Influence of Age and Apical Diameter on the Success of Endodontic Regeneration Procedures

Bishoy Safwat Estefan, BDS,* Kariem Mostafa El Batouty, Phd,* Mohamed Mokhtar Nagy, Phd,* and Anibal Diogenes, DDS, MS, Phd†

Abstract

Introduction: Treatment of immature permanent teeth with necrotic pulp and apical pathosis constitutes a challenge for endodontists. The present study was done to evaluate the effect of age and apical diameter on the regenerative potential of young permanent immature teeth with necrotic pulps. Methods: Immature necrotic permanent maxillary incisors (n = 40) of patients 9–18 years old were divided into 2 groups according to the treatment protocol: group Y (younger age group), 9–13 years and group O (older age group), 14–18 years. Each group was further subdivided into 2 subgroups according to apical diameter, subgroup (n) (narrower diameter) between 0.5 and 1 mm and subgroup (w) (wider diameter) equal to or greater than 1 mm. Revascularization procedures were performed for all patients. Follow-up was done for up to 12 months. Standardized radiographs were digitally evaluated for increase in root length and thickness and decrease in apical diameter. Results: After the follow-up period, most of the cases demonstrated radiographic evidence of periapical healing. Group Y showed significant progressive increase in root length and width and decrease in apical diameter. Subgroup (w) representing wider apical diameter showed significant progress as well. Conclusions: It was found that revascularization procedures can be implemented in any age ranging from 9 to 18 years; however, younger age groups were better candidates for revascularization procedure than older ones. Regarding the apical diameter, regeneration procedures were successful with apical diameters as small as 0.5 mm. However, teeth with preoperative wider diameters (≥1 mm) demonstrated greater increase in root thickness, length, and apical narrowing. (J Endod 2016; ■ :1–6)

Key Words

Age, apical diameter, regeneration

Significance

Pulp regeneration is a biologic treatment modality for immature teeth with open apices. Regenerative ability depends on both age and apical diameter.

Treatment of immature permanent teeth with necrotic pulp and apical pathosis constitutes a challenge for endodontists. Such cases are commonly encountered in children because of trauma, dental anatomic variations (eg, dens evaginatus), and untreated carious lesions. Many of these teeth develop pulpal necrosis before completing root development. Such conditions are challenging not only in root canal debridement and filling but also for the thin dentinal walls increasing the risk of subsequent fracture (1).

Historically, immature apices have been managed with root-end closure through apexification (2, 3). Although these procedures have excellent clinical success for the resolution of infection and its associated symptoms, they do very little for continued root development. Thus, teeth remain with thin dentinal walls after apexification procedures (4). In addition, in highly immature teeth, clinician may elect the long-term use of calcium hydroxide as the method to develop an apical calcific barrier. This technique has several disadvantages because it requires multiple visits during long period of time, requiring compliance, and the long-term use of calcium hydroxide might alter the mechanical properties of dentin, making the tooth more susceptible to fractures (5). Therefore, even if apexification closure is successful, the long-term prognosis is questionable because of eventual root fracture (6).

Recently, the concept of immediate apical plug has been advocated. This technique is performed by placement of artificial apical plug obliterating the apical portion of the canal. Mineral trioxide aggregate (MTA) proved to be excellent candidate for this protocol. This protocol has the advantage of reduced number of visits, higher patient compliance, and high success rate. However, the problem of thin brittle roots was not solved (7–9).

An alternative approach to treating the immature necrotic permanent tooth is to regenerate pulpal tissue, allowing for continued root formation. This treatment modality was introduced as a biological alternative for continued maturation of the entire root rather than the formation of an apical calcific barrier through apexification (10–12).

In regenerative endodontics, one of the goals is to promote continued root development in addition to the crucial resolution of the disease process. Therefore, the advantage of this treatment is continued root lengthening and reinforcement of lateral dentinal walls with deposition of new hard tissue. Revascularization, regeneration, and revitalization are commonly used terms to describe the regrowth of de novo tissue within the root canal space (13–21).
Clinical Research

It has been appreciated in the dental trauma literature that regenerative potential of the dental pulp in replanted immature teeth is influenced by age, stage of root development, and apical diameter (22). Because the patient’s age is directly related to stage of root formation and apical diameter, it is likely a modifying factor in regenerative endodontic procedures. Thus, the aim of this study was to evaluate the effect of age and the apical diameter on the outcomes of the regenerative procedures.

