E-ISSN: 3068-5052
Journal of Regenerative Medicine & Biology Research

ATHENAEUM SCIENTIFIC PUBLISHERS

Review Article

Bioengineering and Alveolar Ridge Preservation: Can Synthetic Growth Factor-Releasing Scaffolds Overcome the Limitations of Autogenous Bone Grafts? A Narrative Review

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Citation: Salas DJS, et al. Bioengineering and Alveolar Ridge Preservation: Can Synthetic Growth Factor-Releasing Scaffolds Overcome the Limitations of Autogenous Bone Grafts? A Narrative Review. J Reg Med Biol Res. 2026;7(3):1-11.

https://doi.org/10.46889/JRMBR.2026.7302

Received Date: 21-08-2026

Accepted Date: 14-09-2026

Published Date: 21-09-2026

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Abstract

Removing a tooth triggers a remodeling response that leaves the alveolar process narrower and shorter than before. Where an implant is planned, that contraction can be the difference between a site that accepts a fixture in its ideal position and one that does not, which is why managing the post-extraction socket has become a discipline in its own right. This narrative review asks a specific question: can synthetic scaffolds engineered to release growth factors in a controlled manner do what autogenous bone does, without the drawbacks autogenous bone brings? To address this, we examined socket-healing biology, the design criteria that govern scaffold performance, the mechanisms by which bioactive molecules are delivered and the clinical data available to date. Searches covered ridge preservation, autogenous grafting, bone tissue engineering, scaffold composition, fabrication methods and growth factor delivery; we retained preclinical work, clinical trials, systematic reviews and consensus documents where they bore directly on the question posed. The evidence indicates that controlled-release constructs improve osteogenesis and vascular ingrowth, limit ridge collapse and spare the patient a donor site, with sequential and sustained-release designs performing particularly well. What the evidence does not yet show is durability: nearly all comparative data come from animal models and the available human studies are too small and too short to establish whether these constructs outperform autogenous bone over time. The rationale is sound and the direction of travel is clear, but adequately powered trials reporting volumetric, histomorphometric and implant-related endpoints together remain the missing piece.

Keywords: Bone Tissue Engineering; Alveolar Ridge Preservation; Controlled Growth Factor Delivery; Synthetic Scaffolds; Autogenous Bone Graft; Smart Biomaterials; Three-Dimensional Printing; Regenerative Dentistry; Implant Site Development; Long-Term Outcomes

Introduction

When a tooth is removed, the body responds with an organized repair sequence aimed at closing the wound and restoring local homeostasis. That sequence is unavoidable and so is its consequence: the alveolar process remodels, losing bone tissue

irreversibly and contracting in both width and height even as new bone forms inside the socket [1]. Healing after extraction should not be read as regeneration of what was there before. Repair and resorption run concurrently and the net result is a smaller ridge. This is why Alveolar Ridge Preservation (ARP) now occupies a central position in implant planning and, more broadly, in prosthetically driven rehabilitation [2].

The healing sequence comprises several overlapping phases rather than a clean sequence: hemostasis, inflammation, vascular ingrowth, deposition of woven bone, conversion to lamellar bone and remodeling that continues well beyond clinical closure. Early on, the clot filling the socket functions as a temporary matrix; inflammatory cells migrate into it and cytokines and growth factors are released locally. Neutrophils and macrophages clear necrotic debris during this inflammatory window while simultaneously orchestrating the reparative response that follows [2]. New vessels then grow into the socket, delivering the oxygen, nutrients and osteoprogenitor cells that osteogenesis requires. Woven bone fills the defect and is subsequently converted, through coupled osteoclastic and osteoblastic activity, into mechanically superior lamellar bone. Because these phases overlap, the timeline varies substantially from one patient to the next [3].

Adequate bone formation inside the socket does not prevent the ridge from contracting. The principal driver is loss of the periodontal ligament and with it the bundle bone that depends on the tooth for its vascular supply. Bundle bone resorbs quickly once that supply is gone and the effect is most pronounced along the buccal wall, whose cortex is typically thin and composed largely of this tissue. How much is lost varies considerably between patients and local anatomy accounts for much of that variation: how thick the buccal plate is, how many socket walls survive extraction and in what condition, the periodontal status of the site, where the root sat within the alveolus and how the alveolar process relates to the underlying basal bone. Sites with thin buccal plates, missing walls or poor basal support lose the most in both dimensions [3]. Pooled data put figures on this: roughly 3.8 mm of horizontal loss and 1.2 mm of vertical loss within six months when a socket is left to heal on its own, with the bulk of that change concentrated in the first three months [4].

