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REVIEW

DIAGNOSTIC PERFORMANCE OF CONE-BEAM COMPUTED TOMOGRAPHY TO DIAGNOSE IN VIVO/IN VITRO ROOT RESORPTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

TERESA BAENA-DE LA IGLESIA[a], ROSA MARIA YAÑEZ-VICO[b], AND ALEJANDRO IGLESIAS-LINARES[b]

[a]School of Dentistry, Complutense University of Madrid, Madrid, Spain
[b]BIOCRAN, Craniofacial Biology and Orthodontics Research Group, School of Dentistry, Complutense University of Madrid, Madrid, Spain

ABSTRACT

Background
This review analyses the diagnostic performance of cone-beam computed tomography (CBCT) for the in vivo/in vitro detection of external root resorption (ERR) and critically analyses current and past methods of measuring or classifying ERR in vivo/in vitro in terms of radiation doses and cumulative radiation risks.

Methods
A diagnostic test accuracy (DTA) protocol was used for a systematic review of diagnostic methods following PRISMA guidelines. The protocol was registered with PROSPERO (ID: CRD42019120513). A thorough and exhaustive electronic search of 6 core electronic databases was performed, applying the ISSG Search Filter Resource. The eligibility criteria were designed [problem-intervention-comparison-outcomes (PICO) statement: Population, Index test, Comparator, Outcome] and methodological quality was assessed by QUADAS-2.

Results
Seventeen papers were selected from a total of 7841 articles. Six in vivo studies were assessed as having a low risk of bias. The overall sensitivity and specificity of CBCT for diagnosis of ERR was 78.12% and 79.25%, respectively. The highest and lowest sensitivity and specificity of CBCT for diagnosis of external root resorption are 42%-98% and 49.3%-96.3%.

Discussion
Most of the selected studies reported quantitative diagnoses with single linear measurements of ERR even though multislice radiographs were available. The cumulative radiation dose (μS) to radiation-sensitive structures, such as the bone marrow, brain and thyroid, was observed to increase using the 3-dimensional (3D) radiography methods reported.

Conclusions
The highest and lowest sensitivity and specificity of CBCT for diagnosis of external root resorption are 42%-98% and 49.3%-96.3%. The minimum and maximum effective doses of dental CBCT for external root resorption diagnosis are 34 μSv and 1073 μSv.

CORRESPONDING AUTHOR. Alejandro Iglesias-Linares, BIOCRAN, Craniofacial Biology and Orthodontics Research Group, School of Dentistry, Complutense University of Madrid, Plaza Ramón y Cajal sn, 28040 Madrid, Spain. Tel.: +34 636 705 246.
E-mail: aleigl01@ucm.es

KEYWORDS

Accuracy, Diagnostic, External root resorption, Cone-beam computed tomography, Radiation dose

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1. INTRODUCTION

Inflammatory external root resorption (ERR) is a pathologic consequence of orthodontic tooth movement leading to transitory or permanent loss of mineral content from dental roots.[1] The incidence of ERR is reported to be 1%-86% in nonorthodontically treated patients and 19%-93% in orthodontically treated patients, according to a 2D radiographic study using periapical radiography. Papers currently available however have reported that 2D radiographs cannot detect root resorption less than 0.6 mm in diameter or 0.3 mm in depth.[2–4]

Cone-beam computed tomography (CBCT) was introduced into dentistry in the early 1990s as an alternative technique of multislice radiography that requires considerably lower doses of radiation than computed tomography (CT).[5] Some authors have suggested that the accuracy of the CBCT method for volumetric measurements of teeth was similar to that of the micro-CT method, and that CBCT could be a suitable method for diagnosing ERR in vivo studies.[6] Nevertheless, although some previous studies described CBCT as the better choice for detecting ERR than routinely used radiographic techniques, there is as yet no conclusive scientific evidence available about the ability of CBCT to detect and quantify loss of root structure in vivo in terms of accuracy, as well as specificity and sensitivity for this type of root resorption.[7–12] A number of diagnostic studies in the literature[13–22] have evaluated the accuracy, specificity and sensitivity of CBCT for detection of root resorption according to criteria such as area under the receiver operating characteristic (ROC) curve, voxel size, field of view (FOV), milliamps, kilovoltage, exposure time, or processing tools such as filters, software, and examiners for the interpretation of ERR, suggesting that, even today, there is no definitive gold standard or single threshold criterion for the diagnosis of ERR.[15]

The main aim of this systematic review is to critically analyze the specificity and sensitivity of CBCT for the in vivo/in vitro diagnosis of external root resorption, as well as to assess the accuracy of CBCT for the detection of incipient ERR lesions. A secondary outcome was to critically analyze current and past methods used to measure or classify ERR in vivo in terms of radiation dose and cumulative radiation risk.

2. MATERIAL AND METHODS

2.1. Methodology and Protocol Registration

A diagnostic test accuracy (DTA) protocol for the systematic review of diagnostic methods was followed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[23,45] The present systematic review was registered with PROSPERO receiving the number (ID: CRD42019120513).

2.2. Sources of Information and Search Query

A systematic and comprehensive electronic search of the PubMed, Cochrane, Embase, Lilacs, Grey Literature, and Web of Science electronic databases (Figure 1) was conducted up to 1 December 2021.

Prepiloted search queries were developed, complemented with the Information Specialists' Sub-Group (ISSG) Search Filters Resource [24] (Supplementary Appendix 1) and used in the different databases. Titles and abstracts retrieved were examined for possible inclusion in accordance with the eligibility criteria. No dates, status or language of publication were excluded.

2.3. Eligibility Criteria

Eligibility criteria were based on the problem-intervention-comparison-outcomes (PICO) statement, following a previously published methodology[23,25]: *Population:* studies analyzing single or multiple tooth-root areas or changes in volume; *Index test:* Cone-Beam Computed Tomography; *Comparator:* gold standard comparison as a micro-CT; *Outcome:* quantification of ERR lesion or root resorption crater (volume, area, total or partial mineral loss). Included were research studies that evaluated simulated and nonsimulated root resorption using 3D X-ray diagnostic methods.

