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D3.3. METHODOLOGICAL GUIDELINES FOR 3D PRINTING WITH TRAINING PURPOSES

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- **Summary**

This deliverable presents good practice guidelines for design and developing 3D model printing for minimally invasive surgery (MIS) training purposes. These printed models have two main applications, their use as a training method for medical and surgical anatomy and as a physical model for basic surgical skills training in a laparoscopic training simulator. This review summarizes aspects such as materials, technologies and applications of 3D printing for use as a training tool in MIS.

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1. Introduction

Three-dimensional (3D) printing technologies can have a wide range of applications in medical and surgical anatomy. In medical education, Fused Deposition Modeling (FDM), Stereolithography (SLA), Selective Laser Sintering (SLS) and MultiJet are used to create 3D anatomical models for teaching and training purposes (Aparicio et al., 2021). These models can be created based on real patient data, allowing students and surgeons to practice procedures on lifelike models before performing them on actual patients.

In surgical planning, 3D printing technologies can be used to create models of a patient's anatomy, which can then be used to plan and practice surgical procedures before the actual surgery takes place. This helps surgeons to visualize the patient's anatomy and plan the best approach to the surgery, reducing the risk of complications and improving patient outcomes.

In this paper, two methods of application of 3D printing in healthcare will be developed. The first one is SMA (Surgical and Medical Anatomy), which could be defined as the use of 3D printing to obtain three-dimensional models of a patient in order to plan a possible surgery. On the other hand, another method is SSTL (Surgical Skills Training in Laparoscopy), where models are printed to simulate the physical and mechanical characteristics of organs so that laparoscopic surgery trials can be performed without harming any patient.

The aim of this deliverable is to present existing technologies and software for 3D printing and provide good practice guidelines for designing and developing 3D model printing for minimally invasive surgery (MIS) training purposes. These guidelines include *Methodological guidelines for Surgical and Medical Anatomy (SMA)*, and *Methodological guidelines for Physical models for basic surgical skills training in laparoscopy (SSTL)*. For that, surgical and medical anatomy, and physical models for basic skills training in laparoscopy are being shortly explained. In a supporting document for Deliverable 3.3. *Methodological guidelines for 3D printing with training purposes*, the details of the literature review on aspects such as materials, technologies and applications of 3D printing for use as a training tool in MIS are provided.

The information presented in this deliverable has been continuously updated during the course of the MIREIA Project.

2. Surgical and Medical Anatomy (SMA)

SMA could be summarized as the design, based on medical images obtained from a patient, of three-dimensional models that allow health personnel to have a more realistic view of the state of a patient's condition with a view to carrying out a surgical intervention.

Using SMAs makes it easier for the professional in charge of performing the surgery to plan more directly what is the most correct way to carry it out, as well as favoring communication with the patient, given that there is the possibility of showing the patient in a simple way what the situation is, providing a more relaxed atmosphere than in the case of not knowing what is wrong or what the surgery is going to consist of.

SMA is being used more and more frequently in hospitals around the world, given the increase in the success of surgeries of various kinds (try to find articles that demonstrate the increased use of this technique, as well as its proven effectiveness).

3. Physical models for basic surgical skills training in laparoscopy (SSTL)

When it comes to basic surgical skills training, silicone and latex are commonly used materials for creating physical models. These models allow aspiring surgeons and medical students to practice various procedures in a realistic and controlled environment. A few examples of physical models for basic surgical skills training are:

- *Suturing and Knot Tying Models:* These models typically consist of a silicone or latex base with pre-made incisions or wounds. They allow learners to practice suturing techniques and knot tying, which are fundamental skills in surgery. The material mimics the texture and feel of human tissue, providing a realistic experience (Goudie et al., 2018)
- *Injection and Venipuncture Models:* Silicone or latex models can be designed to simulate the human skin and underlying structures, such as veins. These models allow trainees to practice injection techniques and venipuncture, which involve inserting a needle into a vein. They provide a realistic feel for needle insertion and the resistance encountered during the procedure (Riedle et al. 2019).
- *Laparoscopic Surgery Simulators:* Laparoscopic surgery involves performing procedures using small incisions and a camera-guided instrument called a laparoscope. Silicone or latex models can be used to create abdominal cavities with simulated organs and structures. Trainees can practice manipulating the laparoscope and performing various surgical tasks, such as suturing or tissue dissection, in a minimally invasive setting (Melo Filho et al. 2021).
- *Anatomical Models:* Anatomical models made of silicone or latex can be used to learn basic surgical anatomy and practice dissection techniques. These models often depict specific body parts or systems, such as the heart, brain, or limbs. They allow trainees to familiarize themselves with the anatomical structures they will encounter during surgery (Turney et al. 2014).
- *Wound Closure Models:* Silicone or latex wound closure models are designed to simulate complex wounds that require more advanced suturing techniques. They can include irregular or curved incisions, representing challenging scenarios surgeons may face in real-life situations. Practising on these models helps develop skills for suturing under more difficult conditions (Warnung et al. 2023).

4. Technologies for 3D printing

3D printing technologies have numerous applications in the medical field, and they are rapidly transforming the way medical professionals approach patient care (Riedle et al. 2019). The use of 3D printing technology to create physical models for surgical skills training has become increasingly popular in recent years. In the case of laparoscopic surgery, 3D printing can be used to create anatomically accurate models of the abdominal cavity, which can be used to train surgeons in basic laparoscopic skills. Moreover, 3D printing can be used to print abnormal anatomy cases, which can be used in training of surgeons with different proficiency levels. (Currently, not all surgeons are “exposed” to

unusual anatomy cases, as these are not too common, and/or the patients with these anatomies might be treated in specialized hospitals.

These 3D models can be created using patient-specific data obtained from CT scans and/or MRI images. The resulting models can then be used to practice various laparoscopic procedures, such as trocar insertion, camera manipulation, instrument handling, and suturing. These models provide a realistic simulation of the anatomical structures found in the abdominal cavity, allowing surgeons to practice and refine their skills before performing actual procedures on patients.

4.1. Fused Deposition Modeling (FDM)

Fused Deposition Modeling (FDM) is a 3D printing technology used to create 3D objects by extruding a thermoplastic material layer by layer, with an approximate minimum layer thickness of 0.05 mm. Overall, FDM technology has revolutionized the way medical and surgical anatomy is taught and practiced, allowing for greater precision and accuracy in patient care.

4.1.1. Filament

For medical and surgical anatomy applications, there are specialized filaments that are commonly used in FDM technology. Sometimes, these filaments are designed to be biocompatible and safe for use in medical applications (Fig. 1).

- **PLA (Polylactic Acid)** - biodegradable, plant-based filament that is often used for surgical training models and medical devices that do not require implantation.
- **ABS (Acrylonitrile Butadiene Styrene)** - strong, durable filament that is commonly used in manufacturing applications. It can be more challenging to print than PLA but produces high-quality, detailed models.
- **PETG (Polyethylene Terephthalate Glycol)** - durable and flexible filament that is resistant to moisture, making it ideal for surgical instruments, trays, and other medical equipment.
- **Nylon** - strong, flexible filaments that, and have good chemical resistance, making them ideal for surgical tool prototypes and anatomical models.
- **TPU (Thermoplastic Polyurethane)** - flexible, rubber-like filament that is often used for prosthetics and other medical devices that require flexibility and elasticity.
- **PCL (Polycaprolactone)** - biodegradable, FDA-approved filament that is often used for medical implants and scaffolds.



Figure 1: FDM ankle bone model using PLA filament.

4.1.2. Pellet

Pellet-based 3D printing is not commonly used for anatomical models. It is, still, in its early stages, and the technology is not yet widely available. However, there is a possibility of using pellet-based 3D printing for creating biocompatible anatomical models. The choice of pellet material would then depend on the specific requirements of the project, and the process for creating 3D models from pellets would differ from traditional 3D printing methods.

4.2. Stereolithography (SLA)

SLA is a 3D printing technology that uses a UV laser to cure a photosensitive resin layer by layer, with an approximate minimum layer thickness of 0.025 mm, creating a solid object. SLA technology has a range of applications in medical and surgical anatomy.

SLA is currently used to create custom implants and prosthetics for patients. By using a 3D printer and patient-specific data, prosthetics and implants can be designed and manufactured to fit perfectly for the individual patient. In addition, SLA technology can be used to create molds for various medical devices, such as hearing aids, dental implants, and orthotics. These molds can be customized to fit the patient's specific needs, improving the effectiveness and comfort of the device.

Objects created using the SLA process are known for their high precision and surface smoothness, making them suitable for a wide range of applications such as jewelry, dentistry, rapid prototyping, engineering, medicine and more (Fig. 2).



Figure 2: SLA heart model using dental resin.

4.2.1. Resin

For anatomical models, there are several types of resins that are commonly used in SLA 3D printing technologies. For example:

- **Bio-Compatible Resins** - specifically designed for medical applications; they are biocompatible, non-toxic, and safe for use in anatomical models. They are often used for creating patient-specific surgical guides, implants, and prosthetics.
- **Clear Resins** - used to produce high-quality, transparent models that are ideal for anatomical models that require detailed visualization of internal structures.
- **Dental Resins** - commonly used in the dental industry for producing dental models, implants, and aligners. They are biocompatible and come in a range of colors.
- **Engineering Resins** - often used for creating high-strength anatomical models, such as those used for biomechanical testing and surgical training.
- **Flexible Resins** - used to produce models that have a soft, rubber-like texture and are ideal for anatomical models that require elasticity and flexibility.

The choice of resin depends on the specific requirements of the project, such as biocompatibility, transparency, strength, and flexibility. It is important to choose a resin

that is safe for use in anatomical models and meets the necessary regulatory requirements for medical use.

Some of the main advantages of SLA include high resolution, accuracy, and surface finish, as well as the ability to produce highly detailed parts. Some of the main disadvantages include the high cost of materials, limited build volume, and the need for post-processing to remove excess resin and cure the final part.

4.3. Selective Laser Sintering (SLS)

SLS is a 3D printing technology that uses a laser to sinter powdered materials together, layer by layer, with an approximate minimum layer thickness of 0.05 mm to create a solid object.

SLS technology is used to create 3D anatomical models, prosthetics, implants, and surgical tools. It can produce objects with high accuracy and is well-suited for producing objects with complex geometries, making it a popular choice for creating custom orthopedic implants or surgical tools. However, SLS technology can be more expensive than FDM and require additional post-processing steps.

The most widely used SLS material is Polyamide 12 (PA 12), also known as Nylon 12. Polyamide powder can be filled with various additives to improve the mechanical and thermal behavior of the produced SLS part. Examples of additives include carbon fibers, glass fibers or aluminum. Materials filled with additives are usually more brittle and can have highly anisotropic behavior (Fig. 3).



Figure 3: SLS heart and backbone with vascularization model using Polyamide.

4.3.1. Dust

The following materials are commonly used in SLS technology for medical applications:

- **Polyamide 11** - also known as Nylon 11, is a thermoplastic material with excellent mechanical properties, including high strength, durability, and impact resistance. It is often used in SLS 3D printing for medical models due to its biocompatibility, making it suitable for applications such as surgical guides and anatomical models.
- **Polyamide 12** - or Nylon 12, is another commonly used material in SLS technology. It offers similar characteristics to Polyamide 11, such as good mechanical properties and biocompatibility. It is often chosen for medical applications due to its resistance to chemicals and sterilization methods, making it suitable for producing functional prototypes and custom medical devices.
- **Polyamide 6** - or Nylon 6, is a versatile thermoplastic with good mechanical strength, toughness, and wear resistance. While it may not be as commonly used in medical applications compared to Polyamide 11 or 12, it can still be employed in SLS technology for certain medical models, such as anatomical prototypes or surgical planning aids.
- **Polypropylene** - a widely used thermoplastic material known for its lightweight nature, chemical resistance, and high impact strength. In SLS 3D printing, polypropylene-based powders are utilized to produce functional prototypes and medical models. PP offers good flexibility and durability, making it suitable for applications like orthotics, prosthetics, and other custom medical devices.
- **Polyurethane Flex** - commonly employed material in medical applications such as creating flexible anatomical models, wearable medical devices, and prosthetic components. Polyurethane flex materials used in SLS 3D printing offer these same properties. Polyurethane (PU) - a class of polymers known for their excellent flexibility, elasticity, and resistance to abrasion.

4.4. Other technologies

In the following sections we will present other less-commonly used technologies.

4.4.1. HP Multi Jet Fusion (MJF)

HP MJF is a 3D printing technology that uses a combination of inkjet printing and fusing techniques to create high-quality, precise, and detailed 3D models, with an approximate minimum layer thickness of 80 µm. It was developed by HP Inc., and is used in a wide range of applications, including product prototyping, manufacturing, and medical and surgical anatomy.

MJF technology works by applying a thin layer of powdered material, such as nylon, to a build platform. An inkjet printhead then applies a layer of liquid agent that fuses the

powder together in the desired pattern. This process is repeated layer by layer until the final 3D model is created.

One of the main advantages of MJF technology is its ability to produce high-quality, detailed 3D models quickly and efficiently. It can produce parts with a resolution of up to 42,2 dots per mm, resulting in parts with smooth surfaces and fine details. In addition, MJF technology allows for the production of parts with variable properties, such as flexibility, color, and texture. It has the potential to revolutionize the way medical professionals approach patient care, allowing for greater precision, accuracy, and customization than ever before.

4.4.2. PolyJet de Stratasys

Stratasys Polyjet is a 3D printing technology that uses inkjet printing technique with droplets of liquid plastic and a UV light cure the plastic to create high-quality, precise, and detailed multi material 3D models, with an approximate minimum layer thickness of 14 μm . It was developed by Stratasys and is used in a wide range of applications, including product prototyping, manufacturing, and medical and surgical anatomy.

This technology works by applying droplets of liquid plastic material, such as BoneMatrix, or TissueMatrix, to a build platform. An UV printhead cures the layer of liquid plastic. This process is repeated layer by layer until the final 3D model is created.

4.4.3. Silicone-based technologies

A recent advancement in additive manufacturing has introduced a groundbreaking technology that allows for the utilization of silicone as a material in 3D printing.

This technology enables the creation of three-dimensional objects using silicone materials without the need for thermal alterations. Lynxter, a leading French company, is leading the way in the field of smart and compact industrial 3D printing solutions for liquids. They have developed 3D printers designed exclusively for liquid additive manufacturing, such as their S300X silicone 3D printer, which specializes in printing objects with this specific material.

The application of 3D printing technology in the medical field has proven to be highly beneficial due to its customisation capabilities and reduced lead times. In particular, 3D printing with silicone has significantly contributed to improving and simplifying medical processes by decreasing the need for manual interventions in the production of orthotics, prosthetics, customized orthopedic devices, suture-forming brackets, medical implants for epithesis and more.

Additive manufacturing is using silicone to facilitate the production of custom devices without the need for manual impressions or molds. In addition, 3D printing with silicone enables the creation of lighter parts with adjustable mechanical properties, such as hardness, strength, damping and anisotropy, by casting the part or varying fill rates. These capabilities cannot be achieved with traditional silicone manufacturing methods, such as molding.

4.5. Summary of technologies for 3D printing

A summary of the features (process and materials) related to the main technologies for 3D printing is shown in Table 1.

Table 1. Summary of the 3D printing technologies.

Technology	Process	Materials
FDM	<u>Fused deposition modeling</u> process, this printing technology is the most fundamental and widely used 3D printing technology.	Different polymers in different formats.
SLA	<u>Stereo-lithography</u> process, in this process the light responsive materials are solidified into a lean layer.	Thermoplastics
SLS	<u>Selective laser sintering</u> process is similar to the SLA method, though materials are solidified by infrared laser.	Ceramics, plastics, and wax.
Other technologies	PolyJet, MultiJet, Silicones	Silicones, polymers...

5. Software

The printing software is in charge of laminating the 3D model and configuring the printing parameters of the 3D printer.

5.1. CAD

Computer-aided design (CAD) software is used to create 3D models, and can be used by designers and artists to create objects of any shape or size. Models created in CAD can be exported in different formats, such as STL, which is the most common format used in 3D printing. To create 3D reconstructions of medical imaging, medical image segmentation - the process of extracting the desired object (organ) from a medical image - is performed.

5.1.1. Segmentation

Segmentation consists of transforming 2D images obtained by means of medical imaging technologies into 3D models, which in this case make it easier for healthcare personnel to observe specific pathologies of the patient, thus avoiding having to look at each 2D image at a glance. This segmentation can generally be carried out in different ways:

- **Manual** - the user, image by image (or slice by slice), selects the parts of interest.
- **Automatic** - the software itself, after providing a grayscale depending on the type of tissue to be selected, is responsible for marking the areas of interest in all images and generating the 3D model.
- **Semi-automatic segmentation** - consists of a mixture of both aforementioned methods, where the area of interest is selected manually in one image and then the software, using artificial intelligence or other assistance methods, selects the areas of interest in the rest of the images based on the one selected manually.

