Original Article

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Clinical outcomes of calcium silicate-based cements with or without calcium chloride as an orthograde apical barrier: a randomised controlled clinical trial

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Objective: Calcium chloride has been used as an accelerator to reduce the setting time, dissolution, and leakage of calcium silicate-based cement materials. Its use has increased successful treatment outcomes. The aim of this study was to evaluate and compare the treatment outcomes of two calcium silicate-based cements with or without calcium chloride (Bio-MA or ProRoot® MTA) as orthograde apical barrier materials in teeth with open apices.

Materials and Methods: Sixty teeth in patients (8–67 years old) were recruited at the Endodontic Clinics of Dental Hospital, Faculty of Dentistry (Phayathai Campus) and Mahachakri Sirindhorn Dental Hospital (Salaya Campus), Mahidol University, Bangkok, Thailand. The teeth were randomly divided into two groups, i.e., Bio-MA or ProRoot® MTA material; the apical barrier was created using standard treatment protocols. Patients were recalled least 6 months after treatment. The treatment outcome was assessed as healed, healing, or disease, based on the clinical and radiographic evaluations. Healed and healing cases were grouped as success. The outcomes of the two materials were analysed and compared using the chi-square test and risk ratio for non-inferiority test.

Results: Fifty-five of 60 teeth, 28 in the Bio-MA group and 27 in the ProRoot® MTA group, were recalled, with a 94.9% recall rate and a median recall period of 17 months (range 6–38 months). Overall, healed and healing cases were 76.4% and 23.6%, respectively with no disease found. The Bio-MA group demonstrated 78.6% healed and 21.4% healing. Whereas, 74.1% healed and 25.9% healing were reported in the ProRoot® MTA group. There was no significant difference in the outcomes between Bio-MA and ProRoot® MTA used as an orthograde apical barrier ($p>0.05$). The non-inferiority analysis indicated that Bio-MA tended to be non-inferior, but the risk ratio was inconclusive.

Conclusion: Clinical outcomes of calcium silicate-based cements with or without calcium chloride in an orthograde apical barrier were highly successful with no significant difference between the materials.

Keywords: apexification, calcium chloride, calcium silicate-based cements, open apex, randomised controlled clinical trial

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Introduction

Teeth with open apices or loss of an apical stop can be found in immature or mature root development. When the dental pulp becomes necrotic before complete root formation, dentine formation and root development are interrupted, resulting in short and thin immature roots [1]. Depending on the stage of root development, the root canal walls may be divergent, parallel, or slightly convergent, and the root apex is relatively

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open and lacks apical constriction. In the teeth with mature roots, an open apex can be caused by pathological root resorption or iatrogenic root canal over-preparation [2].

Endodontic treatment is challenging in the presence of an open root apex due to the risk of extruding irrigation solution, medication, and especially root canal filling. The absence of natural apical constriction makes well-compacted root canal obturation impossible; gutta percha and root canal sealer tend to be pushed out beyond the apex. Apexification is a suitable technique for managing an open root apex by inducing a calcified apical barrier and/or stimulating apical root development [3]. Calcium hydroxide paste has been used as a long-term intracanal medication for apexification due to its effects of hard tissue induction, antibacterial effect, no adverse periapical reaction, and low cost [1]. In contrast, the disadvantages of calcium hydroxide apexification are long and multiple-visit treatment varying from 5–20 months for the induction of an apical calcified bridge [1, 4], unpredictable apical closure, and poor quality of the dentine barrier [1]. Additionally, long-term calcium hydroxide medication may weaken root dentine and increase the risk of root fracture [5, 6]. Due to these shortcomings, calcium silicate cement has been proposed to replace calcium hydroxide for apexification. Mineral trioxide aggregate (MTA), the first-generation calcium silicate-based cement (e.g. ProRoot® MTA, Dentsply, Tulsa, OK, USA), has been used in many endodontic treatment procedures due to its desired properties, including sealing ability, inducing hard tissue formation, biocompatibility, bioactivity, hydrophilic, antibacterial effect, and no cytotoxicity [7, 8]. Calcium silicate-based cement has been used to form an artificial apical barrier after root canal disinfection to reduce treatment visits, prevent extrusion of filling materials, and decrease the risk of root fracture [5].

