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ORIGINAL ARTICLE

Root resorption of endodontically treated teeth following orthodontic treatment: a meta-analysis

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Abstract
Objective The aim of this meta-analysis was to investigate the effect of orthodontic treatment on root resorption of endodontically treated teeth compared to vital teeth.
Materials and methods A literature search was conducted in 18 electronic databases. Review articles and relevant articles were searched for cross-references. Two independent reviewers screened all articles according to predefined inclusion and exclusion criteria and extracted the corresponding data. The pooled estimate of mean difference of root resorption weighted by the fixed-effect model and the corresponding 95 % confidence intervals (CIs) were used to construct a forest plot by implementing the "RevMan 5.1" software. Quality and heterogeneity assessments as well as publication bias evaluation and sensitivity analyses were performed. Inter-reviewer agreement for data selection, data extraction and quality analysis was evaluated by Cohen's kappa.
Results Six out of 1,942 original papers met the inclusion criteria. Four out of six studies were included in the quantitative analysis. Root resorption was less in endodontically treated teeth than in vital teeth (MD=−0.48 mm; 95 % CI=−0.81 to −0.14 mm). The funnel plot indicated no evidence of publication bias, while no data heterogeneity was present (I^2=0 %). However, the overall quality of the included studies was considered as "low."
Conclusions Following orthodontic treatment, endodontically treated teeth exhibit relatively less root resorption than teeth with vital pulps.
Clinical relevance Clinicians should consider orthodontic movement of endodontically treated teeth as a relatively safe clinical procedure.

Keywords External apical root resorption · Root resorption · Endodontics · Orthodontic treatment · Systematic review · Meta-analysis

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Introduction

Root resorption of teeth is an undesirable, particularly complicated and nonreversible pathologic process, which is related to the external layers of cementum, the dentine of the root, or the apex [1, 2].

External apical root resorption has long been recognized as an unwanted side effect of orthodontic tooth movement and a significant number of published articles have confirmed the relationship between orthodontic treatment and external root resorption, especially concerning the incisors, as well as the canines, premolars, and molars [3–6]. This can be attributed to both bone remodeling and to root resorption that take place as a sterile inflammatory process initiated by force application [7]. The degree and severity of the external root resorption associated with orthodontic treatment depends on several factors, with the duration of treatment and the type and magnitude of orthodontic forces playing a major role [1, 8]. Histological studies have reported that root resorption occurs in 90 % of teeth that have been moved orthodontically [9, 10], while 1–5 % of orthodontically moved teeth suffer resorption amounting to one third of the original root length [11]. Orthodontic patients that present a detectable root resorption during the first 6 months of active treatment are more likely to experience resorption in the following 6-month period than those without [12].

Root resorption during orthodontic treatment has been associated with previously endodontically treated teeth, since some authors found that previously endodontically treated teeth exhibit more [13, 14], equal [15], or less root resorption [16, 17]. According to these aforementioned controversial results, it seems that root resorption of endodontically treated teeth compared to vital teeth during orthodontic treatment remains an issue that needs to be investigated in an evidence-based manner.

Among all available study designs, systematic reviews and meta-analyses (MAs) are considered to be the study designs providing the strongest evidence [18]. Thus, the aim of this study was to qualitatively evaluate the currently existing evidence by undertaking a systematic review of the literature and to perform a quantitative synthesis of the corresponding data by means of a MA in order to detect whether there is a difference in the apical root resorption of endodontically treated teeth compared to vital teeth subjected to orthodontic treatment.

Material and methods

This MA was undertaken by following the PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions [19].

Data sources and searches

Electronic searches were conducted for studies published up to January 2012. In addition, the reference lists of the articles eligible for inclusion in this investigation were also manually reviewed. Citations of articles published in journals, dissertations, and conference proceedings were located by searching several electronic databases, using a search strategy appropriately adjusted for each individual database (Table 1).

No restrictions were applied concerning publication year, language, or status. "Gray literature" (i.e., materials that cannot be found easily through conventional channels) was not excluded from our search. When additional information was needed, authors, journal editors, or libraries were contacted.

Study selection

Two reviewers (IIM and AZ) independently screened titles, abstracts, and full-text reports. Any disagreement was resolved by consultation with the third author (MAP) until a final consensus was achieved. Inter-reviewer agreement on study eligibility was assessed by Cohen's kappa. Appropriate studies to be included in the MA fulfilled specific predefined inclusion criteria; only randomized controlled clinical trials (RCTs), quasirandomized controlled clinical trials, and prospective and retrospective controlled clinical trials (CCTs) were included in current investigation (Table 2).

Data extraction

Two reviewers (IIM and AZ) independently extracted relevant data in a pre-designed collection form. Any disagreement was resolved by consultation with the third author (MAP) until a final consensus was achieved. Inter-reviewer agreement on data extraction was assessed by Cohen's kappa.

Quality assessment

Strength of evidence was evaluated with respect to pre-established characteristics [20, 21]. Studies were categorized as of low (0–5 points), medium (6–8 points), or high (9 or 10 points) quality. Inter-reviewer agreement on quality assessment was evaluated by Cohen's kappa.

Assessment of publication bias

Publication bias was evaluated through visual inspection of funnel plot asymmetry [22], which however should be seen as a means of examining "small study effects" and not as a tool to diagnose specific types of bias [23]. In the presence of publication bias, the Begg and Mazumdar's rank correlation test [24] was planned to be conducted to examine the negative correlation between the standardized effect size and the standard errors of these effects, as well as the linear regression-based tests proposed by Egger et al. [25] to quantify the publication bias captured by the funnel plot.