Among the most widely used medical image segmentation software are: MIMICS, from the company Materialize, which allows segmentation of medical images and generating 3D models and subsequently editing them, scaling them, creating surgical guides, etc.; 3D Slicer, which is a free and open source software with a wide variety of applications for the analysis of medical images, not only segmentation; and, finally, InVesalius, another free and open software that allows segmentation of medical images and obtaining 3D models.

5.1.2. Solids

The design of 3D solid models consists of using CAD tools to produce 3D objects from 2D drawings. These objects can range from standard organ simulations to the design of surgical guides.

The use of solid design is usually more related to surgical training, since no specific images of any patient are used, but rather a standardized and manipulable model is used in such a way that no one is harmed, allowing dissections, cuts, sutures, etc. to be performed.

Among the best known solid design software are the following: Solidworks, from the company Dassault Systèmes, which is a 2D and 3D mechanical modeling software in which a great variety of solids can be custom designed, assembled together, scaled and carried out different mechanical tests to study the behavior it would have; Fusion360, from Autodesk, which could be summarized as an all-in-one in the area of 3D design, because it not only allows you to design solids and test them, but also allows you to edit the different solids generated using meshing tools; and Blender, which is a free and open source dedicated to 3D design, but not only of solids, but also of images, animation, etc.

5.1.3. Mesh

3D model editing and meshing is used to modify those 3D models obtained by medical image segmentation or designed from scratch, in order to reduce imperfections as much as possible, with a view to their subsequent 3D printing. Meshing software allows modifications to be made with a greater or lesser degree of accuracy, allows Boolean operations of addition or subtraction of objects or models to each other, to iron out

imperfections that exist on the surface of the models, cut objects in a particular plane, remove unwanted parts, analyze errors in the meshing, etc. It is a very important process since it depends on this step whether a print comes out better or worse or is easier or more complicated to print.

Among the most prominent mesh editing software are the aforementioned "Fusion360" and "Blender", but there is also a free software whose express use is for mesh design and editing, Meshmixer, from Autodesk (like Fusion360), which has a wide variety of design tools that allow smoothing the surfaces of the models, cutting, removing, converting objects into solids, parameterizing, Boolean operations, etc.

5.2. Slicing

Slicing software is used to prepare CAD models for 3D printing (Table 2). The software divides the model into horizontal layers, determines the required print settings (such as print speed and temperature), and generates a G-code file that can be sent to the 3D printer to start printing.

Table 2. Main 3D printing slicer software regarding the 3D printing technologies.

		TECHNOLOGIES FOR 3D PRINTING			
		FDM	SLA	SLS	Others
SOFTWARE	Prusa Slicer	X	X		
	Cura	X			
	Simplify	X			
	Mango 3D	X			
	Lychee 3D		X		
	ChiTuBox		X		
	PreForm		X		

	Sinterit Studio			X	
	Materialize Magics			X	
	HP SmartStream 3D Build Manager				Modified SLS

6. Methodological guidelines

6.1. Surgical and Medical Anatomy (SMA)

Steps to follow to make a surgical planning model (recommendations are attached at the end):

1. Obtain medical images (MRI or CT scan).

To obtain the three-dimensional model from a preoperative study of a patient performed by computed tomography (CT) or magnetic resonance imaging (MRI), medical imaging software is needed to segment the anatomical part to be printed, generating a file in STL or PLY format.

2. Segment the images using 3D model reconstruction software from images taken in all 3 planes.

To perform such segmentation, modeling software such as 3DSlicer or InVesalius can be used. In general, these programmes allow the segmentation to be carried out in three different ways:

Automatic segmentation. This is the most convenient segmentation model to use. To do this, a threshold is selected, which is in charge of marking the gray range we are interested in for the images. In other words, if the aim is to segment a tac by obtaining a three-dimensional model of the bone area, the gray range that the programme must be told to take is greater than if it were a soft area such as an organ. This mode of segmentation is faster, but at the same time less accurate, as the software may not detect certain parts correctly or may cause confusion.

Manual segmentation. Contrary to automatic segmentation, this method is much slower but more accurate. It consists of "drawing" the region of interest in all the 2D images of a plane. It is slower because it is necessary to draw image by image manually, but more accurate because only the part that is really of interest is drawn.

Semi-automatic segmentation. This consists of making use of artificial intelligence to segment those areas that are of interest. To do this, a single image is segmented manually and, subsequently, the programme, using AI, is capable of segmenting the remaining images based on the manually selected area.

3. **Edit the 3D model** obtained by segmenting the medical images .
Editing the model allows any errors in the model resulting from the segmentation to be corrected. It makes it possible to prepare the 3D object for subsequent printing by eliminating any roughness that might exist and make printing difficult, to cut out specific parts of the model, to make surgical guides for future surgery, etc. For the edition of models, the most used softwares are Meshmixer, Blender, 3DBuilder, Mimics... (Images)
4. **Prepare the 3D model for printing once it is edited and free of defects.**
To do this, we have to be clear about what material and printing mode we intend to follow, based on the information previously seen in section 5.2 of this project, as depending on the printing technique, different model lamination software must be used. (Images of each technique).

6.2. Physical models for basic surgical skills training in laparoscopy (SSTL)

The steps to follow to create 3D models to be applied in laparoscopic surgery training are as follows:

1. **Check whether the 3D model is as close to reality as possible.**
First of all, as it is a model that is going to be used for surgical training, it must be as close to reality as possible. To do this, the first step is to get the correct information about the anatomy of the area to be designed, in order to make a design that is as close to reality as possible.
2. **Design the 3D model using CAD design tools.**
Once the bibliography has been reviewed or professionals in the field have been consulted, the model to be made is designed, using CAD design tools such as the following software: Solidworks, Blender, OnShape. As these are design software, initially a series of sketches will have to be made in two dimensions, which will later be rendered in three dimensions. After this, when the design is finished, it must be exported in STL format for subsequent editing.
3. **Edit the previously created solid.**
To do this, using programs such as Meshmixer or Blender, the models are edited by adding necessary elements (such as injuries), eliminating possible imperfections, smoothing roughness, etc. These kinds of programs allow to perform boolean operations of union or subtraction between several objects, which are very useful when simplifying several models. Once finished, the model obtained is exported again in STL format and prepared for printing.

4. **Print the 3D model.**

When it comes to printing the model, depending on the printers available and the purpose of the model, two techniques can be applied:

- Silicone injection: if you only have printers that are not capable of replicating the texture of the areas to be used for training (for example, soft organs), the simplest method could be to print the solid model designed and edited and, also, a box with the negative of said model, so that silicone can be injected between the model and the box (as a mold) so that, when it dries, the silicone is left with the desired shape and texture.
- Printing using PolyJet technology: if this technology is available, the designed model can be printed directly with the desired texture, as it allows different textures to be simulated, adjusting it more exactly to reality.

7. 3D printers companies

Since 3D printing is a field in constant evolution, a list of companies could be more useful than mentioning specific 3D printers (Table 3).

Table 3. 3D printer companies related to the 3D printing technologies.

		TECHNOLOGIES			
		FDM	SLA	SLS	Others Technologies
3D PRINTERS COMPANIES	Prusa	X	X		
	Form		X	X	
	HP				MultiJet
	Sinterit			X	X
	Stratasys				PolyJet
	Ultimaker	X			

	Meltio	X			X
	Dynamical 3D	X			

8. Glossary

ABS: Poly acrylonitrile butadiene styrene

CAD: Computer-Aided Design

CT: Computer Tomography

DICOM: Digital Imaging and Communications in Medicine

HIPS: High impact polystyrene

MRI: Magnetic Resonance Image

PA: Polyamide

PC: Polycarbonate

PDMS: Polydimethylsiloxane

PGA: Polyglutamic Acid

PLA: Polylactic acid

PLC: Poly-L-caprolactone

PLY: Polygon File Format

PMA: Polymethyl acrylate

PMMA: Polymethyl methacrylate

PU: Polyurethane

PUR: Polyurethane rubber

PVA: Polyvinyl Alcohol

ROI: Region Of Interest

SLS: Selective laser sintering

SMA: Surgical and Medical Anatomy

SSTL: Physical models for basic surgical skills training in laparoscopy

STL: StereoLithography

TPE: Thermoplastic elastomer

TPU: Thermoplastic polyurethane

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D3.3. METHODOLOGICAL GUIDELINES FOR 3D PRINTING WITH TRAINING PURPOSES - ANNEX I: SCIENTIFIC LITERATURE REVIEW OF 3D PRINTING FOR MEDICAL AND MIS TRAINING

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Summary

This document is a supporting document for the Deliverable 3.3. *Methodological guidelines for 3D printing with training purposes*, and it consists of details on the literature review of 3D printing for Medical and Minimally Invasive Surgery (MIS) training that focused on aspects such as materials, technologies and applications of 3D printing for use as a training tool in MIS.

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1. ANNEX I: Scientific literature review of 3D printing for Medical and MIS training

1. Methodology

1.1. Search strategy

A structured bibliographical search was conducted in the PubMed database. We used a set of keywords related to 3D printing and MIS training to identify relevant studies published up to September 24, 2021.

The search string used was: ("additive manufactur*[Title/Abstract] OR "3D print*[Title/Abstract]) AND "Training"[Title/Abstract] AND "Surgery"[Title/Abstract]

1.2. Selection of Articles

A series of inclusion and exclusion criteria were considered to select the articles that best applied for our objectives. In general, articles which were about 3D printing in MIS training and written in English were selected. Those papers which subject was incorrect, papers not written in English, abstracts, conference proceedings, and review articles, were not considered for this study.

The articles finally included in this review were analyzed according to the following aspects: (1) applications of 3D printing technology in MIS training, (2) fabrication techniques, and (3) equipment and software for 3D printing.

2. Application in MIS training

2.1. General overview

This section provides the results presented in the articles analyzed with respect to their application in MIS training published up to September 24, 2021. The results are organized with respect to: (a) the surgical specialty, (b) the type of training, and (c) the anatomical structure to be simulated.

2.2. Surgical specialty

Several surgical specialties have been considered, as detailed in Figure 1. The surgical specialties that have shown the greatest application of 3D printed models for training have been neurosurgery, otolaryngology and urology. No studies have been found with the maxillofacial specialty.

It is worth mentioning the study by Marconi et al. (Marconi et al., 2019), where the authors performed 13 cases of robotic abdominal surgery on 3D printed model: 2 splenic artery aneurysm exclusions, 2 living donor nephrectomies, 5 renal tumors and 1 adrenal tumor resection, 2 total mesocolic excisions in right hemicolectomy and 1 vascular morphology anomaly (double renal artery).

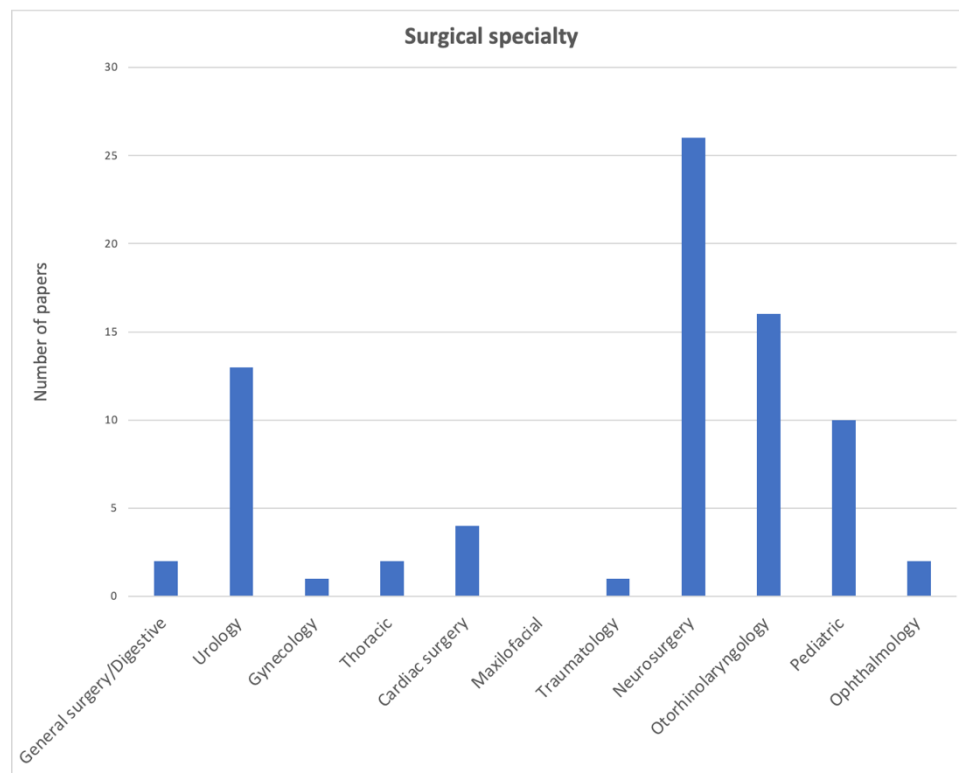


Figure 1. Surgical specialty.

Similarly, the popularity of the use of 3D printed models for training in different minimally invasive techniques has been analyzed (Figure 2). The results show that the use of 3D printed models most often occurs in training of microsurgery and endoscopic techniques .

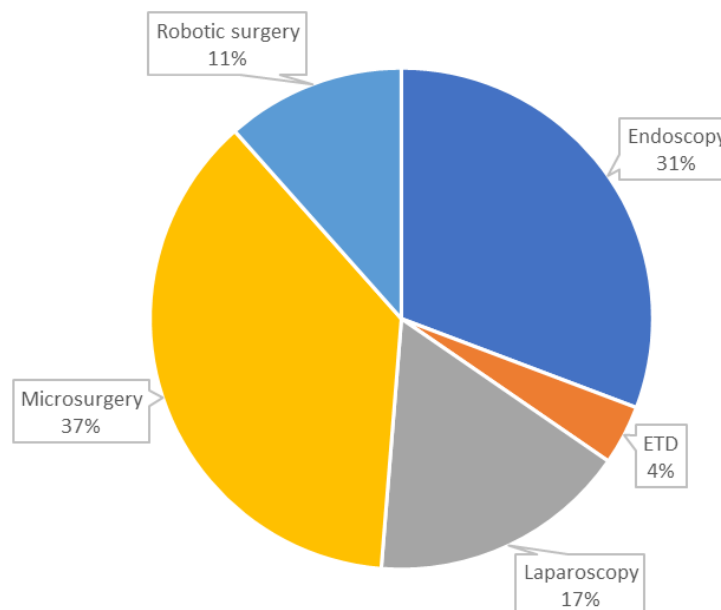


Figure 2. Minimally invasive surgical technique. ETD: endoluminal therapeutic and diagnosis.

The popularity in the use of 3D printed models has been analyzed by surgical spatiality and surgical technique (Figure 3). In this regard, the most widespread application in the use of 3D printed models are for training in neurosurgery using microsurgery and in otorhinolaryngology using endoscopic techniques.

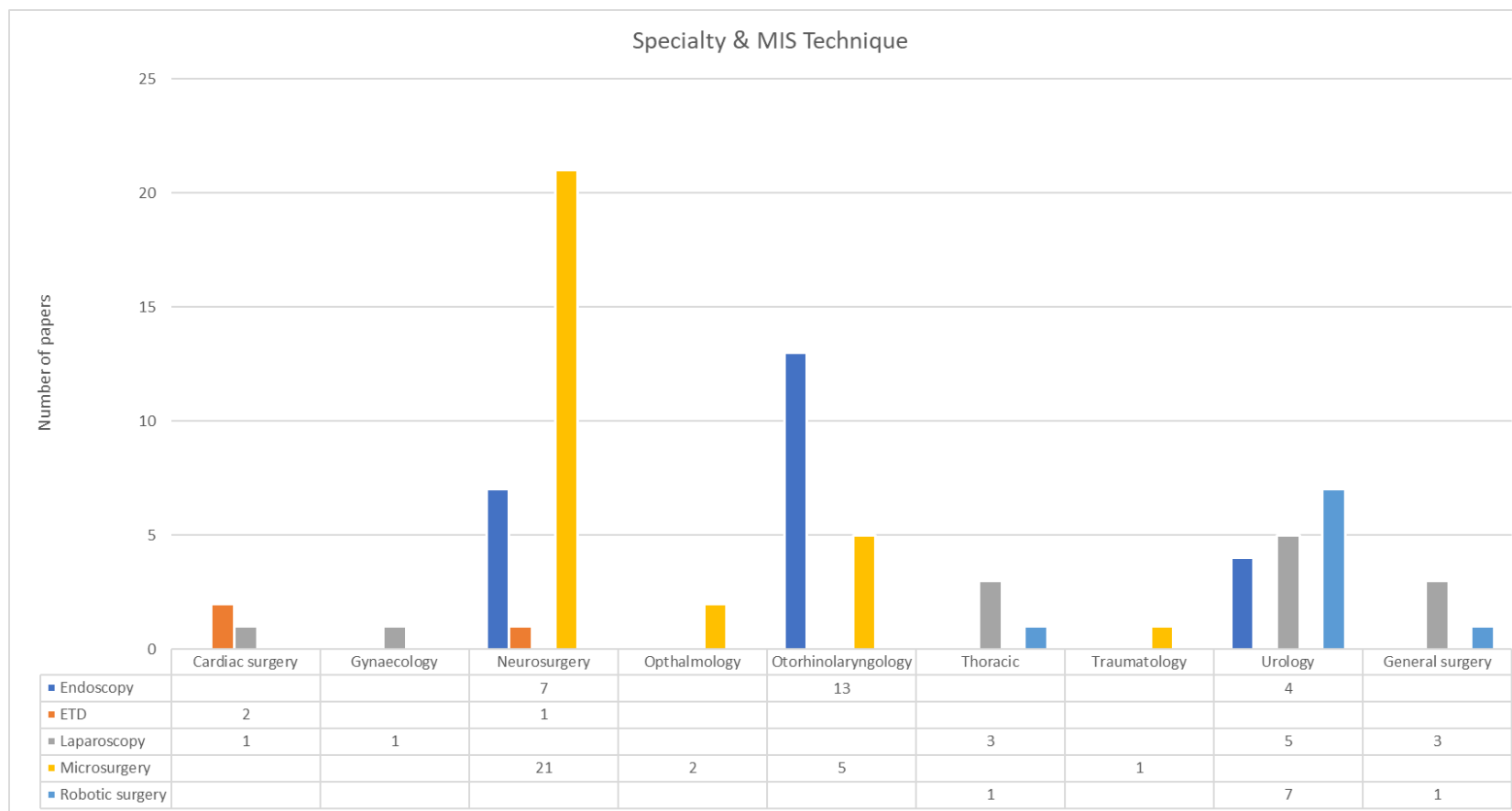


Figure 3. Application of 3D printing models for MIS training with regard to the surgical specialty and the type of minimally invasive technique.

