Title: Adaptation of MTA to dentine walls compared with other root-end filling materials: A systematic review

Running Title: Adaptation of MTA in root-end cavities

Authors: Selen Küçükkaya Eren[a], DDS, PhD, Peter Parashos, MDSc, PhD[b]

[a] Department of Endodontics, Faculty of Dentistry, Hacettepe University, Ankara, Turkey

[b] Melbourne Dental School, Faculty of Medicine Dentistry and Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia

Corresponding Author:

Selen KÜÇÜKKAYA EREN, DDS, PhD

Department of Endodontics,
Faculty of Dentistry, Hacettepe University
Sıhhiye, Ankara/Turkey, 06100
Phone: +903123052260 Fax：+903123104440
e-mail address: selenkkkaya@yahoo.com

Authorship Declaration

All authors have contributed significantly, and are in agreement with the manuscript.

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DR. SELEN KÜÇÜKKAYA EREN (Orcid ID : 0000-0001-5023-1454)

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Abstract

This systematic review analysed the literature comparing marginal adaptation of MTA with other filling materials in root-end cavities. The PubMed, Ovid, Web of Science, SCOPUS, and Cochrane library databases were searched using appropriate keywords related to root-end filling materials and adaptation. Of 38 articles assessed, 20 met the inclusion criteria. No in vivo study was identified. In 10 studies, MTA gave the best marginal adaptation results, but no significant differences were found between MTA and any of the tested filling materials in 7 studies. There was great variability in the study designs including analysed surface, unit of gap measurement and magnification amount during analysis. On the basis of available evidence, MTA presented good marginal adaptation to dentine walls. This review identified the need for the development of standardized methods to evaluate the adaptation property of root-end filling materials in ex vivo studies as well as in clinical studies evaluating outcome.

Keywords: adaptation, endodontic surgery, MTA, systematic review

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Introduction

Endodontic surgery is a viable treatment option when nonsurgical attempts prove unsuccessful or unlikely to result in a better outcome (1). This treatment approach aims to remove diseased tissues and untreated apical ramifications and to provide an apical seal to decrease the risk of apical pathosis (2). Hence, the placement of a root-end filling has been recommended because it can prevent egress of any remaining bacteria or their byproducts and allow for the formation of a normal periodontium across its surface (2, 3).

Traditionally, endodontic surgery was performed using surgical burs for root-end cavity preparation and amalgam for root-end filling (2). Precisely locating, cleaning and filling all the complex apical ramifications were unpredictable. The root-end cavity preparation using burs risked perforation of the root-end and generally lead to insufficient depth and retention of the filling material. Modern endodontic surgical concepts include the use of ultrasonics for root-end cavity preparation and biomaterials for root-end filling (2). The use of ultrasonic tips provides centred and deep root-end cavities with a decreased risk of root perforation (4). According to a recent meta-analysis, root-end cavity preparation with ultrasonics was significantly superior in achieving high clinical success rates when compared with traditional root-end cavity preparation with burs (5). In 1993, mineral trioxide aggregate (MTA), a calcium silicate-based biomaterial was introduced as a root-end filling material (6) and since then has been accepted as the gold standard because it is a biocompatible material with good physical and chemical properties (7). However, MTA has difficult handling characteristics and long setting time that can result in material washout in a moist surgical site (8). Recently, ongoing research for the ideal root-end filling material has lead to new biomaterials that have mostly similar constituents to MTA (9-12).

The sealing ability of a root-end filling material potentially will affect the long-term outcome of

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endodontic surgery (3). The quality of the seal achieved by root-end filling materials has been evaluated by several leakage studies using various methodologies such as dye penetration (13), bacterial penetration (14), radioisotope penetration (15), electrochemical method (16) and fluid transport method (17). However, the clinical relevance of these methodologies is controversial because the results of these in vitro studies do not correlate with clinical outcomes (18), so much so that such research is generally no longer accepted in the mainstream endodontic literature.

