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SYSTEMATIC REVIEW

Activated Irrigation vs. Conventional non-activated Irrigation in Endodontics – A Systematic Review

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ABSTRACT

Objective: Irrigant activation has been claimed to be beneficial in in vitro and clinical studies. This systematic review aims to investigate the clinical efficiency of mechanically activated irrigants and conventional irrigation.

Methods: A literature search (PROSPERO registration number: CRD42018112595) was undertaken in PubMed, Cochrane and hand search. The inclusion criteria were clinical trials, *in vivo/ex vivo* on adult permanent teeth involving an active irrigation device and a control group of conventional irrigation. The exclusion criteria were studies done in vitro, animals and foreign language. Adult patients requiring endodontic treatment of permanent dentition and irrigant activation during the treatment were chosen as the participants and intervention respectively.

Results: After removal of duplicates, 89 articles were obtained, and 72 were excluded as they did not meet the selection criteria. 6 devices (EndoVac, EndoActivator, Ultrasonic, MDA (manual dynamic agitation), CUI (Continuous Ultrasonic Irrigation) and PUI (Passive Ultrasonic Irrigation)) and 6 variables of interest (Post-operative pain, periapical healing, antibacterial efficacy, canal and/or isthmus cleanliness, debridement efficacy and delivery up to working length) were evaluated in the 17 included articles. The risk of bias and quality of the selected articles were moderate. Results showed that mechanical active irrigation reduces post-operative pain. It improved debridement, canal/isthmus cleanliness. It also improved delivery of irrigant up to working length. Bacterial count was more with active irrigation, though not significant. There is no effect on long-term periapical healing.

Conclusion: It may be concluded that mechanical active irrigation devices are beneficial in reducing post-operative pain and improving canal and isthmus cleanliness during Endodontics.

Keywords: Active irrigation, continuous ultrasonic irrigation, EndoActivator, EndoVac, passive ultrasonic irrigation, ultrasonic irrigation, manual dynamic agitation

HIGHLIGHTS

- Irrigant activation proves to be beneficial, in terms of post-operative pain intensity, debridement and canal & isthmus cleanliness. However, no significant benefit can be proved with the available evidence, for activation in terms of antibacterial effect and long term healing of lesions.

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INTRODUCTION

Root canal irrigation plays a pivotal role in Endodontics, to facilitate instrumentation by lubrication, remove debris, microorganisms, smear layer and prevent apical debris packing. Irrigants exert their effects, by mechanical, chemical and biological actions (1). On the mechanical front, streaming forces are delivered to the canal walls. On the chemical front, the active components exert specific actions on the organic and inorganic debris. On the biological front, the antimicrobial action on the organisms in the canal help inactivate or kill them. Root canals are considered "closed systems" (2) where the fluid dynamics of the irrigant plays a major role in ensuring optimal actions. This "irrigation dynamics" (1) refers to how they flow, penetrate and exchange within the root canal walls. Conventional irrigation methods, at best deliver irrigant just 1mm beyond the needle tip. This may help microbes thrive after treatment in the safe havens of root canals, namely the lateral, accessory canals, fins, isthmii and anastomoses. Hence to improvise the cleansing effectiveness of irrigants and thorough removal of microbes, many activation devices are being used.

Activated irrigation may be defined as using a method to agitate and improve the flow of irrigants to the intricacies of root canal system by mechanical or other energy forms. While conventional

irrigation purely depends on the positive pressure of injection and the viscosity of the irrigant to flow in the root canal system. There are many mechanical irrigant activation systems available in the market. Some of them use ultrasonic activation by high frequency (3-6) or low frequency (EndoActivator), or continuous ultrasonic irrigation (CUI) (7), special holding device during ultrasonic like Nusstein's needle holding device (8-10) or sonic energy (RispiSonic file) (3), mechanical brushing actions (Ruddle brush) (4), Canal brush (5) to achieve the activation while others use vibrations (Vibringe) (8), or passive ultrasonic irrigation (PUI-IrriSafe) (9) and positive or negative pressure alternating devices (EndoVac) (11), (RinsEndo) (12) or simply using a technique to manually agitate the irrigant with a high amplitude/frequency (MDA) (13). The irrigation efficacy depends as much on the mode of delivery (1, 14) as the irrigant (15).

Smear layer often is obstinate for removal offering a niche for microbes to thrive post-treatment. Micro brush developed by Ruddle helps in mechanically removing this by its intimate contact with canal irregularities, though it is commercially unavailable. Canal Brush developed by Coltene (Whaledent) is equipped with still smaller bristles to reach curvatures and has the ability to clean the canal even before instrumentation. Complexities of root canal often pose challenge to thorough debridement and Durr Dental introduced RinsEndo to achieve this by hydrodynamic phenomenon of efficient fluid exchange combined with suctioning device. GentleWave delivers a vortex of irrigant that removes debris and smear layer from canal walls. It is a continuous irrigation system (16). Self-contained fluid delivery units like Quantec E (17), promotes debridement during rotary instrumentation by agitation, greater contact with & penetration of irrigant in the walls. Vibringe is a cordless Sonic irrigant delivery cum activation unit, that reduces the overall time and ensures thorough contact of irrigant with the entire canal. Nusstein's needle holding device enables attachment of 25G needle instead of endosonic file to Ultrasonic handpiece. This ensures powerful irrigant activation without breakage of needle. Developed by MicroMega, the Sonic irrigant activation by RispiSonic file, that possesses non-uniform taper, enables activation after preparation. Barbs engage the canal walls to facilitate cleaning. Vertical vibrations delivered by SAF (18), ensures supreme level of cleaning by scrubbing action and disinfection as the file adapts well to the canal walls. Manual Dynamic Agitation (MDA) was introduced by Gu et al. in 2009 (13). The guttapercha cone is used to activate the irrigant manually by delivering at least 100 push/pull stroke/min. This was shown to remove apical vapor lock, improve debridement, cleanliness and antimicrobial action of irrigants.