Calcium hydroxide apexification had a 74–100% success rate [1], and MTA apexification demonstrated a success rate ranging from 77–100% [9]. However, there was no significant difference in the clinical success and apical hard tissue barrier formation between the materials [10, 11]. Currently, MTA orthograde apical barrier (apexification) is preferred due to its reduced treatment time, lower risk of root fracture, and predictable apical barrier formation. However, the shortcomings of MTA, e.g., a 3–4 hour setting time [12] and the relatively high cost, are a concern.

Bio-MA (M-Dent/SCG, Bangkok, Thailand) has been developed from Thai white Portland cement (TWPC). The main compositions are Portland cement and bismuth oxide radiopacifier as in white ProRoot® MTA (WMTA) [13], except for calcium chloride accelerator in Bio-MA, which accelerates the setting reaction [14, 15]. The chemo-physical properties, such as solubility, water sorption, dimensional change, compressive strength, and pH of Bio-MA and WMTA, were not significantly different [13], nor was their sealing ability to dye and bacterial leakage [16, 17]. Moreover, the biocompatibility of Bio-MA was comparable to that of WMTA [18, 19].

The results from *in vitro* and *in vivo* studies have confirmed the excellent properties of Bio-MA and WMTA [13, 14, 18-20]. An *in vitro* study [21] found that adding calcium chloride to WMTA reduced the setting time, solubility and maintained the high pH. It also provided better sealing ability and clinical outcomes. However, the preliminary phase of a randomised controlled clinical trial reported that the outcomes of Bio-MA and ProRoot® MTA as an apical barrier were not significantly different at the 12-month follow-up [22]. Due to the small sample size and short recall period in the preliminary phase [22], the objective of this randomised controlled clinical trial was to

compare the clinical outcomes of two calcium silicate-based cements with or without calcium chloride, Bio-MA and ProRoot® MTA, when used as orthograde apical barriers in open-apex teeth.

Materials and Methods

Case Selection

A non-inferiority, randomised controlled clinical trial was conducted to compare the outcomes of Bio-MA and ProRoot® MTA in orthograde apical barrier following the CONSORT [23] and PRIRATE [24] guidelines. The study protocol was approved by the Institutional Review Board, Faculty of Dentistry and Faculty of Pharmacy, Mahidol University (MU-DT/PY-IRB 2016/DT043). The subjects were recruited at the Endodontic Clinic of Dental Hospital, Faculty of Dentistry (Phayathai Campus) and Mahachakri Sirindhorn Dental Hospital (Salaya Campus) Mahidol University, Bangkok, Thailand. The patients were informed about the benefits, risks, and alternative treatment options before enrolment and signing the consent form. Based on Song *et al*. [25] in 2012, the success rate of ProRoot® MTA for root-end filling was 95%. The laboratory and animal studies of Bio-MA were comparable to that of ProRoot® MTA [13, 14, 18-20], therefore the similar clinical result of Bio-MA was expected. The sample size was calculated by the online statistical software (Sealed Envelope, London, UK) for non-inferiority trial. The non-inferiority limit was set at 15% with a statistical power at 0.8 and a significance level of 0.05. The calculated sample size was 27 teeth per material in each treatment category. To compensate for possible dropouts, the sample size was increased by 10%, thus the sample size was 30 teeth per material. Patients with healthy or well-controlled systemic disease were recruited based on the following criteria.

Inclusion Criteria

1. Immature or mature permanent teeth diagnosed as irreversible pulpitis or pulp necrosis and with or without periapical disease.
2. Immature teeth must have incomplete root formation at stages 4–6 of Moorrees' classification.
3. Mature teeth in which the apical constriction was lost and larger than a #80 file from over-instrumentation or apical root resorption.

Exclusion Criteria

The teeth with one of these conditions were excluded:

1. Unrestorable
2. Horizontal or vertical cracks or fractures
3. External or internal root resorption (except apical resorption)
4. Chronic periodontitis with marginal bone loss more than 5 mm.

