IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 11 Ser.11 (November. 2020), PP 13-24
www.iosrjournals.org

Applications of 3D Printing in Medicine

Dr.BharaniKrishna.T M.D.S [1], Dr.Swagathika Mishra M.D.S [2], Dr. K.v.Chandini M.D.S [3],Dr.M.Sireesha M.D.S [4],Dr. Bhavana Sujanmulk M.D.S [5]Dr.Mohammad Naffizuddin M.D.S [6]

Corresponding Author:Dr.Bharani Krishna.T Senior Resident
Drs.Sudha and Nageswara Rao Siddhartha Institute of Dental Sciences, Vijayawada
Address: Dr.BharaniKrishna.T, Vijayawada, Andhra Pradesh, India

Date of Submission: 12-11-2020 Date of Acceptance: 28-11-2020

The term 3D printing is used to describe a manufacturing approach that builds objects one layer at a time, adding multiple layers to form an object. This process is more correctly described as additive manufacturing, and is also referred to as rapid prototyping or Solid free form technology

This technology is basically an application of Radiology in which the normal 3dimensional objects are viewed in a 2dimensional system,With the advent of this technology the 3dimensional objects are converted into 3dimensional images which are later on printed accordingly with accurate precision.

3D printer definition: It is a machine that makes a 3D solid object based on the input drawings, as a 2D printer prints a letter or picture. It is the same principle used in a 2D printer in which 2D image (letter or picture) is formed by spraying ink onto paper if a digitized file is sent. In a 2D printer, it moves forward and backward (x-axis) and left and right (y-axis). However, in a 3D printer, up and down (z-axis) movement is added here, and a solid object is made on the basis of the input 3D drawing.

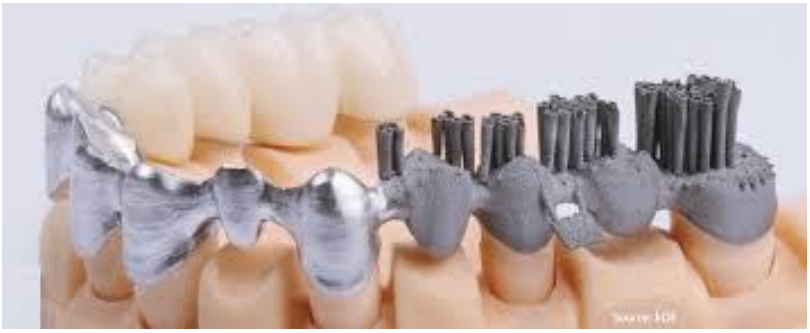
The Key Applications include

1. Dentistry
2. Tissue Engineering and Regenerative Medicine
3. Engineered Tissue Models
4. Medical Devices
5. Anatomical Models
6. Drug formulations
7. Anthropology
8. Forensics

I. Dentistry

Digital dentistry is one of the rapidly expanding segments of the Additive manufacturing technologies. Digital dentistry has been around for over 50 years since CAD/ CAM (computer-aided design/computer-aided manufacture) technology was introduced in the 1970s to replace traditional manual operations. CAD/CAM in dentistry is often associated with subtractive manufacturing, which involves 3D scanning, designing and milling from solid blocks of ceramic. Despite its popularity, subtractive manufacturing does not completely replace the traditional manual methods as it lacks resolution and accuracy. In contrast, 3D printing can create sophisticated components in mass production, which makes it an attractive technique for dentistry. Over the past 5 years, 3D printing technology has changed dentistry dramatically due to the progress in intraoral scanning technology, accessibility of 3D printers and the development of printable biomaterials. It is now possible to create restorations, physical. Today, AM techniques in dentistry are moving primarily into two directions:

1. photopolymerisation
2. powder-based printing



3D-printed Dental Implants

SLA/DLP/MJM use photopolymerisation technology and photosensitive resins filled with reinforced metal or ceramic fillers to create restorations (such as crowns, bridges, veneers, and partial denture frameworks/denture base), physical models, surgical guides/implants and orthodontic aligners/retainers. Photo polymerisation is the most commonly used process in dental applications as it has several advantages, including rapid fabrication, high resolution, low-cost, very fine surface finish and the ability to create complex shapes.

MJM is becoming a leading technology in dentistry as it is capable of building parts with various colours and physical properties since the print heads can be loaded with multiple build materials, allowing the creation of realistic teeth, gum-like texture and nerve canals. However, it should be noted that the parts fabricated using photopolymerisation normally have weaker mechanical properties, and thus the products are generally stone models and temporary restorations.

Powder-based printing techniques, including SLS/ DMLS/SLM/BJ, have been used in dentistry for about 20 years. They commonly utilise biocompatible metal alloys such as cobalt–chrome, titanium and stainless steelalloys to make crowns/bridges, implants and partial denture frameworks. Thecommonly used polymeric materials are pigment-filled polyamide powders, which are used to create dental models and surgical guides, one of the most important parameters in dentistry is the degree of accuracy between the digital model and the printed construct. Clinical studies reveal that the acceptabledegree of accuracy is a relative parameter, and has to be determined for each application. The examination of accuracy and reproducibility of dental models typically include measurements of intercanine distances, intermolar distances, the overjet, the overbite, tooth sizes and arch lengths. For instance, the 3D-printed models, fabricated by three different techniques, MJM, DLP and BJ, were compared with conventional plaster models. Several authors compared tooth sizes and observed no significant difference in the height and width of the crowns of all teeth. They concluded that the 3D-printed dental models should be clinically acceptable . For applications in implant surgery, a clinical study evaluated the accuracy and complications of SLS surgical guides for implant placement.

