Strategies for Enhancing the Mechanical Properties of Hydrogels in Bone Tissue Engineering

Wencao Wang

The College of Information, Mechanical and Electrical Engineering, Shanghai Normal University, Shanghai, China

1000530448@smail.shnu.edu.cn

Keywords: Bone Tissue Engineering; Hydrogels; Mechanical Properties; Enhancement Strategy; Bone Defect Treatment

Abstract: Bone tissue engineering, as an important branch of regenerative medicine, aims to reconstruct functional bone tissue by integrating biomaterials, cells, and bioactive factors, addressing the limitations of traditional bone grafting. Hydrogels are increasingly used in the field of bone tissue engineering due to their biocompatibility, unique swelling properties and relatively simple preparation methods. They can provide a three-dimensional growth environment for cells, mimic the natural extracellular matrix, promote angiogenesis, modulate immune responses, promote cell adhesion, proliferation and differentiation, and serve as a vehicle for drug delivery, thus accelerating bone regeneration. However, hydrogels, as excellent scaffold materials in bone tissue engineering, are often limited in their application for load-bearing tissue repair due to mechanical performance constraints. Specifically, traditional hydrogels demonstrate insufficient mechanical strength and toughness, poor compressive performance, and low fatigue strength, making them inadequate for withstanding the complex stresses involved in the growth and remodeling processes of load-bearing tissues. This research analyzes the existing strategies that can be used to enhance the mechanical properties of hydrogels and discusses their performance in bone tissue engineering, including cross-linking strategies, material composites, and structural regulation. Among these, crosslinking strategies can achieve a compressive strength of 1.5 MPa for hydrogels while maintaining an 80% high water content. Material composites can triple the compressive modulus of gelatin hydrogels and activate osteogenic signaling pathways through ion release. Structural regulation can increase the compressive strength of hydrogels to 2.5 MPa, supporting osteoblast infiltration and angiogenesis. This research may provide new insights for the development of hydrogels with superior mechanical properties.

1. Introduction

Bone defects are common deformities caused by tumors, injuries, and congenital malformations. When a bone defect exceeds the body's self-healing ability and cannot spontaneously regenerate, it poses significant challenges for clinical treatment, necessitating transplant intervention for effective treatment. Autologous bone has been considered the ideal material for bone grafting because of its immune compatibility, good biological properties, and mechanical strength compatibility. However, it also has some drawbacks. For example, a second surgery is required to obtain the bone graft material, the available amount of bone is limited, and the donor site may have complications. Although allogeneic and xenogenic bones are less available and limited, they carry risks of immune rejection and infection. Bone tissue engineering is a regenerative medicine approach that utilizes biomaterials, cells, and growth factors to construct biologically active and functional bone tissue *in vitro*, to repair or replace damaged bone. Biomaterials play a crucial role in this process as scaffolds, providing a site for cell attachment, proliferation, and differentiation, guiding the formation of new bone tissue. The materials used in bone tissue engineering can be roughly categorized based on their sources and properties into natural biological materials, synthetic biological materials, and bioceramic materials.

For natural biological materials, they include collagen, gelatin, cellulose, chitosan and sodium

  DOI: 10.25236/icceme.2025.011

alginate. They possess good biocompatibility and biodegradability, capable of mimicking the extracellular matrix (ECM) of natural bone tissue. It has shown excellent performance in bone tissue engineering. For example, collagen is the main organic component of bone and has good cell affinity. Chitosan, on the other hand, has antibacterial properties, which can reduce the risk of infection. Synthetic biological materials include polylactic acid (PLA), polycaprolactone (PCL), and polyglycolic acid (PGA). These materials have controllable degradation rates and good mechanical properties, and can be fabricated into different shapes and structures using various processing methods. For example, PCL has a longer degradation time, suitable for applications requiring long-term support, while PLA has good biocompatibility and processability. Bioceramic materials including hydroxyapatite (HA), tricalcium phosphate (TCP), and bioactive glass, have compositions and structures similar to natural bone, exhibiting good bioactivity and bone induction capabilities that promote the adhesion, proliferation, and differentiation of bone cells. Hydroxyapatite is the main inorganic component of bone and has excellent bone conductivity. Bioactive glass can form a hydroxyapatite layer on its surface, establishing a strong bond with bone tissue.

