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 – 4, Issue – 3, May - 2021, Page No. : 428 - 437

Smart materials – future stepping stone in dentistry

[1]Dr.Krishnaprasada. L, Professor and HOD, Department of Conservative Dentistry and Endodontics, KVG Dental College and Hospital, Sullia, Karnataka -574327

[2]Dr. Amitha Ponnath, Post Graduate Student, Department of Conservative Dentistry and Endodontics, KVG Dental College And Hospital, Sullia, Karnataka -574327

Corresponding Author: Dr. Amitha Ponnath, Post Graduate Student, Department of Conservative Dentistry and Endodontics, KVG Dental College and Hospital, Sullia, Karnataka -574327

Citation of this Article: Dr. Krishnaprasada. L, Dr. Amitha Ponnath, "Smart materials – future stepping stone in dentistry", IJDSIR- May - 2021, Vol. – 4, Issue - 3, P. No. 428 – 437.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Applications of smart materials in dentistry have been recognized in regular clinical practice. These materials establish to be successful for restoration of teeth in esthetic, function and to preserve the integrity of masticatory muscles. Some are biomimetics and can mimic the natural tooth structures. These materials embrace a favorable future in terms of improved efficiency and reliability and mark the establishment of a new era that is Smart Dentistry.

Keywords: Smart Material , Biomimetic

Introduction

Traditionally materials were designed for long run use within the body or a lot of specifically with in the mouth are thought to survive longer if they are 'passive' and have no interaction with their environment. Materials like amalgams, composites and cements are often arbitrated on their ability to endure without interacting with the oral environment. The recognition of the advantage of fluoride release from materials made them first preference that an 'active' rather than 'passive' material could be attractive.[1]

Based on their interactions with the environment materials used are classified as bio inert (passive), bioactive, and bio responsive or smart materials.[2]

Smart materials are materials that have properties that may be enhanced in a controlled fashion by stimuli, such as stress, temperature, moisture, pH, and electric or magnetic fields. They are highly responsive, have the inherent capability to sense and react according to changes in the environment, hence called "responsive materials".[3,4]

Early smart material applications happening with magnetostrictive technologies. This intricate the use of nickel as a sonar source during World War I to find German U-boats by Allied forces.[5]

Classification of smart materials

1. Passive smart materials that react to external change without external control.

They possess self-repairing or stand-by characteristics.

2. Active smart materials employ a feedback loop to allow them to purpose like a cognitive response over an actuator circuit;
3. Smart materials that intellect change in the environment and respond (e.g., by altering one or more of their property coefficients, tuning their sensing, or actuation capabilities); and
4. Intelligent materials that incorporate the sensing and actuation functions with the control system.

The nature of smart materials

The stimuli, such as stress, temperature, moisture, pH, electric or magnetic fields can alter the properties of smart materials in a controlled fashion . A fundamental feature of smart behaviour comprises an ability to return to the original state after the stimulus has been removed. Present smart materials include piezoelectric materials which produce a voltage when stress is applied or vice versa.

They sense fluctuations in the environment around them and respond in a predictable manner. In general, these properties are:

• Piezoelectric — An electric current is generated, when mechanical stress is applied.

• Shape memory— These materials can remember their original shape and return to it when heated. eg:- NiTi alloys

• Thermo chromic — in reaction to change in temperature these materials change color. Eg. Thermochromic brushes Photochromic —in response to changes in light conditions materials change color. eg: Clinpro™ Sealant(3M)

• Magnetorheological —when placed in a magnetic field these fluid materials become solid.

• PH-sensitive —when the pH of the surrounding media changes these materials swell/collapse.eg: - Smart composites containing ACP (amorphous calcium phosphate).

• Biofilm formation — Presence of biofilm alters the interaction of the surface with the environment.

