JOURNAL OF MATERIALS RESEARCH AND TECHNOLOGY 2021;14:1430–1450

Available online at www.sciencedirect.com

jmr&t Journal of Materials Research and Technology

journal homepage: www.elsevier.com/locate/jmrt

Rveview Article

3D printing technology; methods, biomedical applications, future opportunities and trends

Yahya Bozkurt [a,*], Elif Karayel [b]

[a] Marmara University, Metallurgy and Materials Engineering Department, 34734 Kadikoy, Istanbul, Turkey

[b] Marmara University, Institute of Pure and Applied Sciences, Metallurgy and Materials Engineering Department, 34734 Kadikoy, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 18 March 2021
Accepted 10 July 2021
Available online 16 July 2021

Keywords:
3D printers
Additive manufacturing
Biomedical applications
Biomaterial
Bioprinting

ABSTRACT

3D printer technology is one of the innovations brought by the industrial age. It has been in our lives for many years. It is rapidly developing and used in many sectors like aviation and defence industry. This miracle manufacturing method has been frequently preferred for medical applications in recent years. In this study, 3D printer technology is introduced, various method of 3D printing are mentioned and the use of this technology in biomedical applications is referred. The use of 3D printing in surgery, pharmaceutical industry, disease modelling, development of customized implants and prostheses, organ printing, vet medicine and tissue engineering applications have been explained and this new method compared with traditional methods that used in the biomedical field. In addition, this study includes future opportunities that are expected to become widespread and developed in the future.

1. Introduction

3D printing is to manufacture any 3D data designed with CAD programs using a printer, by adding layers of material to a 3D physical part. 3D printing can be defined as additive manufacturing (AM) or layered manufacturing [1,2]. 3D printing which has some techniques like selective laser sintering (SLS) material jetting, stereolithography (SLA), material extrusion and binder jetting etc. can be used for different materials and areas. It is interesting for many areas due to its success in the production of complex parts and the saving of material and time thanks to high-speed production [3–7]. The effects of the developing technology can be seen in every field, from medicine to industry. 3D printers have become a part of this developing technology. Although it is thought to be a very new technology for us, what is actually new is that they are now more accessible and affordable than before. It is thought that 3D printing will move forward day by day thanks to the different facilities that provides for many different sectors [8–10]. This technology, which is preferred especially for many applications in the field of health, provides great benefits especially for medical imaging [11,12] and dental imaging [13,14], since it can largely manage studies such as medical device design and production that define the patient-specific anatomical structure. Applications using biocompatible materials such as the creation of tissue without any damage with living cells [15,16], blood vessel production [17], dental implants [18,19] and special medical prostheses [20,21] are just some of the contributions of the 3D printer to the biomedical

* Corresponding author.
E-mail address: ybozkurt@marmara.edu.tr (Y. Bozkurt).

https://doi.org/10.1016/j.jmrt.2021.07.050

field. In addition, this technology is also being researched in order to fix or replace defective organs such as kidneys, heart. Moreover, with this technology, organs that will perform the same biological functions as the original organs can be created. Thanks to this technology with organ and tissue printing, the future will be provided for many patients [22,23], and there is now a growing research effort focussing on the use of its research in a variety of biomedical applications [24,25]. 3D printer technology has become a preferred application in many sectors, especially in recent years its use in biomedical applications has attracted attention. In this study, 3D technology is introduced and various 3D method are referred. The superior properties of the method and its use in biomedical applications are mentioned. The use of the method in surgical applications, medical imaging, pharmaceutical industry, production of patient-specific medical prostheses and implants, vet medicine applications, skin engineering and stem cell studies and organ printing were explained. In addition, this study includes the benefits of this technology which is expected to become widespread in the biomedical applications, the current challenges that need to be developed, trends and future opportunities.

2. 3D printer technology

It can be expressed with many definitions such as "additive manufacturing" and "layered manufacturing". Although it has more than one definition, as we explained in our previous study, it is the method of adding main materials to layers that usually overlap to produce parts [26–29]. Printing process basically has some steps, and the first step is modelling. Generally, computer-aided (CAD) software is preferred in 3D modelling of the part to be manufactured. The object to be manufactured can be prototyped on the computer. If, it was previously prototyped by someone else, it could be downloaded to the computer or if the part to be produced is an existing object, it can be produced after scanning. After the modelling step, the model of the part is sliced into printable layers. The last step is printing. During the printing step, an object is manufactured by adding another layer on top of layers. Thus, production takes place in a layered structure. Thanks to this technology, prototyping which takes several months using traditional methods, can be reduced to a few days or hours, saving time and costs, as the requirements of traditional manufacturing such as moulds, a long production line are not needed. In addition, it provides design freedom that enables designers to create parts with geometric and structural complexity, as it is feasible to produce objects that are impossible to produce using conventional methods. Moreover, some limitations in traditional methods are not valid for the technology so the removal of various limitations, the method offers a different way of thinking and the ability by removal of various limitations to directly address people's imagination has been effective in the day-to-day development of this technology [20–32]. In the printing process an idea, a need is first transformed into a model and then into an object and thanks to this system, manufacturing can be performed easily and fastly. Fig. 1 shows the modelling and slicing steps for the printing of the humerus bone, which forms the bone structure of the arm region between the shoulder and the elbow [33,34]. To define the surface of the bone model and send it to the 3D printer in order to print, it must be converted to an STL file. The stereolithography file format, abbreviated as "STL", is obtained by dividing the surfaces of 3D designed models into many triangles in a mathematical order. STL format identify surfaces as a collection of triangles. The surface is created with simple triangles that fit together like a jigsaw puzzle. Thus the step-by-step printing process is performed [33,35–38].

This technology includes many methods in itself. Some of the frequently preferred techniques are powder bed fusion (Selective laser melting, selective laser sintering etc.), material extrusion, SLA etc. The differences between the techniques are on account of the method of processing the layers, the material used. When choosing one of the 3D technology methods, the material and used method properties used should be considered and the most suitable method should be selected [39,40].

3D printing methods can be classified according to the physical state of the main material, solid, liquid or powder. Different methods are used for different types of materials. This classification is shown in Table 1. The advantages and disadvantages of 3D printing methods and the materials that uses in the methods are shown in Table 2 [41–43].

3D printing technology can be applied to metal, ceramic, composite and polymer materials. The most commonly used metal materials are stainless steel [44,45], titanium [46–48], magnesium, aluminium [49–51], Cr–Co [52–54] alloys. In addition, the processing of unique materials such as titanium aluminides can be achieved with EBM. In addition to the benefits it provides, it is thought that the use of more metal alloys will increase in different applications. Metal materials, especially Ti and Cr–Co alloys, are preferred in biomedical applications, mostly because of their mechanical properties, biocompatibility, thermal, magnetic and electrical conductivity and generally high temperature resistance. Although metals have many advantages compared to polymers and other materials due to their properties such as laser absorption power and stability at higher temperatures, it can be said that this method is new for metals, while polymer materials have been used for 3D printing for years [55–59]. Polymer is the first material group produced with this technology and still constitutes a large part of the materials today. Polymers

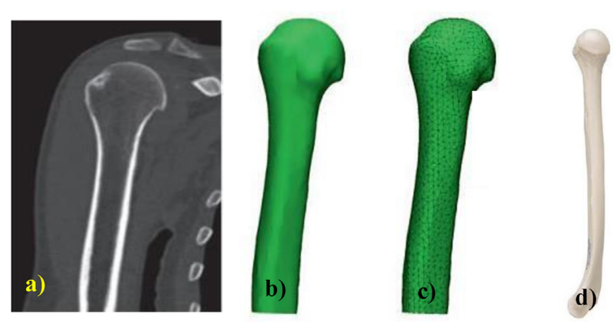

Fig. 1 – Production stages of humerus bone with 3D printer; a) imaging of humerus bone with the help of computerized tomography, b) modelling, c) slicing the model for printing, d) printed humerus bone [33,34].

Table 1 – Classification of 3D printing methods according to the material used and the solid, liquid and powder form of the material [41,42].

3D printing method		Material type			Material			
		Liquids	Powder	Solid	Metal	Ceramic	Polymer	Photopolymers
Powder bed fusion	SLS		x		x	X	x	x
	SLM		x		x		x	
	EBM		x		x	X		
VAT- polymerization	SLA	X				X		x
Directed energy deposition	DED		x		x			x
Material jetting		x						x
Binder jetting		x			x	X	x	

are preferred in various 3D printing technologies, just like using resin as the necessary supporting structure in the SLA method. Acrylonitrile butadiene styrene (ABS), polyamides, polylactic acid (PLA), polycarbonates (PC), resins are the most commonly used polymer materials with this technology. Especially in medical applications, SLA method is preferred for poly(ethylene glycol) diacrylate (PEGDA) and periodontal ligament (PDL) polymers while material extrusion for ABS, polycaprolactone (PCL), polycarbonate (PC), polylactic acid (PLA), poly(lactic acid). SLS technique is preferred for acid-coglycolic acid (PLGA), polyvinyl alcohol (PVA), polyether etherketone (PEEK), and binder spraying methods are preferred for polyvinyl and silica [60–64].

2.1. *Selective laser sintering*

SLS produces solid parts by solidifying powder-like materials layer-by-layer. Parts are produced by laser or another high energy beam on the surface of the powder bed. The method uses laser energy as an energy source to fuse powdered materials into a solid part. In the beginning, the powders are stacked on top of each other, and the powder starts to heat up with laser energy, the powder combines to form a solid object as shown in Fig. 2. The advantage of the method is that it enables the production of parts with a density near to full density. In this way, long postprocessing steps are avoided. Quality and properties of materials and some parameters of a method such as a laser energy density, laser scanning speed, scanning strategy, distance between layers, and bed temperature influence the mechanical properties of the product which manufactured by SLS [65–68]. SLS is similar to SLM process in terms of material addition technique and the energy input it uses. The main difference in the SLS process compared to the SLM process is that the powder material is sintered instead of full melting [69,70]. Since the materials with low heat conduction do not spread the heat around them, their sintering is successful. Therefore, it can be preferred for this method. When the powder properties and system parameters are considered, the process is successful. In addition, the SLS method can be used not only for polymers but also for metals such as Ti, Al, Co, Cr, ceramics or composites [71,72].

2.2. *Selective laser melting*

SLM is PBF method like SLS and EBM methods and powder bed fusion methods contain at least one thermal resource to induce fusion between the powder particles. In SLM method, the part is created layer by layer out of a powder which is heated by a laser source. When the temperature decreases, the molten material begins to solidify. The molten material forms the object while the unmelted powder portion supports the structure. When the process completed and part is built, the residual powder is removed [73]. In the process, the powder layer is shaped by laser scanning, and the object is manufactured owing to laser energy [74]. The machine system that ensures the process is shown in Fig. 3 [75]. SLM process is a printing method commonly used for metals such as Ni, Al, and Ti [76,77]. Especially when compared with the SLS method, it can be said that the SLM method is mostly preferred for metal materials. SLM like other AM techniques provides almost unlimited geometry and flexibility with the optimization of parameters like powder material, powder size, laser energy input, scan strategy scan speed and morphology. In addition, SLM has some advantages such as the use of different materials, relatively low cost [31,78,79]. All printing methods, including SLM, have many advantages. Thus they are accounted for the production of scaffolds and orthopaedic implants. Scaffolds and orthopaedic implants are produced by casting, forging and machining. While these techniques are a standard that is approved to safely and successfully produce scaffolds and implants 3D printing technologies are gradually affecting the production dynamics of customised implants and scaffolds. 3D printing enables the manufacture of complicated parts with hollow structures that cannot be achieved with other traditional methods [80–82].

2.3. *Stereolithography*

SLA is a frequently used variant of VAT polymerisation and is also an important technology for AM. In general, parts are produced using thermoset photopolymer material. Photopolymer is a polymer that changes its mechanical properties and chemical properties by a chemical reaction when exposed to light. Although the light is in generally invisible wavelengths such as ultraviolet (UV) or infrared, that can also be in visible wavelengths. The schematic working principle of SLA is shown in Fig. 4. Its parameters are usually predetermined, not changed. The height of the layer and the resolution of the light source are important parameters for the surface quality. Although it is a preferred method due to its high surface quality and its success in producing detailed parts, it has some disadvantages. Photopolymers are brittle, so their low impact

Table 2 – Materials used in some 3D printing methods, advantages and disadvantages of the various methods [43].

Methods	Materials	Advantages	Disadvantages
Fused deposition modelling	ABS, PLA, Wax blend, Nylon	High speed, high quality, used for a wide range of material	Porous structure for the binder, weak mechanical properties, often required support
Stereolithography	Resin (Acrylate or Epoxy based with proprietary photoinitiator)	Large parts can be built easily, high accuracy and surface finish	Expensive, not well-defined mechanical properties due to the usage of photopolymers
Selective Laser Sintering	Metallic powder, polyamide, PVC	High resolution, high strength	Only metals can be printed, post-processing required due to its grainy roughness
3D Inkjet Printing	Photo-resin or hydrogel	Very good accuracy, very high surface finishes	Fragile parts, poor mechanical the properties

resistance can be a problem. In addition, as they experience loss of mechanical properties over time, their part life is limited. The coating can be done to prolong the service life, but it is still a method with some limitations. Despite these disadvantages, it has success in the production of complex parts owing to the supporting structures. On the other hand, one of the biggest advantages of the method is to ensure that detailed, small and complex parts are produced in the right dimensions and with a very good surface quality. Due to these features, it is used especially in the fields of automotive and medicine. It, is clear that its use will increase in the coming days [83–89]. SLA has been successfully applied to the field of orthodontics and has been used to produce specialised dental implants that can be applied to oral surgery. In addition to these applications, in the treatment of cardiovascular diseases, behavioural and tissue interaction tests and applications to get a better approach to the tissue, neurosurgery, spine surgery and traumatology [90,91].

2.4. *Material extrusion*

In general, the material extrusion process is shortened FFF (Fused Filament Fabrication). Thermoplastic is used as the main material, and as can be understood from the filament expression in the name of the method, the thermoplastic material is mostly in the form of the filament. Some of the critical processing parameters of the method are layer thickness and extrusion tip diameter. Initially used polymers are heated above their glass transition temperatures and are fed into the extruder in the form of a semi-melt filament and then pushed through a nozzle as shown in Fig. 5 [92–94]. The filament is laid on the ground with the movement of the extrusion head, it cools and solidifies. Meanwhile, the platform moves down, and the process is repeated. The filament is deposited on the solidified filament layer so that layered production occurs. When the hot filament is laid on preprinted and cooled filaments, it heats them as well. Thus, the solidified filament layer melts again and merges with the last layer added. The layered structure is provided in this way. When processes are finished, postprocessing is usually required, and layers can be visible on the surface when the part is printed [42,95–98]. Especially promising for the biomedical industry in recent years, extrusion-based printing is also used for many different applications ranging from cell-loaded connections that mimic natural tissues [98].

