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REVIEW ARTICLE

Bio-Active Composite Therapy (BACT) in Regenerative Orthopaedics

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Abstract

Background Bio-Active Composite Therapy (BACT) represents a significant advancement in regenerative orthopaedics, integrating bioactive materials with biological systems to enhance bone and tissue regeneration. This comprehensive approach leverages materials such as hydroxyapatite, bioactive glasses, polymers, and metals to create scaffolds that mimic the extracellular matrix, facilitating cellular activities essential for tissue repair.

Methods A systematic literature review was conducted using databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords such as "Bio-Active Composite Therapy," "regenerative orthopaedics," and "bioactive materials" were employed to identify relevant studies published between 2000 and 2024. Inclusion criteria focused on peer-reviewed articles, reviews, and clinical trials related to the development, application, and evaluation of BACT in bone and soft tissue regeneration. Data extraction emphasized bioactive material types, fabrication techniques, clinical applications, outcomes, and associated challenges. The findings were categorized thematically to synthesize current advancements and identify knowledge gaps.

Results BACT utilizes a diverse range of bioactive materials, with hydroxyapatite and bioactive glasses being predominant due to their osteoconductive and osteoinductive properties. Advanced fabrication techniques, particularly additive manufacturing (e.g., 3D printing), enable the creation of scaffolds with precise geometries and tailored porosity, enhancing cellular adhesion and proliferation. Clinically, BACT has demonstrated efficacy in bone regeneration, cartilage repair, and ligament healing, although biocompatibility and immunotoxicity remain challenges, especially with certain metal oxides like TiO_2. Economic barriers and technical precision in scaffold application also pose significant limitations.

Conclusion BACT holds transformative potential in regenerative orthopaedics by offering tailored, effective treatments for musculoskeletal disorders. Overcoming biocompatibility, safety, and accessibility challenges through interdisciplinary collaboration and technological innovation is essential for its widespread clinical adoption. Future research should focus on optimizing bioactive materials and fabrication methods, alongside rigorous clinical trials to validate long-term efficacy and safety.

Keywords Bio-active composite therapy · Regenerative orthopaedics · Tissue regeneration · Bioactive materials

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Introduction

In the evolving landscape of orthopaedic medicine, the exploration of novel therapeutic strategies that augment the body's inherent regenerative capabilities has emerged as a critical endeavor. Among the spectrum of innovations, Bio-Active Composite Therapy (BACT) has garnered significant attention as a cutting-edge approach for the treatment of musculoskeletal injuries and degenerative conditions [1, 2]. This methodology epitomizes a sophisticated amalgamation of bioactive materials with the principles of regenerative medicine, meticulously engineered to foster tissue repair and facilitate functional recuperation within the orthopaedic framework. The genesis of this approach is deeply rooted in the pioneering discovery of Mesenchymal Stem Cells (MSCs) by A. Caplan in 1989, which unveiled the profound capacity of these cells to repair damaged tissues and organ systems, thereby revolutionizing the prospects of cellular therapy in regenerative medicine [3]. The distinctive attributes of MSCs, encompassing their potential to restore tissue functionality and ensure superior viability with reduced morbidity, have set the foundation for innovative therapeutic paradigms such as BACT [4–6].

BACT represents an intricate and refined approach to regenerative orthopaedics, harnessing the potential of bioactive materials and their composites to drive the repair and regeneration of bone and soft tissues [7]. Central to the efficacy of BACT is the dynamic interplay between these materials and biological entities, aimed at emulating and enhancing the natural healing mechanisms inherent within the body. The composition of BACT is underpinned by a versatile array of materials, including but not limited to hydroxyapatite (HA), bioactive glasses, and a diverse range of polymers and metals. These components are judiciously selected based on their unique properties and contributions to the regenerative matrix, functioning as scaffolds that not only support cellular proliferation and differentiation but also actively participate in the orchestration of tissue regeneration through various biological pathways. Despite the promising strides made in the realm of BACT, there remain significant knowledge gaps that warrant further investigation. Among these is the need for a deeper understanding of the interactions between bioactive materials and the biological milieu, particularly in the context of long-term outcomes and integration with host tissues. Additionally, the optimization of material compositions and configurations to enhance the efficacy and specificity of tissue regeneration presents an ongoing challenge.

The aim of this review article is to provide a comprehensive exploration of BACT within the field of regenerative orthopaedics. By delving into the foundational principles, applications, and recent advancements associated with BACT, we seek to elucidate its transformative potential in redefining the paradigm of musculoskeletal care. Specifically, this article will address the aforementioned knowledge gaps, focusing on the customization of bioactive composite materials for targeted therapeutic applications, and evaluating the clinical implications of BACT in promoting effective and sustainable tissue regeneration. Through this discourse, we venture to foster a nuanced understanding of BACT, highlighting its significance for patients, clinicians, and researchers, and paving the way for future innovations in orthopaedic regenerative medicine.

Methods

A comprehensive literature search was conducted to gather relevant studies, reviews, and clinical trials pertaining to BACT in regenerative orthopaedics. The databases utilized included PubMed, Scopus, Web of Science, and Google Scholar. The search was performed using a combination of keywords and MeSH terms such as "Bio-Active Composite Therapy," "regenerative orthopaedics," "tissue regeneration," "bioactive materials," "hydroxyapatite," "bioactive glasses," "polymers in orthopaedics," and "orthopaedic tissue engineering."