However, the mechanical properties of natural biomaterials are often poor, making it difficult to meet the demands of bone repair. Synthetic biomaterials usually lack cell recognition sites and require surface modifications to improve cell compatibility. Bioceramic materials have high brittleness and low compressive strength. Due to these existing issues, there is a need to develop new bone tissue materials. Hydrogels, as a type of polymer material with a three-dimensional network structure, largely address these problems due to their excellent biocompatibility, controllable shape, high toughness, ease of preparation, and unique porous structure. They are now widely used in the biomedical field, such as drug delivery, tissue engineering, wound dressings, and 3D bioprinting. However, although hydrogels can be used for bone tissue materials and exhibit excellent performance, their mechanical properties still need to be improved during use, limiting their application in load-bearing tissue repair. At the same time, studies indicate that biomaterials that match the mechanical properties of bone are beneficial for the proliferation and mineralization of bone cells, effectively exhibiting good bone conduction and bone induction effects [1, 2]. Therefore, this research mainly analyzes the existing strategies to improve the mechanical properties of hydrogels, thereby enhancing their effectiveness in repairing bone defects.

2. Cross-linking strategies

Crosslinking is one of the core methods to enhance the mechanical properties of hydrogels. Crosslinking can be achieved through physical, chemical, or enzymatic reactions. For example, double network hydrogels introduce two different crosslinked networks, each with significantly different properties—one being a highly crosslinked polyelectrolyte network structure (rigid and brittle), while the other is a loosely crosslinked neutral network structure (soft and tough). The polyelectrolyte network structure provides 'sacrificial bonds' that help dissipate external stress. The flexible neutral network structure fills the polyelectrolyte network, providing a scaffold that maintains the shape of the hydrogel. This significantly enhances the strength and toughness of the material. Additionally, the Diels-Alder reaction has also been used to construct interpenetrating network hydrogels with excellent mechanical properties.

Zhang et al. developed a novel magnesium ion-containing double-crosslinked hydrogel to improve osteogenesis and angiogenesis mediated by bone scaffolds [1]. As shown in Figure 1, this hydrogel was prepared through phot crosslinking by using methacrylated gelatin (GelMA), thiolated chitosan (TCS), and modified polyhedral oligomeric silsesquioxane (POSS) nanoparticles. Subsequently, active Mg^{2+} ions were introduced into the system through coordination with MgS. This innovative design endowed the hydrogel with excellent mechanical strength, stable network structure, and more suitable pore size and degradation properties. In terms of mechanical performance, this hydrogel exhibited significant advantages and could be customized according to demand to meet specific application scenarios. Its mechanism primarily lies in the introduction of POSS and Mg^{2+}, which not only stimulated the osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) but also effectively promoted angiogenesis *in vitro* and *in vivo*. Experimental results indicated that the

prepared GelMA/TCS/POSS-Mg hydrogel could effectively promote cell adhesion, spreading, and proliferation, thereby providing strong support for subsequent bone regeneration at rat cranial defect sites.

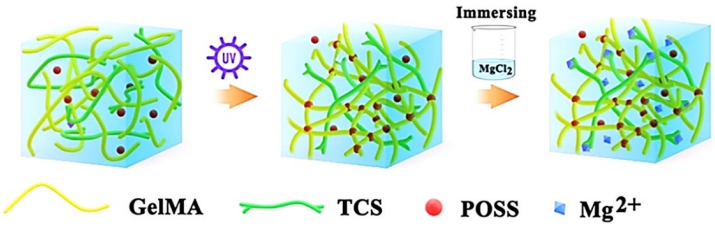

Figure 1: Schematic diagram of the preparation of GelMA/TCS/POSS-Mg hydrogel [1].

Li et al. developed a dual-network hydrogel based on gellan gum (GG) for promoting bone regeneration [2]. This hydrogel was prepared using a one-step mixing method, where GG serves as the first network, while a cross-linking agent-containing polymerizable monomer forms the second network (Figure 2). A synthesized monomer containing phosphate groups, 2-methacrylamidoethyl phosphate (MDP), was introduced into the second network to promote in situ mineralization. After the addition of the second network, the mechanical properties of the hydrogel were significantly improved, including an increase in compressive modulus and ultimate stress compared to the non-cross-linked group. The phosphate groups in the MDP monomer can promote the formation of hydroxyapatite on the surface of the hydrogel, thereby enhancing its mineralization ability, effectively promoting bone mineralization in the mouse osteoblastic cell line MC3T3-E1.

