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CASE SERIES

Management of teeth with open apex and apical periodontitis using MTA and OrthoMTA

ABSTRACT

Aim: *To describe successful managements of teeth with open apex using ProRoot MTA and OrthoMTA.*
Summary: *Teeth with open apex and apical periodontitis present multiple challenges specially in disinfecting the root canal space and providing an artificial apical barrier to achieve an optimal filling of the root canal. In the past decade, Mineral Trioxide Aggregate (MTA) has steadily gain popularity among clinicians to be used as a biocompatible apical stop for apexification of teeth with open apex. With strict adherent to the standard root canal protocol, teeth treated with ProRoot MTA and Ortho MTA in this case series showed satisfactory apical healing radiographically and improvement of signs and symptoms. Studies featuring OrthoMTA in the last ten years showing satisfactory clinical successes in various clinical scenarios such as pulpotomy in primary molars, partial pulpotomy in permanent teeth and apexification in immature apex of permanent teeth have also been listed.*
Key Learning Points
- *Clinicians need to be extra cautious with the aggressive use of endodontic files and have thorough knowledge of standard root canal protocols in establishing the correct working length, advancements in the disinfection procedures, materials, and techniques to be used to create an apical barrier.*
- *The obturation of the root canal space shall focus on the prevention of the extrusion of the root filling material into the periapical tissues and reinforcement of the weakened root against fracture during and after an apical stop is provided.*

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Introduction

The open apex in permanent teeth is mainly resulted when the pulp undergoes necrosis before the competition of root development, often caused by trauma (1), carious exposure (2, 3) and presence of an existing dental anomaly such as dens evaginatus and dens invaginatus that renders the developing tooth susceptible to the pulpal necrosis (4, 5).
Endodontic treatment of a permanent tooth with an open apex poses a different set of challenges compared to the tooth with a mature root apex. Incomplete root and thin dentinal walls make the tooth more susceptible to fracture (6) and compromised crown to root ratio may cause increased mobility (7). An absence of an apical stop can lead to extrusion of irrigating solution and/or sealer into periradicular tissues leading to a negative effect on the apical healing process (8). A wide root apex may also create difficultly in achieving the apical seal during the conventional root canal filling, resulting in apical leakage. To overcome these problems, a hard tissue barrier that allows the optimal filling of the root canal and the strengthening of the weakened root walls against secondary fracture must be formed.
Apexification has traditionally been the treatment of choice to manage teeth with necrotic pulps and open apices. Apexification is a process in which a non-vital, immature, permanent tooth that has lost the capacity for further root development, root end closure is induced to form a calcified root barrier at the root terminus (9).
Calcium hydroxide as an intracanal medicament has been historically used to induce the formation of a hard tissue barrier at the root apex with great success (10-14). The mechanism of action of calcium hydroxide on apical tissue is not clearly understood however, its antimicrobial activity, high pH or its direct effect on the apical and periapical soft tissues have been discussed in the literature (15). The effect of optimal timing and frequency to change the calcium hydroxide dressing on the rate and quality of apical barrier formation is debatable that may vary from changing it every month, every 3 month, every 6-8 months or not at all (16-20).
However, despite its many advantages, there are several limitations relating to the use of calcium hydroxide for apexification such as long time required for hard tissue barrier formation (21), possibility of root canal contamination during the apexification process (10, 13), multiple and repeated "dressings" required to achieve the root apex closure (16, 17, 19, 20), reduced fracture resistance of teeth after the long-term application of calcium hydroxide (22-24),and patient's compliance (25).
Mineral trioxide aggregate (MTA) has steadily gained popularity amongst clinicians in the past three decades as it offers multiple benefits compared to calcium hydroxide in the apexification procedure. The principal components of MTA include tricalcium silicate, tricalcium aluminate, tricalcium oxide and silicate oxide. MTA has been successfully used as root-end filling during apical surgery (26) and repair of root perforations (27, 28). Use of MTA in vital pulp therapy even for the primary dentition has been supported by a systemic review done by Sanz et al. (2020), that shows that hydraulic calcium silicate cements (HCSC) which includes ProRoot MTA when cultured with human exfoliated deciduous teeth (SHEDs) shows cytocompatibility and bioactivity (29). Apexification done with MTA can be completed in one to two visits, saving time, relying less on patient compliance, and greatly reducing the risk of fracture and reinfection of the tooth. MTA is mixed and packed into the apical 3-4mm of the tooth. It reaches a high pH of 10.2 to 12.5 in three hours, possibly inducing hard tissue formation of the apical tissue, similar to that of calcium hy-

droxide (30). ProRoot MTA (Dentsply Tulsa Dental, Tulsa, OK, USA) was launched in the United States in 1999, and was the first commercial product made available. With its wide array of usage and benefits, ProRoot MTA also has some limitations: high material cost, long setting time (which requires additional visits), difficult handling characteristics and tooth discoloration (31-33). As the demand increases and companies attempt to improve and upgrade this Portland cement, many brands of MTA were created. Few of the many are Biodentine (Septodont, Saint-Maur-des-Fosses, France), and OrthoMTA (BioMTA, Seoul, Korea).

Biodentine is a calcium silicate-based material used for crown and root dentin repair treatment, repair of perforations or resorptions, apexification and root-end fillings. The material can also be used in class II fillings as a temporary enamel substitute and as permanent dentine substitute in large carious lesions. Its manufacturer claims that Biodentine has a faster setting time compared to ProRoot MTA, due to calcium chloride as a setting accelerator in the liquid component (34).