Editorials, opinion letters, case series or case reports, and other studies of 2-dimensional methods were excluded.

2.4. Quality Analysis and Risk of Bias Assessment

A validated method for assessing the quality of diagnostic accuracy studies (QUADAS)-2 was used to perform a quality assessment of the included studies.[26] This scale was based on the 4-stage approach proposed by Moher.[26,27]

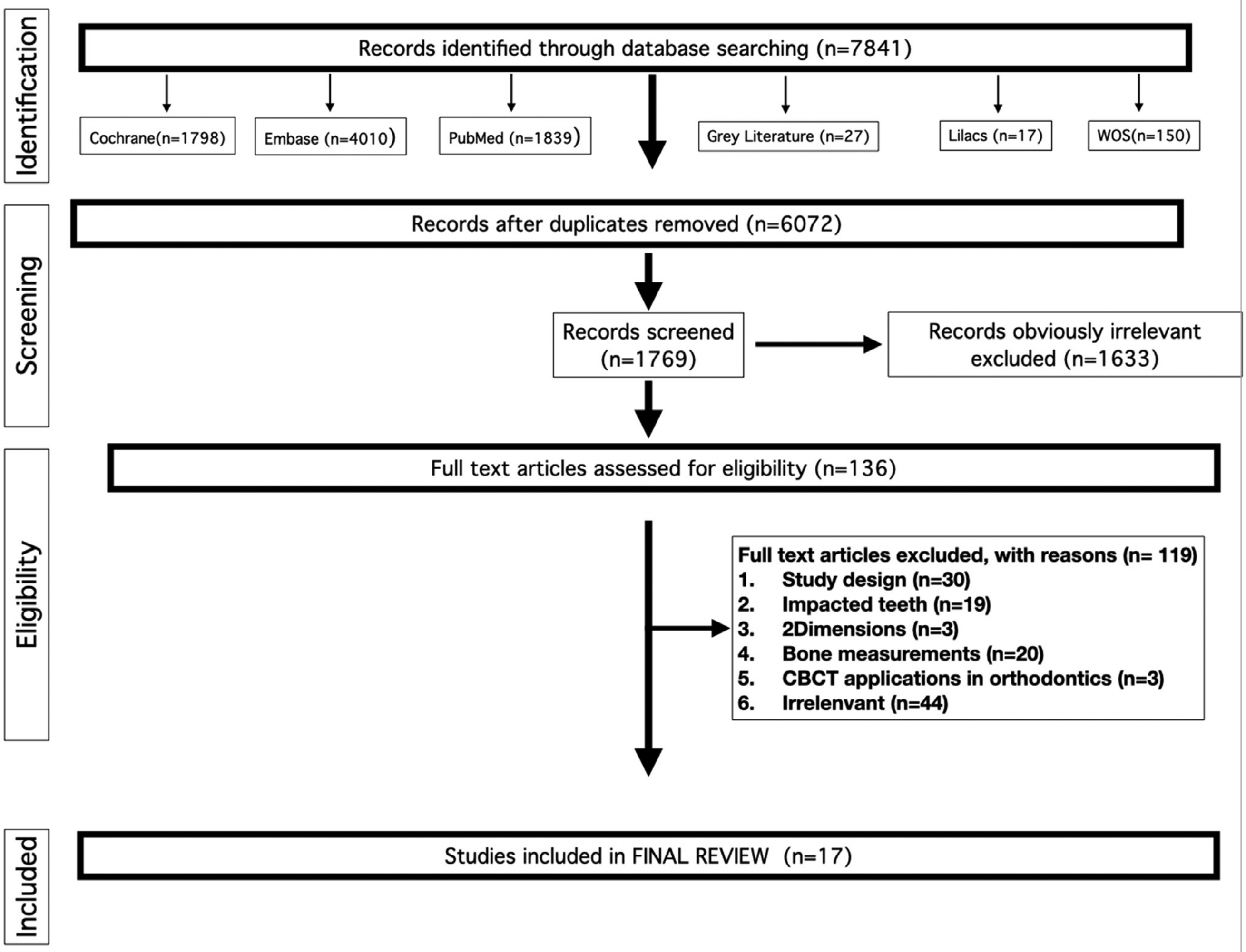
2.5. Data Extraction and Description of Selected Studies

Data were obtained from the literature following a prepiloted data extraction protocol. Two reviewer authors carried out the study inclusion and data extraction and evaluated the risk of bias and eligibility of retrieved studies independently. Any disagreement was solved by discussion with a third reviewer. Kappa coefficient was calculated to evaluate interobserver agreement (Kappa = 0.929).

Briefly, first author, publication date, and country of reference were targeted.

Specifically, the features of external root resorption in different radiographic techniques were scored by adding tooth, type of diagnostic method, kilovoltage, milliamps, exposure time, field of view, voxel size, type of study, whether in vivo or in vitro, examiner, intra-/interexaminer error, ERR measurements (areas, reference standard, grades, units), software

Figure 1. Flow chart.



and image format, and CBCT radiation doses and cumulative radiation risk in relation to well-established cause and effect considerations in pathologies. The sensitivity, specificity and accuracy of the CBCT test against different reference standards or degrees of ERR were also extracted.

2.6. Quantitative Analysis of the Data: Heterogeneity and Selection Bias

For each indicator (Sensitivity and Specificity) a meta-analysis was developed to obtain the global effect measure for 4 papers (Ren, 2013; Sousa, 2017; Deliga, 2018; Deliga, 2019). The estimate was made using a random effects model due to the high I^2 with maximum likelihood (ML) and the DerSimonian method, with 95% confidence intervals for z distribution. The results of the estimates, global effect measure, and confidence intervals were represented in the Forest plot (Figure 4). The relative weight of each article was estimated in the meta-analysis calculations.

The I^2 index of heterogeneity (percentage of variability of the estimated effect that can be attributed to heterogeneity of the true effects) and the corresponding statistical test of nullity of Q was calculated. The consistency of the results of the different studies was explored using a Galbraith plot (Supplementary Appendix 3).

For the study of selection bias, Funnel plot (Supplementary Appendix 5) was represented and Egger's test was performed. The level of significance used in the analyses was 5% ($\alpha = 0.05$).

