Temporomandibular Joint Disorder TMJ Bioengineering Conference



Auditorium of Poblenou Campus

Universitat Pompeu Fabra—Barcelona Carrer de Roc Boronat, 138 08018 Barcelona, Spain

September 12-13, 2016

TMJ Bioengineering Conference - 5

September 12 -September 13, 2016

Auditorium of Poblenou Campus Universitat Pompeu Fabra Barcelona, SPAIN

Welcome!

It is indeed our pleasure to welcome you to Barcelona, Spain, for the fifth Temporomandibular Joint Bioengineering Conference (TMJ5)!

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; 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 Luígí Gallo Míchael Detamore Kyle Allen Lucas Lu Boaz Arzí

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.

Conference Organizer

Program Committee

Alejandro Almarza – Chair Michael Detamore Luigi Gallo Kyle Allen Alejandro Almarza Lucas Lu

Advisory Board

Kyriacos Athanasiou Jeremy Mao Lou Mercuri

Instructions to 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 **10 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



Paul H. Krebsbach, DDS, PhD, is the Roy H. Roberts Professor of Dentistry and Professor of Biomedical Engineering at the University of Michigan. He serves as the Chair of the Department of Biologic and Materials Sciences and Division of Prosthodontics. Dr. Krebsbach received his D.D.S. degree from the University of Minnesota and his certificate in Periodontology and Ph.D. in Biomedical Sciences from the University of Connecticut Health Center. His research program focuses on the cell and molecular biology of mineralized tissues with an emphasis on gene therapydirected osteogenesis and bone marrow stromal cell biology. Dr.

Krebsbach has served on many local and national committees, including chairing the AADR William J. Gies Award Committee and the AADR and IADR Hatton Award Committees, a term on the AADR Constitution Committee and serving on the AADR Board of Directors for 3 years as Treasurer. He served on the American Association for the Advancement of Science Electorate Nominating Committee and completed a term as Member at Large. He currently is a chartered member of the Moss IRB Musculoskeletal Tissue Engineering study section. He is on the editorial boards of the Journal of Bone and Mineral Research and the International Journal of Oral and Maxillofacial Surgery.



Andrew Sidebottom, BDS, FDSRCS, MBChB, FRCS, OMFS, has been a Consultant in Oral and Maxillofacial Surgery at Queens Medical Centre, Nottingham since 2001. He has special interests in TMJ disease and facial deformity and carries out complex Oral and Maxillofacial Surgery at Queens Medical Centre, Nottingham and The Park Hospital, Nottingham. He has provided an Oral Surgery and Dental Implant service at Trent Bridge Oral Surgery Centre from 2008. He has written 2 book chapters, 28 peer reviewed papers and 44 international scientific presentations and is an internationally invited key note speaker on

TMJ replacement. He is secretary for the British TMJ Surgeons Association and a foundation member and President of the European Society for TMJ Surgery (2012-2013). He is the invited specialist adviser for TMJ Replacement for NICE. He is an internationally invited speaker in TMJ surgery, being one of only 8 surgeons in the UK currently providing significant numbers of TMJ Joint Replacements, having written the National Guidelines for TMJ Replacement and is in the top 20 providers of TMJ replacement in the world.



TMJ Bioengineering Conference Program

September 11-13, 2016 (Barcelona, Spain)

CONFERENCE LOCATION:

Campus del Poblenou, School Address Carrer de Roc Boronat,138, 08018 Barcelona, Spain

DAY 1 - September 11, 2016

7:00 PM WELCOME RECEPTION

Location: Hotel Silken Diagonal Barcelona Avenida Diagonal 205 08018 Barcelona 34 934 895 300

DAY 2 - September 12, 2016

8:00 AM BREAKFAST, REGISTRATION, CHECK-IN

8:40 AM OPENING REMARKS

9:00 AM KEYNOTE SPEAKER - Paul Kresbach, DDS, PhD

BIOMECHANICS – PART 1

10:30 AM Cartilage Stiffness and Thickness Distributions Revealed by an Automated Indentation Technique in the Temporomandibular Joint

Sim S, Matuska A, Garon M, Quenneville E, McFetridge P and Buschmann MD Polytechnique Montreal, Quebec, Canada University of Florida, Florida, United

The purpose of this study was to evaluate the capability of an automated indentation technique to reveal the topographical variation of mechanical properties over the entire articular surface of the temporomandibular joint (TMJ), especially the thickness and instantaneous modulus (IM). Mechanical properties of visually normal temporal bones and condyles of a porcine TMJ were mapped ex vivo using a multiaxial mechanical tester (Mach-1 v500css, Biomomentum Inc.). Perpendicular spherical indentations (D=6.35mm) and thickness measurements (needle technique) were performed at ~100 positions over each surface. Data were fit to an elastic model in indentation to extract the IM at each position. High-resolution mappings of the thickness and IM for all surfaces were generated (Fig.1). The cartilage is thicker on the central portion of the condyle while the thickness of the temporal bone is mostly homogenous.