Materials and Methods

Forty patients with immature, non-vital maxillary anterior teeth presenting with or without signs and/or symptoms of periapical pathology were included in this study from the outpatient clinic of the Faculty of Dentistry, Ain Shams University, Cairo, Egypt. A detailed medical and dental history was obtained from each patient’s parents or guardians. Only systemically healthy patients were included in this research. The clinical and radiographic exclusion criteria were teeth with vertical fractures, periodontally involved teeth, and non-restorable teeth. All procedures were performed after obtaining proper institutional review board approval that was based on the regulations of the Ethical Committee of the Faculty of Dentistry, Ain Shams University. Intraoral periapical radiographs revealed immature apices. The age of the patients ranged between 9 and 18 years. Informed consent including the proposed treatment and possible outcomes or complications was signed for each case by the patient’s parents or guardians.

Preoperative radiographs were acquired by using the standardized paralleling technique with the Rinn XCP alignment system (Rinn Corporation, Elgin, IL). Periapical radiographs were digitized by using a transparency scanner (HP Scanjet G3110; Hewlett-Packard Development Co, Palo Alto, CA) for apical diameter measurement via ImageJ software (Imagej v1.44; National Institutes of Health, Bethesda, MD).

Cases were divided into 2 groups (20 patients for each group): group Y (younger age group), aged 9–13 years; and group O (older age group), aged 14–18.

Each group was subdivided according to apical diameter into 2 equal subgroups (n = 10): subgroup (n) narrower range, apical diameter equal to or greater than 1 mm; and subgroup (w) wider range, apical diameter equal to or greater than 1 mm.

Table 1. Summary of Patients’ Demographic Data

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Tooth no.</th>
<th>Age (y)/sex</th>
<th>Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>1</td>
<td>8</td>
<td>9/m</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>9</td>
<td>10/f</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>12/m</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>11</td>
<td>13/f</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>12</td>
<td>Excluded</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>9</td>
<td>14/m</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>9</td>
<td>15/f</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>17/m</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>11</td>
<td>18/f</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>12</td>
<td>Failed</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>13</td>
<td>Excluded</td>
</tr>
</tbody>
</table>

Evaluation

The clinical assessment of pain and/or swelling and standardized radiographic assessment included the following:

Teeth were anesthetized by using local anesthesia without a vasoconstrictor (Scandostan 3% plain; Septodont, Saint-Maur-Des-Fosses, France). After rubber dam isolation, access cavities were prepared, and root canals were irrigated by using 10 mL 2.6% sodium hypochlorite, with circumferential filling of the canal walls by using hand files. The triple antibiotic paste was prepared by using metronidazole (500-mg tablets, Flagyl 500 mg; Aventis, Cairo, Egypt), ciprofloxacin (250-mg tablets, Ciprocin 250 mg; EPICO, Cairo, Egypt), and doxycycline (100-mg capsules, Vibramycin; Pfizer, Cairo, Egypt). The doxycycline capsule content was evacuated in a sterile mortar; a tablet of metronidazole and a tablet of ciprofloxacin were crushed and ground into homogenous powder in the same mortar by using a pestle. Saline drops were added and mixed by using the pestle until a creamy paste was achieved. The canal space was dried by using paper points, and 1 mL prepared paste was injected into the canals by using a sterile plastic syringe with a 20-gauge needle. A sterile cotton pellet was then applied, and the access cavity was sealed by using a temporary restoration (Coltosol F; Coltene Whaledent, Altstatten, Switzerland) for 3 weeks. The final visit was scheduled when the tooth was asymptomatic with no signs of discharge. In cases of persistent infection, 1 or more visits were scheduled for further drainage and chemical disinfection. After anesthesia and proper isolation, the temporary restoration and the cotton pellet were removed. The canal was irrigated with 10 mL NaOCl 2.6%, followed by 17% EDTA for about 1 minute. Canals were then dried with sterile paper points.

