






CASE REPORT

REVISED Case Report: Single visit photo-activated disinfection in regenerative endodontics [version 2; peer review: 2 approved]

Previously titled: Case Report: Photo-activated oral disinfection in regenerative endodontics

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Abstract

Background: Root canal disinfection is considered critical for achieving successful regenerative endodontic procedures. Photo-activated disinfection is a novel disinfection method that can help to achieve the goal of regenerative endodontics. This article reports the clinical and radiographic results after single visit regenerative endodontics using photo-activated disinfection.

Methods: An 8.5-year-old girl complained of fractured upper right central incisor. Pulp necrosis was diagnosed on the basis of clinical findings. The root canal was irrigated with sodium hypochlorite solution (1.5%) followed by saline. Then, the canal was dried with paper points. A combination of a photosensitizer solution and low power laser light were applied. EDTA solution was used as a final irrigant. Bleeding was induced, followed by placement of collagen resorbable matrix and white mineral trioxide aggregate. Two days later, the tooth was sealed and restored with permanent filling.

Results: Clinical findings revealed no pain on percussion or palpation tests. Radiographic examination revealed an increase in root length, an increase of apical root thickness and apical closure at the 12-month follow-up period.





Conclusion: Regenerative endodontics using photo-activated disinfection achieved successful outcomes in the necrotic immature permanent tooth.

Keywords

regenerative endodontics, necrotic tooth, open apex, root canal disinfection


Open Peer Review

Reviewer Status  

	Invited Reviewers	
	1	2
version 2 (revision) 03 Jun 2020	 report	 report
version 1 28 Aug 2019	 report	 report

1. **Gianluca Gambarini**, Sapienza University of Rome, Rome, Italy

Dario Di Nardo, Sapienza University of Rome, Rome, Italy

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: **Abdel Hafiz Abdel Rahim AS:** Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Writing – Original Draft Preparation; **Abdelgawad F:** Methodology, Supervision, Validation, Visualization, Writing – Review & Editing; **Abd Alsamed AM:** Investigation, Software, Supervision, Visualization; **Moheb DM:** Conceptualization, Supervision, Writing – Review & Editing; **Wahab El-Dokky NA:** Supervision, Validation, Writing – Review & Editing

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REVISED Amendments from Version 1

The title was modified. We added more justifications for our idea in the introduction and discussion sections as requested by the reviewer.

Any further responses from the reviewers can be found at the end of the article

Introduction

The term regenerative endodontic procedures (REPs) has been widely endorsed. This term describes all procedures that aim to achieve organized repair of the dental pulp¹. The clinical considerations for REPs include: disinfecting the root canal system; providing a scaffold with periapical tissue laceration to get a blood clot and introduce stem cell activity within the root canal; and sealing the coronal access properly to prevent reinfection^{2,3}.

Antibiotics appear to be suitable intra-canal medication. Triple antibiotic paste (TAP) consisting of metronidazole, ciprofloxacin and minocycline is considered to be a successful regimen in managing the root canal pathogen of necrotic immature permanent teeth⁴. Recently, new methods of disinfection have been described to control the limitations of conventional disinfecting methods by neither diminishing the bacterial number to an adequate level or eliminating the toxicity to periapical stem/progenitors⁵. Other concerns regarding the use of TAP include tooth discoloration and bacterial resistance⁶.

Photodynamic therapy (PDT)/photo-activated disinfection (PAD) is considered one of the optimized single visit approaches⁷. It involves a photosensitizer (photoactive dye) that is activated by exposure to light of a specific wavelength in the presence of oxygen. The energy transferred from the activated photosensitizer to available oxygen leads to toxic oxygen species formation, such as singlet oxygen and free radicals. These very reactive chemical species can destroy proteins, nucleic acids, lipids and other cellular components⁸. Moreover, PAD acts in a selective way. Both photosensitizer and oxygen released during bacterial cell death do not exhibit toxicity to the viable tissues⁹.