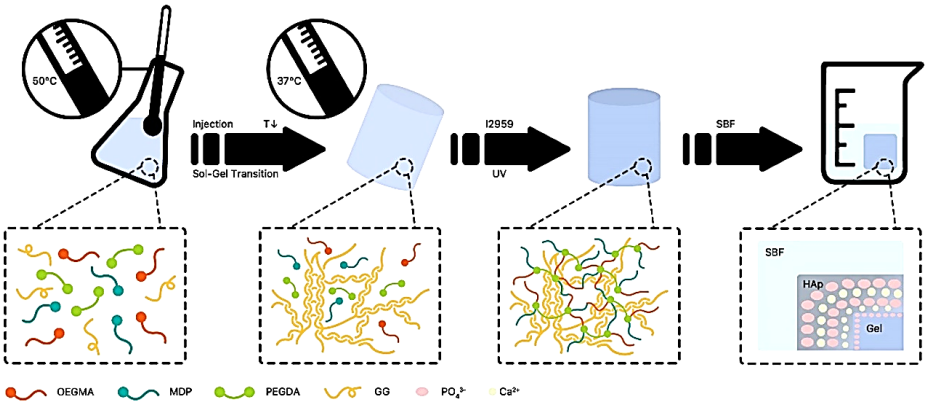

Figure 2: Schematic diagram of the fabrication of injectable p(MDP-co-PEGMA) @GG double network hydrogel [2].

Xu et al. prepared a novel porous polyvinyl alcohol/sodium alginate/hydroxyapatite (PVA/SA/HA) composite hydrogel using a dual crosslinking method [3]. They mixed PVA, SA, and HA in a certain mass ratio and formed a stable three-dimensional network structure through physical and chemical crosslinking. By changing the mass ratio of PVA/SA/HA, the mechanical properties, water content, and porosity of the hydrogel can be regulated. When the weight ratio of PVA/SA/HA was fixed at 42:18:40, the composite hydrogel exhibited optimized compressive modulus (41.74±7.86 kPa), water content (86.99±0.72%), and porosity (79.98±1.61%). These properties make it an ideal candidate for bone repair materials. PVA, SA, and HA could be evenly combined to form a hydrogel with a uniform interpenetrating porous structure. FTIR and XRD results further confirmed the good compatibility and uniform integration among the three. Additionally, in vitro biodegradation and mineralization experiments demonstrated that the hydrogel gradually degraded in PBS solution and formed flaky HA nanocrystals on its surface, which helps promote bone tissue regeneration.

3. Material composites

3.1 Introduction of nanocomposites

Haraguchi et al. expanded the concept of new nanocomposites to the field of hydrogels. Introducing nanomaterials (such as hydroxyapatite, graphene oxide, or nanoclay) into the hydrogel

matrix can significantly enhance its mechanical properties and is widely applied in bone tissue engineering [4]. The following will discuss in detail two strategies for nanocomposites.

The first type is nano-biomaterial ceramic composite hydrogels. It is a type of composite material that combines the advantages of nano-bio ceramics and hydrogels, with broad application prospects in the biomedical field. Bio-ceramics have unique advantages in biocompatibility, biodegradability, and biomechanical properties, making them important materials for bone regeneration and repair. The addition of nano-bio ceramics can significantly improve the mechanical properties of hydrogels and impart biological activity, promoting bone regeneration.

Wang et al. developed a novel gelatin methacrylamide (GelMA)-polyethylene glycol diacrylate (PEGDA)-nano-hydroxyapatite (nHA) composite hydrogel scaffold [5]. By mixing GelMA and PEGDA and adding nHA, a stable crosslinked structure was formed under UV light exposure, where the Ca^{2+} in nHA formed [HO]Ca^{2+}[OH] bridging structures with the hydroxyl groups in GelMA, thereby enhancing stability. In terms of mechanical properties, the addition of nHA can control the mechanical properties of the composite hydrogel and reduce the degradation rate, making it more stable compared to pure GelMA-PEGDA hydrogels. nHA not only provides additional crosslinking points but also enhances the overall network strength by forming bridging structures with the hydroxyl groups in GelMA.