General Information

The preoperative data comprising age, sex, medical history, tooth type, tooth location, number of roots, clinical and radiographic examinations, stage of root development in immature tooth, size of apical foramen, and size of preoperative radiolucency were recorded. The type of endodontic treatment, i.e., primary treatment or retreatment, was defined. The teeth were randomly assigned to a test material using Microsoft Excel 2013 (Microsoft Corp., Redmond, WA, USA). Each patient received one of the materials, ProRoot® MTA or Bio-MA, according to the random order table that was sequentially numbered, opaque, sealed envelopes (SNOSE). To ensure the patients' privacy and bias control, patient's identification was converted into code numbers. The test material types were blinded by a person who did not participate in the experiment.

Treatment Protocol

The treatment protocol was performed by endodontic department faculty and postgraduate students, using an operating dental microscope (Carl Zeiss, Jena, Germany) and rubber dam isolation. The working length was determined using an electronic apex locator (Root ZX, J-Morita, Tokyo, Japan) and radiographic confirmation (X-Mind DC, Aceteon, Via Roma, Olgiate Olona, VA, Italy). The root canals were cleaned and shaped with hand files and/or nickel-titanium rotary files, and irrigated with 17% ethylene diamine tetraacetic acid (EDTA) and 2.5% sodium hypochlorite (NaOCl). To increase disinfection efficiency, passive ultrasonic irrigation with an ultrasonic tip (Irrisafe, Acteon, Merignac, France) was performed. The root canal was medicated with calcium hydroxide powder mixed with distilled water or with ready-mixed calcium hydroxide (UltraCal™ XS, Ultradent, South Jordan, UT, USA) for at least one week. The access cavity was sealed with a temporary filling material (Caviton, GC Corporation, Tokyo, Japan; or IRM®, Dentsply, Caulk, Milford, DE, USA).

At the next visit, if the symptoms persisted, irrigation was performed and the root canal medication was replaced. If the symptoms had subsided, calcium hydroxide intracanal medication was removed using K-file and irrigation with 2.5% NaOCl and 17% EDTA. Bio-MA or ProRoot® MTA was mixed according to the manufacturer's instructions, carried into the root canal with an MTA carrier (MAP System, Dentsply Tulsa Dental, OK, USA), and condensed to the apical area to create an artificial apical barrier. The material was added and plugged with an endodontic plugger and paper points until the apical barrier with an adequate thickness of 4–5 mm was obtained. In cases with a large open apex and periapical bone destruction, a collagen sponge (CollaPlug®, Zimmer Biomet, FL, USA) was used as an apical matrix to prevent extrusion of the material into the periapical tissue. The quantity and the quality of the apical barrier material were evaluated by a periapical radiograph. After the apical barrier was created, a moist paper point was placed on the top of the material to facilitate the setting reaction. The access cavity was then filled with temporary filling material.

At the following visit, light pressure from an endodontic plugger was used to confirm that the material was set. The remaining root canal space was filled with gutta percha and resin-based (AH Plus®, Dentsply, Tulsa, OK, USA) or eugenol-based root canal sealer (MU sealer, M Dent, Bangkok, Thailand). Glass-ionomer cement (Vitrebond™, 3M ESPE, St. Paul, MN, USA; Fuji II LC, or Fuji VII, GC Corporation, Tokyo, Japan) was lined over the gutta percha, and the coronal access was restored with resin composite (Filtek™ Z350, 3M ESPE) and bonding agent (Adper™ Single Bond 2, 3M ESPE). If a complex restoration was needed, the patient was referred to a restorative specialist.

Follow-Up and Outcome Assessment

The outcomes were assessed with a recall period at least 6 months after complete root canal treatment comprising clinical signs and symptoms (pain, tenderness on percussion and palpation, mobility, pocket depth, and quality of restoration) and radiographic evaluations (normal periapical tissue, widening of the PDL space, or any periapical radiolucency).