2.5. *Material jetting*

The material jetting, which is a technology using photopolymers, is based on the curing of the photopolymers under the effect of light. In addition to photopolymer, the wax is also used. The method is to ensure that different materials are printed together. The supporting structures required in some applications are produced from different materials in this method [93,99,100]. Photopolymer or wax are jetted in droplets and cured by UV rays. Curing is the hardening of the base material by cross-linking polymer chains thus the first layer is created. Viscosity is an important parameter as the main substance form is a droplet. High viscosity will make flow difficult and therefore hard to obtain layers. On the other hand

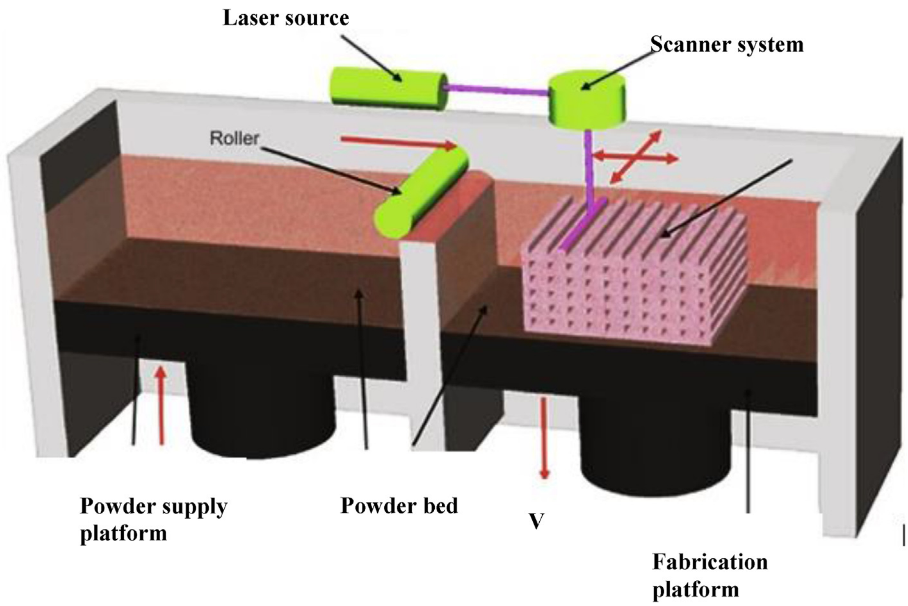

Fig. 2 – Model for SLS method [65].

low viscosity facilitates flow, so layers quickly deposit on top of each other and optimum structure cannot be achieved. In order to obtain a successful structure, the parameters must be optimum [101–105]. The process of solidification of drops is also important for the success of the technique; the improper solidification of the drops can cause unwanted results such as strength loss, deformity. Just as these parameters are important in the successful production of the part, the impact of postprocessing on the surface quality of the part is major. In addition to its success in producing the complex, detailed parts in the desired form and in the correct dimensions, the surface quality of the produced part is high. The printed parts can be coloured as desired, and colouring, processes are easier and less costly than other methods. The process can be accelerated. Besides the advantages, the main material of resin is brittle thereby the mechanical properties of the produced product are low. Also, the type of material used is limited. However, these disadvantages are expected to be improved, and the method developed [105,106].

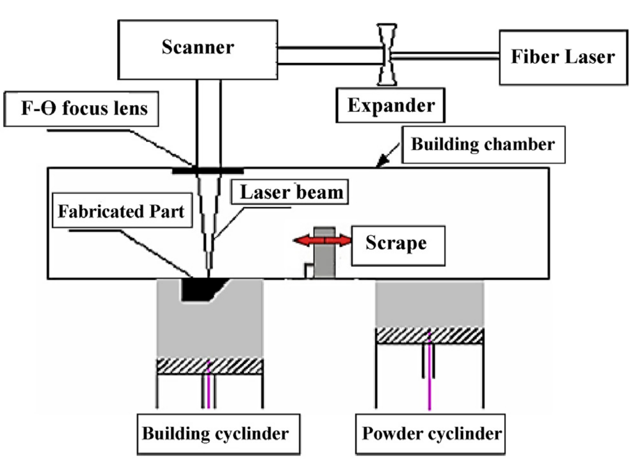

Fig. 3 – SLM working system [75].

2.6. *Binder jetting*

The binder jetting process takes place in the powder bed, as the method name suggests, the binder is used. The reason for using the binder is to ensure that the powder particles are connected. New layers are created on top of the structures that are connected to each other and become layers. Thus, layered manufacturing is realised. This process has the advantages of the previously mentioned powder bed fusion techniques. The parts produced in the powder bed do not require supporting structures owing to the physical support of the powder. Therefore, in this method, the supporting structures are not needed. Also, unused powders can be recycled so that unused powders can be recycled just like in powder bed fusion methods. The functioning of the method also depends on the material. As it was used for the first time, gypsum-based powder and water-based binders can be used. Also, different materials and different binders can be used. In addition, it is possible to manufacture coloured parts like material jetting technology. The powder bed has the advantages of fusion, as well as some advantages in the material jetting method. For example, faster parts can be produced, and material limitation is less. High-quality parts can be produced in metal and ceramic materials. It has many advantages, so the method can be used in many sectors [105–109].

3. 3D printing technology in biomedical applications

Recently the use of 3D printing in the biomedical applications has been interesting for lots of researches, and many

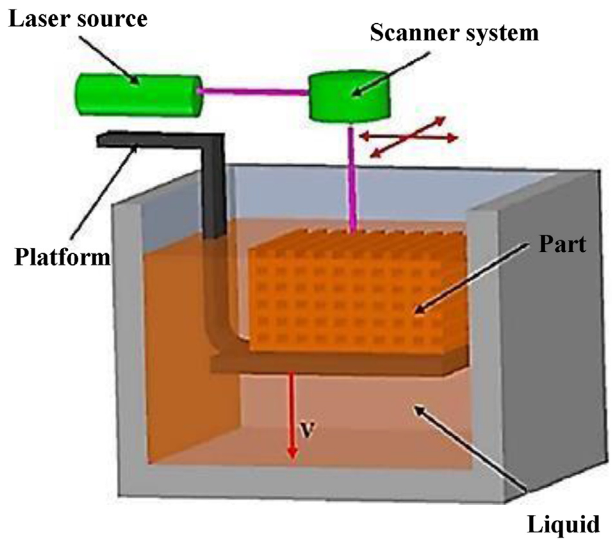

Fig. 4 – Working principles of the SLA method [89].

companies around the world have contributed to the increase in the use of this manufacturing method in the medicine with their laboratories and scientific researches. This technology offers significant benefits for biomedical applications and devices owing to the ability to manufacture the optional product according to specific patient needs. For example, many instruments used in surgery are currently produced by forging or casting methods and by using the mould required for the part, with special surface coating for desiderated surface properties and mechanical properties. These procedures need uneconomic machine and equipment, so distinct implants or patient-specific are unaffordable and seldom produced. Machining of titanium alloys is more difficult as it has low elastic modulus, high mechanical strength and low thermal conductivity compared to 314L stainless steel. For this reason, patient-specific implants are uneconomic to manufacture from these materials. These methods generate large material waste, and it is not possible to manufacture functional grade implants, so it is a miracle opportunity in order to the manufacturing of various functional biomedical equipment. Biomedical is a branch of technology that deals with the production of all material, apparatus and devices that can be used for diagnosis and treatment in medicine. Artificial kidneys, heart, dental implants, knee prostheses, lenses, pacemakers and hip etc. this includes biomedical applications. Printing for these medical applications allows the customised complicated geometry of implants and upon request production, which can result in a significant attenuation in expense and stock. Also, the unit cost remains constant for all product since any special tooling for any product not to be necessary for 3D printing. This expense assessment forms the basis and purpose of this method for biomedical orthopaedic implants. Since this technology has many advantages, its use in biomedical applications is increasing day by day. It is used in biomedical applications such as implants and tissue engineering. It is predicted that its use in these application areas will increase in the near future, as shown in Fig. 6. Today, it is preferred for many different applications, especially in the medical sector, as shown in Fig. 7. Despite some remarkable achievements, the development of organs tissue with this method goes on pose important challenges [110]. From cancer treatment to patient-specific prostheses; In many areas of medicine, inventions strengthened with 3D printing are sought to improve the quality of life or save patients life [111–121].

3.1. *Surgical applications*

Since the 3D printing has an improved imaging system in surgical planning, it ensures a better visualisation of the patient's anatomical structure by surgeons. During surgery, a surgical template helps to precisely guide the surgical procedure, estimate appropriate angles and have a prior opinion of the direction and size of the bone. Under normal conditions, it is difficult to assess the location of blood flow and predict the structure of the bones. Therefore this technology is used today as a guide that provides correct planning and supervision during surgery to provide accurate imaging inside the body. In surgical applications, this method is often used as a surgical guide and surgical 3D modelling as mentioned. The use of this technology as a guide in surgical imaging is shown in Fig. 8. Surgical applications are only a broad definition, including cardiovascular surgery, neurosurgery, orthopaedic surgery, general surgery and plastic and aesthetic surgery so this method is preferred especially in vascular surgery, tumour resections, orthopaedic surgery and neurosurgery etc. Successful use of technology in these areas can improve surgical results and reduce medical errors, thereby increasing patient safety. In addition to these, it is anticipated that the application of this technique both during and before surgery will be beneficial in the training of medical students and surgical assistants. These benefits of technology have not been ignored; the use of 3D printers in surgical applications increases every year and investigations are accomplished to the development of this [121–129]. In one of the studies 3D printing models and rendered images were compared, and as an end of the investigation, it has been established that the use of the printers provides an obvious benefit in examining the patient's anatomy [130]. It enables the anatomical structure of the patient to be viewed during the preoperative planning stage, to simulate the surgical intervention, as well as to test surgical instruments with the help of a 3D model. In general terms, a common belief is that it is useful in surgical applications. It is expected that the number of studies carried out in the coming years, surgical application areas and this technology may improve.

3.2. *Disease modelling*

3D printing technology is used to create a copy of the patient's special anatomy before complex operations or to understand the disease. In this way, the copy of the organ can be examined much more clearly than imaging methods such as tomography, can be made pratice before surgery, and the margin of error can be reduced. In addition, it can be adopted as an easy and fast method in the diagnosis and treatment of the disease. A study is about modelling kidney diseases with printing. Kidney models are modelled with high accuracy, thus planning and simulating complex surgery is provided. This method makes it easier for medical students to understand the disease through

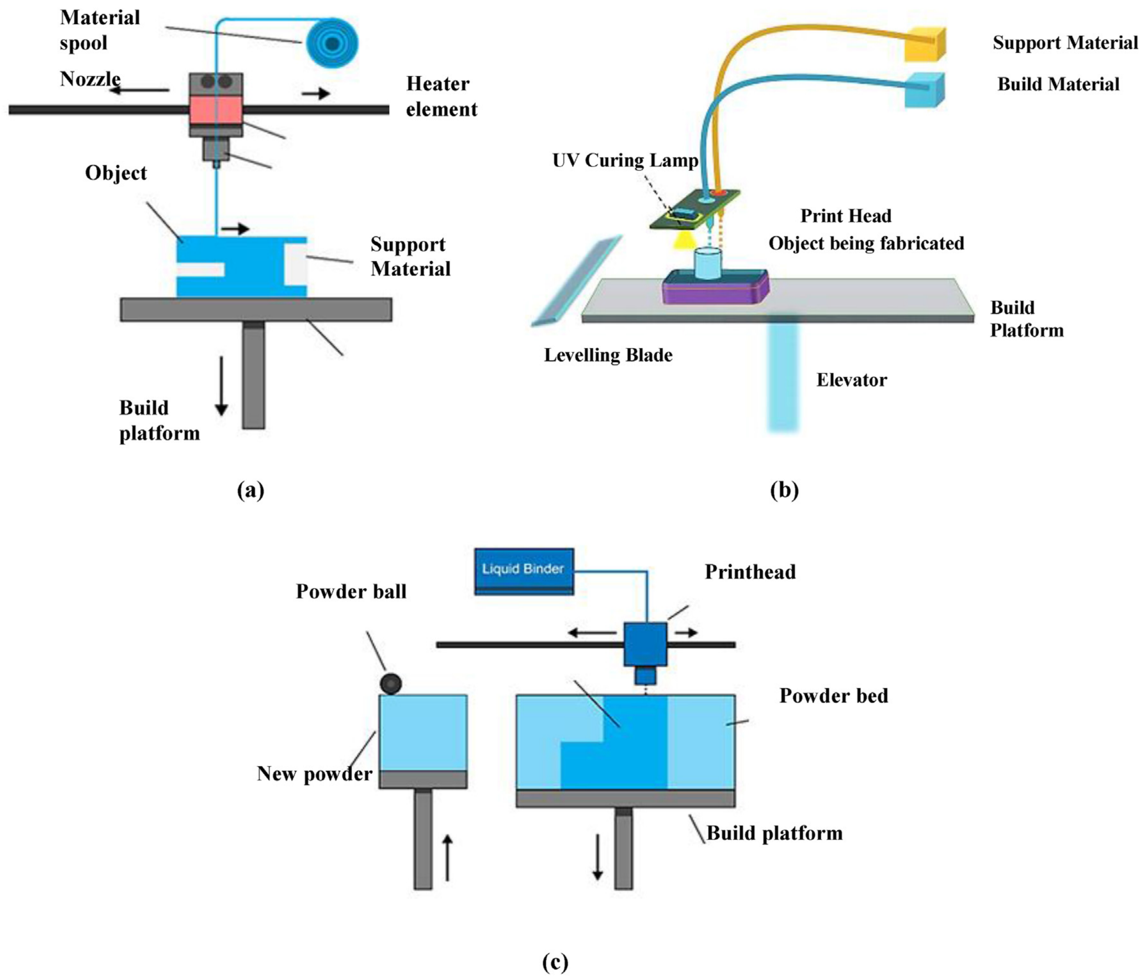

Fig. 5 – Working principles of 3D printing methods; a) Material extrusion technique, b) Material jetting, c) Binder jetting [92–94].

modelling and provides the opportunity to examine complex kidney anatomy and pathology. In today's conditions, the diagnosis of kidney tumours can be made with technological methods such as tomography and MRI, but understanding the relationship between kidney tumours and surrounding renal anatomical structures is quite difficult in some cases. Therefore, modelling has a great role in the diagnosis of kidney tumours and in examining the patient's condition. There are many studies that argue that modelling will be of great benefit not only in the kidney but also in cardiovascular and liver diseases. Traditional imaging methods may not be sufficient, especially in complex surgeries such as cardiovascular surgery because these methods are limited on a flat-screen. Therefore, 3D modelling for many surgeries can provide a complete representation of the anatomy, prevent unexpected findings, and provide personalised treatment. In this way, it can reduce the duration of the operation and the possibility of error and provide patient safety [131–138].

