EFFECTIVENESS, EFFICIENCY AND MOLECULAR MECHANISM OF SURGICAL AND NON-SURGICAL METHODS USED IN ACCELERATED ORTHODONTIC TOOTH MOVEMENT.
PART I: SYSTEMATIC REVIEW AND META-ANALYSIS OF SURGICAL METHODS.

Authors and affiliations

María Antonia Alvarez[a], Carlos Mario Franco[b], Juan Fernando Aristizábal[c], Diego Rey[d], Rubén Manrique[e].

[a]DDS, MSc, Faculty of Dentistry, CES University, Medellín, Colombia.
[b]DDS, MSc, Faculty of Dentistry, CES University, Medellín, Colombia.
[c]DDS, MSc, Faculty of Dentistry, Valle University, Cali, Colombia.
[d]DDS, Faculty of Dentistry, CES University, Medellín, Colombia.
[e]QF, MSc, PhD, CES University, Medellín, Colombia.

Corresponding author

María Antonia Alvarez
Faculty of Dentistry, CES University
Calle 10A # 22 – 04, Medellín, Colombia
Tel: +57 4 4440555
Email: malvarez@ces.edu.co

Summary

Background. Several surgical methods have been developed to accelerate orthodontic tooth movement, in past few years various randomized controlled trials have been published and this controversial topic was in need of an actualization.

Objective. To assess the effectiveness and describe the molecular mechanism involved in surgical methods used in accelerated orthodontics.

Search methods. Electronic database searches (MEDLINE, EMBASE, The Cochrane Library, and LILACS) were performed until June 2018 using controlled terms identified in the articles included in the theoretical framework. Additional controlled and uncontrolled vocabulary was identified using the search tools provided by the databases according to the PICO question.

Selection criteria. Articles were screened for randomized controlled trials using adjunctive surgical methods to accelerate orthodontic tooth movement, i.e. corticotomy, accelerated osteogenic orthodontics, periodontal distraction, corticision, piezopuncture, piezosurgery, piezocision and micro-osteoperforations;

with the following primary outcome measures: velocity of tooth movement; distance of accumulated tooth movement; total treatment time; and levels of inflammatory and bone remodeling markers in saliva or gingival crevicular fluid.
Data collection and analysis. Two independent authors evaluated the included articles using a standardized form to extract data, including quality indicators. Risk of bias was assessed using the Cochrane risk of bias tool.
Results. The searches resulted in 2.043 articles. After application of inclusion criteria, 17 randomized controlled trials were included in this systematic review. Of these, 8 evaluated the effect of corticotomies, 4 of piezocision, 4 of micro-osteoperforations, and 1 of periodontal ligament distraction.
Conclusions. Weak evidence suggests that corticotomy and piezocision are effective in accelerating orthodontic tooth movement in the first months of treatment. Strong evidence suggests that piezocision is unable to reduce the treatment time required to correct mandibular crowding and to perform en-masse retraction. High evidence suggests that micro-osteoperforations is able to accelerate maxillary canine retraction. Weak evidence suggests a positive correlation between stimulation of RAP accelerated tooth movement, however randomized clinical trials are still needed. Corticotomies and minimally invasive surgical procedures are safe to the periodontium.
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Key words: Accelerated tooth movement, Bone Remodeling, Systematic review, Meta-analysis.

Introduction

Conventional orthodontic treatment on average requires less than 2 years to complete(1). This treatment duration is considered extensive, especially by adult patients who increasingly seek for shorter and more efficient treatments(2). Since alveolar bone remodeling is the basis of orthodontic tooth movement(3), several surgical and non-surgical methods have been developed to accelerate this process and thus increase the speed of tooth movement(4,5).

Surgically facilitated orthodontic therapy is a procedure that uses conventional orthodontic forces through a healing wound to accelerate orthodontic tooth movement(6). Frost(7) described wound healing as a complex process characterized by a transient increase in tissue remodeling. He termed this process *regional acceleratory phenomenon* (RAP) and it has been described as the biological basis of surgically accelerated tooth movement(2). Cortical activation is defined as the injury that generates the biochemical changes that in turn induce and potentiate the RAP. It begins with a sterile, cytokine-mediated inflammatory process that increase bone remodeling and triggers transient regional osteopenia, which in turn accelerates orthodontic tooth movement(2,8,9).

