THE UNIVERSITY of TENNESSEE HEALTH SCIENCE CENTER

COLLEGE of DENTISTRY

Department of Orthodontics
875 Union Avenue
Memphis, TN 38163
Phone: (901) 448-1893

AAO Foundation Award Final Report

Type of Award: Orthodontic Faculty Development Fellowship Award (Orhan C. Tuncay Teaching Fellowship Award)

Name(s) of Principal Investigator(s): Ayman Al Dayeh

Title of Project: Deformation and growth of the midfacial sutures during bone anchored maxillary protraction

Period of AAOF Support: July 2015-June 2016. No cost extension until 9/30/2016

Amount of Funding: $ 25,000: 20,000 from the AAOF; $5,000 from UTHS CoD alumni foundation

Summary/Abstract

Introduction: Bone anchored maxillary protraction (BAMP) is a relatively new treatment modality in orthodontics. Despite the increased use of BAMP, little is known about how it works at the tissue level. The main objective of this project was to establish an animal model for BAMP and to collect pilot data on sutural loading during BAMP and its effects on osteoblast differentiation and bone formation at the sutural edges. **Materials and methods:** The study consisted of an *in vivo* and an *ex vivo* part. ***In vivo*:** Four female 6-months minipigs were used. Miniplates were implanted in the maxilla 0.5 cm anterior to the zygomatico-maxillary (ZMS) suture and in the body of the mandible in the canine-1st premolar area. Unilateral protraction force (150-250 gram.force) was applied while the contralateral side served as control. Fluorescent bone labels were injected one-week before, during, and one-week after miniplates insertion. Two weeks after miniplates insertion, animals were anesthetized, strain gauges and displacement transducers (2 per site) were implanted across the ZMS and nasofrontal suture (NFS). Various BAMP forces (100-600 gram.force) were applied bilaterally, while the deformation of the sutures was measured. Animals were then sacrificed and the ZMS and NFS

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were harvested for histological analysis. The analysis included measuring the mineral apposition rate (using fluorescent bone labels) and osteocalcin expression. ***Ex vivo*:** 2 cadaver farm-pig heads were used (~1.5- 2 years old), unknown gender. Sensors were place and sutural deformation was measured similar to the *in vivo* part of the study. Additionally, deformation of the sutures during reverse pull headgear (RPHG) was measured. To assess BAMP effects on the mandible, deformation of the sutures was measured with the mandible restrained in an anterior position and unrestrained. **Results and Discussion**: In most animals, BAMP resulted in bodily protraction of the maxilla as evidenced by tension at the ZMS (in 78% of measured locations) and NFS (55% of locations). However, in some cases we found compression in the dorsal part of the ZMS and in the NFS suggesting upward rotation of the maxilla. The magnitude of sutural deformation increased as protraction force increased and was much higher in the younger *(in vivo*) compared to the older (*ex vivo*) group (236± 211με compared to 58± 32 με for 250 gram.force). *Ex vivo* results showed that deformation of the sutures doubled when the mandible is restrained suggesting that BAMP produces strong posterior force on the mandible. Sutural separation was higher (2.5-folds) in the BAMP compared to RPHG, especially at high protraction forces. Histologically, preliminary analysis showed that BAMP resulted in increased mineral apposition rate (~1.6 times) and osteocalcin expression (~1.4 times) at the protracted ZMS compared to control side. **Conclusion:** Minipigs were established as an animal-model for BAMP. BAMP is more effective than RPHG in maxillary protraction. However, BAMP might induce rotation of the maxilla. Further studies are needed to establish the optimal magnitude and direction of BAMP. Additionally, BAMP effects on the mandible need to be thoroughly investigated.

Response to the following questions:

1. Were the original, specific aims of the proposal realized? The faculty development plan has several objectives at the research, educational and teaching levels.

I. Research Objectives:
   a. Establish an animal model for bone anchored maxillary protraction: objective was achieved.

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b. Measure deformation of ZMS and NFS during BAMP: objective was achieved

c. Histology:

i. Measure bone formation along the sutural edges during BAMP: objective is an ongoing progress, 3 out of 4 animals are analyzed. The objective will be fully achieved by April 2017

ii. Use IHC detection of Ki-67 and osteocalcin to determine the effects of BAMP on cellular proliferation and osteogenesis at the ZM and NF sutures: Because ki-67 can potentially form an irreversible bond with the fixative we are using, we decided to detect another proliferation maker: proliferating cellular nuclear antigen (PCNA). The objective is an ongoing progress: osteocalcin expression was analyzed in 3 out of the 4 animals, PCNA is currently being analyzed. The objective will be fully achieved by April 2017

II. Education: the objective was to pursue additional course work in biostatistics and to take the Tweed study course.

a. I successfully pursued a Certificate in Clinical Research from the Department of Preventive Medicine at the University of Tennessee Health Science Center (UTHSC). The certificate consisted of 4 courses (3 credit-hours each) in biostatistics, epidemiology and research regulations. The coursework was finished in May 2016.

b. Tweed study course: was successfully completed in September 2015.