These activated irrigant delivery systems claim improved irrigant transfer, debridement, minimal periapical extrusion and removal of smear layer or biofilm. Many in vitro and tooth model studies support these claims. However, only clinical studies can elucidate their advantages or superiority over conventional irrigation. Clinical efficiency may be defined as the ability of a clinical procedure to achieve best results in the shortest possible time. While clinical usefulness may be defined as the ease with which a clinical procedure may be performed by both experienced and novice clinicians. Hence this systematic review was undertaken to understand the effectiveness of mechanical irrigant activation devices compared to conventional irrigation methods as reported by published literature of clinical studies.

Objectives

"Are mechanical active irrigation devices clinically beneficial than conventional manual irrigation methods in Endodontics?" was formed to undertake this systematic review which was done according to PRISMA guidelines given in PRISMA checklist (Table 1).

MATERIALS AND METHODS

PICOs

P-Population

Endodontic therapy or root canal treatment or root canal therapy or RCT or endodontic management or endodontic procedure and their synonyms were used.

I-Intervention

Active irrigation or activated irrigation devices or machine assisted or rotary brushes or ruddle brush or canal brush or Quantec E. Other device names and synonyms were used.

C-Comparison

Manual irrigation devices or manual irrigation or syringe irrigation or needles or cannulas or end venting or side venting. Other device names and synonyms were used.

O-Outcomes

Beneficial or adverse reaction or time consumption or ease of use or favourable or good or antimicrobial efficacy. Other synonyms were also used.

S-Study design

Randomized controlled trials, clinical studies (*in vivo*/*ex vivo* studies).

Protocol and registration

This systematic review was done according to PRISMA guidelines and was registered in the PROSPERO (Centre for Reviews and Dissemination, University of York; http://www.crd.york.ac.uk/PROSPERO). Registration number - CRD42018112595.

Eligibility criteria

Healthy adult (16-89 years) (14) patients requiring endodontic treatment were included in the studies selected without any gender or socio-economic discrimination.

Studies in which atleast any one mechanical active irrigation device and one conventional irrigation system has been evaluated were selected.

Studies in which any one or more of the various outcome measures like, reduction in post-operative pain, reduction in cultivable bacteria, canal cleanliness, isthmus cleanliness, debris removal, apical debris extrusion, delivery of irrigant to full working length and long term effects on healing and success were selected.

Randomized controlled trials, clinical studies (*in vivo* and *ex-vivo*) were only selected.

TABLE 1. PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2; Separate document
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	10
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	11
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12

TABLE 1. Cont.

Section/topic	#	Checklist item	Reported on page #
Limitations	25	Discuss limitations at study and outcomelevel (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

Follow up was done from 4h (14, 19) to 19mo (20, 21) in the selected studies.

The search included all studies without any limits for the start date (oldest available literature). Studies reported till June 2019 were included. Articles published in English language or translation available in English, were only selected. Conference proceedings, personal communications and other unpeer-reviewed literature were not included.

Information sources
Pubmed (www.ncbi.nlm.nih.gov) and Cochrane (www.cochranelibrary.com) databases were searched for eligible literature from the oldest available publication till 11th June 2019.

Search
An advanced literature search of all publications was performed without year limit.

Study selection
The databases were searched for relevant publications with the title, abstract and Medical Subject Headings and key words and their combinations as follows: Endodontic therapy OR endodontic treatment OR root canal therapy OR root canal treatment OR RCT OR endodontic procedure (and other synonyms) AND activation device OR active irrigation OR activated irrigation OR active irrigation device OR machine assisted irrigation OR Ruddle Brush OR Canal Brush OR EndoVac OR EndoActivator OR RispiSonic OR Ultrasonic OR Sonic OR passive ultrasonic irrigation OR PUI OR Vibringe OR IrriSafe OR Quantec E OR Self Adjusting File OR SAF OR RinsEndo OR Nusstein's needle holding device OR Gentle Wave (and other synonyms) AND manual irrigation OR needle irrigation OR conventional irrigation OR syringe irrigation OR cannulae OR side vented needles OR end vented needles (and other synonyms) AND Effective OR Efficient OR efficacy OR Cost effective OR beneficial OR adverse reaction OR good OR better OR debriding efficacy OR debris loosening OR antibacterial OR post-operative pain OR post-operative discomfort OR inter-appointment pain OR inter-appointment flare-up OR irrigant extrusion OR debris extrusion OR smear layer removal efficacy OR biofilm removal ability OR apical extrusion OR antimicrobial (and other synonyms). The yielded articles were further assessed after securing full-text and eliminating duplicates. The titles and abstracts were thoroughly screened and they were either included or excluded based on the inclusion criteria: only clinical studies (*in vivo, ex-vivo* and randomized controlled trials) on adult population (permanent teeth) were included; in vitro studies, studies on paediatric patients or deciduous teeth and animal studies were excluded. Studies on Photo or laser activation of irrigants, namely photodynamic therapy (PDT), laser activated irrigation (LAI), photo activated irrigation (PAI), photo activated disinfection (PAD), photo activated chemotherapy (PACT), light activated therapy (LAT), light activated disinfection (LAD), photon induced photo acoustic streaming/ photo activated systems technology (PIPS/PHAST) were also excluded as they significantly differed from the other systems in their activation principle. In photo/laser activated irrigation, light energy exerts its effects in cleaning and inactivating microbes without necessarily improvising the flow of irrigants to the intricacies of root canal system.

Data collection process
The following data were extracted from the included studies: sample size, type of teeth included, activation devices used, controls used, primary outcome results, follow up if applicable and any other secondary inferences.

Data items
Reduction in post-operative pain, reduction in cultivable bacteria, canal cleanliness, isthmus cleanliness, debris removal, apical debris extrusion, delivery of irrigant to full working length and long term effects on healing and success were the variables of interest that were sought for in the selected articles. No assumptions or simplifications were made. The study was fully self-funded by the investigators.