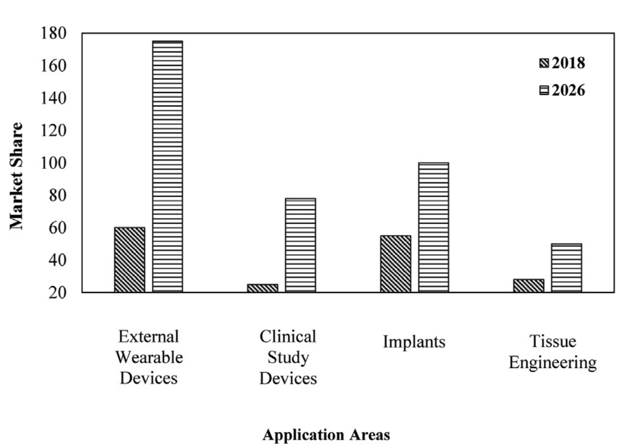

Fig. 6 – Forecast of the increase in the use of 3D printer technology in biomedical applications [113].

3.3. *Medical devices*

3D printer technology is a frequently preferred method in the production of many devices used in the medicine. It is especially used in the production of medical devices that are hard to produce using conventional methods. Also, the production of devices suitable for the anatomical structure of the patient is provided at an affordable cost. For this reason, most of the hearing aids specially produced for the patient, such as

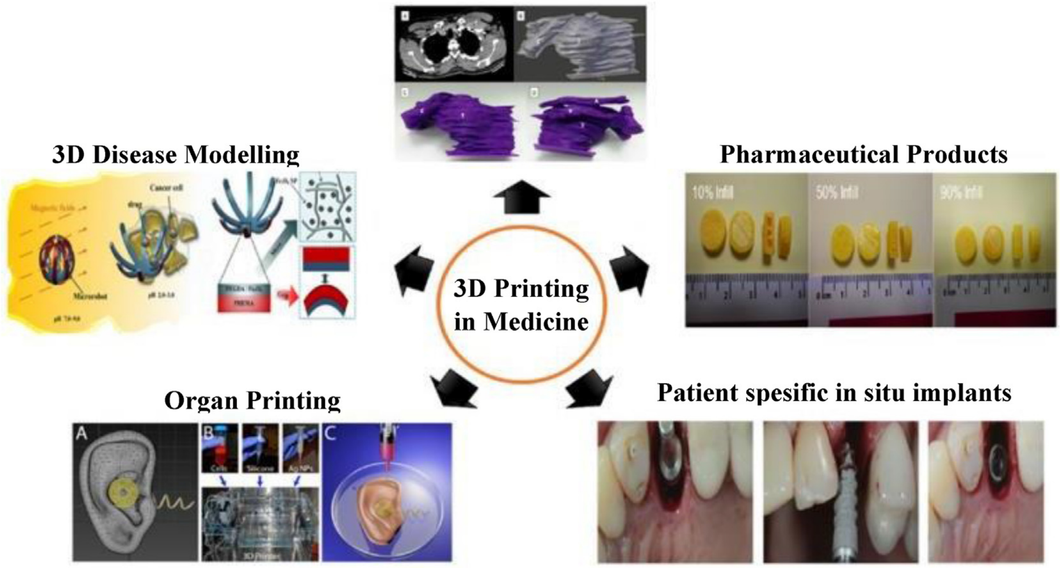

Fig. 7 – Applications of 3D printer in health [115].

hearing aids, which must be suitable for the patient's ear anatomy are produced with this technique [139,140]. In fact, it is said that more than 10 million printed hearing aids were produced worldwide for 2013. Today, much more than this number is produced and used. Thanks to the advantages of this method, hearing aids can be produced in a much shorter time than normal production time. This technology is promising for many medical devices not only hearing aids but also especially eye lenses, stethoscopes and glasses specially designed for the visually impaired [141–143]. The manufacture of many medical types of equipment like hearing aids with printing is very valuable in many aspects such as cost, patient safety and device efficiency. It is anticipated that the use of 3D printers will increase for many of our needs in the near future. In fact, the term medical devices are a broad definition, from the human face and skull surgical transplantation to prostheses, implants and human organs, etc. can contain. Therefore, this topic will be mentioned in the next sections [144,145]. Treatment is a promising technology for 3D printing technology, especially with regard to the demanding paediatric patient population that requires different doses and flexible-dose adjustments. When pharmaceutical production is adopted with this method, besides all its benefits, it can be an alternative to clinical medical research on humans and animals in toxicology tests and cosmetic development. It is predicted that it will be a great benefit even because of this [146,147]. As shown in Fig. 9, the 3D printer can be used to design drugs in desired dimensions and geometries. It can be a solution to the problems encountered in conventional manufacturing and can provide the development of drugs with complex formulations in terms of cost and time [148–157].

3.4. *Patient-specific implants*

The manufacturing of patient-specific prostheses is of great importance in the medical use of 3D printer technology. Personal implant application in dental implant applications provides convenience for healthcare personnel as well as patient comfort. However, the implants produced with traditional methods are accepted as the gold standard thanks to their biological compatibility and superior mechanical properties. They are not able to provide enough aesthetic appearance, they are insufficient as a result of placing the implant with an angulation far from ideal, and they cause areas that cannot be cleaned to prevent the continuity of hygiene, and personalized implants can be produced. One of the advantages of this technology is that it eliminated traditional measurement methods and shortened waiting times. The printing method is frequently preferred in knee joints, tibia bone,

Fig. 8 – Use of 3D printer technology in surgical imaging [127].

Fig. 9 – Drugs with different geometries such as cylinder, torus, film and size produced by 3D printer [157].

femur bone, fibula bone implants and dental implants. For example, hip and knee implants produced by 3D printing are shown in Fig. 10. The tibial tray produced by SLM technique, which is one of the 3D printer methods, is shown in Fig. 10a. Femoral component fabricated by SLM is shown in Fig. 10b, acetabular cup manufactured by AM is shown in Fig. 10c and hip stem built with SLM method is shown in Fig. 10d. Thanks to this technology, it allows an accurate manufacturing specific to the patient with biocompatible. With successful surgical imaging, anatomical information of the patient is obtained, a digital model is created, and complications and errors that may occur in the placement of the implant are prevented. In addition, implants produced specifically for the patient's anatomy increase the chance of success. A printed mould can be used in the production of these implants or can be printed directly [158]. In addition, it can support tissue regeneration depending on the regeneration and growth factors of cells. Furthermore, implants produced with AM can have high fatigue strength and high corrosion resistance [159–166]. One of the types of implants that can be successfully produced with this method is cranial implants. Patients often need cranial implants due to damage to their cranial part as a result of an accident or injury. The reason for using these implants is to protect the brain from possible damage and to improve the cranial appearance and provide psychological support to the patient. Cranial implants are modelled with a 3D printer in accordance with the patient's skull anatomy and produced with this technology using a biocompatible material. This miracle technology is preferred in the production of implants due to provides good mechanical properties and the ability to produce suitable for the patient [167,168]. There are many successful examples of cranial implants produced with 3D printers in the world. One of these examples is the production of implant for Yaşar Ağayev from the Azerbaijani army, who was shot in the head in April 2016. METUM (Turkish abbreviation for Medical Design and Production Center) produced cranial implants with 3D printers for Yasar Ağavey. It is the medical design and manufacturing centre in Turkey. Yaşar Ağayev, who lost half of his skull, could not speak and could not move his left side, was replace with a cranial implant that he produced as a result of METUM's study. Thus, thanks to this implant produced in a printing technology, the damage to the patient's skull is largely eliminated. METÜM and other organisations in different countries continue to create miracles thanks to this technology [168].

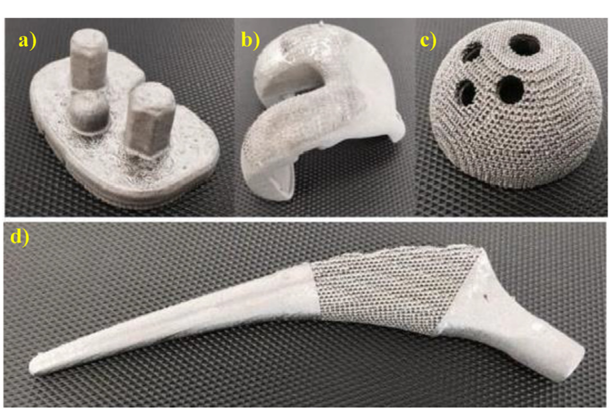

Fig. 10 – Hip and knee implants manufactured by 3D printer technology; a) tibial component, b) femoral component, c) acetabular cup, d) hip stem [162].

3.5. *Patient-specific prostheses*

Prostheses have a very old history and are thought to have been used since ancient Egypt. Generally, prostheses are produced by traditional methods such as casting methods nowadays, 3D printing technology has also been used in order to manufacture prostheses and has to get successful results. Compared to a prosthesis produced with traditional methods, a big difference can't be seen between them compared to the one produced by a 3D printer. 3D technology is more advantageous for personal production. Recently, the wide commercialization of 3D printing in prosthetic designs has provided the opportunity to rapidly prototype a number of desired designs, and they can be tested in a short time at minimum cost. The 3D printer enables the production of prostheses that have the desired mechanical and physical properties and are fully compatible with the patient in a short time. Realistic, suitable for the patient's anatomy, and close to the original mechanical properties, prostheses are produced for the ear, nose, teeth, bone, hand and foot. In addition, using the multi-material printing approach, it is possible to adjust the skin tone of the person who will use the prosthesis in accordance with the skin pigmentation. However, there are some limitations regarding this technology. One of them is that the prosthesis has a harder texture compared to the original skin [169]. And the prostheses are not adjustable; that is they do not grow with the patient, after a patient grows up the prosthesis will not fit for the patient. It is expected that these limitations are eliminated and the usage potential of the technology increases. Another problem that is thought to be a solution is the weight of the prostheses. Especially complex prostheses are heavy. Weight may not seem like an important problem in the short term, but the use of the prosthesis becomes difficult when doing daily activities [170–177]. Prostheses can be produced in different colours to provide the necessary mechanical and physical properties for people of different ages, races, genders and sizes [178].

3.6. *Vet medicine*

3D printing is widely used in human medicine, as mentioned in previous sections, in many surgical applications, especially in vascular surgery, neurosurgery, modelling of diseases, and patient-specific implant and prosthesis design. The benefits of the method are hopeful not only for human medicine but also for veterinary medicine. In most of these investigations, it is used in different application areas in vet. For example, in order to manage view and understand the anatomy of the animal more clearly and the veterinarian's practice before the surgery, imaging with this method is preferred. Thus, the veterinarian can anticipate the possible anatomical differences, reduce the margin of error and ensure the safety of the animal just by planning pre-surgery [179–181]. In one of these, surgical intervention AM to improve a dog's lameness has

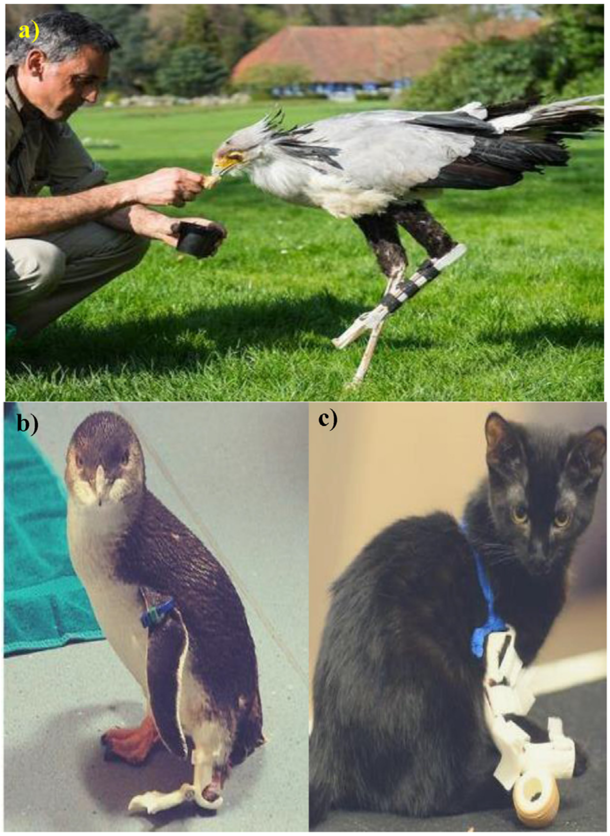

Fig. 11 – 3D printed prostheses for animals: a) Leg prosthesis for secretary bird, b) A prosthesis for a penguin whose foot has been amputated, c) Prosthesis produced for a kitten who is not one of the congenital front legs bones [184,185].

been successful in characterising and planning surgery. In another case, 3D printer was used in the tumour removal surgery of the dog so the defect area was determined the mass was removed with the correct surgical planning and the patient was cured [182,183]. Unfortunately, every year hundreds of animals are disabled through accidents and some medical issues every year. Thanks to these technology prostheses, that are fully compatible with the anatomical structure for animals can be produced, a damaged bone, tissue or muscle can be printed and implanted like the original one. There are many successful examples and studies on this subject. One of them is the use of it in the surgery of the hornbill kept in the Jurong Bird Park zoological collection, which was diagnosed with cancer. This technology was used as a surgical guide, and the damaged muscle was removed with a smooth surgery, and a prosthesis designed with a 3D printer was placed. In this study, it was used for both preoperative imaging and production of prosthesis suitable for the patient, and it was successful [183,184]. Thanks to this technology, prostheses can be designed for many animals; some of these examples are shown in Fig. 11. For example, is a printed prosthesis for a secretary bird whose leg is broken and whose leg amputated due to damage, as shown in Fig. 11a [184]. In another example, a prosthesis with AM is designed for acute penguin whose foot has been amputated. The prosthesis is shown in Fig. 11b. Prostheses are not only produced for animals that have amputated limbs, but also for congenitally missing limbs. For instance, one of the congenital front legs bones of a 4-month-old kitten was missing, so a suitable prosthesis was produced with 3D printing for the offspring. The prosthesis is shown in Fig. 11c [185]. There is no ready-to-use implant in animals, and patient-specific implants are the one way convenient. For this reason, using 3D printing, a perfectly compatible patient-specific implant can be produced in accordance with the anatomy of animals. Moreover, in many situations, necessary implants with complicated shapes will be not possible or uneconomic to production by methods other than AM. In veterinary orthopaedics, AM can mainly be used to create bone models, complex patient-specific implants, and surgical guides. It is expected that the use of this technology in veterinary medicine will increase in the near future [186,187].

