Review Article

Three-dimensional (3D) printing and its applications for aortic diseases

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Abstract: Three-dimensional (3D) printing is a process which generates prototypes from virtual objects in computer-aided design (CAD) software. Since 3D printing enables the creation of customized objects, it is a rapidly expanding field in an age of personalized medicine. We discuss the use of 3D printing in surgical planning, training, and creation of devices for the treatment of aortic diseases. 3D printing can provide operators with a hands-on model to interact with complex anatomy, enable prototyping of devices for implantation based upon anatomy, or even provide pre-procedural simulation. Potential exists to expand upon current uses of 3D printing to create personalized implantable devices such as grafts. Future studies should aim to demonstrate the impact of 3D printing on outcomes to make this technology more accessible to patients with complex aortic diseases.

Keywords: Three-dimensional (3D) printing; segmentation; aortic diseases

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Introduction

Three-dimensional (3D) printing is a rapidly expanding field in medicine. Originally developed in the 1980s, the technology has largely been used in the manufacturing industry until more recently as clinicians and researchers have been applying 3D printing to the medical field (1,2). One of the advantages of 3D printing is the use of additive manufacturing, where consecutive layering of two-dimensional (2D) slices are combined together to form a 3D object (3). This allows for translation of intricate, complex designs using a variety of materials including plastic, metal, wax, rubber, and biomaterial (3,4). It also allows models to be custom made at a relatively low cost without the need for expensive molds or casts (3). The models are derived from 3D reconstructed images, printed, and can be used for surgical planning, such as an endovascular abdominal aortic aneurysm repair (*Figure 1*). There are variety of current and developing uses for the treatment of vascular disease including the creation of models for surgical planning (5-7), education and training (8,9), and vascular device and tissue engineering (10,11).

Principles of 3D printing

3D printing enables rapid prototyping from various imaging modalities (12). The technology has much promise in an age of personalized medicine for treatment planning, particularly in vascular diseases where anatomy can be especially complex (13). The basic procedure for medical 3D printing consists of two steps: (I) reconstructing the medical image into a virtual object on CAD software, and (II) processing and printing the model or device. After these steps, the printed model is ready for surgical use or planning.

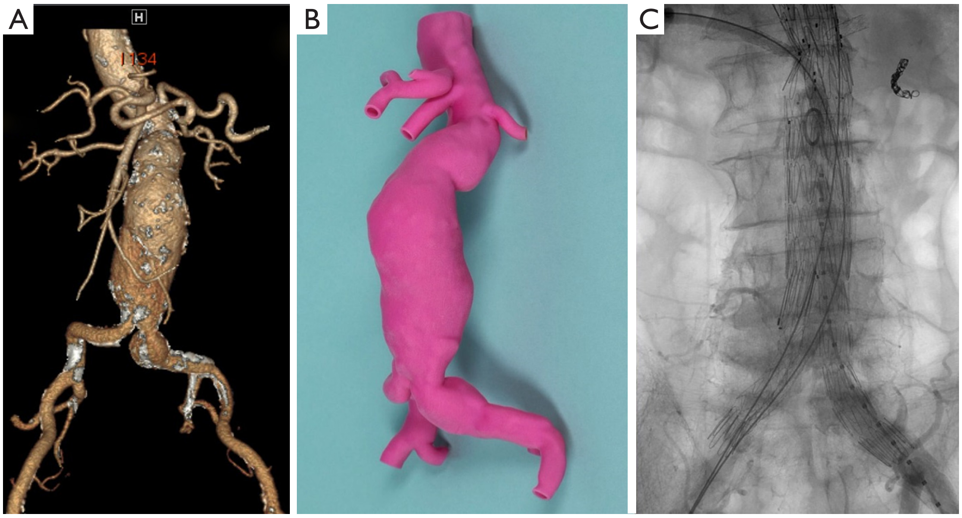

Figure 1 Patient with abdominal aortic aneurysm. (A) 3D reconstructed computed tomography image of large abdominal aortic aneurysm; (B) 3D printed model; (C) post-procedural fluoroscopy after endovascular aneurysm repair.