Studies were selected based on the following inclusion criteria:

- Publications from the year 2000 to 2024.
- Peer-reviewed articles, reviews, and clinical trial reports.
- Studies focusing on the development, application, and evaluation of BACT in bone and soft tissue regeneration.
- Research discussing the biocompatibility, mechanical properties, and biological interactions of bioactive materials used in orthopaedics.

Exclusion criteria encompassed:

- Non-English language publications.
- Case reports, editorials, and opinion pieces without substantial data.
- Studies focusing solely on non-orthopaedic applications of bioactive materials.

Data were extracted from the selected studies, focusing on the types of bioactive materials employed, fabrication techniques, clinical applications, outcomes, and reported challenges.

Bio-Active Composite Therapy: An Overview

BACT represents an advanced regenerative strategy that transcends traditional bioactive material integration with biological systems through a comprehensive approach. This strategy is characterized by the synergistic combination of adipose-derived stem cells (ADSCs), the stromal vascular fraction (SVF), and platelet-rich fibrin (PRF), alongside bio catalyzers such as amino acids, vitamins, and reduced glutathione (GSH) [7]. These components collectively enhance cell intake, survival, and overall tissue regeneration by creating an optimal in situ bioreactor environment for tissue repair, while adhering to stringent legal and ethical standards [7, 8]. BACTs leverage the regenerative potential of cellular and blood components, enriching the regenerative milieu and supporting crucial cellular activities necessary for tissue repair [7, 8].

The transition from basic bioactive composite grafts (BACGs) to the more sophisticated BACTs marks a significant evolution in regenerative medicine. This advancement incorporates minimal grade manipulation (MGM) of tissues, addresses programmed cell death (PCD), and utilizes advanced compounds like bio-active cellular matrices to enhance regenerative efficacy [7]. Additionally, BACTs integrate cutting-edge techniques such as cytokine modulation, meticulous donor site preparation, and the targeting of multi-lineage differentiating stress enduring (MUSE) cells to refine and amplify their therapeutic potential, ensuring a more directed and efficient intervention [7, 9, 10].

At the heart of BACTs are bioactive materials, including hydroxyapatite (HA), bioglass, bioactive glasses, organic polymers, and metals, renowned for their compatibility with bone and other tissues as listed in Table 1 [11]. These materials provide a versatile scaffold that promotes cellular adhesion, proliferation, and differentiation. The composite nature of BACTs facilitates the integration of materials with distinct properties, such as the osteoconductivity of HA, the mechanical strength of titanium, or the biodegradability of polymers. This integration supports not only the physical structure of regenerating tissues but also actively participates in their biological regeneration [11–14]. Through the innovative amalgamation of these elements, BACTs embody a holistic and multifaceted approach to tissue repair and regeneration, showcasing the dynamic and evolving field of regenerative medicine.

The efficacy of BACT in promoting tissue regeneration is multifaceted, deeply rooted in the interaction between the bioactive materials and the biological environment. One primary mechanism is the provision of a scaffold that emulates the extracellular matrix (ECM), facilitating the attachment, proliferation, and differentiation of cells. Materials like HA and bioglass can induce the deposition of apatite layers in physiological fluids, promoting osteoblast adhesion and proliferation—a key step in bone regeneration [11, 14]. Moreover, the degradation products of some bioactive materials can beneficially modulate the local biological environment. For instance, the ionic dissolution products of bioglass are known to stimulate angiogenesis and activate genes associated with bone regeneration, fostering a conducive environment for tissue repair [15].

In addition to providing a physical scaffold and modulating the biological environment, BACT therapies also harness the potential of bioactive molecules and growth factors as shown in Fig. 1. These can be incorporated into the composite materials, enabling controlled release to further enhance the regenerative process [16–19]. The inclusion of bone morphogenetic proteins (BMPs) or growth factors (GFs) within a bioactive scaffold, for example, can significantly enhance osteogenesis and angiogenesis, respectively [8, 13]. Another key mechanism involves the stimulation of stem cell

Table 1 Bioactive Materials in BACT [7, 8]

Components	Form of materials	Significance in BACTs
Adipose-Derived Stem Cells (ADSCs)	Mesenchymal stromal cells from adipose tissue	Enhance cell intake and survival, support tissue repair and regeneration
Stromal Vascular Fraction (SVF)	Heterogeneous mixture of cells from adipose tissue	Enhances the regenerative milieu, supports crucial cellular activities
Platelet-Rich Fibrin (PRF)	Peripheral blood derived orthobiologic	Creates an optimal environment for tissue repair by elaborating growth factors in the medium
Bio catalyzers (Amino acids, Vitamins, Reduced Glutathione [GSH])	Small biomicromolecules	Enhance cell function and survival, improve tissue regeneration
Bioactive Materials (Hydroxyapatite [HA], Bioglass, Bioactive Glasses, Organic Polymers, and Metals)	Biomaterials	Provide a scaffold for cellular adhesion, proliferation, and differentiation
Cytokines	Modulation of pro- and anti-inflammatory cytokines	Refines and amplifies therapeutic potential, supports directed intervention
Multilineage differentiating Stress Enduring (MUSE) Cells	Immune privileged, requiring less number compared to MSCs	Enhances therapeutic precision and efficiency

