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REVIEW

Sticky Bone: Advances and Applications

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Abstract: Sticky bone is a new type of composite biological material in the field of dental implantation and restoration in recent years, which is usually composed of Autologous Fibrin Glue (AFG) or injectable-platelet rich fibrin (i-PRF) is prepared in combination with different types of bone augmentation materials, such as granular or powdered bone substitutes, providing a solution for bone regeneration that integrates growth factor release with bone scaffold functionality. Its unique gel texture ensures precise adhesion at the site of bone defects and does not fall apart due to external forces. This property not only enhances the stability of the bone graft, but also accelerates the regeneration and healing of bone tissue by providing an ideal environment for cell attachment and proliferation. In addition, the bioactivity and plasticity of sticky bone allow it to demonstrate higher adaptability and surgical success when compared to conventional bone grafting methods. Its development potential in bone tissue engineering also opens up new directions for future clinical applications. Overall, sticky bone is becoming a key material for promoting bone regeneration and improving implant success due to its sticky bone, scaffolding function and ability to carry bioactive components. In this paper aims to review the composition, preparation methods, mechanisms of action, and specific applications of sticky bone in oral implantation and related fields.

Keywords: sticky bone, platelet concentrates, bone substitutes, bone regeneration

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Introduction

Background

In the field of oral cavity research, bone tissue regeneration remains a critical area of medical science.[1] As technological advancements continue, researchers strive to discover more effective methods for regenerating bone tissue, which is particularly important in cases involving critical-size bone defects caused by surgery, trauma, or tumor resection.[2] Due to the body's limited capacity to regenerate significant amounts of lost bone, bone augmentation techniques have become essential in repairing such defects.[3] These techniques are designed to stimulate and promote bone tissue growth, thereby restoring both function and structural integrity. A variety of methods are used in bone augmentation, each employing different materials that present distinct applications and benefits.[4] The advancement of these techniques has significantly expanded the possibilities for treating complex bone defects, with the sticky bone technique emerging as particularly promising.

Sticky bone is an innovative bone augmentation material that combines autologous platelet concentrate with bone graft materials to create a bioactive scaffold.[5] This material incorporates modern-day biomaterial science with sophisticated tissue engineering methods. By integrating autologous fibrin gel (AFG) or injected platelet-rich fibrin (i-PRF) into bone graft materials, a highly adhesive bone augmentation product is formed.[6] This combination creates an optimal environment for cell accessory and proliferation, accelerating the procedures of bone regeneration and healing. Furthermore, it enables the exact and complete implantation of the graft in the recipient location, additional improving the efficiency of bone regeneration.[7] The purpose of this paper is to supply a thorough overview of the application and advancement of sticky bone innovation in oral bone tissue regrowth. In this paper, the biological qualities of sticky bone

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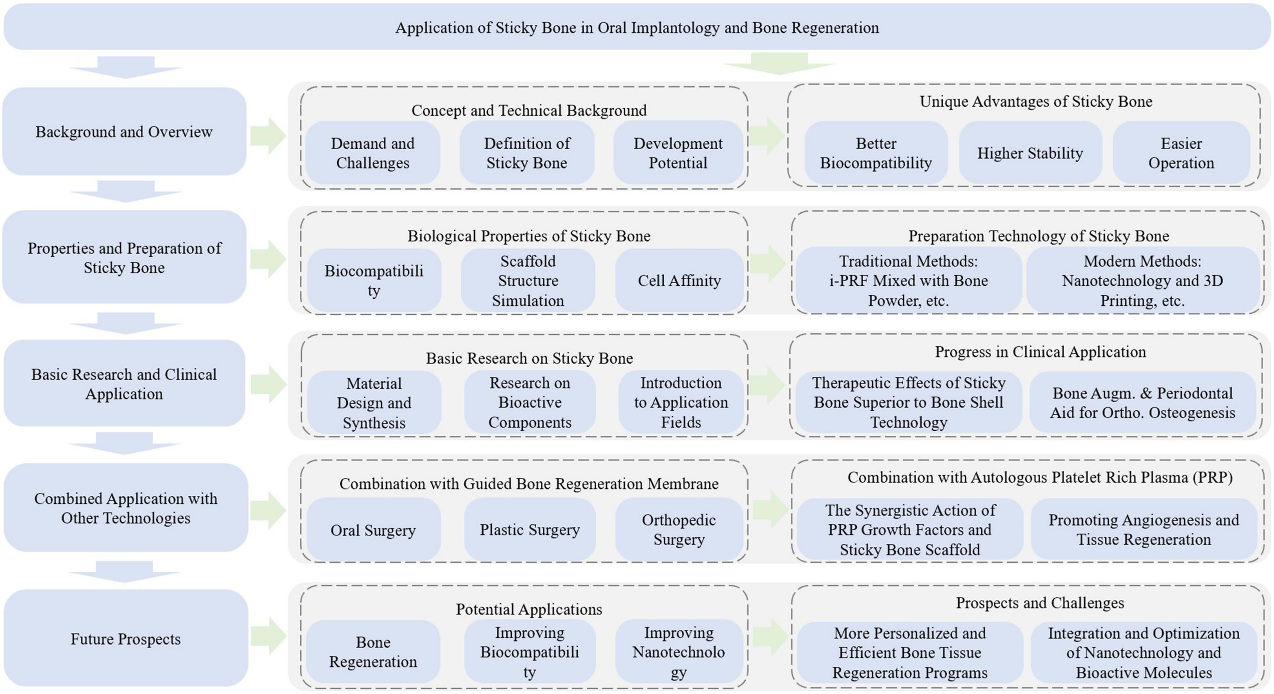

Figure 1 Summary of the basic structure of the article.

and its application in Guided Bone Regeneration (GBR) are discussed and compared to other techniques. By focusing on its adhesive and regenerative properties, this review aims to provide valuable insights into the clinical advancements and challenges in sticky bone technology. Through a methodical evaluation of relevant literature, the advancement history, prospective applications, and obstacles of sticky bone innovation are checked out, providing valuable insights and research instructions for physician in dentistry and associated fields. The overall structure of this article is summarized in Figure 1.

Progress of Sticky Bone Research

Origin of Sticky Bone

Alveolar bone defects can result from different elements, consisting of inflammation, tumors, trauma, or developmental abnormalities, limiting the clinician's ability to restore oral function. To attend to these challenges, bone tissue regeneration treatments are often required.[8] The structural integrity of bone tissue is crucial for preserving oral function, ensuring tooth stability, and maintaining facial aesthetics.[9] In clinical practice, patients frequently experience physiological bone resorption following tooth loss, while traumatic edentulism often leads to substantial bone tissue loss. In many cases, this results in a low or narrow alveolar ridge or localized depressions, which represent a significant portion of clinical cases.[10] Autologous bone grafting is considered the gold standard for alveolar bone regeneration. However, its widespread use is limited by the difficulties of harvesting, surgical trauma, and high graft resorption rates. During bone healing, the graft material must maintain the osteogenic space. Consequently, researchers are actively exploring more effective tissue regeneration materials, making this a key focus of current research.

In this context, Sohn et al[11] first introduced the term "sticky bone" at a conference in Tokyo in 2010, a composite biomaterial created by combining plasma products with bone substitutes (such as allogeneic bone, xenogeneic bone, or non-bone graft materials), sticky bone provides stability to bone grafts in defects, thereby accelerating tissue healing and minimizing graft resorption during healing. This innovation marked a significant milestone in bone regeneration by integrating adhesive properties with bioactive components to promote bone formation.[12] In 2015, Sohn et al[13] defined sticky bone as a fibrin-encapsulated, bio-cured adhesive bone graft network. In this method, autologous fibrin glue (AFG) is mixed with bone graft material, with the individual bone particles being interconnected through a fibrin network. This results in the formation of a viscoelastic scaffold material with a stable three-dimensional structure that resists disintegration, even when subjected to external forces. The authors thoroughly describe the preparation process of sticky bone and its clinical applications in the regenerative repair of bone defects. In the same year, Mourão et al[14] introduced the concept of a "steak for bone grafting" wherein injectable platelet-rich fibrin (i-PRF) is incorporated into bone grafts without the use of anticoagulants or other additives, producing a novel composite biomaterial. More recently, Csonge et al[15] proposed a folding technique that combines bone grafts with self-folding i-PRF. This technique results in a more homogeneous cellular composition compared to traditional platelet-rich fibrin (PRF) prepared using standard centrifugation methods. Additionally, it allows for extended in vivo residence time, thereby enhancing the sustained release of cytokines and growth factors from blood cells, which promotes bone formation.

Properties and Preparation of Sticky Bone

Biological Properties of Sticky Bone

As an innovative material for bone tissue regeneration, sticky bone exhibits a range of biological properties that significantly influence its in vivo performance.[16] These properties can be summarized as biocompatibility, biodegradability, the delivery of bioactive agents, scaffold structure mimicking, and cell affinity, among others.

Biocompatibility Sticky bone materials exhibit exceptional biocompatibility, minimizing immune responses and reducing the risk of rejection. This is attributed to their composition, which incorporates biocompatible polymers and natural bone matrix components. This is primarily due to the fact that sticky bone is generally composed of extremely biocompatible materials, such as eco-friendly polymers or components derived from natural bone matrices. The remarkable biocompatibility of these materials makes sure convenience during implantation and assists in the regeneration and repair of surrounding tissues.[17] For instance, Choi et al[18] introduced a bone-specific, artificial extracellular matrix (aECM) developed as a bioengineered specific niche efficient in restoring totally practical bone tissue. This was attained through the synergistic binding of two bioactive peptides within the matrix, exhibiting biocompatibility. Biocompatibility is a critical factor in the clinical success of sticky bone, as it allows for seamless integration with surrounding tissues, reducing foreign body reactions and rejection while promoting the growth and repair of bone tissue.[19] This ensures that patients experience minimal discomfort or complications post-surgery, aligning with the principles of bone tissue regeneration and ensuring the stability of the implant.

