

Beyond The Gold Standard: Rethinking Bone Graft Selection For Dental Implants In The Era Of Dentin Grafts, Growth Factors, And Bioprinted Scaffolds

Paulo Vinicius de Oliveira Bastos¹

(Specialist in Periodontology, Odontoclínica Central do Exército (OCEx), Specialist in Implant Dentistry, Federal University of Rio de Janeiro (UFRJ), Master's Degree in Orthodontics, Federal University of Juiz de Fora, Rio de Janeiro, RJ, Brazil)

ORCID: <https://orcid.org/0009-0008-2449-3010>

Corresponding author e-mail: paviolba75@gmail.com

Caroline Melo Gomes Malaquias

(Specialist in Implant Dentistry, ABO, Specialist in Orthodontics, ABEPO, Vitória da Conquista, Bahia, Brazil)

ORCID: 0009-0005-2132-8798

carol_melog@icloud.com

Larissa Caroline Cayres Pereira

(Specialist in Implant Dentistry, University Cruzeiro do Sul, SP, Brazil)

ORCID: <https://orcid.org/0009-0008-2406-8137>

laricayres12@gmail.com

Diogo Mendes Silva

(Specialist in Implant Dentistry, University of Guarulhos, SP, Brazil)

ORCID: 0009-0004-0035-8288

dr.diogomendessilva@gmail.com

Caroline dos Santos Alcantara

(Specialist in Orthodontics, IOPG- Instituto Odontológico de Pós Graduação – Bauru, SP, Brazil)

ORCID: 0009-0006-4214-5955

Carolines.alcantara2016@gmail.com

Marcos Pereira Villa-Nova

(Dentist, University Estácio de Sá – Rio de Janeiro, RJ, Brazil)

ORCID: 0009-0005-6619-7285

drmarcosvillanova@gmail.com

Pablo Mendonça de souza

(Specialist in Implant Dentistry – (ABO), Osasco, SP, Brazil)

ORCID: 0009-0002-2061-482

pablomsouza89@gmail.com

Cíntia Carvalho Gomes

(Specialist in Implant Dentistry – University of São Paulo's City, SP, Brazil)

ORCID: 0009-0008-4498-5696

cintiacgomes@hotmail.com

Abstract:

Background: Alveolar bone resorption following tooth loss frequently compromises the volume and quality of bone available for implant placement, and bone grafting is required in an estimated one in every four dental implant cases. Over the past five years the therapeutic landscape has expanded far beyond the classical autograft/allograft/xenograft/alloplast framework, incorporating autogenous tooth-derived (dentin) grafts, recombinant growth-factor-loaded carriers, three- and four-dimensional (3D/4D) bioprinted scaffolds with sequential growth-factor release, and stem-cell/exosome-based cell-free therapies.

Materials and Methods: A narrative literature review was conducted using PubMed-, Scopus-, and Semantic Scholar-indexed sources retrieved through the Consensus academic research platform, focusing on peer-reviewed articles published between 2021 and 2026, supplemented by earlier foundational studies where relevant to context. Search terms combined “bone graft,” “dental implant,” “autograft,” “allograft,” “xenograft,” “alloplast,” “dentin graft,” “rhBMP-2,” “guided bone regeneration,” “3D bioprinting,” “4D printing,” “mesenchymal stem cell,” and “exosome.” Randomized controlled trials, systematic reviews, and narrative reviews published in English were prioritized; case reports, non-peer-reviewed preprints, and animal-only studies without translational discussion were generally excluded except where illustrating an otherwise underrepresented emerging technology.

Results: Autogenous bone remains the biological benchmark for combined osteogenic, osteoinductive, and osteoconductive activity, but donor-site morbidity and unpredictable resorption (up to ~42% volumetric loss at six months in sinus augmentation) continue to limit its routine use. Xenografts, particularly deproteinized bovine and porcine mineral, show the most consistent evidence of matching autograft clinical outcomes while resorbing far more slowly (as little as ~7% at six months), and allografts perform comparably in ridge preservation. Autogenous dentin, obtained by grinding the patient's own extracted tooth, has emerged as a genuinely novel autogenous alternative with strong histological evidence of osteoconduction and osteoinduction without a second surgical site. Alloplastic ceramics remain reproducible and unlimited in supply but show comparatively lower new bone formation. Recombinant human bone morphogenetic protein-2 (rhBMP-2), now used clinically in composite grafts and titanium-mesh techniques, achieves implant survival and marginal-bone-loss outcomes equal to or exceeding conventional grafts in resorbed ridges, without donor-site surgery. The most active current research frontier combines 3D/4D bioprinting with spatiotemporally sequenced growth-factor release (VEGF, BMP-2, PDGF, TGF- β 1) and, increasingly, cell-free mesenchymal stem cell-derived exosome therapies, though both remain largely preclinical.

