Temporomandibular Joint Disorder

TMJ Bioengineering Conference

June 19-21, 2014 Pittsburgh, PA

University Club

At the University of Pittsburgh

123 University Place
Pittsburgh, PA 15260

University of Pittsburgh

Pittsburgh Campus Map

School of Dental Medicine
3501 Terrace St.
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University Club
123 University Place
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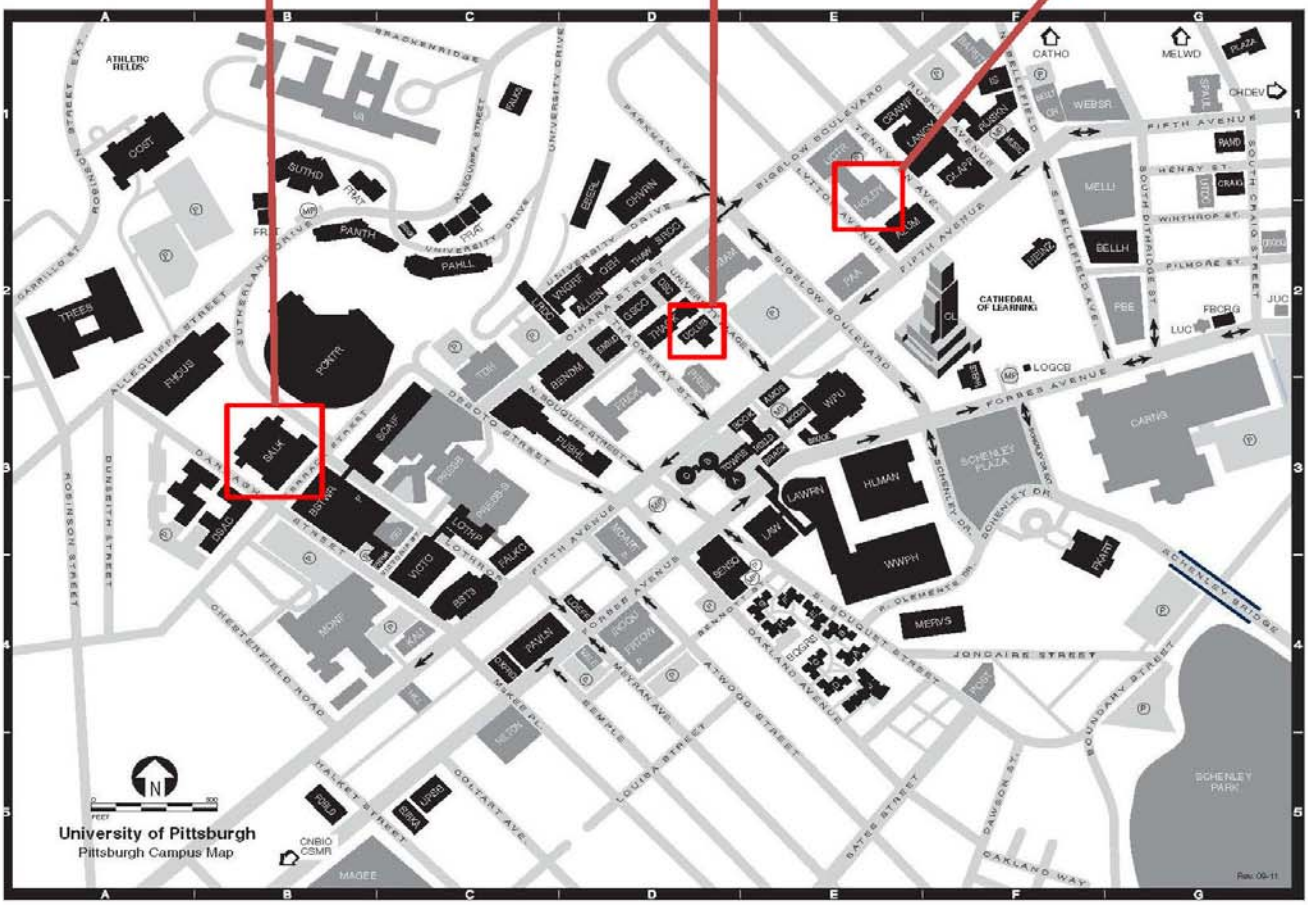

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TMJ Bioengineering Conference - 4

Thursday, June 19 through Saturday, June 21, 2014
University Club
Pittsburgh, PA

Welcome!

It is indeed our pleasure to welcome you to Pittsburgh, PA, for the third Temporomandibular Joint Bioengineering Conference (TMJ4)!

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 our generous sponsors, the program committee, and our local organizers, Diane Turner and Michele Leahy; all of your support is an integral part of maintaining the high quality of this meeting.

Please enjoy the conference!

With our very best wishes.

Sincerely,
Alejandro Almarza, PhD
Michael Detamore, PhD
Kyle Allen, PhD
Boaz Arzi, DVM, DAVDC, DEVDC
The TMJ4 Organizing Committee

General Information

Aims of the Symposium

The *TMJ Bioengineering Conference* 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 challenging problems in clinical management of TMDs, and set new directions in biomechanical and biological research that hold great potential for the future.

Organizing Committee

Alejandro Almarza – Chair
Michael Detamore
Kyle Allen
Boaz Arzi

Advisory Board

Kyriacos Athanasiou
Jeremy Mao

Instructions to Presenters

I. Podium Presenters

The time for presentations will be limited, in favor of more time for discussion. Therefore, the speakers and moderators have been asked to limit the number of slides as well as to adhere to the time allotted for each presentation.

Important Notes:

All speakers are asked to check-in with the projectionist and the session moderators 15 minutes before the start of session in which they will present.

For 15 minute time slots

10 min. presentations each immediately followed by a 5 min. discussion.
Maximum **15 PowerPoint slides** for computer presentation.

Note: In view of time and the large number of talks, there will be no opportunity to use your personal computer or load your PowerPoint file during the symposium.

Featured Keynote Speakers

William Maixner, DDS, PhD is the Mary Lily Kenan Flagler Bingham Distinguished University Professor and Director of the Center for Pain Research and Innovation in the School of Dentistry at the University of North Carolina, Chapel Hill. Dr. Maixner's research program focuses on identifying the pathophysiological processes that underlie pain perception, persistent pain conditions, and related disorders. His current research focuses on genetic, environmental, biological, and psychological risk factors that contribute to the onset and maintenance of chronic pain conditions. A long term goal of his program is to translate new discoveries into clinical practices that improve the ability to diagnose and treat patients experiencing chronic pain. Dr. Maixner received his BA, DDS, and PhD from the University of Iowa. He recently was awarded the New York College of Dentistry Distinguished Scientist Award and the Wilbert E. Fordyce Clinical Investigator Award from the American Pain Society. Dr. Maixner has authored several peer reviewed paper and book chapters in both basic and clinical pain research. He is also co-founder of Algynomics Inc, which has a mission to translate clinical findings in the field of pain into novel diagnostics and therapeutics that will advance the diagnosis and treatment of common pain conditions.

