ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 3, Issue – 2, March - 2020, Page No. : 411 - 417

3D - Printing In Periodontal Regeneration

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Citation of this Article: Dr. Amala.k, Dr Anjalie Prakash, Dr. Angel Fenol, Dr. Rajesh Vyloppillil, Dr. Biju Balakrishnan, Dr. Ashmy Stephen, "3D - Printing In Periodontal Regeneration", IJDSIR- March - 2020, Vol. – 3, Issue -2, P. No. 411 – 417.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Periodontitis is a disease with a broad range of inflammatory and destructive responses leading to loss of periodontium and tooth-supporting bone. The aim of periodontal therapy is to regenerate the periodontium lost due to periodontal disease. Tissue regeneration in the oral cavity is regulated by signaling molecules, cells, and by matrix formation. Maintenance of the integrity of healthy periodontium and regeneration of the periodontium are achieved by a balance between bone formation and bone resorption termed as bone coupling. Traditional regeneration techniques using grafts and membranes were unpredictable and could not achieve complete regeneration. Periodontal tissue engineering focuses on regenerating the form and function of hard and soft tissues using, scaffolds, and cells. Bony defects may vary in size from small intra bony defects to large horizontal and vertical bone defects in periodontal diseases that prove critical for implant rehabilitation. This review focuses on the various materials and methods that are currently being used and which are in the research stage for 3D printing of patient-specific custom-made scaffolds for periodontal regeneration in the last few years' development of 3D printing for medical and dental applications has increased strikingly.

Keywords: 3D Printing, Periodontics, Tissue Regeneration, Periodontal Tissues, Scaffolds

Introduction

Looking at the dental specialties it becomes evident that the attention in 3D printing is mainly focused on applications in oral surgery and prosthodontic, followed by orthodontics, while there are limited numbers of publications on applications in periodontic and endodontic. The ultimate goal of periodontal therapy is the regeneration of the original architecture and function of the periodontal complex. Several techniques and products aimed at achieving periodontal regeneration are currently available for clinical use. Tissue-engineered constructs have potential to induce bone-ligament complex regeneration to treat disease- or trauma-induced damage to periodontal Fabrication of three dimensional (3D) organoids with controlled micro architectures has been shown to enhance tissue functionality. Bioprinting can be used to precisely position cells and cell-laden materials to generate controlled tissue architecture.[2]. Three-dimensional printing of scaffolds, tissue analogs, and organs has been proposed as an exciting alternative to address some of these key challenges in regenerative medicine and dentistry[3] This range of techniques also referred to as solid freeform fabrication or additive bio manufacturing, enables precise positioning of cells and biomaterials in 3D with finely tuned internal and external architectures, while being customizable to patient-specific needs. Three-dimensional printing is a method that is fundamentally derived from additive manufacturing technology. In principle, objects are fabricated by adding materials layer by layer, hence rendering a 3D volumetric structure [3,4]. The printed structures are designed using computer-aided design (CAD) software or from images obtained via computed tomography (CT), magnetic resonance imaging, or X-ray. Traditionally, 3D printing has been primarily used to fabricate scaffolds constituted of synthetic inks (i.e., polymer hydrogels, sintered calcium and phosphate ceramics, inert metals), which are then seeded with living cells and tested in vivo after implantation.[5]

The most widely applied additive manufacturing methods include fused deposition modelling (FDM), selective laser sintering (SLS), Stereolithography (SLA), polyjet printing, and Fused deposition modelling (FDM) printers are the most common to begin with in a medical or dental set-up owing to its wide availability, moderately reliable printing quality, ease of installation, and use and economic affordability It is competent with a number of materials like acrylonitrile butadiene styrene (ABS) and polylactic acid (PLA)[6]. The spooled material is supplied into a hot nozzle, melting and extruding it in the X-Y dimensions, one layer at a time, before the nozzle is elevated or the print bed drops down .It is the printer of choice for the in house production of easily accessible anatomical models, but for complex anatomies there are various other limiting factors. Both SLS and SLA use laser to scan and build the object layer by- layer, while SLS uses powder-based material for printing the object, SLA is based on a liquid resin material). It overcomes the printing resolution and support material limitations of the FDM, however, object shrinkage is a matter of concern[7]. The printer with highest resolution that is commercially available is the polyjet printer where the 3D model is created, one layer at a time, by the printer heads jetting layers of liquid photopolymer onto a build tray, followed by UV light curing [8]The advantages of polyjet printers are a wide choice of printing materials with varieties in density, hardness and flexibility. The disadvantages are the post-print model processing steps. It finds major application in surgical planning on patient-specific 3D models with complicated geometries, surgical stents and guides, phantoms for orthopaedic and cardiac surgeries, and scaffolds for tissue engineering [9]Following the increasing attention toward these 3D printing methods in the last decade, its utilization in tissue engineering, regenerative medicine, and any form of research has emerged as the most investigated fields of interest. In regenerative medicine, the process of combining cells with 3D-printed polymers for creating 3D cell cultures for tissue engineering drug screening or in vitro disease models is gaining wide popularity[10].

