8TH INTERNATIONAL

TMJ Interdisciplinary Research Meeting

April 21-22, 2023

University of Pennsylvania
Philadelphia, Pennsylvania

www.dental.upenn.edu/ITIRM8

Penn Dental Medicine
University of Pennsylvania

Penn Medicine
Center for Temporomandibular Joint Disease

8TH INTERNATIONAL

TMJ Interdisciplinary Research Meeting

Welcome

It is our great pleasure to welcome you to Philadelphia, USA, and the University of Pennsylvania campus for the 8th International TMJ Research Meeting (ITIRM8)!

Once again, we have reunited our friends and colleagues for another lively scientific discussion of state-of-the-art research on the TMJ. We are pleased that this meeting continues to be an attractive venue where students as well as junior and senior level biologists, engineers, and clinicians can get together to exchange ideas, learn from one another, develop friendship and establish collaboration.

Consistent with that theme, this year's program focuses on special topics with accompanying keynote speakers such as markers and cell based therapies, in vivo mechanics, pathophysiology of the TMJ, and bioscaffold based functional tissue engineering.

We would especially like to thank the program committee, all of your support is an integral part of maintaining the high quality of this meeting.

Please enjoy the conference!

Alejandro Almarza, PhD, *Chair*
Boaz Arzi, DVM
Michael Detamore, PhD
Eric Granquist, DMD, MD

AIMS OF ITIRM8

The 8th International TMJ Interdisciplinary Research Meeting provides a forum to discuss state-of-the-art TMJ research. By bringing together leaders as well as budding investigators in our field, we hope to address challenges in the clinical management of TMJ problems affecting function, bring forth an understanding of the embryonic development of the TMJ, start to identify the primary drivers of chronic pain, and set new directions in biomechanical and biological research that hold great potential for future treatments.

CONFERENCE ORGANIZER

Alejandro Almarza
Eric Granquist

PROGRAM COMMITTEE

Alejandro Almarza
Boaz Arzi
Michael Detamore
Eric Granquist

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Friday, April 21

Location: Law Auditorium, Jordan Medical Education Center

8:00 am	**Breakfast/Check in**
9:00 am	**Opening Remarks**
9:15 am	**Keynote Presentation** **"Surgery of the TMJ Past,Present and Future"** Peter Quinn, *University of Pennsylvania School of Dental Medicine*
10:15 am	**Break**

TOTAL JOINT PROSTHETICS

10:30 am	**"Wear and Oxidation Analysis of Explanted TMJR Devices"** Louis Mercuri, *Rush Medical Center*
10:45 am	**"Identifying Structure-Function Relationships Toward Tissue-Engineering of the Temporomandibular Joint Disc Complex in the Yucatan Minipig"** Eston G. Kallins, *University of California, Irvine*
11:00 am	**"Chondromatosis of TMJ. The Prague Experiences"** Vladimír Machoň, *Charles University and Faculty Hospital Prague*
11:15 am	**"Massachusetts General Hospital Surgical and Diagnostic Techniques"** Briana Burris, *Massachusetts General Hospital*
11:30 am	**Lunch**

BIOMECHANICS

1:00 pm	**"Orthognathic Surgery Effects on Masticatory Muscle Activities and Neuromechanics"** Laura Iwasaki, *Oregon Health & Science University*
1:15 pm	**"Identifying Temporomandibular Disorder Morphological Risk Factors via Deep Learning and Multiscale Biomechanical Modeling"** Shuchun Sun, *Clemson University*
1:30 pm	**"Mandibular Osteotomy Rotation Effects on TMJ Energy Density"** Jeff Nickel, *Oregon Health & Science University*
1:45 pm	**"Mechanical Response of TMJ Condylar Cartilage under Dynamic Loading"** X. Lucas Lu, *University of Delaware*
2:00 pm	**Break**

MORE ▶

Friday, April 21 cont'd

GENERAL TOPICS

2:30 pm	**"Improving the Accuracy at Triangle Technique in Arthroscopic Procedure Using a 3D Device"** Leonard D. Moreira, *Private Clinic*
2:45 pm	**"A Systematic Review of Animal Models for Temporomandibular Joint Heterotopic Ossification"** Jason Chen, *Massachusetts General Hospital*
3:00 pm	**"Diagnostic Tool for Temporomandibular Joint Implant: Based on Acoustic Emission"** Jacob Eapen, *University of Illinois at Chicago*
3:15 pm	**Break**
3:45 pm	**"Automatic Classification of Temporomandibular Joint Disorders by MRI Images and Convolutional Neural Networks"** Wen-Liang Lo, *Taipei Veterans General Hospital*
4:00 pm	**"EHPN: A Comprehensive Patient-Specific Prediction Model for Temporomandibular Joint Osteoarthritis Progression"** Najla Al Turkestani, *University of Michigan, School of Dentistry*
4:15 pm	**Open Forum**
5:30 pm	**Reception**
6:00 pm	**Dinner**

Saturday, April 22

Location: Rubenstein Auditorium, Smilow Center for Translational Research

8:00 am **Breakfast/Check-in**

9:00 am **Keynote Presentation**
"TMJ Pain: Models, Mechanisms and Manipulations"
Beth Winkelstein, *University of Pennsylvania School of Engineering and Applied Science*

9:30 am **Break**

MOLECULAR BIOLOGY AND ANIMAL MODELS

10:00 am **"Evaluation of Condylar Remodeling and MMPs from Patient with Temporomandibular Osteoarthritis"**
Eric Granquist, *University of Pennsylvania School of Dental Medicine*

10:15 am **"NG2/CSPG4 Potentiates Endochondral Ossification in Mandibular Condylar Cartilage"**
David Reed, *University of Illinois Chicago*

10:30 am **"TBD"**
Sumit Yadav, *University of Nebraska*

10:45 am **"Signaling Interplays of CD11c+-Myeloid Dendritic Cell-Derived Osteoclast Precursor and Environment/Cytokine-Milieu onto Osteoclastogenesis vs. Bone Remodeling"**
Andy Yen-Tung Teng, *Kaohsiung Medical University (KMU) & KMU-Hospital*

11:00 am **"Single Cell RNAseq of Rat TMJ"**
Sara Trbojevic, *University of Pittsburgh*

11:15 am **Break**

11:30 am **Open Forum**

12:00 pm **Lunch**

TREATMENTS

1:30 pm **"Heterotopic Ossification Following TMJ Replacement With Alloplastic Reconstruction: Retrospective Analysis of Zimmer Biomet and TMJ Concepts"**
Alexander Li, *University of Pennsylvania School of Dental Medicine*

