

AAO Foundation Award Final Report

Type of Award: Orthodontic Faculty Development Fellowship Award (Eugene E. West Memorial Fellowship Award)

Name(s) of Principal Investigator(s): Clarice Nishio

Title of Project: Effects of exogenous retinoic acid and corticotomy on inflammatory process and bone remodeling during tooth movement.

Period of AAOF Support: July 2015 to June 2016. No cost extension until December 31, 2016.

Amount of Funding: \$20,000 from AAOF. Part of this study has also been supported by the Network for Oral and Bone Health Research (RSBO).

Summary/Abstract

This project generated two studies that evaluated the effect of piezo-corticision and 13-cis-retinoic acid (isotretinoin) on the rate of orthodontic tooth movement (OTM), external root resorption (ERR), bone remodeling and the inflammatory process during OTM:

Objective: Assess the effects of piezo-corticision on OTM and ERR in a rat model. ***Method:*** 48 male Wistar rats were divided into 4 groups (n=12): OTM; OTM+ERR; OTM+ERR+piezo-corticision and OTM+piezo-corticision. OTM was performed with a NiTi coil bonded between the upper 1st molar and incisors. ERR was created by scraping a scaler on the root furcation. Piezo-corticision was completed 1mm from the mesio-palatal crest of the upper 1st molar (1.5mm depth). Rats were euthanized at 3 and 7 days after surgery. OTM and ERR were evaluated by micro-CT. ***Results:*** At day 3, there was a significant increase in OTM (μm) in the OTM+piezo-corticision group (219.68 ± 53.6 ; $p < 0.05$) than in the OTM group (154.90 ± 35.6 ; $p < 0.05$). Root length was significantly reduced in the OTM+ERR+piezo-corticision group (2309.27 ± 90.3 ; $p < 0.01$), compared to the OTM+ERR group (2459.74 ± 47 ; $p < 0.01$). No differences were noted at day 7 for OTM or root resorption. ***Conclusion:*** Piezo-corticision increased the rate of OTM and the amount of apical root resorption.

Objective: Appraise the effect of isotretinoin on OTM and wound healing following exodontia. ***Method:*** 16 Wistar rats were divided into 2 groups (n=8): OTM; tooth extraction (TE) of the upper 1st molar + OTM. The experimental animals received isotretinoin (7.5 mg/kg) and the control animals oil solution for 37 days. OTM and bone volume were evaluated by micro-CT and the periodontium healing was assessed by immunohistochemistry (VEGF-C, COX-2, IL-1 β). ***Results:*** The animals submitted to the TE showed a significant decrease in bone volume percentage and increase of OTM. No significant difference in OTM and bone volume was observed between the control and experimental groups. The alveolar bone of the isotretinoin group revealed more medullary spaces with inflammatory, hematopoietic cells, blood vessels, intense immunolabeling for VEGF-C, and faster gingival regeneration. No significant difference was observed with the COX-2 and IL-1 β labelings. ***Conclusion:*** Isotretinoin did not affect OTM or alter maxillary bone volume. However, this exogenous acid may contribute to the acceleration of gingival healing.

Education, Clinical and Teaching plan updates:

i. Education: Throughout 2016, I have attended and presented the results of our studies at important scientific meetings, such as at the 43rd Annual Moyers Symposium and the Workshop on “Personalized and Precision Orthodontic Therapy”, Consortium for Orthodontic Advances in Science and Technology (COAST). The participation at these meetings gave me the opportunity to divulgate internationally our research studies and to represent our Faculty in the science community. It also allowed me to keep current with the latest research tendencies and orthodontic treatments, as well as to exchange experiences with other faculty members.

ii. Clinical: Since August 2014, I have set up a lingual orthodontic clinic in our orthodontic masters program where we were treating patients with only partial lingual braces to correct mild malocclusions. Due to the success of our lingual appliance cases and the practical experience we obtained, we started in 2016 to use full lingual appliances and to treat more severe malocclusions.

One of my overall goals in research is to combine fundamental and clinical studies. Our studies on the effect of piezoelectric periodontal surgery on orthodontic treatment have allowed us to implement this new treatment approach in our clinic. This represents an opportunity for the students to learn different periodontal surgical methods during their graduate program.

iii. Teaching: In 2016, I was awarded the Academy of Academic Leadership Sponsorship Program Award by the American Association of Orthodontists. This two-phase workshop (50 credits) allowed me to refine my teaching skills. I am now applying the knowledge acquired during the workshop to improve the quality of both my didactic and clinical instruction of my students. This experience was of great value, since it illustrated potential avenues for improvement in the educational field. I am currently supervising seven students in their master’s theses, four as principal director and the other three as co-director.

Response to the following questions:

1. *Were the original, specific aims of the proposal realized?*

Yes, the aims of the proposal research have been achieved. However, we have adjusted the number and distribution of the animals in order to optimize the results of the proposed study.

2. *Were the results published?*

A manuscript titled “Effect of exogenous retinoic acid on tooth movement and periodontium healing following tooth extraction in a rat model” (Nishio C.; Rompré P.; Moldovan F.) has been accepted at the Orthodontics & Craniofacial Research journal.

a.) *If so, was AAOF support acknowledged.*

AAOF support was acknowledged in all presented and/or submitted materials.

b.) *If not, are there plans to publish? If not, why not?*

A manuscript using the results from the effect of piezo-corticision on bone remodeling during OTM in a rat model study is under preparation. The delay in manuscript creation and submission stemmed from a delay in obtaining the results of this study.

3. *Have the results of this proposal been presented?*

a.) *If so, when and where? And was AAOF support acknowledged.*

i. Results of the study on 13-cis-retinoic acid were presented at the 2016 Innovators' Workshop on "Personalized and Precision Orthodontic Therapy". Consortium for Orthodontic Advances in Science and Technology (COAST). Palm Beach, FL, United States.

ii. A Table Clinic titled "Effect of exogenous retinoic acid on tooth movement and periodontium healing in a rat model" will be presented at the American Association of Orthodontists (AAO) 2017 Annual Session in San Diego, CA. Application has been accepted.

iii. A Table Clinic titled "Evaluation of the effect of piezo-corticision surgery on root resorption following orthodontic tooth movement in a rat model" at the AAO 2017 Annual Session in San Diego, CA. Application has been accepted.

AAOF and RSBO supports were and will be acknowledged in all presentations.

4. *To what extent have you used, or how do you intend to use, AAOF funding to further your career?*

This was my first funding from the AAOF and it has been invaluable for my development as a junior orthodontic academic. This support allowed me to strengthen my research program and involve our orthodontic residents and dental students in these studies. I plan to secure further AAOF funding to generate more studies on the medications and/or therapy methods to increase the efficiency of orthodontic treatment. This data will be a great asset towards obtaining competitive grants from federal funding entities.