RESULTS

Study selection
The number of studies that were screened, assessed for eligibility and included in the review as well as the studies that were excluded with reasons at every stage have been presented in the flow-chart (Fig 1). A total of 89 articles were retrieved for evaluation after initial search and elimination of duplicates. Of these 35 were done in vitro and hence excluded. Of the 54 articles screened, another 35 were excluded after abstracts were read, as they were done either on animals, or paediatric patients or deciduous teeth or irrelevant to the research question. Of the 19 articles, 2 were excluded as their English translation could not be obtained.

Study characteristics
The data that were extracted regarding study size, PICOS, methodology, type of activation device used, controls used

and variables of interest are presented in Table 2. A total of 6 variables of interest had been evaluated in them. The detailed description of the irrigation devices used is given in Table 3.

Risk of bias within studies

The major and minor criteria for risk of bias are presented in Tables 4a and 4b. The risk of bias was categorized as major and minor and assessed; blinding, method of randomization, allocation concealment and drop-out rate for major; baseline comparison, sample size justification, methodology error and inclusion/exclusion criteria for minor criteria. The risk of bias (average of major and minor criteria) was classified for the selected articles as 3/high (6, 21-26), 2/moderate (20, 27-29) and 1/low (7, 14, 19, 30-32).

Results of individual studies

Heterogeneity of the selected articles prevented calculation of estimates and confidence intervals. However, simple summary data of outcome measure, follow-up and any additional inferences for the intervention groups are presented in Table 5.

Synthesis of results

Quantitative analysis could not be done due to the heterogeneity of results. 6 activation devices/techniques had been evaluated in the 17 selected articles. 6 articles evaluated post-operative pain, 5 evaluated debridement efficacy, canal & isthmus cleanliness, 4 evaluated antibacterial efficacy, 2 evaluated periapical healing as evidenced by radiographic evaluation and 1 evaluated delivery of irrigant up to working length. Post-operative pain reduced significantly by using activated irrigation. Debridement efficacy, canal & isthmus cleanliness and delivery of irrigant to working length were superior in activated irrigation. There was no significant effect on periapical healing with and without activation. Bacterial growth actually increased with activation, though not significant according to 3 articles but 1 study differed, in that activated irrigation was found to be more antimicrobial than conventional.

Risk of bias across studies

Risk of bias and quality assessment across the studies, are presented in Table 6. No publication bias or selective reporting could be identified that could affect the cumulative evidence. After data extraction, the quality assessment of the articles was done according to CEBM evidence ranking based on sample size calculation, randomization, allocation concealment, inclusion/exclusion criteria, blinding, drop-out rate and adequacy of follow-up. The CEBM evidence level ranged between 2 (6, 7, 14, 19, 20, 23-27, 28, 29-32) and 3 (21, 22) for the included articles.

Summary measures

The active irrigation devices used in the selected studies were found to be more effective than conventional irrigation in 12 of the 17 studies. However, there was no difference in the effectiveness in 2 studies. Conventional irrigation was found to be better in 3 studies.

DISCUSSION

Summary of evidence

This review discussed the benefits of activated irrigation over conventional irrigation in terms of clinical efficiency. There

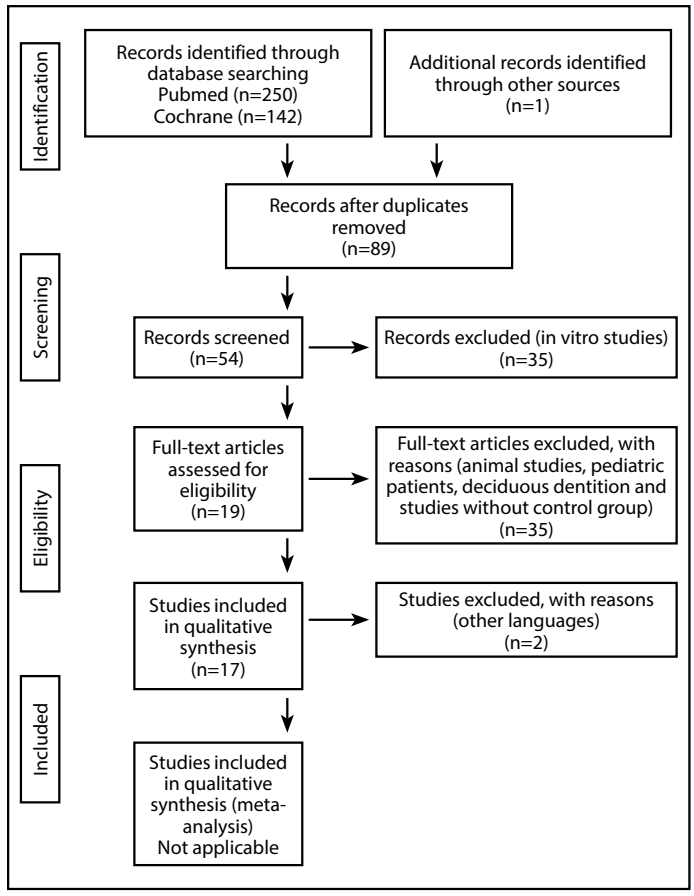

Figure 1. PRISMA 2009 Flowchart
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

are more than 13 different activation devices in the market, yet only 6 have been clinically evaluated and reported at the time of this review. Ultrasonic was the most often reported activation device followed by EndoVac. Three articles reported about EndoActivator and one about MDA. Overall, the activation devices are significantly better than conventional irrigation in one or more parameters evaluated. It appeared that long-term benefits of using activated irrigation over conventional one is negligible as evidenced by radiographic evaluation of periapical healing (20, 21) and post-operative pain after 2 days (7, 14, 31, 32).