Assessing the quality of marginal adaptation is an alternative methodology that indirectly compares the sealing ability of root-end filling materials (19). The presence of marginal gaps between a root-end filling material and root dentine may potentially be responsible for apical leakage (19-21), which may result in apical pathosis (3). Thus, this property is crucially important for the selection of a root-end filling material (22).

To date, studies have reported conflicting results on the adaptation of MTA as a root-end filling (20, 21, 23). Therefore, the aim of this systematic review was to analyse marginal adaptation studies based on contemporary concepts of endodontic surgery using ultrasonic tips for root-end cavity preparation and which compared MTA with other materials.

Literature Search Methodology

Data sources and the search strategy

This systematic review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (24). The free form of the research question was the following: 'Does root-end filling with MTA present better quality of marginal adaptation to dentine walls than other materials in root-end cavities prepared with ultrasonic tips?' The population, intervention, comparison, and outcome (PICO) strategy was used for the structured review question as follows:

P : Fully formed human teeth undergoing root-end surgery with ultrasonic root-end preparation

I : Root-end filling with MTA

C: Root-end filling with other materials

O: Quality of marginal adaptation of the materials to dentine walls

The search strategy covered electronic databases and identified articles published through to 28 September 2017. No publication year or language limits were set. The electronic databases searched were the following: PubMed (MEDLINE), Ovid (MEDLINE), Web of Science (all databases), SCOPUS, and the Cochrane library. The main search terms were apicoectomy, root-end resection,

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root-end filling, marginal adaptation, mineral trioxide aggregate. These keywords and terms were selected from articles published in following three endodontic journals: Journal of Endodontics, International Endodontic Journal and Australian Endodontic Journal. The keywords and terms were enriched during the electronic database searches. The search strategy used is depicted in Table 1.

Screening and selection of the studies

Initially, the titles identified in the searches were screened. If the title indicated possible inclusion, the abstract was then evaluated. In case of any doubt, the full text of the article was read. Following the evaluation of the abstracts, articles considered eligible for the review were identified and all of the full-text articles were assessed. Two reviewers working independently from one another assessed all the citations. Studies were selected for inclusion if they fulfilled all of the following criteria:

1. In vivo or ex vivo studies performed on fully-formed human teeth
2. Studies comparing the marginal adaptation of MTA with other root-end filling materials
3. Studies evaluating the marginal adaptation at the interface of the root-end filling material and dentine in terms of presence of gaps
4. Root-end cavities prepared using surgical ultrasonic tips
5. The assessment method did not involve microleakage.

Studies failing to meet any of these criteria were excluded.

Data extraction

Data extraction for the included studies was completed using a systematic data collection form designed to summarize each study. All aspects of treatment that could potentially affect the study outcomes were identified and included in the data form. Data were extracted by 1 reviewer directly from the full texts of articles and a second reviewer independently verified the extracted data. The following variables were recorded: authors, year of publication, study design (in vivo or ex vivo), type of teeth, tested material, whether the root-end cavity was cleaned before placement of filling material, storage time between the placement of filling materials and analysis, storage in a moist environment after the placement of filling materials, analysed surface (transverse or longitudinal), type of analysis (quantitative or qualitative), evaluation method, unit of gap measurement, magnification amount during analysis and outcomes pertinent to the aim of the review.

Each study was analysed in terms of similarities so that a meta-analysis could be performed. However, because of considerable methodological heterogeneity a meta-analysis was not indicated. Instead, a descriptive analysis of the results of the individual studies was undertaken.

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Quality assessment (Risk of bias)

The methodological quality of each included study was critically evaluated based on the following parameters:

1. Was the calculation of an adequate sample size performed before starting experiments?
2. Were the samples randomly divided into groups?
3. Were the root-end procedures performed by a single operator?
4. Was the experience of the operator who performed the root-end procedures reported?
5. Were the materials prepared and/or used according to the manufacturer's instructions?
6. Were the root-end procedures performed under magnification?
7. Were the analyses performed by evaluator/s blinded to the groups?

