UNIVERSITY *of* MARYLAND
SCHOOL OF DENTISTRY

2024 Research Day
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Oral Presentation

#1. Student Skills Development in Periodontal Instrumentation during the COVID-19 Pandemic: Longitudinal Assessment

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Objectives: Substantial modifications in dental education had to be made because of the COVID-19 pandemic. This study aimed to evaluate student skills development in periodontal instrumentation among three classes during the COVID pandemic via longitudinal assessment.

Methods: The COVID-19 pandemic began at the end of the third year for Class A ($n1 = 126$), the end of the second year for Class B ($n2 = 130$), and the end of the first year for Class C ($n3 = 126$). Onsite simulation-based learning (SBL) was implemented for Classes A and B; Class A had additional in-clinic student-partners practice before the second-year practical examination. Remote SBL was implemented for Class C, utilizing demonstration videos of each instrument. Student performances in the first-year practical, second-year practical, and fourth-year scaling competency examinations were compared using the Friedman test and a two-way repeated ANOVA.

Results: Classes A and C showed no differences in their performances over time while Class B exhibited a significant variation ($p = 0.0003$). Clinical experience in Class A was significantly less than Classes B and C ($p < 0.0001$) attributable to the implementation of social distancing guidelines. The class effect on student performance was significantly dependent on assessment timing ($p = 0.0007$). The remote SBL was favored for the first-year practical while the onsite SBL approach for Class A was favored for the second-year practical. However, there was no difference in the 4th-year scaling performances among the three classes ($p > 0.62$).

Conclusion: While Class A had the least clinical experience, Classes B and C had less preclinical experience than Class A. Nonetheless, all three modified curricula achieved comparable student learning outcomes in periodontal instrumentation.

#2.   Antibiofilm and Degradation-Resistant Ionic Liquid-Based Silane for Dental Resins

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The current dental resins undergo a short life service mainly due to interfacial breakdown by bacterial acid attack and vulnerability to enzymatic or hydrolytic degradation. Here we demonstrated the synthesis of an ester-free ionic liquid-based silane with effects against *Streptococcus mutans*. Furthermore, we developed a resin composite with this versatile silane, generating an antibiofilm and degradation-resistant material. This study aimed to formulate and evaluate resin composites with silica nanoparticles silanized with different concentrations of an experimental ionic liquid-based silane. The ionic liquid-based silane was synthesized with (3-chloropropyl) trimethoxysilane and 1-vinylimidazole, generating an ester-free silane. The silane was characterized by Fourier transform infrared (FTIR), ultraviolet-visible (UV-Vis), and nuclear magnetic resonance (NMR) spectroscopies. Silica nanoparticles were silanized with 1, 2.5, 5, 7.5, and 10 wt.% silane. One group of silica was not silanized for comparison. The silicas were analyzed by FTIR, UV-Vis, NMR, thermogravimetric analysis (TGA), scanning electron microscopy, and transmission electron microscopy. The silicas with different silane concentrations were incorporated at 60 wt.% into a matrix to formulate resin composites. Six resins were formulated: with silica without silane (control) or silica silanized with 1, 2.5, 5, 7.5, and 10 wt.% silane. The resins were evaluated by TGA, immediate and long-term degree of conversion, softening in solvent, immediate and long-term flexural strength, immediate and long-term ultimate tensile strength, antimicrobial activity by counting the colony-forming units and by fluorescence microscopy, and cytotoxicity. The results showed that the silane was successfully synthesized and bonded to the silica nanoparticles. The developed dental resins displayed proper degree of conversion, improved resistance against softening in solvent, physicochemical stability after six months of water storage, antibiofilm property, and biocompatibility. Our outcomes endorse future applications for ionic liquid-based materials due to their structural tunability, which may assist to develop novel biomaterials with improved therapeutic features.

#3.   Bioactive and Therapeutic Dental Restorations

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Objective. Recurrent caries at tooth-restoration margins is a primary reason for restoration failure. The objectives of this study were to: (1) develop novel multifunctional dental resins with antibacterial function and calcium (Ca) and phosphate (P) ion release, and (2) investigate the effects on enamel and dentin demineralization and hardness at the margins under biofilms.

