

## Editorial

# Regenerative Endodontics: A New Treatment Modality for Pulp Regeneration

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Endodontic disease is one of the most common dental diseases. Currently the major treatment modality is root canal therapy (RCT). The American Dental Association reported that approximately 22 million RCT's are performed in the United States each year, with an annual expenditure of 20 to 34 billion dollars [1]. RCT consists of complete removal of the contaminated pulp tissue and filling the pulp space with an inert material. Although the reported success rate of RCT is 78-98% [2,3], RCT in permanent teeth diagnosed with pulpal necrosis and immature root development is very challenging. In these cases, the thin dentinal walls of the root and the open apex limit the application of mechanical instrumentation and obturation. In addition, conventional RCT cannot regenerate new dentin and pulp tissue in these teeth, nor prevent their susceptibility to fracture.

Recently, the potential for successful pulp regeneration therapy is increasing due to accumulated knowledge of the regenerative endodontics. Regenerative endodontics is to create and deliver new tissues to replace the necrotic pulp [4]. Regenerative endodontics applies the principles of regenerative medicine, utilizing a combination of specific stem cells, three dimensional scaffolds and growth factors to regenerate pulp-dentin complex and revitalize teeth. Currently, there are two major concepts in the regenerative endodontics: Guided tissue regeneration and tissue engineering.

The concept of guided tissue regeneration was originally proposed by Dr. Nygaard-Ostby in the 1960s [5]. In 2004 a modified clinical protocol was reintroduced by Dr. Trope [6]. It has now become widely used in endodontic clinics and is known as the "revascularization" or "revitalization" approach. During the first visit, the immature permanent teeth with open apices are treated by minimal instrumentation, disinfection with copious irrigation, and medicated with a mixed antibiotic paste. In the second visit, mechanical irritation of the apex is performed to initiate bleeding into the root canal to the level of cemento-enamel junction. This is followed by the coronal sealing with MTA and glass ionomer or resin restoration. The bleeding delivers stem cells from the apical papilla to the root canal system and the blood clot provides a scaffold to support stem cell proliferation and differentiation. Numerous case reports have shown the continuation of root formation and closure of the apex by this approach. In some cases, the teeth even regain their vitality [7]. Histology studies have found that the regenerated tissues inside

the root canal are not real pulp tissue, but mainly the periodontal tissues including bone and cementum [8]. Presently, the outcome of clinical guided tissue regeneration is still not predictable. If this approach fails to regenerate new tissue, apexification is needed to achieve apex closure in order to perform conventional RCT.

The second concept in the regenerative endodontics is tissue engineering. The modern development of tissue engineering started in the late 1980s when synthetic biodegradable materials were introduced as scaffolds for cell expansion. However, further use in regenerative endodontic was halted due to the lack of isolation of specific dental stem cells. This was until the first human dental pulp stem cells were isolated in 2000 [9]. Currently at least five different types of mesenchymal stem cells have been isolated from the dental tissues, including dental pulp stem cells (DPSC), stem cells of human exfoliated deciduous teeth (SHED), stem cells of the apical papilla (SCAP), dental follicle progenitor cells (DFPC) and stem cells from periodontal ligament [10]. Among these, DPSC, SHED and SCAP show stronger potential for pulp regeneration. In last decade, a variety of biomaterials have been developed as the scaffold to support pulp regeneration. These include natural polymers, synthetic polymers, hydrogels and bioceramics. Scaffolds not only support stem cell proliferation and differentiation, but also can integrate and provide a sustained release of growth factors to guide cell differentiation. Numerous animal models and preclinical studies have shown the success of regenerating pulp-like tissues via tissue engineering in *in vitro* and in *in vivo* settings [11].

The future advancement of pulp regeneration will continuously focus on three essential components: dental stem cells, scaffolds and growth factors. Several major challenges need to be addressed: (1) Microbial control. Since the microorganism and biofilm are the fundamental etiologic factors of endodontic diseases, similar to conventional root canal treatment, microbial control is a key step for the success of pulp regeneration. (2) Spatial and temporal control of the release of growth factors from the scaffold remains as a major challenge when we design a new scaffold for tissue engineering. (3) It still remains a challenge to regenerate a real and functional pulp-dentin complex. A functional pulp-dentin complex would ideally contain an inside soft core highly vascularized with sufficient nerve supply and a peripheral layer of odontoblasts, located against the existing dentin wall, synthesizing matrix to produce new dentin.

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