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David C. Hatcher, DDS, MSc, MRCD received his DDS degree from the University of Washington. Subsequently he completed two years active duty in the U.S. Public Health Service and a one year general practice residency program at the University of Vermont Medical Center. Dr. Hatcher entered the graduate program in radiology at the University of Toronto and was granted a specialty degree in Oral and Maxillofacial Radiology in 1982 and a M.Sc. in 1983. His thesis topic dealt with radiology of tempormandibular disorders. Presently Dr. Hatcher is in private practice in Sacramento, California and has faculty appointments as Clinical Professor at the University of California San Francisco, University of California Los Angeles, University of the Pacific and Roseman University of Health Sciences.

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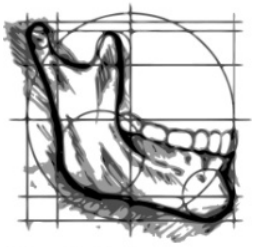

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Department of Bioengineering (UPitt)

http://www.engineering.pitt.edu/bioengineering

PROGRAM

Location: **University Club – Ballroom B**
123 University Place
Pittsburgh, PA 15260

7:30 am **Breakfast, Registration, Check-In**

8:45 am **Opening Ceremony, Welcome & Announcements**
Alejandro Almarza

Keynote Lecture:

9:00 am Genetic Approaches to Unraveling Complex Chronic Pain Conditions – Implications for Translational Pain Medicine
William Maixner

10:00 am **Break**

Podium Session 1: **Assessing Clinical TMJ Pain and Animal Models**
Session Chairs: ***Kyle Allen and Inna Belfer***

10:30 am Pain Assessment and Phenotyping of Orafacial Pain
Belfer I

10:45 am Variations in Biopsychosocial Outcomes in TMJD Based on Pain Severity
King C

11:00 am A Novel Non-Invasive Model of Temporomandibular Joint Pain In the Rat with Tunable Outcomes of Acute & Chronic Pain
Granquist E*, Kartha S, Zhou T, Winkelstein B*

11:15 am Use of a Novel Behavioral Device to Measure Orofacial Mechanical Allodynia in Rats
Rohrs E*, Kapernaros K, Jenkins AC, Neubert JK, Allen KD*

11:30 am Altered Loading, Degeneration, and Pain in a Rabbit Model
Almarza AJ*, Henderson S, Tudares M, Lowe J, Gold M*

12:00 pm **Lunch (Box Lunch-Provided)**

Podium Session 2: **Minimally-Invasive Surgical and Diagnostic Techniques**
Session Chairs: ***Mark Wong***

1:30 pm Ultrasound - Guided Mini-invasive Therapy of Temporomandibular Joint
Levorova J*, Machon V, Foltan R*

1:45 pm Magnetic Capture of Osteoarthritis Biomarkers from Synovial Fluid
Yarmola EG, Shah Y, Kozissnik B, Garraud A, Arnold DP, Dobson JP, ***Allen KD***

2:00 pm Autologous Blood in the Therapy of Temporomandibular Joint Disorders
Machon V*, Levorova J, Hirjak D*

2:15 pm Show Me the Hole and I'd Put the Ball In
McCain JP, ***Hossameldin RH***

2:30 pm **Networking Session**

3:00 pm **Afternoon Break**

Podium Session 3: **TMJ Biomechanics**
Session Chairs: ***Hai Yao***

3:15 pm TMJ Disc Nutrition and Cell Energy Metabolism
Yao H

3:30 pm Effects of Hyaluronic Acid in the Lubrication of TMJ Disc and Condylar Cartilage
Zimmerman BK*, Vorrasi JS, Burris DL, Lu XL*

3:45 pm Mechanobiology Assessment of TMJ Disc Surfaces: A Nanoindentation and TEM Study of Micron Scale Variation
Juran CM*, Dolwick MF, McFetridge PS*

4:00 pm **Discussion of Day's Topics**

4:30 pm **Close**

Location: **University Club – Ballroom B**
123 University Place
Pittsburgh, PA 15260

8:00 am **Breakfast, Registration, Check-In**

Keynote Lecture:

9:00 am Radiology of TMJ Disorders
David Hatcher

10:00 am **Break**

Podium Session 4: **Animal Models of TMJ Degeneration and Restoration**
Session Chair: ***Boaz Arzi***

10:30 am Introduction to Veterinary TMD Research
Arzi B

10:45 am Spontaneous Temporomandibular Joint Disease in Marine Mammals
Verstraete FJM*, Arzi B*

11:00 am Degenerative Changes in Deformed Porcine Temporomandibular Joint Discs Resulting from Displacement
Matuska AM*, Dolwick MF, McFetridge PS*

11:15 am Replacement of the TMJ Meniscus in a Porcine Model Using a Xenogeneic Extracellular Matrix
Chung WL*, Brown BN, Almarza AJ, Badylak SF*

11:30 am **Networking Session**

12:00 pm **Lunch (On your own)**

Podium Session 5: **Finite Element Approaches**
Session Chairs: ***Luigi Gallo and Michel Mesnard***

1:30 pm Models to predict implanted Temporomandibular Joint behavior - Experimental and Numerical Tools
Ramos A*, Mesnard M*

1:45 pm Dynamic Finite Element Modeling of the Temporomadibular Joint
***Nicolella DP**, Wong ME, Treasure TE, Bredbenner TL, Coogan JS*

2:00 pm A Comparative Analysis of Christensen TMJ Concept and BIOMET Concept - A Numerical Study
***Ramos A**, Duarte R, Mesnard M*

2:15 pm The Role of Mechanics in the Development of Degenerative TM Joint Disease: An Update
Gallo LM

2:30 pm **Networking Session**

Podium Session 6: TMJ Tissue Engineering
Session Chair: ***Alejandro Almarza***

3:00 pm Novel Radial Tension and Compression Mechanical Stimulator Design for TMJ Disc Tissue Engineering
***Juran CM**, McFetridge PS*

3:15 pm Isolating Homogenous Cells from Mandibular Condylar Cartilage by LCM Technique
***Basudan AM**, Jin LJ, Yang YQ, Wong R*

3:30 pm Physical and Enzymatic Fixation Methods Enhance Initial Stability and Long-term Integration of Engineered Cartilage in Porcine TMJ Disc Defect Model
***Murphy MK**, Arzi B, Hu JC, Athanasiou KA*

3:45 pm Nanoseeds: Nanoparticle Enhanced Hydrogels as Chemoattractants for Tissue Regeneration
***Karnik SJ**, Mills DK*

4:00 pm **Discussion of Day's Topics**

4:30 pm **Close**

6:00 pm **Dinner**

Location: **University Club – Ballroom B**
123 University Place
Pittsburgh, PA 15260

8:30 am **Breakfast**

Podium Session 7A: TMJ Arthroscopic Technologies and Animal Models
Session Chairs: ***Lou Mercuri and Mildred Embree***

9:30 am Investigation on the Failure Mechanisms of Retrieved Temporomandibular Joint (TMJ) Implants: A Bioengineering Perspective
Kerwell S*, Alfaro M, Pourzal R, Mercuri LG, Sukotjo C, Lundberg H, Mathew MT*

