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Patient-Specific 3D Printed Models for Education, Research and Surgical Simulation

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Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.79667>

Abstract

3D printing techniques are increasingly used in engineering science, allowing the use of computer aided design (CAD) to rapidly and inexpensively create prototypes and components. There is also growing interest in the application of these techniques in a clinical context for the creation of anatomically accurate 3D printed models from medical images for therapy planning, research, training and teaching applications. However, the techniques and tools available to create 3D models of anatomical structures typically require specialist knowledge in image processing and mesh manipulation to achieve. In this book chapter we describe the advantages of 3D printing for patient education, healthcare professional education, interventional planning and implant development. We also describe how to use medical image data to segment volumes of interest, refine and prepare for 3D printing. We will use a lung as an example. The information in this section will allow anyone to create own 3D printed models from medical image data. This knowledge will be of use to anyone with little or no previous experience in medical image processing who have identified a potential application for 3D printing in a medical context, or those with a more general interest in the techniques.

Keywords: 3D printing, tissue-mimicking models, surgical planning, patient-specific phantoms, personalise medicine

1. Introduction

Within recent years there has been exponential growth in healthcare related 3D printing research (as shown in **Figure 1**). This growth is translating into clinical practice as accessibility to 3D printers increases. One of the drivers for the growth 3D printing within healthcare is a trend towards development of ‘personalised’ medicine. Personalised medicine is “a move away from a ‘one size fits all’ approach to the treatment and care of patients with a particular condition, to one which uses new approaches to better manage patients’ health and target therapies to achieve the best outcomes” [1]. 3D printing has been shown to be useful for: patient education [2–4] education for healthcare professionals [5], procedure planning [6, 7] and prosthesis / implant production [8] and is set to be promising in the areas of regenerative medicine and tissue engineering. Before we describe each above-mentioned section, we will highlight the workflow from medical images acquisition to application (see **Figure 2**).

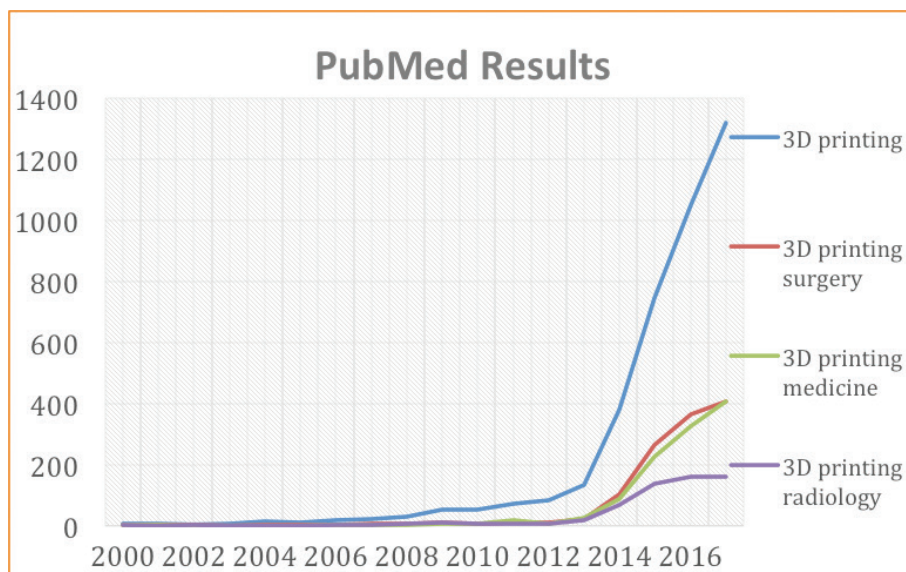


Figure 1. Chart demonstrating the number of citations in PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) per annum from 2000 to 2017 in PubMed using the search terms ‘3D printing’, ‘3D printing surgery’, ‘3D printing medicine’, ‘3D printing radiology’.

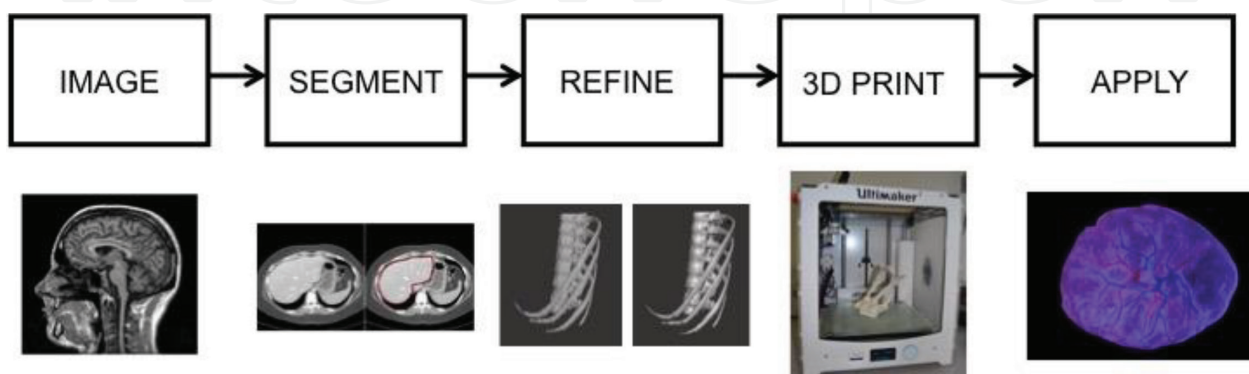


Figure 2. Outline of the workflow from medical images acquisition to application of 3D printed models.

2. Workflow

The use of products derived from 3D mesh models and computer aided design (CAD) techniques in healthcare is rapidly growing. Applications include: planning surgical procedures for hepatic & renal cancer resection; innovative cardiac and vascular device testing for paediatric and adult populations; visualisation of complex head and neck anatomy for neurosurgeons; practicing procedures *ex vivo*; training models and educating clinicians and patients [9–13]. Models of heart [2], renal collecting system [14], kidney [15] and brain [16, 17] have been previously developed. Model production requires knowledge of how to segment the region of interest from medical image data, manipulate the resulting 3D model and prepare stereolithographic (.stl) files for 3D printing.

In this section we present a pipeline that converts medical images of body structures to 3D print models. Particularly, we discuss how to load and manipulate 3D medical image data, use simple processing tools to extract volumes and structures from the images, export those volumes into 3D printing software where they can refine and repair their models. We demonstrate our streamlined processing pipeline on 3D printed model of a lung, which was fabricated using filament deposition-modelling additive printing technique. This model was segmented from medical data using the freely available segmentation software Slicer.

This section will be of interest to students and professionals from medical biomedical and engineering backgrounds that wish to learn basic image processing and volume extraction techniques. The materials will make it possible to develop 3D models from medical images, which can be used as a learning aid to help visualise anatomy. As shown in **Figure 2** the process starts with a 3D medical image, from which a structure will be extracted. The particular nature of the image will inform how it is processed.

2.1. Imaging

The nature of the imaging data depends on the specific imaging technology and the region of interest being imaged (see **Table 1**). Image resolution can vary between 0.1 and 8 mm, while image intensity can be due to density, light absorption of acoustic impedance. The main medical data file types are DICOM, NIFTI and MINC. DICOM is a universal image format and file sharing protocol, suitable for multiple image modalities and very widely used. It is easy to import into most software. NIFTI is a format designed specifically to store neuroimaging data. This format is compatible/viewable with several specific software packages. MINC is a format used with certain brain imaging software.

2.2. Segmentation

The next stage of the image-processing pipeline is segmentation, which refers to the extraction of a specific 3D volume from a set of image data/slices. It is used to locate objects and boundaries in each slice that corresponds to the tissue of interest. As it is done slice by slice, a volumetric data is gradually built up. It can be used to create patient specific, highly accurate models of organs, tissue and pathology. Many software packages are available [10, 18], here we mention only Slicer. The volume can be extracted using basic or advanced segmentation techniques.