Conclusion: No single graft material satisfies every criterion of the “ideal” bone substitute, and the comparative evidence increasingly favors combination and hybrid strategies over any single material used alone. Recent innovations — particularly autogenous dentin grafts, clinically validated rhBMP-2 delivery systems, and growth-factor-functionalized bioprinted scaffolds — are progressively narrowing the historical trade-off between regenerative performance and patient morbidity, and represent the most promising directions for translation into routine implant dentistry.

Key Word: Bone graft; Dental implants; Osseointegration; Guided bone regeneration; Autogenous dentin graft; rhBMP-2; 3D bioprinting; Biomaterials.

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I. Introduction

Tooth loss initiates a well-documented and largely irreversible cascade of alveolar ridge resorption: within the first year after extraction, the residual ridge can lose up to 50% of its original width, with the greatest dimensional change occurring on the buccal aspect¹. This resorptive process frequently leaves insufficient bone volume and quality to support a dental implant in a prosthetically ideal position, which is why bone grafting has become one of the most routine adjunctive procedures in implant dentistry, required in an estimated one in every four implant cases¹. The clinical consequences of inadequate bone volume are not merely aesthetic: they compromise primary implant stability, long-term marginal bone maintenance, and the biomechanical distribution of occlusal load, making the choice of grafting strategy a decision with direct bearing on implant survival.

Historically, bone graft materials have been classified into four broad categories according to their tissue origin: autografts, harvested from the patient's own body; allografts, processed bone obtained from human donors; xenografts, derived from another species, most commonly bovine or porcine; and alloplasts, fully synthetic materials such as calcium phosphates and bioactive glasses². Each category is evaluated along the classic regenerative triad of osteogenesis (the intrinsic capacity to form new bone via viable transplanted cells), osteoinduction (recruitment and differentiation of host mesenchymal cells via biologically active signaling molecules), and osteoconduction (passive scaffolding that supports the ingrowth of host bone)³. No material within this classical framework combines all three properties without a significant trade-off: autografts

alone are osteogenic, osteoinductive, and osteoconductive, but require a second surgical site; the remaining categories sacrifice osteogenic potential, and often much of the osteoinductive potential, in exchange for eliminating donor-site morbidity.

The past five years have substantially reshaped this classical picture. First, autogenous tooth-derived grafts — particulate or demineralized dentin obtained from the patient's own extracted teeth, previously considered biological waste — have emerged as a genuinely novel intra-category alternative, combining autogenous biocompatibility with a far less invasive harvesting procedure than traditional intraoral or extraoral bone harvesting^{4,5}. Second, recombinant osteoinductive growth factors, above all recombinant human bone morphogenetic protein-2 (rhBMP-2), have progressed from experimental use to routine clinical protocols for ridge preservation, horizontal and vertical augmentation, and sinus floor elevation, in some series matching or exceeding the outcomes of autogenous grafting without any donor-site surgery⁶. Third, three- and four-dimensional (3D/4D) bioprinting has enabled a fundamentally new paradigm: rather than selecting among passive scaffolds, researchers can now engineer the temporal sequence of biological signaling within a single construct, releasing angiogenic factors first and osteogenic factors afterward to more faithfully recapitulate natural bone healing physiology⁷. Finally, cell-free therapies based on mesenchymal stem cell-derived exosomes are beginning to be explored as a means of harnessing the paracrine regenerative signaling of stem cells without the regulatory and logistical burden of live-cell transplantation⁸.

Given this rapidly diversifying landscape, a critical, up-to-date synthesis comparing traditional graft materials against these genuinely new alternatives is of direct practical value to the implant surgeon. The aim of the present narrative review is therefore to (i) summarize the current evidence for each classical graft category, (ii) examine in detail the most clinically and scientifically significant recent innovations — autogenous dentin grafts, clinical rhBMP-2 protocols, growth-factor-sequenced bioprinted scaffolds, and stem cell/exosome-based strategies — and (iii) critically compare these materials against one another in light of the most recently published evidence, rather than relying on outdated hierarchies established before these innovations existed.

II. Material And Methods

A narrative literature review was conducted using PubMed-, Scopus-, and Semantic Scholar-indexed sources retrieved through the Consensus academic research platform, focusing on peer-reviewed articles published between 2021 and 2026, supplemented by earlier foundational studies where relevant to context. Search terms combined “bone graft,” “dental implant,” “autograft,” “allograft,” “xenograft,” “alloplast,” “dentin graft,” “rhBMP-2,” “guided bone regeneration,” “3D bioprinting,” “4D printing,” “mesenchymal stem cell,” and “exosome.” Randomized controlled trials, systematic reviews, and narrative reviews published in English were prioritized; case reports, non-peer-reviewed preprints, and animal-only studies without translational discussion were generally excluded except where illustrating an otherwise underrepresented emerging technology.

