

**2016 AAO Annual Session Milo Hellman Research Award, Harry Sicher Research Award, Thomas M. Graber Awards of Special Merit**

The Milo Hellman Research Award, Harry Sicher Research Award and Thomas M. Graber Awards of Special Merit lectures will be held on Sunday May 1 and Monday May 12 in the Orange County Convention Center West Building. Consult the listing below for room number and time of lecture. Continuing education credit is available for attending these lectures.

**Milo Hellman Research Award**

Lecture Information: Sunday, May 1; 10:00am-10:20am; Orange County Convention Center West Building Room 307

**Analysis of Bone Augmentation with Corticotomy-Facilitated Dental Expansion: A Histologic & Micro-CT Study**

Britney Bare, DMD, MS

Texas A&M University Baylor College of Dentistry

**Objective:** A randomized split-mouth experiment was performed to determine the effects of bone grafting, when performed along with corticotomies and buccal tooth movements, on dehiscence formation.

**Methods:** Bilateral full-thickness mucoperiosteal buccal flaps were raised and corticotomies were performed with a piezosurgery unit adjacent to the maxillary 2nd premolars in seven dogs. The experimental (Graft+) side received a demineralized freeze-dried allograft and a resorbable collagen membrane. The 2nd premolars were expanded with archwires for 9 weeks, followed by 3 weeks of consolidation. Soft tissue measurements included probing depths, attachment loss, and recession. Tooth movements were monitored using intraoral, radiographic and model measurements. Bone surrounding the 2nd premolar was evaluated with microCT. New bone formation was analyzed histologically using calcein and alizarin fluorescent labels, and H&E stains.

**Results:** Post-surgical healing progressed normally with no signs of infection. The Graft+ and control (Graft-) 2nd premolars underwent similar amounts of expansion (~2.5 mm intraorally; ~1.7 mm radiographically) and tipping, with no statistically significant side differences. The soft tissue periodontium was not affected on either side. There were bony dehiscences on both the Graft+ and Graft- sides, with slightly but significantly ( $p=0.038$ ) more bone loss over the mesial root on the Graft- side. Bone material density (mg HA/cm<sup>3</sup>) was significantly ( $p=0.028$ ) greater on the Graft+ side. Buccal bone apposition was evident surrounding graft particles and mineralized particulate graft material was present at the apical aspect of the roots on the Graft+ side.

**Conclusions:** Bone grafting does not prevent dehiscence formation because only limited amounts of new bone is formed, primarily at the more apical aspects of the tooth's roots.

**Harry Sicher Research Award**

Lecture Information: Sunday, May 1; 10:20am-10:40am; Orange County Convention Center West Building Room 307

**Bone Mineralization Dependent Craniosynostosis and Craniofacial Shape Abnormalities in the Mouse Model of Infantile Hypophosphata**

John M. DuRussel, MS, DDS, MS

University of Michigan

**Background:** Inactivating mutations in tissue-nonspecific alkaline phosphatase (TNAP) cause hypophosphatasia (HPP), which is commonly characterized by decreased bone mineralization. Infants and mice with HPP can also develop craniosynostosis and craniofacial shape abnormalities, though the mechanism by which TNAP deficiency causes these craniofacial defects is not yet known. Manifestations of HPP are heterogeneous in severity, and evidence from the literature suggests that

much of this variability is mutation dependent. Here, we performed a comprehensive analysis of craniosynostosis and craniofacial shape variation in the *Alpl*<sup>-/-</sup> mouse model of murine HPP as an initial step towards better understanding penetrance of the HPP craniofacial phenotype.

**Methods:** Mouse paws were radiographed and scored to establish severity of the long bone hypomineralization phenotype. Craniosynostosis was identified on micro CT scans of mouse skulls and confirmed by microscopy of dissected samples. Craniofacial shape abnormalities were quantified using digital calipers and by placing landmarks on micro CT scans. Skulls were compared by genotype and by severity of the long bone hypomineralization phenotype through analysis of variance, mixed model, principal component and Euclidean distance matrix analyses.

**Results:** Despite similar deficiencies in alkaline phosphatase, *Alpl*<sup>-/-</sup> mice develop craniosynostosis and a brachycephalic/acrocephalic craniofacial shape of variable penetrance. Only those *Alpl*<sup>-/-</sup> mice with a severe bone hypomineralization defect develop craniosynostosis and an abnormal craniofacial shape.