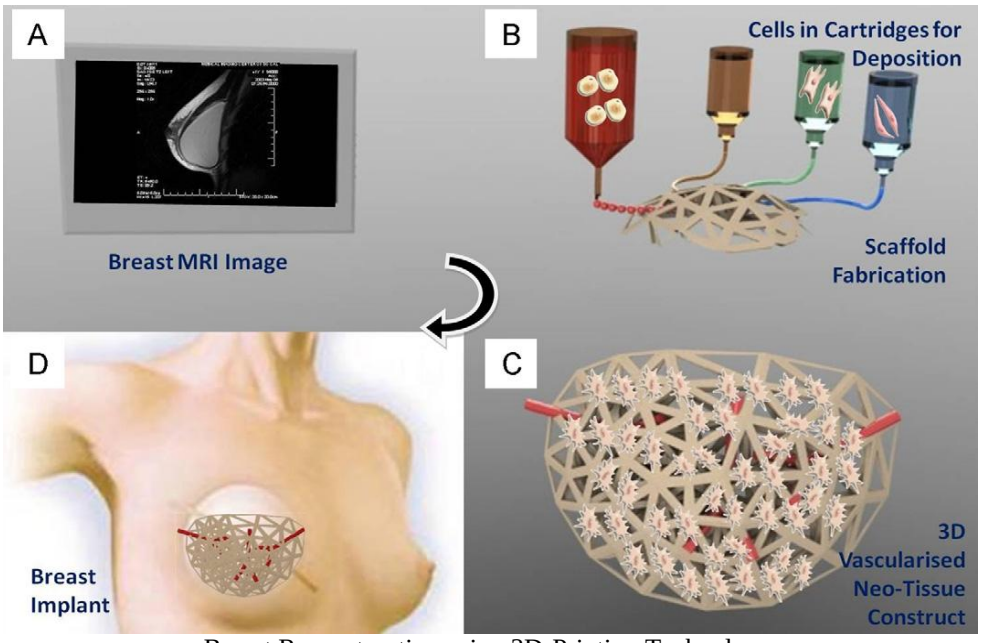
The Authors measured the lateral and angular deviations between virtually planned and placed implants for a total of 60 dental implants and 12 prostheses installed in 12 patients and documented the surgical and prosthetic complications during the 30-month follow-up period. The results showed that both the apical deviations (>2mm) and complication rate (34.4%) were high. In a recent study, the accuracy of implant surgical guides, designed from Kennedy Class 2 (K2) casts and Kennedy Class 3 (K3) casts, fabricated by a conventionaltechniqueandadditivemanufacturingtechniques (SLA and MJM), were compared. The results showed that the conventional guide was the best-fitting guide for the K3 group, whereas the AM guide was the best-fitting guide for K2 group. It was also concluded that **MJM surgical guides were more accurate than those fabricated with SLA**. When the overall performance was considered, conventional guides were reported to work better than most of the AM guides.

Kimet al. examinedthemarginal fitof three-unit fixeddentalprosthesesfabricatedbyDMLS using cobalt-chromium alloy and the conventional lost wax technique using nickel-chromium alloy. They found that the mean values of the gaps were higherforDMLSprostheses,whichwereslightlylarger thantheclinicalacceptancerange. 3D-printed devices will completely replace their conventional counterparts in the near future, and which printing technology will dominate themarket. Perhapsitisfairtosaythatthesedecisions should be made on a case-by-case basis.

Tissue engineering and regenerative medicine

The recent focus of tissue engineering has been two-fold to create functional tissues and organs for implantation and to develop tissue models either to study tissue development and disease or to assess drug toxicity, perform drug screening, or drug mechanistic safety testing. In this section, we focus on tissue engineering scaffolds for the development of functional tissues and organs. Tissue-engineered scaffolds are the most important component in tissue engineering as they provide the structural support for cells to attach,

migrate, proliferate and produce their own extracellular matrix and in some cases even differentiate into a certain phenotype. An ideal scaffold needs to be
Biocompatible,
Bioactive, mechanically strong
Porous with high pore interconnectivity
To allow diffusion of cells, nutrients and waste. In addition, it needs to be biodegradable, with a tunable degradation rate to allow replacement of the scaffold with the newly formed tissue, The scaffolds that serve as space filling or fixation purposes are classified under medical devices as they don't require bioactivity towards cells or tissues, andthey are not required to regenerate tissues.



