DESCRIPTION OF RESEARCH PROJECT

I – Title of the project: Evaluation of the effects of osteoperforation and piezocorticision on canine retraction: Randomized controlled clinical trial.

II - Introduction

Within the field of dentistry, orthodontic treatments are often disregarded or disliked due to their long duration and the negative impact they can have on the patient's physical appearance.[1] Treatment duration can be significantly affected by some procedures, such as canine retractions and the intrusion of teeth. Consequently, this can have a considerable negative impact on patient motivation and can cause or increase the risk of certain side effects associated with the orthodontic treatment, such as root resorption.[2] To address this issue, several procedures have been developed to increase the rate of tooth movement during orthodontic treatment. These accelerated orthodontic procedures have been studied for more than a century. In 1892, surgeons would perform osteotomies around teeth to move the bone segment as a block.[3] Subsequent developments were attributed to Köle during the 1950s, when he introduced a procedure combining the elevation of a mucoperiosteal flap with incisions limited to the cortical bone without entering the medullary space.[4] It was subsequently discovered that corticotomies alone were sufficient to induce an acceleration of teeth movement[5] via a process called Regional Acceleratory Phenomenon (RAP) described a few years earlier by an orthopedist named Frost.[5,6] The RAP induces a remodeling process of the bone, in addition to a transient state of osteopenia. Studies have shown that the rate of dental movement can be as much as two times faster with the RAP.[7,8] Its duration of effect was reported to last for four months but is still unproven.[9,10]

Lately, the research interest has turned towards minimally invasive techniques such as osteoperforation and piezocorticision. These techniques do not require the elevation of a mucoperiosteal flap to induce the RAP, thus reducing the associated comorbidities (discomfort, swelling, hematoma). [11] Osteoperforation has the advantage of being significantly more conservative on the soft and hard tissues since it only consists in making small perforations in the buccal gingiva and cortical bone.[12] On the other hand, piezocorticision has the benefit of allowing hard or soft tissue grafting by a tunnelling technique, if necessary.[13,14,15] The efficiency of piezocorticision is well documented and shows a significant acceleration of dental movement. Furthermore, one study suggested that the vibrations emitted by the knife induce a greater acceleration of tooth movement than traditional corticotomies with rotary instruments.[13] A systematic review comparing both techniques[12] revealed that only one controlled human study was conducted so far to determine the efficiency of osteoperforations. This study showed a significant acceleration of tooth movement (2-3X) as well as an increase of inflammatory markers in the gingival crevicular fluid analysis.[16] Studies conducted on rat subjects also report an increase in the rate of tooth movement over a period of two weeks.[17] Thus, the current research will bear an important role in the literature and will demonstrate which technique, osteoperforation or piezocorticision, is the most efficient in increasing the rate of canine retraction while conserving posterior anchorage.

III – Specific objectives and research hypothesis

Primary objective: Compare the rate of canine retraction following the osteoperforation and piezocorticision procedures.

Secondary objectives:

- Compare the second order movement of the canine (tipping) between the osteoperforation and piezocorticision procedures.
- Compare the amount of root resorption associated with the osteoperforation and piezocorticision procedures.
- Compare the inflammation process between the experimental and the control group by measuring the inflammatory markers in the gingival crevicular fluid.
- Evaluation of the loss of posterior anchorage by measures on the cone beam computed tomography (CBCT) 3-dimensional radiograph and on the casts.
- Evaluation of the pain level and the impact on quality of life following each procedure using the questionnaire of the visual analogue scale (VAS) of pain.

Research hypothesis:

- Primary :
  - The rate of canine retraction will be faster following the piezocorticisions than the osteoperforations.
- Secondary :
  - There will be less tipping of the canine following the piezocorticisions than the osteoperforations.
  - There will be less root resorption following the piezocorticisions than the osteoperforations.
  - The increase in inflammation will be greater following the piezocorticisions than the osteoperforations.
  - The posterior loss of anchorage will be less following the piezocorticisions than the osteoperforations.
  - The pain level and the impact on quality of life will be greater following the piezocorticisions than the osteoperforations.

Null hypothesis: The rate of canine retraction is the same following the piezocorticisions, the osteoperforations and without any surgical procedure.