In both studies on healing, ultrasonic unit was used as the activation device. Mechanically activated irrigation appears to benefit short term parameters like post-operative pain in the first 48h. EndoActivator, (19, 32) EndoVac (14, 31) MDA (32) and Ultrasonic (7, 21) were used in the studies on post-operative pain. Debridement (EndoVac) and cleanliness (Ultrasonic) are superior with activated irrigation according to the selected articles. The evidence for irrigant delivery up to WL (PUI and EndoVac), appears scarce as only 1 article evaluated this parameter.

The 6 systems included in this review are described in Table 3. Simultaneous Ultrasonic instrumentation and irrigation was introduced as early as 1980 by Martin (33). The high frequency

TABLE 2. Study details of articles included in data synthesis

S. no:	Author/year	Sample size	Devices tested	Control used	Parameters evaluated (variables of interest)	Methodology
1	Haidet et al. 1989	60	CaviEndo-Ultrasonic	Standard syringe	Canal & Isthmus Cleanliness	Histological preparation after sectioning of apical 1-3mm; Gomori's one step trichrome method of staining;
2	Archer et al. 1992	42	EnacOsada-Ultrasonic	Standard syringe	Canal & Isthmus Cleanliness	Histological preparation after sectioning of apical 1-3mm; 5µ sections; 0.1mm interval; Gomori's one step trichrome method of staining;
3	Gutarts et al. 2005	36	MiniEndo-Ultrasonic	Standard syringe	Canal & Isthmus Cleanliness	Histological preparation after sectioning of apical 1-3mm; 5µ sections; 0.2mm interval; Gomori's one step trichrome method of staining;
4	Burleson et al. 2007	48	Ultrasonic needle-Mini Endo unit with Aladdin mechanical pump	Syringe (not specified) with Aladdin mechanical pump	Canal and isthmus cleanliness	Histologic preparation and Brown & Brenn staining of cross-sections from the 1-3 mm apical levels; 5µ sections; 0.2mm interval; evaluated for percentage of biofilm/ necrotic debris removal.
5	Carver et al. 2007	31	MiniEndo-Ultrasonic	Standard syringe	Antibacterial efficacy	Brucella Blood Agar; Anaerobic chamber; CFU counting using operating microscope
6	Huffaker et al. 2010	84	Endo Activator	Syringe with 27 Gauge side vent needle	Anti-bacterial efficacy	Anaerobic tube turbidity test at 1 week using bacteriologic sampling of root canals.
7	Gondim et al. 2010	110	EndoVac	Max-I-probe	Post-Operative Pain	Pain levels were assessed at 4h, 24h and 48h according to Borg scale 0-10.
8	Siu et al. 2010	47	EndoVac	Syringe (not specified)	Debridement efficacy	Six histological slides of each 6µm thickness were made from sections at 1 and 3 mm from WL and stained. The slide with the most debris was photographed at each level for each tooth. Median amount of debris at 1mm and 3 mm were assessed.
9	Munoz et al. 2012	30	EndoVac, PUI- IrriSafe	Monoject syringe	Delivery of irrigant to working length (WL) of root canals	Canals were irrigated with 1 ml of IOHEXOL (radiopaque solution) by using the assigned irrigation systems was done and a digital radiograph was taken. With the aid of image editing software the distance between WL and maximum irrigant penetration was measured.
10.	Pawar et al. 2012	52	EndoVac	Syringe with 27-gauge side vented Monoject stainless steel needle	Anti-bacterial efficacy	Anaerobic tube turbidity test at 1 week using bacteriologic sampling of root canals
11.	Paiva et al. 2012		PUI	2% CHX in NaviTip syringe	Antibacterial efficacy	Culturing & PCR; bacteria, archaea & fungi;
12.	Liang et al. 2013	105	Ultrasonic activation	NaviTip 30 Gauge needle	Radiographic evaluation of periapical healing	Ten to 19 months after treatment, the teeth were examined by using Periapical radiography and CBCT. Absence and reduction of the periapical radiolucency were analyzed.

TABLE 2. Cont.

S. no:	Author/year	Sample size	Devices tested	Control used	Parameters evaluated (variables of interest)	Methodology
13.	Ramamoorthy et al. 2015	110	Endo Activator	Syringe with 27 gauge open ended needle	Post-Operative Pain	Pain levels were assessed according to Visual Analogue Scale (VAS). Score (Range 0-7) at 8h, 24h and 48h.
14.	Tang et al. 2015	300	Ultrasonic activation	Syringe (not specified)	Post-Operative Pain and Periapical healing through radiographic follow up	Pain levels were assessed at 24 hours, 6months and 12 months after irrigation protocol according to VAS. Score 0-3. Clinical effective rates were calculated according to PAI (Peri apical index) and Clinical examination
15.	Middha et al. 2017	70	CUI-ProultraPiezoflow	27 gauge needle	Post-operative pain	VAS scale; every day for 1-7days;
16.	Topcuoglu et al. 2018	116	EndoVac	NaviTip syringe	Post-operative pain	VAS scale; 6, 24, 48 & 72h; 1 week;
17.	Topcuoglu et al. 2018	168	EndoActivator, PUI & MDA	NaviTip syringe with side-port needle	Post-operative pain	VAS scale; 6, 24, 48 & 72h; 1 week;