Wilcko and Wilcko developed one of the surgically facilitated orthodontic tooth movement techniques, known as *periodontally accelerated osteogenic orthodontics* (PAOO), which consists in the combination of selective alveolar corticotomy after full-thickness flap elevation with bone grafts and conventional orthodontic forces. PAOO has the ability to accelerate orthodontic tooth movement and gives the possibility for contouring the bone phenotype(8–11). However, this procedure is considered invasive and therefore less accepted by the patients(12). For this reason, a number of different techniques have been developed, including as piezo-surgery(13), corticision(14), piezocision(12), piezopuncture(15), and micro-osteoperforations(16). These approaches aim for a minimally invasive surgical intervention that generates the necessary injury in the cortical bone to activate a response at the alveolar bone and periodontal ligament, which in turn accelerates orthodontic tooth movement.

In recent years, several systematic reviews(17–30) on accelerated orthodontic tooth movement have been published. Two of these reviews evaluated the biological mechanism involved in surgery facilitated orthodontic tooth movement and concluded that there is an increase in regional bone remodeling based on histological data(21,23). However, the authors only included animal studies, excluding recent studies in humans that would provide information more valuable for current clinical practice. The aim of Part I of this review was to systematically search the literature to evaluate the effectiveness and describe the molecular mechanisms involved in surgically facilitated orthodontic tooth movement in humans. In addition, we aimed to answer the following questions: 1) Does surgical methods performed in conjunction with orthodontic treatment significantly increase the speed of tooth movement and shorten the treatment time?; 2) Which molecular mechanisms are involved in surgical methods used in accelerated orthodontics?; and 3) What is the effect of surgical methods used in accelerated orthodontics on periodontal parameters and periodontal biotype?

Material and methods

This systematic review was based on a specific protocol developed following the guidelines outlined in the Cochrane Handbook of Systematic Reviews of Interventions and the PRISMA statement, and registered in the National Institute of Health Research Database (www.crd.york.ac.uk; 42017064638).

Eligibility criteria

Eligibility criteria were determined according to the PICO question and are shown in Table 1.
Exclusion criteria are shown in Table 1.

Search methods for identification of studies
Electronic database searches (MEDLINE, Supplementary Table 1; EMBASE, Supplementary Table 2; the Cochrane Library, Supplementary Table 3; and LILACS, Supplementary Table 4) were performed using controlled and uncontrolled terms identified from articles included in the theoretical framework. Additional controlled and uncontrolled vocabulary was identified using the databases search tools based on the PICO question. The reference lists of all included articles were also searched for relevant studies. The search was restricted to studies published in English and Spanish. No restriction was applied on the date of publication and no filter was used to retrieve specific types of publications. The databases were searched to June 2018.

Data collection and analysis
Two independent authors (M.A.A. and C.M.F.) evaluated the titles and abstracts of the studies that were found through the search strategy and performed a full-text assessment of the potentially eligible studies. Any disagreement regarding the eligibility was resolved by discussion or consultation with a third reviewer (R.M.).

A standardized form was used to extract data from the included studies for the quality assessment. The information extracted included: reference list, study objective, study design, study population, sampling method, interventions, description of the control group, follow-up time, presence of biases, measured results and comments.

Quality assessment and risk of bias
Three authors (M.A.A., C.M.F. and J.F.A.) independently assessed the data quality. The differences were solved by discussion or consultation with a fourth reviewer (R.M.).

The risk of bias was assessed following the Cochrane Collaboration's Tool for Assessing Risk of Bias as described in section 8.5 of the *Cochrane Handbook for Systematic Reviews of Interventions.* The following domains were classified as low, high, or unclear risk of bias on each individual study:

1. Selection bias
    - 1.a. Random sequence generation
    - 1.b. Allocation concealment
2. Performance bias
    - 2.a. Blinding of participants and personnel

2.b. Blinding of outcome assessment

3. Attrition bias

    3.a. Incomplete outcome data

4. Reporting bias

    4.a. Selective reporting

5. Other bias

    5.a. Other sources of bias.