9:45 am TMJ TJR Questions Requiring Further Investigation
Mercuri LG

10:00 am Post-Market Surveillance Study on the Long-Term Survivorship of the Biomet TMJ Replacement Device
Granquist EJ*, Quinn P, Sinn DP, Dattilo DJ, Cillo JE, Boulox G, Louis P, Szymela V, Warner MR, McCain JP, Gonzalez O*

10:15 pm **Break**

Podium Session 7B: TMJ Arthroscopic Technologies and Animal Models
Session Chairs: ***Lou Mercuri and Mildred Embree***

10:45 am Mandibular Kinematics, Maximum Voluntary Bite Force, Pressure Pain Threshold and Oral Health-related Quality of Life in Patients with Alloplastic Temporomandibular Joint Replacement
Linsen SS*, Reich RH, Teschke M*

11:00 am Transient Sclerostin Treatment Induces TMJ Progenitor Cells to Form Cartilage and Ameliorates Pathology in a TMJ Injury Model
Kong D*, Chen M, Gabor J, Iwakoka GM, Patel R, Koslovsky DA, Koch A, Kalajzic, Shi C, Yao H, Sun D, Bi Y, Mao JJ, Embree M*

11:15 am Role of Estrogen and Estrogen Receptor Beta in Mediating Decreased Occlusal Loading Induced TMJ Remodeling
Aronson R*, Greco A, Chen J, Xu M, Wadhwa S*

11:30 am Discussion- Future of Conference

12:00 pm **Closing Remarks**

ABSTRACTS

4001 Replacement of the TMJ meniscus in a porcine model using a xenogeneic extracellular matrix

Chung W, Brown B, Almarza A, and Bradylak S
University of Pittsburgh Medical Center; University of Pittsburgh School of Dental Medicine; UPMC McGowan Institute for Regenerative Medicine

Currently there is no universally accepted algorithm in the treatment of an irreversibly damaged temporomandibular joint (TMJ) meniscus in humans. Furthermore, there is no effective and safe alloplastic alternative to replace such a damaged TMJ meniscus. Several autogenous tissue sources are used by surgeons, but none consistently restore the function of the meniscus long-term. Several recent publications have reported the significant reduction in TMJ pain and improvement of TMJ function after a meniscectomy. However, these patients will inevitably experience varying degrees of degenerative joint disease of the TMJ. Identification of a suitable off-the-shelf disk replacement material would obviate the associated donor site morbidity and avoid subsequent degenerative changes to the TMJ. Ideally, such a material would act as a template for cellular in-growth, integrate with the surrounding host tissues, and eventually restore the native morphology and function of the TMJ meniscus. The present study examines the effectiveness of an extracellular matrix (ECM) device in the porcine model, considered to be the "gold-standard" preclinical model for TMJ research. To date, results from the porcine model have further supported those results obtained in 2 earlier published studies that used a canine model.[1,2]

References: (1) Brown, BN. JOMS. 2012; 70(11):2656-68. (2) Brown, BN. JOMS. 2011;69(12):e488-505.

4003 Effects of Hyaluronic Acid in the Lubrication of TMJ Disc and Condylar Cartilage

Zimmerman BK, Granquist EJ, Vorrasi JS, Burris DL,and **Lu XL**
Department of Mechanical Engineering, University of Delaware

The TMJ disc glides on the mandibular condyle during daily movement. Injection of intra-articular lubricants is frequently utilized to reduce friction and alleviate pain in TMD, but the biomechanical mechanisms underlying such treatment and its effectiveness in reducing friction remains unclear. Using a novel custom-built microtribometer, we evaluated and compared the effectiveness of synovial fluid (SF), hyaluronic acid (HA), and PBS as exogenous lubricants. Testing was performed in the central region in the anterior-posterior direction under 4 normal compression forces and 4 sliding speeds (25, 50, 100, 200 mN; 500, 1000, 2000, and 3000 um/s). During each test, a small amount of either HA, SF, or PBS was added to the central region to serve as a lubricant. We found that 1) Dependence of frictional coefficient on normal force was detected for HA and SF on both condyle and disc; 2) Significant difference between all three lubricants was seen on both tissues, with PBS providing the lowest friction coefficient and HA the highest; 3) No lubricant demonstrated any relationship between frictional coefficient and sliding speed. The results (Fig. 1) suggest that injection of lubricants may have limited tribological effectiveness for healthy tissue during physiologically relevant migrating contact.

4004 A comparative analysis of Christensen TMJ concept and BIOMET concept - A numerical study

Ramos A., Duarte R, and Mesnard M
Biomechanics Research Group, TEMA, Department of Mechanical Engineering, University of Aveiro, Portugal

The objective of this study was to compare the effect of geometry in total temporomandibular implants and load mechanisms, in two TMJ solutions, a Christensen® model, no longer marketed, and a commercial solution, the Biomet® model. Based on specific patient CT scan images with a diseased right disc, two finite element models were created, one with a Christensen implant and the other with the Biomet, on the right side of the mandible and in the same position on the mandible. Simulations considered the five most important muscles acting on the mandible, and evaluated biomechanical changes in the bone structures (skull, mandible and articular disc). Results revealed different behaviour in the BIOMET® implant model and the Christensen® model, and further differences in the mandible condyles. In the right condyle the difference in strains was 40% between the two models with the Christensen model presenting more strain distribution. Both TMJ models influenced distribution in the opposite condyle and here the Christensen model presented less strain distribution. This study shows that replacing the damaged joint by an implant redistributes the loads in a different way from the intact situation. The geometry of the TMJ changes mandible behaviour and load distribution in the opposite condyle.

4006 Novel Radial Tension and Compression Mechanical Stimulator Design for TMJ Disc Tissue Engineering

Juran C and McFetridge P
University of Florida

Under healthy physiologic conditions the Temporomandibular Joint (TMJ) disc is held in tension over the condyle during joint articulation which induces compressive, shear, and rotational loading. *In vitro* tissue engineering technology has demonstrated naturally derived porcine discs decellularized by sodium dodecyl sulfate and modified by laser ablation (LMP) to optimize porosity for cell integration and mass transport provides a framework for functionalization investigations. In these works acellular LMP porcine disc scaffolds were cultured under tensile and compressive stimulation to encourage fibrochondrocyte functionalization of human Mesenchymal Stem cells. Mechanical and cell viability (PicoGreen DNA Quantification, and AlamarBlue Metabolism Assay) results indicate that the scaffold is actively being modified by the cultured cells. Histology (H&E, Masson's trichrome), florescence imaging (Live/DEAD, DAPI), and immunohistochemistry (procolI, procolII, anti-chondroitin sulfate, and anti-aggrecan) show that the ECM fibril alignment is remodeled throughout culture. All stimulation culture conditions showed dramatic mechanical and biochemical improvement over static culture. The frequency of stimulation is shown to play key role in regulating metabolism of cultured cells and the functionalization of those cells especially as it affects biomechanics. These works show manipulating the frequency of compressive/tensile bioreactor stimulation endow the graft with tunable modulation of wound healing properties and cellular activity.