If we analyze the anatomical structures that are usually printed for training according to the surgical specialty (Figure 4), we observe that the skull is the most popular structure, being used for training in neurosurgery and otorhinolaryngology. Other common structures are the head and neck for otolaryngology and the kidneys and urinary system for urological training.

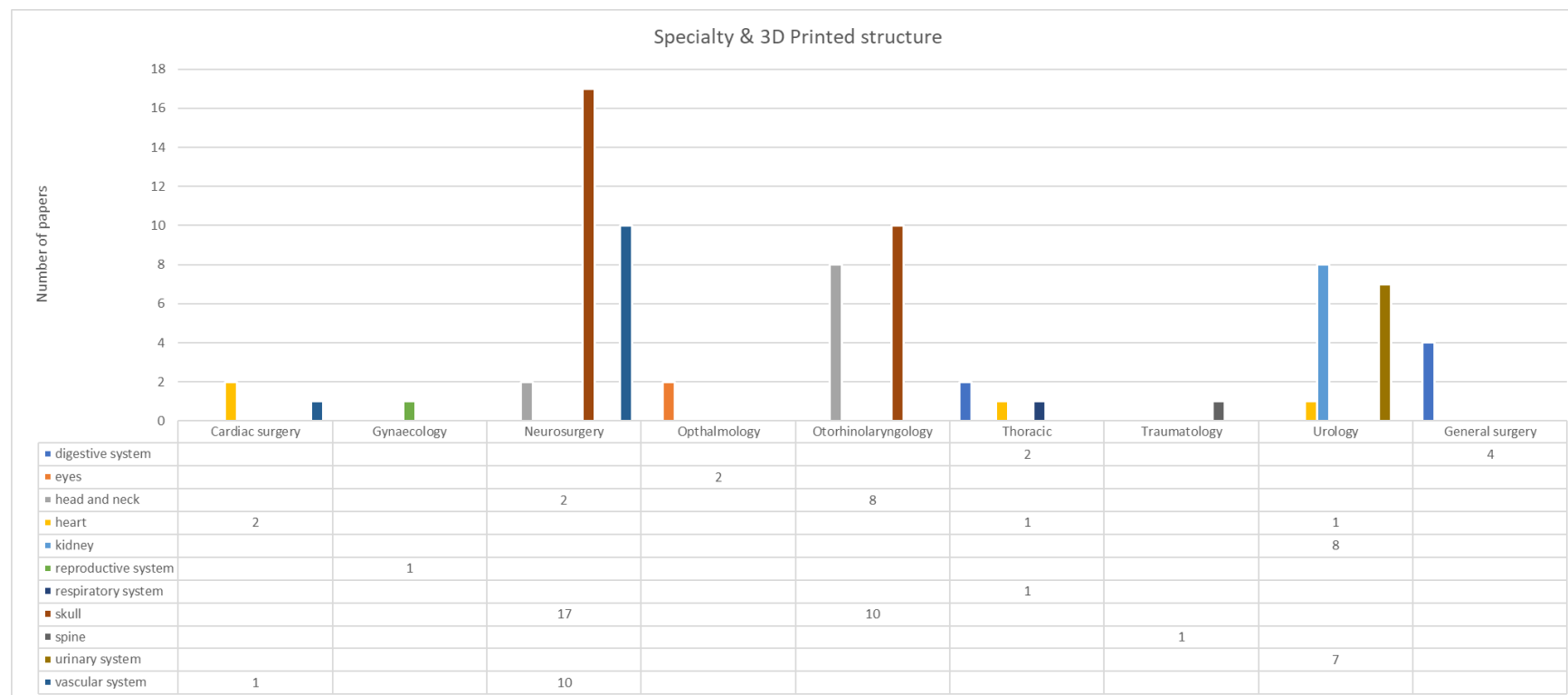


Figure 4. Relationship between 3D printed anatomical structures and the surgical specialty in which it is used for training.

If we look at the type of 3D printed structure (rigid, soft, rigid and soft), we see that the anatomical structure that has been printed most often in rigid and rigid and soft materials is the skull. As for the anatomical structure that has been replicated the most with soft materials is the kidney (Figure 5).

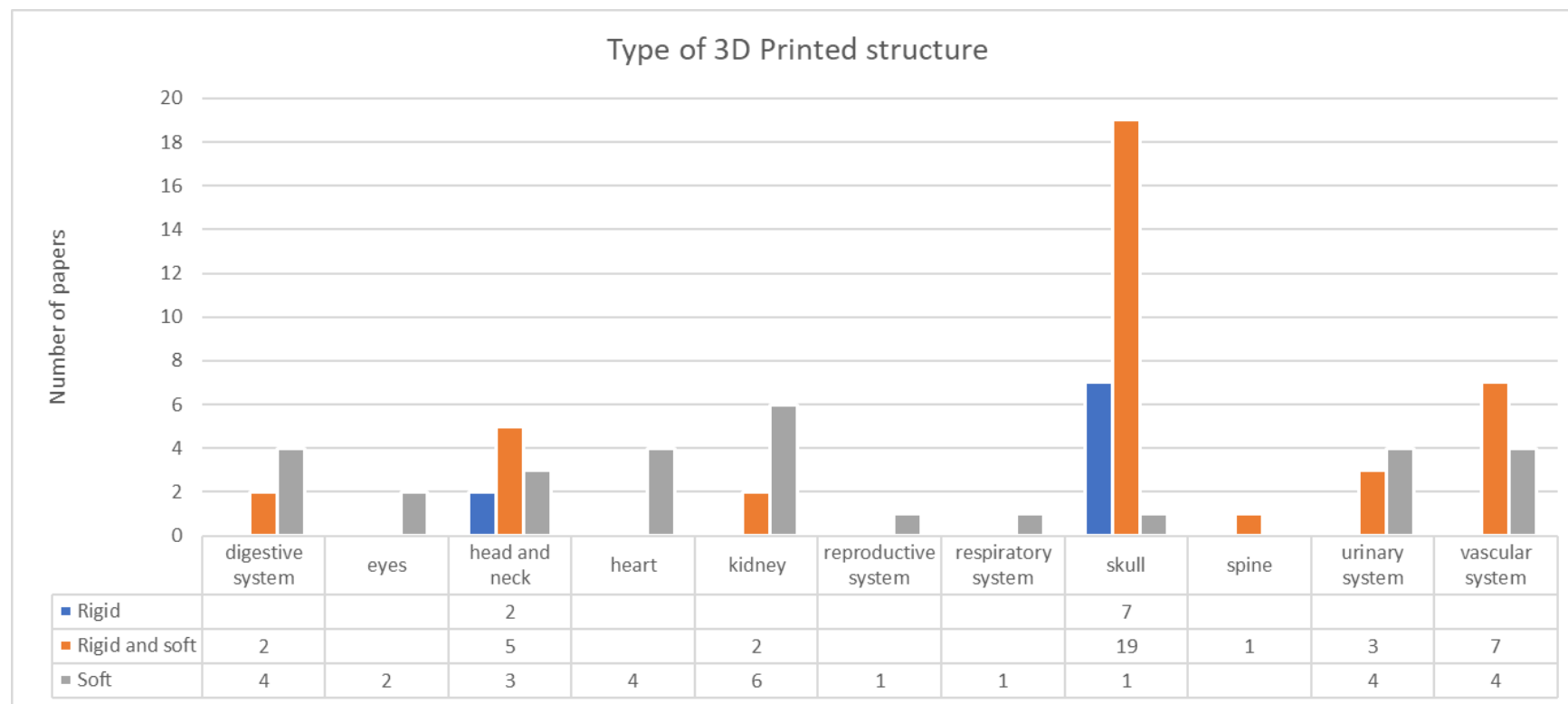


Figure 5. Type of 3D printed structure (rigid, soft, rigid and soft).

The anatomical structures most commonly 3D printed for anatomical training in MIS have been the head and neck for anatomical training in otolaryngology and the urinary system for urology (Figure 6). As for the type of structure, the kidney printed in soft material has been the most used (Figure 7).

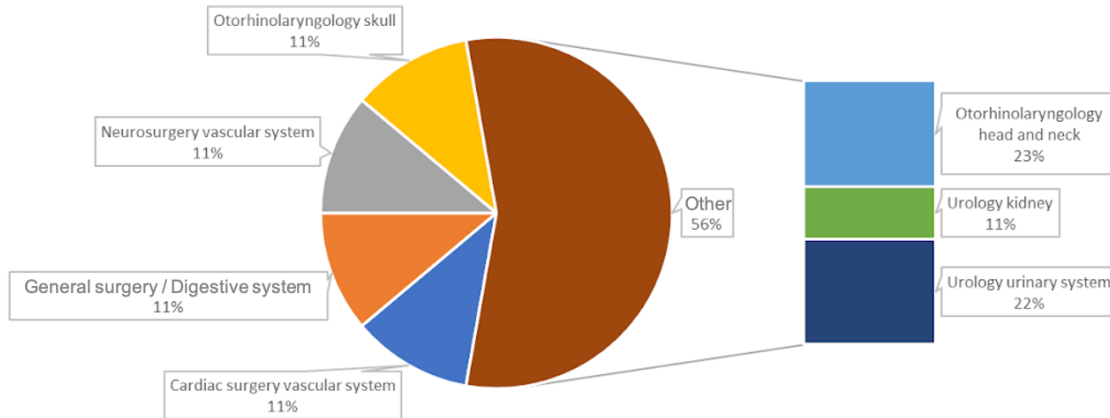


Figure 6. Type of anatomical training. Percentage of articles including this information.

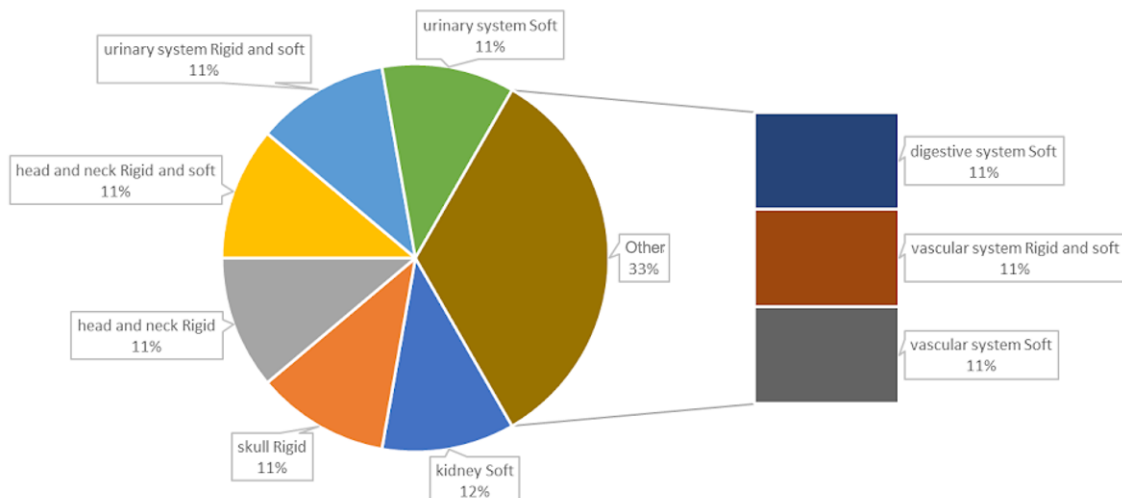


Figure 7. Type of 3D printing according to the anatomical structure for anatomical formation. Percentage of articles including this information.

The anatomical structures that have been most commonly 3D printed for hands-on MIS training have been the skull and vascular system for neurosurgery, as well as the skull for otolaryngology (Figure 8). Regarding the type of structure, the vascular system printed in rigid and soft material and the kidney printed in soft material have been the most used (Figure 9).

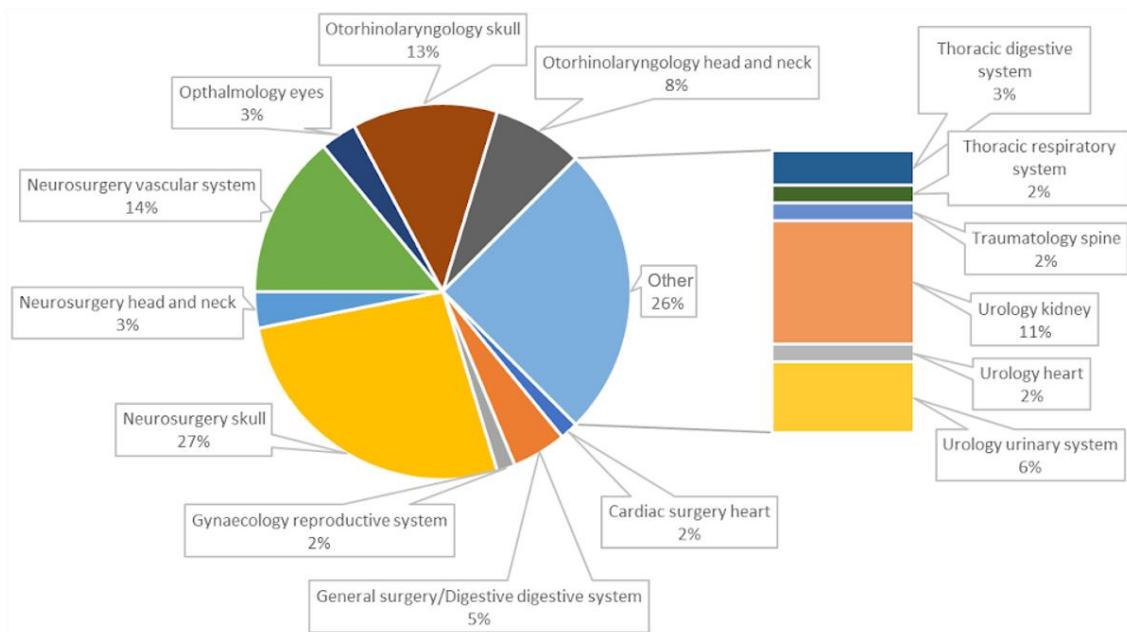


Figure 8. Type of hands-on training.