A sterile hand file size #50 was used with sharp strokes into the periapical tissue 2 mm beyond the apex until bleeding was evident at the cervical portion of the canal. An MTA orifice plug was used to seal the canal orifice covered by a moist cotton pellet. After 1 week, adhesive composite resin was used to seal the access cavity.

After treatment, patients were recalled for follow-up every 3 months for up to 1 year.
1. An increase in root length
2. An increase in root thickness
3. A decrease in apical diameter

All measurements were performed blindly by 2 examiners and averaged.

**Figure 1.** Representative cases. (A) Preoperative radiograph representing group O(n); (B) radiograph of same case in group O(n) after 12 months of follow-up; (C) preoperative radiograph representing group O(w); (D) radiograph of same case in group O(w) after 12 months of follow-up; (E) preoperative radiograph representing group Ia; (F) radiograph of same case in group Y(n) after 12 months of follow-up; (G) preoperative radiograph representing group Y(w); (H) radiograph of same case in group Y(w) after 12 months of follow-up.

**Increase in Root Length**

A measuring scale was set in the ImageJ software (ImageJ v1.44) by measuring a known clinical dimension to its radiographic dimension. The scale was calculated as the number of measured pixels per millimeter length. Root lengths were measured as a straight line from
the cementoenamel junction to the radiographic apex of the tooth in millimeters. Pretreatment and follow-up root lengths were measured, and the difference in root length was calculated (4). The percentage of increase in length was calculated as follows:

\[
\text{Percentage of increase in length} = \frac{\text{postoperative length} - \text{preoperative length}}{\text{preoperative length}} \times 100
\]

**Increase in Root Thickness**

By using the preset measurement scale, the level of the apical third was determined and fixed from the cementoenamel junction. The root thickness and the pulp width were measured at this level in millimeters. Dentin thickness was measured by subtracting the pulp space from the whole root thickness (4).

Measurements were performed preoperatively and postoperatively at the same fixed level. The difference in thickness was calculated. The percentage of increase in dentin thickness was calculated as follows:

\[
\text{Dentin Thickness} = \text{root thickness} - \text{pulp width}
\]

\[
\text{Percentage of increase in thickness} = \frac{\text{postoperative thickness} - \text{preoperative thickness}}{\text{preoperative thickness}} \times 100
\]

**Decrease in Apical Diameter**

By using the preset measurement scale, the diameter of the apical foramen was measured in millimeters. Measurements were performed preoperatively and postoperatively. The difference in apical diameter was calculated (23).

The percentage of apical closure was calculated as follows:

\[
\text{Percentage of apical closure} = \frac{\text{postoperative apical diameter} - \text{preoperative apical diameter}}{\text{preoperative apical diameter}} \times 100
\]

Data were collected, tabulated, and statistically analyzed by using statistical analysis software SPSS (Statistical Packages for the Social Sciences 20.0; IBM, Armonk, NY). Two-way analysis of variance was performed. The Tukey post hoc test was used in case of significance.

**Results**

Patients’ demographic data are summarized in Table 1. A total of 5 patients were excluded from the study because of inadequate compliance and failure to recall. Two cases were excluded from group Y(n), 1 case was excluded from group Y(w), 1 case was excluded from group O(n), and 1 case was excluded from group O(w). The percentages of recall for groups Y(n), Y(w), O(n), and O(w) were 80%, 90%, 90%, and 90%, respectively. Clinical and radiographic examination during the follow-up period showed signs and symptoms of failure in 2 of the 35 recalled cases, with overall success rate of 94.3%). One case belonged to group Y(w), and the other case belonged to group O(n). The failed cases were reevaluated, and the treatment plan was shifted to MTA apexification. Representative cases are shown in Figure 1.

**Increase in Root Length**

Statistical analysis showed no significant difference between the subgroups (n) and (w) in both age groups Y and O through the whole follow-up period (Table 2). Younger age groups [Y(n) and Y(w)] showed significantly greater increase (1.09 ± 0.5 and 1.26 ± 1.08 mm, respectively) in root length than in older age groups [O(n) and O(w)] (0.45 ± 0.19 and 0.45 ± 0.3 mm, respectively).