The software used to perform the meta-analysis was R Core Team 3.5.1 (2018). (R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.)

3. RESULTS

3.1. Studies Chosen and Included for the Systematic Review

As of 1 December 2021, a total of 7841 articles were identified in the initial literature search across the 6 major electronic databases (Figure 1). After cross-checking reference lists, no further potentially eligible primary studies were found in addition to those finally selected. After discarding on the basis of titles and duplicates, 1769 papers were left for full text review. After reviewing these articles, 136 papers were examined further and, after screening for inclusion and exclusion criteria, 17 papers met all criteria.[1,4–6,13–22,34–36] These 17 papers were included in the final systematic review, all of them published between 2009 and 2020 (Tables 1 and 2).

One hundred and nineteen articles were excluded because their study designs were systematic reviews or case reports, 2-dimensional diagnostic techniques were used or different outcomes were examined, such as diagnosis of impacted teeth or alveolar bone measurements without using CBCT to examine root resorption lesions, as fully detailed in Supplementary Appendix 2.

Eight of the included papers were *in vivo* experimental research studies, and the other 9 were experimental in vitro assessments of simulated root resorption cavities of different diameters. The *in vivo* and *in vitro* studies were classified and summarized independently in Tables 1 and 2 for further analysis and comparison of results.

3.2. Extracted Data From Studies

3.2.1. Type and radiation dose of equipment used

The range of effective doses in dental CBCT has been described as in a range from 34 to 1073 μSv per complete CBCT scan. This data was calculated following the International Commission on Radiological Protection (ICRP) in 2007. There is no available data since 2015.[28,29] Effective doses vary widely between manufacturers. The NewTom 3 G effective dose (30-78 μSv) has been described as the lowest, while, conversely, the CBMercuRay has been described as delivering the maximum effective dose at 283-1073 μSv[28,30–33] (Tables 1 and 2).

The studies described a substantial variety of radiographic equipment for assessment of ERR. The majority of in vitro studies used iCAT®,[14,18,19,22,34] 3D Accuitomo® [35,36] or Scanora 3D® [34–36] with tube voltages ranging from 80 kVp to 120 kVp, exposure times between 3.7 and 20 seconds, and milliamps between 3 and 36 mA (Table 2). Most of the in vivo studies used 3D Accuitomo® [5,20,36] and iCAT®[21]. Nevertheless in selected studies, different CBCT equipment was used, for example, Galileos 3D®,[36] Kodak®,[36] Picasso Trio®,[36] ProMax®,[36] Hitachi®,[13] Kavo 3D®,[15] NewTom 3G®,[16] and CBMercuRay®[1] (Table 1).

3.3. Criteria and Methods Used for Quantification/Assessment of External Root Resorption

Only 3 studies reported quantitative measurements of ERR in terms of absolute volume of resorption craters (in mm^3).[6,15,16] The DICOM (Digital Imaging and Communication in Medicine) format was used for storing CBCT image files. Professional medical imaging processing software, Mimics or Dolphing,[14] was used for tissue segmentation, 3-dimensional (3D) reconstruction and volumetric measurement.

Four papers[4,35,36] used an adapted 3D version of the ERR classification proposed by Ericson and Kurol (Ericson et al., 2000) for the 2D analysis, converting the categories into a 4-category range: none; slight (0.15, 0.20, and 0.30 mm); moderate (0.60 and 1.0 mm); and severe (1.50, 2.00, and 3.00 mm). Finally, others categorized ERR findings subjectively using a mixed method of the form: "no root resorption," "mild resorption" (only if the contour was damaged), "moderate resorption" (some loss of the root area, including apex, amounting to less than 2 mm), and "severe resorption" (at least one-third of the root was missing), following the criteria and methodology proposed for 2D analysis by Levander and Malmgren[37] and adding the buccal, palatal, mesial, and distal surfaces (Tables 1 and 2).

3.4. Sensitivity and Specificity

Sensitivity, considered as the probability that a test result will be positive when the pathology is present [true positive rate VP/(VP + FN)]. Specificity, defined as the probability that a test result will be negative when the pathology is not present [true negative rate; VN/(VN + VP)].[15]

Sensitivity and specificity of in vitro studies for diagnosis of external root resorption ranged from 42% with a half scan with iCAT[19] to 85.42%-98.96%, as described by Alqerban,[36] who used 6 CBCTs (Picasso Trio, Kodak, Galileos, 3D Accuitomo XYZ, Scanora, Promax) (Table 2). Specificity and sensitivity were not reported in any of the in vivo studies described (Table 1). The highest sensitivity and specificity of CBCT for diagnosis of ERR was 98.96% and 97.60%, respectively (Tables 1 and 2).

3.5. Quality of Included Studies

Of the 17 included studies, the quality assessments of in vivo studies were distributed as follows: 6 were low-risk,[1,4–6,16,21] one was unclear[20] and one had a high risk of bias[13]. The studies that presented a low risk of bias had a larger sample size than the studies with a high risk of bias (29, 40 samples). In contrast, the studies with unclear risk of bias had a similar sample size to those with low risk of bias (12-160).

Table 1. Characteristics of the included studies (in vivo).