IV – Experimental design, data acquisition and analysis methodology

a) **Type of research:** Prospective randomized controlled clinical trial.

b) **Characteristics of participants *:***

Sample size :

- Sample size: 15 patients for the control group and 15 patients for the experimental group. A sample size of 10 subjects has a power of 80% to show a difference between the speed of retraction of the piezocorticision 1.0±0.2/12 weeks and the osteoperforation 0.8±0.2mm/12 weeks, thus a speed 20% higher for the piezocorticision, with a bilateral alpha of 0.05 and a paired sample T-test. A sample size of 15 also allows to show a difference between the experimental and control group (speed of 0.5±0.2mm/12 weeks), with a power of more than 80% based on an independent-sample T-test We will recruit 15 subjects per group to compensate for the possible attrition. The sample will be 50% male, 50% female.

- Experimental group: Bilateral maxillary canine retraction after first premolar extraction with piezocorticision procedure on one side and osteoperforation on contralateral side using a split mouth design.
-Control group: Bilateral maxillary canine retraction after first premolar extraction without any surgical procedures.

Inclusion criteria:

- Dental and/or skeletal Cl I and II requiring maxillary first premolar extraction.
- Young adults 16 years and older.
- Good overall health.
- Complete adult dentition.
- Cooperative.
- Acceptable hygiene.
- Absence of any periodontal disease (gingivitis, periodontitis).

Exclusion criteria:

- Non-cooperative, fearful patients or patients with intellectual disability.
- Patients requiring the regular use of nonsteroidal anti-inflammatory drugs (NSAID).
- Use of antibiotics in the last 6 months.
- Previous or current use of bisphosphonates, corticosteroids or immunosuppressive drugs.
- Smokers.
- Patients suffering from uncontrolled systemic diseases (ex. diabetes type I and II).
- Presence of oral or maxillofacial malformations (ex. cleft palate) or dental pathologies (ex. ankylosis, abscess).

***Recruitment modalities**:* Patient selection and recruitment will take place at the Graduate orthodontics clinic of the "Université de Montréal".

c) **Materials and methods**

Materials

- CBCT machine
- Piezotome (Piezosurgery®) to perform the piezocorticision procedure.
- Osteoperforation tool (Propel Excellerator; Propel Orthodontics)
- SPEED™ self ligating orthodontic brackets (Strite Industries Limited) + Nickel-Titanium (Ni-Ti) closed coil spring, medium force (150g)[18] (Medium Sentalloy; GAC International Inc).
- Orthodontic force gauge. (Dynamometer).
- Visual analogue scale of pain questionnaire.
- Periotron 8010 and PerioCol paper strips (Oraflow Inc).

Methods

- Submission of research proposal for ethics approval.
- Recruitment of patients according to inclusion and exclusion criteria and procurement of informed consent.
- Group randomization using randomized block design.
- Pre-treatment periodontal screening consisting of a 6-point probing around each tooth, measuring of the depth of sulcus and of the distance between the marginal gingiva and the cementoenamel junction.
- Pre-treatment panoramic and cephalometric X-ray, dental impressions, intraoral and extraoral picture and elaboration of treatment plan.
- Bonding of maxillary and mandibular orthodontic brackets and initial alignment and levelling of arches.
- Surgical guide fabrication.
- Pre-retraction CBCT.
- First premolar extraction with patient's general dentist.
- Piezocorticision or osteoperforation one week following premolar extraction.
    - Preoperative rinsing with Chlorhexidine 0.12% (Peridex™) 15 mL for 60 seconds.
    - Topical anesthesia using Benzocaine 20% for 2 minutes.
    - Buccal infiltration of the maxillary canine with lidocaine, epinephrine 1 :100 000 (1,8 mL)
    - For the piezocorticision procedure (Dr. Thomas Nguyen): Using the surgical guide, vertical incisions are performed on the buccal mucosa, mesial and distal to the canine, starting 2 mm below the interdental papilla followed by piezocorticision cuts 3 mm deep, extending to the apex of the tooth.[13]
    - For the osteoperforation procedure (Khang Le): Using the surgical guide, four osteoperforations are performed mesial and distal to the canine along the root. All perforations are 3 mm apart and 5 mm deep.[19]
    - Prescription: Acetaminophen 500 mg q6h PRN if pain and chlorhexidine mouthwash 0.12%, 2X/day X14 days.
- Canine retraction on 0.018 X 0.025 stainless steel (SS) wire using a medium force Ni-Ti closed coil spring with force application from the canine to the molar(s), delivering a force of 150g measured with a gauge.
- Follow up every two weeks for adjustment of forces with the gauge and digital impressions.
- When the canine has reached the desired position, the post-retraction CBCT is taken.
- Evaluation of the pain level of both experimental sides and of the control group using the questionnaire of the VAS immediately after the premolar extraction, then each day for 7 days following the surgeries and the first day after each adjustment of the spring.
- Collection of gingival crevicular fluid samples on the distobuccal corner of the canine at 0,1, 3, 8 weeks and at the end of treatment to analyze the concentration of cytokines, IL-I, RANKL, OPG and the RANKL/OPG ratio.
- The amount of tooth movement will be measured on the digital dental casts from the tip of the canine to the third rugae palatinae.[20]
- The amount of anchorage loss will be measured on the CBCT using the distance from the nasopalatine foramen to the projection of the mesiobuccal cusp of the first molar on the palatal suture .[21]