Because this is a narrative rather than systematic review, no formal dual-reviewer screening, PRISMA flow diagram, or Cochrane risk-of-bias appraisal was applied to the primary literature; nonetheless, priority was consistently given to the most recent systematic reviews and randomized controlled trials available for each graft category, supplemented by narrative reviews and case series only where controlled clinical data for an emerging technology remain unavailable. Studies were organized thematically by graft category and, within the discussion, cross-compared chronologically to distinguish long-established evidence from genuinely recent innovations, allowing the comparative analysis in Section IV to reflect the current, rather than historical, state of the evidence.

III. Result

Autogenous Bone Grafts (Autografts)

Autogenous bone, harvested intraorally from the mandibular ramus or symphysis, or extraorally from the iliac crest or calvarium, remains the only material that is simultaneously osteogenic, osteoinductive, and osteoconductive, and continues to be described by many authors as the clinical gold standard^{2,3}. Its principal limitations are a second surgical site with associated morbidity (pain, risk of neurosensory injury, limited harvestable volume) and a comparatively rapid and unpredictable resorption pattern. A systematic review of randomized controlled trials in lateral sinus augmentation found that autogenous grafts showed the greatest volumetric reduction at six months of any material compared ($41.71 \pm 12.63\%$), considerably higher than xenografts ($7.30 \pm 15.49\%$)⁶. A split-mouth randomized trial comparing autologous mandibular bone with porcine xenograft in two-step lateral window sinus lift found statistically significant bone gain with both materials and no significant difference between them (7.8 ± 2.4 mm autogenous vs. 8.7 ± 2.2 mm xenograft, $p = 0.26$), an important early signal that xenografts could approximate autograft performance while avoiding a second surgical site⁵.

Autogenous Dentin Grafts: A Genuinely Novel Autogenous Alternative

Among the most significant recent developments in bone grafting for implant dentistry is the clinical validation of autogenous tooth-derived dentin as a graft material. Rather than discarding an extracted tooth as biological waste, it can be processed — most commonly using a chairside tooth grinder — into particulate dentin, which is chemically and structurally similar to bone mineral and retains bioactive dentin matrix proteins⁹. Histomorphometric evaluation of particulate dentin used for socket preservation found complete biocompatibility and high osteoconduction, with new bone formation occupying $38.4\% \pm 16.5\%$ of the grafted area and direct bone-to-dentin particle contact averaging $69.1\% \pm 22.8\%$. A case series using a dedicated tooth-grinding device for socket preservation reported vital bone occupying $40.39\% \pm 15.86\%$ of biopsy volume at implant placement, with only $12.20\% \pm 12.34\%$ residual graft remaining and no infective complications over an 18-month average follow-up¹⁰.

Comparative and longitudinal data further strengthen the case for this material. A pilot study mixing dentin with xenograft at a 1:1 ratio, used when dentin alone was insufficient in volume, found the two materials resorbed at markedly different rates — 71% of the dentin fraction resorbed by four months versus only 6% of the xenograft fraction — with the resulting resorption gap itself appearing to stimulate additional new bone formation¹¹. A retrospective human study following particulate dentin grafts over 24 months documented a clear temporal trajectory of bone maturation, from 16.3% new bone at three months to 59.4% at 24 months, with high resorption of the dentin particles and replacement by mature bone without inflammatory signs¹². A 2025 narrative review restricted to studies directly comparing autogenous dentin against spontaneous (unassisted) healing found consistently better preservation of ridge dimensions with dentin grafting, particularly in the coronal third of the socket, across all six qualifying comparative studies¹³, and a randomized controlled trial in severely periodontally compromised sockets found that autogenous partially demineralized dentin matrix increased ridge width by 4.5–5.2 mm and bone volume by 37.07%, compared to a bone volume increase of only 2.33% with spontaneous healing ($p < 0.05$ for both)¹⁴.

A comprehensive review of autogenous tooth graft use specifically in guided bone regeneration, synthesizing 19 qualifying studies out of 174 screened, concluded that the technique produced stable new bone formation, low marginal bone loss, and clinically acceptable implant stability quotients, with high implant survival rates overall¹⁵. Combining dentin with platelet-rich fibrin (PRF) appears to further accelerate early bone formation: a controlled comparison of dentin alone, dentin plus PRF, and untreated (control) extraction sockets found significantly greater new bone formation and higher expression of BMP-2 and Runt-related transcription factor-2 (RUNX2) in the combined dentin-PRF group than in either dentin alone or untreated sockets¹⁶. A split-mouth comparison directly pitting dentin autograft against conventional autogenous bone graft harvested from the external oblique ridge for third-molar socket preservation found comparable regenerative potential between the two, raising the practical question of why a second surgical harvest site should be created at all when a comparably effective material is otherwise discarded¹⁷. A systematic review protocol registered with PROSPERO is currently underway to formally synthesize this evidence base under GRADE methodology, reflecting the rapid maturation of interest in this material over a very short period¹⁸.