After collecting these items, the studies were classified with a high, moderate, or low risk of bias. Studies that failed to report 5 items or more were classified as high risk, studies that failed to report 3-4 items were classified as moderate risk, and studies that failed to report 2 items or less were classified as low risk.

Results

The electronic systematic searches yielded a total of 235 studies from all the databases. Of these, 70 were identified in Web of Science, 58 in Scopus, 50 in Pubmed, 50 in Ovid, and 7 in the Cochrane library. After removal of duplicates and data screening based on title and abstract, a total of 38 citations were selected for full-text reading. No additional studies were identified after the cross-reference analysis. Following the full-text reading, 18 studies were excluded, and the reasons for exclusion were the following: using burs for root-end cavity preparation (25-34), no comparison of MTA with another filling material (35-39), inadequate detail regarding root-end cavity preparation (40, 41) and one study had exactly the same data as a previously published study (42). Finally, 20 studies were found to be eligible for inclusion in this systematic review. Of these, 19 were in English (9-12, 20, 21, 23, 43-54) and 1 study was in Portuguese (55), which was translated by the principal author. All of the included studies were ex vivo studies, no in vivo studies were identified.

The literature review was organized into two sections: (i) methodologies of marginal adaptation studies, and (ii) comparative analysis of root-end filling materials.

Methodologies of marginal adaptation studies

The summary of characteristics of the included studies is shown in Table 2. The methodology, type

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of preparation of the samples, the chosen surface for analysis and the type of analysis varied in these studies. Of the 17 SEM studies, 5 performed a replication technique to obtain acrylic copies of natural teeth (9, 12, 20, 21, 44) while 11 analysed natural teeth (11, 43, 45-51, 53, 55) and 1 used both natural teeth and replicas (54).

The analysis in the studies was either qualitative or quantitative, or both. In 2 studies qualitative analysis was performed by interpreting the images in terms of the presence or absence of gaps (23, 47) while in 4 studies scoring scales indicating the distribution of gaps in relation to cross-sectional quadrants were used (48, 50, 53, 55). In 15 studies, quantitative analysis was performed by measuring the gap amounts (9-12, 21, 43-46, 49, 50, 52-54, 56). In 1 study, the margin types were categorized as continuous, overfilled, underfilled and non-continuous and the percentages were calculated according to a formula (20). In 9 studies, image analysis programs were used to measure the length, width, area or volume of gaps (10, 12, 20, 21, 45, 49, 52-54).

Comparative analysis of root-end filling materials

The main outcomes are summarized in Table 2 and the classification of the materials is shown in Table 3. In 7 studies, MTA was associated with the best marginal adaptation (21, 43, 45, 46, 50, 52, 55), whereas 2 associated it with the worst results (23, 54). In 3 studies, MTA presented similar marginal adaptation results with a resin composite material (44), calcium silicate cement clinker (49), and intermediate restorative material (IRM) (11) while showing better performance than the remaining filling materials. No significant difference was found between MTA and any of the tested filling materials in 7 studies (9, 12, 20, 47, 48, 51, 53). According to 1 study, Biodentine showed better adaptation than MTA while MTA was better than glass ionomer cement (GIC) (10). In 9 studies, the colour of MTA was not specified (11, 12, 20, 21, 43, 44, 48, 51-53, 55).

Risk of Bias

All 20 included studies were assessed for the risk of bias (Table 4) and only 1 (5%) showed low risk of bias, whereas 4 (20%) presented medium risk. The majority of the studies (75%) showed high risk.