Modality	“Type”	Intensity from:	Resolution
CT	Structural	Photoelectric coefficient \approx Density	0.5 - 1.5 mm
MRI	Structural/ Functional	Proton Relaxation Time	0.3 - 1.0 mm
SPECT/PET	Structural/ Functional	Particle emission from radioisotope	3.0 - 8.0 mm
Ultrasound	Structural	Reflections from changes in acoustic impedance	0.3 - 0.5 mm
Photoacoustic	Structural	Absorption of laser light by chromophores	\sim 0.1 mm (depth dependent)

Table 1. Main imaging modalities, CT-computed tomography, MRI-magnetic resonance imaging, SPECT/PET-single photon emission computed tomography/positron emission tomography

2.2.1. Basic techniques

- Manual segmentation

User identifies boundaries and manually draws around the shapes using a paintbrush tool.

- Thresholding

Pixels are partitioned depending on grayscale value. This effectively converts a grey-scale image to a binary image with one intensity representing tissue to be included in the model and the other representing that which should be excluded. This is most effective when the target tissue is a different intensity to the background.

- Cropping

Restricting the segmentation to a certain volume of space (**Figure 3**).

2.2.2. Advanced techniques

- Edge based methods—region growing

‘Seeds’ are positioned by the user and grow to fill regions defined by boundaries in the image. Works well when regions are well defined for example contrast enhanced medium to large arteries. If the data is noisy or edges are not clear, the segmentation may ‘leak’.

- Parametric models—snakes

The algorithm attempts to model the edges by minimising an energy term. This is minimised when the contour is on the object boundary and when the contour is as regular and as smooth as possible. It is useful for interpreting incomplete images and is robust to noise, but it can be slow to compute.

- Expectation maximisation (EM)

The algorithm finds the maximum likelihood of label distribution in a probabilistic manner. This framework is highly complex but can be a powerful tool for modelling the data accurately (Figure 4).

2.3. Refinement

Following segmentation of the 3D volume the next stage is refinement, which refers to the wide range of techniques used to convert a rough 3D segmentation into a finished, printable model. The full range of possible refinement techniques is too large to be described effectively, but key methods include:

- Repairing

Errors and discontinuities can sometimes arise in the segmentation & exporting process, which need to be repaired before printing

- Smoothing

Staircasing errors resulting from the resolution of the original medical image can be mitigated by smoothing the surface of the mesh model

- Appending

The segmentation will often only be one component of a final model. To convert the model into a final, useable form it is often necessary to combine it with other structures to, or subtracting volumes from, the mesh.

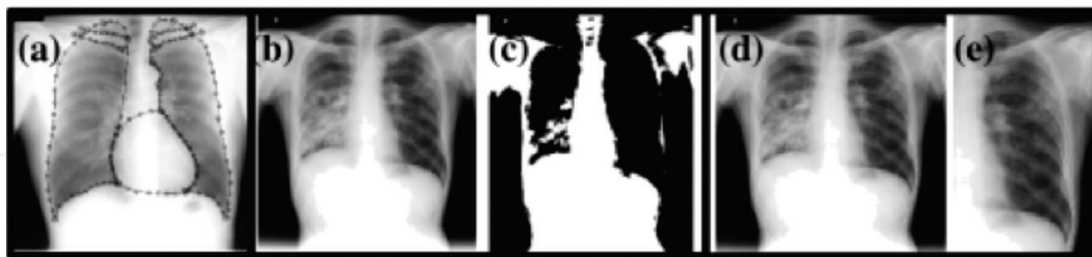


Figure 3. Examples of basic segmentation tools: (a and b) manual, (c) thresholding, (d and e) cropping.

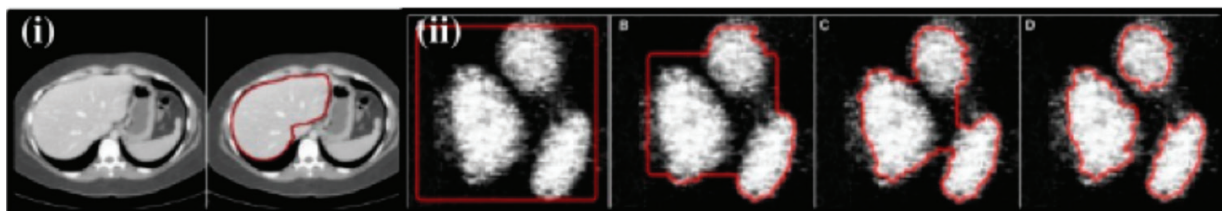


Figure 4. Advance segmentation tools: (i) region growing, (ii) parametric models—snakes.

Mesh refinement can be performed using a variety of freely available software, including FreeCAD [19], MeshLAB [20], and Blender [21]. In the worked example below, extensive use is made of the Meshmixer [22], which is an easy to use mesh viewing and manipulation software, with several essential mesh refinement tools.

2.4. 3D printing

There are many different printing techniques, with many more different synonyms. It is beyond the scope of this chapter to give a complete description of every printing technique, therefore in this section we present a broad overview of current technologies. Almost all 3D printing technologies can be categorised into one of three main groups:

1. Extrusion printing
2. Photopolymerisation
3. Powder binding techniques

The first group of 3D printers extrude a material via a print head nozzle. The material is molten and deposited on the layer underneath, where it hardens again. The most commonly used materials are thermoplastics (polylactic acid (PLA), acrylonitrile butadiene styrene (ABS)), which are deposited with a technique called “Filament Deposition Modelling”. Other techniques of note are “Wire and Arc Additive Manufacturing” (used for industrial scale metal prints), as well as “Material Jetting” (which utilises inkjet print heads). Using these techniques, a multitude of materials can be printed, including metal alloys, chocolate, and even wood or ceramic composites.

The second group of 3D printers selectively solidifies photopolymers. These are liquid materials that harden by exposure to light, typically ultraviolet light delivered via a laser. There are two key technologies: “Stereolithography” and “Poly Jetting”. As the name of this group implies, these techniques can only print plastics. Another important technique is “digital light processing”, which is very similar to Stereolithography, except that it uses a different kind of illumination.

The third group of 3D printers binds granules of the material by gluing or melting them. This method offers the widest choice of materials: glass, ceramics, many metals, and plastics. The technologies associated with this group are “Binder Jetting” and “Laser Sintering/Melting”. More information about 3D printing techniques can be found on Ref. [18].

In order to print any model the file format (typically .stl or .obj) should be transformed into a language that the printer can understand (typically .gcode format). Freely available slicing software such as “Ultimaker Cura” or “Preform” help to perform this step. It converts the geometry of the model into a long series of coordinates, which the printer interprets to control the movement of an extruder or laser heads. Finally, the support material settings, print speed, temperature and other parameters should be optimised before starting to 3D print. To better understand this process, a worked example of the development of a lung model is described in the next section.

