Applications and Research Progress of Biomaterials for Treating Infected Bone Defects

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Infected bone defects represent a challenging clinical condition that requires simultaneous infection control and bone structure reconstruction. Traditional antibiotic therapy and bone grafting each have inherent limitations. With advances in regenerative medicine and tissue engineering, biomaterials have garnered increasing attention in this field. This review systematically summarizes the research progress of inorganic biomaterials, polymeric biomaterials, and composite biomaterials in the repair of infected bone defects, covering their antibacterial mechanisms, osteogenic properties, and functional integration strategies. The clinical applications of these materials as adjuncts to established surgical techniques, including the induced membrane technique and bone transport, are also reviewed. Current challenges and future directions, including intelligent responsive materials and immunomodulatory strategies, are discussed to provide insights for the development of next-generation biomaterials for infected bone defect repair.

Keywords: infected bone defects; biomaterials; bone tissue engineering; bone regeneration

Introduction

Bone tissue, one of the important structural tissues of the human body, plays a key role in maintaining body shape, supporting movement and protecting vital organs. It is also an important microenvironment for bone marrow hematopoiesis [1]. The skeleton is a highly dynamic complex structure composed of organic matrix and inorganic mineral components, including osteoblasts, osteoclasts, osteocytes, extracellular matrix (ECM), vascular network and immune cells [2]. These complex structures and cell compositions maintain the metabolic balance of bone tissue and provide a degree of self-repair and regenerative capacity [3]. In clinical practice, bone defects caused by trauma, infection, tumors, or degenerative diseases are very common [4,5]. Although bone tissue has some self-healing potential, defects that exceed the body's intrinsic repair capacity result in so-called critical-sized bone defects. At this time, relying solely on the body's regeneration is often insufficient to achieve complete repair, and treatment through surgical intervention and bone reconstruction techniques is required [6].

Infected bone defects are complex orthopedic conditions, usually secondary to open wounds, postoperative infection after internal fixation of fractures, or chronic osteomyelitis [7]. When pathogenic microorganisms invade bone tissue, they can trigger a persistent inflammatory response and lead to destruction of bone tissue structure [8]. At the same time, bacteria can form biofilm structures on the bone surface or implant surface, making the microorganisms more resistant to the body's immune response and antibiotic treatment, thus making it difficult to completely eliminate the infection [9]. Long-term infection not only affects the normal metabolism of bone tissue but may also cause complications such as osteonecrosis, nonunion, and recurrent infection. In severe cases, it can even develop into chronic osteomyelitis or systemic infection, which seriously affects the patient's quality of life and can be life-threatening [10,11]. At present, the treatment of infection-related bone defects usually requires a comprehensive intervention strategy, among which controlling infection and reconstructing bone defects are the two core goals of treatment. Sufficient surgical debridement is an important step in the treatment of bone infection. In the treatment of chronic osteomyelitis or fracture-related infection, surgery is required to thoroughly remove necrotic bone tissue, infected soft tissue and potential bacterial biofilm, and remove unstable implants to reduce local bacterial load and improve tissue blood supply environment [12,13]. However, bone loss caused by the debridement process, initial trauma and infection itself often leads to or exacerbates bone defects, which highlights the necessity and urgency of seeking efficient bone defect reconstruction solutions while effectively controlling infection [14].

In the treatment of infected bone defects, the main clinical approach is to use systemic or local antibiotics to inhibit the growth of pathogens. However, because bone tissue has

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a relatively limited blood supply, intravenous administration often fails to maintain sufficient drug concentrations at the site of infection, and long-term systemic administration may also lead to drug toxicity and increased bacterial resistance [15]. Therefore, achieving sustained and effective antibacterial effects locally while promoting bone tissue regeneration has become an important research direction in the treatment of infected bone defects. Traditional reconstruction strategies, including autologous bone grafting, allogeneic bone grafting, the induced membrane technique, and bone transport, have been reported to be constrained by donor site morbidity, limited graft availability, immune rejection risks, and lengthy treatment durations [4,7,16,17,18].

In recent years, with advances in regenerative medicine and tissue engineering, the application of biomaterials in the treatment of infected bone defects has gradually attracted widespread attention. However, traditional bone substitutes still have several limitations, including inadequate mechanical strength, asynchronous degradation rates with bone regeneration, and insufficient osteoinductive capacity.

