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REGENERATIVE DENTISTRY VERSUS SYNTHETIC BIOMATERIALS: A COMPARATIVE REVIEW OF BIOLOGICAL AND ENGINEERED APPROACHES TO ORAL TISSUE REPAIR

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ABSTRACT

Objective: This review compares regenerative dentistry, which seeks to restore diseased or damaged oral tissues using the body's own biological processes, with the long-established approach of replacing lost tissue with synthetic biomaterials. The aim was to critically appraise the evidence for biologically driven regeneration of the dentin-pulp complex, periodontium and alveolar bone relative to conventional synthetic alternatives, and to identify where the two approaches converge.

Methods: A narrative literature review was conducted using PubMed, Scopus and Web of Science, focusing on publications from 2017 to 2025, supplemented by earlier landmark studies where they remain clinically relevant. Sources covering dental pulp stem cell therapy, calcium silicate bioceramics, guided tissue and bone regeneration membranes, enamel matrix derivative, platelet concentrates and polymer-based scaffolds were selected for their methodological relevance to the pulp-dentin complex, periodontium and alveolar bone.

Results: Regenerative strategies, including dental pulp stem cell transplantation and enamel matrix derivative, have shown biologically authentic tissue formation and favourable clinical outcomes in pilot and randomised trials, but remain constrained by cost, technical complexity and variable long-term evidence. Synthetic biomaterials, particularly calcium silicate bioceramics and resorbable polymer membranes, offer predictable handling, regulatory maturity and lower cost, though they generally repair rather than truly regenerate tissue architecture. Hybrid strategies that combine synthetic scaffolds with biological signalling molecules or autologous cells appear to outperform either approach in isolation. Conclusion: Regenerative and synthetic strategies are complementary rather than mutually exclusive. Material selection should be guided by defect type, patient factors and the balance between biological fidelity and clinical practicality, with hybrid bioactive constructs representing the most promising direction for future clinical practice.

Keywords: Regenerative Dentistry; Synthetic Biomaterials; Tissue Engineering; Dental Pulp Stem Cells; Calcium Silicate Bioceramics; Guided Tissue Regeneration.

1 INTRODUCTION

Restorative dentistry has traditionally relied on inert, bonded synthetic materials to replace tissue lost to caries, trauma or periodontal disease. Regenerative dentistry instead aims to restore oral health by replacing diseased or damaged tissue with biologically functional, integrated counterparts, a fundamentally different philosophy from repair with bonded restorative materials [1]. The oral cavity contains a complex array of tissues that are frequently diseased, including the dental pulp, the periodontal ligament, the alveolar bone and the mineralised tooth itself, and regeneration of each presents distinct scientific and clinical challenges [1].

Functional biomaterials for regenerative dentistry are increasingly classified according to their biological role rather than their chemical origin, spanning osteoconductive ceramics, osteoinductive growth-factor carriers, and cell-instructive polymeric scaffolds [2]. Within this landscape, a persistent clinical question is whether biologically derived regenerative approaches, such as stem cell transplantation, growth-factor concentrates and extracellular-matrix-derived proteins, offer meaningful advantages over synthetic biomaterials such as calcium phosphate ceramics, resorbable polymers and non-resorbable membranes, which have decades of regulatory approval, manufacturing consistency and clinical familiarity behind them [3][4].

The rationale for this review is that clinicians are increasingly required to choose between, or to combine, biologically active regenerative therapies and conventional synthetic materials when managing pulpal, periodontal and osseous defects, yet comparative appraisals that weigh both approaches against the same clinical endpoints remain scarce. The objective of this review is therefore to compare the evidence base for regenerative dentistry and synthetic biomaterials across three principal domains of oral tissue repair, the dentin-pulp complex, the periodontium, and alveolar bone, and to evaluate the hypothesis that hybrid strategies combining biological signalling with synthetic scaffolding outperform either approach used in isolation.

2 MATERIALS AND METHODS

This review followed a narrative rather than systematic design, appropriate for synthesising a broad and methodologically heterogeneous body of literature spanning stem cell biology, materials science and clinical periodontics and endodontics. The electronic databases PubMed, Scopus and Web of Science were searched for English-language articles published between January 2017 and September 2026, using combinations of the terms "regenerative dentistry", "synthetic biomaterials", "dental pulp stem cells", "calcium silicate bioceramics", "guided tissue regeneration", "guided bone regeneration", "enamel matrix derivative", "platelet-rich fibrin" and "tissue engineering scaffolds". Reference lists of retrieved reviews were hand-searched for additional relevant primary studies and systematic reviews.

Studies were included if they reported clinical, pre-clinical or systematic-review-level evidence directly comparing, or independently evaluating, regenerative biological therapies or synthetic biomaterials for pulp-dentin, periodontal or alveolar bone repair. Case reports, non-peer-reviewed sources and studies not available in English were excluded. Because this is a narrative comparative review rather than a primary clinical or laboratory investigation, no human or animal subjects were recruited by the author, and no institutional ethical approval or informed consent was required for its preparation. Where included studies involved human participants, ethical approval and informed consent were reported by the original investigators in the cited primary sources.