The IM is much higher in the lateral side of both surfaces and its topographic variation is more important in the condyle. A reproducibility analysis (5 attempts) revealed an Intraclass Correlation Coefficient of 0.97 for IM. Similar regional differences in mechanical properties have already been reported but never at such high spatial resolution. These findings support the use of this non-destructive technique in TMJ articular surface characterization.

10:45 AM Distribution of masticatory muscle activity during non-symmetrically loaded open-close movements

van Sluijs RM, Koolstra JH, Wojczynska A, Gallo LM Department of Functional Anatomy, Academic Centre for Dentistry Amsterdam (ACTA), Research Institute MOVE, University of Amsterdam and VU University, Amsterdam, The Netherlands Clinic for Masticatory Disorders and Complete Dentures, Center for

In daily life the masticatory system is regularly loaded in a non-symmetrical fashion, for example during tasks such as chewing and biting. The aim of the current study was to gain insight into the coordination of such non-symmetrically loaded movements. We hypothesized that when unilaterally loaded the masticatory muscles would

be recruited to minimize and equalize load in the temporomandibular joints (TMJs). Symmetrical jaw closing movements were analyzed with non-symmetrical loads of varying weight attached to the lower dentition. When looking at symmetry of muscle activation on the working and balancing side we found that during non-symmetrically loaded movements the temporalis muscle is significantly more active on the working side (p<0.05). No such asymmetry was found for the masseter muscle. The space between the bony surfaces of the TMJ was significantly smaller on the working side during non-symmetrically loaded movements (p<0.05). This implies that the cartilage in this joint was more compressed leading to a higher joint reaction force. Our findings do not support our hypothesis that masticatory muscles play a protective role during non-symmetrically loaded movements. The question which biologically important objective the central nervous system adopts when regulating masticatory muscle activity remains to be investigated.

11:00 AM Cartilage response to a sliding load depends on indenter radius

Schäti ORi^{1,2}, Colombo V¹, Torzilli PA², Gallo LM¹

^I Center of Dental Medicine, University of Zurich, Zurich, Switzerland ²Hospital for Special Surgery, New York, USA

Objective: To correlate the mechanical and cellular response of cartilage to dynamic reciprocating sliding motion when loaded with spherical indenters with different radii. Methods: Cartilage explants were subjected to a reciprocating sliding load using a 17.6 mm or 30.2 mm spherical ball for 2000 cycles at 10 mm/s and 4 kg axial load. Cartilage deformation was recorded and contact mechanics parameters were calculated according to Hertzian theory. After mechanical loading, cartilage samples were collected and analyzed for extracellular matrix (ECM) collagen damage and proteoglycan (PG) loss, and gene regulation of common matrix proteins and enzymes. The biological response was correlated with the mechanical parameters. Results: Significantly higher ECM deformation, strain and contact stress and lower dynamic effective modulus (p=0.0002) were found for explants loaded with the smaller diameter indenter whereas contact radius and stress remained unaffected. Mechanical loading with the 17.6 mm indenter induced no visible ECM damage but did result in increased PG loss and induce significant upregulation of aggrecan, fibronectin, cartilage oligomeric matrix protein (COMP) collagen type II, MMP-3 and ADAMTS-5 genes as compared to the 30.2 mm indenter. Conclusion: Sliding loads that increase ECM load/stress and deformation/strain were found to induce enzyme-mediated catabolic processes in articular cartilage explants. These observations provide further understanding of how changes in cartilage contact mechanics under dynamic conditions can affect the cellular response of chondrocytes. This knowledge has potential value to understand degenerative joint disease associated to joint surface incongruity as well as for the development of and improvement of tissue-engineered constructs for cartilage repair.

11:15 AM Viscoelastic characterization and numerical simulation of the whole TMJ disc for static and dynamic loadings.

Barrientos E¹, Pelayo F¹, Tanaka E², Lamela MJ¹, Canteli¹, de Vicente JC³

¹Department of Construction and Manufacturing Engineering, University of Oviedo, Spain. ²Department of Orthodontics and Dentofacial Orthopedics, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan. ³Department of Surgery and Medical Surgical Specialities, University of Oviedo, Spain.