Study	Sample		Radiography						Type of study	Examinator		Method assessments						ERR measurements				Image format
	Type	Size	Type	kVp	mA	Exposure time	FOV	Voxel Size		Type	Number	Error intra	Error inter	Test	Precision	Sensitivity	Specificity	Areas	Reference standard	Grades	Units	
Lund et al. 2010	IC,IL,C,PM,1 M	26	CBCT: 3D Accuitomo	75kV	4.5-5mA	17.5sec	60x60 mm	–	*in vivo*	–	1	0.75-0.78	–	Kappa	95%	–	–	apical,bucal,distal,lingual,mesial,palatal	Modified Malmgrem et al.:bucal,palatal/lingual and mesial/distal	Irregular=0	mm	DICOM
	I,C,2PM,1M	10							*in vitro*			0.77-1.0								Minor=1		
																				Severe=2		
																				Extreme=3		
Alqerban et al.	Impacted maxillary C	89	CBCT: Accuitomo	80kV	3mA	18sec	30x40 mm	0.125mm	*in vivo*	Dental practitioners	3	–	0.26-0.66	Kappa	–	–	–	apical, cervical or middle third	Ericson and Kurol	None	mm	JPEG
2011			Scanora	85kV	15mA	3.7sec	75x100mm	0.2mm	*in vivo*	Postgraduates	8	–	0.24-0.74		–	–	–			Slight		
			Panoramic: Soredex	65kV	15mA	15sec	–	–	*in vivo*			–	0.17-0.64		–	–	–			Moderate		
																				Severe		
Wang et al.	PM	27	CBCT: MCT-1	80kV	5mA	–	–	0.125mm	*in vivo*	–	2	0.740	0.999	ICCs	95%	–	–	apical,bucal,distal,lingual,mesial,palatal	microCT measurements	3D images reconstructed with CBCT	mm^3	DICOM
2011			microCT: Scanco Medical	70kV	0.144 mA	–	–	0.037mm	*in vitro*			–	0.998		–	–	–					
Oberoi et al.	Impacted C	29	CBCT: Hitachi MercuRay	120kV	15mA	–	12 inches	0.376mm	*in vivo*	–	1	–	–	–	–	–	–	apical,bucal,distal,lingual,mesial,palatal	Ericson and Kurol	None	mm	DICOM
2012																				Slight		
																				Moderate		
																				Severe		
Li et al.	M	12	CBCT: NewTom3G	110kV	15mA	36sec	9 inches	0.2-0.4mm	*in vivo*	–	2	P>0.05	P>0.05	t test	–	–	–	apical,bucal,distal,lingual,mesial,palatal	Hounsfield units	initial-final volume	mm^3	DICOM
2013																						
Kim et al.	PM	94	CBCT: CBMercuRay	120kV	15mA	9.6sec	149.5 x149.5mm	0.292mm	*in vivo*	–	1	–	–	t test	95%	–	–	–	–	crown, tooth and root length	mm	–
2013									*in vitro*													
Alamadiet al.	Extracted deciduous C	34	CBCT: 3D Accuitomo	–	–	–	60x60 mm	–	*in vitro*	–	2	p<0.05	0.88	t test	–	–	–	bucal,distal,lingual and mesial	Histological resorption	Modified Malmgrem et al	mm	–
2017			Periapical RX	–	–	–	–	–	*in vivo*			–	–	Cohen´s Kappa	–	–	–					
			Panoramic: Scanora	–	–	–	–	–				–	–		–	–	–					
Lago et al	IC,IL,II	200	CBCT: iCAT	120kV	36mA	40 sec	22x16 mm	0.4mm	*in vivo*	–	2	0.95-0.99	0.90-0.99	ICC	82-99%	–	–	tooth length	SD=0.37-0.67mm	T_2-T_1*	mm	–
2018			Periapical: Rx Dabi Atlante Unit	70kV	8mA	0.11-0.31sec	–	–	*in vivo*			–	–		–	–	–			*T_2 six months after the beginning *T_1 before the beginning		

Study	Effective Dose (µSv)		Bone Marrow (µSv)		Bone Surface (µSv)		Skin (µSv)		Oesophagus (µSv)		Brain (µSv)		Thyroid (µSv)		Salivary glands (µSv)		Remainder (µSv)	
	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	CH
Lund et al. 2010	257	430	267	244	831	940	152	307	140	253	176	2039	1498	4265	5487	6622	776	1004
Alqerban et al. 2011	257	430	267	244	831	940	152	307	140	253	176	2039	1498	4265	5487	6622	776	1004
	68	–	86	–	94	–	55	–	–	–	255	–	296	–	1568	–	221	–
Wang et al. 2011	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Oberoi et al. 2012	421	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Li et al. 2013	103	311	100	71	269	182	113	22	54	44	878	430	477	595	2076	531	301	85
Kim et al. 2013	421	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Alamadiet al. 2017	257	430	267	244	831	940	152	307	140	253	176	2039	1498	4265	5487	6622	776	1004
	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Lago et al 2018	34-206	115	79	115	176	190	41	81	43	53	238	391	353	1001	1859	2045	256	302
	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

ERR:external root resorption; IC:central incisor; IL:lateral incisor; C:canine; PM:premolar; M:molar; II:inferior incisor; CBCT:cone beam computer tomography; microCT:micro computed tomography; DICOM: digital imaging and communications in medicine; JPEG: joint photographic experts group; TIFF:tagged image file format; intra: intraexaminator; iter:interexaminator; ICC:intraclass correlation coefficient; mm:millimeters; mm^3:cubic millimeters; µSv:microsievert.
A:adult; Ch: child.–: no refered.

Table 2. Characteristics of the included studies (in vitro).

