

## AAO Foundation Award Final Report

**Type of Award:** Orthodontic Faculty Development Fellowship Award (Subtenly, Baker, Eastman Teaching Fellowship Award)

**Name of Principal Investigator:** Clarice Nishio (Université de Montréal)

**Name of Co-investigator and Mentor:** Isabelle Villemure (École Polytechnique de Montréal) and Florina Moldovan (Université de Montréal)

**Title of Project:** “Effect of Vitamin D on bone morphometry and on stability of orthodontic tooth movement (OTM) in rats”.

**Period of AAOF Support:** July 2017 to June 2018. No cost extension until May 31, 2019.

**Amount of Funding:** \$20,000 from AAOF.

### **Summary/Abstract**

**Introduction:** Vitamin D (VitD,  $1.25(\text{OH})_2\text{D}$ ) is part of a group of fat-soluble secosteroids and plays a fundamental role in bone metabolism. Although some studies on VitD have demonstrated that it increases the rate of orthodontic tooth movement (OTM), there is a lack of evidence regarding its effect on bone morphometry and its influence on the long-term stability of orthodontic treatment.

**Objective:** To evaluate the effect of VitD on the rate and stability of OTM and on bone morphometry.

**Materials and Methods:** 32 male 250g Sprague Dawley rats were assigned into 4 groups: control gavage (CG); experimental gavage (EG); control injection (CI) and experimental injection (EI). The rats of the EG group received the calcitriol ( $1.25(\text{OH})_2\text{D}_3$ ) by gavage once every other day (100 ng/kg body weight). An oral saline solution in an identical volume and frequency was given to the CG group. The EI group received an injection of  $1.25(\text{OH})_2\text{D}_3$  (20  $\mu\text{l}$  of  $10^{-10}\text{M}$ ) locally in the submucosal palatal area of the root bifurcation of the 1<sup>st</sup> molar, once every 2 days. The CI received a 0.1 M saline solution in a dose identical to that of the VitD solution. Treatment with VitD or saline started 10 days before the beginning of the OTM and continued until the day of euthanasia. OTM was performed with a NiTi coil of 50cN bonded between the upper 1<sup>st</sup> molar and incisors for 7 days. Micro-CT scanning was carried out at 5 time points: T0 (before administration of VitD), T1 (start of OTM), T2 (end of OTM), T3 (7 days post-OTM), T4 (30 days post-OTM). For OTM stability, we evaluated the shortest distance ( $\mu\text{m}$ ) between the 1<sup>st</sup> and 2<sup>nd</sup> molar surfaces in both sagittal and occlusal views from uCT images. For bone morphometry assessment, the following parameters were measured: bone volume (BV;  $\text{mm}^3$ ), tissue volume (TV;  $\text{mm}^3$ ), bone volume percent ( $\text{BVP} = \text{BV}/\text{TV}$ ; %), total porosity (%) and connectivity density ( $1/\text{mm}^3$ ). Pairwise comparisons with Brunner-Langer test were used to compare groups for each measure time of OTM rate and stability. An ANOVA test was used to compare the early (T3-T2) and late (T4-T3) relapse and t-test was used to compare groups for each parameter of bone morphometry.

**Results:** No difference was found on the OTM rate between all groups at T2 ( $P = 0.24$ ), T3 ( $P = 0.60$ ) and T4 ( $P = 0.22$ ). The OTM rate ( $P = 0.039$ ) and overall relapse ( $P = 0.029$ ) were significantly greater in the control gavage group (figure 1). Recurrence of OTM was greater at T3 than T4 for all groups ( $p < 0.001$ ) (figure 2). The experimental groups showed significant increases of percent bone volume, bone mineral density and decrease of total porosity when compared to the control groups ( $P < 0.05$ ) (figure 3). A significant increase of connectivity density was observed when the VitD was locally injected ( $P < 0.05$ ).

**Conclusion:** Although systemic VitD administration decreased the OTM rate, it also contributed to an increase in the OTM stability. The significant increase of bone mineral density and the percent bone volume promoted by the VitD not only generated more resistance to orthodontic tooth movement, but also prevented the relapse of OTM in the long term by improving the bone quality of the periodontal support.

**Clinical application:** In North America, a deficiency of VitD is especially marked during winter due to the short days and the lack of sun exposure. An economical and simple solution to remedy this condition is the use of VitD supplements. Our findings suggest that patients could take supplements of VitD in the last phase of orthodontic treatment in order to increase the OTM stability. Either forms of administration of VitD supplementation (capsules or local injection) proved to be effective in preventing OTM relapse in the long term. Our study provided an insight into the effect of VitD on bone morphometry. This vitamin had a positive impact on the quality of bone by increasing both the percent bone volume and bone mineral density and by decreasing the total porosity.

