Review

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Artificial vascular models for endovascular training (3D printing)

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Abstract: The endovascular technique has led to a revolution in the care of patients with vascular disease; however, acquiring and maintaining proficiency over a broad spectrum of procedures is challenging. Three-dimensional (3D) printing technology allows the production of models that can be used for endovascular training. This article aims to explain the process and technologies available to produce vascular models for endovascular training, using 3D printing technology. The data are based on the group experience and a review of the literature. Different 3D printing methods are compared, describing their advantages, disadvantages and potential roles in surgical training. The process of 3D printing a vascular model based on an imaging examination consists of the following steps: image acquisition, image post-processing, 3D printing and printed model post-processing. The entire process can take a week. Prospective studies have shown that 3D printing can improve surgical planning, especially in complex endovascular procedures, and allows the production of efficient simulators for endovascular training, improving residents' surgical performance and self-confidence.

Keywords: 3D printing; endovascular; patient-specific; simulations; training.

Abbreviations: 3D printing, three-dimensional printing; angioCT scan, computed angio-tomography scan; CT, computed tomography; DICOM, Digital Imaging and Communication in Medicine; MRI, magnetic resonance imaging; STL, stereolithography.

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Introduction

The endovascular technique has led to a revolution in the care of patients with vascular disease; however, acquiring and maintaining proficiency over a broad spectrum of procedures is challenging for experienced surgeons and surgeons under training [1, 2], as the rapid innovation process of the endovascular material demands frequent update and technical training [3]. Although the importance of training based on simulations is well documented in several studies [4–10], the use of simulators is still limited [3], and the cost of the simulator is probably the main reason [10–12]. Therefore, affordable simulators are the key to make simulations a routine [11].

Three-dimensional (3D) printing, also known as additive manufacturing or rapid prototyping, is a growing technology that is changing the manufacturing industry [13]. The process consists of creating 3D objects through deposition of successive layers of different materials, based on a computer file. 3D printing offers many advantages over traditional manufacturing, including the ability to create objects with complex internal structures, improved versatility, and customisation and lower space requirements [12]. The cost of 3D printers has recently decreased, and the availability of 3D printing services has increased. Itagaki [13] showed the feasibility of producing a 3D-printed splenic aneurysm using Internet-based services (www.shapeways.com, www.imaterialise.com) at a low cost.

The combination of 3D printing and imaging examinations offers a great opportunity for the progress of medical science [14–16], as it allows the visualisation of diseases with complex anatomy [12] and the creation of models in different materials, which can be used for surgical planning and training [7, 17, 18]. Furthermore, 3D printing allows a patient-specific simulation, which is more efficient than generic simulation [8, 19].

Methods

We performed electronic searches in PubMed to collect studies on 3D printing technology and its applications in endovascular training. Several searches were performed using the combination of different terms: 3D printing and/or endovascular training and/or surgical planning. The only limit defined was language: only reports in Portuguese or English were considered. Titles and abstracts were screened to exclude irrelevant or duplicate abstracts. Then, the included articles underwent a full-text review. We initially found 409 results, which were narrowed down to 190 after the analysis of abstracts (duplicated articles and researches deemed irrelevant to surgical practice were excluded). This set of results was then reviewed to form a set of 58 full-text articles used for the final analysis. In addition, the websites of the 3D printers were searched for technical information.

Process to create 3D-printed vascular models for endovascular training

The process to produce 3D-printed vascular models based on image examinations consists of four steps: image acquisition, image post-processing, 3D printing and printed object post-processing (Figure 1). Depending on the size and complexity of the vascular model, it can take up to 48 h just to 3D print it. It is reasonable to expect 1 week for the completion of the entire process.

Image acquisition

Data for generating medical 3D-printed models are typically acquired with computed angio-tomography scan (angioCT) or magnetic resonance imaging (MRI) [12, 15]. For vascular models, image post-processing is less complex for angioCT scan data [15]. An ideal computed tomography (CT) acquisition should be free of image artefacts and have isotropic voxel resolution, high image contrast between the anatomy of interest and neighbouring tissues, and low noise. A slice thickness of 0.5–1.5 mm is adequate. Acquired data are saved in Digital Image and Communication in Medicine (DICOM) format.

Image post-processing

Image post-processing can be performed using several different software programs, as shown in Table 1.

For DICOM post-processing, the authors’ choices were iNtuition Unlimited software (Aquarius, TeraRecon, San Mateo, CA, USA), OsiriX software (Pixmeo, Geneva, Switzerland), or Horos software (The Horos Project, sponsored by Nimble Co LLC d/b/a Purview, Annapolis,