Discussion

Endodontic surgery has undergone many changes over the past decades with the use of microscopes, microinstruments and biomaterials. These advancements have been adopted widely and represent contemporary procedures that produce more predictable outcomes compared with traditional techniques. Therefore, to highlight the studies that were designed according to contemporary concepts, the criteria were set to include studies that prepared the root-end cavities with ultrasonic tips and exclude the ones that used burs. In addition, as the introduction of MTA is a benchmark of modern

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endodontic surgery (2), only the studies that used MTA as one of the root-end filling materials were included in the present review.

Although adaptation of the filling materials was the common outcome measured in the the included studies, it was not feasible to perform a meta-analysis due to the heterogeneity among the studies. The unit of gap measurement varied which was defined as either score, length, width, depth, area, volume or percentages of one of these units. Also, the analyses were performed under different magnification between 10x and 2000x. Furthermore, the analysed surfaces (transverse or longitudinal) also varied among the studies. This variability made comparison difficult.

In this systematic review, SEM analysis was the most commonly used technique for the evaluation of marginal adaptation of root-end filling materials (9-12, 20, 21, 43-51, 54, 55). The main reasons for its popularity is its ability to provide high magnification and good resolution. However, the process of SEM preparation may affect the results because of the high vacuum evaporation and dehydration of the coating process of biological samples that can cause development of artefacts such as cracks in hard tissues and separation or lifting of the filling materials from the surrounding tooth structure (25). To overcome these problems, the replication technique was used by some of the included studies (9, 12, 20, 21, 44, 54). In this technique, an impression of the resected root-end is taken and an epoxy resin is poured into the impression to obtain a resin replica that may be more resistant than natural teeth to the preparation procedures. Another drawback of SEM evaluation is that it gives no three dimensional information and therefore only linear or area analysis can be performed. One study used a 3D profilometer that provided colour axonometric images of the surface representing each depth with different colours (45). However, a 3D model of the total volume of the root-end filling material cannot be obtained with 3D profilometry. According to that study, 3D profilometry produced similar results to the SEM regarding the marginal adaptation (45). Only 1 study evaluated adaptation using micro-CT, and MTA presented better quality than Super-EBA (52).

Based on the results of the present review, MTA was superior in terms of marginal adaptation by showing good performance in most of the studies (9, 11, 12, 20, 21, 43-53, 55). The success of MTA can be related to its bioactivity by promoting apatite deposition in tissue fluid which improves the sealing ability and contributes to filling the marginal porosities around restorations (57). Besides bioactivity, another property of a root-end filling material can also affect the marginal adaptation is viscosity. Materials with low viscosity can penetrate into irregularities and open dentinal tubules on the prepared surfaces (58, 59). However, penetration into tubules is not only dependant on the viscosity of the material but also on the particle size of the material. Fine particles of MTA have the potential to penetrate into open tubules (60). Despite the favorable results in most of the studies, in 2 studies MTA presented inferior adaptation results compared with other materials (23, 54). The different results among the studies could be related to the variability in the study designs. The storage

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time and storage conditions following the placement of filling materials may affect the results of the adaptation analysis. It was well-established that MTA requires moisture and time for its complete setting (7). As shown in Table 2, the filling materials were stored in a moist environment for at least 24 hours in most of the studies. Importantly, the materials were not stored in a moist environment in the 2 studies that associated MTA with inferior results (23, 42). In most of the studies, the materials were prepared according to the manufacturers' instructions. The differences in the preparation of the materials including different powder-liquid ratios, curing periods and mixing techniques could also affect adaptation. Marginal adaptation of the filling materials to dentine walls may not be only dependent on the material properties, but also on the condition of the cavity surfaces. Although ultrasonic tips work under continuous irrigation, debris may persist in the cavity after the preparation procedure (61). To obtain a clean root-end cavity free from dentine chips and gutta-percha, it may be necessary to perform additional irrigation after root-end cavity preparation. In only 6 studies included in the present review, the root-end cavities were cleaned before the placement of the materials (10, 20, 21, 23, 46, 47). According to the outcomes of these studies, it is not possible to directly correlate the cleanliness of root-end cavity and marginal adaptation quality of the materials.