Breast Reconstruction using 3D-Printing Technology

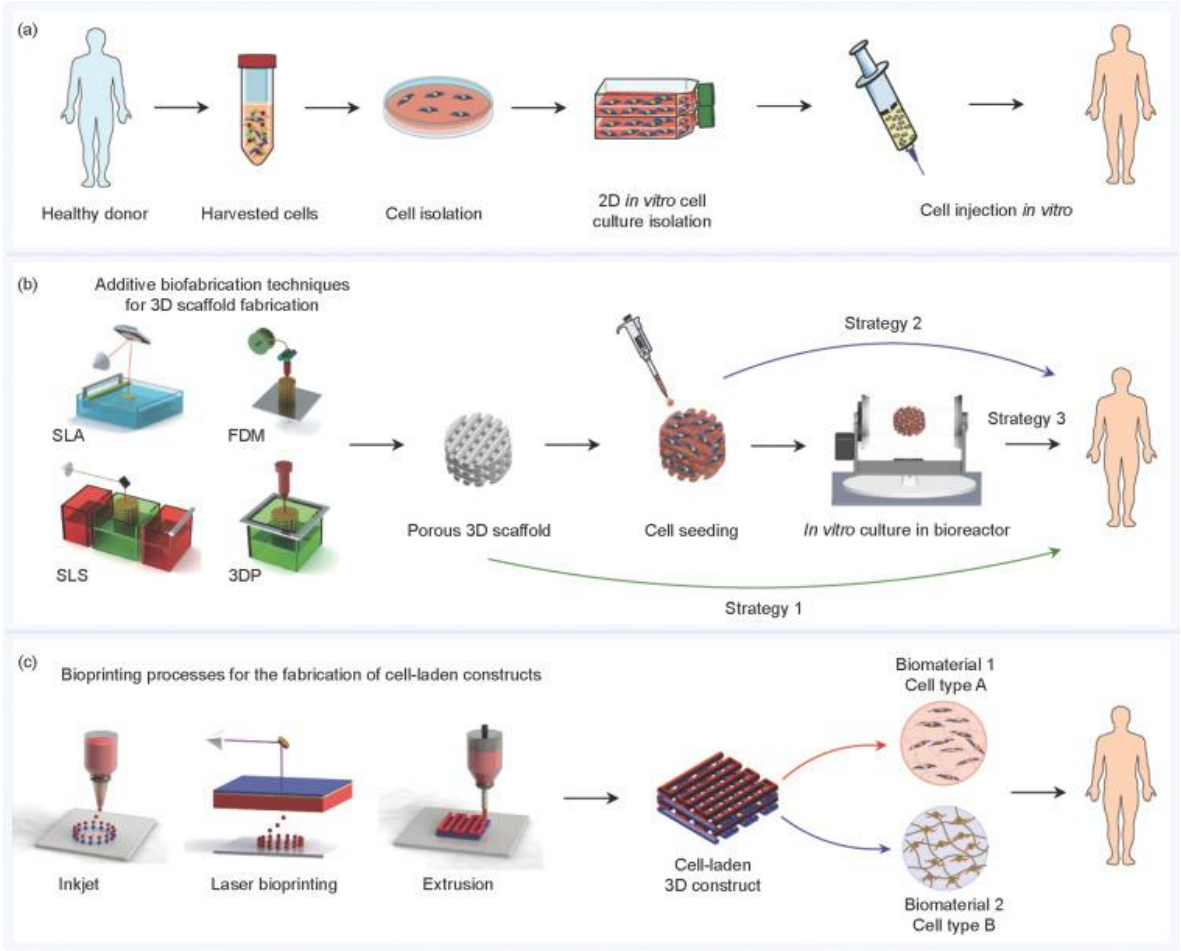
The conventional fabrication methods, such as porogen leaching, freeze-drying, moulding and electrospinning, have been widely used to produce tissue engineering scaffolds. However, due to their inability to create spatially tunable properties, including porosity, architecture, mechanics, bioactivity and distribution of cells, they are not the best options for creating tissue-mimicking constructs. Over the past 15 years, AM has attracted widespread interest as an alternative manufacturing technique since it offers many advantages, including precise control of overall size and shape, structural architecture(porosity and pore distribution), material composition and chemistry (i.e. mechanics and degradation), and multi-cellular composition in 3D space. In addition, custom design, on-demand fabrication, high reproducibility, and high throughput are other advantages as compared with conventional techniques. In general, an AM approach for tissue-engineered scaffolds requires cells to be incorporated either post-printing by seeding the cells into the scaffold or pre-printing by encapsulating the cells into the ink formulation. The most commonly used printing methods for creating scaffolds described in the first approach are FDM, SLS/DMLS, BJ and **vat polymerisation**. The latter approach is known as 'bioprinting', whichcanbefurthercategorised as scaffold-based and scaffold-free bioprinting. The scaffold-based approach commonly utilises cell-laden hydrogels, andthemainAMtechnologiesareDIW, MJM, vat polymerisation, and LIFT. In comparison, the scaffold-free approach uses high-densitycellsuspensionsintheformofcellpelletsor tissue spheroids, with or without a carrier polymer, and reliesoncell-cellinteractionsandcellfusionrequiringa periodofmaturationinbioreactors. Theworld's first FDA-approved 3D-printed medical devices provider, 4WEB Medical, introduced their DMLS truss implants made of titanium alloy with web structures. The patented truss design is advertised to distribute force and transfer strain to adjacent osteogenic cells, and thus accelerate bone healing. The company recently announced that more than 10000 patients had been implanted with customised truss implants between 2013 and 2016. Another leading medical supplier, Stryker, released the titanium posterior lumber cage in2016. Thisspinalimplantismadeof titaniumalloy andbuiltbyDMLStechnology.Thecompany claims that the interconnected porous structure of the implants provides sufficient blood flow and cell migration. Although bioprinting is still in its very early stage ofdevelopmentandfarfromclinics, thereisagrowing interestinbioprintingleading toexcitingandpromisingoutcomesfor the future. To date, a variety of bio-printed

tissues have been reported, including skin, blood vessel, cartilage, bone, ear, osteochondral interface, cardiac tissue, kidney, and liver.

In 2015, 3D Bioprinting Solutions, a Russian-based company, announced successful implantation of bio-printed functional thyroid glands into mice. A US-based biotech startup is developing breast reconstruction for breast cancer survivors by inkjet printing patients' own cells. The first product for the company will be nipple reconstruction, and the long-term goal is filling lumpectomy voids with regenerated tissues. Recently, L'Oreal has partnered with a French biotech startup, Poietis, to explore the possibility of beating hair loss through bioprinting hair follicles utilising LIFT technology. They believe that it takes continued collaboration and innovation for the 3D printing industry to revolutionise the future of the tissue engineeringfield.