The complex geometry of the temporomandibular joint (TMJ) implies that testing of circular TMJ specimens, as separately extracted from different disc regions, is not sufficiently representative. This way of specimen cutting causes damage on the tissue and prevents to ensure the natural continuity and compatibility of the boundary conditions between the different disc regions. In particular, internal flow of the fluid in the disc is discarded. Therefore, in order to achieve a more realistic mechanical characterization of the TMJ disc, a different test methodology must be considered. With this aim, a specific, novel testing fixture tool is developed to be applied in the tests by considering the whole TMJ disc specimens, allowing the condylar and fossa surfaces to be reproduced in order to match the TMJ disc geometry. Ten porcine discs are used in the investigation. Dynamic and static compressive properties all over the whole discs are studied. On the other hand, a finite element model is used for an inverse material characterization and the experimental data is used to implement and validate a numerical model that improves understanding of the loading transmission occurring in the TMJ.



Figure 1. Finite element model of the test and whole disc test.

ANIMAL MODELS

11:45 PM

Assessment of minipig TMJ structure-function relationships supports its suitability for human comparative studies

Vapniarsky n, Aryaei A, Arzi B, Hatcher DC, Hu J, Athanasiou KA

Traditionally, farm pigs have been deemed suitable for maxillofacial research due to similarities to humans (e.g., skull size and omnivorous physiology). However, the fast growth rate and operational difficulties associated with the farm pig's size (e.g., anesthesia, surgical approach, maintenance) limit their use. The slower growth rate and overall smaller size of minipigs are attractive, though full characterization of the minipig TMJ disc is lacking. In this study, we performed extensive structural and functional characterization of the minipig TMJ disc (TMJD), including morphology, histology, ultrastructural analysis (SEM), and biochemical and biomechanical assays. Despite being 1/5 to 1/10 of the farm pig's weight at skeletal maturity, the minipig's TMJ disc was of a comparable size, 2.0 cm2 (farm pig and human TMJ discs are 2.6 and 2.9 cm2, respectively). The minipig disc contained 24.3% collagen and 0.84% glycosaminoglycans per wet weight (WW) (farm pig and human TMJ discs are 24.9% and 24.6 % for collagen and 0.37% and 0.53% for GAG respectively). The instantaneous (Ei) and relaxation (Er) compressive moduli averaged over the whole disc at 20% strain were 765 kPa and 35 kPa, respectively. These functional relationships were similar to those in farm pigs and humans (Ei: 1134.2 kPa and 1315.9 kPa; Er: 31.7 kPa and 37.4 kPa respectively). As with the human and farm pig, the regions of the minipig TMJ disc that were stiffest in compression were the anterior and posterior regions, with Ei values of 1480 and 1540 kPa at 20% strain, respectively. In addition to parameters previously characterized for the human and farm pig TMJ discs, we also investigated anisotropy using bidirectional tensile testing, and collagen crosslinking using HPLC. The compositional and functional similarities of the minipig disc to humans, combined with its size and ease of handling, make it an attractive model over the farm pig for biomedical research.

12:00 PM The Temporomandibular Joint of dolphins and porpoises

Arzi B, McDonald M, Vapniarsky N, Staszyk C, Leale DM, Woolard KD, Verstraete FJM

The temporomandibular joint (TMJ) in cetaceans (infraorder Cetacea) is largely uncharacterized. We aimed to describe the macroscopic, microscopic, biochemical and biomechanical features of the TMJ of six species of the odontocetes (parvorder Odontoceti). Furthermore, we aimed to elucidate the structure-function relationship of their TMJs and their possible role in echolocation. We obtained TMJ specimens from fresh cadaver heads acquired from strandings. The species evaluated were Risso's dolphin, harbour porpoise, Pacific white-sided dolphin, longbeaked common dolphin, short-beaked common dolphin, and common bottlenose dolphin. Following macroscopical evaluation, the TMJs were investigated for their histological, mechanical and biochemical properties. The TMJs of the studied odontocetes were found to be fundamentally different from other mammals. Macroscopically, the TMJs lacked the typical joint cavity found in most mammals and were essentially a syndesmosis. Histological and microstructural analysis revealed that the TMJ discs were composed of intersecting fibrous connective tissue bundles separated by adipose tissue, blood vessels and nerve fibers. The collagen fiber composition was primarily collagen type I with lesser amounts of collagen type II. Sulfated glycosaminoglycan (sGAG) content was lower compared to other studied mammals. Finally, mechanical testing demonstrated the disc was stronger and stiffer in the dorsoventral direction than in the mediolateral direction. In conclusion, the spatial position of the TMJ, the absence of an articulating synovial joint and the properties of the TMJ discs all reflect the unique suction-feeding mechanism adopted by odontocetes for underwater foraging. In addition, the presence of unique adipose globules, blood vessels and nerves throughout the discs may indicate a functional need beyond food prehension. Instead the disc may play a role in neurological sensory functions such as echolocation.