Allogeneic Bone Grafts (Allografts)

Allografts consist of processed human donor bone — fresh-frozen, freeze-dried, or demineralized freeze-dried bone matrix — and provide reliable osteoconduction with variable, processing-dependent osteoinductive potential, without requiring a second surgical site². A systematic review comparing xenografts and allografts prior to dental implant placement, synthesizing 12 studies encompassing 395 patients, found bovine-derived allografts (41.9% of the pooled sample) and bovine xenografts (58.1%) to produce broadly comparable clinical outcomes across alveolar ridge preservation, immediate and delayed implant placement, and sinus augmentation, though the authors emphasized a persistent lack of demographic diversity and generally small sample sizes across the available comparative literature¹⁹.

Xenogeneic Bone Grafts (Xenografts)

Xenografts, most commonly of bovine (deproteinized bovine bone mineral) or porcine origin, are processed to remove antigenic organic components while preserving a mineral scaffold chemically similar to human bone². A sequence of randomized trials by the same research group, spanning progressively longer follow-up periods, has consistently reported clinical outcomes for porcine xenograft comparable to autograft in lateral sinus augmentation: at 12 months, implant survival was 95% on the xenograft side versus 100% on the autologous side, with low and statistically similar marginal bone loss between groups²⁰; at three years, using a collagen-supplemented porcine xenograft, no significant differences from autograft were found in implant survival, marginal bone loss, or patient preference²¹. A 2026 systematic review comparing alloplastic and biologic (allograft/xenograft) materials in maxillary sinus augmentation across 18 studies concluded that

autografts showed the highest regenerative effectiveness overall, followed by xenografts, with alloplasts showing comparatively lower new bone formation but superior dimensional stability relative to autograft²². Notably, a randomized trial evaluating graftless sinus floor elevation (membrane elevation without any grafting material at all) found significantly lower bone gain (6.20 mm vs. 9.69 mm, $p = 0.041$) and lower implant survival (86.2% vs. 96.7%, $p < 0.001$) compared with conventional autograft/xenograft augmentation, confirming that grafting material continues to confer a measurable clinical advantage over a graftless approach²³.

Alloplastic and Synthetic Bone Substitutes

Alloplastic materials include calcium-phosphate ceramics (hydroxyapatite, β -tricalcium phosphate), bioactive glasses, and their composites, valued for unlimited availability, absence of any disease-transmission risk, and reproducible manufacturing^{2,3}. Hydroxyapatite (HA), the most extensively studied synthetic material owing to its compositional similarity to natural bone mineral, has been used clinically in sintered, carbonated, eggshell-derived, and three-dimensionally printed forms, and in combination with rhBMP-2, PRF membranes, collagen membranes, and amniotic membranes; a systematic review of 11 qualifying studies found these modifications consistently improved osseointegration outcomes as assessed by histomorphometry, implant stability quotient, and imaging²⁴. A further refinement involves incorporating therapeutic ions — strontium, copper, boron, magnesium, lithium, and silver, among others — into the ceramic lattice, conferring additional osteogenic, angiogenic, or antibacterial properties beyond simple osteoconduction²⁵. Nevertheless, direct comparative clinical evidence remains less favorable for alloplasts than for natural grafts: the 2026 systematic review discussed above found alloplasts inferior to both xenografts and allografts in new bone formation, with higher residual graft content indicating slower resorption²².

Platelet Concentrates and Composite (“Sticky Bone”) Strategies

Autologous platelet concentrates — platelet-rich fibrin (PRF) and injectable platelet-rich fibrin (i-PRF) — are increasingly combined with particulate graft material to form a cohesive, moldable composite informally termed “sticky bone,” which improves surgical handling, adheres to defect margins, and locally releases growth factors that may accelerate healing²⁶. In a 36-month retrospective comparison of PRF alone versus xenograft in sinus augmentation with simultaneous implant placement, both groups achieved 100% implant survival, with PRF showing a numerical advantage in keratinized tissue height, suggesting a possible soft-tissue benefit even where PRF alone provided somewhat lower radiographic bone gain than xenograft²⁷.