II. Engineered Tissues Models

Engineered human tissue models are becoming increasingly attractive as pre-clinical platforms for studying diseases and predicting the effectiveness of novel therapeutics, due to their potential for reducing, or even completely eliminating, the use of animal subjects. Traditional models, such as patient-derived xenograft models, involve biopsy from the patient, separation and expansion of diseased cells (such as cancer cells), and engrafting into immune deficient mice to develop disease-bearing mice. This lengthy process requires the use of animals and is not cost-effective. Thus, significant effort has been devoted to the development of animal-free in vitro models using conventional fabrication techniques. However, conventional fabrication techniques produce over simplified constructs, often leading to unrealistic cell microenvironments, hindering the accuracy of models. The use of 3D printing mitigates this inaccuracy by allowing researchers to fabricate more sophisticated, and thus more biomimetic, in vitro tissue models. Below, we discuss the most commonly studied cancer, liver and skin models. The tumour microenvironment, or tumour stroma, is considered extremely important in regulating tumour progression and metastasis. The tumour stroma consists of various types of non-malignant cells, including fibroblasts, epithelial, immune and vascular cells, along with the extracellular matrix (ECM). 3Dprinted models precisely mimicking tumour microenvironments are ideal for pre-clinical models. In this regard, various 3D printing techniques, including LIFT, droplet-based, extrusion-based and vat photo polymerisation, were used to create physiological models for mimicking the cancer microenvironment. Xu et al. demonstrated a dual ejection system to bio print a 3D co-culture model using human ovarian cancer cells (OVCAR-5) and normal fibroblasts which were patterned in a controlled fashion (such as cell density and cell-cell distance). They showed that the microprinted OVCAR-5 formed 3D acini with structures and growth kinetics resembling similar in vivo



Tissue Engineered 3D Models.

Grolman et al. developed a co-cultured hydrogel fiber model by bioprinting MDA-MB 231 breast cancer cells(within the shell)and macrophages (in the core) to study the interactions of cancer cells with surrounding stromal cells. Sun Lab used a micro extrusion printing process to construct a cervical tumor model with HeLa cells embedded in gelatin/alginate/fibrinogen hydrogels. Their results revealed that HeLa cells in the 3D-printed model showed higher metalloproteinase (MMP) protein expression, and improved cell proliferation rate, and greater chemo resistance than those in 2Dculture.

Ling et al. developed high-throughput fabrication of 3D MCF-7 human breast cancer cellular spheroids using bioprinting. And also 3D projection printing to create a honeycomb branched structure within a hydrogel with three different channel widths to study the effect of channel size on the behaviour of HeLa cells. They found that the change in channel width has a greater effect on the morphology of the non-cancerous cell lines while it only affects the migration speed of HeLa cells. Despite the current efforts to create a cancer microenvironment, multicellular systems are still required to create complete cancer microenvironments comprising tumour cells, non-cancer cells, immune cells and vascular cells.

Liver tissue engineering is an emerging field in drug testing, and high-throughput drug screening as theliveristheprincipalsiteofdrugmetabolism andis highly sensitive to drug toxicity. The liver is a complexorganwhichiscomposedof80%hepatocytes and 20% non-parenchymal cells, arranged into lobules with a hexagonal shape. Researchers have madeprogressinrecapitulatingthecomplexityofliver architecture by3Dprinting technology. For instance, Ma et al. utilised DLP-based 3D printing to precisely organise the human-induced pluripotent stem cell-derived hepatic progenitor cells (hiPSCHPCs) and the supporting cells into a hexagonal pattern. Chang et al. bio-printed a liver micro-organ model consisting of hepatocytes (HepG2) encapsulated in alginate to study drug metabolism. In their study, they combined an extrusion-based direct cell-writing process and micromoulding techniquetocreatea3Dmicrofluidicchamberwhich perfused a prodrug into the synthetic liver system. Matsusaki et al. demonstrated a layer-by-layer assembly process using inkjet printing to construct micrometre-size multilayers consisted of hepatocytes and endothelial cells on a chip. This simplified 3D liver tissue showed great potential for the evaluation of drug toxicity. Medical research companies are also utilising 3D bioprinting to create engineered human tissue models for pharmaceutical applications. For instance,

Organovo (Organovo Holdings Inc., USA) developed a 3D bioprinted human liver tissue model for pre-clinical drug testing to assess organ-levelresponsestoclinicaldrug-induced toxicity in vitro. For this purpose, bioinks comprising parenchymal cells (without a carrier) or non-parenchymal cells (15□× 107 cells ml−1 formulated in a carrier hydrogel) were loaded into separate heads of the bio printer and deposited in a two-compartment planar geometry. The non-parenchymal cells comprisetheborderregionsofeachcompartment, whereas the parenchymal cells filled each compartment. Following fabrication, tissues were allowed to mature in cultureforatleast3weekspriortoinitiationof experiments. In addition to cancer and liver models, 3D bioprinting is also used to develop skin tissue models. In 2013, theEuropeanUnion(EU)bannedtheuseofanimalsfortestingcosmeticproducts.Thishasexpedited the development of engineered 3D in vitro skin tissue modelstoreplaceanimaltesting.3Dinvitroskinmodels provide a new gateway to assess the toxicity, absorptionandefficacyoftopicaldrugsandcosmetics. For example, Lee et al. demonstrated the feasibility of building an in vitro skin model. Using an eightchannel droplet-based printer, keratinocytes and fibroblasts were printed within a collagen matrix representing the epidermis, the dermis layer and the dermal matrix of the skin respectively. In 2011, Koch et al. reported a multi-cellular skin tissue analogue using LIFT, Fibroblastandkeratinocytesembedded in acollagen matrix was printed layer by layer to mimic the dermis and epidermis layers. The results showed that the printed cells proliferated and formed a tissue through intercellular adhesion and communication. Althoughmostofthecurrentresearchwasfocused on optimising printing parameters to promote cell proliferation and tissue formation, the printed models showed great potential in helping to understand the pathophysiology of skin diseases as well as drug/ cosmetics testing. Cosmetic companies are actively making investments in this technology. **We would like to note that vascularisation is a majorbottleneckforthecurrent3Dbioprintedtissues with regard to modellingand transplantation**. The lack of blood vessels to transport nutrients, oxygen, and waste limits the size of the 3D-printed tissues and shortens their lifespan. The diffusion length of nutrientsandoxygenatetypicalengineeredconstruct is approximately 200 microns. This means that cells located at a distance more than 0.2mm away from the source will eventually undergo hypoxia and apoptosis. Although 3D-printed human-scale constructs are recently reported, to date, there is not a single3D-printedhuman-scalelivingtissueconstruct. The thickness of the printed tissues is usually only including skin, blood vessel, cartilage, bone, ear, osteochondral interface, cardiac tissue, kidney, and liver.

