

Dentinal tubule penetration of bioceramic-based versus epoxy resin-based root canal sealers: a systematic review and meta-analysis

ABSTRACT

An ideal endodontic treatment involves filling the root canal system with a sealer that penetrates the dentinal tubules and remains intact. Hence, this systematic review aimed to appraise and analyse the dentinal tubule penetration of bioce-ramic-based and epoxy resin-based root canal sealers.

Articles published between January 1990 and March 2022 were searched in seven online databases (Google Scholar, PubMed, Web of Science – Core collection, Scopus, Cochrane Library, EBSCO, and Open Grey). Only in-vitro studies evaluating dentinal tubule penetration of bioceramic-based and epoxy resin-based sealers were selected. The OHAT risk of bias (RoB) tool was employed to analyse the RoB of each article. A two-arm meta-analysis based on the DerSimonian-Laird random-effects model was used to assess the standardised weighted mean differences in dentinal tubule penetration for both sealer types.

Although bioceramic-based root canal sealers exhibit inferior dentinal tubule penetration than epoxy resin-based sealers, future well-designed studies with standardised evaluation tools and a more control of confounding variables should be conducted.

Galvin Sim Siang Lin^{1*} Daryl Zhun Kit Chan¹ Jia Zheng Leong² Ing Zheng Kan³ Wong Mun Xuan⁴

Vincent Tee⁵

¹Department of Dental Materials, Faculty of Dentistry, Asian Institute of Medicine, Science and Technology (AIMST) University, 08100, Bedong, Kedah, Malaysia.

²Petaling Dental Clinic, Ministry of Health Malaysia, 71600, Kuala Klawang, Negeri Sembilan, Malaysia.

³Bukit Minyak Dental Clinic, Ministry of Health Malaysia, 14000, Bukit Mertajam, Penang, Malaysia.

⁴Pertang Dental Clinic, Ministry of Health Malaysia, 72300, Jelebu, Negeri Sembilan, Malaysia.

⁵Department of Internal Medicine, School of Medical Sciences, University Sains Malaysia, Health Campus, 16150, Kubang Kerian, Kelantan, Malaysia.

Received 2022, February 3 Accepted 2022, May 26

KEYWORDS biomaterial, calcium silicate, endodontics, confocal laser scanning microscopy, scanning electron microscopy

Corresponding Author

Dr. Galvin Sim Siang Lin | Head of Department, Department of Dental Materials, Faculty of Dentistry, Asian Institute of Medicine, Science and Technology (AIMST) University, 08100, Bedong, Kedah | Malaysia. Tel: +6010-9305602 | Email: galvin@aimst.edu.my

Peer review under responsibility of Società Italiana di Endodonzia 10.32067/GIE.2021.35.02.60

Società Italiana di Endodonzia. Production and hosting by Ariesdue. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).



Introduction

oot canal sealers play a crucial role in the long-term success of endodontic treatment. Undeniably, core obturation material itself cannot fill the entire three-dimensional canal space due to the presence of lateral canals, accessory canals, canal irregularities and minor discrepancies that exist between root dentinal walls and the obturating material (1, 2). To achieve a hermetic and fluid-tight seal, endodontic sealers are used to seal off voids in the root canal systems (3, 4). A well-obturated root canal system can prevent bacteria reinvasion and their antibacterial activity significantly reduces the number of bacteria remaining in the canals which in turn provides a predictable success in endodontic treatment (5). Furthermore, the penetration of sealers into chemo-mechanically prepared root canals is of utmost importance for maximising the adaptability and sealing ability of the root canal filling (6, 7).

In the past decades, various root canal sealers have been constantly developed and marketed based on their major constituents, including zinc oxide eugenol, glass ionomer, epoxy resin, methacrylate resin, calcium hydroxide, silicone, and bioceramic-based root canal sealers (8). Recently, bioceramic-based root canal sealers have received considerable attention in the practice of endodontics. Bioceramics in endodontics was first introduced by Torabinejad in the 1990s (9), of which mineral trioxide aggregates (MTA) is a ceramic cement based on the hydraulic powders of tricalcium silicate and dicalcium silicate. Bioceramic-based endodontic sealers can be further classified into calcium silicate-based (iRoot SP, EndoSequence BC Sealer), MTA-based (MTA Fillapex, Endo CPM Sealer, ProRoot Endo Sealer), and calcium phosphate-based (iRootSP and EndoSequence BC, Bio-C Sealer) (10). They exhibit several advantages such as having an alkaline pH, effective antibacterial ability, biocompatibility, no shrinkage and are chemically stable in the biological milieu (11).