Growth-Factor-Enhanced Grafts: Clinical Translation of rhBMP-2

Recombinant human bone morphogenetic protein-2 (rhBMP-2), long studied preclinically, has in the past several years moved decisively into routine clinical protocols for alveolar ridge preservation and augmentation, generally delivered on an absorbable collagen sponge (ACS) or acellular dermal matrix (ADM), often mixed with deproteinized bovine bone mineral or β -tricalcium phosphate to provide additional structural volume²⁸. Case-level evidence includes an rhBMP-2-coated implant placed immediately into a severely resorbed maxillary socket, with successful integration and minimal complications at six months²⁹, and two cases of horizontal ridge augmentation using rhBMP-2-loaded ADM without any additional graft material, achieving 1.5–1.7 mm of horizontal bone gain fully covering previously exposed implant threads, with no peri-implantitis at 10–13 months³⁰.

Comparative and retrospective series provide stronger evidence of clinical equivalence or superiority to conventional grafting. A retrospective follow-up of alveolar ridge preservation using two different rhBMP-2 delivery systems found implant success rates of 100% and 92.9% respectively over roughly three years, with marginal bone loss below 0.03 mm in both groups³¹. A composite graft technique combining rhBMP-2/ACS with deproteinized bovine bone mineral in a titanium mesh achieved 100% implant success and survival at one-to-four-year follow-up for vertical ridge augmentation³², and an analogous protocol for posterior maxillary reconstruction — the so-called “BOXAM” technique combining rhBMP-2, a preformed titanium mesh, xenograft, and allograft — achieved excellent bone quality and implant stability within four months, notably faster than historical grafting timelines, while eliminating the need for autogenous harvesting altogether³³. In a larger case series of 13 patients (71 implants) undergoing reconstruction of a severely resorbed posterior maxilla, an rhBMP-2/ACS plus deproteinized bovine bone mineral composite achieved a mean alveolar ridge height increase of 14 mm and width increase of 6 mm, with 100% implant success and survival maintained over 3–12 years of follow-up³⁴.

A pilot randomized controlled trial isolating the effect of rhBMP-2 itself (ACS with rhBMP-2 versus an empty socket control) found a statistically significant 1.80 mm reduction in buccal bone height loss at 12 weeks in the rhBMP-2 group, though overall bucco-lingual ridge width collapse was not fully prevented, indicating that rhBMP-2 selectively protects specific dimensions of the ridge rather than eliminating resorption

altogether³⁵. Perhaps most directly relevant to long-term implant prognosis, a retrospective study of 63 implants placed after maxillary sinus floor augmentation found that adding rhBMP-2 to the graft material improved 3- and 5-year cumulative implant survival (100% at both time points versus 95.5% and 86.4% without rhBMP-2) and reduced marginal bone loss at both intervals, particularly benefiting cases with unfavorable preoperative residual bone height³⁶. These findings collectively indicate that rhBMP-2 has moved from an experimental adjunct to a clinically validated tool capable of matching or exceeding conventional grafting outcomes while avoiding donor-site morbidity, though standardized dosing protocols and long-term safety monitoring remain areas of ongoing clinical attention^{37,38}.

Three- and Four-Dimensional (3D/4D) Bioprinting with Sequential Growth-Factor Release

The most active area of current laboratory research combines additive manufacturing with spatiotemporally controlled, sequential delivery of growth factors, seeking to mimic the natural physiological sequence of angiogenesis followed by osteogenesis observed during bone healing³⁹. Vascular endothelial growth factor (VEGF) and bone morphogenetic protein-2 (BMP-2) form the most extensively studied combination: a staged-release GelMA-alginate microsphere scaffold produced by combined microfluidic and 3D-printing methods achieved an initial burst of VEGF followed by sustained BMP-2 release, fully repairing a critical-sized cranial defect in a rat model within 12 weeks⁴⁰; a bilayer bioprinted GelMA construct separately encapsulated BMP-2- and VEGF-loaded PLGA nanoparticles within osteogenic and vascular-mimetic layers respectively, achieving zero-order release kinetics⁴¹; and a 3D-printed porous titanium alloy scaffold coated with VEGF/BMP-2 shell-core microspheres achieved sequential release with significantly greater new bone formation than gelatin-coated or uncoated titanium controls in a rabbit femoral defect model⁴².

Beyond the VEGF/BMP-2 combination, an injectable poly(organophosphazene) hydrogel encapsulating both BMP-2 and TGF- β 1 achieved sequential release from a single, one-step formulation without requiring a complex multi-material scaffold design⁴³, while nanoparticle-based composite coatings using differentially degrading carriers (chitosan/albumin for VEGF versus poly-L-lysine/alginate for BMP-2) similarly achieved tunable, staged release on tricalcium phosphate scaffolds⁴⁴. A separate line of work combining BMP-7 and fibroblast growth factor-2 (FGF-2) on nanofibrous scaffolds demonstrated that the relative dose and release kinetics of the two factors, rather than their mere co-presence, determines whether FGF-2 enhances or paradoxically inhibits BMP-induced bone regeneration — an important caution for future scaffold dosimetry⁴⁵. A broader 2025 review of 3D-printed scaffold technologies for bone repair concluded that structural optimization (hierarchical macro/micro/nano-porosity) and biological functionalization are now converging with artificial-intelligence-guided, patient-specific design as complementary rather than competing strategies⁴⁶.