Biodegradability Most sticky bone materials are biodegradable, meaning they gradually degrade and are absorbed by the body without leaving any residual material. This process is crucial for bone tissue regeneration, as the sticky bone weakens in tandem with the formation of new bone and is ultimately metabolized by the body. The use of biodegradable materials eliminates the need for secondary surgeries, reduces patient discomfort, and poses no long-term health risks. Ragit et al[20] compared the efficacy of concentrated growth factor-enriched bone graft matrix (sticky bone) with hydroxyapatite-enhanced Beta TCP and bioresorbable membranes in treating class II furcation defects. They concluded that the sticky bone group demonstrated significant improvements in clinical parameters, attributed to its biodegradability. A greater percentage of defects were converted from class II to class I, indicating a regenerative potential comparable to combination therapies.[21]

Delivery of Bioactive Agents Sticky bone can be designed to carry bioactive agents such as growth factors, cytokines, or therapeutic drugs. These materials can release substances that promote bone cell proliferation, differentiation, and extracellular matrix production after implantation. In this way, sticky bone not only provides structural support but also actively participates in the biological regulation of bone tissue regeneration. Bioactive biomaterials may be derived from natural sources, such as bovine bone mineral matrix, hyaluronic acid, collagen, gelatin, fibronectin, agarose, alginate, chitosan, and silk, or they can be synthetically produced, such as ceramics, metals, polymers, hydrogels, and composites. Among these, ceramic-based materials (eg, bioactive glass, microcrystalline glass, calcium phosphate, ceramics, and cements) are the most widely used due to their similarity to bone minerals.[22] Sticky bone supports bone regeneration by delivering bioactive agents such as growth factors, cytokines, and therapeutic molecules through its fibrin-based matrix. This promotes osteoblast adhesion, proliferation, and differentiation, while its viscoelastic scaffold maintains structural integrity under mechanical stress.

Mimicking Scaffold Structure for Bone Tissue Engineering An ideal scaffold for bone tissue engineering should provide not only mechanical support but also promote osteogenesis, osteoconduction, and even osteoinduction. Addressing various structural complexities and engineering challenges is essential.[23] The architecture of sticky bone scaffolds is designed to mimic the structure of natural bone tissue, offering both structural support and guidance to facilitate new bone formation.[24] This bone matrix-like structure enhances cell adhesion and migration while creating an optimal microenvironment for cell growth, which in turn supports the directional growth and differentiation of osteocytes.[25] Figure 2 highlights how engineered scaffold designs, through surface modifications and structural optimization, can enhance cell adhesion and promote bone regeneration. These design principles are closely aligned with the objectives of sticky bone scaffolds, providing valuable insights into their theoretical and practical applications. The scaffolds enhance cell attachment through surface modifications and optimize their structure using precisely controlled fabrication techniques, such as three-dimensional (3D) printing, providing support and guidance similar to natural bone tissue,[26] which is a key feature of the sticky bone design. The definition of the scaffold's topological features is heavily influenced by precisely controlled fabrication techniques, such as advanced 3D printing technologies. Through 3D printing, surface roughness and fiber orientation, particularly interconnected pore structures, can be manipulated to generate complex 3D architectures.[27] By mimicking the micro- and nanostructural characteristics of bone tissue, it becomes possible to regulate key cellular functions such as migration, adhesion, proliferation, and differentiation, thereby fostering bone regeneration. In addition to biochemical signals, physical stimuli in the environment, such as electrical and magnetic factors, can also influence cellular behavior and further promote bone regeneration. As demonstrated in previous studies,[28] bone tissue exhibits piezoelectric properties, enabling it to generate charges or potentials in response to mechanical stimuli, which in turn supports bone growth. In the context of bone tissue regeneration, the combination of magnetoelectric scaffolds and the restoration of the physiological and electrical microenvironment can further regulate cell fate and optimize the design of biomaterials. The structure and function of sticky bone as a material that mimics the microenvironment of bone tissue may help to stimulate the natural piezoelectric response of bone tissue and promote bone repair.[29] Moreover, the adaptable nature of sticky bone allows it to conform to bone defects of varying shapes and sizes, forming a structure similar to that produced by 3D printing. This adaptability provides clinicians with greater flexibility in adjusting the material, enabling them to customize it to meet the specific needs of individual patients, ultimately improving the outcomes of bone regeneration.[30]

Sticky bone surfaces exhibit excellent cell affinity, supporting bone cell adhesion. This property helps with the adhesion and proliferation of bone cells on the material's surface, promoting the formation of new bone tissue, particularly advantageous for clients going through rehabilitation. Chang[31] demonstrated that the advancement of bone scaffolds with boosted mechanical properties and improved cellular affinity, attained through 3D printing innovation, enables better integration with cells, thus reducing the risk of patient rejection.

The combination of these biological properties makes sticky bone an ideal material for bone tissue regeneration, using appealing new methods for dealing with bone defects in both oral and other skeletal applications.

Preparation Method of Sticky Bone

Sticky bone is normally developed by integrating biocompatible matrix materials with scaffolding residential and bioactive substances, such as growth factors.[32] The composition ratio and preparation process play critical roles in determining the properties of the material. Conventional techniques include blending biomaterials with carriers, followed by biotechnological processes, consisting of polymerization or cross-linking, which impart viscosity and plasticity to the product. Current advances in nanotechnology and bioengineering have caused developments in sticky bone preparation, making it more precise and manageable to fulfill diverse medical requirements.

Several factors affect the manufacture of sticky bone, consisting of the type of centrifugation devices, centrifugation specifications, extraction site of the liquid post-centrifugation, the kind of bone substitute, and the mixing ratio of bone augmentation product and liquid. Currently, there is no standardized guideline for production.[33,34] In bone regrowth, the most typical treatment includes utilizing autologous fibrin gel (AFG) mixed with bone meal particles. AFG preparation starts with smooth centrifuge tubes, which are spun at 2,400– 2,700 rpm for two minutes to gather the leading layer of liquid AFG for later usage. The centrifugation is then continued for an additional 12 minutes after equilibrating the tubes.

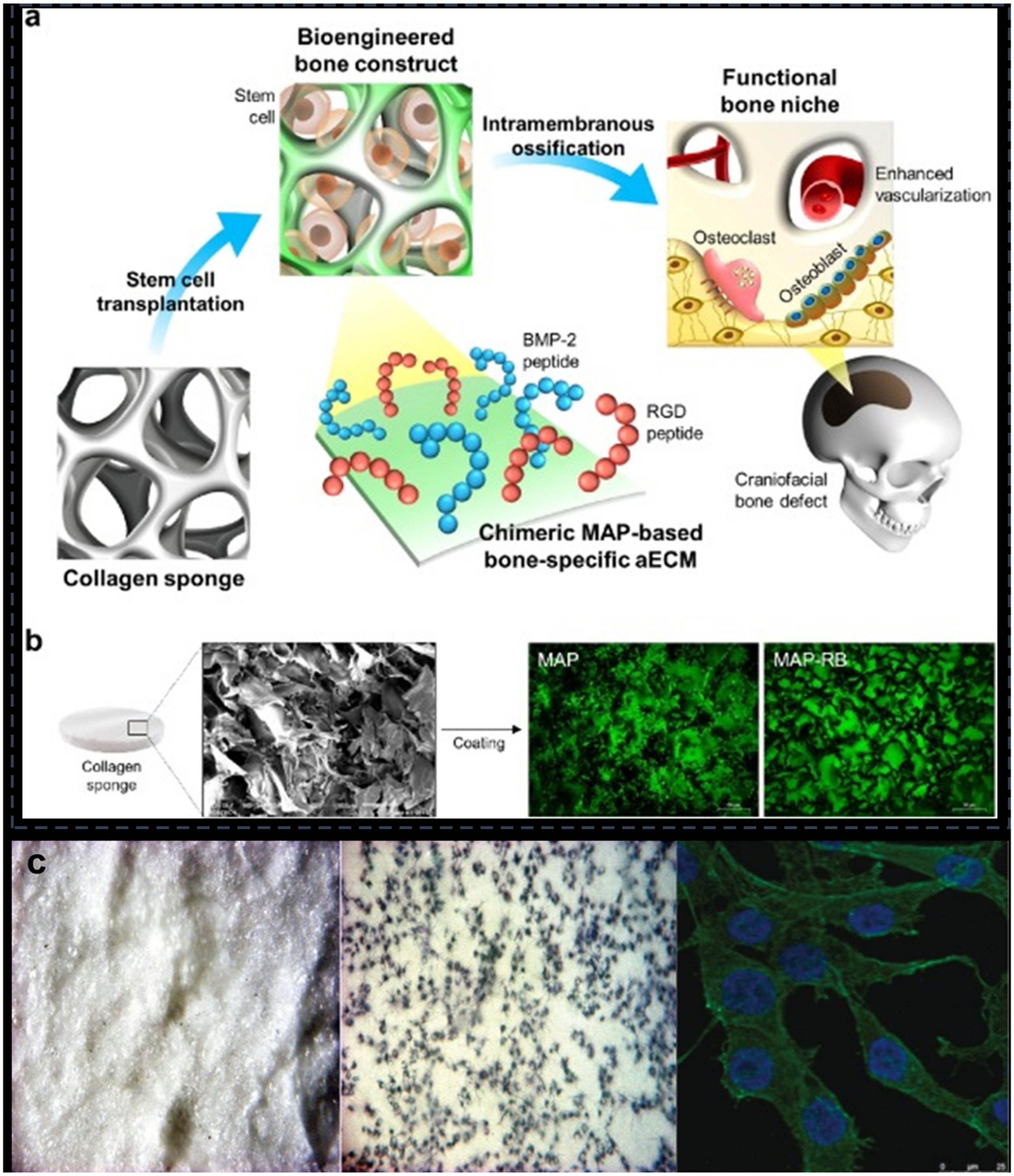

Figure 2 Design principles of "sticky bone" scaffolds and their potential for bone regeneration. (**a**) Schematic representation of the bone healing process mediated by stem cells within a MAP-based bone-specific aECM. (**b**) Scanning electron microscopy (SEM) images of bare collagen sponges and fluorescence images of MAP and MAP-RB-coated collagen sponges, reproduced from Choi BH, Jo YK, Zhou C et al, Sticky bone-specific artificial extracellular matrix for stem cell-mediated rapid craniofacial bone therapy, Applied Materials Today 18 (2020) 100,531. © *2019 Elsevier Ltd. All rights reserved.*[18] (**c**) Osteoblast-like MG-63 cells attached to 3D-printed bone scaffolds, reproduced from Chang CH, Lin CY, Liu FH et al, 3D Printing Bioceramic Porous Scaffolds with Good Mechanical Property and Cell Affinity. PLoS One. 2015 Nov 30;10(11):e0143713. © 2015 Chang et al, This is an open-access article distributed under the terms of the Creative Commons Attribution License.[31]

After this second round of centrifugation, the venous whole blood in the tube separates into three layers: the PPP layer at the top, the CGF fibrin clot in the middle, and the RBC layer at the bottom. This action makes sure the pureness and quality of fibrin drawn out from the client's own blood. The AFG is then combined with bone meal particles to complete the procedure.