Bioprinting using cell ink based bio printers or spheroid /microtissue-based systems has been developed to generate artificial "tissues" and shown to allow the setup of complex 3D in vitro models[11] A multitude of materials is used to fabricate cell-laden 3Dprinted scaffolds, for example, chitosan[12] calcium silicate complex[13] and controlled release polymeric materials with bioactive agents[14]. 3D printing has been used in application of generating optimal volumes of human bone and skin grafts in vitro [15]This is gaining immense potential to replace the current strategies of procuring autografts

The entire process of additive manufacturing technology is divided into four steps: (1) producing a digital 3Dmodel designed with a software or using intraoral scans or computed tomography data. (2)making and slicing of the 3D model into many two-dimensional layers. (3) printing the final 3D end product layer by layer. (4) final processing of the printed object [16]In this review we aim to draw together the dental experimental, clinical, and future educational aspects of 3D printing in the field of Periodontics under one roof which has not been done in the past.

Three-Dimensional Printing

Three-dimensional printing is a method that is fundamentally derived from additive manufacturing technology. In principle, objects are fabricated by adding materials layer by layer, hence rendering a 3D volumetric structure (Derby 2012). The printed structures are designed using computer-aided design (CAD) software or from images obtained via computed tomography (CT), magnetic resonance imaging, or X-ray. Traditionally, 3D printing has been primarily used to fabricate scaffolds constituted of synthetic inks (i.e., polymer hydrogels, sintered calcium and phosphate ceramics, inert metals), which are then seeded with living cells and tested in vivo after implantation. More recently, however, direct printing of living cells, cell-laden biomaterials, and scaffold-free cell aggregates also has been increasingly studied with a much greater level of complexity. Although a wide range of commercial printers is available in the market and reported in the literature, most current systems fall under 1 of 3 categories: inkjet printers, laser-based printers, or micro extrusion printers. Common to all of these systems is coordinated motion of stages in the X, Y, and Z directions, while an automated system dispenses a bio ink via different mechanisms.

Different Technologies of 3D Printers

Though the basic technology of 3D printers is same, that is, automated, additive manufacturing process, there are various principles on which the 3D printers work.

The technologies under consideration here are as follows:

- Stereolithography (SLA)
- Direct Light Processing (DLP)
- Fused Deposition Modelling (FDM)
- Inkjet Powder Printing
- Selective Laser Sintering (SLS)/Direct Metal Laser Sintering (DMLS)

Stereolithography (SLA) Technique

It is one of the first techniques to be commercialized. Printers using this method employ a perforated platform located beneath a container of a liquid UV-curable polymer (photopolymer), together with a UV laser. A laser beam light is used to trace and 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.

Direct Light Processing (DLP) Technique

It is an optical technique which uses a light projector operating at UV wavelengths to project voxel (volumetric pixel) data into a photopolymer, which causes the resin to cure and solidify. Each voxel dataset is made up of voxels with dimensions as small as 16 x 16 x 15 μmm in the X, Y and Z directions. The German company Envision TEC uses this technique

Fused Deposition Modelling (FDM) Technique

This technology was invented by Scott Crump in 1988. It is based on material extrusion in which a semi liquid material, typically a heated thermoplastic, is deposited by a computer controlled print head. It uses 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, depositing material to complete each layer before the base moves downward and the next layer begins. Once completed, the support material is removed or dissolved and the component is ready for use

Inkjet Powder Printing

It involves selectively bonding successive layers of a powdered material together. Glue or binder is applied from an inkjet-style print head to bond successive powder layers together. The most frequently used powder is a gypsum based composite that needs to have 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-colour 3D objects to be created with a resolution of up to 600 x 540 dpi

Selective Laser Sintering (SLS)/Direct Metal Laser Sintering (DMLS)

This uses 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 support the object as it is constructed. When SLS is used directly to produce metal objects, the process is called "direct metal laser sintering"

3d In Periodontics

Another area of dentistry in which 3D printing is used is periodontology with the focus being on regenerative Periodontology in research and 3D-printed guides for esthetic gingival correction. The periodontium is a complex tissue. Different tissue has different properties and tissue regeneration in the oral cavity.