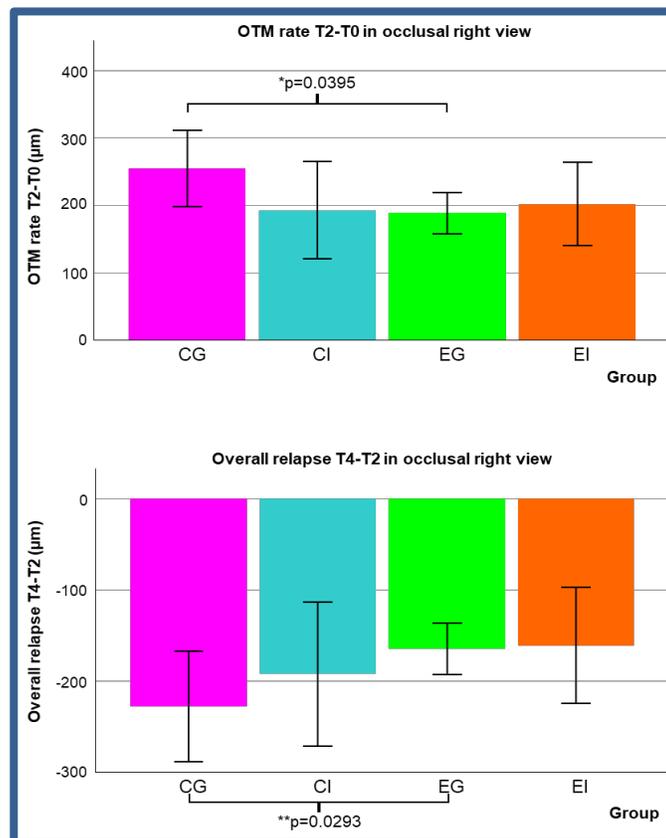


Figure 1: Orthodontic tooth movement rate and overall relapse

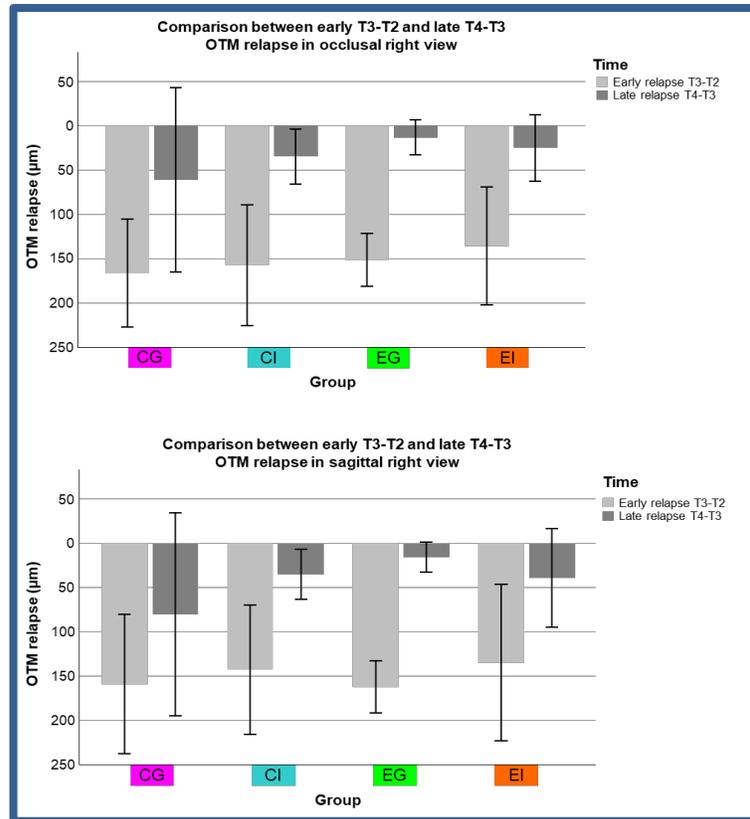


Figure 2: Orthodontic tooth movement relapse

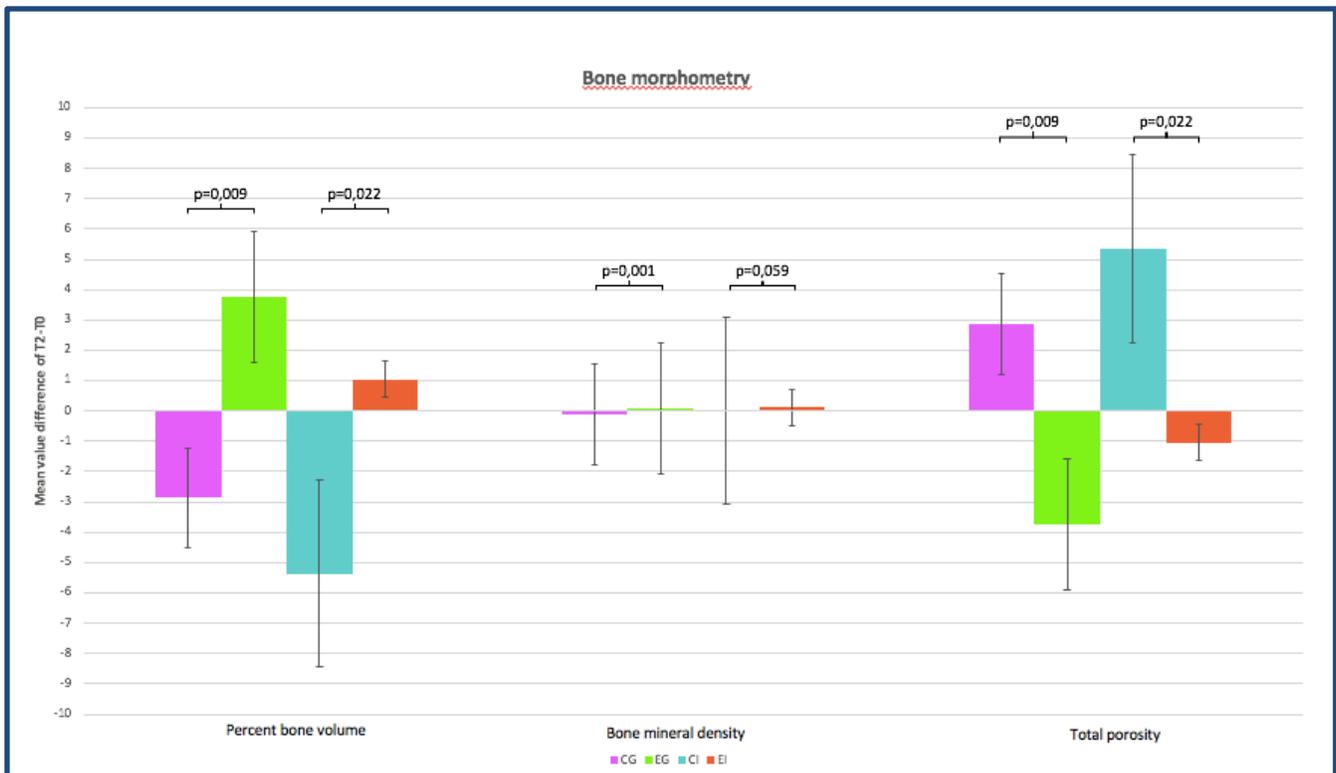


Figure 3: Assessment of bone morphometry

### **Education, Clinical and Teaching plan updates:**

The development plan of this project consisted of four axes: education (15%), teaching (15%), clinical skills (20%) and research (50%). The education, clinical and teaching plan updates are:

- i. Education: In 2019, I succeeded in obtaining tenure with a promotion from assistant professor to associate professor. I have been participating in diverse committees and academic activities in the Faculty of Dentistry, such as member of the research committee, the scientific committee, the selection committees for candidates for both the DDS program and the orthodontic graduate program.
- ii. Clinical: One of my objectives in research is to combine fundamental and clinical studies. I have been developing studies on the effect of piezoelectric periodontal surgery on orthodontic treatment and on the assessment of dental malocclusion in patients with systemic disease, such as attention deficit and hyperactivity disorder. The data from these clinical studies have generated several manuscripts.
- iii. Teaching: In 2017, I was awarded the Arto and Sona Demirjian Teaching Excellence Award in Dentistry by the Faculty of Dentistry, Université de Montréal. The students under my research supervision have attended and presented the results of our studies at important scientific meetings, such as at the annual sessions of the American Association of Orthodontists and at the *Journées de l'orthodontie à Paris*. Some of them have been awarded scholarships and prizes for best poster presentations. The participation at these meetings has given us the opportunity to divulgate internationally the results of our studies and to represent our Faculty within the scientific community.

### **Response to the following questions:**

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

Yes, the objectives of the proposed research have been achieved. We have adjusted the sample size of the animals in order to optimize the results of the proposed study.