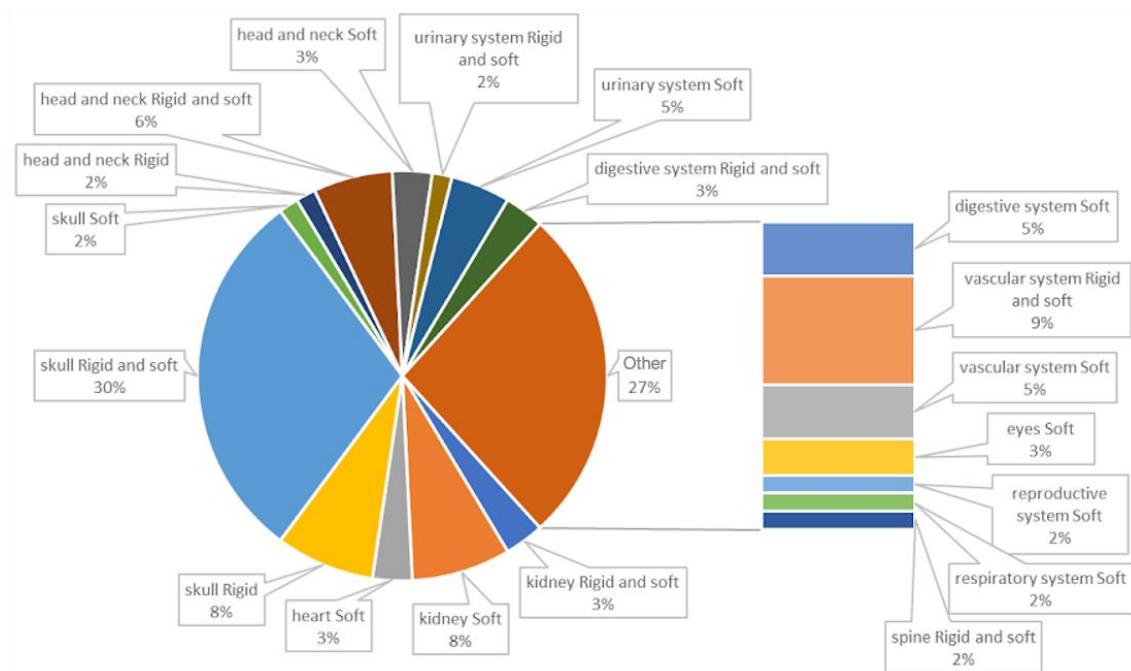


Figure 9. Type of 3D printing according to the anatomical structure for anatomical formation.

2.3. Recommendations

As an initial and fundamental step in the use of 3D printing in MIS training, it is recommended to use advanced medical imaging technology to obtain high-resolution

images, such as computed tomography (CT) or magnetic resonance imaging (MRI). These technologies should be able to distinguish similar densities of different tissues, and this is essential to adequately simulate tissue characteristics (Coelho et al., 2021). In addition, the quality of the materials is very important to simulate the different structures, so it is advisable to use high resolution multi-material printers (Alrasheed et al., 2017). On the other hand, since 3D printing of these models is sometimes a complex process, it is recommended that this is carried out by qualified technologists (Maddox et al., 2018).

Many studies represent soft or rigid anatomical structures, but most of them recommend future developments and improvements to include complex or advanced features in their models. They focused their interest mainly on two approaches: 1) to increase the current effort in the analysis and measurement of human tissue that is highly determinant for each specific formation and, 2) to develop new formation models with this specific mechanical behavior that will be closely related to new materials or a better use of the current ones. Importantly, several researchers set out to improve their studies in the future with additional and better grouped subjects that can test their 3D printed models. In this sense, studies conducted at a single center or by a few surgeons propose future experiments with more participants from several institutions. The results could be better if the studies were performed by many surgeons from a wide variety of centers.

In general, rigid models are more advanced and allow their application to a wide variety of MIS training activities. Rigid anatomical structures, such as the skull, are the most widespread for both anatomical and hands-on MIS training. These 3D printed models have been mainly employed for training in neurosurgery as well as otolaryngology. The surgical techniques most commonly used in these training applications have been microsurgery and endoscopy. This wide application of these types of structures for MIS training may be largely due to the ease of creating these models by additive printing as they are rigid structures, with the sole exception of small anatomical structures that can be complex to model and print. Therefore, the use of additive printing is recommended for the development of rigid anatomical models for use in both anatomical and hands-on MIS training. Perhaps, one of the main challenges for these structures is to achieve adequate material behavior when they are intended to be used in milling tasks for hands-on training, for example in neurosurgery.

With regard to soft anatomical structures, it seems that the most widespread are those that present a semi-rigid behavior, as is the case of the kidney. In this case, more flexible anatomical structures such as the liver are avoided. This may be due to the high degree of complexity involved in finding a material that can offer behavior similar to that found in these structures. The most common technique for the fabrication of soft anatomical structures such as the kidney is usually the use of molds. In this sense, the molds are created by additive manufacturing techniques in rigid material, mainly by obtaining the negative mold from the anatomical structure previously segmented from the preoperative imaging study. The resulting mold is finally filled with a material that simulates the behavior of the tissue to be simulated, such as silicone. Although 3D printing is the main focus of this guide, we have detected that molding is still widely used to obtain soft models. Therefore, 3D printing is recommended to produce better or customized molds for generating silicone-based structures.

Among the main limitations of 3D printed models for use in MIS training, both rigid and soft, are usually the lack of some typical human tissue behaviors such as bleeding, fluid appearance or pulsatile sensation, and that sometimes tissues may have a behavior

(mechanical properties) when interacting with surgical instruments that is not very close to reality. However, both of them are positively scored by clinicians asked through a survey or other kind of subjective/qualitative tool.

As aspects to highlight in the use of 3D printed models for MIS training, we will point out that the use of these training tools allows training in a controlled environment, replacing and reducing the use of experimental animals for the initial phases of surgical training. Therefore, the use of these 3D printed models is recommended as tools to fulfill the 3Rs (Replacement, Reduction and Refinement) principle in animal experimentation oriented to MIS training. On the other hand, it has been shown that the use of these models eases the learning curve in the performance of MIS tasks and procedures. Therefore, the use of 3D printed models is recommended to assist in the improvement of MIS competencies during the early stages of training.

2.4. Guidelines

In general, 3D printed training models can belong to two fields, on the one hand models for anatomical learning (anatomical models), and on the other hand models for practical training (hands-on models). In order to achieve a suitable model, two characteristics should be taken into account: fidelity (a facsimile of reality) and behavioral simulation (replicating functions or some functional aspects). In order to create models with both features, a compromise between fidelity (facsimile) and behavior (mimicking) is required (Figure 10).

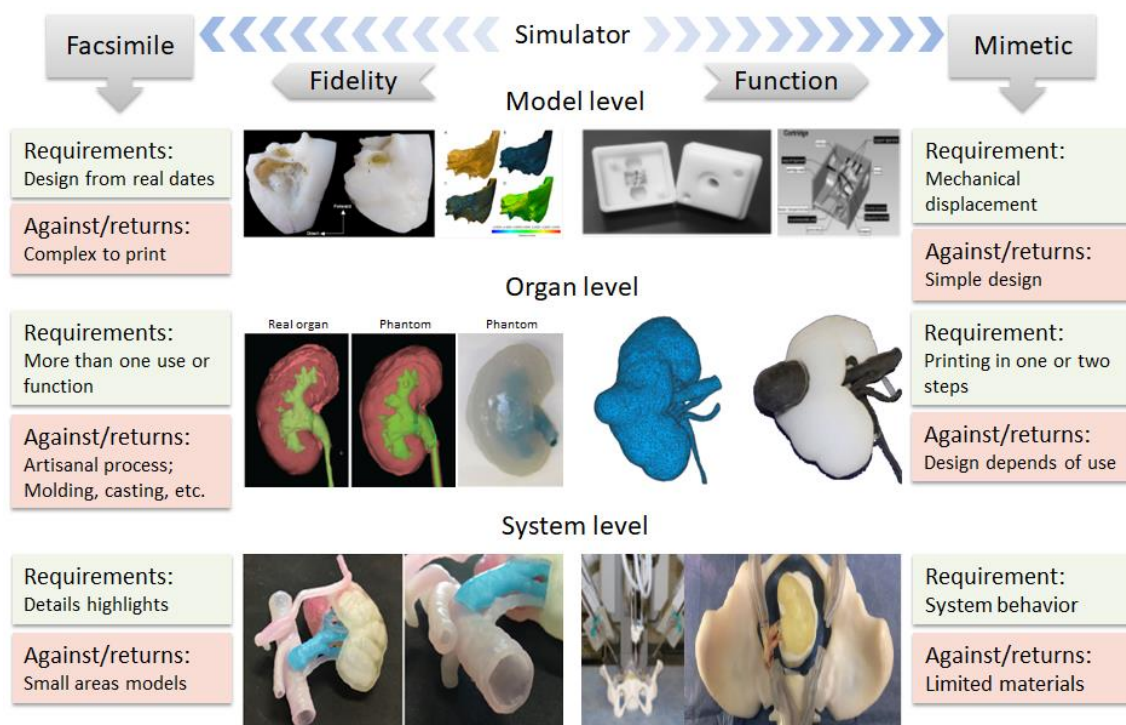


Figure 10. General scheme of the type of material to be used if an anatomically reliable model (fidelity) or a functional model is desired (mimetic). The models are arranged by anatomical (model level), organ and system levels.

The fidelity of the models implies that the model fits real parameters and can be customized models for patients; on the other hand, there are models that seek to replicate some biomechanical properties or functions. In the case of printed models, if we opt for fidelity, we have to sacrifice part of the functionalities. That is why the models have different levels of detail, depending on the area covered, so we have models at the level of anatomical area, organs and systems. Within each level each model will conform to certain parameters, which establish a compromise relationship between them. Some of these parameters are the printing speed, the realism of the model with respect to the biomechanical behavior, among others. Thus, being realistic could mean having to work with small areas or even reducing the size of the model. On the other hand, being faithful to the behavior of the model could imply having to work with few (small number of) materials.

Step 1. Choose the type of MIS training application

With the above in mind, the first step in determining the type of material we can use for the development of the 3D-printed model for MIS training is to decide on the application we are going to focus our model on. That is, whether it is an anatomical training application or a hands-on training model.

1. 2.4.1. Anatomical models obtained from a mold (SMA)

In this case, the aim is to develop an anatomical model with aesthetic and sensory perception characteristics similar to the real ones. The more aspects are presented in the model, the more stages are necessary and the development of models becomes more artisanal. In these cases, 3D printing becomes an auxiliary procedure with which to produce the most precise details. To do this, it is necessary to follow a series of steps for the materials that make up each of its elements.

Step 1. Mold manufacturing

For the manufacturing of the mold on which the materials that form part of the model will be injected, we should use a mechanically resistant material such as Polymethyl methacrylate (PMMA).

Step 2. (Optional) Fabrication of the removable material

This part of the model should be manufactured with a material that can easily be removed once the model is created, such as thermoplastic (e.g., wax) or hydrosoluble (e.g., PGA) materials. Its main application is the creation of structures (e.g., blood vessels) or internal cavities in the model.

Step 3. Fabrication of the tissue

In order to create the external tissues of the anatomical model (e.g., parenchyma), which are usually soft tissues, we can use materials such as hydrogels (PVA) or silicones (PDMS).

Step 4. Final assembly

For the final assembly, the internal structures (Step 2) will be placed inside the mold (Step 1). Then, the mold will be filled with the material that composes the tissue of the anatomical structure (Step 3). Finally, if necessary, the internal structures will be removed from the model.

2. 2.4.2. General anatomical models (SMA)

For models that are of a broader nature, in which several anatomical systems are collected, in which certain peculiarities are to be emphasized in detail, the system requires materials of different behaviors, which means that different 3D printing techniques are required, which work with different materials.

Step 1. Choose model layers and materials

For these types of models, it is necessary to know the layers of the models. Each of these layers usually corresponds to a type of anatomical structure or tissue.

Depending on the characteristics of these anatomical structures we will use different materials:

- Highly elastic structures (e.g., skin): Elastomeric silicones or elastomeric photoresin
- Semi-rigid structures (e.g., muscles): Rigid silicones, Thermoplastic polyurethane (TPU), elastic photoresists
- Stiff structures (e.g., bones): Rigid photoresists, Polylactic acid (PLA), photoresist composites
- Spongy structures (e.g., organs): Soft photoresists, Polyurethane (PU), TPU

In general, anatomical models seek the visual representation of anatomical elements, organs or systems, which implies that they should be a scheme/summary of the information that the student has to receive, mainly visually. This is why the realism of the design is critical, although with the aim of improving perception it is usually resorted to designing models that allow representing different aspects of the parts that make up the model (Figure 11). Those anatomical models, that represent both the form, and replicate

certain anatomical details, require a manufacturing process that consists of several steps that gives it a certain degree of complexity.

3. 2.4.3. Materials for anatomical training models (SSTL)

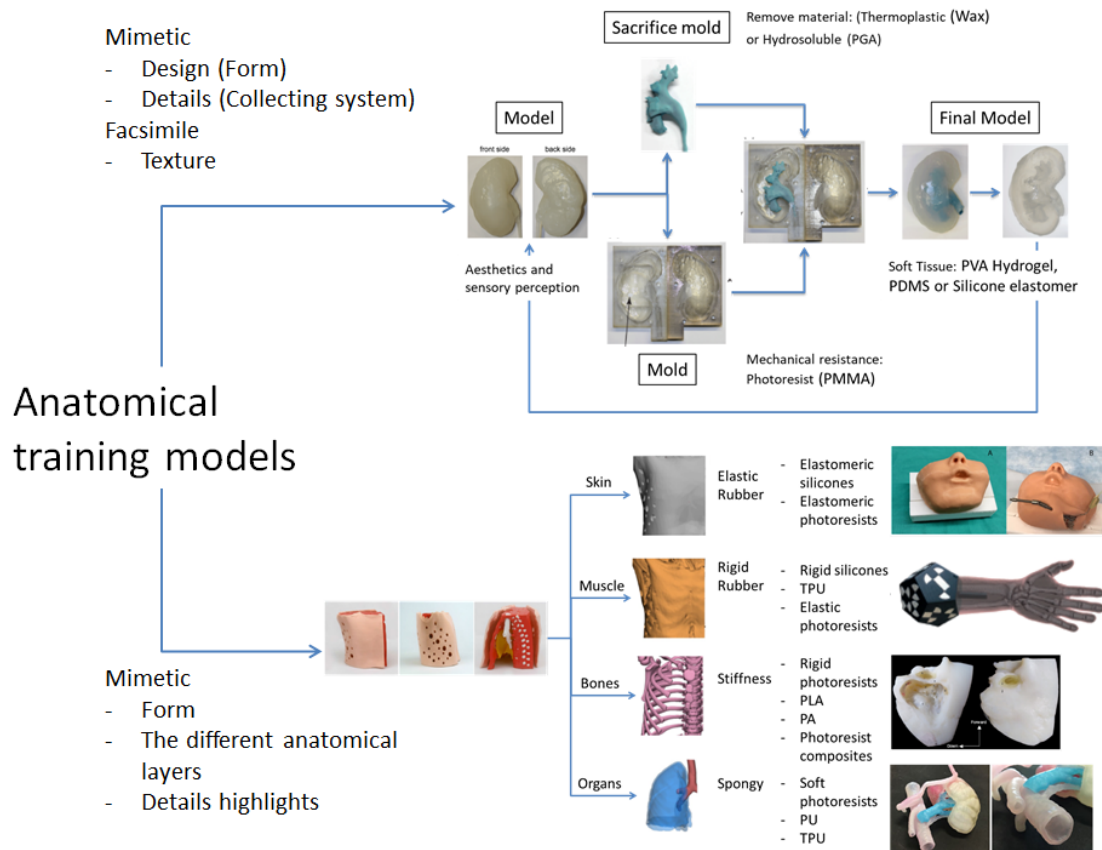


Figure 11. Workflow for the development of 3D printed models for anatomical training according to the expected reliability and functionality characteristics.

Step 1. Choose features of the 3D printed anatomical model

The first step in order to make the right choice of materials for the development of the 3D printed model is to determine the features that the model should meet (Figure 11). These features will focus mainly on anatomical similarities with respect to the real anatomical structure to be imitated, appearance, texture, among others.

3. Fabrication techniques

Review of the literature showed that published studies use a variety of fabrication techniques. The most widely used is Fused Deposition Modeling (FDM), followed by ColorJet Printing (CJP)/polyjet (see Figure 12). The popularization of the latter technique

is due to its ease of use, in addition to the possibility of producing models in different materials or colors in a single print and without the need for additional post-processing. Stereolithography (SLA) is also used in about one in ten articles, mainly because of its higher resolution. Selective Laser Sintering (SLS) is used in about one in twenty papers, due to its excellent resolution and good mechanical properties of the resulting parts. Finally, molding, in which other materials are first used to produce the molds, is also very common. In addition, it is worth mentioning that a surprisingly high number of studies do not specify the techniques used (N/A).

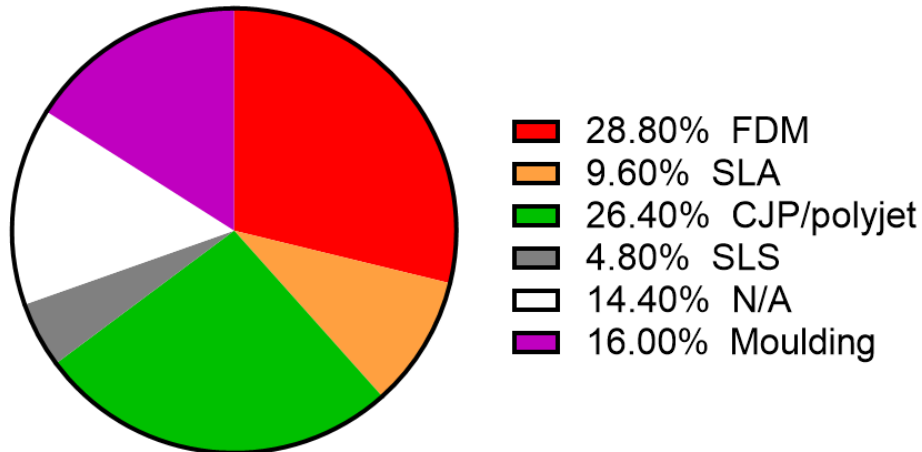


Figure 12. Fabrication techniques used to create the models. FDM: Fused Deposition Modeling; SLA: Stereolithography; CJP: ColorJet Printing; SLS: Selective Laser Sintering; N/A: techniques not specified by the authors.