• Ion release and recharging- The advantageous effect of fluoride release of dental materials has been researched for many years, products even with high initial fluoride release tend to quickly lose their ability to release fluoride in important amounts. The smart behavior of materials containing GIC salt phases deals some long-term solutions by the sustained re-release of fluoride after initial recharging which may be much more important than the initial burst.[6-8]

Smart materials in dentistry

Smart memory alloy (SMA)

The shape memory alloys (SMAs) refer to the manner of a material changing shape or remembering a particular shape at a particular temperature (i.e. its transformation or memory temperature). Materials that can only demonstrate the shape change or memory effect once are known as one-way SMAs. However, some alloys are skilled to show a two-way effect in which they recall two shapes, one below and one above the memory temperature. The alloy undergoes a solid-state phase transformation at the memory temperature. The change in structure is known as thermo elastic martensitic transformation, occurs as the material has a martensitic microstructure below transformation temperature, characterized by a zig-zag arrangement of the atoms, known as twins. The martensitic structure is soft and is deformed by removing the twinned structure. Above the memory temperature the material has an austenitic structure, which is stronger. To transform from the martensitic to the austenitic shape the material is heated through the memory temperature, cooling down reverts the alloy to the martensitic state.[9]

In endodontics, NiTi files offer super flexibility, durability, and torqueability as associated to the stainless steel files. Its important application is in the field of orthodontics. [10]Superelasticity of wires along with shape memory applies continuous, gentle forces that are within physiological range over a longer period with less discomfort. At mouth temperature wires that display shape memory behavior contain copper and or chromium in addition to nickel.

Self-healing composites

The first self-repairing or self-healing synthetic materials reported shows some resemblances to resin-based dental materials. As this is an epoxy system that contains resin filled microcapsules, if a crack occurs in the epoxy composite material, some of the microcapsules disintegrate near the crack and they release the resin. The cracks are subsequently filled by resin and reacts with a Grubbs catalyst that is dispersed in the epoxy composite, resulting in a polymerization of the resin and a repair of the crack. The self-repairing mechanism based on microcapsules disintegration may have a promising future and composites repaired in that way may perform better than those repaired with macroscopic repair approaches.[11]

Smart Ceramics

CERCON was introduced in market since 1995. The strength and technology of CERCON permit the bridge to be created while not stainless steel or metal. The zirconia-based all ceramic material is created from one unit with no metal. The overall product is metal-free, biocompatible life like restoration with a strength that helps resist crack formation, the unappealing dark margins and artificial grey shadows from the underlying metal are no longer a problem.

Smart Impression Material

These materials exhibit following characteristics:

- Hydrophilic to get a void-free impression.
- Shape memory repels distortion for more accurate impression during elastic recovery and toughness resists tearing.
- Snap - set behavior those resulting in precise fitting restorations without distortion.
- Reduced working and setting times by at least 33%.
- Low viscosity

Smart Glass Ionomer Cement (RMGIs)

It's associated to the ability of a gel structure to absorb or release solvent rapidly in response to a stimulus that can be temperature, change in pH etc. The smart ionomer imitates the behavior of human dentin. These smart characteristics are exhibited by resin-modified glass ionomer cement, compomer or giomerare. Ex. GC Fuji IX EXTRA[13]

Smart Prep Burs

They are polymer burs that remove only infected dentin. It avoids overcutting of tooth structure compared to conventional burs. Carious dentin are selectively removed by smart burs leaving the healthy dentin intact. On contact with harder materials the polymer cutting edges wear down, such as healthy dentin and becomes blunt Eg: SS White diamond and carbide preparation kit.[14]

Smart Sutures

Sutures are fabricated of thermoplastic polymers that have both shape memory and biodegradable properties, applied loosely in its temporary shape and the ends of the suture are fixed. The suture shrinks and tightens the knot above the thermal transition temperature, applying the optimum force. The thermal transition temperature is close to body temperature, it's clinical significance in attachment a knot with correct stress in surgery. They are made of plastic or silk threads enclosed with temperature sensors and microheaters, which can detect infections. Eg: Novel MIT Polymer

Pheromone guided smart antimicrobial peptide

A new class of pathogen selective molecule called specifically (or selectively) Targeted Antimicrobial Peptides (STAMP) have been developed based on the fusion of a species-specific targeting peptide domain with a wide spectrum antimicrobial peptide domain. These “smart” material peptide is targeted against the killing of Streptococcus mutans, the principal microorganism responsible for dental caries. Utilizing Competence Stimulating Peptide (CSP), a pheromone produced by S.mutans, it can be eliminated from multi-species biofilm without affecting the nation-cariogenic microorganisms. Their molecules have the potential to be established into “probiotic” antibiotics that will selectively eliminating pathogens while preserving the protective benefits of a healthy oral flora[15].