One observer was calibrated prior to the radiographic assessment of periapical lesions by interpreting 20 periapical radiographs twice with a 2-week interval. The intra-observer reliability was statistically analysed by Cohen's kappa. Preoperative, immediate post-operative,

and recall radiographs were adjusted to obtain similar contrast and brightness with Adobe Photoshop software (Adobe Systems Inc., San Jose, CA, USA). Before interpreting and comparison, all the images had the difference in radiographic angles minimized using TurboReg plugin of ImageJ software (National Institutes of Health, Bethesda, MD, USA). The periapical lesion area was measured and compared by the ImageJ software. The outcome assessment was based on the clinical and radiographic findings.

The outcome assessment was defined following the criteria of Freidman *et al*. [26] that included "healed, healing, and disease". Healed was defined as both the clinical and radiographic presentations were normal. Healing was diagnosed when a normal clinical presentation combined with radiographic radiolucency reduction was observed. Disease was the outcome when a radiolucency had emerged or persisted without change, including when the clinical presentation was normal, or clinical signs or symptoms were present including when the radiographic presentation was normal.

The evaluated unit was the whole tooth. The outcome was considered as disease if another root of the multi-rooted tooth presented any symptoms or periapical lesion, including when the root treated with Bio-MA or ProRoot® MTA was normal. A tooth with a root fracture because of a thin root canal wall or incomplete root formation that was not associated with the tested materials was excluded from the study.

Statistical Analysis

The clinical outcomes of Bio-MA and ProRoot® MTA as orthograde apical barriers were analysed and compared by the chi-square test with a significance level of 0.05. Healed and healing cases were grouped and categorized as 'success', and cases with disease was categorized as 'failure' for the binary analysis of the outcome. The risk ratio between Bio-MA and ProRoot® MTA was calculated with 95% confidence interval and tested for the non-inferiority test. The Statistical Package for the Social Sciences (SPSS) version 18.0 (IBM Corp, Somers, City, NY, USA) was used for statistical analysis.

Results

Sixty teeth were initially included in this study. However, 5 teeth were excluded due to a crack (1 tooth), lost to follow-up (3 teeth), and being unrestorable (1 tooth). The remaining 55 teeth were divided as follows: 28 in the Bio-MA group and 27 in the ProRoot® MTA group (Figure 1). The recall rate was 94.9%, and the median follow-up period was 17 months, ranging from 6–38 months. Furthermore, 98.18% (54/55 teeth) were followed up at 12–38 months, and 1.82% (1/55 teeth) were followed up at 6–11 months. The study comprised 29 males and 26 females from 8–67 years old with the median age of 21 years old. Most of the teeth were immature upper anterior teeth with preoperative lesions, and their root development was in Moorrees' stages 4–6. The majority of the endodontic treatment was primary treatment. The preoperative data demonstrated a similar distribution of the collected factors between the two material groups (Table 1).