Summary measures and approach to synthesis

1. Assessment of heterogeneity

We analyzed the heterogeneity of the included studies to evaluate the possibility of performing a quantitative synthesis or meta-analysis. We assessed the clinical heterogeneity by examining the characteristics of the study and treatment protocol, and the similarities of the participants, setting, interventions, materials, data collection method, and measures used to assess the outcomes of treatment. The statistical heterogeneity was assessed using the I2 statistic.

2. Data synthesis

We pooled the data of the articles that had similar study populations, interventions, and outcomes. The intervention effect was expressed as weighted mean differences (WMD). For continuous outcomes, we used 95% CI. Finally, we used random-effect models for meta-analyses.

3. Summary of results

We created a table to highlight the main characteristics (Table 2) and the results (Table 3) of the included studies.

Results

Description of studies

The electronic database search resulted in 2039 references. Four additional articles were identified through other sources. After removal of duplicates, a total of 889 articles were screened by title and abstract. Full-text evaluation of 31 potentially relevant studies was performed. After further assessment, 14 studies were excluded.

Finally, 17 randomized controlled trials (RCTs) were included in this review (16,31–46) (Figure 1).
Of the 17 RCTs included, 8 had not been included in previous systematic reviews(37,38,41–46).

Risk of bias within the studies

There is no homogeneity among the studies regarding the risk of bias. Five out of the 17 included studies presented with low risk of bias in most of the evaluation criteria. The all of the studies showed a high potential risk in terms of performance bias, most likely due to impossibility of blinding. Overall, the quality of the studies is acceptable. (Supplemental Table 5 and Table 4)

Qualitative synthesis

In order to conduct the qualitative analysis, all included studies were divided into 4 groups according to the intervention used to accelerate the orthodontic tooth movement. The analysis was made based on the outcomes proposed in the eligibility criteria. Table 3 provides a detailed view of the outcomes of the included studies.

1. Corticotomy. This intervention was performed in 8 studies(31–38) by doing a mucoperiosteal flap elevation in the area of interest, followed by vertical cuts and/or perforations on the alveolar bone to accomplish bone activation(31–33,36). Additionally, some studies placed bone grafts in the operated area(33,35,37,38). A meta-analysis was not performed because some of the data was missing or could not be compared.

- *Accumulative tooth movement.* One split-mouth RCT with unclear risk of bias(32) investigated the effect of corticotomy on the accumulative tooth movement in maxillary canine retraction. The authors found that the accumulative canine retraction was significantly higher in the experimental side vs. the control side at 1, 2, 3 and 4 months after surgery (P=0,01).

- *Rate of tooth movement.* Four split-mouth RCTs investigated the effect of corticotomy on the rate of maxillary canine retraction. Of these, three were at unclear risk of bias(31,32,36) and one at high risk of bias(33). Abbas et al.(31) found that the rate of canine crown tip were greater (P<0,05) in the corticotomy side compared to the control side at 2, 4, 6, 8, 10 and 12 weeks after surgery. Another study(36) also found a higher rate of tooth movement in the experimental side from week 1 to 12 (P<0,05).

Aboul-Ela et al.(32) reported a higher rate of anteroposterior movement of the canines (*P*<0,01) in the experimental side compared to the non-operated side at all measurement times (Month 1, 2, 3, and 4) after the intervention. Similarly, Jahanbakshi et al.(33) found that the velocity of tooth movement was significantly higher in the experimental side compared to the control side from month 1 to month 4, with a pooled rate of canine retraction of 1,8 ± 0,17 mm/month vs. 1,1 ± 7,39 mm/month (*P*<0,001).

- *Treatment duration.* Four parallel-group RCTs, three with high risk of bias(34,35,38) and one with unclear risk of bias(37), investigated the effect of corticotomy on the treatment time needed for en masse retraction of anterior teeth after premolar extraction, on the treatment time needed for mandibular decrowding, and the total treatment time from bracketing to debonding. Bhattacharya et al.(34) found that the en masse retraction time after premolar extraction was significantly higher in the control group as compared to the corticotomy group (*P*<0,001). Shoreibah et al.(35) reported a reduced treatment duration in the experimental group compared to the controls when correcting mandibular crowding from the beginning of treatment until debonding (17,5 weeks vs. 49,0 weeks); and Abbas and Moutamed(38) reported an accelerated mandibular decrowding in the experimental group compared to the controls (74,5 ± 7,7 days vs. 141,7 ± 21,3 days). However, these studies did not show *P*-values. Aristizabal et al.(37) evaluated the total treatment time of a comprehensive orthodontic treatment and found no statistical difference between the experimental group and the controls (8,20 ± 4,49 months vs. 13,40 ± 6,26 months; *P*=0,17).