With the emerging use of bioceramics in endodontics, numerous studies have been conducted to assess the material's performance as a root canal sealer. The ability to provide a good seal by means of dentinal tubule penetration is one of the most widely used methods for monitoring the effectiveness of these biomaterials in endodontic applications. Root canal sealers can penetrate into the dentinal tubules, forming a physical barrier, enhancing root filling retention, and encasing residual microorganisms (12). It has also been suggested that if a sealer can penetrate the tubules far enough, it will have a greater antibacterial effect (13). Nonetheless, the depth and consistency of the sealer penetration into root dentine tubules are influenced by physical and chemical parameters such as particle size, solubility, viscosity, and surface tension (12).

To the best of the authors' knowledge, there is still no unanimity in the literature when comparing the dentinal tubule penetration of bioceramic-based sealers to other types of sealers (14-17). Data and findings from related research topics can be summarised and contrasted through systematic review and meta-analysis, offering the highest level of clinical evidence to assist clinicians in obtaining the information they require (18). In addition, the authors also questioned whether bioceramic-based root canal sealers can achieve better dentinal tubule penetration than epoxy resin-based sealers. Hence, the current review aimed to answer the critique and comprehensively compare and evaluate the dentinal tubule penetration of bioceramic and epoxy resin-based root canal sealers.

Review

Protocol and registration

The current systematic review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol (19), and it was registered in the Prospective Register of Systematic Reviews (PROSPERO), University of York, with the registration number, CRD42021275860. The focused question was formulated using the PICOS



framework, which includes the Population (P), Intervention (I), Comparison (C), Outcome (O), and Study design (S).

The PICOS criteria were: (P) Root canal treated teeth, (I): Bioceramic-based root canal sealers, (C) Epoxy resin-based root canal sealers, (O) Dentinal tubule penetration, and (S) *in-vitro* experimental studies. Therefore, the PICOS question was "Do bioceramic-based root canal sealers have greater dentinal tubule penetration in root canal treated teeth than epoxy resin-based root canal sealers?". In this context, bioceramic sealers include calcium silicate-based, mineral trioxide aggregate-based, and calcium phosphate-based materials (10).

Search strategy

Four investigators (JZL, DZKC, IZK, WMX) used seven online databases to search for articles published between January 1990 and March 2022 (Google Scholar, PubMed, Web of Science - Core Collection, Scopus, Cochrane Library, EBSCO, and Open Grey). Two other investigators (GSSL, VT) independently reviewed the reference lists of relevant papers from the electronic search and keyed into a computer software (End-Note X9, Thomson Reuters). Deduplication of articles was accomplished using the software, and the titles of the remaining articles were recorded for the next screening stage. The keywords used for each database are 'dentinal tubule penetration', 'dentine tubule penetration', 'dentinal tubular penetration', 'dentine tubular penetration', 'dentine penetration', 'dentinal penetration', 'calcium silicate', 'calcium phosphate', 'bioceramic', 'mineral trioxide aggregate', 'MTA', 'root canal sealer' and 'endodontic sealer'. During the search, the Boolean operators 'AND' and 'OR' were employed to combine these keywords.

Study selection

Following the removal of duplicate publications, two investigators (JZL and DZKC) independently filtered the studies based on the title and abstract. Subsequently, another two investigators (IZK, WMX) conducted a thorough full-text assessment based on the inclusion and exclusion criteria. The inclusion criteria in choosing the articles are:

- Bioceramic-based and epoxy resin-based root canal sealers
- Studies evaluating the sealer penetration to root dentinal tubules

• In-vitro studies using extracted teeth The exclusion criteria are:

- Other types of root canal sealer (zinc oxide eugenol-based, calcium hydrox-ide-based etc.)
- Using artificial tooth model
- Heat obturation (warm gutta-percha obturation etc.)
- Animal studies, prospective or retrospective studies, randomised or non-randomised controlled trials, expert opinions, reviews, case reports and case series
- Poor data reported No mean and standard deviation of the sealer penetration depths
- Experiments that focused on different obturation techniques, irrigating solutions, and smear layer removal

Calibrations between investigators were performed to assess interrater reliability. The average concordance was determined using the Kappa value to compare the investigators' decisions on inclusion and exclusion (20). Any conflicts that arose throughout the search were addressed and resolved with the assistance of the fifth investigator (GSSL).

Data extraction

The following variables were extracted from each article using a customised Google Spreadsheet form to aid comparability: authors, year of publication, type of study, sample size, tooth type, types of final irrigation, types of sealers, mechanical instrumentation, storage condition, thickness of sample, tubule penetration assessment tool, area of testing, obturation technique and the general results. One investigator (GSSL) double-checked the data's accuracy, and any disputes were settled by consensus among all authors.

Risk of bias assessment

The risk of bias (RoB) for each included study was assessed using the Office of



Figure 1 The PRISMA flowchart search strategy.