Including AFG into bone meal assists in rapid solidification, normally within 5 to 10 minutes, due to its bioadhesive homes. This characteristic allows the mixture to adhere rapidly to bone defect sites throughout implantation, forming a "sticky bone" with noteworthy strength and strength. The development of this sticky bone not just supplies a favorable environment for osteoblast development but also efficiently fills bone flaws, promoting the regeneration of new bone tissue.[35]

This procedure of mixing AFG with bone powder is not only simple but also highly controllable, providing clinicians with a practical and efficient method of preparing bone regeneration material. Figure 3 demonstrates the preparation process of sticky bone step by step. The underlying principle of blood coagulation involves converting soluble fibrin into insoluble fibrin, which imparts the mixture with its "sticky" nature, allowing it to better accommodate patient-specific differences. This adaptability enhances the success rate of bone regeneration and presents a more reliable, innovative option for clinical applications. Future studies aiming to optimize and refine this technique are expected to further increase its potential in the field of bone regeneration.

D Scaffold Fabrication Strategies

Due to the key role of 3D scaffolds in reproducing the complex structural and mechanical properties of natural bone tissues in biomimetic scaffold systems, their preparation strategies are discussed in depth in this section. The evolution of 3D scaffold fabrication techniques has been instrumental in overcoming the limitations of traditional bone graft materials, particularly in achieving a balance between structural integrity and bioactive functionality.[36] Sticky bone, with its unique adhesive and regenerative properties, benefits significantly from advances in scaffold design, which enhance its clinical adaptability and regenerative efficacy.[37]

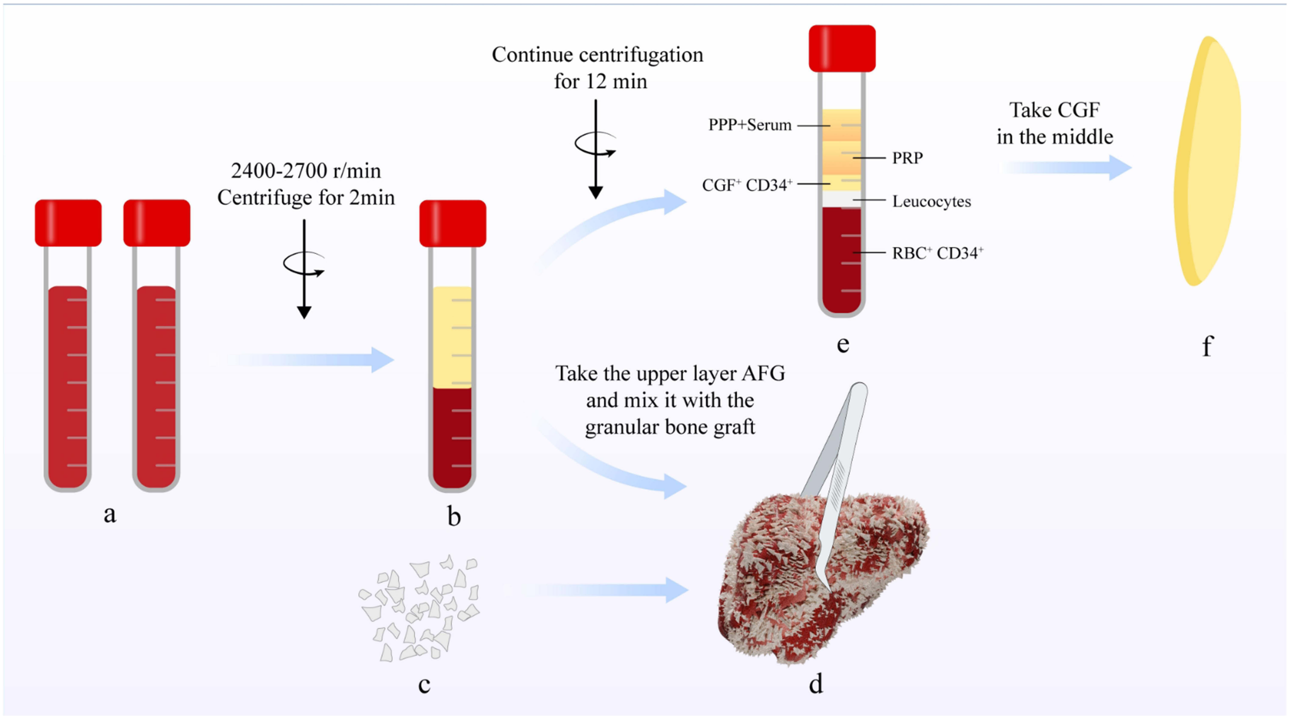

Figure 3 Preparation process of sticky bone; (**a**) venous blood; (**b**) centrifuged to obtain AFG (upper layer); (**c**) granulated bone graft material; (**d**) AFG and granulated bone graft material polymerised to form sticky bone; (**e**) centrifuged tube is divided into an upper plate poor plasma (PPP) layer, an intermediate concentrated growth factors (CGF) layer, and a bottom layer of red blood cell (RBC) layer; (**f**) CGF compressed into CGF membrane.

At the heart of these advances is 3D printing or bioprinting, a technology that allows for precise control of scaffold structures using materials such as PLGA, hydroxyapatite (HA), and bioinks such as GelMA and alginate. By tailoring pore sizes (100–500 μm) and geometries, 3D-printed scaffolds optimize cell infiltration and vascularization, as demonstrated by Choi et al[18] who integrated MAP-coated collagen sponges to enhance osteoblast adhesion (Figure 2a and b). While 3D printing and bioprinting have demonstrated significant potential in creating patient-specific scaffolds with precise geometries and functional properties, alternative strategies also offer complementary benefits to address specific challenges, such as mechanical strength, scalability, and biocompatibility (Table 1).

For example, electrostatic spinning provides an effective way to generate nanofibrous scaffolds that mimic the natural extracellular matrix (ECM) by using materials such as PCL, collagen, and filipin proteins.[44,45] These scaffolds provide a high surface area for cell adhesion and facilitate localized drug delivery, as seen in the study by Huang et al[46] who found that electrospun PCL membranes bound to platelet-rich plasma (PRP) accelerated periodontal regeneration. Despite these advantages, the fragility of electrospun silk scaffolds and their limited pore connectivity limit their use in mechanically demanding environments.

Similarly, freeze-drying is a cost-effective and scalable technique to produce porous scaffolds from materials such as chitosan, alginate and β-TCP.[47] These materials are particularly suitable for filling irregular bone defects because their interconnected pores promote nutrient diffusion and angiogenesis.[39] For example, sticky bone scaffolds enriched with AFG prepared by freeze-drying have been successful in the repair of mandibular cysts, although variability in pore distribution and degradation rates poses a challenge in standardizing results.[40]

In addition to these approaches, innovations such as magnetoelectric scaffolds may further expand the range of applications for viscoelastic bone,[28] incorporating Fe_3O_4 nanoparticles into bioceramics, which offer unique advantages by mimicking the inherent piezoelectric properties of bone. These scaffolds stimulate osteoblast differentiation under mechanical stress and allow magnetic fields to control drug release, providing dynamic therapeutic modulation.[41] Although promising, their long-term biosafety and manufacturing complexity require further investigation.

The greatest advances in 3D scaffold biomaterials have come from hybrid strategies that integrate multiple fabrication techniques into a single unified structure. By combining the structural precision of 3D-printed PLGA or PLGA/HA frameworks with the bioactivity of electrostatically spun nanofibers containing i- PRF, researchers have created structures that provide both mechanical stability and sustained release of growth factors.[42] In a typical case, this composite scaffold achieved up to 92% new bone density in a maxillary sinus lift model (Figure 4a).[12] The synergistic effect of the precise geometry produced by this printing and the dynamic, cell-friendly microenvironment generated by sticky bone provides a powerful way to meet the dual demands of strength and biology.[30]

Table 1 3D Scaffold Fabrication Strategies

Technique	Materials	Key Advantages	Limitations	Applications	Ref
Sticky Bone Scaffold	AFG/i-PRF; Bone substitutes	Seamless defect integration; Sustained growth factor release	Mechanical instability; Preparation complexity	Alveolar augmentation, sinus lifting	[12,35]
3D Printing	PLGA, HA, GelMA	Precision pore design; Patient-specific grafts	Limited bioink strength; Scalability challenges	Customized bone grafts	[18,26]
Electrospinning	PCL, Collagen	ECM-mimetic nanofibers; Drug delivery potential	Fragility; Poor pore connectivity	GBR membranes, periodontal repair	[27,38]
Freeze-Drying	Chitosan, β-TCP	Cost-effective; Interconnected pores	Irregular pore distribution; Degradation variability	Cystic defect filling	[39,40]
Magnetoelectric Scaffolds	Fe_3O_4, Bioceramics	Piezoelectric stimulation; Controlled drug release	Biosafety concerns; Complex fabrication	Jaw joint reconstruction	[28,41]
Hybrid Techniques	PLGA/HA, 3D +Electrospinning	Multiscale functionality; Enhanced mechanical/bioactive synergy	High cost; Technical complexity	Craniofacial regeneration	[42,43]

