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Review

Fabrication of polymer-based bone scaffolds—Conventional vs. advanced methods

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Abstract: This review comprehensively summarizes various preparatory methods of polymeric bone scaffolds using conventional and modern advanced methods. Compilations of the various fabrication techniques, specific composition, and the corresponding properties obtained under clearly identified conditions are presented in the commercial formulations of bone scaffolds in current orthopedic use. The gaps and unresolved questions in the existing database, efforts that should be made to address these issues, and research directions are also covered. Polymers are unique synthetic materials primarily used for bone and scaffold applications. Bone scaffolds based on acrylic polymers have been widely used in orthopedic surgery for years. Polymethyl methacrylate (PMMA) is especially known for its widespread applications in bone repair and dental fields. In addition, the PMMA polymers are suitable for carrying antibiotics and for their sustainable release at the site of infection.

Keywords: bone scaffold; polymer; polymethyl methacrylate; tissue engineering; orthopedic surgery

1. Introduction

Bones are dense connective tissues with a solid, calcified outer layer (cortical bone) that comprises more than three-fourths of the bone's mass. Cortical bone has a relatively low porosity, ranging from 5% to 10%. The soft inner spaces of bone (usually described as cancellous or trabecular bone) form the remaining one-fourth of the bone mass. Cancellous bone has a high porosity, ranging from 60% to 90%, and contains the bone marrow, which consists of blood stem cells, adipose cells, osteoblasts, and osteocytes. From these, the osteoblasts are essential for the deposition and mineralization of the extracellular matrix of new bone, while osteocytes are the supporters of bone matrix calcification. In addition, specific growth factors and proteins, mainly residing in the extracellular matrix of bone, regulate cellular activity and stimulate the intracellular environment.

Bone possesses a high compressive strength of 170 MPa but a low tensile strength of 104–121 MPa and a very low shear stress strength of 51.6 MPa [1,2]. This means that bone can be fractured given that torsion force is exerted. In other words, bone is more sensitive to pulling or torsion than pushing. Though bones are naturally brittle (80% of CaP), a significant degree of elasticity is shown due to collagen. However, the likelihood of human bones failing due to mechanical problems, injuries, diseases, infections, and tumors increases with age. This means that wrong movement of the body or diseases like osteoporosis [3–5], scoliosis [6–8], and osteomyelitis [9–11] can cause the bones to fracture or deteriorate.

Naturally, bones can regenerate in case of minor injury and continuously remodel

throughout adulthood [12–14]. These bone injuries heal without forming scar tissue while regenerating the bone with its pre-existing properties. In addition, the regenerated bone is indistinguishable from the uninjured bone. However, significant injuries involving the load-bearing bone require orthopedic surgery to place a bone graft over the defective bone site to encourage new bone growth while preventing other tissues from interfering with osteogenesis. During osteogenesis, the osteoblasts (cells with single nuclei that form the bone) originating from the bone graft enhance the growth of new bone. This is conducted through osteoinduction and osteoconduction processes. Osteoinduction is the recruitment of immature cells and stimulation of these cells to develop into bones [15–17]. Osteoconduction is when bone grows on a surface—a phenomenon seen in the case of bone implants [18]. Polymers are unique synthetic materials [19–43] that are extensively used in various industrial applications [44–50]. Likewise, it is primarily used for bone and scaffold applications. This paper provides various fabrication techniques and their potential use in orthopedic surgery.

2. Tissue engineering

Tissue engineering combines cells, materials, engineering methods, and suitable biochemical and physic-chemical factors to improve or replace biological functions [52,53]. The main goal of tissue engineering is to regenerate and replace the structural and functional of the injured bone beyond its natural healing capacity [53]. For this to happen, external regenerative materials such as scaffolds, cell growth factors, or a combination of either are required [54]. Tissue engineering uses undifferentiated cells seeded within the scaffold, which defines the geometry of the replacement tissues and provides environmental indications to promote the development of new tissues, as demonstrated in **Figure 1** [55]. However, the interaction between the cell and the material used to develop the scaffold plays a vital role in tissue engineering. This is because the developed scaffold must mimic the properties of the injured bone structurally and bio-functionally. Therefore, it is essential to understand the requirements and properties of the injured bone before designing the scaffold [56–58].

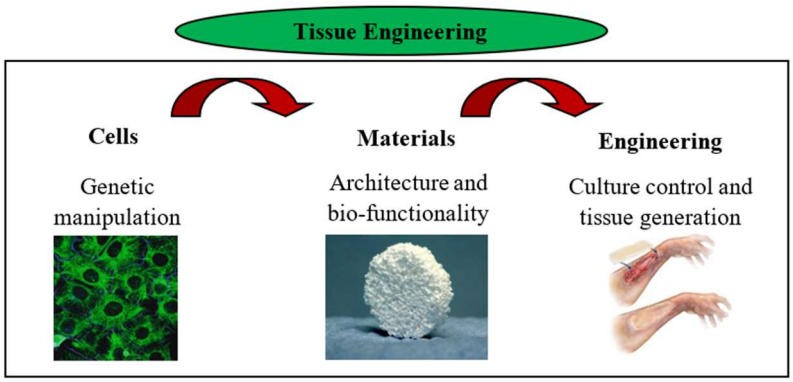

Figure 1. Schematic illustration of tissue engineering process.

3. Bone scaffolds and their requirements

Scaffolds are materials developed to perform in the body as devices able to

support and possibly induce a complex pattern of events whose final goals are tissue repair and tissue function recovery [59–61]. Generally, the application of scaffolds can be summarized as:

- Allow cell attachment and migration.
- Deliver and retain cells and biochemical factors.
- Enable diffusion of vital cell nutrients and expressed products.
- Exert specific mechanical and biological influences to modify the behavior of the cell phase.

However, to achieve the goal of tissue engineering and bone regeneration, scaffolds must meet some specific requirements [62,63]. The scaffold should be biocompatible to integrate well within the tissue host without provoking any immune reaction and biodegradable into carbon dioxide and water forms. In addition, scaffolds should possess an open pore and be fully interconnected with highly porous structures [64,65]. These are the fundamental characteristics for providing space for cells to migrate and vascularize the tissue. In other words, the pore size of the scaffold is used to regulate cell survival, growth, and differentiation. Hence, the minimum pore size required is considered to be 100 μm due to the cell size, migration conditions, and transport [66,67]. However, pore sizes bigger than 300 μm are recommended to improve the new bone formation and to develop a net of capillaries. More on the effects of pore size on tissue regeneration is summarised in **Table 1**. Furthermore, the larger the surface area to volume ratio available, the more cell interactions will occur [68]. Scaffolds should also have the mechanical strength to retain their structure after implantation, mainly for the load-bearing tissues, as depicted in **Table 2**. Moreover, the scaffolds should be osteoinductive to recruit and stimulate the differentiation pathway of the stem and develop osteoblast cells to the defective bone [69].

Table 1. Effect of pore size on tissue regeneration [2].

Tissue formation/cell growth	Required pore size (μm)
Neovascularization	5
Fibroblas ingrowth	5–15
Regeneration of adult mammalian skin	20–115
Regeneration of bone	100–350
Osteoid ingrowth	40–100
Hepatocytes ingrowth	20
Fibrovascular tissue	500

Table 2. Mechanical properties of human tissues.

	Tensile strength (MPa)	Compressive strength (MPa)	Young's modulus (GPa)	Fracture toughness (MPa.m$^{1/2}$)
Cancellous bone	-	4–12	0.02–0.5	-
Cortical bone	60–160	130–180	3–30	2–12
Cartilage	3.7–10.5	-	0.7–15.3 (MPa)	-
Ligament	13–46	-	0.065–0.541	-
Tendon	24–112	-	0.143–2.31	-

In summary, a scaffold is required to match bone properties closely. However, achieving all these properties in one material is a complex challenge due to the lack of strength associated with porosity. Therefore, to make it possible, the scaffold materials must be optimized from the atomic level through the macroscale to the nanoscale structure with respect to the cellular response [70].

