Advanced Scaffolds for Dental Pulp and Periodontal Regeneration

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KEYWORDS

• Biomaterials • 3D printing • Dental pulp • Pulpitis • Periodontitis • Scaffolds • Regenerative endodontics • Guided tissue regeneration

KEY POINTS

- No current therapy exists that promotes regeneration of the pulp-dentin complex in cases of pulp necrosis.
- Antibiotic pastes used to eradicate root canal infection have been shown to negatively affect stem cell survival.
- Three-dimensional easy-to-fit antibiotic-eluting nanofibers, combined with injectable scaffolds, enriched or not with stem cells and/or growth factors, may lead to an increased likelihood of achieving predictable dental pulp regeneration in humans.
- Periodontitis is an aggressive disease that impairs the integrity of tooth-supporting structures and may lead to tooth loss.
- The latest advances related to membranes' biomodification to endow needed functionalities (eg, antimicrobial capacity) and technologies (additive manufacturing) to engineer patient-specific membranes/constructs to amplify both hard and soft tissue periodontal regeneration are presented.

INTRODUCTION

Caries and periodontitis are major disorders affecting teeth and their ancillary structures and, if not properly managed, may lead to tooth loss.[1,2] Recent estimates from the National Health and Nutrition Examination Survey show that, in the United States, nearly 8% of adults (aged 20–64 years) and 17% of seniors (aged ≥65 years) have periodontitis, whereas caries affects 37% of children (aged 2–8 years) in their

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deciduous teeth and 58% of adolescents (aged 12–19 years) in their permanent dentition. From these statistics, it becomes immediately clear that these two conditions remain a significant public health problem and require better strategies for disease prevention and clinical management.

A challenging problem for endodontists and pediatric dentists is the clinical management of immature (open apex) permanent teeth with necrotic pulp resulting from trauma or bacterial infection.[3] Over the years, the therapy of choice has followed the principles of apexification; that is, disinfection treatment with calcium hydroxide followed by root canal sealing with gutta-percha. However, the last decade has brought forward new prospects regarding dental pulp regeneration, thanks to evoked bleeding (EB), an approach that has been found to induce dentinal wall thickening and root end closure.[3–6] Nonetheless, despite the aforementioned clinical and histologic observations, the regenerative outcome of this patient-dependent and unpredictable therapy remains elusive.[6–11] Several aspects, including but not limited to the use of very cytotoxic antibiotic pastes, have been thought to account for the unsystematic success.[4] To circumvent the characteristic toxicity associated with commonly used antibiotic pastes and sodium hypochlorite, a more biocompatible strategy has recently been developed by our laboratory. A series of studies[3,12–20] have stressed the practicality and translational prospects of three-dimensional (3D) easy-to-fit antibiotic-eluting nanofibers as a localized, intracanal drug delivery strategy that, combined with injectable scaffolds, enriched or not with stem cells and/or growth factors (GFs), may lead to an increased likelihood of achieving predictable dental pulp regeneration in humans.

Considered to be one of the most aggressive chronic inflammatory oral diseases, periodontitis affects the integrity of both soft and hard tissue, and, in severe cases of tissue destruction, can result in tooth loss.[21] Originally, the principles of guided tissue regeneration have been followed to restore the architecture and functionality of the periodontal system. In essence, an occlusive biocompatible polymer-based membrane is used as a barrier to prevent epithelial and connective tissue migration into the regenerating site. In this way, slower migrating progenitor cells, located in the remaining periodontal ligament (PDL), are able to recolonize the root area and differentiate into new periodontal tissues.[22] Based on varying levels of clinical success with this approach, the last decade has witnessed significant advancement toward the generation of membranes with therapeutic properties. The work reported in the literature has included not only antimicrobials and inorganic particles (eg, calcium phosphates) but also biomolecules (eg, GFs) in the fabrication of membranes with therapeutic functions.[21,23] More recently, the combination of known materials and biomolecules with advanced technologies,[24–31] particularly 3D printing, has permitted translation of the first patient-specific scaffold modified with recombinant human platelet-derived growth factor-BB (rhPDGF-BB) for treating large periodontal defects.[26]

This 2-part review offers an update on progress related to advanced biomaterials for dental pulp and periodontal regeneration. To provide a better understanding of the regenerative strategies described herein, a concise but informative summary on dental stem cells is presented. The first part provides a short background on the EB strategy, the significance of a biocompatible disinfection, and major highlights on the use of scaffolds, stem cells, and GFs in dental pulp regeneration. The second part highlights the newest advances regarding the development of membranes with therapeutic properties and technologies, such as additive manufacturing, to engineer patient-specific membranes/scaffolds to amplify hard and soft tissue periodontal regeneration.