3.1. General overview of fabrication techniques

The entire set of articles was examined for the description of the materials used to fabricate the 3D models. Of the 272 articles considered for this review, 95 articles were selected for this purpose.

The subset of papers revealed a variety of techniques and materials used to produce the models. In addition, a variety of tests were conducted to assess the quality, fidelity and functionality of the models. Several papers did not specify information on the materials or technology used.

Some of the reasons for implementing or using 3D printing techniques in the medical/surgical field are to develop realistic models for medical and surgical training and/or to use the models for planning the surgical strategy and to facilitate diagnosis and training in the detection of diseases and pathologies. For this, it is very important to achieve models that replicate the sensations of real tissues.

3.2. Materials

A wide variety of materials have been used to produce the models. In general, it has been observed that the larger the set of materials used to produce a model, the more complex and accurate the model is. The different materials make it possible to introduce, for

example, different mechanical properties. That is, the creation of sections with different tactile sensations or behavior during the simulation of the anatomical structure.

Regarding the most commonly used materials, according to the data extracted from the manufacturing techniques (Figure 13), they are the powders used in the CJP/polyjet techniques. Most of these materials are the property of each 3D printer manufacturer, so it is often impossible to know exactly their composition or synthesis process.

PLA and ABS, thermoplastic materials for FDM printing, are frequently used, possibly due to their ease of use and wide availability, as they are the most commonly used materials in entry-level 3D printing. Other thermoplastics for FDM, such as hips, polycarbonate, polyurethane, polycaprolactone and thermoplastic elastomers, are used less frequently. A common material for creating support structures in FDM is polyvinyl alcohol (PVA), which is easy to remove due to its solubility in water.

Resins are also frequently used for SLA. As with CJP/polyjet materials, they are usually supplied by the manufacturer, who does not reveal their chemical composition. However, resins with different mechanical properties (toughness, elasticity, etc.) are available, which makes it possible to produce model sections with different behavior.

SLS materials, such as nylon or polyamide, are rarely used.

Silicone is often used to be cast in molds produced by 3D printing. Silicone produces a tactile experience similar to that of soft tissue, and is easy to mold and remove very quickly.

Finally, in a number of papers, the authors did not specify the materials they used to create the models.

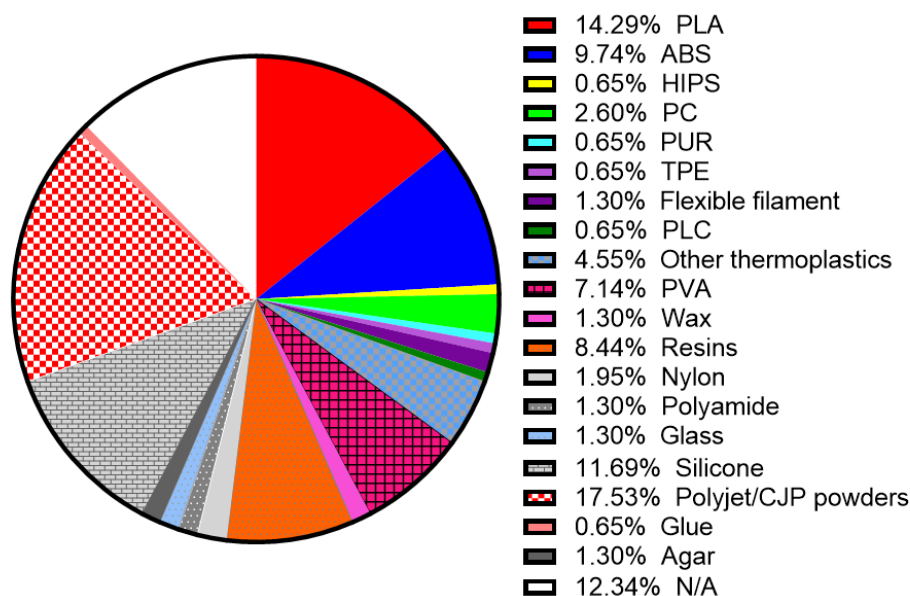


Figure 13. Fabrication techniques used to create the models. PLA: Polylactic acid; ABS: Polyacrylonitrile butadiene styrene.

Materials used for creating models can be classified according to the type of material (Figure 14). Thermoplastic materials are the most frequently used, followed by

CJP/polyjet powders. The third group in frequency are molding materials, such as silicone. Resins and support materials are also frequently used. We also note that in some cases materials of biological origin, such as eggs or animal organs, are introduced into 3D printed models. For example, calf brains were introduced inside 3D printed skulls so that surgeons could practice on the model.

In addition, only 3% of the studies used transparent materials to produce the models.

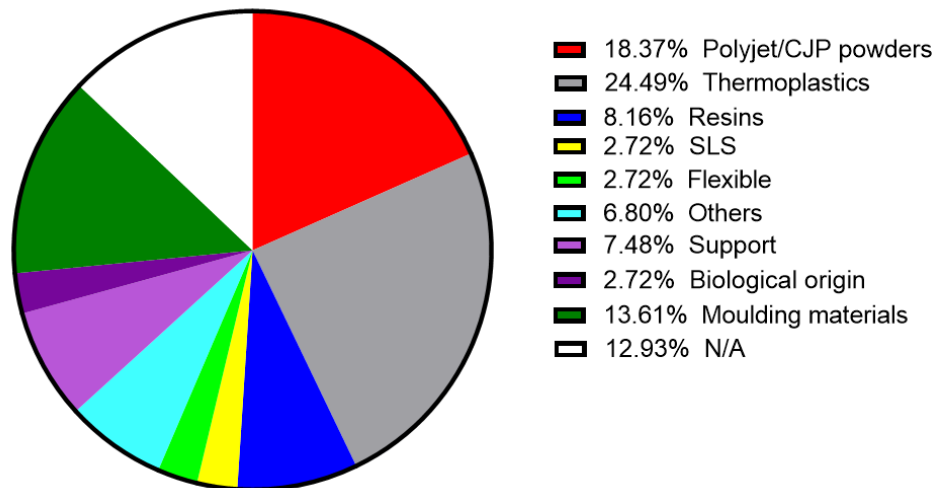


Figure 14. Material categories used in the creation of the models. SLS: Selective laser sintering.

From the point of view of models for practices, it is difficult to determine a particular list of materials that need to be used. Depending on the model, different behaviors or properties may be needed (Figure 15), meaning that different materials might need to be used.

3.2.1. Materials for hands-on training models

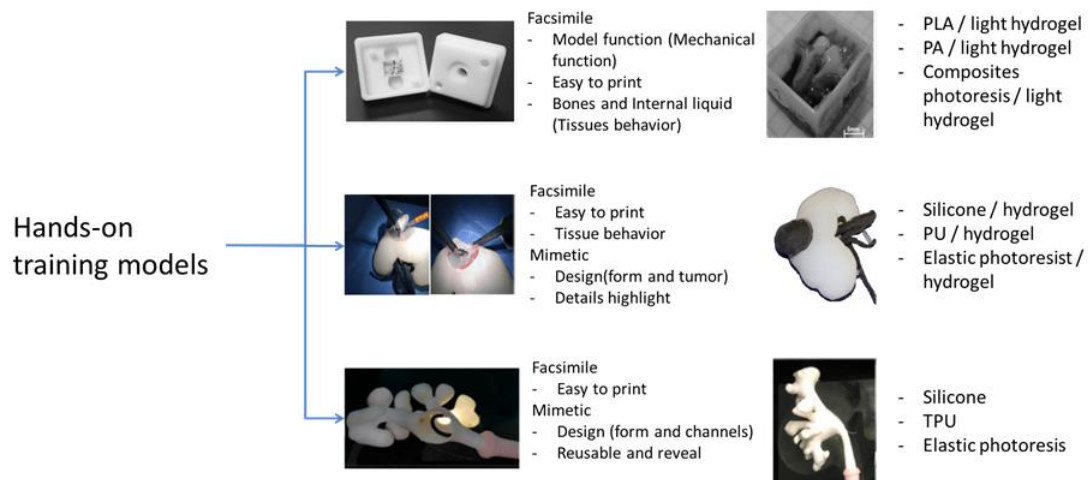


Figure 15. Workflow for the development of 3D printed models for hands-on training according to the expected functionality.

4. 4.4 Pre and postprinting processes

A small number of studies (7 out of 95) reported steps required before or after the printing process. These steps (Figure 16) included mixing coloring agents with the materials, preparing the materials for printing/moulding (e.g., mixing with curing agents), and, in one case, introducing a contrast agent into the material.

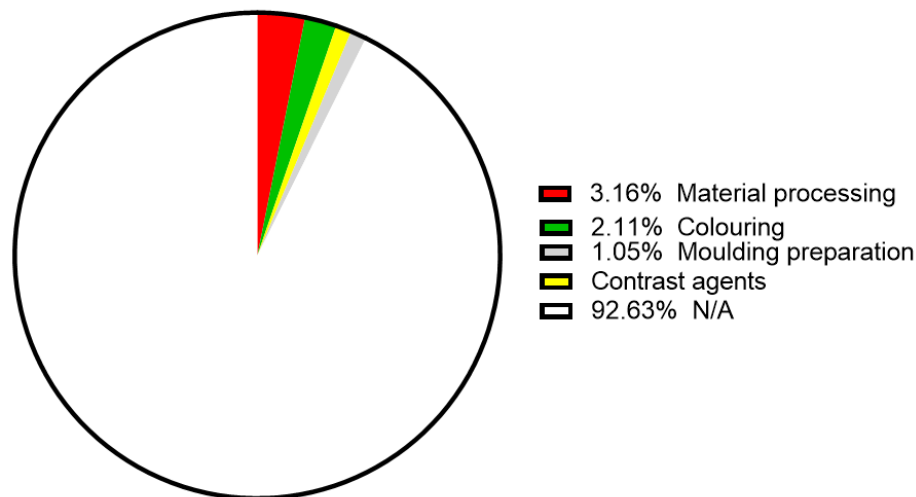


Figure 16. Pre-processing steps performed before the printing process, as found in the literature.

A larger number of articles report on the post-printing process. The most frequent process (Figure 17). is the removal of the support material, either manually (in the case of FDM thermoplastics) or using a chemical bath (e.g., water to dissolve PVA supports). The second most common process is the pouring of silicone or other materials onto the 3D printed parts that are used as a mold. Other common processes are the manual addition of parts (e.g., materials of animal origin, as mentioned above), coloring of parts to highlight different anatomical structures, cleaning of parts (e.g., to remove uncured resin residues on SLA-printed parts) or removal of excess powder in polyjet or SLS printing.

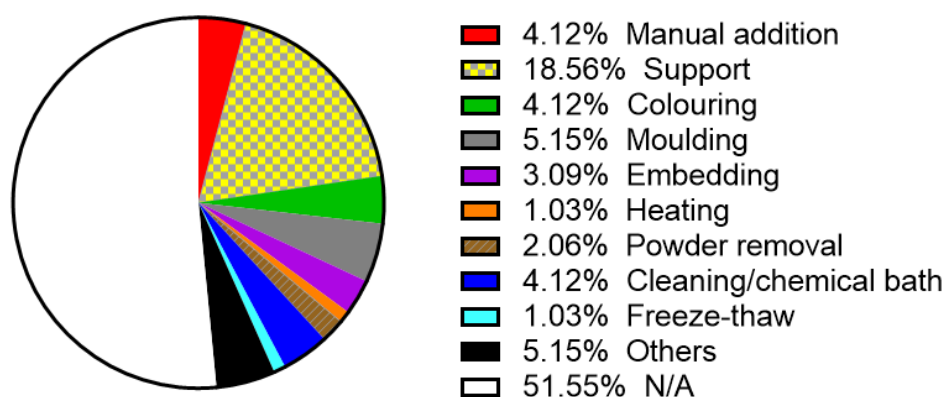


Figure 17. Post-printing processing steps performed after the printing process, as found in the literature.

1. 4.4.1 Printing parameters

The number of articles reporting the printer configuration parameters used to print the models is very low (Table 1). The scarce information jeopardizes the reproducibility of the results described in the articles, and prevents the expert reader from assessing the quality of the fabrication procedure.

The most reported parameter, z-resolution/layer height, remained in the range of tens of micrometers for SLA and SLS, and 100-500 μm micrometers for FDM and CJP/polyjet.

Table 1. Frequency of reporting printing parameters.

Parameter	Papers reporting the parameter value (%)
Resolution/layer height	23
Thickness of the outer perimeter	1
Nozzle temperature (FDM)	4.3
Bed temperature (FDM)	1
Printing speed (FDM)	2
Nozzle size (FDM)	2
Filling % (FDM)	2
Laser power (SLA)	0
Exposure time (SLA)	0
Laser power (SLS)	0
Temperature (SLS)	0

2. 4.4.2 Testing of the models

Several types of tests were performed to evaluate the quality, fidelity and functionality of the developed 3D models (Figure 18). The most common way to evaluate the model was to ask physicians, with different levels of experience and familiarity with the model, to perform a specific surgical task or procedure on the model and then fill out a questionnaire on its fidelity and functionality to simulate a specific surgery. In other cases, the evaluation was performed qualitatively without performing surgery, by means of a visual or tactile evaluation by expert surgeons.

As for the properties of the models themselves, some studies performed accuracy tests by quantifying the geometric parameters in the 3D printed model and comparing them with the values obtained in the images from which they were segmented. In a small number of cases, the models were also subjected to mechanical tests to quantify the mechanical parameters and compare them with those of the tissues they simulated. In a small number

of papers, the models were tested for use with diagnostic imaging techniques (e.g., ultrasound or fluoroscopy).

Finally, the models were also tested by evaluating the surgical performance of novice surgeons performing a specific surgical task for the first time. In two cases, the procedure was also recorded and some evaluation metrics were quantified during the first time the model was used and after several performances, such as the reduction in total time required to complete the procedure.

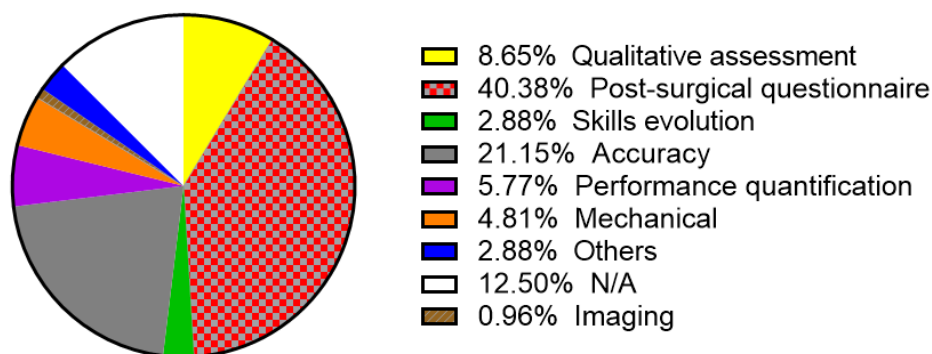


Figure 18. Methods to test the performance of the 3D printed models.

3.3. Guidelines

3.3.1. Planification

Step 1. To choose the functionalities of the model

The first step in the development of the training model is to determine the functionalities to be achieved with the model for hands-on training. The set of these functionalities will determine the design and the materials to be used for the different elements of the model.

Step 2. To choose the materials

As we have just mentioned, the set of materials to be used for the manufacture of the model will depend on the functionalities to be met.

We may need a model, that from the point of view of aesthetics is not quite realistic, but if it reproduces certain details or functions, such as the presence of components with a certain movement, or environments with certain conditions of pH, humidity, etc. In this case, materials such as PLA and photoresist composites can be used in combination with light hydrogels.

There are models that require a certain degree of realism, even customization (patient, pathology), but it is not needed that they reproduce even the slightest size. In these models what is sought is that they are quick to produce, and that it presents in a schematic way

the points of interest. Materials such as silicones, PU or elastic photoresist in combination with hydrogels can be used for these models.

Finally, there is a group of models that need to be as accurate as possible in their realism from a design point of view. These models are usually asked to be resistant, in addition to allowing monitoring and highlighting in some way the evolution of the model. Materials such as silicone, TPU or elastic photoresist can be used for these models.

