ABSTRACT

Introduction: This article describes the regenerative endodontic procedures applied in 3 cases of maxillary incisor necrosis that resulted in continuous root development, dentinal wall thickening, and cervical level biological repair of the access openings that was verified radiographically in 2 cases and clinically in 1 case. Methods: Three maxillary central incisors in 2 different patients were rendered necrotic after having dentin enamel fracture traumatic dental injuries. All teeth were treated with single- or multiple-visit regenerative endodontic procedures. Results: The 5- and 9-year follow-up evaluations revealed similar continuous root development, dentin wall thickening, and hard tissue biological repair of the wide access cavities. In the 9-year follow-up case, the calcium silicate cement was removed because of unacceptable discoloration. The hard tissue biological repair was visualized under the microscope and checked for its continuity with the axial walls, its resistance to displacement, and the presence of possible gaps. The repair tissue seemed to be yellowish in appearance with some brown niches of irregular texture, did not have detectable gaps, was firmly connected with the axial dentinal walls through a demarcated white line, and resisted all displacement forces applied. The tooth was restored with bonded composite resin restoration after internal bleaching. Conclusions: Cervical-level hard tissue repair of the access opening after the application of regenerative endodontic procedures in necrotic immature maxillary incisors might reinforce the weakened tooth structure to a great extent and warrants further investigation.

KEY WORDS

Apical repair; cervical level access repair; dental trauma; healing pattern; regenerative procedures

SIGNIFICANCE

The cervical level biological repair of the access opening in necrotic immature teeth might be feasible after regenerative endodontic procedures. A regenerative protocol that can induce such a healing pattern might strengthen the immature tooth and warrants further scientific investigation and modulation.
Apexification protocols with MTA offered the advantage of shortened treatment time and improved patient compliance, but most of all they facilitated the rapid placement of a bonded restoration for the fragile immature root. Although advances with MTA and bonded restorations went some way toward a better outcome, both apexification methods required a wide access cavity preparation that weakened and destabilized the tooth structure further and condemned the immature roots to the cessation of further root development. Moreover, the dental tissues removed from the cervical level of the roots during wide access cavity preparation could only be restored with artificial materials and not repaired or regenerated. Thus, the problem of strengthening the immature root had remained largely unsolved.

Recently, revitalization procedures were introduced for the induction of continued root development and dentin wall thickening of the necrotic immature root that might strengthen the tooth structure. Although the biological goals of these procedures can be achieved, the outcome of the treatment is not always predictable, and the strengthening effect of the different healing patterns reported is questionable. With unpredictable and questionable outcomes, clinicians are reluctant to incorporate regenerative endodontic procedures in their everyday practice, and they ask for more evidence and better biological outcomes.

The aim of this article is to report the regenerative endodontic procedures followed in 3 cases of maxillary incisor immature tooth necrosis that resulted not only in continued root development and dentin wall thickening but also in formation of a cervical level hard tissue biological repair of the access cavity in close continuity with the axial walls, as verified clinically in 1 case. A regenerative protocol that can induce such a healing pattern might strengthen the immature root and deserves further scientific investigation.

**CASE REPORTS 1 AND 2**

A 9-year-old male patient was referred for evaluation and possible treatment of teeth 8 and 9. In the dental history it was reported that the patient had an impact injury after a fight with his brother 6 months earlier, and both teeth suffered an enamel-dentin fracture with no pulp involvement. Both teeth remained asymptomatic, and no treatment was sought since then. A week before presenting to the pediatric hospital (Fig. 1A), the patient had an impact injury after a fall. In the dental history it was reported that the patient had an impact injury after a fall. The patient had an impact injury after a fall.

On clinical examination at the second visit both teeth were asymptomatic, with the vestibular intraoral swelling and the sinus tract resolved (Fig. 1C). The patient was anesthetized by using local anesthesia without vasoconstrictors (3% mepivacain; 3M ESPE, St Paul, MN). The rubber dam was placed and stabilized with Wedjets (Coltene, Altstätten, Switzerland). The operation field was disinfected by using 2% chlorhexidine scrub. The pulp cavities were accessed with a sterile diamond bur (Endo-Access Bur; Dentsply Maillefer, Ballaigues, Switzerland), and the contaminated content of both canals was rinsed away with copious sterile saline irrigation through a slotted end needle.

