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Review

3D-Printing in surgery: Beyond bone structures. A review

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ABSTRACT

Additive manufacturing (AM), otherwise known as 3D-Printing (3DP) or rapid prototyping (RP), is the fabrication of an object from zero by means of depositing materials layer by layer. 3DP allows the creation of complex geometrical objects such as human anatomy. 3DP applications in a surgical setting have mainly been described for anatomical models (surgical planning, simulation and education), customized implants, prostheses and surgical guides. In order to 3DP for surgical planning, Digital Imaging and Communications in Medicine (DICOM) images are converted to Standard Tessellation Language (STL) files. This process is called segmentation. Segmentation of bone structures is nowadays quite automated, whilst this becomes a challenge when dealing with other anatomical parts such as organs or soft tissues. This review explores what can be done in 3DP for surgical planning beyond bone structures, the current available technology, and clinical applications, limitations of printers and materials and ongoing research.

Introduction

Additive manufacturing, otherwise known as 3D-Printing (3DP) or rapid prototyping (RP), is the fabrication of an object from zero by means of depositing materials layer by layer [1]. As opposed to traditional methods of creating an object by subtracting material from a raw piece of material, known as subtractive manufacturing (SM), 3DP allows the creation of complex geometrical objects. As human anatomy is quite complex, 3DP has expanded the possibilities of using this technology in medicine for multiple purposes and especially in surgical disciplines. In order to 3DP for surgical planning, Digital Imaging and Communications in Medicine files (DICOM), obtained from Computer Tomography (CT) or Magnetic Resonance images (MRI), are converted. Among other file formats, into a Standard Tessellation Language (STL) file that can be 3DP. This process is called segmentation. First 3DP applications for surgery were published in 1999 by maxillofacial surgeons, demonstrating already shorter surgical times in the group where 3DP was used [2]. In these more than 20 years, technology related to 3DP has exponentially grown following Moore's law [3]. This is specially the case for bone specialties where for many surgeries 3DP has become the gold standard for surgical planning. This is mainly because the process of bone segmentation (3D virtual reconstruction of the images) is quite simple and automated and because 3DP hard anatomy structures such as the bone is a lot easier than 3DP soft materials. Unfortunately, this is not the case for other areas of the anatomy such as organs or other soft tissues. By reviewing the literature, it is easy to identify at a glimpse that 3DP published papers outside the scope of bone related surgeries, represent less than a 1% [4]. Nevertheless, new technological developments in segmentation software, 3D Printers and new 3DP materials that intend to mimic human anatomy, are allowing non bone-related surgical disciplines to join the advantages of 3DP in surgery. You will find in this review what can be done in 3DP surgical planning beyond the bone.

Soft tissue segmentation: from DICOM images to 3D virtual planning

Historically, preoperative planning has been based on the study of 2D images obtained from MRI and/or CT. For the study of soft tissue, MRI is usually the acquisition technique of choice for radiologists, as it allows better characterization of tissues, without exposing the patient to ionizing radiation [5,6]. However, in complex cases or in cases combining soft and bone tissue, a combination of both, CT and MRI are used for a more accurate anatomical reconstruction [7]. The development of imaging techniques is rapidly evolving, being now capable of obtaining multi-parametric and multimodal data from different imaging techniques, advancing to more realistic anatomical reconstructions and tissue characterization, opening the way for

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Fig. 1. 3DP SurgicalPlanning Process.

high-reality phantoms. Different imaging modalities may also be used for image acquisition and virtual planning reconstructions such as positron emission tomography (PET), single-photon emission computed tomography (SPECT), ultrasound (US), and mammography [8].

In the last decades, the above-mentioned important improvements in imaging techniques have come with great advances in post-processing software, allowing the generation of 3D virtual models in an accurate manner [8]. The advanced capabilities of MRI and CT to acquire volumetric data sets with isotropic voxels have resulted in the increased use of new techniques such as Three-Dimensional Volume Rendering (3DVR) and the maximum intensity projection (MIP) for complex cases in routine radiological practice, moving from 2D images to 3D imaging planning [9,10]. 3D planning has been reported in several studies to improve the visualization of anatomical structures and their spatial relationship to vessels, tumors or other compromised structures, providing more accurate information than 2D images [11,12].