3.3.2. Pre-processing

INPUT: STL or PLY 3D model

Step 1. To import the segmented 3D model into a CAD software

Carry out all the necessary steps for the import of the 3D model of the anatomical structure of interest segmented in the previous phases into the CAD software. This will allow for performing post-processing tasks on the 3D model.

Step 2. Optimization of the 3D model

The objective of this step is to optimize the segmented 3D model extracted from the previous phase. For this purpose, smoothing methods will be applied. In some cases, it would be also necessary to re-design some parts of the 3D model which could present design errors or do not have enough anatomical details.

Step 3. (Optional) Mold generation

In case what is intended to be 3D printed is a mold for the creation of the anatomical model, it is required to obtain the negative mold of this model. For this purpose, Boolean subtraction methods are generally used.

Step 4. Validation with medical professionals

Before proceeding to print the 3D model, it is recommended to validate the design obtained with medical professionals. In some cases, it may be necessary to return to step b to make adjustments to the design as recommended by medical professionals.

Step 5. To export the surface meshes

Once we have the 3D model optimized and edited, the surface meshes of the model will be exported to a standard 3D printing format (e.g., STL or PLY).

OUTPUT: STL or PLY 3D model

5. 3.3.3. 3D printing & model fabrication

Once we have the final 3D model to be printed and the materials to be used (see guidelines on the selection of materials for 3D printing of this report), the last step is to configure the printer to be used and proceed to print the model (Figure 19).

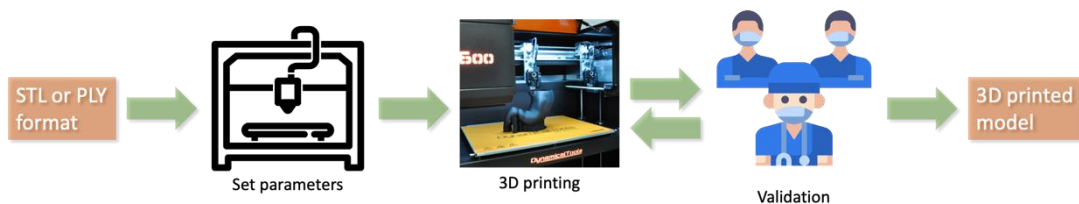


Figure 19. Flow diagram for the 3D printing and model fabrication phase.

INPUT: STL or PLY 3D model

Step 1. Configuring the 3D printing machine

The parameters of the 3D printer will be adjusted depending on the characteristics of the printer, the model to be printed, the type of material to be used (see guidelines on the selection of materials for 3D printing of this report), the expected level of detail, the printing time required, among other aspects.

Step 2. Printing 3D models or molds

During the printing process there are some additional steps to follow depending on the type of model to be printed. For 3D models, once printed, if necessary, the support material used for the printer during the printing process should be removed.

In the case of molds, used to cast soft-tissue models in various materials, they should be filled with the corresponding material (depending on the main training application) and removed the necessary parts (e.g., casting).

Step 3. Validation

Once the model is printed, it is necessary to carry out several types of validations:

- Validate the differences in geometry between the printed model with the designed 3D model and the initial DICOM study.
- Validation of the mechanical properties of the printed model with respect to the real anatomy.
- Validate if the printed model is suitable for medical professionals in terms of mechanical properties, esthetics and interaction.

OUTPUT: 3D printed model

1. 3.4. Recommendations

In this section we reviewed the medical publicized in recent years in the field of 3D printing, aimed at the development of simulation models both for the clinical study of medical pathologies, as well as for the practice and improvement of the skills of professionals in the medical-surgical field. In that data compilation, neither the field nor the medical modality in which the models were used, was critical for the study. So the number of models that were found, as well as the systems-organs that they simulate, were very diverse, making it clear that the current state of the art in the field of 3D printing model development is broad, and giving notions of the potential that 3D printing techniques present when developing models for the simulation and / or viewing of pathologies, with which to design the strategies to follow in order to achieve the highest degree of success in the interventions carried out by professionals from different medical fields.

Although, the main objective of the considered studies is undoubtedly to simulate the mechanical-sensory behavior that the doctor perceives during the interventions of the patients, with different techniques or equipment, a relevant part of the studies also focus on the design of models that are not so realistic from a sensory point of view, but rather focus on simulating operating conditions, such as duct sizes as well as key elements of organs and / or pathologies, in order to simulate movements / maneuvers to be performed when using certain types of intervention techniques, with which to exercise muscle memory.

A large number of the models that have been found are focused on the manufacturing training of laparoscopic techniques. In these cases, what has been seen is that the greatest possible realism is sought, so in most of the works they focus on the development of models with pathologies or damages such as cysts, tumors, abnormal morphologies, etc. For this reason, it is common to use models obtained from patients through medical analysis methods.

In most of the works on which we have focused our study, in relation to 3D printing techniques, as we can see on 1.3.1 the fused material deposition (FDM) techniques are the most used followed by CJP/Polyjet techniques.

From the point of view of the customized models manufacturing to specific clinical cases or techniques or for the development of organ or body region training models, the most used printers are based on FDM's. In the case of FDM machines, they are common to use as auxiliary techniques in tandem with other techniques and/or for print masks/molds, with molding the organs, the different components of the organs or part of the body region. The most common use for FDM is to print rejecting or sacrificial components, so for many of these cases are interesting to use soluble materials.

On the other hand, if the training models have structures with more complexity, with small details or/and require the identification of the different components/parts on complex systems such as the tilting or urinary systems, the CJP/Polyjet is the most used printing techniques as alternative to FDM. In these cases, what is sought to simulate is to achieve models of high precision in detail and the identification of the different parts that make up the models, and to a lesser extent the similarity in the mechanical behavior of

the model. This is so due to the limitation in the materials-inks available. In these cases, commercial resins are usually used, with a reserved composition from the most common houses, although the tendency is to adjust to those of the equipment brand itself. And both pigments are usually used from the origin, as in the case of color-jet (CJP) or expressly colored for the studies on which this report is based, the most frequent use being the polyjet equipment. The models printed by CJP/Polyjet techniques may be supported by FDM techniques, in the cases where a temporary component is required that have to be removed from the model, to keep some critical details or structures saved from a post processing treatment, as alternative to the wax.

From the point of view of the organs-systems, many of the simulator-models have been developed for medical techniques training, followed by models for the testing of surgical methods such as the removal of foreign bodies. The models of the urinary-renal system are the predominant one and the vascular and cranial systems are the next in frequency.

As the largest number of models are used for the training of laparoscopy techniques, the greatest possible realism is sought, which is why most of the works focus on the development of models with pathologies or damages such as cysts, tumors, abnormal morphologies, etc., so it is common to use models obtained from patients by medical analysis methods.

Models that seek greater realism in mechanical behavior, from the point of view of the perception of the physician/student, silicone is used as the main manufacturing material followed by polyurethane foams (PU), in particular to simulate tissues with structural activity such as skin, muscle or connective tissue. To work with this kind of materials the more appropriated technique are the molding techniques, therefore to fabricate the simulators, it is easiest to print by FDM the molds with the required specifications.

Attending to the simulation of the mechanical behavior of tissues with a spongier character such as the organs textures (kidney, lung, central nervous system...) the most spread-out materials are the mixtures in different proportions of silicones and hydrogels. The proportion that will be used for each of the components depends on the degree of rigidity of the tissue at simulate, the components of the nervous system are usually formed mainly by hydrogels being those of PVA the most used presenting the highest degree of satisfaction, while for tissues similar to the kidneys, a silicone model or to a lesser extent polyurethane foam (PU) of the organ is used, with the inner coated with a hydrogel. As alternative to PVA hydrogel are other materials such as Agar.

On other hands, only in those cases in which the model to simulate must have a behavior similar to that of bone, the more appropriated technique is the SLA, since it is a technique that uses photocurable resins in which the formulations can be present agents of a ceramic nature, such as hydroxyapatites or metal oxides such as alumina.

Regarding the methods of testing the models, we observed that qualitative assessment and post-surgical questionnaires represent around 50% of the tests, while the accuracy of the models was only quantified in roughly 20% of the papers, and the mechanical properties in less than 5%. This represents a paradox, as the models should accurately reproduce both the geometrical features and the mechanical properties of the organs they represent. Therefore, introducing both accuracy quantification and mechanical testing of the models as standard tests is strongly recommended.

2. 4. 3D printing equipment and SW

In this section we will review the type of 3D printing equipment most commonly used for printing 3D models for MIS training, as well as software for designing and preparing the models for printing. Finally, we will indicate some recommendations to consider for future developments in this area.

1. 4.1 Equipment

A wide variety of companies with a 3D printer on the market were analyzed in the selected articles. A total of 98 articles mentioned the printer company with which they had 3D printed (Figure 20), of which Stratasys (LTD, Eden Prairie, Minnesota, USA) stands out above the rest with a total of 34 articles mentioning that they had used their printers, followed far behind by 3D Systems (Rock Hill, Southern California, USA) with 14 mentions, Ultimaker (Utrecht, The Netherlands) with 11 and Formlabs (Inc., Somerville, MA, USA) with 8 mentions. The remaining articles are distributed among 15 other different companies.

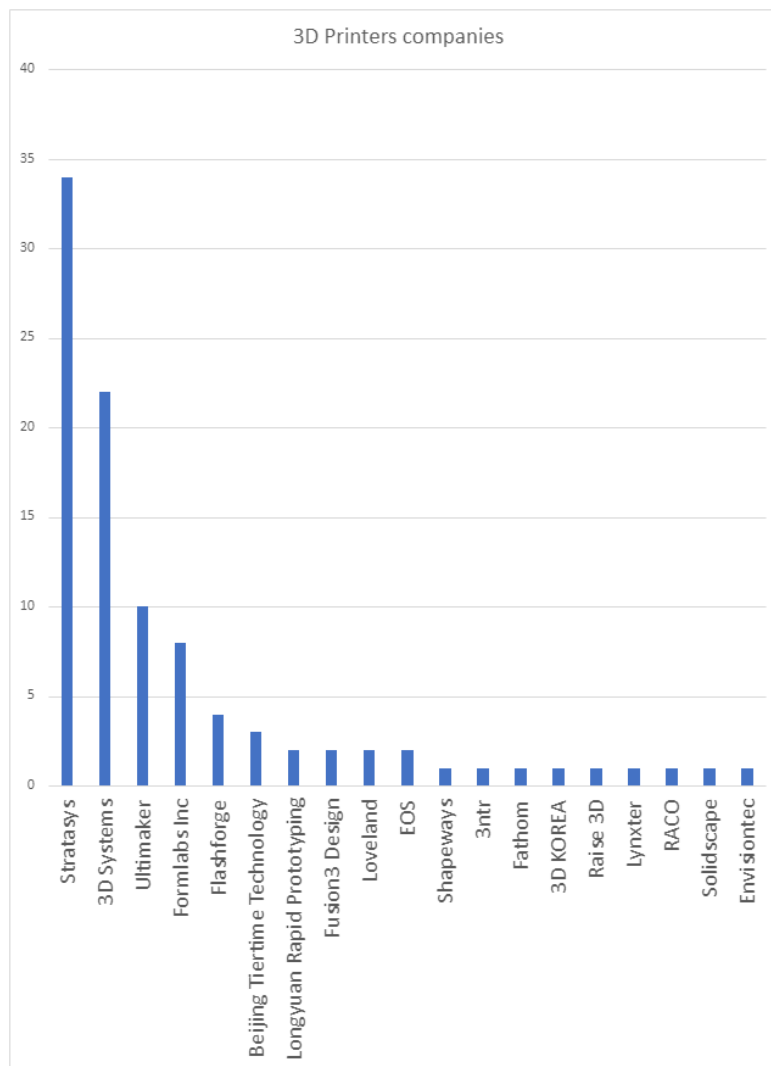


Figure 20. Overview of the 3D Printers companies.

Given the large number of articles (34) using Stratasys 3D printers, we proceed to break down their different printer models (Figure 21), highlighting the use of the Objet 500 Connex model with 8 mentions, followed by three mentions of the Objet 350 Connex, Objet 260 Connex, Objet 30, Objet J750 and Objet Connex models without specifying the specific model.

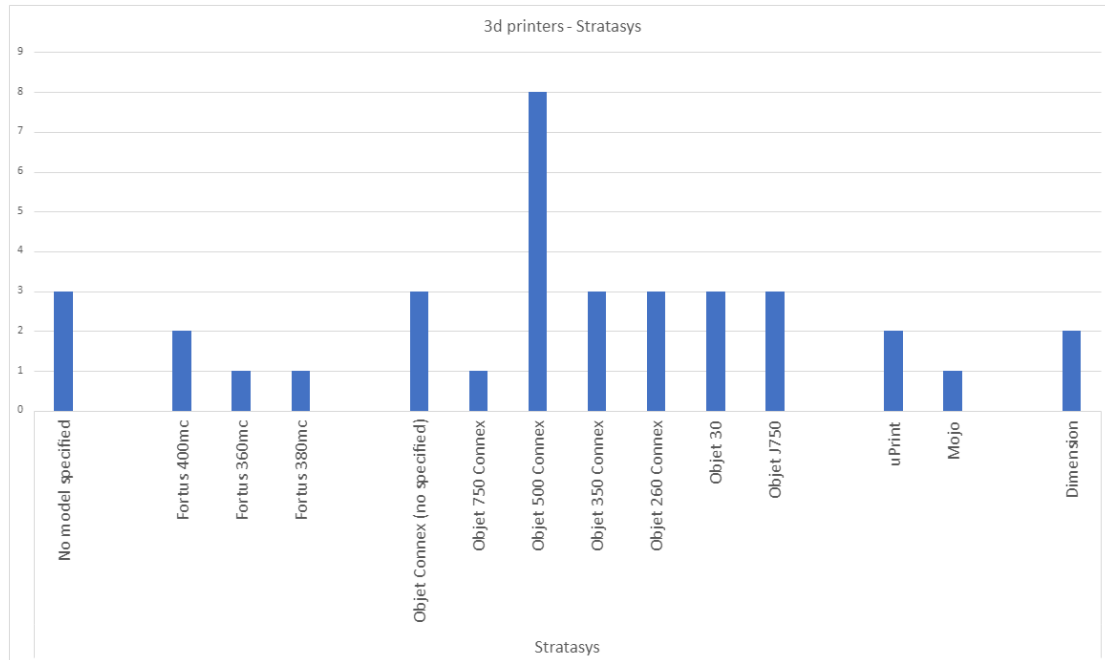


Figure 21. 3D Printers from Stratasys.

The particular models of the 3D Systems company were also broken down, appearing in 22 articles (Figure 22). We will highlight the ProJet 660Pro model with 5 mentions, followed by the ZPrinter 450 with 4 and the ColorJet Printing with 3.

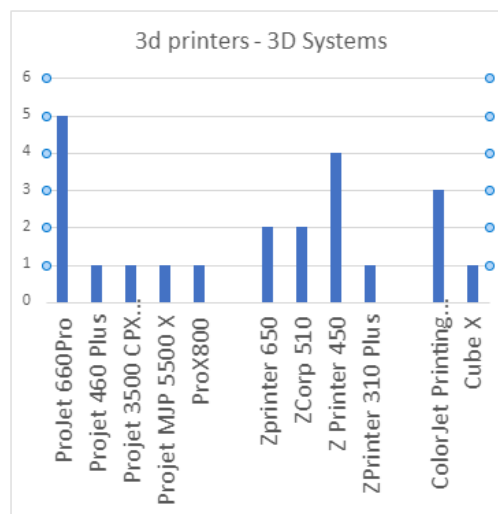


Figure 22. 3D Printers from 3D Systems.

The Ultimaker company appeared in 10 articles (Figure 23). Specifically, the Ultimaker 3 Extended and Ultimaker 2 Extended printers were used in 3 studies each. Other Ultimaker 3D printer models were used in four other studies.

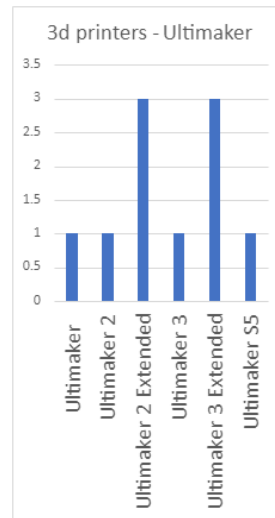


Figure 23. 3D Printers from Ultimaker.

The rest of the articles are distributed among different 3D printer models from various companies in the industry (Figure 24), highlighting Formlabs which was mentioned in 8 articles (of which 6 mentioned the Form 2 printer), FlashForge (Zhejiang Flashforge 3D Technology Co, Ltd, Jinhua, China) with 4 mentions, Beijing Tiertime Technology with 3, Longyuan Rapid Prototyping (Longyuan Rapid Prototyping Ltd, Beijing, China) with 2, Fusion 3 (Fusion3 Design, Greensboro, NC, USA) with 2, Loveland (Loveland, Colorado, USA) with 2 and EOS (EOS GmbH, Munich, Germany) with 2 mentions. Other studies, while mentioning that a 3D printer was used, do not specify the model or the corresponding company.