No significant differences were found among calcium silicate-based materials in 3 studies (9, 12, 53). This can be explained by the similar composition and characteristics of calcium silicate-based materials such as dimensional stability, porosity and particle size (62-64). On the other hand, in 1 study, Biodentine presented better adaptation results than MTA (10), while in another MTA showed better adaptation than Biodentine (11). Conflicting results could be related to the methodological differences. In the former study (10), the filling materials were evaluated under 10x magnification with confocal laser scanning microscopy in terms of the amount of gap area while in the latter study (11), the evaluation was performed under 1000x magnification using SEM in terms of the amount of gap width. Furthermore, the influence of the operator could affect outcomes. Importantly, none of the included studies reported details regarding the operator experience or calibration of the operator before the experiments and the majority of them (85%) failed to report that the procedures were performed by a single operator.

In clinical outcome studies, MTA exhibited a higher healing rate than resin composite fillings (65), while presented similar success rates to Super EBA or IRM when used as root-end filling materials (66-68). Moreover, the clinical performance of MTA was comparable to another calcium silicate-based material in a randomized controlled study (69). Based on the findings of the present review, Super-EBA or IRM presented inferior marginal adaptation than MTA in the 5 included studies (21, 43, 49, 52, 55), while no significant difference was found among the materials in 4 studies (11, 20, 47, 48). In 1 study, Super EBA and IRM were associated with better outcome compared with MTA in terms of adaptation (23). Consequently, the adaptation property of a filling material may not

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be a significant factor affecting clinical outcome, which implies that other clinical factors exist that contribute to controlling intraradicular infection. A recent systematic review that aimed to clarify the clinical effect and safety of different materials for root-end filling revealed that more high-quality randomized controlled trials are required to determine the benefits of any one material over another (70). As no in vivo study was identified in the present systematic review, clinical studies are necessary to obtain information on the relation between the clinical outcome and the adaptation property of root-end filling materials. It should be noted that there are difficulties in performing such studies including patient factors (health, habits, age and gender) and tooth-related factors (type, quality of previous endodontic treatment, status of present restoration, the presence and size of the lesion), which are usually beyond the operator's control unlike the treatment-related factors (material selection and surgical technique) (71). These factors must be considered in the planning of clinical studies. Moreover, experience and expertise of the operator could be one of the key factors influencing the success or failure of endodontic surgery (72). Hence, standardization of study design and outcome criteria should increase the quality of work and provide more powerful data regarding outcomes.

Overall, MTA adapted well to dentine walls in most studies. However, standardization in the design of these studies is lacking. The literature is also lacking on the clinical relevance of adaptation of root-end filling materials but does imply the existence of other, as yet unidentified factors, that affect biological outcome.

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Table 1. Example of the search strategy (Pubmed)

No.	Search strategy	Results
1	(((((((((apicoectomy)) OR (apicectomy)) OR (root-end resection)) OR (root end resection)) OR (pulpectomy)) OR (pulpotomy)) OR (root canal therapy)) OR (root canal filling materials)) OR (endodontics)	39063
2	((((obturation material)) OR (obturation)) OR (filling)) OR (filling material)	58504
3	((((((retrograde)) OR (retro-filling)) OR (retro filling)) OR (retrofilling)) OR (root-end)) OR (root end)	69938
4	((((((marginal)) OR (adaptation)) OR (fit)) OR (discrepancy)) OR (gap)) OR (gaps)	728704
5	(mineral trioxide aggregate) OR (MTA)	6813
6	#1 AND #2 AND #3 AND #4 AND #5	50

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Table 2. Descriptive data of included studies