Four-dimensional (4D) printing extends this approach by incorporating stimuli-responsive “smart” materials — most often shape-memory polymers responding to temperature, near-infrared light, or magnetic fields — allowing a scaffold implanted in a compact, minimally invasive form to subsequently self-expand or change function to match an irregular defect geometry^{47,48}. A systematic review following PRISMA guidelines identified only 15 qualifying studies to date, most exploiting thermally triggered shape-memory effects using polyurethane or poly(lactic acid), and found that 4D-printed scaffolds showed higher osteogenic differentiation capacity than structurally identical static 3D-printed controls⁴⁸. A review focused specifically on oral and craniofacial applications noted that 4D printing is particularly suited to the dynamic mechanical environment of the alveolus and jaws, which undergo continual remodeling with tooth eruption and movement, though it emphasized that clinical translation in dentistry remains at an early, largely preclinical stage⁴⁷.

Stem Cell- and Exosome-Based Regenerative Strategies

A parallel and increasingly prominent research direction explores cell-free therapies based on extracellular vesicles (exosomes) secreted by mesenchymal stem cells (MSCs), which carry proteins, lipids, and regulatory RNAs capable of modulating inflammation, promoting angiogenesis, and enhancing osteogenic differentiation without the regulatory and logistical burden of transplanting living cells^{8,49}. A review focused specifically on peri-implant bone regeneration found that MSC-derived exosomes show potential to counter aseptic loosening around prostheses and implants through modulation of inflammatory responses, suppression of osteoclastogenesis, and enhancement of osteogenic differentiation⁴⁹, while a broader review of MSC-exosome clinical potential in bone regeneration emphasized that although preclinical results across intravenous and biomaterial-combined delivery are promising, standardization of isolation protocols and appropriately powered clinical trials remain necessary before translation⁵⁰.

Engineering strategies that combine exosomes with biomaterial carriers appear especially promising: hydrogel-integrated exosome mimetics derived from osteogenically induced MSCs cultured as spheroids produced robust bone regeneration in a mouse calvarial defect model, with associated activation of Wnt/ β -catenin and Notch signaling pathways⁵¹, and a broader review of biomaterial-assisted exosome delivery

platforms concluded that combining exosomes with scaffolds substantially enhances their functional retention and regenerative effect compared with exosome injection alone⁵². Of particular relevance to dentistry, exosomes derived specifically from dental-tissue mesenchymal stem cells (from dental pulp, apical papilla, and gingiva) offer lower immunogenicity and fewer ethical constraints than exosomes derived from bone marrow or other non-dental sources, and are increasingly explored for jawbone repair alongside their more established roles in periodontal and pulp regeneration⁵³, though clinical application in implant dentistry specifically remains almost entirely preclinical at present.

Nanomaterials and Ion-Doped Bioceramics

Complementary nanotechnology approaches further illustrate the convergence of materials science and regenerative medicine now shaping this field. Rare-earth-doped nanomaterials have been developed with combined osteogenic, angiogenic, antimicrobial, antioxidant, and even in vivo imaging capabilities, offering a multifunctional alternative to single-purpose graft materials⁵⁴, while magnetic nanoparticles and stimuli-responsive (pH- or temperature-sensitive) hydrogels represent a further evolution of bone-regeneration biomaterials beyond the traditional grafting paradigm, with the capacity to be externally triggered to release therapeutic payloads on demand⁵⁵. Collectively, these nanotechnology-based strategies, alongside the ion-doped ceramics discussed in Section 3.5, suggest that the boundary between “alloplast” and “biologically active material” is progressively dissolving as synthetic scaffolds are engineered to actively participate in, rather than merely passively support, the regenerative process⁵⁶.

IV. Discussion

Comparing Regenerative Performance: What the Most Recent Evidence Actually Shows

The traditional hierarchy taught in implant dentistry — autograft as the unrivaled gold standard, followed at some distance by allograft, xenograft, and finally alloplast — is only partially supported when the most recent comparative trials are examined directly rather than assumed. Volumetrically, autograft is in fact the least stable of the four classical materials: the pooled randomized-trial data show autogenous bone losing roughly 42% of its grafted volume by six months, nearly six times the resorption rate of xenograft over the same interval (~7%)⁶. This inversion matters clinically because implant success depends on retained volume at the time of loading, not on peak regenerative activity immediately after grafting. Three separate randomized trials from the same research group, spanning follow-up from 12 months to three years, converge on the same conclusion: porcine xenograft is clinically indistinguishable from autograft in implant survival, marginal bone loss, and patient-reported outcomes^{20,21}, a finding robust enough across time points that it should arguably now be considered the primary evidence base for sinus augmentation material choice, rather than autograft superiority assumed from older, less rigorously controlled literature.