- *Molecular mechanism.* Only one parallel-group RCT, which was at unclear risk of bias(37), attempted to describe the biological mechanisms involved in surgically facilitated orthodontics. The authors analyzed the urinary deoxypyridinoline (DPD), but due to the great inter- and intra-group variance of this bone resorption biomarker, no conclusion could be drawn. However, an increased bone turnover was noted 2 days after surgery in most patients of the experimental group; DPD increased between T1 and T2 and decreased in T3 almost to baseline level. In most of the control subjects, the DPD remained stable across all measurements.

- *Periodontal parameters.* Five studies, two split-mouth RCTs with unclear risk of bias(31,32), and three parallel-group RCTs with high(35,38) and unclear risk of bias(37), investigated this outcome. Except for the gingival index scores, which were found to be significantly higher (*P*<0.05) at the end of the treatment on the operated side compared to the non-operated side(32), no differences were found in any of the evaluated periodontal parameters among these studies.

2. Piezocision. This intervention was performed in 5 studies(31,39–42) by doing gingival microincisions in the area of interest, followed by vertical cuts on the alveolar bone through the gingiva to accomplish bone activation. A meta-analysis was not performed because some of the data was missing or could not be compared.

- *Accumulative tooth movement.* One split-mouth RCT, which was at unclear risk of bias, investigated the effect of piezocision on the accumulative tooth movement of canine retraction compared to conventional orthodontic tooth movement. Aksakalli et al.(39) found that the accumulative canine retraction was higher in the experimental side compared to the control side after 4 weeks, although it is uncertain whether this difference is statistically significant.

- *Rate of tooth movement.* A split-mouth RCT at unclear risk of bias(31) and a parallel-group RCT at low risk of bias(41) investigated the effect of piezocision on the rate of maxillary canine retraction and the rate of en masse retraction, respectively. Abbas et al.(31) found that the rates of canine crown tip were greater (P<0,05) in the piezocision side compared to the control side at 2, 4, 6, 8, 10, and 12 weeks after surgery. Tunçer, et al.(41) reported that the retraction rate was slightly higher in the experimental group at all time points, except for day 90, when the rates evened. However, the difference between the groups was not statistically significant (P>0,05).

- *Treatment duration.* One split-mouth RCT at unclear risk of bias(39) and three parallel-group RCTs at high(40) and low risk of bias(41,42) investigated the effect of piezocision on the total treatment time, treatment time needed for canine retraction, and time needed for en masse retraction of anterior teeth and for anteroinferior alignment.

Charavet et al.(40) reported a significantly lower treatment duration from the beginning of treatment until debonding in the experimental group compared to the control group (310 days vs. 540 days; P<0,0001). Similarly, Aksakalli et al.(39) showed that the treatment duration for space closure after premolar extraction and canine retraction was lower in the experimental group than in the control group (3,54 ± 0,81 months vs. 5,59 ± 0,94 months), although no P-value was reported.

Tunçer et al.(41) reported that treatment duration for en masse retraction of anterior teeth was similar in both the experimental and control group (9,33 ± 4,10 months vs. 9,27 ± 2,55 months; P=0,958). Likewise, Uribe, et al.(42) found that the treatment duration for correcting mandibular crowding was similar in both the experimental and control group (102,1 ± 34,7 days vs. 112,0 ± 46,2; P=0,52).

- *Molecular mechanism.* One parallel-group RCT at low risk of bias(41) aimed to describe the biological response involved in piezocision-assisted orthodontics in miniscrew supported en-masse retraction cases. In this study, the authors evaluated the concentration of receptor activator of nuclear factor kappa-B ligand (RANKL) in gingival crevicular fluid (GCF) samples at the beginning of retraction (before piezocision) (T1), on day 28 (T2) and at the end of retraction (T3). This bone biomarker showed an unlike pattern between groups, the experimental group showed a decrease at T2-T1 followed by an increase at T3-T2 and the control group showed a steady increase at both time intervals. However, the difference between groups was not statistically significant (*P*>0,05).