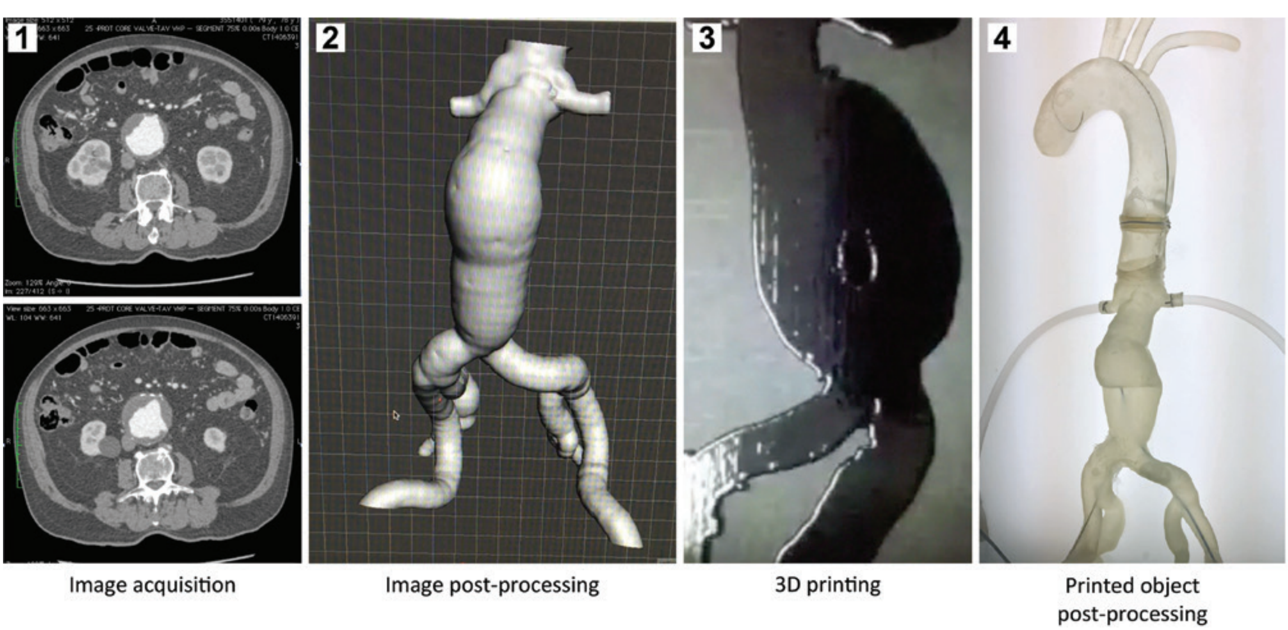

Figure 1: Steps to produce a 3D-printed aneurysm.
1, Images from an angioCT; 2, abdominal aorta after image post-processing; 3, 3D printing process; 4, post-processed 3D-printed aneurysm.

Table 1: Software programs available for image post-processing.

Software programs for DICOM file processing	References
Mimics® (Materialise NV, Leuven, Belgium)	Biglino et al. [20], Wilasrusmee et al. [21], Håkansson et al. [22], Yuan et al. [23], Mafeld et al. [18], Dong et al. [24], Koleilat et al. [25], Taher et al. [26]
OsiriX (Pixmeo SARL, Bernex, Switzerland)	Marro et al. [12], Tam et al. [27], Takao et al. [28]
Vitrea 3D Station (Vital Images, Inc., Minnetonka, MN, USA)	O'Hara et al. [29], Russ et al. [30]
iNtuition software (TeraRecon Inc., Foster City, CA, USA)	Koleilat et al. [25]
Vascular Modeling Toolkit (VMTK, Orobix, Bergamo, Italy)	Meess et al. [31]
Software programs for STL file processing	
3-matic® (Materialise NV, Leuven, Belgium)	Biglino et al. [20], Mafeld et al. [18], Koleilat et al. [25]
MeshLab (Visual Computing Lab – ISTI-CNR, Rome, Italy)	Marro et al. [12]
Blender (Blender Foundation, Amsterdam, the Netherlands)	Itagaki [13]
Google SketchUp (Trimble Inc., CA, USA)	Govsa et al. [32]
Magics (Materialise NV, Leuven, Belgium)	Yuan et al. [23]
Meshmixer software (Autodesk, San Rafael, CA, USA)	O'Hara et al. [29], Takao et al. [28], Russ et al. [30], Meess et al. [31]

MD, USA). The first step was to generate a reconstruction of the region of interest based on the contrast inside the arterial lumen. After that, the vascular reconstruction was extracted from the surrounding tissue (manually or using specific tools, such as extracting the central line in TeraRecon) and exported as a stereolithography (STL) file. Thereafter, we chose Mesh Mixer (Mesh Mixer 2.8; Autodesk Inc., San Rafael, CA, USA) or Magics Software (Magics, 3-matic®; Materialise NV, Leuven, Belgium) for STL processing. These programs allow the user to smooth the surface of the vascular structure and to correct errors in the mesh. A wall thickness was digitally produced, and the space occupied by the lumen was subtracted to create the primary hollow models, as shown in Figure 2.

3D printing

Recent advances in 3D printing technology have led to the development of new resources, making the use of a wide variety of materials from plastic to metals possible. It is possible to directly 3D print hollow flexible models, which is a one-step process; therefore, it is faster and more accurate than the commonly used lost wax technique [27]. The choice of the 3D printer depends on the application. Figure 3 shows some 3D printers available. Some of the following characteristics should be considered: cost, accuracy, speed and materials available [12].

Industrial machines, such as Connex from Stratasys [33], are versatile (have a great number of printing materials available and allow the combination of different

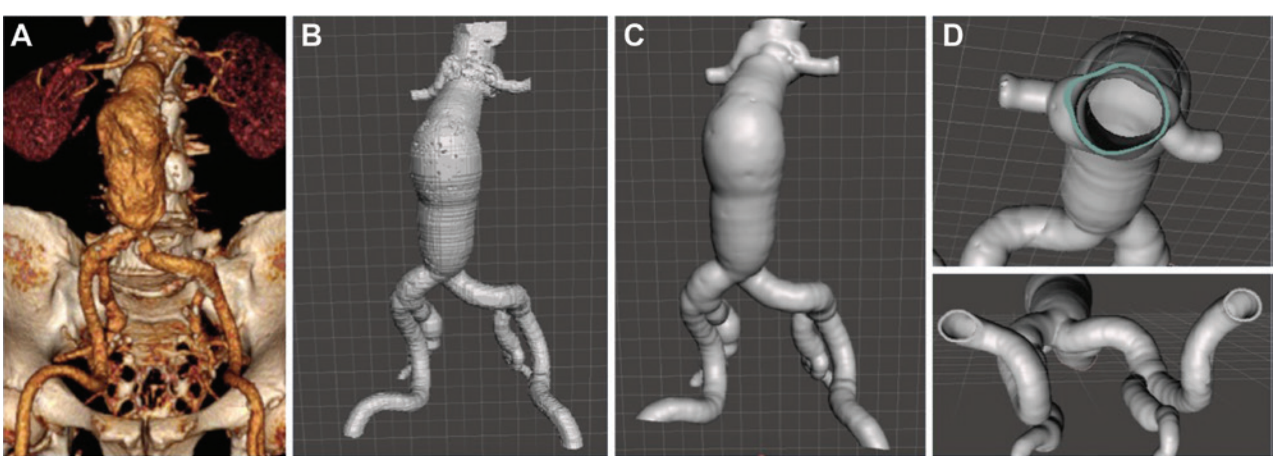

Figure 2: Image post-processing.
(A) Reconstruction of the aorta based on the contrast inside the arterial lumen – DICOM file. (B) Aorta after conversion of DICOM to STL file. (C) Surface of the aorta smoothed. (D) Wall of the aorta digitally thickened to 1.5 mm.