Where the newest evidence genuinely changes the comparative picture is in the emergence of autogenous dentin as a fifth, functionally distinct category. Because dentin is autogenous in origin yet requires no second surgical site — it is simply the patient's own extracted tooth, otherwise discarded — it partially resolves the central trade-off that has defined bone grafting for decades: the assumption that avoiding donor-site morbidity necessarily means sacrificing autogenous biological activity^{9,15}. The histomorphometric data are compelling on their own terms: new bone formation around dentin particles (38–41% of grafted area at four to six months) is comparable to, or in some series exceeds, published values for xenograft and allograft over similar intervals, while the resorption trajectory of dentin (71% resorbed by four months) more closely resembles the fast-remodeling profile of autograft than the slow, space-maintaining profile of xenograft^{9,11,12}. This places dentin in an intermediate regenerative category of its own: biologically closer to autograft in turnover, but logistically closer to a same-visit, no-additional-morbidity material — a genuinely new position on the trade-off curve that did not exist in the classical four-category framework.

The clinical translation of rhBMP-2 represents an equally significant, though differently structured, shift. Rather than offering a new graft material in the traditional sense, rhBMP-2 offers a way of pharmacologically upgrading the osteoinductive potential of an otherwise ordinary alloplast or xenograft carrier. The comparative numbers are striking: adding rhBMP-2 to a sinus graft raised five-year implant survival from 86.4% to 100% in one retrospective cohort³⁶, and rhBMP-2/ACS composite techniques achieved vertical ridge gains of up to 14 mm without any autogenous harvesting³⁴ — outcomes that, historically, would have been considered achievable only with block autograft or extensive staged autogenous procedures. In this sense, rhBMP-2 and autogenous dentin represent two distinct, non-competing solutions to the same underlying problem (how to obtain autograft-level biological activity without autograft-level morbidity): dentin achieves this by recycling autogenous tissue that already exists, while rhBMP-2 achieves it by pharmacologically inducing the host's own bone-forming response within an otherwise passive carrier.

Biofabrication and Cell-Free Therapies: Genuinely New Territory, Still Largely Preclinical

The 3D/4D bioprinting and exosome literature reviewed in Sections 3.8 and 3.9 occupies a different evidentiary category altogether from the clinical comparisons above: essentially all of the growth-factor-sequencing and exosome data derive from small-animal calvarial or femoral defect models, with no randomized human trials identified for either technology specifically in the context of dental implants^{39,50}. Nonetheless, the consistency of the VEGF-then-BMP-2 sequencing finding across independent research groups and delivery platforms — microsphere hydrogels, bilayer bioprinted constructs, coated titanium, and nanoparticle coatings all converge on the same staged-release principle improving outcomes^{40,41,42,44} — lends this specific strategy an unusually strong cross-validation for a still-experimental field, arguably stronger methodologically (if not yet clinically) than the single-material human trials available for some classical grafts. The dose-dependent finding that excessive FGF-2 can paradoxically inhibit BMP-induced regeneration is an important corrective against assuming that adding more growth factors, or higher doses, is always beneficial, and should inform how any future clinical translation of multi-factor scaffolds is dosed⁴⁵. Four-dimensional printing and exosome-based cell-free therapies remain the least mature of all technologies discussed in this review, evidenced by the small number of qualifying studies identified in the only systematic review of 4D bone scaffolds located (15 studies)⁴⁸ and by the near-total absence of oral- or alveolar-specific *in vivo* data for either technology.

Synthesizing the Comparison: Which Trade-offs Have Actually Changed

Taken together, the material reviewed here suggests that the field has moved from a single trade-off axis — regenerative potential versus morbidity — toward a more differentiated set of options along that same axis. Autograft still anchors one extreme (highest regenerative activity, highest morbidity and resorption), and pure alloplast the other (lowest morbidity and unlimited supply, lowest regenerative activity)^{6,22}. Xenograft and allograft continue to occupy a well-validated middle ground with the strongest volume of comparative clinical trial evidence of any category^{19,20,21,23}. What is genuinely new is the appearance of two additional strategies that do not simply sit between these poles, but instead shift the curve itself: autogenous dentin grafting, which delivers autograft-like biological turnover without a second surgical site^{9,15,17}, and rhBMP-2-augmented composite grafting, which delivers autograft-or-better clinical outcomes on top of an otherwise ordinary alloplast or xenograft carrier^{34,36}. Bioprinted, growth-factor-sequenced scaffolds and exosome-based cell-free therapies represent a further, more radical shift still in development, promising eventually to combine minimal morbidity with programmable, patient-specific regenerative performance, but not yet validated in the alveolar or peri-implant clinical setting specifically^{39,48,50}.