Several *in vitro* studies have shown that PDT is effective in root canal disinfection¹⁰⁻¹². A clinical study by Johns *et al.*¹³ reported successful outcomes for using PAD in root canal treatment of completely formed root. The case report by Johns *et al.*¹⁴ was the first to document pulp revascularization using PDT and platelet-rich fibrin. Root lengthening, continued thickening of the canal walls and apical closure were demonstrated at 10-month follow-up¹⁴.

This article reports the successful use of PAD in regenerative endodontics as a novel and effective disinfection method, which might present a solution to the problems associated with triple antibiotic paste¹⁴.

Case report

An 8.5-year-old Egyptian girl came to the outpatient clinic of Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University with the chief complaint of fractured upper right central incisor due to trauma one and half months previously (Figure 1A and B). The patient's medical history was non-contributory. On clinical examination (which included a visual examination for any abnormalities, palpation of labial vestibule, percussion test and sensibility test), the tooth was sensitive to percussion, which was determined by tapping the tooth with the back of the mirror. The surrounding soft tissue had no tenderness to finger palpation and the tooth had no response to the hot test in comparison to the contralateral tooth. Preoperative radiographic examination revealed a wide root canal with an open apex (Figure 2A) using conventional periapical radiograph.

The case was managed by single visit regenerative endodontic procedure using PAD after obtaining written informed consent from the parents (including usage of data and publication) and assent from the child. The procedure was performed according to the American Association of Endodontics (AAE) guidelines¹⁵, except PAD instead of TAP was used. A 1.8ml carpule of mepivacaine 3% (Mepivacaine hydrochloride, Alexandria Co. for Pharmaceuticals, Egypt) was administered by infiltration. A rubber dam was applied, followed by access cavity preparation and tooth length detection. Gentle, copious irrigation was done using 20ml NaOCl (1.5% NaOCl 20ml/canal for five minutes). NaOCl of lower concentration was advised and then flushed with saline (20ml/canal for minutes), using irrigating needle located about 1mm from root end then the canal was dried using paper points.

Aseptim solution (SciCan Ltd, Denfotex Light Systems Ltd, Inverkeithing, Scotland) was applied to the canal, followed by a low power laser diode red light system (Aseptim system, SciCan Ltd, Denfotex Light Systems Ltd, Inverkeithing, Scotland) with a specific wavelength (635nm) to activate the aseptic solution for 150 seconds. Canals was washed with saline to remove the aseptic solution. Gentle, copious, irrigation with 20ml of 17% EDTA was applied. Dryness with paper points to remove excess EDTA was done. Bleeding was initiated into the canal system by rotating a K-file at 2mm beyond the apical foramen. A resorbable matrix (Collacote dressing Zimmer Biomet, USA) was placed over the blood clot. Then, white mineral trioxide aggregate (MTA) (Angelus, Brazil) was placed over the matrix with placement of a moistened pellet of cotton and glass ionomer (Figure 2B). After two days, the tooth was double sealed using glass ionomer cement (Kromoglass 2, LASCOD- Italy) and composite restoration 3M composite (3M, America Inc).

Clinical examination of the patient revealed no adverse signs and symptoms at three, six-, nine- and 12-month follow-up periods (Figure 1C and 1D). Radiographic examination revealed an increase in root length and root thickness at six months (Figure 2C) and complete root closure at 12 months (Figure 2D)



Figure 1. **A)** front view of preoperative intra-oral photo of traumatized upper right central incisor; **B)** occlusal preoperative photo; **C)** three month follow up; and **D)** 12-month follow-up.