Experimental Approaches

The term additive biomanufacturing, signifying the application of 3D printing[17] in manufacturing 3D-printed scaffolds to support tissue regeneration in a defect is popularly used in periodontics. The concept behind using this technology is to restore the periodontal tissue and bone defects by supplying the surrounding tissue with growth factors, genetically modified cells, or bioactive proteins [18.]However, damage to the periodontal tissue can also lead to difficulties with the implant placement or cause implant loss as the remaining tissue does not provide sufficient support for osseointegration. 3D printing has its main role in the application in procedure called guided tissue regeneration. It is done as a controlled tissue regeneration to prevent the in growth of rapidly regenerating tissues such as the oral epithelium into the defect and slow-growing bone tissue for regeneration [19.]Advancements in 3D-printed membrane structure, improving its integrity and function in the oral cavity, making it more resistant to the occlusal forces, are being effectuated [20.]3D printing techniques is used in application in tissue regeneration based on the basis of the defect area. A CT scan of the defect in a patient serves as template for the creation of 3D objects.**.** Improved regeneration of the alveolar tissue using 3D polycaprolactone (PCL) scaffolds has been shown**.** With the invention of 3D-printed biphasic scaffolds, it is now possible to utilize and guide multiple periodontal cell types during the healing process. Various other investigations on animals like mice have been noted that the biphasic frameworks have advantages over scaffolds which are produced without the exact specification of a printed mold. The methods that have been used have provided predictable orientation, improved organization of the periodontal ligament, and controlled tissue infiltration. Complex clinical cases have been reported where individualized 3Dprinted scaffolds have been applied for periodontal regeneration [21]Various Studies that uses bioprinting of periodontal cells in hydrogels have proven the feasibility of the technology in vitro [22.]However, in addition to tissue engineering strategies, the technology can also be applied for other purposes**.** Also scaffold-free approaches of bioprinting seem feasible as spheroids **[23]** and more complex micro tissues have been generated successfully from periodontal ligament and gingival cells.

Clinical Approaches

3D printing is popular in esthetic surgeries in the anterior region of the oral cavity [24.]Patient specific areas can be printed and used for gingivectomy procedures and smile designing. Such templates are known for their precision. Educational and training models based on computerized tomographic scans of patients have been developed and used for better surgical skills [25.]Through the use of individualized products, advantages over conventional methods can be created in the area of periodontal tissue regeneration and surgeries.

Educational Approaches

Dental students have been trained either on dental models, or directly on patients for periodontal examination, scoring, and indexing procedures [26.]That has caused a lot of difficulties, leading to patient discomfort such as pain and bleeding. It would be a good approach to print 3D models simulating gums, periodontal tissues, and defects with respective tissue characteristics to develop a better proprioception before operating the patient. Additive manufacturing also encourages printing models of patients with gingival aesthetic defects to be trained using these models and preventing procedural 3D printing has the capacity to revolutionize dentistry. The different technologies have been applied for a variety of purposes in the field of dentistry. The main focus is on surgical planning and the indirect production of implants are by printing the moulds for these objects and 3D printing is used to create personalized tissue engineering scaffolds for usage in oral surgery. Because the print object is produced according to the image of the patient, the print can be altered to optimally fit the anatomical landmarks and anatomy thereby accuracy of aligners or implants can be improved. The problem that requires further research is the limitation of the available material assortment in particular when moving beyond the canonical polymers as well as the improvement of printing speed and post processing requires. All the materials to be used must meet the dental and technical requirements and biocompatibility standards. Therefore it is of great interest to establish new, printable materials for dentistry that meet all these requirements, as the expansion of the material range also opens up new door for clinical applications of 3D printing in dentistry. 3D printing has a high potential for education as witnessed above in all the major disciplines of dentistry. It gives the performing surgeon a better perception of the bone and teeth as compared to the stereotype typhodont or acrylic models. With the advancement in materials and technology, the flexibility to manipulate the physical characteristics of additively manufactured materials, the trainees have the opportunity to develop better operative and proprioceptive skills[27]**.** 3D printing based technologies have a great potential to transform treatment methodology, and educational system of dentistry ameliorating oral health care.

Conclusion and Future Perspective

3D printing has the capacity to revolutionize dentistry. The different technologies have been applied for a variety of purposes in the field of dentistry. The main focus is on doing surgical planning and the indirect production of implants by printing the molds for these objects. And also 3D printing is used to create personalized tissue engineering scaffolds for usage in oral surgery. Experimental approaches has got the application of 3D printing for the production of scaffolds which serve as carriers for growth factors or other bioactive molecules as well as cells. But the results of previous studies show that 3D printing has many advantages, that is used in the fabrication of fixation splints in oral surgery or in orthodontic models. The print object is produced according to the image of the patient, and it can be tailored to optimally fit the anatomical conditions and hence the accuracy of aligners or implants can be improved. The problem that requires further research is the limitation of the available material assortment in particular when moving beyond the canonical polymers as well as the improvement of printing speed and post processing requires. And the used materials must meet the dental and technical requirements and biocompatibility standards. It is a great deal to establish new, printable materials for dentistry that meet these requirements, as the expansion of the material range also opens up new possibilities for clinical applications of 3D printing in dentistry. 3D printing has a high potential for education as witnessed above in all the major disciplines of dentistry. It gives the surgeon a better subjective perception of the bone and teeth as compared to the stereotype typhodont or acrylic models. With the advancement in materials and technology, the flexibility to manipulate the physical characteristics of additively manufactured materials, the trainees have the opportunity to develop better operative and proprioceptive skills .Overall, 3D printing based technologies have a tremendous potential to transform research, treatment methodology, and educational streams of dentistry ameliorating oral health care.

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