12:15 PM Animal model for temporomandibular joint research: morphological, histological and biomechanical characterization of the sheep joint disc

Angelo DF, Salvado F, Morouço P, Alves N, Gonzalez R, Monje F, Fernandes R, Ferreira J, Santos F, Pinho M

Large animal models may be more appropriate to perform trials involving the temporomandibular joint (TMJ). The aim of this work was to make a morphological, histological and biomechanical characterization of sheep TMJ. Results showed that sheep condylar process and mandibular fossa are anatomically similar to the same human structures. TMJ disc has an elliptical perimeter, thinner in the center than in periphery. Peripheral area acts as a ring structure supporting the central zone. The disc cells display both fibroblast and chondrocyte-like morphology. Marginal area is formed by loose connective tissue, with some chondrocyte-like cells and collagen fibers in diverse orientations. Discs obtained a tensile modulus of 3.97±0.73 MPa and 9.39±1.67 MPa, for anteroposterior and

mediolateral assessment. The TMJ discs presented a compressive modulus (E) of 446.41 ± 5.16 MPa and their maximum stress value (σ max) was 18.87 \pm 1.33 MPa. Obtained results suggest that these animals should be considered as a prime model for TMJ research and procedural training. Further investigations in the field of oromaxillofacial surgery involving TMJ should consider sheep as a good animal model due to its resemblance of the same joint in humans.

12:30 PM

Behavioral Changes Associated with Cutaneous, Myogenic, and Arthrogenic Capsaicin-mediated Hypersensitivity in the Rat

MINIMALLY-INVASIVE SURGICAL AND DIAGNOSTIC TECHNIQUES

2:00 PM Microparticle Drug Delivery Systems in the Management of TMJ Disorders

Mercuri LG

Department of Orthopedic Surgery, Rush University Medical Center & Institute of Biomaterials, Tribocorrosion and Nanomedicine, Chicago, IL, USA

Temporomandibular joint (TMJ) disorders are a heterogeneous group of diseases that cause progressive joint degeneration leading to chronic pain and reduced quality of life. Both effective pain reduction and restoration of TMJ function remain unmet challenges. Intra-articular injections of corticosteroids and hyaluronic acid are currently used to manage chronic pain, but these methods require multiple injections that increase the risk of iatrogenic joint damage and other complications. The emerging field of nanobiology aims through novel strategies to develop methods for sustained, intra-articular release of drugs, growth factors and other pro-regenerative signals aimed at reducing TMJ pain and disability. Current methods of intra-articular drug delivery are complicated by rapid degradation and clearance of injected pharmacologic agents, so that frequent injections and high concentrations are necessary. An innovative way to maintain a therapeutic concentration over longer time periods is the administration of depot formulations. Despite their clinically proven efficacy, these depot formulations suffer from a significant drawback, which limits their use. Actually, due to their crystalline nature, some drugs can generate inflammatory conditions upon injection, leading to crystal- induced arthritis, observed in 10% of the patients. The development of novel nanobiology systems for sustained anti-inflammatory drug release will increase the residence time of medications within the joint, reducing the need for repeated intra-articular injections and thus minimizing iatrogenic damage. Tighter control over release kinetics would reduce the required medication dosage and decrease the risk of side effects.

2:15 PM Twenty years of surgical management of advanced degenerative arthritis of temporomandibular joint with metal fossa-eminence hemijoint replacement prosthesis: 1996 - 2016

Keller EE, Baltali E

We would like to present our experience with temporomandibular joint with metal fossa- eminence hemi-joint replacement prosthesis. As a group we published 3 surgical followup articles on TMJ hemi-joint replacement to treat patients with advanced osteoarthritis, total number of 219 patients, including data on 289 joints. As well as kinematic study articles providing condylar motion, rotation and mandibular body motion providing data on 63 patients (68 joints). Over twenty years our research evolved from prospective chart studies to retrospective followups with kinematic motion recordings of the mandibular body. We matched our motion data with CT scans to obtain 3D animation of the whole mandibular body relative to the scull. Research provided some insight to the surgical technique we used. As a result a novel design custom hemi-joint TMJ prosthesis was designed and developed. Which is currently being used with a high patient satisfaction rating (8.4/10).