4. Bone scaffold preparation techniques—Conventional methods

Conventional, non-designed manufacturing techniques are used to fabricate an interconnected porous structured scaffold [71]. Some methods include solvent casting/particulate leaching, freeze-drying, phase inversion, and electrospinning. However, they lack precision when controlling the pore size, geometry interconnectivity, and spatial distribution of pores [72,73].

4.1. Solvent casting and particulate leaching

Solvent casting on its own is an attractive method in the polymer field due to its ability to obtain films with high quality [74,75]. Aside from being a relatively simple technique, the film's thickness, uniformity, and distribution can easily be controlled [76]. However, solvent-casting techniques can fabricate a scaffold in combination with particulate leaching. In this technique, the first stage involves dissolving the polymer into chloroform and casting it in a petri dish filled with porogen (sodium chloride, ammonium bicarbonate, or glucose). The composite is then placed in a dust-free environment to evaporate the solvent and washed with distilled water to remove the porogen. Here, the properties of the developed scaffold, such as porosity and pore size, can be controlled by the amount of salt added and salt crystals, respectively [77]. However, homogenous distribution of the salt into the polymer is difficult to attain because the density of the polymer and salt is different. Other factors, such as casting temperature and drying conditions, can also affect the properties of the scaffold. To overcome this limitation, researchers have suggested adding a centrifugation stage to improve the pore uniformity and interconnectivity of the scaffold, as shown in **Figure 2** [78]. In these studies, the polymer solution mixed with salt was centrifuged and dried (air-dried and vacuum-dried), followed by salt leaching in distilled water, resulting in the fabrication of an interconnected porous scaffold with porosity >90% [79].

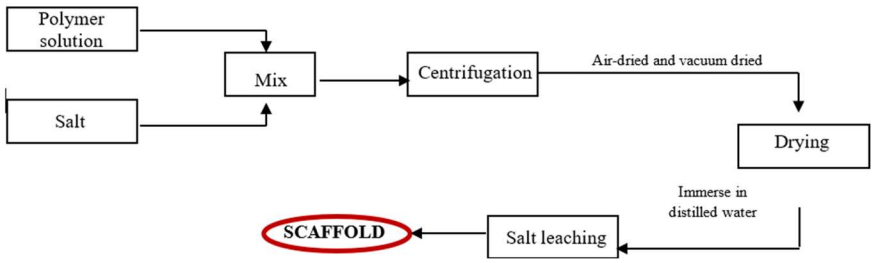

Figure 2. Schematic diagram for fabrication of scaffold using solvent casting and particulate leaching in addition to centrifugation stage.

4.2. Freeze-drying

In this technique, the polymer solution is mixed homogeneously with an acid (acetic acid) before the sublimation of ice using freeze drying, causing the formation

of ice crystals, as shown in **Figure 3** [80–82]. The freezing temperature and rate can control the pore size properties of the developed scaffold. For instance, a scaffold freeze-dried pore size at −20 °C and −196 °C was 200–250 µm and 80–100 µm, respectively [45,46,83–88]. However, in another research, the addition of an annealing stage after freeze-drying (low temperature) has been shown to increase the pore size from 96–150 µm to 85–325 µm (~40% increase). This is due to the rise in temperature of the frozen suspension, which increased the ice crystal growth rate [89].

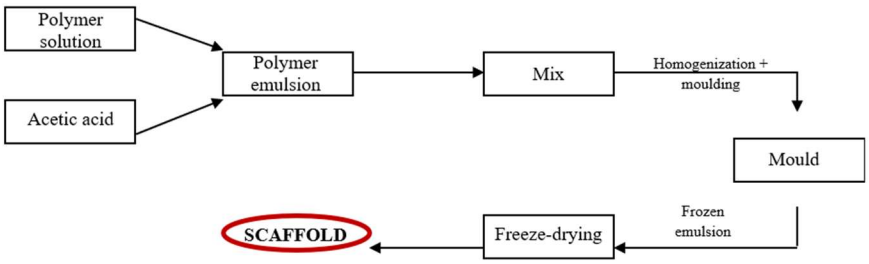

Figure 3. Schematic diagram for fabrication of scaffold using freeze-drying.

4.3. Phase inversion

Phase inversion is an effective technique for developing porous scaffolds by combining mass transfer and liquid phase separation, as depicted in **Figure 4** [61,90–93]. Initially, the mixed solution of polymer dissolved in a solvent and ethanol (non-solvent) would be cast or molded. Then, the dried casted gel will be induced to phase separation by immersing it into the non-solvent used [94]. After the extraction of the remaining solvent, the developed scaffold will be dried in a controllable environment. However, the drying stages can be avoided using supercritical fluid [95], such as carbon dioxide [96], which is biocompatible (non-toxic, non-corrosive, and non-flammable) and affordable [97]. The polymer solution is poured into a container and placed inside a heated high-pressure vessel. The supercritical fluid is pumped into the vessel with a high-pressure pistol. The fabrication of the scaffold was completed once the phase separation took place. A porous structure can be developed without any remaining solvent in this process. Nonetheless, the overall properties of the developed scaffold depend on the solubility and diffusivity of the supercritical fluid in the polymer. The phase separation technique has produced micro-patterned nanofibrous sheets (50–500 nm) with properties comparable to those obtained by electrospinning. The pore interconnectivity can increase when the phase inversion technique is combined with the particulate porogen leaching method, which can further be used for bone tissue regeneration applications [98].

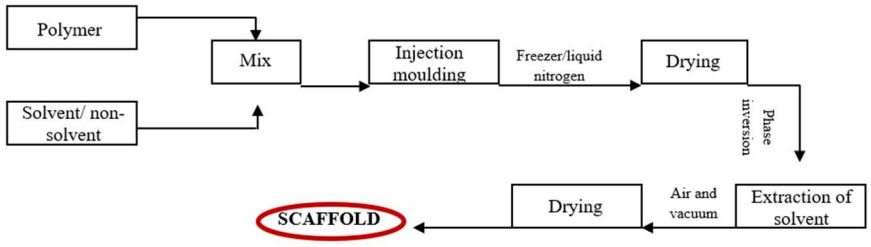

Figure 4. Schematic diagram for fabrication of scaffold using thermally induced phase inversion.

4.4. Electrospinning

Electrospinning, though not a new technique, has recently become significant in developing nanostructures in the form of fibers that can be used for scaffolds [99–105]. The basic tools required to fabricate this scaffold via the electrospinning technique include three components: a syringe, high voltage, and a collector plate, as shown in **Figure 5**. The polymer or composite solution prepared is poured into the syringe at a slow flow rate. Then, the tip of the needle is connected to the positive electrode of the high voltage, whereas the negative electrode is connected to the collecting plate. Finally, the polymer/composite is ejected from the syringe to the collecting plate as non-woven fibrous structures. These non-woven fibrous structures have unique characterization with a high surface area to volume ratio, flexible surface functionality, and mechanical properties superior to large fibers [105,106]. In addition, the pore size can be manipulated using either the properties of the polymer or composite solution prepared, the voltage applied, the processing temperature, or the distance between the collecting plate and the syringe [107–109]. However, the maximum pore size obtained through this technique is 10 μm, which is relevant to applications related to hindering cell infiltration [110]. The porosity can be increased by either removing one of the composite components used or using phase separation technology during electrospinning [111].