Having the same indications as MTA, Bio-C is a ready-to-use bioactive reparative putty. Besides having a setting time of less than 120 minutes, its bioceramic formulation and high alkalinity induces tissue regeneration, setting expansion, chemical adhesion to dentine and inhibits bacterial infiltration. An in vitro study by Rodríguez-Lozano et al. (2020) (35) showed the cytocompatibility and high bioactive potential of Bio-C Repair and TotalFill BC RRM putty that can promote the osteo- and cementogenic differentiation of human periodontal ligament stem cells. Similarly, Ghilotti et al. (2020) (36) showed adequate attachment of hDPCS to the vital pulp materials, indicating excellent biocompatibility of Bio-C Repair similar to BioDentine and ProRoot MTA.

Recently, a newly developed MTA, OrthoMTA claims to be as biocompatible as ProRoot MTA, but without hexavalent chromium, a carcinogenic heavy metal. In addition, due to its bioactive characteristic: releasing calcium ions through the apical foramen, OrthoMTA neutralizes the apical tissue. This results in the formation of an interfacing layer of hydroxyapatite (Hap) between the OrthoMTA and the canal wall. Hap prevents microleakage and induces regeneration of the apical periodontium (BioMTA http://www.biomta.com/shop/eng/product_1.php?).

However, in apexification the long-term survival of the teeth is questionable due to its thin and prone-to-fracture dentinal walls (23). Regenerative endodontics procedure (REP) presents a viable treatment alternative for these teeth. By utilizing the key elements of tissue engineering: growth factors, stem cells and scaffold, REP allows healing of the teeth by complete restoration of pulpal function and subsequent completion of root development (38). REP presents a promising future in the world of endodontics based on largely reported successful clinical cases and studies (39-43). However, the generally recognized current protocol of REP suggested by American Association of Endodontics (44) too presents with its own sets of limitation, such as inability to invoke bleeding, sub-optimal barrier placement (e.g. MTA), and coronal staining (45). Therefore, careful case selection is imperative in determining case success, and further research is warranted to explore alternative methods and materials to further improve clinical outcomes.

Therefore, this case series describes the successful management of teeth with open apex using MTA and OrthoMTA and lists various studies done on the properties of OrthoMTA.

Report

#Case1

A healthy 57-year-old patient was re-

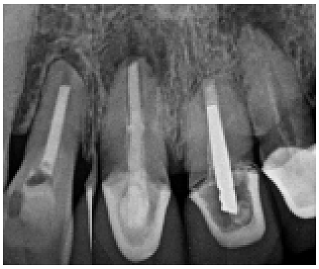

Figure 1
Preoperative radiograph showing teeth 12,1 1, 21 and 22 with previous endodontic treatments and radiolucent periapical lesions adjacent to the wide apices of teeth.

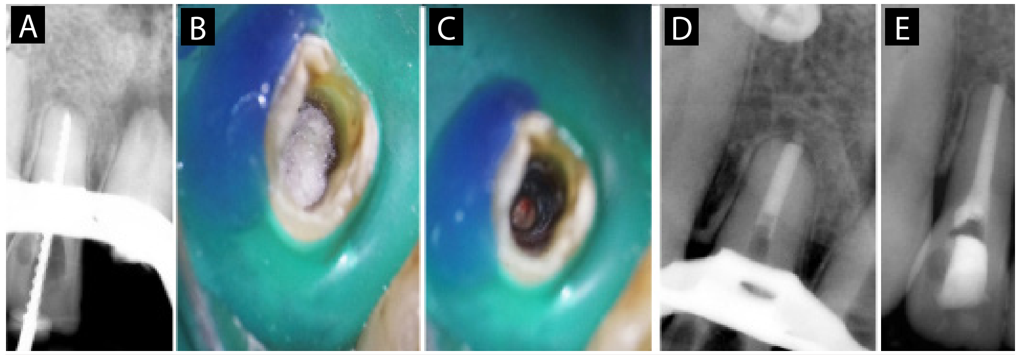

Figure 2
A) radiological working length determination, **B)** collagen sponge placement, **C)** apex view after the placement of the collagen sponge beyond the apex to create a barrier (tooth 11), **D)** 4 mm MTA cement placement control, (E) The rest of the canal was filled with injectable thermoplasticized gutta-percha (tooth 12).

ferred to the dental clinic for the treatment of the upper incisors. The patient had a history of orthodontic treatment and orthognathic surgery for maxilla in the year 1991. The teeth 12,11, 21 and 22 had previous endodontic treatments performed 15 years back and tooth 21 had a history of Endodontic surgery in 2008. Percussion and palpation tests were negative for teeth 12, 11, 21 and 22, with physiologic mobility.

Radiographic examination showed radiolucent periapical lesions adjacent to the wide apices of teeth 12, 11, and 22 (Figure 1). A common diagnosis of asymptomatic apical periodontitis was made for the latter teeth. After explaining all treatment options (retreatment and apexification with MTA, Endodontics surgery), risks and benefits, an informed consent was obtained from the patient and the decision was to attempt a non-surgical endodontic treatment with MTA apexification on teeth 12, 11 and 22.

First Appointment

The root canal system of the three teeth was accessed after local anesthetic injection with 4% articaine hydrochloride with epinephrine 1:200,000 (Septanest, Septodont, France) under rubber dam isolation. Each root canal was desobturated using D2 files (Dentsply Maillefer, Ballaigues, Switzerland) in the coronal/middle third of the canal then gently irrigated with 5 mL of 3% sodium hypochlorite (NaOCl) (Coltene/Whaledent, GnbH, USA). The rest of the canal was desobturated using manual K-files Dentsply Maillefer, Ballaigues, Switzerland) then the working length was established with both electronic apex locator (Root ZX (J. Morita, Tokyo, Japan) and reconfirmed using the intraoral periapical radiograph (Figure 2A).