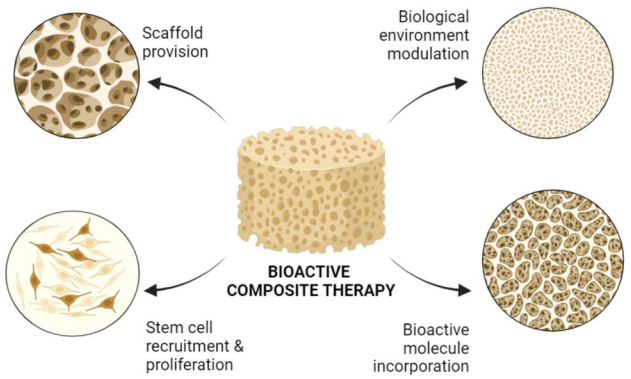


Fig. 1 Mechanism of action of BACT

recruitment and differentiation. Bioactive composites can influence the fate of resident stem cells or those introduced as part of the therapy, enhancing the regeneration of bone and other tissues as these cells differentiate into osteoblasts, chondrocytes, or other cell types under the influence of the scaffold's biochemical cues [8, 20].

By embedding bioactive molecules within the composite matrix, localized and sustained release of therapeutics can be achieved, enhancing the regenerative process while minimizing systemic side effects [21, 22]. This approach allows for the targeted delivery of anti-inflammatory agents, antibiotics, or other drugs that support the healing process [23]. In orthopaedic domain, the versatility of BACT is particularly evident. For bone tissue engineering, the composites are designed to support bone in-growth, provide mechanical stability, and degrade at a rate compatible with new tissue formation. This ensures the restoration of function without the long-term presence of a foreign body [12, 24]. In cartilage repair, the emphasis is on mimicking the ECM's mechanical and biochemical properties to support chondrocyte function and cartilage synthesis [25].

Clinical Applications of BACT in Orthopaedics Bone

Bone regeneration and repair via Bioactive Composite Tissue (BACT) involves employing scaffolds composed of biomaterials that are biocompatible, biodegradable, and possess suitable mechanical properties. These scaffolds offer a temporary structure to facilitate new tissue formation, essential for bone tissue engineering. The design of these scaffolds is crucial, as the mechanical properties of bone can significantly vary, emphasizing the need for scaffolds that closely mimic the natural bone structure for optimal integration and functionality. The materials range from metals, natural and synthetic polymers, to ceramics, each selected for their specific benefits in promoting bone healing and regeneration. This multidisciplinary approach merges materials science, biology, and engineering to enhance the body's innate healing capacity for large bone defects. Significant research, including studies by Ling et al. [20] and Zocci [8], highlights the potential of composites in reducing immunotoxicity concerns associated with orthopaedic implants and enhancing the recruitment and differentiation of progenitor cells into osteoblasts through BACT, thereby promoting bone regeneration and repair [26].

Cartilage

In cartilage repair, bioactive glasses such as Bioglass® 45S5, BonAlive®, and 19-93B3 play a pivotal role. Investigated in various forms—bulk materials, powders, composites, and porous scaffolds—these materials are celebrated for their bone-forming capability, antibacterial properties, degradability, and potentials in soft tissue regeneration and wound healing. The literature underscores their promising avenue for cartilage regeneration and repair, necessitating further research to fully harness their osteogenic and angiogenic potential [27]. Ohba et al. advocate for a multidisciplinary approach in optimizing bioactive factors for cartilage regeneration, emphasizing the development and use of bioactive composite materials designed to mimic the natural extracellular matrix, thereby presenting a viable strategy for cartilage restoration [23].

Ligament and Meniscus

The application principles of BACT in bone and cartilage regeneration also extend to the healing of ligament and meniscus injuries. Despite the scarcity of dedicated research on specific outcomes and optimization strategies for BACT in these areas, the importance of bioactive molecules and scaffolding materials that encourage cellular ingrowth, differentiation, and extracellular matrix formation is recognized. Similar to muscle tissue engineering, these components highlight the need for cellular migration, proliferation, and extracellular matrix formation. In clinical practice, various surgical and nonsurgical methods utilizing BACT aim to enhance natural healing processes and potentially reduce recovery periods for ligament and meniscus injuries, emphasizing the utility of BACT in not only bone and cartilage repair but also in the healing of tendon and ligament injuries [7, 25].

BACT distinguishes itself from other regenerative therapies in orthopaedics through its bespoke tailoring of bioactive components to meet the specific needs of the repair site, exemplified by the selective employment of composites in bone regeneration. This specificity, combined with the capacity to integrate multiple bioactive cues within a single treatment modality, underscores BACT's unique position. Furthermore, the intersection of materials science, bioengineering, and molecular biology in BACT's development

facilitates the creation of advanced treatment modalities capable of addressing multifaceted orthopaedic challenges. This includes the fabrication of scaffolds that not only provide structural support but also actively participate in the healing process, through the release of growth factors or by promoting stem cell recruitment and differentiation, marking a significant advancement in the field of orthopaedic regenerative therapy [12, 25].

Challenges and Limitations

Despite the promising advancements in BACT, several critical limitations must be acknowledged. The clinical validation of many bioactive composites remains limited, with most studies confined to in vitro experiments or small-scale animal models, lacking the robust longitudinal human clinical trials necessary for comprehensive evaluation of long-term efficacy and safety. This gap between laboratory findings and clinical implementation represents a significant barrier to widespread adoption of BACT in standard orthopaedic practice.

