Root Canal Revascularization:
The Beginning of a New Era in Endodontics

By Su-Min Lee, DDS, MS, DScD and Bekir Karabucak, DMD, MS
Penn Dental Medicine, Dept. of Endodontics

Traumatic injury, pulp exposure with anatomic anomaly, such as dens invaginatus or evaginatus, or caries of an immature permanent tooth can cause pulpal necrosis and interrupted root development. Arrested root development can result in a poor crown-root ratio, an open apex, a root with very thin walls, and an increased risk of fracture. Treating an immature tooth with necrotic pulp has been a real challenge to dentists. Large immature canals without physiologic apical closure are difficult to debride and the thin dentinal walls make the tooth susceptible to cervical root fracture. In addition, restoring immature teeth with thin dentin walls is a challenge and placing implants is not advised in young patients as the cranio-facial skeleton is still growing.

The traditional treatment of immature teeth with necrotic pulps relied on apexification procedures involving long-term, Ca(OH)2-based intracanal medicament with multiple visits or on one-step apexification, placing an apical plug of MTA. Even though these treatments have a high success rate of 95% and 94% respectively, they do not regenerate the physiology of the pulp-dentin complex, nor do they allow for further root formation. A greater alternative in such cases would be performing a revascularization procedure. This therapy involves removal of the diseased or necrotic pulp tissue and ultimately replacing it with healthy pulp tissues to revitalize the teeth, which optimally translates to a complete restoration of pulpal function and subsequent completion of the root development.

What is the Biological Basis for a Root Canal Revascularization Procedure?
Induction of periapical bleeding into the canal space is the most important and necessary step in a revascularization procedure of immature permanent teeth with necrotic pulps. Blood clots in the canal space serve as a matrix or scaffold to promote pulp tissue wound healing. Provoked periapical bleeding brings mesenchymal stem cells from the periapical area into the canal space. Furthermore, blood contains many platelet-derived growth factors. Therefore, induced periapical bleeding brings a fibrin scaffold, mesenchymal stem cells, and blood-derived bioactive growth factors, which are three key elements for pulp-tissue engineering into the canal space.

Root canal revascularization is performed in immature teeth with pulpal necrosis and ultimately leads to:
• Elimination of clinical symptoms/signs and resolution of apical periodontitis
• Thickening of the canal walls and/or continued root maturation
• Regaining vitality/positive response to vitality testing

Therefore, the primary goal of revasculization therapy and traditional non-surgical root canal therapy is actually similar. The difference between the two procedures is that the disinfected root canal space in revascularization therapy is filled with the host’s own vital tissue, and the canal space in traditional therapy is filled with biocompatible foreign materials. Furthermore, revascularization therapy has a distinctive secondary goal, which is increased root length and the maturation of root development, and thus, may confer a better long-term prognosis (Figure 1). In addition, successful regeneration of the pulp-dentin complex would most likely result in vital tissue capable of mounting an immune response and signaling tissue damage by sensory neurons.

What are the Clinical Considerations for a Root Canal Revascularization Procedure?
A revascularization procedure should include appropriate case selection, with a strict disinfection protocol and use of antimicrobial paste to achieve complete asepsis and blood clot formation in the canal space, followed by placement of an MTA or BC putty barrier over the blood clot, with a final restoration and follow-up at regular intervals (Table 1 and 2).

1. CASE SELECTION
• Young patient
• Tooth with immature apex and necrotic pulp
• Pulp space not needed for post/core, final restoration
• No known allergies to antibiotics if intended for use
• Compliant patient (parent/guardian)

2. DISINFECTION CONTROL
Disinfection of the root canal system is a crucial step in a revascularization procedure as mechanical instrumentation is contraindicated due to the fragility of the thin root walls, requiring a disinfection protocol restricted to the use of irrigant solutions and intracanal medications. Sodium hypochlorite (NaOCl) at concentrations between 2.5–5.25% has been used. In a revascularization procedure, the lower concentrations (1.25–2.5%) of NaOCl are advised to minimize cytotoxicity to stem cells in the apical tissues. However, it should be emphasized that pulp revascularization is more favorable in a bacteria-free environment, which requires a clean and disinfected root canal system prior to cell colonization. There is a particular combination of...
antibiotics which effectively disinfects root canal systems and increases revascularization of avulsed and necrotic teeth. This combination includes metronidazole, minocycline, and ciprofloxacin, which is known as triple antibiotic paste (TAP). Studies have shown that calcium hydroxide (Ca(OH)_2) can be applied as the intracanal medicament as well. Ca(OH)_2 is antimicrobial at concentrations that do not induce stem cell toxicity and is widely available. However, case reviews have shown that root development may not be as prominent in Ca(OH)_2 cases as in TAP cases.