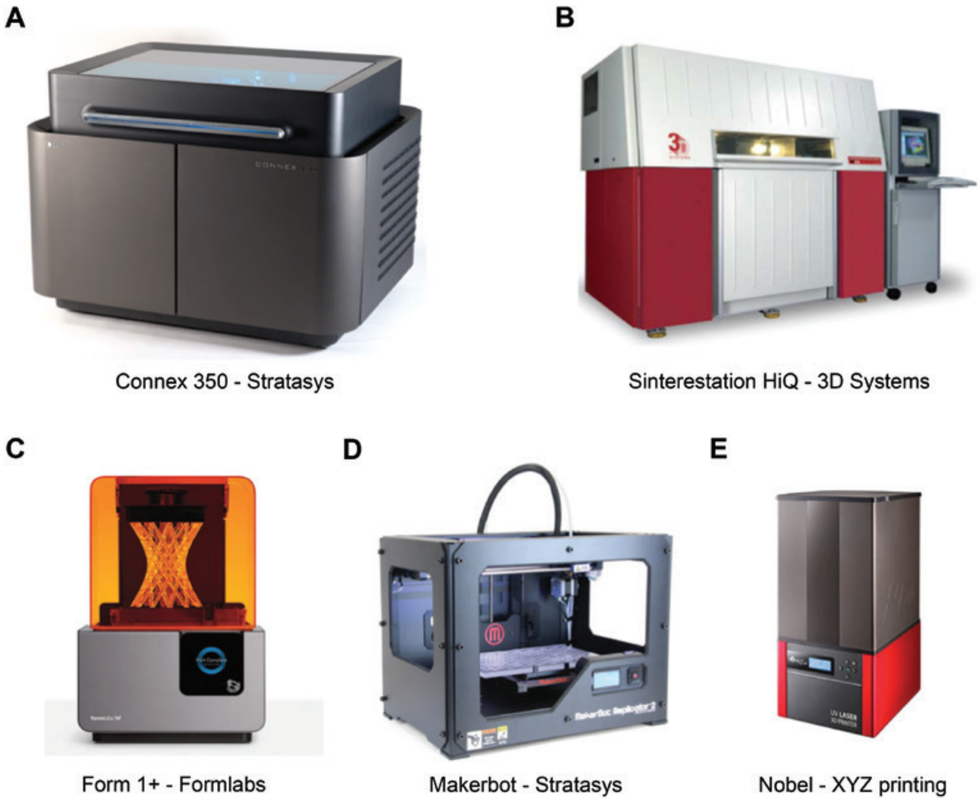

Figure 3: Examples of 3D printers available for the production of vascular models.
A and B are industrial machines. C, D and E are desktop machines. The pictures were collected from the websites (www.stratsys.com, www.3dsystems.com, www.formlabs.com and www.xyzprinting.com). The companies agreed to the use of the pictures.

materials in the same object), accurate (has a layer resolution of 16 μm) and have a big printing platform (up to 490 × 390 × 200 mm). Nevertheless, the cost of the 3D printer and the resins is high (one 3D printer costs around US$270,000.00, and the cost to 3D print an aneurysm is US$1670.00). Desktop machines, in general, have smaller printing platforms, smaller accuracy and limited materials available. Therefore, they cost less (Form1+, US$3000.00; MakerBot, US$2118.00; Nobel, US$2214.00), which makes their use outside study protocols feasible [19]. The companies Stratasys, Formlabs and MakerBot informed the cost of the 3D printers through invoices. The cost of the materials was calculated by two different 3D printing companies, based on the mean quantity of the material necessary for one aneurysm.

The characteristics of some 3D printers previously tested for producing models for endovascular training are shown in Table 2.

The 3D printing materials are specific to each 3D printer and are not interchangeable. In general, the characteristics desired for endovascular training are transparency (for training with no need for radiation), good resistance (to avoid leakages and ruptures during the training sessions) and good navigability of the endovascular material (for precision during the deployment of the stent graft and the use of the endovascular material).

It is possible to produce a simulator for training in endovascular aneurysm repair (EVAR) using Connex (Stratasys), Form1+ (Formlabs), MakerBot and Nobel (XYZ Printing) 3D printers. The properties of the materials are shown in Table 3.

Unfortunately, no 3D printing material has all the properties required for endovascular training: insufficient transparency or resistance are the main problems. Most flexible resins available (e.g. Tango Plus from Stratasys, the flexible resin from Formlabs and the flexible resin from XYZ Printing) allow a single training session to be performed, due to the poor resistance of the material, which makes ruptures and leakages frequent. It is possible to reproduce the vascular model in silicone to overcome this issue. For this reproduction, a solid model is made (using a low-cost fused deposition modelling printer such as MakerBot or Sinterstation HiQ printer) and reproduced in silicone. Nevertheless, the process is not simple; knowledge of the material, skills and a good infrastructure are necessary. However, in a test of different materials (shown

Table 2: 3D printers tested for the production of endovascular training models.