Methods. Dimethylaminohexadecyl methacrylate (DMAHDM) and nanoparticles of amorphous calcium phosphate (NACP) were incorporated into resins. Four groups were tested: (1) Commercial control, (2) Experimental control (0% DMAHDM+0% NACP), (3) antibacterial group (3% DMAHDM+0% NACP), (D) antibacterial and remineralizing group (3% DMAHDM+30% NACP). Mechanical properties and ion release were measured. Colony-forming units (CFU), lactic acid and polysaccharide of biofilms were evaluated. Demineralization of tooth with restorations was induced via biofilms. Enamel and dentin hardness was measured.

Results. Incorporating DMAHDM and NACP into resins did not compromise the mechanical properties ($P>0.1$). Ca and P ion release was increased at cariogenic pH. Biofilm acid and polysaccharides were greatly decreased via DMAHDM ($P<0.05$). Under biofilm acids, enamel and dentin hardness at the margins was substantially reduced, indicating lesion formation. The antibacterial resins diminished lactic acid and polysaccharides of biofilms, reducing CFU by 4 logs. For enamel, NACP composite remineralized tooth lesions. The new composite produced marginal enamel hardness that was 2-fold greater than commercial control. For dentin, the new composite preserved marginal dentin, yielding dentin hardness 41% greater than commercial fluoride-release composite group. For tooth roots, the bioactive endodontic sealer regenerated root dentin minerals, and increased root dentin hardness to match that of sound dentin.

Conclusions. Novel bioactive and therapeutic multifunctional resins are promising to inhibit recurrent caries at tooth-restoration margins and overcome the primary reason for restoration failures. The new resin also has great potential for endodontic applications to strengthen tooth roots and prevent root fractures.

#4.   Analyzing claims data to determine access to and utilization of oral healthcare services among the Medicare population

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Background: The population of Medicare-eligible adults in the U.S. is increasing. Despite the importance of oral health to overall health, traditional fee-for-service (FFS) Medicare does not usually cover dental services. In contrast, most Medicare Advantage (MA) plans offer dental benefits, and enrollment in MA has been greatest among groups that experience oral health inequities. The primary objective of this research is to analyze claims data to explore characteristics of traditional FFS Medicare dental encounters, and to determine whether MA is expanding access to oral healthcare services.

Methods: Centers for Medicare & Medicaid Services (CMS) Medicare FFS claims from 2019-2021 were analyzed to identify and characterize oral health-related encounters. CMS 2019 MA plan benefits and enrollment data was used to assess the prevalence and likelihood of having MA plans offering dental coverage among beneficiaries by sociodemographic factors.

Results: A total of 2,098,056 oral health encounters were identified through FFS Medicare claims from 2019-2021, with dental treatment/procedures accounting for only about 3% of annual encounters. Among 21,219,195 beneficiaries with MA coverage in 2019, 32.7% had an MA plan with no dental coverage, 14.0% had a plan offering preventive dental coverage, and 53.3% had a plan offering comprehensive dental coverage. Racial/ethnic minority MA beneficiaries had higher odds of having dental coverage compared to non-minority beneficiaries, with Hispanics displaying the highest odds ratio (aOR=1.71 [95%CI=1.70, 1.72]). Dual-eligible MA beneficiaries displayed higher odds of having dental coverage compared to non-dual-eligible beneficiaries (aOR =2.77 [95% CI=2.76, 2.77]).

Conclusions: Analyses identified that a small percentage of traditional FFS Medicare oral health encounters were related to dental treatment/procedures. Additionally, beneficiaries who were racial/ethnic minorities and beneficiaries with lower incomes were more likely to have MA plans offering dental coverage than their counterparts. MA could, therefore, potentially help to improve access to oral healthcare services for Medicare beneficiaries who have historically experienced oral health inequities.

