401 N. Lindbergh Blvd.
St. Louis, MO 63141
Tel.: 314.993.1700, #546
Toll Free: 800.424.2841, #546
Fax: 800.708.1364
Cell: 314.283.1983
E-Mail: rhazel@aaortho.org

AAO Foundation Final Report Form
(a/o 3/6/2016)

Please prepare a report that addresses the following:

Type of Award: Biomedical Research Award

Name(s) of Principal Investigator(s): Petros Papagerakis

Title of Project: Evaluation of Orthodontic Apical Root Resorption Using Biomarkers in Gingival Crevicular Fluid and Whole Saliva

Period of AAOF Support: 07/01/2013 to 05/31/2016

Amount of Funding: $25,000

Summary/Abstract (250 word maximum):

External apical root resorption (EARR) is the most common sequelae of orthodontic treatment and may result in severe tooth mobility or tooth loss if not diagnosed early. Radiographs are the standard method for diagnosing EARR, which increases patient exposure to ionizing radiation and fails to measure the rate of root loss. We hypothesized that dentin and cementum protein biomarkers are significantly increased in gingival crevicular fluid (GCF) and whole saliva (WS) from orthodontic patients exhibiting ≥ 2mm EARR and tested their expression in GCF and WS over time in actively treated patients. Our study in WS showed that DSPP, CEMP1, CAP, and DMP1 were 100%, 100%, 91.7% and 63.4% detectable, respectively. The cementum proteins had very low detectability in GCF compared to WS. Detectability of DSPP, CEMP1, CAP, and DMP1 in WS and GCF samples showed no obvious correlation between the two different fluids being assayed. Therefore, WS samples should be considered as a supplement to GCF samples when assaying these proteins. Furthermore, subjects had elevated levels of DSPP, CEMP1 and CAP as tooth movement levels increased in GCF samples more evidently than in WS. There was a continual increase in CAP protein concentrations up to week 13 in GCF and WS samples for both the maxillary incisors and maxillary molar regions. These results aid to form the hypothesis that resorption of cementum may release CAP into the GCF and can serve as a potential biomarker for monitoring cementum resorption. However, more research is necessary to confirm this hypothesis.

Response to the following questions:

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

2. Were the results published?

   a. If so, cite reference/s for publication/s including titles, dates, author or co-authors, journal, issue and page numbers –
      No publication was made.

   b. Was AAOF support acknowledged?
      N/A

   c. If not, are there plans to publish? If not, why not?
      The initially obtained data is difficult to publish because of the reasons previously described in our annual reports (please see summary below).

      Reasons of not publishing the initial data
      Although the results of this study prove promising, no definitive results can be made comparing WS to GCF protein levels at this time. A continuation of this study to increase sample size and power will be necessary to validate the clinical relevance of these proposed biomarkers. However, we will need an extensive large sample size to be able to get significant results, which may be very difficult to get.

      Plans for future publication of the last part of the study (proteomics analysis)
      As we mentioned above since none of these four selected proteins showed statistically significant differences, we did extend our analysis by using proteomics analysis of 10 samples 5 with documented root resorption and 5 controls undergoing similar treatment). This analysis was able to detect significant changes (over 4 fold) of 14 different proteins some of which are known to be involved in inflammation and tissue remodeling. Although further confirmation is necessary, we believe that this analysis may allow us to discover more reliable biomarkers that could be used in future follow up studies. This part of the study will be submitted for publication in the next 1-3 months.

3. Have the results of this proposal been presented?

   a. If so, list titles, author or co-authors of these presentation/s, year and locations
      The data of this project were presented at the University of Michigan as part of a MS Thesis in Orthodontics by Dr. Ehler (the resident working in this project) in June 2015.

   b. Was AAOF support acknowledged?
      Yes

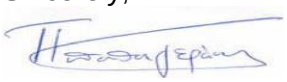
   c. If not, are there plans to do so? If not, why not?
      We may also present the proteomics analysis data to a future Orthodontics meeting. If so, we will acknowledge the AAOF support.

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

Once validated the data of the proteomics analysis will be used for a R21 NIH application. We also may use these data for promoting a prognostic test for severe root resorption patients.

Thank you very much for your support.

Sincerely,



Petros Papagerakis, BDS, MS, PhD Assistant Professor
Department of Orthodontics and Pediatric Dentistry University of Michigan,
Ann Arbor
petrosp@umich.edu