Innovations

3d matrices in periodontal regeneration a new vista

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Abstract:
Technology has become an essential part of dentistry in recent years that led to the development of devices and tools to improve treatment methods and teaching in the fields of end odontics, implant, craniofacial, maxillofacial, orthognathic, and periodontal treatments. 3D Bioprinting is an evolving technology in the field of regenerative medicine that allows the fabrication of living tissues using the living cells by the printing process. Since, periodontitis has become more prevailing disease among the population; there is a requirement for increased periodontal regenerative procedures to restore normal healthy periodontium for the patients. The 3D printing technologies have the advantages of high material utilization and the capability to manufacture a single complex geometry; nevertheless, they have the demerits of high cost and time-consuming post processing. The development of new materials and technologies will be the future trend of 3D printing in dentistry, and there is no denying that 3D printing will have a vivid future.
Keywords: *Periodontitis, Bioprinting, Regeneration, Scaffold, Computer Aided Design.*

Introduction

Technology has become an essential part of dentistry in recent years, which has led to the development of devices and tools to improve treatment methods and teaching in the fields of end odontics, implants, craniofacial, maxillofacial, or thognathic, and periodontal treatments. [1] The expanded use of technology or "digital workflow" in dentistry comprises of three elements; acquisition of data through scanning, processing of data using computer-aided design software (CAD), and use the information to develop objects using computer-aided-manufacturing.[2] Previously, subtractive manufacturing, or milling, was used to build objects with some precision, but it was time-consuming, resulting in wastage of material and limited application in complex anatomy. To get the better of these problems, three-dimensional (3D) printing was introduced. [3] 3D printing is the term used to delineate additive manufacturing approach that constructs material layer by layer. It utilises information from CAD software that measures thousands of cross sections to build the exact replica of each product. [4]

3D printed scaffolds are currently being traversed in techniques such as guided bone regeneration (GBR), guided tissue regeneration (GTR), vertical bone augmentation, sinus augmentation, and preservation of the cavity, showing undulating results regarding their success. ([5] The great attention that three-dimensional (3D) printing currently receives around the world cannot go unseen by dentists. The term "3D printing" was coined at MIT in 1995. [6]

History of 3D Bioprinting

Bioprinting is a technique that is employed to design complex biological structures using bioink. After the contrivance of stereo lithography by Hull CW in 1983, the concept of printing human organs was developed. Before time, the machine discovered by Hull used UV lasers to engrave the layers of acrylic into shapes, which are then assembled to form objects. The major disadvantage was that the printer uses written codes to engrave the acrylic, so only simple shapes were generated. Later, in 1986, Hull discovered the 3D printing technology and also outlined the materials that go into the printers. [7]

Then, in 2003, Thomas Boland, a scientist from the University of El Paso, invented his own designed 3D bioprinter, which uses bioinks to print live tissues. [8] In 2004, Dr. Forgacs launched his own bioprinter, which during his uprising caused a great change in the scientific community. It was the first device that allowed 3D direct biodegradation, i.e., using live cells without the requirement to build scaffolding. [9] In 2006, Noble Prize winner Dr. Shinya Yamanaka discovered that mature cells acquired from cultures can be reorganised again into a stem cell state. [10] This created a revolution in the field of regenerative medicine and also in 3D bioprinting. In 2009, one of the first commercial bio printers from Organovo-NovoGen MMX was created. They aimed at a "scaffold-free" printing process. In 2010, the first blood vessel was printed by Organovo, the bioprinting company, and today the revolution continues on.