Pre-processing medical images with CAD software

While commercial and manufacturing industries have widely adopted 3D printing since its invention, integration of 3D printing in medicine has been challenging. This lag has arisen because in manufacturing, design involves planning models and conceiving them on a screen with CAD software; conversely, in medicine, most 3D printing involves reverse engineering—creating objects which already exist physically in the patient (14). Therefore, converting data in the form of a stack of computed tomography (CT) or magnetic resonance imaging (MRI) slices into an STereoLithography (STL) file format readable by a CAD software requires pre-processing (15).

Pre-processing, usually performed by a visualization software, extracts anatomical information from the combination of image slices (14). Moreover, by segmenting, or creating thresholds in the image based upon density, users can create volumes of interest and selectively reconstruct specific anatomical structures or display them in different colors when printed (16).

Segmentation in these programs often involves manually shading 2D anatomical features slice-by-slice to identify the correct volume of interest through which the CAD software "interpolates" the region (13). For instance, as a blood vessel shifts in location on a 2D slice, users shade the area known to encompass the relevant structure. Attempts at semi-automated or completely automated segmentation have been made, but not enough progress has been shown for implementation (17).

Segmentation often creates 3D models that are not topologically sound for printing; several tools exist to correct for these structural issues, while maintaining the accuracy of the model (18). First, by finding connections between continuous voxels, topological corrections can connect disconnected, topologically non-viable parts to enable printing (19). Moreover, local least squares and Laplacian smoothing techniques increase feasibility of printing by removing unnecessary details to reduce printing time and model contiguous anatomical features (20,21).

After the 3D model has been created in CAD software, a 3D model file, or STL file, is generated and uploaded to the appropriate printer type (13,14).

3D printing medical models and devices

Once CAD software has a virtual object for printing, the user must select the type of 3D printing most appropriate for use. This consideration depends on the purpose of the device or model, therefore several key factors, including technique, cost, resolution, and materials, often determine which type of 3D printing method is used (2,3,22). The main types of 3D printing are (I) stereolithography (SLA); (II) selective laser sintering (SLS); (III) inkjet; (IV) fused deposition modeling (FDM); (V) sheet lamination (SL); and (VI) tissue engineering methods (12).

SLA

SLA is the most ubiquitous and common type of 3D printing, as it was the first type of additive manufacturing for 3D printing (3). An SLA apparatus creates 3D objects by polymerizing a bath, or "vat" of photosensitive polymer resin or hydrogels on a modeling platform with a laser (13). The resin crosslinks and forms bonds when exposed to specific wavelengths of light, often in the UV range, delivered by the laser, which causes the liquid to harden layer-by-layer (i.e., additively) (3,12). While the use of photosensitive material allows for high resolution and relatively quick printing, the materials must have this photosensitivity. Thus, the materials used in SLA are more limited than other techniques (23). Although the cost is decreasing, the occasional need for thermal processing of the photosensitive material has often been cited as a barrier for low-cost printing (12,22). Nonetheless, SLA has become widely accepted as the easiest method for printing surgical models quickly and accurately.

SLS

SLS is an alternative to the traditional SLA techniques, as SLS does not use photosensitive layers of liquid resin, but instead relies upon powder which solidifies into layers upon irradiation with a CO_2 laser (3,13). Repeated layers of hardened powder eventually construct the object over time (24). However, since SLS uses powder to construct the object, the final product is porous and requires sand-blasting for processing (12). While the printed device or model will have high accuracy and resolution, this porosity is often not desirable, and the equipment for the printing and subsequent sand-blasting is also expensive and time-consuming (3,13). However, the number of materials available for rapid prototyping through SLS makes it attractive in specific circumstances.