The second type is nano-clay based hydrogels. It is a type of composite material that combines the advantages of nano-clay and hydrogels, with broad applications in biomedical engineering and environmental protection. Compared to other nanoparticle materials, nano-clay particles still exhibit good biocompatibility at higher concentrations, and their degradation products are not only non-toxic but also beneficial for osteogenic differentiation. Hydrogels themselves are polymers with a three-dimensional network structure that can absorb a large amount of water, and the addition of nano-clay can significantly improve the mechanical properties, thermal stability, and adsorption performance of hydrogels.

Liu et al. developed an injectable gelatin/alginate/Laponite nanocomposite hydrogel to promote bone healing in a rat cranial critical-sized defect model [6]. This hydrogel is prepared by mixing gelatin, alginate, and Laponite, capable of forming a stable three-dimensional network structure *in vivo*, thus mimicking the composition and structure of natural ECM. The preparation process involves mixing a gelatin solution with a Laponite dispersion, followed by the addition of sodium alginate solution and a crosslinking reaction. Laponite acts as a reinforcing agent, improving the mechanical properties and stability of the hydrogel, making it more suitable for applications in bone tissue engineering. The hydrogel possesses good mechanical properties, can withstand certain pressure without rupture, while maintaining flexibility and injectability. The hydrogel promotes cell proliferation and differentiation by providing a microenvironment similar to natural ECM. Rat bone marrow mesenchymal stem cells (rBMSCs) encapsulated within the hydrogel can survive and significantly proliferate in vitro. Hydrogels loaded with rBMSCs can significantly promote bone healing at the site of the cranial defect in rats, demonstrating better outcomes compared to hydrogels without cells, and without any side effects.

3.2 Introduction of conductive materials

By introducing conductive materials into hydrogels, conductive hydrogels can be prepared that combine the biocompatibility of hydrogels with the excellent electrical properties of conductive materials. These conductive hydrogels not only possess good physical properties but also suitable electrical properties, allowing for efficient transmission of electrical signals to cells, thereby promoting effective communication between cells, which is especially important for excitable tissues such as nerves and muscles. Some conductive materials, such as carbon-based materials, can adsorb proteins and serve as load-bearing materials, thereby enhancing the mechanical properties of the hydrogel, making it more suitable for bone repair and regeneration. Available conductive materials can be classified into metal nanoparticles, carbon-based materials, and conductive polymers. Hybrid hydrogels synthesized with metal particles have excellent physicochemical properties, bone inductivity, and osteogenic potential, showing great research prospects in the field of bone tissue

engineering. Various metal nanoparticles, such as gold, silver, and copper, have been widely studied for bone tissue engineering to enhance the performance of hydrogels.

Celikkin et al. primarily investigated the enhancement of X-ray attenuation properties of 3D printed gelatin methacryloyl (GelMA) hydrogels by introducing gold nanoparticles (AuNPs) of varying sizes and concentrations, thereby improving their imaging visibility and biocompatibility in bone tissue engineering [7]. The GelMA hydrogel used in the study was prepared by reacting gelatin with methacrylic anhydride, followed by dissolving it in deionized water to form a homogenous solution. To further enhance the X-ray attenuation capacity of the hydrogel, AuNPs of different sizes and concentrations were incorporated, and 3D printing was performed using photopolymerization techniques to construct scaffold materials with specific structures. The mechanical properties of the GelMA hydrogel were significantly improved after the addition of AuNPs, particularly in terms of elastic modulus. This enhancement effect is attributed to the interactions between AuNPs and GelMA molecular chains, as well as the uniform dispersion of AuNPs within the hydrogel matrix. Specifically, the presence of AuNPs increased the crosslinking density within the hydrogel, thereby enhancing its overall mechanical strength and stability.