The local mechanical environment contributes as well. Once the tooth is gone, the physiological loading transmitted through the periodontal ligament disappears, which disrupts the signals governing bone homeostasis and tips the balance toward osteoclastic activity in the early healing period. Mineralization proceeds inside the socket while resorption acts on the outer cortical surface at the same time [2]. A radiograph showing good intrasocket fill therefore says nothing definitive about ridge dimensions, since the two processes are driven by different mechanisms operating on different surfaces. Three-dimensional imaging has added a further complication: thickening of the overlying soft tissue can partially conceal buccal bone loss, so that clinical inspection understates the true hard tissue deficit [5].

For implant-supported rehabilitation the consequences are direct. A contracted ridge constrains three-dimensional implant positioning, compromises primary stability, makes later augmentation more likely and undermines the peri-implant soft tissue support on which esthetic outcomes depend. Randomized data confirm that sockets left to heal spontaneously lose more bone in both planes than sockets treated with guided bone regeneration or socket-sealing protocols [6] and meta-analysis indicates that ARP retains a measurable margin of width and height relative to unassisted healing [7]. The intervention is not free, however. Whether it is justified in a given case depends on complication rates, biomaterial cost and how likely preservation is to genuinely spare the patient a later augmentation procedure [8].

Current consensus reflects this, recommending individualized socket management based on site morphology, buccal plate condition, periodontal phenotype and the planned prosthesis [9]. Since the anatomical factors governing resorption are already fixed before the tooth comes out [3], remodeling belongs in the treatment plan as an anticipated event rather than in the postoperative notes as a complication. Taken together, these biological realities define what any regenerative strategy must overcome and frame the bioengineering approaches examined in the sections that follow.

Autogenous Bone Grafts: Biological Properties and Practical Limitations

Bone taken from the patient's own skeleton remains the material against which every alternative is measured. The reason is straightforward: no other graft delivers all three biological requirements for bone formation at once — osteogenesis, osteoinduction and osteoconduction [10]. Each of these means something distinct. Osteogenesis describes bone laid down directly by viable osteoblasts and osteoprogenitor cells carried within the transplanted tissue. Osteoinduction describes the

recruitment of undifferentiated mesenchymal stromal cells and their commitment to an osteoblastic phenotype, a process driven by bone morphogenetic proteins (BMPs) and related signaling molecules. Osteoconduction describes the provision of a surface along which vessels and bone-forming cells can advance and on which mineralized tissue is deposited [11]. An autograft supplies all three. Substitute materials typically manage one, occasionally two.

This distinction matters because osteoinduction is claimed far more often than it is demonstrated. Under the strict definition, a material qualifies only if it induces bone formation at an ectopic site, a threshold met by demineralized bone matrix, recombinant BMPs and a handful of bioactive materials. Hydroxyapatite and Beta-Tricalcium Phosphate (β-TCP), despite frequent characterization to the contrary, function almost entirely as osteoconductive scaffolds [12]. Autogenous bone also contains its own growth factor reservoir, bound within the mineralized matrix and gradually released as remodeling proceeds. That reservoir includes BMP-2 and BMP-7 alongside Transforming Growth Factor-Beta (TGF-β), Platelet-Derived Growth Factor (PDGF), insulin-like growth factor and vascular endothelial growth factor (VEGF), all present in physiologically calibrated proportions. Because these molecules are autologous, they pose no immunogenic risk and, importantly, act in concert across successive healing phases rather than as a single isolated stimulus [13].

Clinically, autogenous bone is harvested either as particulate or as block grafts. Intraorally, the mandibular symphysis, the ramus and the maxillary tuberosity are the usual sources; when greater volume is needed, surgeons turn to the iliac crest, the calvarium or the tibia. The material is used for ridge preservation, horizontal and vertical augmentation, periodontal regeneration and implant site development and it incorporates into the recipient bed faster than most alternatives [14]. In ARP specifically, however, autogenous bone is rarely used alone; more often it forms one component of a composite graft, paired with a slowly resorbing substitute that holds the space [15].