2.4.1. Working example – Lung

1. Obtain DICOM imaging data (For example, from the Osirix website [23]).
2. Run 3D slicer software (Download and install [24]).
3. Load the DICOM data into the scene (DCM > Import > Select data > Load)
4. The default setting is to have four views of the data. You can scroll through the slices using the sliders above each view. For segmentation, it's easiest to just see one view, so select the grey squares icon on the taskbar and set the view to Green slice only
5. Scroll through the slices using the slider at the top of the view. We are going to be segmenting the lung on the left hand side of the view (this is actually the right lung). Find the slice at which the lung first becomes visible (A: 50.371 mm in the top right corner)
6. Open the segmentation editor (Modules > Segmentation > Editor) and select OK to choose the standard colour scheme for the label map.
7. Select the Level Tracing Effect Tool in the 'Edit Selected Label Map' toolbox.
8. Use the tool to hover over the slice until the region of interest is outlined and left click to label the region.
9. Use the slider or the scroll wheel on your mouse to go to the next slice (A: 50.957 mm) and repeat the process – hover over the region of interest until it is outlined correctly, then left click to label this region.
10. Repeat on each slice in the volume where the lung is visible (up to A: 211.824 mm), highlighting and labelling the lung in each slice. Allow some time for this stage. Ensure that this is accurate – the segmentation technique has a tendency to leak or to not highlight the entire region. Use the EraseLabel and PaintEffect tools to correct errors of this form by removing leaks and filling in holes.
11. Convert the label map on each slice into a 3D volume using the ModelMaker tool. (Modules > Surface Models > Model Maker)
12. In the Model Maker module, ensure that the Input Volume is set to have the same name as your label. Change the Model Name to 'lung' or another suitable name, then select Apply to run the module.
13. Export the model as a stereolithography file (.stl). Click File then Save. Your model should be listed as a .vtk file (lung.vtk). Ensure that the box next to this file is ticked, the other files on the list do not need to be ticked at this point. Change the file format in the drop down menu to .stl, and choose a suitable directory where the model can be saved. Click Save to export the data.
14. Open Meshmixer, free Mesh refinement software [22].

15. Import your model (File > Import > Select your model from the directory > Open). You should now be able to see your lung model. There will be some errors, which we can fix in this refinement stage such as holes, non-manifold surfaces, rough edges etc. Basic commands: middle and left button on the mouse to translate, Alt and left click to rotate, scroll using middle button on mouse to zoom in and out.
16. There are a number of filters that can be used to improve the quality of the model. Firstly, repair any holes using the inspector tool. (Analysis > Inspector > Auto repair all)
17. Then use the RobustSmooth tool (Sculpt > Brushes > RobustSmooth). You can set the strength, size and depth of the brush according to the application. It is best to start with a low strength and a larger size, then increase the strength and reduce the size as the structure becomes smoother. Move the brush over the surface of the model in a continuous way, not spending too much time on a particular area. You should be able to see that the surface becomes visually smoother as you do this. Make sure that you save multiple versions so that is possible to go back a step if you are not happy with the result at any stage.
18. The Flatten and Inflate brushes are also useful if there are unphysical holes that need to be filled in – use inflate to fill the holes then flatten and smooth so that the surface is continuous.
19. Once you are happy with the model, export the volume as a .stl file for final processing and printing. (File > Export > Save)

3D printed model of a lung was fabricated by an extruded thermo-plastic polymer printer (Ultimaker2;Ultimaker,Chorley,England) using PLA filament material (PolyMax;Polymakr, Changshu, China). The Ultimaker printer is a fused deposition modelling (FDM) printer, which works by depositing layers of print material from a nozzle, which moves in the horizontal plane, onto a print bed, which moves vertically (**Figures 5–12**). The Polymax material was chosen due to its relatively low cost, availability, and predicted ultrasonic reflectiveness. The enhanced PLA allows higher build quality and a reduced print failure rate. The STL file for a lung model was loaded into the Ultimaker CURA 3D printing software. This software allows selection of print options and generates the gcode files used by the

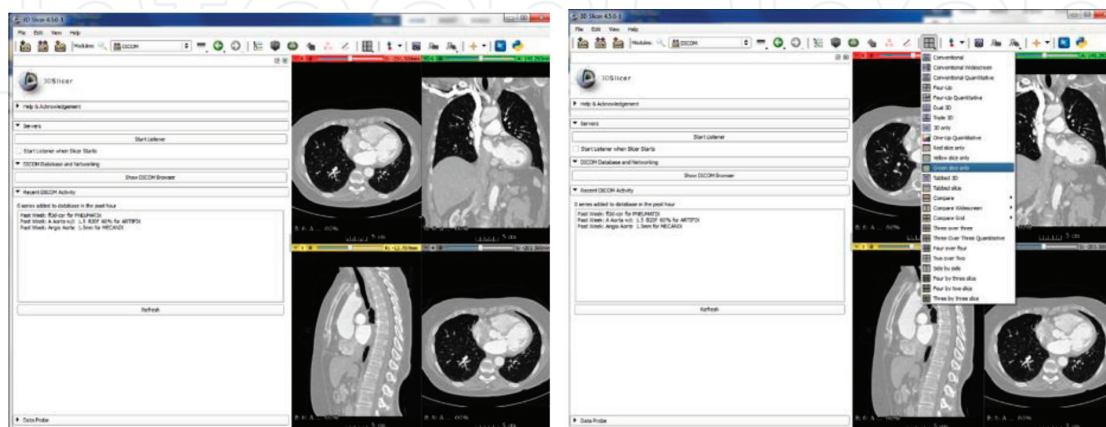


Figure 5. Steps 3–4: Importing the imaging data.

Ultimaker printer. Due to the dimensional constraints of the Ultimaker printer, the model was printed at 90% size compared to the original CT image. The completed lung print is shown in **Figure 13**.

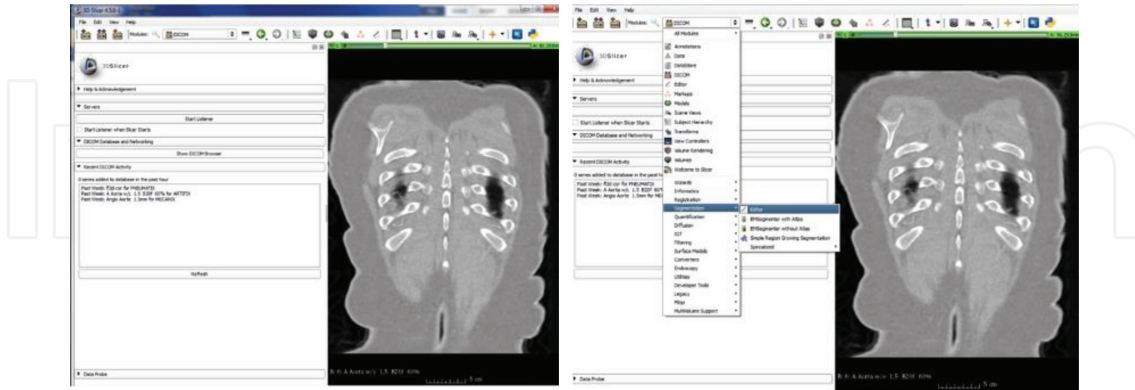


Figure 6. Steps 5–6: Finding the correct slice and open the segmentation editor.

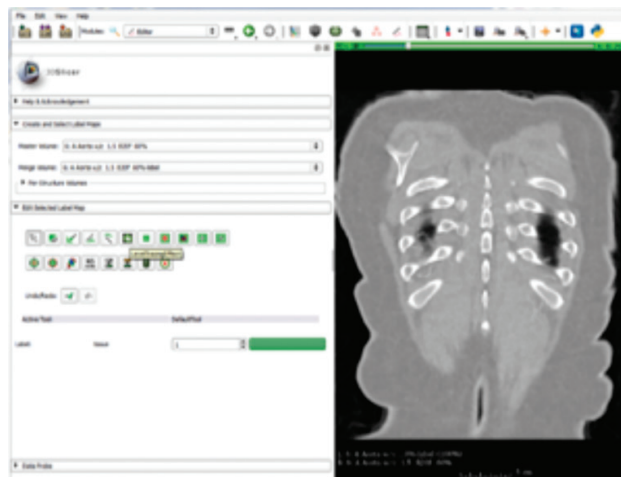


Figure 7. Step 7: Selecting the level tracing effect tool.