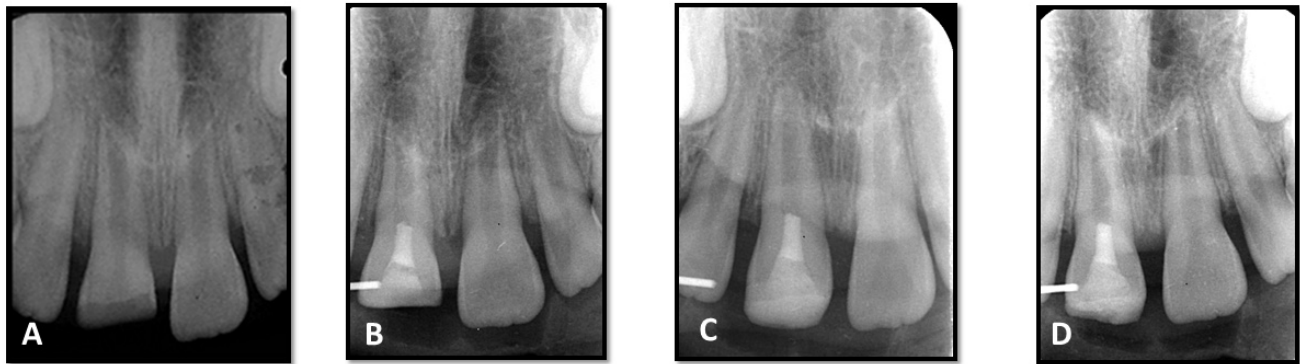


Figure 2. **A)** preoperative periapical radiograph; **B)** immediate postoperative radiograph after mineral trioxide aggregate coronal plug application; **C)** follow up radiograph at six months; and **D)** follow-up radiograph at 12 months.

using digital radiography (Digora™ Optime UV) and digital software (Soredex, Finland). An individual acrylic XCP (Extension Cone Paralleling) index was prepared by registering the bite and placed around the XCP plastic tip for radiographic standardization during follow up (Table 1).

Discussion

This case report documents the successful application of a novel and innovative disinfection technique in regenerative endodontics for management of a necrotic immature permanent tooth in a single visit, although a longer follow up period is recommended.

Root canal system disinfection is an integral step in the success of REPs. Chemical disinfection of the root canal is dependent on bacteriostatic/bactericidal properties of the agents as well as avoid harming the patient's stem cells³. Copious and

gentle irrigation was done using 20ml NaOCl. The use of NaOCl at lower concentrations was advised (1.5% NaOCl) with the irrigating needle adjusted to be 1mm from the root end to reduce the cytotoxicity to stem cells and to minimize the possibility of irrigant extrusion into the periapical tissues¹⁵. Furthermore, 1.5% NaOCl was effective in bacterial reduction of root canals as reported by Trevino *et al.*¹⁶.

The PAD technique was effective in removing high bacterial concentrations from infected root canals¹⁷. Aseptic solution was applied to the canal and agitated in the canal for 60 seconds using an endodontic file to ensure maximum penetration of the dye, since it is essential that the aseptic solution comes in close contact with the bacteria, otherwise the photosensitivity process does not occur¹⁸. The photosensitizer stains the bacterial cells in soft and hard tissues and the photo-activated cells release molecular oxygen causing disruption of the bacterial

Table 1. The patient's timeline of symptoms, treatment and follow-up periods.

Timeline	Event	Findings
0	Patient comes to the clinic. Patient's medical history obtained. Clinical and radiographic examination performed.	Fractured necrotic traumatized upper right central incisor, sensitive to percussion and no response to hot test with a wide root canal and an open apex
0	Regenerative endodontic procedure using photo-activated oral disinfection	
+ 2 days	Composite restoration	
+ 3 months	1 st Follow up (clinical assessment)	No pain, no swelling (symptom free)
+ 6 months	2 nd Follow up (clinical and radiographic assessment)	No pain, no swelling (symptom free) Increase in root length and dentin root thickness, and no adverse radiographic evidence.
+ 9 months	3 rd follow up (clinical assessment)	No pain, no swelling (symptom free).
+ 12 months	4 th follow up (clinical and radiographic assessment)	No pain, no swelling (symptom free). Complete apical root closure

cell wall. Photosensitizer and oxygen released during bacterial cell death are not reported to produce any toxicity to normal cells⁹. Moreover, PAD is a newer antimicrobial strategy that involves the combination of a non-toxic PS or dyes and a non-harmful visible light source to disinfect the root canal. Low power laser in itself is not particularly lethal to bacteria, but is useful for photochemical activation of oxygen-releasing dyes¹⁹.

