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PERSPECTIVE ARTICLE

Regeneration or Repair? Evaluating Foreign Material in Periodontal Healing

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The possibility of periodontal regeneration was first observed as a spontaneous phenomenon, with the natural filling of infrabony defects following the debridement of root surfaces [1]. The interest in experimentally inducing regeneration was then achieved by creating conditions for a submerged environment, followed by the foundational notions on cell exclusion, which led to current applications [2–4].

The revolutionary impact of regeneration lies in the fact that a healthy but reduced periodontium, with mucogingival deformities, was widely accepted as the inevitable new baseline after periodontal therapy. Periodontal regeneration, however, introduced the potential to reverse the biological clock of the affected site, restoring lost periodontium in a coronal direction.

Various techniques have been used in the effort to achieve periodontal regeneration, including particulate bone, barrier membranes, biological agents, combinations thereof, and others. While these approaches may yield similar clinical outcomes, histological evidence highlights critical differences. For instance, residual traces of certain materials are frequently integrated within newly formed bone.

This finding opens the door to important reflections on the nature of regenerated tissue. Some techniques promote or guide spontaneous regeneration, wherein healing occurs naturally after scaling and root planing, microsurgical approaches, biological agents, or resorbable barrier membranes alone. In these cases, no residual particles are found incorporated within the regenerated bone after tissue maturation. In "spontaneous" regenerative processes, all radiographic defect fill and histological bone gain arise from new, native bone formation (Figure 1).

In contrast, scaffold-based approaches, such as those utilizing particulate bone grafts alone or in combination with other approaches, provide immediate radiopacity and may leave residual traces within the regenerated bone (Figure 2).

A current concern in the scientific community is the tendency to classify all regenerative techniques under a single umbrella term, "regeneration," despite significant biological differences. In cases where regeneration is achieved through techniques that maximize spontaneous healing potential, the newly regenerated bone closely resembles native bone upon radiographic examination, surgical reexposure, and histological analysis. Spontaneous regeneration, with or without the application of barrier membranes or biological agents, is a rapid process that accomplishes the stabilization of the blood clot within days and the filling of regenerated tissue within weeks. Conversely, in cases of scaffold-dependent regeneration, involving particulate bone grafts, residual bone particles may be encapsulated by native bone, fibrous tissue, or a combination of both. Histologically, these particles may be found near the root surface in contact with the periodontal ligament or superficially near the crest. Often, they do not fully resorb and remain visible on radiographs for many years, sometimes appearing as residual particles. Clinically, upon reentry, the consistency of the newly formed tissue does not always match that of native bone. The use of bone biomaterials slows down the wound healing process compared to graftless

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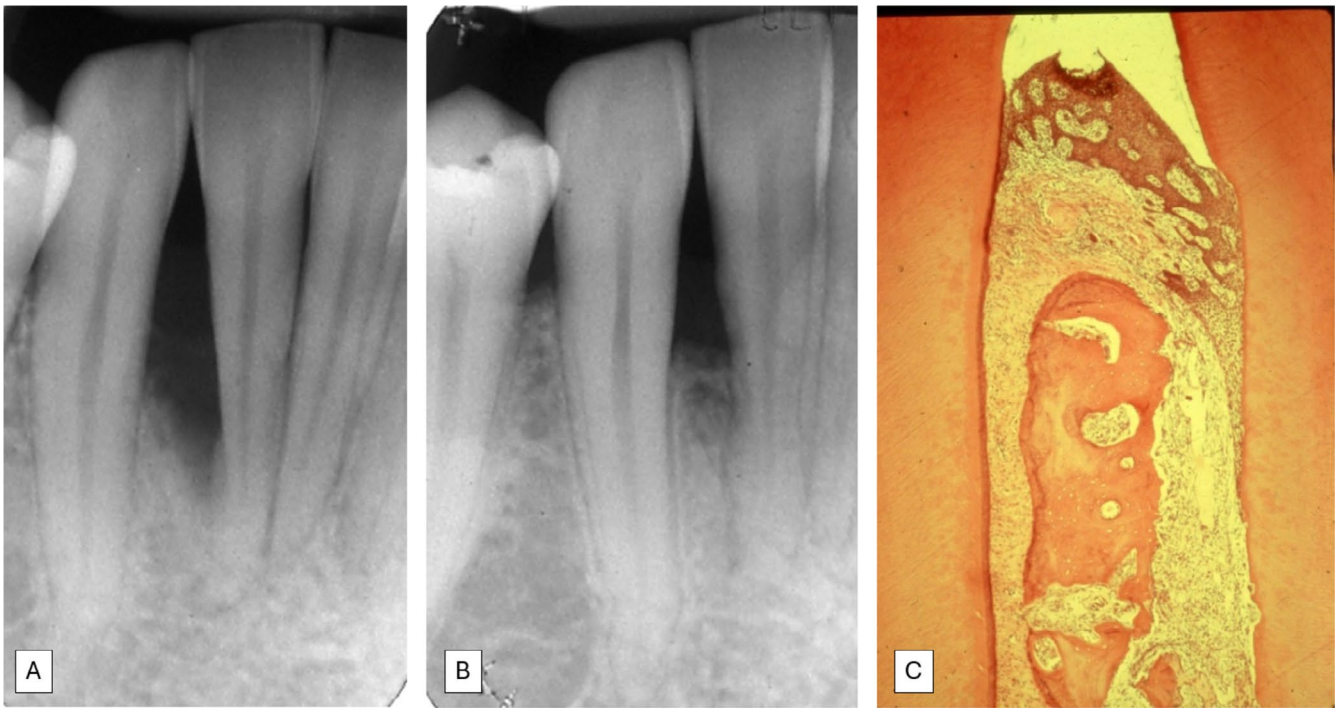