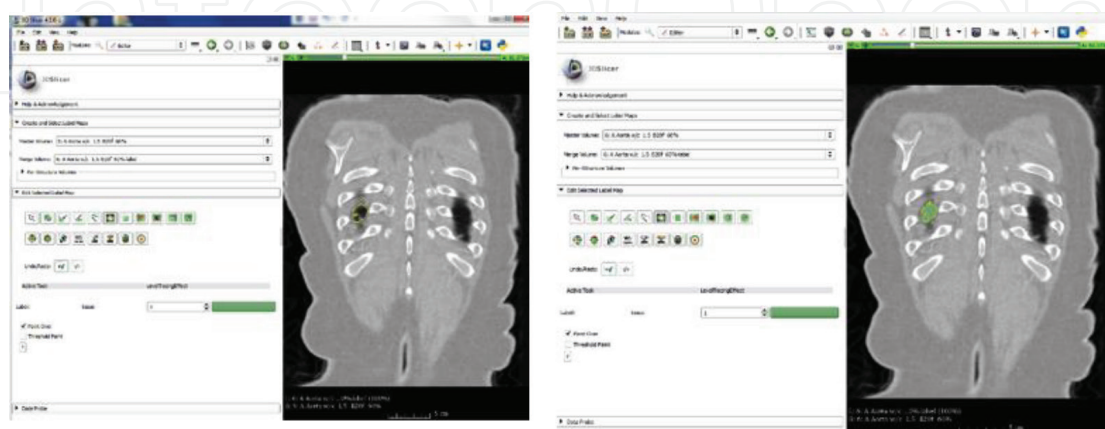


Figure 8. Step 8: Labelling the region of interest.

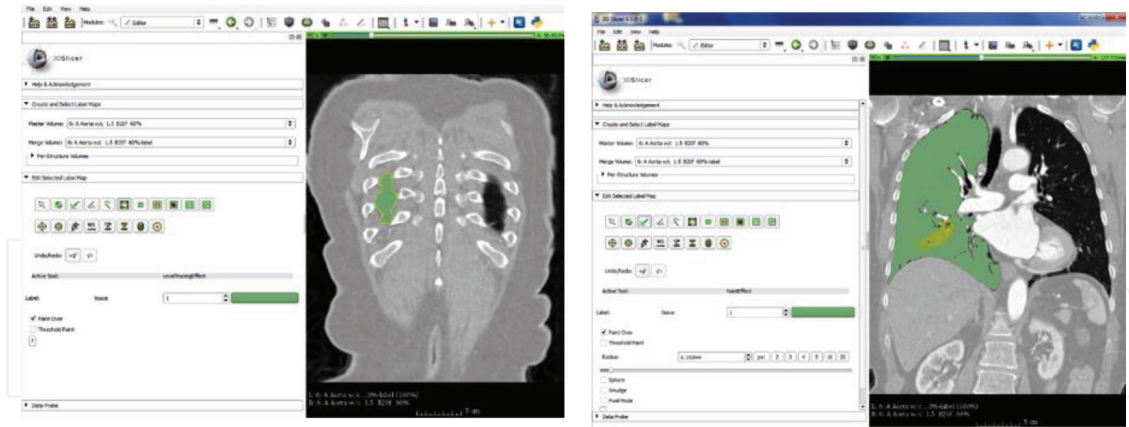


Figure 9. Steps 9–10: Continue labelling the region of interest.

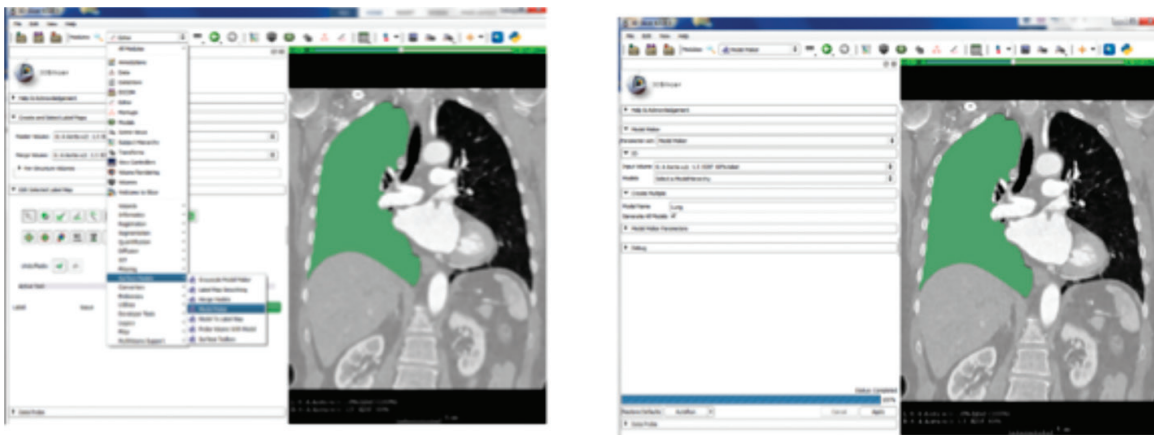


Figure 10. Steps 11–12: Creating a 3D volume using ModelMaker tool

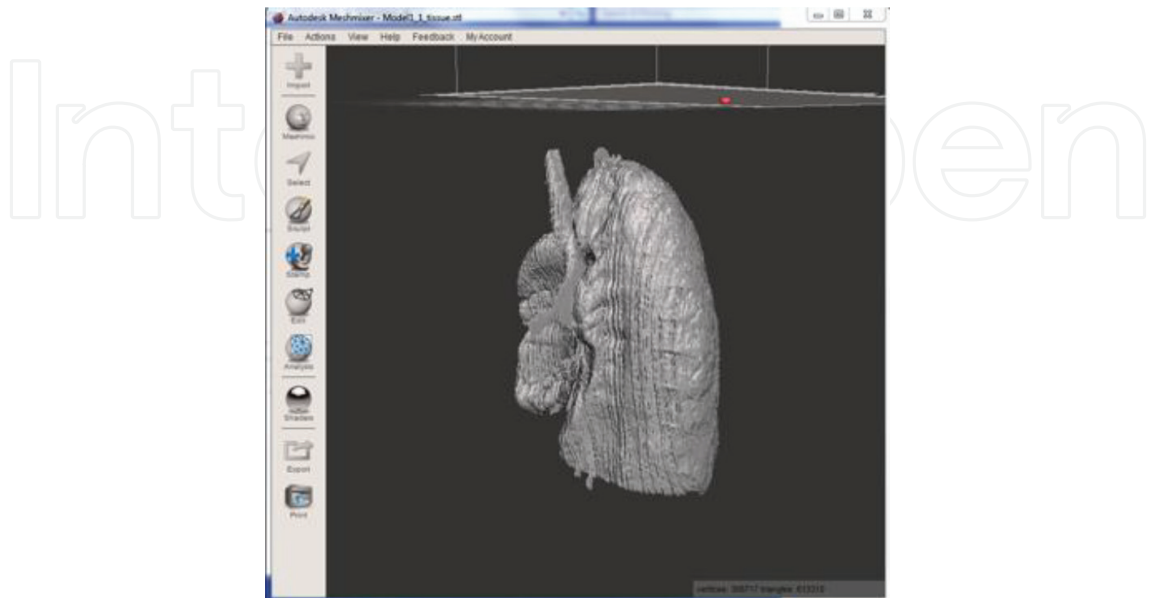


Figure 11. Step 15: Importing the model to Meshmixer software.