The limitations are equally well documented. A second surgical site must be opened, which lengthens the procedure and brings postoperative pain, swelling, sensory disturbance that may prove transient or permanent and a quantifiable infection risk [16]. Intraoral volume is finite and often inadequate for larger defects, while extraoral harvesting considerably increases morbidity [10]. Autografts also resorb during remodeling, sometimes substantially and often unpredictably, so vigorous early regenerative activity does not guarantee volume years later [16]. In the post-extraction socket, this is a particular concern, because the graft is asked to resist a resorptive process that is most aggressive precisely where the bone is thinnest, at the buccal plate [17].

Such constraints explain the persistent search for substitutes. Three categories exist. Allograft material comes from human donors and is processed through tissue banks. Xenograft material is animal-derived, most often bovine or porcine. Alloplasts are manufactured synthetically and include hydroxyapatite, β-TCP and bioactive glass. Each provides osteoconduction and demineralized allograft adds a measure of osteoinduction, but none contains living osteogenic cells [13]. Systematic reviews of ARP show that these materials perform measurably differently on both dimensional and histomorphometric endpoints, while a Cochrane review found the evidence too weak to name any single technique superior for implant site development [18,19]. Consensus documents therefore advise selecting material according to the defect rather than adopting a preferred products and clinical guidance identifies ARP as most worthwhile when implant placement will be delayed, when the buccal plate is thin or already compromised and when esthetic demands are high [20,21]. Autogenous bone consequently remains the biological benchmark and the stated aim of bone tissue engineering has been to replicate its threefold biological activity without opening a donor site [15,22].

Tissue Engineering Strategies for Alveolar Ridge Preservation

Conventional grafts, as outlined above, are limited by donor-site morbidity, unpredictable resorption, restricted supply, and, for allogeneic and xenogeneic material, lingering immunological questions. Bone tissue engineering emerged in response to these constraints, aiming to produce a single material that is biocompatible, osteoconductive, osteoinductive and controllably biodegradable [23]. Laboratory progress has been considerable. Clinical validation has not kept pace: relative to the volume of constructs described in preclinical work, very few have undergone controlled evaluation in patients [24].

Three components underpin contemporary strategy: a cell source, a scaffold and signaling molecules. Osteoblasts, mesenchymal stromal cells and osteoprogenitor cells supply the osteogenic capacity. The scaffold provides a three-dimensional framework that offers temporary mechanical support and an organized surface on which cells adhere, migrate, proliferate and deposit

matrix. Signaling molecules act as the regulatory layer, governing cell recruitment, proliferation, differentiation, osteogenesis and angiogenesis [25]. Several intracellular cascades mediate these effects, BMP/Smad signaling, the Wnt/β-catenin axis, Notch and the mitogen-activated protein kinase pathways and it is their coordinated activation that determines whether a progenitor cell commits to the osteoblastic lineage [26].

Any scaffold intended for the alveolus must reconcile several competing demands. Biocompatibility comes first: the construct must permit adhesion, proliferation and integration with adjacent tissue without cytotoxicity, sustained inflammation or an adverse immune reaction. It must degrade into harmless products at a pace that keeps step with the bone replacing it. It must also hold the regenerative space against functional loading and soft-tissue pressure throughout healing [25]. These demands pull against one another. Greater porosity improves biological performance but weakens the structure; greater density strengthens it but impedes tissue ingrowth [27]. Composite and hybrid designs, pairing a load-bearing component with a bioactive one, represent the usual compromise [23].

Internal architecture is as important as composition. Pore dimensions and their distribution determine how readily cells migrate, how effectively nutrients and oxygen diffuse and how far vessels and bone advance into the construct; pore interconnectivity determines whether that advance reaches the full depth of the scaffold or stops at its surface. Diameters in the range of 100 to 400 μm are generally considered favorable for both osteogenesis and vascularization [28]. Degradation kinetics likewise need to track the pace at which bone forms: lose the scaffold too early and structural support disappears before the new tissue can bear load; lose it too slowly and residual material occupies volume that bone should have claimed [29].