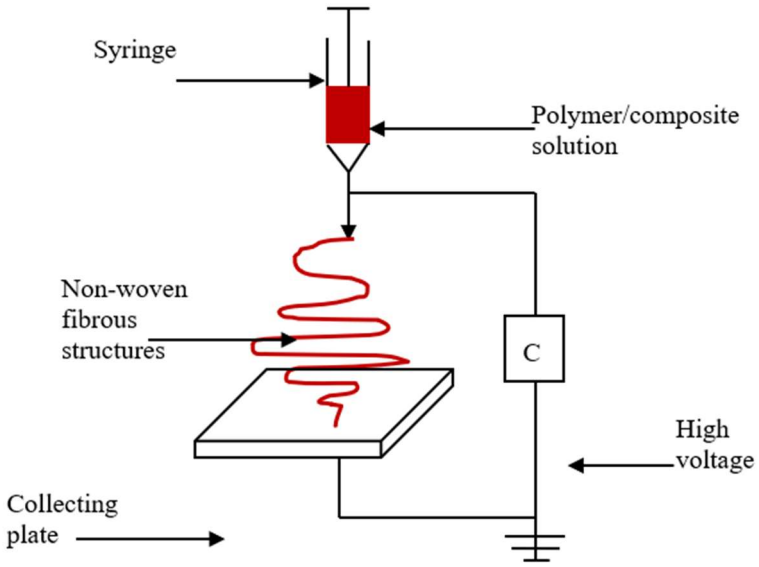

Figure 5. Schematic diagram for fabrication of scaffold using electrospinning.

5. Bone scaffold preparation techniques—Advanced methods

5.1. Computer-aided tissue engineering (CATE)

Advanced techniques, also known as designed manufacturing techniques in cooperation with computer-aided tissue engineering (CATE), have been known for a while [112–116]. This technique integrates advanced imaging technologies such as computer tomography (CT), magnetic resonance imaging (MRI), computer-aided design (CAD) technology, and rapid prototyping (RP) with tissue engineering applications, as shown in **Figure 6** [117–119]. Generally, CATE consists of two major

processes: 1) non-invasive imaging data acquisition, where an image or scan of 3D tissue structural view is produced using CT or MRI, and 2) 3D reconstruction, where the physical model of the image is fabricated using CAD followed by RP and finally used for tissue implementation [120,121].

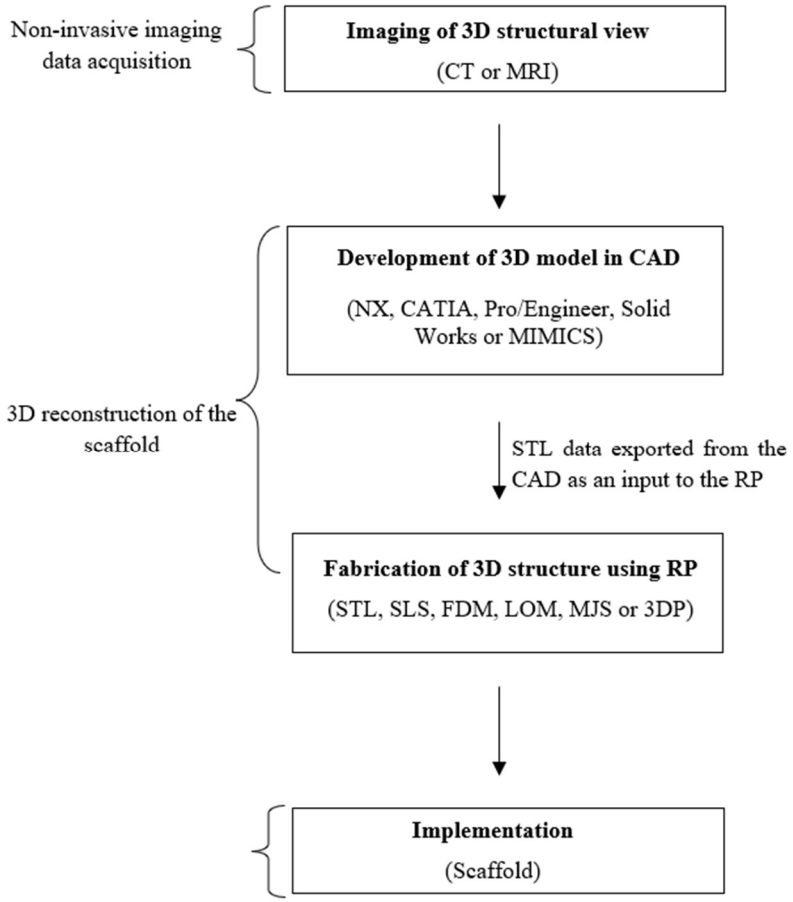

Figure 6. Schematic diagram for fabrication of scaffold using CATE.

5.2. Computed tomography (CT)

Computed tomography (CT) is one of the techniques employed to construct a 2D or 3D image of any tissue inside the body using special X-ray equipment with computer programs [122–126]. CT scanning has been used for many studies, including bone mass and morphology, growth and development analysis, mechanical loading and unloading, and evaluation of fracture healing [127]. The most crucial step in this technique is image acquisition, involving the preparation and positioning of the sample, the selection of scanning medium, the determination of the X-ray energy required, the voxel size and image resolution needed, and the recognition of the area of interest for the study [128]. Then, the image obtained is filtered to reduce signal noise while maintaining its resolution. Furthermore, the mineralized and non-mineralized structures in the image are separated using a segmentation process for analysis [129].

There are main advantages to using CT: 1) allows direct 3-D measurement of any morphology; 2) compared to the 2D image, a larger volume is studied; 3) it is faster than histologic analysis; and 4) the evaluation is non-destructive; hence can be used

for other studies [130]. On the other hand, CT uses X-rays in the form of ionizing radiation, which can be harmful. However, compared to the naturally occurring radiation everyone is exposed to daily, a 1-time low dose of CT radiation exposure is equivalent to 6 months of natural radiation. That being said, there are still three ways to reduce the overall exposure to radiation doses: 1) reduce the number of CT scans prescribed; 2) reduce the CT dose used in a person; and 3) whenever practical, replace CT use with MRI, such as for imaging the liver. As a result, the most recent CT machines, known as multi-slice CT or multi-detector CT scanners, take the image in a spiral manner rather than individual parts of the body, making it faster, producing better 3D images with fewer CT scans, and detecting minor irregularities.

5.3. Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) is the other technique besides CT used to scan part of the body using a magnetic field and radio waves [131–133]. Due to its non-invasive and non-radiant nature and high resolution, MRI is preferred for in vivo assessments [134–136]. Unlike CT, MRI produces a magnetic field that temporarily releases hydrogen atoms into the body. That being said, the movement limiting its applications can easily affect MRI scanners. Furthermore, the images might suffer geometric distortions caused by variations in the magnetic field strength [137,138].

5.4. Computer-aided design (CAD)

Computer-aided design (CAD) is widely used to design an approach that provides a powerful tool to model 3D scaffold geometries [139–143]. CAD designs the model using constructive solid geometry (CSG) or boundary representation (B-Rep). CSG models are designed using boolean operations, whereas B-Rep uses software like NX (Siemens PLM Software), CATIA (Dassault Systemes), Pro/Engineer (PTC), SolidWorks (Dassault Systemes), and MIMICS (Materialize Gmbh) to design the model [144]. Developing a CAD scaffold is well-suited when combined with rapid prototyping techniques to fabricate the physical scaffolds [145].

5.5. Rapid prototyping (RP)/Solid freeform fabrication (SFF)

Rapid prototyping (RP), also known as the solid freeform fabrication (SFF) technique, is a controllable 3D structure designed layer by layer [146–149]. Designing a scaffold using this technique allows excellent reproducibility and the possibility of designing a structure that mimics the natural bone structure to be replaced [150]. Some of the RP techniques employed include stereolithography (STL), selective laser sintering (SLS), fused deposited modeling (FDM), laminated object manufacturing (LOM), multiphase jet solidification (MJS), and three-dimensional printing (3DP) [59,151,152].