Inkjet

While SLA and SLS use photosensitive materials, either in the liquid or solid form, inkjet techniques use methods similar to 2D desktop inkjet printers (3,13). Since they use the same mechanisms as desktop inkjet printers, the first 3D inkjet printers were simply commercial printers "modified" to print in 3D (12). Like SLS, inkjet printing uses powder, but rather than using laser irradiation, this modality congeals the powder with drops of binding solution, often deposited using piezoelectric phenomena (3). While the user can easily manipulate the cartridges for the binding solution and powder type, and the price of materials is cheaper than previously described methods, inkjet printing compromises accuracy and resolution. It also requires both powder and a binding solution to create layers.

FDM

FDM, as its name suggests, does not use irradiation or binding solution to create solid objects; instead, the printing process involves a nozzle extruding, or "depositing" a semi-solid filament onto the printer's base, which then solidifies with application of heat (3,25). The nozzle has few restrictions on its range of movement, which allows FDM to create the same shapes as other non-deposited 3D printing methods (25). By depositing the material rather than solidifying material (e.g., resin) in a base or tray, FDM minimizes waste material and thereby reduces cost. However, only certain materials are able to be deposited, and a major limitation inherent in the deposition technique is accuracy (3,25).

SL

SL takes a completely different approach than the aforementioned techniques and instead bonds sheets of material together to form objects from synthetic polymers or paper (13). SL takes a hybrid approach between subtractive and additive manufacturing to increase building speed. Sheets are added together in layers, but then are cut and pasted to make the object. Since the sheets are held together in manufacturing, no supports are necessary, unlike in SLA and SLS techniques. However, removing the sheets that have been cut off, or "subtracted", can be difficult, especially for hollow structures. This tedious process makes SL methods non-ideal for surgical models.

Surgical planning

The evolution of radiographic imaging has allowed surgeons to better prepare and plan surgical approaches. As cross-sectional imaging has rapidly advanced in the last decade, high-resolution 3D images can routinely be obtained which help visualize complex vascular anatomy. However, even with this improvement in technology, the 3D image is still limited to viewing on a 2D screen. With 3D modeling the individual complexities of a patient's anatomy can be seen and felt at every angle (3).

Models can be made of any area of interest to aid in surgical planning. In particular, cases involving complex abdominal aortic anatomies have demonstrated the utility of 3D printing. The use of 3D modeling was used to successfully plan stent-grafting for an aortic aneurysm with sharp neck angulation (5). In another study of endovascular abdominal aortic aneurysm repairs, 1 in 5 fenestrated endografts were modified after testing their suitability in an aortic model, potentially decreasing adverse events associated with misaligned fenestrations of aortic branches (6). 3D modeling has also shown useful in planning aortic arch interventions, such as stenting of aortic arch hyperplasia (26). One case-study discussed perioperative planning for repair of a calcified, aneurysm extending from the ascending to the descending aorta. The 3D model allowed the team to discuss various therapeutic options and anticipate any pitfalls for a complex, high-risk procedure (27). However, no large scale clinical trials exist evaluating the use of 3D modeling on patient outcomes.

In addition to great vessel pathology, 3D printing has also been used in the treatment of other visceral vessel diseases. 3D modeling was used to plan the optimal combination of guide catheter and microcatheter to successfully treat a patient with multiple splenic artery aneurysms. The team was able to preserve splenic function and minimize the need for repeat angiograms (28). 3D printing has also been described as an intraoperative reference for robotic resection of a celiac trunk aneurysm (29). Modeling other visceral vessel aneurysms has been described, including left gastric, right epigastric, gastroduodenal and posterior superior pancreaticoduodenal aneurysms (30).

Training and education

The use of 3D modeling for vascular simulations can provide training and education in either normal or complex anatomy. In one study, general surgery residents who prepared for endovascular abdominal aneurysm repairs (EVAR) using both 3D CT images and a 3D model performed better on a perioperative case-scenario questionnaire than residents who used only 3D CT images and no model (31). Models also provide an ideal format for training. It eliminates risk to patients, allows trainees to engage with the procedure on their own time, and also allows for practice on rare pathologies that experienced surgeons may only encounter a limited number of times in their careers (32). It can also provide the haptic feedback which may be lacking in virtual reality simulations and has been shown to improve anatomical knowledge in students (13,33). In addition to provider education, 3D models have been demonstrated as a useful tool for preoperative patient education (9,34,35).