2:30 PM Correlation Between Arthroscopic Findings of TMJ Synovitis, Serology, and Synovial Biospy Outcomes

Hossameldin RH, McCain JP

Lecturer of Oral and Maxillofacial Surgery, Faculty of Oral and Dental Medicine , Cairo University , Egypt

Introduction: TMJ disorders include non-inflammatory osteoarthropathies, primary arthritides. To distinguish from other forms of observed inflammatory polyarthritis, serological tests and synovial biopsy are suggested. <u>Aim</u>: is to evaluate the specificity of serological results in reaching an early diagnosis of arthritis when correlated to synovial biopsy outcome, and arthroscopic findings. <u>Methods</u>: A prospective clinical study included 142 patients with unilateral TMJ disorders who underwent primary arthroscopy at Baptist Hospital, Miami, FL in the period from January 2010 to February 2013. Preoperative arthritis blood serology testing was done Selected seropositive patients were subjected to synovial tissue biopsy during arthroscopic procedure. Statistical analysis was performed using one sample Chi-square test. <u>Results</u>: The study included 142 unilateral joint patients. 29 joints were

seropositive and 113 joints negative which is significantly different P = 0.001. 15 seropositive patients were biopsied. Arthritis positive biopsy was seen in 3 patients, negative in 12 patients being significantly different P = 0.001. Arthroscopic synovial tissue inflammation was noticed in all seropositive patients, except 2 patients, being positive in all 3 seropositive, positive biopsy patients. Conclusions: Current study suggests that synovial biopsy and diagnostic arthroscopic findings provide additional and valuable diagnostic tools to isolate TMJ as being involved with arthritis.

2:45 PM

Preoperative predictors for successful outcome after temporomandibular joint arthroscopy

Ulmner M, Weiner CK, Lund B

Department of Oral- and Maxillofacial Surgery, Karolinska University Hospital, Stockholm Department of Dental Medicine, Karolinska Institute, Stockholm

<u>Aim</u>: To scrutinize if preoperative variables can predict treatment outcome. <u>Material and Methods</u>: Consecutive patients were asked to participate. Exclusion criteria were prior discectomy or age under 18. All patients were subjected to a standardized clinical investigation before and after surgery. Criteria for successful outcome was maximum interincisal opening (MIO) of \geq 35 mm and visual analog scale (VAS) values of TMJ functional pain and impairment of \leq 3 and/or \geq 40% improvement 6 months after surgery. <u>Results</u>: Of the 41 included patients (4 males, 37 females), 34 (83 %) were successful or significantly improved. Success in relation to diagnose was 85% for chronic closed lock, 71% for osteoarthritis and 87% for systemic arthritis. In the successful group mean MIO was significantly improved from preoperative 30.5 mm to postop 42.2 mm (p<0.005). No significant correlation be between outcome, previous trauma, joint hypermobility, duration of symptoms, and preoperative VAS values could be seen. Un-successful cases were on average 10 years younger (34 years) compared to favorable surgical outcome (45 years). <u>Discussion</u>: No preoperative variables could predict the outcome of the surgery in contrast to a previous retrospective study were female gender, low age, general anxiety/depression and severely reduced MIO correlated to non-successful outcome.

3:00 PM Arthroscopic Repositioning And Suturing Of The Temporomandibular Joint Disc - A New Design.

da Silva PA ,Moreira LD, Freire FS, Heladio R, Motta L São Leopoldo Mandic School of Dentistry - Campinas -SP- Brazil

Different disc repositioning and suturing techniques have been described from the classic technique of McCain et al in 1992. Although there were different designs of the suture technique, all have in common the previous anterior release and disc mobilization and all of techniques have excellent results when well indicated. The aim of this study was to present a new design of the arthroscopic suture. The present technique was first tested in biomodels and after the determi- nation of the landmarks were applied in 6 patients (9 ATM) with symptomatic disc displacement with pain and limited mouth opening, refractory to medical treatment. Patients were followed for 12 months with magnetic resonance image (MRI) at 6 and 12 months. As criterion of success was considered the improvement of symptoms and a



suitable position in the disc in MRI. The success rate was 83% (5 patients) and 89% (8 well positioned discs). New arthroscopic suturing technique showed itself effective, with results similar to other techniques, can be considered as a new alternative. Further studies with larger samples and a long-term follow-up are necessary for consolidation of the effectiveness of this technique.