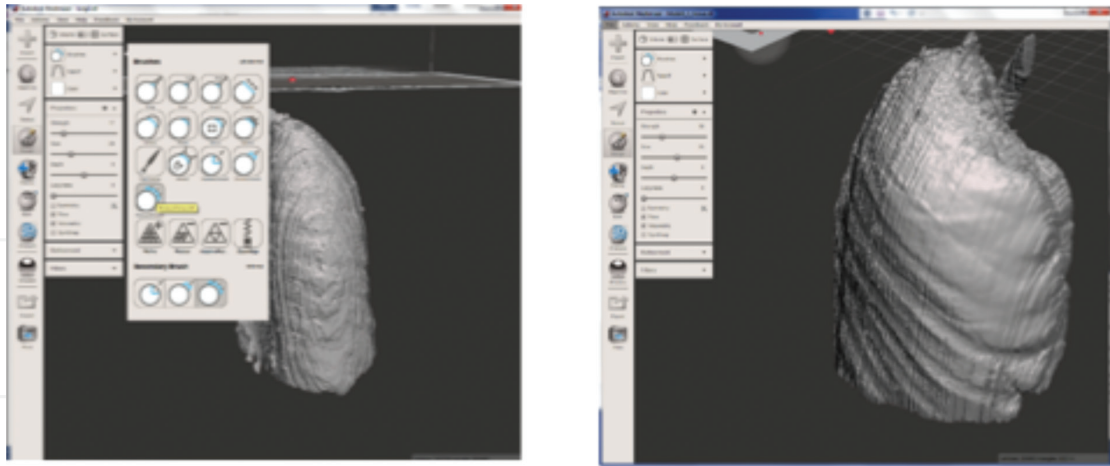


Figure 12. Steps 16–17: Repair holes and smoothing, step 19 exporting the smoothed model as a .stl file.



Figure 13. Final 3D printed model of a lung painted with acrylic paint.

3. Applications

The following sections will describe in details the following applications: Patient Education (Section 8), Healthcare Professional Education (Section 3), Intervention Planning (Section 4), Other Applications: Implants (Section 5.1) and (Tissue Engineering) (Section 5.2).

3.1. Patient education

Guidance from both the American Medical Association [25] and the General Medical Council in the UK [26] strongly advocates a collaborative approach by physicians with their patients.

It is vital that patients are provided with the relevant knowledge allowing them to engage fully in their care and to give their informed consent to treatment [27]. Information that should be given includes an explanation of the clinical condition, the proposed procedure including the anticipated post-procedural course and its benefits, risks and alternatives [27]. This information is usually communicated verbally, sometimes with the aid of diagrams or showing patients' their 'scan'. However, physicians and surgeons undergo years of training in normal human anatomy and pathology to develop an understanding of disease processes. Diseases are assessed by increasingly complex imaging modalities such as multi-phase contrast enhanced computed tomography and multisequence magnetic resonance imaging. It also takes many years to understand the vast amount of information presented in such 2D images and then conceptualise them in 3D. Consequently, patients find medical images difficult to interpret and do not enhance understanding [2]. Although many patients access additional information about their condition on the internet, this information is also often of poor quality [28].

3D printed models are proving a useful aid enhancing patient understanding of their disease. In complex diseases, replicas of the area of interest which patients can see and manipulate are thought to help understanding of the relative locations of anatomical structures, the specific areas of abnormality and the degree to which they are abnormal and what a proposed treatment (e.g. surgery) would entail [2]. A study of more than 100 parents of children with congenital heart disease in which patient-specific 3D printed models of the disease were produced and used during outpatient consultations found that 3D printed models can enhance engagement with parents and improve communication between cardiologists and parents, potentially impacting on parent and patient psychological adjustment following treatment [29]. A similar study has shown statistically significant improvements in confidence, knowledge and satisfaction amongst adolescents after consultations in which the main features of their congenital heart disease was presented using a 3D printed heart model based on their medical imaging data [29]. Similar data exists for other organ systems too. For example, a study of 7 children and 14 parents found that 3D printed patient specific livers models significantly improved parental understanding of basic liver anatomy and physiology, tumour characteristics, the planned surgical procedure, and surgical risks [30].

3.2. Healthcare professional education

3D printing is useful for education of healthcare professionals from undergraduate to expert level. It has been shown that complex anatomy is better understood from physical 3D models than 2D images. 3D printed models of segmental liver anatomy are superior to 3D virtual and 2D images for teaching anatomy and preparing for surgery [4]. The days of the traditional method of teaching surgeons and other interventional physicians known as "See One, Do One, Teach One" are gone. This method is no longer ethical or applicable mainly because of concerns for patient safety [31]. It has been replaced with competency-based training. Part of this change has been adoption of simulation-based education [32]. 3D printing can provide high fidelity and realistic models for simulation of procedures. There are numerous reports of 3D printing for simulation. For example, a recent study used box trainers and 3D-printed stomachs to assess medical students, general surgery residents, and adult and paediatric general surgeons

performing a laparoscopic pyloromyotomy surgical procedure for hypertrophic pyloric stenosis, a common neonatal condition. There was a significant improvement in Global Operative Assessment of Laparoscopic Skills and Task Specific Assessments. Users felt the model accurately simulated a laparoscopic pyloromyotomy and would be a useful tool for beginners [33].

3.3. Intervention planning

Use of 3D printing is being explored for planning radiological and surgical intervention in many body systems. For example, a systematic review of 3D printed kidney models found an excellent demonstration of 3D relationships between renal tumours and adjacent anatomical structures and encouraging findings with regards to the role in surgical planning [34]. Similarly, in the liver a systematic review of 3D printing has found that models have served as valuable tools in preoperative planning of surgical or interventional procedures for treatment of malignant hepatic tumours [35]. However, there are few quantitative studies and further studies with inclusion of more cases are needed [34]. 3D-printed spine models have been shown to be useful in preparing for complex spinal surgery. Using 3D-printed spine models for preparation has been reported to allow successful performance of complex en bloc resections of primary cervical tumours [36]. In addition to open surgical procedures, 3D printing has been reported useful for planning minimally invasive and particularly endovascular interventional radiology procedures. For example; 3D-printed aortic have been used for design, planning, and/or optimization of fenestrated stent grafts [37], intracranial arteriovenous models have been found to be beneficial for radiosurgery treatment planning [38] and 3D printed models have been used to plan embolization aneurysms with challenging anatomy in the splenic artery [39] and arteriovenous malformations in the brain [40].

The most common medical application of 3-D printing is surgical guides—patient specific templates used intraoperatively to guide drilling or cutting. Using a guide specific to the patient has been shown to systematically reduce the operation time, as well as improved clinical outcomes in orthopaedic and maxillofacial surgery [41]. Another increasingly common methodology is the presurgical contouring or shaping of implants using 3D printed anatomical representations, as opposed to during the surgery itself [42, 43]. This is of particular interest in maxillofacial surgery, where a number of studies have shown reduced surgery time and improved surgical outcomes [44–46]. Similarly, bespoke 3D printed tools have been applied post surgically, through the design of bespoke external fixations for tibial fracture reduction [47].

3.4. Implants

3D printed objects can also be directly implanted into the patient to further take advantage of the ability to create bespoke, precise models. Patient specific implants (PSI) and have seen increasing interest in recent years, with numerous implants receiving FDA clearance in the first half of 2018 alone, in the wake of publication of the FDA guidance on additive manufacturing [48]. Biocompatibility is one of the major challenges of these implants, and has the devices are often made from materials which have received clinical approval previously, namely titanium and polyether ether ketone (PEEK) [41].

Using custom implants are widely accepted in maxillofacial and dental reconstruction surgery [49], in part due to the complexity of the bone and soft tissue reconstructions required. Titanium meshes have been used to create support patches to aid the repair of significant skeletal lesions [50], and splints for mandibular reconstructions [51–54]. Bespoke implants have helped reduce post-operative cosmetic deformities, which are commonly associated with these surgeries [55].

The most common PSI are those created for cranioplasty to restore cranial anatomy either after surgery or repair cranial defects, as opposed to the standard treatment of autologous bone. Implants constructed out of titanium, PEEK and polymethylmethacrylate (PMMA) have all been successfully implemented surgically, and the process is becoming common practice in a number of centres [56–58]. Overall a review of custom cranial implants found the all were found to accurate and reduce operating room time, with the overwhelming majority demonstrated improvement in clinical outcomes, arising from the improved anatomical verisimilitude [41].