3.7. *Tissue engineering and stem cell technology*

Tissue Engineering (TE) includes the application of engineering principles and life sciences together for tissue regeneration, regulation and continuity of organ functions. It aims to produce living cells in in vitro environment on support scaffolds made up of biomaterials and place them in the damaged area of the body. Its main purpose is to produce three-dimensional functional artificial tissues and organs by using cell, tissue scaffold, instead of damaged organs that have become unable to perform their duties [188–190]. Bioprinting is an evolving technology with various applications in making functional tissue structures to replace injured or diseased tissues. It is based on the principle of precise positioning of biological materials and living cells layer by layer. During the bioprinting process, a solution of biomaterials or a mixture of several biomaterials is usually used in the form of a hydrogel that encapsulates the desired cell types to create tissue structures. Hydrogels containing cells are printed in defined shapes. And the polymers in the hydrogels are joined together or cross-linked so that the printed gel becomes stronger. Bioinks can be made from natural or synthetic biomaterials alone or a combination of the two as hybrid materials. Biological materials must be biocompatible with materials related to the ink and the printer itself. Some of the methods used for 3D bioprinting of cells are photolithography, magnetic 3D bioprinting, stereolithography and direct cell extrusion [191–197]. The pre-process, methods used in technology and applications of the bioprinting are shown in Fig. 12 [198].

TE generally involves the use of material referred to as scaffold. The scaffold is designed as a means of transport for the transport of cells to a specific area, providing structural support for newly formed tissue. Tissue scaffolds are of great importance in preserving their chemical and biological properties and cell viability. Scaffolds should be biocompatible, have a porous structure and provide mechanical support to the cells. However, the necessary conditions for scaffolding can't be obtained with traditional methods. For example, adequate control of the ideal pore mesh and pore size can't be achieved, and non-ideal scaffolds are produced. 3D printing is used to solve this problem, and controlled pore size and pore structure can be obtained thanks to this technology. The desirable mechanical properties can be obtained by controlling the pore in the

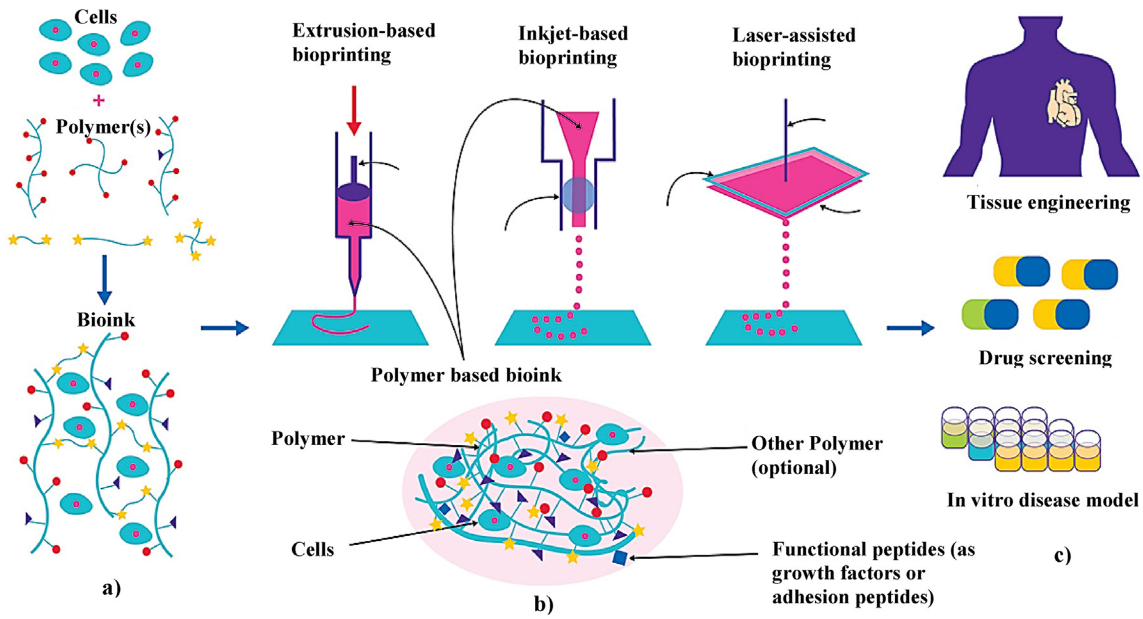

Fig. 12 – 3D Bioprinting; a) Bioinks are formed by combining various biocompatible materials and cultured cells; b) Various methods used in the process; c) Applications areas [198].

scaffolds produced with printers. The very porous structure reduces the strength and the desired strength can't be obtained, while the non-porous structure is not suitable. Therefore, the desired mechanical and physical properties are achieved through 3D printer production. Pore control is not only provided in scaffolds, but also scaffolds compatible with bone tissue can be produced. Successful experiments have been carried out for cell-free tissue scaffolds, cartilage, bone and skin printing studies produced with this technology [199–206]. In one of the studies on this subject, TE models with high bioactivity have been developed with bioprinting. The study aims to produce BC/PCL composite scaffold with a 3D printer. It has been concluded that bioprinting is a useful technology for many areas of health, as well as showing great potential for TE and regenerative medicine [206]. The scaffolds produced with AM can also repair the damaged nervous system in spinal cord injuries that are still not successfully treated [207]. In addition to these developments, there are many studies and many successful experiments. Artificial tissue production instead of joint, cartilage and skin losses due to injuries, diseases and accidents are important developments for the healthcare industry. Artificial tissue production instead of joint, cartilage and skin losses due to injuries, diseases and accidents are important developments for the healthcare industry. The classical processes of tissue engineering are shown in Fig. 13 [208].

A stem cell is a host cell that can renovate itself and grow into one or more cells in its tissue. Stem cells can not only differentiate into adult cells of tissue-specific stem cells, but can also turn into unexpected cells, so they hold promise for regenerative medicine. In addition, stem cells provide a renewable source of cells because they are constantly growing. Moreover, some stem cells provide an internal repair that is they divide to renew cells during illness or injury. Thus, it plays a role in the regeneration of all tissues and organs that are sick or damaged. By transforming into the needed cell type; repairs organ and tissue damage or loss due to disease, injury and other reasons. Thanks to this feature, it is used in the treatment of many diseases that may result in death and some types of cancer. Stem cells can be transformed into blood or muscle cells and can be produced by 3D printing. Thanks to the 3D printer, adipose tissues, blood vessels using stem cells can be produced, thus providing a deeper perspective on metabolic diseases and potentially replacing damaged tissues. In addition, cell behaviour, environment, tissue formation and architecture can be better understood. It is also thought that it will be used for many applications from tissue production to clinical applications in the future. Especially with this technology, many patients will be hopeful with stem cell production [209–214]. Unfortunately, stem cell donation is not enough today, and many patients die while waiting for a transplant. In the future, it is hoped that the production of stem cells will be done much faster and more effectively with the 3D printer, and thus the treatment of many diseases will be much easier. Until it makes this process much easier, please let us be a stem cell donor to save someone's life.

3.8. *Organ printing*

Recent developments have enabled biocompatible materials, cells, to be 3D printed on living tissues. Bioprinting is developed to produce tissues and organs appropriate for organ transplantation. Bioprinting includes additional complexities such as material selection, growth and differentiation factors, cell types, and technic difficulties living cells compared to non-bioprinting. This technology has been applied to production and tissues, involving multilayer heart tissue, cartilage and bone structures. In addition, highly efficient printed tissue models have been developed for drug discovery, toxicology and various research. As we move towards printing complex

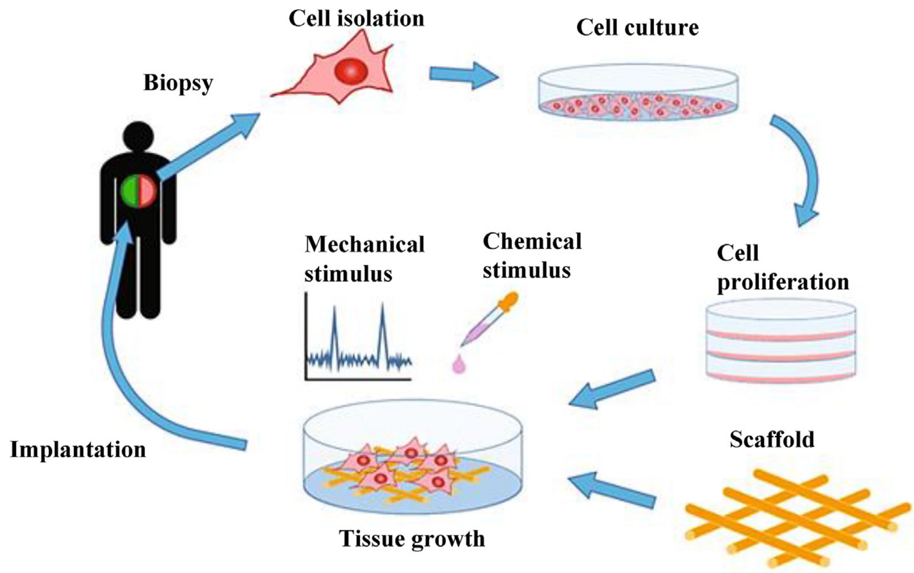

Fig. 13 – Classic flow of tissue engineering applications [208].

tissues, various problems such as cell and material requirements, tissue maturation and functionality will be encountered, and different research will be needed to overcome these difficulties and transform this technology into regenerative medicine because the possibilities of this technology are too many to ignore in the medical field. One of them is the benefit that organ printing with the 3D printer will add to organ donation. Unfortunately, organ donation is still insufficient despite the increase in volunteer donors. The average donation is not even a third of those in need [215]. Solving this problem requires long-term solutions by creating or generating living organs from one's own cells, as with solutions to other major engineering challenges. Despite the medical benefits of 3D printer and advances in tissue engineering, several problems need to be solved to make organ pressure a reality. Even if the organ is imitated with a 3D printer, it is very difficult to perform its original function. The most important challenge is the assembly of vascular structures, a problem faced by most tissue engineering technologies. 3D thick tissue or organs designed without a circulatory system cannot receive enough nutrients, waste removal and gas exchange required for maturation during circulation which causes cell viability problems and malfunction of organs produced by 3D printing. But on the one hand, one of its biggest advantages is the potential to use patient-specific cell resources, and the tissue produced minimizes the possibility of organ rejection. When some of its limitations and problems are solved, AM will bring revolutionary innovations in the field of medicine and save many lives. Therefore, many researchers are working on organ printing with 3D printers. Organ production with it can't yet produce organs that can perform exactly the same functions as the original, but organs very close to the original can be produced by examining the patient's anatomical structure as shown in Fig. 14 [215–224]. For example, Zein et al. produced the first fully printed liver known in their study. By using it in the preoperative planning stage, they have achieved better preoperative surgical planning, and by examining the livers of patients and donors, they have successfully developed synthetic fibres with 3D printed networks of vessels and bile structures. They were able to produce a living transparent 3D liver that allows detailed visualization of vascular and bile structures, as shown in Fig. 14a. With this method, the liver produced for the patient was compared with the natural liver taken from the donor, and the success of the study has been proven. There are still many limitations, but it is clear that these studies are of great importance for the future [225]. Organ printing with this technology can be used not only for organ donation but also to produce and examine a replica of the sick organ in order to better understand the patient's disease. One example of this situation is shown in Fig. 14b. A 3D printed physical anatomical kidney model was created using tomography images of the patient with kidney cancer. The 3D printed model facilitated the preoperative planning, while successfully controlling the cancer, the cancerous tumour tissue was removed, and the operation was successfully completed [226]. Another successful example concerns the ability of organs produced with AM to perform some functions. In this study, an auricle containing electronics that provides alternative abilities to human hearing was produced with this technique. Despite the complex curved structure of the ear consisting of cartilage, a bionic ear was produced in accordance with the anatomical geometry, as shown in Fig. 14c [227].

4. Current challenges and future opportunities

In today's world that changes and develops day by day, the needs required by the age and the technology used to meet these needs are also developing. 3D printing technology, which has many successful examples in the different areas where it is used, offers great opportunities for the future. It is hoped that it will be effective in solving some of the problems we encounter recently. One of the best examples of this situation is

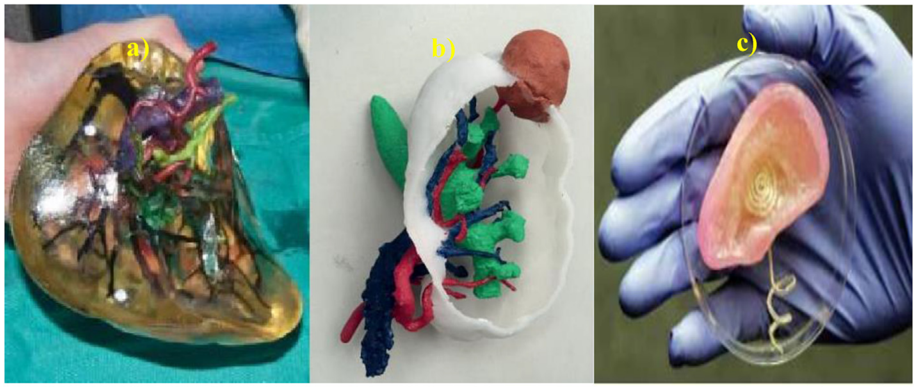

Fig. 14 – 3D printing organs: a) The first fully 3D printed liver known, b) Kidney model produced by additive manufacturing for surgical planning according to tomography image data, c) Bionic ear that have hearing manufactured with a 3D printer [225–227].