Medical devices

AM has several advantages over traditional manufacturingtechniques,whichmakeitveryattractivewhere medical devices are considered. Firstly, AM allows for the fabrication of custom-designed medical devices and surgical tools by using the patient's own medical image; devices are thus matched anatomically to the patient. It also allows the creation of personalised surgicalinstrumentsto fitthehandsofa surgeon. Secondly, AM(Additive manufacturing) is able to develop complex geometric structures which are not possible with conventional techniques. It also allows on-demand fabrication in remote locations with relatively low costs, and further reducing the prices associated with packaging, transportation, and storage. The applications of AM in medical devices, include:

(i) surgical instruments,
(ii) implants,
(iii) prostheses
(iv) orthoses,
(v) hearingaids

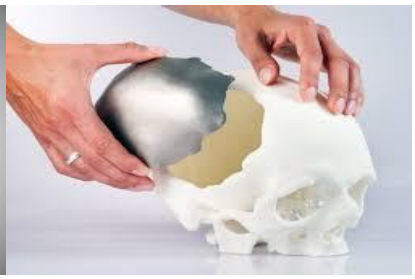
Several medical institutions have successfully fabricated and utilised 3D-printed surgical instruments, includingintraoperativeguides, scalpelhands, needle drivers, retractors, tissue forceps and haemostats, for a variety of applications, such as spine, craniomaxillofacial, orthopaedics ,urology, tumourremoval, hip and knee surgery. Recently, Kunz et al. used an FDM 3D printer to create patient-specific surgical guides made of acrylonitrile butadiene styrene (ABS) to repair an articular cartilage defect of a patient's knee during a mosaic arthroplasty operation. Orthopaedic surgeons have used SLS-printed resection guides from polyamide for hip endoprosthetic operations, and they found that the 3D-printed guides enabled easier, faster and precise procedures. Maeda et al. explored the clinical feasibility and performance of a 3D-printed endoscopic device (printed by using biocompatible photopolymers with an MJM printer), which enabled efficient cell sheet coverage for preventing severe oesophagal stenosis after endoscopic submucosal dissection. Another example demonstrated the use of an SLA-printed fibular cutting guide for mandibular reconstruction. In addition, Rankin et al. printed a PLA army/navy surgical retractor using an FDM printer. They showed that the surgical retractor could be sterilised by glutaraldehyde (an FDA-approved chemical sterilant), could endure 13.6kg of tolerance (much higher than the required force), and cost only $0.46 per unit, which is much cheaper than the cost of a stainless steel device are devices intended to replace missing body parts. There are three major 3D printing uses in Orthopaedics are

1 foot orthoses (FO)

2.Ankle–foot orthoses (AFO)
3. prosthetic sockets.

Currently, the commonly used materials for fabrication of Orthopaedic devices include polyamide, ABS, PC, PP and the primary 3D printing techniques are SLS, FDM and MJM Only a few cases employed SLA, which is probably due to the brittleness and low resistance to stress of the SLA-printed parts. Other 3D-printed Orthopaedic products include wrist splints, robotic exoskeletons for patients with neuromuscular impairment prosthetic hands, arms, feet and legs. In aesthetic reconstruction, such as the face, nasal and ear prostheses, AM (SLA, FDM, BJ, orSLS) technology is typically used or fabrication of highly detailed moulds to cast a silicone-based prosthesis with a natural appearance. In addition to academic and clinical research, many commercial manufacturers have emerged, such as Create Orthopaedic 3DMedScan, 3D Orthotics, and Peacocks, providing services relating to 3D-printed customised O&P.

Non-profit organisations such as e-NABLE and Limitless Solutions are dedicated to providing advanced 3D-printed prostheses at an affordable price. e-NABLE offers open-source CAD designs for 3D-printable prosthetics and assembly instructions as well as resources of the current state-of-the-art in 3Dprinted prosthetics.Another advantage of AM is that it allows on-demand fabrication of medical devices, which makes it a potentially attractive fabrication technique for remote areas. In fact, various groups have been exploring 3D printing applications for space missions, the military and in areas with limited resources.

3D-Pubic prosthesis 3D-cranium

3D-Auricular prosthesis

In 2014, researchers from the Center for Innovative Technologies and Public Health explored the feasibility of creating ABS surgical instruments using FDM for potential use in long-duration space missions. Thirteen boardcertified surgeons underwent simulated surgical tasks (prepping, draping, incising and suturing) using the printed devices including sponge sticks, towel clamps, scalpel handles and toothed forceps. The study aimed to evaluate multiple aspects of the capability of 3Dprinted devices regarding the instrument fabrication speed and mechanical properties, surgical completion time and instrument performance compared with conventionaldevices. *Theauthorsdidnotobserveany substantial differences between the 3D-printed and conventional instruments when completion time and functional performance were considered. However, the printing parameters, such as part thickness and printing orientation, were shown to be important forincreasingtheload-bearingcapacityofthe devices*. The same group developed another study to validate the feasibility of using FDM-printed ABS surgical instruments by Mars analogue crew members with no prior surgical experience. For limited-resource settings, a non-profit organisation, to print simple medical supplies (such as umbilical cord clamps) for use in local clinics. 3D printing is becoming a viableoption inruralareaswiththe increasing availability of solar-powered printers and open-source software andCAD designs. Finally, 3D printing has played an important role inreshapingthehearingaidindustry. Similartodental manufacturing, the process of hearing aid production consistsofmultiplelabour-intensivestepsrangingfrom moulding, curing and trimming to drilling. This processissignificantlyshortenedby3Dprinting, andnow consists

of impression scanning, virtual sculpting and printing, whichtakeslessthana day.3Dprinting is primarily used to produce the plastic shells which hold a microphone, a digital processor, an amplifier, speakerandabattery.

