Review Article

Tissue Engineering Strategies in Periodontal Regeneration: An update

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ABSTRACT

Three-dimensional (3D)-printing nowadays is commonly applied in tissue engineering. This brief review provides importance of 3D printing techniques & approaches in regenerating ligament-bone complexes by regulating spatiotemporal cell organizations. Some techniques currently being used to produce scaffolds are 3D Printing, Fused Deposition Modelling (FDM), Stereolithography and Selective Laser Sintering (SLS). These tissue engineering strategies will help in enhancing the knowledge regarding regeneration of tooth supporting structures.

Keywords: 3D printing, scaffold, regeneration

INTRODUCTION

Periodontium consists of periodontal ligament which attaches cementum of the tooth to the alveolar bone. Neurovascular elements occupy major portion of periodontal ligament (PDL) space. It helps in distributing cyclic masticatory forces by relative motion between the tooth and the bone. [1] These forces allow continuous adaptation of the Bone-PDL-Cementum complex. [1,2] Angulated PDLs with spatiotemporal organizations between the teeth and the alveolar bone helps to withstand masticatory stress and force distributions. It also optimizes mineralized tissue remodeling for tooth-periodontium complexes thus adding to the functionalization and revitalization of tooth-supportive biofunctional structures. [3] One of major critical requirement for micron-scaled multiple tissue regeneration and functional restoration is spatiotemporal compartmentalization. [4] However various kinds of inconsistencies in multiple tissue interfaces or the loss of their supportive functions can be induced by numerous diseases or traumatic injuries of the musculoskeletal systems. [5]

Periodontitis, a highly prevalent infectious disease, commonly induces tissue destruction of the periodontal complex in humans. [6] Lipopolysaccharide (LPS) secreted by gram –ve bacterial species can stimulate cytokines to signal precursor cells to differentiate and activate osteoclastic cells or the periodontal inflammatory process by bacterial biofilm. [7,8] Current therapeutic knowledge is limited to sub-micron-scaled interfaces and systemic compartmentalization which can periodontal structures and functions for the re-establishment of different tooth-supportive functions. [3]

Heat-Mediated 3D Fabrication

Various techniques such as Selective Laser Sintering, Fused Deposition Modelling and 3-D Plotting are included under Heat-Mediated 3D Fabrication.

Selective Laser Sintering/melting

University of Texas developed Selective Laser Sintering/melting in the year 1989. This technique incorporates CO2 laser beam. On the surface of a powder bed, it selectively fuses powdered material by scanning cross-sections generated from a 3D digital description of the part. The powder bed is lowered by one layer thickness after scanning cross section and a new layer of material is applied on top and till the completion the process is repeated. [10] The fabrication of scaffolds to automatically shape external architectures and porous interior is enabled by selective laser sintering technique. Recently, for making of custom craniofacial implants, use of Selective Laser Sintering has got FDA clearance to process medical grade Polyether Ether Ketone (PEEK). [11]

Fused Deposition Modeling (FDM)

A moving nozzle is used in this method to extrude a fiber of polymeric material from which the physical model is built layer by layer. Polylactic Acid (PLA) due to its biocompatibility and good thermal & physical properties is mainly used for FDM. Human fibroblasts were cultured for proliferation and production of extracellular matrix. [12] Hutmacher et al. found it compatible with that of human cancellous bone by evaluating compressive strength of each printed group. [13] In the XY-plane, FDM exhibits high pattern resolution but in the Z-direction it is limited by the diameter of the extruded polymer filament that helps in defining corresponding pore height and layer thickness. High processing temperature limits the use of biomaterials in this method. However, FDM capabilities are achieving newer horizons with innovations such as Multi-phase jet solidification (MJS) that allows extrusion of multiple melted materials simultaneously. [14]