To overcome these limitations, researchers have increasingly focused on biomaterials, aiming to develop repair strategies that better meet the treatment needs of infected bone defects. Related research strategies are no longer limited to simple structural filling, but are dedicated to endowing materials with more suitable biological functions through various pathways. For example, local anti-infection barriers are constructed by loading antibiotics or metal ions to compensate for the inadequacy of systemic medication, while the adhesion, proliferation, and differentiation of osteoblast-related cells are actively regulated by modifying the surface morphology of materials, optimizing pore size, or incorporating bioactive factors such as bone morphogenetic proteins, thereby accelerating the bone repair process. These different directions of biomaterial research and development provide new options and insights for clinical treatment from the perspectives of controlling infection, inducing osteogenesis, and improving mechanical support [19,20]. Therefore, systematically reviewing the surgical treatment strategies for infected bone defects and the research progress of related biomaterials is of great significance for optimizing clinical treatment plans. This article reviews recent progress in bone reconstruction techniques for infected bone defects and the application of biomaterials in infection control and bone repair. It also provides an outlook on future research directions, aiming to offer a reference for clinical treatment and the development of new materials.

Pathological Process and Treatment Implications of Infected Bone Defects

Bone healing is a well-orchestrated process that proceeds through three overlapping phases: inflammation phase, repair phase, and remodeling phase [21]. Following injury, pro-inflammatory cytokines are rapidly released, and the hematoma formed locally serves as a temporary scaffold that recruits inflammatory cells and bone marrow mesenchymal stem cells (BMSCs) to the defect site via signaling axes such as Stromal Cell-Derived Factor-1/C-X-C motif chemokine receptor 4(SDF-1/CXCR-4) [22,23]. The recruited BMSCs subsequently undergo osteogenic differentiation through intramembranous or endochondral ossification, leading to the formation of cartilaginous and hard callus that is eventually remodeled into lamellar bone [24]. This orderly regenerative cascade is severely disrupted when pathogenic microorganisms colonize the defect. Staphylococcus aureus, the most prevalent pathogen in bone infections [2], establishes persistent local infection through multiple complementary mechanisms. The bacterium invades and survives within osteoblasts via fibronectin-binding protein-mediated interactions with α5β1 integrin on the cell membrane, effectively transforming these bone-forming cells into pathogen reservoirs [25,26]. Concurrently, S. aureus adhering to bone or implant surfaces secretes extracellular polymeric substances to form dense biofilms that act as both physical barriers against antimicrobial agents and as sources of bacterial dissemination to distant sites [2]. Persistent infection further induces the formation of staphylococcal abscess communities encased within fibrin pseudocapsules that shield bacteria from immune clearance.

These pathological processes collectively reshape the local microenvironment into a state that is hostile to bone regeneration. Persistently elevated pro-inflammatory cytokines, including Interleukin-1 beta (IL-1β) and Tumor Necrosis Factor-alpha (TNF-α), enhance osteoclast activity and bone resorption while simultaneously suppressing osteoblast differentiation through disruption of the Bone Morphogenetic Protein-2 (BMP-2) signaling pathway [27,28]. The resulting imbalance between excessive bone resorption and impaired bone formation represents the fundamental reason why infected bone defects fail to heal. This hostile microenvironment also limits the efficacy of systemic antibiotic therapy due to poor local blood supply and renders conventional bone grafts highly susceptible to bacterial recolonization. These challenges have driven the development of biomaterials that can simultaneously address infection control and bone regeneration—materials that should ideally integrate osteoconductivity to guide new bone ingrowth, osteoinductivity to actively stimulate osteogenesis, and the capacity to resist or eliminate local infection [29,30].

Application of Biomaterials in the Treatment of Infected Bone Defects

Inorganic Biomaterials

Inorganic biomaterials play an important role in the field of bone tissue engineering. Their composition is usually similar to that of natural bone minerals, thus providing good structural support and bioactive environment for new