3:15 PM Temporomandibular Custom Hemi-joint Replacement Prosthesis: Prospective Clinical and Kinematic Study

Keller, EE, Baltali, E, Liang X, Zhao K, Huebner MA, An K

<u>Aims</u>: To evaluate the clinical outcome of Patients who underwent surgery to receive a novel custom temporomandibular hemijoint fossa/eminence implant prosthesis. <u>Methods</u>: Fifty four patients that fulfill the inclusion criteria were selected to enroll this prospective cohort study. Patients were followed up by a visual analog scale questionnaire in pre-operatively as well as 3 (T1), 6(T2), and 12(T3) months after surgery. They were asked to evaluate pre to post changes in study variables and their overall satisfaction with the surgical result. <u>Results</u>: All study variables were statistically significant at the p<.001 level, indicating significant improvement in jaw-facial pain experience and intensity, chewing ability, jaw opening, and joint noise from the preoperative assessment to the post-operative assessments. There were also no statistically significant changes among postoperative time points. Average patient reported overall satisfaction with the surgery was 8.2(T1), 8.4(T2) and 8.3(T3) with median value being 9 on a 10 point scale. <u>Conclusions</u>: Temporomandibular hemiarthroplasty with custom metal fossa-eminence prosthesis provides predictable and satisfactory results in patients.

BIOMECHANICS – PART II

4:00 PM Comparison of mandibular kinematics and maximum voluntary bite force in mandibulectomy patients with and without reconstruction of the mandible of the custom implant.

Linsen S, Oikonomou A, Martini M, Teschke M

Purpose: Mandibular continuity defects with and without reconstruction alter jaw kinematics, occlusal forces, and mastication. The purpose was to analyze the mandibular patterns and maximum voluntary bite force in mandibulectomy patients without and with reconstruction (bone graft, alloplastic total TMJ replacement (TJR)). Material and Methods: Condylar range of motion during opening, incisal range of motion during opening and lateral excursion, deflexion and mandibular rotation angle during opening, and maximum voluntary bite force were evaluated in 11 patients each without reconstruction, with osseous reconstruction, and with alloplastic TMJ TJR. Results: Results show significant (P =.017) wider condylar translation in patients with osseous reconstruction versus patients with TMJ TJR and significant higher maximum voluntary bite forces in patients with osseous reconstruction (P =.001) and patients with TJR (P =.022) compared with nonreconstructed patients. Significant higher deflexion during opening (P =.002) was found in the nonreconstructed group (P =.002 vs osseous reconstruction, P =.014 vs TMJ TJR). Conclusion: Both reconstructed and nonreconstructed patients (both osseous and TMJ TJR) having better overall function than nonreconstructed patients.

4:15 PM An innovative temporomandibular joint prosthesis is necessary

MESNARD M, RAMOS A

Université de Bordeaux, Institut de Mécanique et d'Ingénierie, Bordeaux, Fr.; ² University of Aveiro, Dept. of Mechanical Engineering, Aveiro, Pt.

TMJ implants currently on the market consist of either custom-made solutions or stock models. In both, the concept and fixation methodology are the same. This fixation is applied laterally on the mandible ramus with screws in different places and positions, causing bending in the implant and the mandible bone. The joint is created between a hemisphere and a plate, the fossa component is made of UHMWPE, also fixed by screws. Here, we point out some critical aspects of the actual concept, using in vitro experimental and numerical models. These results identify the most important positions for the screw fixation, and conclude that 3 screws determine the connection behavior between implant and condyle. The bending of the lateral plate is critical for fatigue and screws proximally. The fossa component in the stock implants presented here does not fit to the bone of the fossa, which increases the load on the 3 fixing screws. Results from numerical models show that the stock implant changes the behavior in both the implanted and the opposite condyles, and that the size and geometry of the implant head change the condyle contact point. Stress values in the contact point are high, causing wear and osteolisis in the bone connection.