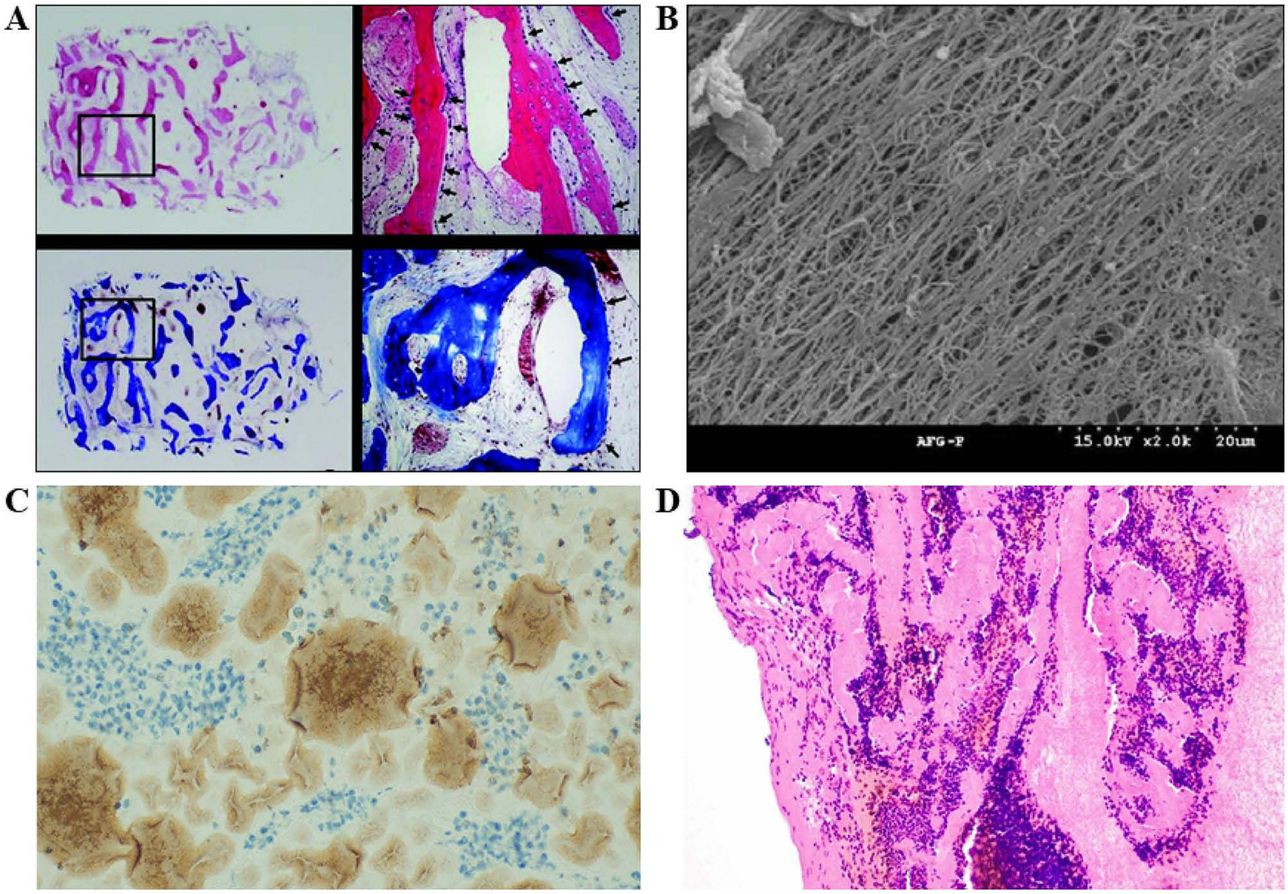

Figure 4 (**A**) sticky bone promotes maxillary sinus bone regeneration, reproduced from Sohn DS, Heo JU, Kwak DH et al. Bone Regeneration in the Maxillary Sinus Using an Autologous Fibrin-Rich Block With Concentrated Growth Factors Alone. Implant Dentistry 20(5):p 389–395, October 2011. *Copyright © 2011, © 2011 Lippincott Williams*.[12] active new bone formation is seen in hematoxylin and eosin stain and in Masson's Trichrome stain. Arrows show a large number of osteoblasts visible along the new bone. (**B**) SEM image of a strong cross-linked fibrin network of sticky bone.,[13] (**C** and **D**) homogeneous aggregation of leukocyte and platelet populations in folded F-PRF, reproduced from Csönge L, Bozsik Á, Tóth-Bagi Z, Gyuris R, Kónya J. Regenerative medicine: characterization of human bone matrix gelatin (BMG) and folded platelet-rich fibrin (F-PRF) membranes alone and in combination (sticky bone). Cell Tissue Bank. 2021 Dec;22(4):711–717 © The Author(s) 2021. Creative Commons Attribution 4.0 International License.[15]

Biomimicry Methods in Bone Tissue Engineering

In bone tissue engineering, the design and application of biomimetic methods are distinctive, and together they provide multidimensional design ideas for the construction of high-performance sticky bone materials, but there is still a need for refinement between their technical properties and clinical applications. In the field of bone tissue engineering, biomimetic design strategies are divided into four main categories: structural biomimicry, biochemical biomimicry, mechanical biomimicry, and conductive biomimicry. Each strategy aims to simulate the natural bone regeneration microenvironment through physical structure, chemical signaling, mechanical stimulation, or electrochemical conditions, thereby synergistically promoting cell infiltration, vascularization, and osteogenic differentiation.

Structural biomimicry is the process of mimicking the 3D scaffolding structure of natural bone by constructing multi-scale interconnected pores and bone-like surface topology, which significantly enhances the depth of cellular infiltration and the rate of vascular invasion, thus optimizing the healing effect.[48] However, the preparation of their high-precision pores often relies on complex and expensive 3D printing or phase separation techniques, and the pores may collapse or change in size during in vivo degradation, affecting long-term mechanical stability and permeability.[49] In the future, scaffold structures can be optimized by introducing gradient structures, bionic surface topology, and using computer-aided design (CAD) and artificial intelligence (AI) to improve the efficiency of cell infiltration, angiogenesis, and bone regeneration.[50]

Biochemical biomimicry is achieved by loading the scaffold with collagen peptides, integrin-binding sequences, and growth factors such as BMP-2 and VEGF, and utilizing nanocarriers or microcapsules to achieve spatiotemporal controlled release, precisely driving osteoblast adherence, proliferation, and differentiation, as well as promoting neovascularization.[51] However, exogenous factors are susceptible to enzymatic degradation in vivo, and the release rate is difficult to accurately master. High concentrations of proteins may also induce local inflammation or immune responses, so it is necessary to find a balance between stability and biological activity.[52] In the future, targeted release of growth factors may be achieved through the development of intelligent response systems, such as pH or temperature sensitive carriers. In addition, combining the sticky bone strategy to enhance the ability of cell adhesion and osteogenic differentiation by constructing artificial extracellular matrix is also a direction worth exploring.[53]

Mechanical biomimicry can simulate the mechanical microenvironment at different stages of healing by adjusting the elastic modulus and viscoelastic properties of scaffolds or applying dynamic mechanical loading in the bioreactor to activate mechanical signaling pathway, guide stem cells to osteogenic differentiation, and reduce stress shielding.[54] However, it is still challenging to accurately reproduce the complex multi-stage load pattern in vivo while maintaining long-term mechanical properties, which requires continuous optimization of material ratio and process conditions. In the future, dynamic mechanical loading system can be introduced to simulate the mechanical changes during bone healing and promote the mechanical sensing and differentiation of cells. In addition, the three-dimensional culture and functionalization of scaffolds combined with bioreactor technology is also a key way to improve the mechanical bionic effect.[55]

Conductive biomimetic strategies integrate conductive components into scaffolds to mimic the electrical properties of natural bone tissue, promoting bone regeneration.[56] Conductive scaffolds can not only transmit electrical signals, but also respond to external electrical stimulation to activate intracellular calcium channels and promote osteogenic differentiation and angiogenesis. In addition, the conductive scaffold can regulate the immune response, inhibit the inflammatory response, and improve the repair efficiency under electrical stimulation.[57] However, current conductive biomimetic materials still face some challenges, such as biocompatibility, long-term electrophysiological safety, and complex fabrication processes. Future research should focus on optimizing the biocompatibility of conductive materials, ensuring their safety for long-term use, and developing simple preparation methods to facilitate their clinical application.[58]

The integration of four biomimetic strategies - structural, biochemical, mechanical and conductive - into a single scaffold allows for synergistic interaction of structural, chemical, mechanical and electrochemical signals in the same structure. This approach not only enhances the osteoconductive properties of scaffolds, but also provides a comprehensive and flexible framework for the multifunctional design of next-generation sticky bone materials. By combining these strategies, scaffolds can more effectively guide bone regeneration and integration. Future bone tissue engineering should move toward multimodal biomimetic strategies considering structural, chemical, mechanical, and electromagnetic factors for more efficient and safer bone regeneration and repair.

Feasibility and Durability of Sticky Bone

Sticky bone offers ease of application in surgical settings, with its versatility allowing it to adapt to various bone defect morphologies. This flexibility enhances surgical outcomes and expands its potential for clinical use in complex bone defects. Its adhesive properties allow the material to firmly attach to the bone surface, reducing the complexity of surgical manipulation and providing the surgeon with greater operational flexibility.[38] Figure 4 illustrates the application of sticky bone in maxillary sinus bone regeneration and its structural features under SEM. Due to its plasticity and compatibility with biological tissues, sticky bone is well-suited for a broad range of oral bone defects, including those resulting from alveolar bone resorption, traumatic edentulism, and other causes, highlighting its wide applicability.[59] The biodegradable nature of sticky bone materials enables a controlled balance between persistence and degradation by adjusting the rate of biodegradation. This function enables the material to support and direct bone tissue regrowth while avoiding premature deterioration, ensuring the long-term effectiveness of treatment.[38] Furthermore, sticky bone can integrate bioactive substances, such as growth aspects, which are capable of sustained release with time.[60] This sustained release system promotes the growth and distinction of osteoblasts, consequently boosting new bone formation.

Comparison with Conventional GBR

Traditional bone implanting approaches often count on matrix products developed for bone tissue engineering, that include naturally obtained bone compounds such as calcined bone, decalcified bone matrix, and deproteinized bone matrix, in addition to reassembled xenogeneic bone matrices. Furthermore, polymeric products like collagen, fibrin, chitin, alginate derivatives, and coral-derived bone have been utilized.[61] In some cases, calcium phosphate cement combined with exogenous nerve development elements is used to prepare artificial bone products that promote bone development.[62] While these innovations offer certain advantages in bone tissue regeneration, they likewise present various limitations and obstacles.

In contrast, the sticky bone strategy provides considerable benefits over traditional GBR methods. Sticky bone innovation offers an innovative technique to bone tissue healing by utilizing and stimulating the body's natural regenerative processes.[63] Its key feature is the elimination of the need for a second surgical site, which is also seen in many conventional bone graft materials. However, sticky bone is unique in that it can provide a sticky scaffold that creates an ideal environment for osteoblast proliferation and differentiation. This not only shortens patient recovery time but also reduces the pain and complications often associated with donor site surgeries in conventional bone grafting procedures.[43,64] Furthermore, sticky bone technology is adaptable to individual patient differences, allowing for personalized treatment and improving the overall success rate by tailoring the procedure to each patient's unique needs. This adaptability makes it a promising solution not only for oral applications but also for bone regeneration in other parts of the body.[65]

Excluding these factors, sticky bone offers greater flexibility in the repair of various bone defects. By utilizing adhesive scaffolds or materials, sticky bone technology creates an optimal environment for bone cell growth, facilitating bone tissue regeneration. Unlike traditional bone grafting methods, this technique activates the body's natural regenerative mechanisms. Sticky scaffolds not only provide structural support but also regulate osteoblast proliferation and differentiation through biological signals, thereby accelerating bone tissue formation. This approach can provide a more steady solution for localized bone defects.[6]

Clinically, sticky bone has actually yielded impressive outcomes, offering patients with a more secure and more effective approach to bone tissue repair work. With ongoing technological developments and additional research, guided bone regeneration is poised to become an essential direction in the future of bone tissue engineering and regenerative medicine.

Progress of Clinical Application of Sticky Bone

Clinical History of Sticky Bone

Over the past few decades, GBR methods have advanced considerably, progressing from initial experimental research studies to widespread medical applications. Early research mostly focused on animal designs, intending to stimulate bone tissue growth through the implantation of numerous biological materials or the application of growth elements. The success of these initial experiments laid the groundwork for the advancement of GBR, advancing the method to a more mature phase and allowing its entry into scientific trials. The sticky bone technique has since emerged as a superior option for guided bone regeneration. A study by Barbu et al[63] compared sticky bone and the shell technique in horizontal bone augmentation, revealing that while both methods produced substantial results, sticky bone transcended in terms of treatment time and postoperative recovery.