Advances in automatic segmentation and image processing using Computer-Aided Design (CAD) files have also opened the way for the generation of 3D virtual and printable models in an accurate manner [13,14]. This new process of surgical planning including segmentation and 3DP can be summarized in 8 steps: 1; image acquisition, 2; segmentation and conversion to STL format, 3; CAD simulation, 4; generation of 3D printable models, 5; 3DP, 6; post-processing, 7; quality and cleaning control and final 8; surgery (Fig. 1). The first step of the above-mentioned process is image acquisition (mainly from MRI or CT Scan). The second is segmentation, in which DICOM files are converted to a CAD- STL file. Once segmentation is completed, these files are used for 3D visualization and virtual surgical simulation (Fig. 2). Steps 2 and 3 require using specific imaging and CAD software. Nowadays, many different softwares are available; with or without CE or FDA clearance for medical use, and proprietary or open-source solutions [15]. Once the surgery is virtually simulated, if the clinical team considers that having a 3DP version of the case can be of help, the process is continued with the 3DP of the anatomical model (steps 4 and 5). This process requires the conversion and preparation of the CAD model to a printable format understandable by the 3DP machine. The software used is normally the one provided by the 3D printer vendor. Once 3DP, the model is post-processed, cleaned and washed for a better surface finish (steps 6 and 7). Finally, the 3DP models are delivered to the surgeon for surgical planning as well as for other purposes such as resident training and patient experience (Fig. 3) [16,17].

While bone structures in 3DP are straightforward and economically affordable, soft tissue structures are a costly and time-consuming process that clearly needs to be improved [18].

It is also important to mention that these 3D models can be sterilized and brought to the OR so the surgeons can check them at any time during surgery. In this case, it is important to know the specifications of the 3DP materials as the sterilization process involves high temperatures that can affect the model. This is further explained in this article [19].

All data gathered during the segmentation process can be used in new emerging technologies such as Virtual Reality (VR), Augmented Reality (AR) and Mixed Reality (XR) improving the surgical planning experience [20–23]. In the latter, mixing the virtual model with real anatomy offers the user the ability to interact with digital projections of surgical targets.

Present 3DP soft tissue technology

As a starting point, it is necessary to mention that soft tissues have a viscoelastic behavior, which shows a mix between a viscous and an elastic property. That is why, for achieving an excellent mimicking, it is necessary to find 3D-printable materials able to reach the softness of the soft living tissues. The applications of 3DP technologies in surgical planning is a relative novelty, but the use of soft materials is more recent.

Anyway, the use of hard materials to perform 3D-printed surgical planning prototypes opened the way to the use of soft materials, which is still limited due to technological and cost reasons.

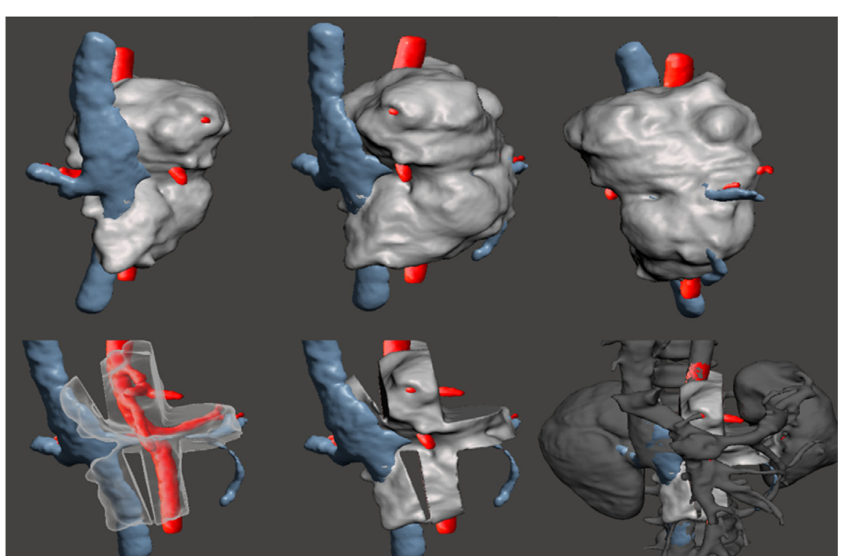

Fig. 2. 3D virtual reconstruction and tumor resection simulation in a complex neuroblastoma.