10 mL of NaOCl was delivered using EndoVac system and activated with EndoActivator (Dentsply Tulsa Dental, Tulsa, OK, USA) for 1 min. Calcium hydroxide paste (mixture of $Ca(OH)_2$ powder (Merck, Darmstadt, Germany) with sterile water) was placed in the canal and gently packed with paper points. The access cavity was sealed with Cavit (3M Espe, St. Paul, MN, USA).

Second Appointment

After two weeks, the patient came for treatment completion. Teeth were similarly anesthetized and isolated with a rubber dam. Calcium hydroxide paste was removed with copious irrigation with 5 mL of NaOCl using Endovac system. Apical gauging was done using K-files (Dentsply Maillefer, Ballaigues, Switzerland)

Tooth 22 had an apex of 90/100, tooth 11 an apex superior to 140/100, and

tooth 12 an apex of 120/100. The final irrigation protocol was performed by a continuous delivery of solutions as follows: 5 mL of 17% ethylenediamine-tetraacetic acid (EDTA) (produits dentaires, Switzerland), 5mL of 3% NaOCl (Coltene/Whaledent, GnbH, USA) followed by a 5mL of distilled water followed by an activation with endoactivator (Dentsply Tulsa Dental, Tulsa, OK, USA) for 1 min for each solution.
Canals were dried and collagen sponge (Etik Collagene Aceton, Merignac, France) was placed beyond the apex and compressed with a #70 K-file (Figure 2B and 2C). This procedure was performed under microscope (CJ-Optik GmbH & Co. KG, Aßlar, Germany) to control the sponge placement. Immediately after, the mineral trioxide aggregate (MTA) cement was inserted into the apical third of the canal. The teeth were filled with 4 mm of white ProRoot MTA® (Dentsply International) mixed with sterile water in a 0.26 WP ratio using MTA gun system (Dentsply Maillefer, Ballaigues, Switzerland) (Figure 2D). After the placement of the first millimetre, an X-ray control was taken to control the placement of the MTA cement. The MTA plug placement was also performed under microscope. A wet paper point was placed inside each canal then the teeth were closed with Cavit (3M Espe, St. Paul, MN, USA) and temporary crowns.

Third Appointment

The patient was recalled 48 hours after the appointment to finish the treatment. Rubber dam isolation was placed, and the paper points were removed from the canals. The MTA setting was assessed using the hand plugger. Following, the rest of the canal was filled using injectable thermoplasticized gutta-percha (Kerr Sybron Endo, Orange, CA, USA) (Figure 2E). Access cavity was sealed with Cavit and temporary crowns were placed. Patient was referred to her general dentist to complete the prosthetic treatment.

Follow Up

One-month post-operative radiograph showed well obturated root canals of teeth 12, 11, 21 and 22 with reduction in the size of periapical radiolucency (Figure 3B). In the18 month follow-up, the teeth were asymptomatic. Clinical examination showed physiological mobility and absence of sensitivity to percussion and palpation. The follow-up radiographs revealed a satisfactory periapical healing (Figure 3C).

#Case2

A 38-year-old male reported to the clinic with a concern of pain on biting in his lower left back tooth for past few days. Clinical examination showed a temporary restoration on tooth 35

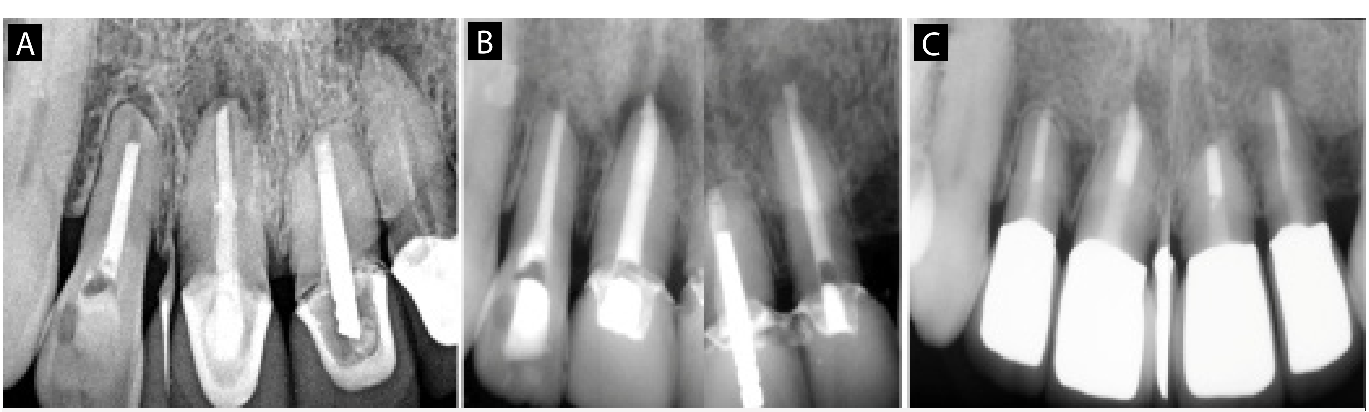

Figure 3
A) Pre-operative radiographs of maxillary incisors, **B)** post-operative radiographs, **C)** eighteen months follow-up radiographs showing a satisfactory periapical healing of teeth 12, 11, 21 and 22.

Figure4
A) In intraoral periapical radiograph showing tooth 35 with large peri-apical lesion with an open apex. **B)** Completion on tooth 35 root canal filling using OrthoMTA. **C)** Three months follow up radiograph showing tooth 35 with complete resolution of the periapical lesion. **D)** Thirty months follow up radiograph tooth 35 showing satisfactory healing.

sis with symptomatic apical periodontitis was made and root canal therapy with the management of open apex using OrthoMTA was advised.

