Proceedings of the 4th International Conference on Materials Chemistry and Environmental Engineering
DOI: 10.54254/2755-2721/63/20240995

Mechanistic study on the role of 3D-Printed biomimetic coral bone scaffolds in bone defect repair

Zeyu Liu[1], Wenjie Dong[2], Zihao Shi[2], Jie Pei[1], Tengfei Ma[1], Kun Fu[1,3]

[1]First Affiliated Hospital of Hainan Medical University, Hainan Medical University, Haikou, China
[2]The First Affiliated Hospital of Hainan Medical University, Hainan Medical University, Haikou, 571199, China

[3]fukun2015@126.com

Abstract. With the continuous innovation and development of 3D printing technology, 3D-printed biomimetic coral bone scaffolds have demonstrated significant potential in the field of bone defect repair. This paper aims to explore in-depth the mechanistic study of 3D-printed biomimetic coral bone scaffolds in bone defect repair, by systematically reviewing relevant literature and analyzing their potential mechanisms in promoting bone growth and improving the success rate of bone defect repair. Firstly, this paper introduces the fabrication process and material characteristics of 3D-printed biomimetic coral bone scaffolds. Secondly, the paper discusses the mechanisms of 3D-printed biomimetic coral bone scaffolds in terms of biocompatibility, biomechanical performance, as well as their roles in vascularization and bone formation. Finally, the paper outlines future research directions for 3D-printed biomimetic coral bone scaffolds, including further optimization of material properties, improvement of printing precision, and expansion of clinical applications.

Keywords: 3D printing, biomimetic coral bone scaffolds, bone defect repair, bone formation mechanisms

1. Introduction

In recent years, with the rapid development of medical technology, the field of bone defect repair is undergoing a revolutionary transformation. As one of the pioneers in this revolution, 3D printing technology has attracted widespread attention. In this transformative landscape, biomimetic coral bone scaffolds, as innovative repair materials, have become a focal point due to their unique structure and biocompatibility. This review aims to delve into the mechanistic study of 3D-printed biomimetic coral bone scaffolds in bone defect repair, with the anticipation of providing a scientific theoretical basis for future treatments of bone defects.

Bone defects, whether caused by trauma, infection, tumor resection, or other diseases, are common clinical issues that significantly impact patients' quality of life and physical functions. Traditional treatment methods, such as bone grafts and allografts, can alleviate bone defects to some extent but are still constrained by limitations such as donor scarcity and rejection reactions [1]. Therefore, finding a customizable, biocompatible, and well bone-integrating repair material is urgently needed. The rise of 3D printing technology offers a novel approach to address this challenge. Through this technique, we can precisely customize the shape and structure of bone scaffolds to better accommodate individual patient differences. Biomimetic coral bone scaffolds, characterized by a porous structure and excellent biocompatibility, are widely applied in bone defect repair. Their biomimetic microstructure not only provides an ideal environment for cell implantation but also promotes angiogenesis and the growth of bone cells [2].

In this paper, we will explore the key mechanistic roles of 3D-printed biomimetic coral bone scaffolds in bone defect repair, providing a scientific foundation for future research and clinical applications. In-depth research in this field will drive bone defect repair technology towards a more personalized and efficient direction, ultimately delivering better treatment outcomes and quality of life for patients.

2. Literature Review

The treatment of bone defects using 3D-printed artificial coral bone scaffolds is a promising research area. Studies indicate that 3D-printed bone scaffolds, such as those made from tricalcium phosphate bioglass and hydroxyapatite/tricalcium phosphate, can effectively induce bone growth and integration, thereby enhancing bone regeneration [3-4]. These scaffolds can be customized based on the specific clinical conditions of patients, offering personalized treatment approaches [4-5]. Additionally, 3D-printed bone cement implants have been successfully used to treat bone defects in the distal humerus, showcasing the potential of this technology in complex bone defect reconstruction. Recent advancements in bone tissue engineering have witnessed positive outcomes in the repair of bone defects using 3D-printed artificial coral bone scaffolds [5]. The effectiveness of 3D-printed scaffolds in enhancing bone ingrowth, integration, and promoting efficient bone repair has been demonstrated. These scaffolds, composed of tricalcium phosphate bioglass and biomimetic oxygen-enriched structures, have been proven to sustainably release oxygen, thereby enhancing the survival, growth, and osteogenic differentiation of bone marrow mesenchymal stem cells [6]. Relevant literature further discusses the processes of 3D-printing porous ceramic scaffolds and the selection of bone repair materials, emphasizing the importance of optimizing scaffold design and highlighting the potential prospects of 3D printing technology in this field [7].