- *Periodontal parameters.* Two split-mouth RCTs at unclear risk of bias(31,39) and one parallel-group RCT at high risk of bias(40) investigated these parameters. None of these studies found differences between the groups in any of the evaluated periodontal parameters.

3. Micro-osteoperforation. This intervention was performed in 2 parallel-group RCTs at unclear(16) and low risk of bias(43), and 2 split-mouth RCTs at low risk of bias(44,45). Micro-osteoperforations were made in the area of interest through the gingiva to accomplish bone activation, without any flap or incision. Of these four studies, three could be compared and a meta-analysis was performed.

- *Accumulative tooth movement.* Alikhani et al.(16), Kundi(43), Khan et al.(44) and Alkebsi et al.(45) evaluated the effect of micro-osteoperforations on accumulative tooth movement of maxillary canine retraction. Micro-osteoperforations were performed distal to the experimental canine in the experimental group, but not in the control group. Both maxillary canines were retracted, and movement was measured after 28 days. Alikhani et al.(16), Kundi(43), and Khan et al.(44) reported that the accumulative tooth movement was significantly larger in the experimental group compared to the controls (*P*<0,05). In contrast, Alkebsi et al.(45) found no statistically significant difference in the accumulative tooth movement between the micro-osteoperforation and the control side at month 1(*P*=0,77), month 2 (*P*=0,50) and month 3 (*P*=0,76).

- *Molecular mechanism.* Alikhani et al.(16) attempted to investigate the biological mechanisms involved in surgically facilitated orthodontics with micro-osteperforations. The authors evaluated the inflammatory response by measuring the levels of 8 proinflammatory cytokines (IL-1α, IL-1β, IL-6, IL8, TNFα, CCL2, CCL3, CCL5) in the GCF samples obtained from the distobuccal sites of the canines at different time points (Before retraction, 24 hours, 1 day, 7 days and 28 days). Protein analysis showed a statistically significant increase in the level of the 8 cytokines after

24 hours in both the experimental and control groups, when compared with their levels before retraction (*P*<0,05). At 24 hours and at 7 days, the levels of IL-1α, IL-1β, IL8, TNFα, CCL3, CCL5 were significantly higher in the experimental group than in the control group (*P*<0,05). At day 28, the levels of IL-1α and IL-1β were still significantly higher in the experimental group than in the control group (*P*<0,05). Although the other proinflammatory cytokines (IL8, TNFα, CCL2, CCL3, CCL5) were elevated in the experimental group compared to the control group, these differences were not shown to be statistically significant (*P*>0,05).

- *Periodontal parameters.* One split-mouth RCT at low risk of bias(45) investigated this outcome by evaluating the periodontal index and plaque index, and found no differences in any of the evaluated parameters between the groups at baseline and after 3 months (*P*=1.000).

4. Periodontal ligament distraction. This intervention was performed in one split-mouth RCT at high risk of bias(46). The authors evaluated the effect of periodontal ligament distraction on the rate and accumulative tooth movement of maxillary canine retraction after premolar extraction compared to conventional orthodontic tooth movement. The rates of canine retraction were greater (*P*=0,002) in the experimental side compared to the control side at 1st and 2nd month after surgery; however no statistically significant difference was found at 3rd month. The accumulative tooth movement was significantly larger in the experimental side compared to the control side at 3-month follow-up (*P*=0,002).

Quantitative synthesis of included studies

Three studies could be compared and a meta-analysis was performed for quantitative synthesis of micro-osteoperforations for one month follow-up period(43–45).

1. Micro-osteoperforations. The effect of micro-osteoperforation on accumulative tooth movement (mm) of canine retraction was assessed in three studies eligible for meta-analysis. All these studies evaluated canine retraction in a first premolar extraction space. The meta-analysis was suggestive of a higher accumulative tooth movement with micro-osteoperforations compared to controls for the first month of retraction (WMD=0.70; 95% CI: 0.10, 1.30; I-squared= 97,2% *P*=0,000). The overall quality of evidence supporting this intervention was high (Figure 2).