undoubtedly the masks produced with this method to protect from the coronavirus pandemic, which has been on the agenda all over the world recently. Lack of protective face masks is a major problem during pandemic crises, especially for people working in healthcare, such as doctors, nurses and paramedics. Therefore, printed masks are produced for healthcare professionals who are struggling with the COVID-19 epidemic that emerged in Wuhan, affected the whole world in a short time. Unfortunately, millions of people have been infected with coronavirus today, and thousands of people have died, for this reason so many studies are carried out to protect against the virus. One of the measures to be taken to protect against the virus is the use of personal masks. Due to the increasing demand for masks, various problems arise in the production and distribution of masks. As a potential solution to this problem, this technology is used in the production of masks. In this way, globally accessible masks are produced in a shorter time. In addition, it is also possible to produce masks just as personal prostheses and implants can be produced. The face mask produced with this method is shown in Fig. 15. The modelled personalized face mask is shown in Fig. 15a, and a printed face mask is shown in Fig. 15b. It can be used in the production of protective clothing, gloves, goggles, face shields and other equipment designed to protect not only masks but also from the spread of the disease. With CAD-CAM programs, any type of mask can be modelled within 10 min and printed in a short time. Therefore, compared to traditional methods, production can be made in a shorter time with lower labour costs. It also prevents waste through manufacturing on demand. The benefits of this technology during the crisis period have attracted attention due to its contribution to the fight against the epidemic and to providing a greener and more environmentally friendly future [228–235]. In addition, this technology is promising for cancer which is one of today's major health problems and the second cause of death in the world. Cancer cases increase with each passing year, and many people die because of this illness. In consequence, cancer treatment researches and early detection and targeted therapies have gained great importance. Differences between individuals are a serious problem in cancer treatment as each patient responds differently to existing drug treatments. 3D models are used for better understanding of the illness and for the necessary treatment to be more efficient. It facilitates complex treatments with models that closely mimic real conditions, so that problems encountered in cancer patients can be solved. In addition to these benefits, thanks to the produced tumour model, the doctor can be analysed, and it used in surgical planning, and more efficient treatment can be provided [236–239]. It is also thought that the efficiency of chemotherapy used in cancer treatment will increase. It is a very difficult process and can be dangerous for almost all patients. Chemotherapy, which has many side effects, including vomiting and heart failure, is actually treated using toxic drugs. To avoid these side effects of chemotherapy, Steve Hetts, a neuroradiologist at the University of California in San Francisco, developed the 3D sponge project. The sponge has been tested on pigs and has been successfully completed. The task of the sponge is to absorb the medicine before it enters the body. In this way, the drug becomes active where it should be active, and other organs are not damaged. In the test performed on pigs, it has been observed that the amount of drug administered to the body is reduced by 64%, it is thought that the same results will be achieved in humans. The use of the sponge produced with this technology will reduce the strong side effects of chemotherapy and prevent it from harming other organs [240]. In addition to cancer research, it is also promising for the treatment of congenital disorders or birth defects. For example, Lioufas et al. [241] used a 3D printer to treat eight and 14-month-old children born with a cleft palate. Anatomically accurate models were developed with the SLA method, and the operations were successfully completed. In the study, the use of this method in the education of medical students is recommended because it facilitates preoperative planning and offers practical opportunities. Moreover, in the near future, it may be possible to print 3D copies with materials that mimic the colour, physical and mechanical properties of living human tissue. It also has significant potential in drug development, treatment testing, medical research, wound healing, and even organ transplantation. Organ transplantation applications can't be performed at the moment because the technology is still insufficient for the design of an organ that is exactly the same as the original organ of the patient, has the entire vascular system and can perform all the functions of the

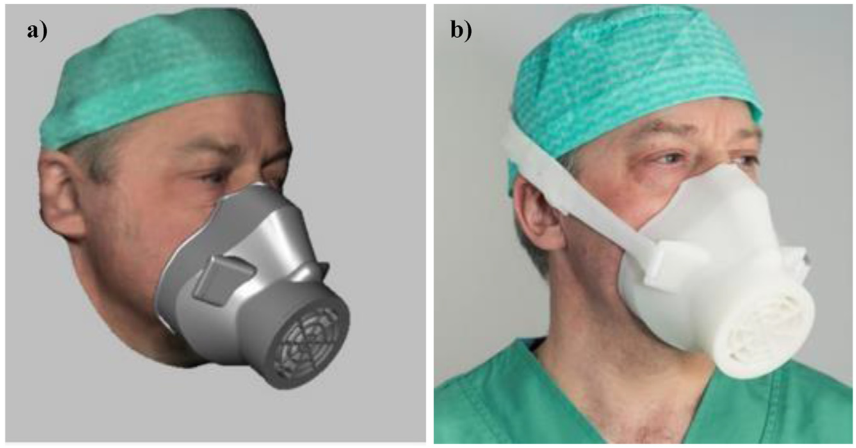

Fig. 15 – The face mask custom-made with a 3D printer; a) 3D facial mask modelling, b) Custom made 3D printed face mask [229].

original organ. The patient's organ can be modelled similarly but is not able to function. However, it is expected that this situation will change in the future, that organs that can fulfil their functions can be produced and used in organ transplantation, thus saving the lives of many people. These examples are just some of its future opportunities, a few years ago what the 3D printer can do now seemed to be imaginary things we could only see in science fiction movies, but that has changed. Therefore, It is believed that this technology will open new doors in the future [242,243].

5. Conclusion

3D printer technology can provide the production of complex-shaped parts that are difficult to produce with traditional methods, can produce easier and faster with less cost, and its use and prevalence in different sectors are increasing due to these advantages. It is especially used in the biomedical field thanks to its advantages, and it is preferred for different applications in this field every day. Some of these applications are included as surgical applications using biomodels or templates, modelling and imaging for a better understanding of diseases, manufacturing medical devices, patient-specific implant and prosthesis applications, vet medicine applications, tissue engineering applications, pharmaceutical industry applications and organ bioprinting which is currently in the testing stage. Thanks to the use of this technology especially in the modelling and diagnosis of diseases, it is possible to model, diagnose and monitor the course of cancer which is one of the health problems of our age. In addition, produced 3D models increase the accuracy of the operation compared to radiographic and clinical examination. This development is of great benefit not only for surgeons but also for veterinarians and medical school students. Furthermore, this method is preferred in the production of personalised prostheses and implants. The quality of life of many patients has increased with implants and prostheses, which can be produced in desired sizes and colours modelled according to the patient's anatomy. The use of this miracle technology in the pharmaceutical sector and bioprinting applications is not widespread yet and continues to be tested and developed, but it is thought to bring revolutionary developments when it becomes widespread. When developed in the near future, it will bring revolutionary innovations to the medical field and can save many lives. From cancer treatment to birth defects treatment, from functional prostheses; In all areas of medicine, inventions powered by 3D printing are sought to provide patients with high quality of life and a longer life.

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.

REFERENCES

[1] Murr LE. Frontiers of 3d printing/additive manufacturing: from human organs to aircraft fabrication. J Mater Sci Technol 2016;32:987–95. https://doi.org/10.1016/j.jmst.2016.08.011.
[2] Kumar A, Sharma A, Mohanty UK, Simhambhatla S. Advances in welding technologies for process developments. Additive manufacturing with welding. India. 2019.
[3] Coykendall J, Cotteler MJ, Haldowsky J, Mahto M. 3D opportunity for aerospace and defense, A Deloitte series on additive manufacturing1; 2014. p. 3–6.
[4] Cotteleer M, Joyce J. 3D opportunity additive manufacturing paths to performance, innovation and growth. Deloitte Review. 2014.
[5] Sames WJ, List FA, Pannala S, Dehoff RR, Babu SS. The metallurgy and processing science of metal additive manufacturing. Int Mater Rev 2016;61:315–60. https://doi.org/10.1080/09506608.2015.1116649.
[6] Wong KV, Hernandez A. A review of additive manufacturing, vol. 2012. International Scholarly Research Network Mechanical Engineering; 2012. https://doi.org/10.5402/2012/208760.

[7] Vayre B, Vignat F, Villeneuve F. Designing for additive manufacturing. 45th CIRP conference on manufacturing systems. 2012. 2012. p. 632–7.

[8] Horn TJ, Harrysson OLA. Overview of current additive manufacturing technologies and selected applications. Sci Prog 2012;95:255–82. https://doi.org/10.3184/003685012x13420984463047.

[9] Pinkerton AJ. Lasers in additive manufacturing. Opt Laser Technol 2015;78:25–32. https://doi.org/10.1007/s40684-017-0037-7.

[10] Horvath J. Mastering 3D printing, California. 2014.

[11] Squelch A. 3D printing and medical imaging. J Med Radiat Sci 2018;65:171–2. https://doi.org/10.1002/jmrs.300.

[12] Marro A, Bandukwala T, Mak W. Three-dimensional printing and medical imaging: a review of the methods and applications. Curr Probl Diagn Radiol 2016;45:2–9. https://doi.org/10.1067/j.cpradiol.2015.07.009.

[13] 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. https://doi.org/10.1371/journal.pone.0178540.

[14] Shah S, Chong B, Chong S. 3D imaging, 3d printing and 3D virtual planning in endodontics. Clin Oral Invest 2018;22:641–54. https://doi.org/10.1007/s00784-018-2338-9.

[15] Jammalamadaka U, Tappa K. Recent advances in biomaterials for 3D printing and tissue engineering. J Funct Biomater 2018;9:22. https://doi.org/10.3390/jfb9010022.

[16] Patra S, Young V. A review of 3d printing techniques and the future in biofabrication of bioprinted tissue. Cell Biochem Biophys 2016;74:93–8. https://doi.org/10.3390/jfb9010022.

[17] Esmaeili S, Shahali M, Kordjamshidi A, Torkpoor Z, Namdari F, Samandari SS, et al. An artificial blood vessel fabricated by 3D printing for pharmaceutical application. Nanomed J 2019;6:183–94. https://doi.org/10.22038/NMJ.2019.06.00005.

[18] Oliveira TT, Reis AC. Fabrication of dental implants by the additive manufacturing method: a systematic review. J Prosthet Dent 2019;122:270–4. https://doi.org/10.1016/j.prosdent.2019.01.018.

[19] Chen J, Zhang Z, Chen X, Zhang C, Zhang G, Xu Z. Design and manufacture of customized dental implants by using reverse engineering and selective laser melting technology. J Prosthet Dent 2014;112:1088–95. https://doi.org/10.1016/j.prosdent.2019.01.018.

[20] An Y, Jin, Plott J, Wensman J, Shih A. Additive manufacturing of custom orthoses and prostheses – a review. Procedia CIRP 2015;36:199–204. https://doi.org/10.1016/j.procir.2015.02.125.

[21] Gao C, Wang C, Jin H, Wang Z, Li Z, Shi C, et al. Additive manufacturing technique-designed metallic porous implants for clinical application in orthopedics. RSC Adv 2018:25210–27. https://doi.org/10.1039/C8RA04815K.

[22] Miao S, Castro N, Nowicki M, Xia L, Cui H, Zhou X, et al. 4D printing of polymeric materials for tissue and organ regeneration. Mater Today 2017;20:557–91. https://doi.org/10.1016/j.mattod.2017.06.005.

[23] Ringeissen BR, Spargo BJ, Wu PK. Cell and organ printing, U.S.A. 2010.

[24] Thomas DJ, Singh D. 3d printing in medicine and surgery, Philadelphia. 2019.

[25] Schubert C, Langeveld MC, Donoso LA. Innovations in 3D printing: a 3D overview from optics to organs. Br J Ophthalmol 2014;98:159–61. https://doi.org/10.1136/bjophthalmol-2013-304446.

[26] Karayel E, Bozkurt Y. Additive manufacturing method and different welding applications. J Mater Res Technol 2020;9:11424–111438. https://doi.org/10.1016/j.jmrt.2020.08.039.

[27] Niaki MK, Nanino F. The management of additive manufacturing, Birmingham, U.K. 2017.

[28] Bourell D, Campbell I. Additive manufacturing: rapid prototyping comes of ages. Rapid Prototyp J 2004;10:7–10.

[29] Sürmen HK. Additive manufacturing technologies and applications. J Uludağ Univ Eng 2019;24. https://doi.org/10.17482/uumfd.519147.

[30] Kloski LW, Kloski N. Getting starting with 3D printing, Canada. 2016.

[31] Quan Z, Wu A, Keefe M, Qin X, Yu J, Suhr J, et al. Additive manufacturing of multi-directional preforms for composites: opportunities and challenges. Mater Today 2015;18:503–11. https://doi.org/10.1016/j.mattod.2015.05.001.

[32] Huang SH, Liu P, Mokasdar A, Hou L. Additive manufacturing and its societal impact: a literature review. Int J Manuf Technol 2012;67:1191–203. https://doi.org/10.1007/s0017-012-4558-5.

[33] Rybicki FJ, Grant GT. 3D printing in medicine a practical guide for medical professionals, Canada. 2017.

[34] 3D Models. Humeros bone produced by 3d printing. https://www.free3d.com/tr/3d-model- humerus-bone-4370.html. [Accessed 25 August 2020].

[35] Hu J. Study on STL-based slicing process for 3d printing. Solid freeform fabrication symposium. 2017.

[36] Segerman H. 3D printing for mathematical visualization. Mathematical Entertainments 2012;34:56–62. https://doi.org/10.1007/s00283-012-9319-7.

[37] Hager I, Golonka A, Putanowicz R. 3D printing of buildings and building components as the future of sustainable construction. Procedia Eng 2016;151:292–9. https://doi.org/10.1016/j.proeng.2016.07.357.

[38] 5 vital things to know about STL file format in 3D printing. https://www.cmac.com.au/blog/5-vital-things-about-stl-file-format-3d-printing. [Accessed 1 June 2021].

[39] Bhushan J, Grover V. Additive manufacturing: current concepts, methods, and applications in oral health care. 2019. Switzerland.

[40] Thompson MK, Moroni G, Vaneker T, Fadel G, Campbell IR, Gibson L, et al. Design for additive manufacturing: trends, opportunities, considerations, and constraints. CIRP Ann 2016;65:737–60. https://doi.org/10.1016/j.cirp.2016.05.004.

[41] Attaran A. The rise of 3D printing: the advantages of additive manufacturing over traditional manufacturing. Business Horizon 2017;60:677–88.

[42] Redwood B, Schöffer F, Garret B. The 3D handbook technologies, design and applications. Amsterdam: 3D HUBS; 2017.

[43] Han T, Kundu S, Nag A, Xu Y. 3D printed sensors for biomedical applications: a review. Sensors 2019;19(7):1706.

[44] Kong D, Ni X, Dong C, Lei X, Zhang L, Man C, et al. Bio-functional and anti-corrosive 3D printing 316L stainless steel fabricated by selective laser melting. Mater Des 2018;152:88–101.

[45] Baek SW, Song EJ, Kim JH, Jung M, Baek UB, Nahm HS. Hydrogen embrittlement of 3-D printing manufactured austenitic stainless steel part for hydrogen service. Scr Mater 2017;130:87–90.

[46] Tunchel S, Blay A, Kolerman R, Mijiritsky E, Shibli JA. 3D printing/additive manufacturing single titanium dental implants a prospective multicenter study with 3 years follow up. Int J Dent 2016;6:1–9. https://doi.org/10.1155/2016/8590971.

[47] Popov VV, Kamskii GM, Kovalevsky A, Dzhenzhera G, Strokin E, Kolomiets A, et al. Design and 3D printing of titanium bone implants brief review approach and clinical cases. Biomed Eng Lett 2018;8(4):337–44. https://doi.org/10.1007/s13534-018-0080-5.