FIGURE 1 | Periodontal regeneration via guided tissue regeneration. (A) Preoperative radiographic evaluation of a localized deep infrabony defect extending near the apex of a vital lateral incisor. (B) One-year postoperative radiographic examination demonstrating successful periodontal regeneration, evidenced by bone fill, radiographic appearance comparable to native bone, and improved tooth prognosis. (C) Histological section illustrating periodontal regeneration, showing a periodontal compartment indistinguishable from a native periodontium, with new bone, cementum, and periodontal ligament, and no residual particles integrated within the regenerated tissues. A–C represent different patients. Courtesy of Prof. P. Cortellini for (A, B) and of Prof. S. Nyman for (C).

counterparts. However, several features have contributed to establishing them as necessary, such as the improved clinical and histomorphometric outcomes; their scaffolding function in non–self-supporting morphologies; and their role in cell homing whereby a biological agent is absorbed onto the graft material which in turn acts as a sustained-release device [5, 6].

This distinction calls for a reconsideration of historical definitions of regeneration and repair. Repair has been defined as "the healing of a wound by tissue that does not fully restore the architecture or function of the original part," whereas regeneration has been described as "the reproduction or reconstitution of a lost or injured part in a manner similar or identical to its original form [...] including the formation of new bone, cementum, and a functionally oriented periodontal ligament at a site deprived of its original attachment apparatus" [7, 8]. Historically, repair has been associated with histological healing via long junctional epithelium, whereas regeneration has required histological evidence of newly formed cementum, periodontal ligament, and native bone. However, these definitions do not specifically account for the presence of residual particles [9, 10]. While such materials may allow new cementum and periodontal ligament formation—thus meeting the traditional definition of regeneration—they also create a tissue composition that does not fully replicate the pre-disease state due to the permanence of residual particles. Modern long-term studies often combine data from patients treated with various regenerative techniques, making it difficult to accurately assess the clinical performance of individual approaches. Given these considerations, several critical questions arise:

- Should regenerative outcomes with and without particle retention be classified under the same category of "regeneration," or should they be distinguished as separate entities?
- Should the official definitions of regeneration and repair be updated to account for the presence of residual graft particles?
- When assessing clinical endpoints, do these two categories of regeneration yield different long-term outcomes?

Modifying the preexisting taxonomy in periodontology is always a delicate task. Currently, there is no robust evidence to support that regeneration with or without residual particles leads to meaningful long-term implications for host tissue physiology, metabolism, surrogate measurable outcomes (clinical attachment level, bone levels, and probing depth), as well as final endpoints (tooth loss and disease recurrence). Also, the official definition of regeneration allows for the inclusion of outcomes that are "similar," though not necessarily identical, to the original histological tissue. The use of the term "similar" is a key semantic element of the current definition, as it would allow the presence of residual particles within the concept of regeneration. As such, it is advisable to adopt a cautious approach. Any official alteration of the existing definitions of repair and regeneration should be preceded by extensive professional dialog, evidence of clinical relevance, and engagement with professional organizations to assess the actual need for terminology clarification. Studies are warranted to determine whether various regenerative therapies differ in their long-term clinical outcomes, thus