Discussion

Orthodontists have focused on accelerating orthodontic tooth movement to reduce the treatment time and risks associated with its duration. Since bone remodeling is the biological basis of dental movement, different surgical and non-surgical methods have been developed for these purposes.

To date, several systematic reviews on accelerated orthodontic tooth movement have been published, but to the best of our knowledge this is the first to include human studies on methods for accelerating orthodontic tooth movement and the molecular mechanisms involved in these processes. In this review, we systematically searched the literature for the best evidence on seven types of surgical interventions.

In this systematic review we included 17 RCTs, which evaluated four types of interventions and five outcomes.

Does conventional orthodontic treatment combined with surgical interventions significantly increase the speed of tooth movement and shorten the treatment duration compared to conventional orthodontics alone?

Seventeen studies evaluated surgical approaches to accelerate orthodontic tooth movement. Four studies, most of them with unclear risk of bias(31–33,36), evaluated the speed of tooth movement after corticotomy and showed that this method can accelerate maxillary canine retraction approximately twice as fast as conventional orthodontic movement during the first two months of treatment. Although the differences in canine retraction remained stable between groups in the following month of treatment, the difference started to decrease by the end of the third month. Finally, control groups and experimental groups ended up with similar speed of tooth movement. This reduction pattern of the difference between groups, could be associated with the decrease of the effect of RAP. According to Frost, the RAP typically lasts about four months in bone (7).
Regarding piezocision and accelerated maxillary canine retraction, similar results were obtained by one study with unclear risk of bias(39). However, when the effectiveness of corticotomy in accelerating canine distalization was compared to that of piezocision, a study with unclear risk of bias reported that corticotomy exhibited grater rates of canine movement(31).
The difference in the effectiveness between corticotomy and piezocision can be attributed to the divergence in the extension of the surgical intervention. Cortical activation is the injury that generates the biochemical changes that in turn induce and potentiate the normal healing process known as RAP(2). Since piezocision does not require flap elevation–which increases the inflammatory response of the underlying bone–(47)and the extension of corticotomies are greater when performed with burs than with piezoelectric scalpels(48), it is reasonable to assume that a more conservative intervention results in a milder RAP.

Micro-osteoperforations (MOPs) were evaluated in four studies(16,43–45). One of them with unclear(16) and two with low(43,44) risk of bias, reported that MOPs on average, increase the rate of canine retraction by 2–3 fold when compared to the controls. However, the measurements were made only until day 28 in all three studies, which hinders the possibility of comparing their long-term effectiveness with other surgical techniques. In contrast, a study that used 3D digital model measurements and that made a three month follow up, found no significant difference in tooth movement between the MOPs and control sides from baseline to months 1-3(45).

One study with high risk of bias evaluated interseptal bone reduction(46) and showed that it can enhance the rate of canine retraction if interseptal bone is sufficiently reduced at the first and second month. But again, the difference in the amount of canine movement between the groups decreased with time, resulting in no statistically differences by the end of the third month.

Five studies(34,38,39,41,42) aimed to determine the time needed to perform different tooth movements using corticotomy and piezocision. One study with high(34) risk of bias, evaluated the effect of corticotomy on en-masse retraction of upper anterior teeth after premolar extraction and found a statistically significant reduction in the treatment time required to close extraction spaces; on the other hand, one study with low risk of bias(41) evaluated the effect of piezocision on en-masse retraction time as well, and found that this technique was ineffective in accelerating this type of movement. Another study with unclear risk of bias(39) found that piezocision reduced the time of maxillary canine distalization, although no *P* value was given(39). The remaining two studies evaluated the time needed to align the lower mandibular teeth using corticotomy and piezocision. The first study(38). which was at high risk of bias, showed that corticotomy reduced the time of mandibular decrowding. However, no *P* value was given. The second study(42), which was at low risk of bias, showed no statistically significant difference between piezocision and conventional orthodontics in the time required to correct mandibular crowding.