TABLE 3. Description of the devices tested in this review

Name of the devices	Manufacturer	Description of mechanism of action
Ultrasonic Activation- CaviEndo	Dentsply International/York/PA/.USA	First ultrasonic unit designed for both prophylaxis and endodontics. It is a magnetostrictive ultrasound unit. It has a switch, prophy/endo mode selection switch, power control dial with LED indicators, water supply control dial with LED indicators, Air pressure valve window.
Ultrasonic Activation- OsadaEnac	ENAC/USA	It's an ultrasonic endodontic system based on Quartz Piezoelectric vibrator system. It is automatically tuned to provide stable 30KHz ultrasonic oscillation. It has a handpiece-hose assembly, handpiece holder, footswitch, water hose with filter & connector. Simultaneous root canal enlargement with U files and swirling irrigation for debridement, root canal obturation without water, restoration removal, flush cleaning of periodontal pockets and pits& fissures, root-end preparations with angled diamond coated files are the functions of this unit.
CUI- Ultrasonic Activation- Proultra PiezoFlow	Dentsply Tulsa Dental Specialties, Tulsa, OK/USA	This unit is designed to deliver continuous irrigation. It provides superior cleaning power by facilitating introducing irrigants into root canal structure, dentinal tubules & isthmuses. It can disrupt biofilms. It enhances the action of NaOCl even if applied for 1min.
Ultrasonic Activation- Mini Endo Unit	SybronEndo/USA/	The MiniEndo II is a compact ultrasonic cleaning unit designed specifically for endodontic applications. It is operated and controlled by microprocessors designed to deliver just the right amount of power and amplitude at the tip to successfully complete endodontic procedures.
PUI- IrriSafe	Satelec (R&D), France	Its exclusive design helps to remove the smear-layer and to kill the bacteria, even in difficult-to-reach areas (apical third) or in curved canals. It can be used safely, without any risk of damaging the apical structure. Driven by the Newtron range of piezoelectric generators, IrriSafe generates micro-cavitation and micro-currents that spread through the canal system. The thinnest diameter is recommended for the

TABLE 3. Cont.

Name of the devices	Manufacturer	Description of mechanism of action
		majority of the clinical cases (IRR 20), the largest instrument can be used for the treatment of juvenile canals (IRR 25). The instrument should vibrate freely inside the root canal lumen. IrriSafe is available in two lengths, from IRR20/21 or IRR20/25 and, IRR25/21 or IRR25/25. IrriSafe is inserted 2 mm short of the working-length and it can be pre-shaped, if necessary. 20 ml of the irrigant solution is injected into the canal with a syringe. IrriSafe is activated for 10 seconds, at the recommended color coded power level moving the instrument with a ¼-pull-stroke and backwards: it drives the debris and the smear layer back to the surface.
MDA	NA	This is not a gadget, but a method of manually activating irrigant using GP cones with 100 push/pull/min amplitude.
EndoActivator	Dentsply Tulsa Dental Specialties, Tulsa, OK/USA	The EndoActivator is designed to safely and vigorously energize intracanal irrigants using sonic energy. It has strong, flexible medical grade uncoated & non cutting polymer tips for Single patient use. It creates fluid hydrodynamics, improves debridement and the disruption of the smear layer and biofilm
EndoVac	Discus Dental, Culver City, CA	The EndoVac system is regarded as an apical negative pressure irrigation system composed of three basic components: A Master Delivery Tip (MDT), the Macrocannula, and the Microcannula. The MDT delivers irrigant to the pulp chamber and evacuates the irrigant concomitantly. Both the macrocannula and microcannula are connected via tubing to a syringe of irrigant and the highspeedsuction of a dental unit. The Macrocannula is made of sflexible polypropylene with an open end of 0.55 mm in diameter, an internal diameter of 0.35 mm, and a 0.02 taper, used to suction irrigants up to the middle segment of the canal. Lastly, the Microcannula is made of stainless steel and has 12 microscopic holes disposed in four rows of three holes, laterally positioned at the apical 1 mm of the cannula. Each hole is 0.1 mm in diameter, the first one in the row is located 0.37 mm from the tip of the microcannula, and the distance between holes is 0.2 mm. The microcannula has a closed end with external diameter of 0.32 mm can be used in canals that are enlarged to size 35 or larger, and should be taken to the working length (WL) to aspirate irrigants and debris. During irrigation, the MDT delivers irrigant to the pulp chamber and siphons off the excess irrigant to prevent overflow. The cannula in the canal simultaneously exerts negative pressure that pulls the irrigant from its fresh supply in the chamber by the MDT, down the canal to the tip of the cannula, into the cannula, and out through the suction hose. Thus, a constant flow of fresh irrigant is being delivered by negative pressure to working length.

TABLE 4a. Major criteria for Risk of bias assessment for selected articles

S. No:	Reference	Method of randomization	Allocation concealment	Blinding	Drop out rate
1	Haidet et al. 1989	Yes	Not mentioned	Single	NA; 1.7% due to loss of tooth during sectioning
2	Archer et al. 1992	Yes	Not mentioned	Not mentioned	No drop-out
3	Gutarts et al. 2005	Yes	Not mentioned	Single	No drop-out
4	Burleson et al. 2007	Yes	No	Single	No drop-out
5	Carver et al. 2007	Yes	Not mentioned	Single	No drop-out
6	Gondim et al. 2010	Yes	Yes	Double	No drop-out
7	Huffaker et al. 2010	Yes	No	Double	NA; 11.9% due to loss of tooth during sectioning
8	Siu et al. 2010	Yes	No	Single	No
9	Munoz et al. 2012	No	No	No	No
10.	Pawar et al. 2012	Yes	Yes	Single	No
11.	Paiva et al. 2012	Yes	No	Not mentioned	6.25%
12.	Liang et al. 2013	Yes	No	No	No
13.	Ramamoorthi et al. 2015	Yes	Yes	Single	Yes
14.	Tang et al. 2015	No	No	No	No
15.	Middha et al. 2017	Yes	Yes	Not mentioned	No drop-out
16.	Topcuoglu et al. 2018	Yes	Not mentioned	Single	2.6%
17.	Topcuoglu et al. 2018	Yes	Not mentioned	Single	No drop-out