Scaffold materials divide conventionally into natural and synthetic. Natural polymers closely mimic the native extracellular matrix. Collagen supports adhesion, migration and osteogenic activity via integrin-binding motifs; chitosan is biocompatible, degradable and readily blended with other materials; gelatin preserves the cell-binding sequences that encourage adhesion and proliferation; and hyaluronic acid, itself a matrix constituent, contributes to migration, remodeling and angiogenesis [30]. Their weaknesses include modest mechanical performance that varies between production batches and degradation rates that resist precise control [30]. Even so, constructs built on these polymers have performed creditably in periodontal and peri-implant applications, where the objective involves regenerating several tissue types in coordination rather than simply restoring bone volume [31].

Synthetic materials offer much tighter control over architecture, mechanical strength and degradation profiles. With poly(lactic-co-glycolic acid) (PLGA), altering the lactide-to-glycolide ratio adjusts how quickly the polymer breaks down, making it a common vehicle for bioactive molecules. Polycaprolactone (PCL) offers mechanical robustness and slow degradation, characteristics well matched to fabricated porous structures. Among ceramics, β-TCP and hydroxyapatite provide osteoconduction and a composition close to bone mineral, while bioactive glass stimulates osteoblastic activity and promotes angiogenesis through the ions it releases as it dissolves [27]. Since no individual material satisfies every criterion, composites have gained ground. One nanofibrous construct developed specifically for alveolar bone regeneration combined bioactive glass and carboxymethyl chitosan with short PCL fibers and exhibited both anti-inflammatory and osteogenic behavior; dual-phase designs, meanwhile, can release two bioactive molecules from a single construct on separate timescales [29,32].

Fabrication methods have developed alongside the materials themselves. Electrospinning generates submicron and nanoscale fibers that echo the fibrillar architecture of native matrix while offering an exceptionally favorable surface-area-to-volume ratio for cell attachment [32]. Modifying surfaces at the nanoscale or chemically functionalizing them, enhances protein adsorption, cell-material interactions and local retention of osteogenic signals; these techniques can be applied to additive-manufacturing constructs [33]. Three-dimensional printing allows resorbable, patient-specific scaffolds to be produced with a defined external shape and a reproducible internal pore structure, an advantage that matters most in irregular or multi-wall alveolar defects. Feeding cone-beam computed tomography data into computer-aided design and manufacturing means the construct can be matched to the individual defect before the patient reaches surgery [34].

Collectively these advances have changed what a scaffold is understood to be: no longer a passive filler that maintains space, but an active regenerative device. The open question is not manufacturing capability, which has been demonstrated [34], nor whether such constructs can be functionalized to modify cell behavior, which has also been demonstrated [33]. The question is whether

their performance in an actual human post-extraction socket warrants displacing a material whose regenerative capacity is already established. Work in multi-tissue applications suggests that engineered constructs convince most when they reproduce biological signaling rather than architecture alone and the scarcity of constructs that have reached controlled clinical trials remains the field's defining weakness [24,31]. The following section addresses the feature that most sharply separates these devices from conventional grafts: controlled growth factor delivery.

Controlled Growth Factor Delivery: Mechanisms and Bioengineering Advances

How well a growth factor works depends not only on what the molecule does biologically but on where it is, how much of it is present and when. Administered as a simple bolus, it diffuses away from the defect quickly, forcing the use of supraphysiological doses and those doses have been linked to ectopic bone formation, edema and inflammatory complications. Delivery systems can address this: they shield the molecule from proteolysis, hold it at the site and meter the rate at which responding cells encounter it [35]. In bone the argument is especially strong, since osteogenesis and angiogenesis are coupled processes directed by coordinated signaling rather than by any one molecule acting alone [36].

The major factors contribute in complementary ways. BMP-2 is the most powerful osteoinductive agent currently in clinical use and pushes mesenchymal stromal cells toward the osteoblastic lineage; BMP-7 likewise supports osteoblast differentiation and bone formation. PDGF largely drives cell recruitment, proliferation and angiogenesis. Neovascularization depends on VEGF. Fibroblast Growth Factor-2 (FGF-2) promotes proliferation and early vascular responses. TGF-β regulates matrix production and cellular differentiation [36]. Because these signals belong to different stages of healing, systems that present them in a biologically plausible order outperform those that release everything simultaneously. Biomimetic delivery built around VEGF has shown this, with new bone formation responding to the timing of presentation rather than total dose [37].