3D printer	Connex 350	Form 1+	Nobel	MakerBot	Sinterstation HiQ
Technology	Polyjet Industrial machine	Stereolithography Desktop machine	Stereolithography Desktop machine	Fused deposition modelling Desktop machine	Selective laser sintering Industrial machine
Printing platform (mm)	340×340×200	125×125×165	128×128×200	295×195×165	381×330×457
Layer resolution (μm)	16	25–100	25	100	70
Advantages	High-resolution, large printing platform, possibility of material combination	Low cost, high resolution		Low cost	Large printing platform, good printing speed
Disadvantages	High cost, materials with insufficient transparency and/or resistance	Small printing platform		No flexible or translucent material available	No flexible or translucent material available
Materials available	Transparent, biocompatible, rigid opaque, rubber like, polypropylene like	Photopolymer resins: transparent, white, resistant, flexible, castable dental SG	Photopolymer resins: standard, castable, flexible, rigid, tough	PLA filament, ABS filament, absorbable filament	DuraForm PA, DuraForm GF, DuraForm EX, DuraForm Flex, DuraForm AF, LaserForm A6 and CastForm materials
Webpage	http://www.stratasys.com/3d-printers/production-series/connex3-systems	https://formlabs.com/3d-printers/form-1-plus/	https://www.xyzprinting.com/en-US/product/nobel-1-0	https://www.makerbot.com/replicator/	http://ntk-mt.ru/pdf/ds_sinterstation_hiq_rev.pdf

ABS, acrylonitrile butadiene styrene; PLA, poliatic acid; SG, surgical guides.

in Table 2) in a simulator for EVAR training, silicone was the only flexible material capable of resisting the training sessions with no leakages or ruptures [19].

Printed model post-processing

After 3D printing, the object needs to be post-processed. Each material requires different work [19].

If the Polyjet technology is used (e.g. Connex 3D printer from Stratasys), the support material has to be removed with a water jet. Ruptures may occur during the cleaning process and have to be repaired (using the resin itself or glue). The vascular models should be exposed to ultraviolet light for 24–48 h to improve transparency. Figure 4 shows the process.

If STL technology is used (e.g. Form1+ from Formlabs, Nobel from XYZ Printing, Projet from 3D Systems), pillars are produced to sustain the vascular model during the printing process (shown in Figure 5). These pillars have to be removed. In general, the printing area is small and the vascular models have to be produced in two or three parts, which can be assembled together using the resin and a proper laser. For curing purposes, the vascular models should be exposed to ultraviolet light for 24–48 h.

If a solid model is 3D printed, it can be reproduced in silicone in several different ways: the lost wax technique can be used, or silicone can be directly applied on the surface of the solid model, cured under rotation and heat, and thereafter cut, removed from the solid model and restored. A soluble resin can be used to produce a solid vascular model, and then silicone is applied on the surface of the soluble model and cured, and afterwards the soluble resin is removed by submerging it in a solution produced with caustic soda and water.

Production of a patient-specific simulator for training in endovascular procedures

After post-processing, the vascular models should be connected to a pulsatile flow system to improve the navigability of the endovascular material and to allow the procedure to be performed under antegrade flow. There are commercially available pumps and generic silicone vascular models (e.g. http://www.elastrat.ch/models/assets/files/Products%20PDF/Pump-Tank%203 lt.pdf). A 3D-printed model can be incorporated in a generic silicone model, as shown in Figure 4. Although no 3D printing materials show all the properties required for training,

Table 3: Materials available for producing transparent vascular models for endovascular training.

Material	Typical properties of the material			Major limitation during training session[f]
	Shore	Elongation at break (%)	Tensile strength (MPa)	
TangoPlus[a]	A 26–68	170–220	0.8–1.5	Transparency and resistance
Vero Clear[b]	D 83–86	10–25	50–65	Transparency and navigability
TangoPlus and Vero Clear[c]	A 57–63	75–85	2.5–4.0	Transparency
Flexible Resin Formlabs[d]	A 80–90	90	5.95–6.5	Resistance
Flexible Resin XYZ Printing	–	–	–	Transparency and Resistance
Silicone[e]	A 30	470	5	Navigability

[a]Polyjet Material Rubber FLX930. [b]Polyjet Material Standard Plastic RGD810. [c]Polyjet Digital Material Tango Plus + Vero-Clear Shore 60. [d]Formlabs Flexible Photopolymer Resin for Form1+. [e]Dow Corning Silastic [34]. [f]According to our previous study [19], analysing transparency, resistance and navigability.

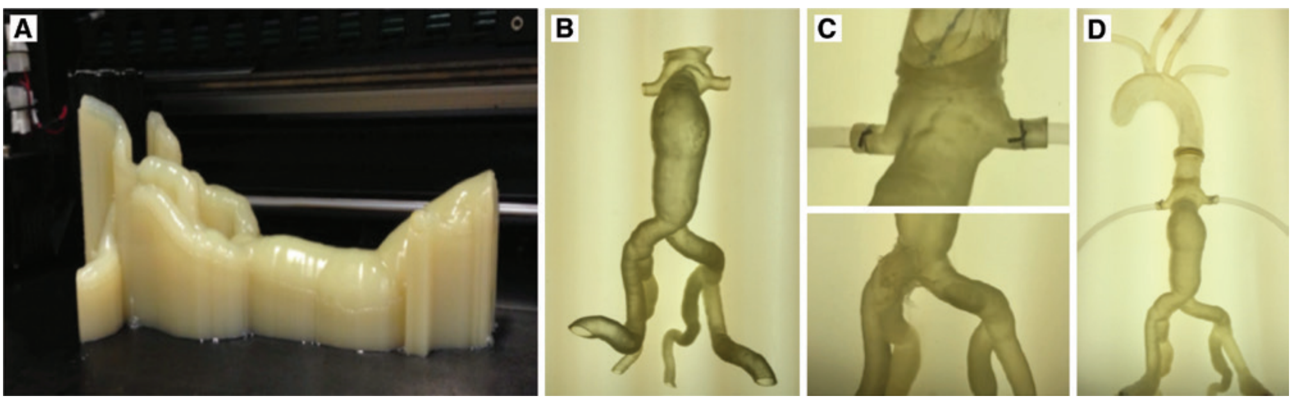

Figure 4: Post-processing of the aneurysms in Material 1.
(A) 3D-printed aneurysm with the support material. (B) 3D-printed aneurysm after removing the support material. (C) Areas reinforced with silicone. (D) 3D-printed aneurysm connected to the simulator.

the simulators produced using 3D-printed models allowed efficient patient-specific training prior to endovascular procedures [19].