The working length was estimated with a working length radiograph and an ISO 100 K-file. The file was placed coronal to the length estimated from the preoperative periapical radiograph (to avoid damage to the apical papilla). There was no further instrumentation of the root canal walls. The wide canals of both teeth were rinsed with 10 mL of 1.5% NaOCl solution through a 27-gauge fluted end needle fitted 2 mm short of working length.

The canals were dried with capillary suction fitted 2 mm short of working length. A double antibiotic mixture powder containing equal parts of ciprofloxacin and metronidazole had been prepared by the compound pharmacy. The powder had been kept in the refrigerator. Just before use, the powder was mixed with sterile water to a slurry consistency (approximately 1000 mg/mL solution is needed to create a pasty slurry consistency) and placed inside both canals with a lentulo spiral rotating 2 mm short of working length.

**Anesthesia and rubber dam isolation were performed as in the first visit.**

The temporary restorations were removed from both teeth with a sterile diamond bur, and the double antibiotic mix was rinsed away with copious sterile saline irrigation through a slotted end needle. The root canals were rinsed with 20 mL of 1.5% NaOCl through a 27-gauge fluted end needle fitted 2 mm short of working length.

The canals were dried with capillary suction fitted 2 mm short of working length. The Endo-Vac macro-cannula (Kerr Dental, Bioggio, Switzerland) was fitted 1 mm short of working length, and negative pressure irrigation with 10 mL of 1.5% NaOCl was performed in each tooth. The canals were flooded with 1.5% NaOCl and left inside the canals non-agitated for 30 minutes.

The canals were dried with capillary suction from the NaOCl solution and were flooded with 17% EDTA through an Endo-Vac macro-cannula fitted in working length. The EDTA 17% was left for 10 minutes and then rinsed away with sterile water. The canals were dried with capillary suction fitted 2 mm short of working length. Bleeding was induced by mechanical irritation of the periapical tissues and rotational movement of a sterile apically pre-curved size 40 K-file. The canals were allowed to fill with blood to the level 2 mm below the cementoenamel
junction and waited for 15 minutes for a clot to be formed.

- An MTA barrier of 4-mm thickness (MTA Angelus, Londrina Brazil) was placed over each blood clot with an MTA applicator.
- The MTA material was adapted over the blood clot with a micro-brush and a dry sterile cotton pellet.
- MTA material was protected with injectable gutta-percha, and the MTA remnants were removed with a grit blast of bisodium carbonate sandblasting.
- The access cavities were rinsed with water, the gutta-percha plug was removed with an excavator, and both teeth were restored with glass ionomer (Fuji IX GP).
- A postoperative radiograph was taken to be used as baseline for future evaluations (Fig. 2B).
- The patient was referred for the restoration of both teeth with composite resin.

The patient returned for the scheduled follow-up appointment 4 months later. The clinical (Fig. 1C) and radiographic evaluations (Fig. 2C) revealed asymptomatic maxillary central incisors with resolution of the periapical pathosis and signs of continued root maturation. The cervical discoloration resulting from the MTA material was minimal and had been masked sufficiently with the composite resin restorations.

The 5-year follow-up clinical evaluation revealed healthy soft and hard tissues and favorable esthetics (Fig. 1E and F). The radiographic examination revealed a characteristic healing pattern with complete periapical healing, hard tissue repair of the access cavity in contact with the MTA coronal barrier, continuous root development, dentinal wall thickening, and apical closure (Fig. 2D–F). No response to electric vitality testing was recorded.