[48] Pei X, Zhang B, Fan Y, Zhu X, Sun Y, Wang Q, et al. Bionic mechanical design of titanium bone tissue implants and 3D printing manufacture. Mater Lett 2017;208:133–7.
[49] Aboulkhair NT, Simonelli M, Parry L, Ashcroft I, Tuck C, Hague R. 3D printing of aluminium alloys additive manufacturing of aluminium alloys using selective laser melting. Prog Mater Sci 2019;106.
[50] Gill SS, Kaplas M. Comparative study of 3D printing technologies for rapid casting of aluminium alloy. Mater Manuf Process 2009;24(12):1405–11.
[51] Martin JH, Yahata BD, Hundley JM, Mayer AJ, Schaedler TA, Pollock TM. 3D printing of high-strength aluminium alloys. Nature 2017;549:365–9.
[52] Ganbold B, Heo SJ, Koak JY, Kim SK. Human stem cell responses and surface characteristics of 3D printing Co-Cr dental material. Materials 2019;12(20):3419.
[53] Barazanchi A, Li KC, Amleh BA, Lyons K, Waddell NJ. Mechanical properties of laser sintered 3D-printed cobalt chromium and soft-milled cobalt chromium. Prosthesis 2020;2(4):313–20.
[54] Kazantseva NV, Ezhov JV, Davydov DI, Merkushev AG. Analysis of structure and mechanical properties of Co-Cr-Mo alloy obtained by 3D printing. Phys Met Metallogr 2019;120:1172–9.
[55] Dietrich DM, Kenworthy M, Cudney EA. Additive manufacturing change management best practices. U.S.A: CRC Press; 2019.
[56] Jayanath S, Achuthan A. A computationally efficient hybrid model for simulating the additive manufacturing process of metal. Int J Mech Sci 2019;160:255–69.
[57] Milewski JO. Additive manufacturing of metal from fundamental technology to rocket nozzles,medical implants and custom jewelry. U.S.A: Springer; 2017.
[58] Kumar LJ, Pandey PM, Wimpenny DI. 3D printing and additive manufacturing technologies. Singapore: Springer; 2019.
[59] Yang L, Hsu K, Baughman B, Godfrey D, Medina F, Menon M, et al. Additive manufacturing of metals: the technology, materials, design and production. Birmingham, U.K: Springer; 2017.
[60] Gebhart A. Understanding additive manufacturing. Germany: HANSER; 2012.
[61] Devine DM. Polymer-based additive manufacturing biomedical applications. Switzerland: Springer; 2019.
[62] Sing S, Ramakrishna S, Berto F. 3D printing of polymer composites:a short review. Compos B Eng 2017;42:442–58.
[63] Ziolkowska PS, Labowska MB, Detyna J, Michalak I, Gruber P. A review of fabrication polymer scaffolds for biomedical applications using additive manufacturing techniques. Biocybern Biomed Eng 2020;40(2):624–38.
[64] Culmone C, Smit G, Breedveld P. Additive manufacturing of medical instruments: a state-of-the-art review. Addit Manuf 2019;27:461–73. https://doi.org/10.1016/j.addma.2019.03.015.
[65] Stansbury JW, Idacavage MJ. 3d printing with polymers: challenges among expanding options and opportunities. Dent Mater 2016;32:54–64. https://doi.org/10.1016/j.dental.2015.09.018.
[66] Shirazi SFS, Gharehkhani S, Mehrali M, Yarmand H. A review on powder-based additive manufacturing for tissue engineering: selective laser sintering and inkjet 3D printing. Sci Technol Adv Mater 2015;16. https://doi.org/10.1088/1468-6996/16/3/033502.
[67] Shuai C, Zhuang J, Peng S, Wen X. Inhibition of phase transformation from ß- to a-tricalcium phosphate with addition of poly (L-lactic acid) in selective laser sintering. Rapid prototyp J 2014;20:369–76. https://doi.org/10.1108/RPJ-03-2013-0037.
[68] Kolan KC, Leu MC, Hilmas GE, Velez M, Mech J. Effect of material, process parameters, and simulated body fluids on mechanical properties of 13-93 bioactive glass porous constructs made by selective laser sintering. Behav Biomed Mater 2012;13:14–24. https://doi.org/10.1016/j.jmbbm.2012.04.001.
[69] Poyraz Ö, Kuşhan MC. Investigation of the effect of different process parameters on laser additive manufacturing of metals. J Fac Eng Archit Gazi Univ 2018;33:729–42.
[70] Gibson A, Rosen DW, Stucker B. Additive manufacturing technologies: 3D printing, rapid prototyping and direct digital manufacturing. 2014. New York, ABD.
[71] Mani M, Feng S, Lane B, Donmez A, Moylan S. Measurement science needs for real-time control of additive manufacturing powder bed fusion processes. 2015. p. 2–7. https://doi.org/10.6028/NIST.IR.8036. Technical Report.
[72] Spears TG, Gold SA. In-process sensing in selective laser melting SLM additive manufacturing. Integr Mater Manuf Innov 2016;5:2–8. https://doi.org/10.1186/s40192-016-0045-4.
[73] Sahini D, Ghose J, Kumar SJ, Behera A, Mandal A. Additive manufacturing applications for metals and composites. U.S.A: IGI Global; 2020. p. 187–209. https://doi.org/10.4018/978-1-7998-4054-1.ch010.
[74] Meier H, Haberland C. Experimental studies on selective laser melting of metallic parts. Werkstofftech 2008;39. https://doi.org/10.1002/mawe.200800327.
[75] Wang D, Yang Y, Liu R, Xiao D, Sun J. Study on the designing rules and processability of porous structure based on selective laser melting. J Mater Process Technol 2013;213:1734–42. https://doi.org/10.1016/j.jmatprotec.2013.05.001.
[76] Zhang J, Song B, Wei Q, Bourell D, Shi Y. A review of selective laser melting of aluminium alloys: processing microstructure property and developing trends. J Mater Sci Technol 2019;35(2):270–84.
[77] Louvis E, Fox P, Sutcliffe CJ. Selective laser melting of aluminium components. J Mater Process Technol 2011;211(2):275–84.
[78] Zhang B, Li Y, Bai Q. Defect formation mechanisms in selective laser melting: a review. Chin J Mech Eng 2017;30:515–27. https://doi.org/10.1007/s10033-017-0121-5.
[79] Yap CY, Chua CK, Dong ZL, Liu ZH, Zhang DQ, Loh LE, Sing SL. Review of selective laser melting: materials and applications. Appl Phys Rev 2015. https://doi.org/10.1063/1.4935926.
[80] Chus CK, Leong KF. 3D printing and additive manufacturing: principles and applications, Singapore. 2017.
[81] Thijs L, Verhaeghe F, Craeghs T, Humbeeck JV, Kruth JP. A study of the microstructural evolution during selective laser melting of Ti–6Al–4V. Acta Mater 2010;48:3303–12. https://doi.org/10.1016/j.actamat.2010.02.004.
[82] Dobrzànski LA, Danikiewicz ADD, Franczak AA, Dobrzànski LB, Szindler M, Gawel TG, editors. Porous selective laser melting Ti and Ti6AL4V materials for medical applications, Zagreb; 2017.
[83] Murr LE. Metallurgy of additive manufacturing: examples from electron beam melting. Addit Manuf 2015;15:40–53. https://doi.org/10.1016/j.addma.2014.12.002.
[84] Bartolo PJ. Stereolithography: materials, proses and applications, Portugal. 2011.
[85] Liu B, Gong X, Chappel W. J, Applications of layer-by-layer polymer stereolithography for three-dimensional high-frequency components. IEEE Trans Microw Theor Tech 2004;52:2567–75. https://doi.org/10.1109/TMTT.2004.837165.
[86] Robles JALA, Hernandez CC, Cavazos JOF, Siller HR, Rodriquez CA, Lopez JIM. Hydrostatic high-pressure post-processing of specimens fabricated by DLP, SLA, and FDM: an alternative for the sterilization of polymer-based

biomedical devices. Materials 2018;11:1–12. https://doi.org/10.3390/ma11122540.

[87] Borello J, Nasser P, Iatridis J, Costa KD. 3D printing a mechanically-tunable acrylate resin on a commercial DLP-SLA printer. Addit Manuf 2018;23:374–80. https://doi.org/10.1016/j.addma.2018.08.019.

[88] Wang X, Jiang M, Zhou Z, Gou J, Hui D. 3D printing of polymer matrix composites: a review and prospective. Compos B Eng 2017;110:442–58. https://doi.org/10.1016/j.compositesb.2016.11.034.

[89] Melchels PWF, Feijen J, Grijpma DW. A review on stereolithography and its applications in biomedical engineering. J Biomater 2010;31:6121–30. https://doi.org/10.1016/j.biomaterials.2010.04.050.

[90] Kaza Stawicki SP, Yellapu V, Rembalsky J, Roma N, Delong WG. Int J Acad Med 2018;4:252–9. https://doi.org/10.4103/IJAM.IJAM_54_18.

[91] Jin Y, He Y, Fu JZ, Gan W, Lin Z. Optimization of tool-path generation for material extrusion based additive manufacturing technology. Addit Manuf 2014;1–4:32–47. https://doi.org/10.1016/j.addma.2014.08.004.

[92] About Additive Manufacturing, Material Extrusion. https://www.lboro.ac.uk/research/amrg/about/the7categoriesofadditivemanufacturing/materialextrusion/. [Accessed 2 June 2021].

[93] Sireesha M, Lee J, Kiran ASK, Babu VJ, Kee BBT, Ramakrishna S. A review on additive manufacturing and its way into the oil and gas industry. RSC Adv 2018;8:1–9. https://doi.org/10.1039/C8RA03194K.

[94] About Additive Manufacturing. Binder jetting. https://www.lboro.ac.uk/research/amrg/about/the7categoriesofadditivemanufacturing/binderjetting/. [Accessed 3 June 2021].

[95] Park SI, Rosen DW, Choi SK, Duty CE. Effective mechanical properties of lattice material fabricated by material extrusion additive manufacturing. Addit Manuf 2014;1:12–23. https://doi.org/10.1016/j.addma.2014.07.002.

[96] Masood SH, Wang H, Lovenitti P, Harvey EC. Application of fused deposition modeling rapid prototyping system to the development of microchannels. Rapid Prototyp J 2016;22:281–99. https://doi.org/10.1117/12.454606.

[97] Konta AA, Pina MG, Serrano DR. Personalised 3D printed medicines: which techniques and polymers are more successful? Bioengineering 2017;4:16. https://doi.org/10.3390/bioengineering4040079.

[98] Pranzo D, Larizza P, Filippini D, Percoco G. Extrusion-based 3d printing of microfluidic devices for chemical and biomedical applications: a topical review. Micromachines 2018;9:374. https://doi.org/10.3390/mi9080374.

[99] Placone JK, Engler AJ. Recent advances in extrusion-based 3D printing for biomedical applications. Progress report, https://doi.org/10.1002/adhm.201701161; 2017.

[100] Yap YL, Wang C, Sing SW, Dikshit V, Yeong WY, Wei J. Material jetting additive manufacturing: an experimental study using designed metrological benchmarks. Precis Eng 2017;50:275–85. https://doi.org/10.1016/j.precisioneng.2017.05.015.

[101] Gibson I, Rosen DW, Stucker B. Additive manufacturing technologies: rapid prototyping to direct digital manufacturing. 2nd ed 2015. Singapore.

[102] Wang L, Gardner DJ. Contribution of printing parameters to the interfacial strength of polylactic acid in material extrusion additive manufacturing. Prog Addit Manuf 2018;3:165–71.

[103] Nichetti D, Zloczower IM. Influence of parameters on material processability in extrusion processes. Polym Eng Sci 2004;39(5):887–95. https://doi.org/10.1002/pen.11478.

[104] Elliat H, Urbanic J. Determining the relationships between the build orientation, process parameters and voids in additive manufacturing material extrusion processes. Int J Adv Manuf Technol 2019;100:683–705. https://doi.org/10.1007/s00170-018-2540-6.

[105] Braconnier DJ, Jensen RE, Peterson AM. Processing parameter correlations in material extrusion additive manufacturing. Addit Manuf 2020;31:100924. https://doi.org/10.1016/j.addma.2019.100924.

[106] Sachs EM, Cima MJ, William P, Barancazio D, Cornie J. Three-dimensional printing: rapid tooling and prototypes directly from a CAD model, England. 1992.

[107] Xu X, Meteyer S, Perry N, Zhao YF. Energy consumption model of Binder-jetting additive manufacturing processes. Int J Prod Res 2014;53:7005–15. https://doi.org/10.1080/00207543.2014.937013.

[108] Gokuldoss PK, Kolla S, Eckert J. Additive manufacturing processes: selective laser melting, electron beam melting and binder jetting—selection guideline. Materials 2017;10:1–12. https://doi.org/10.3390/ma10060672.

[109] Feilden E, Thesis. Additive manufacturing of ceramics and ceramic composites via robocasting, vol. 24. Imperial College London; 2017. https://doi.org/10.25560/55940.

[110] Ventola CL. Medical applications for 3D printing: current and projected uses. P&T 2014;39:704–11.

[111] Alali AB, Butler PME, Griffin M. Three-dimensional printing surgical applications. Eplasty 2015;15:352–63.

[112] Ni J, Ling H, Zhang S, Wang Z, Peng Z, Benyshek C, et al. Three-dimensional printing of metals for biomedical applications. Mater Today Bio Dergisi 2019;3:1–18. https://doi.org/10.1016/j.mtbio.2019.100024.

[113] 3D printing healthcare market outlook 2026. https://www.alliedmarketresearch.com/3D- printing-healthcare-market. [Accessed 26 August 2020].

[114] Kalaskar DM. 3D printing in medicine, United Kingdom. 2017.

[115] Zadpoor AA. Design for additive bio-manufacturing: from patient-specific medical devices to rationally designed meta-biomaterials. Int J Mol Sci 2017;18:1607. https://doi.org/10.3390/ijms18081607.

[116] Hu Q, Sun XZ, Parmenter CDJ, Fay MW, Smith EF, Rance GA, et al. Additive manufacture of complex 3D Au-containing nanocomposites by simultaneous two-photon polymerization and photoreduction. Sci Rep 2017;7:17150. https://doi.org/10.1038/s41598-017-17391-1.

[117] Mchugh KJ, Nguyen TD, Linehan AR, Yang D, Behrens AM, Rose S, et al. Fabrication of fillable microparticles and other complex 3D microstructures. Science 2017;359:1138–42. https://doi.org/10.1126/science.aaf7447.

[118] Yan Q, Dong H, Su J, Han J, Song B, Wei Q, et al. A review of 3D printing technology for medical applications. Engineering 2018;4:729–42. https://doi.org/10.1016/j.eng.2018.07.021.