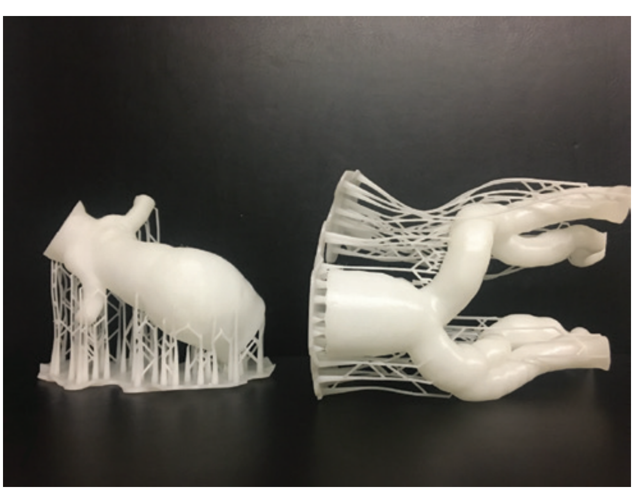

Figure 5: Pillars produced during the printing process of the Form1+ 3D printer.
Test with an opaque material and an aneurysm produced in two parts.

Applications of 3D-printed vascular models

Surgical training

Simulation-based training is not a substitute for clinical practice; however, it offers a consistent method of instruction that allows skill development and assessment. It is more efficient than simple demonstrations (because the resident can truly practice the procedure), more accurate (a patient-specific condition can be reproduced) and less expensive than training in animals. Simulations avoid the exposure of patients to unnecessary risks, and avoid ethical and legal issues related to teaching and learning processes inside a hospital [34]. University hospitals can use simulators to assess the surgical skills of residents during their training, identifying their difficulties in order to improve the program.

Senior residents in the United States reported limited experience and low self-confidence in performing complex endovascular procedures. Residents who performed simulation-based training reported an increase in self-confidence; nevertheless, only 25% of residents in the United States had access to this kind of training [10]. Among educators, there is a concern that graduated residents are not ready to independently perform all vascular surgery procedures in their field [10].

Training in patient-specific simulators, produced with 3D-printed vascular models, improves the residents' surgical performance (reducing fluoroscopy time, total procedure time and amount of contrast used) and increases their self-confidence [19].

Surgical planning

Preoperative planning is a crucial part of endovascular procedures [21, 35–37]. The choice of stents and grafts is based on CT images; however, in complex cases, there can still be considerable uncertainty [7, 15, 26]. 3D-printed vascular models can be created from CT data and used to test the device selection to assist in the preoperative planning [25–27, 31].

Tam et al. [38] conducted a pilot study to investigate the role of 3D-printed models in surgical planning and clinical decision making for cases with aortic aneurysms with challenging anatomical features (e.g. short, angulated or conical necks). They analysed 28 endovascular operators who planned six different cases. After planning the procedure based on the patients' angioCT, the surgeons were presented with the equivalent 3D-printed models and asked to review their decisions. The plan changed in 20% of the cases, and the level of confidence increased in 43% [38].

3D aortic models are also a valuable tool to test a custom-made stent graft before implantation, and may avoid adverse events associated with misaligned fenestrations and unconnected aortic branches. Taher et al. [26] analysed 60 patients who underwent fenestrated endovascular aortic repair and observed that 21.7% of the stent grafts were modified after the surgeon tested the stent graft in a 3D-printed aortic model.

Similarly, Koleilat et al. [25] assessed the accuracy of the measurements obtained with automated 3D centreline reconstruction from imaging data compared with 3D-printed aortic models. They found substantial differences in inter-observer measurements compared with 3D-printed aortic models and concluded that vessel angles are not accurately measured. This may lead to an eclipsing phenomenon, which may contribute to branched or fenestrated vessel failure and re-intervention.

Itagaki [13] manufactured a vascular model to assist surgical planning prior to endovascular treatment of a patient with multiple splenic artery aneurysms. He used free software and low-cost printing services, and concluded that the models produced are useful in preoperative planning and intraoperative guidance.

In addition, 3D-printed vascular models significantly improve the ability of trainees to properly plan for complex endovascular procedures such as EVAR [21]. Therefore, a simulator produced using 3D-printed vascular models is a good tool to teach procedural planning. Surgeons under training have the opportunity to plan the procedure on the patients' CT and test their tactics on the simulator, which allows for a better understanding of endovascular material behaviour.

Discussion

Increased emphasis on patient outcome and quality improvement has led to the use of 3D printing technology in the medical field, especially in school hospitals, where surgeries are performed by surgeons under training [39].

The effect of residents' involvement in perioperative outcomes is a topic of debate and has been evaluated across different surgeries [39, 40]. Iannuzzi et al., analysing lower-extremity amputation, concluded that resident involvement increased the odds of major morbidity, operative time and the risk of intraoperative transfusions [41]. Scarborough et al. noticed that resident involvement in lower-extremity bypass was an independent risk factor for graft failure [42]. DiDato et al. [39] analysed the effect of resident involvement in EVAR, and concluded that it was not associated with major adverse perioperative outcomes. However, it was associated with an increased operative time and length of stay, and therefore may lead to increased resource utilisation and cost [39].

The increased operative time related to residents' involvement in EVAR was reversed with patient-specific training in a school hospital in Brazil. During 1 year, the residents trained for all steps of the surgery using a simulator produced with 3D printing technology, which led to an improvement in residents' surgical performance (total procedure time was reduced by 29%, fluoroscopy time by 31% and time for contralateral limb gate cannulation by 54%) and increased their self-confidence [19]. These findings agree with a systematic review published by See et al. in 2016 [43], which reported a reduction in surgical metrics (procedure time and fluoroscopy time) after the technical training of the residents because the residents became more familiar with the procedure. The reduction in fluoroscopy time and total procedure time is an important issue in a procedure that exposes the patient and the surgical team to ionizing radiation [44, 45].