Engineering of personalized aortic devices

3D printing has also enabled providers to create patient specific devices and tissues as a treatment strategy. One prominent example, the personalized external aortic root support (PEARS), is an alternative to aortic root replacement in where a replica of the patient's aorta is created. The 3D model is then used as template onto which a medical-grade polymer mesh fabric is fitted which follows the exact aortic contours. This device makes an ideal external support for the expanding aortic aneurysms of Marfan's disease (10,36). The precision of the mesh allows it to be fully incorporated while maintaining aortic valve competence (37,38). Treasure *et al.* reported early outcomes with PEARS were better than published results for standard of care aortic root replacement operations with no deaths, cerebrovascular, aortic or valve-related events 1.4–8.8 years following the procedure in 30 patients (39). Expanded use of this device is ongoing (37).

Vascular tissue bioprinting

Current research efforts are directed towards developing functioning 3D printed vascular tissue. In general, vascular tissue has been constructed either using scaffold-based or scaffold-free methods (40). Scaffold-based bioprinting incorporates cells into hydrogel or decellularized matrices, while scaffold-free methods exploit functions such as cell sorting and tissue fusion (41). Some success has been reported with scaffold-based vascular structures (42), however, their clinical utility has been limited by chronic inflammation, thrombosis, rejection, and degradation (11,43). Using scaffold-free techniques, Itoh *et al.* described tubular structures developed from multicellular spheroids. The grafts underwent remodeling and endothelialization after implantation into the abdominal aorta of rats (44). Using 3D bioprinted mouse embryonic fibroblast Kucukgul *et al.* (45) developed a self-supported, biomimetic human aorta. Further research is needed to develop the vascular tissue bioprinting for clinical use. Fully functioning vascular networks have proven to be difficult in 3D printing engineering and is a major milestone in the development of 3D printed organs (46).

Future considerations

As the technology continues to develop, 3D printing holds the potential to revolutionize the future of medicine. Its current clinical applications can be expanded through streamlining the 3D printing process, reducing costs, and increasing access. Although 3D printing is relatively inexpensive compared to equivalent manufacturing methods, it largely remains confined to university-scale hospital systems that can afford the hardware, software, and recurring material costs required (47). Lower costs may follow increasing demand, making 3D printing resources more readily available in smaller communities. In addition, further research is needed to establish the cost-effectiveness of using 3D models as part of a treatment plan. Currently, no large randomized clinical trials exist to evaluate the effect of 3D printing on patient outcomes. This data will be especially important to meet federal and state regulations and when seeking reimbursement from insurers (48). The United States Food and Drug Administration (FDA), the agency which oversees medical devices, published draft guidance in 2016 on the Technical Considerations for Additive Manufactured Devices, which can be found on their website: http://www.fda.gov.

One largely anticipated future development is the bioprinting of complex organs to be used for transplantation and research. Despite much promising progress already made, more advancement is necessary, in particular due to the challenges of printing vascular networks (2). As bioprinting continues to develop, there is potential to use personalized biomaterial to treat a variety of aortic diseases, such as aneurysms, coarctation, and connective tissue disorders. *In vitro* organ models also have the potential to be used for pharmaceutical research and drug discovery (49,50). Researchers also envision devices which can print biomimetic structures on demand to be used to repair damaged structures (51).

Conclusions

3D printing has become a useful tool to many clinicians and researchers. A variety of applications currently employ 3D printing for the treatment of aortic vascular disease, including pre-procedural planning, training, and creation of personalized aortic grafts. Advances in the accessibility of 3D printing, as well as continued research in 3D-printed vascular networks, has the potential to revolutionize the treatment of aortic diseases.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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