6. Summary and future direction

This review comprehensively summarized various fabrication techniques of bone scaffold preparation techniques and their potential use in orthopedic surgery. Polymethylmethacrylate remains one of the most enduring materials in orthopedic surgery. It has a central role in the success of total joint replacement and is also used

in newer techniques such as percutaneous vertebroplasty and kyphoplasty. The use of bone scaffolds is nowadays an important aid in the orthopedic field, both in situations in which it is necessary to fix a fracture in patients with severe osteoporosis ("augmentation") and in cases where it must ensure greater stability in the system of the prosthetic hip, knee, and shoulder. In cases of prosthetic infection, joint antibiotic-loaded spacers are used, and PMMA has gained favor as a vehicle for the delivery of antibiotics. Antibiotic-loaded acrylic cement in joint replacement provides short- to medium-term protection against prosthetic infection. It aims to overlap with and replace the prophylaxis provided by peri-operative intravenous antibiotics. Recently, new materials such as bioglass and porous cement have been developed, which seem to provide good results in clinical trials. These materials exploit their potential biological value, allowing the bone to integrate within the acrylic cement structure and favoring the mechanical and biological stability of the bone cement system. For future development of these materials (PMMA, antibiotic-loaded cement, glass, and porous cement), the aim is to improve osseointegration to promote better mechanical stability and better biological integration on the interface of bone cement.

Bone scaffold research focuses on better mechanical quality and biocompatibility. Biomaterials, such as calcium phosphates and hydroxyapatite, more efficiently induce bone growth. Advances in the biocompatibility of PMMA bone scaffolds might be achieved by introducing osteogenic agents, such as bone morphogenic proteins or transforming growth factors, to scaffold surfaces that contact the surrounding bone. PMMA for vertebroplasty has greater stiffness than vertebral cancellous bone, causing higher incidences of fracture of neighboring vertebral bodies.

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References

1. Turner CH, Wang T, Burr DB. Shear Strength and Fatigue Properties of Human Cortical Bone Determined from Pure Shear Tests. Calcified Tissue International. 2001; 69(6): 373-378. doi: 10.1007/s00223-001-1006-1
2. Lee H, Liao JD, Guo YS, et al. Biomimetic Design for a Dual Concentric Porous Titanium Scaffold with Appropriate Compressive Strength and Cells Affinity. Materials. 2020; 13(15): 3316. doi: 10.3390/ma13153316
3. Lin JT, Lane JM. Osteoporosis. Clinical Orthopaedics and Related Research. 2004; 425: 126-134. doi: 10.1097/01.blo.0000132404.30139.f2
4. Marcus R, Dempster DW, Cauley JA, Feldman D. Osteoporosis. Academic Press; 2013.
5. Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. The Lancet. 2011; 377: 1276-1287. doi: 10.1016/S0140-6736(10)62349-5
6. Brooks H, Azen S, Gerberg E, et al. Scoliosis. The Journal of Bone & Joint Surgery. 1975; 57(7): 968-972. doi: 10.2106/00004623-197557070-00015

7. MacLennan A. Scoliosis. The British Medical Journal. 1922; 2(3227): 864-866.
8. Rogala EJ, Drummond DS, Gurr J. Scoliosis. The Journal of Bone & Joint Surgery. 1978; 60(2): 173-176. doi: 10.2106/00004623-197860020-00005
9. Calhoun JH, Manring MM. Adult Osteomyelitis. Infectious Disease Clinics of North America. 2005; 19(4): 765-786. doi: 10.1016/j.idc.2005.07.009
10. Lew DP, Waldvogel FA. Osteomyelitis. New England Journal of Medicine. 1997; 336(14): 999-1007. doi: 10.1056/nejm199704033361406
11. Waldvogel FA, Vasey H. Osteomyelitis: The Past Decade. New England Journal of Medicine. 1980; 303(7): 360-370. doi: 10.1056/nejm198008143030703
12. Ramesh N, Moratti SC, Dias GJ. Hydroxyapatite–polymer biocomposites for bone regeneration: A review of current trends. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2017; 106(5): 2046-2057. doi: 10.1002/jbm.b.33950
13. Dimitriou R, Jones E, McGonagle D, et al. Bone regeneration: current concepts and future directions. BMC Medicine. 2011; 9(1). doi: 10.1186/1741-7015-9-66
14. Soucacos PN, Johnson EO, Babis G. An update on recent advances in bone regeneration. Injury. 2008; 39: S1-S4. doi: 10.1016/S0020-1383(08)70009-3
15. Cornell CN, Lane JM. Current Understanding of Osteoconduction in Bone Regeneration. Clinical Orthopaedics and Related Research. 1998; 355S: S267-S273. doi: 10.1097/00003086-199810001-00027
16. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. European Spine Journal. 2001; 10(0): S96-S101. doi: 10.1007/s005860100282
17. Kuzyk PRT, Schemitsch EH. The basic science of peri-implant bone healing. Indian Journal of Orthopaedics. 2011; 45(2): 108-115. doi: 10.4103/0019-5413.77129
18. Chang BS, Hong KS, Youn HJ, et al. Osteoconduction at porous hydroxyapatite with various pore configurations. Biomaterials. 2000; 21: 1291-1298. doi: 10.1016/S0142-9612(00)00030-2
19. Krishnan MR, Alsharaeh E. Potential removal of benzene-toluene-xylene toxic vapors by nanoporous poly(styrene-r-methylmethacrylate) copolymer composites. Environmental Nanotechnology, Monitoring & Management. 2023; 20: 100860. doi: 10.1016/j.enmm.2023.100860
20. Krishnan MR, Alsharaeh EH. Polymer gel amended sandy soil with enhanced water storage and extended release capabilities for sustainable desert agriculture. Journal of Polymer Science and Engineering. 2023; 6(1): 2892. doi: 10.24294/jpse.v6i1.2892
21. Krishnan MR, Alsharaeh EH. Facile fabrication of thermo-mechanically reinforced polystyrene-graphene nanocomposite aerogel for produced water treatment. Journal of Porous Materials. 2024; 31: 1363-1373. doi: 10.1007/s10934-024-01602-y
22. Krishnan MR, Alsharaeh EH. High-performance functional materials based on polymer nanocomposites—A review. Journal of Polymer Science and Engineering. 2023; 6(1): 3292. doi: 10.24294/jpse.v6i1.3292
23. Krishnan MR, Rajendran V. Sulfonated mesoporous polystyrene-1D multiwall carbon nanotube nanocomposite as potential adsorbent for efficient removal of xylene isomers from aqueous solution. Characterization and Application of Nanomaterials. 2023; 6(2): 3516. doi: 10.24294/can.v6i2.3516
24. Krishnan M, Michal F, Alsoughayer S, et al. Thermodynamic and Kinetic Investigation of Water Absorption by PAM Composite Hydrogel. In: Proceedings of the SPE Kuwait Oil & Gas Show and Conference; 13-16 October 2019; Mishref, Kuwait. doi: 10.2118/198033-ms
25. Krishnan MR, Aldawsari YF, Alsharaeh EH. Three-dimensionally cross-linked styrene-methyl methacrylate-divinyl benzene terpolymer networks for organic solvents and crude oil absorption. Journal of Applied Polymer Science. 2020; 138(9). doi: 10.1002/app.49942
26. Krishnan MR, Aldawsari Y, Michael FM, et al. 3D-Polystyrene-polymethyl methacrylate/divinyl benzene networks-Epoxy-Graphene nanocomposites dual-coated sand as high strength proppants for hydraulic fracture operations. Journal of Natural Gas Science and Engineering. 2021; 88: 103790. doi: 10.1016/j.jngse.2020.103790
27. Krishnan MR, Aldawsari Y, Michael FM, et al. Mechanically reinforced polystyrene-polymethyl methacrylate copolymer-graphene and Epoxy-Graphene composites dual-coated sand proppants for hydraulic fracture operations. Journal of Petroleum Science and Engineering. 2021; 196: 107744. doi: 10.1016/j.petrol.2020.107744
28. Krishnan M, Chen HY, Ho RM. Switchable structural colors from mesoporous polystyrene films. In: Proceedings of the ACS 252nd. National Meeting; 18-26 August 2016; Philadelphia, Pennsylvania, USA.