Two studies with high(35) and unclear(37) risk of bias evaluated the total treatment duration using corticotomy. The first study(35) suggests that corticotomy significantly reduces the time from the beginning of treatment until de-bonding, but no *P* value was given. In contrast, the second study(37) reported no statistically significant difference in the total treatment time, although the authors found a reduction in the treatment time in the experimental group, but the difference was not statistically significant (*P*=0,17). With regard to the effect of piezocision in the treatment duration, one study with unclear risk of bias(40) reported that the overall treatment time was significantly lower in the test group than in the control group (P<0,00001), the control group exhibited a 43% increase in the mean treatment time compared with the experimental group.

Since there were substantial methodological differences between all these studies, it is difficult to interpret their results. This heterogeneity did not make it possible to perform a meta-analysis for each intervention. Although we could observe that corticotomy accelerate different orthodontic tooth movements, including maxillary canine retraction, en masse retraction of upper anterior teeth, and alignment of anterior lower teeth. However, the studies that evaluated these outcomes were at unclear risk of bias(31–33,36,38), and since the acceleratory effect of this surgical intervention decreased with time and all of the studies evaluated these movements for a short period of time, their effectiveness in the long-term acceleration of tooth movement is still questionable.

On the other hand, according to one unclear risk of bias study(37), the corticotomy was unable to significantly reduce the total treatment time of a comprehensive orthodontic treatment; but according to one high risk of bias studies(35), the corticotomy was effective in reducing the total time of treatment. These results reflect the conflicting findings of the corticotomy in the total treatment time, which hampers the possibility of drawing solid conclusions.

Regarding the effect of piezocision and MOPs on accelerating the tooth movement, the findings were contradictory, however the studies about piezocision that were executed with high quality standards and were at low risk of bias(41,42) showed ineffectiveness of this intervention in accelerating en-masse retraction(41), and no significant difference in the time required to correct mandibular crowding(42). Nevertheless, it is important to bear in mind that these results may be due to the limited extent of the injury performed during the piezocision. It would be very important to compare the effectiveness of the piezocision with different extensions of the surgical injury. With respect to MOPs it is difficult to drawing solid conclusions, because three studies with low risk of bias(43–45) showed contradictory results, however the meta-analysis was suggestive of a higher accumulative tooth movement with micro-osteoperforations compared to controls for the first month of canine retraction.

Which molecular mechanisms are involved in surgically facilitated orthodontic tooth movement?

Three studies evaluated the molecular mechanisms involved in accelerated orthodontic tooth movement. The first study(16), which was at unclear risk of bias, analyzed 8 inflammatory cytokines and chemokines from GCF samples of patients with MOPs. At 24 hours the levels of the 8 inflammatory markers (IL-1α, IL-1β, IL-6, IL8, TNFα, CCL2, CCL3, CCL5) were significantly higher in the experimental group than in the control group (*P*<0,05). At day 28, the levels of IL-1α and IL-1β were still significantly higher in the experimental group than in the control group (*P*<0,05). Although the levels of the rest of cytokines and chemokines were higher at day 28 in the experimental group compared to the control group, the differences were not statistically significant. These findings are consistent with the inflammatory phase of the regional acceleratory phenomenon, which explains the accelerated movement after surgery. The second study(37), which was at unclear risk of bias and evaluated the effect of corticotomy, aimed to correlate urinary DPD levels with the rate of bone resorption. Since the results showed a great variance between individuals and between groups, no conclusions could be drawn, however the DPD value in the experimental group increased 2 days after surgery and then decrease 6 months after surgery, while in the control group the DPD values remained stable. This findings could be also consistent with the accelerated bone remodeling phase of the regional acceleratory phenomenon RAP.

The findings in these two RCT studies could be consistent with the positive correlation between stimulation of RAP and an increased orthodontic tooth movement. The RAP was first described by Frost in the 80’s(7), and then the term was coined by the Wilcko brothers to explain the molecular mechanism that occurs in surgically facilitated orthodontic tooth movement(2). The injury caused by corticotomy is the necessary stimulus to activate RAP, which is characterized by an initial inflammatory phase that triggers osteoclastogenesis via RANK/RANKL, which in turn increases bone remodeling and thus tooth movement. This phenomenon is transient and decreases with time, which is consistent with the decreasing difference over time in the cytokine and chemokine levels between the groups(16).