Extracted data were organised thematically by tissue target (dentin-pulp complex, periodontium, alveolar bone) and by material class (biological/regenerative versus synthetic), and were qualitatively synthesised with attention to biological mechanism, reported clinical outcomes, and practical limitations such as cost, regulatory status and technique sensitivity.

3 RESULTS AND DISCUSSION

3.1 Regeneration of the Dentin-Pulp Complex

Conventional management of irreversible pulpitis or pulp necrosis relies on pulpectomy and obturation with inert, synthetic filling materials, which seals the root canal system but does not restore vital tissue. Regenerative endodontic procedures instead attempt to re-establish a functional pulp-dentin complex through cell homing or direct cell transplantation [6]. In a pilot clinical study, autologous transplantation of mobilised dental pulp stem cells into pulpectomised teeth produced no adverse events, a robust positive electric pulp test response at four weeks, magnetic resonance imaging signal intensity comparable with normal pulp at twenty-four weeks, and radiographic evidence of functional dentin formation in three of five treated patients [5]. A subsequent systematic review of clinical studies using stem or progenitor cell transplantation for dentin-pulp regeneration similarly reported favourable radiographic and

clinical outcomes, although the authors emphasised marked heterogeneity in cell source, scaffold choice and outcome measures across trials [6]. A 2023 update on clinical trials using dental stem cells likewise concluded that, despite encouraging safety data, standardised protocols and larger controlled trials are still needed before such therapies can be considered routine [7].

By contrast, calcium silicate-based bioceramics, including mineral trioxide aggregate (MTA), Biodentine, Bioaggregate and iRoot BP Plus, represent the dominant synthetic approach to pulp capping, pulpotomy and regenerative endodontic scaffolding. These materials are not living tissue substitutes but bioactive synthetic cements that release calcium ions, promote hydroxyapatite formation, and stimulate reparative dentin bridging when placed in contact with vital pulp [8]. Comparative clinical data indicate that Biodentine offers a shorter setting time and easier handling than MTA while achieving broadly similar or superior rates of dentine bridge formation, whereas iRoot BP Plus has demonstrated pulp-capping success rates as high as ninety per cent at three-year follow-up with no reported tooth discolouration [8]. Polymer-based instructive scaffolds, most often collagen or fibrin-based hydrogels, are frequently used as carriers within regenerative endodontic procedures to control scaffold porosity and viscosity and to support cell attachment, effectively bridging the synthetic and biological categories rather than sitting cleanly within either [14].

Taken together, the dentin-pulp evidence suggests that cell-based regeneration can produce tissue with functional and imaging characteristics closer to native pulp, but at present carries higher cost, technical complexity and a smaller evidence base than calcium silicate bioceramics, which remain the more clinically mature and reproducible option for most cases of vital pulp therapy.

3.2 Periodontal Regeneration: Biological Proteins versus Barrier Membranes

Two principal strategies dominate periodontal regeneration: guided tissue regeneration (GTR) using barrier membranes, and biologically active enamel matrix derivative (EMD), a protein extract intended to recapitulate the signalling events of periodontal development. A systematic review comparing early wound healing after regenerative periodontal surgery with EMD or GTR found that both approaches carry distinct advantages and disadvantages, with no clear consensus favouring one technique for early wound stability [11]. Randomised controlled data summarised in the periodontal literature indicate that EMD and GTR produce broadly comparable clinical attachment gain in intrabony defects, and that combining EMD with a synthetic bone graft can further improve outcomes relative to EMD alone in selected multicentre trials [11].

Synthetic and biologically derived barrier membranes used in GTR and guided bone regeneration (GBR) span non-resorbable expanded polytetrafluoroethylene (e-PTFE), resorbable synthetic polymers such as polylactic acid and polylactic-co-glycolic acid, and naturally derived collagen membranes. A comprehensive review of GTR and GBR biomaterials concluded that membrane choice materially affects the exclusion of non-osteogenic cells from the healing defect and, in turn, bone and tissue regeneration outcomes, with resorbable collagen membranes increasingly favoured for their handling properties and avoidance of a second surgical removal procedure [12]. A related review of barrier membranes for periodontal GBR similarly identified collagen membranes as the most extensively used resorbable option, while noting that non-resorbable membranes still offer superior space maintenance for larger defects, at the cost of increased exposure risk and the need for a removal procedure [13].

Adjunctive biological approaches, including platelet concentrates such as advanced platelet-rich fibrin (A-PRF), have also been investigated for periodontal and osseous regeneration. Systematic review evidence indicates that A-PRF, an autologous, growth-factor-rich blood preparation, can be a useful additive to hard-tissue management protocols in oral surgery, and case series data suggest a possible benefit in the treatment of medication-related osteonecrosis of the jaw when combined with conventional therapy [9][10]. Mesenchymal stem cell-based periodontal therapy has likewise been assessed in a systematic review and meta-analysis of five randomised controlled trials, which found statistically significant improvements in clinical attachment level and pocket probing depth relative to stem-cell-free therapy, although effects on gingival recession were not significant and the authors called for larger, more standardised trials before routine clinical adoption [15].