Material integration poses another substantial challenge, as achieving seamless incorporation of bioactive composites with host tissues involves complex biological interactions that are difficult to predict and control. The interface between implanted materials and surrounding tissues often presents complications related to mechanical mismatch, inadequate vascularization, and inconsistent degradation rates, which can compromise the overall success of the regenerative process. Furthermore, variations in patient-specific biological responses to bioactive materials add another layer of complexity to standardizing these therapies for broad clinical application.

At the forefront of considerations for BACTs is their biocompatibility and safety. The interaction between bioactive composites and the biological environment they are introduced to is complex and can lead to unforeseen adverse reactions. Studies have demonstrated how different composites, exhibit varying levels of toxicity in vivo [12]. These findings underscore the critical importance of selecting materials that are not only effective in their therapeutic role but also compatible with body tissues to avoid inducing toxic responses. Furthermore, the nuanced immune responses elicited by these materials highlight the variability in biocompatibility across individuals, suggesting that what works for one patient may not be suitable for another. This variability necessitates a robust screening process for bioactive composites, ensuring they do not induce oxidative DNA damage or alter antioxidant enzymes adversely, as observed with TiO2 treatments in mice [12]. Such detailed understanding and testing are imperative to advance BACTs from experimental stages to safe, widely accepted medical treatments.

The application of BACTs is not without its technical and surgical challenges. The precision required in their application is high, given the complexity of accurately evaluating these therapies' efficacy and safety. Techniques such as in vitro mineralization testing using simulated body fluid and in vivo experiments on model organisms like mice are pivotal in assessing the potential of BACTs [12]. However, translating these benchtop findings into successful clinical treatments involves overcoming significant hurdles, including the customization of therapies to individual patient needs, the variability in disease states, and anatomical differences among patients. Moreover, the surgical application of these composites requires not just precision but also a deep understanding of the materials' behaviour within a biological context. For instance, the correct placement and integration of bioactive scaffolds within bone or tissue, ensuring they promote regeneration without compromising the surrounding structures, present a complex challenge. This complexity necessitates a multidisciplinary approach, bringing together expertise from materials science, biology, and clinical medicine to ensure the successful application of BACTs.

The economic implications of BACTs cannot be overstated. The research and development phase of these therapies involve substantial financial investment, primarily due to the sophisticated materials and cutting-edge technologies employed. This investment often translates into high costs for the end therapies, potentially making them inaccessible to a broad segment of patients. The study findings from El-Bassyouni et al., not only reflect the scientific and medical considerations but also hint at the underlying economic challenges in making these therapies widely available [12]. Accessibility extends beyond cost to include the availability of specialized equipment and expertise required to apply these treatments. The disparity in healthcare infrastructure globally means that even if these therapies become economically viable, their application may be limited to regions with the necessary technological and professional resources. This disparity raises ethical considerations about the equitable distribution of advanced medical treatments and underscores the need for strategies aimed at broadening the accessibility of BACTs, ensuring that advancements in regenerative medicine benefit a wide patient population.

Addressing the biocompatibility and safety concerns of BACTs requires a concerted effort in research to elucidate the mechanisms of interaction between bioactive composites and biological systems. Rigorous testing protocols and longitudinal studies are essential to ensure that these therapies do not pose long-term health risks to patients. Furthermore, the development of standardized testing frameworks could facilitate the comparison of bioactivity and toxicity levels across different materials, aiding in the selection of the most suitable composites for clinical applications. On the technical and surgical front, advancements in imaging and surgical

techniques, coupled with the development of customizable bioactive materials, could alleviate some of the challenges related to the precise application of BACTs. Moreover, training programs and workshops for surgeons and medical professionals on the nuances of BACT application would play a crucial role in bridging the gap between theoretical knowledge and clinical practice.

Economically, the exploration of cost-effective production methods and materials could make BACTs more accessible. Policies and funding mechanisms that support research and development in this field could also play a significant role in offsetting the initial high costs associated with these therapies. Additionally, global health initiatives aimed at technology transfer could help in making these advanced treatments available beyond high-income countries, ensuring wider accessibility.

Future Directions

The trajectory of bone tissue engineering and the integration of novel bioactive materials into orthopaedic practice are pivoting towards an exciting future. As advancements in bioactive glasses (BG), polymer composites, and additive manufacturing (AM) technologies such as 3D printing continue to evolve, the focus is increasingly on the exploration of their potential applications across a range of orthopaedic diseases, the need for orthopaedic surgeons to adapt and learn these new technologies, and the importance of rigorous clinical trials to validate their efficacy and safety.

The advent of bioactive materials, including bioactive glasses and their composites with bioresorbable polyesters, has led to the development of scaffolds with patient-specific designs and tailored mechanical and biological properties crucial for bone defect healing [28, 29]. The future direction should emphasize the optimization of these materials and AM techniques as shown in Fig. 2 to produce scaffolds that not only fit anatomically but also possess the desired degradation behaviours and promote effective bone regeneration in a broader spectrum of orthopaedic conditions.