[119] Schmauss D, Gerber N, Sodian R. Three-dimensional printing of models for surgical planning in patients with primary cardiac tumors. Thorac Cardiovasc Surg 2013;145:1407–8. https://doi.org/10.1016/j.jtcvs.2012.12.030.

[120] Shilo D, Emodi O, Blanc O, Noy D, Rachmiel A. Printing the future—updates in 3d printing for surgical applications. Rambam Maimonides Med J 2018;9.

[121] Qiu K, Haghiashtiani G, McAlpine MC. 3D printed organ models for surgical applications. Annu Rev 2018;11:287–306. https://doi.org/10.1146/annurev-anchem-061417-125935.

[122] Hoang D, Perrault D, Stevanovic M, Ghiassi A. Surgical applications of three-dimensional printing: a review of the current literature & how to get started. Ann Transl Med 2016;4:456. https://doi.org/10.21037/atm.2016.12.18.

[123] Aimar A, Palermo A, Innocenti B. The role of 3D printing in medical applications: a state of the art. J Healthc Eng 2019;10:1–10. https://doi.org/10.1155/2019/5340616.

[124] Li C, Cheung TF, Fan VC, Sin KM, Wong CWY, Leung G. Applications of three-dimensional printing in surgery. Surg Innov 2016;24:1–7. https://doi.org/10.1177/1553350616681889.

[125] Tack P, Victor J, Gemmel P, Annemans L. 3D-printing techniques in a medical setting: a systematic literature review. Biomed Eng Online 2016;115:1–21. https://doi.org/10.1186/s12938-016-0236-4.

[126] Chae MP, Rozen WM, McMenamin PG, Findlay MW, Spycal RT, Smith DJH. Emerging applications of bedside 3D printing in plastic surgery. Front Surg 2015;2. https://doi.org/10.3389/f.surg.2015.00025.

[127] 3D printed models used to plan kidney cancer surgery. https://www.medicaldevice- network.com/news/3d-printed-kidney-tumuor-removal/. [Accessed 28 August 2020].

[128] Zheng B, Wang X, Zheng Y, Feng J. 3D printout models vs. 3D-rendered images: which is better for preoperative planning? J Surg Educ 2018;73. https://doi.org/10.1016/j.jsurg.2016.01.003.

[129] Sun Z, Liu D. A systematic review of clinical value of three-dimensional printing in renal disease. Quant Imaging Med Surg 2018;8:311–25. https://doi.org/10.21037/qims.2018.03.09.

[130] Sun Z, Lee SY. A systematic review of 3-D printing in cardiovascular and cerebrovascular diseases. Anatol J Cardiol 2017;17:423–35. https://doi.org/10.14744/AnatolJCardiol.2017.7464.

[131] Giannopoulos AA, Mitsouras D, Yoo SJ, Liu PP, Chatzizisis YS, Rybicki FJ. Applications of 3D printing in cardiovascular diseases. Nat Rev Cardiol 2016;13:701–18. https://doi.org/10.1038/nrcardio.2016.170.

[132] Cantinotti M, Valverde I, Kutty S. Three-dimensional printed models in congenital heart disease. Int J Cardiovasc Imaging 2017;33:137–44. https://doi.org/10.1007/s10554-016-0981-2.

[133] Yap YL, Tan YSE, Tan HKJ, Peh ZK, Low XY, Yeong XY, et al. 3D printed bio-models for medical applications. Rapid Prototyp J 2017;23:227–35. https://doi.org/10.1108/RPJ-08-2015-0102.

[134] Ma X, Liu J, Zhu W, Tang M, Lawrence N, Yu C, et al. 3D bioprinting of functional tissue models for personalized drug screening and in vitro disease modeling. Adv Drug Deliv Rev 2018;132:235–51. https://doi.org/10.1016/j.addr.2018.06.011.

[135] Perica ER, Sun Z. A systematic review of three-dimensional printing in liver disease. J Digit Imaging 2018;31:692–701. https://doi.org/10.1007/s10278-018-0067-x.

[136] Kim GB, Lee S, Kim H, Yang DH, Kim YH, Kyung YS, et al. Three-dimensional printing: basic principles and applications in medicine and radiology. Korean J Radiol 2016;17:182–97. https://doi.org/10.3348/kjr.2016.17.2.182.

[137] Banks J. Adding value in additive manufacturing: researchers in the United Kingdom and Europe look to 3D printing for customization. IEEE Pulse 2013;6:22–6. https://doi.org/10.1109/MPUL.2013.2279617.

[138] Lipson H. New world of 3-D printing offers "completely new ways of thinking": Q&A with author, engineer, and 3-D printing expert Hod Lipson. IEE Pulse 2013;6:12–4.

[139] Dodziuk H. Applications of 3D printing in healthcare. Kardiochirurgia i Torakochirurgia Polska/Polish Journal of Thoracic and Cardiovascular Surgery 2016;13(3):283–93. https://doi.org/10.5114/kitp.2016.62625.

[140] Auricchio F, Marconi S. 3D printing: clinical applications in orthopaedics and traumatology. EOR 2016;1:123–7. https://doi.org/10.1302/2058-5241.1.000012.

[141] 3D printing technology for improved hearing. https://www.sonova.com/en/story/innovation/3d-printing-technology-improved-hearing. [Accessed 2 September 2020].

[142] Mertz L. Dream it, design it, print it in 3-d: what can 3-d printing do for you? IEEE Pulse 2013;4:15–21. https://doi.org/10.1109/MPUL.2013.2279616.

[143] Choonara YE, du Toit LC, Kumar P, Kondiah PPD, Pillay V. 3D-printing and the effect on medical costs: a new era? Expert Rev Pharmacoecon Outcomes Res 2016;16:23–32. https://doi.org/10.1586/14737167.2016.1138860.

[144] Lepowsky E, Tasoglu S. 3D printing for drug manufacturing: a perspective on the future of pharmaceuticals. Int J Bioprinting 2017;4:119. https://doi.org/10.18063/ijb.v1i1.119.

[145] Jamroz W, Szafraniec J, Kurek M, Jachowicz R. 3D printing in pharmaceutical and medical applications – recent achievements and challenges. Pharm Res 2018;35:176. https://doi.org/10.1007/s11095-018-2454-x.

[146] Preis M, Öblom H. 3D-printed drugs for children—are we ready yet? AAPS Pharm Sci Tech 2017;18. https://doi.org/10.1208/s12249-016-0704-y.

[147] Klingmann V, Spomer N, Lerch C, Stoltenberg I, Frömke C, Bosse HM, et al. Favorable acceptance of mini-tablets compared with syrup: a randomized controlled trial in infants and preschool children. J Pediatr 2013;163:1728–32. https://doi.org/10.1016/j.jpeds.2013.07.014.

[148] Trenfield ST, Goyanes A, Telford R, Wilsdon D, Rowland M, Gaisford S, et al. 3D printed drug products: non-destructive dose verification using a rapid point-and-shoot approach. Int Pharm J 2018;549:238–92. https://doi.org/10.1016/j.ijpharm.2018.08002.

[149] Yu DG, CWhite CB, Yang YC, Zhu LM, Welbeck EW, Yang XL. A novel fast disintegrating tablet fabricated by three-dimensional printing. Drug Dev Ind Pharm 2009;35:1530–6. https://doi.org/10.3109/03639040903059359.

[150] Preis M, Breitkreutz J, Sandler N. Perspective: concepts of printing technologies for oral film formulations. Int J Pharm 2015;494:578–84. https://doi.org/10.1016/j.ijpharm.2015.02.032.

[151] Trenfield SJ, Awad A, Goyanes A, Gaisford S, Basit AW. 3D printing pharmaceuticals: drug development to frontline care. Trends Pharmacol Sci 2018;39:440–51. https://doi.org/10.1016/j.tips.2018.02.006.

[152] Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med 2015;372:793–5. https://doi.org/10.1056/NEJMp1500523.

[153] Alomari M, Mohamed FH, Basit AW, Gaisford S. Personalised dosing: printing a dose of one's own medicine. Int J Pharm 2015;494:568–77. https://doi.org/10.1016/j.ijpharm.2014.12.006.

[154] Awad, Trenfield SJ, Goyanes A, Gaisford S, Basit AW. Reshaping drug development using 3D printing. Drug Discov Today 2018;23:1547–55. https://doi.org/10.1016/j.drudis.2018.05.025.

[155] Sabna K, Anroop N, Nimer A. 3D printing technology in drug delivery: recent progress and application. Curr Pharm Des 2018;24:5039–48. https://doi.org/10.2174/1381612825666181206123828.

[156] Gayones A, Wang J, Buanz A, Pacheco RM, Telford R, Gaisford S, et al. 3D printing of medicines: engineering novel oral devices with unique design and drug release characteristics. Mol Pharm 2015;12:4077–84.

[157] Arun M, Sathishkumar N, Kumar KN, Ajai SS, Aswin S. Mater Today: Proc. 30;2020.

[158] Thomas DJ. 3D printing durable patient specific knee implants. J Orthop 2017;14:182–3. https://doi.org/10.1016/j.jor.2016.12.015.

[159] Nadagouda MN, Rastogi Y, Ginn M. Surgical management of proximal femoral metastasis: fixation or hip replacement? A 309 case series. Curr Opin Chem Eng 2020;28:152–7. https://doi.org/10.1016/j.coche.2020.05.007.

[160] Tan ETW, Ling JM, Dinesh SK. The feasibility of producing patient-specific acrylic cranioplasty implants with a low-cost 3D printer. J Neurosurg 2015;13:1–7. https://doi.org/10.3171/2015.5.JNS15119.
[161] Sing SL. Selective laser melting of novel titanium-tantalum alloy as orthopaedic biomaterial, Singapore. 2019.
[162] Dawood A, Marti BM, Jackson VS, Darwood A. 3D printing in dentistry. Br Dent J 2015;219:521–9. https://doi.org/10.1038/sj.bdj.2015.914.
[163] Popov VV, Kamskii GM, Kovalevsky A, Dzhenzhera G, Stokin E, Kolomiets A, et al. Design and 3D-printing of titanium bone implants: brief review of approach and clinical cases. Biomed Eng Lett 2018;8:337–44. https://doi.org/10.1007/s13534-018-0080-5.
[164] Mok SW, Nizak R, Fu SC, Ho KWK, Qin L, Saris DBF, et al. From the printer: potential of three-dimensional printing for orthopaedic applications. J Orthop Transl 2016;6:42–9. https://doi.org/10.1016/j.jot.2016.04.003.
[165] Singh S, Prakash C, Ramakrishna S. 3D printing of polyether-ether-ketone for biomedical applications. Eur Polym J 2019;114:1–13. https://doi.org/10.1016/j.eurpolymj.2019.02.035.
[166] Chen X, Xu L, Li X, Egger J. Computer-aided implant design for the restoration of cranial defects. Sci Rep 2017;7:1–10. https://doi.org/10.1038/s41598-017-04454-6.
[167] April fights survivor's skull replaced with 3D -printed implant. https://en.azvision.az/news/73640/april-fights-survivor%E2%80%99s-skull-replaced-with-3d- printed-implant-photos.html. [Accessed 15 September 2020].
[168] Vujaklija A, Farina D. Expet Rev Med Dev 2018;15:1745–2422. https://doi.org/10.1080/17434440.2018.1494568.
[169] Honigmann P, Sharma N, Okolo B, Popp U, Msallem B, Thieringer FM. Patient-specific surgical implants made of 3D printed PEEK: material, technology, and scope of surgical application. Biomed Res Int 2018;2018:1–8. https://doi.org/10.1155/2018/4520636.
[170] Mohammed MI, Gibson I. Conference 2016 annual international solid freeform fabrication symposium. 2016. Texas.
[171] Birbara NS, Otton JM, Pather N. 3D modelling and printing technology to produce patient-specific 3D models. Heart Lung Circ 2019;28:302–13. https://doi.org/10.1016/j.hlc.2017.10.017.
[172] Weber DJ, Hao M, Urbin MA, Schoenewald C, Lan N. Biomedical Information Technology. 2020. p. 687–715. https://doi.org/10.1016/B978-0-12-816034-3.00021-3.
[173] Durfee WK, Laizzo PA. Engineering in medicine. 2019. p. 527–43.
[174] Elmansy R. Designing the 3D-printed prosthetic hand. DMI J 2015;26:24–31. https://doi.org/10.1111/drev.10311.
[175] Schmidt R, Coons G, Chen V, Gmeiner T, Ratto M. Autodesk conference. 2015.
[176] Mills DK. Future medicine: the impact of 3D printing. J Nanomater Mol Nanotechnol 2015;4:1–3. https://doi.org/10.4172/2324-8777.1000163.
[177] Manero A, Smith P, Sparkman J, Dombrowski M, Courbin D, Kester A, et al. Implementation of 3D printing technology in the field of prosthetics: past, present and future. J Environ Res Public Health 2019;16:1–15. https://doi.org/10.3390/ijerph16091641.
[178] Hespel AM, Wilhite R, Hudson J. Invited review-applications for 3d printers in veterinary medicine. Vet Radiol Ultrasound 2014;55:1–9. https://doi.org/10.1111/vru.12176.
[179] Haleem A, Javaid M, Suman R. Additive manufacturing applications in orthopaedics: a review. J Clin Orthop Taruma 2019;58:171–3. https://doi.org/10.1016/j.jcot.2018.04.008.
[180] Reilly MO, Reese S, Herlihy T, Geoghegan T, Cantwell CP, Feeney RNM, et al. Fabrication and assessment of 3D printed anatomical models of the lower limb for anatomical teaching and femoral vessel access training in medicine. Anat Sci Educ 2016;9:71–9. https://doi.org/10.1002/ase.1538.
[181] Dismukes DI, Fox DB, Tomlinson JL, Essman SC. Use of radiographic measures and three-dimensional computed tomographic imaging in surgical correction of an antebrachial deformity in a dog. J Am Vet Assoc 2008;232:68–73. https://doi.org/10.2460/javma.232.1.68.
[182] Kim SE, Shim KM, Jang K, Shim JH, Kang SS. Three-dimensional printing-based reconstruction of a maxillary bone defect in a dog following tumor removal. In Vivo 2018;32:63–70. https://doi.org/10.21873/invivo.11205.
[183] Xie S, Cai B, Rasidi E, Yen CC, Hsu C, Chow WT, et al. The use of a 3D-printed prosthesis in a Great Hornbill (Buceros bicornis) with squamous cell carcinoma of the casque. PloS One 2019;14. https://doi.org/10.1371/journal.pone.0220922.
[184] Bird of prey gets 3D-printed prosthetic leg. https://www.dw.com/en/bird-of-prey-gets- 3d-printed-prosthetic-leg/a-38364472. [Accessed 17 September 2020].
[185] 3D printed prosthetic: 8 Incredible animal prostheses. https://www.sculpteo.com/blog/2018/05/02/3d-printed-prosthetics-8-incredible-animal- prostheses/. [Accessed 17 September 2020].
[186] Popov VV, Kamskii GM, Demyanetz AK, Kovalevsky A, Usov S, Trofimcow D, et al. Additive manufacturing to veterinary practice: recovery of bony defects after the osteosarcoma resection in canines. Biomed Eng Lett 2019;9:97–108. https://doi.org/10.1007/s13534-018-00092-7.
[187] Sendemir A, Seçkin UD, Uyanıkgil Y, Gördün C. 3D bioprinting and cultivation of keratinocytes for skin tissue engineering. Dicle Med J 2018;45:9–18. https://doi.org/10.5798/dicletip.407239.
[188] O'Brien FJ. Biomaterials & scaffolds for tissue engineering. Mater Today 2011;14:88–95. https://doi.org/10.1016/S1369-7021(11)70058-X.
[189] Kim LY, Seo SJ, Moon HS, Yoo MK, Park LY, Kim BC, et al. Chitosan and its derivatives for tissue engineering applications. Biotechnol Adv 2008;26:1–21. https://doi.org/10.1016/j.biotechadv.2007.07.009.
[190] Mano JF, Silva GA, Azevedo HS, Malafaya PB, Sousa RS, Silva SS, et al. Natural origin biodegradable systems in tissue engineering and regenerative medicine: present status and some moving trends. J R Soc Interface 2007;4:999–1030. https://doi.org/10.1098/rsif.2007.0220.
[191] Chua CK, Yeong WY. Bioprinting principles and applications. Singapore: World Scientific Publishing Co; 2015.
[192] Deo K, Singh DA, Peak CW, Gaharwar AK, Alge DL. Bioprinting 101:Design, fabrication, and evaluation of cell-laden 3D bioprinted scaffolds. Tissue Eng Part A 2020;5–6:318–38. https://doi.org/10.1089/ten.TEA.2019.0298.
[193] Mahfouzi SH, Tali SHS, Amoabediny G. 3D bioprinting for lung and tracheal tissue engineering: criteria, advances, challenges and future directions. Bioprinting 2021;(21). https://doi.org/10.1016/j.bprint.2020.e00124.
[194] Ozbolat IT, Peng W, Ozbolat V. Application areas of 3D bioprinting. Drug Discov Today 2016;21(8):1257–71. https://doi.org/10.1016/j.drudis.2016.04.006.
[195] Seol YJ, Kang HW, Lee SJ, Atala A, Yoo JJ. Bioprinting technology and its applications. Eur J Cardiothorac Surg 2014;46(3):342–8. https://doi.org/10.1093/ejcts/ezu148.
[196] Parak A, Pradeep P, Toit LC, Kumar P, Choonara YE, Pillay V. Functionalizing bioinks for 3D bioprinting applications. Drug Discov Today 2019;24(1):198–205. https://doi.org/10.1016/j.drudis.2018.09.012.