3Dprintingisprimarilyusedfor in-the-ear (ITE), in-the-canal (ITC) and completely-in-the-canal(CIC)hearingaidmodelsasthesemodels requireaperfect fitinthe patient'sear. Theearlyperiodof manufacturing activity relied on SLS technology. However, the printed shells were changing colour with time and displaying high surface roughness, which limited the use of SLS.

In late 2002, companiesrapidly adapted SLA technology due to the development of biocompatible materials suitable for SLA. Today, the hearing aid market is dominated by six major companies, including Phonak (Sonova Company, Switzerland). Approximately 99% of the hearingshellsproducedworld-widearecurrentlyfabricatedusing SLA. Readers are referred to an excellent case study of 3D printing in the hearing aidindustryforfurtherinformation

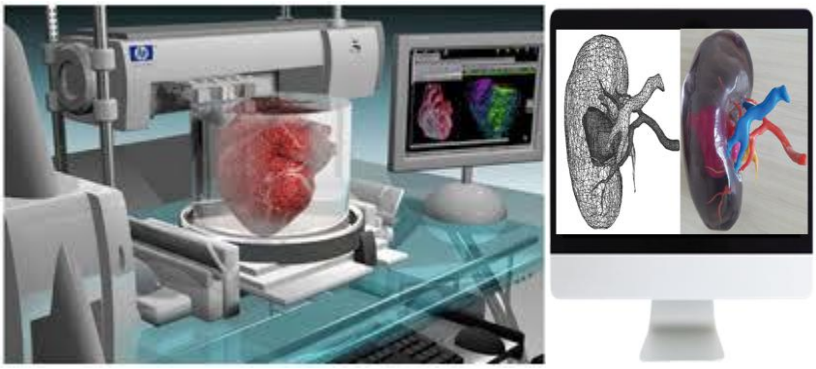
Anatomical models

Pre-surgical planning and training are of paramount importance for a successful surgical outcome .3D-printedanatomicalmodelsarebecoming increasingly popular, as they can be easily printed on demand from a medical image (such as CT and MRI). AM is currently the most commonly used fabrication technique for anatomical models, which serve in pre-surgical planning and surgical education. The pre-surgical planning process includes decision-making, visualisation of tissue anatomy, simulation of the surgical process, selection and manipulation of surgical equipment, anddemonstrationofmodelsto patient. Although 3D-printed surgical models date as far back in the early 1990s, they have only recently become rapidly popular due to easyand cost-effectiveaccessibilityofAMtechnology. Thelargestgrowthhasbeen incraniomaxillofacial and cardiothoracic surgery.

Other surgical applications employing 3D-printed models include spinal surgery,neurology, lung surgery, hepatobiliary surgery, urology, vascular surgery, transplantation, tumoursurgery,anaesthesia and plastic surgery. In addition, 3D-printed models are particularly valuable for helping surgeons in complex and rare cases, For example, A 4-month-old baby suffering from kidney failure successfully received an adult kidney from her father with the aid of 3D-printed anatomical models. In this case, the huge size discrepancy between the father's kidney and the child's abdomen imposed a high risk for the child and great challenge for the surgeons. To conduct the transplant, models of the child's abdomen (including the liver, pelvis, lateral abdominal walls and blood vessels) and the father's kidney were 3D-printed. The models helped the surgeons to visualise the recipient's anatomy and available space, to determine the location of the suturing site and to optimise the surgical procedures. Increasing evidence shows that the use of 3D-printed surgical models has led to an increase in the confidence of surgeons and their success rate, a decrease in operating time and enhanced doctor-patient communication. Beyond the spectrum of surgical modelling, studies have also shown greater anatomical learning experience and outcome for students using 3D-printed models compared with those utilising textbooks and 3D computer-basedmodels.

Inaddition, anatomicalmodelsofferareal**hands-on**experience for surgical anatomy education and planning. This is particularly important for programs which may have limitedaccesstohumancadaveric models. There are several 3D printing technologies available to produce medical models. The choice of the printing method and material is dependent on the desired properties of the models, such as resolution, accuracy, colour and long-term stability. Single-colour modelsaretypicallymadewith SLS andSLA techniques. FDM-printed models are cost-effective but usually exhibit rough surfaces and low resolution. BJ can produce multi-colour prints with colours highlighting different regions of the model. In addition to incorporating a varietyofcolours,MJMcansimulatethetextureofsoftand hard tissues with pre-determined mechanical propertiesofthematerials.Forexample,Zeinetal printed liver replicas in rubber-like photopolymers using a Stratasys Connex350 printer (MJM) . The models exhibited different colors for the vascular and biliary networks within a transparent liver parenchyma, which closely mimicked the native livers from three pairs of donors and recipients who underwent living donor liver transplantation (LDLT).

Materialise, a leading provider of 3D printing software and services, has launched Anatomy Print, an online portal for users to upload patient data and receive anatomical models .