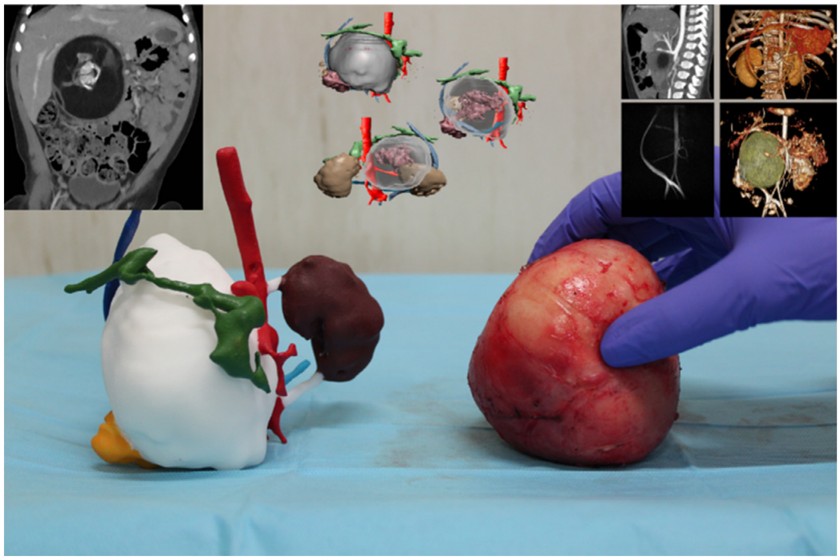

Fig. 3. A 3DP case of a fetus in the operating room. Notice the complex anatomical relations of a displaced IVC and major abdominal aortic branches.

Using hard materials limits the benefits of applying 3DP to surgical planning for visualization purposes. A commonly cited example of this is the surgical planning prototype manufactured in 2004 using SLA (Vat Photopolymerisation) in order to prepare an operation of head-conjoined twins. It's same size as the real case, made it perfect to visualize the complexity of vessels, and other anatomic references involved in the separation process [24].

First introduction of soft material in 3D Printing surgical planning applications was made in an indirect way: by 3D printing casts with filament desktop 3D printers (FFF, Fused Filament Fabrication) and then using them to reproduce a soft organ by filling these casts with some soft material (hydrogels, silicones). For example, in Forte et al. [25], a cast 3D printed using FFF technology was used to cast a composite hydrogel in order to reproduce the softness of a human brain.

PBF (Powder Bed Fusion) is another technology used for health applications. It is the most used technology for materializing surgical guides, and its ability to 3D print parts without supports. The easily removable powder solves the problem of supporting overhanging geometry of parts. For 3D-printed models for surgical planning, the hardness of polymers used limits, as it has been said, the application of PBF models to visualization purposes, as for example complex disposition of vessels, etc.

A bigger step beyond was given thanks to Material Jetting Additive Manufacturing technology, developed by Stratasys© company with the name of Polyjet©, and also known as Jetted Photopolymer. The drops come out of the print-head (commonly an adapted 2Dprinting inkjet print-head) and solidify by chemical reaction (UV light in the printing camera). Three reason exists for the success of this technology related to 3DP of oncologic surgical planning prototypes:

- Ability of PolyJet© technology to print in multimaterial, allowing the differentiation at least between tumors and other structures (organs, blood vessels, etc.), being this multi-materiality associated with colours and hardness.
- Availability of soft materials in order to reproduce the tumors on which resection were being tested.
- Availability of translucent materials (closest to transparent materials, which are not available with low hardness) in order to try to visualize the blood vessels trapped in the mass tumor represented as translucent.