Data synthesis

Data were summarized and considered suitable for pooling if the corresponding studies used similar interventions in the same way and reported similar outcomes. The pooled estimate of mean difference (MD) of root resorption weighted by the fixed-effect model and the corresponding 95 % confidence intervals (CIs) were used to construct a forest plot by implementing the "RevMan 5.1" [26], a specific software for performing systematic reviews and meta-analyses provided by the Cochrane Collaboration.

Heterogeneity assessment

To assess heterogeneity, the I^2 statistic was calculated, which is considered as a useful statistic for quantifying inconsistency [27]. I^2 is defined according to the following formula [27, 28]:

$$I^2 = [(Q - df)/Q] \times 100\%,$$

Table 1 The electronic databases searched, the search strategies used, and the corresponding results

Electronic database	Search strategy used	Extend of search	Hits
MEDLINE searched via PubMed on 24 November 2011 www.ncbi.nlm.nih.gov/sites/entrez/	(((resorpt*) OR (resorbt*)) AND (orthodont*)) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh]) OR ("clinical trial"[tw]) OR (singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw]) OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study OR evaluation studies OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]))	In all fields	757
EMBASE searched via ScienceDirect on 8 December 2011 www.embase.com	((resorpt*) OR (resorbt*)) AND (orthodont*)	Limited to Embase	413
Cochrane Database of Systematic Reviews searched via The Cochrane Library on 8 December 2011 www.thecochranelibrary.com	(orthodontic) and (resorption)	In all fields	19
Cochrane Central Register of Controlled Trials searched via The Cochrane Library on 08.12.2011 www.thecochranelibrary.com	(Orthodontic) and (resorption)	In all fields	52
Google Scholar Beta searched on 11 January 2012 www.scholar.google.com	Orthodontic resorption	Title only	298
Web of Science searched on 6 January 2012 http://scientific.thomson.com/products/wos/	[((Randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh]) OR ("clinical trial"[tw]) OR [(singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])] OR (placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study OR evaluation studies OR follow-up studies[mh] OR prospective studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw])]) and Topic = (orthodont*) and Topic = (resorpt*)	Refined by subject areas: dentistry, oral surgery medicine or radiology, nuclear medicine, medical imaging or biophysics or research experimental medicine	122
Evidence-based medicine searched on 9.12.2011 http://ebm.bmjjournals.com	Orthodont* and resorpt*	In all fields	0
Scopus searched on 21 December 2011 www.scopus.com	(ABS(resorpt*) AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal)) AND (ABS(orthodont*) AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal))	Subject areas: dentistry, medicine, biochemistry, genetics and molecular biology, health professions, immunology and microbiology, pharmacology, toxicology and pharmaceutics	847
LILACS database searched on 9 December 2011 http://bases.bvs.br	(orthodontic) AND (resorption)	In all fields	97
Bibliografia Brasileira de Odontologia searched on 12 December 2011 http://bases.bvs.br	(orthodontic) AND (resorption)	In all fields	74
Ovid database searched via Heal-link on 6 January 2012 http://ovidsp.ovid.com/autologin.html	(orthodont*) AND (resorpt*)	Journal subsets: clinical medicine, life and biomedical sciences, life sciences, health professions and medical humanities; limited to abstracts, original articles and articles with abstracts Ovid databases: Journals@Ovid Full	185

Table 1 (continued)

Electronic database	Search strategy used	Extend of search	Hits
		Text, Your Journals@Ovid via HEAL-Link	
Bandolier searched on 12 December 2011 http://www.jr2.ox.ac.uk/Bandolier	Orthodontic AND resorption	In all fields	1
Atypon Link searched on 12 December 2011 http://www.atypon-link.com/	orthodont* and resorpt*	In all fields	1
African Journals Online searched on 12 December 2011 www.ajol.info	orthodontic AND resorption	In all fields [a]	1
Digital dissertations searched via UMI ProQuest on 6 January 2012 http://proquest.umi.com/pqdweb?RQT=302&cfc=1	(orthodont*) AND (resorpt*)	Citation and abstracts searched (databases: dissertations and theses)	269
Conference Paper Index searched via Cambridge Scientific Abstracts on 21 December 2011 http://journals.cambridge.org/action/search	(orthodontic) AND (resorption)	In all fields	3
metaRegister of Controlled Trials (all registers active and archived) searched on 21 December 2011 http://www.controlled-trials.com/mrct/	(orthodont*) AND (resorpt*)	In all fields[a]	7
German National Library of Medicine (ZB MED) searched on 06.01.2012 http://www.medpilot.de	(orthodont*) AND (resorpt*)	Limits: keywords only, MEDLINE excluded	3
Sum			3,149

[a] Indicates limited search capabilities.

where Q is the chi-squared statistic and df is its degrees of freedom.

This describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling

Table 2 Eligibility criteria used in this meta-analysis

Criteria category	Inclusion criteria	Exclusion criteria
Outcome	Studies investigating apical root resorption of endodontically treated teeth compared to vital teeth subjected to orthodontic treatment	Investigations not relevant to the subject of this study
Study design	Randomized controlled clinical trials	Prospective uncontrolled clinical trials
	Quasirandomized controlled clinical trials	Retrospective uncontrolled clinical trials
	Prospective controlled clinical trials	Unsupported opinion of expert
	Retrospective controlled clinical trials	Editor's choices
		Books' abstracts
		Conferences' abstracts
		Cross-sectional surveys
		Narrative reviews
		Systematic reviews
		Meta-analyses
		Animal studies
		Replies to the author/editor
		Studies on molecular biology, histology or genetics
		In vitro studies
		Case series without a control
		Case reports
		Case-control observational studies
		Studies with missing English abstract or/and having no abstract at all
		Ongoing studies
Participants' characteristics		Clinical trials with inadequate sample size groups

error (chance) [29]. I^2 is independent of the number of studies and quantifies heterogeneity on a scale of 0–100 %. Heterogeneity was defined as low (25 %), moderate (50 %), or high (75 %) [25]. In addition, although the Q value was also calculated, only its significance was taken into consideration.