Smart seal Obturation System

The C Point system , is a point-and-paste root canal filling technique that consists of premade, hydrophilic endodontic points and an attendant sealer. These are available in different tip sizes and tapers and deliberated to expand laterally without expanding axially, by absorbing residual water from the instrumented canal space. Trogamid T and Trogamid CX are two proprietary nylon polymers seen in inner core The polymer coating is a cross-linked copolymer of acrylonitrile and vinyl pyrrole, which are polymerized and cross-linked by means of allyl methacrylate and a thermal initiator. The lateral growth happens non-uniformly, with the expandability depending on extent to which the hydrophilic polymer is prestressed (i.e., contact with a canal wall will reduce the rate or extent of polymer expansion). They reduce the possibility of reinfection with the nonisotropic lateral expansion that enhances the sealing ability of the root canal filling.[16]

Smart Coatings for Dental Implants

A “smart coating” helps surgical implants bond more closely with bone and ward off infection, resulting in less risk of rejection of dental implants. A crystalline layer created next to the implant and an amorphous outer layer encompassing bone. Bone growth is encouraged by the amorphous layer that dissolves over time and releases calcium and phosphate. The bone grows into the coating resulting in improved bonding osseointegration. This bonding also makes the implant more functional, because the bonding helps the bone and the implant to share the load.[17]

Smart Fibers for Laser Dentistry

Hollow core photonic crystal fibers (PCFs) are used for delivery of high-fluence laser radiation. Nd: YAG laser radiation is transmitted through a core diameter of approximately 14 micrometers and is focused on a tooth surface to ablate dental tissue. 1.06-micrometer laser radiation was supported with the single fundamental mode regime. The same fiber is also used to transmit emission from plasmas, which is produced by laser pulses on the tooth surface in the backward direction for detection and optical diagnostics.[18]

Biomimetic and bionic smart scaffold

In recent times, using the principles of biomimetics smart artificial bone scaffolds were ready to mimic the composition and structural characteristics of natural bone, nano-assembly technology and additive manufacturing techniques.[19] On scaffold specific molecular recognition signals (growth factors,peptides and genes)were immobilized . Biomimetic porous poly(lactideco-glycolide) (PLGA) microspheres coupled with peptides were used to build biomimetic environments for tissue engineering.[20]

Immune-Sensitive Smart Scaffolds

To avoid or reduce the potential immunological response between the host immune system and foreign scaffolds, it is necessary to develop sensible immunomodulatory biomaterials that are skillful of directional the host response towards tolerance of the foreign scaffolds or regulate immunological microenvironments to spice up cell survival. Immune cell activation and infiltration could be satisfactory with surface modification of scaffolds.[21] ECM-like injectable gelatin microspheres were synthesized via the self-assembly of heparin-modified gelatin nanofibres.[22-24] Interleukin 4 (IL4) was integrated into the scaffold by binding the domains with heparin to protect it from denaturation and degradation and also helped prolong its sustained release to modulate the macrophage polarization. The nanofibrous heparin-modified gelatin microspheres (NHG-MS) could spatiotemporally supply the anti-inflammatory cytokine IL4 to polarize the proinflammatory M1 macrophages into an anti-inflammatory M2 phenotype, thus facilitating osteogenic differentiation and bone formation. The osteoimmunomodulatory ability of the scaffold was able by the amino functionalization. β-tricalcium phosphate (β-TCP) was coated on Mg scaffolds to modulate the detrimental osteoimmunomodulatory properties.[29] β-TCP-coated Mg scaffolds induced macrophages shift to the extreme M2 phenotype, which instigated the release of anti-inflammatory cytokines and osteoinductive molecules by the macrophages.[28]

Shape-memory smart scaffolds

An external stimulus, such as temperature change, an electric or magnetic field, and light can stimulate Shape-memory polymers (SMPs) return from a deformed shape to their original shape. [25-27] For the repair of bone defects ,BMP2-loaded shape-memory porous nanocomposite scaffold (SMP scaffold) that consist of of chemically crosslinked polycaprolactone and hydroxyapatite (HA) nanoparticles was made-up. The three-dimensional (3D)-printing technologies, four dimensional (4D)-printed hierarchy scaffolds were created employing a series of novel SMPs, demonstrating excellent biocompatibility and tunable shape-changing effects. The smart polymeric scaffolds offered finely tunable recovery and showed excellent attachment, proliferation and differentiation of MSCs.[30,31]