TABLE 4b. Minor criteria for Risk of bias assessment for selected articles

S. No:	Reference	Sample justified	Baseline comparison	Inclusion/exclusion criteria	Method error
1	Haidet et al. 1989	Yes	Yes	Yes	No
2	Archer et al. 1992	Yes	Yes	Yes	No
3	Gutarts et al. 2005	Yes	Yes	Yes	No
4.	Burleson et al. 2007	No	Not applicable	Yes	No
5	Carver et al. 2007	Yes	Yes	Yes	No
6.	Siu et al. 2010	No	Not applicable	Yes	No
7.	Huffaker et al. 2010	No	Yes	Yes	No
8.	Gondim et al. 2010	Yes	Yes	Yes	No
9.	Munoz et al. 2012	No	Yes	Yes	No
10.	Pawar et al. 2012	No	Yes	Yes	No
11.	Paiva et al. 2012	Yes	Yes	Yes	No
12.	Liang et al. 2013	No	Yes	Yes	No
13.	Ramamoorthi et al. 2015	Yes	Yes	Yes	No
14.	Tang et al. 2015	No	Yes	Yes	No
15.	Middha et al. 2017	Yes	Yes	Yes	No
16.	Topcuoglu et al. 2018	Yes	Yes	Yes	No
17.	Topcuoglu et al. 2018	Yes	Yes	Yes	No

and low amplitude of ultrasonic energy effectively delivers and activates the irrigant to loosen debris and bacteria from canal walls. Introduced by Ruddle, Sharp and Machtou, EndoAcivator is based on Sonic energy and agitates irrigant vigorously to disrupt smear layer and biofilm by hydrodynamic phenomenon resulting in cavitation and acoustic streaming. This results in deep cleaning and disinfection. Kerr introduced EndoVac which is the pioneer in apical negative pressure generation to pull the irrigant down the root canal, then up using micro cannula placed as close as 0.2 mm from apex and macro cannula placed at coronal one third of the canal and delivery of irrigant using master delivery tip. Further, the micro-pores in the cannulae ensure thorough cleaning of canal walls and accessory canals and prevention of clogging. IrriSafe is a Passive ultrasonic irrigation system that facilitates transmission of micro currents and cavitation to the irrigant with its blunt tip. It removes smear layer, microorganisms and debris without violating apical constriction. Further when PUI is used, a smooth oscillating wire transmits the energy to the irrigant by ultrasonic wave (28, 30, 22). This produces a stream and cavitation, which helps in reducing deformities in the canal walls. The irrigant flow may be chosen as either continuous or intermittent (34). According to one study, debris elimination was significantly higher in PUI groups and no differences were found between irrigating solutions or Irrisafe tip size. The study concluded that Irrigation with conventional syringe in the initial preparation stage, followed by 10% EDTA and a final phase of passive ultrasound irrigation (PUI) with intermittent flush and Irrisafe tips, is effective for cleaning root canals, independently of the use of CHX or NaOCl as final irrigant (35).

Endodontic irrigants may extrude and cause pain both intra and post-operatively affecting the overall quality of the treatment. The incidence is approximately 30% (36). Though extrusion of irrigant is the main reason for post-operative pain, conventional needle irrigation delivers irrigant just 1 mm beyond

TABLE 5. Outcome assessment

Author	Variables of Interest assessed	Evaluation period for outcome assessment & Outcome							
		Immediate	4h	8h	24h	2W	6 Mo	10-19 Mo	12 Mo
Haidet et al. 1989	Canal cleanliness Isthmus cleanliness	1mm-Ultrasonic>Syringe 3mm-Ultrasonic=Syringe 1&3mm- Ultrasonic> Syringe							
Archer et al. 1992	Canal cleanliness Isthmus cleanliness	Ultrasonic>Syringe							
Gutarts et al. 2005	Canal cleanliness Isthmus cleanliness	1mm-Ultrasonic>Syringe 3mm-Ultrasonic=Syringe 1&3mm-Ultrasonic> Syringe							
Burleson et al. 2007	Canal cleanliness	syringe vs. ultrasonic 1mm: 33% vs. 83%; 2mm: 31% vs. 86%; 3mm: 45% vs. 91%.							
	Isthmus cleanliness	1mm: 80% vs. 95%; 2mm: 92% vs. 99%; 3mm: 95% vs. 100%							
Carver et al. 2007	Antibacterial efficacy	Ultrasonic – 80%-ve culture; Syringe–20% -ve culture CFU-Ultrasonic<Syringe							
Siu et al. 2010	Median amount of debris	3mm: EV: 0.09% S: 0.07%. 1mm: EV: 0.05% S: 0.12%							
Huffaker et al. 2010	Cultivable bacteria	S: 52% EA : 60%							
Gondim et al. 2010	Post-operative pain (Borg)		MP: 1.72 EV: 0.39			MP: 1.45 EV: 0.31	MP: 0.50 EV: 0.18		
Munoz et al. 2012	Mean distance from irrigant delivery to WL	M: 1.51 +- 0.43 mm EV: 0.42 +-0.30 mm PUI: 0.21+-0.25 mm							
Pawar et al. 2012	Microbial growth	EV: 17.4% S: 9.1 %							

TABLE 5. Cont.