If the TAP is used:

- consider sealing pulp chamber with a dentin bonding agent [to minimize risk of staining],
- mix 1:1:1 metronidazole: minocycline: ciprofloxacin in a lower concentration (0.01-0.1 mg/ml) to avoid stem cell toxicity; these lower concentrations appear as a liquid form and are no longer a paste.

### 3. INDUCTION OF INTRACANAL BLEEDING AND CREATION OF BLOOD CLOT IN THE CANAL

Upon confirming the absence of clinical signs and symptoms, the second appointment focuses on removing the antimicrobial medicament, and releasing growth factors from the dentin by irrigating with 17% ethylenediaminetetraacetic acid (EDTA), and forming a blood clot in the canal. At the second appointment, the use of local anesthetic without a vasoconstrictor may better facilitate stimulation of apical bleeding. Induction of bleeding to facilitate healing is a common practice done in surgical procedures. A blood clot can act as a natural fibrin scaffold for cell attachment, proliferation, and differentiation to facilitate the regeneration and repair of tissues into the canal. Stem cells from the apical papilla in immature tooth and mesenchymal stem cells from bone marrow of the jaw migrate into the root canal and produce dentin-pulp complex-like tissue and deliver abundant growth factors within the blood clot, such as platelet-derived growth factor, which will aid in revascularization. Hemorrhage is induced by over instrumentation with either endodontic files or an endodontic explorer, penetrating slightly into the periapical tissue. This procedure induces bleeding into the canal. Blood coming into the canal should be left untouched coming into the canal should be left untouched.

### Table 1. Steps to accomplish root canal revascularization

**FIRST TREATMENT VISIT**

1. Local anesthesia, rubber dam isolation, access
2. Copious, gentle irrigation with 20ml 1.5% NaOCl using an irrigation system that minimizes the possibility of extrusion of irrigants into the periradicular space. (e.g., needle with closed end and side vents)
3. Dry canals with paper points
4. Measure the working length of the canals with a file inside the canals using an apex locator and a radiograph (Do not merely reply on an apex locator; it is not reliable in teeth with a blunderbuss apex)
5. Place antibiotic paste or calcium hydroxide. If the triple antibiotic paste is used mix 1:1:1 metronidazole:minocycline: ciprofloxacin and fill the canal from the apex to the CEJ using a similar closed end needle.
6. Seal the access with a temporary material such as Cavit or glass ionomer cement

**SECOND TREATMENT VISIT (TWO TO FOUR WEEKS AFTER FIRST VISIT)**

1. Assess response to initial treatment. If there are signs/symptoms of persistent infection, consider additional treatment with the antimicrobial, or an alternative antimicrobial. Recall the patient in about 3-4 weeks as before
2. Anesthesia with 3% mepivacaine without vasoconstrictor, rubber dam, isolation
3. Copious, slow irrigation with 20ml 17% EDTA, followed by normal saline, using a similar closed end needle.
4. Dry canals with paper points
5. Mark a file 2-mm longer than the working length, and use it to stir the tissue 2 mm beyond the apical foramen to cause bleeding in the root canal. Allow 15 minutes for the blood to pool in the root canal up to CEJ
6. Stop bleeding up to CEJ
7. Place CollaPlug/CollaCote at 3mm below CEJ optionally
8. Place 3-4mm of a MTA or BC putty directly above the blood clot or collagen plug
9. Overlay MTA or BC putty with reinforced glass ionomer and place permanent restoration

**FOLLOW-UP**

Clinical and radiographic exam

- No pain or soft tissue swelling (often observed between first and second appointments)
- Resolution of apical radiolucency (often observed 6-12 months after treatment)
- Increased width of root walls (this is generally observed before apparent increase in root length and often occurs 12-24 months after treatment)
- Increased root length
- Apical closure

Recall in 3, 6, 12, 24 months

If the periapical radiolucency has increased in size, revascularization may not be indicated and the treatment plan will have to change to an apexification

### Table 2. ADA CDT Codes for pulpal regeneration procedures

**FIRST PHASE OF TREATMENT**

D3351 debridement and placement of antibacterial medication

**INTERIM PHASE OF TREATMENT (REPEAT OF FIRST PHASE)**

D3352 interim medication replacement (this is to be used if patient is still symptomatic)

**FINAL PHASE**

D3354 pulpal regeneration- (completion of regenerative treatment in an immature permanent tooth with a necrotic pulp); does not include final restoration
for 15 minutes so that the blood would clot in the canal and stopped at a level just below CEJ. MTA or BC putty is then placed over the blood clot.