4007 Mechanobiology assessment of TMJ disc surfaces: A Nanoindentation and TEM study of micron scale variation

Juran C, Dolwick MF and McFetridge
University of Florida

The Temporomandibular Joint (TMJ) disc is a mechanically robust tissue with a structurally dense ECM matrix which supports the functional loading of the joint. These works hypothesize that the structural complexities of the superior and inferior TMJ disc surfaces seen in imaging investigations and the robust mechanical ability of the meniscus may be due to depth-dependent regional or layered differences through the intermediate surface zones. To test this hypothesis we utilized ultra-nanoindentation in conjunction with Transmission Electron Microscopy to detail structural attributes that influence disc function. This study demonstrates the central zone of the disc is structured in isometric depth-dependent layers, each of which provide different mechanical function over the bulk tissue's properties. Within 20μm of the inferior surface, imaging shows limited cellular populations with little depth-dependent structural variation. Nanoindentation findings show the inferior surface is stiffer and offers comparatively less energy dissipation than the superior surface. The superior surface presents three distinct mechanical and structural layers each responsible for different mechanical characteristics supporting the action of articulation within the TMJ. These works focus on the fine mechanobiology of the surface layers of the TMJ disc, properties imperative for future tissue engineering efforts focused on restoring function to the joint.

4008 Degenerative changes in deformed porcine temporomandibular joint discs resulting from displacement

Matuska AM, Dolwick MF, McFetridge PS
J Crayton Pruitt Department of Biomedical Engineering, University of Florida, Gainesville, FL

The etiology of TMJ pathologies are poorly understood. One of the most common disorders, disc displacement, often results in adaptive disc remodeling in response to aberrant disc mechanical loading. It is generally though that over time, loss of mechanical integrity in the retrodiscal tissues results in disease progression; however no quantitative biomechanical evaluation currently exists in literature. Porcine TMJ discs are frequently studied as they are the most similar anatomically and functionally of all animal species to human discs. Porcine discs were collected with deformed gross morphology indicative of anterior disc displacement. Routine histology demonstrated loss of smooth biconcave shape as well as increased cellularity and loss of ECM organization compared to morphologically healthy discs (Figure 1). This mirrors histological findings in past studies of deformed human TMJ discs, indicating similarity in porcine and human TMJ adaptive remodeling. This study seeks to determine how tensile and compressive biomechanical properties of retrodiscal and discal tissues differ between deformed and morphologically healthy discs. The results will establish how the disc is remodeled in response to irregular loading, thus providing insight into clinical approaches to treat or prevent the progression of disc displacement.

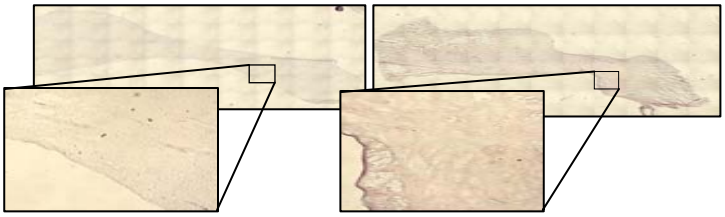


Figure 1. Histology of morphologically healthy (left) and deformed (right) porcine TMJ disc.

4009 Isolating homogenous cells from mandibular condylar cartilage by LCM technique

Basudan A, Jin LJ, Yang YQ and Wong R
The University of Hong Kong

Aim: The tissue-engineered mandibular condylar cartilage **(**MCC) should ideally mimic the native zonal structure to achieve a functional condylar replacement. This study attempted to optimize a working protocol for isolating homogenous cell populations from MCC by using laser capture micro-dissection (LCM) technique. **Methods**: Frozen sections were prepared after harvesting MCC tissues from three SD rats. Cells from four identified zones were separately isolated (10 samples/zone) using LCM technique. tRNA was extracted for qPCR, and 3′/M ratio of GAPDH was calculated to evaluate RNA quality. **Results:** The morphology of tissue sections was preserved allowing accurate identification of all four zones of MCC, namely fibrous, proliferative, mature and hypertrophic chondrocytes zones. This improved morphology extended the range of cell types isolated via LCM technique. The average of the 3′/M GAPDH ratios, a better guide to RNA quality for small-quantity LCM-samples, was 1.46±0.41, 1.49±0.27, 1.75±0.50, and 1.60±0.43 for fibrous, proliferative, mature, and hypertrophic samples, respectively. **Conclusion:** The present study shows that the optimized LCM protocol could allow isolation of homogenous cells from various zones of MCC separately, thereby generating accurate molecular and genetic data for further study on tissue-engineered mandibular condylar cartilage.

4010 Nanoseeds: Nanoparticle Enhanced Hydrogels as Chemoattractants for Tissue Regeneration

Karnik, SJ, **Mills DK**
Center for Biomedical Engineering and Rehabilitation Sciences, and School of Biological Sciences, Louisiana Tech University, Ruston, LA

Halloysite nanotubes (HNTs) have the ability to be doped with bioactive molecules and then release them in a controlled and sustained manner. In our project, the ability of growth factor doped HNTs to act as chemoattractants and recruit osteoblast and mesenchymal stem cells (MSCs) was studied. HNT were loaded with BMP-2, VEGF, and Pleiotropin and added to chitosan or alginate hydrogels. The resulting nanocomposite ('Nanoseeds') were seeded into a 24 well culture dish containing a type I collagen gel. Osteoblasts or MSCs were tagged with a membrane-impermeant dye and then added to the center of each gel. Osteoblast and MSC migration and cellular response was studied for 21 days. Cell migration was tracked using fluorescent microscopy, image analysis and CellTrack image tracking software. For osteogenic assays, samples were fixed at 1, 7, 14 and 21 days and stained with Von Kossa, Alizarin red and Alkaline Phosphatase to assess differentiation and maturation of the cells towards the osteoblastic lineage. Cells appear to migrate towards doped HNTs, differentiate as they migrate and produce a mineralized matrix. Results suggest that this system might be used as an implantable in vivo signaling system guiding regenerative cells to injury sites and advance the repair process.

4011 "Show me the hole and I'd put the ball in"

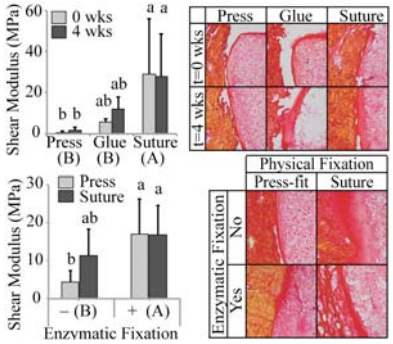
McCain JP, **Hossameldin RH**
FIU School of Medicine, Miami, FL

Various modalities in temporomandibular joint (TMJ) arthroscopic surgery have shown high success rates in regards to their indications. Still further advanced modalities are required to polish and upgrade such a valuable; minimally invasive diagnostic and therapeutic treatment option in the management of internal derangements and degenerative joint diseases. Such advancements are met in different elements of treatment starting with preoperative testing modalities in order to reach proper treatment planning and education of TMD treatment cascade, walking through new medications, devices and modifications used in different surgical procedures. Quoting Lanny Johnson; the pioneer famous orthopedic arthroscopic surgeon saying *"Show me the hole and I'd put the ball in"*, we clearly demonstrate the ability to negotiate the joint arthroscopically with all types of advanced modalities, yet the future dictates the use of growing revolutionary tissue engineering technology in order to obviate the need to end up with open surgery and/or total joint replacement. We are now prepared to deliver regenerative products in TMJ at any site arthroscopically.
All such advanced modalities are meant to end up with one purpose, which is reaching a brighter future meeting the ultimate goal of treating all TMD patients through the treatment cascade primarily arthroscopically.