Similarly, Chandra et al[66] compared sticky bone with autologous bone ring grafting in the treatment of type II bone defects. Although the autologous bone ring grafting group demonstrated better outcomes in terms of bone density, buccal/lingual bone height, implant stability, and tissue volume on biopsy, the sticky bone group also achieved notable bone regeneration. Such studies underscore the significance of sticky bone as a key biomaterial in GBR, owing to its unique adhesive properties and bioactivity. Its application not only highlights the potential of biomaterials in promoting bone regeneration but also offers new insights and opportunities for the future development and clinical use of bone tissue regeneration techniques.[67]

A study by Wang et al[68] examined the impact of a digital workflow on improving hard tissue thickness through adhesion and demonstrated that combining sticky bone with a digital workflow significantly contributed to bone augmentation at the neck of the implant.

Some other researchers have also successfully applied sticky bone in different contexts, Joshi et al[32] used it in alveolar ridge augmentation for Seibert class III defects, and Dayashankara Rao et al[69] demonstrated that the combined use of i-PRF and modified platelet-rich fibrin enhanced alveolar ridge bone formation and reduced bone resorption. Additionally, they found that labial bone graft thickness was notably higher in the group utilizing digital guides with sticky bone. Similarly, research by Sureshbabu et al[70] reported satisfactory outcomes in treating large bone defects with sticky bone. Building on previous studies, it can be concluded that sticky bone significantly enhances the formation of blood vessels and woven bone, which is crucial for alveolar ridge preservation and bone regeneration following tooth extraction. Sticky bone has shown positive effects in promoting both angiogenesis and osteogenesis, while also improving alveolar ridge morphology.[71]

Basic Research on Sticky Bone

Sticky bone is an emerging biomedical material developed to possess adhesive properties and promote bone tissue regeneration, with a focus on its application in bone regeneration. Experimental studies have highlighted its unique biological properties and clinical potential. Research on sticky bone primarily concentrates on the following key areas:

Material Design and Synthesis

In the field of sticky bone material research, scientists are focusing on the design and synthesis of innovative materials that demonstrate excellent biocompatibility, adhesion, and mechanical properties. Achieving these goals requires extensive investigation into the selection of specific biomaterials, as well as precise control over their structure and chemical functionality. Advances in nanotechnology have helped with the development of products with customized residential or commercial properties, offering significant potential for applications in tissue engineering and medical prosthetics.[72] A key location of focus is understanding the immune action triggered by these materials.[73] Sticky bone can be engineered to minimize the danger of immune rejection while likewise preventing infection, which might arise from an insufficient immune response.[74]

Given that sticky bone is used in vivo, its anti-infection properties are a crucial research focus.[7] Materials with enhanced antibacterial features can effectively prevent infections at the implantation site, either through anti-bacterial coverings or the release of antimicrobial substances, therefore enhancing surgical success rates.[75] Consequently, mindful design and regulation of the chemical structure and structure of materials used in sticky bone are important for effectively regulating the immune system. In the field of oral implantology, increasing attention is being paid to the incorporation of nanostructures on the surface of implants.[76] This method boosts the bonding between the implant and surrounding bone tissue, enhancing both the stability and biocompatibility of the implant. These advancements are important for increasing the success rate of oral implant surgeries and promoting client recovery.[77] Incorporating such advances not only improves the mechanical properties and longevity of sticky bone, but also aligns with the ongoing trend of developing bioactive materials,[78] enabling sticky bone to better interact with the body's immune and healing processes, thus ensuring more effective and sustainable treatments.

Nanotechnology applications are not the only location experiencing quick developments; tissue engineering techniques are also progressing. Techniques like bioprinting are being utilized to create tissues with particular structures and functions. In the style and synthesis of materials, scientists are concentrating on how scaffolds can be engineered to enhance tissue adhesion. A primary focus in tissue engineering research consists of mesenchymal stem cells, osteoblasts, and extracellular matrix proteins. Efforts are centered on optimizing scaffold interactions with these biological components to enhance tissue repair and regeneration procedures.[79]

The mechanical durability of materials occupies an equally important place in fundamental research on sticky bone. The strength and stability of materials straight affect surgical results and long-lasting treatment success. Sticky bone should have the ability to hold up against the forces and stresses come across during surgery while supplying sufficient assistance for fracture fixation and bone defect repair work.[80] Recent studies have highlighted the importance of incorporating organic-inorganic composites to optimize bone adhesive performance. Experimental evidence reveals that polyacrylic acid (PAA) demonstrates enhanced structural integrity in bone graft applications when synergistically paired with bioceramic components like tetracalcium phosphate (TTCP).This combination not only strengthens interfacial bonding durability but also increases weight distribution efficiency in load-bearing scenarios. The molecular interaction between PAA's carboxyl groups and TTCP-derived calcium ions facilitates cross-linked network formation, creating a stress-resistant composite architecture that maintains mechanical stability during dynamic physiological conditions. This chemical synergy effectively addresses historical challenges in achieving both robust adhesion and fracture resistance in biomedical adhesives.[81]

The development of sticky bone materials has also benefited from bioinspired strategies, which enhance the mechanical durability and functionality of the material. Kim et al demonstrated the potential of mussel-inspired adhesives in improving the cohesion and mechanical strength of bone grafts. By incorporating recombinant mussel adhesive proteins (rMAP) with hyaluronic acid (HA), these materials exhibited superior mechanical properties, including enhanced resistance to blood displacement and better cohesion, all of which are essential for sticky bone to maintain its structure during surgery[82]. This bioinspired approach significantly improves the performance of sticky bone in clinical settings, where the material must endure blood exposure and mechanical stress during fracture fixation and bone regeneration.

Additionally, Chiu et al explored a supercritical carbon dioxide (SCCO2)-derived bone graft putty that combines bone graft powder and acellular dermal matrix (ADM) powder. This putty demonstrated excellent cohesiveness and retained its mechanical stability even when exposed to saline and blood.[83] The enhanced durability of such materials ensures that they can maintain their integrity and provide stable support for bone defects, aligning well with the goals of sticky bone in offering a malleable yet durable material for bone repair.

In summary, the mechanical durability of sticky bone is a critical factor in its success as a biomaterial for bone regeneration. Advances in material compositions, such as organic-inorganic composites and bioinspired adhesives, have significantly enhanced the mechanical properties of sticky bone, enabling it to withstand the stresses encountered during surgical procedures and support long-term healing. This progress ensures that sticky bone materials provide both immediate and lasting benefits in fracture fixation and bone defect repair. In addition, ensuring that the modulus of elasticity of the sticky bone is consistent with that of the surrounding bone is important to minimize postoperative pain and improve surgical outcomes.[84] As this field continues to evolve, a much deeper understanding of sticky bone products and tissue engineering will lead the way for ingenious medical repair methods, ultimately using more secure and more efficient treatment choices for patients.

Bioactive Components

In recent years, research trends in the field of bone regeneration have gradually shifted towards a deeper integration of bioactive components into sticky bone to promote osteoblast expansion and bone tissue regeneration. This approach centers on the incorporation of growth factors and cytokines into sticky bone structures to enhance their bioactivity and support bone healing. For example, a retrospective study conducted by Barbu et al[63] demonstrated that the use of concentrated growth factor-enriched bone graft matrix (sticky bone) in horizontal ridge augmentation resulted in adequate bone ridge widths compared with the bone shell technique, thus providing an appropriate bone environment for implant placement. This study emphasizes the potential of sticky bone in enhancing bone regeneration. To achieve these goals, scientists are investigating ways to use smart functional biomaterials, especially those sensitive to environmental stimuli, which have been widely studied for their ability to adapt to dynamic conditions outside the body. For example, Li et al[85] developed a self-promoting electroactive mineralized scaffold (sp-EMS) that generates weak currents through spontaneous electrochemical reactions, which activates voltage-gated calcium channels, enhances ATP-induced actin reorganization, and ultimately achieves osteogenic differentiation of MSCs through activation of the BMP2/Smad5 pathway. In addition, the electroactive interface of sp-EMS inhibits bacterial attachment and activity through electrochemical products and co-generated reactive oxygen species. These smart materials are able to respond to environmental changes and precisely release bioactive components at different stages of healing, thus providing precise therapeutic support.

Biocompatibility refers to the interaction between a material and a living organism, encompassing its effects on tissues, cells, and the organism as a whole.[86] Heiss et al[87] discussed bone adhesives in trauma and orthopedic surgery, emphasizing the importance of selecting materials that promote cell adhesion and proliferation, which can significantly enhance new tissue formation and accelerate the healing process. However, such materials may also induce inflammatory responses, potentially causing tissue damage or implant rejection. Ongoing research, including a broader range of clinical cases, aims to identify precise application methods tailored to different bioactive components, providing a stronger foundation for the future development of sticky bone.[88] In addition, minimizing inflammation during surgery involving sticky bone is a central focus of basic research,[89] as it ensures a positive interaction with surrounding tissues. Adopting an integrated approach to bioactive materials research will facilitate the transition to more practical, individualized solutions for orthopedic treatments, leading to innovative advancements in the field.

Biosignaling Microenvironment

In bone tissue engineering, the core goal of constructing biomimetic sticky bone materials is to accurately mimic the biosignaling microenvironment of natural bone tissue to promote bone regeneration. This microenvironment dynamically regulates cellular behavior through a multidimensional biophysical signaling network, especially during the differentiation of bone stem cells (BMSCs) to osteoblasts.[90] It has been shown that the ECM not only serves as a physical support for cell attachment, but also drives the expression of osteogenesis-related genes and bone matrix mineralization through integrin-mediated signaling (eg, binding of α2β1 to type I collagen) and activation of the focal adhesion kinase (FAK) and Src family kinase pathways.[91] This mechanism of cell-ECM interaction suggests that adhesive bone materials need to mimic the biochemical properties of the natural bone matrix, such as enhancing cell adhesion by surface modification of ECM-derived peptides such as FNIII7-1, in order to directionally guide the osteogenic differentiation of BMSCs.[92]

Mechanical properties of the ECM, especially stiffness, are critical for cell fate regulation.[93] The high stiffness microenvironment of mineralized ECM significantly promotes the differentiation of BMSCs toward osteogenesis by activating the YAP/TAZ transcription factor with the Runx2 signaling axis.[94] This mechanism provides key insights into the construction of sticky bone - for example, GelMA/DNA dual network hydrogels coordinate the spatiotemporal activation of integrin-FAK signaling with the MAPK pathway by mimicking the mechanical gradient from an early soft matrix to mineralized high stiffness during bone repair, thereby avoid pathological outcomes such as fibrosis or ectopic mineralization.[95]

Furthermore, the activation of the PI3K-AKT pathway via integrin α7 by immobilized nanohydroxyapatite (nHAP) further suggests that the physical state of the material, such as the immobilization design, has a decisive influence on mechanical signaling.[96] This emphasizes the need for sticky bone to replicate not only the biochemical cues of the natural bone matrix, but also its mechanical properties, in order to effectively promote bone regeneration.