Electromechanical-stimulus smart scaffolds

Efforts were made to develop smart electrically active biomaterials and scaffolds, representing potential for bone engineering by providing electrical stimulation to cells to promote tissue formation. 3D fibrous scaffolds was made-up with piezoelectric polyvinylidene fluoride-trifluoroethylene (PVDF-TrFE) into flexible.[32] The scaffolds stimulated MSC differentiation and tissue formation when undergoing dynamic loading, which mimicked the physiological loading conditions in structural tissues. Piezoelectric HA/barium titanate ($BaTiO_3$) composite was fabricated and exposed to a dynamic loading device that simulated the force of human motion. A similar piezoelectric effects on human bone growth, modelling and reconstruction was observed when cyclic loading was functional on HA/$BaTiO_3$, the electrical stimulated osteoblast proliferation and growth.[33]

Smart drug delivery for bone tissue engineering

Bioactive factors, including small molecules, cytokines, peptides, proteins and genes, can be loaded in drug delivery systems (DDS).[35] These smart systems can have controlled drug release and exert synergistic effects from multiple loaded drugs to boost osteoblast proliferation and differentiation to stimulate bone regeneration.

Stimuli-responsive smart materials were proven to enable minimally invasive drug delivery and monitoring. A novel pH-responsive bacterial cellulose-g-poly acrylic acid co-acrylamide hydrogel with a highly porous morphology was developed as an oral controlled release drug delivery carrier.[34] The intelligent hydrogel was demonstrated to display remarkable pH-responsive modifications in swelling behaviour, with reduced swelling in acidic media and maximum swelling at pH 7. Another poly (ethylene glycol) hydrogel was loaded with drugs by β-eliminative linkers and established tunable capability in drug release and the hydrogel erosion rate.[37] The farnesol-loaded nanoparticles, composed of 2-dimethylamino ethyl methacrylate, butyl methacrylate and 2- propylacrylic acid were synthesized with a pH-responsive drug release capability due to micro environmental triggers.[36]They were tuned to expedite the drug release when the local cariogenic biofilm micro environmental pH became acidic at pH 4.5. [38]

Smart multifunctional nanoparticle-based DDSS

Mesoporous silica nanoparticles (MSNs) had variable pore structures and large active surface areas, which facilitated the attachment of different functional groups to accomplish precisely controlled drug release and targeted delivery. These nanoparticles were reported with smart features to better react to the biological environment and meet the on-demand therapeutic and diagnostic determinations of diseased and damaged tissues. Bone-forming peptide-1 (BFP-1)-laden MSNs (pep@MSNs) were encapsulated into arginine-glycine-aspartic acid-treated alginate hydrogel (RA), which was referred to as pep@MSNs-RA.[42]MSNs contained many uniform and homogeneous pore channels and thus applied as an excellent drug carrier for BFP-1. The smart pep@MSNs designated a continuous peptide release pattern in the appropriate growth stage of hMSCs upon demand, with the initial osteo-inducing time likely on the fourth day.[42]

Biomimetic DDSS

Biomimetic hydrogels, micelles, liposomes, dendrimers, polymeric carriers and nanostructures were established.[39,40] They mimicked the natural ECM to provide a desirable cellular environment to support cell growth and biodegradation.[41] Furthermore, biomimetic peptide-based, self-assembly hydrogels (RADA16) were used as intraosseous delivery vehicle for BMP2 into defects. This promotes osteoblastic differentiation of BMSCs and bone remodelling. Associated with traditional 3D-printed scaffolds, biomimetic lotus root-like structures could productively induce blood vessels and new bone tissues to grow into the inner locations of the biomimetic materials and successfully promote bone defect healing.[43]

Smart biomaterials to promote dental and periodontal regeneration

Nano composite polycaprolactone-based membranes with amoxicillin were produced, which provided antibacterial and osteoconductive properties. Other alternative agents, such as chitosan, could also be incorporated into the membrane.[45,46] Moreover, chitosan could entrap biomolecules by crosslinking and ionic complexation and was thus used as a drug and growth factor carrier in periodontal regeneration. Smart materials were designed to target the macrophages in a binding manner to control the inflammation and enhance the innate regeneration. It was found that human exfoliated deciduous teeth (SHEDs)could promote the classically activated M1 (promote inflammation) to alternative M2 (inhibit inflammation), thereby decreasing the local inflammation and enhancing periodontal regeneration.[44]