Dickers *et al.*²⁰ stated that the average temperature rise was lower than the 7 degrees C safety level for periodontal injury. Moura-Netto *et al.*²¹ reported that studies on tissue engineering using stem cells from human exfoliated deciduous teeth have yielded promising results. Laser phototherapy is able to influence the proliferation and differentiation of these cells

Blood clot formation inside the canal is considered a scaffold and a source of growth factors. Inducing bleeding to promote blood clot formation is a commonly used method in many of the reported cases^{22–25}. A resorbable matrix (collagen wound dressing) should be carefully placed on the top of the blood clot to serve as an internal matrix and ease the placement of MTA¹⁵. White MTA was applied to act as a coronal plug and achieve effective coronal seal. It was the most frequently chosen material in published regenerative endodontic studies^{26–29}.

Regenerative endodontic procedures were completed during a single visit because PAD is considered one of the optimized single visit disinfection approaches. A successful single-visit regenerative endodontic therapy of an immature permanent tooth with a chronic apical abscess was published by Shin *et al.* They stated that a single-visit revascularization procedure has some advantages. It eliminates subsequent appointments to

access the root canal environment, thus reducing the possibility of further bacterial contamination of the root canal. It also diminishes the detrimental consequences of poor patient compliance with regular follow-up evaluation²³. Topçuoğlu and Topçuoğlu reported that a single-visit regenerative endodontic procedure may be a favorable treatment option for an asymptomatic immature tooth with a necrotic pulp and no periapical lesion³⁰

No adverse clinical signs and symptoms were noted during follow up periods, which is considered as a primary goal for regenerative endodontics as reported by AAE¹⁵. Apical closure and increasing apical dentin thickness were observed at the 12-month follow-up period. This case report demonstrates that PAD is a promising method for controlling infection in a single visit regenerative endodontic procedure. Further randomized clinical studies are needed to assess this disinfection technique.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent for publication of their clinical details and clinical images was obtained from the parents of the patient.

Acknowledgements

I dedicate this work to the soul of Prof. Mervat Abdelmonem Rashed, Professor of Pediatric Dentistry, Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University that her death prevents her to see the result of this report.

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Open Peer Review

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Version 2

Reviewer Report 04 September 2020

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Gianluca Gambarini

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I approve the revised manuscript in the present form.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 10 June 2020

<https://doi.org/10.5256/f1000research.25673.r64237>

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Mohamed Mokhtar Nagy 

Endodontic Department, Faculty of Dentistry, Ain Shams University, Cairo, Egypt

The authors addressed the required comments. The article is suitable for indexing.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Endodontic regeneration

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 30 March 2020

<https://doi.org/10.5256/f1000research.22088.r61455>

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**Mohamed Mokhtar Nagy**

Endodontic Department, Faculty of Dentistry, Ain Shams University, Cairo, Egypt

The manuscript focuses upon two main issues which are single visit regeneration and photo activated disinfection.

1. The title lacks the "the single visit concept".
2. The title states "oral" disinfection, this would be better as "canal" disinfection.
3. The introduction and discussion did not include the justification of the idea of single visit regeneration.
4. The introduction and discussion did not include the possible effects of laser as heat generation and effects on stem cells.
5. The manuscript did not state radiographic standardization during follow up.
6. The discussion did not justify the supposed mechanism of root canal disinfection by laser (PAD).

Is the background of the case's history and progression described in sufficient detail?

Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

No

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Endodontic regeneration

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 04 Apr 2020

Shaimaa Abdel Hafiz, Fayoum University, Fayoum, Egypt

We are pleased to submit the new version of **Case Report: Photo-activated oral disinfection in regenerative endodontics**. We appreciate the constructive criticisms of the reviewer that helped us to improve our manuscript. Herein we address their concerns. All changes appear by track changes in the revised version. Hope you find our replies satisfactory.

