24]. Both these approaches are more advanced than FDM and polyjet and not used as often in applications with cardiology. However, with the advanced technology used DLP and CLIP, these approaches could potentially serve to improve the rate of the 3D model creation and subsequent development, further advancing the field of cardiology and cardiovascular treatments.

6. Discussion

6.1. Image integration from multiple imaging modalities

Because a single modality cannot satisfy the need of cardiology, multiple imaging modalities are routinely being used. The continuous x-ray imaging provided by fluoroscopy has its use in diagnosing and in interventional cardiology.. Along with its real-time imaging capabilities, fluoroscopy allows for patients to be imaged from different angles which can be coregistered with cardiac MRI or CT. repositioned during the exam, a characteristic not seen in CMR and CT, and exposed to lower doses of ionizing radiation. Despite the value of this imaging modality, fluoroscopy faces challenges in comparison to others in the areas of availability, economic factors that make fluoroscopy less desirable, and operator dependency [25].

Specifically, in the field of cardiology, the use of 3D multi-modal image integration can overcome limitations seen in 2D angiography for the visualization of vascular structures and increase the reliability of diagnoses. For instance, combining 3D images from modalities such as CT and CMR with live fluoroscopy has proven to be a solid roadmap for the guidance of CHD diagnostic and interventional procedures [26]. By implementing this multi-modal approach, several benefits, including the improved interventional efficacy, reduction in overall radiation exposure, and reduction in procedural time are seen [26]. Considering the potential complexity of congenital cardiac anatomy, multiple imaging modalities are often needed to get a complete image of patient-specific structures when developing a management plan for CHD. Developing a common platform for the integration of the individual imaging modalities together is necessary in order to take advantage of the different strengths highlighted by each approach [27].

6.2. Augmented reality, live image integration, and 3D printing

Augmented reality (AR) has great potential to enhance precision medicine and value-based care models at point-of-care health systems. We envision the combined services of 3D printing, multimodality live image integration, and AR will open new possibilities in clinical treatment and application. Clinical adoption of these emerging technologies requires work of an interdisciplinary team (engineering, computer science, and clinical medicine).

7. Conclusions

3D printing in cardiology plays an important role in the advancement of cardiovascular treatments. By developing 3D printed models of various materials and increasing complexity, a better understanding of the heart anatomy and its relationship with disease pathologies can be gained. This can be applied in educational settings to teach students more efficiently or in clinical settings for the development of optimized surgical procedures and transplants. The basic process of 3D printing in cardiology is the same as in other medical specialties. However, there are ways to optimize the process. This includes choosing the right imaging modality to gather the best resolution images for the target area of the heart, combining multiple imaging modalities to create a multimodal image acquisition approach, utilizing open-source tools to refine the meshed geometry obtained after image segmentation, and selecting the right 3D printing approach for the application. Additionally, further development of AI-based image segmentation has the potential to fundamentally transform current segmentation practices. By focusing on optimizing the individual steps to the 3D printing process, 3D printing in cardiology has the potential to advance further and faster than it has in the past decades, providing more breakthroughs in efficient, effective, and patient-specific treatment of cardiovascular diseases.

Conflict of interest

The authors have no relevant financial interests or conflicts to disclose.

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