Overall, the materials that were closer with respect to the soft living tissues were those materials from the "Tango" PolyJet© family: For example, Meisel et al. [26] manufactured multi-material structures with different VeroWhite© and TangoBlackPlus© compositions. However, they carried out several DMA tests, and viscoelastic properties found (storage and loss modulus), were very high, in the range of MPa, in comparison to soft tissues viscoelastic properties, which are in the range of 2–20 kPa [27–31].

Apart from oncologic surgical planning, where 3D-printing tumours with soft material is one of the main focus, softness of some of the 3D-printable photopolymeric resins used has captured the interest of other medical specialties linked to soft living tissues:

- Liver: in Zein et al. [32], a 3D printed liver was used to reproduce a cirrotic liver of a 42-year-old man which needed a transplantation. The purpose in this case and other cases (performed from a total of three donors and three possible recipients) was to avert unnecessary surgery in patients with potentially unsuitable anatomy, and thereby decrease the complications of liver transplant surgery.
- Heart: in Yang et al. [33], a 3D printed heart was reproduced with different colours and softness, facilitating the identification of different parts in the surgical planning model. Conceived to be an excellent model for visualization thanks to its different coloured zones, it was also soft as long as the "Tango" materials family from Stratasys used is conceived for this purpose.
- Kidney: the work performed by Kusaka et al. [34] is similar to the previous one, but materializing a kidney instead of a heart. Again, the ability of printing one part with different colours and hardness is approaching the models to a mimic copy of soft living tissues, at least with a better solution than most of the hard mono-material 3D printing techniques.

More cases related to other soft human tissues could be outlined, and in fact some of the present authors used Polyjet© technology in recent years in order to perform surgical planning over 3D printed prototypes, trying to mimic real parts as best as possible. In Krauel and Fenollosa-Artés et al. [35], three different prototypes for different oncologic cases were additive manufactured using the Polyjet technology, and were complemented with other prototypes made by Powder Bed Fusion and FFF technologies, boosting the potential of all present available AM technologies to perform surgical training. In this way, interventions of two high-risk stage-4 neuroblastoma and a mediastinal synovial sarcoma were helped by a set of different 3D-printed models: for every case, several prototypes were made and were ready one week before the intervention so the surgical team

Table 1
Differences between the present AM technologies related to 3D printed surgical planning prototypes.

AM Technology	Properties				
	Multi- color	Casting Technique	Price	Transparency	Hardness
Vat Photopolymerisation	No	No	Average	Medium	Medium
FFF	Yes	Yes	Low	No	Medium
PBF	By colouring	Yes	Average	No	Hard
Jetted Photopolymer	Yes	No	High	Yes	Soft

could take advantage from rehearsing with them and visualize the complexity of the encased vessels within the tumours. In the operating room, a high degree of tumor resection was achieved in all the cases.

Overall, the AM technologies mentioned, can lead today to the manufacture of surgical planning models with different properties as is presented in Table 1.

3DP research and new materials

Best current 3DP technologies, despite all the background exposed, have significant limitations in terms of reproducing soft parts. They are also very expensive, and hospitals avoid their use due to this fact. As an example, a rigid 3D printed part reproducing an anatomical reference of the body (made of PLA filament on a standard open-source desktop 3D printer) costs less than 1/10 compared to the same 3D printed part using Jetted Photopolymer technology, which allows soft materials and multi-color models. So, even if present technology is the best we have so far for mimicking soft tissues and a good rehearsal experience in terms of trying to mimic soft tissues for a good rehearsal experience, surgeons generally only ask for rigid visualization 3D printed prototypes as they are affordable for most health care systems.