1:45 pm **"Regenerative Engineering of a Biphasic Patient-Fitted Temporomandibular Joint Prosthesis"**
David S. Nedrelow, *University of Oklahoma*

2:00 pm **"CRISPR to Modulate Inflammation"**
Joshua Stover, *University of Pittsburgh*

2:15 pm **"Developing a Minimally Invasive Therapy for Restoring Cartilage Homeostasis and Chondrocyte Identity"**
Millie Embree, *Columbia University*

2:30 pm **Closing Remarks**

Peter D. Quinn, DMD, MD

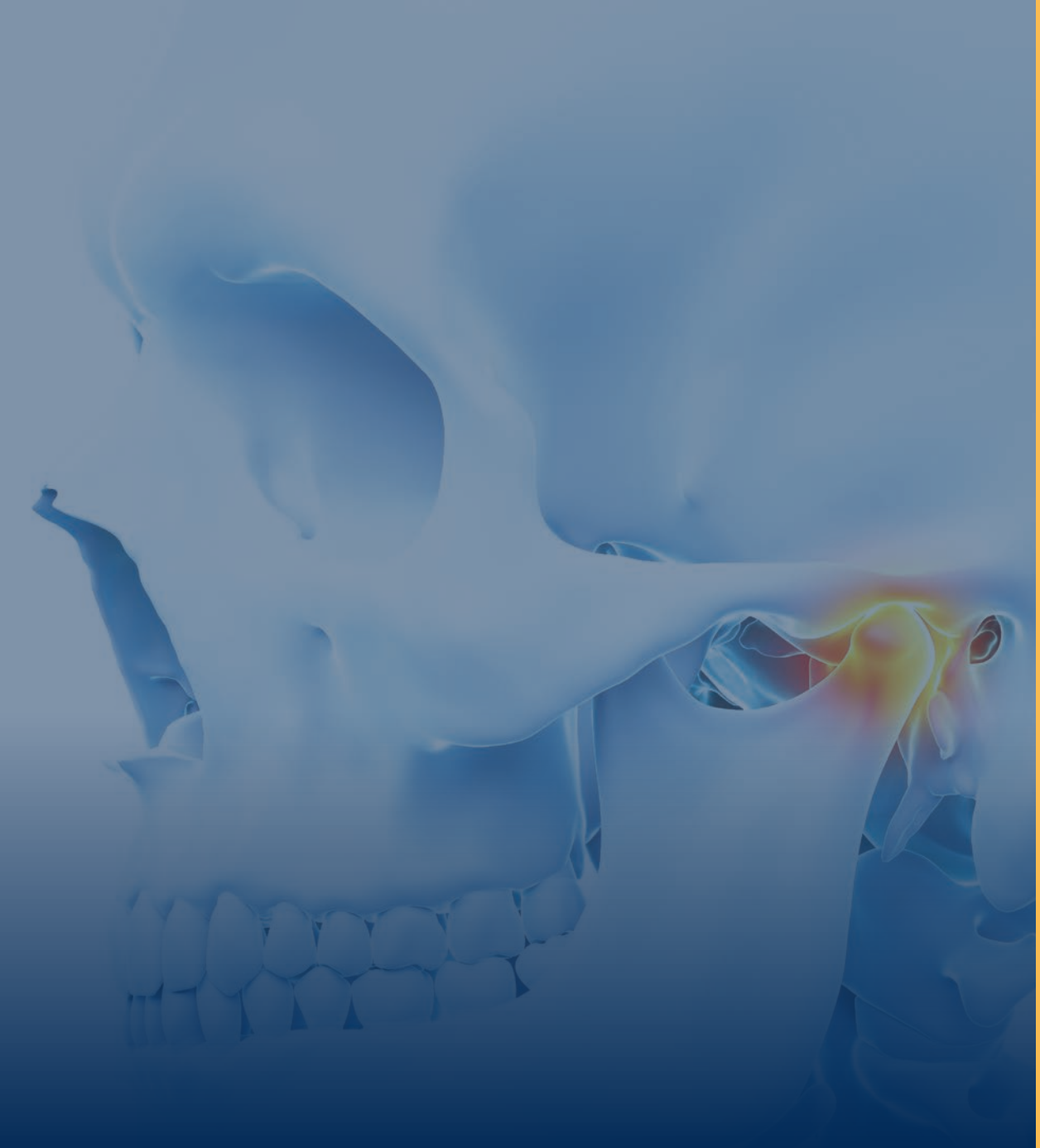
Peter D. Quinn is the Schoenleber Professor of Oral & Maxillofacial Surgery/ Pharmacology at Penn Dental Medicine. Dr. Quinn served as Chair of the Department of Oral & Maxillofacial Surgery/Pharmacology at Penn Dental Medicine from 1986 to 2008. His primary research interests are in the alloplastic reconstruction of the temporomandibular joint and vascular malformations of the maxillofacial skeleton maxillofacial skeleton. He was a principal investigator in a ten-year clinical trial for the development of the only FDA-approved stock prosthesis for reconstruction of the temporomandibular joint. Dr. Quinn has completed a surgical atlas for temporomandibular joint surgery, which has been published by Elsevier.

Beth A. Winkelstein, PhD

Beth A. Winkelstein's pioneering research focuses on the mechanisms of bodily injury — especially injuries from sports, automobile accidents or degenerative diseases that produce persistent pain in the neck and spine — and has been supported by the National Institutes of Health, the National Science Foundation and the Department of Defense, among many others, including a Presidential Early Career Award from the NSF.

The author of Orthopaedic Biomechanics (2012) and more than a hundred papers and book chapters, she serves as editor of the Journal of Biomechanical Engineering and is a Fellow of the Biomedical Engineering Society, American Institute for Medical and Biological Engineering and American Society of Mechanical Engineers, which awarded her its Y.C. Fung Young Investigator Award in 2006.

At Penn, she served as associate dean for undergraduate education in the School of Engineering and Applied Science and before that as chair of the Graduate Group in Bioengineering and as a Penn Fellow, the cross-University program for select faculty members to develop leadership skills, build alliances across disciplines and gain deeper knowledge of University governance. In partnership with Dean Dennis DeTurck of the College of Arts and Sciences, she led Penn's multi-year grant from the American Association of Universities to improve the quality of teaching in science, technology, engineering and mathematics, especially through new techniques of active in-class learning.