Smart sensitive materials to selectively inhibit acid-producing bacteria

pH sensitive quaternary pyridinium salts (QPS) were established, for which the antibacterial potency is boosted by low pH and can be controlled by varying the pH between 4 and 8. It selectively suppresses the growth of acidogenic bacteria within a multispecies biofilm. This molecule,(E)-1-hexadecyl-4-((4 methacryloyloxyphenyldiazenyl-pyridinium bromide (termed Azo-QPS-C16), can alter its antibacterial potency within pH 4–8. Therefore, the biocidal activity of Azo-QPS-C16 can have limited triggering by acidic metabolic products of bacteria, which, in turn, leads to the killing of these bacteria.[49]

Smart resins that respond to ph

Smart Composites

It is a light activated alkaline, when intraoral pH values drop below the critical pH of 5.5 it releases calcium, fluoride and hydroxyl ions and counteract the demineralization of the tooth surface and help in remineralization [47]. The material can be effectively cured in bulk thickness up to 4mm. Suggested for the restoration of class I and class II lesions in both primary and permanent teeth.

Smart composites that contain amorphous calcium phosphate are one of the most soluble of the biologically important calcium phosphates, exhibiting the most rapid transformation to crystalline hydroxyapatite. When assimilated into specially designed and formulated resins to make a composite material, will have prolonged time release nature to act as a source for calcium and phosphate which will be useful for preventing caries.[48]

Smart materials to modulate biofilm species towards a healthy composition

Broad spectrum of antimicrobial effects is exhibited by quaternary ammonium methacrylates. QAMs disrupts the bacterial membranes. For extended function QAMs can be co-polymerized with the resin matrix to anchor itself into the polymer network. Several other QAMs were successively developed, including quaternary ammonium poly ethylenimine, methacryloxylethyl cetyl dimethyl ammonium chloride (DMAE-CB), dimethylaminododecyl methacrylate (DMADDM). DMADDM can suppress the cariogenic S. mutans and stimulate the growth of non-cariogenic species.[50-52]

Conclusion

As the field of dentistry is dependent on the use of different materials, the use of smart materials abilities better reliability and long-term efficiency because of their potential to select and execute specific functions intelligently in response to various local changes in the environment, thereby significantly improving the quality of dental treatment. With the introduction of such materials the profit for the patient and the excellence of dental therapy will undergo a significant improvement. Adequate knowledge of biomaterials is essential for their application in clinical practice particularly in restorative dentistry. To indorse biocompatibility of a material, animal experiments, tissue culture, clinical studies and Prospective and retrospective track record of usage reports are mandatory, for key of success.

Reference

1. McCABE JF, Yan Z, Al Naimi OT, Mahmoud G, Rolland SL. Smart materials in dentistry—Future prospects. Dental materials journal. 2009;28(1):37-43.
2. Badami V, Ahuja B. Biosmart materials: Breaking new ground in dentistry. The Scientific World Journal. 2014 Jan 1;2014.
3. McCabe JF, Yan Z, Al Naimi OT, Mahmoud Get al.Smart materials in dentistry.-Aust Dent J. 2011; 56(1): 3–10.
4. Gautam P, Valiathan A.Bio-Smart Dentistry: stepping into the future.Trends0Biomater Artif Organs. 2008; 21(2): 94-7.
5. Gupta V. Smart materials in dentistry: A review. International Journal for Advance Research and Development. 2018;3(6):89-96.