29. Krishnan MR, Almohsin A, Alsharaeh EH. Syntheses and fabrication of mesoporous styrene-co-methyl methacrylate-graphene composites for oil removal. Diamond and Related Materials. 2022; 130: 109494. doi: 10.1016/j.diamond.2022.109494
30. Krishnan MR, Omar H, Yazeed Y, et al. Insight into Thermo-Mechanical Enhancement of Polymer Nanocomposites Coated Microsand Proppants for Hydraulic Fracturing. SSRN Electronic Journal. 2022. doi: 10.2139/ssrn.4243574
31. Krishnan MR, Rajendran V, Alsharaeh E. Anti-reflective and high-transmittance optical films based on nanoporous silicon dioxide fabricated from templated synthesis. Journal of Non-Crystalline Solids. 2023; 606: 122198. doi: 10.1016/j.jnoncrysol.2023.122198
32. Krishnan MR, Li W, Alsharaeh EH. Ultra-lightweight Nanosand/Polymer Nanocomposite Materials for Hydraulic Fracturing Operations. SSRN Electronic Journal. 2022. doi: 10.2139/ssrn.4233321
33. Krishnan MR, Omar H, Almohsin A, et al. An overview on nanosilica–polymer composites as high-performance functional materials in oil fields. Polymer Bulletin. 2023; 81(5): 3883-3933. doi: 10.1007/s00289-023-04934-y
34. Krishnan MR, Li W, Alsharaeh EH. Cross-linked polymer nanocomposite networks coated nano sand light-weight proppants for hydraulic fracturing applications. Characterization and Application of Nanomaterials. 2023; 6(2): 3314. doi: 10.24294/can.v6i2.3314
35. Krishnan MR, Almohsin A, Alsharaeh EH. Thermo-Mechanically Reinforced Mesoporous Styrene-Co-Methyl Methacrylate-Graphene Composites for Produced Water Treatment. SSRN Electronic Journal. 2022.
36. Aldosari MA, Alsaud KBB, Othman A, et al. Microwave Irradiation Synthesis and Characterization of Reduced-(Graphene Oxide-(Polystyrene-Polymethyl Methacrylate))/Silver Nanoparticle Nanocomposites and Their Anti-Microbial Activity. Polymers. 2020; 12(5): 1155. doi: 10.3390/polym12051155
37. Krishnan MR, Almohsin A, Alsharaeh EH. Mechanically robust and thermally enhanced sand-polyacrylamide-2D nanofiller composite hydrogels for water shutoff applications. Journal of Applied Polymer Science. 2023; 141(7). doi: 10.1002/app.54953
38. Almohsin A, Michal F, Alsharaeh E, et al. Self-Healing PAM Composite Hydrogel for Water Shutoff at High Temperatures: Thermal and Rheological Investigations. In: Proceedings of the SPE Gas & Oil Technology Showcase and Conference; 21-23 October 2019; Dubai, United Arab Emirates. doi: 10.2118/198664-ms
39. Almohsin A, Alsharaeh E, Michael FM, Krishnan MR. Polymer-Nanofiller Hydrogels. US Patent, US11828116B2, 31 October 2023.
40. Almohsin A, Alsharaeh E, Krishnan MR. Polymer-Sand Nanocomposite Lost Circulation Material. US Patent, US11828116B2, 28 November 2023.
41. Almohsin A, Alsharaeh E, Krishnan MR, Alghazali M. Coated Nanosand as Relative Permeability Modifier. US Patent, US11827852B2, 28 November 2023.
42. Almohsin A, Krishnan MR, Alsharaeh E, et al. Preparation and Properties Investigation on Sand-Polyacrylamide Composites with Engineered Interfaces for Water Shutoff Applications. In: Proceedings of the Middle East Oil, Gas and Geosciences Show; 19-21 February 2023; Manama, Bahrain. doi: 10.2118/213481-ms
43. Keishnan MR, Michael FM, Almohsin AM, et al. Thermal and Rheological Investigations on N,N'-Methylenebis Acrylamide Cross-Linked Polyacrylamide Nanocomposite Hydrogels for Water Shutoff Applications. In: Proceedings of the Offshore Technology Conference Asia; 2-6 November 2020; Kuala Lumpur, Malaysia. doi: 10.4043/30123-ms
44. Krishnan MR, Aldawsari YF, Alsharaeh EH. 3D-poly(styrene-methyl methacrylate)/divinyl benzene-2D-nanosheet composite networks for organic solvents and crude oil spill cleanup. Polymer Bulletin. 2021; 79(6): 3779-3802. doi: 10.1007/s00289-021-03565-5
45. Krishnan MR, Lu K, Chiu W, et al. Directed Self-Assembly of Star-Block Copolymers by Topographic Nanopatterns through Nucleation and Growth Mechanism. Small. 2018; 14(16). doi: 10.1002/smll.201704005
46. Ho RM, Krishnan MR, Siddique SK, Chien YC. Method for Fabricating Nanoporous Polymer Thin Film and Corresponding Method for Fabricating Nanoporous Thin Film. US Patent, US11059205B2, 13 July 2021.
47. Alsharaeh EH, Krishnan MR. Method of Making Mutlilayer Soil with Property for Extended Release Water for Desert Agriculture. US Patent, US10772265B1, 15 September 2020.
48. Tasleem S, Bongu CS, Krishnan MR, et al. Navigating the hydrogen prospect: A comprehensive review of sustainable source-based production technologies, transport solutions, advanced storage mechanisms, and CCUS integration. Journal of Energy Chemistry. 2024; 97: 166-215. doi: 10.1016/j.jechem.2024.05.022

49. Michael FM, Krishnan MR, Fathima A, et al. Zirconia/graphene nanocomposites effect on the enhancement of thermo-mechanical stability of polymer hydrogels. Materials Today Communications. 2019; 21: 100701. doi: 10.1016/j.mtcomm.2019.100701
50. Michael FM, Krishnan MR, AlSoughayer S, et al. Thermo-elastic and self-healing polyacrylamide -2D nanofiller composite hydrogels for water shutoff treatment. Journal of Petroleum Science and Engineering. 2020; 193: 107391. doi: 10.1016/j.petrol.2020.107391
51. Vacanti CA. The history of tissue engineering. Journal of Cellular and Molecular Medicine. 2006; 10(3): 569-576. doi: 10.1111/j.1582-4934.2006.tb00421.x
52. Chapekar MS. Tissue engineering: challenges and opportunities. Journal of Biomedical Materials Research. 2000; 53: 617-620. doi: 10.1002/1097-4636(2000)53:6<617::AID-JBM1>3.0.CO;2-C
53. Atala A, Lanza R. Methods of Tissue Engineering. Gulf Professional Publishing; 2001.
54. Stock UA, Vacanti JP. Tissue Engineering: Current State and Prospects. Annual Review of Medicine. 2001; 52(1): 443-451. doi: 10.1146/annurev.med.52.1.443
55. Black CRM, Goriainov V, Gibbs D, et al. Bone Tissue Engineering. Current Molecular Biology Reports. 2015; 1(3): 132-140. doi: 10.1007/s40610-015-0022-2
56. Shafiee A, Atala A. Tissue Engineering: Toward a New Era of Medicine. Annual Review of Medicine. 2017; 68(1): 29-40. doi: 10.1146/annurev-med-102715-092331
57. Patrick CW, Mikos AG, McIntire LV. Prospectus of Tissue Engineering. In: Patrick CW, Mikos AG, McIntire LV, Langer RS (editors). Frontiers in Tissue Engineering, 1st ed. Pergamon; 1998. pp. 3-11. doi: 10.1016/b978-008042689-1/50003-0
58. Ikada Y. Tissue Engineering: Fundamentals and Applications. Elsevier; 2011.
59. Abdelaziz AG, Nageh H, Abdo SM, et al. A Review of 3D Polymeric Scaffolds for Bone Tissue Engineering: Principles, Fabrication Techniques, Immunomodulatory Roles, and Challenges. Bioengineering. 2023; 10(2): 204. doi: 10.3390/bioengineering10020204
60. Hutmacher DW. Scaffolds in tissue engineering bone and cartilage. Biomaterials. 2000; 21: 2529-2543. doi: 10.1016/S0142-9612(00)00121-6
61. Guarino V, Causa F, Netti PA, et al. The role of hydroxyapatite as solid signal on performance of PCL porous scaffolds for bone tissue regeneration. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2008; 86B(2): 548-557. doi: 10.1002/jbm.b.31055
62. Gómez S, Vlad MD, López J, et al. Design and properties of 3D scaffolds for bone tissue engineering. Acta Biomaterialia. 2016; 42: 341-350. doi: 10.1016/j.actbio.2016.06.032
63. Mirkhalaf M, Men Y, Wang R, et al. Personalized 3D printed bone scaffolds: A review. Acta Biomaterialia. 2023; 156: 110-124. doi: 10.1016/j.actbio.2022.04.014
64. Wu S, Liu X, Yeung KWK, et al. Biomimetic porous scaffolds for bone tissue engineering. Materials Science and Engineering: R: Reports. 2014; 80: 1-36. doi: 10.1016/j.mser.2014.04.001
65. Qu H, Fu H, Han Z, et al. Biomaterials for bone tissue engineering scaffolds: a review. RSC Advances. 2019; 9(45): 26252-26262. doi: 10.1039/c9ra05214c
66. Lichte P, Pape HC, Pufe T, et al. Scaffolds for bone healing: Concepts, materials and evidence. Injury. 2011; 42(6): 569-573. doi: 10.1016/j.injury.2011.03.033
67. Chocholata P, Kulda V, Babuska V. Fabrication of Scaffolds for Bone-Tissue Regeneration. Materials. 2019; 12(4): 568. doi: 10.3390/ma12040568
68. Wang C, Huang W, Zhou Y, et al. 3D printing of bone tissue engineering scaffolds. Bioactive Materials. 2020; 5(1): 82-91. doi: 10.1016/j.bioactmat.2020.01.004
69. Alonzo M, Alvarez Primo F, Anil Kumar S, et al. Bone tissue engineering techniques, advances, and scaffolds for treatment of bone defects. Current Opinion in Biomedical Engineering. 2021; 17: 100248. doi: 10.1016/j.cobme.2020.100248
70. Polo-Corrales L, Latorre-Esteves M, Ramirez-Vick JE. Scaffold Design for Bone Regeneration. Journal of Nanoscience and Nanotechnology. 2014; 14(1): 15-56. doi: 10.1166/jnn.2014.9127
71. Cao S, Zhao Y, Hu Y, et al. New perspectives: In-situ tissue engineering for bone repair scaffold. Composites Part B: Engineering. 2020; 202: 108445. doi: 10.1016/j.compositesb.2020.108445
72. Collins MN, Ren G, Young K, et al. Scaffold Fabrication Technologies and Structure/Function Properties in Bone Tissue Engineering. Advanced Functional Materials. 2021; 31(21). doi: 10.1002/adfm.202010609