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Studies	Tooth type	Materials	Cavity cleaning	Storage time after root-end filling	Storage in moisture
Peters&Peters, 2002 (20)	human maxillary and mandibular molars	ProRoot MTA, Super EBA	Y	24h	Y
Gondim et al, 2003 (21)	human canine teeth	ProRoot MTA, Super EBA, IRM	Y	24h	Y
Xavier et al, 2005 (45)	human single-rooted teeth	MTA Angelus, Super EBA, Vitremer	N	immediately	N
Tobón-Arroyave et al, 2007 (23)	human single-rooted maxillary and mandibular teeth	ProRoot WMTA, Super EBA, IRM	Y	30 min	N
Costa et al, 2008 (54)	human single-rooted teeth	WMTA Angelus, white, a calcium silicate cement clinker, Vitremer, GC Fuji Ortho LC, silver amalgam without zinc	N	immediately	N
Gomes et al, 2009 (55)	maxillary molar teeth	MTA, Super EBA, ZOE, Ketac-CEM, N-	N	immediately	N

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		Rickert, IRM, Amalgam			
Rosales-Leal et al, 2011 (44)	single-rooted anterior teeth	ProRoot MTA, Clearfil AP, Cavalite, Amalgam, Vitrebond, IRM	N	24h	Y
Munhoz et al, 2011 (45)	human maxillary canine teeth	WMTA Angelus, Sealer 26	N	36h	Y
Shahi et al, 2011 (46)	human single-rooted teeth	ProRoot GMTA, ProRoot WMTA, white calcium silicate cement clinker, gray calcium silicate cement clinker	Y	48h	Y
Almeida et al, 2012 (47)	human maxillary and mandibular canine teeth	WMTA Angelus, Super EBA	Y	immediately	N
Oliveira et al, 2013 (48)	human single-rooted maxillary anterior teeth	ProRoot MTA, IRM, Amalgam, Super EBA, Epiphany/Resilon	N	24h	Y
Rosa et al, 2014 (49)	human maxillary	WMTA Angelus, a calcium silicate	N	1 week	Y

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	molars	cement clinker, Super EBA			
Shokouhinejad et al, 2014 (9)	human single-rooted teeth	ProRoot WMTA, Endosequence Root Repair Putty, Endosequence Root Repair Paste	N	1 week	Y
De Conto et al, 2014 (50)	human single-rooted mandibular incisors and canines	WMTA Angelus, Vitremer	N	2 weeks	N
Ravichandra et al, 2014 (10)	human mandibular premolar teeth	Biodentine, ProRoot WMTA, Glass ionomer cement type II	Y	1 week	Y
Soundappan et al, 2014 (11)	maxillary central incisors	ProRoot MTA, IRM, Biodentine	N	5 days	Y
Mokhtari et al, 2015 (51)	human single-rooted teeth	ProRoot MTA, a ceramic-based material (experimental)	N	24h	N
Bolhari et al, 2015 (12)	human single-rooted teeth	ProRoot MTA, Biodentine, Bioaggregate, CEM	N	96h	Y

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Kim et al, 2016 (52)	human single-rooted teeth	ProRoot MTA, Super EBA	N	24h	Y
Küçükkaya Eren et al, 2017 (53)	human maxillary central incisors	MTA Angelus, Biodentine, CEM	N	24h	Y

Y: reported in the article; N: not reported in the article

NA: not applicable

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Table 2. (continued)

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Studies	Analyzed surface	Analysis type	Method	Unit of gap measurement	Magnification amount	Main findings
Peters&Peters, 2002 (20)	Transverse	Quantitative	SEM	percentage (length)	200x	No difference was found among materials
Gondim et al, 2003 (21)	Transverse	Quantitative	SEM	mm^2 (area)	300x	ProRoot MTA presented the best adaptation results
Xavier et al, 2005 (45)	Transverse	Quantitative	SEM	μm (width)	1800x	MTA Angelus presented the best adaptation results
Tobón-Arroyave et al, 2007 (23)	Longitudinal	Qualitative	Stereomicroscopy	score	50x	ProRoot WMTA was associated with the worst results
Costa et al, 2008 (54)	Transverse	Quantitative	SEM	N	230x	Both glass ionomer cement showed