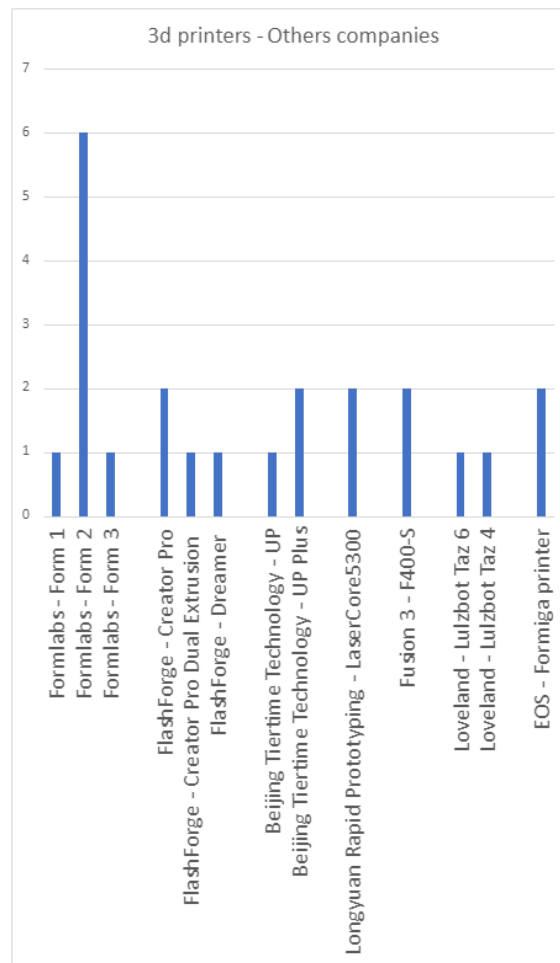


Figure 24. 3D Printers from other companies.

2. 4.2 Software

The printing software will be in charge of laminating the 3D model and configuring the printing parameters of the 3D printer. As for the mentions in the articles that referred to the specific software to perform the printing, only 11 specified the software that was used to print the 3D model (Figure 25), highlighting the Ultimaker Cura software (Ultimaker B.V., Geldermalsen, The Netherlands) with 5 mentions and the remaining 6 articles are distributed among 6 different software.

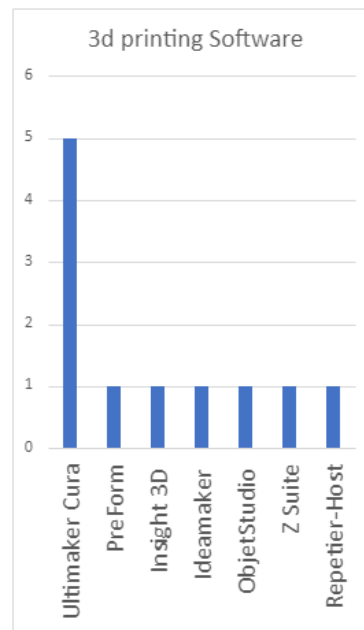


Figure 25. 3D Printing software.

1. 4.2.1 Import Software

To obtain the three-dimensional model from a preoperative study of a patient performed by computed tomography (CT) or magnetic resonance imaging (MRI), medical imaging software is needed to segment the anatomical part to be printed, generating a file in STL or PLY format. This approach encompasses the vast majority of the articles reviewed, accounting for almost 74% of the total (Figure 26). Another approach to obtaining a three-dimensional model is based on CAD design from the medical image measures. This approach is less used, accounting for 9% of the total. 17% of the articles did not specify how the three-dimensional model was obtained.

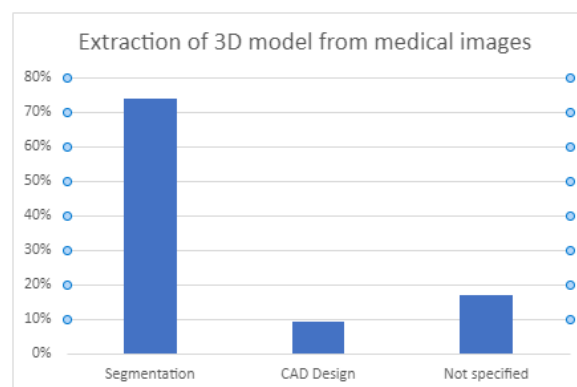


Figure 26. Extraction of 3D models from medical images.

A total of 71 articles specified in particular with which software the import of the preoperative study was performed to create the 3D model (Figure 27), highlighting the software Materialise Mimics (Materialise, Leuven, Belgium) with 35 mentions, followed by 3D Slicer (Open Software, Boston, Massachusetts, USA) with 11, OsiriX (Pixmeo SARL, Bernex, Switzerland) and InVesalius (Centro de Tecnologia da Informação

Renato Archer, Campinas, Brazil) with 4, MITK (Institute of Automation, Chinese Academy of Sciences, China) and Amira (Thermo Fischer Scientific, MA, USA) with 3, TeraSalius (Thermo Fischer Scientific, MA, USA) with 3, and TeraSalius (TeraSalius, China, USA) with 3, and TeraSalius (TeraSalius, China, USA) with 3. USA) with 3, TeraRecon (TeraRecon, San Matteo, CA, USA) and MeVisLab (MeVis Medical Solutions AG, Bremen, Germany) with 2 and the rest distributed among 7 different software.

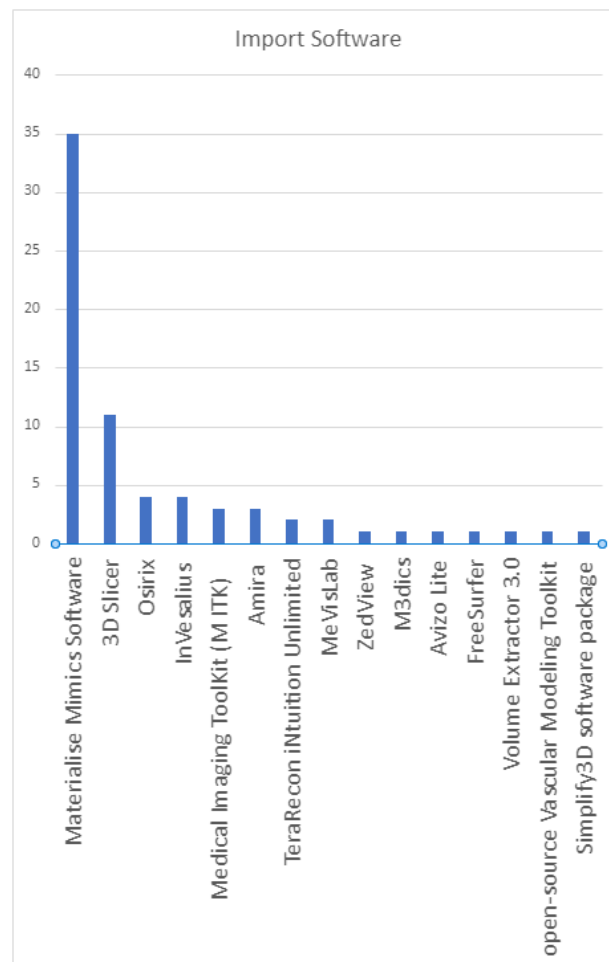


Figure 27. Import software.

2. 4.2.2 Modelling Software

Once the 3D model has been obtained in STL or PLY format, a subsequent process will be necessary in which the model will be cleaned, smoothed and modified for the specific use it is to be given. These software applications are also used to make the necessary corrections to make fillable molds by means of holes or negative molds. The Meshmixer and Materialise 3-Matic (Materialise NV, Leuven, Belgium) programs were the most commonly used, with a total of 11 articles mentioning their use (Figure 28). Solidworks (SOLIDWORKS Corp., Waltham, MA, USA) had a total of 7 mentions, Meshlab (Visual Computing Lab, ISTI-CNR, Italy) 6 mentions and Blender (Blender Foundation, Amsterdam) 5 mentions. The rest of the 18 papers used 12 different computer programs to perform post-processing of the 3D model.

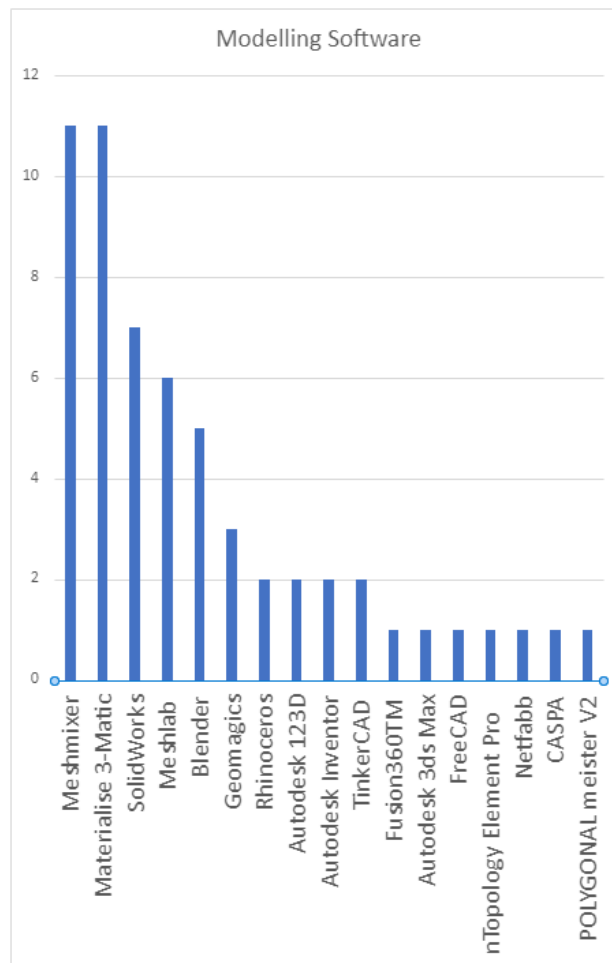


Figure 28. Modelling software.

3. 5. General guidelines

1. 5.1 Data collection

The first step is to perform a medical imaging study (CT, MRI) in order to record the anatomy of the structure to be analyzed for subsequent 3D fabrication (Figure 29).

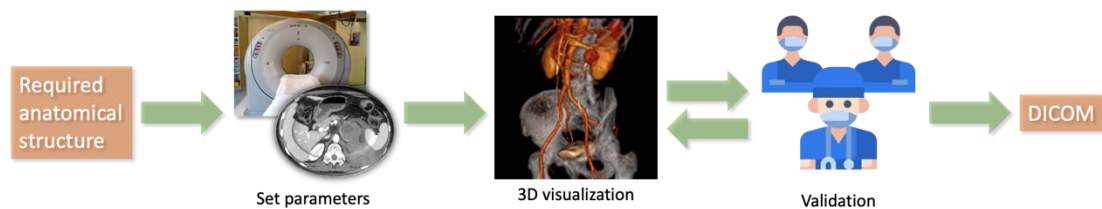


Figure 29. Flow diagram for the data collection phase.

INPUT: Anatomical structure to replicate

Step 1. To configure the parameters of the medical imaging equipment

Before conducting the medical imaging study, it is necessary to establish the appropriate parameters of the imaging equipment to be used (e.g., CT scan, MRI). These parameters will be established in collaboration with the medical professionals (e.g., radiologists) and will largely depend on the anatomical area of the patient and the characteristics of the specific anatomical structure to be analyzed.

Step 2. Validation of the medical imaging study

The medical imaging study obtained will be validated with the medical professionals in terms of resolution, number of slices and definition of the desired anatomical structure. If necessary, the study will be repeated.

Step 3. To export the medical image study to DICOM format

In order to be able to work with the medical image study in the following phases, it will be exported in a standard medical image format such as DICOM.

OUTPUT: DICOM file

CT/MRI Scanner

Obtaining the preoperative study by computed tomography or magnetic resonance imaging is usually the first step in order to proceed to extract the medical image, segment it, postprocess it and finally print the resulting 3D model. A total of 24 articles specified with which specific model the medical image was obtained (Figure 30). 11 articles used Siemens devices (Siemens, Munich, Germany), of which 7 used the CT-SOMATOM model, 1 the CT-AXIOM and 2 the MRI-MAGNETOM, leaving one without specifying which specific Siemens model was used. Philips (Philips, Amsterdam, The Netherlands) appeared in 6 articles with different models: EPIQ with 2 mentions, IE33 with 2. 2D Xtra vision and QLAB10 had 1 mention each. General Electric (General Electric healthcare, Chicago, Illinois, USA) appeared in 5 articles and Toshiba in two.

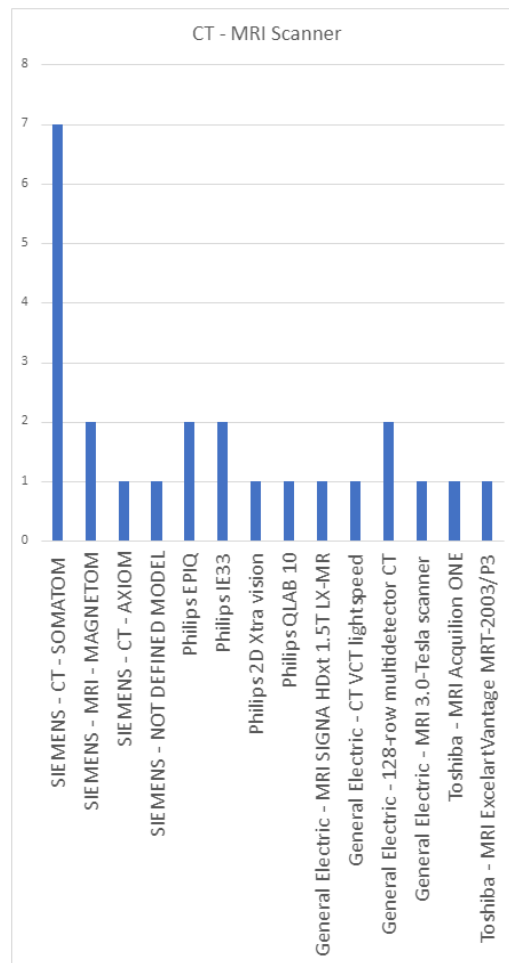


Figure 30. CT/MRI Scanners.

2. 5.2 Segmentation & Volume Rendering

During this phase, the anatomical structure of interest will be segmented (Figure 31).

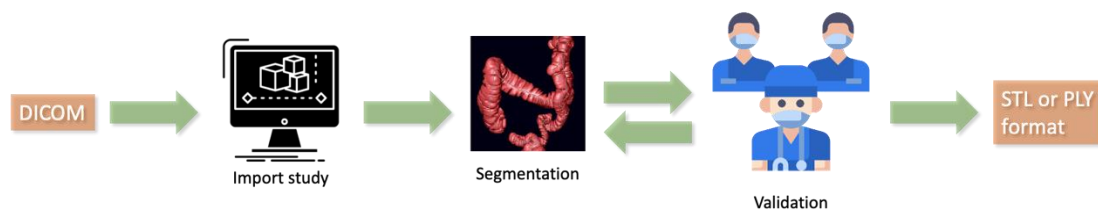


Figure 31. Flow diagram for the segmentation and volume rendering phase.

INPUT: DICOM

Step 1. To import the DICOM imaging study into the segmentation software

The first step is the import of the medical imaging study (DICOM) into the CAD software with which the segmentation process is to be carried out (e.g., 3D Slicer).

Step 2. Segmentation of the anatomical structures of interest

To perform the segmentation of the anatomical structure of interest, segmentation techniques such as thresholding or region growing, among others, will be applied. The election of these segmentation techniques, or their combination, will depend on the characteristics of the tissue to be segmented (see Table 2).

Once the anatomical structure of interest has been segmented, a 3D volume rendering is performed.

Step 3. Validation of the segmented 3D model

Once the volumetric representation of the segmented anatomical structure is available, it is validated with the medical professionals. This validation will analyze whether the differences in geometry between the segmented 3D model and the DICOM dataset are adequate.

Step 4. To export the segmented 3D model to STL or PLY format

Once the 3D model has been validated, it is exported to a file format commonly used for 3D printing and computer-aided design (CAD), such as STL or PLY.

OUTPUT: STL or PLY format

3. 5.3 Manual model optimization & Mold design

The main objective of this phase is to optimize the design of the 3D model extracted from the previous phases and, if necessary, to design the mold for the fabrication of the training model (Figure 32).