A multicentre, prospective, randomised trial in Europe showed that patient-specific rehearsal prior to EVAR reduced perioperative errors and the number of angiograms required to deploy the stent graft. Therefore, it may improve patient safety and procedural efficiency [5].

The CT scan measurements for programming endovascular procedures are based on a centreline of flow. However, even modern workstations cannot accurately predict the treatment lengths in patients with severe aortoiliac tortuosity [46]. These patients tend to show a substantial shorten due to a combination of remodelling of the native aorta, stent-graft conformability, and stiffness of guidewires and delivery systems used in endovascular surgeries. The arterial deformations caused by the endovascular equipment depend on multiple factors, such as the morphology of the arteries, the state and degree of calcification of the arterial wall, and the type of device used. Today, their prediction relies mainly on the surgeon's experience [47].

3D printing can be a valuable tool to predict the deformations of the arteries due to the insertion of the endovascular material, which can help improve surgical plans, avoiding complications and use of unnecessary material [26, 47], especially prior to complex surgeries such as implantation of fenestrated aortic grafts. Planning and construction of fenestrated stent grafts for complex aortic anatomies are challenging: the exact fit and positioning of the graft are paramount to allow cannulation of the aortic branches [26].

A retrospective study at Stanford University Medical Center showed a 30% cost increase in EVAR when the use of stent graft extensions was necessary, compared to cases where the standard number of pieces was used (mean device-related cost US$13,220 vs. US$17,107, $p<0.01$); the authors concluded that appropriate preoperative planning and device selection can minimize the cost [48]. Improvement in surgical planning and surgical efficiency can make the use of simulators cost-effective. The cost to produce 3D-printed models (Itagaki, US$50.34–232.03; Torres and De Luccia, US$200.00–1200.00) seems reasonable compared to the cost of the endovascular material [13, 19]. Nevertheless, a study designed to analyse cost reduction after simulations is necessary to confirm this conclusion.

An important limitation of training using 3D-printed models is the need for endovascular material for training purposes, which is wasteful and adds to the cost of training [11]. However, endovascular materials that are close to expiration are generally collected and incinerated. This material may be donated to hospitals where training protocols are implemented. In addition, some endovascular material can be recapped and deployed several times. Moreover, in complex cases, the company may produce a non-sterile prototype for training purposes, which is already commercially available for Terumo Anaconda fenestrated grafts, for example [26].

Currently, there are virtual-reality simulators that overcome the need for endovascular material for training. Numerous studies have shown good results with endovascular training using virtual-reality simulators [4, 5, 8, 11, 49–52]. However, virtual-reality simulators are expensive devices [11, 50, 53] that are prone to technical failure and require regular calibration and maintenance [11].

Virtual-reality simulators and 3D-printed models are both interesting and promising technologies. Virtual-reality simulators have proven useful in choosing the C-arm angle and offer quantitative data for performance analysis [4]. 3D-printed models may help in understanding the behaviour of the endovascular material in three dimensions, inside a specific anatomy. In addition, 3D-printed models can be directly manipulated and inspected, which can help identify some details that were not noticed on the CT scan. Both technologies have shown good results for training and surgical planning [4, 5, 19]; the choice depends on the institution infrastructure, budget and personal preferences.

The traditional apprenticeship model training was stated by Halsted in 1904 and basically consists of supervised training with progressive exposure of the residents to the procedures [11]. Although patient safety is assured by the presence of a senior surgeon [39], this teaching method may not be valid in the modern practice of vascular surgery [54–56]. Simulation-based training offers a consistent method of instruction that allows skill development and assessment. Simulations avoid the exposure of patients to unnecessary risks, and avoid ethics and legal issues [34]. 3D-printed vascular models allow the production of simulators for endovascular training, which can improve procedural efficiency and patient safety.

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Author Statement

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Author Contributions

Inez Torres: performed the research, wrote the manuscript; Nelson De Luccia: reviewed the manuscript.

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Supplementary Material: The article (https://doi.org/10.1515/iss-2018-0020) offers reviewer assessments as supplementary material.

Reviewer Assessment

Inez Torres* and Nelson De Luccia

Artificial vascular models for endovascular training (3D printing)

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Reviewers' Comments to Original Submission

Reviewer 1: Karolis Tijunaitis

Jun 05, 2018

Reviewer Recommendation Term:	Accept with Minor Revision
Overall Reviewer Manuscript Rating:	95

Custom Review Questions	**Response**
Is the subject area appropriate for you?	5 - High/Yes
Does the title clearly reflect the paper's content?	5 - High/Yes
Does the abstract clearly reflect the paper's content?	5 - High/Yes
Do the keywords clearly reflect the paper's content?	5 - High/Yes
Does the introduction present the problem clearly?	5 - High/Yes
Are the results/conclusions justified?	4
How comprehensive and up-to-date is the subject matter presented?	4
How adequate is the data presentation?	5 - High/Yes
Are units and terminology used correctly?	5 - High/Yes
Is the number of cases adequate?	3
Are the experimental methods/clinical studies adequate?	4
Is the length appropriate in relation to the content?	5 - High/Yes
Does the reader get new insights from the article?	5 - High/Yes
Please rate the practical significance.	5 - High/Yes
Please rate the accuracy of methods.	4
Please rate the statistical evaluation and quality control.	5 - High/Yes
Please rate the appropriateness of the figures and tables.	5 - High/Yes
Please rate the appropriateness of the references.	5 - High/Yes
Please evaluate the writing style and use of language.	5 - High/Yes
Please judge the overall scientific quality of the manuscript.	5 - High/Yes
Are you willing to review the revision of this manuscript?	Yes

Comments to Authors:
The manuscript ISS-2018-0020 entitiled "Artificial vascular models for endovascular training (3D Printing)" is a review article analysing 3D printing value for endovascular training.