**Increase in Root Thickness**

Statistical analysis demonstrated no significant difference between the subgroups (n) and (w) in age group Y (increase 0.5 ± 0.24 and 0.61 ± 0.38 mm, respectively). However, in age group O subgroup (n), a significantly lower increase in root thickness was observed (0.14 ± 0.11 mm) (Table 3).

**Decrease in Apical Diameter**

Group Y(w) showed the highest decrease in apical diameter at the follow-up period, followed by group Y(n) and O(w). Conversely, group O(n) (older age group with narrower diameter) showed the least significant change in apical diameter (Table 4).

**TABLE 2. Increase in Length in Millimeters for All Groups during Different Follow-up Periods**

<table>
<thead>
<tr>
<th>Group</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>0.21 ± 0.2a</td>
<td>0.18 ± 0.12ab</td>
<td>0.41 ± 0.27ab</td>
<td>0.29 ± 0.18ab</td>
<td>1.09 ± 0.5a</td>
</tr>
<tr>
<td>Ib</td>
<td>0.36 ± 0.28a</td>
<td>0.43 ± 0.4b</td>
<td>0.25 ± 0.21b</td>
<td>0.22 ± 0.14a</td>
<td>1.26 ± 1.08a</td>
</tr>
<tr>
<td>Ila</td>
<td>0.13 ± 0.11b</td>
<td>0.17 ± 0.1a</td>
<td>0.08 ± 0.03c</td>
<td>0.05 ± 0.02b</td>
<td>0.43 ± 0.19b</td>
</tr>
<tr>
<td>llb</td>
<td>0.12 ± 0.1b</td>
<td>0.08 ± 0.06a</td>
<td>0.15 ± 0.1c</td>
<td>0.1 ± 0.01b</td>
<td>0.45 ± 0.3b</td>
</tr>
<tr>
<td>P value</td>
<td>.02</td>
<td>.036</td>
<td>.007</td>
<td>.001</td>
<td>.001</td>
</tr>
</tbody>
</table>

**TABLE 3. Increase in Thickness in Millimeters for All Groups during Different Follow-up Periods**

<table>
<thead>
<tr>
<th>Group</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>0.09 ± 0.09a</td>
<td>0.08 ± 0.07a</td>
<td>0.04 ± 0.02a</td>
<td>0.29 ± 0.18a</td>
<td>0.5 ± 0.24a</td>
</tr>
<tr>
<td>Ib</td>
<td>0.09 ± 0.08a</td>
<td>0.19 ± 0.13b</td>
<td>0.11 ± 0.09b</td>
<td>0.22 ± 0.14a</td>
<td>0.61 ± 0.38b</td>
</tr>
<tr>
<td>Ila</td>
<td>0.02 ± 0.01b</td>
<td>0.05 ± 0.02c</td>
<td>0.02 ± 0.02c</td>
<td>0.05 ± 0.02b</td>
<td>0.14 ± 0.11b</td>
</tr>
<tr>
<td>llb</td>
<td>0.18 ± 0.16c</td>
<td>0.11 ± 0.12b</td>
<td>0.06 ± 0.03c</td>
<td>0.1 ± 0.01b</td>
<td>0.45 ± 0.23a</td>
</tr>
<tr>
<td>P value</td>
<td>.004</td>
<td>.027</td>
<td>.002</td>
<td>.015</td>
<td>.001</td>
</tr>
</tbody>
</table>

Significant at P ≤ .05. Different letters indicate significant difference.
**Discussion**

Endodontic treatment of immature permanent teeth with necrotic pulp, with or without apical pathosis, poses several clinical challenges (1). There is a risk of inducing dentin wall fracture or extending gutta-percha or other restorative materials into the periapical tissue during compaction of the root canal filling. Recently, regenerative endodontics has gained much attention as a biologically based treatment alternative. Regenerative approaches differ from apexification procedures in that they can allow for further root maturation in length and thickness by regenerating vital tissue (10–12).

Thorough disinfection of the root canal that is followed by stimulation of residual stem cells gave the way to ingrowth of de novo pulp-like tissue (revascularization procedure), which can induce formation of new hard tissue on the existing dentin wall and continued root development (14). Revascularization is considered a simple protocol by which pulp regeneration is enhanced by the use of the blood clot as a scaffold for autogenous release stem cells, as stated by Lovelace et al (24).