The integration of semiconducting metal oxides like silicon dioxide (SiO2), titanium dioxide (TiO2), and zirconium dioxide (ZrO2), despite the challenges such as TiO2's immunotoxicity, hints at a promising avenue for enhancing scaffold bioactivity and cellular response. Future studies should focus on overcoming these challenges through material

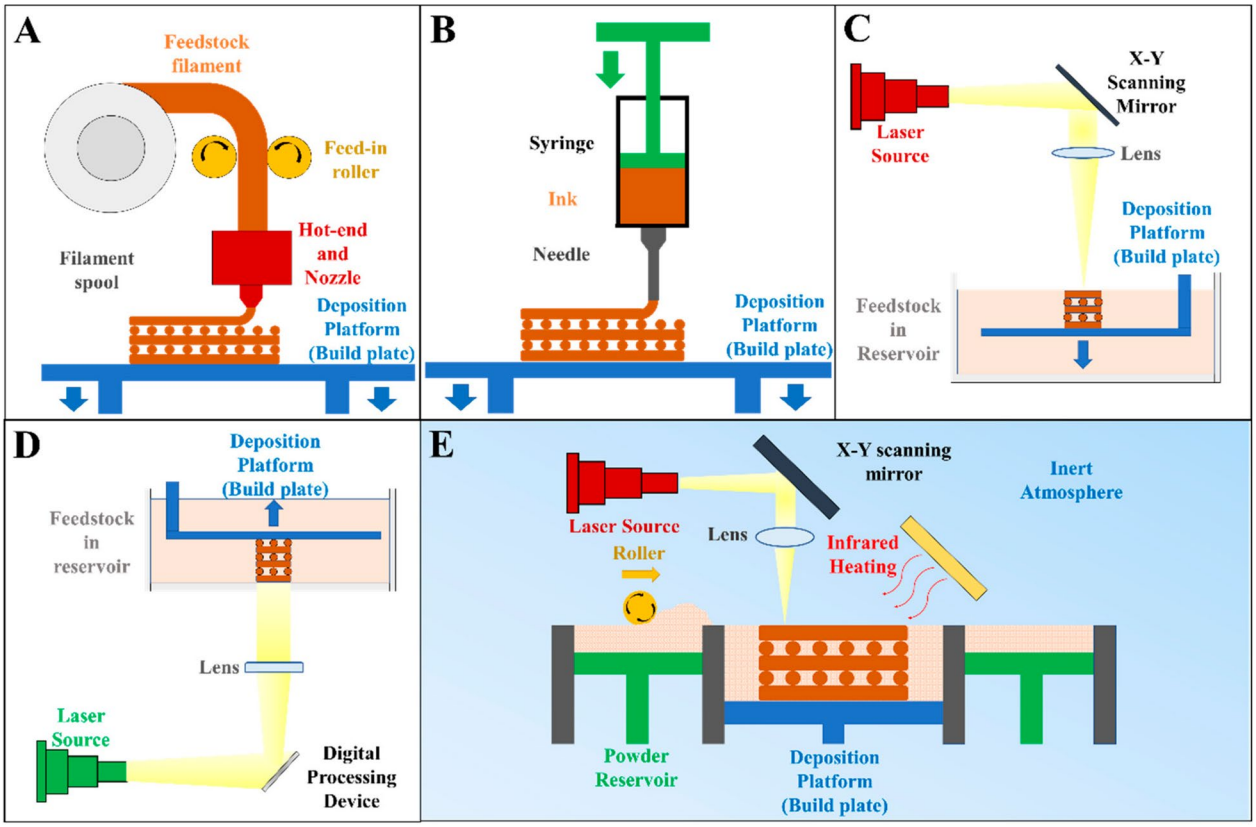


Fig. 2 Schematic view of typical AM technologies applied to fabricate bioactive polymer composites. **A** Melt extrusion; **B** direct ink writing; **C** stereolithography; **D** digital light processing; and **E** selective laser sintering. Adapted from He et al. [28]

innovation and composite synthesis, aiming for a balanced enhancement of biocompatibility and functionality [11, 12, 15, 24, 30].

Furthermore, the potential of hydroxyapatite (HA)-based materials and the advent of bioactive polymers and peptides underscore a significant shift towards organic–inorganic hybrid composites. These materials offer a novel approach for enhancing osteogenic differentiation and proliferation, indicating a pivotal area for future research and application in various bone-related diseases [13, 14, 23, 25].

Technological advancements in scaffold fabrication, particularly through 3D printing and nanotechnology, have revolutionized the creation of structures mimicking the native extracellular matrix. Future directions in this domain should leverage these technologies for the development of scaffolds with even higher precision in mimicry and functionality. This includes the spatial deposition of materials and cells, and the manipulation of material surfaces at the molecular level to enhance bioactivity and interaction with biological tissues [7, 8, 20].

The progression of bioactive materials and tissue engineering constructs (BACT) from the laboratory to clinical application necessitates an expanded focus on clinical trials. These trials are essential for assessing the long-term efficacy, safety, and bioactivity maintenance of these innovations. Future studies should prioritize the design and execution of long-duration clinical trials to comprehensively evaluate the interactions between bioactive composites and the human body [12, 30].

Lastly, the successful integration of BACT into orthopaedic practice requires a concerted effort from an interdisciplinary team comprising materials scientists, bioengineers, and orthopaedic surgeons. The ongoing education and training of orthopaedic practitioners in the latest materials and AM technologies are crucial for the effective implementation of these advancements in treating orthopaedic diseases. This collaborative approach will not only accelerate the development of effective BACT but also ensure their practical applicability and relevance in real-world clinical scenarios [7, 8].

The future of orthopaedics, through the lens of bone tissue engineering and novel bioactive materials, promises a transformative impact on the treatment of various bone-related conditions. By focusing on these future directions, the field can achieve significant advancements in patient care, leveraging the synergistic potential of interdisciplinary collaboration, technological innovation, and rigorous clinical validation.