Several platforms have been engineered to achieve such control. Microspheres and nanoparticles encapsulate the factor, protect it from degradation and release it as the carrier polymer erodes or as the molecular interactions holding it weaken [35]. Hydrogels provide a hydrated, matrix-like environment suited to localized delivery and can be injected directly into irregularly shaped defects; one injectable formulation carrying BMP-2 and TGF-β1 achieved sequential release of both factors and was progressively replaced by regenerated bone, demonstrating that a single construct can coordinate distinct signaling phases [38]. Silk-based hydrogels co-delivering VEGF165 and BMP-2 have been tested for maxillary sinus floor elevation, showing that dual delivery is feasible within a recognized maxillofacial indication [39]. Beyond these, layer-by-layer coatings, covalently functionalized surfaces and materials that respond to local stimuli, pH shifts, enzymatic activity and mechanical loading represent the more sophisticated end of current development.

Release kinetics consequently matter as much as the choice of molecule. A burst profile delivers a high initial concentration but empties the reservoir rapidly and may expose surrounding tissue to unnecessarily high local levels. Sustained profiles hold biologically active concentrations for longer and can lower the total dose needed [37]. Sequential profiles most closely mimic natural healing, supplying angiogenic and chemotactic cues during early repair and then following with prolonged osteogenic stimulation [38]. Cascaded systems push this further still: one pH-responsive composite hydrogel released VEGF early, exploiting the acidity of the injury environment, while mesoporous silica nanoparticles sustained BMP-2 delivery over a longer interval; the resulting microenvironment was both better vascularized and more osteogenic than either factor produced alone [40].

Evidence specific to the alveolar ridge is now emerging. Working in a canine extraction-socket model, investigators incorporated BMP-2 at low dose into biomimetic calcium phosphate and recorded significantly less loss of buccal height and ridge width than in controls, together with gains in bone mineral density, bone volume fraction and trabecular number and histological confirmation of increased new bone volume [41]. The same low-dose approach, delivered from functionalized calcium phosphate cement, has been assessed in lateral ridge augmentation, where it generated substantial mineralized tissue around implants and produced thicker trabeculae than either the cement alone or autogenous bone in the identical model [42]. Dual-delivery strategies have already shown benefit in sinus augmentation [39], suggesting the principal transfers across intraoral indications.

Read together, these findings mark a shift away from passive graft substitution toward scaffolds that are, in effect, biologically programmable. Synchronizing degradation with angiogenic, proliferative and osteogenic signaling may reproduce the natural

healing sequence more faithfully than any single-phase material can, while reducing the required growth factor dose and the dose-related risks that accompany it [40]. Two caveats are essential, however. The comparisons with autogenous bone have been conducted in animals rather than patients and the canine socket differs from the human one in healing rate, loading conditions and infection risk [41]. Further, the most encouraging results have come from defects with intact walls, whereas the compromised sockets that stand to benefit most from preservation are precisely those where maintaining space is hardest [42]. Properly designed human trials remain a prerequisite before these systems can be described as predictable alternatives to autogenous grafting.

Clinical Performance: Volumetric Stability and True Bone Regeneration

Judging ARP by the external contour of a healed site is insufficient. A technique earns its place only if it limits collapse in both planes and, at the same time, yields living bone able to receive an implant and hold up under function. Autogenous grafts and controlled-release synthetic scaffolds therefore need comparison across dimensional and biological endpointstogether and network meta-analysis has shown that these two do not necessarily move in the same direction. The materials that best maintain ridge dimensions are not always those producing the greatest proportion of newly formed bone [43].

Autogenous bone holds its reference position because of its regenerative capacity, but that capacity comes at an identifiable cost. Opening a donor site may add postoperative discomfort and morbidity [44] and patient-reported data document pain and other donor-site concerns when autogenous harvesting is compared head-to-head with allogeneic alternatives [45]. The graft itself remodels and resorbs once placed, so early regenerative vigor does not necessarily produce optimal volume maintenance when the material is used on its own [44].

Volume maintenance and genuine regeneration are not the same thing and conflating them has consequences. Histomorphometry looks directly at what the tissue is made of, separating living newly formed bone from leftover biomaterial and from non-mineralized connective tissue. What it repeatedly reveals is that a ridge which appears well maintained radiographically often contains a smaller fraction of vital bone than its appearance implies [43]. Radiographic fill and apparent density should therefore be interpreted with corresponding caution. One clinical trial acknowledged this openly, noting that computed tomography detects newly formed bone poorly during early healing when density remains low and identifying the absence of histomorphometric assessment as a limitation of its own design [46].