Health Assessment and Translation (OHAT) Risk of Bias Assessment Tool from the National Toxicology Programme (NTP) (21). The OHAT assessment tool was also modified to account for *in-vitro* experimental study designs. A list of ten domains was used to identify potential bias, and a supplementary category for 'other potential threats to internal validity'. However, only questions 1, 2, 5, 6, 7, 8, 9, 10 and 11 were applied to evaluate experimental studies. The 11th question labelled 'other bias' by OHAT, allows for the incorporation of other possible risks to internal validity (e.g., statistical methods). Each RoB question was addressed on a four-point scale: 'definitely high (DH)', 'probably high (PH)', 'probably low (PL)', and 'definitely low (DL)'. 'NR' was assigned when insufficient information can be retrieved or not reported from the selected study. The assessments were completed independently by two investigators (JZL, DZKC). Any differences were also resolved by discussion with the third investigator (GSSL).

Statistical Analysis

After evaluation, all the included studies were deemed eligible for quantitative analysis. Data were entered into the Cochrane Collaboration Review Manager software (RevMan5.4, The Cochrane Collaboration, Oxford, England) and statistical analysis was performed with the significance threshold set at *P*=0.05, whereas the confidence intervals (CI) set at 95%. A two-arm meta-analysis based on the Der-Simonian-Laird random-effects model was used to assess the standardised weighted mean differences in dentinal tubule penetration (um) of both bioceramic-based and epoxy resin-based root canal sealers. Due to limited data available, sealers from the same origin and root sections were pooled together (Appendix 1). The effect size was calculated based on the sample



	Biod	eramic	Epoxy resin				Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total Weight IV, Random, 95% Cl			IV, Random, 95% Cl
Arikatla SK et al. 2018	205.92	114.21	10	309.55	138.22	10	16.8%	-0.78 [-1.70, 0.13]	
Chen H et al. 2017	31.82	12.41	12	34.01	9.07	12	17.4%	-0.19 [-1.00, 0.61]	
El Hachem et al. 2018	876.52	275.99	32	775.72	207.66	32	18.6%	0.41 [-0.09, 0.90]	
Sigadam A et al. 2020	1,031.91	231.58	13	656.63	175.97	13	16.8%	1.77 [0.84, 2.70]	
Toursavadkohi S et al. 2018	1,524.6	355	15	962.51	119.77	15	16.9%	2.06 [1.16, 2.97]	
Vandana G et al. 2021	1,215.66	73.65	10	937.83	74.76	10	13.6%	3.59 [2.07, 5.10]	
Total (95% CI)			92			92	100.0%	1.04 [0.02, 2.07]	•
Heterogeneity: Tau ² = 1.40; Chi ² = 43.73, df = 5 (P < 0.00001); I ² = 89%									
Test for overall effect: Z = 2.00	(P = 0.05)								Favours [Bioceramic] Favours [Epoxy resin]

Figure 2

Two-arm meta-analysis showing the weighted mean differences of dentinal tubule penetration among bioceramic-based and epoxy resin-based sealers.

size for each study that included more than one group of bioceramic-based root canal sealers, and then pooled across the groups. Furthermore, studies that evaluated dentine tubule penetration at various root sections were pooled together to obtain the overall estimated mean values. The Higgins' I^2 statistic was also used to evaluate the degree of data heterogeneity across studies, with $I^2 < 30\%$ = acceptable heterogeneity, I^{2} 30-60%=moderate heterogeneity, and I^2 >60%=substantial heterogeneity (22). Subgroup analysis was conducted to assess the effect of obturation techniques and evaluation tools on the tubular penetration depth of root canal sealers. The publication bias was detected using Egger's test.

Review data

Study Selection

A total of 4,275 articles were identified during the initial search, with 2,130 duplicates being eliminated. Subsequently, 1,993 articles were excluded based on their titles and abstracts, while 146 articles were discarded based on the inclusion and exclusion criteria following full text assessment. Finally, only 6 articles were selected for qualitative and quantitative analyses. The average Kappa score for preliminary article screening (titles and abstracts) and the second screening (fulltext assessment) was 0.73 and 0.70, respectively, indicating a 'strong' agreement (24). Figure 1 depicts the reasons for eliminating the articles.

Study Characteristics

Table 1 lists the characteristics of the in-

cluded studies, all of which were published between 2017 and 2021 and employed an *in-vitro* experimental study design. Four studies used mandibular premolars (6, 23-25), while the other two used central incisors (7, 26). Except for Toursavadkohi S *et al.* (26), all the studies used crown down techniques during cleaning and shaping. Furthermore, only two studies used a single cone approach for obturation (7, 25), whereas the other four studies used lateral condensation approach.

Risk of bias assessment

Table 2 presents the risk of bias assessment using the OHAT critical appraisal tool. All included studies were assigned a 'DL' for domains 7, 8, 9, 10 and 11. Meanwhile, all the studies were given 'PH' for both domain 2 and domain 6 due to insufficient information establishing that samples were appropriately concealed and that the investigators were blinded during the experiments. On the other hand, Domains 1 and 5 were rated as either 'PL' or 'DL'.