4012 Physical and enzymatic fixation methods enhance initial stability and long-term integration of engineered cartilage in porcine TMJ disc defect model

Murphy, MK, Arzi B Hu JC and **Athanasiou KA**
Department of Biomedical Engineering, Department of Orthopaedic Surgery, University of California Davis

The clinical outcome of neocartilage in addressing TMJ pathologies depends largely on integration with surrounding tissue. The present study investigated physical and enzymatic fixation methods toward improving initial stability and long-term integration of costochondral cell neocartilage in 5 mm dia. intermediate zone TMJ disc defects. First, it was hypothesized that physical fixation (suture or glue) would enhance shear stiffness and strength of the integration interface, compared with press-fit upon implantation and following 4 wks *in vitro*. Second, it was hypothesized that a crosslinking regimen ($CuSO_4$, OH-lysine, lysyl oxidase) would enzymatically enhance shear stiffness and strength of the integration interface following 8 wks culture, and combined physical/enzymatic fixation would further enhance interface mechanical properties. Sutures significantly enhanced the interface shear stiffness and strength at t=0 and 4 wks, compared with press-fit. Toward enhancing long-term integration, enzymatic fixation significantly enhanced shear stiffness following 8 wks. However, combined physical/enzymatic fixation led to no significant differences over enzymatic fixation alone. At 4 and 8 wks, increased collagen staining was apparent at the interface in accordance with mechanical results. Physical and enzymatic fixation methods may be used to enhance neocartilage stability and long-term integration, respectively in a porcine TMJ disc defect model.



4013 Ultrasound - guided miniinvasive therapy of temporomandibular joint

Levorova J, Machon V and Foltan R
Dept of Oral Maxillofac.Surgery, Charles University and Faculty Hospital Prague, Czech Republic

Miniinvasive therapy of temporomandibularjoint (TMJ) disorders is based on intraarticular- or periarticular medicament injection (hyaluronic acid, corticoids, autologous blood or plateled rich plasma application) or TMJ arthrocenthesis. The issue is that both these methods are “blind“ – the only way to assure the needle inserted intraarticulary is the aspiration of aplicated fluid. Authors present ultrasound-guided needle insertion in TMJ in the process of miniivasive therapy.

4014 Autologous blood in the therapy of temporomandibular joint disorders

Machon V, Levorova J and Hirjak D
Dept of Oral Maxillofac.Surgery, Charles University and Faculty Hospital Prague, Czech Republic

Intraarticulary blood application is one option of miniinvasive therapy of temporomandibularjoint disorders. Autologous blood application is currently possible as “whole blood“ (in the therapy of TMJ hypermobility) or as platelet rich plasma (PRP - in the therapy of TMJ osteoarthritis). Autors present experience with intraarticular blood application in the therapy of temporomandibular disorders.

4015 Investigation on the Failure Mechanisms of Retrieved Temporomandibular Joint (TMJ) Implants: A Bioengineering Perspective

Kerwell S, Alfaro M, Pourzal R, Mercuri LG, Sukotjo C, Lundberg H and **Mathew MT**
University of Illinois at Chicago and Rush University Medical Center

To manage end-stage temporomandibular joint disorders (TMD), surgeons resort to alloplastic temporomandibular joint replacement (TMJ TJR) to increase patient mandibular function and mitigate pain. To extend TMJ TJR longevity, understanding the degradation process and failure mechanisms of these implants is important. However, failure mechanisms for these implants are not clearly defined because, as compared to orthopedic TJR devices, fewer TMJ TJR devices are implanted annually. The role of corrosion and wear on the failure of implants is reported, however no systematic study on retrieved TMJ TJR is made. Therefore, the aim of this study is to investigate and compare degradation mechanisms of unsuccessful metal-on-metal, metal-on-polymer, and titanium-nitride coated TMJ TJR to control TMJ TJR implants by analyzing alloy microstructure. Surfaces were imaged using the SmartScope measuring system, white light interferometry and scanning electron microscopy (SEM). Substantial surface damage was observed in contact zones between the condyle and fossa; damage included pitting corrosion, evidence of deposited corrosion products, specific wear patterns and scratches. In summary, the study demonstrated the role of wear and corrosion interactions on the early failure of TMJ TJR devices. This study provides data that can guide future material composition and functional design improvements for TMJ TJR devices.

4016 Spontaneous Temporomandibular Joint Disease in Marine Mammals

Verstrate FJM and Arzi B
Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California - Davis

Museum skulls specimens of stranded southern sea otters (n=1,008), California sea lions (n=495) and northern elephant seals (n=104), were examined macroscopically according to defined criteria for the presence, severity and characteristics of temporomandibular joint osteoarthritis (TMJ-OA). Overall 4.1% of the southern sea otters and 63.5% of the California sea lions specimens had findings consistent with TMJ-OA. There was no significant association between age and sex with the presence or severity of TMJ-OA. The most prominent TMJ-OA changes were the presence of subchondral bone defects, increased porosity of the articular surface and peri-articular osteophytes. Both the condylar process of the mandible and the mandibular fossa were affected. In northern elephant seals there were 3 cases of bony defects in the mandibular fossa, consistent with osteochondritis dissecans. TMJ-OA occurs in southern sea otters and northern elephant seals but the incidence in California sea lions is particularly high. Although the significance of the high incidence of this disease in the latter species remains elusive, the occurrence and severity of TMJ-OA detected in this study may play an important role in the species' morbidity and mortality.

4017 Investigation on the Failure Mechanisms of Retrieved Temporomandibular Joint (TMJ) Implants: A Bioengineering Perspective

Kerwell S, Alfaro M, Pourzal R, Mercuri LG, Sukotjo C, Lundberg H and Mathew MT
University of Illinois at Chicago and Rush University Medical Center

To manage end-stage temporomandibular joint disorders (TMD), surgeons resort to alloplastic temporomandibular joint replacement (TMJ TJR) to increase patient mandibular function and mitigate pain. To extend TMJ TJR longevity, understanding the degradation process and failure mechanisms of these implants is important. However, failure mechanisms for these implants are not clearly defined because, as compared to orthopedic TJR devices, fewer TMJ TJR devices are implanted annually. The role of corrosion and wear on the failure of implants is reported, however no systematic study on retrieved TMJ TJR is made. Therefore, the aim of this study is to investigate and compare degradation mechanisms of unsuccessful metal-on-metal, metal-on-polymer, and titanium-nitride coated TMJ TJR to control TMJ TJR implants by analyzing alloy microstructure. Surfaces were imaged using the SmartScope measuring system, white light interferometry and scanning electron microscopy (SEM). Substantial surface damage was observed in contact zones between the condyle and fossa; damage included pitting corrosion, evidence of deposited corrosion products, specific wear patterns and scratches. In summary, the study demonstrated the role of wear and corrosion interactions on the early failure of TMJ TJR devices. This study provides data that can guide future material composition and functional design improvements for TMJ TJR devices.