6. Shaw A, McCabe JF, Carrick TE. Fluoride release from glass ionomers and 0compomers. J Dent. 1998; 26:355–360.
7. Momoi Y, McCabe JF. Fluoride release from light-activated glass ionomer0restoration cement. Dent Mater. 1993; 9:151– 154.
8. McCabe JF, Carrick TE, Sidhu SK. Determining low levels of fluoride released 0from resin-based dental materials. Eur J Oral Sci. 2002; 110:380–384.
9. Gautam, Valiathan A. Bio-smart Dentistry: stepping into the future. Trends Biomater. Artif.Organs.2008; 21(2):9-97.
10. Revathi M, Rao CVN, Lakshmi Narayanan.Revolutions in endodontic instruments--a review. Endodontology. 2001; 13:43- 47
11. Jandt KD, SiguschBW.Future perspectives of resin-based dental materials. Dental Materials.2009; 25(8): 1001–1006.
12. Terry DA, Leinfelder KF, Lee EA, James A. The impression: A blueprint for restorative success. Int Dent SA.2006; 8:12-21.
13. Dube M, Ponnappa KC. Smart ART!!. Journal of International Oral Health. 2009 Dec 1;1(1).
14. Dammaschke T, Schafer E. Efficiency of the polymer bur smart prep compared with conventional carbide bud bur in dentin caries excavation. Operative Dentistry.2006; 31(2): 256-60.
15. Eckert R, He J, Yarbrough DK, Qi F, Anderson MH, Shi W. Targeted killing of Streptococcus mutans by a pheromoneguided “smart” antimicrobial peptide. Trends -----Antimicrob Agents Chemother 2006; 50:3651-7.
16. Economides N, Gogos C, Kodonas K, Belts C, Kolokouris I. An ex vivo comparison of the push-out bond strength of a new endodontic filling system 000(Smartseal) and various guttapercha filling techniques. Odontology.2012; 100(2):187–191.
17. Bai X, More K, Rouleau CM, Rabiei A. Functionally graded hydroxyapatite coatings doped with antibacterial components.ActaBiomaterialia. 2010;6(6): 2264–2273.
18. Konorov SO, Mitrokhin VP, Fedotov AB, BiryukovDAS et al. Hollow-core photonic-crystal fibers for laser dentistry. Phys Med. Biol. 2004; 49(7): 1359-1368.
19. Wu, T., Yu, S., Chen, D. & Wang, Y. Bionic design, materials and performance of bone tissue scaffolds. Materials 10, 1187 (2017).
20. Mittal, A., Negi, P., Garkhal, K., Verma, S. & Kumar, N. Integration of porosity and bio-functionalization to form a 3D scaffold: cell culture studies and in vitro degradation. Biomed. Mater. 5, 045001 (2010).
21. Li, W. A. et al. The effect of surface modification of mesoporous silica micro-rod scaffold on immune cell activation and infiltration. Biomaterials 83, 249–256 (2016).
22. Liu, X. & Ma, P. X. Phase separation, pore structure, and properties of nanofibrous gelatin scaffolds. Biomaterials 30, 4094–4103 (2009).
23. Liu, X. et al. Biomimetic nanofibrous gelatin/apatite composite scaffolds for bone tissue engineering. Biomaterials 30, 2252–2258 (2009).
24. Sachar, A. et al. Osteoblasts responses to three-dimensional nanofibrous gelatin scaffolds. J. Biomed. Mater. Res. A 100, 3029–3041 (2012).
25. Buckley, P. R. et al. Inductively heated shape memory polymer for the magnetic actuation of medical devices. IEEE Trans. Biomed. Eng. 53, 2075–2083 (2006).