ABSTRACTS

8TH INTERNATIONAL

TMJ

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EHPN: A Comprehensive Patient-Specific Prediction Model for Temporomandibular Joint Osteoarthritis Progression

Al Turkestani N[1], Li T[2], Bianchi J[3], Gurgel M[1], Benavides E[4], Soki F[4], Mishina Y[5], Fontana M6, Rao A[7], Cevidanes L[1]

[1]Orthodontics & Pediatric Dentistry, University of Michigan, School of Dentistry
[2]Department of Biostatistics, University of North Carolina
[3]Pediatric Dentistry and Orthodontics, University of Pacific
[4]Department of Periodontics and Oral Medicine, University of Michigan, School of Dentistry
[5]Department of Biologic and Materials Science, University of Michigan, School of Dentistry
[6]Department of Cariology, Restorative Sciences and Endodontics, University of Michigan, School of Dentistry
[7]Department of Computational Medicine & Bioinformatics, University of Michigan

Introduction/Rationale: To test risk predictors and validate a comprehensive patient-specific prediction model for temporomandibular joint (TMJ) osteoarthritis (OA) progression. **Materials and Methods:** We acquired clinical, biological and CBCT imaging data of 92 subjects, 46 TMJ OA and age and sex matched healthy controls at baseline, and clinical and imaging data for 74 subjects recalled at 2-3 years follow-up interval. Health status of participants was categorized into healthy, improved, same or worsened based on changes in levels of pain related symptoms, radiographic signs and three-dimensional morphological changes of the condyles. We evaluated the performance of 6 feature selection methods, that eliminate redundant and irrelevant variables, and 8 statistical and machine learning approaches [Generalized linear model elastic net (Glmnet), Glmboost, High-dimensional Discriminant Analysis, Single-hidden-layer neural networks, Random Forest, Extreme Gradient boosting, Support Vector Machine and Linear Discriminant Analysis (LDA)]. Nested 10-fold cross-validation was adopted to rigorously avoid overfitting due to sample size. Areas Under the receiver operating characteristic Curve (AUC), accuracy, precision and F1 score were utilized to compare models' predictions on independent datasets. **Results:** A novel EHPN (Ensemble via Hierarchical Predictions) Glmboost model combined the top performing 18 models with different feature selection methods, achieving AUC= 0.72, accuracy= 0.87, precision= 0.99 and F1=0.82. The integration of clinical, imaging and biological markers improved the models' performance in predicting TMJ OA progression. The top contributing features included: clinical variables (headache, back pain, restless sleep, age, mouth opening), objective quantitative imaging markers (joint space, articular fossa Bone Surface/Bone volume, and condylar High Grey Level Run Emphasis (HGLRE), ShortRunHGLRE) and biological markers in saliva (Osteoprotegerin, MMP7, Angiogenin, VEGF) and serum (BDNF, ENA78). **Conclusions:** This comprehensive study identifies risk predictors for TMJ OA progression. The new predictive model may be employed in cost-effectiveness research towards applying it for early prognosis in clinical practice. **Clinical Significance:** Current understanding of the TMJ OA pathogenesis has shifted from a simple mechanical wear-tear model to a complex and multifactorial condition. Despite the availability of different and well-established treatment options for TMJ OA, to date no clinically approved treatment is available to reverse or regenerate the damage within the TMJ structure. Thus, identifying patients at risk for disease progression is crucial for early assessment, timely intervention, enhancing the prognosis and reducing the need for surgical management.

Metal Allergy Testing in Patients Listed for Temporomandibular Joint Replacement at Massachusetts General Hospital

Burris BJ[1], Johnson H[2], Yu J[3], McCain JP[4]

[1]Clinical Fellow in the Department of Surgery, Division of Oral and Maxillofacial Surgery, Massachusetts General Hospital, Harvard Medical School, Harvard School of Dental Medicine
[2]Dermatology, Massachusetts General Hospital, University of Minnesota Medical School
[3]Dermatology, Massachusetts General Hospital, Harvard Medical School
[4]Surgery, Oral and Maxillofacial Surgery, Massachusetts General Hospital, Harvard Medical School, Harvard School of Dental Medicine

Introduction/Rationale: Patients with temporomandibular joint (TMJ) arthropathies (i.e end-stage degeneration, invasive pathology, or developmental anomalies) may be candidates for total joint replacement (TJR). Metal allergy testing is conducted beforehand to guide the choice of prosthesis. Our aim was to determine the agreeability between the lymphocyte transformation test (LTT) and skin patch test (SPT) for detection of metal allergy. **Materials and Methods:** Retrospective analysis of patients who presented to Massachusetts General Hospital with TMJ arthropathies requiring TJR and were referred for LTT and SPT, from 2018-2022. **Results:** Of the 31 patients included, the mean age was 45.2 years. 87.1% were female and 90.3% self-identified as White. Of the fourteen patients who completed both the LTT and SPT, 21.4% self-reported a history of metal allergy, while 50% self-reported a history of jewelry allergy. The results of LTT and SPT were discordant with regards to aluminum, cobalt, chromium, molybdenum, zirconium, or iron. 41.7% of patients who tested positive for nickel at any concentration on LTT also tested positive for nickel on SPT. 100.0% of patients who tested positive for vanadium at any concentration on LTT also tested positive for vanadium on SPT. The sensitivity and specificity of LTT were 46.2% and 83.8%, respectively. **Conclusions:** In patients planned for TMJ TJR, there is the most agreement between LTT and SPT on vanadium allergy, followed by nickel allergy. There is no agreement on other metal allergies. **Clinical Significance:** When compared to SPT, LTT has a low sensitivity and high specificity.