First Appointment

After obtaining the written consent, the treatment was carried out. The area was anesthetised using 2% lignocaine with epinephrine 1:200,000 (inibsa, Barcelona, Spain) and tooth was isolated using the rubber dam. Old temporary restoration was removed, and an access cavity was modified using endo access burs (Dentsply Maillefer, Ballagues, Switzerland)), pulp chamber roof was completely removed. The working length was confirmed using the intra-irrigating solution. Thereafter, obturation of the entire root canal with OrthoMTA was planned. In this appointment, non-setting calcium hydroxide (Voco GmbH, Germany), an intracanal medicament was placed into the root canal and the cavity was temporarily restored with Cavit (3M Espe, St. Paul, MN, USA).

Second Appointment

The patient was recalled after one-week, old temporary dressing was removed, canal was irrigated with 5 ml of 3% NaOCl (Coltene/Whaledent, GnbH, USA), saline and 17% ethylenediaminetetraacetic acid (EDTA) (PULPDENT, Watertown, MA, USA) each for 1 minute ensuring no extrusion of any irrigating solution. The mastercone radiograph was taken to reconfirm the extension of root canal filling material. OrthoMTA (BioMTA, Seoul, Republic of Korea, Figure 5) was mixed according to the manufacturer's instruction and placed in the canal using the MTA gun. The compactor with the established working length was used to place OrthoMTA (BioMTA, Seoul, Republic of Korea) upto the working length of the root canal following the manufacturer's instruction. The hand plugger was used to compact OrthoMTA (BioMTA, Seoul, Republic of Korea) in the canal with the controlled working length. The excess OrthoMTA (BioMTA, Seoul, Republic of Korea) was removed from the canal orifice area and a damped cotton pel-

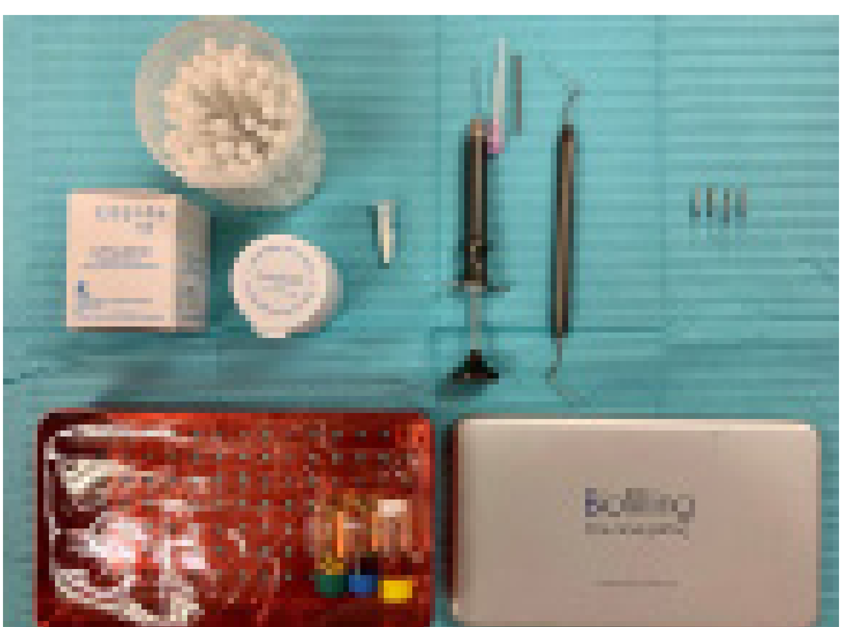

Figure 5
Biomaterial intracanal grafting kit including OrthoMTA, gun, compactors and plugger.

let was placed covering the OrthoMTA (BioMTA, Seoul, Republic of Korea) in the pulp chamber area (Figure 4B). A temporary restoration using Cavit Cavit (3M Espe, St. Paul, MN, USA) was placed to close the access cavity and recalled after a day for further treatment.

Third Appointment

The patient was recalled 24 hours after the second appointment, old temporary dressing was removed, canal was irrigated with 5 ml of 3% NaOCl (Coltene/Whaledent, GnbH, USA), saline and 17% ethylenediaminetetraacetic acid (EDTA) (Pulpdent, Watertown, MA, USA) each for 1 minute ensuring no extrusion of any irrigating solution. old temporary restoration was removed, and the hardness of OrthoMTA (BioMTA, Seoul, Republic of Korea) was assessed. The root canal filling was solidified and thereafter, the access cavity was restored suing composite resin (3M ESPE, St.Paul, MN, USA). the patient was recalled for periodic follow ups.

Follow up visit

The patient was recalled for follow up after one month to assess the clinical signs and symptoms such as absence of tenderness to percussion or palpation, swelling, locally deep periodontal probing defect, tooth mobility and condition of coronal seal. An intraoral radiograph was taken to assess the reduction/absence of periapical lesion. The clinical and radiographic findings of the follow up visit suggested satisfactory healing process (Figure 4C). The follow up was done at regular interval up to 30 months to ensure the positive outcome of the treatment (Figure 4D).

#Case3

A 20-year-old male reported to the clinic with a concern of caries and mild pain on biting in his upper front teeth. Clinical examination showed a restoration on tooth 11 and deep caries on tooth 12. The tooth 11 was tender on percussion with no mobility. Periodontal examination showed healthy gingival tissue around the tooth. Radiographic examination showed tooth 11 with open apex and large peri-radicular radiolucency and coronal radiolucency on tooth 12 suggesting dentinal caries (Figure 6A). After considering the clinical and radiographical findings the diagnosis of pulpal necrosis with symptomatic apical periodontitis was made and root canal therapy with the management of open apex using OrthoMTA was advised for tooth 11 and composite resin restoration for tooth 12.