Various carbon-based materials have been used in the construction of hydrogel composite scaffolds for bone tissue engineering, including carbon nanotubes (CNTs), graphene oxide (GO), and graphene quantum dots (GQDs). CNTs possess excellent mechanical, thermal, and electrical properties, which can significantly enhance the strength and modulus of hydrogel composites. CNTs can promote the adhesion and proliferation of bone-related cells and induce osteogenic differentiation. GO has a large specific surface area and modifiable surface functional groups, which can load drugs and growth factors to achieve targeted regulation of bone regeneration. GO can also regulate the polarization state of macrophages, promoting the improvement of the bone immune microenvironment and accelerating bone repair. GQDs have good biocompatibility and optical properties, making them suitable as carriers for biological imaging and drug delivery, while also promoting angiogenesis and bone formation, accelerating the regeneration of bone tissue.

Zhou et al. primarily explored the ability of GO as a growth factor delivery vehicle to enhance the chondrogenic differentiation of human mesenchymal stem cells (hMSCs) within a three-dimensional hydrogel [8]. GO sheets were allowed to absorb transforming growth factor β3 (TGFβ3), and these TGFβ3-loaded GO sheets were then integrated into a collagen hydrogel matrix. Subsequently, human mesenchymal stem cells were encapsulated in this collagen hydrogel containing the GO-TGFβ3 complex to assess its promoting effect on chondrogenic differentiation (Figure 3). GO was able to efficiently absorb and stabilize TGFβ3, reducing its release, thereby continuously stimulating the phosphorylation of Smad2 within cells, enhancing the expression levels of cartilage-related genes, and promoting the deposition of cartilage-specific extracellular matrices. This mechanism ensures the effectiveness of TGFβ3 during prolonged culture without the need for further supplementation.

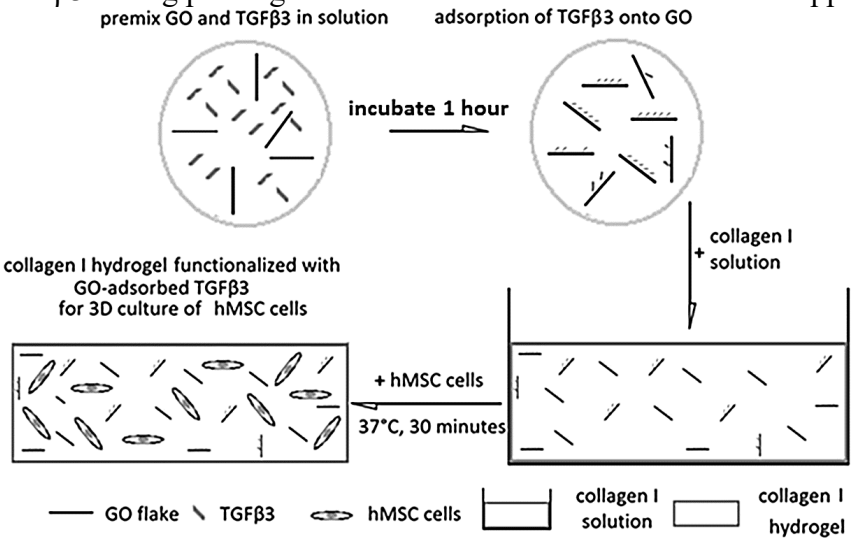

Figure 3: Schematic diagram of GO-TGFβ3 composite collagen hydrogel preparation [8].

Introducing conductive polymers into hydrogels is a promising strategy in bone tissue engineering. Conductive polymers commonly used in bone tissue engineering include polypyrrole (PPy), polyaniline (PANi), and polythiophene derivatives. These polymers can be used alone or in combination with other materials (such as nanomaterials and bioceramics) to further optimize the performance of the hydrogels.

The conductive hydrogel of GelMA-PANi is developed [9]. This composite hydrogel is prepared by incorporating PANi clusters into the photo-polymerized GelMA hydrogel. PANi is synthesized by dissolving aniline and ammonium persulfate in hydrochloric acid solution, and then dispersed into the GelMA solution to form a uniform mixture. This method ensures good compatibility between PANi and GelMA, allowing the subsequent photo-polymerization process to create a stable hydrogel structure. The conductivity of PANi arises from the conjugated double bonds in its chemical structure, which facilitate the flow of electrons. When PANi is embedded in the GelMA matrix, it not only imparts conductive properties to the hydrogel but may also influence the behavior of encapsulated cells through electrical stimulation, such as promoting mineralization or differentiation.