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						better adapatation than MTA
Gomes et al, 2009 (55)	Transverse	Qualitative	SEM, Optical microscopy	score	50x, 150x	MTA presented the best adaptation results
Rosales-Leal et al, 2011 (44)	Transverse	Quantitative	SEM	µm (width)	N	ProRoot MTA and Clearfil AP presented the best adaptation results
Munhoz et al, 2011 (45)	Transverse	Quantitative	SEM, 3D profilometry	µm (depth) and μm^2 (area)	50x, 150x	WMTA Angelus presented the best adaptation results
Shahi et al, 2011 (46)	Transverse	Quantitative	SEM	µm (width)	16x	ProRoot GMTA

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						presented the best results and followed by white calcium silicate cement clinker
Almeida et al, 2012 (47)	Transverse	Qualitative	SEM	N	70x, 500x	No difference was found among materials
Oliveira et al, 2013 (48)	Transverse	Qualitative	SEM	score	100x, 500x	No difference was found among materials
Rosa et al, 2014 (49)	Longitudinal	Quantitative	SEM	percentage (area)	100x	WMTA Angelus and calcium silicate cement clinker presented the best adaptation results

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Shokouhinejad et al, 2014 (9)	Transverse, longitudinal	Quantitative	SEM	μm (width)	30x, 500x	No difference was found among materials
De Conto et al, 2014 (50)	Transverse, longitudinal	Quantitative, qualitative	SEM, Digital radiography	μm, score	2000x	WMTA Angelus presented the best adaptation results
Ravichandra et al, 2014 (10)	Transverse	Quantitative	CLSM	μm^2 (area)	10x	Biodentine presented the best results and followed by ProRoot WMTA
Soundappan et al, 2014 (11)	Transverse	Quantitative	SEM	μm (width)	1000x	ProRoot MTA and IRM presented the best adaptation results

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Mokhtari et al, 2015 (51)	Transverse	Quantitative	SEM	N	N	No difference was found among materials
Bolhari et al, 2015 (12)	Transverse	Quantitative	SEM	µm (width)	200x	No difference was found among materials
Kim et al, 2016 (52)	Three dimensional analysis	Quantitative	Micro-CT	percentage (volume)	NA	ProRoot MTA presented superior adaptation
Küçükkaya Eren et al, 2017 (53)	Longitudinal	Quantitative, qualitative	SEM	percentage (area), score	130x	No difference was found among materials

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NA: not applicable

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Table 3. Detailed information regarding the tested materials in included studies

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Tested materials	Classification of materials	Manufacturers' details
Amalgam	A liquid mercury and metal alloy mixture	1. Logic+^{TM} SDI, Bayswater, Vic., Australia 2. Amalcap, Vivadent, Liechtenstein
Bioaggregate	Calcium silicate-based cement	Innovative BioCeramix, Vancouver, Canada
Biodentine	Calcium silicate-based cement	Septodont, Saint-Maur-des-Fosses, France
Cavalite	Compomer	Kerr, Rastatt, Germany
CEM	Calcium silicate-based cement	Bionique Dent, Tehran, Iran
Clearfil AP	Composite resin	Kuraray, Osaka, Japan
Endosequence Root Repair Putty/Paste	Calcium silicate-based cement	Brasseler, Savannah, GA, USA
Epiphany/Resilon	Synthetic polymer-based root canal filling material	Pentron Clinical Technologies, Wallingford, CT, USA
Fuji Ortho LC	Glass ionomer cement	GC America Inc., Alsip. IL, USA
Glass ionomer cement type II	Glass ionomer cement	GC United Kingdom, Coopers Court, Newport Pagnell, UK
Gray calcium silicate cement clinker	Calcium silicate-based cement	Sufiyan Cement company, Tabriz, Iran
IRM	Zinc oxide based cement	1. LD Caulk Co., Mildford, DE, USA