Statistical Analysis

The mean and standard deviation of the dentinal tubule penetration (μ m) of bioceramic and epoxy-resin based root canal sealers are shown in Table 2. Two-arm meta-analysis revealed that the overall standardised weighted mean difference of dentinal tubule penetration was 1.04 (95% CI: 0.02 to 2.07), with epoxy resin-based sealers demonstrating significantly deeper tubular penetration (P=0.05) compared to bioceramic-based sealers (Figure 2). The P of the weighted mean differences of dentinal tubule penetration was 89%, implying that the included



	Table 1
Characteristics	of the selected studies

Author	Year	Type of studies	Sample size	Tooth type	Type of final irrigation	Type of sealers	Mechanical Instrumentation	Storage condition	Thickness of sample	Tubule penetration assessment tool	Area of testing	Obturation technique	General results
Arikatla SK et al.(23)	2018	In-vitro	30	Mandibular premolars	DW	AH Plus, MTA Plus, BioRoot RCS	Protaper rotary NiTi files up to F3	100% humidity at 37 °C for 1 week	n/a	CLSM	3 mm and 6 mm from root apex	LC	AH Plus sealer has shown significantly higher depth of penetration and minimum gaps than bioceramic sealers
Chen H et al.(24)	2017	In-vitro	50	Mandibular premolars	DW	RealSeal SE, AH Plus, iRoot SP, Cortisomol	Protaper rotary NiTi files up to F3	100% humidity at 37 °C for 10 days	n/a	SEM	2, 5, and 8 mm from root apex	LC	Maximum penetration was exhibited by RealSeal SE, followed by AH-Plus, iRoot SP, and Cortisomol
Vandana G et al.(25)	2021	In-vitro	20	Mandibular premolars	DW	AH Plus, EndoSequence BC	Protaper rotary NiTi files up to F3	100% relative humidity at 37 °C for 24 hours	1 mm	CLSM	3, 6, and 9 mm from root apex	SC	EndoSequence BC showed more depth of penetration than AH Plus.
Toursavadkohi S et al.(26)	2018	In vitro	50	Central incisors	DW	AH 26, Easy-Seal, Sure-Seal	Step-back with a #40 master apical file	incubated for 2 weeks	1 mm	SEM	3 and 6 mm from root apex	LC	Tubular penetration of AH 26 sealer is less than that of Easy-Seal and Sure-Seal at 3-mm and 6-mm sections.
El Hachem et al.(7)	2018	In-vitro	96	Maxillary central incisors	DW	EndoSequence BC, AH Plus, NTS	Protaper rotary NiTi files up to F4	37 °C at 100% humidity for 2 weeks	2 mm	CLSM	1 mm and 5 mm from root apex	SC	BC Sealer and NTS demonstrated better tubule penetration results than the AH Plus sealer.
Sigadam A et al.(6)	2020	In-vitro	65	Mandibular premolars	DW	Endomethasone, AH-Plus, Roekoseal, MTA Fillapex, EndoSequence BC	Protaper rotary NiTi files up to F4	n/a	1 mm	CLSM	Coronal, middle, and apical 1/3	LC	EndoSequence BC showed the highest penetration into dentinal tubules.

n/a: not available; DW: Distilled water; CLSM: Confocal laser scanning microscope; SEM: Scanning electron microscope; LC: Lateral condensation; SC: Single cone

studies for quantitative analysis had significant heterogeneity. Sensitivity analysis (Appendix 2) was performed, and the largest and smallest weighted mean differences of dentinal tubule penetration were 250.79µm [CI: (59.68, 441.90)] and 122.00µm [CI: (-27.29, 271.29)] when Arikatla SK et al. (23) and Toursavadkohi et al. (26) were excluded, respectively. Subgroup analyses were conducted to evaluate different obturation techniques and evaluation tools on the dentinal tubule penetrations of root canal sealers (Appendix 3). No significant difference in tubular penetration depth was found when compared between single cone and lateral compaction obturation techniques (P=0.147). Nevertheless, there was a significant difference (P=0.018) in the evaluation tools, with the scanning electron microscope demonstrating greater tubular penetration than the confocal microscope. The effect of the sample sizes of each study on the dentinal tubule penetration depth was evaluated using meta-regression. There was no statistically significant difference (P=0.611), indicating that the sample size of each study had no direct effect on the degree of data heterogeneity. Egger's test using funnel plot (Figure 3) suggested that no evidence of significant publication bias was observed (P=0.06), with a fairly equal distribution of included studies on each side of the line.