4. Structural regulation

Fibers with higher stiffness than isotropic matrices can enhance the mechanical properties of hydrogels. Compared to ordinary hydrogels, the fiber network-reinforced hydrogels have a structure that is closer to the extracellular matrix, thereby improving cell function and indicating broad application prospects.

Dubey et al. developed a highly tunable bioactive fiber-reinforced hydrogel for guiding bone regeneration (GBR) [10]. This composite material was prepared by integrating a highly porous poly(ε-caprolactone) (PCL) fiber mesh with well-controlled three-dimensional structure into a methacrylated gelatin hydrogel loaded with bioactive amorphous magnesium phosphate. A PCL fiber mesh was manufactured using melt electrospinning technology, and then it was embedded in a methacrylated gelatin hydrogel containing amorphous magnesium phosphate to form a fiber-reinforced hydrogel. The hydrogel exhibited significantly enhanced mechanical properties with increased mechanical strength and stiffness. This is mainly attributed to the additional support structure provided by the PCL fiber mesh, which formed an effective interface with the hydrogel. The presence of amorphous magnesium phosphate not only further improved the mechanical properties of the hydrogel but also promoted enhanced osteogenic potential. The PCL fiber mesh can delay the degradation of the hydrogel, preventing soft tissue invasion while providing a mechanical barrier that allows time for slowly migrating progenitor cells to participate in bone regeneration. These progenitor cells can differentiate into osteoblasts, thus promoting bone tissue formation. The amorphous magnesium phosphate component in the hydrogel may stimulate osteogenic-related gene expression by releasing bioactive substances such as magnesium ions, thereby enhancing the effects of bone regeneration. This hydrogel is expected to be an ideal candidate for next-generation GBR membranes. It can serve not only as a physical barrier to prevent soft tissue ingrowth into bone defect areas but also promote the regeneration of bone tissue through its bioactive characteristics. This is of significant importance for treating bone damage caused by periodontitis and other conditions requiring guided bone regeneration.

Xu et al. primarily discussed the material properties of fiber-reinforced layered hydrogel nanocomposites and their effects on the osteogenic differentiation of bone marrow stromal cells (BMS cells) [11]. A poly(L-lactide) (PLLA) fiber mesh was prepared through electrospinning technology, and it was coated with a poly(lactic acid-co-ethylene glycol fumarate) (PLEOF) hydrogel precursor solution. Subsequently, these meshes were stacked and pressed together, followed by crosslinking treatment to form a layered fiber-reinforced composite. To enhance the osteoconductivity of the material, HA nanocrystals were added to the precursor solution, and acrylamide-terminated arginine-glycine-aspartic acid (RGD) peptides were conjugated to the hydrogel phase to promote BMS cell adhesion and osteogenic differentiation. The Young's modulus of the composite under dry and wet conditions was significantly higher than that of the individual fiber mesh or PLEOF/HA hydrogel, and its modulus value was within the reported range of wet cancellous bone, indicating

good mechanical strength and biomechanical compatibility.

5. Conclusions

The mechanical properties of hydrogels in bone tissue engineering are enhanced through three methods: cross-linking strategies optimization, material compounding and structural regulation. In terms of cross-linking strategies, the synergistic application of physical cross-linking (such as hydrogen bonds and ionic interactions), chemical cross-linking (such as acrylate group copolymerization), and dynamic covalent cross-linking (such as Schiff-base bonds and boronate ester bonds) effectively improves the mechanical strength and fatigue resistance of hydrogels, while matching the bone regeneration rate through controllable degradation characteristics. The material compounding strategy introduces components like nano-bioceramics, nano-clays, metallic nanoparticles, carbon-based materials, or conductive polymers to construct a composite system that integrates biomimetic mineralization and energy dissipation mechanisms, significantly enhancing the compressive modulus and interfacial bonding capacity of hydrogels. Structural regulation techniques such as integrating PCL fiber networks, gradient stiffness regulation, and mimicking biomimetic layered structures further optimize the stress distribution and nutrient transfer efficiency of hydrogels, providing a chemotactic microenvironment for cells.