Types of 3D Printing Technological Models

- Fused deposition modelling (FDM)
- Stereo lithography (SLA)
- Selective laser sintering (SLS)-Direct metal laser sintering (DMLS)
- Digital Light Projector (DLP)
- Photopolymer Phase Change Inkjets (Polyjet)

Stereolithography (SLA) Technique

It is one of the most widely commercialised techniques. Printers using this method make use of a perforated platform located beneath a container of a liquid UV-curable polymer (photopolymer), together with a UV laser. A beam of laser light is employed to trace the initial slice of an object on the surface of the liquid, causing a very thin layer to harden. The platform is then lowered, and another slice is traced and hardened; this process is repeated until the complete object has been printed. [11,12]

Direct Light Processing (DLP) Technique

It is an optical technique that employs a light projector operating at UV wavelengths to project voxel (volumetric pixel) data into a photopolymer, which gives rise to the resin curing and solidifying. Each voxel dataset is made up of voxels with measurements as small as 16 x 16 x 15 μmm in the X, Y, and Z directions. Envision TEC: A German company uses this technique. [11]

Fused Deposition Modeling (FDM) Technique

Scott Crump invented this technology in 1988. It is based on material extrusion, in which a semiliquid material, typically a heated thermoplastic, is deposited by a computer-controlled print head. It employs two materials: the modelling material, which constitutes the finished piece, and a gel-like support material, which acts as the scaffolding. Material filaments are fed from the printer's material bays to the print head, which moves in X and Y coordinates, laying material to complete each layer before the base moves downward in the Z-axis and the next layer begins. Once completed, the support material is withdrawn or dissolved, and the component is ready for use. [11,12]

Inkjet Powder Printing

It entails selectively bonding successive layers of a powdered material together. Glue or binder is coated by an inkjet-style print head to bond successive powder layers together. The most frequently used powder is a gypsum-based composite that requires having its surface coated after printout if a robust object is required. It is also known as "binder jetters''. Some binder jetting printers can jet both the binder and coloured inks from several separate print heads, allowing full-color 3D objects to be created with a resolution of up to 600 x 540 dpi. [11,12].

Selective Laser Sintering (SLS)

This makes use of heat rather than a binder to bond powdered materials together and produces objects by laying down a fine layer of powder and using a laser selectively to fuse some of its particles together. During the printing process, non-bonded powder granules hold up the object as it is constructed. Direct metal laser sintering is the process in which the SLS is used directly to produce metal objects.[11,12]

Steps in 3D Bioprinting

Prebiotics:

It is the first step in the process where the structure to be printed is designed and modelled as a 3D structure using Computed Tomography (CT) and MRI(Magnetic Resonance Imaging) scans. Every fine detail is recorded and tomographic reconstruction is done on the images so that they are printed in layer by layer fashion. Later, the bioinks are prepared by isolating them from living tissues and allowing them to multiply.

Bioprinting:

It is the printing process where the designed structures have to be printed using the printers. Here the bioinks are introduced to the printer cartridges and, based on the digital model, the cells are accumulated in a layered fashion.

Post-Bioprinting:

The post-bioprinting process involves maintaining the mechanical integrity and function of the 3D printed structure. They control the remodelling and the growth of tissues by sending signals, and recently, the evolution of bioreactor technologies has caused rapid tissue maturation, vascularization of tissues, and increased the durability of the transplants. Depending on the kind of tissue, the bioreactors differ. [13]

List of bioinks that are used in the 3d bioprinting process (Gopinathan J and NOH I, 2018)

BIOINKS	Description	Advantages	Disadvantages
Agarose	It is a marine polysaccharide taken from seaweed. The disaccharides D-galactose and 3,6 anhydro L-galacto pyranose form the backbone of this agarobiose.	Due to its gel-forming property, it has a wide range of use in the biomedical field. It has good mechanical strength. Biocompatible	It provides limited support to cell growth. Poor cell adhesion, not degradable.
Alginate	It is a natural polymer derived from brown algae. also known as algin or alginic acid). composed of monomers such as alpha L-guluronic acid and (1-4) beta D-mannuronic acid.	It has a good gel forming property and good flexural strength. They imbibe water and other molecules by capillary forces, enabling cell growth.	It has slow degradation kinetics. Poor cell adhesion
Chitosan	It is a cationic polysaccharide which is derived from the natural biomaterial chitin found in the cells of shrimp and other crustaceans.	highly biocompatible. anti-bacterial properties. biodegradable forms stable hydrogels with good cell affinity, mechanical strength.	It has a slow gelation rate.
Collagen	It is the main structural protein component of the extracellular matrix. found in skin and connective tissues.	It has good biomimetic properties. biocompatible It allows cell remodeling.	It has poor mechanical properties and therefore needs to be cross-linked with other biomaterials.
Fibrin	Fibrin is synthesized from fibrinogen by enzymatic action with thrombin. It is a protein found in blood.	good biocompatibility. Biodegradable.	It has a weak mechanical property. It has limited printability.
Cellulose	It is a polysaccharide obtained from cellulose. CMCs are used as hydrogels by modifying their cellular properties.	This has improved cell viability. biocompatible Blending with bioglass, it has good mechanical properties.	lack of shear thinning properties and structural shrinkage on drying.