Conclusions

The present systematic review and meta-analysis aimed to comprehensively



Table 2

Evidence table on the mean and standard deviation of the dentinal tubule penetration (μ m) of bioceramic and epoxy-resin based root canal sealers with the risk of bias of each included study based on JBI risk of bias assessment tool

Study	Voor	Sample	Seale	rs	Dentine 1 Penetra (mean ±	ubule tion SD)	Obturation	Evaluation	RoB (Domain)									
	Tear	group	Bioceramic- based	Epoxy resin-based	Bioceramic- based	Epoxy resin- based	Technique	Tool	1	2	5	6	7	8	9	10	11	
Arikatla SK et	2018	10	MTA Plus,		205.92	309.55		LC CLSM [וח	рн	וח	рн	וח	וח	וח	וח	וח	
al.(23)	2010	10	BioRoot RCS	AITTIUS	(114.21)	(138.22)	10					<u> </u>						
Chen H et	2017	12	iRoot SP	AH Plus	31.82	34.01	10	SEM	וח	рн	וח	рн	וח	וח	וס	וח		
al.(24)	2017	12			(12.41)	(9.07)	10					<u> </u>						
Vandana G et	2021	10	10	EndoSequence	AH Plus	1215.66	937.83	50	CLSM	PL	рн	PL	рн	DL	וח	וח	וח	
al.(25)	2021			BC	AITTIUS	(73.65)	(74.76)	30					<u> </u>					
Toursavadkohi	2018	15	Suro Soal	AH 26	1524.60	962.51		SEM	PL	PH	PL	БЦ		וח	DL	DL	DL	
S et al.(26)	2018	1.5	Sule-Seal		(355.00)	(119.77)						FII						
El Hachem et	2018	20	20	EndoSequence		876.52	775.72	80	CLEM	ы	БЦ	וח	БЦ		ы	ы		
al.(7)	2018	52	BC	ALLEIUS	(275.99)	(207.66)	30	GEOINI	L.	FII					DL			
Sigadam A et	2020	12	2 EndoSequence	AH Plus	1031.91	656.63	10	CLSM	וח	БЦ		ЬП		וח	וח			
al.(6)	2020	12	BC		(231.58)	(175.97)												

SD: standard deviation; LC: lateral condensation; SC: single cone; CLSM: confocal laser scanning microscopy; SEM: scanning electron microscopy; DH: definitely high; PH: probably high; PL: probably low; DL: definitely low. Domain 1: Was administered dose or exposure level adequately randomized?

Domain 2: Was allocation to study groups adequately concealed? Domain 5: Were experimental conditions identical across study groups?

Domain 5: Were experimental control binded to the study group during the study? Domain 7: Were outcome data complete without attrition or exclusion from analysis? Domain 8: Can we be confident in the exposure characterization?

Domain 9: Can we be confident in the outcome assessment (including blinding of assessors)?

Domain 10: Were all measured outcomes reported?

Domain 11: Were there no other potential threats to internal validity (statistical method)?





evaluate the dentinal tubule penetration of bioceramic-based root canal sealers as compared to epoxy resin-based sealers in order to provide valuable insight with reliable evidence-based findings. An excellent adaptation of filling materials to the root canal walls is required for optimal obturation which can be achieved by solidly compacting gutta-percha and sealer into a homogeneous mass (17). The creation of sealer tags into dentinal tubules may also aid in the adaptation and retention of filling material to the root dentinal wall (27). Based on the current two-arm meta-analysis, epoxy resin-based sealers showed a significantly deeper dentinal tubule penetration than bioceramic-based sealers.

The epoxy resin-based sealer used among all included primary studies was AH Plus, except for one study that used AH 26 (26). AH Plus is extensively utilised due to its physicochemical properties, simplicity of handling, and frequent use as a "gold standard" or control in several studies (7, 28, 29). The strong covalent bonds between the amino group of root dentine and the epoxy ring of resin can form micro-mechanical lock within the root dentinal walls, leading to a high bond strength of epoxy resin-based sealer (8). Several studies have found that an epoxy resin-based sealer possesses superior tubular penetration due to its high flow rate and capillary action in the dentinal tubules, permitting the sealer to be drawn into the tubules rather than by hydraulic forces induced during root canal filling (23, 24, 30, 31). However, one should highlight that epoxy-resin based sealers are hydrophobic and will shrink due to polymerisation. It was also reported that the penetration depth of epoxy resin-based sealers could have been restricted due to residual moisture in the root canal after drying (32). Hence, it is still conceivable to state that the epoxy resin-based sealer's capacity to penetrate and adapt to dentinal walls may be hampered by moisture in the root canals (33). Therefore, future studies should emphasise the manipulation of epoxy-based resin matrix to enhance its hydrophilic

characteristic and reduce shrinkage. On the other hand, bioceramic-based sealers were claimed to exhibit smaller particle size, greater fluidity, and hydrophilicity which allow them to form more sealer tags when in contact with the dentinal walls, resulting in greater sealer penetration and adaptation (27, 34). Bioceramic-based sealers have also been discovered to show high hydraulic conductivity which can form tag-like structure 'mineral infiltration zone' and obstruct dentinal tubules (1), allowing for greater bond strength and tubular penetration (35). However, such scientific theories contradict the current findings, which could be due to the methodology design, since most included studies kept the samples at 100% humidity, leading to increase the solubility of bioceramic-based sealers over epoxy resin-based sealers (36). One technique to improve the sealing capacity and tubular penetration of bioceramic-based sealers is the employment of ultrasonic activation during root canal obturation which can increase the flowability of the sealer materials (37, 38). Furthermore, the mixing procedure of root canal sealers could be a critical aspect in dentinal tubule penetration. Premixed bioceramic-based sealers displayed higher tubular penetration than the conventional powder-liquid form when compared with epoxy resin-based sealers (27, 39). Additionally, inconsistencies in results across the literature may be attributable to differences in the size and number of dentinal tubules, and evaluating specific root sections may not be a reliable way to extrapolate sealer penetration throughout the root canals (31).