Exploring the integration of novel bioactive materials in orthopaedics, particularly within the realm of bone tissue engineering, reveals significant advancements in the utilization of bioactive glasses (BG) and their polymer composites. These materials have shown immense potential as scaffolds for bone defect healing, with additive manufacturing (AM) technologies such as 3D printing playing a pivotal role in fabricating scaffolds that exhibit complex geometries tailored to fit specific anatomical requirements and desired degradation behaviours. The use of AM for bioactive glass and its polymer composites enables the creation of well-defined shapes and intricate porous structures, essential for supporting effective bone defect healing. These advancements are critical in producing scaffolds with patient-specific designs and the on-demand spatial distribution of biomaterials, which are pivotal for facilitating the regeneration of bone tissue [29].

Moreover, the combination of bioresorbable polyesters and bioactive glasses marks a significant development in orthopaedic applications. These composite implants and scaffolds for bone tissue engineering embody an attractive approach to achieving scaffolds with the desired mechanical and biological properties. The challenge lies in forming complex interconnected pore structures with the addition of inorganic phases, which are crucial for facilitating bone regeneration. The integration of these materials into scaffolds for bone tissue engineering indicates a promising direction towards enhancing the efficacy of bone defect healing, leveraging the synergistic benefits of bioactive glasses' osteoinductive properties and the biodegradable nature of polyesters as shown in Fig. 3 [28].

These findings underscore the necessity for continued research and development in the field of bone tissue engineering, focusing on the synthesis of novel bioactive materials and the optimization of fabrication techniques. The goal is to achieve scaffolds that not only support bone regeneration but also actively participate in the healing process by directing cellular behaviour and promoting the integration of the scaffold with the native bone tissue.

Future Bioactive Materials

At the core of advancing BACT lies the exploration and integration of novel bioactive materials apart from the traditional bioactive molecules listed in Fig. 4. Recent studies underscore the potential of semiconducting metal oxides like silicon dioxide (SiO2), titanium dioxide (TiO2), and zirconium dioxide (ZrO2) for their distinct properties including biocompatibility, bioactivity, and the ability to promote cellular responses conducive to tissue regeneration [11, 12, 30]. Despite TiO2's pronounced immunotoxicity implications, ongoing research is pivoting towards harnessing its superior catalytic properties while mitigating adverse biological effects. Concurrently, the synthesis of SiO2 and ZrO2 composites with optimized ratios emerges as a promising strategy to enhance material performance without compromising biocompatibility [15, 24].

The quest for innovative materials extends into the domain of hydroxyapatite (HA)-based biomaterials and