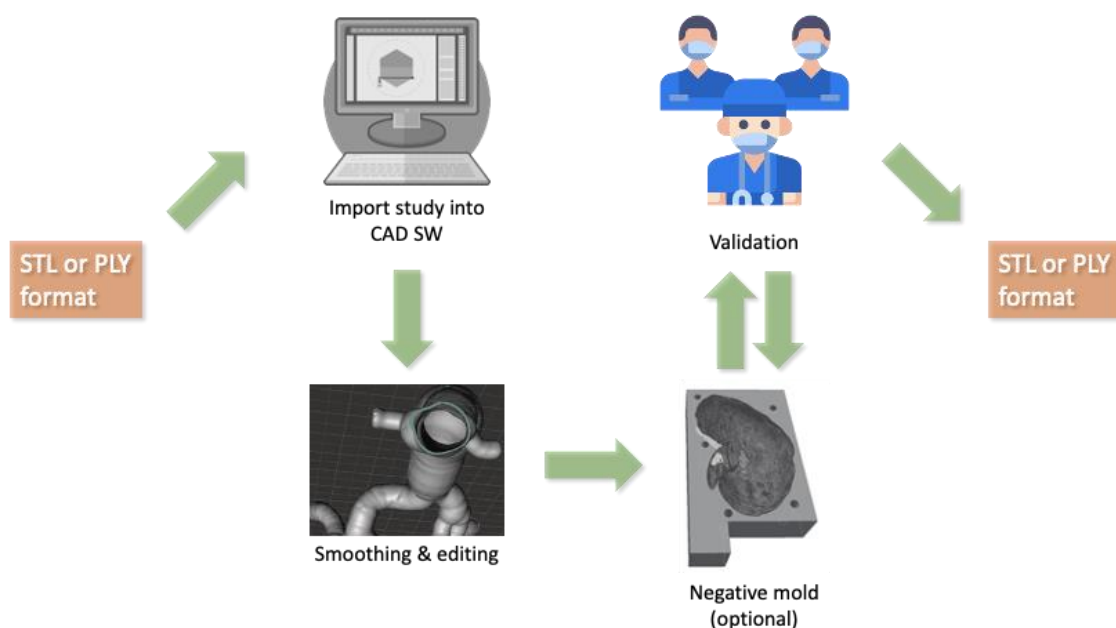


Figure 32. Flow diagram for the manual model optimization and mold design phase.

4. 6. General recommendations

Technical recommendations have been compiled for the import of models from medical images (especially technical aspects for segmenting the anatomy) describing the parameters and tools necessary for a correct segmentation of the three-dimensional model (Table 2).

Table 2. Recommendations for importing 3D models from medical images.

Software	Recommendation
3d Slicer	Trace the annular curve by rotating the image cutting planes around the annulus in <u>10-degree increments</u> , generating a set of points that are then smoothed using <u>Fourier smoothing</u> and resampled to a smooth curve to define the annular boundary.
3d Slicer	<u>Segmentation of the middle cranial fossa structures</u> (including the facial nerve canal and membranous labyrinth) using <u>a combination of thresholding</u> (automated selection of voxels based on Hounsfield Unit thresholds) <u>and manual contouring</u> (manual drawing of anatomical borders on each CT slice).
3d Slicer	In order to <u>evaluate both the shape and position of each structure</u> in the model as a whole, <u>point-surface distances</u> (shortest node distances between two frames) were calculated using algorithms based on the <u>VTK visualization toolkit</u> .
Invesalious	Employ a <u>Boolean subtraction operation</u> of two solid parts <u>to design outer molds</u> . Add an inlet and an outlet to allow for mold filling.
Materialise Mimics	Medical images of the mitral valve are manually segmented using pixel intensity threshold settings. The <u>pixel intensity</u> was set at 170 units <u>to reduce the occurrence of blood spots and artifacts</u> while maintaining the integrity of soft tissue structures.
Materialise Mimics	For segmentation, <u>bone tissues were separated from the paranasal sinus and skull base regions using Hounsfield unit thresholds</u> , and the segmented bone was stored as a Mimics (mask) object. Some soft tissues, such as the nasal concha and mucosal tissues, required manual editing with the Mask Edit component. To visualize the 3D printed model of the right-sided paranasal sinus, the right-sided paranasal sinus model was segmented into several flake-shaped models with unequal thickness in the coronal direction, and the neighboring flake-shaped models were connected through the rotating axis structures.
Materialise Mimics	The anatomical structure of the middle cerebral artery was segmented by a <u>semi-automated thresholding process</u> , segmenting the tissue with a <u>density ranging from 2848 to 12807 Hounsfield units</u> .

Materialise Mimics	<u>The skull structure can be separated from the external nose, nasal cavity and paranasal sinuses using the segmentation module tools. Similarly, the nasal cavity and paranasal sinuses can be segmented into various cuboid components, such as the septum, lateral walls and nasopharynx.</u>
Materialise Mimics	<u>The segmentation of the airway can be performed by means of a threshold-based algorithm.</u>
Materialise Mimics	<u>The craniofacial skeleton can be segmented in axial slices with the thresholding tool, and then isolated with the region growing tool.</u>
Materialise Mimics	<u>Structures with a significant intensity/density contour could be semi-automatically delineated from surrounding structures, while structures with an unremarkable intensity/density contour and fine structures could be artificially delineated from surrounding structures.</u>
MeVisLab	<u>The Voxelize Inventor Scene module allows the computation of a voxel representation of the scene.</u>
MIST	<u>Semi-automatic intensity thresholding (beyond 300 Hounsfield units), region growing and manual slice-by-slice contouring in orthogonal triplanar view can be employed as segmentation methods the orbital lamellae of the ethmoid bone, the anterior wall of the sphenoid sinus and the body of the sphenoid bone.</u>
Not specified	<p><u>Skull segmentation from a CT study could be performed with an initial neighborhood filter connected with seed points placed in various regions of the CT bone anatomy. The resulting skull mask can be postprocessed in STL format using a marching cubes algorithm. Similarly, the STL can be postprocessed by applying a geometry-preserving Taubin smoothing followed by quadratic edge collapse decimation to reduce the number of edges and faces in the mesh.</u></p> <p>The resulting bone STL can be cropped as needed to prepare it for 3D printing. For <u>vascular anatomy</u>, the CT study can be subjected to a <u>multi-level Hessian vesselness calculation</u>, a common and well-documented general method for enhancing tubular regions of a 3D image. From the enhanced image, a procedure identical to the above can be carried out, starting with neighborhood connected filtering, to generate the final model.</p>
ZedView	<u>Bone structures can be semi-automatically segmented from the surrounding tissues using a threshold of CT values from 600 to 2390 Hounsfield Units. To remove excess materials from the enclosed spaces after 3D printing, small drainage holes (5 mm) can be manually designed in the 3D model prior to printing.</u>

Table 3 provides technical recommendations for the post-processing of the 3D models obtained from the import. This describes the parameters and tools necessary for a correct post-processing of the model, mainly methods for cleaning the model, smoothing it and approaches for the realization of the negative or positive molds to be filled with a different material than the one used for the impression.

Table 3. Recommendations for the post-processing of the 3D models.

Software	Recommendation
Materialise 3-Matic	Trimming and drawing tools within CAD software can be used to manually manipulate the 3D volume into the shape of an artificial mitral valve (MV) with anterior leaflets, posterior leaflets, and commissures. Similarly, Boolean subtraction methods can be used to obtain a negative cast of the 3D MV model.
Materialise 3-Matic	The "hollow" function can be applied followed by manual adjustment using the "trim (cut)" function to exclude insignificant structures and reveal the most significant structures, reducing the printing cost. Smoothing of the resulting surface can be carried out by "local smoothing" function.
Autodesk Meshmixer	To smooth edges and correct segmentation imperfections, post-processing of the images can be carried out using a computer-aided design and drafting (CADD) program.
Autodesk Meshmixer	To smooth the surface of the aorta, the aorta can be digitally thickened (up to 1.5 or 2 mm) and the space occupied by the lumen subtracted to create the hollow primary model.
Autodesk Meshmixer	To smooth the bone surfaces and simplify the geometries of the 3D model, the "Sculpt" tool can be used in combination with the "Robust Smooth Brush" tool. The selection of the region of interest (ROI) can also be carried out by deleting the other parts by editing with the "Plane cut" tool.
Autodesk Meshmixer	The mesh shape of the virtual model can be converted to a solid body using the Mesh to B-Rep conversion tool. The mold for a kidney can be created using a box in which an inverse geometry is developed with the target body using the cut operation. Three solid tubes can be used to facilitate unidirectional filling of the kidney.
MeshLab	Mesh models can be cleaned up using a Poisson filter to smooth and fill holes in the virtual models and to finalize the computer-aided design file.
MITK	Once the model has been obtained in STL format, it is recommended to carry out a post-processing for noise removal, smoothing and meticulous filling.

Technical recommendations for 3D printing have been compiled describing parameters, information on materials and the manufacture of molds for filling (Table 4).

Table 4. Recommendations for the post-processing of the 3D models.

Topic	Recommendation
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Material	<u>PolyJet printers require more expensive materials and equipment compared to other printers, but the accuracy is high. In addition, the hardness can be adjusted by combining several types of materials with different elongations and hardness. The higher the proportion of Vero material (or the lower the proportion of Agilus material), the higher the hardness.</u>
Materials	<u>Bone components can be 3D printed using HIPS-X gypsum filament (1.75 mm, Spectrum, USA), which are found to be sufficiently radiopaque for medical-surgical training applications. The wall thickness of each bone can be taken as 2 mm, and a fill density of 10%.</u>
Materials	<u>The bladder/bladder neck model can be printed with resin and coated with a thin layer of silicone to give a realistic feeling of tissues.</u>
Materials	<u>The SLA printers provided the highest scores, high accessibility, more consistent lifetime, portability and relatively low cost. All SLA printers used laser polymerization of the resin: a fine laser is used to cure (harden), layer by layer, the liquid acrylic resin with high resolution (150 mm in the X and Y dimensions, 50 mm in the Z dimension).</u>
Materials	<u>The transparency of the VeroClear material makes it possible to check the mold filling.</u>
Materials	Two commercial PolyJet materials (Stratasys): <ul style="list-style-type: none"> - VeroCyan RGD841 or VeroMagenta RGD851: <u>rigid photopolymers with an elongation at break of 10%-25%.</u> - TangoPlus FLX930: <u>deformable photopolymer with an elongation at break of 170%-220%.</u>
Molds	<u>For the different components of the brain, a two-part mold can be created which is then filled with a casting silicone.</u>
Molds	<u>The negative skin mold can be printed in polylactic acid (PLA) and the Boolean subtraction technique can be implemented to create the negative mold for the facial skin overlay.</u>
Molds	<u>The silicone neonatal esophageal atresia and tracheoesophageal fistula models can be created using a 3D printed injectable mold.</u>
Molds	<u>Negative volume molds can be created with 3D modeling software, then fabricated with a 3D printer and finally cast with silicone rubber.</u>
Molds	<u>The mold for a kidney can be created using a box in which an inverse geometry is developed with the target body using the cut operation. Three solid tubes can be used to facilitate unidirectional filling of the kidney.</u>
Parameters	<u>A paranasal sinus (skull base model) model can be printed with a layer thickness of 1.2 mm and a printing speed of 50 mm/s.</u>

Parameters	The parameters set for the printer of the <u>external nose, nasal cavity, and paranasal sinuses (including the septum, lateral walls, and nasopharynx) models</u> were as follows: 0.1 mm layer thickness, 100% infill, 0.4 mm printer head diameter, 210°C nozzle temperature, 30 mm/second printing speed, retraction on, cooling fan on, 0.8 mm shell thickness.
Parameters	<p>If the print requires <u>high resolution</u>, the <u>Layer Height</u> is the <u>most important factor to consider</u>, while <u>the Shell Thickness controls the overall strength of the model</u>. The Shell Thickness controls the thickness of the print's side walls. Fill Although Shell Thickness is the main factor that determines the print strength, to create an evenly strong print, the Bottom/Top Thickness must also be considered. Not only does the <u>Fill Density affect the strength of the model</u>, but applying fill density will supply internal support for the top layers to be printed on.</p> <p><u>Speed and temperature not only control the overall print time, but can have a major effect on the overall print quality and even the success of the print.</u> Both <u>Printing Temperature and Bed Temperature</u> are parameters that determine the success of the print. If these two factors are not properly controlled, it can cause issues with extrusion and bed adhesion.</p> <p>Support is not required for every print, but <u>selecting an appropriate Support Type can solely determine the success of a print</u>. Support structures are used as scaffolding to provide a surface to print on for overhanging parts of a print. Depending on the geometry of the print, a type of Platform Adhesion (brim or raft) may be needed to provide a solid base for the print to build on.</p> <p>Filament Inputting the correct filament Diameter is necessary for proper extrusion to occur. <u>Flow % is usually increased when printing with flexible materials that are difficult to extrude</u>. Advanced settings typically remain unchanged but advanced users can adjust them based on the specific requirements of a print.</p>
Postprocessing	During post-processing, <u>water-soluble support material can be removed from the 3D printed model by placing the model in hot water</u> . The resulting model is then gently <u>brushed and dried to remove the residual support material</u> .

Technical recommendations have been compiled for the comparison between printed 3D models and real anatomical models (Table 5), ranging from 3D computer programs to manual measurements of important landmarks.

Table 5. Recommendations for comparison between printed 3D models and real anatomical models.

Measurement method	Recommendation
Automatic method	Accuracy could be investigated by fusion of the original temporal bone and the model using a <u>Ziostation2 workstation</u> (Ziosoft Inc., Tokyo, Japan).
Automatic method	<u>Dimensions</u> of each valve could be measured virtually in <u>QLab</u> (Philips Medical, Andover, MA) and 3D Slicer.
Automatic method	A Bland–Altman analysis could be used to evaluate the STLfile and printed phantom using <u>MedCalc software</u> (trial version 18.2.1). 95% confidence interval. Furthermore, the order of accuracy of the three types was as follows: CJP > Polyjet > FDM.
Automatic method	<u>Quantitative error analysis</u> could be performed using the <u>part comparison tool in Mimics</u> between the CAD files from the original CT and the created 3D model, confirming that the fabrication process provides an accurate, standardized model.
Automatic method	Using the <u>PSS software</u> (trial version 25.00; IBM), the <u>Bland–Altman analysis</u> could be conducted to compare the STL file and 3D-printed phantoms using XLSTAT 2020 software.
Automatic method	The following anatomical characteristics of the middle cerebral artery were measured using MeshLab software (ISTI-CNR, Pisa, Italy).
Automatic method	Using <u>Geomagic ControlAnalysis tools</u> , a global comparison of meshes between bone (segmented skull base and sinuses bone) and materials can be performed by calculating the average distance between all vertices of the two recorded meshes (rigid registration) <u>to evaluate the overall accuracy</u> . To do this, the meshes are overlapped as much as possible to eliminate differences in position and orientation. The resulting geometric differences are then compared by measuring the average distance between vertices. This result can be visualized as a color map of the distances.
Automatic method	The <u>Cloud Compare freeware</u> (http://www.danielgm.net/cc/) can be used to compare the printed 3D model and the real anatomical one.
Automatic method	Using <u>CloudCompare v2.6.1 software</u> , two separate meshes in the STL files are manually aligned by selecting three marker points in each mesh. The three marker points are selected to be the relatively sharp endpoints quantitative analysis was made of the inner structure by determining the differences between the 3D printed and the CT model using a 3D triangular mesh maximum error of 2 mm and a mean error of around 0.6 mm.
Automatic method	To assess the differential image processing between the 3D CAD data and the printed model, the 3D evaluation software <u>SpGauge 2014.1</u> (Armonicos Co., Ltd., Shizuoka, Japan) can be used.

Manual & automatic method	Accuracy was determined using <u>Ultratech digital calipers (GeneralTools, NewYork, NY)</u> for the patient and the 3D printed model, and the "markup caliper tool" on the CT scan using <u>IMPAX software (AGFA Healthcare, Belgium)</u> .
Manual method	<u>Qualitative comparison</u> of the digital 3D reconstructions based on manual CT segmentation and the anatomical reality.
Manual method	The 3D CAD model of the anatomical model is created from the dimensions measured with the use of a <u>digital Vernier Caliper</u> .
Manual method	Manual measurements using a tool <u>microscope (Leica optical Microscope, DM series)</u> .
Manual method	The written and marked plans can be measured for accuracy and time to completion.

5. Glossary

ABS: Poly acrylonitrile butadiene styrene

CAD: Computer-Aided Design

CT: Computer Tomography

DICOM: Digital Imaging and Communications in Medicine

HIPS: High impact polystyrene

MRI: Magnetic Resonance Image

PA: Polyamide

PC: Polycarbonate

PDMS: Polydimethylsiloxane

PGA: Polyglutamic Acid

PLA: Polylactic acid

PLC: Poly-L-caprolactone

PLY: Polygon File Format

PMA: Polymethyl acrylate

PMMA: Polymethyl methacrylate

PU: Polyurethane

PUR: Polyurethane rubber

PVA: Polyvinyl Alcohol

ROI: Region Of Interest

SLS: Selective laser sintering

SMA: Surgical and Medical Anatomy

SSTL: Surgical Skill Training in Laparoscopy

STL: STereoLithography

TPE: Thermoplastic elastomer

TPU: Thermoplastic polyurethane

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