2.1. Preparation Process, Material Characteristics, and Innovations of 3D-Printed Biomimetic Coral Bone Scaffolds

The preparation process and material characteristics of 3D-printed biomimetic coral bone scaffolds are crucial factors for the successful application of this technology in bone defect repair. The successful preparation of 3D-printed biomimetic coral bone scaffolds begins with the selection of materials. Commonly used materials include biodegradable polymers, bioceramics, and bioactive substances. These materials need to exhibit excellent biocompatibility, compatibility with human tissues, and gradual degradation over a specific period. The preparation process starts with Computer-Aided Design (CAD), where a digital model defines the scaffold's geometric shape and internal structure. This step forms the basis for personalized fabrication, allowing customized design based on the specific bone defect conditions of patients to enhance repair effectiveness [8]. Utilizing layer-by-layer manufacturing technology, the digital model is segmented into layers and printed layer by layer. 3D printing technology precisely overlays materials according to the predefined CAD model, achieving accurate three-dimensional structural preparation. This step determines the final form and internal structure of the scaffold. After preparation, the scaffold may undergo post-processing steps, such as removing residual scaffold materials and surface polishing, ensuring a smooth, non-toxic surface with appropriate mechanical properties. The uniqueness of biomimetic coral bone scaffolds lies in their porous structure, simulating the microstructure of natural coral bones. This porous structure provides an ideal environment for cell growth, aiding in the attachment, growth, and differentiation of bone cells. The biocompatibility of the printing material is crucial to ensure that the scaffold does not induce noticeable immune reactions or rejection when implanted in the body. The selection of biodegradable materials promotes gradual scaffold degradation and integration with surrounding tissues. Materials must possess sufficient biomechanical properties to withstand bone loads and provide necessary mechanical support. Biomaterials like bioceramics often exhibit good biomechanical properties, adapting to the mechanical requirements of bone tissue. Some scaffolds may contain bioactive substances, such as growth factors or drugs, to promote cell proliferation, differentiation, or inhibit inflammatory reactions, thereby accelerating the healing process of bone defects [9]. These scaffolds, designed with high precision of microstructures through 3D printing technology, mimic the porosity and complex structure of natural coral. This design provides an ideal growth environment for cells, promoting cell adhesion and proliferation while creating favorable conditions for vascularization and bone formation [9]. The use of biocompatible materials in 3D-printed biomimetic coral bone scaffolds reduces the risk of immune rejection, facilitating strong integration with surrounding tissues. Moreover, the biodegradable nature of the scaffold means it gradually degrades into biologically acceptable byproducts, evolving alongside new bone tissue and reducing the need for secondary surgeries. The scaffold surface can be coated with bioactive substances such as growth factors and extracellular matrix components. These substances play a crucial role in the repair process, guiding cell differentiation, proliferation, and tissue regeneration, thereby promoting vascularization and bone tissue formation. Scaffold design not only considers microstructure but also focuses on its biomechanical properties [10]. The scaffold provides appropriate mechanical support, simulating the mechanical environment of natural bones, activating the biological response of surrounding bone cells and aiding in the bone formation process. 3D printing technology allows the customization of scaffolds based on a patient's specific anatomical structure and the shape of the bone defect. This personalized customization capability enhances the precision of treatment, enabling the scaffold to better adapt to the specific needs of the patient [10]. Overall, 3D-printed biomimetic coral bone scaffolds, through meticulous preparation processes and excellent material characteristics, provide a viable solution for personalized and efficient bone defect repair. These features enable the scaffold to better adapt to the physiological and anatomical structures of patients, thereby improving the success rate of treatment.