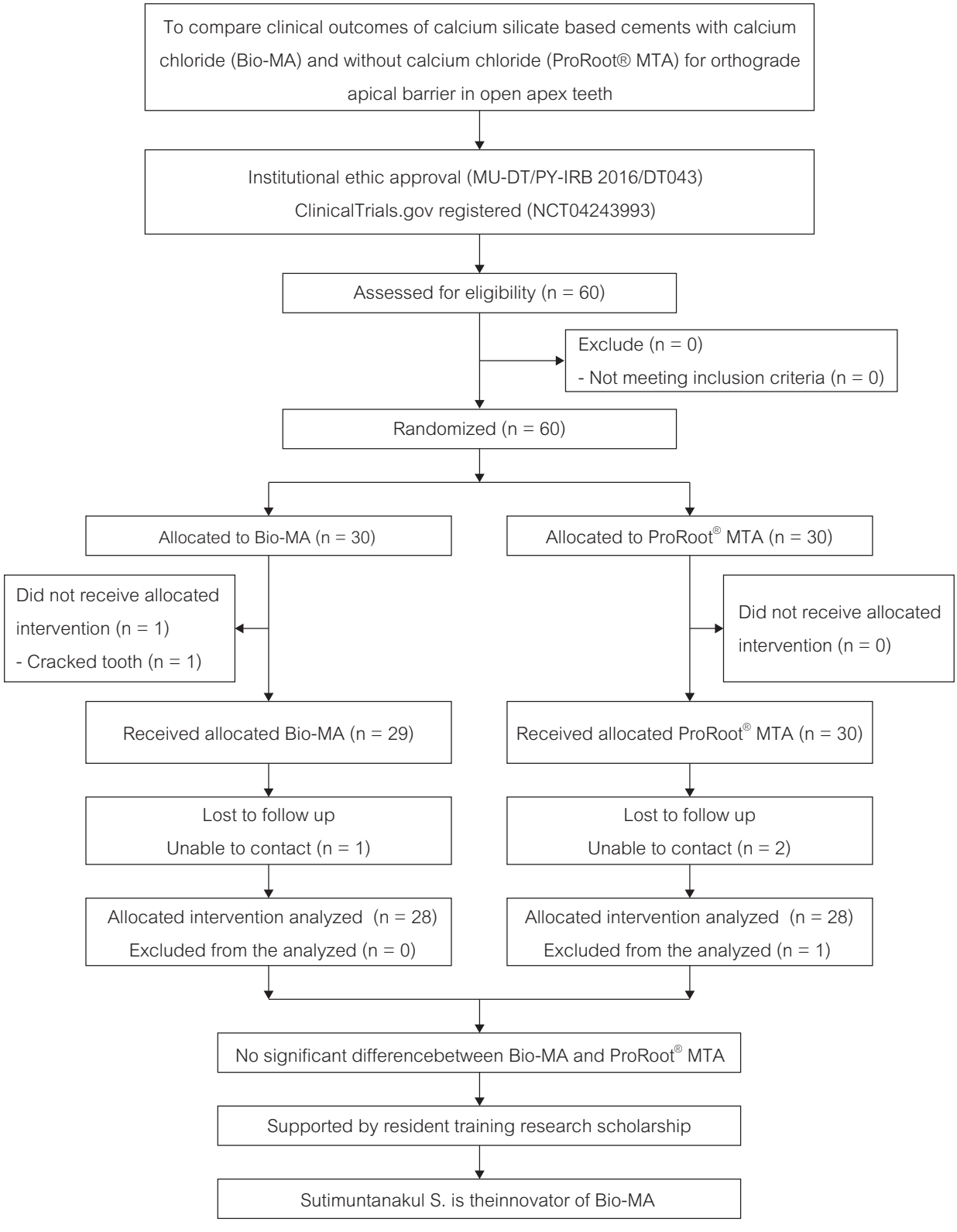

Figure 1 Flow diagram of the orthograde apical barrier with Bio-MA and ProRoot® MTA according to the CONSORT (2010) and PRIRATE (2020) guidelines

Table 1 The pre-operative data distribution of the teeth receiving an orthograde apical barrier with Bio-MA and ProRoot® MTA groups.

	Bio-MA n=28		ProRoot® MTA n=27		Total n=55		p value
	n	%	n	%	n	%	
Sex							0.227
Male	17	60.70	12	44.40	29	52.70	
Female	11	39.30	15	55.60	26	47.30	
Age							0.469
≤45	25	89.30	22	81.50	47	85.50	
>45	3	10.70	5	18.50	8	14.50	
Tooth type							0.808
Anterior	21	75.00	21	77.80	42	76.40	
Posterior	7	25.00	6	22.20	13	23.60	
Tooth location							0.686
Maxilla	23	82.10	21	77.80	44	80.00	
Mandible	5	17.90	6	22.20	11	20.00	
Pre-op periapical radiolucency							0.620
Absent	5	17.85	3	11.10	8	14.50	
≤5 mm	12	42.85	10	37.00	22	40.00	
>5 mm	11	39.30	14	51.90	25	45.50	
Stages of root development							0.469
4-6	25	89.30	22	81.50	47	85.50	
7	3	10.70	5	18.5	8	14.50	
Type of treatment							0.695
Primary treatment	22	78.60	20	74,1	42	76.40	
Retreatment	6	21.40	7	25.90	13	23.60	

Cohen's kappa of intra-observer reliability for radiographic calibration was 0.88, indicating almost perfect agreement [27]. The outcome of apexification in 55 teeth was 100% successful, including healed and healing teeth. No disease was found in either group. Overall, the healed and healing cases were 76.4% (42/55) and 23.6% (13/55), respectively. Healed and healing cases in the Bio-MA group were 78.6% (22/28) and 21.4% (6/28), while in the ProRoot® MTA group, healed and healing cases were 74.1% (20/27) and 25.9% (7/27), respectively (Table 2).