Growth factor-enhanced systems are intended to deliver regeneration while sparing the donor site. An American Academy of Periodontology best-evidence review of biologics in ridge preservation and reconstruction reported encouraging histomorphometric findings for recombinant human BMP-2 (rhBMP-2) and recombinant human PDGF-BB, while noting that superiority on clinical and radiographic measures was not consistently established [47]. A randomized trial combining rhBMP-2 with β-TCP found significantly less loss of alveolar height and width at twelve weeks than with β-TCP alone [46]. More recently, a pilot study using an absorbable collagen sponge as the rhBMP-2 carrier also reported better preservation of buccal bone height at twelve weeks than untreated sockets [48]. Short-term dimensional preservation is thus reasonably well supported. Durable regeneration is a different claim and a twelve-week endpoint cannot substantiate it.

Implant-related outcomes reveal whether preserved bone is functionally sound. In one clinical study, implants were placed after ARP using two different rhBMP-2 delivery systems; the implant stability quotient rose between primary and secondary measurements in both groups, with no meaningful difference between delivery systems and comparable healing intervals [49]. Survival at approximately three years reached 100% and 92.9%, respectively. Notably, however, additional surgery was still needed at some sites because of insufficient bone height or width, indicating that growth factor-assisted ARP does not reliably eliminate the need for secondary augmentation [49].

The overall position is therefore mixed. Controlled-release scaffolds avoid harvesting and show encouraging results across dimensional, histomorphometric and implant-related measures and consensus assessments of regenerative technology in the craniomaxillofacial region reach a similar conclusion: the biology is persuasive, but the clinical evidence is uneven [50]. Human data do not currently demonstrate ridge preservation that is more predictable or more durable than autogenous grafting and the small pilot cohorts and abbreviated follow-up typical of this literature cannot detect late resorption [48]. What is required are longer studies reporting volumetric stability, bone density, percentage of vital bone, residual biomaterial, secondary augmentation requirements, implant stability and implant survival within a single cohort, only then can short-term radiographic

preservation be shown to correspond to stable, functional bone [47].

Limitations, Emerging Directions

Bioengineering and smart biomaterials are widely expected to reshape regenerative dentistry and the ambition behind that expectation is considerable. Nanotechnology, additive manufacturing and synthetic scaffold design are converging on constructs that do more than occupy a defect — they direct the biological response occurring within it [51]. Groups worldwide continue to extend these capabilities and the materials emerging are increasingly characterized as devices rather than fillers, since a single construct may now combine structural, biochemical and in some cases responsive functions [52].

Biological and technical constraints nonetheless stand between this potential and its realization. Vascularization is the principal biological bottleneck: however favorable a construct's architecture, cells at its center will not survive if perfusion cannot reach them quickly enough and biocompatibility and osseointegration with host bone impose additional ceilings [51]. The mechanical domain presents an analogous difficulty, since a construct is asked to remain stable under function while breaking down on a schedule that suits oral tissue regeneration — two requirements that regularly conflict [53].

Cost and manufacturability form a second cluster of obstacles. Bringing a personalized scaffold to production requires characterizing, testing and approving new materials, which is both expensive and slow; adding growth factors introduces complexity that has largely kept advanced constructs at laboratory scale, because maintaining consistent performance during scale-up is difficult [54]. Sophistication drives cost upward, which threatens access in lower-income settings and widens the distance between what can be built and what can actually be used [55]. Standardization compounds this. Sterilization protocols for these devices remain unsettled and while many additive manufacturing materials already hold regulatory and public health recognition, low-temperature sterilization takes longer, costs more and lies beyond the reach of many dental practices [54].

Regulatory pathways constitute a further barrier. The moment a material incorporates growth factors, genes, cells or other bioactive components, it stops being classified as a simple device; the approval route becomes markedly more demanding, with corresponding increases in required evidence and time to market [56]. This burden goes some way toward explaining why combination products move from preclinical promise to clinical availability far more slowly than the underlying science alone would suggest [57].