III. Teaching and service: teaching and service objectives were to be achieved through fulfilling departmental and college assignments in these fields.

a. Teaching: I was involved in directing and instructing several course. These duties exposed me to various aspects pertaining to teaching such as curriculum development, course design, competencies development and testing, lecture design and presentation, exam writing and overall management of the courses and students. My performance in most of these courses was ranked as "exceeds expectations" by my Department chair and were received and evaluated highly by the students. Below is a detailed list of the courses I participated in during the 2015-2016 academic year, along with the students' level and my involvement in each course:

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Course name	Role/ students	Duties/ Performance
MDS (Orthodontics) Research and Manuscript	Director/ 1st year Orthodontics' residents	Supervised and chaired several Masters' thesis projects. Helped develop my skills in students and research projects management.
Graduate Craniofacial Growth	Director/ instructor; 1st year Orthodontics' and Pediatric Dentistry residents	Helped develop course curriculum and delivered several lectures. Performance was ranked as "exceeds expectation" by the Department Chair
Orthodontics-Periodontics seminar	Director/ instructor, 2nd year Orthodontic and Periodontics residents	I developed this course in 2014. The curriculum, content and exams were revised and updated. The course was highly received by residents, my performance was ranked as exceeds expectation by the Department Chair
American Board of Orthodontics exam preparation class	Director/ instructor, 2nd year Orthodontic residents	This was a trial course. I developed the curriculum and content of this course. The course was received highly by the residents and they recommended it for the upcoming classes
Advanced Clinical Orthodontics	Director, instructor; fourth year dental students elective	I developed this course in 2014. The curriculum, content and exams were revised and updated. The class was expanded from 6 to 8 students with over 20 active clinica cases. The class was highly received by the students
Craniofacial Growth and Human Development	Director instructor; first year dental students	I developed some of the course content, lectures and exam questions. The class was received well by the students and was ranked average-above average on an objective scale

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b. Services: My involvement in several committees helped expose me to the decision making process in the College of Dentistry. Below is a list of my administrative and service duties during the academic year 2015-2016

i. Director of undergraduate program in the Department of Orthodontics:

ii. Member in the following committees:

1. Curriculum committee, 2014-2017
2. Guest member in the Quality Assessment and Assurance committee, 2014-2017
3. Member in the Student Appeal Committee, 2014-2017

2. Were the results published?

a.) If so, was AAOF support acknowledged

b.) If not, are there plans to publish? If not, why not? A manuscript with preliminary results was submitted to the Moyers pre-symposium proceedings on May 2016, the submission is still pending. AAOF support was acknowledged. I am planning to expand the *ex vivo* part of the study (3-4 more animals) before submission to publication. I am planning to have a final manuscript ready for publications before June 2017.

3. Have the results been presented?

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

i. Preliminary results were presented at the Moyers presymposium in University of Michigan, March 2016.

ii. Preliminary results were presented at the Southern Association of Orthodontists (SAO) annual meeting in Sandestin, FL, October 2016.

AAOF support was acknowledged in both.

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

This was my first grant through the AAOF. I am planning to use the AAOF funding again in the future to generate pilot data concerning the relation between mechanical loading and sutural growth. Such pilot data will be a great asset as I seek additional research grants through other entities such as the NIDCR.

Sincerely,

11/10/2016

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Review comments

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We thank the reviewer for their comments and questions. Below are our responses.

1. **It seems that 3 animals (invivo) were used, originally 4 were proposed and it was acknowledged that 4 was a small sample size, 3 is even smaller. There is an ex-vivo component included now.**

   The project was supported by two sources: AAOF ($20,000) and the UTHSC College of Dentistry alumni award ($5,000). A total of four animals were used in the study: 3 from the AAOF funding and one from the UTHSC alumni award. Since the experiment supported by the UTHSC alumni was finished after the AAOF proposal submission but before the AAOF funding period started, we thought to only include the part of the study supported by the AAOF in the final report. We apologize for the confusion. The final report is now revised to include results from the 4 animals used. Numbers were updated to reflect the additional results. Regarding the *ex-vivo* part of the study, because of the small sample size and limited age range in the *in-vivo* part, we thought to supplement it by an *ex-vivo* part. Sensors that were acquired in the *in-vivo* part were utilized in the ex-vivo part. The ex-vivo part is an ongoing process and additional pigs of various age groups will be investigated over the coming few months.

2. **Was Ki-67 histology not completed or reported?**

   In the initial application it was proposed to use Ki-67 to assess the cellular proliferation at the sutures. After further investigation, it appears that the fixative solution used in the study (Prefer ®, a Glyoxal-based fixative) might form an irreversible bond with Ki-67 antigen, rendering its detection difficult even with antigen retrieval. As a result, we decided to instead use immunohistochemical detection of proliferating cellular nuclear

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antigen (PCNA) as a marker for cellular differentiation. As a result there was some delay in starting the PCNA part, only two animals have been processed so far, the data analysis has not been performed yet. The histological part of the study (mineral apposition, PCNA, Osteocalcin) is still preliminary and we are planning to have the final results by April 2017.

3. **Description of teaching and service objectives and if they were achieved should be provided in the report in terms of outcomes described in the proposal and this would be helpful.**

It was planned to achieve Teaching and Service objectives through fulfilling departmental and college duties in these fields. No clear outcome measurement was suggested in the proposal. As a result we used Department Chair and student evaluation as teaching outcome measure. A detailed description of involvement in these activities is now added to the final report.