Table 2 Clinical outcomes of the orthograde apical barrier the Bio-MA and ProRoot® MTA groups.

Outcomes	Bio-MA n=28		ProRoot® MTA n=27		Total n=55	
	n	%	n	%	n	%
Healed	22	78.60	20	74.10	42	76.40
Healing	6	21.40	7	25.90	13	23.60
Disease	0	0.0	0	0.0	0	0.0

Representative cases are presented in Figures 2 and 3. There was no significant difference between the healed and healing rates in the two material groups ($p>0.05$). The clinical outcomes of the pre-operative factors of the orthograde apical barrier with Bio-MA and ProRoot® MTA are described in Table 3. The risk ratio between ProRoot® MTA and Bio-MA was 0.884 at the 95% confidence interval (0.488–1.603). The non-inferiority trial analysis indicated that Bio-MA tended to be noninferior, however, the confidence interval was inconclusive because the lower limit of the confidence interval for the risk ratio overlapped with the 15% non-inferiority limit (Figure 4).

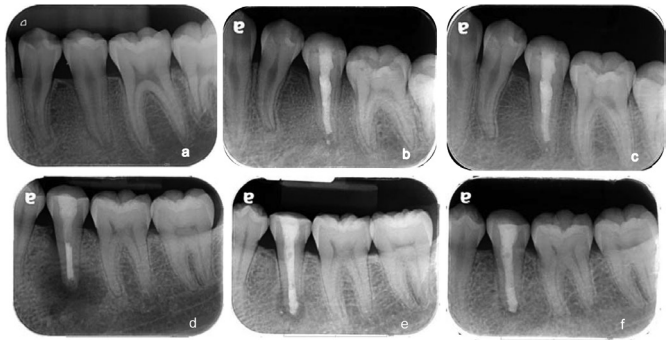

Figure 2 Two representative cases of an orthograde apical barrier with Bio-MA. Preoperative radiographs of a mandibular left second premolar (a), Bio-MA orthograde apical barrier (b), Periapical lesion healed at the 15-month recall (c). Pre-operative radiographs of a mandibular left second premolar (d), Bio-MA orthograde apical barrier (e), Periapical lesion healing at the 14-month recall (f).

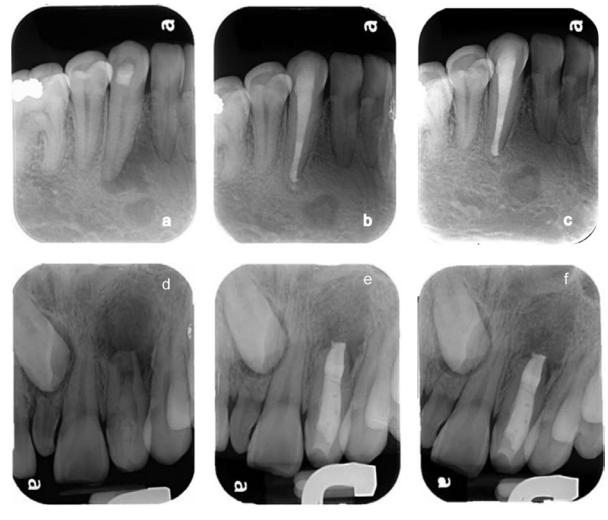

Figure 3 Two representative cases of an orthograde apical barrier with ProRoot® MTA. Preoperative radiographs of a mandibular right canine (a), ProRoot® MTA orthograde apical barrier (b), Periapical lesion healed at the 24-month recall (c), Preoperative radiographs of a maxillary left lateral incisor (d), ProRoot® MTA orthograde apical barrier (e), Periapical lesion healing at the 12-month recall (f).