Response to comments of Reviewer:

1. The title lacks the "the single visit concept".

Single visit photo-activated disinfection in regenerative endodontics. The title was modified.

2. The title states "oral" disinfection, this would be better as "canal" disinfection

I omit the word oral because the most common terminology used in literature is Photo-activated disinfection and according to the remaining title it represents the site of disinfection applied on. So its preferable to state Photoactivated disinfection as mentioned in published literature of endodontics field (1-5).

3.

The introduction and discussion did not include the justification of the idea of single visit regeneration

For introduction:

Photodynamic therapy (PDT)/photo-activated disinfection (PAD) is considered one of the optimized single visit approaches (6). This part was added to introduction section. Several *in vitro* studies have shown that PDT is effective in root canal disinfection (1,2,7). A clinical study by Johns *et al.* (3) reported successful outcomes for using PAD in root canal treatment of completely formed root. The case report by Johns *et al.*(4) was the first to document pulp revascularization using PDT and platelet-rich fibrin. Root lengthening, continued thickening of the canal walls and apical closure were demonstrated at 10-month follow-up (4).All of these mentioned studies applied the PAD system in single visit. As mentioned in introduction section.

For Discussion:

Regenerative endodontic procedures were completed during a single visit because PAD is considered one of the optimized single visit disinfection approaches (6). A successful single-visit regenerative endodontic therapy of an immature permanent tooth with a chronic apical abscess was published by Shin *et al.* (8), They stated that a single-visit revascularization procedure has some advantages. It eliminates subsequent appointments to access the root canal environment, thus reducing the possibility of further bacterial

contamination of the root canal. It also diminishes the detrimental consequences of poor patient compliance with regular follow-up evaluation (8). Topçuoğlu and Topçuoğlu (9) reported that a single-visit regenerative endodontic procedure may be a favorable treatment option for an asymptomatic immature tooth with a necrotic pulp and no periapical lesion (9). This part was added to discussion section

4. The introduction and discussion did not include the possible effects of laser as heat generation and effects on stem cells.

For introduction:

Moreover, PAD acts in a selective way. Both photosensitizer and oxygen released during bacterial cell death do not exhibit toxicity to the viable tissues (10). This part was added to introduction section.

For Discussion:

Photosensitizer and oxygen released during bacterial cell death are not reported to produce any toxicity to normal cells(10).

Dickers et al. (11) stated that the average temperature rise was lower than the 7 degrees C safety level for periodontal injury. Moura-Netto et al.(12)reported that studies on tissue engineering using stem cells from human exfoliated deciduous teeth have yielded promising results. Laser phototherapy is able to influence the proliferation and differentiation of these cells. This part was added to discussion section.

5. The manuscript did not state radiographic standardization during follow up

An individual acrylic XCP (Extension Cone Paralleling) index was prepared by registering the bite and placed around the XCP plastic tip for radiographic standardization during follow up. This part was added to the case report section.

6. The discussion did not justify the supposed mechanism of root canal disinfection by laser (PAD).

Response:

The photosensitizer stains the bacterial cells in soft and hard tissues and the photo-activated cells release molecular oxygen causing disruption of the bacterial cell wall (10). Moreover, PAD is a newer antimicrobial strategy that involves the combination of a non-toxic PS or dyes and a non-harmful visible light source to disinfect the root canal. Low power laser in itself is not particularly lethal to bacteria, but is useful for photochemical activation of oxygen-releasing dyes (13). This part was added to discussion section.

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Competing Interests: No competing interests were disclosed.

Reviewer Report 10 March 2020

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The article presents a case of apicogenesis performed by gold standard methodologies. The novelty is the use of a photoactivated disinfectant instead of a triple antibiotic paste. Since NaOCl and EDTA used are sufficient to remove all the tissues that could avoid a proper regeneration of the apex, the effectiveness of the light activated disinfectant is doubtful.