Light Mediated Fabrication

Stereolithography

An UV laser is used for solidifying the exposed polymer regions keeping the remaining areas in liquid form. The movable table then drops by a sufficient amount to cover the solid polymer with another layer of liquid resin. The desired shape is created by repeating the process. As with SLS, stereolithography has limited resolution which is approximately 250 µm, although small-spot laser systems have demonstrated the production of smaller (70 µm) features.[15] Laser-Based Stereolithography and Digital Light Projection Stereolithography are the two different methods applicable under irradiation. The laser-based method incorporates a direct approach in which a computer-manipulated laser beams which fabricates structures in a vector-by-vector, bottom-up manner. Procedure of digital light projection involves UV light source projection on a transparent surface at the bottom of a vat, which holds the photosensitive resin. Upon light exposure, an entire layer of material is simultaneously polymerized. In initial attempts involving this approach, a physical mask was applied to define the specific pattern to be illuminated during Light Projection Stereolithography. [16] Significant freedom of design is enabled by Stereolithography and is capable of fabricating minimum features sizes on the micrometer scale. While some Stereolithography systems produces structures with ≤5 µm features, most commercial systems have produced structures with ≥50 µm features. [17]

Adhesive –Mediated Fabrication

3-D printing

The first report based on periodontal tissue regeneration by 3D Printing have demonstrated a promising results towards manufacturing and designing of complicated, unpredictable geometries. [9]
The main advantage of this technique is it does not require any additional mould to produce an implant directly from 3D data in one step. The matrices are produced by 3D printing to which patient-derived cells are embedded implanted into the body. 3D printing not only manufactures ceramics but also different types of scaffolds from

polymers. [18] In one of the human based case reports, treatment of large periodontal defects using a patient specific scaffolds by 3D printing for regeneration of periodontal complex have been attempted. [19] Chen Ho Park et al conducted a study where demonstration of different angulated microgroove patterns was shown to control the orientation of ligamentous cell bundles using 3D printing scaffolds which gave high manufacturing reproducibility. This simple strategy provides the topographical platform to precisely form functional architectures for 3D organizations of fibrous connective tissues. [3]

MATERIALS

Various materials for 3DP materials include calcium polyphosphate and PVA, HA and TCP, TCP, TCP with SrO and MgO doping. Rests are HA and apatite–wollastonite glass ceramic with water-based binder, calcium phosphate with collagen in binder, PLGA, and Farringtonite powder (Mg3 (PO4)2). Materials used in indirect 3DP gelatin preforms replaced with PCL and chitosan. [20]

Table 1: Forms and Examples of materials used for 3D printing. [22]

Form	Examples	3D-printing processes
Solidifiable fluid	Temperature sensitive polymers, Photopolymer resins, hydrogels, ceramic paste, ion cross-linkable, etc.	Stereolithography (SLA) Digital light processing (DLP) Micro-extrusion Polyjet
Non-brittle filament	Thermoplastics, e.g., ABS, PLA, and PCL	Fused deposition Modeling (FDM)
Laminated thin sheet	Paper, Plastic sheet, Metal foil	Paper lamination technology (PLT) Laminated object manufacturing (LOM) Ultrasonic consolidation (UC)
Fine powder	Plastic fine powder, ceramic powder,	Electron beam melting (EBM), Laser engineered net saping (LENS), Selective laser sintering/melting (SLS/SLM)

Notes: ABS-acrylonitrile-butadiene-styrene; PLA-polylactic acid; PCL-polycaprolactone.

Pressure Assisted Microsyringe

The Interdepartmental Research Centre "E.Piaggio" at the University of Pisa developed the pressure-assisted microsyringe (PAM) technique. This technique incorporates deposition of hydrogels and polymers of broad range with the use of microsyringes. A stage controlled microsyringe delivery system through a 10–20 µm glass capillary needle deposits a stream of polymer dissolved in solvent. [21]

Future Perspectives

Since the description of 'medical device' may get restructured as with growing trends and technologies of 3D bioprinting, further delay in standardizing this technique may complicate routine work. Implementing and transferring theoretical knowledge into regular practice may simplify dental systems and can lead to more precise work.