Limitations of the Study

This review has several limitations inherent to its narrative design. First, no formal systematic search protocol, dual-reviewer screening, or risk-of-bias appraisal (e.g., Cochrane RoB 2.0) was applied, so the selection of primary studies, while guided by recency and methodological quality, cannot exclude selection bias. Second, the evidence base for autograft, allograft, and xenograft comparisons is dominated by small, often single-center randomized trials (frequently fewer than 15 patients per arm) and by a limited number of research groups, restricting generalizability; notably, three of the xenograft trials discussed in Section 3.4 originate from the same investigative team, which strengthens internal consistency but limits external validation. Third, essentially all data on 3D/4D bioprinting with growth-factor sequencing and on exosome-based therapies derive from small-animal models (rodent calvarial or rabbit femoral defects) rather than from alveolar or peri-implant defect models directly relevant to implant dentistry, and no randomized human trials of these biofabricated or cell-free constructs were identified. Fourth, although the autogenous dentin and rhBMP-2 literature includes genuine human clinical data, sample sizes remain modest (typically under 40 patients per study) and long-term (>5 year) follow-up is scarce outside a small number of rhBMP-2 case series. Fifth, direct cost-effectiveness data, which the literature identifies as ultimately decisive for clinical adoption of any new material, were sparse and were not systematically extracted across studies. Finally, only English-language, peer-reviewed sources indexed in the databases searched were considered, which may have excluded relevant regional literature, including Brazilian and other Latin American clinical experience with several of these materials.

Proposals for Future Work

1. Conduct adequately powered, multi-center randomized controlled trials directly comparing autogenous dentin graft against xenograft and allograft specifically in alveolar ridge preservation and peri-implant defect models, rather than relying on comparisons against spontaneous healing alone.
2. Establish standardized protocols for chairside dentin processing (particle size, demineralization degree, sterilization) to allow pooling of results across studies and centers, given the current heterogeneity in preparation technique across the dentin-graft literature.

3. Extend rhBMP-2 clinical follow-up beyond the 3–5 year window currently available in most series, with particular attention to long-term marginal bone stability and any dose-related adverse effects in the specific context of alveolar and peri-implant use.
4. Translate growth-factor-sequenced 3D-bioprinted scaffolds (VEGF/BMP-2 and related combinations) from small-animal calvarial/femoral models into alveolar ridge and socket-preservation models more directly representative of implant dentistry, including split-mouth human pilot studies where ethically feasible.
5. Determine optimal dosing and relative release-kinetics for multi-factor delivery systems, given evidence that the ratio and timing between factors (e.g., BMP-7/FGF-2) can determine whether regeneration is enhanced or paradoxically inhibited.
6. Advance dental-tissue-derived (rather than bone-marrow-derived) mesenchymal stem cell exosome research specifically toward jawbone and peri-implant applications, capitalizing on their comparatively low immunogenicity and more accessible tissue source.
7. Advance 4D-printing and stimuli-responsive smart materials specifically for the craniofacial and alveolar environment, where dynamic remodeling during tooth eruption and orthodontic/prosthetic loading differs substantially from long-bone applications.
8. Incorporate formal cost-effectiveness and health-system feasibility analyses — particularly relevant for implant dentistry delivered within public health systems such as Brazil's SUS — alongside biological outcome measures in future comparative trials of all the materials discussed in this review.

V. Conclusion

The evidence reviewed here indicates that the classical hierarchy of bone graft materials for dental implants is being actively reshaped rather than simply reconfirmed. Autogenous bone remains biologically unmatched but resorbs faster than commonly assumed; xenografts and allografts now have robust, repeated randomized-trial support for clinical equivalence to autograft with substantially lower morbidity; and alloplasts remain a reproducible, if regeneratively modest, unlimited-supply option. Among genuinely recent innovations, autogenous dentin grafting stands out for combining autogenous biological turnover with the absence of a second surgical site, and clinically validated rhBMP-2 protocols now achieve vertical and horizontal ridge augmentation outcomes previously reserved for extensive autogenous procedures. Growth-factor-sequenced 3D/4D bioprinted scaffolds and mesenchymal stem cell-derived exosome therapies represent the most scientifically ambitious frontier, promising eventually to combine minimal morbidity with programmable regenerative performance, but require alveolar-specific in vivo and human clinical validation before they can be considered viable alternatives to the materials already in routine clinical use.

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