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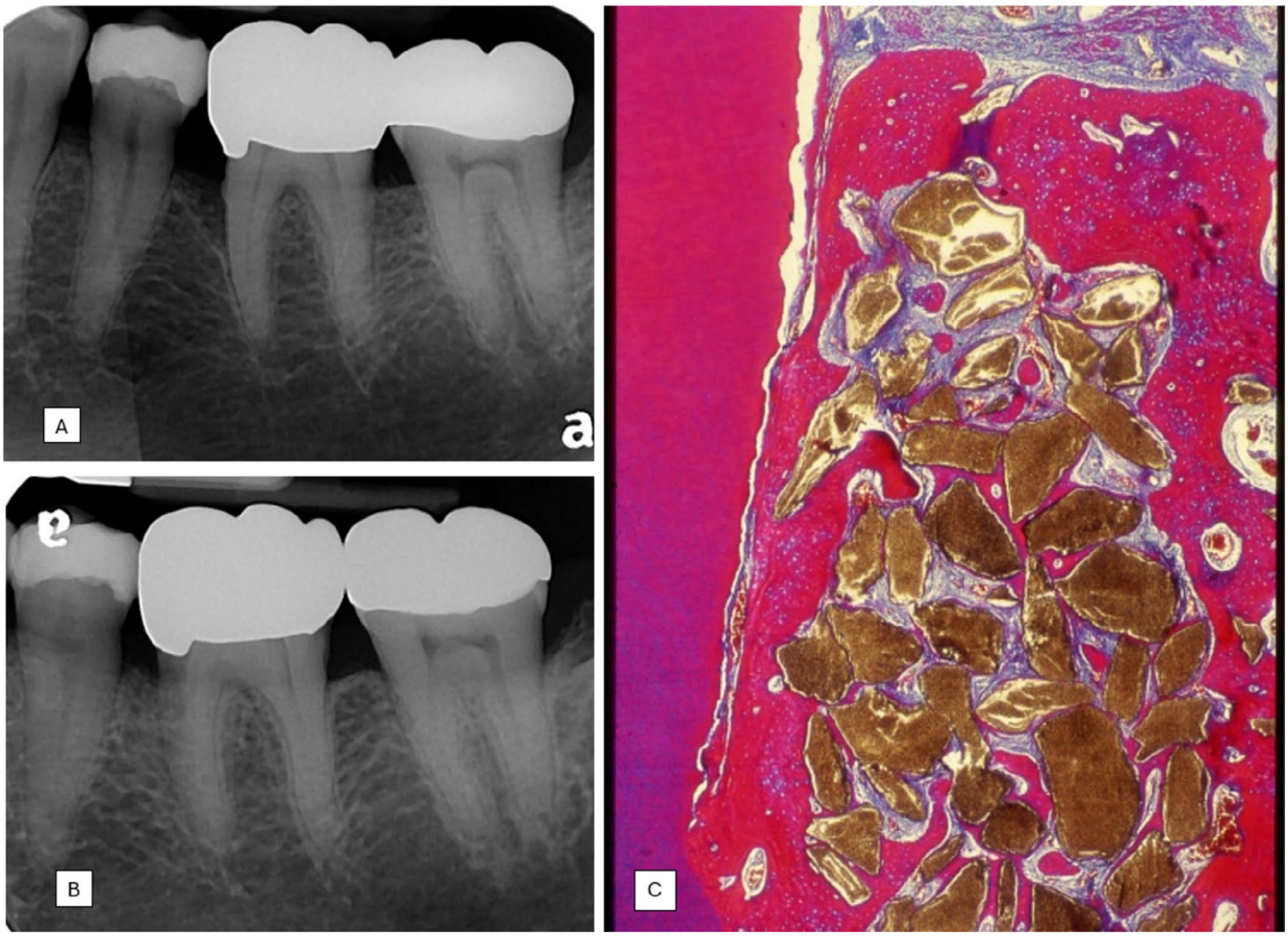


FIGURE 2 | Periodontal regeneration using a combination approach with xenograft bone particulate and guided tissue regeneration. (A) Preoperative radiographic evaluation showing a localized infrabony defect on the mesial root of a mandibular molar, with visible radiographic calculus within the root concavity. (B) Six-month postoperative radiograph demonstrating successful outcomes, indicated by complete radiographic bone fill. However, the regenerated bone retains a particulated appearance due to the presence of graft material. (C) Histological section showing the persistence of residual particles embedded within the newly formed bone matrix. A–C represent different patients. Courtesy of Prof. G. Bowers for (C).

clarifying whether this biological distinction holds meaningful implications for patient care.

Author Contributions

Both authors significantly contributed to the ideation, realization, and writing of the study. Both authors approved the last version before submission.

Disclosure

Artificial intelligence statement: The content reported in the manuscript is original and produced by the authors. Language artificial intelligence software was used solely to improve language clarity and grammar. This manuscript used NLP (ChatGPT) for proofreading an entirely human-generated text, but no other use of AI was made.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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