REFERENCES

1. Nanci, A. Ten Cate's Oral Histology. Mosby; 2007.
2. Wagle N, Do NN, Yu J, Borke JL. Fractal analysis of the PDL-bone interface and implications for orthodontic tooth movement. Am J Orthod Dentofacial Orthop 2005;127(6):655–61.
3. Chan Ho Park , Kyoung-Hwa Kim , Yong-Moo Lee, William V. Giannobile and Yang-Jo Seol, 3D Printed, Microgroove Pattern-Driven Generation of Oriented Ligamentous Architectures. Int. J. Mol. Sci. 2017, 18, 1927.
4. Park, C.H.; Kim, K.H.; Rios, H.F.; Lee, Y.M.; Giannobile, W.V.; Seol, Y.J. Spatiotemporally controlled microchannels of periodontal mimic scaffolds. J. Dent. Res. 2014, 93, 1304–1312.
5. Lu, H.H.; Thomopoulos, S. Functional attachment of soft tissues to bone: Development, healing, and tissue engineering. Annu. Rev. Biomed. Eng. 2013, 15, 201–226
6. Pihlstrom, B.L.; Michalowicz, B.S.; Johnson, N.W. Periodontal diseases. Lancet 2005, 366, 1809–1820
7. Taba, M., Jr.; Kinney, J.; Kim, A.S.; Giannobile, W.V. Diagnostic biomarkers for oral and periodontal diseases. Dent. Clin. N. Am. 2005, 49, 551–571.

8. Darveau, R.P. Periodontitis: A polymicrobial disruption of host homeostasis. Nat. Rev. Microbiol. 2010, 8, 481–490.
9. Rasperini, G.; Pilipchuk, S.P.; Flanagan, C.L.; Park, C.H.; Pagni, G.; Hollister, S.J.; Giannobile, W.V. 3D-printed bioresorbable scaffold for periodontal repair. J. Dent. Res. 2015, 94, 153S–157S.
10. S. Yang et al. The design of scaffolds for use in tissue engineering. Part II. Rapid prototyping techniques. Tissue Engineering, 8:1–11, 2002.
11. Nickels L. World's first patient-specific jaw implant. Metal Powder Report. 2012; 67:12–4.
12. D.W. Hutmacher. Scaffold design and fabrication technologies for engineering tissues–state of the art and future perspectives. J. Biomater. Sci. Polym. Ed., 12(1):107–124, 2001.
13. Hutmacher DW, Schantz JT, Lam CX, Tan KC, Lim TC. State of the art and future directions of scaffold-based bone engineering from a biomaterials perspective. J Tissue Eng Regen Med. 2007 Jul-Aug; 1(4):245-60.
14. D.W. Hutmacher, M. Sittinger, and M.V. Risbud. Scaffold-based tissue engineering: rationale for computeraided design and solid free-form fabrication systems. Trends Biotechnol, 22(7):354–362, 2004.
15. S. Yang et al. The design of scaffolds for use in tissue engineering. Part II. Rapid prototyping techniques. Tissue Engineering, 8:1–11, 2002.
16. Nakamoto T, Yamaguchi K. Consideration on the producing of high aspect ratio micro parts using UV sensitive photopolymer. Proceedings of 7th International Symposium on Micro Machine and Human Science 1996; 53–58.
17. Gittard SD, Narayan RJ. Laser direct writing of micro and nanoscale medical devices. Exp Rev Med Dev. 2010;7:343–56.
18. Leukers B, Gülkan H, irsen SH, Milz S, Tille C, Schieker M, et al. Hydroxyapatite scaffolds for bone tissue engineering made by 3D printing. J Mater Sci Mater Med. 2005;16:1121-4.
19. Rasperini, G.; Pilipchuk, S.P.; Flanagan, C.L.; Park, C.H.; Pagni, G.; Hollister, S.J.; Giannobile, W.V. 3D-printed bioresorbable scaffold for periodontal repair. J. Dent. Res. 2015, 94, 153S–157S.
20. Recent advances in 3D printing of biomaterials Chia and Wu Journal of Biological Engineering (2015) 9:4
21. G. Vozzi et al. Fabrication of PLGA scaffolds using soft lithography and microsyringe deposition. Biomaterials, 24:2533–2540, 2003.
22. 3D Printing—Review Design and 3D Printing of Scaffolds and Tissues Jia An, Joanne Ee Mei Teoh, Ratima Suntornnond, Chee Kai Chua. Engineering 2015, 1(2): 261–268

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