STUDY	SAMPLE		RADIOGRAPHY						TYPE OF STUDY	EXAMINATOR					ERR MEASUREMENTS							SOFTWARE	TYPE OF IMAGE	EFFECTIVE DOSE (μSv)		BONE MARROW (μSv)		BONE SURFACE (μSv)		SKIN (μSv)		OESOPHAGUS (μSv)		BRAIN (μSv)		THYROID (μSv)		SALIVARY GLANDS (μSv)		REMAINDER (μSv)	
	Type	Size	Type	kVp	mA	Exposure time	FOV	Voxel Size		Type	Number	ERROR intra	ERROR inter	Test	Precision	Sensitivity	Specificity	Areas	Reference standard	Grades	Units			A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	Ch	A	CH
Alqerban et al.																																									
2009	IL	8	CBCT: 3D Accuitomo XYZ	80kV	3mA	18sec	40x30mm	0,125mm	*in vitro*	Postgraduates	8	–	–	McNemar	–	95%	75%	Apical, Cervical	Ericson and Kurol	None	mm	OneDemand3D	DICOM	257	430	267	244	831	940	152	307	140	253	176	2039	1498	4265	5487	6622	776	1004
			Scanora	85kV	15mA	3,7sec	75x100mm	0,133mm	*in vitro*	orthodontic		–	–		–	94%	75%	or middle third		Slight				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Panoramic: Cranex Tome 2D	65kV	15mA	15sec	15x30mm	–	*in vitro*	trainees		–	–		–	78%	38%			Moderate				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Periapical: Soredex	70kV	7mA	0,12sec	–	–	*in vitro*			–	–		–	–	–			Severe				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Alqerban et al.	Maxillary																																								
2011	left IL	8	CBCT: 3D Accuitomo XYZ	80kV	3mA	18sec	30x40mm	0.125mm	*in vitro*	Dental radiologists	2	P>0.05	P<0.001	McNemar	95%	93.75%	87.50%		Ericson and Kurol	None	mm	OneDemand 3D	DICOM	257	430	267	244	831	940	152	307	140	253	176	2039	1498	4265	5487	6622	776	1004
			Galileos	85kV	7mA	3.4-14sec	120x150mm	0.29mm	*in vitro*	Orthodontic instructors	2	–	–		–	87.50%	70.83%			Slight				68	39	86	26	94	91	55	25		22	255	185	296	384	1568	589	221	91
			Kodak 9000	85kV	10mA	10sec	3.7x50mm	0.076-0.2mm	*in vitro*	Postgraduates orthodontic	8	–	–		–	86.46%	91.67%	Apical, Midapical or Middle third of the root		Moderate				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Picasso Trio	85kV	5mA	15sec	70x120mm	0.2mm	*in vitro*	residents		–	–		–	85.42%	95.83%			Severe				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			ProMax 3D	84kV	12mA	18sec	80x80mm	0.16mm	*in vitro*			–	–		–	98.96%	58.33%							131	277	98	318	341	1118	70	222	19	112	86	2829	333	2154	3865	3706	514	145
			Scanora	85kV	8-15mA	2.25-4.5sec	75x100mm	0.13-0.35mm	*in vitro*			–	–		–	95.83%	95.83%																								
Ponder et al.	Teeth	25	CBCT: iCAT low resolution	120kV	18.6mA	20sec	–	0.4mm	*in vitro*		2	0.98-1.0	0.98-1.0	Pearson	95%	–	–		MicroCT	3D images	mm	Image J: volumetric	DICOM	34-89	115	79	115	176	190	41	81	43	53	238	391	353	1001	1859	2045	256	302
2013			iCAT high resolution	120kV	36.52mA	40sec	–	0.2mm	*in vitro*			–	–		–	–	–	Apical,Bucal, Distal, Lingual, Mesial, Palatal	measurements	reconstructed		Dolphin: linear		48-206	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Panoramic: Gendex GX770	70kV	7mA	0.4sec	–	0.018mm	*in vitro*			–	–		–	–	–			with CBCT				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			MicroCT: Locus SP	80kV	80mA	1.6sec	–	–	*in vitro*			–	–		–	–	–				mm³			–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Ren et al	PM	160	CBCT: Kavo 3D	120kV	18.54mA	8.9sec	80mm	0.3mm	*in vitro*	Postgraduate	2	0.74	0.001	Kappa	98.8%	75.8%	96.3%		Levander	None	mm³	iCAT view		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2013			Periapical: Kodak 2100	60kV	7mA	0.1sec	–	–		orthodontic		–	–	–	–	67.5%	82.5%	Apical,Bucal Distal, Lingual Mesial, Palatal	and	Mild	mm	software		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
										residents									Malmgren	Moderate																					
																				Severe																					
Creanga et al.	Teeth	120	CBCT: Planmeca Promax 3D	84kV	14mA	12sec	–	0.2mm	*in vitro*	Oral radiology	4	–	0.63	Kappa	95%	69%	91%			Definitely NR		Romexis	DICOM	131	277	98	318	341	1118	70	222	19	112	86	2829	333	2154	3865	3706	514	145
2015			Prostyle intra machine	60kV	8mA	0.16-0.4sec	–	–	*in vitro*			–	0.33		–	51%	83%	Apical,Bucal Distal, Lingual Mesial, Palatal		Probably NR			TIFF	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
																				Unsure																					
																				Probably R																					
																				Definitely R																					
Takeshita et al	PM	40	CBCT: iCAT	120kV	36.2mA	–	60x60mm	0.125mm	*in vitro*	Radiologist	6	0.878	0.878	Kappa	–	–	–	–	–	Change definitely		Xoran CAT	DICOM	79	115	79	115	176	190	41	81	43	53	238	391	353	1001	1859	2045	256	302
2015			Panoramic Orthoralix 9200	–	–	–	–	–				0.728	0.728		–	–	–			Change probably present				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Periapical digital Dental XRay	70kV	8mA	0.4sec	–	–				0.809	0.809		–	–	–			Uncertain		CDR DICOM		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Periapical conventional	–	–	–	–	–				0.813	0.813		–	–	–			Change probably absent				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
																				Change definitely absent																					
Sousa et al.	Anterior	100	CBCT: iCAT																																						
2017	teeth		half scan 180º	120kV	5mA	2sec	80x80mm	0.4mm	*in vitro*	Oral and maxillofacial	3	–	0.63-0.71	Kappa	64%	42%	84%	Apical third	–	Definitely NR	mm³	Xoran CAT	DICOM	34-89	115	79	115	176	190	41	81	43	53	238	391	353	1001	1859	2045	256	302
			full scan 360º	120kV	5mA	4-7sec	–	0.12-0.40mm		radiologist residents		–	–		62%	54%	69%			Probably NR				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			microCT: Sky Scan	80kV	0.12mA	–	–	0.015mm				–	–		80%	81%	79%			Unsure				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
																				Probably R																					
																				Definitely R																					
Deliga et al.	I,C,PM, M	126	CBCT: iCAT	120kV	5mA	26.9sec	–	0.25mm	*ex vivo*	Radiologist	2	0.8-1.0	0.8-1.0	Kappa	73%	78.1%	59.5%		microCT values	present-absent cavity	mm³	Xoran	DICOM	34-206	115	79	115	176	190	41	81	43	53	238	391	353	1001	1859	2045	256	302
2018			microCT: SkyScan 1172	100Kv	0.1mA	–	–	–		Orthodontist		–	–		100%	100%	100%	Apical,Bucal Distal, Lingual Mesial, Palatal				CTvox 3.1.1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
			Periapical: VistaScan no.2	60kV	7mA	0.17-0.25sec	–	–				–	–		97.2%	97.2%	97.6%						TIFF	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Deliga et al.	I,C,PM, M	126	CBCT: iCAT X generation	120kV	8mA	26.7sec	80mm	0.20mm	*ex vivo*	Oral radiologist	3	0.8-1.0	0.8-1.0	Kappa	60.3%	60.8%	60%		microCT values	Small cavities	mm³	CTvox 3.1.1	DICOM	34-206	115	79	115	176	190	41	81	43	53	238	391	353	1001	1859	2045	256	302
2019			Orthophos XG	85kV	6mA	20sec	80mm	0.16mm				–	–		56.7%	56.5%	56.5%	Apical,Bucal Distal, Lingual Mesial, Palatal		Medium cavities				36	–	33	–	156	–	18	–	10	–	31	–	90	–	1036	–	131	–
			Scanora 3D	90kV	13mA	13 sec	75mm	0.25mm				–	–		46.7%	44.1%	49.3%			large cavities				68	–	86	–	94	–	55	–		–	255	–	296	–	1568	–	221	–
			microCT:SkyScan 1172	100kV	0.1mA	–	–	–				–	–		100%	100%	100%							–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