[197] Hong N, Yang G, Lee J, Kim G. 3D bioprinting and its in vivo applications. J Biomed Mater Res 2017;106(1). https://doi.org/10.1002/jbm.b.33826.
[198] 3D Bioprinting: Bioink Selection Guide. https://www.sigmaaldrich.com/TR/en/technical-documents/technical-article/cell-culture-and-cell-culture-analysis/3d-cell-culture/3d-bioprinting-bioinks. [Accessed 4 June 2021].
[199] Mota C, Puppi D, Chielline F, Chielline E. Additive manufacturing techniques for the production of tissue engineering constructs. J Tissue Eng Regen Med 2012;9. https://doi.org/10.1002/term.1635.
[200] An J, Teoh JEM, Suntornnord R, Chua CK. Design and 3D printing of scaffolds and tissues. Engineering 2015;2:261–8. https://doi.org/10.15302/J-ENG-2015061.
[201] Bose S, Vahabzadeh S, Bandyopadhyay A. Bone tissue engineering using 3D printing. Mater Today 2013;16:496–503. https://doi.org/10.1016/j.mattod.2013.11.017.
[202] Melches FPW, Domingos MAN, Klein TJ, Malda J, Bartolo PJ, Hutmacher DW. Additive manufacturing of tissues and organs. Prog Polym Sci 2012;37:1079–104. https://doi.org/10.1016/j.progpolymsci.2011.11.007.
[203] Giannitelli SM, Mozetic P, Trombetta M, Rainer A. Combined additive manufacturing approaches in tissue engineering. Acta Biomater 2015;24:1–11. https://doi.org/10.1016/j.actbio.2015.06.032.
[204] Madrid APM, Vrech SM, Sanchez MA, Radriguez AP. Advances in additive manufacturing for bone tissue engineering scaffolds. Mater Sci Eng C 2019;100:631–44. https://doi.org/10.1016/j.msec.2019.03.037.
[205] Tytgat L, Damme LV, Hoorick JV, Declercq H, Thienpont H, Ottevaere H, et al. Additive manufacturing of photo-crosslinked gelatin scaffolds for adipose tissue engineering. Acta Biomater 2019;94:340–50. https://doi.org/10.1016/j.actbio.2019.05.062.
[206] Altun E, Ekren N, Kuruca SE, Gunduz O. Cell studies on Electrohydrodynamic (EHD)-3D-bioprinted bacterial cellulose\polycaprolactone scaffolds for tissue engineering. Mater Lett 2019;234:163–7. https://doi.org/10.1016/j.matlet.2018.09.085.
[207] Bedir T, Ulag S, Ustundag CB, Gunduz O. 3D bioprinting applications in neural tissue engineering for spinal cord injury repair. Mater Sci Eng C 2020;110:1–10. https://doi.org/10.1016/j.msec.2020.110741.
[208] Kim BW. Clinical regenerative medicine in urology. South Korea: Springer; 2018.
[209] Jaidev LR, Chatterjee K. Surface functionalization of 3D printed polymer scaffolds to augment stem cell response. Mater Des 2019;161:44–54. https://doi.org/10.1016/j.matdes.2018.11.018.
[210] Tasnim N, Vega LDL, Kumar SA, Abetseth L, Alonzo M, Amereh M, et al. 3D bioprinting stem cell derived tissues. Cell Mol Bioeng 2018;11:219–40. https://doi.org/10.1007/s12195-018-0530-2.
[211] Kolesky DB, Truby RL, Gladman AS, Busbee TA, Homan KA, Lewis JA. 3D bioprinting of vascularized, heterogeneous cell-laden tissue constructs. Adv Mater 2014;26:3124–30. https://doi.org/10.1002/adma.201305506.
[212] Wu J, Xie L, Lin XZY, Chen Q. Biomimetic nanofibrous scaffolds for neural tissue engineering and drug development. Drug Discov Today 2017;9:1375–84. https://doi.org/10.1016/j.drudis.2017.03.007.
[213] Javaid M, Haleem A. 3D printing applications towards the required challenge of stem cells printing. Clin Epidemiol Global Health 2020;8:863–7. https://doi.org/10.1016/j.cegh.2020.02.014.
[214] Wang X, Zhang M, JMa J, Xu M, Chang J, Gelinsky M, et al. 3D printing of cell-container-like scaffolds for multicell tissue engineering. Engineering 2020;22(9):1375–84. https://doi.org/10.1016/j.eng.2020.08.001.
[215] Kumar P, Rajak DK, Abubakar M, Syed GMA, Hussain M. 3D printing technology for biomedical practice: a review. J Mater Eng Perform 2021;192. https://doi.org/10.1007/s11665-021-05792-3.
[216] Miranov V, Boland T, Trusk T, Forgacs G, Markwald RR. Organ printing: computer-aided jet-based 3D tissue engineering. Trends Biotechnol 2003;21:157–61. https://doi.org/10.1016/S0167-7799(03)00033-7.
[217] Miranov V, Kasyanov V, Drake C, Markwald RR. Organ printing: promises and challenges. Regen Med 2007;3:93–103. https://doi.org/10.2217/17460751.3.1.93.
[218] Murphy SV. 3D bioprinting of tissues and organs. J Nat Biotechnol 2014;32:773–85. https://doi.org/10.1038/nbt.2958.
[219] Fedorovich NE, Alblas J, Hennink WE, Öner FC, Dhert WJA. Organ printing: the future of bone regeneration? Trends Biotechnol 2011;29:601–6. https://doi.org/10.1016/j.tibtech.2011.07.001.
[220] Miranov V, Kasyanov V, Markwald RR. Organ printing: from bioprinter to organ biofabrication line. Curr Opin Biotechnol 2011;22:667–73. https://doi.org/10.1016/j.copbio.2011.02.006.
[221] Park JH, Jang J, Lee JS, Cho DW. Current advances in three-dimensional tissue/organ printing. Tissue Eng Regen Med 2016;13:612–21. https://doi.org/10.1007/s13770-016-8111-8.
[222] Rezende RA, Kasyanov V, Mironov V, Silva JVL. Organ printing as an information technology. Procedia Eng 2015;110:151–8. https://doi.org/10.1016/j.proeng.2015.07.023.
[223] Gopinathan J, Noh I. Recent trends in bioinks for 3D printing. Biomater Res 2018;22. https://doi.org/10.1186/s40824-018-0122-1.
[224] Zein NN, Hanouneh LA, Bishop PD, Samaan M, Eghtesad B, Quantini C, et al. Three-dimensional print of a liver for preoperative planning in living donor liver transplantation. Liver Transpl 2013;19:1304–10. https://doi.org/10.1002/lt.23729.
[225] Fan G, Meng Y, Zhu S, Ye M, Li M, Li F, et al. Three-dimensional printing for laparoscopic partial nephrectomy in patients with renal tumors. Int Med Res 2019:1–9. https://doi.org/10.1177/0300060519862058.
[226] Mannoor MS, Jiang Z, James T, Kong YL, Malatesta KA, Soboyejo WO, et al. 3D printed bionic ears. Nano Lett 2013;13:2634–9. https://doi.org/10.1021/nl4007744.
[227] Bauncher H, Fontanarosa PB, Livingson EH. Sourcing personal protective equipment during the COVID-19 pandemic. J Am Med Assoc 2020;323:1912–4. https://doi.org/10.1001/jama.2020.5317.
[228] Swennen GRJ, Pottel L, Haers PE. Custom-made 3D-printed face masks in case of pandemic crisis situations with a lack of commercially available FFP2/3 masks. Int J Oral Maxillofac Surg 2020;49:673–7. https://doi.org/10.1016/j.ijom.2020.03.015.
[229] Ishack S, Lipner SP. Applications of 3D printing technology to address COVID-19–related supply shortages. Am J Med 2020;133:771–3. https://doi.org/10.1016/j.amjmed.2020.04.002.
[230] Choong YYC, Tan HW, Patel DC, Choong WTN, Chen CH, Low HY, et al. The global rise of 3D printing during the COVID-19 pandemic. Nat Rev Mater 2020;5:637–9. https://doi.org/10.1038/s41578-020-00234-3.
[231] Tino R, Moore R, Antoline S, Ravi P, Wake N, Lonita CN, et al. COVID-19 and the role of 3D printing in medicine. 3D Print Med 2020;6:1–8. https://doi.org/10.1186/s41205-020-00064-7.
[232] Wesemann C, Pierall Si, Fretwurst T, Nold J, Nelson K, Schmelzeisen R, et al. 3-D printed protective equipment

during COVID-19 pandemic. Materials 2020;13. https://doi.org/10.3390/ma13081997.
[233] Amin D, Nguyen N, Roser SM, Abromowicz S. 3D printing of face shields during COVID-19 pandemic: a technical note. J Oral Maxillofac Surg 2020;78:1275–8. https://doi.org/10.1016/j.joms.2020.04.040.
[234] Flanagan ST, Ballard DH. 3D printed face shields: a community response to the COVID-19 global pandemic. Acad Radiol 2020;27:905–6. https://doi.org/10.1016/j.acra.2020.04.020.
[235] Serrano DR, Terres MC, Lalatsa A. Applications of 3D printing in cancer. J 3D Print Med 2018;2:115–27. https://doi.org/10.2217/3dp-2018-0007.
[236] Haleem A, Vaishya R, Javaid M. 3D printing applications for the treatment of cancer. Clini Epidomol Global Health 2020. https://doi.org/10.1016/j.cegh.2020.03.022.
[237] Knowlton S, Onal S, Yu CH, Zhao JJ, Tasoglu S. Bioprinting for cancer research. Trends Biotechnol 2015;33:504–13. https://doi.org/10.1016/j.tibtech.2015.06.007.
[238] Bahcecioglu G, Basara G, Ellis BW, Ren X, Zorlutuna P. Breast cancer models: engineering the tumor microenvironment. Acta Biomater 2020;106:1–21. https://doi.org/10.1016/j.actbio.2020.02.006.
[239] Fong ELS, Harrington DA, Carson MCF, Yu H. Heralding a new paradigm in 3D tumor modeling. Biomaterials 2016;108:197–213. https://doi.org/10.1016/j.biomaterials.2016.08.052.
[240] UC Berkeley develops drug sponge to soak up chemotherapy side effects. https://www.pharmaceutical-technology.com/news/drug-sponge-soaks-up-chemotherapy- effects/. [Accessed 30 September 2020].
[241] Lioufas PA, Quayle MR, Leong JC, Mcmenamin PG. 3D printed models of cleft palate pathology for surgical education. Plast Reconstr Surg Glob Open 2016;4:1029. https://doi.org/10.1097/GOX.0000000000001029.
[242] Ghillan A, Chiriac AP, Nita LE, Rusu AG, Neamtu L, Chiriac VM. Trends in 3d printing processes for biomedical field: opportunities and challenges. J Polym Environ 2020;28:1345–67. https://doi.org/10.1007/s10924-020-01722-x.
[243] Choi J, Kwon OC, Jo W, Lee HJ, Moon MW. 4d printing technology: a review. 3D Print Addit Manuf 2015;2. https://doi.org/10.1089/3dp.2015.0039.

Prof. Yahya Bozkurt received his PhD degree in Technical Education Faculty, Metal Education Department from Marmara University, Institute of Pure and Applied Sciences. Currently, he is full professor at Metallurgy and Materials Engineering Department since 2018. At the same time, he is head of Mechanical Metallurgy Department and a member of the faculty board. His research areas; welding technologies, solid state welding, manufacturing methods, 3D printing technology and additive manufacturing.

Elif Karayel started Metallurgical and Materials Engineering education in Kocaeli University (Turkey) 2015. She continued part of her undergraduate education in the Thessaly University, Greece and graduated from Kocaeli University in 2020. She is a master student in Marmara University, Turkey. She studied on additive manufacturing applications. Her current research activities include the development of additive manufacturing (3D printing), welding technologies, materials science and engineering.