Apart from the expected evolution of proprietary Jetted Photopolymer technology (where no cost reduction is foreseen), research and technological improvements in other additive manufacturing technologies are considering cost as a key issue, as this factor has a direct impact on the expansion of the use of surgical planning prototypes. Anyway, present limitations come not only from the side of cost:

- Photopolymerizable resins, that allow nice 3DP models for anatomical visualization, are very difficult to sterilize for its use in the operating room. They are materials that mostly fail to keep their shape over 45 °C, and therefore would not be suitable to be subjected to sterilization procedures that involve higher temperatures.
- As it has been cited, soft material and transparency are not compatible for photopolymer resins, something that is possible for other materials such as silicones or gels.
- The softest resins, with hardness values about 35 Shore A, are not soft enough to mimic real softness of living tissues, which commonly needs lower (softer) Shore scales (Shore OO, OOO) to be characterized. For example, Tejo-Otero et al. [36] measured that the Shore hardness of liver tissue is in the range of 15–20 Shore 00. Due to this, a commonly used trick for volumes as a full organ or tumor needed to be soft, is to materialize a shell of 2–4 mm, and then, in the 3D printing process, fill the inside volume with easy removable supporting material. Other issues arise due to this technique, such as loss of transparency or exaggerated difference related to hardness or cutting sensation when comparing boundaries and inside volume.

Consequently, from the need to 3DP prototypes able to overcome all these limitations, the first step in research has been the study of soft living tissues through the eyes of engineering, trying to capture which parameters and values are needed by surgeons in order to get the best rehearsal experience. That is, put into values what "mimicking" means, and go beyond obvious parameters as softness is. Doing so, the next step is to find industrial materials (available or new) and research how to make them 3D-printable, creating if necessary, new additive manufacturing technology.

A suggested list of these parameters [37] - apart from hardness/softness - includes density, viscoelasticity, bulk (K), elastic/Young (E) and shear (G) modulus. Other parameters or characterization methods such as Warner-Blatzer shear test or penetration tests that takes in consideration what is done when in surgery like the "cutting feeling" cited by surgeons or dissection difficulties.

As a result, characterization of relevant soft living tissues under the light of preparing the path to mimic 3D printed parts for surgical planning purposes has been researched using methodologies such as Dynamic Mechanical Analysis (DMA) [38].

- Soft printable materials: silicones and hydrogels are being researched as long as they can be formulated to meet similar hardness to soft tissues. Silicones tend to be more stable than hydrogels, which start to lose water after being consolidated, so surgical planning must be done within the first 24 h after the model has been 3D printed. Other materials explored are thermopolymer polyurethane (TPU) in monomeric liquid form. All these materials, as long as they have liquid consistency before being processed, need another AM technology to become 3D printed soft parts. This technology is a kind of Material Extrusion AM Technology known as Robocasting or Direct Ink Writing (DIW). DIW 3D printers are commonly similar to FFF Desktop 3D printers where the filament has been replaced by a syringe or a similar device to pump liquids to a nozzle. Conversion from liquid to solid is performed by different ways: most commonly by mixing two components to induce catalysis when extruded, or using photocatalysts and then UV light in the printing chamber, as it is made in SLA or Jetted Photopolymer technologies. Fig. 4 shows a bespoken DIW 3D printer while printing a bi-component silicone, and Fig. 5 shows different hydrogel materials with which surgeons rehearsed for finding suitable materials. Apart from the mechanical properties the feeling and feedback from a surgeon needs to be taken into consideration.

DIW technology alone is not capable of printing complex multi-material prototypes needed for surgical planning. Therefore, research on combining more than one technology is going on. For example, combining in a 3D-printer different filaments and liquids is a very interesting path, due to expected limited cost and the capability to use a variety of materials meeting mimicking requirements of different soft and hard tissues present in most of the surgical planning scenarios.

As an example, Fig. 6 shows a special 3D-printer with a tool-changer that uses 4 different filaments (e.g. red soft TPU filament for vessels, water-soluble PVA for supports, white PLA for anatomic references, and another TPU filament for other soft parts) and one print-head for silicone using a progressive-cavities pump with pressurized feeding system.