73. Roseti L, Parisi V, Petretta M, et al. Scaffolds for Bone Tissue Engineering: State of the art and new perspectives. Materials Science and Engineering: C. 2017; 78: 1246-1262. doi: 10.1016/j.msec.2017.05.017
74. Thadavirul N, Pavasant P, Supaphol P. Development of polycaprolactone porous scaffolds by combining solvent casting, particulate leaching, and polymer leaching techniques for bone tissue engineering. Journal of Biomedical Materials Research Part A. 2013; 102(10): 3379-3392. doi: 10.1002/jbm.a.35010
75. Sola A, Bertacchini J, D'Avella D, et al. Development of solvent-casting particulate leaching (SCPL) polymer scaffolds as improved three-dimensional supports to mimic the bone marrow niche. Materials Science and Engineering: C. 2019; 96: 153-165. doi: 10.1016/j.msec.2018.10.086
76. Prasad A, Sankar MR, Katiyar V. State of Art on Solvent Casting Particulate Leaching Method for Orthopedic ScaffoldsFabrication. Materials Today: Proceedings. 2017; 4(2): 898-907. doi: 10.1016/j.matpr.2017.01.101
77. Koyyada A, Orsu P. Recent Advancements and Associated Challenges of Scaffold Fabrication Techniques in Tissue Engineering Applications. Regenerative Engineering and Translational Medicine. 2020; 7(2): 147-159. doi: 10.1007/s40883-020-00166-y
78. Zhang Z, Feng Y, Wang L, et al. A review of preparation methods of porous skin tissue engineering scaffolds. Materials Today Communications. 2022; 32: 104109. doi: 10.1016/j.mtcomm.2022.104109
79. Suamte L, Tirkey A, Barman J, et al. Various manufacturing methods and ideal properties of scaffolds for tissue engineering applications. Smart Materials in Manufacturing. 2023; 1: 100011. doi: 10.1016/j.smmf.2022.100011
80. Fereshteh Z. Freeze-drying technologies for 3D scaffold engineering. In: Deng Y, Kuipe J (editors). Functional 3D Tissue Engineering Scaffolds. Elsevier; 2018. pp. 151-174. doi: 10.1016/b978-0-08-100979-6.00007-0
81. Kazimierczak P, Benko A, Palka K, et al. Novel synthesis method combining a foaming agent with freeze-drying to obtain hybrid highly macroporous bone scaffolds. Journal of Materials Science & Technology. 2020; 43: 52-63. doi: 10.1016/j.jmst.2020.01.006
82. Putra DFA, Aji BB, Ningsih HS, et al. Preparation and Characterization of Freeze-Dried β-Tricalcium Phosphate/Barium Titanate/Collagen Composite Scaffolds for Bone Tissue Engineering in Orthopedic Applications. Ceramics. 2023; 6(4): 2148-2161. doi: 10.3390/ceramics6040132
83. Samitsu S, Zhang R, Peng X, et al. Flash freezing route to mesoporous polymer nanofibre networks. Nature Communications. 2013; 4(1). doi: 10.1038/ncomms3653
84. Krishnan MR, Samitsu S, Fujii Y, et al. Hydrophilic polymer nanofibre networks for rapid removal of aromatic compounds from water. Chem Commun. 2014; 50(66): 9393-9396. doi: 10.1039/c4cc01786b
85. Krishnan MR, Chien YC, Cheng CF, et al. Fabrication of Mesoporous Polystyrene Films with Controlled Porosity and Pore Size by Solvent Annealing for Templated Syntheses. Langmuir. 2017; 33(34): 8428-8435. doi: 10.1021/acs.langmuir.7b02195
86. Cheng CF, Chen YM, Zou F, et al. Li-Ion Capacitor Integrated with Nano-network-Structured Ni/NiO/C Anode and Nitrogen-Doped Carbonized Metal–Organic Framework Cathode with High Power and Long Cyclability. ACS Applied Materials & Interfaces. 2019; 11(34): 30694-30702. doi: 10.1021/acsami.9b06354
87. Chien YC, Huang LY, Yang KC, et al. Fabrication of metallic nanonetworks via templated electroless plating as hydrogenation catalyst. Emergent Materials. 2020; 4(2): 493-501. doi: 10.1007/s42247-020-00108-y
88. Lo TY, Krishnan MR, Lu KY, et al. Silicon-containing block copolymers for lithographic applications. Progress in Polymer Science. 2018; 77: 19-68. doi: 10.1016/j.progpolymsci.2017.10.002
89. Mi A, Guo L, Guo S, et al. Freeze-casting in synthetic porous materials: Principles, different dimensional building units and recent applications. Sustainable Materials and Technologies. 2024; 39: e00830. doi: 10.1016/j.susmat.2024.e00830
90. Hajihasani Biouki M, Mobedi H, Karkhaneh A, et al. Development of a simvastatin loaded injectable porous scaffold in situ formed by phase inversion method for bone tissue regeneration. The International Journal of Artificial Organs. 2018; 42(2): 72-79. doi: 10.1177/0391398818806161
91. Duarte ARC, Mano JF, Reis RL. Dexamethasone-loaded scaffolds prepared by supercritical-assisted phase inversion. Acta Biomaterialia. 2009; 5(6): 2054-2062. doi: 10.1016/j.actbio.2009.01.047
92. Duarte ARC, Mano JF, Reis RL. Supercritical phase inversion of starch-poly(ε-caprolactone) for tissue engineering applications. Journal of Materials Science: Materials in Medicine. 2009; 21(2): 533-540. doi: 10.1007/s10856-009-3909-8
93. Duarte ARC, Mano JF, Reis RL. The role of organic solvent on the preparation of chitosan scaffolds by supercritical assisted phase inversion. The Journal of Supercritical Fluids. 2012; 72: 326-332. doi: 10.1016/j.supflu.2010.12.004