bone formation [19,31]. Calcium-phosphate bioceramics are the most widely studied inorganic bone repair materials. Their main representatives include hydroxyapatite (HA) and tricalcium phosphate (TCP) [32]. These materials, highly similar to natural bone minerals in chemical composition, have good biocompatibility and osteoconductivity, and have better mechanical strength [33]. HA can provide a microenvironment for osteoblasts to attach and proliferate, promote osteoblast differentiation and new bone formation, while TCP can be gradually degraded *in vivo* and replaced by new bone tissue, which is conducive to the long-term reconstruction of bone tissue [34,35]. The osteoconductivity of these ceramics is facilitated by the gradual release of calcium and phosphate ions during degradation, which not only provides essential mineral building blocks for new bone formation but also creates a local ionic microenvironment conducive to osteogenic differentiation [35]. Calcium-phosphate ceramic powder is usually processed into the required shape by dry pressing, slurry molding or three-dimensional (3D) printing, and then the density and mechanical strength are improved by high-temperature sintering, finally obtaining a porous scaffold suitable for bone defect repair [36]. Pearson's team [37] built a model using New Zealand white rabbits. The results showed that in the infected bone defect model, the bone mineralization rate and bone mineral density of the porous HA scaffold were significantly better than those of autologous bone grafts, suggesting that it can be used as an effective alternative to autologous bone. In terms of clinical research, Sasaki et al. [38] mixed β-TCP with autologous cancellous bone in equal proportions and applied it to the induction membrane technique to treat infected bone nonunion of the lower extremities. The median time for bone healing after surgery was 6 months, which preliminarily confirmed the feasibility of β-TCP as an autologous bone volume-enlarging material in the repair of infected bone defects. Notably, although calcium phosphate ceramics lack inherent antibacterial properties, they can be used as a delivery platform for antibiotics or other antibacterial components due to their porous structure and good carrier properties. This strategy also provides a foundation for the subsequent development of composite biomaterial systems with both anti-infective and osteogenic functions.

Bioactive glass is another inorganic bone repair material with significant application potential. In physiological fluid environments, it can release various ions such as silicon, calcium, and phosphorus, and form a hydroxyapatite layer similar to natural bone minerals on the surface of the material, thereby promoting the bonding between bone tissue and the material [39]. With its excellent bioactivity and osteoconductivity, bioactive glass has been widely used in bone tissue engineering scaffolds and bone defect filling. In addition to promoting bone regeneration, bioactive glass also has antibacterial potential and can serve as a drug carrier for loading antibiotics or antibacterial molecules, enabling sustained local drug release in bone defects and improving infection control [40]. Lindfors et al. [41] reported that bioactive glass S53P4 showed good tolerability and preliminary efficacy in the treatment of chronic osteomyelitis. A retrospective study compared the therapeutic effects of S53P4 and autologous bone grafting in patients with infected nonunion. The results showed that there were no significant differences between the two groups in terms of infection control rate, bone healing rate and functional recovery, suggesting that bioactive glass can effectively control infection while filling defects and is expected to become a suitable alternative to autologous bone grafting [42]. However, there are still some limitations in the application of single bioactive glass. For example, burst release may occur during drug release, which may shorten the effective treatment time. Whether this limitation truly compromises clinical efficacy remains unclear, as most existing studies have not systematically correlated release kinetics with infection recurrence rates. For this reason, researchers often improve the drug release behavior through material compositing or surface modification to prolong the duration of its antibacterial effect.

In recent years, the doping of inorganic biomaterials with metal ions to endow them with antibacterial properties has become a major research focus. Silver (Ag), zinc (Zn) and strontium (Sr) ions have all been shown to have some antibacterial or osteogenic effects [43,44]. The antibacterial action of silver ions involves multiple mechanisms, including disruption of bacterial cell membrane integrity, generation of reactive oxygen species that induce oxidative stress, and interference with intracellular protein and DNA function, ultimately leading to bacterial death [35]. Zinc ions can promote osteoblast proliferation and regulate the expression of bone-related genes to enhance bone formation capacity in bone tissue repair, and can also exert a bactericidal effect by inducing the production of reactive oxygen species. It is expected to serve a dual function in the treatment of infected bone defects. In addition, strontium ions can further improve the bone repair process by regulating immune cell function and promoting angiogenesis [45].

Overall, inorganic biomaterials show promising applications in the treatment of infected bone defects. Through strategies such as structural design, ion doping, and drug loading, these materials can be endowed with dual antibacterial and osteogenic functions. However, single inorganic materials still have limitations in terms of mechanical properties, degradation rate, and bioactivity. Therefore, in practical applications, they often need to be combined with polymeric materials or bioactive molecules to construct more comprehensive multifunctional material systems that better meet the clinical requirements for treating infected bone defects.