Clinical Application

In the clinical application of sticky bone, its potential is not only reflected in the field of dentistry, but also widely extended to other medical fields. The application of sticky bone in the field of dentistry, especially in oral implantology, alveolar bone restoration, and periodontal therapy, is considered to have significant advantages. By combining with other therapeutic materials, sticky bone can effectively promote bone regeneration, increase the stability of implants, and accelerate the healing of periodontal tissues.

In addition to the oral field, sticky bone also shows a wide range of applications in other medical fields. Especially in orthopedics, plastic surgery and neurosurgery, sticky bone plays an important role in bone defect repair, trauma healing and facial reconstruction. Its superior biocompatibility and mechanical properties make it an ideal material for repairing defects and promoting tissue regeneration.

Next, we will discuss in detail the specific clinical applications of sticky bone in the oral field and other medical fields.

Clinical Applications and Findings in the Oral Field

Numerous clinical trials and research studies have actually highlighted the considerable impact of sticky bone in numerous medical contexts. Current years of clinical practice have demonstrated that sticky bone offers exceptional results compared to traditional bone replacement materials, especially in oral medication. Sticky bone has achieved more significant application results than bone substitute materials alone, including oral implant surgery, alveolar bone defect repair, maxillary sinus elevation, and periodontal treatment.

In oral implantology, sticky bone is primarily utilized for bone enhancement, alveolar ridge conservation, and maxillary sinus floor lifting. A medical group led by Jung carried out a 12–14 year follow-up study of 58 patients who went through GBR with synthetic bovine bone. They found that the success rate of implantation surgeries using the GBR technique remained high, regardless of whether resorbable or non-resorbable membranes were used, with no significant difference between the two types of membranes.[97] Another study, led by Sunmida, applied 3D technology to the GBR technique in 26 patients, using customized titanium devices and conventional titanium mesh. This approach proved to be time-efficient and safe for bone augmentation across a variety of bone defects. The study concluded that guided bone regeneration is more effective than traditional bone grafting methods in preserving the patient's original bone structure, reducing the risk of donor site complications, and enhancing the long-term stability of implants.[98] The use of granular bone substitute material as a scaffold for GBR has certain limitations, particularly in larger procedures. Loose bone augmentation material can be challenging to maintain, and the graft morphology may collapse during the healing process. In contrast, sticky bone's cohesive structure offers greater stability and ease of manipulation. With the aid of digital technology, the volume and shape of sticky bone can be customized to fit the specific dimensions of bone defects, enabling personalized bone augmentation solutions. However, it is important to note that granular bone replacement material itself does not possess bone-inductive properties.[99]

In the repair of alveolar bone defects, the application of sticky bone can provide a more stable space for bone grafting, promoting the rapid healing of both soft and hard tissues while minimizing bone loss and resorption during the healing process.[100] In a study by Cortellini et al,[101] 10 patients with horizontal alveolar ridge defects were evaluated after mucosal bone grafting. Radiographic analysis revealed significant increases in alveolar ridge width—by an average of 4.6 ± 2.3 mm, 5.3 ± 1.2 mm, and 4.4 ± 2.3 mm at 2 mm, 6 mm, and 10 mm from the ridge crest, respectively. Additionally, alveolar ridge volume increased by 1.05 ± 0.7 cm^3, with graft resorption limited to 15.6% ± 6.7%. These findings indicate that sticky bone significantly enhances bone augmentation in horizontal alveolar ridge defects.

Rupawala et al[102] investigated the healing process of mandibular third molar extraction sockets and observed that, compared to areas where sticky bone was not used, patients experienced reduced pain and swelling in the treated area, along with smoother gum recovery. Bone tissue formed more rapidly, and bone density was higher. Moreover, the degree of alveolar bone resorption was lower, leading to improved treatment outcomes. Similarly, sticky bone has shown promising results in maxillary sinus lift procedures. Research indicates that its application enhances the clinical effectiveness of maxillary sinus lifts by promoting early angiogenesis in bone grafts, reducing inflammation, minimizing postoperative pain, and stimulating tissue regeneration, all of which contribute to improved postoperative healing.[103]

Taher et al[19] investigated a minimally invasive "three-in-one" treatment approach, which integrates maxillary molar extraction, maxillary sinus elevation, and alveolar ridge preservation (ARP). Patients delayed implant placement for 7 to 21 months following maxillary molar extraction, and the peri-implant soft and hard tissues were evaluated 8 to 12 months post-implantation. Their findings demonstrate that making use of sticky bone efficiently accelerates neovascularization, promotes the distinction and expansion of surrounding cells, and enhances new bone formation within the implant site. In addition, sticky bone improves implant stability, facilitating much easier fixation and supporting both vascularization and the recovery of difficult and soft tissues.

In the field of periodontology, sticky bone is primarily used in cases of gingival economic downturn and periodontally accelerated osteogenic orthodontics (PAOO). PAOO is a surgical technique that combines selective alveolar osteocorticotomy with bone grafting products to boost orthodontic results. This method has been shown to effectively avoid alveolar dehiscence and gingival recession around buccally likely mandibular anterior teeth.[104,105] Furthermore, when compared to using a coronally repositioned flap alone, sticky bone shows superior effectiveness in promoting healing. Its primary role during gingival recovery is to enhance clot stability, promote osteoblast expansion, and assistance soft tissue development.[28] In adult patients with a thin gum biotype and buccal bone problems, the application of sticky bone has actually been shown to increase alveolar bone thickness, decrease the period of orthodontic treatment needed for tooth crowding, and lower the threat of gingival recession. In addition, in the management of large periapical lesions, sticky bone has demonstrated substantially much faster healing of the periapical location, with its restorative efficacy confirmed through radiographic evidence.[70]

Bone grafting is a commonly made use of method in oral and maxillofacial surgery to fix bone defects triggered by maxillofacial defects, jaw fractures, and other etiologies.[106] It plays a pivotal function in implant surgery and alveolar bone defect repair work. By utilizing biological scaffolds and growth elements, the reconstruction and remediation of the facial skeleton can be carried out with increased precision, yielding both functional and aesthetic outcomes. This approach provides a more individualized and efficient treatment choice for clients.

Sticky bone is mostly used in the repair of oral and maxillofacial bone problems. Beyond its capacity to restore bone stability, sticky bone has demonstrated the ability to promote soft tissue regeneration and may even affect the phenotype of oral tissues. Clinical trials, such as those performed by Kyyak et al[107] have actually revealed that sticky bone technology not only enhances bone regrowth at defect websites however also substantially reduces recovery time, minimizes patient pain, and enhances surgical success rates. The effective implementation of sticky bone technology has led to notable improvements in patient outcomes and has catalyzed a series of advancements in the field of medicine, particularly in advancing guided bone regeneration strategies. Figure 5 presents representative examples of sticky bone applications in guided bone regeneration and periodontal treatments.

In summary, the biomimetic design of sticky bone needs to break through the static limitation of traditional materials and focus on the spatial and temporal coupling of dynamic biosignal networks. Through the integration of ECM biochemical modification, mechanical adaptation and advanced manufacturing technology, we can construct a smart material system that can respond to local microenvironmental changes, and ultimately achieve a high degree of matching with the natural bone regeneration process, so as to provide efficient and personalized solutions for clinical bone repair. Looking ahead, as research into sticky bone continues and the technology goes through more improvement, its medical applications are likely to broaden, offering clients more advanced and tailored treatment choices. The continuous advancement of this field promises to further stimulate medical development, with sticky bone anticipated to play an increasingly considerable role in oral care, contributing to more detailed and enhanced health care services for patients.

Clinical Applications and Findings in Other Areas of Medicine

Beyond dentistry, sticky bone has demonstrated its potential for a wide range of applications in other medical fields, particularly in orthopedics, plastic surgery and neurosurgery. Due to its excellent biocompatibility, plasticity and ability to promote bone healing, sticky bone is gradually becoming an important option for the treatment of bone defects and tissue repair.

In the field of orthopedics, sticky bone is mainly used for post-traumatic bone defect repair, such as fracture repair, bone grafting and bone structure reconstruction in spinal surgery.[108] Its excellent mechanical properties and stability help to restore the integrity of bone structure, reduce joint stiffness and muscle atrophy, and promote the regeneration of bone tissue. The application of sticky bone as a bone repair material can reduce the risk of traditional bone grafting and avoid the limitation of bone source donor, as well as reduce the patient's recovery time and surgical trauma.[102]

In plastic surgery, sticky bone is widely used for facial reconstruction and soft tissue repair. It can be used to repair facial bone defects due to trauma, disease, or congenital defects, such as zygomatic, mandibular, or nasal bone repairs.[17,109] Its excellent adaptability allows it to be personalized to the shape and size of the patient's bone defect, ensuring the best possible restoration. In plastic surgery, sticky bone not only provides a bony scaffold, but also promotes angiogenesis, accelerates post-operative healing, and improves the patient's appearance and functional recovery.[110]

The application of sticky bone in the field of neurosurgery is mainly focused on the repair of cranial defects. Cranial defects are usually caused by trauma, tumor resection, or congenital diseases, and traditional repair methods often face problems such as poor material compatibility and lack of stability.[111] By virtue of its good biocompatibility and bone