First Appointment

After obtaining the written consent, the treatment was carried out. The area was anesthetised using 2% lignocaine with epinephrine 1:200,000 (inibsa, Barcelona, Spain) and an access cavity was prepared under rubber dam isolation. The working length

Figure 6
A) Preoperative intra-oral radiogrpah showing open apex on tooth 11 with large peri-apical radiolucency and coronal radiolucency on tooth 12. **B)** Establishing the working length. **C)** Obturation done using OrthoMTA. **D)** Three months follow up showing satisfactory periapical healing and closure of root apex, **(E)** Thirty months follow up radiograph tooth 12 showing complete resolution of peri-apical lesion.

was established using the intraoral periapical radiograph (Figure 6B) and the size of the apical end of the canal was gauged to size 140. The canal was circumferentially filed using Hand K files (Dentsply Maillefer, Ballagues, Switzerland), disinfected with 5 ml of 3% NaOCl (Coltene/Whaledent, GnbH, USA) and saline each for 1 minute ensuring no extrusion of any irrigating solution. Thereafter, obturation of the entire root canal with OrthoMTA was planned. In this appointment, non-setting calcium hydroxide (Voco GmbH, Germany), an intracanal medicament was placed into the root canal and the cavity was temporarily restored with Intermediate Restorative Material (IRM, Dentsply Sirona, Konstanz, Germany).

Second Appointment

The patient was recalled after one-week, old temporary dressing was removed, canal was irrigated with 5 ml of 3% NaOCl (Coltene/Whaledent, GnbH, USA), saline and 17% EDTA (Pulpdent, Watertown, MA, USA) each for 1 minute ensuring no extrusion of any irrigating solution. The mastercone radiograph was taken to reconfirm the extension of root canal filling material. OrthoMTA (BioMTA, Seoul, Republic of Korea) was mixed according to the manufacturer's instruction and placed in the canal using the MTA gun as described in case 1 (Figure 6C) and the patient was recalled after a day for further treatment.

Third Appointment

The patient was recalled after 24 hours, old temporary restoration was removed, and the hardness of OrthoMTA (BioMTA, Seoul, Republic of Korea) was assessed. The root canal filling was solidified and thereafter, the access cavity was restored suing composite resin (3M ESPE, St.Paul, MN, USA). the patient was recalled for periodic follow ups to assess the clinical signs and symptoms such as absence of tenderness to percussion or palpation, swelling, locally deep periodontal probing defect, tooth mobility and condition of coronal seal. An intraoral radiograph was taken to assess the reduction/absence of periapical lesion. The clinical and radiographic findings of the follow up visit suggested satisfactory healing process (Figure 6D). A thirty month follow up radiogrpah showed complete healing of the periapical lesion (Figure 6E).

Discussion

Appropriate management of open apex largely depends on the vitality of the tooth. Through detailed history taking, pulp sensibility tests, supported by radiographical evidence, an accurate diagnosis can be obtained. For teeth with viable pulpal status, vital pulp therapy is the primary treatment option (46). This will allow continued physiological development and formation of the root. For irreversibly inflamed or necrotic pulp, current evidence shows two treatment options such as root-end closure by apexification or pulpal regeneration (46). To achieve root-end closure, large interest has been expressed in the use of mineral trioxide aggregate and MTA like materials such as OrthoMTA.

The literature has shown satisfactory clinical successes of OrthoMTA in various clinical scenarios such as pulpotomy in primary molars, partial pulpotomy in permanent teeth and apexification in immature apex of permanent teeth (Table 1). Despite it being newly developed, OrthoMTA is very much comparable to ProRoot MTA in terms of biocompatibility, mineralization -inducing potential, fracture resistance, and marginal adaptation. In an in vitro research by Kum et al. (2013) (47) using RNA isolation and revers transcription-polymerase chain reaction, osteopontin levels were increased in incubated cells in both ProRoot MTA and Ortho MTA groups. However, Kim et al. (2014) (89) reported increased cytotocixity with OrthoMTA compared to ProRoot MTA and Endocem MTA. This finding was supported

Table 1
Studies showing various parameters and outcomes using OrthoMTA in last ten years