Overall, the periodontal evidence suggests that biologically active proteins and cell therapies can match or modestly exceed the clinical attachment gains achieved with synthetic barrier membranes alone, but that synthetic membranes remain indispensable for mechanical space maintenance, particularly in larger or non-contained defects, and that the two approaches are most often used in combination rather than as substitutes for one another.

3.3 Alveolar Bone Regeneration: Autografts, Synthetic Substitutes and Scaffold Engineering

Autologous bone grafting remains the biological gold standard for alveolar bone regeneration because autografts possess intrinsic osteogenic, osteoconductive and osteoinductive properties and are fully biocompatible, eliminating the risk of immune rejection associated with allogeneic or synthetic substitutes [11]. However, donor-site morbidity, limited graft volume and the need for a second surgical site have driven interest in both autologous alternatives, such

as demineralised autologous dentin matrix derived from extracted teeth, and synthetic bone substitutes, including calcium phosphate ceramics, bioactive glasses and resorbable polymer scaffolds [1].

Polymer-based scaffolds occupy an important intermediate position in bone and dental tissue engineering. Natural polymers such as collagen, chitosan and alginate offer inherent biocompatibility and bioactivity, while synthetic polymers such as polylactic acid and polycaprolactone provide tunable mechanical strength and controllable degradation rates that natural polymers alone often cannot match [3]. Hybrid scaffolds that combine natural and synthetic polymers, sometimes further functionalised with bioactive molecules or nanoparticles, have been proposed specifically to reconcile the biocompatibility of natural materials with the mechanical reliability and reproducibility of synthetic ones, and are increasingly framed as the direction of travel for the field rather than a niche solution [3][4].

Drug-delivery-enabled biomaterials extend this hybrid logic further. A review of nanoparticles, hydrogels, scaffolds and additive-manufacturing platforms for dental applications concluded that dual-function materials, capable of both structurally supporting tissue regeneration and locally delivering therapeutic agents such as antibiotics or growth factors, are transforming dental treatment from a purely restorative discipline into one centred on personalised, biologically integrated regeneration, while also highlighting that regulatory and long-term safety data for many of these platforms remain immature relative to conventional synthetic grafts [4].

The comparative picture for alveolar bone is therefore one of complementarity rather than competition: synthetic ceramics and polymers supply predictable mechanical scaffolding, radiographic volume maintenance and manufacturing consistency, whereas autologous and biologically derived materials supply the cellular and molecular signals needed for true osseous regeneration rather than mere space filling, with the strongest evidence favouring composite or hybrid constructs over either material class in isolation.

3.4 Comparative Considerations: Biological Fidelity, Practicality and Cost

Across all three tissue domains, a consistent pattern emerges. Regenerative biological therapies, whether cell-based, protein-based or platelet-derived, more closely recapitulate native tissue architecture and cellular composition, but are typically constrained by higher cost, batch-to-batch biological variability, technique sensitivity, and a comparatively immature regulatory and clinical trial base [5][6][7]. Synthetic biomaterials, by contrast, offer manufacturing consistency, predictable handling characteristics, established regulatory pathways and, in many cases, decades of long-term clinical follow-up, but they generally achieve tissue repair rather than the full biological regeneration that living, cell-based approaches aim to deliver [1][8].

This distinction has practical implications for material selection. For small, contained defects where biological fidelity is paramount, such as vital pulp therapy in a young permanent tooth or a narrow intrabony periodontal defect, the additional cost and complexity of a regenerative biological approach may be justified. For larger, less contained defects where mechanical space maintenance and predictable volumetric outcomes are the priority, such as extensive alveolar ridge augmentation, synthetic scaffolds and membranes remain the more practical first-line choice. The most consistent finding across the reviewed literature, however, is that hybrid strategies, synthetic scaffolds functionalised with bioactive proteins, growth factors or autologous cells, tend to outperform either a purely biological or a purely synthetic approach used alone, supporting the hypothesis proposed in the introduction to this review [2][3][14].

4 CONCLUSION

Regenerative dentistry and synthetic biomaterials are best understood as complementary rather than competing paradigms. Cell-based and protein-based regenerative therapies for the dentin-pulp complex and periodontium have demonstrated biologically authentic tissue formation and encouraging clinical outcomes, but remain limited by cost, technique sensitivity and an evidence base that, while growing, still relies heavily on pilot studies and small trials. Synthetic biomaterials, particularly calcium silicate bioceramics and resorbable polymer membranes, offer clinical maturity, manufacturing consistency and regulatory familiarity, but generally achieve structural repair rather than true biological regeneration. The most promising direction identified across the dentin-pulp, periodontal and alveolar bone literature is the convergence of the two paradigms into hybrid, bioactive constructs that combine the mechanical reliability of synthetic scaffolds with the signalling and regenerative capacity of biological agents. Clinicians selecting between these approaches should weigh defect size and containment, biological fidelity requirements, cost, and the maturity of the supporting evidence, while future large-scale randomised trials are needed to define which patient and defect characteristics most favour a regenerative, synthetic, or hybrid strategy.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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