Scanning electron microscope (SEM) and confocal laser scanning microscope (CLSM) are both useful assessment tools to investigate and examine features such as surface topography, porosity, and particle size of dental materials, as well as the evaluation of dentinal tubule penetration of root canal sealers (7, 23, 40). Subgroup analysis in the present review showed that SEM demonstrated greater sensitivity in detecting tubular penetra-



tion compared to CLSM. This could be due to SEM's higher magnification level, which offers more detailed information. allowing investigators to appreciate dentinal tubules and the surface appearance of sealer materials, even when tubular density is low (17, 41). However, SEM possesses several drawbacks, including a lack of accurate identification at lower magnifications and the creation of artefacts during sample preparation for analysis (41). Furthermore, novice investigators may have difficulty interpreting SEM images since it is sometimes impossible to distinguish between the dentine and sealer present in canals due to the lack of fluorescent markers (42).

Conversely, CLSM allowed optical portions beneath the surface of dentine to be viewed without the need for special specimen processing such as removing the smear layer (34, 43). Moreover, CLSM creates fewer artefacts and does not cause dehydration of the sample. It also gives a thorough image of interfacial adaption and sealer dispersion using fluorescence, allowing for adequate analysis, due to its strong contrast (44). Thus, a standardised evaluation tool that can evaluate the three-dimensional tubular penetration is warranted in the future to allow better comparability among similar studies. The present results also revealed that no significant difference was observed when comparing dentinal tubular penetration using single cone versus lateral condensation technique, implying that the obturation technique utilised may not have a direct impact on sealer penetration in the root canal. Nevertheless, it should be noted that heat may have an adverse effect on the properties of most bioceramic-based sealers, notably their flowability, setting time, and adhesion to dentinal walls (45, 46). As a result, studies that employed heat obturation approaches were excluded from the current review to mitigate bias and offer a well-standardised meta-analysis.

The strength of the current review is that it adopts a systematic approach to evaluate the currently available studies on dentinal tubule penetration among bio-

ceramic-based and epoxy resin-based root canal sealers. Despite this, clinical decision-making in providing definitive endodontic treatment remains challenging as direct extrapolation of the findings into clinical setting is not always practicable. Nevertheless, the current study also demonstrated several flaws. First, the results may be skewed due to the pooling of data from all three-thirds of the root regions. Previous studies have shown that maximum tubule penetration occurs in the root canal cervical third region, with a gradual decrease in the middle third and apical third (27, 34). This is mainly attributed to the histological characteristics of the apical root dentine, which include a high degree of sclerosis and poorly permeable dentinal structures with fewer dentinal tubules (30). Another factor to consider is the canal shape, which can range from round to oval (47). When employing the single cone obturation technique for oval-shaped canals, it has been advocated that auxiliary gutta-percha cones be used to enhance the hydraulic force in all directions and push the sealer into the tubules (48). Moreover, the number of primary studies eligible for inclusion in the current analvsis is still limited, and pooling MTA and non-MTA bioceramic sealers could lead to bias since their element compositions varied despite similar classification. The current review demonstrated greater

dentinal tubule penetration among epoxy resin-based sealers as compared to bioceramic-based sealers. Besides, greater tubular penetration was observed using scanning electron microscope, but the type of obturation technique had no effect on the penetration depth. Future well-designed studies with standardised evaluation tools and more control of confounding variables should be conducted to provide more reliable results.

Clinical Relevance

Although bioceramic-based root canal sealers are considered a promising advancement in endodontics, the current systematic review revealed that bioce-



ramic sealers demonstrated inferior tubular penetration to root dentine walls as compared to epoxy resin-based sealers. Nevertheless, the current review paves the way for future research to establish a standardised experimental methodology and clarify the clinical outcomes of using these sealers.

Conflict of Interest

All authors declare no conflicts of interest.

Acknowledgements

Not applicable.