Sensitivity analyses

Additional meta-analyses were conducted to explore the influence of study design, trial quality, sample adequacy, blinding, method error analysis, publication date, and removal of individual studies on the effect size.

Results

Literature flow

Initially, the search yielded 3,149 records. After subtraction of duplicates, 1,938 titles remained, while four additional articles were identified through manual searching (n=1,942). In total, 1,931 records were excluded for various reasons after implementation of the specific exclusion criteria. Of the remaining 11 articles, the full text was not accessible for four studies, even after attempts were made to contact the authors, journal editors and university libraries containing the title. Finally, one study did not use a proper control group, and thus it was excluded. Consequently, only six studies remained for final qualitative evaluation. Because two of the studies used data of the same subgroup of teeth [30, 31], they were counted as one study in quantitative synthesis. Furthermore, one additional study [32] used a different methodology (presented below) as the other included studies in the qualitative synthesis, and therefore it was excluded from the data pooling. In total, four studies were included in quantitative synthesis.

The selection procedure, the number of excluded studies, and the corresponding reasons for exclusion are provided in Fig. 1 and Table 3. The kappa scores before reconciliation for study selection, data extraction, and quality evaluation procedures were 0.799, 1.000, and 0.656, respectively. According to Landis and Koch [33], these kappa scores indicated substantial, almost perfect and substantial inter-reviewer agreement, respectively.

Description of studies and baseline characteristics

The characteristics of the studies included in the MA are presented in Table 4.

The sample of 39 pairs of endodontically treated teeth and its contralateral vital controls in two of the articles [30, 31] originates from a larger sample of 343 patients examined in the two studies by the same authors. In the first study, the prevalence and severity of apical root resorption of maxillary anterior teeth is evaluated and any differences between subgroups of patients with and without a history of earlier orthodontic treatment are analyzed [30]; while in the second, the risk factors of root resorption of maxillary teeth in adult patients who had undergone orthodontic treatment are investigated [31]. The subgroup of endodontically treated teeth is common for the two studies and therefore is used only once in the present study. Moreover, the sample in these articles [30, 31] included incisors and canines, while the rest of the articles used only incisors in their samples. However, after contacting the authors [30, 31], they kindly provided all their detailed data (including the incisors) used in their study. Thus, the sample used in the present study originated from these two studies consisted of 28 endodontically treated incisors (15 centrals and 13 laterals) and their contralateral vital controls. Finally, Llamas-Carreras et al. [32] used a distinctively different methodology, since they used all types of teeth, while the measurements were carried out on digital panoramic radiographs. Moreover, they measured the proportion of root resorption of the teeth and not the tooth lengths as the other included studies. Due to these reasons, the data of this study could not be pooled, and thus it was not included in the quantitative synthesis.

In total, the amount of root resorption of 107 endodontically treated incisors was measured before (T1) and after treatment (T2), while 107 contralateral vital teeth of the former served as control group. The amount of root resorption was measured by measuring the tooth length in periapical radiographs.

Quality assessment

The overall quality of the studies included in the MA was evaluated as “Low.” All five studies were retrospective controlled clinical trials of low quality (Tables 4 and 5). In all of the studies, the sample was deemed as adequate, since 15 or more patients were included in each group. In three studies, a method error analysis was used, while no study assessed the possible impact of confounding factors.

Assessment of publication bias

The funnel plot exhibited a symmetrical distribution, indicating that there is no evidence of publication bias of the data of the source studies (Fig. 2), and thus no other statistical evaluations of publication bias, such as