On the other hand, one study at low risk of bias(41). evaluated the effect of piezocision on the biological response of accelerated tooth movement, by means of receptor activator of nuclear factor kappa-B ligand (RANKL). RANKL concentration showed an unlike pattern, but the difference between groups was not significant. These results may be compatible with the conservative extent of the surgical injury during the piezocision procedure, which did not made the sufficient bone stimuli for the RANKL to increase.

To date, this is the only evidence available of the molecular mechanism involved in surgically facilitated orthodontic tooth movement in humans. To determine the duration of RAP after surgical methods, it is imperative to investigate what happens after the levels of inflammatory markers increase, which bone resorption and bone formation markers are expressed, as well as the time they remain elevated.

What is the effect of surgically facilitated orthodontic tooth movement on periodontal parameters and periodontal biotype?

Eight studies evaluated the effect of accelerated orthodontic tooth movement on periodontal parameters. Five studies, most of them at unclear risk of bias(31,32,35,37,38), evaluated the effect of corticotomy on periodontal parameters. Of these, two(31,32) evaluated plaque index, gingival index, probing depth, attachment level, and gingival recession index when corticotomies were performed with submarginal flap elevation. The remaining three studies evaluated probing depth(35,37,38) and gingival recession(37) when corticotomies were performed with intracrevicular full-thickness flap elevation. All these studies showed no statistically significant difference in plaque index, attachment loss, gingival recession index, and probing depth between the operated and non-operated groups. However, one study(32) showed that gingival index scores, which assess the qualitative changes in the gingiva (no inflammation to severe inflammation), were significantly higher on the experimental side compared to the control side at the end of the study; this difference between groups may be due to the difficulty of performing adequate oral hygiene in the operated area.

Four studies evaluated the effect on periodontal parameters of minimally invasive surgical procedures in the acceleration of tooth movement, such as piezocision(31,39,40) and MOPs(45). These studies showed no significant differences in any of the periodontal parameters.

The existing evidence suggests that corticotomies and minimally invasive surgical procedures do not cause detrimental effects on the periodontium. This can be attributed to the fact that all studies included patients who had adequate oral hygiene before treatment (16,31-46), and some of them implemented measures that aimed to preserve the periodontium, such as a strict oral hygiene of the patient. Also, the fact that the marginal bone was not incised during surgery could be associated with this finding. Furthermore, the flap design (intrasulcular flap, submarginal flap or non-flap techniques), did not influence the preservation of the periodontium.

Conclusions

. Weak but statistically significant evidence suggests that corticotomy is effective in accelerating orthodontic tooth movement in the first two months of treatment.
. Weak but statistically significant evidence suggests that piezocision is able to accelerate orthodontic tooth movement in the first month of treatment. However, strong evidence suggest that this surgical method does not reduce the treatment time required to correct mandibular crowding and to perform en-masse retraction.
. High and statistically significant evidence suggest that micro-osteoperforations is able to accelerate maxillary canine retraction for the first 28 days of treatment.
. Weak but statistically significant evidence suggest that periodontal ligament distraction is able to accelerate maxillary canine retraction.
. Weak evidence suggests a positive correlation between stimulation of RAP and an increased orthodontic tooth movement in humans, however randomized clinical trials evaluating inflammatory and bone remodeling markers at different time points of treatment are still needed.
. Corticotomies and minimally invasive surgical procedures do not cause detrimental effects on the periodontium.

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The authors declare not to have any conflict of interest.

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Figure legends

Figure 1. Flow chart of study selection.

Figure 2. Meta-analysis for micro-osteoperforations. Random-effects meta-analysis of rate of canine retraction with micro-osteoperforations vs. controls for an assessment period of 28 days.

Table legends

Table 1. Eligibility criteria according to the PICOS question

Table 2. Characteristics of Included studies
OTM: Orthodontic Tooth Movement.
NR: Not Reported in the study protocol.

Table 3. Results of included studies
NE: Not Evaluated.

Table 4. Risk of bias summary for included studies
+: Low risk of bias
?: Unclear risk of bias
-: High risk of bias
By an agreement of the authors, the quality of the studies was classified according to the risk of bias rating in each of the 7 domains. Studies with one or more minus signs and only one plus sign are considered at high risk of bias. Studies with one or more question mark and two or three plus signs are considered at unclear risk of bias. Studies with plus signs only, except at the third domain were considered at low risk of bias.