4018 TMJ TJR Questions Requiring Further Investigation

Mercuri LG
Institute of Biomaterials,Tribocorrosion and Nanomedicine;Department of Orthopedic Surgery, Rush University Medical Center,Chicago

End-stage TMJ disease often requires replacement to regain mandibular function and form. Whether future TMJ replacement lies in the use of either total or partial autogenous or bioengineered tissue, alloplastic components, or any combination thereof, the following questions must be investigated: 1. What are the functional loading forces on the normal TMJ? On a unilateral and bilateral TMJ TJR? Where and when are they the greatest? The least? 2.What are the most common complications of TMJ TJR? Same as orthopedic TJR? If not, why? 3. Does TMJ TJR tribocorrosion contribute to the development or enhancement of any of these complications or vice versa? 4. Are the tribocorrosion biochemical and/or electrochemical environmental changes seen around orthopedic TJR devices the same, or are they unique to TMJ TJR devices? 5. How would failed TMJ TJR tribocorrosion biochemical and/or electrochemical environmental changes affect a future autogenous and/or bioengineered tissue partial or total TMJ TJR? This presentation will discuss these issues in detail and offer some potential research objectives for each.

4019 Magnetic Capture of Osteoarthritis Biomarkers from Synovial Fluid

Yarmola EG, Shah Y, Kozissnik B, Garraud A, Arnold DP, Dobson JP and Allen KD
University of Florida, J. Crayton Pruitt Family Department of Biomedical Engineering

Introduction: Diagnosis of early-stage joint degeneration remains a significant challenge. Promising biomarkers of joint degeneration have been identified in urine and serum; however, serum- and urine-level changes are not specific to an affected joint and may not be detectable at the earliest disease stages. Moreover, direct synovial fluid aspiration is challenging in small joints, such as the TMJ. As such, human synovial fluid samples from the TMJ are often diluted due to arthocentesis, and synovial fluid samples from small animal models are often impossible to acquire. Here, a magnetic nanoparticle-based technique that can enable the recovery of proteins from small joints is described. **Methods:** Cross-linked C-telopeptide of type II collagen (CTXII) antibodies were conjugated to 1 μm polystyrene particles containing superparamagnetic iron oxide nanoparticles within the particle core. Antibody-coupled particles were incubated in 30 μL of synovial fluid for 1 hr at room temperature. Then, particles were collected on an NdFeB magnetic microneedle. The microneedle was then place in PBS (20 μL), heated to 90°C for 5 mins, cooled, and the needle was removed. The PBS sample was then centrifuged and analyzed for CTXII. **Results and Discussion:** Magnetic collection was able to collect about 15% of the CTXII from the starting solution. Moreover, using antibody-ligand binding relationships, the initial concentration of CTXII within the synovial fluid was approximated. Average CTXII concentration for a sample analyzed via magnetic capture was comparable to a direct ELISA on a synovial fluid aliquot, thought the experimental error was increased by 20-30% for magnetic capture. Increased experimental error was anticipated, as additional processing during magnetic capture is necessary relative to a direct ELISA. Nonetheless, these data demonstrate that initial biomarker concentrations within a SF sample can be determined using our magnetic capture technique. While some refinement remains, magnetic capture could enable the recovery of biomarkers from a degenerated joints without the need to remove synovial fluid, thereby facilitating biomarker analysis in smaller joints and from animal models of TMJ degeneration.

4020 Use of a Novel Behavioral Device to Measure Orofacial Mechanical Allodynia in Rats

Rohrs, EL, Kapernaros K, Jenkins AC, Neubert JK and Allen KD
J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL

Background: Chronic constriction injury of the infraorbital nerve (CCI-ION) causes heightened thermal sensitivity in the orofacial regions of rats. In this study, a novel device was engineered to assess mechanical sensitivity in a rat CCI-ION model. **Methods:** Unilateral and bilateral CCI-ION surgery was performed in Sprague-Dawley rats (250g, females), whereby unilateral left (n=3), unilateral right (n=3), bilateral (n=5), and sham (n=4) surgeries were performed. Following surgery, animals were placed in a cage with a bottle of sweetened condensed milk. To engage the bottle, animals had to accept a mechanical stimulus (dental wire) on its face. Willingness to accept the award was tracked via a lickometer. Deflection of wires was tracked via flexiforce sensors, thereby detecting preferential loading to a side of the face. All animals were tested pre-surgery and every 3 days post-surgery out to 4 weeks. **Results:** Unilateral CCI-ION surgery resulted in deviations from centered, but direction did not associate with the side of CCI-ION surgery. Total sensor deflection increased in all animals, indicating animals were preferentially loading the caudal aspects of the head post-surgery. While these deviations were unexpected in sham animals, we hypothesize that residual chromic gut particles given off as the suture is passed over the nerve during the sham surgery may have caused local inflammation of the ION; histological investigations are ongoing to confirm this hypothesis. **Conclusion:** While results deviated from our expectations, our behavioral device detected measurable changes to orofacial mechanical stimuli following CCI-ION surgery. Future plans will examine changes in orofacial mechanical sensitivity resulting from TMJ degradation. While pain and dysfunction are the primary reasons TMJ disorder patients seek treatment, TMJ pain and dysfunction are challenging to assess in preclinical rodent models. Recently, a rodent behavioral assay of orofacial sensitivity was developed [1]. Here, animals contact a thermode while they drink from a bottle of sweetened milk. Since the animal must tolerate the heat applied via the thermode (non-noxious, 37-57° C) to accept the reward, the frequency of reward acceptance at different temperature can assess thermal orofacial sensitivity. We recently developed a similar assay to assess mechanical sensitivity using an array of flexible cantilever strain gauges. Here, animals must accept pressure from the cantilever strain gauges in order to accept the award. Touch pressure applied to the orofacial region is recorded during reward acceptance, providing data on mechanical sensitivity. We also recently developed an instrumented toy to measure gnawing activity in rats. Here, thin film strain gauges are potted inside soft silicone, creating an “instrumented toy” that can be covered with hard candy or yogurt coatings. This treat can be used in place of the sweetened condensed milk or as an independent measure of jaw function in the rat. [1] Neubert et al. Pain 2005.