d) Measures and variables: The rate of canine retraction (mm/12 weeks), the amount of tipping, the amount of root resorption, the amount of posterior loss of anchorage, the level of inflammation and the level of pain.

e) Statistical analysis: The Shapiro-Wilk test will be used to determine if the data follows the normal distribution law. A paired sample T-test and the Wilcoxon test will be used to compare the piezocorticision and the osteoperforation within the same subject for the speed of retraction, the amount of tipping, the amount of root resorption and the posterior loss of anchorage. A mixed model analysis for repeated measures (Brunner-Langer method) will be used to compare the evolution of the level of pain and the level of inflammation between the two groups through time.

V- Expected results: We are expecting a marked increase in the rate of canine retraction with the piezocorticision and osteoperforation procedures (two times faster than the control group). The canine retraction will be faster on the piezocorticision side than the osteoperforation side. Finally, we are expecting a more noticeable reduction in the root resorption, tipping movement and in the loss of posterior anchorage in the piezocorticision side than the osteoperforation side.

VI- Schedule

Research protocol: May 2017.
Literature review: July 2017.
Scientific committee: August 2017.
Ethics committee: December 2017.
Recruitment of patients: December 2017 to January 2018.
Data collection: January 2018 to December 2018.
Redaction of the memoir: January to July 2019.

VII – Limitations of the research: Firstly, we will only be evaluating the efficiency of the piezocorticision and osteoperforation procedures in the specific and localized case of canine retraction. Hence, these results cannot directly be extrapolated to all types of orthodontic treatments. Secondly, the concomitant extraction of the first premolar will be contributing to the overall RAP phenomenon and thus, could confuse the analysis of our results and exaggerate the amount of reported inflammation. Finally, it is possible that we will not be able to compare the inflammatory effects of the osteoperforation and piezocorticision due to the dynamic nature of the gingival crevicular fluid and the physical proximity of both experimental sites. Still, this information will be valuable to better understand the effect of these approaches on the biological response.

VIII – Responsibilities of the student

- Establish the research protocol.
- Create the consent form and obtain informed consent.
- Perform the orthodontic examination and the pre-treatment and post-treatment periodontal screening.
- Perform the osteoperforations and the orthodontic treatment.
- Coordinate treatment sequence with the general dentist, the radiology and periodontology department.
- Collection of gingival crevicular fluid and inflammatory marker analysis at 0, 1, 3, 8 weeks and final.
- Gathering and analysis of the clinical, radiological and biological data.
- Redaction of the memoir.

External contributors :

- Dre Clarice Nishio: Guidance of research and supervision of orthodontic treatment.
- Dr. Robert Durand: Piezocorticision.
- Dr. Thomas Nguyen: Piezocorticision / calibration for pre-treatment and post-treatment periodontal screening.
- Dr. Daniel Turgeon: CBCT
- Dr. Jeff Wang, U Michigan: Analysis of gingival crevicular fluid.
- M. Pierre Rompré: Statistics.

IX – Source of financing

We will apply for internal funding from the Faculty of dentistry of the “Université de Montréal”.

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