Neurosurgery also has the potential to benefit from 3D printing due to complexity of the anatomical considerations, with meticulous planning required due to the associated risks. Therefore a reduction of surgery time would be a considerable benefit in these cases [59]. Xu et al. [60] fabricated a 3D titanium alloy axial vertebral body that was implanted for upper cervical spinal reconstruction following a C2 Ewing sarcoma resection. A bespoke vertebral body has also been successfully implanted for reconstruction after removal of a T9 Primary bone tumour [61].

Beyond reconstructing bone and rigid structures, 3D printing methods have been developed to create bioresorbable structures, which can be used as temporary stents and splints [62, 63]. For example, a bespoke bioresorbable airway splint was successfully implanted into a child with tracheobronchomalacia [8, 64].

3.5. Tissue engineering

There are numerous applications for 3D printing technology being developed. A promising area for the integration of 3D printing technology is tissue engineering. Tissue engineering is set to provide a solution to the unmet demand for tissues and organs for regenerative medicine. This will be achieved using a combination of stem cell, bio-materials, and engineering technologies. Experts in this field believe radical improvement to tissue engineering could come from 3D printing [8]. One main problems with the synthetic scaffolds currently used is the inability to adequately mimic in vivo microarchitecture. Advances in 3D printing technology may allow production of scaffolds, which do not suffer from this problem [8].

4. Limitations

While 3D printing in healthcare is becoming more prevalent and technological advancements appear promising across a wide spectrum of applications, there are some drawbacks which must be taken into consideration. The technology is evolving and long-term evidence for the benefit of 3D printing for various applications is unknown. The potential risks of basing decisions on or carrying out procedures with poorly executed models (due to errors at any stage of the model production pipeline) is yet unknown. Another challenge is the considerable time it takes to complete the pre-print component of the pipeline. While surgery is the

most complicated and expensive part of the treatment process, the increase in pre-surgical time may outweigh some of the costs saved in reducing surgery. Detailed cost effectiveness studies, which consider the increase in manufacturing capabilities and pre surgical time, as well as the reduction in operation time and improved patient outcomes, are necessary to truly evaluate the impact of 3D printing on healthcare costs. Improving the segmentation and model design stages of the pipeline will strengthen the case for 3D printing as a cost effective healthcare technology and are therefore crucial areas of research. For example, when state-of-the-art convolutional neural networks for automatic organ segmentation are packaged for non-expert users [65] model production time may decrease. A final consideration is the range of materials available for 3D printing. Currently materials often lack the ability to mimic both the mechanical and imaging (ultrasound, optical, electrical and X-ray) properties of biological structures. Tuning the electrical or optical properties during phantom construction has been demonstrated in rigid plastic, are not readily transferrable to flexible materials. Further the choice between these properties is mutually exclusive, as the additives used control one property change the other [66–70]. Multimodal phantoms are an area of active research and gel wax which can be tuned to have specific optical and ultrasound imaging properties looks to be a promising material [71].

Obtaining regulatory approval has been previously outlined as a significant barrier for the widespread implementation of 3D printing technologies in medicine [72]. While these challenges are still largely in place, the publication of the FDA guidance [48] has shown a clear pathway for full regulatory approval with these devices, with over 100 devices having undergone pre-market approval.

5. Conclusion

3D printing is permeating nearly every aspect of medicine from education, from before treatment begins in improving education and communication, through to improving surgical planning and reducing surgery times. As the technology becomes ubiquitous, there is increased demand for extracting the relevant anatomy from medical imaging data. This places further emphasis on the tools used to automatically create representative geometry and process them in a form, which is ready to be printed. There is of course, further emphasis on demonstrating the reliability of the technologies themselves, to reduce the time taken to produce the models, and the level of expertise to use them. The review presented here gives an overview of the myriad applications of 3D printing in medicine. The workflow to create the anatomical models along with a worked example would be helpful to medical and surgical students who need access to anatomical models, and also to students from associated fields who wish to gain a hands-on understanding of surgical training and planning.

Acknowledgements

This work was supported by Medical image computing for next-generation healthcare technology grant [EP/M020533/1], British Society of Interventional Radiology Bursary Knowledge

Exchange and Innovation Fund [KEI2017-02-01], the MRC (MR/J01107X/1), an Innovative Engineering for Health award by the Wellcome Trust [WT101957], and the Engineering and Physical Sciences Research Council (EPSRC) [NS/A000027/1].

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References

- [1] NHS England » Personalised medicine. <https://www.england.nhs.uk/healthcare-science/personalisedmedicine/>.2017
- [2] Biglino G, Capelli C, Wray J, Schievano S, Leaver L-K, Khambadkone S, et al. 3D-manufactured patient-specific models of congenital heart defects for communication in clinical practice: Feasibility and acceptability. *BMJ Open*. 2015;**5**:e007165-e007165. DOI: 10.1136/bmjopen-2014-007165
- [3] Javan R, Herrin D, Tangestanipoor A. Understanding spatially complex segmental and branch anatomy using 3D printing: Liver, lung, prostate, coronary arteries, and circle of Willis. *Academic Radiology*. 2016;**23**:1183-1189. DOI: 10.1016/J.ACRA.2016.04.010
- [4] Kong X, Nie L, Zhang H, Wang Z, Ye Q, Tang L, Huang WLJ. Do 3D printing models improve anatomical teaching about hepatic segments to medical students? A randomized controlled study. *World Journal of Surgery*. 2016;**40**:1969-1976. DOI: 10.1007/s00268-016-3541-y
- [5] Nikitichev DI, Barburas A, McPherson K, Mari J-M, West SJ, Desjardins AE. Construction of 3-dimensional printed ultrasound phantoms with wall-less vessels. *Journal of Ultrasound in Medicine*. 2016;**35**:1333-1339. DOI: 10.7863/ultra.15.06012
- [6] Javan R, Zeman MN. A prototype educational model for hepatobiliary interventions: Unveiling the role of graphic designers in medical 3D printing. *Journal of Digital Imaging*. 2018;**31**:133-143. DOI: 10.1007/s10278-017-0012-4

- [7] Sheth R, Balesh ER, Zhang YS, Hirsch JA, Khademhosseini A, Oklu R. Three-dimensional printing: An enabling technology for IR. *Journal of Vascular and Interventional Radiology*. 2016;**27**:859-865. DOI: 10.1016/j.jvir.2016.02.029
- [8] Fishman JM, Wiles K, Lowdell MW, De Coppi P, Elliott MJ, Atala A, et al. Airway tissue engineering: An update. *Expert Opinion on Biological Therapy*. 2014;**14**:1477-1491. DOI: 10.1517/14712598.2014.938631
- [9] Evans LV, Dodge KL, Shah TD, Kaplan LJ, Siegel MD, Moore CL, et al. Simulation training in central venous catheter insertion: Improved performance in clinical practice. *Academic Medicine*. 2010;**85**:1462-1469. DOI: 10.1097/ACM.0b013e3181eac9a3
- [10] Bücking TM, Hill ER, Robertson JL, Maneas E, Plumb AA, Nikitichev DI. From medical imaging data to 3D printed anatomical models. *PLoS One*. 2017;**12**:e0178540. DOI: 10.1371/journal.pone.0178540
- [11] Robertson J, Hill E, Plumb A, Choong S, West S, Nikitichev D. 3D printed ultrasound phantoms for clinical training. *IS&T's 32nd Int. Conf. Print. Fabr., Manchester*: 2016
- [12] Nikitichev DI, Xia W, Daher B, Wong RYJ, David AL, Desjardins AE, et al. Placenta vasculature 3D printed imaging and teaching phantoms. *IS&T's 32nd Int. Conf. Print. Fabr.*; 2016
- [13] Rengier F, Mehndiratta A, von Tengg-Kobligk H, Zechmann CM, Unterhinninghofen R, Kauczor H-U, et al. 3D printing based on imaging data: Review of medical applications. *International Journal of Computer Assisted Radiology and Surgery*. 2010;**5**:335-341. DOI: 10.1007/s11548-010-0476-x
- [14] Turney BW. A new model with an anatomically accurate human renal collecting system for training in fluoroscopy-guided percutaneous nephrolithotomy access. *Journal of Endourology*. 2014;**28**:360-363. DOI: 10.1089/end.2013.0616
- [15] Kusaka M, Sugimoto M, Fukami N, Sasaki H, Takenaka M, Anraku T, et al. Initial experience with a tailor-made simulation and navigation program using a 3-D printer model of kidney transplantation surgery. *Transplantation Proceedings*. 2015;**47**:596-599. DOI: 10.1016/j.transproceed.2014.12.045
- [16] Naftulin JS, Kimchi EY, Cash SS. Streamlined, inexpensive 3D printing of the brain and skull. *PLoS One*. 2015;**10**:e0136198. DOI: 10.1371/journal.pone.0136198
- [17] Prados F, Nikitichev DI, Vercauteren T, Ourselin S. Patient-Specific 3D Printable Anatomical Brain Models from a Web App. *Hawaii USA: ISMRM*; 2017
- [18] 3D-MED. n.d. <http://www.3d-med.uk/> [Accessed: June 8, 2018]
- [19] FreeCAD. n.d. <http://www.freecadweb.org/> [Accessed: January 1, 2016]
- [20] MeshLab. n.d. <http://www.meshlab.net/> [Accessed: June 8, 2018]
- [21] Blender. n.d. <https://www.blender.org/> [Accessed: January 1, 2016]
- [22] Weblet Importer. n.d. <http://www.meshmixer.com/> [Accessed: June 8, 2018]