94. Seyed Hakim R, Maghsoud Z, Halabian R. Fabrication and evaluation of polycaprolactone/olive oil scaffolds by phase inversion for tissue engineering. European Polymer Journal. 2021; 150: 110394. doi: 10.1016/j.eurpolymj.2021.110394
95. Duarte ARC, Mano JF, Reis RL. Supercritical fluids in biomedical and tissue engineering applications: a review. International Materials Reviews. 2009; 54(4): 214-222. doi: 10.1179/174328009x411181
96. Yang DZ, Chen AZ, Wang SB, et al. Preparation of poly(L-lactic acid) nanofiber scaffolds with a rough surface by phase inversion using supercritical carbon dioxide. Biomedical Materials. 2015; 10(3): 035015. doi: 10.1088/1748-6041/10/3/035015
97. Duarte ARC, Mano JF, Reis RL. Preparation of starch-based scaffolds for tissue engineering by supercritical immersion precipitation. The Journal of Supercritical Fluids. 2009; 49(2): 279-285. doi: 10.1016/j.supflu.2008.12.008
98. Papenburg BJ, Bolhuis-Versteeg LAM, Grijpma DW, et al. A facile method to fabricate poly(l-lactide) nano-fibrous morphologies by phase inversion. Acta Biomaterialia. 2010; 6(7): 2477-2483. doi: 10.1016/j.actbio.2009.12.051
99. Yoshimoto H, Shin Y, Terai H, Vacanti J. A biodegradable nanofiber scaffold by electrospinning and its potential for bone tissue engineering. Biomaterials. 2003; 24: 2077-2082. doi: 10.1016/S0142-9612(02)00635-X
100. Yu Y, Hua S, Yang M, et al. Fabrication and characterization of electrospinning/3D printing bone tissue engineering scaffold. RSC Advances. 2016; 6(112): 110557-110565. doi: 10.1039/c6ra17718b
101. Prabhakaran MP, Venugopal J, Ramakrishna S. Electrospun nanostructured scaffolds for bone tissue engineering. Acta Biomaterialia. 2009; 5(8): 2884-2893. doi: 10.1016/j.actbio.2009.05.007
102. Wang Z, Wang Y, Yan J, et al. Pharmaceutical electrospinning and 3D printing scaffold design for bone regeneration. Advanced Drug Delivery Reviews. 2021; 174: 504-534. doi: 10.1016/j.addr.2021.05.007
103. Maji K, Pramanik K. Electrospun scaffold for bone regeneration. International Journal of Polymeric Materials and Polymeric Biomaterials. 2021; 71(11): 842-857. doi: 10.1080/00914037.2021.1915784
104. Lin W, Chen M, Qu T, et al. Three-dimensional electrospun nanofibrous scaffolds for bone tissue engineering. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2019; 108(4): 1311-1321. doi: 10.1002/jbm.b.34479
105. Qi Y, Lv H, Huang Q, et al. The Synergetic Effect of 3D Printing and Electrospinning Techniques in the Fabrication of Bone Scaffolds. Annals of Biomedical Engineering. 2024; 52(6): 1518-1533. doi: 10.1007/s10439-024-03500-5
106. Khajavi R, Abbasipour M, Bahador A. Electrospun biodegradable nanofibers scaffolds for bone tissue engineering. Journal of Applied Polymer Science. 2015; 133(3). doi: 10.1002/app.42883
107. Andric T, Wright LD, Taylor BL, et al. Fabrication and characterization of three-dimensional electrospun scaffolds for bone tissue engineering. Journal of Biomedical Materials Research Part A. 2012; 100A(8): 2097-2105. doi: 10.1002/jbm.a.34045
108. Jang JH, Castano O, Kim HW. Electrospun materials as potential platforms for bone tissue engineering. Advanced Drug Delivery Reviews. 2009; 61(12): 1065-1083. doi: 10.1016/j.addr.2009.07.008
109. Yang C, Shao Q, Han Y, et al. Fibers by Electrospinning and Their Emerging Applications in Bone Tissue Engineering. Applied Sciences. 2021; 11(19): 9082. doi: 10.3390/app11199082
110. Bhattarai DP, Aguilar LE, Park CH, et al. A Review on Properties of Natural and Synthetic Based Electrospun Fibrous Materials for Bone Tissue Engineering. Membranes. 2018; 8(3): 62. doi: 10.3390/membranes8030062
111. Li W, Laurencin CT, Caterson EJ, et al. Electrospun nanofibrous structure: A novel scaffold for tissue engineering. Journal of Biomedical Materials Research. 2002; 60(4): 613-621. doi: 10.1002/jbm.10167
112. Sun W, Darling A, Starly B, et al. Computer-aided tissue engineering: overview, scope and challenges. Biotechnology and Applied Biochemistry. 2004; 39(1): 29-47. doi: 10.1042/ba20030108
113. Sun W, Lal P. Recent development on computer aided tissue engineering-a review. Computer Methods and Programs in Biomedicine. 2002; 67: 85-103. doi: 10.1016/S0169-2607(01)00116-X
114. Giannitelli SM, Accoto D, Trombetta M, et al. Current trends in the design of scaffolds for computer-aided tissue engineering. Acta Biomaterialia. 2014; 10(2): 580-594. doi: 10.1016/j.actbio.2013.10.024
115. Top N, Şahin İ, Gökçe H, et al. Computer-aided design and additive manufacturing of bone scaffolds for tissue engineering: state of the art. Journal of Materials Research. 2021; 36(19): 3725-3745. doi: 10.1557/s43578-021-00156-y
116. Di Gravina GM, Loi G, Auricchio F, et al. Computer-aided engineering and additive manufacturing for bioreactors in tissue engineering: State of the art and perspectives. Biophysics Reviews. 2023; 4(3). doi: 10.1063/5.0156704
117. Zenobi E, Merco M, Mochi F, et al. Tailoring the Microarchitectures of 3D Printed Bone-like Scaffolds for Tissue Engineering Applications. Bioengineering. 2023; 10(5): 567. doi: 10.3390/bioengineering10050567