A Systematic Review of Animal Models for Temporomandibular Joint Heterotopic Ossification

Chen JE[1], Handa S[2], Rosén A[3], Keith DA[4], Guastaldi FPS[4]

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[2]Oral & Maxillofacial Surgery, Orofacial Pain, Massachusetts General Hospital, Harvard School of Dental Medicine
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[4]Oral & Maxillofacial Surgery, Massachusetts General Hospital, Harvard School of Dental Medicine

Introduction/Rationale: There are few animal models for the study of temporomandibular joint heterotopic ossification (TMJ-HO). The aim of this systematic review was to assess the available literature where TMJ-HO was directly studied or observed through animal protocols. **Materials and Methods:** Studies from *PubMed*, *Web of Science*, and Cochrane Library were selected by two independent reviewers with the following MeSH terms: "((heterotopic ossification) OR (heterotopic calcification) OR (heterotopic mineralization) OR (heterotopic bone) OR (ectopic bone) OR (ankylosis) OR (osteophyte) OR (osteophytosis) OR (bone cyst) OR (bone spur) OR (myositis ossificans)) AND (TMJ) AND (animal)". A manual search was also performed through the databases, study references, and relevant journals. ARRIVE guidelines were assessed to evaluate methodology and reproducibility of selected studies. SYRLCE's risk of bias tool was also adapted to determine internal validity. **Results:** 24 publications were included after study identification and screening. Heterotopic ossification was surgically or chemically induced through single or combined defects in the condyle, articular disc, and temporal bone in animal models (mice, n=5; rats, n=4; rabbit, n=2; goat, n=1; sheep, n=8; pig, n=2; dog, n=1; monkey, n=1) specific for TMJ-HO (n=4), ankylosis (n=9), osteoarthritis (n=10), status post TMJ replacement (n=1), and status post bilateral sagittal split osteotomy (n=1). **Conclusions:** Heterotopic ossification of the TMJ is difficult to study due to its multifactorial etiology, pathogenesis, and symptoms. There remains a need for more accurate and reproducible animal models as well as a consolidated classification system for TMJ-HO. **Clinical Significance:** At present, TMJ-HO is not fully understood, and several facets of the disease remain unclear. An established classification system that is supported by empirical data, collected through animal experiment protocols, will help formulate proper therapeutic guidelines and prevent clinical mismanagement.

Diagnostic Tool for Temporomandibular Joint Implant: Based on Acoustic Emission

Eapen J[1], Keaty W[2], Sun Y[2], Mercuri LG[3], Mathew MT[4], Ozevin D[2]

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[2]Department of Civil, Materials and Environmental Engineering, UIC, University of Illinois at Chicago
[3]Department of Orthopedic Surgery, Rush University Medical Center
[4]Department of Restorative Dentistry, University of Illinois at Chicago

Introduction/Rationale: Temporomandibular joint (TMJ) injuries are prevalent problem in the US today especially in young people [1]. The FDA received 680 Medical Device Reporting's (MDRs) related to TMJ implants from 2014-2018 [2]. Due to the increase in MDRs of TMJ implants there is a great need to identify and treat implant issues before the condition worsens. The absence of a proper functioning of TMJ can be detrimental to a person's l livelihood and may affect a person's ability to eat, speak and take medications. Currently, the common way to see if a person has a TMJ implant issue is through Computed Tomography Scan or Magnetic resonance imaging scan. These imagining procedures are expensive, require prior authorization, resulting in late diagnosis and other complications. Acoustic emissions (AE) are a phenomenon of ultrasound and sonic wave and generation by materials as they undergo deformation and fracture processes[3]. Since the number of TMJ implants are expected to increase in the future, a new cost-effective and effective diagnostic device is needed. **Materials and Methods:** Preliminary tests were performed using a tribometer customized for the purpose. A bone block with similar density to that of a skull and a ramus component of a custom TMJ replacement device made of Ti6Al4V containing 3 Ti6Al4V screws (S1, S2, S3) were selected as materials. The TMJ implant was stimulated to study different conditions (well function, partial-functional, and total-failed), the three groups that were designed for this study includes: (i) 3 fixed screws (control group), (ii) loosened S1 (360°) with fixed S2 and S3, and (iii) all 3 screws loosened. During the experiment, an AE sensor was attached to each screwhead and the TMJ was controlled to move at 1 Hz with 5N normal force with the tribometer. **Results:** The AE signals were successfully detected on each screw. Group (i) shows that the amplitude of the fixed screws is 61ff1dB, (ii) has an amplitude of 59ff1dB for the fixed screw and 63.3ff1.5dB for the loosened screw, and (iii) presents an amplitude of 67.7ff2.5dB for the loosened screws. The friction coefficient was calculated to be approximately 0.2ff0.05 based on the friction force for all groups which is similar to those in other studies [4]. From this experiment it was observed that the loosened screws exhibit higher AE amplitudes than the tightened ones. **Conclusions:** This pilot study found that tightened screws displayed a lower AE amplitude than loose screws, which could be used to detect early TMJ device fixation screw loosening. This is an ongoing investigation. Detailed studies with TMJ simulators are in progress. **Clinical Significance:** The clinical significance of this project is that a clinician will be able to diagnose and treat a person suffering from TMJ screw loosening and start treatment early. The significance of using AE instead of traditional methods like MRI and CT. Is that AE provides a more cost-effective approach. It also allows the clinician to get the results faster and not need prior authorization from insurance companies. This will also be a more safe approach when compared to using CT scans.

Orthognathic Surgery Effects on Masticatory Muscle Activities and Neuromechanics

Iwasaki LR1, Liu Y[2], Liu H[1], Nickel J[1]

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[2]Epidemiology and Public Health, East Tennessee State University

Introduction/Rationale: The objective of this investigation was to test the effects of orthognathic surgery on muscle force activation patterns and neuromechanics **Materials and Methods:** Pre- (T1) and post-surgery (T2) cone-beam computed tomography images were collected from consenting subjects aged ≥15 years. Anatomical data were used to measure surgical changes in anteroposterior mandibular position and occlusal plane angle (FH-OP), and to calculate T1 and T2 masticatory muscle forces (N) during canine biting at a given magnitude and a comprehensive range of biting angles relative to occlusal plane via numerical modeling. Principal Component Analyses (PCA) identified jaw muscle forces that accounted for changes in T2-T1 temporomandibular joint (TMJ) loads. Regression analyses tested the correlations between surgical changes in mandibular position, FH-OP, and muscle forces. **Results:** Of 148 cases screened, 28 females and 16 males provided complete records. T2-T1 differences in masticatory muscle forces varied by anteroposterior and FH-OP surgical changes. PCA T2-T1 changes in jaw muscle forces had moderate (PCA1, ipsilateral, λ=4.59; η2=0.071) to large (PCA2, contralateral, λ=1.49; η2=0.31) effects on TMJ loads. Correlations between surgical changes and ipsilateral masseter (PCA1, 0.23 ≤ R2 ≤ 0.47), contralateral masseter (PCA2, 0.17 ≤ R2 ≤ 0.46), and ipsilateral lateral pterygoid (PCA1, 0.42 ≤ R2 ≤ 0.47) muscle forces depended on biting angle. **Conclusions:** T2-T1 differences in muscle activities for the same canine biting magnitude and angle were affected by surgical changes in mandibular position and occlusal plane angle. These changes in masticatory muscle force activation patterns for the same biting conditions likely reflected the activation of different subpopulations of periodontal mechanoreceptors resultant to post-surgical changes in neuromechanics. **Clinical Significance:** Orthognathic surgery of the mandible has the potential to change the muscle activation patterns during loading of the mandible, and thereby change the TMJ loads