Polymer Biomaterials

Polymer biomaterials play an important role in the field of bone tissue engineering. They usually have good biocompatibility, biodegradability and processability, and can provide a suitable microenvironment for cell adhesion, growth and tissue regeneration. Among them, chitosan and its derivatives, as well as hydrogel materials, have become major research focuses in this field due to their unique physicochemical properties and biological functions. Chitosan is a natural polysaccharide derived from chitin. It has good biocompatibility, biodegradability and low toxicity, and is widely used in the biomedical field [46]. Its molecules contain positively charged amino groups, which can interact electrostatically with negatively charged bacterial cell membranes, destroy cell membrane structure and inhibit bacterial growth, and exhibit intrinsic antibacterial activity [47]. In addition to antibacterial effects, chitosan can also promote bone tissue regeneration. Studies have shown that chitosan can provide cells with a microenvironment similar to the extracellular matrix, promote osteoblast adhesion and proliferation, and induce the expression of bone-related genes (such as osteopontin, osteocalcin and alkaline phosphatase), thereby promoting bone formation [48,49]. Meanwhile, the chitosan oligosaccharides produced during the degradation of chitosan have biological activity, which can promote wound healing and reduce inflammatory response, further enhancing their application potential in bone tissue repair [50]. However, natural chitosan has poor water solubility under neutral or alkaline conditions, and its osteogenic induction ability is relatively limited. To address these limitations, researchers have developed a variety of chitosan derivatives through chemical modification strategies such as quaternization, carboxymethylation, sulfation, and phosphorylation [46]. These derivatives significantly improve water solubility, antibacterial activity, or synergistic ability with growth factors while retaining the fundamental biological characteristics of chitosan, thereby laying the foundation for its further functional applications. A substantial portion of the antibacterial assessments for chitosan derivatives have been performed in planktonic culture systems, whereas the clinical challenge of chronic bone infection centers on biofilm eradication—a distinction that is not always addressed in material characterization studies.

Hydrogels are another important class of polymeric biomaterials. Hydrogels are formed by the physical or chemical cross-linking of hydrophilic polymers to form a three-dimensional network structure, which can absorb and retain a large amount of water or biological fluid while maintaining structural integrity [51]. These materials have good biocompatibility, degradability, high porosity, and can simulate the microenvironment of the natural extracellular matrix, so they have attracted much attention in the field of bone tissue engineering, especially in the repair of infected bone defects [52]. In terms of antibacterial function, hydrogels can act through a contact-killing mechanism. Specifically, the introduction of quaternary ammonium salts or guanidine groups into the hydrogel network enables the material surface to carry a positive charge, which directly disrupts the bacterial cell membrane upon contact, and achieves a long-lasting antibacterial effect without relying on drug release. In terms of bone repair, hydrogels can provide a three-dimensional scaffold for bone marrow mesenchymal stem cells and promote osteogenic differentiation by mimicking the physicochemical cues of the extracellular matrix [53]. Studies have shown that gelatin-based hydrogels can support the adhesion and proliferation of osteoblasts and induce the expression of bone-related genes such as alkaline phosphatase and osteocalcin [54,55]. Additionally, the unique three-dimensional network structure and good permeability of hydrogels enable them to serve as reservoirs for active substances, a property that makes it possible to achieve multifunctional synergistic therapy by loading antibacterial drugs or growth factors.

In general, natural and synthetic polymers each have their own advantages and limitations. To compensate for the shortcomings of single materials in terms of mechanical properties, bioactivity, or antibacterial efficacy, researchers are increasingly combining them with other functional components to construct more comprehensive bone repair systems.

Composite Biomaterials

In research on infected bone defect repair, single materials often struggle to simultaneously meet the requirements for anti-infection, bone regeneration, and mechanical support. Therefore, in recent years, researchers have increasingly combined inorganic biomaterials with polymeric materials to construct multifunctional scaffolds that integrate the advantages of different materials, aiming to achieve synergistic antibacterial and osteogenic effects. Inorganic materials typically possess good osteoconductivity and bioactivity, while polymeric materials exhibit excellent processability, biodegradability, and drug delivery capabilities. Through rational design of composite structures, a suitable repair microenvironment can be formed in the bone defect area, while simultaneously achieving the sustained release of local antibacterial drugs, thereby improving the overall treatment efficacy of infected bone defects.