**CASE REPORT 3**

An 8-year-old female patient was referred for evaluation and possible treatment of tooth 9. In the dental history it was reported that the patient had an impact injury after a bicycle accident 6 months earlier, and both maxillary central incisors suffered a dentin-enamel fracture with no pulp involvement. Both teeth were restored with composite resin restorations by the pediatric dentist and had remained asymptomatic since then. A week before presenting to the clinic, tooth 9 was rendered painful, and a swelling developed. The patient had then sought treatment at the emergency clinic of the Pediatric Hospital, where antibiotics were administered for 1 week (500 mg amoxicillin every 8 hours) without any other intervention. At the time of the appointment the antibiotics regimen was completed, but the tooth was still slightly percussion and palpation painful. Clinical examination revealed a vestibular intraoral swelling associated with tooth 9 (Fig. 3C). Periodontal probing was within normal limits. No reaction was recorded on thermal and electrical sensibility tests only for tooth 9. The radiographic examination revealed periapical radiolucency associated with the immature
A diagnosis of pulpal necrosis with acute apical abscess was established. After presenting and discussing all treatment alternatives with the patient’s parents, a decision was made to attempt revitalization endodontic procedures for the immature necrotic maxillary incisor. A signed informed consent was obtained.

**Revitalization Protocol**

- The patient was anesthetized by using buccal infiltration anesthesia without vasoconstrictors (3% mepivacaine; 3M ESPE).
- The rubber dam was placed and stabilized with Wedjets. The operation field was disinfected by using 2% chlorhexidine scrub.
- The pulp cavity was accessed with a sterile diamond bur (Endo-Access Bur; Dentsply Maillefer). After accessing the wide canal, purulent drainage was noticed (Supplementary Video 1). The tooth was left to drain until the drainage became hemorrhagic and ceased. The contaminated content of the wide canal was rinsed away with copious sterile saline irrigation through a slotted end irrigation needle.
- The working length was estimated with a working length radiograph with an ISO 100 K-file.
- No further instrumentation of the root canal walls was performed.
- The wide canal was rinsed with 20 mL of 1.5% NaOCl solution through a 27-gauge slotted end needle fitted 2 mm short of working length.
- The canal was dried with capillary suction fitted 2 mm short of working length.
- The Endo-Vac macro-cannula was fitted 1 mm short of working length, and negative pressure irrigation with 20 mL of 1.5% NaOCl was performed.
- The canals were flooded with 1.5% NaOCl and left inside the canals non-agitated for 30 minutes.
The canal was dried with capillary suction from the NaOCl solution, and it was flooded with 17% EDTA through an Endo-Vac macro-cannula fitted in working length.

The EDTA 17% was left for 10 minutes and then rinsed away with sterile water.

The canal was dried with capillary suction fitted 2 mm short of working length.

Bleeding was induced by mechanical irritation of the periapical tissues and rotational movement of a sterile apically pre-curved size 40 K-file.

The canal was allowed to fill with blood to the level 2 mm below the cementoenamel junction and waited for 15 minutes for a clot to be formed.

An MTA barrier of 4-mm thickness (MTA Angelus) was placed over the blood clot with an MTA applicator.

The MTA material was adapted over the blood clot with a micro-brush and a dry sterile cotton pellet.

MTA material was protected with injectable gutta-percha, and the MTA remnants were removed with a grit blast of bisodium carbonate sandblasting.

The access cavity was rinsed with water, the gutta-percha plug was removed with an excavator, and the tooth was temporarily restored with glass ionomer (Fuji IX GP). A radiograph was taken to evaluate the coronal plug (Fig. 3B).

The patient was scheduled 14 days later for evaluation and permanent composite resin restoration.

The patient returned for the scheduled follow-up appointment 14 days later. The clinical evaluation revealed an asymptomatic maxillary central incisor, but the sinus tract was still present. The temporary restoration was removed, and the MTA was checked for proper setting. The dentin in contact with MTA had been rendered grey. The discoloration was removed in part with a diamond bur, and the