Identifying structure-function relationships toward tissue-engineering of the temporomandibular joint disc complex in the Yucatan minipig

Kallins EG, Donahue RP, Hu JC, Athanasiou KA

Department of Biomedical Engineering, University of California, Irvine

Introduction/Rationale: Anterior displacement of the temporomandibular joint (TMJ) disc complex (i.e., the TMJ disc and its six attachments) is frequently attributed to the two posterior attachments. As a direct result of this pathology, partial- or full-thickness defects develop in the lateral aspect of the TMJ disc. Tissue-engineering is poised to improve treatment for not only these partial- or full-thickness defects, but also, potentially, anterior disc displacement via implantation of biomimetic constructs. **Materials and Methods:** This study seeks to identify tissue-engineering design criteria for the two posterior attachments and lateral disc via structural, mechanical, biochemical, and crosslinking assays in the well-accepted Yucatan minipig model. **Results:** Under tension, this study found that the posterior inferior attachment (PIA) was 2.13-times stiffer and 2.30-times stronger than the posterior superior attachment (PSA). Collagen in both attachments was predominantly aligned mediolaterally, exhibiting anisotropy indices (ratio of Young's modulus in anteroposterior vs. mediolateral direction) of at least 2.78; however, the lateral disc was much more anisotropic, with an anisotropy index of 7.74. Among the three tissues, the PSA was the most heterogeneous, having a higher proportion of fat vacuoles. The PIA and lateral disc were more collagenous by dry weight (DW) than the PSA by 1.93- and 1.91-times, respectively. Compared to the PSA, the PIA was also 1.78-times higher in crosslinking per DW. In terms of glycosaminoglycan per DW, the lateral disc was significantly higher by 1.48- and 5.39-times in the PIA and PSA, respectively. **Conclusions:** These results indicate that the attachments are less fibrocartilaginous than the disc, while still contributing to the TMJ disc complex's mechanical stability during articulation. These findings also support the biomechanical function of the PIA and PSA; the stiffer PIA appears to anchor the disc to the mandibular condyle during articulation, while the softer PSA allows translation over the articular eminence. **Clinical Significance:** This characterization study seeks to give tissue engineers gold-standard design criteria for which to aim for when engineering biomimetic implants for addressing pathologies of the TMJ disc complex, including anterior disc displacement and resulting lateral defects, toward relieving pain and improving function for the many patients with TMJ afflictions.

Heterotopic Ossification Following TMJ Replacement With Alloplastic Reconstruction: Retrospective Analysis of Zimmer Biomet and TMJ Concepts

Li AYZ[1], Wu BW[2], Francois KR[1], Radley BD[3], Quinn PD[1], Granquist EJ[1], Giannakopoulos HE[1]

[1]Department of Oral and Maxillofacial Surgery, University of Pennsylvania School of Dental Medicine
[2]Department of Oral and Maxillofacial Surgery, New York University Langone Health
[3]Department of Oral and Maxillofacial Surgery, University of Florida Health Jacksonville

Introduction/Rationale: Heterotopic ossification (HO) of the temporomandibular joint (TMJ) is a rare pathologic process that involves formation of extraskeletal bone due to unidentified complications such as trauma. This is a retrospective cohort study to review all cases in which patients that have undergone alloplastic TMJ reconstruction from 2011-2021 at the Hospital of University of Pennsylvania for HO identification. Two FDA-approved alloplastic implants, Zimmer-Biomet© (stock) and TMJ Concepts© (custom), are currently used for TMJ total joint replacement. This study aims to determine the HO prevalence between the two competing alloplastic implants, and to perform statistical analysis to identify risk factors for developing HO. **Materials and Methods:** The selected cohort included patients who have had at least one TMJ replacement and/or revision during the surgical catalog period from 2011 to 2021, determined by CPT billing codes 21243 (arthroplasty, TMJ, with prosthetic joint replacement). Patients that were not treated by attendings from Penn Center for TMD as well as those that passed away were excluded from the selected cohort. **Results:** A total of 373 TMJ replacements (TMJR) and TMJ revisions (TMJREV) were performed in 262 patients, with an average age of 45 years. The majority of patients who underwent TMJR/TMJREV did not have inciting incidents nor previous TMJ surgeries. The prevalence of HO was found to be in 8.4% of all patients, with the most common location in the mandibular condyle (90.9%). The preliminary diagnosis of myofascial pain (P=0.002, RR=0.268 [0.110-0.656]) and the need for TMJREV (P<0.001, RR=34.8 [11.631-104.118]) were statistically significant risk factors for not developing and developing HO, respectively. **Conclusions:** There is no statistical difference between stock and custom prostheses for HO prevalence. Patients who underwent TMJ total joint replacement have low likelihood in contracting HO. **Clinical Significance:** The TMJ may be at an increased risk of developing HO compared to other joints in the human body due to its small joint space and unique anatomy. HO is a difficult pathology to control and treat. The pathogenesis of HO is complicated in the TMJ as it may involve trauma, inflammation, and hypoxia. Successful TMJ reconstruction requires multidisciplinary care including oral and maxillofacial surgeons, pain specialists, internists, physical therapists, and general dentists in order to optimize patient outcome.

Automatic classification of temporomandibular joint disorders by MRI images and convolutional neural networks

Lo W

Department of Oral and Maxillofacial Surgery, Taipei Veterans General Hospital

Introduction/Rationale: In this study, magnetic resonance imaging (MRI) of the temporomandibular joint collected in Division of Oral and Maxillofacial Surgery, Taipei Veterans General Hospital. Classification and analysis of severity stages of temporomandibular joint disease using convolutional neural networks. **Materials and Methods:** In such a grayscale series of images, the articular disc cartilage at the junction of the temporal bone and the condyles probably contains the most important features. You Only Look Once (YOLO) deep learning technology is used to identify the articular disc cartilage area and crop the image. Read the image in HSV format after removing surrounding noise. Store the image information in the V value. Reduce the subject's age information and left-right ear information to one dimension using principal component analysis and store it in the H value. **Results:** A six-category convolutional neural network was developed to identify severe stages in patients with temporomandibular joint (TMJ) disease. The prediction accuracy was 81.72%. **Conclusions:** The model can reduce the time spent on clinical imaging diagnosis, thereby improving the quality of care. **Clinical Significance:** It can assist clinical specialists by automatically identifying TMJ disorders.