First author	Year	Country	Objective	Sample type	Sample size	Experimental groups	Outcome
Song et al. (50)	2011	Korea	To evaluate the influence of root canal filling material composed of MTA on tubular penetration	Human teeth	50	1. Angelus Fillapex MTA sealer 2. Gutta-percha 3. Portland cement 4. OrthoMTA 5. ProRoot MTA	OrthoMTA group showed deepest penetration of particles in the dentinal tubule with no significant difference with other groups (p>0.05)
Chang et al. (51)	2011	Korea	To investigate and compare the levels of arsenic(As), chromium (Cr), hexavalent chromium (Cr6+), and lead (Pb) in Ortho MTA and ProRoot MTA	-	-	1. OrthoMTA 2. ProRoot MTA	OrthoMTA and ProRoot MTA meet the ISO specification 9917-1 regarding the safety limits of As and Pb and are safe biomaterials when the purity of As, Cr6+, and Pb is considered
Lee et al. (101)	2012	Korea	To compare the cyto-toxicity of four root-end filling materials	MG-63 cells derived from a human osteosarcoma	-	1. Fuji II GIC (Glass Ionomer Cement) 2. IRM (Intermediate Restorative Material) 3. OrthoMTA 4. ProRoot MTA	ProRoot MTA and GIC showed good biocompatibility. However, OrthoMTA showed lower biocompatibility compared with ProRoot MTA and GIC
Kum et al. (52)	2013	Korea	To investigate the levels of cadmium (Cd), copper (Cu), iron (Fe),manganese (Mn), nickel (Ni) and zinc (Zn) in Ortho MTA and ProRoot MTA.	-	-	1. Ortho MTA 2. ProRoot MTA	Ortho MTA had lower levels of Cd, Cu,Fe, Mn and Ni than ProRoot MTA
Kum et al. (47)	2013	Korea	To compare the elemental constitution, morphological characteristics, particle size distribution, biocompatibility, and mineralization potential of Ortho MTA and ProRoot MTA	-	-	1. Ortho MTA 2. ProRoot MTA	The morphology of OrthoMTA powders was similar to that of ProRoot MTA. The constituent elements of both MTAs were calcium, silicon, and aluminum. The mean particle sizes of OrthoMTA and ProRoot MTA were 4.60 and 3.34 mm, respectively. Both MTAs had equally favorable in vitro biocompatibility
Chang et al. (48)	2014	Korea	To evaluate the biocompatibility, inflammatory response, and odontoblastic potential of Biodentine, Ortho-MTA, Angelus-MTA, and IRM on human dental pulp cell (HDPCs)	-	-	1. Biodentine 2. Ortho-MTA 3. Angelus-MTA 4. IRM	The biocompatibility, inflammatory response, and odontoblastic differentiation of OrthoMTA were similar to Bio-dentine
Ghorbanzadeh et al. (103)	2014	Iran	To compare the marginal adaptation of MTA and MTA-like materials as root-end fillings after incubation in phosphate buffer saline (PBS), a synthetic tissue fluid, for either 1 week or 2 months	Human single-rooted teeth	72	1. ProRoot MTA 2. Ortho- MTA 3. Retro MTA	There was no difference between the marginal adaptation of ProRoot MTA, OrthoMTA, and RetroMTA as root-end filling materials
Kang et al. (100)	2015	Korea	To determine the clinical efficacy of the newly developed OrthoMTA and RetroMTA, compared to Pro-Root MTA for pulpotomy in primary teeth	Human primary teeth	143	1. OrthoMTA 2. RetroMTA 3. ProRoot MTA	The success rates of RetroMTA, OrthoMTA and ProRoot MTA were almost similar, indicating that pulpotomy with these material can be carried out success-fully in primary molars
Kim et al. (89)	2014	Korea	To compare the biological properties of OrthoMTA and Endocem MTA with those of ProRoot MTA	Preosteoblast like cell line MC3T3-E1	-	1. OrthoMTA 2. Endocem MTA 3. ProRoot MTA	Pro-Root MTA appeared to be superior to OrthoMTA and Endocem MTA in terms of biological properties although Endocem MTA exhibited the shortest setting time and presented lower cytotoxicity.
Soram et al. (104)	2016	Korea	To evaluate the effects of three acids on the microhardness of set OrthoMTA and root dentin, and cytotoxicity on murine macrophage	Human teeth	40	1. 10% citric acid (CA) 2. 5% glycolic acid (GA) 3. 17% ethylenediaminetetra-acetic acid (EDTA) 4. Saline	Tested acidic solutions reduced microhardness of root dentin. Five minutes application of 10% CA and 5% GA significantly reduced the microhardness of set OrthoMTA (p<0.05) with lower cellular cytotoxicity compared to 17% EDTA
Kang et al. (105)	2017	Korea	To evaluate and compare the clinical applicability of various MTA materials as partial pulpotomy materials in permanent teeth	Human teeth	104	1. ProRoot MTA 2. Ortho-MTA 3. RetroMTA	ProRoot MTA, OrthoMTA and RetroMTA had favorable clinical and radiographic results after one year.

Table 1
Studies showing various parameters and outcomes using OrthoMTA in last ten years

Rahoma et al. (106)	2018	Saudi Arabia	To measure the push-out bond strength of three types of mineral trioxide aggregate (MTA) materials in root dentin	Human maxillary central incisors	30	1. OrthoMTA 2. MTA Angelus 3. ProRoot MTA	OrthoMTA, MTA Angelus, and ProRoot MTA materials showed similar push-out bond strength values in root dentin
Mousavi et al. (107)	2018	Iran	To evaluate the sealing ability of ProRoot MTA, Biodentine, and OrthoMTA as the root canal obturation materials using the fluid infiltration method	Human mandibular premolars	66	1. Negative group 2. Positive group (gutta- percha) 3. ProRoot MTA 4. Biodentine 5. OrthoMTA	OrthoMTA, ProRoot MTA and Biodentine showed similar sealing ability
Khedmat et al. (111)	2018	Iran	To assess the antibacterial activities of OrthoMTA, RetroMTA, and ProRoot MTA	Fusobacterium nucleatum (Fn), Porphyromonas gingivalis (Pg), and Prevotella intermedia (Pi)	-	1. Ortho-MTA 2. RetroMTA 3. ProRoot	OrthoMTA had the highest antibacterial activity against Pi. The mean number of CFU/ml of Fn in the presence of ProRoot MTA and RetroMTA was significantly lower than that in positive controls ($p<0.05$). ProRoot MTA and OrthoMTA both had equal significant antibacterial effect against Pg compared to positive controls
Aslan et al. (108)	2018	Turkey	To evaluate the forces required to fracture roots obturated with different calcium silicate based materials, after applying a fractured instrument removal simulation	Human mandibular premolars	75	1. ProRoot MTA 2. Ortho- MTA 3. Biodentine 4. Endocem MTA	Any of the tested materials could be chosen to reinforce the root after the removal of a fractured instrument
Kang et al. (109)	2018	Korea	To compare the inflammatory response and mineralization-inducing potential of three calcium silicate cements	Dog's teeth	44	1. ProRoot MTA 2. OrthoMTA 3. Endocem MTA	ProRoot MTA and OrthoMTA resulted in reduced pulpal inflammation and more complete calcific barrier formation, whereas Endocem MTA caused a lower level of calcific barrier continuity with tunnel defects
Kim et al. (102)	2019	Korea	To evaluate the initial cytotoxicity of four different commercially available MTA materials	Bone-marrowderived human mesenchymal stem cells (hMSCs)	-	1. Endocem MTA 2. Ortho MTA 3. ProRoot MTA 4. MTA Angelus	100% extracts from completely set MTAs showed similar cell viability with the control group without cytotoxicity. However, all four MTA products tested during setting showed severe cytotoxicity at original and 50% extracts
Ballal et al. (53)	2020	Switzerland	To evaluate the influence of ProRoot MTA and OrthoMTA as an obturating material on the fracture resistance of endodontically treated teeth	Human maxillary central incisors	30	1. Ortho- MTA 2. ProRoot MTA 3. Positive control	OrthoMTA showed the highest fracture resistance and showed better tubular biomineralization when compared to ProRoot MTA
Bolbolian et al. (110)	2020	Iraq	To compare microleakage of resin modified glass ionomer and OrthoMTA used as an intra-orifice barrier in non-vital bleaching	Human mandibular premolars	36	1. OrthoMTA 2. RMGIC (Resin Modifies Glass Ionomer Cement) 3. Positive group 4. Negative group	OrthoMTA had less leakage than RMGIC but both materials can be used as suitable barriers for internal tooth bleaching