Predicting how delivered growth factors will behave in a given patient also remains difficult. Effective regeneration depends on local factor concentration, receptor availability and the biochemical condition of the recipient tissue and the same molecule may either promote or disturb cell behavior depending on those variables. Safety concerns tied to supraphysiological dosing continue to constrain clinical application and it is not yet possible to state confidently that any particular combination of scaffold, cells and signaling molecules will regenerate tissue predictably in an individual [58]. Absent standardized protocols, results from different research groups also resist direct comparison [56].

The evidence base is itself the most consequential limitation. Long-term randomized trials comparing graft materials are scarce, particularly for newer composite and bioactive constructs and much of what exists derives from animal models observed over short periods [55]. Reviews and meta-analyses are plentiful but largely aggregate the same restricted pool of primary clinical data and surveys of materials science progress in oral and maxillofacial grafting keep identifying the identical gap between what is published in the laboratory and what is confirmed in patients [53].

Artificial intelligence has begun addressing part of this. Predictive models can simulate how a particular scaffold composition and architecture will behave biologically, permitting candidate designs to be screened computationally before anything is fabricated and allowing anticipated healing outcomes to be compared across alternatives [57]. Applied to patient-specific planning, such tools accelerate selection of a configuration suited to the individual defect and can compress both the design cycle and the operation itself, though their outputs still require validation against clinical rather than simulated endpoints [52].

Three-dimensional bioprinting ranks among the more transformative of these technologies, since computer-aided design and manufacturing allow a scaffold's geometry to be customized precisely to the defect and supplying a construct that needs no intraoperative shaping shortens operating time [59,62]. The aim is to approximate the architecture of the patient's own bone.

Hydroxyapatite and β-TCP feature commonly because they support bone growth and integration and incorporating stem cells into printed constructs has been investigated as a means of enhancing regeneration, although whether those cells survive within the printed matrix remains a critical determinant of effectiveness [59].

Several biological strategies are developing alongside these fabrication advances. Gene therapy delivered through biomaterial platforms represents a viable route to alveolar bone preservation; immobilizing BMP genes on implant surfaces has enhanced peri-implant bone regeneration while sidestepping the high protein doses that carry adverse effects [58]. Exosome-based delivery offers a cell-free alternative, using nanoscale extracellular vesicles to carry osteogenic proteins, angiogenic factors and immunoregulatory molecules into the defect, combining biological potency with a safety profile more favorable than cell transplantation [60,61]. Early work in dental and maxillofacial applications indicates that this promotes healing and tissue regeneration, though standardizing isolation and dosing remains unresolved [61].

Conclusion

Immunomodulatory and stimuli-responsive biomaterials represent a further conceptual departure. Rather than evading the host immune response, immunomodulatory constructs are designed to steer it, encouraging a reparative macrophage phenotype that favors regeneration and integration. Stimuli-responsive scaffolds extend the same logic to release, discharging their payload only when defined local conditions are met. pH-keyed systems exploit the acidity characteristic of inflamed tissue. Enzyme-responsive systems take advantage of fluctuating matrix metalloproteinase activity in injured tissue, so that proteolysis itself triggers BMP-2 release and the osteogenic marker expression that follows in pre-osteoblasts. Mechanically responsive systems detect stress, pressure and strain, reproducing the dynamic loading environment of natural bone.

Returning to the question with which this review opened, the answer the present evidence supports is a qualified negative. Synthetic scaffolds with controlled growth factor delivery preserve ridge dimensions and generate vital bone without a donor site, a substantial clinical advantage; smart, responsive constructs may eventually deliver signals with a precision autogenous bone cannot match. However, greater long-term predictability has not been demonstrated. Autogenous bone retains its benchmark status because its behavior over years, resorption included, is documented in human patients, whereas comparative data for bioengineered constructs remain largely preclinical, short-term or both. The realistic objective for the coming decade is therefore not to replace lost bone but to induce the host to regenerate its own reliably. Progress toward that objective will be measured in adequately powered clinical trials reporting volumetric, histomorphometric and implant-related endpoints together, not in further preclinical demonstration.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding Statement

This research did not receive any specific grant from funding agencies in the public, commercial or non-profit sectors.

Acknowledgement

The authors have no acknowledgments to declare.

Data Availability Statement

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

Ethical Statement

The project did not meet the definition of human subject research under the preview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

Not applicable.

Authors' Contributions

All authors contributed equally to this paper.

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