Mechanical Response of TMJ Condylar Cartilage under Dynamic Loading

Lu XL[1], Porter A[1], Santare M[1], Han L[2], Peloquin J[3]

[1]Mechanical Engineering, University of Delaware
[2]Biomedical Engineering, Drexel University
[3]Biomedical Engineering, University of Delaware

Introduction/Rationale: A primary biomechanical function of TMJ condylar cartilage is shock absorption through energy dissipative deformation to reduce concussion on the brain. In this study we hypothesized that the unique bilayer structure of TMJ condylar cartilage endows a low dynamic stiffness, especially under small stress and high frequency loads, to minimize the impact from TMJ daily movements, i.e., eating and talking. **Materials and Methods:** To test the hypothesis, we compared the mechanical responses of porcine TMJ condylar cartilage and knee joint cartilage under dynamic loading. A constant load at 0.2 N was first applied to the sample in an unconfined compression setup. Young's modulus was calculated with the equilibrium strain. A cyclic sinusoidal loading of 6 N was then applied at 0.1-20 Hz. Cauchy normal stress and stretch ratio were calculated based on an incompressible material assumption. Dynamic modulus was obtained from the slope of stress-strain curve at each frequency. **Results:** The equilibrium Young's modulus of TMJ condylar cartilage under unconfined compression was approximately 60% lower than that of knee cartilage. For TMJ tissue, the dynamic modulus increased with loading frequency, but this correlation diminished at high stress levels (> 0.6 MPa). At low stresses, dynamic modulus of the TMJ cartilage was lower than that of the knee (10.6±4.0 vs 14.9±2.6 MPa at 10 Hz), but the opposite was true at higher stresses (22.0±7.8 vs 16.8±3.0 MPa at 10 Hz). **Conclusions:** It is critical to note that dynamic moduli were obtained when the knee and TMJ tissues were under the same initial loading, but different initial strains (15% vs 41%). Thus, the dynamic moduli of TMJ could be even lower than the knee at similar initial deformation. **Clinical Significance:** The study indicates that during daily activities, such as talking, TMJ cartilage provides better shock absorption than knee cartilage, potentially reducing impact on the brain

Chondromatosis of TMJ. The Prague experiences

Machon V

Oral Maxillofac Surgery, Charles University and Faculty Hospital Prague

Introduction/Rationale: Chondromatosis is a metaplasia of the synovial membrane, when it gradually leads to the formation of cartilaginous bodies in the joint space. **Materials and Methods:** The author recorded a total of 35 cases of chondromatosis in the years 2009-2022 (24 women, 11 men, average age 54.7 years). **Results:** The dominant symptom was pain (82% of patients), followed by crepitation (45%) and swelling of the preauricular landscape (20%). 51% of patients were treated arthroscopically, 49% of patients with open surgery. Recurrence was noted in 3 patients (8%). **Conclusions:** The authors present the individual phases of the disease, the possible solutions, on a set of patients. **Clinical Significance:** The authors present the individual phases of the disease, the possible solutions, on a set of patients.

Wear and Oxidation Analysis of Explanted TMJR Devices

Mercuri LG[1], Yuh C[1], Hall DJ[1], Cordero KE[2], Pourzal R[1]

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Introduction/Rationale: Total temporomandibular joint replacement (TMJR) is the salvage treatment for end-stage TMJ pathology. Unlike total hip (THR) and knee replacements (TKR), limited knowledge exists on the in vivo wear behavior. Here, we assessed in vivo generated polyethylene wear and oxidation in retrieved TMJR fossae. **Materials and Methods:** We examined 24 surgically-retrieved TMJR fossae (duration: 57.4 months (range 0.2-240)). Damage features on the surface were recorded and laser scanning confocal microscopy was used to measure linear wear penetration of the fossae. Fossae were then sectioned for the measurement of polyethylene oxidation indices (OIs) through the component thickness using FTIR spectroscopy. **Results:** 17/24 of the fossa surfaces had distinct round/oval wear scars (d=1-6 mm). Three fossae exhibited no wear. Two had uniform wear not confined to a distinct scar. Primary wear features (Figure1) included polishing, protuberances, and fine scratches. The mean maximum linear wear was 87.35fff1110.17sm. Wear and time in situ were linearly correlated (R2 =0.47, p=0.001, Figure2), with a linear wear rate of 0.82 sm/month. Most fossae exhibited consistent OIs through the thickness (Table1). Samples with distinct wear scars tended to have a higher OI within the wear region at the subsurface, with OI increasing with longer time in situ. **Conclusions:** Mild wear and minimal oxidation were observed in surgically-retrieved TMJR fossae. The observations of protuberances are interesting because it is also common in tibial liners. Potential explanations for this pattern include the nonconforming surface conditions and the lack of pure sliding. Patterns of oxidation found in fossa wear scars were consistent with observations reported in TKR literature. Overall, the wear and oxidation behavior appear mild, however "normal" benchmarks for TMJR wear and oxidation have yet to be established. **Clinical Significance:** As the number of TMJR procedures is rising, fundamental knowledge of wear mechanisms associated with implant design/material is essential to guarantee implant longevity.

Improving the Accuracy at Triangle Technique in Arthroscopic Procedure Using a 3D Device

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Introduction/Rationale: Do a surgery technique in arthroscopic procedure needs handling arthroscope and a cannula, but to do this is not so easy and the surgeon have to follow a long time a learning curve, that depend of the hability of the surgeon triangle using his knowledge and long training and expertise. Using a 3d technology, this long curve could be shorter, getting easier the way of training all endoscopic Surgeons. **Materials and Methods:** Device generation workflow is fully digitally using a CAD CAM software a cannula scanning or measurements are taken and now we can do in software a device that embrace our cannula models and put then in a triangle position **Results:** First we could print the model generated by software and fit the cannulas. Now we can check if they are intersecting and now we can see in our plastic model how it works so we can see by the endoscope that the punctures and the triangle technique is working very well. **Conclusions:** Using this 3d triangle technique device to improve the accuracy in arthroscopic procedures in many levels of difficulty is real. **Clinical Significance:** Use this 3d device to prepare more surgeons to do minimally invasive technique surgery in patients with TMJ disorders.