#5. **Unraveling Temporomandibular Disorder Comorbidities: Dissecting Sex-Based Brain Mechanisms in Chronic Pain Conditions**

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Temporomandibular disorder (TMD) and irritable bowel syndrome (IBS) are two Chronic Overlapping Pain Conditions (COPCs) that present with significant comorbidity. Both conditions are more prevalent in women and are exacerbated by stress. While peripheral mechanisms might contribute to pain hypersensitivity for each individual condition, mechanisms underlying the comorbidity are poorly understood, complicating pain management when multiple conditions are involved. In this study, longitudinal behavioral and functional MRI-based brain changes have been identified in an animal model (masseter muscle inflammation followed by stress) that induces de novo Comorbid visceral Pain Hypersensitivity (CPH) in rats. In particular, the data indicated that increased activity in the insula and regions of the reward and limbic systems are associated with more pronounced and longer lasting visceral pain behaviors in females, while the faster pain resolution in males may be due to increased activity in descending pain inhibitory pathways. Analysis of functional connectivity of insula and machine learning approaches using functional MRI is underway. These findings suggest the critical role of brain mechanisms in chronic pain conditions and that sex may be a risk factor for developing COPCs.

#6. Identification of sex-dependent biomarkers of fMRI-active brain regions in a rat model of comorbid pain hypersensitivity using MSI

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Chronic pain conditions affect over 100 million people in the United States. Chronic overlapping pain conditions that include temporomandibular disorder (TMD) and irritable bowel syndrome (IBS) are predominant in women and are exacerbated by stress. The overlapping nature of these conditions, sex-dependence, and stress-linked mechanisms of these conditions make adequate treatment difficult. We used a rat model of comorbid pain to induce chronic visceral pain hypersensitivity (CPH). To gain insights into the sex-dependency of this model, we evaluated brain activity by functional magnetic resonance imaging (fMRI) and during colorectal distention followed by MSI. Rats were injected with complete Freund's adjuvant into both masseter muscles followed by restraint stress for 2 hours/day for 4 days alternating nose-up or nose-down at a 45° angle in 15-minute blocks. Colorectal distention was performed during fMRI collection. Scans were collected at baseline, 1, and 7 weeks and brains were subsequently removed and frozen. Cryosections were prepared based on targeted locations from the fMRI results. Sections were prepared for MSI with matrix and negative ion mode lipid data was collected at 50um spatial resolution and stained (Nissl) for reference. CPH persisted longer in females (at least 7 weeks) than it did in males (resolved after 1 week). One week after stress, several candidate subregions of interest were identified as having greater activity in females over males. These included the insula, nucleus accumbens, anterior cingulate cortex (ACC), and hippocampus. A custom algorithm was used to encircle uniformly sized brain subregions and were termed functional regions of interest (fROIs). The most striking differences among fROIs were phosphatidylglycerol (PG) lipids with greater intensity in male ACC than female; however, a panel of lipids showed greater intensities in female ACC. Using this approach, we identified a panel of region-specific and sex-dependent lipid changes that are being evaluated for mechanistic links to pain-stimulated brain activity.

#7. Targeting hepatoma-derived growth factor attenuates the rise of resistance to EGFR tyrosine kinase inhibitor in non-small cell lung cancer xenograft tumors

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Constitutively active mutant epidermal growth factor receptor (EGFR) is one of the major oncogenic drivers in non-small cell lung cancer (NSCLC). It has been reported that 15% to 50% of NSCLC harbor mutant EGFR. Targeted therapy using EGFR tyrosine kinase inhibitor (TKI) is the first line choice in patients with metastatic or recurring disease. However, despite the high response rate, most patients have a partial response and resistance to TKI develops eventually. Options after failure of second line third generation EGFR TKIs such as osimertinib are limited. Thus, improving EGFR targeted therapy is an unmet need. Although the mechanism of resistance in relapsed tumors has been extensively studied, the factors that enable the tumor cells to survive initial TKI exposure and transform from TKI-sensitive to TKI-resistant are not fully elucidated.