Table 3 Clinical outcomes of pre-operative factors of the orthograde apical barrier with Bio-MA and ProRoot® MTA.

	Healed		Healing / Disease	
	n	%	n	%
Sex				
Male	22	75.90	7	24.10
Female	20	76.90	6	23.10
Age				
≤45	38	80.90	9	19.10
>45	4	50.00	4	50.00
Tooth type				
Anterior	32	76.20	10	23.80
Posterior	10	76.90	3	23.10
Tooth location				
Maxilla	34	77.30	10	22.70
Mandible	8	72.70	3	27.30
Pre-op periapical radiolucency				
Absent	8	100.00	0	0.00
≤5 mm	20	90.90	2	91.10
>5 mm	14	56.00	11	44.00
Stages of root development				
4-6	38	80.90	9	19.10
7	4	50.00	4	50.00
Type of treatment				
Primary treatment	36	85.70	6	14.30
Retreatment	6	46.20	7	53.80

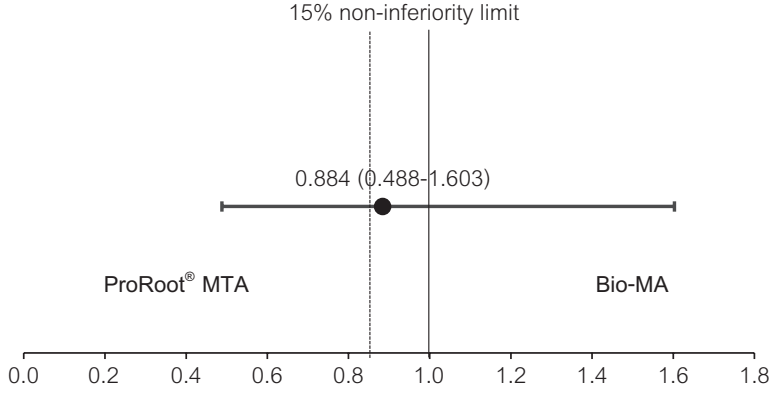

Figure 4 Non-inferiority analysis with 15% non-inferiority limit comparing the risk ratio between Bio-MA and ProRoot® MTA in orthograde apical barrier. The 95% confidence interval line ranges overlap with the non- inferiority margin of 15%. Bio-MA tended to be noninferior, however, the analysis was inconclusive.

Discussion

In this study, the overall success outcome, comprising the healed and healing rate of ProRoot® MTA and Bio MA was 100%, which was higher than the 84–98.1% success rate in other studies [2, 9, 28, 29]. The highly successful treatment outcome may be due to our exclusion criteria, in which the teeth with pre-operative cracks or root resorption were excluded [30]. Moreover, the standardized treatment protocols were performed by endodontists or postgraduate students, who had more experience than general practitioners in another study [28]. The treatment protocol using multiple-visits allowed for prevention of over-instrumentation, disinfection of the root canal with NaOCl, EDTA irrigants, and using calcium hydroxide medication for at least 1 week. The apical-plug material was at least 4 mm thick to provide an adequate apical seal [31]. Every step of the procedures contributed to the highly successful treatment outcome.

Bio-MA is a calcium silicate-based cement whose chemo-physical properties, sealing ability, and biocompatibility are similar to ProRoot® MTA. Furthermore, Bio-MA has a faster setting time [13]. Compared with ProRoot® MTA, Bio-MA also contains calcium chloride [14, 15], which accelerates the setting time of the material. Calcium chloride induces partial precipitation in the tricalcium silicate hydrate gel that promotes more water permeation and rapid hydration reaction. This effect improves the sealing ability by decreasing the setting time. It also increases calcium ion release and keeps the pH high to promote better healing [21]. The setting time of Bio-MA is shorter than ProRoot® MTA [14,32], which may improve its sealing ability and clinical outcomes. Tungsuksomboon, *et al*. [22] reported a 77.8% healed rate of Bio-MA when used as an orthograde apical barrier with a 12-month recall period in a small sample size (n=19), where the outcome was not significantly different from that of ProRoot®MTA. The results of this study were consistent with the present study, i.e., no significant difference in apexification was found between the two materials. In our study, prior to placing the calcium silicate-based cement apical barrier, the periapical inflammation was controlled by root canal disinfection to ensure that the materials were not dissolved by tissue fluid or inflammatory exudate during setting and provided a good sealing ability [33]. However, the shorter setting time of Bio-MA in this study did not significantly affect the clinical outcome of apexification. Further research is required to ascertain its efficiency in other treatments, such as perforation repair or pulp capping in vital pulp therapy.