Applications in Periodontics

Periodontal Applications of Three-Dimensional Printing

Uses of 3D printing in periodontology comprise bioresorbable scaffolds for periodontal repair and regeneration, socket preservation, bone and sinus augmentation procedures, guided implant placement, periimplant maintenance, and implant education. [14]

Guided Bone and Tissue Regeneration

Recent advancements in the field of tissue engineering have opened the way to the development of "3D printed" scaffolds. These multiphasic scaffolds, comprised of both hard (bone and cementum) and soft tissue (gingiva and PDL) components of the periodontium, are not only determined for the particular tissue but are also competent mechanically. [15] With the uprising demand for tissue regeneration, these scaffolds have been investigated in various periodontal procedures such as socket preservation, guided tissue and bone regeneration, sinus, and vertical bone augmentation.[15,16]

The purpose of these scaffolds is to enhance the formation of bone, PDL, cementum, and reestablishment of connections between them. Among various materials, poly caprolactone has been extensively used as a scaffold material due to its documented successful outcomes in bony regeneration. The perks of these scaffolds include 3D architecture that closely resembles the extracellular matrix, resulting in better regenerative capabilities.[17]

A literature search disclosed that most of the studies done were preclinical, in vivo, in vitro, or case reports describing promising results in the field of periodontal regeneration. Rasperiniet al.[18] initially reported the use of a 3Dprinted scaffold in a human periodontal defect (labial soft and hard tissue dehiscence). The results of this case report showed beneficial results for up to 12 months but failed afterward. Lei et al.[19] also reported a 15-month follow-up case of guided tissue regeneration making use of 3D-printed scaffold and platelet-rich fibrin in the management of bony defect around maxillary lateral incisor. He reported a sufficient reduction in pocket depth and bony fill. In a randomised clinical trial by Sumida et al., they used a 3D-printed custom-made device for bone defect repair and reported reduced procedure time and the need for fewer screws for retention than the commercial mesh group. [20] There is a deficiency of randomised control trials and clinical studies with long-term followup.

Sinus and Bone Augmentation

The advantages of 3D printing are the capacity to replicate the bony architecture and form a macro-porous internal structure of the graft with minimal wastage of material because of the additive manufacturing technique. Other benefits include no ethical concerns; ample availability due to alloplastic material; less risk of infection transfer; and less chair-side time of surgery. [21] There is a dearth of randomised control trials. However, multiple case reports and in vivo studies have reported successful outcomes after the use of 3D scaffold for sinus and bone augmentation. Studies have reported the successful use of various materials for printing bone grafts, including monolithic monetite (dicalcium phosphate anhydrous) and biphasic calcium phosphate. [22]

Three-Dimensional Printing for Implants Placement

Implant placement is a technically challenging procedure and, if not done properly, can lead to various complications such as poor esthetics, damage to anatomically important structures, infections, and implant failure. [23] With the help of 3D printing, guided implant placement can avert these complications by the fabrication of surgical guides. It helps in accurate 3D placement of implants, thus preventing undesirable damage to anatomic structures and reducing time.

Two protocols of guided implant surgery have been reported in the literature: static and dynamic. The static guide, also called stereolithographic guide, uses the static surgical template and does not allow any changes in planned implant position during surgery, whereas the dynamic approach utilises motion tracking technology and permits any switch in implant positioning. The guides are produced using photo polymerization techniques. [24] The static approach is more commonly used as it is less costly and less technique-sensitive, and both protocols have comparable failure rates. Surgical guides can be supported by teeth, mucosa, bone, and pins or mini implants based on the intraoral condition like partially dentate or edentulous and the need for extensive bone surgery. Tahmaseb et al. reported in a systematic review that the use of mini-implants resulted in enhanced accuracy in implant placement and immediate loading is possible.