ERR:external root resorption; IC:central incisor; IL:lateral incisor; C:canine; PM:premolar; M:molar; II:inferior incisor; CBCT:cone beam computer tomography; microCT:micro computed tomography; DICOM: digital imaging and communications in medicine; JPEG: joint photographic experts group; TIFF:tagged image file format; intra: intraexaminator; iter:interexaminator; ICC:intraclass correlation coefficient; mm:millimeters; mm³:cubic millimeters; μSv:microsievert.NR:no resorption; R:resorption; A:adult; Ch:child.

Table 3. Quality analysis and risk of bias (in vivo) [QUADAS-2].

STUDY	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Lund	☺	☺	☺	☺	☺	☺	☺
Alqerban A	☺	☺	☺	☺	☺	?	?
Wang	☺	☺	☺	?	☺	☺	☺
Oberoi	☺	☹	☹	☹	☹	?	?
Li	☺	☺	?	☺	☺	☺	?
Kim	☺	☺	☹	☺	☺	?	?
Alamadi	☺	?	?	☺	☺	?	?
Lago	☺	?	☺	☺	☺	?	☹

☺ Low risk; ☹ High risk; ? Unclear risk

Table 4. Quality analysis and risk of bias (in vitro) [QUADAS-2].

STUDY	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Alqerban	☹	☺	?	☺	☺	☺	☺
Alqerban B	☹	☺	☺	?	?	?	?
Ponder	☹	☺	☺	?	☺	☺	☺
Ren	☹	☺	☺	☺	?	☺	?
Creanga	☹	?	☺	☺	?	☺	?
Takeshita	☹	?	?	☹	☹	?	?
Sousa	☹	☺	☺	?	☹	☺	?
Deliga	☹	☺	☺	?	☺	☺	☺
Deliga	☹	☺	☺	☺	☺	☺	?

☺ Low risk; ☹ High risk; ? Unclear risk

In terms of applicability, 4 were classified as having low applicability concerns[5,6,12,17] and in 3 others the concerns were unclear.[1,4,20] Only one had high applicability concerns.[13] The results were different in the in vitro studies, no patients were analyzed in the samples.[14,15,17–19,22,34–36] Results in detail of the QUADAS-2 quality assessment are presented in Figures 2 and 3.

3.6. Meta-Analysis: Sensitivity and Specificity Across Studies

All the studies included in the meta-analysis reported the *Sensitivity* value. Descriptively, the dispersion of sensitivity values (S) was quite important. It ranged between 42% in Sousa and 97.2% in Deliga 2018.

Figure 2. QUADAS-2 diagram (in vivo).

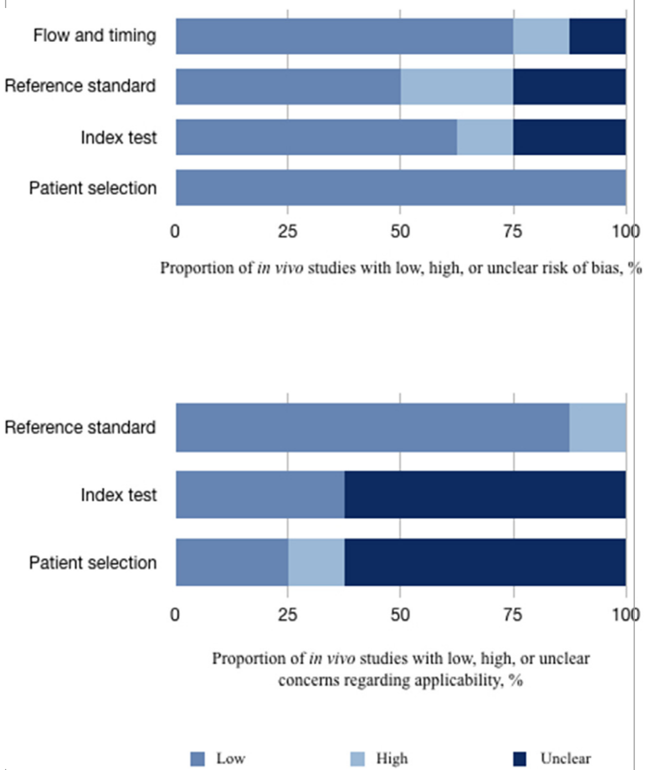
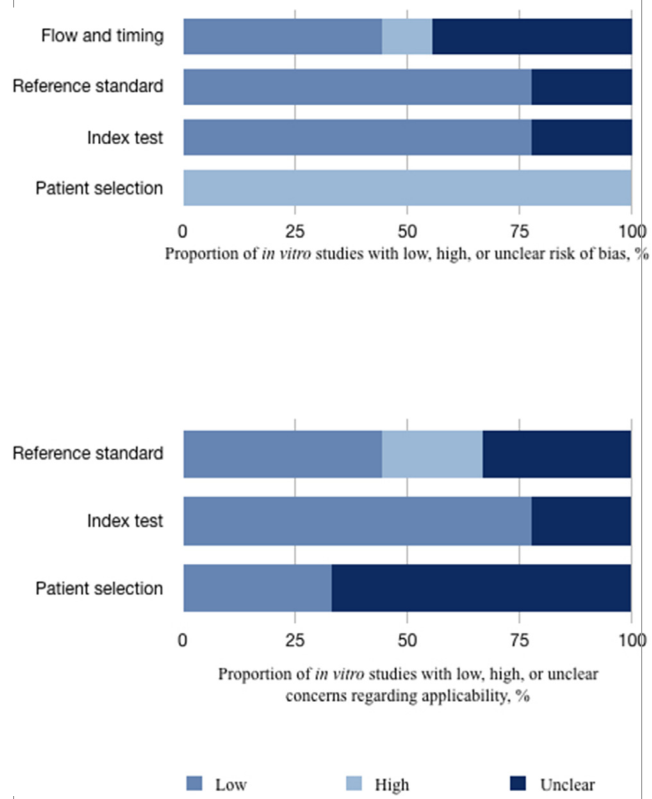