118. Bardini R, Di Carlo S. Computational Methods for Biofabrication in Tissue Engineering and Regenerative Medicine - a literature review. Computational and Structural Biotechnology Journal. 2024; 23: 601-616. doi: 10.1101/2023.03.03.530995
119. Bermejillo Barrera MD, Franco-Martínez F, Díaz Lantada A. Artificial Intelligence Aided Design of Tissue Engineering Scaffolds Employing Virtual Tomography and 3D Convolutional Neural Networks. Materials. 2021; 14(18): 5278. doi: 10.3390/ma14185278
120. Foresti R, Rossi S, Pinelli S, et al. Highly-defined bioprinting of long-term vascularized scaffolds with Bio-Trap: Complex geometry functionalization and process parameters with computer aided tissue engineering. Materialia. 2020; 9: 100560. doi: 10.1016/j.mtla.2019.100560
121. Sahai N, Gogoi M. Computer aided designing and finite element analysis for development of porous 3D tissue scaffold - a review. International Journal of Biomedical Engineering and Technology. 2020; 33(2): 174. doi: 10.1504/ijbet.2020.107712
122. Fernández MP, Witte F, Tozzi G. Applications of X-ray computed tomography for the evaluation of biomaterial-mediated bone regeneration in critical-sized defects. Journal of Microscopy. 2019; 277(3): 179-196. doi: 10.1111/jmi.12844
123. Noroozi R, Tatar F, Zolfagharian A, et al. Additively Manufactured Multi-Morphology Bone-like Porous Scaffolds: Experiments and Micro-Computed Tomography-Based Finite Element Modeling Approaches. International Journal of Bioprinting. 2022; 8(3): 556. doi: 10.18063/ijb.v8i3.556
124. Liu Y, Xie D, Zhou R, et al. 3D X-ray micro-computed tomography imaging for the microarchitecture evaluation of porous metallic implants and scaffolds. Micron. 2021; 142: 102994. doi: 10.1016/j.micron.2020.102994
125. Dixit K, Gupta P, Kamle S, et al. Structural analysis of porous bioactive glass scaffolds using micro-computed tomographic images. Journal of Materials Science. 2020; 55(27): 12705-12724. doi: 10.1007/s10853-020-04850-w
126. Rawson SD, Maksimcuka J, Withers PJ, et al. X-ray computed tomography in life sciences. BMC Biology. 2020; 18(1). doi: 10.1186/s12915-020-0753-2
127. Olăreț E, Stancu IC, Iovu H, et al. Computed Tomography as a Characterization Tool for Engineered Scaffolds with Biomedical Applications. Materials. 2021; 14(22): 6763. doi: 10.3390/ma14226763
128. Farina E, Gastaldi D, Baino F, et al. Micro computed tomography based finite element models for elastic and strength properties of 3D printed glass scaffolds. Acta Mechanica Sinica. 2021; 37(2): 292-306. doi: 10.1007/s10409-021-01065-3
129. Verykokou S, Ioannidis C, Soile S, et al. The Role of Cone Beam Computed Tomography in Periodontology: From 3D Models of Periodontal Defects to 3D-Printed Scaffolds. Journal of Personalized Medicine. 2024; 14(2): 207. doi: 10.3390/jpm14020207
130. Vanlenthe G, Hagenmuller H, Bohner M, et al. Nondestructive micro-computed tomography for biological imaging and quantification of scaffold–bone interaction in vivo. Biomaterials. 2007; 28(15): 2479-2490. doi: 10.1016/j.biomaterials.2007.01.017
131. Yang A, Wang Y, Feng Q, et al. Integrating Fluorescence and Magnetic Resonance Imaging in Biocompatible Scaffold for Real-Time Bone Repair Monitoring and Assessment. Advanced Healthcare Materials. 2023; 13(6). doi: 10.1002/adhm.202302687
132. Washburn NR, Weir M, Anderson P, et al. Bone formation in polymeric scaffolds evaluated by proton magnetic resonance microscopy and X-ray microtomography. Journal of Biomedical Materials Research Part A. 2004; 69A(4): 738-747. doi: 10.1002/jbm.a.30054
133. Zhao M, Li X, Fu F, et al. Magnetic resonance imaging-three-dimensional printing technology fabricates customized scaffolds for brain tissue engineering. Neural Regeneration Research. 2017; 12(4): 614. doi: 10.4103/1673-5374.205101
134. van der Zande M, Sitharaman B, Walboomers XF, et al. In Vivo Magnetic Resonance Imaging of the Distribution Pattern of Gadonanotubes Released from a Degrading Poly(Lactic-Co-Glycolic Acid) Scaffold. Tissue Engineering Part C: Methods. 2011; 17(1): 19-26. doi: 10.1089/ten.tec.2010.0089
135. Sajesh KM, Ashokan A, Gowd GS, et al. Magnetic 3D scaffold: A theranostic tool for tissue regeneration and non-invasive imaging in vivo. Nanomedicine: Nanotechnology, Biology and Medicine. 2019; 18: 179-188. doi: 10.1016/j.nano.2019.02.022
136. Huang J, Lv Z, Wang Y, et al. In Vivo MRI and X-Ray Bifunctional Imaging of Polymeric Composite Supplemented with GdPO4·H2O Nanobundles for Tracing Bone Implant and Bone Regeneration. Advanced Healthcare Materials. 2016; 5(17): 2182-2190. doi: 10.1002/adhm.201600249

137. Stuckey DJ, Ishii H, Chen QZ, et al. Magnetic Resonance Imaging Evaluation of Remodeling by Cardiac Elastomeric Tissue Scaffold Biomaterials in a Rat Model of Myocardial Infarction. Tissue Engineering Part A. 2010; 16(11): 3395-3402. doi: 10.1089/ten.tea.2010.0213
138. Chesnick IE, Fowler CB, Mason JT, et al. Novel mineral contrast agent for magnetic resonance studies of bone implants grown on a chick chorioallantoic membrane. Magnetic Resonance Imaging. 2011; 29(9): 1244-1254. doi: 10.1016/j.mri.2011.07.022
139. Heljak MK, Kurzydlowski KJ, Swieszkowski W. Computer aided design of architecture of degradable tissue engineering scaffolds. Computer Methods in Biomechanics and Biomedical Engineering. 2017; 20(15): 1623-1632. doi: 10.1080/10255842.2017.1399263
140. Lacroix D, Planell JA, Prendergast PJ. Computer-aided design and finite-element modelling of biomaterial scaffolds for bone tissue engineering. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences. 2009; 367(1895): 1993-2009. doi: 10.1098/rsta.2009.0024
141. Fang Z, Starly B, Sun W. Computer-aided characterization for effective mechanical properties of porous tissue scaffolds. Computer-Aided Design. 2005; 37(1): 65-72. doi: 10.1016/j.cad.2004.04.002
142. Sun W, Starly B, Darling A, et al. Computer-aided tissue engineering: application to biomimetic modelling and design of tissue scaffolds. Biotechnology and Applied Biochemistry. 2004; 39(1): 49-58. doi: 10.1042/ba20030109
143. Ramin E, Harris RA. Advanced computer-aided design for bone tissue-engineering scaffolds. Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine. 2009; 223(3): 289-301. doi: 10.1243/09544119jeim452
144. Sahai N, Saxena KK, Gogoi M. Modelling and simulation for fabrication of 3D printed polymeric porous tissue scaffolds. Advances in Materials and Processing Technologies. 2020; 6(3): 530-539. doi: 10.1080/2374068x.2020.1728643
145. Naing MW, Chua CK, Leong KF, et al. Fabrication of customised scaffolds using computer-aided design and rapid prototyping techniques. Rapid Prototyping Journal. 2005; 11(4): 249-259. doi: 10.1108/13552540510612938
146. Quadrani P, Pasini A, Mattioli-Belmonte M, et al. High-resolution 3D scaffold model for engineered tissue fabrication using a rapid prototyping technique. Medical & Biological Engineering & Computing. 2005; 43(2): 196-199. doi: 10.1007/bf02345954
147. Chua CK, Leong KF, An J. Introduction to rapid prototyping of biomaterials. Rapid Prototyping of Biomaterials. Published online 2020: 1-15. doi: 10.1016/b978-0-08-102663-2.00001-0
148. Sing SL, Tey CF, Tan JHK, et al. 3D printing of metals in rapid prototyping of biomaterials: Techniques in additive manufacturing. In: Rapid Prototyping of Biomaterials. Elsevier. 2020: 17-40. doi: 10.1016/b978-0-08-102663-2.00002-2
149. Ansari AI, Sheikh NA. Bone Tissue Regeneration: Rapid Prototyping Technology in Scaffold Design. Journal of The Institution of Engineers (India): Series C. 2022; 103(5): 1303-1324. doi: 10.1007/s40032-022-00872-2
150. Sun F, Wang T, Yang Y. Hydroxyapatite composite scaffold for bone regeneration via rapid prototyping technique: a review. Rapid Prototyping Journal. 2021; 28(3): 585-605. doi: 10.1108/rpj-09-2020-0224
151. Sharma P, Joshi D, Dhanopia A, et al. A review of rapid prototyping and its applications. SKIT Research Journal. 2020; 10(1): 89. doi: 10.47904/ijskit.10.1.2020.89-97
152. Leong K, Cheah C, Chua C. Solid freeform fabrication of three-dimensional scaffolds for engineering replacement tissues and organs. Biomaterials. 2003; 24: 2363-2378. doi: 10.1016/S0142-9612(03)00030-9