- [23] OsiriX DICOM Viewer | DICOM Image Library n.d. <http://www.osirix-viewer.com/resources/dicom-image-library/> [Accessed: June 8, 2018]
- [24] 3D Slicer. n.d. <https://www.slicer.org/> [Accessed January 1, 2016]
- [25] Informed Consent. American Medical Association. <https://www.ama-assn.org/delivering-care/informed-consent>. 2018
- [26] General Medical Council. Consent guidance: Sharing information and discussing treatment options. n.d. http://www.gmc-uk.org/guidance/ethical_guidance/consent_guidance_sharing_info_discussing_treatment_options.asp. [Accessed: June 14, 2017]
- [27] Ripley BA, Tiffany D, Lehmann LS, Silverman SG. Improving the informed consent conversation: A standardized checklist that is patient centered, quality driven, and legally sound. *Journal of Vascular and Interventional Radiology*. 2015;**26**:1639-1646. DOI: 10.1016/j.jvir.2015.06.007
- [28] Pass JH, Patel AH, Stuart S, Barnacle AM, Patel PA. Quality and readability of online patient information regarding sclerotherapy for venous malformations. *Pediatric Radiology*. 2018;**48**:708-714. DOI: 10.1007/s00247-018-4074-3
- [29] Biglino G, Koniordou D, Gasparini M, Capelli C, Leaver L-K, Khambadkone S, et al. Piloting the use of patient-specific cardiac models as a novel tool to facilitate communication during clinical consultations. *Pediatric Cardiology*. 2017;**38**:813-818. DOI: 10.1007/s00246-017-1586-9
- [30] Yang T, Tan T, Yang J, Pan J, Hu C, Li J, et al. The impact of using three-dimensional printed liver models for patient education. *The Journal of International Medical Research*. 2018;**46**:1570-1578. DOI: 10.1177/0300060518755267
- [31] Kotsis SV, Chung KC. Application of see one, do one, teach one concept in surgical training. *Plastic and Reconstructive Surgery*. 2013;**131**:1194-1201. DOI: 10.1097/PRS.0b013e318287a0b3
- [32] Nataraja RM, Webb N, Lopez P-J. Simulation in paediatric urology and surgery. Part 1: An overview of educational theory. *Journal of Pediatric Urology*. 2018;**14**:120-124. DOI: 10.1016/j.jpuro.2017.12.021
- [33] Williams A, McWilliam M, Ahlin J, Davidson J, Quantz MA, Bütter A. A simulated training model for laparoscopic pyloromyotomy: Is 3D printing the way of the future? *Journal of Pediatric Surgery*. 2018;**53**:937-941. DOI: 10.1016/j.jpedsurg.2018.02.016
- [34] Sun Z, Liu D. A systematic review of clinical value of three-dimensional printing in renal disease. *Quantitative Imaging in Medicine and Surgery*. 2018;**8**:311-325. DOI: 10.21037/qims.2018.03.09
- [35] Perica ER, Sun Z. A systematic review of three-dimensional printing in liver disease. *Journal of Digital Imaging*. 2018. DOI: 10.1007/s10278-018-0067-x
- [36] Cho W, Job AV, Chen J, Baek JH. A review of current clinical applications of three-dimensional printing in spine surgery. *Asian Spine Journal*. 2018;**12**:171-177. DOI: 10.4184/asj.2018.12.1.171

- [37] Bastawrous S, Wake N, Levin D, Ripley B. Principles of three-dimensional printing and clinical applications within the abdomen and pelvis. *Abdominal Radiology*. 2018;**43**: 2809-2822. DOI: 10.1007/s00261-018-1554-8
- [38] Conti A, Pontoriero A, Iati G, Marino D, La Torre D, Vinci S, et al. 3D-printing of arteriovenous malformations for radiosurgical treatment: Pushing anatomy understanding to real boundaries. *Cureus*. 2016;**8**:e594. pp. 1-12. DOI: 10.7759/cureus.594
- [39] Itagaki MW. Using 3D printed models for planning and guidance during endovascular intervention: A technical advance. *Diagnostic and Interventional Radiology*. 2015;**21**:338-341. DOI: 10.5152/dir.2015.14469
- [40] Dong M, Chen G, Li J, Qin K, Ding X, Peng C, et al. Three-dimensional brain arteriovenous malformation models for clinical use and resident training. *Medicine (Baltimore)*. 2018;**97**:e9516. pp. 1-5. DOI: 10.1097/MD.00000000000009516
- [41] Tack P, Victor J, Gemmel P, Annemans L. 3D-printing techniques in a medical setting: A systematic literature review. *Biomedical Engineering Online*. 2016;**15**:115. pp. 1-21. DOI: 10.1186/s12938-016-0236-4
- [42] Ghai S, Sharma Y, Jain N, Satpathy M, Pillai AK. Use of 3-D printing technologies in craniomaxillofacial surgery: A review. *Oral and Maxillofacial Surgery*. 2018;**22**:249-259. DOI: 10.1007/s10006-018-0704-z
- [43] Chana-Rodríguez F, Mañanes RP, Rojo-Manaute J, Gil P, Martínez-Gómiz JM, Vaquero-Martín J. 3D surgical printing and pre contoured plates for acetabular fractures. *Injury*. 2016;**47**:2507-2511. DOI: 10.1016/j.injury.2016.08.027
- [44] Keller EE, Baltali E, Liang X, Zhao K, Huebner M, An K-N. Temporomandibular custom hemijoint replacement prosthesis: Prospective clinical and kinematic study. *Journal of Oral and Maxillofacial Surgery*. 2012;**70**:276-288. DOI: 10.1016/j.joms.2011.06.202
- [45] Gil RS, Roig AM, Obispo CA, Morla A, Pagès CM, Perez JL. Surgical planning and microvascular reconstruction of the mandible with a fibular flap using computer-aided design, rapid prototype modelling, and precontoured titanium reconstruction plates: A prospective study. *The British Journal of Oral & Maxillofacial Surgery*. 2015;**53**:49-53. DOI: 10.1016/j.bjoms.2014.09.015
- [46] Park SW, Choi JW, Koh KS, Oh TS. Mirror-imaged rapid prototype skull model and pre-molded synthetic scaffold to achieve optimal orbital cavity reconstruction. *Journal of Oral and Maxillofacial Surgery*. 2015;**73**:1540-1553. DOI: 10.1016/j.joms.2015.03.025
- [47] Qiao F, Li D, Jin Z, Hao D, Liao Y, Gong S. A novel combination of computer-assisted reduction technique and three dimensional printed patient-specific external fixator for treatment of tibial fractures. *International Orthopaedics*. 2016;**40**:835-841. DOI: 10.1007/s00264-015-2943-z
- [48] Press Announcements - Statement by FDA Commissioner Scott Gottlieb, M.D., On FDA ushering in new era of 3D printing of medical products; provides guidance to manufacturers of medical devices; n.d.