2.2. Mechanisms of Action in terms of Biocompatibility and Biomechanical Performance of 3D-Printed Biomimetic Coral Bone Scaffolds

3D-printed biomimetic coral bone scaffolds typically employ materials such as biodegradable polymers and bioceramics, known for their excellent biocompatibility. The compatibility between scaffold materials and surrounding tissues prevents noticeable immune rejection reactions, contributing to the long-term stability of the scaffold within the body. The microstructure and surface treatment of the scaffold's surface are crucial for cell adhesion and biocompatibility. The porous structure provides a larger surface area, facilitating cell attachment and proliferation. Surface treatments, such as coating with bioactive substances or nano-scale surface modifications, can further enhance the biocompatibility of the scaffold. The gradual degradation of biodegradable scaffold materials implanted in the body allows them to be gradually replaced by newly formed bone tissue. This degradation property reduces the stimulus to surrounding tissues from the implant while promoting bone tissue regeneration. Well-compatible scaffolds promote interactions with surrounding tissues and the vascular system. The bioactive portion on the scaffold's surface attracts and promotes cell adhesion, proliferation, and differentiation, thereby accelerating the healing process of bone defects [11]. 3D printing technology allows for the design of the scaffold's internal structure, better simulating the microstructure of natural bones. Well-designed porous structures not only improve the biomechanical performance of the scaffold but also provide sufficient pore space to promote cell invasion and the formation of new blood vessels. The selection of materials with good strength and toughness ensures that the scaffold can withstand bone loads and provide necessary mechanical support. High-strength materials, such as bioceramics, are often used to guarantee the stability of the scaffold under load conditions. The biomechanical performance of the scaffold needs to adapt to the mechanical environment of bone tissue, including parameters like elastic modulus and compressive strength. This helps the scaffold to work in harmony with surrounding bone tissues, preventing issues caused by mechanical mismatch. The biomechanical performance of the scaffold not only depends on its static characteristics but also includes biomechanical stimuli to cells and tissues. Moderate biomechanical stimuli help regulate cell activities and promote bone regeneration. By optimizing biocompatibility and biomechanical performance, 3D-printed biomimetic coral bone scaffolds can effectively play a significant role in bone defect repair, promoting the regeneration and healing of bone tissues. This comprehensive mechanism positions the scaffold as an innovative treatment method that holds promise to replace traditional bone transplantation methods [12].

2.3. Mechanisms of 3D-Printed Biomimetic Coral Bone Scaffolds in Angiogenesis and Osteogenesis Promotion

The 3D-printed biomimetic coral bone scaffold plays a crucial role in promoting angiogenesis and the osteogenic process. The detailed mechanisms of action in these two aspects are elaborated as follows: The porous structure of the biomimetic coral bone scaffold simulates the microstructure of natural coral, providing an ideal three-dimensional environment that facilitates the invasion of endothelial cells and the occurrence of angiogenesis. The rational design of the porous structure enables the scaffold to offer sufficient surface area, promoting the growth of new blood vessels. The scaffold's surface may be coated with bioactive substances such as growth factors or extracellular matrix components, guiding and stimulating the migration and proliferation of endothelial cells in surrounding tissues. The release of bioactive substances continuously promotes the process of angiogenesis after the implantation of the scaffold within a specified period [13].