The composite system of calcium phosphate ceramics and natural polymer materials has been widely studied. The composite material of HA and chitosan has also shown good application potential in bone tissue engineering. Tang et al. [56] constructed a chitosan composite scaffold and applied it to a rabbit ulnar bone defect model, and the results showed that the composite scaffold could promote new bone formation and improve the bone defect repair effect, suggesting that chitosan composite material has good application potential in bone tissue engineering. In addition, chitosan material can promote the mineralization process

by chelating calcium ions, thereby further improving the osteogenic capacity of the material. Chen et al. [57] constructed a chitosan-based composite scaffold and verified it in an animal skull defect model. The results showed that the composite material could promote bone tissue regeneration and improve the bone repair effect [57]. Furthermore, Oftadeh's team [58] prepared an electrospun conductive scaffold by combining hydroxyapatite nanoparticles with conductive polymers, and seeded human bone marrow mesenchymal stem cells on the scaffold *in vitro* while applying electrical stimulation. Studies have found that hydroxyapatite and electrical stimulation have a functional synergistic effect in osteogenic differentiation. The combined effect of the two can significantly upregulate the expression levels of osteogenic markers such as osteocalcin, alkaline phosphatase, osteopontin and Runx2, suggesting that hydroxyapatite may participate in the early differentiation of stem cells into osteogenic progenitor cells, while electrical stimulation helps differentiated cells to further mature [58]. Similarly, Zhao et al. [59] loaded bone morphogenetic protein-2 onto a calcium-deficient hydroxyapatite porous scaffold and coated the scaffold surface with sulfated chitosan to improve the release characteristics of growth factors. In a rat skull defect model, the proportion of bone morphogenetic protein-2 released by the composite system was significantly higher than that in the uncoated group, and the degree of new bone formation was also more obvious eight weeks after the operation, indicating that sulfated chitosan coating can effectively regulate the release behavior of growth factors and enhance the osteogenic effect *in vivo* [59]. These studies show that composites of calcium phosphate ceramics and natural polymers can improve the mechanical compatibility and degradation behavior of materials while further enhancing the osteogenic activity of the system through biophysical stimulation or regulated growth factor release. This approach provides a diversified design space for the performance optimization of composite materials. In inorganic-polymer composite systems, constructing scaffolds with antibacterial and bone-regenerative functions through the incorporation of drugs or growth factors has also become an important research direction. Pacheco et al. [60] prepared silica-calcium phosphate nanocomposite materials in their study and used them as a synergistic delivery system for vancomycin and bone morphogenetic protein-2. Fourier transform infrared spectroscopy analysis revealed that the composite material can form a stable interaction with vancomycin molecules, thereby achieving effective drug loading and sustained release. Further experiments showed that the nanocomposite system can promote bone regeneration-related processes while inhibiting bacterial growth, showing its application potential in the treatment of infected bone defects. The above studies show that incorporating antibacterial drugs or osteogenic growth factors into the inorganic-polymer composite system can endow the material with dual functions—local anti-infection activity and active induction of bone regeneration, without compromising the mechanical properties of the scaffold.

In recent years, composite systems constructed from bioactive glass and polymer materials have gradually become a major research focus because polymer incorporation may improve the mechanical properties of bioactive glass. Gentile et al. [61] introduced bioactive glass (CEL2) in different proportions into a chitosan/gelatin blend system, prepared a composite scaffold with an interconnected porous structure by freeze-drying, and used genipin for cross-linking to enhance its mechanical strength and thermal stability. The results showed that as the content of bioactive glass increased, the compressive modulus of the composite scaffold gradually increased. *In vitro* experiments confirmed that the composite scaffold did not negatively impact the metabolic activity of periosteal stem cells and could promote their osteogenic differentiation. In addition, the introduction of bioactive glass also improved the stability of the scaffold in aqueous solution and endowed the material with good bioactivity. This strategy of combining inorganic active components with natural polymers not only improved the mechanical properties of the scaffold but also enhanced the osteogenic ability of the system [61]. In recent years, researchers have also introduced antibacterial nanomaterials into composite scaffolds to further enhance their anti-infection properties. Sun et al. [62] constructed a BMP-2/AgNP /collagen composite scaffold and evaluated its biological properties. The results showed that the composite material exhibited significant antibacterial activity *in vitro*, while not adversely affecting the adhesion and proliferation of bone marrow mesenchymal stem cells. BMP-2 released from the material could promote osteogenic differentiation, thereby enhancing bone tissue regeneration while inhibiting infection. This study shows that simultaneously introducing antibacterial nanoparticles and osteogenic growth factors into the composite material can achieve a synergistic effect between antibacterial and osteogenic functions. Overall, the composites of bioactive glass and polymer can compensate for the limited mechanical properties of bioactive glass alone while expanding its biological functions through the incorporation of antibacterial components or growth factors, providing a flexible material-design platform for repairing infected bone defects.