**Conclusions:** These results indicate that variability of the HPP phenotype is not entirely dependent upon the type of genetic mutation and level of residual alkaline phosphatase activity. Additionally, despite a severity continuum of the bone hypomineralization phenotype, craniofacial skeletal shape abnormalities and craniosynostosis occur only in the context of severely diminished bone mineralization in the *Alpl*<sup>-/-</sup> mouse model of HPP.

### **Thomas M. Graber Awards of Special Merit**

Lecture Information: Sunday, May 1; 10:40am-11:00am; Orange County Convention Center West Building Room 307

#### **Screw-Type Device Diameter and Orthodontic Loading Influence Adjacent Bone Remodeling**

J. Christian Francis, DDS, MS  
University of Kentucky

**Introduction:** The purpose of this study was to evaluate the effect of diameter and orthodontic loading of a screw-type device on supporting bone remodeling.

**Methods:** Anchorage devices (n=70) with 1.6, 2.0, 3.0 & 3.75mm diameters were placed into edentulous sites in skeletally mature beagle dogs following premolar extraction and healing. In a split-mouth design, devices on one side were loaded (2N) utilizing calibrated coil springs. Epifluorescent bone labels were given i.v. prior to sacrifice. Bone-implant sections (~ 70 micrometers) were prepared using undecalcified methods. Bone formation rate (BFR, %/yr) and other histomorphometric variables were assessed using imaging software.

**Results:** The BFR varied by jaw. The mean BFR ranged from 10.93%/yr. to 38.91%/yr. The BFR was significantly ( $p<0.05$ ) lower in bone adjacent to the 1.6mm diameter screws compared to bone adjacent to the 2.0, 3.0, and 3.75mm diameter screws. BFR was lower adjacent to loaded 1.6mm screws compared to non-loaded 1.6mm screws ( $p<0.01$ ) or loaded 2.0-3.75mm diameter screws ( $p<0.01$ ). No significant differences in BFR were noted, regardless of loading condition, between the 2.0, 3.0, and 3.75mm diameter screws.

**Conclusion:** We detected a dramatic reduction in a critical biologic parameter, bone remodeling, in a controlled experimental design. While orthodontic loading of 2N did not alter bone remodeling associated with screws of 2.0mm diameter or larger, it did decrease bone remodeling adjacent to the 1.6mm screws. 2.0mm diameter or larger machined screws may be more likely to maintain a healthy bone-implant interface under typical orthodontic forces.

Lecture Information: Monday, May 2; 10:00am-10:20am; Orange County Convention Center West Building Room 307

### **Elevation of a Full-Thickness Mucoperiosteal Flap Alone Accelerates Orthodontic Tooth Movement**

Kelly Martinez Owen, DDS, MS

Texas A&M University Baylor College of Dentistry

**Objectives:** To determine if the elevation of a full-thickness mucoperiosteal flap alone, without cortical cuts, decreases the amount of bone around teeth and accelerates mesial tooth movements.

**Methods:** The mandibular second premolars of seven beagle dogs were extracted and, on one randomly selected side, a full-thickness mucoperiosteal buccal flap extending from the distal of the 3rd premolar to the mesial of the first premolar was elevated. The other side did not receive flap surgery. The mandibular 3rd premolars were protracted with orthodontic appliances. Tooth movements were analyzed biweekly over an eight-week period with calipers and radiographs. The amount and density of bone were analyzed using  $\mu$ CT; bone remodeling was evaluated with histologic sections.

**Results:** Experimental tooth movements measured intraorally between cusp tips were significantly greater (25%) than control tooth movements. The approximate center of resistance measured radiographically also moved significantly more ( $\square$  31%) on the experimental than control side. The experimental premolar tipped more than the control premolar (10.5 $\square$  vs 8.7 $\square$ ), but the difference was not statistically significant. The medullary bone volume fraction mesial to the 3rd premolar was significantly less (9.1%) and the bone was significantly less dense (9.8%) on the experimental side than on the control side. Histology showed no side differences in the number of osteoclasts or osteoblasts evident in the medullary bone.

**Conclusions:** Elevation of a full-thickness mucoperiosteal flap alone (i.e. without injury to bone) decreases the amount and density of medullary bone surrounding the tooth and accelerates tooth movements.