The porous structure not only provides channels for the invasion of endothelial cells but also, through the interaction between cells and scaffold materials, activates a series of cellular signaling pathways. Angiogenesis typically involves complex interactions between cells, including endothelial cells, fibroblasts, and immune cells. The structure and chemical properties of the scaffold may guide the directional growth of newly formed blood vessels inside the scaffold, contributing to the formation of a vascular system connected to the vascular network in the surrounding tissues. The biodegradable nature of the biomimetic coral bone scaffold allows it to be gradually replaced by surrounding bone tissue without triggering significant inflammatory reactions. The biomechanical performance of the scaffold needs to adapt to the mechanical environment of bone tissue, aiding in stimulating bone cell activity. Moderate biomechanical stimuli promote the proliferation and differentiation of bone cells, contributing to bone formation. The ceramic components in the biomimetic coral bone scaffold may contain minerals such as calcium and phosphorus, catalyzing the mineralization process in surrounding tissues and promoting osteogenesis. The release of bioactive substances and the interaction between the scaffold and surrounding cells can activate various cellular signaling pathways, including Wnt, BMP, and FGF, which play a regulatory role in bone formation. The porosity of the scaffold is one of its key features, facilitating the settlement of endothelial cells and osteoblasts. The porous structure of the scaffold simulates the structure of natural bone tissue, providing an excellent attachment point and growth space for cells. This microenvironment activates cell signaling pathways, initiating the biological processes of angiogenesis and bone tissue regeneration. The selection of scaffold materials also plays a critical role. Biocompatible materials can harmoniously coexist with surrounding tissues, reduce immune reactions, and promote cell adhesion and proliferation. Additionally, scaffold materials may include bioactive substances such as growth factors and extracellular matrix components, guiding cell differentiation into osteoblasts and endothelial cells. By simulating the structure of coral, the scaffold provides appropriate biomechanical properties, offering mechanical support to surrounding bone tissue and stimulating bone cells. This mechanical stimulation helps regulate the expression of genes related to bone formation, driving the osteogenic process [14-16]. In summary, the 3D-printed biomimetic coral bone scaffold, through its unique structure and chemical properties, regulates cell behavior, guides angiogenesis, and activates signaling pathways related to bone formation. It plays a synergistic role in bone defect repair, promoting the regeneration and healing of bone tissue.

3. Conclusion

The 3D-printed biomimetic coral bone scaffold demonstrates tremendous potential in repairing bone defects. Through an investigation of its mechanisms, we have revealed its crucial role in promoting osteogenesis and angiogenesis. Firstly, the scaffold's microstructure serves as the foundation for its success. The porous structure, mimicking that of natural coral, provides an ideal growth environment for cells. These minute pores and channels simulate the structure of natural bone tissue, offering a favorable platform for cell adhesion, proliferation, and differentiation. This structural feature activates key signaling pathways, guiding the proliferation of osteoblasts and the growth of endothelial cells. Secondly, the selection of scaffold materials is of paramount importance. The use of biocompatible materials reduces immune rejection reactions, facilitating the integration of the scaffold with surrounding tissues. Additionally, the incorporation of bioactive substances, such as growth factors and extracellular matrix components, promotes cell differentiation and tissue regeneration. These substances, when combined with the scaffold, further accelerate the healing of the bone defect area by regulating the biological behavior of cells [17].

The scaffold also influences the regeneration of bone tissue by providing mechanical support. Its design incorporates appropriate biomechanical properties to offer the necessary support and stability for surrounding bone tissues. This mechanical stimulation aids in activating bone cells and regulating the expression of relevant genes, expediting the osteogenic process [18]. In summary, the 3D-printed biomimetic coral bone scaffold, with its ingeniously designed microstructure, excellent biocompatibility, introduction of bioactive substances, and provision of mechanical support, synergistically contributes to bone defect repair. The development of this technology brings new hope to clinical orthopedics, offering an innovative and feasible method for the treatment of bone defects. However, despite significant progress, further research and practical application are still needed in clinical settings to refine its effectiveness and ensure safety and reliability, ultimately benefiting patients.

Funding

This work was supported by the 2024 Key Project of the Joint Innovation of Health and Medical Technology in Hainan Province (SQ2023WSJK0297). Zeyu Liu and Wenjie Dong are joint first authors of this article.

References

[1] Yang Y, Chu L, Yang S, et al. Dual-functional 3D-printed composite scaffold for inhibiting bacterial infection and promoting bone regeneration in infected bone defect models[J]. Acta biomaterialia, 2018, 79: 265-275.

[2] Huang W, Shan Q, Wu Z, et al. Retrievable covered metallic segmented Y airway stent for gastrorespiratory fistula of carina or main bronchi[J]. The Journal of Thoracic and Cardiovascular Surgery, 2021, 161(5): 1664-1671. e2.