In an effort to provide more transparency regarding the decision, five aspects of paper were rated. Below are the scores received by your manuscript:
Novelty = 4
Clinical Impact = 5
Scientific Impact = 4
Definitive = 4
Interesting to the Specialty = 5
(1 = Not at all, 3 = Average, 5 = Completely)
****
A. General Evaluation
Well written manuscript for the most part.
B. Specific Remarks
B1. It might be good to discuss briefly cost effectiveness of 3D printing in training process and case planning, because a wide application depends whether this method is gonna be approved as a cost effective.
B2. Paragraph "Introduction": (www.shapeways.com e www.imaterialise.com) e change to comma.
B3. In the sentence "...insufficient transparency or resistance are the main problem." Please change problem to problems.
B4. Paragraph 3D printing sentence "In addition, directly 3D-printing a hallow aneurysm is a one-step process; therefore, it is faster and more accurete" sounds a bit out of context. It might be better to change its place.
B4. Paragraph "Printed model post-processing" - citations are missing.
B5. In the sentence: "Although no 3D printing materials show ..." please write a comma after although.
B6. Table 1 and Table 2 are shown twice
P.S.
I suggest adding definitions for all figures
9–16% of complications are associated with access injuries. It is usually related to inexperience with closure device systems. Possibility to involve the whole procedure in 3D models simulation from groin puncture to closure with closure devices would have sufficiently reduced operative time and operative success.

Reviewer 2: anonymous

Jun 20, 2018

Reviewer Recommendation Term:	Accept with Minor Revision
Overall Reviewer Manuscript Rating:	N/A
Custom Review Questions	**Response**
Is the subject area appropriate for you?	5 - High/Yes
Does the title clearly reflect the paper's content?	5 - High/Yes
Does the abstract clearly reflect the paper's content?	5 - High/Yes
Do the keywords clearly reflect the paper's content?	5 - High/Yes
Does the introduction present the problem clearly?	5 - High/Yes
Are the results/conclusions justified?	5 - High/Yes
How comprehensive and up-to-date is the subject matter presented?	4
How adequate is the data presentation?	4
Are units and terminology used correctly?	4
Is the number of cases adequate?	5 - High/Yes
Are the experimental methods/clinical studies adequate?	3
Is the length appropriate in relation to the content?	5 - High/Yes
Does the reader get new insights from the article?	5 - High/Yes
Please rate the practical significance.	5 - High/Yes
Please rate the accuracy of methods.	4
Please rate the statistical evaluation and quality control.	4
Please rate the appropriateness of the figures and tables.	4
Please rate the appropriateness of the references.	4
Please evaluate the writing style and use of language.	4
Please judge the overall scientific quality of the manuscript.	5 - High/Yes
Are you willing to review the revision of this manuscript?	Yes

Comments to Authors:

This is a comprehensive review of current application of 3D-printing in generating training models for endovascular surgery.
There are some minor remarks:
It appears that the process for literature search is not structured. It would improve the quality oft he manuscript if the author can add a short passage in methods regarding the algorithm for search/retrieval/selection of references.
The same applies for the author's selection of post-processing software. It is suggested that the author either states the software mentioned as a personal experience/choice or (better) provides a comprehensive list of currently available segmentation and postprocessing software (open source and commercially).
In the manuscript, pricing for 3D printers and production costs is given. Here, the conditions/assumptions of production need to be clarified in order to enable comparison.
Figure 3: source and copyright of figures needs to be stated.
Figures 4 and 6 are redundant

Authors' Response to Reviewer Comments

Jul 02, 2018

Reviewer #1:

The manuscript ISS-2018-0020 entitiled "Artificial vascular models for endovascular training (3D Printing)" is a review article analysing 3D printing value for endovascular training.
In an effort to provide more transparency regarding the decision, five aspects of paper were rated. Below are the scores received by your manuscript:
Novelty = 4
Clinical Impact = 5
Scientific Impact = 4
Definitive = 4
Interesting to the Specialty = 5
(1 = Not at all, 3 = Average, 5 = Completely)
****
A. General Evaluation
Well written manuscript for the most part.
Thank you very much for your comments; they certainly helped to improve this article.

B. Specific Remarks
B1. It might be good to discuss briefly cost effectiveness of 3D printing in training process and case planning, because a wide application depends whether this method is goanna be approved as a cost effective.
This is certainly a very important issue, therefore this paragraph was added to the discussion:
A retrospective study at Stanford University Medical Center showed a 30% cost increase on EVAR, when the use of stent graft extensions was necessary, compared to cases where the standard number of pieces was used (mean device-related cost US$13,220 vs. US$17,107, $p < 0.01$); the authors concluded that appropriate preoperative planning and device selection can minimize the cost [41]. The improvement in surgical planning and surgical efficiency can make the use of simulators cost-effective. The cost to produce 3D printed models (Itagaki et al US$50.34 to US$232.03; Torres et al US$ 200.00 to US$1,200.00) seems reasonable comparing to the cost of the endovascular material [19,42], nevertheless a study designed to analyse cost reduction after simulations is necessary to confirm this conclusion.
B2. Paragraph "Introduction": (www.shapeways.com e www.imaterialise.com) e change to comma.
It was changed.
B3. In the sentence "...insufficient transparency or resistance are the main problem." Please change problem to problems.
It was changed.
B4. Paragraph 3D printing sentence "In addition, directly 3D-printing a hallow aneurysm is a one-step process; therefore, it is faster and more accurete" sounds a bit out of context. It might be better to change its place.
This sentence was moved to the beginning of the section 3D printing, a few more comments were added to put it in context.

It is possible to directly 3D print hollow flexible models, which is a one-step process; therefore, it is faster and more accurate than the commonly used lost wax technique.
B4. Paragraph “Printed model post-processing” - citations are missing.
The post-processing work description was based basically on the author experience. The detailed description was not found prior to our research. Due to limited number of words, the process was only shortly described in our published paper. Nevertheless, the citation was added: After 3D-printing, the object needs to be post-processed. Each material requires different work [19].
B5. In the sentence: “Although no 3D printing materials show ...” please write a comma after although.
A comma was added.
B6. Table 1 and Table 2 are shown twice
I am sorry, that was probably a mistake when the files were uploaded. Extra attention will be payed during the process.