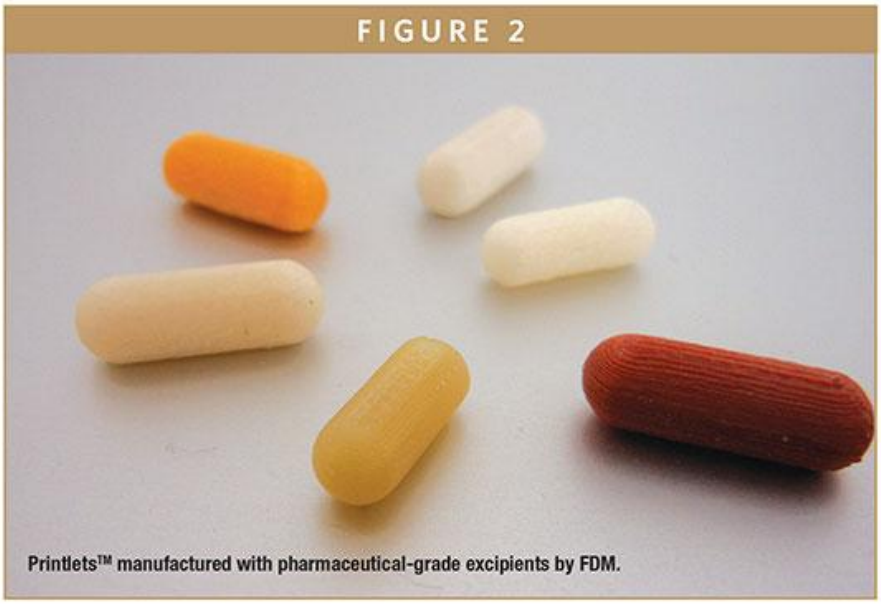


3D-printed HumanHeart and kidney

Fasotec,aJapanese-basedcompanyacquiredby Stratasys, developed 'Biotexture Wet Models' in 2015, which realistically mimic a soft, moist organ model . The company also provides models of liver, lung, bladderandurethraltube. Note that there are still several limitations associated with 3D printing technology. First, the models created by SLS, SLA, FDM and BJ are not practical for performing dissection exercises astherespective printable materials are generally too hard or brittle. Second, there is a limitation in printable wall thickness and hole size for these models determined by the printing method, the geometry of the model and the selected print material. Therefore for some models features such as thin septations within the paranasal sinusescannotbeaccuratelyfabricated

Drug formulation

A drug product is a dosage form comprising active pharmaceutical ingredients (API) and inactive substances (excipients), and can be in the form of pills, liquids, patches or implantable devices. They usually require a sophisticated design including compositionalandstructuralvariationsforcontrolleddrug release, better patient compliance and long-term stability. Due to its ability to create complex objects, 3Dprintinghasbeengraduallyadoptedbythe pharmaceutical industry over the past decade. The drugs are produced using the company's trademark technology called 'Zip Dose', which involves depositing aqueous fluid to bind powder blends layer-by-layer, leading to the formationofsolidyethighlyporoustablets. Thehighly porous structure is claimed to be responsible for the superior disintegration characteristics of the tablets. Other complex structures and shapes with accurate dose distribution are also produced by using 3D printing to tune drug release kinetics. In addition, the potential to provide personalised medication based on apatient's age, body weight and other clinical parameters is one of the key advantages of 3D printing compared with traditional manufacturing. 3D printing technology also allows on-demand production of medicine, such that drug products can be printed for emergency use or for immediate use of formulations with sensitive components to eliminate deteriorationduring storage.



A tremendous amount of research on drug formulation using 3Dprinting techniques can be found in the literature, yet so far there is only one FDA-approved 3D-printed drug available in the market. The techniques used for drug development are droplet-based printing, including MJM and BJ, and extrusion-based printing, including DIW and FDM. In the BJ process, the drugs are incorporated in the powder bed or in the liquid binder. By carefully tuning parameters including powder particle size, binder flow rate and translational speed, a variety of complex designs including core-shell, layered, multi-compartment and porosity/concentration gradient designs have been reported. These complex designs have been applied to fabricate fast-dissolving or controlled-release (e.g. zero/first-order or pulsatile release) dosages for single or multiple drugs. Nonetheless, this approach still exhibits several disadvantages that limit its application. These disadvantages are poor mechanical properties, along post-drying time, the potential presence of a residual organic solvent, poor resolution and low drug loading.

Some of these inherent limitations can be overcome with the use of FDM. In the FDM process, two main approachesareusedtoloadthedrugsintopolymerfilaments. The firstapproachistoimmerse filamentsinan organic solution containing the drug, followed by drying. Thisapproachallowsdrugstopassivelydiffuseinto the filamentsandbetrappedinsidethepolymer matrix. The second approach is to combine drugs and excipients through hot-melt extrusion to directlyfabricatedrug-loadedfilaments. Themajorchallengeofthefirstmethodistheextremely low dose infill percentage, typically less than 2% w/w.Incontrast, hot-meltextrusioniscapableof achieving high drug loading. With appropriate rheological and heat transfer properties of the drug-loaded filaments, the FDM process has been used to print products with various geometries, complex internal structures and multiple drugs. The final product printed by FDM technology typically exhibits high precision and good mechanical strength, even with hollow or porous structures. In addition, FDM has also been used to print templates with various patterns for creating complex-shaped tablets with controllable drug release profiles. However, available pharmaceutical-grade printable polymers are rather limited, and the drugs may be susceptible to thermal degradation during the extrusion or printing process.

Alternatively, degradation can be prevented in the DIW process where the polymer paste is deposited by varying the syringe pressure, thus allowing printing without or with less heat. The drugs can be easily mixed into the polymer carrier to form a viscous paste with appropriate rheological characteristics fordispensing. Thistechnologyhas beenused for the development of a variety of novel controlled-release drugsincludingmulti-layeredtablets,multi-drugtabletswithdifferentcompartmentsseparatedby a semi-permeable membrane and local drug-delivery patches.

Anthropology

RP models can be very beneficial to the anthropologist. RP allows for replication of jawbone and teeth so that moulding, measuring, and dissecting of the remains can be done without causing harm. In cases where only one or two specimens exist, the RP models allow the original model to be safely locked away without hindering research done on the specimen. The models that are built can also be used to show changes in evolution.