4021 Role of estrogen and Estrogen receptor beta in mediating decreased occlusal loading induced TMJ remodeling

Aronson R , Greco A, Chen J, Xu M, Wadhwa S
Columbia University College of Dental Medicine

Temporomandibular (TMJ) joint disorders predominantly afflict women. Defects in mechanical loading induced TMJ remodeling are believed to be a major etiological factor in TMJ degenerative diseases. We have previously found that decreased occlusal loading (incisor trimming and soft diet administration) caused a decrease in col2 expression in female but not in male WT mice. The goal of this study was to examine the role of estrogen and Estrogen Receptor (ER) beta in mediating this effect. *Materials and Methods*- 21 day old male WT (n=12) and ER beta KO (n=12) mice were treated with placebo (n=12) or estradiol (100ng /g body weight) and were exposed to either normal loading (n=12) or decreased occlusal loading (n=12) for 4 weeks. Histomorphometry of the mandibular condyle was performed. *Results*- Decreased occlusal loading caused a significant decrease in the size of the superficial zone in male WT and ER beta KO treated with either placebo or estradiol compared to normal loading controls. However, decreased occlusal loading caused a significant decrease in the pre-hypertrophic zone thickness only in male WT treated with estradiol. *Conclusion*- Decreased occlusal induced sex differences in Col2 expression is mediated by an estrogen -estrogen receptor beta pathway. Inflammation of the surrounding tissues or cases of ankylosys are problems regarding current graft repair of jaw joints. Using cell-based repair strategies incurs both the chance and the task of creating a self-renewing implant and inducing cell that may stabilize the irritated joint via secreted signaling molecules. However, an adequate nutrition and a stable phenotype have to be guaranteed. In order to address these questions, we have compared the physiology of disc cells to fibrocartilage (meniscus) and hyaline (knee articular, condylar) cartilage tissues. The disc showed a variable but outstanding physiology, more close to connective tissues than to other cartilages. The results are transferred to cell-seeded graft cultures using oriented collagen fibre scaffolds under mechanical stimulation in a special bioreactor, which stimulated scaffolds by simultaneously compressing and stretching the carrier. We also investigated the development of different cartilage cell types on a range of matrix components, which can influence differentiation and may help in achieving and stabilizing the desired phenotype. Gene expression profiles were monitored in order to describe cellular reactions. Using inhibitors of the insulin, mTor and PI3K pathways we examined possible interactions of cell development with mitogenic factors in the medium which can delay the onset of differentiation.

4022 Mandibular kinematics, maximum voluntary bite force, pressure pain threshold and oral health-related quality of life in patients with alloplastic temporomandibular joint replacement

Linsen SS, Reich RH and Teschke M
Department for Prosthodontics, Bonn Dental School, Bonn, Germany

Purpose: The purpose was to analyze the mandibular kinematics (condylar range of motion during opening and retrusion; incisal range of motion during opening and lateral excursion), maximum voluntary bite force, pain pressure threshold (PPT) and oral health-related quality of life (VAS) in patients with alloplastic total joint replacement (TJR).
Materials and Methods: 35 patients with different diagnoses resulting in condylar hypomobility (17 patients, 32 joints) and condylar instability (18 patients, 21 joints) requiring TJR from 2006 through 2013 were enrolled in the study. Data were recorded preoperatively and 2, 6, 12 months and subsequently once a year postoperatively. For ordinal data comparison at different time points, the Wilcoxon signed-ranks test was used. **Results:** Analysis of kinematic data showed a statistically significant increase in incisal range of motion during opening but a decrease in all other kinematic data. Analysis of maximum voluntary bite force and VAS (facial pain intensity, temporomandibular joint pain, mandibular function, and diet) revealed a significant improvement over the observed time. PPT of the joint and temporal muscle of the operated side increased. **Conclusions:** Even after successful alloplastic TJR, a complete restoration of normal joint function is not achievable. Nevertheless alloplastic TJR appears to decrease pain, improve function and diet, and decrease psychological discomfort. The biomechanical integrity of the stomatognathic system and the ability of the patient to triturate food could be improved by alloplastic temporomandibular joint (TMJ) replacement.

4023 A Novel Non-Invasive Model of Temporomandibular Joint Pain In the Rat with Tunable Outcomes of Acute & Chronic Pain

Granquist E, Kartha S, Zhou T and Winkelstein B
School of Dental Medicine; School of Engineering & Applied Science; University of Pennsylvania

TMJ pain presents many clinical challenges due to inability to predict which cases will resolve and which will become chronic. Existing animal models use invasive approaches to induce pathology and/or pain but do not replicate all disease states. This study aimed to develop a non-invasive rat model that induces either resolving or sustained TMJ pain. Separate groups of female Holtzman rats underwent repeated mouth opening for 1 hour daily for 7 days using a load of 2N (n=4), 3.5N (n=4), or no opening (sham; n=2). Orofacial sensitivity was assessed daily during and after the loading phase in the TMJ region using von Frey filaments to measure the threshold for eliciting a response. The mechanical threshold decreased from baseline immediately from 37.5±3.9g to 6.6±1.4g for 3.5N and 9.1±3.4g for 2N; both were significantly lower ($p<0.0001$) than sham responses during the period of loading. Thresholds in the 2N group returned to sham and baseline levels by day 13. However, TMJ sensitivity was sustained ($p<0.0001$) in the 3.5N loading group for at least another 14 days. Additional studies are needed to define when sensitivity resolves. However, this work provides a useful platform for understanding those mechanisms which may be contributing to pain maintenance.

4026 TMJ Disc Nutrition and Cell Energy Metabolism

Yao H
Clemson-MUSC Bioengineering Program, Clemson University and Medical University of South Carolina

The normal adult human TMJ disc is a large avascular structure, and the nutrients required by disc cells are supplied by blood vessels and synovial fluid at the margins of the disc. The balance between the rate of nutrient transport through the matrix and the rate of consumption by the disc cells establishes a concentration gradient across the disc. The concentration levels of essential nutrients, such as oxygen and glucose, can profoundly affect disc cell viability, matrix synthesis, and response to inflammatory factors. In this presentation, we will discuss our recent works in 1) studying nutrient transport properties in the TMJ disc and its relationship with tissue structure/composition and mechanical loading, 2) investigating the effect of nutrient levels on the energy metabolic rates of TMJ disc cells, and 3) examining the impact of the nutrient environment on TMJ disc cell homeostasis. Our results suggest that a steep nutrient concentration gradient might exist in TMJ discs and this nutrient environment is uniquely vulnerable to pathological mechanical loadings. Deviation from physiological nutrient levels in the TMJ disc due to the lack of nutrient supply may initiate tissue remodeling and matrix degradation.