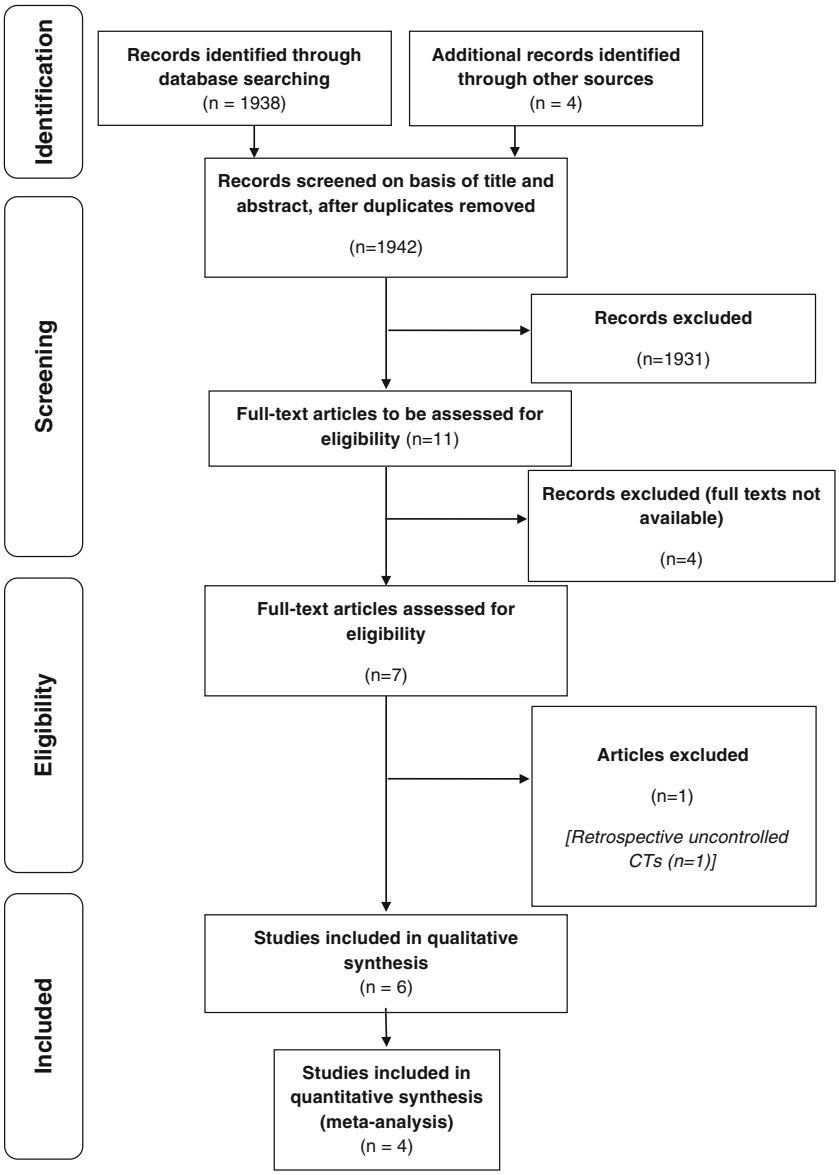

Fig. 1 Flow diagram of the studies retrieved through the selection process

the Begg and Mazumdar's rank correlation test [24] or the linear regression-based tests by Egger et al. [25] were performed.

Data synthesis and heterogeneity assessment

Root resorption was significantly less in endodontically treated teeth than in teeth with vital pulp (MD: −0.48 mm, 95 % CI: −1.32 to −0.22 mm; P=0.005; Fig. 3). Heterogeneity of the source data was low (I^2=0 %).

Sensitivity analysis

Sensitivity analysis indicated relative robustness of results. With regard to the outcomes, only minor changes were observed, which were nonsignificant. In addition, no "reversal of effect direction" was noted. Finally, concerning the importance of individual studies, no changes were found. The only possible exception in robustness was observed after the removal of the study by Spurrier et al. [34], which seemed to increase the MD of root resorption between the two tooth groups by 0.79 mm.

Discussion

The electronic search and the corresponding selection procedure yielded only a few studies appropriate for inclusion, due to the fact that in this MA a precise protocol was followed to minimize possible selection bias. This may be indicative of the lack of original high-quality studies in the currently existing literature concerning the issue of root resorption during orthodontic treatment of endodontically treated teeth.

Table 3 Number of the excluded articles in this meta-analysis according to the exclusion criteria

Exclusion criteria	Number of excluded articles
Investigations not relevant to the subject of this study	1,907
Prospective uncontrolled clinical trials	0
Prospective clinical trials with inadequate sample size groups	1
Retrospective uncontrolled clinical trials	1
Unsupported opinion of expert	0
Editor's choices	1
Books' abstracts	0
Conferences' abstracts	1
Cross-sectional surveys	0
Reviews	8
Systematic reviews	0
Meta-analysis	0
Animal studies	9
Replies to the author/editor	0
Studies on molecular biology, histology or genetics	0
In vitro studies	0
Case series without a control	0
Case reports or reports of cases	4
Case-control observational studies	0
Studies with missing English abstract or/and having no abstract at all	0
Ongoing studies	0
Full-text unavailable	4
Total	1,936

The results of this investigation indicate that there are differences between the amount of root resorption in endodontically treated teeth and in teeth with vital pulps. Root resorption was significantly less in endodontically treated teeth than in vital teeth and the pooled MD of root resorption between these two groups was −0.48 mm (95 % CI=−0.81 to −0.14 mm; P=0.005), although this difference (−0.48 mm) might be considered of little clinical importance. Further, in three of the studies included in this MA that performed a method error analysis, the mean error for the tooth length measurements was 0.34 mm in two of the studies [30, 31], and 0.32 and 0.18 mm for the measurements of the endodontically treated teeth and the control teeth, respectively, in the third study [34], amounts comparable but less than the MD found in current evaluation.

The result of the present study agrees with the result of several studies which found significant less root resorption in endodontically treated teeth subjected to orthodontic treatment as compared to vital ones [16, 30, 31, 34].

Other studies have shown no significant differences in root resorption between vital and root-filled teeth [17, 32, 35–37]. However, two of these studies [35, 36] were conducted in animals, while one study [32] used teeth of all types (incisors, canines, premolars, molars), a fact that could be considered as a confounding factor, since maxillary incisors have been shown to exhibit a greater amount of root resorption during orthodontic treatment, compared to other tooth types [38, 39].

In contrast to the results of this investigation, two studies have shown loss of cementum to be greater in endodontically treated teeth, although there was no difference in radiographic root length between vital and root-filled teeth [14, 40]. However, both of these studies were conducted in animals. One additional study [13] found also a greater frequency of root resorption in the endodontically treated teeth compared to the vital controls; however, the majority of the cases included had received severe dental injury such as intrusion, extrusion, and replantation.

It has been suggested that the dental pulp plays an important role in the processes of root resorption and remodeling of cementum is associated with orthodontic tooth movement [16, 41]. The results of the present study comply with such a suggestion, but they do not offer direct evidence.

Although we initially planned to investigate all the possible factors that may affect root resorption of endodontically treated teeth subjected to orthodontic treatment, there were some drawbacks in the source studies that did not allow any further analysis of these factors.