Lecture Information: Monday, May 2; 10:20am-10:40am; Orange County Convention Center West Building Room 307

### **The Investigation of Primary Failure of Eruption (PFE) Etiology: A Functional and In Silico Approach**

Heather M. Hendricks, DDS, MS

University of North Carolina - Chapel Hill

The genetic basis of PFE (OMIM ID: 125350) was interrogated using molecular functional studies. PFE is a diagnosis that conveys a poor prognosis in the eruption/ function of teeth. Treatment with a continuous archwire worsens the condition. Two aims tested the hypothesis that PTH1R mutations result in loss of function due to altered protein structure: to determine 1) the fate of a functional PTH1R mutation and 2) the resulting PTH1R protein structure of each functional mutation.

**Methods:** We used IFA for COS7 cells transfected with either the WT or 1092delG PTH1R mutation sequence to compare the fate of the expressed protein and performed in silico analysis of the WT PTH1R and 4 different functional PTH1R mutations.

**Results:** Functional studies (IFA) showed a variation in expression between the WT and mutant PTH1R. Further, in silico analysis showed structural differences between WT and mutant PTH1R proteins, particularly in the regions of the 3rd intracellular loop and the 6th transmembrane domain required for efficient PTH1R function.

**Conclusion:** PTH1R mutations identified in PFE likely result from diminished function due to truncation of the protein, lack of efficient G-protein interactions and putatively attenuated signal transduction.

Lecture Information: Monday, May 2; 10:40am-11:00am; Orange County Convention Center West Building Room 307

**Association of APOE- $\epsilon$  Isoforms and Reduced BMI Values in Obstructive Sleep Apnea Patients with a Convex Dento-Facial Profile**

Lucy Lee Wachs, DMD, MS  
University of Kentucky

**Objective:** The goal of this study was to determine the relationships between AHI, BMI, dento-facial classification/facial convexity, and genetic variations within APOE in patients diagnosed with obstructive sleep apnea (OSA).

**Materials and Methods:** 168 Caucasian non-edentulous patients diagnosed with moderate-to-severe OSA (via polysomnography scored using standard criteria) (110 males and 58 females) were enrolled in the study at one of two separate accredited sleep clinics. Skeletal classification was determined by clinical facial/profile exam. Lateral photographs were obtained and analyzed for facial convexity and to support clinical exam diagnosis. Buccal cells were collected in saliva and genomic DNA was isolated with the Oragene-DNA Collection Kits. Examined SNPs included the APOE- $\epsilon$ 1-4 allele-defining single nucleotide polymorphisms (SNPs), rs429358 and rs7412. APOE alleles were determined by the SNPs genotyped, and the resulting allelic combinations based on known APOE genotypic haplotypes. The Shapiro Wilks  $W$  test was used to determine whether the continuous variables being tested were normally distributed. ANOVA was performed for parametric, and the Wilcox/ Kruskal-Wallis Rank sums test for non-parametric continuous data. The Tukey-Kramer HSD, or the Steel-Dwass test, was applied for multiple comparisons of parametric and non-parametric data respectively as applicable. Stepwise logistic regression analysis applying the p-value threshold stopping rule was utilized to test for associations between the test variables in a linear model. Statistical significance was set a priori at  $p < 0.05$ .

**Results:** There was no difference in AHI amongst the three (orthognathic, retrognathic, prognathic) skeletal classifications. No statistically significant correlation between AHI and facial convexity was observed within the overall cohort ( $p=0.2$ ), or when separating out facial convexity case by skeletal classification (orthognathic  $p=0.13$ , retrognathic  $p=0.63$ , and prognathic  $p=0.47$ ). BMI was significantly smaller in the retrognathic group compared with the non-retrognathic combined group ( $p=0.0004$ ). There was no association with AHI or BMI with any APOE haplotype. There was no association with APOE $\epsilon$  alleles and skeletal classification with all classes ( $p=0.27$ ). However, when comparing the retrognathic versus non-retrognathic groups with APOE $\epsilon$  haplotypes, the E3/E4 haplotype was statistically significant compared to the other haplotypes in the retrognathic group ( $p=0.012$ ). Facial convexity was statistically significant with the APOE $\epsilon$  haplotypes E2/E2 and E4/E4 versus E2/E3, E3/E3, E4/E3, and probable E2/E3 haplotypes ( $p=0.017$ ; power =0.7).

**Conclusion:** A retrognathic profile and increased convexity seem to be associated with OSA independent of BMI. Even though there was no association of BMI with APOE $\epsilon$  haplotypes, the retrognathic group had a statistically significant greater distribution of the APOE e3/e4 haplotype compared to the others than the non-retrognathic group in a group of OSA patients.