Composite hydrogel systems have also attracted increasing attention in recent years for the repair of infected bone defects. Hydrogels have a high-water-content structure and good biocompatibility, and can be used as cell and drug delivery platforms. By combining them with inorganic nanoparticles or bioceramics, their mechanical properties and bioactivity can be enhanced. In their study, Wang et al. [63] introduced polymethyl methacrylate (PMMA) bone cement into the Hydroxypropyltrimethyl ammonium chloride chitosan (HACC) (quaternized chitosan) based hydrogel system and further incorporated nano-hydroxyapatite (nano-HA) to construct a composite hydrogel. The experi-

mental results showed that the composite material not only has good antibacterial properties but can also form a stable scaffold structure in the bone defect area, thereby achieving the dual functions of infection control and bone repair [63]. In their study, Lee et al. [64] used succinylated chitosan hydrogel to fix bone graft materials. *In vivo* experiments confirmed that it could stably maintain β-tricalcium phosphate particles in the transplant area for up to 6 weeks. Based on this, the authors proposed that the hydrogel system may also serve as a delivery carrier for bioactive drugs [64]. This study indicates that integrating a delivery-carrier function with a hydrogel structure may play an important role in the repair of infected bone defects. A practical consideration that is rarely addressed in such studies is whether the hydrogel can be injected through a standard cannula and remain intact under the mechanical forces present during early postoperative mobilization. Meanwhile, many researchers have further explored the application of hydrogels as drug-controlled release platforms. Tao et al. [65] constructed a chitosan -based thermosensitive hydrogel and loaded vancomycin to prepare a nanoparticle/gel local drug delivery system. The composite hydrogel has a high drug encapsulation rate and can achieve continuous release of vancomycin within 26 days. In a rabbit osteomyelitis model, the hydrogel not only showed good anti-infection properties but also promoted the repair of bone defects [65]. In addition to drug delivery, hydrogels can also serve as stem cell carriers for bone tissue regeneration. Huang et al. [66] prepared a biomimetic thermosensitive gel scaffold using chitosan, nano-hydroxyapatite and collagen as raw materials, loaded rat bone marrow mesenchymal stem cells into the scaffold and injected it into the body. The results show that the loaded stem cells could survive in the gel for at least 28 days, and the inflammatory response caused by the composite system was milder than that of the simple gel, providing a biocompatible microenvironment for the survival and function of stem cells in the body [66]. Together, these studies show that hydrogels, with their three-dimensional network structure and tunable physicochemical properties, can not only immobilize bone graft materials to maintain local structural stability but also serve as drug or cell delivery carriers, demonstrating broad application potential in the regeneration and repair of infected bone defects.

Overall, composite biomaterials, by integrating multiple functional units such as inorganic materials, polymers, and antibacterial components, demonstrate significant advantages in the treatment of infected bone defects. Inorganic components provide excellent osteoconductivity and structural support, polymers endow the scaffold with superior processability and drug delivery capabilities, while antibacterial nanocomponents effectively inhibit bacterial growth. The synergistic effect of these multiple functions makes composite materials promising for applications in infection control, bone regeneration, and tissue integration. However, most studies are still in the experimental stage, and their long-term safety, degradation behavior, and clinical translational efficacy require further investigation. In the future, optimizing material structure design and combining advanced manufacturing technologies such as 3D printing may enable the construction of more efficient and personalized composite biomaterial systems to better meet the clinical needs of infected bone defect treatment.

A summary of the key biomaterial categories discussed in Sections Inorganic Biomaterials, Polymer Biomaterials and Composite Biomaterials, along with their representative examples, primary antibacterial and osteogenic mechanisms, and corresponding references, is provided in Table 1.