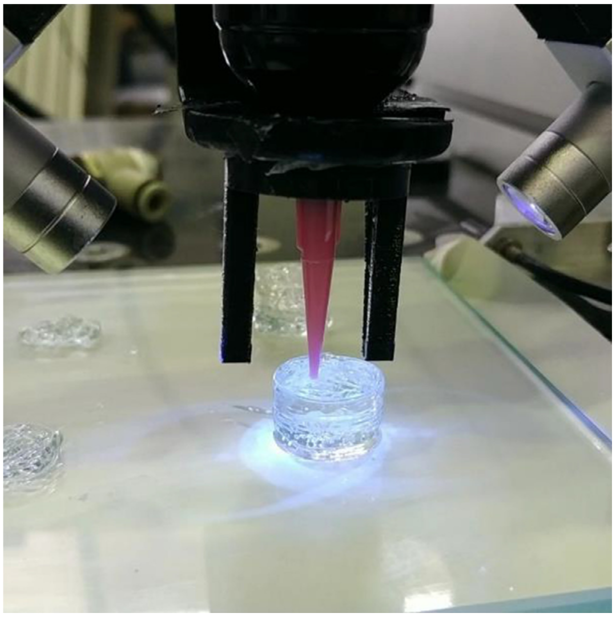

Fig. 4. Silicone DIW 3D-printer designed and manufactured by CIM UPC, aimed to 3D-print human wind-pipe mimic models for medical research purposes. A controlled-pressurized syringe extrudes a photocurable silicone.

Clinical applications

3DP applications in a surgical setting have mainly been described for anatomical models (surgical planning, simulation and education), customized implants, prostheses and surgical guides. In surgeries other than bone structures, the majority of articles refer to anatomical models of specific organs such as the liver or for complex or unique cases [39–42]. Usually, the models are 3DP so the treating team can thoroughly study the case; understand complex anatomy and foresee potential complications. This has become important in oncological cases or rare cases that a surgeon might encounter only once in a lifetime. In oncology, models are used to assess the feasibility of resection, safety, margins and surgical approach. In conventional surgical planning, bi-planar DICOM images are reviewed, thus, only the sense of sight is used. In 3DP surgical planning, the surgeon plays and touches the model, consequently combining the sense of sight with the sense of touch. This is known as the theory of *"touch to learn"* that has demonstrated a better comprehension and knowledge consolidation of important surgical anatomy aspects helping surgeons to analyze critical steps of surgical procedures [43]. These models, though, have some limitations that have been previously mentioned, mainly due to the hardness and rigid properties of available 3DP materials. Some improvements have been published in this aspect though, using silicones and hydrogels that allow some sort of surgical dissection [35,38].

Simulation is also another critical aspect of surgical training, especially in laparoscopic procedures. Different 3DP models of abdominal laparoscopic surgical techniques have been published and 3DP technologies allow the creation of more realistic models based on real cases replicas [43].

In addition to these pure surgical planning aspects, 3DP anatomical models have helped patients and their families to better understand their condition and the surgical procedure to be performed. 3DP models break the barrier of a brain not trained to interpret biplanar DICOM images and therefore persons involved in the case