Firstly, it has been suggested that traumatized teeth, either previously endodontically treated or not, exhibit a greater tendency towards root resorption [42], while orthodontic movement has been suggested to worsen the tendency to root resorption in previously traumatized teeth [13, 42, 43]. Dental injury could be a possible confounding factor in the present study; however, there is a lack of randomized clinical trials investigating patients with previously traumatized teeth undergoing orthodontic treatment. In general, data about the influence of previous dental trauma on root resorption during orthodontic treatment are few and conflicting. One study has shown that the average decrease in root length of traumatized teeth undergoing orthodontic treatment was 1.07 mm compared to 0.64 mm for un-injured teeth [4]. Brin et al. [44] studied the reaction of previously traumatized teeth to the application of orthodontic forces and found moderate root resorption in 27.8 % of previously injured teeth receiving orthodontic treatment compared to 7.8 % in the orthodontic treatment only group and 6.7 % in the trauma only group, while an increased frequency of root resorption was noted in teeth that had experienced multiple episodes of trauma. The authors suggested that previous trauma may be predictive of an increased risk of root

Table 4 Characteristics of the studies included in the qualitative evaluation

Nr	Study[a]	Source	Study design	Initial sample size (M/F)	Average Age in yrs (SD)	Type of teeth	Type of Measurement	Measurement method	Appliances used in orthodontic treatment and (Magnitude of the force exerted)	Orthodontic treatment duration	Timing of endodontic therapy	Materials used in endodontic therapy	Reported effects
1	Esteves et al. [17]	Electronic searching (Pubmed, Google Scholar, Scopus, Ovid)	rCCT	16 (NR/NR)	NR	Central incisors	Greatest length (from incisal edge to apex of root)	Periapical radiographs [With positioner. Magnification corrected according to Spurrier et al. (1990) [34]]	Brackets (NR)	≥1 Year 8 months	>1 Year prior to orthodontic treatment	NR	No statistically significant difference ($p>0.05$)
2	Kreia et al. [45]	Electronic searching (Google Scholar, LILACS, Bibliografia Brasileira de Odontolgogia)	rCCT	20 (NR/NR)	NR	Maxillary incisors	Total length (from incisal edge to apex of root)	Periapical radiographs measurements. (Magnification corrected from plaster casts.)	NR (NR)	NR	NR	NR	No statistically significant difference ($p=0.05$)
3	Llamas-Carreras et al. [32]	Electronic searching (Google Scholar, Scopus, Ovid)	pCCT	77 (21/56)	32.7 (±10.7)	Maxillary and mandibular incisors, canines, premolars and molars	Proportion of root resorption (endodontically treated/vital)	Digital panoramic radiographs (Measured digitally. Magnification standardized using crown length measurements)	Multiband/bracket (NR)	26.8± 8.9 months	Prior to orthodontic treatment, exact time not specified	NR	No statistically significant difference
4	Mirabella and Årtun [30][b]	Electronic searching (Google Scholar, Scopus, Web of science)	rCCT	39[c] (NR/NR)	34.5 (±9.0)	Maxillary anterior teeth (central incisors, lateral incisors, canines)	Method I: tooth length (from incisal edge to apex of root) Method II: (Magnification corrected by crown length)	Periapical radiographs (paralleling long cone technique) (Magnification corrected by measuring crown length)	Multibonded appliances with 0.022×0.028 in. bracket slots (NR)	2.0±0.7 year	NR	NR	Less resorption of the endodontically treated teeth ($P<0.05$)
5	Mirabella and Årtun [31][b]	Electronic searching (Pubmed, Google Scholar, Scopus)	rCCT	39[c] (NR/NR)	34.5 (±9.0)	Maxillary anterior teeth (central incisors, lateral incisors, canines)	Tooth length (from incisal edge to apex of root)	Periapical radiographs (paralleling long cone technique) (Magnification corrected by measuring crown length)	Multi-bonded appliances with 0.022×0.028 in. bracket slots (NR)	2.0±0.7 year	NR	NR	Less resorption of the endodontically treated teeth ($P<0.05$)
6	Spurrier et al. [34]	Electronic searching (Pubmed, Google Scholar, Scopus)	rCCT	43 (21/22)	13,9 (NR)	Incisors	Tooth length (from incisal edge to apex of root)	Periapical radiographs. (Magnification corrected by measuring crown length)	Multibands, brackets (NR)	2 years 1 month	Prior to orthodontic treatment, exact time not specified	NR	Vital incisors resorbed more than endodontically treated incisors ($P<0.05$)

rCCT retrospective controlled clinical trial, *pCCT* prospective controlled clinical trial, *M/F* male/female, *NR* nor reported

[a] Authors in alphabetical order

[b] Both studies by Mirabella and Årtun [30, 31] used the same subgroup of endodontically treated teeth and vital control teeth, so the data were included only once in the quantitative synthesis

[c] The group in the original articles [30, 31] consisted of 39 teeth (central and lateral incisors and canines), while in the present study only data from central and lateral incisors were used ($n=28$)

Table 5 Quality evaluation of the studies included in the MA

Number	Study[a]	Study design	Sample size	Selection description	Valid measurement methods	Method error analysis	Blinding in measurements	Adequate statistics provided	Confounding factors	Score	Judged quality standard
1	Esteves et al. [17]	0	1	0	1	0	0	1	0	3	Low
2	Kreia et al. [45]	0	1	0	1	0	0	1	0	3	Low
3	Mirabella and Årtun [30]	0	1	0	1	1	0	1	0	4	Low
3	Mirabella and Årtun [31]	0	1	0	1	1	0	1	0	4	Low
5	Spurrier et al. [34]	0	1	1	1	1	0	1	0	5	Low
Overall estimate										4	Low

[a] Authors in alphabetical order

The following eight variables were evaluated: study design (RCT = 3 points; prospective study = 1 point; retrospective study = 0 point); sample size (adequate = 1 point; partly inadequate = 0.5 point; inadequate = 0 point); selection description (adequate = 1; partly inadequate = 0.5; inadequate = 0); valid measurement methods = 1 point; use of method error analysis = 1 point; use of blinding in measurements = 1 point; Confounding factors estimated in analysis = 1 point. In summary, a study could maximally score 10 points and was categorized of low (0–5 points), medium (6–8), or high (9–10) quality

resorption during orthodontic treatment, although they concede a small sample size and a heterogeneous collection of injuries may render findings inconclusive [44]. Malmgren et al. [15] however found that traumatized teeth did not have a greater tendency to root resorption than un-injured teeth, although they suggest previously traumatized teeth with signs of root resorption prior to orthodontic treatment may be more prone to root resorption during treatment.