Clinical Applications

Clinically, treatment strategies differ for bone defects of different sizes. For defects smaller than 2 cm, acute shortening or primary bone grafting is usually used for repair; for defects of 2–6 cm, induced membrane technology, post-acute shortening lengthening, or bone transport can be used; for large defects exceeding 6 cm, bone transport technology is mainly used for reconstruction. Although the above techniques have been widely used in clinical practice, each has its inherent limitations—the healing reliability of induced membrane technology in high-risk infection environments remains uncertain, acute shortening often results in limb length discrepancies requiring secondary surgery, and bone transport faces problems such as long external fixation cycles, delayed healing at the joint points, and pin tract infections [67]. These shortcomings provide an entry point for biomaterial-based intervention. By leveraging the local anti-infection properties of biomaterials or their ability to promote osteogenesis, treatment outcomes may be further optimized within the existing surgical framework. In recent years, advances in tissue engineering and biomaterials research have enabled some inorganic and composite material systems to show preliminary application potential in the surgical treatment of chronic osteomyelitis and infected bone defects.

The clinical application of biomaterials in infected bone defect repair can be understood along a spectrum of increasing functional complexity. At the most fundamental level, osteoconductive materials have been employed as void fillers that provide structural support without necessarily carrying additional therapeutic agents. Sasaki et al. [38] mixed β-TCP with autologous cancellous bone in approximately equal proportions as a filling material in the induced membrane technique for treating infected long bone nonunion, and observed good bone healing. The researchers concluded that β-TCP could serve as a supplement or volume-expanding material for autologous bone grafting. Romanò's team [68] further demonstrated that bioactive glass S53P4, when used alone to fill defects after debridement of chronic osteomyelitis, achieved infection control rates comparable to those of antibiotic-loaded hydroxyapatite/calcium sulfate and tricalcium phosphate

Table 1. Summary of biomaterials for the treatment of infected bone defects.

Material category	Representative examples	Key mechanisms
Inorganic Biomaterials		
Calcium phosphate ceramics	HA, β-TCP	Osteoconductive scaffold; gradual Ca^{2+}/PO_4^{3-} release supports mineralization; lacks intrinsic antibacterial activity; can serve as an antibiotic carrier
Bioactive glasses	S53P4, CEL2	Surface HA layer formation; alkaline ion release raises local pH and osmotic pressure for antibacterial effect; drug carrier capability
Metal ion-doped materials	Ag^+, Zn^{2+}, Sr^{2+}	Ag^+: membrane disruption, ROS generation, protein/DNA damage; Zn^{2+}: osteoblast promotion + ROS-mediated antibacterial; Sr^{2+}: immunomodulation and angiogenesis
Polymeric Biomaterials		
Chitosan and derivatives	CS, HACC, CMC, SCS, PCS	Intrinsic antibacterial via electrostatic membrane disruption; ECM-like microenvironment for osteoblast adhesion; SCS enhances BMP-2 bioactivity
Hydrogels	Gelatin-based, CS-based	Contact-killing via quaternary ammonium/guanidine groups; 3D scaffold for BMSCs; reservoir for antibiotics and growth factors
Composite Biomaterials		
CaP–polymer composites	HA/CS, TCP/PLGA/SCS, HA/conductive polymer	Combined osteoconductivity and processability; growth factor delivery; biophysical stimulation (e.g., electrical) synergize with CaP
Bioactive glass–polymer composites	CEL2/CS/gelatin, BMP-2/AgNP/collagen	Improved mechanical properties; antibacterial nanoparticle incorporation; sustained drug release
Multifunctional hydrogels	PMMA/HACC/nano-HA, CS/Vancomycin thermogel, CS/nano-HA/collagen/BMSC	Antibiotic and cell co-delivery; injectability for irregular defects; contact-killing + release-based antibacterial

HA, hydroxyapatite; TCP, tricalcium phosphate; CS, Chitosan; HACC, Hydroxypropyltrimethyl ammonium chloride chitosan; CMC, Carboxymethylcellulose; SCS, Sodium cellulose sulfate; PCS, Polycarbosilane; PLGA, Poly (lactic-co-glycolic acid); BMP-2, Bone Morphogenetic Protein-2; BMSC, bone marrow mesenchymal stem cell; ROS, Reactive oxygen species; ECM, extracellular matrix; 3D, three-dimensional.

combined with demineralized bone matrix. This finding is noteworthy because it suggests that certain inorganic biomaterials can exert meaningful antibacterial effects through their intrinsic surface chemical properties, potentially reducing reliance on locally delivered antibiotics.