The outcome of revascularization procedures remains somewhat unpredictable and multifactorial. The aim of this study was to evaluate the effect of preoperative apical diameter and age on the outcomes of regenerative endodontic procedures. The evaluation was based on the increase in root length thickness and the decrease in apical diameter. The choice of age as a factor represented the healing capacity of the individual (29, 30).

Disinfection of the root canal used the disinfection protocol described by Sato et al (25) and Hoshino et al (26), which was adopted in many studies implementing the revascularization procedures. The use of the triple antibiotic paste in this study resulted in resolution of the disease within 3 weeks in the great majority of patients (33 patients). However, there were some patients who required additional application of the medication (7 patients), and some patients who had systemic manifestation of the infection had to take orally administered antibiotics. In addition, 17% EDTA was used to remove the smear layer, which allowed for better cell adhesion to dentin and enhanced the release of the dentin growth factors (27, 28).

The increase in root length and thickness among all groups was noticed after 1-year follow-up in most of the cases with variable records. The root length was increased probably via the deposition of mineralized tissue along the dentinal walls, which might be intracanal cementum or bone-like tissue as stated by many authors (16, 23). However, the nature of the tissues formed was not evaluated in this study, which focused on clinical outcomes. Nonetheless, the younger age group showed significant increase in length independent of the apical diameter when compared with older age group. This might be attributed to greater stem cell regenerative potential seen in younger individuals (29, 30).

The results on the increase in root thickness were similar to the root length results except for the older age group with wider apical diameter, which were similar to the younger age group. The older group with narrower diameter was significantly lower in root thickness increase. This might indicate the apical diameter is a second factor governing the progress of revascularization process. The new tissue such as cementum or bone itself would not grow into the canal space through the apical foramen. Cementoblasts or osteoblasts migrate into the canal space and produce cementum or bone. The sizes of cementoblasts and osteoblasts (10–100 μm) are much smaller than those of many blood vessels entering the apical foramen.

Thus, the apical diameter at the time of treatment completion appears to be a strong predictor of root development. Also, it was found that the greatest narrowing of the apical diameter occurred in the younger patients. For the older patient group, the narrowing was more limited than in the younger patients, and it occurred more predictably when the apical diameter was greater than 1 mm preoperatively.

**Conclusions**

Under the circumstances of this study, it was found that revascularization procedures can be implemented in any age ranging from 9 to 18 years; however, younger age groups were better candidates for revascularization procedures than older age groups. Regarding the apical diameter as the second factor in the predictability of the procedure outcomes, regeneration procedures were successful with apical diameters as small as 0.5 mm. However, teeth with preoperative wider diameters (>1 mm) in both groups demonstrated greater increase in root thickness, length, and apical narrowing.

**Acknowledgments**

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

**References**


**TABLE 4.** Decrease in Apical Diameter in Millimeters for All Groups during Different Follow-up Periods

<table>
<thead>
<tr>
<th>Group</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>la</td>
<td>0.11 ± 0.09*</td>
<td>0.06 ± 0.05*</td>
<td>0.11 ± 0.04*</td>
<td>0.14 ± 0.11*</td>
<td>0.42 ± 0.24*</td>
</tr>
<tr>
<td>lb</td>
<td>0.27 ± 0.22*</td>
<td>0.29 ± 0.13b</td>
<td>0.32 ± 0.21b</td>
<td>0.23 ± 0.14a</td>
<td>1.11 ± 0.56a</td>
</tr>
<tr>
<td>lla</td>
<td>0.03 ± 0.02c</td>
<td>0.02 ± 0.02b</td>
<td>0.03 ± 0.02c</td>
<td>0.05 ± 0.04b</td>
<td>0.13 ± 0.09c</td>
</tr>
<tr>
<td>llb</td>
<td>0.18 ± 0.17a</td>
<td>0.09 ± 0.07a</td>
<td>0.19 ± 0.13a</td>
<td>0.22 ± 0.16a</td>
<td>0.68 ± 0.41a</td>
</tr>
</tbody>
</table>

P value | .0031 | .48 | .12 | .005 | ≤.001

Significant at P ≤ .05. Different letters indicate significant difference.