Regenerative Engineering of a Biphasic Patient-Fitted Temporomandibular Joint Prosthesis

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Introduction/Rationale: Temporomandibular joint (TMJ) osteoarthritis, trauma, or congenital anomalies (e.g., hemifacial microsomia) may be indications for a TMJ condylar prosthesis. Current TMJ prosthesis biomaterials; however, do not accommodate patient growth over time. Regenerative implant strategies are necessary to treat growing patients who have TMJ tissue degradation. **Materials and Methods:** capable of regenerating bone and cartilage regions. The TMJ scaffold was assembled from two parts: (1) a 3D-printed porous scaffold comprised of polycaprolactone and hydroxyapatite (PCL-HAp), and (2) a hydrogel comprised of photocrosslinkable pentenoate-modified hyaluronic acid (PHA), polyethylene glycol (PEGDA), and devitalized cartilage (DVC). TMJ tissues were characterized after en bloc (i.e., condyle, disc, and fossa) resection from a pilot in vivo study where two different regenerative TMJ prosthesis designs (i.e., with and without hydrogel) were orthotopically implanted in goats for 6 months. Microcomputed tomography renderings were processed to present five viewpoints for each case. **Results:** Regions of both bone growth and resorption were evident along the implant's boundaries. Gross morphological analysis suggested TMJ disc outcomes were variable from perforated to nearly pristine, and some with granulation tissue. Histology and immunohistochemistry staining demonstrated fibrous growth evident inside the condylar implant's porous architecture. Soft tissues surrounding the implant exhibited a highly aligned fibrous structure. In cases from both groups with and without hydrogel, cartilage-like tissues were regenerated on the anterior, functioning surface of the condyle with positive collagen type II and alcian blue staining for glycosaminoglycans. **Conclusions:** In summary, the current study offered in vivo evidence of tissue regeneration using an acellular scaffold for TMJ condyle restoration. Future work aims to develop implants that can elicit more reproducible tissue regeneration. **Clinical Significance:** This research aims to expanded access to TMJ implant treatment for patients who are growing, exhibit metal hypersensitivity, or for other reasons are not appropriate candidates for currently used bioinert TMJ prostheses

Mandibular Osteotomy Rotation Effects on TMJ Energy Density

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Introduction/Rationale: Recently published data reported >40% mandibular condyle volume loss after mandibular orthognathic surgery. Mandibular surgery has the potential to rotate the mandibular condyle (proximal segment) relative to the glenoid fossa due to the use of rigid fixation, potentially increasing the mechanical work per volume of cartilage (energy density, mJ/mm3) during movement of the mandible. The objective of this research was to determine the effects of osteotomy related proximal segment rotation on the energy density variables of stress-field i) aspect ratio, iii) translation distance (mm), iii) velocity of translation (mm/s), and iv) cartilage volume (mm3). **Materials and Methods:** According to IRB oversite, twenty adult subjects (10 women, 10 men) consented to the use of their data. Three-dimensional anatomical geometries were derived from CBCT data. Subjects produced dynamic stereometry recordings during symmetrical closing. Baseline values of energy density variables were determined for subjects' right and left TMJs. This was followed by in silico rotation modification of right and left mandibular condyle relative to the glenoid fossa. These modifications involved a series of ff19 degree rotations about X (dorso-ventral), Y (rostral-caudal), and Z (transverse) axes. For each modification, dynamic stereometry calculations were performed to determine the rotation effects on the energy density variables. ANOVA determined if there were significant changes in the variables compared to baseline. **Results:** Statistically significant effects were seen for Z axis dorsal rotation of the proximal segment. There were no sex differences, where dorsal rotations significantly increased aspect ratio by 1.4x ($p< 0.001$), decreased cartilage volume by 28% ($p< 0.01$), and increased aspect ratio relative to cartilage volume by 1.9x ($p< 0.001$). **Conclusions:** Mandibular osteotomy related Z axis dorsal rotation of the proximal segment can significantly increase energy densities through changes in stress-field aspect ratio and cartilage volume during symmetrical movement of the mandibular condyle. **Clinical Significance:** Orthognathic surgery of the mandible requires control of rotation of the mandibular condyle in order to prevent increased mechanical work per volume of cartilage during function.

NG2/CSPG4 potentiates endochondral ossification in mandibular condylar cartilage

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Introduction/Rationale: NG2/CSPG4 regulates cartilage degeneration during temporomandibular joint osteoarthritis (TMJ OA) and the mechanical activation of the ERK 1/2 signaling pathway, a regulator of OA progression and endochondral ossification. The objective of this study is to determine if NG2/CSPG4 controls signaling pathways regulating endochondral ossification in mandibular condylar cartilage. **Materials and Methods:** Primary mandibular fibrochondrocytes were isolated from 10-14 day old control (c57 BL 6J) and NG2/CSPG4 knockout mice and cultured with and without osteogenic differentiation media. Mineralization was quantified by alizarin red staining, RT-qPCR, and total RNAseq. The transcriptional heterogeneity of skeletally mature control and NG2/CSPG4 knockout tissues was further characterized by single-cell RNAseq (SC-RNA-seq). Cell calls and UMI counts were generated with Cell Ranger (version 6.1.1). Quality control, normalization, and clustering were done in the Seurat R Package toolkit (version 4.0.6). Genes for each sub-population were analyzed using a gene ontology enrichment analysis (ShinyGO v0.76.2). **Results:** Total RNAseq analysis illustrates that NG2/CSPG4 knockout cells are associated with the "ossification" enrichment set (factor 0.1; $p < 8e-06$; $n = 4$/genotype). RT-qPCR analysis illustrates that NG2/CSPG4 knockout cells have significantly lower expression of BMP2, GREM1, and PTHrP ($p < 0.05$; $n = 4$). Culturing with osteogenic differentiation media resulted in alizarin-positive staining in control but not NG2/CSGP4 knockout cells. SC-RNA-seq analysis illustrates that NG2/CSPG4 knockout tissues generate an overlapping but transcriptionally distinct cluster, with the control cluster mapping to the "bone mineralization" enrichment set and the knockout cluster mapping to the "cartilage development" enrichment set (fold enrichment >8; -log10 FDR 7; n = 1/genotype). **Conclusions:** Together, these findings demonstrate that NG2/CSPG4 is implicated in the differentiation of cells undergoing endochondral ossification in mandibular condylar cartilage. **Clinical Significance:** NG2/CSPG4 has proven to be an effective theragnostic target for some cancers. The therapeutic potential of NG2/CSPG in the musculoskeletal system is untested, but could be a target for modulating cartilage biomineralization.