4:30 PM Mevalonate Pathway and The Prevention of PTOA

Lv M, Zhou Y, Fan S, Wang L, Lu X University of Delaware

Mevalonate pathway is the target of two classes of medications, statins and bisphosphonates. Statins can deposit in the liver and reduce the synthesis of cholesterol by inhibiting the mevalonate pathway in cells. Bisphosphonates, as calcium chelators, can attach on the bone and interrupt the bone resorption by osteoclasts. Interestingly, both statins and bisphosphonates showed strong protection effects for cartilage in various OA animal models. Statins also reduced the incidence of OA in several clinical trials. Using DMM mouse model, we found that bisphosphonate can rescue the cartilage from degeneration after DMM surgery and the protection effect may beyond the inhibition of subchondral bone loss. Our in vitro tissue culture studies, interestingly, found that bisphosphonates can directly reduce the loss of GAG content and mechanical integrity of damaged cartilage explants without the presence of bone tissue. This finding was confirmed by using two types of bisphosphonates and different cartilage injury models. Moreover, bisphosphonates enhanced the beneficial effects of dynamic loading for the in vitro culture of cartilage. In all tests, the expressions of anabolic genes in chondrocytes were promoted by bisphosphonate, with catabolic genes suppressed. Similar protective effects were found for statins using the in vitro cartilage explant model. We further hypothesized that the chondro-protective function of bisphosphonate and statin is related to the inhibition of mevalonate pathway in chondrocytes. In our explant model, when bisphosphonate was replaced by alternative mevalonate pathway inhibitors (GGTI and FTI), similar protective effects on chondrocytes were observed. Meanwhile, the chondro-protective activity was abrogated when two downstream derivative molecules (GGOH and FOH) in mevalonate pathway were supplemented together with bisphosphonate. In summary our study implies that mevalonate pathway in chondrocytes could be a new target for OA prevention.

Administration of the statin or bisphosphonate may reduce the risk of OA development after joint trauma.

4:45 PM The role of elastin fibers in the temporomandibular joint disc: structural- functional study

Fazaeli S^{1,3}, *Ghazanfari* S^{2,3}, *Everts* V^{1,3}, *Smit* T^{2,3}, *Koolstra JH*^{1,3} ¹Department of Oral Cell Biology and Functional Anatomy – Academic Center for Dentistry Amsterdam, University of Amsterdam and VU University Amsterdam, Amsterdam, the Netherlands. ² Department of Orthopaedic Surgery - VUmc, Amsterdam the Netherlands. ³ MOVE Research Institute Amsterdam.

The Temporomandibular Joint (TMJ) disc is a fibrocartilaginous structure, composed of collagen fibers, elastin fibers and proteoglycans. Despite the crucial contribution of elastin fibers in load- bearing properties of convective tissues, its biomechanical role in the TMJ disc has been disregarded. Therefore, in this study, the structural-functional role of elastin fibers in the TMJ disc was investigated using a combination of biochemically enzymatic treatment and biomechanical tests. Porcine TMJ discs were digested with elastase to perturb the elastin fiber network. The treated and control samples were mechanically loaded before and following the enzymatic digestion. Further, the samples were biochemically analyzed to quantify their collagen, glycosaminoglycans (GAG) and elastin fiber networks. The energy dissipative properties of the disc was increased noticeably. Biochemical analysis demonstrated considerable reduction of elastin content while the collagen and GAG variation was negligible. Also, immunohistochemical analysis showed clear structural changes and fragmentation of elastin fibers with partial effect on collagenous network. The results indicated that elastin fibers are minor in numbers , nevertheless, they enhance the mechanical integrity of the disc and contribute in restoration of the disc form after load removal.

5:00 PM BREAK

TMJ TISSUE ENGINEERING – PART I

5:30 PM In-vivo Regenerative Potential of Various Polymeric Scaffolds in Osteochondral TMJ Defects

Chin AR, Taboas JM, Gao J, Wang Y, Kumta P, Almarza AJ

Over 15 million Americans suffer from temporomandibular joint disorders (TMDs), of which approximately 10% are affected with damage of the mandibular condylar cartilage (MCC) and subchondral bone [1]. Tissue engineering approaches with biodegradable polymeric scaffolds can be employed to regenerate the TMJ joint tissues. The goal of this study was to assess the regenerative potential of acellular polymeric scaffolds in a novel fibrocartilage defect model in the goat MCC. Poly (glycerol sebacate) (PGS) [2] and gelatin [3] are polymeric scaffold sponges that may provide a substrate for cell infiltration and remodeling. Bilateral osteochondral defects were created in the condyle of mature Spanish Boer goats. A 1mm diameter drill was used to create an osteochondral defect of the mandibular condyle once inside the joint space. PGS, and gelatin scaffolds were then inserted inside the defect. An empty scaffold control was used for comparison. All groups were allowed to heal for 3 months. From histology, the PGS only sponge group appeared to have robust regeneration of fibrocartilage with cellular infiltration, collagen and glycosaminoglycan presence. These results suggest that both synthetic and natural sponges are capable to providing a template for new tissue growth in the MCC of the TMJ.

[1] E. Tanaka, M.S. Detamore, L.G. Mercuri "Degenerative Disorders of the Temporomandibular Joint: Etiology, Diagnosis, and Treatment", Journal of Dental Research; [2] C.K Hagandora, J Gao, Y Wang, A.J Almarza "Poly (dycerol sebacate): a novel scaffold material for temporomandibular joint disc engineering", Tissue Eng Part A; [3] J.M Taboas, R.D Maddox, P.H Krebsbachm S.J Hollister "Indir ect solid free form fabrication of local and global porous, biomimetic and composite 3D polymer-ceramic scaffolds", Biomaterials.