**FIGURE 3** — (A) Preoperative periapical radiograph of tooth 9. (B) Postoperative periapical radiograph of tooth 9. (C) Preoperative clinical image of the buccal infection. (D) One-year follow-up periapical radiograph showing periapical lesion healing. (E) Three-year follow-up periapical radiograph showing periapical lesion healing, continuous root development, dentin wall thickening, and cervical level hard tissue biological repair of the access opening. (F and G) Eight-year follow-up clinical image and periapical radiograph during the orthodontic treatment.
tooth was restored with composite resin. The patient was recalled after 1 month for a detailed clinical evaluation of the tooth. The sinus tract had been resolved, and the tooth was asymptomatic and functional. Periodontal probing was within normal limits. No radiograph was taken, and the patient was scheduled for long-term clinical and radiologic follow-ups. The 1-, 3-, and 8-year follow-up radiographs revealed continuous root development, dentin wall thickening, and hard tissue biological closure of the access cavity over time (Fig. 3D, E, and G). The clinical evaluation at the 8-year follow-up examination revealed healthy soft tissues and a grey cervical discoloration (Fig. 3F). The tooth had been subjected to orthodontic movement. After the removal of the orthodontic appliances, a decision was made to manage the discoloration (Fig. 4A and C). The tooth was isolated with rubber dam, and the composite resin was removed, exposing the calcium silicate cement underneath. The discoloring cement was removed with ultrasonics under microscopic visualization, and the hard tissue biological repair of the access cavity was exposed. The repair tissue was yellowish with some brown niches and seemed irregular and firmly connected with the axial walls through a well-demarcated white line (Fig. 4D and F). A periodontal probe was used to assess the stability of the hard tissue bridge to displacement forces. The hard tissue seemed compact and stable (Supplementary Video 2). A self-etching bonding agent (One coat; Coltene) was used over the repaired access cavity, and a thin layer of flowable composite (Brilliant; Coltene) was placed. Internal bleaching was performed with 35% hydrogen peroxide gel (Opalescence Endo; Ultradent Products, Inc, South Jordan, UT) for 5 days. The tooth was restored with composite resin. The 10-year follow-up clinical and radiographic evaluations revealed healthy tissues and satisfactory esthetic result (Fig. 4B and E).

**FIGURE 4**– (A) Nine-year follow-up radiograph after completion of orthodontic movement. (B) Ten-year follow-up periapical radiograph showing periapical tissue healing, continuous root development, and cervical level hard tissue repair of the access opening. (C) Nine-year follow-up clinical view of the greyish cervical discoloration. (D and F) Clinical images of cervical level biological hard tissue repair of access opening; original magnification, ×16 and ×20, respectively. (E) Ten-year follow-up clinical image showing favorable esthetic result.
DISCUSSION

The strengthening of immature necrotic teeth is considered a major challenge in dentistry. Incompletely formed teeth with thin dentin walls have been shown to experience higher incidences of cervical root fracture, which lead to reduced long-term overall prognosis. Faced with these situations, clinicians have attempted to use bonded composite restorations and fiber posts to reinforce the remaining roots\(^\text{16}\). Although apexification procedures with bonded composite restorations and fiber posts offered favorable outcomes\(^\text{17}\), the replacement of missing tissues with artificial means cannot possibly compete with the biological replacement of the missing tissues with natural dental structures.

Recently, regenerative endodontic procedures were introduced to restore the damaged tissues and strengthen the immature necrotic teeth. Regenerative endodontic procedures are defined as biologically based procedures aiming at the elimination of the infection (primary goal, essential), continuous root development/dentin wall thickening (secondary goal, desirable), and regeneration of the pulpal-dentinal complex within a previous empty but infected root canal space (tertiary goal)\(^\text{18}\). Irrespective of the regenerative objectives that can be accomplished, all regenerative protocols require a wide access cavity to gain access to the wide canal. Usually this access cavity is restored at the cervical level of the root with biocompatible/bioactive calcium silicate cement combined with a composite resin restoration. The coronal placement of the calcium silicate cement in regenerative endodontic procedures precludes the use of fiber posts and might hinder the reinforcement of the immature tooth at the cervical level.

Interestingly enough, most of the regenerative literature focused on the continuous root development and the dentin wall thickening potential of the different regenerative protocols to strengthen the root, and little attention was given to the cervical area.

Although the biological repair of the access cavity in the cervical root level with hard tissue bridge is reported among the favorable outcomes of regenerative endodontic procedures\(^\text{19}\), it is not included in the goals of regenerative endodontic procedures. However, cervical level access opening repair might be a more important biological outcome than continuous root development and dentin wall thickening, leading to true strengthening of the immature teeth.