2. *Were the results published?*

The manuscript about the effect of Vitamin D on bone morphometry and on stability of orthodontic tooth movement in rats is in preparation.

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

AAOF support was acknowledged in all presented and submitted materials.

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

The delay in manuscript preparation and submission stemmed from a delay in obtaining the results of this study. We are working on more complementary data from this study in order to strengthen the manuscript allowing submission to a journal with a high impact factor.

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

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

i. An e-poster titled “Effect of Vitamin D on the rate and stability of orthodontic tooth movement (OTM) in rats” was presented at the American Association of Orthodontists (AAO) 2018 Annual Session in Los Angeles, CA by the DDS student Dr. Marie-Pascalie Gratton.

ii. A poster titled “Effect of Vitamin D on the rate and stability of orthodontic tooth movement (OTM) in rats” was presented at the Annual Research Day of the *Réseau de Recherche en Santé Buccodentaire et Osseuse* (RSBO) and at the 34<sup>th</sup> Annual Research Congress of Graduate and Postdoctoral Students in Research at CHU Sainte-Justine Research Center by the DDS student Dr. Marie-Pascalie Gratton.

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?*

The AAOF funding has been fundamental in the development of my academic career. This second financial support from the AAOF has allowed me to involve a DDS undergraduate student, Dr. Marie-Pascalie Gratton, in this research project. This opportunity stimulated the interest of an undergraduate dental student not only in scientific research but also in orthodontics. This study is the master's thesis that Dr. Gratton is concomitantly completing along with her DDS program. I plan to secure further funding to produce more studies on therapy methods and medications, in order to improve the outcomes of orthodontic treatment. The results of this study will be an asset in helping develop clinical trials using Vitamin D as a mineral supplement in the final phase of orthodontic treatment.