In any case, it should be stated that it is difficult to properly record and quantify the intensity, location, and type of previous teeth injuries. Of the studies that met the inclusion criteria to be considered in the present MA, two studies [17, 45] do not mention if the teeth included were previously injured, while in the study of Spurrier et al. [34] it is stated that "the extent to which either tooth may have been traumatized was not known." All anterior teeth included in Llamas-Carreras et al.'s study [32] had received trauma. In the remaining two studies [30, 31], although the history of traumatic injury was recorded, the severity of the trauma was not recorded and it is also not specifically mentioned if the endodontically treated teeth included in the study were injured. Thus, because of the lack of related data, no useful conclusion could be drawn regarding the effect of dental injury to the root resorption of orthodontically moved vital or root-filled teeth.

Further, the discussion of the type of materials used for endodontic treatment is important, since they could influence possible inflammatory reactions. For example, Ca(OH)2-based materials have been shown to have a favorable effect on periapical tissue healing and repair of orthodontic root resorption in endodontically treated dogs' teeth [46], while apical foramen widening combined with Ca(OH)2-containing sealer have been shown to be more favorable to the healing of chronic periapical lesions than other sealers [47]. Moreover, the periapical histological repair was found to be better in the teeth with Ca(OH)2 root canal dressing before obturation than in teeth with immediate obturation [48]. The presence of other materials, such as zinc oxide and eugenol, induces chronic periapical inflammation because of the toxicity to the tissues [49, 50], while root canal treatment performed with iodoform-containing root canal filling material was found to accelerate root resorption in root canal-treated primary molars compared with homologous teeth without endodontic treatment [51]. However, none of the included studies in the MA mentioned the materials used in endodontic treatment, and thus a further investigation of the results of this evaluation concerning this factor could not be performed.

In addition, the timing of the endodontic therapy was not mentioned in all studies. Timing of endodontic

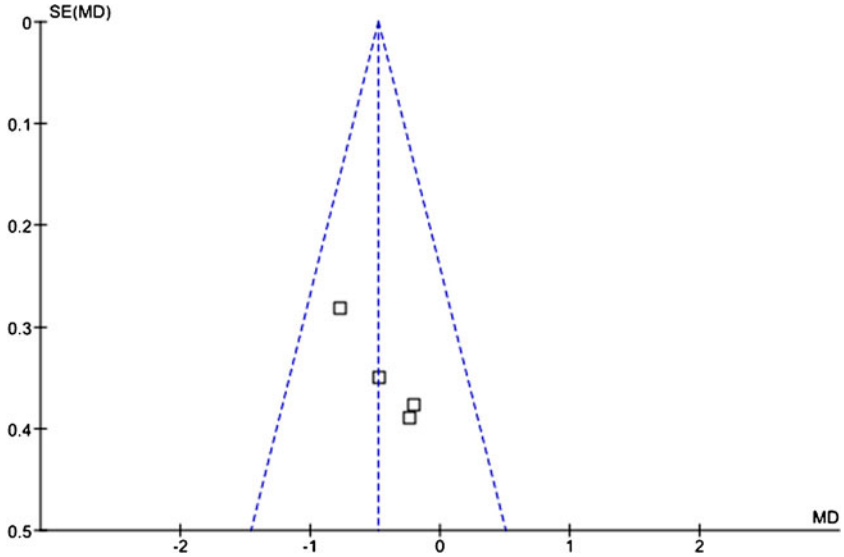

Fig. 2 Funnel plot for the mean difference of root resorption between the endodontically treated teeth and the control group of teeth with vital pulp. The funnel plot exhibits a symmetrical distribution, which indicates that there is no evidence of publication bias of the data of the source studies

therapy related to the onset of orthodontic treatment is of potential interest because the periapical environment of teeth with apical periodontitis may exhibit inflammatory reaction, and consequently bone and root resorption [52] and higher concentrations of bacterial endotoxin [53]. While periapical lesions can heal completely in as early as a 1–3 months time after endodontic treatment [54, 55], incomplete healing can be found in 7.6 % of cases up to 5 years after endodontic treatment [54]. The presence of inflammatory factors could be a matter of concern for orthodontic movement, since it can contribute to an increased inflammatory reaction and root resorption [34] with possible implications for the healing process. Nevertheless, the timing of the endodontic therapy was mentioned only in three of the included studies [17, 32, 34]. Two studies [32, 34] mention that root canal treatment was completed prior to the start of orthodontic treatment without specifying the exact time, while Esteves et al. [17] state that all root canal treatments were completed more than a year before the start of orthodontic treatment.

The strengths of this investigation include the fact that a precise protocol was used with predetermined inclusion criteria concerning study design. In addition, there was no evidence of publication bias, as well as low heterogeneity of the data of the source studies. Finally, sensitivity analysis showed relative robustness of the results.

However, there are also some limitations that diminish in a way the results of this MA, such as the small number of original studies that were possible to be included in the MA, as well as their low quality. Moreover, the pooled sample possibly included previously traumatized teeth, which might be considered as a confounding factor, due to the possible susceptibility of such teeth to root resorption [14].