In this article, we report the regenerative protocols applied in 3 cases of immature maxillary incisor necrosis that, in addition to continuous root development and dentin wall thickening, also resulted in hard tissue repair of the wide access cavities after 5- and 9-year follow-up periods. In the last case, the cervical MTA plug was removed because of esthetic reasons. The hard tissue biological repair was visualized under the microscope and checked for its continuity with the axial walls, its resistance to displacement, and the presence of defects. The repair tissue seemed to be yellowish in appearance with some brown niches, of irregular texture, firmly connected with the axial dentinal walls through a demarcated white line, and resisted all displacement forces applied. This tissue is suggested to provide true fortification of the immature root and might be more important biological outcome than continuous root development and dentin wall thickening.

On the basis of the best available evidence, a protocol that provides the most favorable outcome has yet to be determined\(^\text{20}\). This is attributed to the high variability of the clinical protocols applied during regenerative endodontic procedures\(^\text{21}\). Even similar regenerative protocols applied by the same operator in the same patient have been reported to result in different biological outcomes\(^\text{12}\) or induce different healing patterns\(^\text{13}\). Patterns of healing might differ according to the nature of the initial injury and the timing before intervention. Moreover, the patterns of healing can differ according to tooth type, stage of root maturation, type of coronal barrier, disinfection protocol used, and type of intracanal dressing in multiple-visit cases\(^\text{11}\).

Although antibiotics were used as intermediate dressing for most multiple-visit published case reports, recent publications advocate the use of calcium hydroxide\(^\text{20,22,23}\). Recently, the European Society of Endodontontology published a position statement on revitalization procedures suggesting that the use of antibiotics should be replaced with calcium hydroxide intermediate dressing\(^\text{18}\).

The main concerns for the use of antibiotic pastes during revitalization procedures are treatment-related (crown discoloration, stem cell toxicity, fracture resistance, reduction of dentin) and patient-related (sensitization, bacterial resistance). With regard to the stem cell toxicity, an in vitro study has demonstrated that concentrations of triple antibiotic paste, modified triple antibiotic paste, or a double antibiotic paste (DAP) exceeding 1–6 mg/mL were detrimental to stem cells from the apical papilla when in direct contact\(^\text{24}\). Indeed, this raises some concerns when highly concentrated pasty polyantibiotic mixtures are used. However, for calcium hydroxide dressings, although they exert some antibacterial effects in the root canal system, their antibacterial and anti-biofilm effects remain controversial\(^\text{25,26}\). Recently, there is growing evidence that the most important reason for regenerative failure is persistent biofilm infection, and that improvement of disinfection procedures could shift failing regenerative cases to favorable healing patterns\(^\text{27}\). In the regenerative protocol described in cases 1 and 2, a double antibiotic simple mixture was used to a pasty slurry consistency (approximately 1000 mg/mL solution) that is considered toxic for the stem cells. However, the possible benefit of improved disinfection outweighed the risks of DAP toxicity to the stem cells from the apical papilla. Moreover, the risk was minimized by controlling the level of the placement of the DAP and avoiding extrusion of the antibiotic and direct contact with the cells in their apical niches. Inside the canal space the most detrimental factor is effective disinfection and not the toxicity to stem cells that are not yet there. Removal of all antibiotic paste remnants and dentin conditioning before scaffolding are essential steps to shift the intracanal environment to an environment friendly to cell growth and differentiation after the use of antibiotics.

In the present article, both multiple-visit and single-step protocols resulted in favorable biological repair consisting of continuous root development, dentinal wall thickening, and biological repair of the radicular access opening that might account for the true fortification of the necrotic immature teeth.

CONCLUSIONS

The biological repair of the access cavities observed here is suggested to be as important as continuous root development and dentin wall thickening for the long-term prognosis of regenerative endodontic procedures. A regenerative protocol that can induce such a healing pattern might strengthen the immature root and deserves further scientific investigation and modulation.

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The authors deny any conflicts of interest related to this study.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version at www.jendodon.com (https://doi.org/10.1016/j.joen.2019.07.003).
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