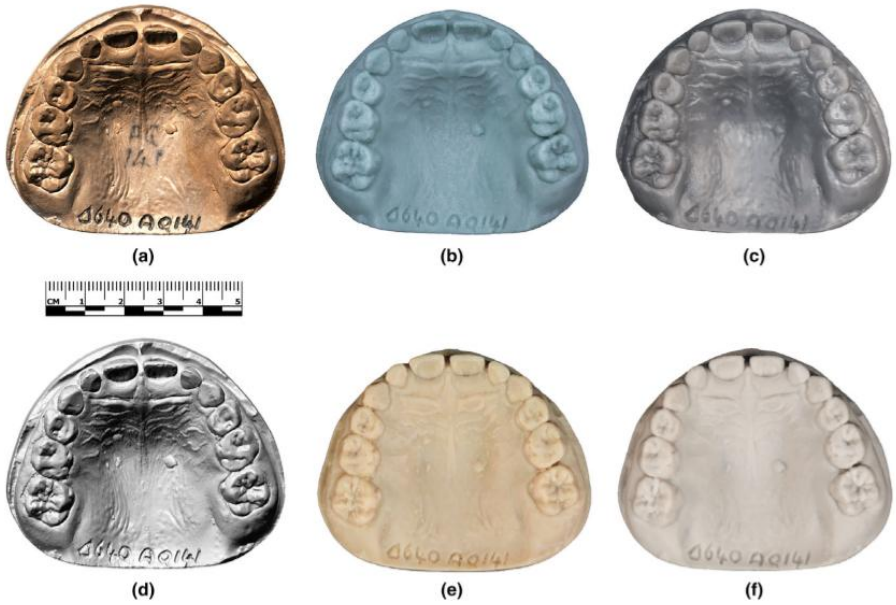


FIGURE 2 Three-dimensional polygonal and rapid prototype models of the upper jaw (a, textured polygonal model; b, FDM print; c, SLA print; d, monochromatic polygonal model; e, material-jetting print; f, binder-jetting print) [Color figure can be viewed at wileyonlinelibrary.com]

Forensics

It is extremely important to keep or reconstruct the scene to investigate a crime. Rapid Prototyping is a valuable tool in the criminal investigation. RP models can be kept as evidence in criminal investigation and helpinvestigators findmore clues.RP models can be used to preserve evidence before it further deteriorates. They are accurate enough to see the effects of wounds. Furthermore, accurate predictions of the forces, implements and other key events can be determined using these models. RP allows the production of simulated bones, so actual physical models are something tangible that could be presented in a court proceeding. These models could help recreate the scene in the courtroom as well as shine some light on what really happened.

References

[1]. Emanuel Ambu,Rodriguez 3d Radiology In Dentistry Vol 3
[2]. Current and emerging applications of 3D printing in medicine Chya-Yan Liaw and Murat Guvendiren
[3]. RaynaT and Striukova L 2016 From rapid proto typing to home fabrication:how 3D printing is changing business model innovation Technol Forecast
[4]. Ventola CL 2014 Medical applications for 3D printing:current and projects Duses Pharma Therapeutics
[5]. Murphy SV and Atala A 2014 3D bioprinting of tissues and organs Nat.Biotechnol
[6]. Schweiger J,Beuer F,Stimmelmayr M,Edelhoff D, Magne PandGüth JF 2016 Histo anatomic 3Dprinting of dental structures
[7]. Jones DB,Sung R,Weinberg C,Korelitz T and Andrews R 2015Three-dimensional modelling may improve surgical education and clinical practice Surg Innov.
[8]. McGurk M,Amis A A,Potamianos P and Goodger NM 1997 Rapid proto typing techniques for anatomical modelling in medicine.
[9]. Siolas D and Hannon GJ 2013 Patient derived tumor xenografts:transforming clinical samples into mouse models Cancer Research.
[10]. Goyanes Aetal 2015 3D printing of medicines:Engineering novel oral devices with unique design and drug release characteristics.
[11]. Van Noort R 2012 The future of dental devices is digital Dent Mater.
[12]. Leong KF,Cheah CM and Chua CK 2003 Solid free form fabrication of three dimensional scaffolds for engineering replacement tissues and organs Biomaterials
[13]. Sobral JM,Caridade SG,Sousa RA,Mano JF and ReisRL 2011Three-dimensional plotted scaffolds with controlled pore size gradients effect of scaffold geometry on mechanical performance and cell seeding efficiency Acta Biomater
[14]. Melchels FPW, Barradas AMC,Van Blitters wijk CA, DeBoer J,Feijen J and Grijpma DW 2010 Effects of the architecture of tissue engineering scaffolds on cell seeding and culturing Act a Biomater
[15]. ZeinI, Hutmacher DW,TanK C and Teoh SH 2002 Fused deposition modelling of novel scaffold architectures for tissue engineering applications
[16]. Almela, T, Al-Sahaf, S, Brook, I. M, Khoshroo, K., Rasoulianboroujeni, M., Fahimipour, F., et al. (2018). 3D printed tissue engineered model for bone invasion of oral cancer. Tissue Cell
[17]. Anssari Moin, D., Derksen, W., Verweij, J. P., van Merkesteyn, R., and Wismeijer, D. A novel approach for computer-assisted templateguided autotransplantation of teeth with custom 3D designed/printed surgical tooling.
[18]. Bhargav,A.,Sanjairaj,V.,Rosa,V.,Feng,L.W.,andFuhYh,J.(2017).Applications of additive manufacturing in dentistry: a review. J. Biomed. Mater. Res. B Appl. Biomater.

[19]. Bottino, M. C., Pankajakshan, D., and Nör, J. E. (2017). Advanced scaffolds for dental pulp and periodontal regeneration. Dent. Clin. North Am.
[20]. Chen, Y.-W., Shen, Y.-F., Ho, C.-C., Yu, J., Wu, Y.-H. A., Wang, K., et al. (2018).Osteogenic and angiogenic potentials of the cell-laden hydrogel/mussel in spired calcium silicate complex hierarchical porous scaffold fabricated by 3D bioprinting.

Dr.BharaniKrishna.T, et. al. "Applications of 3d Printing in Medicine." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(11), 2020, pp. 13-24.