References

- Lin GSS, Ghani N, Noorani TY et al. Dislodgement resistance and adhesive pattern of different endodontic sealers to dentine wall after artificial ageing: an in-vitro study. Odontology 2021;109:149-56.
- 2 Lin GSS, Nik Abdul Ghani NR, Noorani TY et al. Apical Sealing Ability of Different Endodontic Sealers Using Glucose Penetration Test: A Standardized Methodological Approach. Cumhuriyet Dent J 2020;23:79-87.
- 3 Abdelrahman MH, Hassan MY. A comparative evaluation of the sealing ability of two calcium silicate based sealers and a resin epoxy-based sealer through scanning electron microscopy and bond strength. Braz J Oral Sci 2021;20:e214073.
- 4 De-Deus G. Research that matters root canal filling and leakage studies. Int Endod J 2012;45:1063-4.
- 5 Nair U, Ghattas S, Saber M et al. A comparative evaluation of the sealing ability of 2 root-end filling materials: an in vitro leakage study using Enterococcus faecalis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:e74-7.
- 6 Sigadam A, Satish R K, Sajjan GS et al. Comparative evaluation of sealer penetration depth into radicular dentinal tubules using confocal scanning microscope: an in vitro study. International Journal of Dental Materials 2020;02:69-74.
- 7 El Hachem R, Khalil I, Le Brun G et al. Dentinal tubule penetration of AH Plus, BC Sealer and a novel tricalcium silicate sealer: a confocal laser scanning microscopy study. Clin Oral Investig 2019;23:1871-6.
- 8 Komabayashi T, Colmenar D, Cvach N et al. Comprehensive review of current endodontic sealers. Dent Mater J 2020;39:703-20.
- 9 Lee SJ, Monsef M, Torabinejad M. Sealing ability of a mineral trioxide aggregate for repair of lateral root perforations. J Endod 1993;19:541-4.
- 10 Al-Haddad A, Che Ab Aziz ZA. Bioceramic-Based Root Canal Sealers: A Review. Int J Biomater 2016;2016:9753210.
- 11 Raghavendra SS, Jadhav GR, Gathani KM et al. Bioceramics in endodontics - a review. J Istanb Univ Fac Dent 2017;51:S128-S37.
- 12 Mamootil K, Messer HH. Penetration of dentinal tubules by endodontic sealer cements in extracted

teeth and in vivo. Int Endod J 2007;40:873-81.

- 13 Wang Z, Shen Y, Haapasalo M. Dentin extends the antibacterial effect of endodontic sealers against Enterococcus faecalis biofilms. J Endod 2014;40:505-8.
- 14 Akcay M, Arslan H, Durmus N et al. Dentinal tubule penetration of AH Plus, iRoot SP, MTA fillapex, and guttaflow bioseal root canal sealers after different final irrigation procedures: A confocal microscopic study. Lasers Surg Med 2016;48:70-6.
- 15 Al-Haddad A, Abu Kasim NH, Che Ab Aziz ZA. Interfacial adaptation and thickness of bioceramic-based root canal sealers. Dent Mater J 2015;34:516-21.
- 16 Reynolds JZ, Augsburger RA, Svoboda KKH et al. Comparing dentinal tubule penetration of conventional and 'HiFlow' bioceramic sealers with resin-based sealer: An in vitro study. Aust Endod J 2020;46:387-93.
- 17 Sonu KR, Girish TN, Ponnappa KC et al. "Comparative evaluation of dentinal penetration of three different endodontic sealers with and without smear layer removal" - Scanning electron microscopic study. Saudi Endod J 2016;6:16-20.
- 18 Aromataris E, Fernandez R, Godfrey CM et al. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc 2015;13:132-40.
- 19 Page MJ, McKenzie JE, Bossuyt PM et al. The PRIS-MA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
- 20 McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb) 2012;22:276-82.
- 21 Office of Health Assessment and Translation (OHAT) Risk of Bias Assessment Tool [Internet]. National Toxicology Programme (NTP). [cited April 2022]. Available from: https://ntp.niehs.nih.gov/ntp/ohat/ pubs/riskofbiastool_508.pdf.
- 22 Alqaderi H, Lee CT, Borzangy S et al. Coronal pulpotomy for cariously exposed permanent posterior teeth with closed apices: A systematic review and meta-analysis. J Dent 2016;44:1-7.
- 23 Arikatla SK, Chalasani U, Mandava J et al. Interfacial adaptation and penetration depth of bioceramic endodontic sealers. J Conserv Dent 2018;21:373-7.
- 24 Chen H, Zhao X, Qiu Y et al. The Tubular Penetration Depth and Adaption of Four Sealers: A Scanning Electron Microscopic Study. Biomed Res Int 2017;2017:2946524.
- 25 Vandana G, Neelam R, Ambar W. R et al. An In Vitro Evaluation of Depth of Tubular Penetration of Ah plus and Endosequence Bioceramic Sealer: A Confocal Laser Scanning Microscopic Investigation. Ann Romanian Soc Cell Bio 2021;25:3297-306.
- 26 Toursavadkohi S, Zameni F, Afkar M. Comparison of Tubular Penetration of AH26, EasySeal, and SureSeal Root Canal Sealers in Single-Rooted Teeth Using Scanning Electron Microscopy. Journal of Research in Dental and Maxillofacial Sciences 2018;3:27-32.
- 27 Caceres C, Larrain MR, Monsalve M et al. Dentinal Tubule Penetration and Adaptation of Bio-C Sealer and AH-Plus: A Comparative SEM Evaluation. Eur Endod J 2021;6:216-20.
- 28 Viapiana R, Moinzadeh AT, Camilleri L et al. Porosity and sealing ability of root fillings with gutta-percha and BioRoot RCS or AH Plus sealers. Evaluation by three ex vivo methods. Int Endod J 2016;49:774-82.
- 29 Patil SA, Dodwad PK, Patil AA. An in vitro comparison