Author	Variables of Interest assessed	Evaluation period for outcome assessment & Outcome								
		Immediate	4h	8h	24h		2W	6 Mo	10-19 Mo	12 Mo
Paiva et al. 2012	Antimicrobial efficacy	Culture- CHX Syringe -14% +ve ; PUI–23% +ve; PCR- CHX Syringe-43% +ve ; PUI–54% +ve;								
Liang et al. 2013	Reduction of lesion								Ultrasonic 95.1 % Syringe 88.4%.	
Ramamoorthy et al. 2015	Post-operative pain (VAS) Mean pain score			EN: 5.4 EA: 3.7		EN: 3.1 EA: 1.4	EN: 0.8. EA: 0.3			
Tang et al. 2015	Post-operative pain (VAS & customized grading)					Ultrasonic with NaOCl: (n=120): 0 (n=99); 1 (n=15), 2 (n=4), 3 (n=2) Ultrasonic with Active Ag^{++}: (n=122): 0 (n=103), 1 (n=14), 2 (n=4), 3 (n=1) Syringe: (n=188): 0 (n=71), 1(n=26), 2 (n=17), 3(n=4)				
	Clinical effective rates according to PAI:							Ultrasonic with NaOCl: 80.83% Ultrason-ic with Active Ag^{++}: 81.15% Syringe: 74.58%		Ultrasonic with NaOCl:85% Ultrasonic with Active Ag^{++}: 88.52% Syringe: 77.97%
Middha et al. 2017	Post-operative pain					CUI – 31% Syringe – 51%	No difference	No difference	No difference	
Topcuoglu et al. 2018	Post-operative pain				6h: Syringe>EV	24h: Syringe>EV	48h: Syringe>EV	72h: No difference	1w: No difference	
Topcuoglu et al. 2018	Post-operative pain				6h: MDA>other groups	24h: MDA>other groups	48h: No difference	72h: No difference	1w: No difference	

EN: Endodontic needle, EA: EndoActivator, NaOCl: Sodium hypochlorite, VAS: Visual analog scale, PAI: Periapical index, MP: Max I probe, S: Syringe, M: Monoject, PUI: Passive ultrasonic irrigation, MDA: Manual dynamic agitation, CUI: Continuous ultrasonic irrigation

TABLE 6. Risk of bias and quality assessment across studies

S. No:	Reference	Randomization	Allocation concealment	Blinding	Inclusion/ exclusion criteria	Completeness of follow up	Sample size calculation	CEBM Level of evidence	Risk of bias Cumulative risk (Average of Major and Minor criteria)
1	Haidet et al. 1989	Yes	No	No	Yes	NA	Not mentioned	2	3 (high)
2	Archer et al. 1992	Yes	No	No	Yes	NA	Not mentioned	2	3 (high)
3	Gutarts et al. 2005	Yes	No	No	Yes	NA	Not mentioned	2	3 (high)
4	Burleson et al. 2007	Yes	No	Yes	Yes	NA	Not mentioned	2	2 (moderate)
5	Carver et al. 2007	Yes	No	No	Yes	NA	Not mentioned	2	3 (high)
6	Siu et al. 2010	Yes	No	Yes	Yes	NA	Not mentioned	2	2 (moderate)
7	Huffaker et al. 2010	Yes	No	No	Yes	NA	Mentioned	2	2 (moderate)
8	Gondim et al. 2010	Yes	Yes	Yes	Yes	Yes	Mentioned	2	1 (low)
9	Munoz et al. 2012	No	No	No	Yes	NA	Not mentioned	3	3 (high)
10.	Pawar et al. 2012	Yes	Yes	Yes	Yes	NA	Not mentioned	2	1 (low)
11.	Paiva et al. 2012	Yes	No	No	Yes	NA	Not mentioned	2	3 (high)
12.	Liang et al. 2013	Yes	No	No	Yes	Yes	Not mentioned	2	2 (moderate)
13.	Ramamoorthi et al. 2015	Yes	Yes	Yes	Yes	Yes	Mentioned	2	1(low)
14.	Tang et al. 2015	No	No	No	Yes	Yes	Not mentioned	3	3 (high)
15.	Middha et al. 2017	Yes	Yes	Yes	Yes	Yes	Mentioned	2	1 (low)
16.	Topcuoglu et al. 2018	Yes	Yes	Yes	Yes	Yes	Mentioned	2	1 (low)
17.	Topcuoglu et al. 2018	Yes	Yes	Yes	Yes	Yes	Mentioned	2	1 (low)

CEBM: Centre for Evidence-based medicine, NA: Not applicable

the needle tip which is unlikely to cause extrusion unless the canal is large and apex is open. Studies showed that conventional needle irrigation produced greater post-operative pain as evidenced by VAS scores in 5 of the 6 studies (7, 19, 21, 31) and Borg scale in 1 study (14). Also the need and quantum of analgesic consumption was more with conventional needle irrigation (92% vs. 58%). However, 1 study showed that MDA produced more pain than EndoActivator and conventional needle. They also concluded that EndoActivator and conventional needle produced statistically similar postoperative pain levels (32). EndoActivator, (19, 32) EndoVac (14, 31) and Ultrasonic unit (7, 21) were used as the activation devices in these studies. The reason for the increased pain levels with conventional needle-syringe irrigation can be explained by the fact that positive pressure produces greater hydraulic pressure which may result in post-operative pain. In fact, Myers and others reported that positive pressure of conventional irrigation extruded greater weight of debris apically (29, 37). Further, the inability to completely reach full working length can leave behind vital/ necrotic pulpal remnants and microbes that could contribute to the reported post-operative pain.

In general, curved canals extrude less irrigant while canals with resorption extrude more. Syringe and slotted needles extrude the maximum amount of irrigant (38). EndoVac generally has been shown to extrude the least and prevent vapor lock (39). Sonic and ANP extrude less than syringe with side port needle or PUI with continuous flow (40, 41). EndoVac & EndoActivator were comparable in irrigant extrusion and were significantly lower than PIPS/PHAST and Max I Probe (42). However Ultrasonic was found to be the best in efficiency and safety (43). Another study concluded that no significant differences in debridement efficacy were observed in teeth prepared with hand instruments or ultrasonics alone; Ultrasonication after hand instrumentation was the most efficient method (44). Further ultrasonic activation increases the substantivity of chlorhexidine (45). In a study by Rodriguez-Figueroa and others, spectrophotometric evaluation of irrigant extrusion was carried out following EndoActivator, PUI or conventional syringe. No significant difference was found between the three groups, though EndoActivator extruded slightly more irrigant than PUI (46). According to another study, phenomena of cavitation and acoustic streaming were investigated in an ultrasonic endodontic unit. Under scanning electron microscopy no difference in the surface debris was observed between the two techniques, although less smear was apparent in the ultrasonic groups. Transient cavitation does not play a role in canal cleaning; however, acoustic streaming does appear to be the main mechanism involved (47).