26. Mohr, R. et al. Initiation of shape-memory effect by inductive heating of magnetic nanoparticles in thermoplastic polymers. Proc. Natl Acad. Sci. USA 103, 3540–3545 (2006).
27. Lendlein, A., Jiang, H., Junger, O. & Langer, R. Light-induced shape-memory polymers. Nature 434, 879–882 (2005).
28. Hu, Z., Ma, C., Rong, X., Zou, S. & Liu, X. Immunomodulatory ECM-like microspheres for accelerated bone regeneration in diabetes mellitus. ACS Appl. Mater. Interfaces 10, 2377–2390 (2018).
29. Chen, Z. T. et al. Osteoimmunomodulatory properties of magnesium scaffolds coated with b-tricalcium phosphate. Biomaterials 35, 8553e8565 (2014).
30. Liu, X. et al. Delivery of growth factors using a smart porous nanocomposite scaffold to repair a mandibular bone defect. Biomacromolecules 15, 1019–1030 (2014).
31. Miao, S., Zhu, W., Castro, N. J., Leng, J. & Zhang, L. G. Four-dimensional printing hierarchy scaffolds with highly biocompatible smart polymers for tissue engineering applications. Tissue Eng. Part C Methods 22, 952–963 (2016)
32. Damaraju, S. M. et al. Three-dimensional piezoelectric fibrous scaffolds selectively promote mesenchymal stem cell differentiation. Biomaterials 149, 51–62 (2017).
33. Tang, Y. et al. Fabrication and in vitro biological properties of piezoelectric bioceramics for bone regeneration. Sci. Rep. 7, 43360 (2017).
34. Liu, D., Yang, F., Xiong, F. & Gu, N. The smart drug delivery system and its clinical potential. Theranostics 6, 1306–1323 (2016).
35. Sun, G. & Mao, J. J. Engineering dextran-based scaffolds for drug delivery and tissue repair. Nanomedicine (Lond.) 7, 1771–1184 (2012).
36. Horev, B. et al. pH-activated nanoparticles for controlled topical delivery of farnesol to disrupt oral biofilm virulence. ACS Nano 9, 2390–2404 (2015).
37. Mohd Amin, M. C., Ahmad, N., Pandey, M. & Jue Xin, C. Stimuli-responsive bacterial cellulose-g-poly(acrylic acid-co-acrylamide) hydrogels for oral controlled release drug delivery. Drug Dev. Ind. Pharm. 40, 1340–1349 (2014).
38. Li, F., Zhu, Y. & Wang, Y. Dual-responsive drug delivery system with real time tunable release behavior. Micro. Mesopor. Mater. 200, 46–51 (2014).
39. Sant, S., Hancock, M. J., Donnelly, J. P., Iyer, D. & Khademhosseini, A. Biomimetic gradient hydrogels for tissue engineering. Can. J. Chem. Eng. 88, 899–911 (2010).
40. Sheikhpour, M., Barani, L. & Kasaeian, A. Biomimetics in drug delivery systems: a critical review. J. Control Release 253, 97–109 (2017).
41. Lee, N., Robinson, J. & Lu, H. Biomimetic strategies for engineering composite tissues. Curr. Opin. Biotechnol. 40, 64–74 (2016).
42. Luo, Z. et al. Time-responsive osteogenic niche of stem cells: a sequentially triggered, dual-peptide loaded, alginate hybrid system for promoting cell activity and osteo-differentiation. Biomaterials 163, 25–42 (2018).
43. Phipps, M. C., Monte, F., Mehta, M. & Kim, H. K. W. Intraosseous delivery of bone morphogenic protein-2 using a self-assembling peptide hydrogel. Biomacromolecules 17, 2329–2336 (2016).
44. Gao, X. et al. Immunomodulatory role of stem cells from human exfoliated deciduous teeth on periodontal regeneration. Tissue Eng. Part A https://doi.org/ 10.1089/ten (2018).
45. Basile, M. A. et al. Functionalized PCL/HA nanocomposites as microporous membranes for bone

regeneration. Mater. Sci. Eng. C Mater. Biol. Appl. 48, 457–468 (2015).

46. Xu, C., Lei, C., Meng, L., Wang, C. & Song, Y. Chitosan as a barrier membrane material in periodontal tissue regeneration. J. Biomed. Mater. Res. B Appl. Biomater. 100, 1435–1443 (2012).
47. Xu HH, Weir MD, Sun L, Takagi S, Chow LC. Effects of calcium phosphate nanoparticles on calcium phosphate composite. J Dent Res. 2007; 86:378-83.
48. Skrtic D, Antonucci JM, Eanes, ED. "Amorphous calcium phosphate-based bioactive polymeric composites for mineralized tissue regeneration,"Journal of Research of the National Institute of Standards and Technology.2003;108 (3):167–182.
49. Yang, Y. et al. pH-sensitive compounds for selective inhibition of acid-producing bacteria. ACS Appl. Mater. Interfaces 10.1021/acsami. 8b01089 (2018).
50. Imazato, S. et al. An in vivo evaluation of bonding ability of comprehensive antibacterial adhesive system incorporating MDPB. Dent. Mater. 23, 170–176 (2007).
51. Imazato, S. Bioactive restorative materials with antibacterial effects: new dimension of innovation in restorative dentistry. Dent. Mater. J. 28, 11–19 (2009).
52. Cheng, L. et al. Dental plaque microcosm biofilm behavior on calcium phosphate nanocomposite with quaternary ammonium. Dent. Mater. 28, 853–862 (2012).