Figure 3. QUADAS-2 diagram (in vitro).



The meta-analysis estimated an overall estimated sensitivity of 0.69 (95% CI 0.46-0.92) (Figure 4).

The weight of the different articles in the global estimation was (in percentage and in the order in which they appear in the graph): 25.1, 24.5, 25.5, 24.7.

$I^2 = 98.1\%$ was obtained, that is, most of the variability is between-studies. It is a very high level of heterogeneity ($Q = 178.1$; $P < .001$), making the estimate not very robust.

The Galbraith plot showed that the large level of heterogeneity is not attributable to a particular study (all within confidence bands) (Supplementary Appendix 3).

Finally, the Funnel plot (Supplementary Appendix 5) to detect possible publication bias. The most precise studies (upper part) were those that report the greatest sensitivity. However, among the imprecise ones, there was a lack of studies that report high sensitivity values. This result was considered not relevant since the funnel plot asymmetry only implies small-study effects, which could be attributed to several factors other than publication bias. Therefore, for similar sample sizes across items, the graph simply reflected that association.

The overall estimated *Specificity* was 0.85 (95% CI 0.68-1.00) (Figure 4). The weight of the different articles: 25.6%, 24.6%, 25.6%, and 24.2%. The level of heterogeneity was also very high ($I^2 = 98.5\%$; $P < .001$). In that case, there was an article (Deliga 2019) closer to the lower confidence band (the most heterogeneous of the set) (Supplementary Appendix 3).

Regarding publication bias, the interpretation was similar to that of sensitivity. As the sample size was similar, the increase in the specificity value was also associated with greater imprecision (Supplementary Appendix 5).

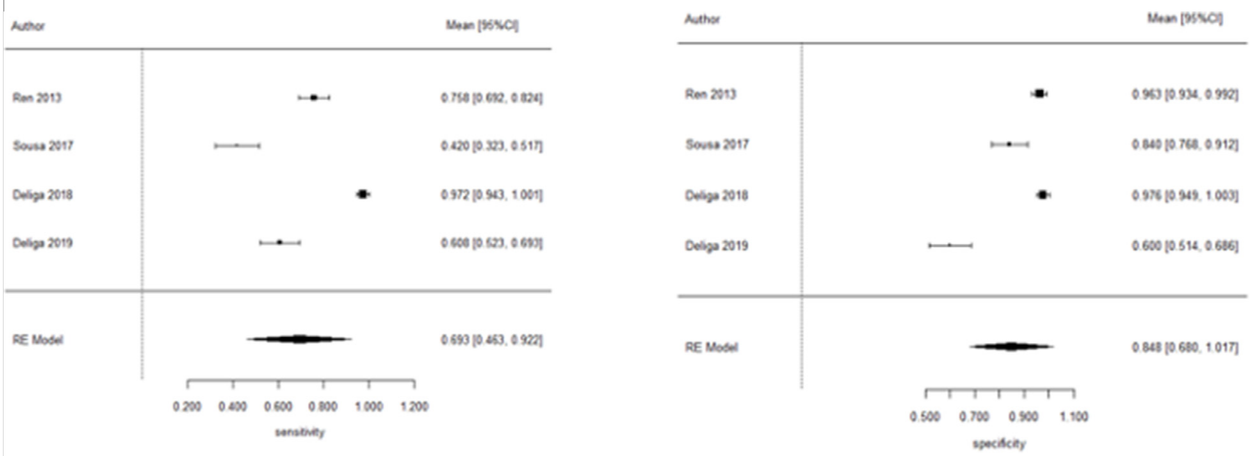
The overall estimated PPV was 0.75 (95% CI 0.28-1.00) and NPV was 0.81 (95% CI 0.56-1.00) (Supplementary Appendix 4). The level of heterogeneity was also very high ($I^2 = 99.1\%$; $P < .001$) ($I^2 = 96.4\%$; $P < .001$), respectively.

Only with 2 articles (Deliga, 2018 and Deliga, 2019) it did not make no sense to explore heterogeneity or publication bias.

4. DISCUSSION

At present, we only have systematic reviews and meta-analyses comparing CBCT and periapical X-rays for simulated ERR in vivo/in vitro, which is why we have no gold stan-

Figure 4. Sensitivity and specificity forest plot.