The title of the article is on regenerative endodontics, that is a procedure that aims to regenerate dental pulp, but no evidences of regeneration are presented in the article instead of the production of new dentine, which is obtainable with a simple apicogenesis procedure and also without the use of triple antibiotic paste.

The overall novelty of the article is doubtful and the evidences of the regeneration of pulp are not explained at all. Dentine formation and the closure of the apex are evidences that could be obtained with gold standard techniques that do not involve the use of other expensive appliances like diode lasers.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Endodontics

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response () 12 Mar 2020

Shaimaa Abdel Hafiz, Fayoum University, Fayoum, Egypt

We appreciate the comments of the reviewer. Herein we address the concerns of the

reviewer.

1- The article presents a case of apicogenesis performed by gold standard methodologies. The novelty is the use of a photoactivated disinfectant instead of a triple antibiotic paste. Since NaOCl and EDTA used are sufficient to remove all the tissues that could avoid a proper regeneration of the apex, the effectiveness of the light activated disinfectant is doubtful.

Response:

- Apicogenesis is a root complementation therapy performed in teeth with pulp vitality and consists in the removal of infected coronal pulp, maintenance of vital root pulp and its protection with biocompatible material (1).

Pulpal necrosis was diagnosed on the basis of clinical findings in our case report as mentioned in the methods section of abstract. So regenerative endodontic procedure was applied for necrotic tooth with open apex as recommended by American Association of Endodontists (AAE)(2).

- Naocl and EDTA may be sufficient to remove all necrotic tissues but in this case report, it was mentioned that the procedure was performed according to the American Association of Endodontics (AAE) guidelines (2), except PAD instead of TAP was used. The AAE guidelines recommend using intracanal medication in adjunctive to the irrigants.

- There are several in vitro and in vivo studies proved the effectiveness of PAD system in root canal disinfection. And this article mentioned some of them (4-9).

2-

The title of the article is on regenerative endodontics, that is a procedure that aims to regenerate dental pulp, but no evidences of regeneration are presented in the article instead of the production of new dentine, which is obtainable with a simple apicogenesis procedure and also without the use of triple antibiotic paste.

Response:

- Regenerative Endodontics is defined as a biologically-based procedure designed to predictably replace damaged, diseased or missing structures, including dentin and root structures as well as cells of the pulp-dentin complex, with living viable tissues, preferably of the same origin, that restore the normal physiologic functions of the pulp-dentin complex (10)

- The term regenerative endodontic procedures (REPs) has been widely adopted and refers to all procedures that aim to attain organized repair of the dental pulp and include future therapies yet to regenerative endodontic treatment of necrotic immature permanent teeth resulting in continued root development, increased thickness in the dentinal walls and apical closure. evolve in the field of regenerative endodontics (3).

3-

The overall novelty of the article is doubtful and the evidences of the regeneration of pulp are not explained at all.

Dentine formation and the closure of the apex are evidences that could be obtained with gold standard techniques that do not involve the use of other expensive appliances like diode lasers.

Response:

- Regenerative endodontic treatment of necrotic immature permanent teeth resulting in continued root development, increased thickness in the dentinal walls and apical closure as mentioned by AAE.

- AAE Clinical Considerations for a Regenerative Procedure (2) stated that the degree of success of Regenerative Endodontic Procedures is largely measured by the extent to which it is possible to attain primary, secondary, and tertiary goals:

1. Primary goal: The elimination of symptoms and the evidence of bony healing.
2. Secondary goal: Increased root wall thickness and/or increased root length (desirable, but perhaps not essential)
3. Tertiary goal: Positive response to vitality testing (which if achieved, could indicate a more organized vital pulp tissue).

- Root canal system disinfection is an integral step in the success of REPs (2). Antimicrobial approaches to disinfect root canals have been proposed that include Photo-activated disinfection (PAD) as it offers a means of destroying bacteria remaining after using conventional irrigants in endodontic therapy (4).

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Competing Interests: No competing interests were disclosed.

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