A step beyond simple void filling is the deliberate design of materials as local drug delivery systems. Here, the inorganic porous architecture serves not merely as a scaffold but as a reservoir for antibiotics, enabling sustained high-concentration release directly at the infection site. Jiamton et al. [69] reported that vancomycin-, gentamicin-, or fosfomycin-impregnated microporous nano-hydroxyapatite microspheres achieved a treatment success rate of approximately 98% in patients with chronic osteomyelitis, with elevated local antibiotic concentrations and low systemic exposure. The same group extended this strategy to large-segment infected defects by using vancomycin-impregnated calcium sulfate/calcium phosphate composites as bone graft expanders in the second stage of the induced membrane technique; all patients achieved radiographic union without infection recurrence or fixation failure at the final follow-up. These results demonstrate that integrating drug delivery functionality into osteoconductive carriers can address the dual challenge of infection control and bone regeneration within a single procedure.

Moving further along the functional spectrum, bioactively enhanced materials aim not only to fill and disinfect but also to actively accelerate the biological processes of bone repair. This approach is particularly relevant for bone transport, where the protracted consolidation phase and high incidence of docking site nonunion remain significant clinical burdens. Huang et al. [70] compared antibiotic-loaded calcium sulfate-assisted bone transport with traditional bone transport in 85 patients with large post-traumatic tibial defects. The material-assisted group demonstrated a significantly shorter external fixation index, higher limb function scores, and lower rates of axis deviation, docking site nonunion, and infection recurrence. Complementary evidence from a preclinical study by Lin et al. [71] showed that a biodegradable intramedullary implant delivering BMP-2 achieved 100% union at the docking site in a rat femoral bone transport model, compared with only 12.5%–25% in the control group, along with superior bone volume frac-

tion and mechanical properties. Collectively, these studies illustrate how the clinical application of biomaterials has progressed from passive structural replacement toward active biological augmentation, with each level of functional complexity addressing a distinct set of clinical needs.

Overall, existing clinical evidence suggests that various biomaterials have demonstrated certain safety and efficacy in the surgical treatment of infected bone defects. These materials either rely on their intrinsic antibacterial properties or function as local drug delivery systems by loading antibiotics, thereby contributing to infection control while providing osteoconductive scaffolds and offering a useful supplementary strategy to traditional autologous bone grafting. Among the clinical studies reviewed, those reporting successful adoption have generally used materials that can be prepared intraoperatively with minimal additional procedural steps, suggesting that ease of use may be as critical to clinical translation as antimicrobial or osteogenic potency.

Conclusions

The treatment of infected bone defects requires simultaneous infection control and bone reconstruction, and biomaterials have emerged as a promising adjunct to established surgical techniques. This review has examined the current landscape of inorganic, polymeric, and composite biomaterials developed for this purpose. Across these categories, a clear trajectory has emerged: the field is moving from passive structural fillers toward multifunctional systems that integrate antibacterial activity, osteoconductivity, and controlled drug delivery within a single construct. Inorganic materials provide a reliable osteoconductive foundation and have achieved the most advanced clinical translation to date, whereas polymeric materials offer unparalleled versatility as delivery platforms through chemical modification and tunable degradation. Composite systems bridge the gap between these two classes, though their clinical adoption remains at an early stage.

However, several challenges persist. The mismatch between material degradation and new bone formation rates, the difficulty of achieving sustained antibacterial release without early burst, and the scarcity of standardized large-animal models continue to impede direct comparisons across material systems and slow clinical translation. The evidence reviewed here suggests that future progress may depend less on discovering entirely new materials than on the intelligent integration of existing components through spatiotemporally controlled release strategies, immunomodulatory designs that harness host responses, and manufacturing approaches that prioritize intraoperative practicality. As the field matures, closer alignment between material design and specific clinical scenarios, rather than reliance on a one-size-fits-all solution, will be essential for realizing the potential of biomaterial-assisted repair of infected bone defects.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

RXS and DPL designed the research study. RXS performed the literature retrieval. RXS and DPL conducted the literature analysis. RXS drafted the article. Both authors contributed to the critical revision of the manuscript for important intellectual content. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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