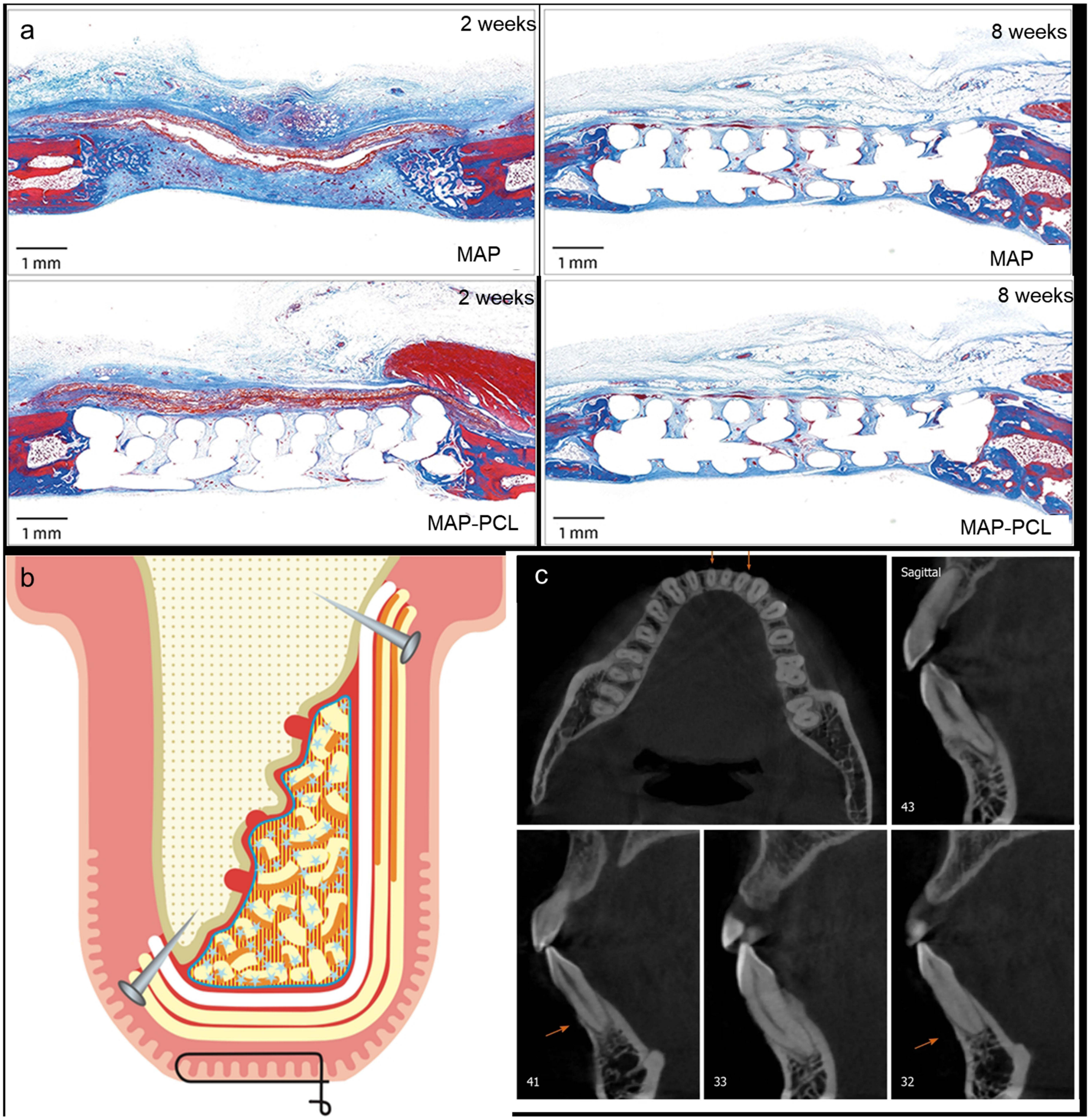

Figure 5 (**a**) MAP-loaded membranes applied in this rabbit cranial GBR model, reproduced from Song WK, Kang JH, Cha JK et al. Biomimetic characteristics of mussel adhesive protein-loaded collagen membrane in guided bone regeneration of rabbit calvarial defects. J Periodontal Implant Sci. 2018 Oct 24;48(5):305–316. Copyright © 2018. Korean Academy of Periodontology. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License,[97] (**b**) Effect of leukocyte- and platelet-rich fibronectin (L-PRF) blocks used for horizontal bone augmentation in the maxilla, reproduced from Cortellini S, Castro AB, Temmerman A et al. Leucocyte-and platelet-rich fibrin block for bone augmentation procedure: A proof-of-concept study, Journal of clinical periodontology 45(5) (2018) 624–634. Copyright 2018, Wiley and Sons,[101] and (**c**) Sticky bone applied for the treatment of gingival recession and periodontal assisted accelerated osteogenic orthodontics, reproduced from Xu M, Sun XY, Xu JG. Periodontally accelerated osteogenic orthodontics with platelet-rich fibrin in an adult patient with periodontal disease: A case report and review of literature. World J Clin Cases. 2021 Feb 26;9(6):1367–1378. ©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved. Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license,[105] arrows show buccal lateral bone wall defects at 32 and 41 anterior to the use of sticky bone.

healing promotion properties, sticky bone can provide sturdy support for cranial bone defects, reduce postoperative complications and accelerate the healing process.[112]

Overall, the application of sticky bone in various medical fields provides new solutions for bone repair and tissue regeneration, especially in complex clinical situations, where the flexibility and bioactivity of sticky bone make it an ideal material. However, there are significant differences in healing rate and complication rate among different groups, such as young adults and old people, patients with bone health and osteoporosis, and patients with or without systemic diseases. In the future, hierarchical analysis should be used to clarify the best indications and expected efficacy of sticky bone for various types of patients, so as to provide personalized guidance for clinical decision-making. With further research, the clinical applications of sticky bone are expected to expand further, providing more personalized and efficient treatment options.

Combined Therapies

In the research and clinical application of sticky bone, the use of a single material has gradually transitioned to the combined application of multiple biomaterials in order to achieve better bone repair results. Among them, the combination of sticky bone with guided bone regeneration membrane (GBR membrane) and autologous platelet concentrate (PRP) has become an important trend in current clinical practice.[113]

Sticky Bone Coupled with GBR Membranes

Sticky bone and GBR membranes are regularly utilized in mix across different surgical disciplines. Due to their complementary properties, the concurrent application of sticky bone and GBR membranes has actually been revealed to make the most of the therapeutic result while making sure client safety.[114] This synergistic approach is particularly relevant in fields such as stomatology, plastic surgery, and orthopaedic surgery. In oral surgery, the combined use of sticky bone and GBR membranes is especially common. During these procedures, GBR membranes are used to cover the bone graft area, while sticky bone is applied to fill the bone defect. This technique has been demonstrated to enhance the rate of bone defect healing and improve the stability of bone grafts.[97] Figure 6 showcases the preparation and SEM characterization of PLGA-grafted hybrid membranes, highlighting their potential to enhance guided bone regeneration in conjunction with sticky bone. These membranes enhance bone healing by providing a structural framework for cell attachment and proliferation. The research team monitored postoperative outcomes through systematic clinical observation and imaging evaluation to ensure the success of the bone grafting procedures. For instance, the use of poly(lactic-co-glycolic acid) copolymer grafted hyaluronic acid bilayer films in GBR has proven effective in treating periodontal defects, providing a valuable therapeutic option in oral surgery.[115]

In plastic surgery, the use of sticky bone has demonstrated remarkable success. This technique is particularly effective in facial plastic surgery, where sticky bone and guided bone regeneration (GBR) membranes are applied to cover the surgical area, facilitating the repair of zygomatic or mandibular defects. Postoperative follow-up, CT imaging, and bone mineral density analysis have been employed to evaluate the regenerative impact of this combined approach on facial bone structures. In one particular case, a chitosan membrane was developed through liquid nitrogen quenching and freeze-drying, followed by cross-linking with sodium tripolyphosphate (TPP). The resulting uneven chitosan membrane, reinforced by TPP, showed boosted tensile strength, supplying a more natural and efficient option for bone repair work in plastic surgery.[117]

In orthopaedic surgical treatment, the mix of sticky bone and GBR membranes has actually also yielded outstanding clinical results, particularly in fracture healing and bone problem repair.[116] This technique encompasses numerous applications, including fracture stabilization and defect restoration, substantially widening the scope of orthopedic treatment. Researchers kept track of the development of bone regrowth and client functional recovery through regular medical examinations, X-ray, and MRI evaluations. For instance, bone tissue engineering has actually revealed fantastic guarantee by producing local beneficial conditions for regeneration through the use of bone scaffolds, growth elements, or cells.[118] These materials, with exceptional osteoconductivity, biocompatibility, and bioactivity, can forming three-dimensional scaffolds that promote cell adhesion, proliferation, and angiogenesis. This regenerative capability is vital for orthopaedic surgery, contributing to more resilient and thorough treatment results for clients.[86]

This series of cases highlights the versatile application of sticky bone in stomatology, cosmetic surgery, and orthopaedic surgery, offering important useful insights and effective examples for advancing bone regrowth research in the medical field.