Conclusions

The results of this MA should be interpreted with some caution, due to the small number and the low quality of included studies although every attempt was made to avoid misleading errors. Under the current limitations, the following conclusions can be drawn:

- Following orthodontic treatment, endodontically treated teeth exhibit relatively less root resorption than teeth with vital pulps, although the overall amount of this resorption might be of little clinical importance.

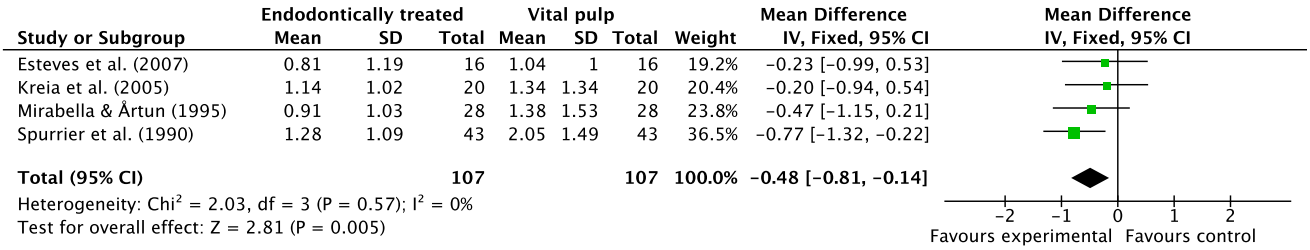

Fig. 3 Forest plot using the fixed-effect model for the mean difference of root resorption and the corresponding confidence intervals between the endodontically treated teeth and the control group of teeth with vital pulp. Root resorption was shown to be significantly less in endodontically treated teeth than in teeth with vital pulp, while heterogeneity of the source data was low

- Clinicians should consider orthodontic movement of endodontically treated teeth as a relatively safe clinical procedure.

The investigation of root resorption of orthodontically treated root-filled teeth compared to vital teeth by well-designed RCTs could be very useful. Such high-quality studies could produce strong evidence to further support the results of the current investigation, as well as to answer the questions that remained unanswered in this MA due to the lack of appropriate data.

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Conflict of interest The authors declare no conflict of interest.

References

1. Bakland LK (1992) Root resorption. Dent Clin North Am 36:491–507
2. Brezniak N, Wasserstein A (2002) Orthodontically induced inflammatory root resorption. Part 1: the basic science aspects. Angle Orthod 72:175–179
3. Levander E, Malmgren O (1988) Evaluation of the risk of root resorption during orthodontic treatment: a study of upper incisors. Eur J Orthod 10:30–38
4. Linge BO, Linge L (1983) Apical root resorption in upper anterior teeth. Eur J Orthod 5:173–183
5. Kaley J, Phillips C (1991) Factors related to root resorption in edgewise practice. Angle Orthod 61:125–132
6. Apajalahti S, Peltola JS (2007) Apical root resorption after orthodontic treatment: a retrospective study. Eur J Orthod 29:408–412
7. Weiland F (2006) External root resorptions and orthodontic forces: correlations and clinical consequences. Prog Orthod 7:156–163
8. Beck BW, Harris EF (1994) Apical root resorption in orthodontically treated subjects: analysis of edgewise and light wire mechanics. Am J Orthod Dentofacial Orthop 105:350–361
9. Harry M, Sims M (1982) Root resorption in bicuspid intrusion. A scanning electron microscope study. Angle Orthod 52:236–258
10. Stevnik A, Mjor I (1970) Pulp and dentine reactions to experimental tooth intrusion. A histological study of the initial changes. Am J Orthod Dentofacial Orthop 57:370–385
11. Reitan K (1974) Initial tissue behavior during apical root resorption. Angle Orthod 44:68–82
12. Artun J, Smale I, Behbehani F, Doppel D, Van't Hof M, Kuijpers-Jagtman AM (2005) Apical root resorption six and 12 months after initiation of fixed orthodontic appliance therapy. Angle Orthod 75:919–926
13. Wickwire NA, McNeil MH, Norton LA, Duell RC (1974) The effects of tooth movement upon endodontically treated teeth. Angle Orthod 44:235–242
14. Gong XY, Jian XC, Lei YH, Yao ZY, Hong T, Ma DY (2007) An experimental study of the effects of root-canal treatment on orthodontic movement in cat cuspids. Shanghai Kou Qiang Yi Xue 16:206–210
15. Malmgren O, Goldson L, Hill C, Orwin A, Petrini L, Lundberg M (1982) Root resorption after orthodontic treatment of traumatized teeth. Am J Orthod 82:487–491
16. Satoh I (1990) Root resorption of vital and endodontically treated teeth in orthodontic movement. Kanagawa Shigaku 24:601–617
17. Esteves T, Ramos AL, Pereira CM, Hidalgo MM (2007) Orthodontic root resorption of endodontically treated teeth. J Endod 33:119–122
18. Papadopoulos MA (2003) Meta-analysis in evidence-based orthodontics. Orthod Craniofac Res 6:112–126
19. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 6:e1000100
20. Antczak AA, Tang J, Chalmers TC (1986) Quality assessment of randomized control trials in dental research. I. Methods. J Periodontal Res 21:305–314
21. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ (1996) Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 17:1–12
22. Light RJ, Pillemer DB (1984) Summing up: the science of reviewing research. Harvard University Press, Cambridge
23. Sterne JAC, Egger M, Smith GD (2001) Investigating and dealing with publication and other biases. In: Egger M, Davey Smith G, Altman DG (eds) Systematic reviews in health care: meta-analysis in context. BMJ Publication Group, London, pp 189–208
24. Begg CB, Mazumdar M (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50:1088–1101
25. Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315:629–634
26. Review manager (RevMan) [computer program]. Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2011. Available at www.ims.cochrane.org/revman. Accessed 8 August 2011
27. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21:1539–1558
28. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327:557–560
29. Higgins JP, Green S (eds) Cochrane handbook for systematic reviews of interventions 4.2.6 [updated September 2006]. http://www.cochrane.org/resources/handbook/hbook.htm. Accessed 6 October 2006
30. Mirabella AD, Årtun J (1995) Prevalence and severity of apical root resorption of maxillary anterior teeth in adult orthodontic patients. Eur J Orthod 17:93–99
31. Mirabella AD, Årtun J (1995) Risk factors for apical root resorption of maxillary anterior teeth in adult orthodontic patients. Am J Orthod Dentofacial Orthop 108:48–55
32. Llamas-Carreras JM, Amarilla A, Solano E, Velasco-Ortega E, Rodríguez-Varo L, Segura-Egea JJ (2010) Study of external root resorption during orthodontic treatment in root filled teeth compared with their contralateral teeth with vital pulps. Int Endod J 43:654–662
33. Landis JR, Koch GG (1977) The measurement of observer agreement for categorical data. Biometrics 33:159–174
34. Spurrier SW, Hall SH, Joondeph DR, Shapiro PA, Riedel RA (1990) A comparison of apical root resorption during orthodontic treatment in endodontically treated and vital teeth. Am J Orthod Dentofacial Orthop 97:130–134
35. Huettner RI, Shore B, Young RW (1955) The movability of vital and devitalized teeth in the *Macacus* rhesus monkey. Am J Orthod 41:594–603
36. Mattison GD, Delivanis HP, Delivanis PD, Johns PI (1984) Orthodontic root resorption of vital and endodontically treated teeth. J Endod 10:354–358
37. Llamas-Carreras JM, Amarilla A, Espinar-Escalona E, Castellanos-Cosano L, Martín-González J, Sánchez-Domínguez