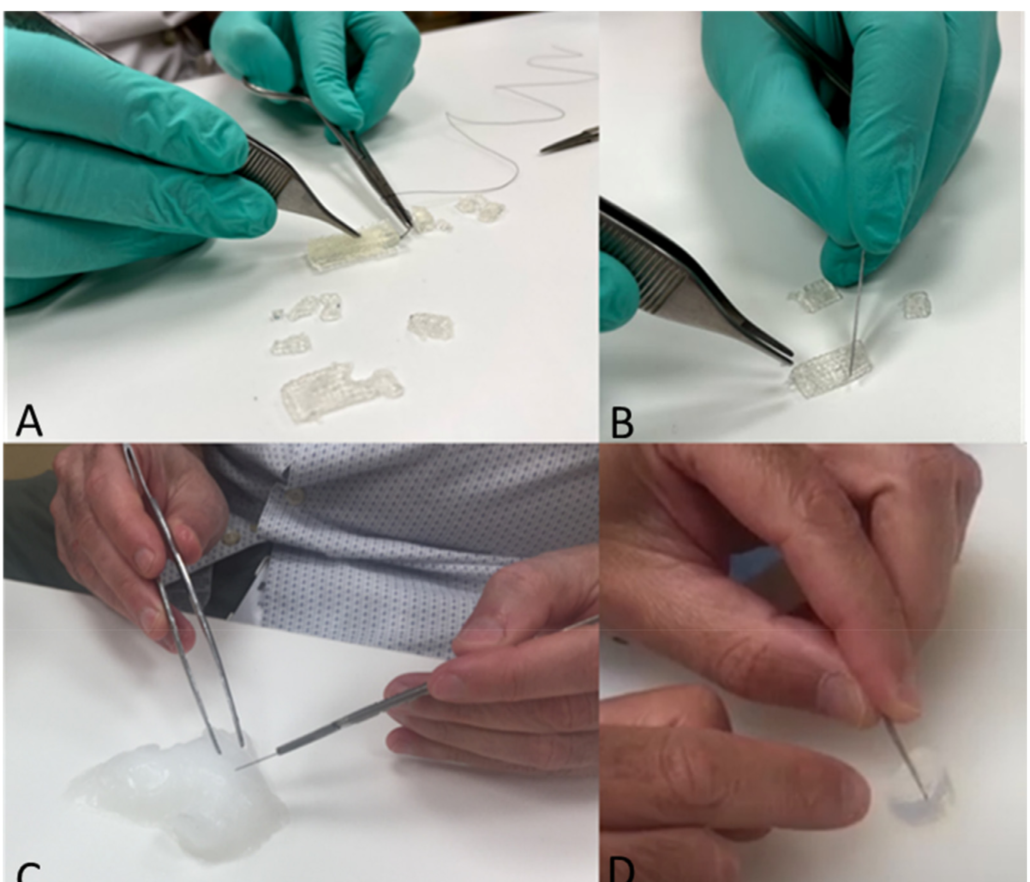

Fig. 5. Surgeon rehearsing with different materials: (A-B) GelMA. (C) CH of PVA and PHY. (D) Agarose gel.

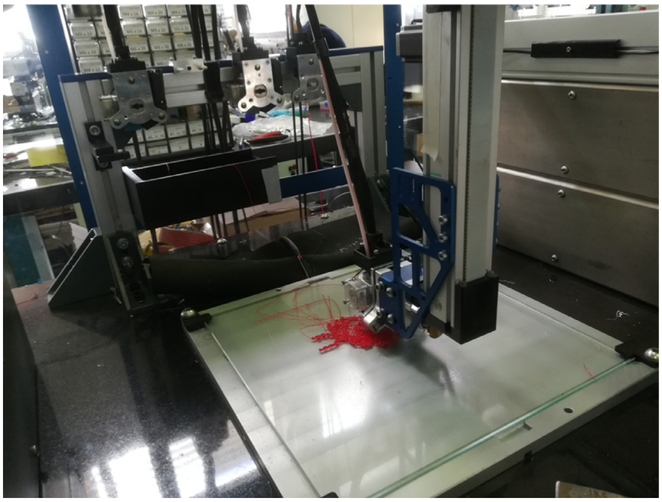

Fig. 6. Multi-material "QuirofAM Project" 3D-printer developed at CIM UPC under HSJD design specifications, combining FFF and DIW technologies to advance on 3DP anatomical models.

(patient included), are placed at the same level of understanding allowing thus for better communication among teams.

Conclusions

3DP in medicine is a fast moving discipline. Health care professionals, engineers and researchers are continuously innovating and expanding its applications. At this moment, main limits for a widespread use of this technology in surgery beyond bone structures are; organ and soft tissue segmentation process, 3DP materials and its cost, and 3D printing systems processing soft and multi-material models. Nevertheless, more and more articles are showing the applications of this technology in soft tissue scenarios. It is also important to mention that, once segmentation has been done, CAD and STL files can be used for virtual reality purposes such as virtual surgical planning or augmented reality. 3DP motto to convince professionals from the health sector is "if you can dream it you can 3DP".

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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