by Lee et al. (2012) (101) study, stating ProRoot MTA has higher biocompatibility compared to OrthoMTA. Nonetheless, Kim et al. (102), Chang et al. (48), Kum et al. (47) and Kang et al. (109) reported that Ortho MTA is equally favorable in cell biocompatibility when compa-red to other calcium silicate cements (CSCs). In addition to biocompatibility and sealing ability, Khedmat et al. (37) demonstrated that OrthoMTA has antibacterial effects against bacteria involved in endodontic periodontal infections. Arising concerns regarding heavy metal content in MTA has led to few studies investigating the issue. The manufacturer of OrthoMTA claims that it has similar components as ProRoot MTA but less heavy metal contents than ProRoot MTA. Chang et al. (2011) (51) and Kum et al. (2013) (52) concluded that both OrthoMTA and ProRoot MTA meet the ISO specification 9917-1 regarding the safety limits of As and Pb, and the latter stating that OrthoMTA has lower levels of Cd, Cu, Fe, Mn and Ni than ProRoot MTA.

In case reports two and three use of OrthoMTA has shown positive outcomes

with successful healing of the periapical lesion. This could be because, in addition to the properties explained earlier, OrthoMTA or BioMTA as an orthograde root canal grafting material forms an interfacial hydroxyapatite layer between Ortho MTA and the root canal wall and prevents microleakage and entombs the remaining bacteria by intratubular mineralization.
Endodontically treated teeth are usually weak because of loss of tooth structure due to caries, access cavity preparation, and instrumentation of the root canal and with the right obturating material and techniques, fracture resistance of the tooth can be greatly enhanced. Ballal et al. (2020) (53) stated that among OrthoMTA, ProRoot MTA and the control group, Ortho-MTA demonstrated the highest fracture resistance and better tubular biomineralization.
Due to the presence of fracture-prone thin dentinal wall, disinfection of the root canal system relies solely on chemical disinfection using irrigants and intracanal medicament. Therefore, careful selection of irrigants/intracanal medicaments is imperative to ensure successful outcomes. Non-setting calcium hydroxide was placed as an inter-appointment intracanal medicament as it is showed to effectively disinfect the canal system against common endodontic pathogens (54). This highly alkaline medicament with a pH of around 12.5, releases hydroxyl ions in an aqueous environment potentially causes damage to the bacterial cytoplasmic membrane, protein denaturation, and damages DNA. Although the mechanism of action is not clearly understood, the antimicrobial action of calcium hydroxide has been documented in many studies (55-58). However, it remains controversial as some authors reported ineffectiveness of calcium hydroxide (49, 59, 60).
3% Sodium hypochlorite was used as an irrigating solution to disinfect the root canal and rinse off the intracanal medicament placed in the previous appointment. NaOCl used in various concentration (0.5-5.25%) has shown to be an excellent non-specific proteolytic and antimicrobial agent to disinfect the root canal system (61-63). A systemic review by Arruda et al. (2009) (64)showed that there is insufficient research done on the time of irrigation, concentration or volume of NaOCl solution that is optimal in endodontic treatment without causing significant changes in the mechanical properties of dentin. Moreover, extreme caution must be exercised when using this cytotoxic irrigant, especially in cases of open apex. Many reports describe clinical complications arising from accidents such as injection of NaOCl into periapical tissue, maxillary sinus, splashing into eyes, leakage of NaOCl through the rubber dam causing severe mucosa/cutaneous chemical burns (65-71). In addition, rare case reports of hypersensitivity and allergy towards NaOCl has also been reported (72-74). To prevent extrusion of NaOCl into periapical tissue, EndoVac system was utilized in this case report. This system applies suction to pull irrigant down the root canal, instead of excessive digital pressure applied through conventional irrigating syringe. Careful working length determination through an apex locator and reconfirming it with the introoral periapical radiograph is recommended in open apex cases. Standard operating procedure such as rubber dam isolation, straight line access, maintaining the working length 2 mm short of root end, loose placement of irrigating needles in the canal and constant in and out movements of irrigating needle must be strictly adhered to avoid potential tissue damage (75).
Smear layer which consists of dentine, pulp remnants, odontoblastic processes and bacteria is formed on canal walls after instrumentation. It is said to inhibit tubular penetration of sealant material during canal obturation (76). Many researchers support the usage of EDTA 17% as a chelating agent to remove this

inorganic layer which cannot be removed by NaOCl alone (76-79) .Using scanning electron microscope, Niu et al. (2012) (80) showed that final irrigation with 3% NaOCl following treatment with 17% EDTA produces clean and exposed dentinal tubule orifices, as compared to EDTA or NaOCl alone.