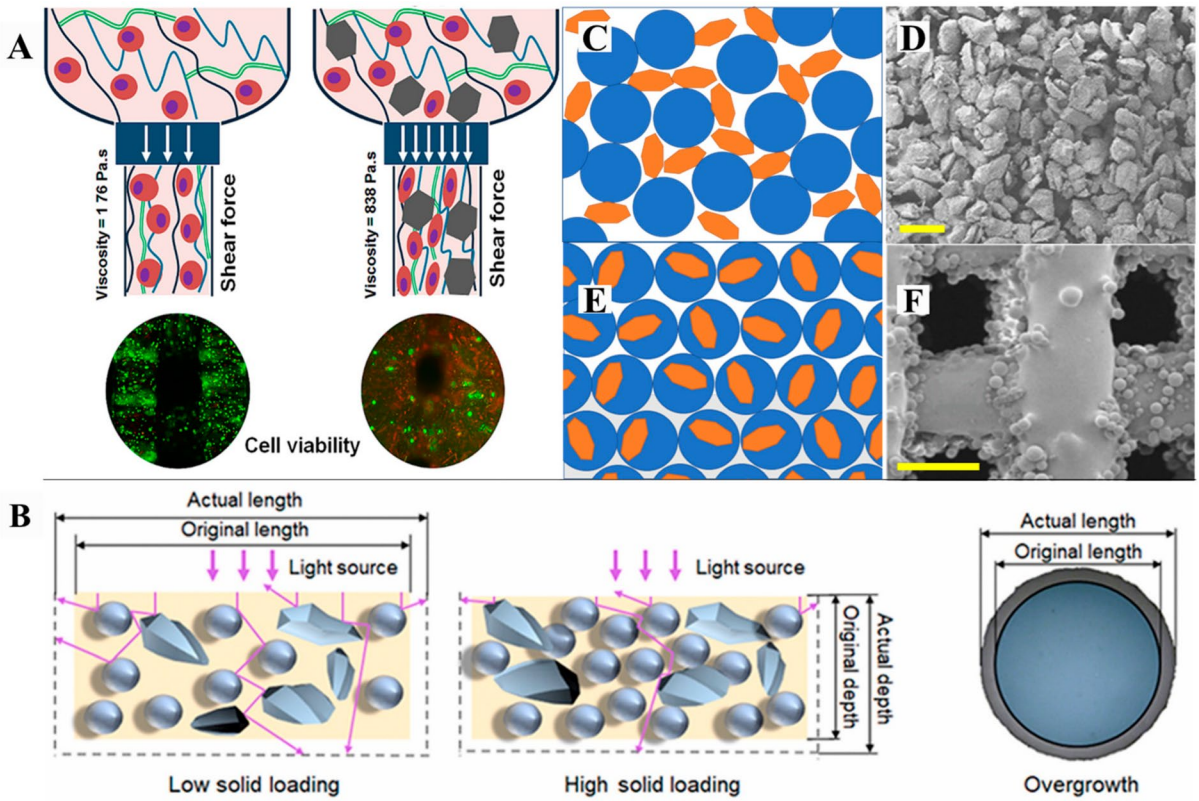


Fig. 3 Influence of bioactive glass addition on the quality of additive manufacturing. **A** BG addition led to increased viscosity and shear force during material extrusion, which impaired cell viability. Adapted from Ojansivu et al.[31] **B** Schematic view of light diffraction due to the presence of bioactive glass particles, as well as the consequent variation in cured depth and width of the fabricated products. Adapted from Li et al.[32] **C–F** Scheme and corresponding SEM images of the SLS-fabricated composites using a simple mixture (**C**, **D**) or composite microsphere (**E**, **F**) as feedstock. Orange polygonal particles represent bioactive glass, and blue spheres represent polymer. Scale bar = 500 μm. Adapted from Sun et al. [33] and He et al. [29]

bioactive glasses, both heralded for their osteoinductive capabilities and potential to support bone regeneration through the provision of a conducive scaffold for cellular attachment and proliferation [13, 14]. Moreover, the advent of bioactive polymers and peptides illustrates a novel approach to augmenting osteogenic differentiation and proliferation, signifying a strategic pivot towards organic–inorganic hybrid composites [23, 25].

The fabrication of bioactive composites has been revolutionized by advancements in technology, notably 3D printing and nanotechnology as shown in Fig. 5. These techniques offer unprecedented precision in scaffold architecture, enabling the creation of structures that closely mimic the native extracellular matrix and promote effective tissue integration and regeneration. For instance, 3D bioprinting allows for the spatial deposition of bioactive materials and cells in predefined patterns, facilitating the development of scaffolds with tailored mechanical properties and biological functions [7, 8]. Nanotechnology, on the other hand, introduces the capability to manipulate material surfaces at the molecular level, enhancing their bioactivity and interaction with biological tissues. These advancements are pivotal in the quest for scaffolds that not only support but actively participate in the regenerative process, by directing cellular behaviour and facilitating tissue repair [20].

The progression of BACT from bench to bedside necessitates a rigorous framework of clinical trials to thoroughly assess their long-term efficacy and safety. While in vitro and animal studies have laid the foundational understanding of the immunotoxicity and bioactivity of various composites [12, 30], the translation of these findings into clinical applications requires a more comprehensive evaluation. Clinical trials, particularly those extending over long durations, are crucial for understanding the long-term interactions between bioactive composites and the human body, including potential immunogenic responses, degradation behaviours, and the maintenance of bioactivity over time. Such studies will be instrumental in establishing the parameters for the successful integration of BACT in therapeutic protocols, ensuring they meet the stringent criteria for patient safety and therapeutic efficacy.

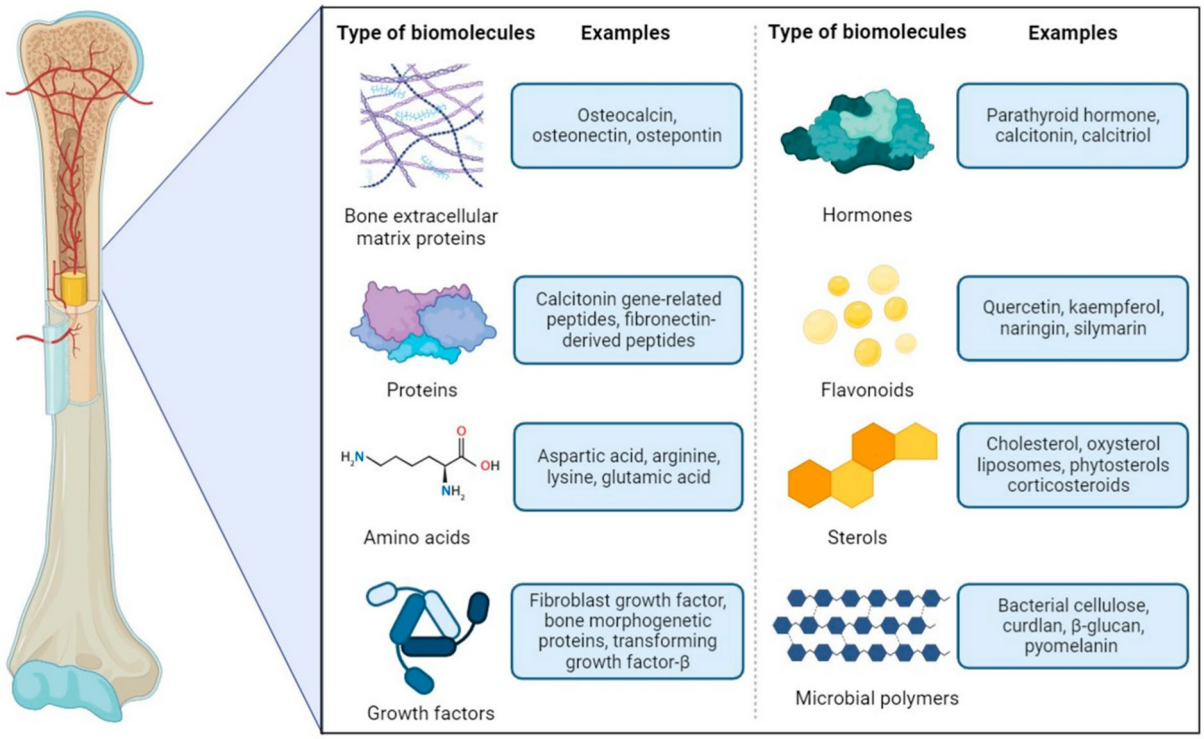


Fig. 4 Current bioactive molecules used in BACT. Adapted from Szwed-Georgiou et al.[21]