Use of three dimensional printing for periim plant maintenance

Implant surfaces are distinct and require special attention while cleaning and maintaining them. 3Dprinted implant models can be used to educate patients about implant maintenance to patients. [25]

Use of three-dimensional printing for implant education

3D printing can be used for teaching purposes that include patient understanding of the procedure before giving consent for implant placement on a 3Dprinted model. It helps to alleviate the anxiety of patients. These models also help in the training of undergraduate and postgraduate students with regard to implant treatment planning, placement of implants without affecting the nearby anatomic structures. [25]

Other uses in dentistry:

- **Oral surgery:**

- Anatomical models can be constructed which can be used as a new perspective for surgical treatment planning and simulation
- To produce customised reconstruction plates and morphological reconstruction of bony defect area for cases of fractures and reconstruction surgery.
- To design and build a customised non-absorbable barrier of titanium mesh.
- To do mock surgeries.[26]

- **Implantology**

3D printed dental implants seems to constitute a successive clinical option for replacement of single tooth gap in both jaws.[27] Digital Light Processing is a useful method for printing customised zirconia dental implants with sufficient dimensional accuracy. Customized dental implants printed using Selective laser melting (SLM) method depicted increased density, strength and ample dimensional accuracy. In cases where conventional implants cannot be used, 3D printed customised subperiosteal implants can be used. [28]

- **Orthognathic Surgery**

Digital study models prove to be a finer alternative to conventional plaster study models in the treatment planning for malocclusion patients. [29] A new technique for fabrication of surgical wafers involves simulated repositioning of digital model images using intra-oral scanners and then fabrication of a computer-generated wafer using orthodontic software packages, which is connected to 3D printing technology for dental model fabrication.

- **Digital Orthodontics**

The Invisalign System realigns the patient's teeth digitally to produce a series of 3D printed models for the construction of aligners, where the patient will receive a new set of aligners every 2 weeks and reposition the teeth over a period of time. [30]

- **Prosthodontics**

In a review article, Silva et al. discussed the utilisation of the method of "robocasting" to manufacture fixed partial dentures. Robocasting is a 3D printing fabrication method in which an object is printed in a layer-by-layer fashion onto a level substrate directly from a digital file. The paste used in Robocasting is composed of ceramic particles and typically 47% solid and 1-2 % organic material. This paste is capable of producing fine filaments and drying with minimal shrinkage. [31]

- **Maxillofacial Prostheses:**
- for replacement and reconstruction of zygomatic bones, temporal bones including ear ossicles, calvarial bones, and mandibles.
- used in soft tissue reconstruction of the head and neck.
- These are more suitable following trauma or tumour resection. With the emergence of 3D implants, the cosmetic defects associated with these surgeries have decreased remarkably. [30]

Shortcomings of 3D Bioprinting

Though 3D bio printing technology has been available for many long years, the expensiveness of the 3D bio printers, high energy consumption, the operation and maintenance cost, clearance from the ethical board as it advocates the use of cells, and also the requirement of a trained operator have been shown to be barriers for its development. [32]

Conclusion

3D printing has transformed the field of periodontology. Numerous uses of this technology have been reported in the literature in various fields, including 3Dprinted scaffolds for socket preservation, periodontal repair and regeneration, sinus and bone augmentation, periimplant maintenance, and implant education. 3Dprinted scaffolds manifest foreseeable upshot for bone and tissue regeneration as well as sinus and bone augmentation. Implant placement using a 3D printed surgical template improves the accuracy and reduces the incidence of complications, surgical time, postoperative pain, and swelling. 3Dprinted models have an encouraging role as an educational tool. However, there are some curbing factors, such as increased cost and increased time. Although the use of 3D printing is of prime focus for Periodontists, documented literature is restricted to preclinical studies, case reports, and few clinical trials. Future implications need further virtous quality randomized control trials. [33]

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