We demonstrated here EGFR mutant patient-derived xenograft (PDX) tumors responded partially to osimertinib despite near complete inhibition of EGFR activation. Signaling in AKT/mTOR and MAPK pathways could be reactivated following initial inhibition. As a result, many tumor cells escaped drug killing and regained growth following about 35 days of continuous osimertinib dosing. However, when an antibody to hepatoma-derived growth factor (HDGF) was given concurrently with osimertinib, tumors showed complete or near complete responses, and there was significant prolongation of progression-free survival of tumor bearing mice. Immunohistochemistry and western blot analysis of tumors collected in the early stages of treatment suggests increased suppression of the AKT/mTOR and MAPK pathways could be a mechanism leading to enhanced efficacy of osimertinib when it is combined with anti-HDGF antibody.

These results suggest that HDGF could be critically involved in promoting acquired resistance to TKI in NSCLC PDX tumors. Blocking HDGF signaling could be a potential means to enhance EGFR targeted therapy of NSCLC that warrants further advanced preclinical and clinical studies.

#8. Risk Factors for Infection Recurrence After Surgical Resection of Advanced Stage Osteonecrosis of the Mandible

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Background: Advanced stage osteoradionecrosis (ORN) and medication-related osteonecrosis of the jaw (MRONJ) are challenging disease entities requiring multimodal therapy including surgical resection. However, risk factors associated with infection recurrence are poorly understood.

Purpose: The purpose of this study was to identify risk factors associated with infection recurrence following resection of advanced stage ORN or MRONJ of the mandible.

Study Design & Methods: This was a retrospective cohort study including patients who underwent segmental mandibulectomy for management of ORN or MRONJ between 2016 and 2021 at the University of Maryland Medical Center. Subjects who did not have margin viability data were excluded. The primary predictor variable was viability of resection margins on histopathologic analysis (viable or nonviable). Secondarily, other risk factors categorized as demographic (age, sex, race), medical (comorbidities), and perioperative (reconstructive modality, antibiotic duration, microbiological growth) were evaluated. The primary outcome variable was time to infection recurrence defined as time from surgical resection to clinical diagnosis of a fistula tract, abscess, or persistent inflammatory symptoms necessitating surgical intervention. Descriptive and bivariate statistics were used to identify associations between risk factors and time to infection recurrence. A significant level of $P \leq .05$ was considered significant.

Results: The cohort consisted of 57 subjects with a mean age of 63.3 +/- 10.0 years (71.9% Male, 75.4% White) treated for ORN (47.4%) or MRONJ (52.6%). A total of 19/57 (33%) subjects developed a recurrence of infection with 1- and 2-year survival of 75.8 and 66.2%, respectively. Nonviable resection margins were associated with earlier time to infection recurrence ($P \leq .001$, hazard ratio (HR) = 11.9, 95% confidence interval (CI) = 3.84 to 36.7) as was younger age ($P = .005$, HR = 0.921, 95% CI = 0.869 to 0.976) and atypical pathogen growth on culture ($P = .002$, HR = 8.58, 95% CI = 2.24 to 32.8).

Conclusions: Histopathologic margin viability was associated with earlier time to infection recurrence following resection of advanced stage ORN or MRONJ of the mandible. A multidisciplinary approach between surgeon, infectious disease specialist, and pathologist is essential to evaluate risk factors and formulate a patient-specific treatment plan in the management of this disease. Additional studies are needed to identify interventions that may improve outcomes in this demographic.

#9. Accuracy of virtual attachments removal for fabrication of thermoplastic orthodontic retainers

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Virtual attachment removal (VAR) is a process used in digital dentistry to prefabricate retainers by removing attachments from a digital scan before the removal of clear aligner attachments. This study aims to evaluate the accuracy of VAR in the maxillary arch. 110 teeth were analyzed from a sample of 54 maxillary scans from 25 subjects. Models with attachments were virtually debonded using Meshmixer® and superimposed over the control group in MeshLab. Vector Analysis Module was used to calculate 3D distances on the buccal surfaces between the superimposed models. The VAR protocol showed no statistical differences in the root mean square between different tooth segments with an overall tendency for inadequate attachment removal. No difference between the groups were found when the number of attachments was used as a main factor. The VAR technique is precise enough for the fabrication of retainers from printed dental models in a clinical setting. Future studies are being performed to analyze mechanical properties and tracking of these retainers fabricated with VAR protocol.