The formation of a natural apical hard tissue barrier is necessary to provide a biological seal. Traditional calcium hydroxide dressings that were used to induce the apical hard tissue barrier have a high clinical success rate of 74–100% [1]. The disadvantages of calcium hydroxide apexification is increased treatment time [1] and might adversely affect root dentine's mechanical properties, increasing the risk of tooth fracture [5, 6, 34, 35]. Moreover, the apical hard tissue barrier formed was porous and irregular [1]. Thus, MTA was used to create the apical barrier, and it demonstrated a significantly shorter treatment time with better outcome than calcium hydroxide [36]. ProRoot® MTA and Bio-MA with calcium chloride in the current study provided evidence to support using calcium silicate-based cement as an apical barrier material.

In a wide-open apex tooth, calcium silicate-based cement can be easily extruded. Adapting the material to the apical root dentine walls is a challenge due to not having a barrier to resist material compaction. To create a physical apical

barrier, a resorbable material, e.g., collagen sponge (CollaPlug®) or calcium sulphate is placed into the root apex prior to placing the calcium silicate-based cement [37]. The physical apical barrier allows minimal extrusion and better adaptation of the material to the root canal walls. In our study, the teeth with extruded calcium silicate-based cement in both groups comprised 13 teeth healed and 4 teeth healing. There were no any adverse effects from the material extrusion [38], and the periapical tissue healing was not affected. The extruded material permitted deposition of cementum over the material surface and reattachment of the periodontal ligament [39].

There were no pre-operative factors in this study that had an impact on the treatment outcome of the orthograde apical barrier, except for the pre-operative lesions. The pre-operative lesions had significantly delayed the periapical healing, which was consistent with the results in a prior study [28]. Most of the teeth had preoperative periapical lesions and were randomly distributed in the two experimental groups to reduce the difference in data distribution and case selection bias. A study [36] reported that the duration for the complete healing of a periapical radiolucency was 4.6±1.5 months after placing an MTA apical barrier in the teeth with a preoperative lesion greater than 3 mm. Thus, clinical outcomes of an MTA apical barrier after at least a six- month follow-up could be predicted if the periapical lesion is small. However, approximately 45% of the preoperative lesions in our study were larger than 5 mm; only 3 of 47 cases were completely healed within 6 months after treatment. Moreover, one-fourth of the cases were still in the healing phase at the recall. These results implied that a 6- or 12-month follow-up period might be insufficient for the complete healing of large periapical lesions [40]. These results indicate that it is important to recall the persistent lesions until they have healed or to determine the necessity of additional treatment.

This randomised clinical trial study was performed at the highest clinical evidence level to ensure sample size balance and elimination of selection bias. Although the non-inferiority analysis revealed a non-inferiority tendency, the calculated confidence interval was in the range of inconclusive. To achieve a conclusive result, a longer follow-up time with a larger number of cases will be required.

Conclusion

With a 94.9% recall rate and an average 17-month recall period, the clinical outcomes in the calcium silicate-based cements with or without calcium chloride groups had a 100% success rate (healed and healing). The outcomes of the Bio-MA group were 78.6% healed and 21.4% healing, while the ProRoot® MTA group had 74.1% healed and 25.9% healing cases. No disease was found in either group. There was no significant difference between the healed and healing rates of the materials with or without calcium chloride. The non-inferiority analysis indicated that Bio-MA tended to be non-inferior to ProRoot® MTA.

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Conflict of interest

Sutimuntanakul S. is a developer of Bio-MA.

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