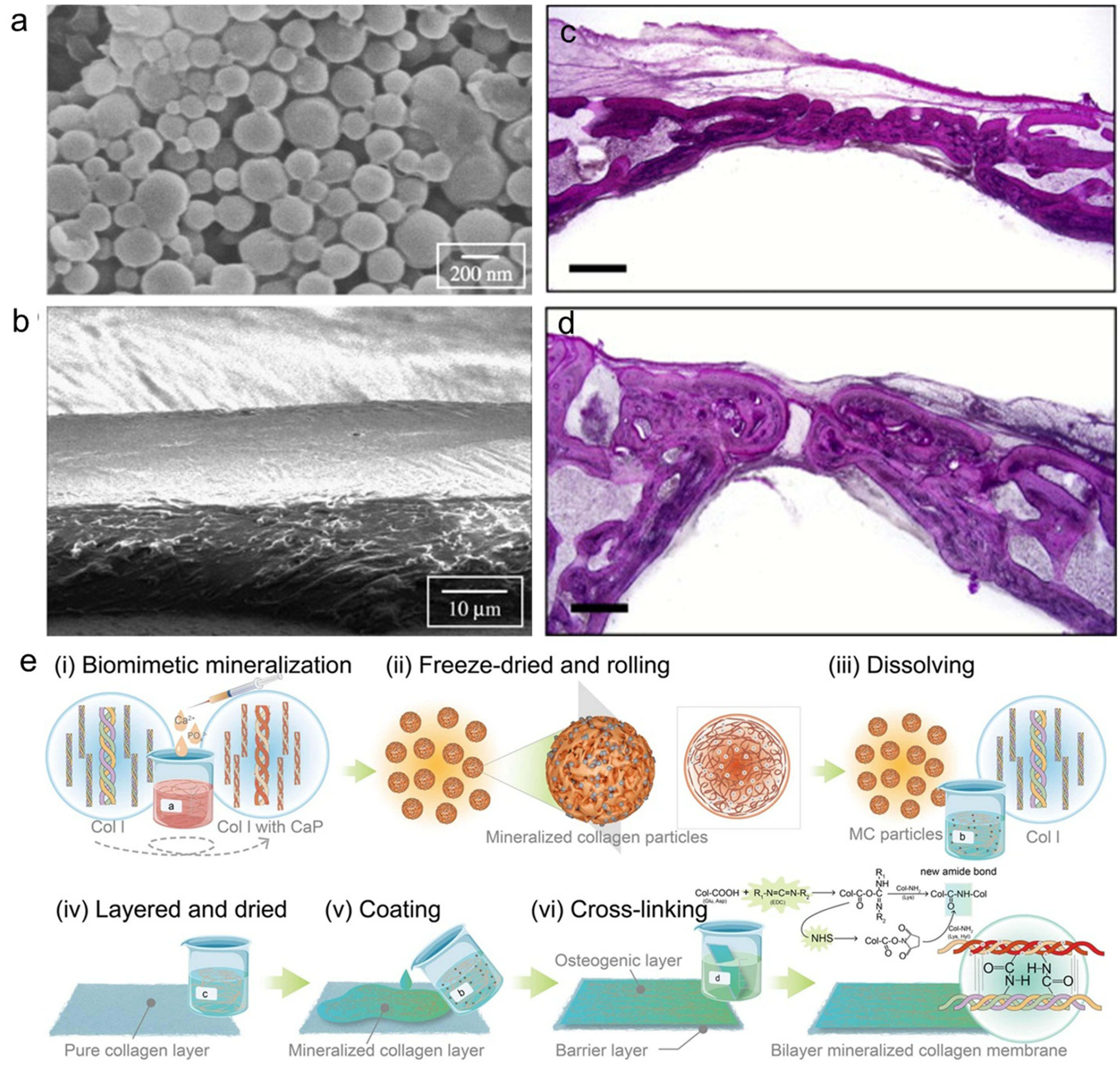

Figure 6 (**a** and **b**) SEM images of poly(lactic acid)-poly(glycolic acid) (PLGA) membranes and PLGA-grafted hyaluronic acid hybrid membranes, (**c** and **d**) for guided bone regeneration applications, reproduced from J.K. Park, (J) Yeom, E.J. Oh et al, Guided bone regeneration by poly (lactic-co-glycolic acid) grafted hyaluronic acid bi-layer films for periodontal barrier applications, Acta Biomaterialia 5(9) (2009) 3394–3403. Copyright 2009, Elsevier,[115] (**e**) Preparation process of a novel double-sided osteochondral membrane (MC/Col membrane) that can promote bone regeneration, reproduced from Peng F, Zhang X, Wang Y. et al, Guided bone regeneration in long-bone defect with a bilayer mineralized collagen membrane. *Collagen & Leather* 5, 36 (2023). Copyright 2023, Springer Nature.Creative Commons Attribution 4.0 International License;[116] In e (i)acidic collagen with CaP biomimetic mineralization; (ii)Freeze-dried and rolling; (iii) Dissolve to MC particles and Col I; (iv)Layered and dried; (v) Coating; (vi) Cross-linking.

The integrated use of sticky bone and GBR membranes has actually shown distinct benefits in particular bone flaw repair circumstances, especially by accelerating healing, enhancing postoperative stability, and lowering donor site problems. However, the technique still faces challenges related to procedural complexity and cost, necessitating further studies with larger sample sizes and extended follow-up periods to better define its clinical indications and long-term efficacy.

This approach has several key advantages, firstly, it improves the rate of healing, sticky bone helps to fill the bone defect and promotes the formation of a more complete bone structure; secondly, it also provides structural support, the

GBR membrane provides a supportive framework to guide the growth of osteoblasts, which helps to speed up the healing process and improves the postoperative stability; and at the same time, it can enhance the stability, the combination of sticky bone and the GBR membrane provides a synergistic approach for the repair of bone defects. The sticky bone enhances the adhesive stability of the graft, while the GBR membrane acts as a barrier to direct osteoblast migration and prevent fibrous tissue invasion. The combination of sticky bone and GBR membrane is less traumatic to the donor site than traditional bone grafting methods, thereby reducing the risk of postoperative complications.[119–121]

Despite its numerous advantages, the combination of sticky bone with GBR membranes presents certain drawbacks. One significant challenge is the increased complexity: this approach requires more advanced surgical techniques and meticulous postoperative management, which can elevate the difficulty of the procedure and complicate the rehabilitation process. Another concern is cost: both sticky bone and GBR membrane materials are expensive, and their combined application can further raise the overall cost of surgery, which may impose financial burdens on patients. Additionally, the long-term impacts stay unpredictable; while short-term outcomes have actually been appealing, the long-lasting efficacy of this combined approach requires validation through further studies and extended follow-up, particularly throughout diverse illness conditions and patient populations.[122,123]

Combined Application of Sticky Bone and Autologous Platelet Concentrate

The preparation of autologous PRP normally includes collecting whole blood from the patient, followed by the enrichment of platelets, development factors, extracellular matrix, and other components through centrifugation and similar methods. This procedure normally includes steps such as centrifugation, the elimination of non-essential parts from the plasma, and the adjustment of concentration levels.[124] Given that PRP is originated from the patient ‘s own blood, it carries minimal threat of immune responses or transmission of infectious diseases. From a biological activity point of view, platelets are abundant in growth elements, such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and fibroblast growth factor (FGF). These growth factors play a vital role in bone regrowth by promoting cell expansion, differentiation, and matrix synthesis, thereby accelerating the healing process.[125] Beyond their direct impacts on osteocytes, the development factors in PRP likewise modulate the immune response, preventing the release of inflammatory mediators and lowering local inflammation, which further supports wound healing.

Theoretically, the increase in autologous growth factors and secreted proteins concentrated in platelet-rich preparations may significantly enhance the wound healing process, particularly in individuals with degenerative tissue or biological damage. By elevating the levels of growth factors, platelet focuses are expected to speed up numerous phases of healing, consisting of decreasing inflammation, promoting angiogenesis, promoting cell proliferation and differentiation, and improving collagen synthesis.[126] This theoretical foundation recommends that the application of platelet concentrates might play an important function in tissue repair, particularly in patients experiencing tissue structural damage due to degenerative diseases, trauma, or persistent inflammation. The enriched cytokines and growth elements may speed up the natural process of tissue repair work and regeneration by modulating essential signaling paths and helping with cell-to-cell interactions. In clinical practice, using platelet concentrates is becoming an appealing healing strategy, especially for speeding up injury recovery and promoting tissue regrowth, using more efficient medical interventions for patients.[127]

The mix of PRP with sticky bone has been shown to enhance the bioactivity of regenerative products. In this technique, the development consider PRP connect with the scaffold structure of sticky bone to produce a synergistic impact, which accelerates osteoblast adhesion, proliferation, and differentiation, therefore promoting bone tissue regeneration.[128] This approach decreases rejection by increasing the bioactivity of the products, making them more suitable with human physiology. Furthermore, platelet concentrates promote angiogenesis and tissue regeneration, expediting wound healing. In combination with sticky bone, they fill and repair bone defects more effectively, reducing healing time.[129] Another key advantage of combining PRP with sticky bone is the ability to tailor treatment to individual patient needs. By adjusting the concentration of PRP and the material properties of sticky bone, personalized treatments can be developed to suit different patients’ physiological conditions and clinical requirements.[130] Additionally, platelet concentrates improve the biological integrity of the surgical site, decreasing the risk of infection and other complications. This combination also lowers the likelihood of postoperative

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complaints and enhances surgical success. Overall, the synergistic application of sticky bone and autologous platelet concentrates holds considerable clinical potential in the field of bone regeneration, offering a more comprehensive and effective approach to promoting bone tissue repair. It provides patients with more individualized and advanced treatment options. This combined method is supported by a strong academic foundation and opens new avenues for research in the treatment of bone defects, particularly in oral implantation and other surgical fields. Looking forward to the future, intelligent ideas can be introduced into viscous bone, such as loading micro/nanoparticles sensitive to pH, temperature, or bioelectric field in the fibrin network to achieve the precise release of growth factors and drugs. At the same time, combined with the synergistic effect of chemical and biological signals, it is expected to accelerate angiogenesis and optimize the inflammatory microenvironment, thereby promoting collaborative repair.

Conclusions

As an innovative biomaterial, sticky bone has great potential in guiding bone regeneration. Its unique adhesive properties and excellent compatibility with biological tissues make it an ideal choice for enhancing bone repair. Firstly, sticky bone provides robust structural support, creating a conducive environment for bone cell adhesion and proliferation. This facilitates the formation of new bone tissue and accelerates the healing process, which is particularly important in the treatment of fractures and bone defects. Secondly, sticky bone has the capacity to integrate bioactive components into its matrix. By incorporating growth factors, cytokines, and other bioactive molecules, sticky bone can guide and stimulate bone cell activity at the microscopic level, further enhancing bone regeneration. This precise modulation of bioactivity enables sticky bone to offer distinct advantages in directing bone regeneration, providing patients with more individualized and efficient treatment options.

Additionally, the application of sticky bone in bone tissue engineering is an area of growing interest. Through techniques such as nanotechnology, the surface structure of sticky bone can be engineered to more closely mimic the microenvironment of natural bone tissue. This biomimetic design is expected to improve the integration between sticky bone and surrounding bone tissue, facilitating smoother and more natural bone formation.

Clinically, sticky bone has shown significant efficacy in a variety of applications including alveolar ridge augmentation, maxillary sinus lift, periodontal defect repair and horizontal bone regeneration. In addition to stomatology, emerging applications in orthopaedics and craniofacial surgery highlight its versatility. Adaptive digital workflows for sticky bone further enable personalized bone augmentation, shorter procedure times, and improved outcomes, while optimized bioactive components can increase guided bone regeneration precision, and combined with nanotechnology can further enhance its clinical potential. These features not only offer new possibilities for surgical applications, such as traditional implants, but also open up unprecedented opportunities for advancing bone tissue engineering and regenerative medicine. Future research should focus on the standardization of the preparation process, including the volume of blood collected, centrifugation speed and time, and the optimization of the ratio of the bone substitute material to AFG/i-PRF to ensure reproducibility and consistency; further study of the spatial and temporal release kinetics of the bioactive factors, so as to achieve precise and controlled release of the factors to optimize the bone regeneration effect; and systematic evaluation of the safety, efficacy and long-term follow-up results of the standardized sticky bone regimen by means of a large-sample, multi-center, randomized, controlled, or prospective study. To systematically evaluate the safety, efficacy and long-term follow-up of standardized sticky bone protocols through large-sample randomized controlled or prospective studies, in order to promote their widespread use in dental, craniofacial and orthopaedic surgery. As research into the properties of sticky bone deepens and clinical experience continues to accumulate, it has the opportunity to further transform bone regeneration strategies to provide safer and more effective solutions for complex bone defects. And as multidisciplinary innovations continue to converge, sticky bone will further enhance its place in bone tissue engineering and individualized medicine.

Ethical Approval

This study did not involve human or animal subjects. Therefore, ethical approval was not required.

Informed Consent

This study is a review of existing literature and does not involve human participants or the collection of new data. Therefore, informed consent was not required.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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