4027 Post-Market Surveillance Study on the Long-Term Survivorship of the Biomet TMJ Replacement Device

Granquist EJ, Quinn P, Sinn DP, Dattilo DJ, Cillo JE, Boulox G, Louis P, Szymela V, Warner MR, McCain JP, Gonzalez O
University of Pennsylvania, Emory Healthcare Hospital, University of Alabama at Birmingham, Allegheny General Hospital, Advanced Facial & Oral Surgery, Miami Oral & Maxillofacial Surgery, and Facial Oral Surgery Associates

In February 2011, the FDA issued a post-market surveillance order to all manufactures of TMJ implants to determine the revision rates and etiology of revision for these devices. The objective of this Post Market Analysis FDA overseen trial is to evaluate these questions. Three arms and seven sites were employed in this multi-center trial: a prospective observational arm to evaluate survivorship, a retrospective arm to determine demographics and clinical information, and a prospective arm to study the explanted devices for modes and causes of failure. This abstract reports preliminary data from 484 joints (145 bilateral:194 unilateral) enrolled in the prospective observational arm to evaluate survivorship. Mean length of follow-up was 6.2 years. The overall second surgery rate was 3.5% (1.4% revision rate and 2.1% reoperation rate). The mean time for revision after the initial implant was 4.7 years. Patient satisfaction was 87.5%. This data is preliminary, however, we have enrolled a high number of joints and the revision rate remains low. These results are consistent with findings in the IDE trial, published revision rates on the Biomet TMJ Replacement System, and are considerably lower when compared to published orthopedic revision rates of 6% at 5 years (1.3 revisions/100 component years)

4028 Models to predict implanted Temporomandibular Joint behavior - Experimental and numerical tools

Ramos A and Mesnard M
Biomechanics Research Group, TEMA, Department of Mechanical Engineering, University of Aveiro, Portugal

Finite element models (FEM) and experimental procedures (EP) have been used to determine stresses and strains on the bone surface. These two approaches can be used for biomechanical analyses. The FEM should be sufficiently refined to represent accurately the geometry and mechanical behaviour of the structure that they simulate. This abstract introduces a study using both, numerical and experimental approaches of an implanted temporomandibular condyle to analyse the condyle biomechanics. The functional loading cases took into account the reaction on the condyle and the five main masticatory muscles. The FEM of the mandible and of the cranium were obtained from human cadaveric bones using CT scan and geometry acquisition. The 3D models were generated as tetrahedral finite element meshes. The strains were measured with EP using electric resistance strain gauges applied on the external surface of the mandible (inside and outside). The mechanical response is shown and discussed in terms of strains, principal numerical and measured strains. This comparative study proved that FE models can reproduce experimental strains within an overall agreement of 10%. The FE models correctly reproduced bone strains under different load configurations and therefore can be used for the design of a novel TMJ prosthesis.

4029 Variations in Biopsychosocial Outcomes in TMJD Based on Pain Severity

King, CD
University of Florida College of Dentistry, Department of Community Dentistry & Behavioral Science

Temporomandibular disorder (TMD) is a common facial pain condition, which is associated with a number of negative outcomes including poor sleep, maladaptive psychological functioning, and higher risk of co-morbid pain conditions. Studies have reported that symptom presentation in TMD is heterogeneous, and based on several stratification schemes, subgroups can be observed. Heterogeneity in TMD suggests different underlying mechanisms contributing to presentation of TMD. One method to subgroup individuals with TMD is by the severity of clinical pain. Investigations into variations in biopsychosocial outcomes have not been properly evaluated. In the current talk, recent data showing differences in self-reported pain-related outcomes, psychological functioning, and sleep will be discussed, which differ as a function of the severity of self-reported pain. Overall, current evidence suggests that the severity of TMD pain might have relevance to presentation of impaired psychological, sleep and other clinically relevant pain outcomes. Future studies are needed to confirm and strengthen current findings. Dysfunction in certain domains implicates multiple mechanisms underlying TMD particularly in patients with more severe clinical pain, which has treatment implications. Furthermore, treatment interventions that reduce the severity of TMD-related pain may also be associated with improved function in the above mentioned domains.

4030 Altered Loading, Degeneration, and Pain in a Rabbit Model

Almarza, A
University of Pittsburgh, Department of Bioengineering, Department of Oral Biology, Center for Craniofacial Regeneration, McGowan Institute for Regenerative Medicine

The aims of the study were to determine the effects of altered occlusion on in the rabbit on endpoints of nociception used in small rodents and correlate changes in nociception with remodeling of the condylar cartilage. Unilateral molar dental splints were used to alter TMJ loading. Changes in nociceptive threshold were assessed with a mechanical probing of the TMJ region. C-Fos in the nucleus caudalis was assessed with standard anatomical immunohistochemical techniques. Retrogradely labeled TMJ afferents were studied with patch clamp electrophysiological techniques. Remodeling of TMJ condyles was assessed by histology. While variable, there was an increase in mechanical sensitivity in splinted rabbits. The increase in c-Fos+ cells in splinted rabbits was also significant (86±8 cells/section vs. 64±15 cells/section, $p<0.05$). The rheobase (364±80 pA) and action potential threshold (-31.2±2.0 mV) were higher in TMJ afferents from splinted rabbits compared to control (99±22 pA and -38.0±2.0 mV, $p<0.05$). There was significant remodeling in the condylar fibrocartilage layers as manifest by a change in glycosaminoglycan distribution and a loss of defined cell layers. Changes in excitability and action potential waveform were consistent with compensatory changes of TMJ afferents for an overall increase in afferent drive associated with joint degeneration. These compensatory changes may reflect pain adaption processes many patients with TMJ disorders experience.

4031 The Role of Mechanics in the Development of Degenerative TM Joint Disease: An Update

Gallo LM, Nickel JC, Iwasaki LR, Gonzales YM, Colombo V, Schaetti OR
University of Zurich, Center of Dental Medicine, Clinic KFS-KAB

Degenerative joint disease in the TMJ can be ascribed to cartilage fatigue due to mechanical work (biomechanical effect) as well as to a mechanically-induced biological reaction causing tissue catabolism (mechanobiological effect). Latest studies have been assessing both effects using models based on *in vivo* data in which plowing forces play a significant role. Plowing through cartilaginous tissue has been measured by means of dynamic stereometry, i.e. virtual anatomical models from TMJ magnetic resonance imaging coupled with jaw tracking data. Mechanical work per volume (i.e. energy density in mJ/mm³) has been estimated based on numerical modeling in female and male subjects without and with disc displacement. Energy density appears to differ between diagnostic groups and gender, being higher in females and symptomatic TMJs. Other studies have analyzed cartilage breakdown and gene expression consequent to plowing in live cartilage explant models with TMJ-specific mechanical loading data. Catabolic genes, in particular MMP-3 and MMP-13, but also lubricin appear to be expressed especially due to increased tractional loads and plowing velocities. Both lines of research need a further deep refinement in order to shed light on the initiation and progression of degenerative joint disease.

4032 Pain Assessment and Phenotyping of Orafacial Pain.

Belfer, I
University of Pittsburgh/UPMC,Departments of Anesthesiology & Human Genetics

Orafacial pain, particularly Temporomandibular disorders (TMD)-associated pain, is among the most common human pain conditions causing personal suffering and significant clinical and public health challenge. This pain may be temporary but often it lasts for many years. The precise causes of chronic TMD pain are poorly understood and need more investigation. Genetic approaches applied to orafacial pain research may help identify important biological factors that may contribute to the risk for or protection against chronicity and recurrence. It is highly likely that the interactions among genes, psychosocial and psychophysical factors will shape orafacial pain processing and perception. Recent findings indicate a progress in bridging gaps of knowledge on orafacial pain genetics; however, some inconsistency has been reported. This may be caused by differences in the design of genetic studies, mainly in the methods of pain assessment and phenotyping. Dr. Belfer will describe and discuss current techniques and methodologies used for comprehensive phenotyping of TMD-related pain, and relevance of pain phenotypes for genetic studies.