Although MTA has been the material of choice for apexification due to its biocompatibility, over extrusion of the material can impede periapical healing and prolong patient discomfort. A controlled condensation pressure of MTA that normally produces a uniform apical plug and good seal might cause the material to be pushed through the apex in an immature open apex tooth (81, 82). Acting as an apical barrier, a collagen sponge was pushed through the apex and compacted in place prior to the placement of MTA in case report 1. The extra radicular membrane improved the adaptation of the MTA in the open apex tooth, achieving a good seal. However, Zou et al. (2008) (83) reported no significant difference in either leakage or overfilling of MTA when internal matrix is used for the repair of furcation perforations. Therefore, it is a matter of the dentist's personal preference as there are few successful case reports showing favorable prognosis with the usage of a collagen sponge apical barrier (84-86). The use of magnification and illumination play an essential role in managing these kinds of cases to ensure the adequate placement of collagen sponge and MTA.

A waiting period of 24 hours was given after the placement of MTA in the canal as MTA has a long setting time (20, 31, 87-89). Manufacturer's instructions have stated that the ProRoot MTA and OrthoMTA sets in 4-6 hours and 3-5 hours respectively. However, Kim et al. (2014) reported that ProRoot MTA and OrthoMTA has a setting time of 318.0±56.0 and 324.3±2.1 minutes respectively in an in vitro study (89), significantly different from the said instructions. Therefore, to ensure that the MTA has completely solidified prior to obturation or coronal restoration, a two-visit endodontic visit was performed in all three case reports. A damp cotton pellet was placed on top of the newly placed MTA as it provides the moisture MTA needed for a proper set. This was demonstrated by an in vitro study by Craig D. Johnson (2010) (90) in which MTA with the placement of a moist cotton pellet showed significantly lesser penetration resistance for 6 hours and set significantly ($P<0.05$) slower than MTA without the moist pellet. However, the MTA without the moist pellet was significantly ($P<0.05$) softer than the MTA with the moist pellet at day 1 and 3.

In all three case reports treated with ProRoot MTA and OrthoMTA, the follow up was done up to thirty months to ensure the successful outcome of these treatment modalities. This time-period is an accordance to Travassos et al. (91) who recommended a period of two to five years to observe complete repair. By providing follow-ups, clinicians can deduce and solve the post-operative problem which can adversely affect a patient's quality of life in the long run (92).

Future Direction

Apexification with calcium hydroxide and MTA barrier technique fails to induce continued root maturation which makes the tooth susceptible to root fracture. Hence, an ideal outcome for such a tooth should be regeneration of pulp like tissue into the root canal capable of continuing normal root maturation. Regenerative endodontic therapy has been defined as "biologically based procedures designed to replace damaged structures, including dentin and root structures, as well as cells of the pulp-dentin complex'' (41).

A very specific environment must be created for revascularization of the pulp to take place. The absence of intracanal infection and presence of a scaffold (e.g., blood clot or platelet-rich plasma) conducive to tissue ingrowth, and a permanent coronal seal (e.g., MTA or resin-modified glass-ionomer) are very crucial in REP. Similar to conventional retrograde endodontic therapy , disinfection of the root canal system is paramount to the success of REP. Due to its thin weakened dentinal wall, disinfection relies less on mechanical instrumentation but rather relies heavily on the use of chemicals, consisting of irrigating solutions and intracanal antibiotic dressings. A combination of antibiotics, specifically ciprofloxacin, metronidazole and minocycline has been shown to properly kill common endodontic pathogens in the infected root canal (93). The blood clot can be created by instrumenting the tooth beyond apex to approximately 1-2 mm to permit bleeding into root canal system. Multiple theories for the mechanism of revascularization have been proposed and discussed.

Remaining vital pulp cells (94), stem cells from the dental pulp (95), periodontal ligament (96), or mesenchymal stem cell from the bones (97) could be the ones responsible for the differentiation into odontoblast. The newly formed odontoblast lay down atubular dentin at the apical end, causing elongation of root and thickening of the dentinal walls, reinforcing and strengthening the root. Not only that, platelet-derived growth factor, vascular endothelial growth factor (VEGF), platelet-derived epithelial growth factor, and tissue growth factor found in the blood clot, could play an important role in regeneration. These growth factors causes the fibroblasts, odontoblasts, cementoblasts etc from the immature, undifferentiated mesenchymal cells in the newly formed tissue matrix to be stimulated to differentiate, grow, and mature (98).

Tatullo et al. (2019) (99) showed cell proliferation, cells viability, and gene expression for osteogenic and odontogenic differentiation when Human periapical cyst mesenchymal stem cells (hPCy-MSCs) derived from inflammatory periapical cysts were seeded on mineral doped bioactive scaffold.

This study is one among the many research making new discoveries and advancement in the evolving world of regenerative dentistry.

Conclusions

This case series showed the successful management of teeth with open apex with periapical lesions using ProRootMTA and OrthoMTA. In all three cases, the tooth restored showed complete resolution of pain and satisfactory healing of periapical lesion radiographically. Clinicians need to have a thorough knowledge of standard root canal protocols to be followed in the managing open apex cases and understanding of ProRoot MTA and OrthoMTA materials to achieve clinical and radiographical success.

Clinical Relevance

Clinicians need to know how to handle teeth with open apex and apical periodontitis as it may present multiple challenges specially in disinfecting the root canal space and providing an artificial apical barrier using Mineral Trioxide Aggregate (MTA) and OrthoMTA.

Conflict of Interest

The authors declare that they have no conflict of interests.

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All authors conceived the original idea, designed, treated these cases, and wrote the manuscript.
All authors have read, reviewed, and approved the manuscript.

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