The integrated application of the above strategies has achieved multiple breakthroughs. High-strength hydrogel scaffolds can effectively bear physiological loads and maintain the morphological stability of bone defect sites. Bioactive composite systems promote osteogenic differentiation of stem cells by regulating osteogenic-related signaling pathways (such as BMP-2/Smad axis). Structured designs guide new bone tissue to grow in specific directions by simulating the anisotropic characteristics of natural bone matrix. However, existing research still needs to focus on the long-term safety *in vivo*, such as the biocompatibility of degradation products and the risk of chronic inflammation. Clinical translation must address the standardization of scalable preparation processes and establish personalized hydrogel manufacturing technology based on patient-specific defect morphology. Future research directions should focus on elucidating the coupling mechanisms of multimodal mechanical-biological signals, the intelligent design of dynamic responsive hydrogels, and validating their efficacy in repairing large bone defects through multicenter clinical trials, ultimately facilitating the transition of this technology from laboratory to clinical application.

References

[1] Zhang, X., Huang, P., Jiang, G., Zhang, M., Yu, F., Dong, X., Wang, L., Chen, Y., Zhang, W., Qi, Y., Li, W., & Zeng, H. (2021). A novel magnesium ion-incorporating dual-crosslinked hydrogel to improve bone scaffold-mediated osteogenesis and angiogenesis. Materials Science and Engineering: C, 121, 111868.

[2] Li, A., Xu, H., Yu, P., Xing, J., Ding, C., Yan, X., ... & Li, J. (2020). Injectable hydrogels based on gellan gum promotes in situ mineralization and potential osteogenesis. European Polymer Journal, 141, 110091.

[3] Xu, M., Qin, M., Zhang, X., Zhang, X., Li, J., Hu, Y., ... & Huang, D. (2020). Porous PVA/SA/HA hydrogels fabricated by dual-crosslinking method for bone tissue engineering. Journal of Biomaterials Science, Polymer Edition, 31(6), 816-831.

[4] Haraguchi K., Takehisa T. Nanocomposite hydrogels: A unique organic-inorganic network structure with extraordinary mechanical, optical, and swelling/de-swelling properties. Advanced materials, 2002, 14(16), 1120-1124.

[5] Wang, Y., Cao, X., Ma, M., Lu, W., Zhang, B., & Guo, Y. (2020). A GelMA-PEGDA-nHA composite hydrogel for bone tissue engineering. Materials, 13(17), 3735.

[6] Liu, B., Li, J., Lei, X., Miao, S., Zhang, S., Cheng, P., ... & Pei, G. (2020). Cell-loaded injectable gelatin/alginate/LAPONITE® nanocomposite hydrogel promotes bone healing in a critical-size rat

calvarial defect model. RSC advances, 10(43), 25652-25661.

[7] Celikkin, N., Mastrogiacomo, S., Walboomers, X. F., & Swieszkowski, W. (2019). Enhancing X-ray attenuation of 3D printed gelatin methacrylate (GelMA) hydrogels utilizing gold nanoparticles for bone tissue engineering applications. Polymers, 11(2), 367.

[8] Zhou, M., Lozano, N., Wychowaniec, J. K., Hodgkinson, T., Richardson, S. M., Kostarelos, K., & Hoyland, J. A. (2019). Graphene oxide: A growth factor delivery carrier to enhance chondrogenic differentiation of human mesenchymal stem cells in 3D hydrogels. Acta biomaterialia, 96, 271-280.

[9] Sawyer, S. W., Dong, P., Venn, S., Ramos, A., Quinn, D., Horton, J. A., & Soman, P. (2017). Conductive gelatin methacrylate-poly (aniline) hydrogel for cell encapsulation. Biomedical Physics & Engineering Express, 4(1), 015005.

[10] Dubey, N., Ferreira, J. A., Daghrery, A., Aytac, Z., Malda, J., Bhaduri, S. B., & Bottino, M. C. (2020). Highly tunable bioactive fiber-reinforced hydrogel for guided bone regeneration. Acta biomaterialia, 113, 164-176.

[11] Xu, W., Ma, J., & Jabbari, E. (2010). Material properties and osteogenic differentiation of marrow stromal cells on fiber-reinforced laminated hydrogel nanocomposites. Acta biomaterialia, 6(6), 1992-2002.