- [49] Ballard DH, Trace AP, Ali S, Hodgdon T, Zygmunt ME, DeBenedictis CM, et al. Clinical applications of 3D printing: Primer for radiologists. *Academic Radiology*. 2018;**25**:52-65. DOI: 10.1016/j.acra.2017.08.004
- [50] Horn D, Engel M, Bodem JP, Hoffmann J, Freudlsperger C. Reconstruction of a near-total nasal defect using a precontoured titanium mesh with a converse scalping flap. *The Journal of Craniofacial Surgery*. 2012;**23**:e410-e412. DOI: 10.1097/SCS.0b013e31825cef78
- [51] Metzger MC, Hohlweg-Majert B, Schwarz U, Teschner M, Hammer B, Schmelzeisen R. Manufacturing splints for orthognathic surgery using a three-dimensional printer. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2008;**105**:e1-e7. DOI: 10.1016/j.tripleo.2007.07.040
- [52] Cohen A, Laviv A, Berman P, Nashef R, Abu-Tair J. Mandibular reconstruction using stereolithographic 3-dimensional printing modeling technology. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2009;**108**:661-666. DOI: 10.1016/j.tripleo.2009.05.023
- [53] Shan X-F, Chen H-M, Liang J, Huang J-W, Cai Z-G. Surgical reconstruction of maxillary and mandibular defects using a printed titanium mesh. *Journal of Oral and Maxillofacial Surgery*. 2015;**73**:1437.e1-1437.e9. DOI: 10.1016/j.joms.2015.02.025
- [54] Zhou L, Shang H, He L, Bo B, Liu G, Liu Y, et al. Accurate reconstruction of discontinuous mandible using a reverse engineering/computer-aided design/rapid prototyping technique: A preliminary clinical study. *Journal of Oral and Maxillofacial Surgery*. 2010;**68**:2115-2121. DOI: 10.1016/j.joms.2009.09.033
- [55] Mitsouras D, Liacouras P, Imanzadeh A, Giannopoulos AA, Cai T, Kumamaru KK, et al. Medical 3D printing for the radiologist. *Radiographics*. 2015;**35**:1965-1988. DOI: 10.1148/rg.2015140320
- [56] Rammos CK, Cayci C, Castro-Garcia JA, Feiz-Erfan I, Lettieri SC. Patient-specific polyetheretherketone implants for repair of craniofacial defects. *The Journal of Craniofacial Surgery*. 2015;**26**:631-633. DOI: 10.1097/SCS.0000000000001413
- [57] Fiaschi P, Pavanello M, Imperato A, Dallolio V, Accogli A, Capra V, et al. Surgical results of cranioplasty with a polymethylmethacrylate customized cranial implant in pediatric patients: A single-center experience. *Journal of Neurosurgery. Pediatrics*. 2016;**17**:705-710. DOI: 10.3171/2015.10.PEDS15489
- [58] Lethaus B, Bloebaum M, Koper D, Poort-ter Laak M, Kessler P. Interval cranioplasty with patient-specific implants and autogenous bone grafts—Success and cost analysis. *Journal of Cranio-Maxillo-Facial Surgery*. 2014;**42**:1948-1951. DOI: 10.1016/j.jcms.2014.08.006
- [59] Mobbs RJ, Coughlan M, Thompson R, Sutterlin CE, Phan K. The utility of 3D printing for surgical planning and patient-specific implant design for complex spinal pathologies: Case report. *Journal of Neurosurgery. Spine*. 2017;**26**:513-518. DOI: 10.3171/2016.9.SPINE16371
- [60] Xu N, Wei F, Liu X, Jiang L, Cai H, Li Z, et al. Reconstruction of the upper cervical spine using a personalized 3D-printed vertebral body in an adolescent with Ewing sarcoma. *Spine (Phila Pa 1976)*. 2016;**41**:E50-E54. DOI: 10.1097/BRS.0000000000001179

- [61] Choy WJ, Mobbs RJ, Wilcox B, Phan S, Phan K, Sutterlin CE. Reconstruction of thoracic spine using a personalized 3D-printed vertebral body in adolescent with T9 primary bone tumor. *World Neurosurgery*. 2017;**105**:1032.e13-1032.e17. DOI: 10.1016/j.wneu.2017.05.133
- [62] Ware HOT, Farsheed AC, Akar B, Duan C, Chen X, Ameer G, et al. High-speed on-demand 3D printed bioresorbable vascular scaffolds. *Materials Today Chemistry*. 2018;**7**:25-34. DOI: 10.1016/j.mtchem.2017.10.002
- [63] van Lith R, Baker E, Ware H, Yang J, Farsheed AC, Sun C, et al. 3D-printing strong high-resolution antioxidant bioresorbable vascular stents. *Advanced Materials Technologies*. 2016;**1**:1600138. DOI: 10.1002/admt.201600138
- [64] Zopf DA, Hollister SJ, Nelson ME, Ohye RG, Green GE. Bioresorbable airway splint created with a three-dimensional printer. *The New England Journal of Medicine*. 2013;**368**:2043-2045. DOI: 10.1056/NEJMc1206319
- [65] Wang G, Li W, Zuluaga MA, Pratt R, Patel PA, Aertsen M, et al. Interactive medical image segmentation using deep learning with image-specific fine-tuning. 2017. DOI: 10.1109/TMI.2018.2791721
- [66] Avery J, Aristovich K, Low B, Holder D. Reproducible 3D printed head tanks for electrical impedance tomography with realistic shape and conductivity distribution. *Physiological Measurement*. 2017;**38**:1116-1131. DOI: 10.1088/1361-6579/aa6586
- [67] McDermott B, McGinley B, Krukiewicz K, Divilly B, Jones M, Biggs M, et al. Stable tissue-mimicking materials and an anatomically realistic, adjustable head phantom for electrical impedance tomography. *Biomedical Physics & Engineering Express*. 2017;**4**:15003. DOI: 10.1088/2057-1976/aa922d
- [68] Zhang J, Yang B, Li H, Fu F, Shi X, Dong X, et al. A novel 3D-printed head phantom with anatomically realistic geometry and continuously varying skull resistivity distribution for electrical impedance tomography. *Scientific Reports*. 2017;**7**:4608. DOI: 10.1038/s41598-017-05006-8
- [69] Dempsey LA, Persad M, Powell S, Chitnis D, Hebden JC. Geometrically complex 3D-printed phantoms for diffuse optical imaging. *Biomedical Optics Express*. 2017;**8**:1754-1762. DOI: 10.1364/BOE.8.001754
- [70] Bentz BZ, Chavan AV, Lin D, Tsai EHR, Webb KJ. Fabrication and application of heterogeneous printed mouse phantoms for whole animal optical imaging. *Applied Optics*. 2016;**55**:280-287
- [71] Maneas E, Xia W, Ogunlade O, Fonseca M, Nikitichev DI, David AL, et al. Gel wax-based tissue-mimicking phantoms for multispectral photoacoustic imaging. *Biomedical Optics Express*. 2018;**9**:1151-1163. DOI: 10.1364/BOE.9.001151
- [72] Malik HH, Darwood ARJ, Shaunak S, Kulatilake P, El-Hilly AA, Mulki O, et al. Three-dimensional printing in surgery: A review of current surgical applications. *The Journal of Surgical Research*. 2015;**199**:512-522. DOI: 10.1016/j.jss.2015.06.051