Identifying Temporomandibular Disorder Morphological Risk Factors via Deep Learning and Multiscale Biomechanical Modeling

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Introduction/Rationale: Temporomandibular disorders (TMD) affect an estimated 11.2 to 12.4 million adults in the United States and contribute to the larger burden of chronic pain causing $560-635 billion in associated annual costs. Despite this high incidence and economic burden, TMD etiology is poorly understood, limiting clinical treatment and prevention. Characterization of etiological risk factors and the temporomandibular joint (TMJ) biomechanical environment critically informs risk analysis and targeted intervention development. Deep learning enables systematic risk factor identification, while multiscale biomechanical modeling provides mechanistic explanation; combining these complementary methodologies improves translational confidence. **Materials and Methods:** We propose a hybrid approach combining deep learning and multiscale biomechanical modeling to systematically identify TMD morphological risk factors and elucidate mechanistic relationships between risk factors and the TMJ mechanobiological environment. Machine learning models were trained to predict TMD status based on mandible geometry segmented from CBCT, and critical areas for making the prediction were exported. Multiscale biomechanical model was built based on cadaver dissection data to study the relationship between the identified morphological features and TMJ mechanobiological environment. **Results:** Our CBCT-derived 3D convolutional neural network predicted TMD status, with individually-unique combinations of condylar, ramus, and chin regions as prediction foundation. Biomechanical modeling result showed that mandibular size is correlated with joint force and condyle shape is correlated with contact behavior. Mandibular size determines the TMJ disc energy density, nutrient availability, and ATP production; and condyle shape determines TMJ disc energy density. Overall, people with small mandible and flat condyle are most susceptible for TMD. **Conclusions:** In this study, we proposed a novel hybrid approach that combined 3D explainable deep learning and multiscale biomechanical modeling to investigate the etiology of temporomandibular disorder (TMD). Our approach successfully identified morphological risk factors and elucidated mechanistic relationships within the temporomandibular joint (TMJ) biomechanical environment. This method addressed major limitations of deep learning in medical applications and demonstrated increased translational confidence and methodological accessibility for smaller clinical datasets. The potential for this hybrid approach to be applied to other musculoskeletal systems highlights its versatility and value in advancing the field. **Clinical Significance:** The clinical significance of our hybrid approach lies in its potential to improve the understanding of TMD etiology, ultimately benefiting patients by informing targeted and preventive TMD care. By identifying morphological risk factors and uncovering their mechanistic relationships within the TMJ biomechanical environment, our method can contribute to better diagnostic accuracy and personalized treatment strategies. The increased translational confidence and methodological accessibility provided by this approach make it a valuable tool for smaller clinical datasets and extend its potential to be utilized in the study of other musculoskeletal systems, ultimately benefiting a broader range of clinical applications.

Signaling interplays of CD11c+-myeloid dendritic cell-derived osteoclast precursor and environment/cytokine-milieu onto osteoclastogenesis vs. bone remodeling

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Introduction/Rationale: Bone remodeling-vs.-osteoclastogenesis involves the pivotal-pathways towards bone repair-&-loss, where the RANKL-RANK/OPG-triad signals via TRAF6/adaptor-complexes to downstream in osteoclast/OC, OC-precursors/OCp and immune-cells onto the environmental milieu at osteo-immune interface. We pioneered the characteristic OCp from myeloid-CD11c+-dendritic-cell-precursors (DDOC) in response to RANKL and osteotropic-cytokines (i.e., TNF-β, TGF-β, etc.), where we explored to study how signal-interactions of TGFβ-&-IL-17 in DDOC lacking TRAF6-signaling for osteoclastogenesis/bone-resorption. **Materials and Methods:** We employed established protocols to generate CD11c+DDOC-cells lacking the TRAF6-signaling in BM/splenic-cells of β6-wk-C57BL/6-chimeric mice post-lethal-irradiation & reconstituted with BM/fetal-liver cells of TRAF6(-/-)-mice, then-subjected to co-cultures with/without naïve-CD4+T-cells (or mRANKL:50-100ng/ ml) and Aggregatibactor Actinomycetemcomitans/JP2-strain sonicate-Ag (Aa-Ag), where exogenous rmTGFβ or mIL-17 vs. anti-TGFβ-neutralizing-Mab was added individually in-vitro, followed by enumerating surface- areas of TRAP+-CD11c+DC/mm2 in resorptive-pits. In parallel, CD11c+-DDOC from WT-TRAF6(+/+)-mice- BM/splenic-cells (w/wt rmM-CSF-&-rmRANKL) were set as controls for the statistics (i.e., student-t-test or ANOVA). **Results:** The results showed that: i) TRAF6/transduced-signaling was essential for RANKL/RANK-associated (WT)-DDOC-mediated osteoclastogensis; ii) rmTGF-β added into TRAF6(-/-)-derived-DDOC co-cultured with RANKL-&-Aa-Ag significantly rescued the reduced TRAP(+)-DDOC/OC activity detected in resorptive-pits (p=0.006); whereas, adding rmIL-17 unexpectedly further enhanced such rescued TRAP(+)-DDOC/OC activity measured (p=0.041), higher than that detected above, suggesting that TGF-β individually or with-IL-17 synergistically, mediated TRAF6-independent rescue-signaling onto effector, DDOC; iii) conversely, addition of anti-TGF-β-neutralizing-Mab in co-cultures of ii), or replacing rmRANKL with naïve-CD4+T-cells & Aa-Ag, significantly reduced TRAP(+)-DDOC/OC activity on resorptive-pits (p=0.008) as depicted in ii), indicating that IL-17/IL-17Rs signaling for the functional activity of DDOC/OCp, required TGF-β in the environmental milieu, regardless the RANKL/TRAF6-signaling or other inter-players expressed in-situ/nearby. **Conclusions:** These new findings suggest that such non-discriminative signaling via TGFβ-&-IL-17 for rescue-effector in CD11c+DDOC/OCp may underpin new insight for the alternative pathway of osteoclastogenesis, which will require further study for its in-vivo significance through animal-models and human conditions; including the periodontitis and articular-joint disorders (i.e., arthritis & TMJ-joint disease). **Clinical Significance:** These findings and new rationale may provide novel approaches for a better understanding of the disease pathogenesis, including periodontitis and articular-joint disorders (i.e., arthritis & TMJ-joint disease).

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