P.S.
I suggest adding definitions for all figures
The Figures have legends, as shown below, maybe the legends were lost with the problem of the tables. I am not sure if I understood your comment, I hope this is the correct answer.
FIGURE LEGENDS
Figure 1: Steps to produce a 3D-printed aneurysm. 1: Images from an angioCT; 2: Abdominal aorta after image post-processing; 3: 3D printing process; 4: Post-processed 3D-printed aneurysm
Image post-processing. (A) Reconstruction of the aorta based on the contrast inside the arterial lumen - DICOM file. (B) Aorta after conversion of DICOM to STL file. (C) Surface of the aorta smoothed. (D) Wall of the aorta digitally thickened to 1.5 mm
Figure 3: Examples of 3D printers available for the production of vascular models. A and B are industrial machines. C, D and E are desktop machines
Figure 4: Post-processing of the aneurysms in Material 1: A) 3D-printed aneurysm with the support material. B) 3D-printed aneurysm after removing the support material. C) Areas reinforced with silicone. D) 3D-printed aneurysm connected to the simulator
Figure 5: Pillars produced during the printing process of the Form 1 + 3D printer. Test with an opaque material and an aneurysm produced in two parts

9–16% of complications are associated with access injuries. It is usually related to inexperience with closure device systems. Possibility to involve the whole procedure in 3D models simulation from groin puncture to closure with closure devices would have sufficiently reduced operative time and operative success.
This is a very important point. Currently most of the endovascular simulators are part task simulators, where the access to femoral arteries and the use of closure devices is not practiced. There are low fidelity simulators build to train this specific steps alone. It would certainly be interesting to have both things combined. The 3D printed simulators are being developed and there is a lot to improve. This is a good information for further tests. Thank you very much.

Reviewer #2:
This is a comprehensive review of current application of 3D-printing in generating training models for endovascular surgery.
Thank you very much for your comments; they certainly helped to improve this article.

There are some minor remarks:
It appears that the process for literature search is not structured. It would improve the quality of the manuscript if the author can add a short passage in methods regarding the algorithm for search/retrieval/selection of references.
This comment is absolutely pertinent. To address this problem, a paragraph was added. I hope it helped to make the review process clear.
We performed electronic searches on PubMed to collect studies on 3D printing technology and its applications in endovascular surgery training. Several searches were performed using combination of different terms: 3d printing and/or endovascular training and/or surgical planning, The only limit defined was language: only reports in Portuguese or English were considered. Titles and abstracts were screened to exclude irrelevant or duplicate abstracts. Then, included articles underwent a full-text review. We initially found 409 results, which were narrowed down to 190 after abstracts analysis (the authors excluded duplicated articles and researches deemed irrelevant to surgical practice). This set of results was then reviewed to form a set of 58 full-text articles used for the final analysis. In addition, the 3D printers’ website was searched for technical information.

The same applies for the author's selection of post-processing software. It is suggested that the author either states the software mentioned as a personal experience/choice or (better) provides a comprehensive list of currently available segmentation and postprocessing software (open source and commercially).

This is important information; therefore Table 1 was added to the article.

Table 1: Softwares available for image post-processing

Softwares for DICOM file processing References

Mimics® (Materialise NV, Leuven, Belgium) Biglino et al. [51]; Wilasrusmee et al. [23]; Hakansson et al. [52]; Yuan et al. [53]; Mafeld et al. [18]; Dong et al. [54]; Koleilat et al. [29]; Taher et al. [27]

OsiriX (Pixmeo SARL, Bernex, Switzerland) Marro et al. [12]; Tam et al. [20]; Takao et al. [55]

Vitrea 3D Station (Vital Images, Inc., Minnetonka, MN) O'hara et al. [56]; Russ et al. [57]

iNtuition software (TeraRecon, Inc, Foster City, Calif) Koleilat et al. [29]

Vascular Modeling Toolkit (VMTK, Orobix, Bergamo, Italy) Meess et al. [30]

Softwares for STL file processing References

3-matic® (Materialise NV, Leuven, Belgium) Biglino et al., Mafeld et al. [18]; Koleilat et al. [29]

MeshLab (Visual Computing Lab - the ISTI-CNR, Roma, Itália) Marro et al. [12]

Blender (Blender Foundation, The Netherlands, v 2.67 for Windows) Itagaki et al. [42]

Google SketchUp (Trimble Inc., CA, USA) Govsa et al. [58]

Magics (Materialise NV, Leuven, Belgium) Yuan et al. [53]

Meshmixer software (Meshmixer, Autodesk, San Rafael, CA, USA) O'hara et al. [56]; Takao et al. [55]; Russ et al. [57]; Meess et al. [30]

Besides, the information of the author's choice was added on the text:

For DICOM post-processing, the author's choice were iNtuition Unlimited software (Aquarius, TeraRecon, San Matteo, CA, USA), OsiriX software (Pixmeo, Geneva, Switzerland) or Horos software (The Horos Project, sponsored by Nimble Co LLC d/b/a Purview, Annapolis, MD, USA).. Thereafter, the authors have chosen Mesh Mixer (Mesh Mixer 2.8, Autodesk, Inc.) or Magics Software (Magics, 3-matic®, Materialise®) for STL processing.

In the manuscript, pricing for 3D printers and production costs is given. Here, the conditions/assumptions of production need to be clarified in order to enable comparison.

The companies Stratasys, Formlabs and Makerbot informed the cost of the 3D printers through invoices. The cost of the materials was calculated by two different 3D printing companies (3Dux and Anacon), based on the mean quantity of the material necessary for one aneurysm.

This information was added to the manuscript

Figure 3: source and copyright of figures needs to be stated.

This information was added to Figure 3:

Figures were collected from the companies' website (www.stratsys.com; www.3dsystems.com; www.formlabs.com; www.xyzprinting.com). The companies agreed with the use of the Figures.

Figures 4 and 6 are redundant

Figure 6 was excluded.