4. EFFECTIVE CORONAL SEAL, FINAL RESTORATION AND FOLLOW-UP

Once the intracanal infection is controlled and a physical scaffold to promote cell growth and differentiation has been achieved, the next important step is a coronal seal to prevent reinfection. In revascularization after inducing a blood clot, MTA or BC putty is placed over the blood clot. A small piece of CollaCote may be placed at the pulp chamber to support the MTA cement, which is to be placed over it. This is followed by the placement of a wet cotton pellet and temporary filling material. The patient is then recalled after 2-3 weeks, and if the tooth is asymptomatic, the direct placement of resin restoration after MTA or BC putty is set. Additional placement with glass ionomer/resin provides a double seal, further securing the sealing ability and the integrity of the filled access.

Periodic follow-up of clinical cases of revascularization is mandatory to verify clinical success and observe the maturation of the root. If after several rounds of intra-canal irrigation and medication the clinical symptoms show no sign of improvement, i.e., a persistent presence of sinus tract, soft tissue swelling and/or pain, an apexification procedure should then be carried out.

What are the Outcomes of Root Canal Revascularization Procedures?

The majority of human case studies have shown good clinical outcomes (absence of clinical signs and symptoms, radiographic evidence of resolution of periapical infections, continued root development and increased canal wall thickness) for immature permanent teeth with pulp necrosis following a revascularization procedure. Our group’s recent retrospective study demonstrated that 75% of cases (21 of 28 cases) showed successful healing of apical periodontitis with continued root development. An additional four cases (14%) presented with periapical healing during the observation period. However, three failed cases (11%) presented coronal leakage from fractured restoration or inflammatory root resorption within a month from initiating the revascularization procedure.

For obvious reasons, there is limited information on the exact histological nature of the tissue in the root canal following a revascularization procedure in humans. However, two recent reports describe the presence of pulp-like tissue in human teeth extracted following revascularization procedures. In dogs, deposition of cementum- and bone-like tissues was observed after revascularization procedures, suggesting differentiation of periodontal ligament tissue versus pulp tissue. Based on case studies, the healing progression following a revascularization procedure will vary depending on the initial presentation. Radiographic evidence of apical healing typically precedes continuation of root development. However, radiographic evidence of the maturation of root development may take more than two years. Figure 2 shows a traumatized maxillary incisor 25 months after a revascularization procedure that remains asymptomatic and functional with complete periapical healing, apical closure, and arrest of external inflammatory root resorption, but minimal increase in root length, a clinical outcome that should be considered acceptable.

Summary

Root canal revascularization, one of the regenerative endodontic procedures, is a treatment revolution in dentistry – the era in which root canal therapy brings diseased teeth back to life, rather than leaving a “non-vital” or dead tooth in the mouth. Endodontists’ knowledge in the fields of pulp biology, dental trauma, and tissue engineering can be applied to deliver biologically based regenerative endodontic treatment of necrotic immature permanent teeth resulting in continued root development, increased thickness in the dentinal walls, and apical closure. These developments in regeneration of a functional pulp-dentin complex have a promising impact on efforts to retain the natural dentition, the ultimate goal of endodontic treatment.

ABOUT THE AUTHORS

Penn Dental Medicine’s Department of Endodontics has conducted clinical outcomes studies to evaluate the probability of long-term success of revascularization procedures and to determine which factors have a detrimental impact on the outcome. Dr. Su-Min Lee has further focused on researching demonstrating the availability and delivery of mesenchymal stem cells into the root canal system via intracanal bleeding and the correlation with clinical outcomes. She is also conducting in vitro and in vivo studies regulating the inflammatory niche and optimizing the immunomodulatory function of resident dental pulp stem cells to suppress inflammation and guide tissue regeneration in the case of pulpotis. Dr. Bekir Karabucak, the Interim Chair in the Dept. of Endodontics, has researched infection control to provide favorable conditions for stem cells and biomolecules to regenerate pulp tissue in a previously necrotic and infected root canal space, which is critically important to the success of the regenerative endodontic treatment.

Figure 2. (A) Preoperative radiograph of tooth #8. (B) Postoperative radiograph of tooth #8. (C) Eight-month follow-up after revascularization procedure. A radiograph shows resolution of apical periodontitis. (D) Twenty-five-month follow-up after revascularization procedure. A radiograph shows arrest of external inflammatory root resorption and increased thickness of the root canal wall.