B, López-Frías FJ (2011) External apical root resorption in maxillary root-filled incisors after orthodontic treatment: a split-mouth design study. Med Oral Patol Oral Cir Bucal 17(3):e523–e527
38. Remington DN, Joondeph DR, Artun J, Riedel RA, Chapko MK (1989) Long-term evaluation of root resorption occurring during orthodontic treatment. Am J Orthod Dentofacial Orthop 96:43–46
39. Sameshima GT, Sinclair PM (2001) Predicting and preventing root resorption: part I. Diagnostic factors. Am J Orthod Dentofacial Orthop 119:505–510
40. Mah R, Holland GR, Pehowich E (1996) Periapical changes after orthodontic movement of root-filled ferret canines. J Endod 22:298–303
41. Bender IB, Byers MR, Mori K (1997) Periapical replacement resorption of permanent, vital, endodontically treated incisors after orthodontic movement: report of two cases. J Endod 23:768–773
42. Hamilton RS, Gutmann JL (1999) Endodontic-orthodontic relationships: a review of integrated treatment planning challenges. Int Endod J 32:343–360
43. Hines FB (1979) A radiographic evaluation of the response of previously avulsed teeth and partially avulsed teeth to orthodontic movement. Am J Orthod Dentofacial Orthop 75:1–19
44. Brin I, Ben-Bassat Y, Heling I, Engelberg A (1991) The influence of orthodontic treatment on previously traumatized permanent incisors. Eur J Orthod 13:372–377
45. Kreia TB, Tanaka O, Lara F, Camargo ES, Maruo H, Westphalen VPD (2005) Avaliação da reabsorção radicular após a movimentação ortodôntica em dentes tratados endodonticamente/Evaluation of root resorption after orthodontic treatment in endodontically treated teeth. Rev Odonto Ciênc 20:50–56
46. de Souza RS, de Souza V, Holland R, Gomes-Filho JE, Murata SS, Sonoda CK (2009) Effect of calcium hydroxide-based materials on periapical tissue healing and orthodontic root resorption of endodontically treated teeth in dogs. Dent Traumatol 25:213–218
47. Borlina SC, de Souza V, Holland R, Murata SS, Gomes-Filho JE, Dezan Junior E, Marion JJ, Neto Ddos A (2010) Influence of apical foramen widening and sealer on the healing of chronic periapical lesions induced in dogs' teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 109:932–940
48. Tanomaru Filho M, Leonardo MR, da Silva LA (2002) Effect of irrigating solution and calcium hydroxide root canal dressing on the repair of apical and periapical tissues of teeth with periapical lesion. J Endod 28:295–299
49. Yesilsoy C, Koren LZ, Morse DR, Kobayashi C (1988) A comparative tissue toxicity evaluation of established and newer root canal sealers. Oral Surg Oral Med Oral Pathol 65:459–467
50. Tanomaru-Filho M, Tanomaru JM, Leonardo MR, da Silva LA (2009) Periapical repair after root canal filling with different root canal sealers. Braz Dent J 20:389–395
51. Moskovitz M, Tickotsky N, Ashkar H, Holan G (2012) Degree of root resorption after root canal treatment with iodoform-containing filling material in primary molars. Quintessence Int 43:361–368
52. Holland R, Valle GF, Taintor JF, Ingle JI (1983) Influence of bony resorption on endodontic treatment. Oral Surg Oral Med Oral Pathol 55:191–203
53. Schein B, Schilder H (1975) Endotoxin content in endodontically involved teeth. J Endod 1:19–21
54. Calişkan MK, Sen BH (1996) Endodontic treatment of teeth with apical periodontitis using calcium hydroxide: a long-term study. Endod Dent Traumatol 12:215–221
55. Caliskan MK, Turkun M (1997) Periapical repair and apical closure of a pulpless tooth using calcium hydroxide. Oral Surg Oral Med Oral Pathol 84:683–687