P	SE	IC 95%		I^2	Q_H (p-value)	Egger (p-value)
0,69	0,12	0,46	0,92	98,1%	<0,001***	<0,001***

*p<0,05; **p<0,01; ***p<0,001

Meta-analysis result for Sensitivity: estimated probability (p), standard error (SE), 95% confidence interval, I^2 index and Cochran's Q statistic (p-value) for heterogeneity; Egger's test (p-value) for publication bias

P	SE	IC 95%		I^2	Q_H (p-value)	Egger (p-value)
0,85	0,09	0,68	1,00	98,5%	<0,001***	<0,001***

*p<0,05; **p<0,01; ***p<0,001

Meta-analysis result for Specificity: estimated probability (p), standard error (SE), 95% confidence interval, I^2 index and Cochran's Q statistic (p-value) for heterogeneity; Egger's test (p-value) for publication bias

dard for comparison with in vivo clinical trials.[9] To date, no studies have published analyses of actual root lesions, apart from the extremely sharp irregular cavities created with burs *in in* vitro CBCT studies.[1,4,14,15,17–20,22] The area of the ERR lesions diagnosed in orthodontic treatment were most frequently described as being less than 2 mm;[38] consequently, we examined in greater depth those papers that provided information about simulated external root resorption using sections of 2 mm or less in stratified analysis. On the other hand, the naturally created type of root resorption crater has a different shape and is more difficult to analyze than the artificially simulated one. This led Deliga[22] to question the adequacy of the sensitivity and specificity data derived from research into radiographic/tomography methods described in their studies. Due to the close correlation between sensitivity and specificity, neither of the 2 indicators should be considered separately as a measure of diagnostic accuracy.

The method used in the different papers varied according to whether they were in vitro or in vivo. Both simulated and real ERR were categorized according to Ericson and Kurol (none, slight, moderate, and severe) or Malmgrem (irregular, minor, severe, extreme) and described the location and area according to whether the lesion appeared on a buccal, palatal, mesial, or distal surface. Only in vivo papers analyzed and compared real and simulated lesions using a 3D method such as micro-CT as gold standard. None of the in vivo papers analyzed either sensitivity or specificity. Whereas in vitro papers were easily able to compare CBCT measurements according to different parameters, such as dosage, field of view, and so on, the in vivo papers could only compare real ERR with one CBCT measurement with ex vivo ERR, or with another CBCT unit or micro-CT.

The QUADAS-2 tool enabled us to incorporate QUADAS sources of bias and variation in diagnostic accuracy in systematic reviews into the original tool. The first signaling question ("Was a consecutive or random sample of patients enrolled?") was unclear because no patients were included in in vitro studies. The question, "If a threshold was used, was it specified?" was not used because it was not applicable to the diagnosis of external root resorption. The case-control study design was difficult to avoid, and in all in vitro studies, the domain referring to patient selection was considered to be at high risk of bias because the guidelines were set by the QUADAS-2 tool. Furthermore, clinical applicability is more realistic because ERR is frequently identified using panoramic radiography but with use of a different radiographic testing method, such as CBCT or periapical radiography, on affected teeth to determine the root lesions more accurately.

Because there are different types of systematic reviews, we analyzed quality assessment with QUADAS-2 because it is the best method for a DTA review; QUADAS-2 is better than the Critical Appraisal Skills Program (CASP) diagnostic checklist, the Centre for Evidence-Based Medicine (CEBM) diagnostic study appraisal worksheet or JBI critical appraisal tools. Our systematic review is a DTA review, not an interventional, observational, or qualitative review.[25] The main bias found in this DTA systematic review has been the absent or inappropriate reference standard, as well as demographic features.[44]

CBCT methods are not being used at their maximum resolution in order to minimize the radiation dose delivered to patients,[19] although even at maximum resolution, the effective dose of CBCT is equivalent to a few days or up to a couple of months of background radiation, depending on the type of radiology equipment and clinical protocol used. In everyday life, average exposure to normal background radiation is about 2400 μSv per year (European Commission, 2007) and the maximum effective dose of dental CBCT is 1073 μSv. At the effective dose used in dental radiology, radiation does involve an increased risk of cancer (5% per 1000 mSv increase),[39] although this is not very high, there needs to be very good justification for its application. In addition, the consequences of using effective doses of radiation are known to be greater in children than adults because of the shorter distance between the chin and thyroid gland. In a meta-analysis of effective doses in 9 CBCT cases, there were large differences between children and adults, especially in the bone narrow, esophagus, brain, thyroid, and salivary glands,[29] drawing attention to the ethical commitment and concluding statements of the 2007 European Commission.[40,41] This is not just an age-dependent effect; critical epigenetic differences in the genome in the population should also be taken into account. In this context, Miousse et al. reported that epigenetic alterations were one of the driving forces of radiation-induced carcinogenesis after observing decreases in long interspersed nucleotide element 1 (LINE-1) DNA methylation in the hematopoietic system of the mouse after radiation.[42,43]

Some limitations that still need to be addressed include the heterogeneity of included studies, the differences between CBCT systems and their parameters, and the diagnostic ability of examiners.[10–12] The radiography equipment, exposure parameters, and radiation doses vary in both in vitro and in vivo studies, which could affect the overall results. Further studies, especially clinical trials, are crucial for more precise conclusions.

It is our responsibility to ensure that dentists see that there is a significant difference between "diagnostic" and "aesthetic" in terms of risk. This is a compelling reason for research into radiation dose. The National Commission on Radiation Protection and Measurements (NCRPM) introduced a modification to the concept of ALARA (as low as reasonably acceptable) reflecting the fact that the major controllable source of exposure to radiation in the United States is the diagnostic imaging test. The new concept, ALADA means "as low as diagnostically acceptable." For this new concept to be implemented, evidence-based clinical trials are necessary to specify the optimal image quality for a diagnosis, as well as the exposure and radiation dose necessary to meet the main objectives.

As a summery, from a clinical illustrative perspective, we should keep in mind that considering a 0.20 voxel size, around 2.46-3.11 mm^3 would be the smallest ERR lesion that could be detectable with 115-206 μSv (child-adult) of radiation dose, with a sensitivity of 60.8% and a specificity of 60% using a CBCT.[34] We would need more randomized clinical trials (RCTs) to demonstrate what is the minimum radiation dose necessary to diagnose the minimum ERR with the highest possible resolution.

CONCLUSIONS

The highest and lowest sensitivity and specificity of CBCT for diagnosis of external root resorption are 42%-98% and 49.3%-96.3%. The minimum and maximum effective doses of dental CBCT for external root resorption diagnosis are 34 μSv and 1073 μSv. There is a wide range of variation in sensitivity and specificity of CBCT for diagnosis of external root resorption, therefore more studies are needed in order to clarify the lowest radiation dose necessary to correctly diagnose the minimum ERR with CBCT.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jebdp.2022.101803.

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