[3] Dutta S D, Hexiu J, Patel D K, et al. 3D-printed bioactive and biodegradable hydrogel scaffolds of alginate/gelatin/cellulose nanocrystals for tissue engineering[J]. International Journal of Biological Macromolecules, 2021, 167: 644-658.

[4] Liu Y, Ma Y, Zhang J, et al. MBG-modified β-TCP scaffold promotes mesenchymal stem cells adhesion and osteogenic differentiation via a FAK/MAPK signaling pathway[J]. ACS applied materials & interfaces, 2017, 9(36): 30283-30296.

[5] Ryan E J, Ryan A J, González-Vázquez A, et al. Collagen scaffolds functionalised with copper-eluting bioactive glass reduce infection and enhance osteogenesis and angiogenesis both in vitro and in vivo[J]. Biomaterials, 2019, 197: 405-416.

[6] Niu H, Ma Y, Wu G, et al. Multicellularity-interweaved bone regeneration of BMP-2-loaded scaffold with orchestrated kinetics of resorption and osteogenesis[J]. Biomaterials, 2019, 216: 119216.

[7] Wang M, Li H, Yang Y, et al. A 3D-bioprinted scaffold with doxycycline-controlled BMP2-expressing cells for inducing bone regeneration and inhibiting bacterial infection[J]. Bioactive Materials, 2021, 6(5): 1318-1329.

[8] Hasan A, Waibhaw G, Saxena V, et al. Nano-biocomposite scaffolds of chitosan, carboxymethyl cellulose and silver nanoparticle modified cellulose nanowhiskers for bone tissue engineering applications[J]. International journal of biological macromolecules, 2018, 111: 923-934.

[9] Wang H, Deng Z, Chen J, et al. A novel vehicle-like drug delivery 3D printing scaffold and its applications for a rat femoral bone repairing in vitro and in vivo[J]. International journal of biological sciences, 2020, 16(11): 1821.

[10] Dang M, Koh A J, ** X, et al. Local pulsatile PTH delivery regenerates bone defects via enhanced bone remodeling in a cell-free scaffold[J]. Biomaterials, 2017, 114: 1-9.

[11] Kolanthai E, Sindu P A, Khajuria D K, et al. Graphene oxide—a tool for the preparation of chemically crosslinking free alginate–chitosan–collagen scaffolds for bone tissue engineering[J]. ACS applied materials & interfaces, 2018, 10(15): 12441-12452.

[12] Pan S, Yin J, Yu L, et al. 2D MXene‐integrated 3D‐printing scaffolds for augmented osteosarcoma phototherapy and accelerated tissue reconstruction[J]. Advanced Science, 2020, 7(2): 1901511.

[13] Zhang Q, Ma L, Ji X, et al. High‐strength hydroxyapatite scaffolds with minimal surface macrostructures for load‐bearing bone regeneration[J]. Advanced Functional Materials, 2022, 32(33): 2204182.

[14] Tang W, Lin D, Yu Y, et al. Bioinspired trimodal macro/micro/nano-porous scaffolds loading rhBMP-2 for complete regeneration of critical size bone defect[J]. Acta biomaterialia, 2016, 32: 309-323.

[15] Hasan A, Waibhaw G, Saxena V, et al. Nano-biocomposite scaffolds of chitosan, carboxymethyl cellulose and silver nanoparticle modified cellulose nanowhiskers for bone tissue engineering applications[J]. International journal of biological macromolecules, 2018, 111: 923-934.

[16] Figueiredo L, Pace R, d'Arros C, et al. Assessing glucose and oxygen diffusion in hydrogels for the rational design of 3D stem cell scaffolds in regenerative medicine[J]. Journal of tissue engineering and regenerative medicine, 2018, 12(5): 1238-1246.

[17] Yang S, Li X, Liu P, et al. Multifunctional chitosan/polycaprolactone nanofiber scaffolds with varied dual-drug release for wound-healing applications[J]. ACS Biomaterials Science & Engineering, 2020, 6(8): 4666-4676.

[18] Wang L, Li D, Huang Y, et al. Bionic Mineralized 3D‐Printed Scaffolds with Enhanced In Situ Mineralization for Cranial Bone Regeneration[J]. Advanced Functional Materials, 2023: 2309042.