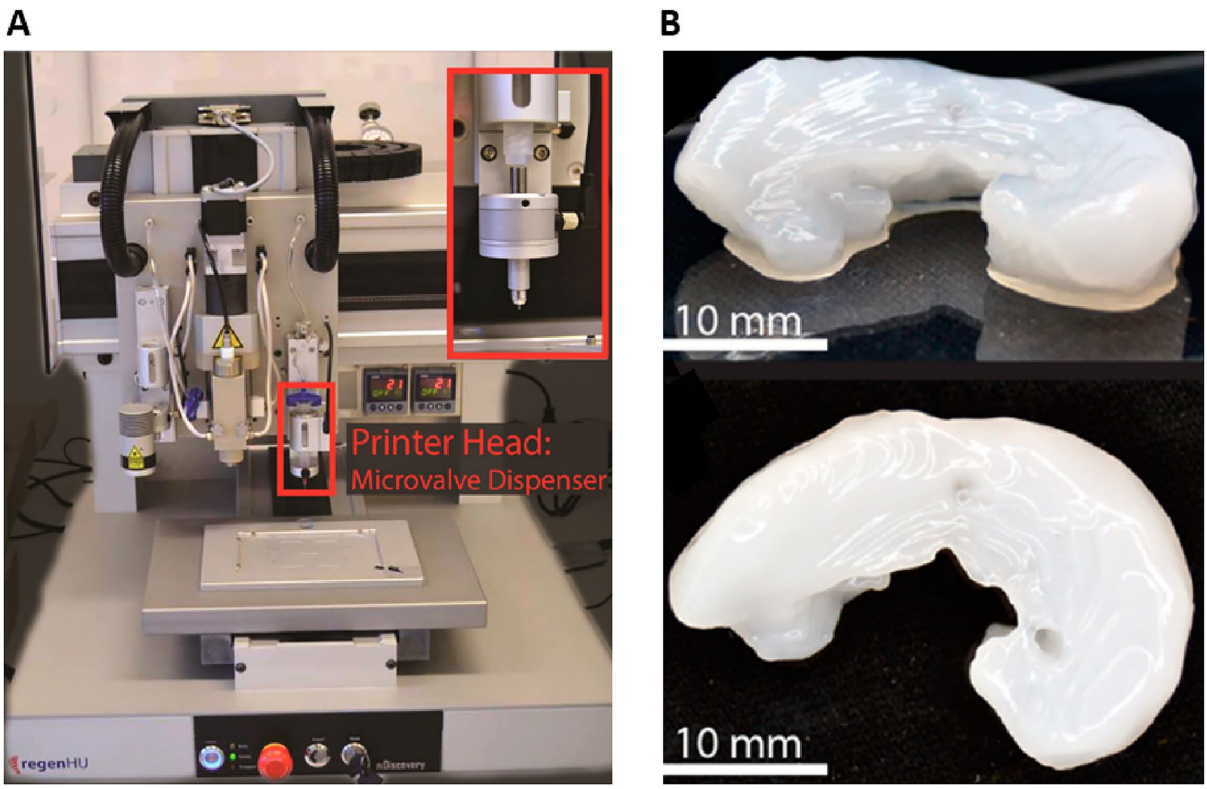


Fig. 5 **A** The 3D Discovery (Switzerland) bioprinter with microvalve print-head shown **B** 3D printed knee meniscus using NFC/A ink. Adapted from Markestedt et al.[34]

The multifaceted nature of BACT underscores the necessity for interdisciplinary collaboration, bridging the expertise of materials scientists, bioengineers, and orthopaedic surgeons. The synthesis of novel bioactive materials demands a deep understanding of chemistry and materials science, while their application within biological systems requires insights from biology and medicine. The optimization of fabrication techniques, such as 3D printing and nanotechnology, calls for engineering prowess. Furthermore, the successful implementation of BACT in clinical settings necessitates the clinical acumen of orthopaedic surgeons, who can provide vital insights into the practical requirements and challenges of regenerative therapies [35, 36]. This collaborative approach will not only accelerate the development of effective BACT but also ensure their relevance and applicability in addressing real-world clinical needs [7, 8].

Conclusion

BACT emerges as a transformative approach in regenerative orthopaedics, offering novel pathways for the repair and regeneration of musculoskeletal tissues. The exploration and integration of innovative bioactive materials, alongside advancements in fabrication technologies underscore the potential of BACT to address complex orthopaedic challenges. However, the realization of BACT's full potential necessitates overcoming challenges related to biocompatibility, safety, and accessibility, underscoring the importance of multidisciplinary collaboration and rigorous clinical evaluation. As we advance, the continued development and refinement of BACT hold promise for ushering in a new era of personalized, effective treatments within musculoskeletal disorders, thereby enhancing patient outcomes and quality of life.

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Data availability All data is contained within the manuscript.

Declarations

Conflict of Interest Nil.

Ethical Standard Statement This article does not contain any studies with human or animal subjects performed by any of the authors.

Informed Consent For this type of study informed consent is not required.

Usage of AI AI has been used to grammar correction and language editing.

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