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		2. Dentsply, Konsztanz, Germany
MTA Angelus	Calcium silicate-based cement	Londrina, PR, Brazil
Calcium silicate cement clinker	Calcium silicate-based cement	Votorantin, Sao Paulo, SP, Brazil
ProRoot MTA	Calcium silicate-based cement	Dentsply Maillefer, Ballaigues, Switzerland
Sealer 26	Resin based sealer	Dentsply Ind. e Com. Ltda., Petropolis, RJ, Brazil
Super EBA	Zinc oxide based cement	Harry J. Bosworth, Skokie, IL, USA
Vitrebond	Glass ionomer cement	3M ESPE, St. Paul, MN, USA
Vitremer	Glass ionomer cement	3M ESPE, St. Paul, MN, USA
White calcium silicate cement clinker	Calcium silicate-based cement	1. CPB40, Votorantin, São Paulo, SP, Brazil 2. Tehran cement Company, Tehran, Iran

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Table 4. Bias risk of individual studies

Studies	Sample size calculation	Teeth randomization	Single operator	Operator experience
Peters&Peters, 2002 (20)	N	Y	N	N
Gondim et al, 2003 (21)	N	Y	Y	N
Xavier et al, 2005 (45)	N	Y	N	N
Tobón-Arroyave et al, 2007 (23)	N	Y	Y	N
Costa et al, 2008 (54)	N	Y	N	N
Gomes et al, 2009 (55)	N	Y	N	N
Rosales-Leal et al, 2011 (44)	N	Y	N	N
Munhoz et al, 2011 (45)	N	N	N	N

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Table 4. (continued)

Shahi et al, 2011 (46)	N	Y	N	N
Almeida et al, 2012 (47)	N	Y	N	N
Oliveira et al, 2013 (48)	N	Y	N	N
Rosa et al, 2014 (49)	N	Y	N	N
Shokouhinejad et al, 2014 (9)	N	Y	N	N
De Conto et al, 2014 (50)	N	Y	N	N
Ravichandra et al, 2014 (10)	N	Y	N	N
Soundappan et al, 2014 (11)	N	Y	N	N
Mokhtari et al, 2015 (51)	N	Y	N	N
Bolhari et al, 2015 (12)	N	Y	N	N
Kim et al, 2016 (52)	N	Y	Y	N
Küçükkaya Eren et al, 2017 (53)	N	Y	N	N

Y, reported in the article; N, not reported in the article

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Studies	Manufacturer's instructions	Magnification used during specimen preparation	Blinding of the evaluator	Classification
Peters&Peters, 2002 (20)	N	Y	N	High
Gondim et al, 2003 (21)	Y	Y	N	Moderate
Xavier et al, 2005 (45)	Y	N	N	High
Tobón-Arroyave et al, 2007 (23)	Y	Y	Y	Low
Costa et al, 2008 (54)	Y	N	N	High
Gomes et al, 2009 (55)	Y	N	N	High
Rosales-Leal et al, 2011 (44)	N	N	N	High
Munhoz et al, 2011 (45)	N	Y	Y	High
Shahi et al, 2011 (46)	N	N	N	High
Almeida et al, 2012 (47)	Y	Y	Y	Moderate
Oliveira et al, 2013 (48)	Y	N	N	High
Rosa et al, 2014 (49)	Y	N	Y	Moderate
Shokouhinejad et al, 2014 (9)	Y	N	N	High
De Conto et al, 2014 (50)	Y	N	N	High
Ravichandra et al, 2014 (10)	Y	N	N	High
Soundappan et	Y	N	N	High

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al, 2014 (11)				
Mokhtari et al, 2015 (51)	Y	N	N	High
Bolhari et al, 2015 (12)	Y	N	N	High
Kim et al, 2016 (52)	N	Y	Y	Moderate
Küçükkaya Eren et al, 2017 (53)	Y	N	N	High

Y, reported in the article; N, not reported in the article

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