Bacterial growth by anaerobic tube turbidity test following access, instrumentation and test irrigation was carried out by 2 studies (9, 48), CFU by 2 studies (25, 26), staining by 1 study (27) and PCR by 1 study (26). Activated irrigation actually showed greater bacterial growth. This may be due to loosening of microbes from smear layer and biofilm over a greater surface area by the activation process. However the difference was not significant. The studies used ultrasonic (25-27) EndoActivator (28) and EndoVac (30) as activation devices.

Only 1 study evaluated irrigant delivery to working length (22). Iohexol solution irrigation followed by radiographic assessment proved that EndoVac & PUI-IrriSafe achieved greater delivery to working length than conventional irriga-

tion, though PUI was superior to EndoVac, it was not statistically significant (22). Canal/isthmus cleanliness was reported by 4 studies (6, 23, 24, 27) and debridement efficacy by 1 study (29).

PUI-IrriSafe has been found to produce cleaner canals than EndoActivator, as its vibration frequency (30 KHz) is greater (46). The dentin debris removal can be achieved within 3min of PUI usage (37). If NaOCl is used as irrigant, then the greatest antibacterial efficacy can be achieved with PUI (49). Moreover, a 3-cyclical activation with PUI of 20s each was shown to produce the equivalent cleanliness and bacterial reduction achievable with LAT (9). According to one study, decalcifying agents ethylenediaminetetraacetic (EDTA), etidronic (EA) and peracetic acid (PA) when used in conjunction with sodium hypochlorite (NaOCl) as root canal irrigants, were all able to remove or prevent a smear layer. However, they eroded the dentine wall differently (50). Histopathological staining ex-vivo revealed that activation of irrigant using Ultrasonic-CaviEndo (23)/OsadaEnac (24)/MiniEndo unit (6, 27) improved canal and isthmus cleanliness especially in the apical 3rd. In a study on whether passive ultrasonic irrigation using finger spreaders was more effective than standard files in removing debris after root canal instrumentation it was found that 3 minutes of activation with a file had significantly less debris remaining than 1 minute of activation with a spreader. When comparing apical, middle, or coronal thirds between groups, no significant differences were found. The use of a nonfluted spreader did not improve debris removal (51).

Debridement efficacy was assessed by histopathological staining *ex vivo*. It was greater for activation with EndoVac than conventional irrigation especially at the apical third (29). EndoVac was found to achieve better cleaning at the apical third with less exposure time of only 150 seconds (40). Manual dynamic irrigation was found to leave 21% debris in isthmii of all the specimens tested while apical negative pressure irrigation left only 1.6% debris in isthmii of 70% of the specimens tested. But canal cleanliness was similar in both the groups (41). EndoVac was found to remove maximum debris from apical third than tip vented or side vented needle irrigation (43). However at 3 mm from WL, there was no significant difference between EndoVac & needle irrigation (52). Ultrasonic activation of irrigant was found to be similar to LAI and PIPS in debris removal. However, a combination of EDTA and NaOCl irrigation with conventional syringe produced slightly better debris removal in one study (78% vs. 91%) (53).

None of the studies evaluated debris extrusion with activation or otherwise. When apical preparation size is increased, debris extrusion anyway increases, irrespective of activation or irrigant type (54). However, in another study, it was shown that EndoVac did not increase apical extrusion with increasing apical preparation size. But, needle irrigation extruded significantly more at smaller preparation sizes and the extrusion increased exponentially with increasing apical size (55). When preparation is done till working length, extrusion is comparatively more than when it is done 1 mm short. This is more common with conventional files than small-headed files like CanalMaster (56).

Long-term evaluation of endodontic treatment success, as evidenced by radiograph, has not been able to correlate irrigation method to the size of periapical lesion (20, 21). A number of variables such as presence of pre-operative symptoms, pre-operative lesion size, Master Apical File size, presence/absence of flare-ups during treatment also did not have a bearing on the method of irrigation and lesion reduction. Liang et al. evaluated lesion reduction using IOPA and CBCT after Ultrasonic activation of irrigant or conventional irrigation. They evaluated presence/absence of sinus tract, pain, swelling, tenderness to palpation/percussion, length and density of root canal obturation and quality of coronal restoration as outcome measures. Lesion was qualified if it was twice the width of periodontal ligament (PDL) space and/or presence of disruption of lamina dura (LD). Lesion size outcome was categorized in to 4 groups: Absence; Reduction/Enlargement (20% difference from original size); Uncertain. Both irrigation methods did not show significant difference in the volume of lesion or master cone size, the only two parameters that affected healing. Others like gender, length/density of root canal filling did not affect healing. 26% of teeth with smaller pre-operative lesions healed completely while 80-100% reduction of lesion size was captured in 64% of teeth evaluated by CBCT. They also found that when master cone size was increased from <45# to ≥50#, healing reduced in frequency by 50%. Tang et al. used PAI to qualify healing as clinically effective rates. There was no significant difference in healing evaluated at the end of 19 months between ultrasonic and conventional irrigation.

From the data collected, it is evident that mechanical activation of irrigants improves their delivery to working length, apical canal and isthmus cleanliness, overall debridement and substantially reduce post-operative pain. However, limited studies support the superiority of activation devices in delivery of irrigant up to working length. Hence more controlled clinical trials are required to confirm this. Moreover, many of the activation devices have not been evaluated clinically and this systematic review investigated only 6 devices/techniques that have been clinically studied and reported.

CONCLUSIONS

Within the limitations of this systematic review, it can be concluded that the use of mechanical active irrigation devices is beneficial in root canal treatment. Mechanical active irrigation devices are clinically efficient in delivering the irrigant upto the working length without causing post operative pain and ensuring canal and isthmus cleanliness.

Disclosures

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