of bond strengths of Gutta-percha/AH Plus, Resilon/ Epiphany self-etch and EndoREZ obturation system to intraradicular dentin using a push-out test design. J Conserv Dent 2013;16:238-42.

- 30 Balguerie E, van der Sluis L, Vallaeys K et al. Sealer penetration and adaptation in the dentinal tubules: a scanning electron microscopic study. J Endod 2011;37:1576-9.
- 31 Schmidt S, Schafer E, Burklein S et al. Minimal Dentinal Tubule Penetration of Endodontic Sealers in Warm Vertical Compaction by Direct Detection via SEM Analysis. J Clin Med 2021;10:4440.
- 32 Gibby SG, Wong Y, Kulild JC et al. Novel methodology to evaluate the effect of residual moisture on epoxy resin sealer/dentine interface: a pilot study. Int Endod J 2011;44:236-44.
- 33 Lee JK, Kwak SW, Ha JH et al. Physicochemical Properties of Epoxy Resin-Based and Bioceramic-Based Root Canal Sealers. Bioinorg Chem Appl 2017;2017:2582849.
- 34 Wang Y, Liu S, Dong Y. In vitro study of dentinal tubule penetration and filling quality of bioceramic sealer. PLoS One 2018;13:e0192248.
- 35 Gandolfi MG, Silvia F, H PD et al. Calcium silicate coating derived from Portland cement as treatment for hypersensitive dentine. J Dent 2008;36:565-78.
- 36 Jafari F, Jafari S. Composition and physicochemical properties of calcium silicate based sealers: A review article. J Clin Exp Dent 2017;9:e1249-e55.
- 37 Kim JA, Hwang YC, Rosa V et al. Root Canal Filling Quality of a Premixed Calcium Silicate Endodontic Sealer Applied Using Gutta-percha Cone-mediated Ultrasonic Activation. J Endod 2018;44:133-8.
- 38 Hwang JH, Chung J, Na HS et al. Comparison of bacterial leakage resistance of various root canal filling materials and methods: Confocal laser-scanning microscope study. Scanning 2015;37:422-8.
- 39 Patri G, Agrawal P, Anushree N et al. A Scanning Electron Microscope Analysis of Sealing Potential

and Marginal Adaptation of Different Root Canal Sealers to Dentin: An In Vitro study. J Contemp Dent Pract 2020:21:73-7.

- 40 Ayad MF, Farag AM, Garcia-Godoy F. Effect of lactic acid irrigant on shear bond strength of Epiphany adhesive sealer to human dentin surface. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2010;109:e100-e6.
- 41 Chandra SS, Shankar P, Indira R. Depth of penetration of four resin sealers into radicular dentinal tubules: a confocal microscopic study. Journal of endodontics 2012;38:1412-6.
- 42 Patel D, Sherriff M, Ford TP et al. The penetration of RealSeal primer and Tubliseal into root canal dentinal tubules: a confocal microscopic study. Int Endod J 2007;40:67-71.
- 43 Jeong JW, DeGraft-Johnson A, Dorn SO et al. Dentinal Tubule Penetration of a Calcium Silicate-based Root Canal Sealer with Different Obturation Methods. J Endod 2017;43:633-7.
- 44 Song D, Yang SE. Comparison of Dentinal Tubule Penetration between a Calcium Silicate-Based Sealer with Ultrasonic Activation and an Epoxy Resin-Based Sealer: A Study Using Confocal Laser Scanning Microscopy. Eur J Dent 2022;16:195-201.
- 45 Eid D, Medioni E, De-Deus G et al. Impact of Warm Vertical Compaction on the Sealing Ability of Calcium Silicate-Based Sealers: A Confocal Microscopic Evaluation. Materials (Basel) 2021;14:372.
- 46 Qu W, Bai W, Liang YH et al. Influence of Warm Vertical Compaction Technique on Physical Properties of Root Canal Sealers. J Endod 2016;42:1829-33.
- 47 Celikten B, Uzuntas CF, Orhan AI et al. Evaluation of root canal sealer filling quality using a single-cone technique in oval shaped canals: An In vitro Micro-CT study. Scanning 2016;38:133-40.
- 48 McMichael GE, Primus CM, Opperman LA. Dentinal Tubule Penetration of Tricalcium Silicate Sealers. J Endod 2016;42:632-6.