5:45 PM Extracellular Matrix-Based Device for Reconstruction of the Temporomandibulat Joint Disc

Brown BN¹, Chung WL¹, Cheetham J², Almarza AJ¹, Badylak SF¹ ¹ University of Pittsburgh; ²Cornell University

The present study examined the use of an extracellular matrix (ECM) device for reconstruction of the temporomandibular joint (TMJ) disc in a porcine model following discectomy. Animals (n=60) were sacrificed at 2, 4, 12, and 24 weeks and remodeling assessed by histologic examination, MRI imaging, biochemical and biomechanical analysis (tension and compression). The device was replaced by a structure highly resembling native tissue by 4 weeks in greater than 50% of animals. Immunolabeling showed that mononuclear macrophages mediated the early stages (2-4 weeks) of tissue remodeling. The histologic appearance of the remodeled implant at later times (>4 weeks) was characterized by dense, aligned fibrocartilage containing spindle-shaped cells within the area of articulation. Formation of peripheral muscular and tendinous attachments resembling those in native tissue was also observed. The biomechanical properties of the remodeling tissue approached that of native tissue over the course of remodeling. Protection of condylar surfaces in ECM implanted animals was observed regardless of formation of new TMJ disc tissue. This device fills a need for which there are currently no effective treatments, may represent a simple and effective "off-the-shelf" solution for TMJ disc reconstruction, and is being considered

for first-in-human trials to begin in late 2016.

6:00 PM Hydrogels for controlled drug delivery and tissue engineering of the Temporomandibular Joint

Talaat WM^{1,2}, *Haide M*^{3,4}, *Kawas SA*¹, *Kandi N*⁶, *and Harding DRK*⁶ 1Department of Oral and Craniofacial Health Science, College of Dental Medicine, University of Sharjah, Sharjah, UAE; 2Department of Oral and Maxillofacial Surgery, College of Dentistry, Suez Canal University, Ismaillia, Egypt; 3Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, University of Sharjah, Sharjah, UAE; 4Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, 5Department of Chemistry, Faculty of Women, Ain Shams University, Heliopolis, Cairo, Egypt; and Institute of Fundamental Sciences, Massey University, Palmerston North, New Zealand.

Intra-articular injections of hyaluronic acid (HA) and corticosteroids have been commonly used in treating Temporomandibular disorders. However, rapid clearance from the joints is a critical concern that is negotiated by frequent dosing, which is not without complications. This study aimed to investigate the suitability of four different hydrogelation systems based on alginate, carboxymethyl cellulose, nanocellulose and chitosan for intra-articular controlled release of drugs in the rabbit TMJ. A series of hydrogels were prepared and several parameters were investigated to select the formulation with optimum characteristics. Chitosan β -glycerophosphate was selected for further drug (HA) loading. HA concentrations were measured using Hyaluronan Quantikine Elisa Kit. The mean concentration of HA in the experimental joints after 7 days was significantly higher than the control (P<0.001). No morphological changes were observed. In conclusion, the chitosan-based thermosensitive hydrogel can be considered a promising controlled drug release system to the TMJ that would potentially overcome many of the current shortcomings of intra-articular formulations. We are currently investigating both in vitro and in vivo release of HA from Ch/b-GP hydrogel at different time points and assessing its efficiency for controlled release of other drugs as well as its utilization in tissue engineering strategies for TMJ regeneration.

6:15 PM Regenerative Medicine for the TMJ: Past, Present and Future

Detamore, MD University of Oklahoma

6:30 PM Comparison of custom hemijoint replacement prosthesis which is made of the different materials. Finite element analysis.

Tekin U, Bolat IE, Atıl F, Koçyigit ID, Önder ME Kırıkkale University, Oral and Maxillofacial Surgery Department

Introduction: Two types of hemijoint fossa prosthesis are available as a stock or custom in the literature. All prosthesis was made of Chrome-Cobalt-Molybdenum (Cr-Co-Mo). The purpose of this study was to evaluate the durability and stress distribution of hemijoint prosthesis which is made of different types of materials such as Cr-Co-Mo, Titanium- 6Alumunium- 4 Vanadium (Ti-6Al-4V) and Polyether ether ketone (PEEK) by using finite element model analysis. <u>Material Methods:</u> A three-dimensional (3D) finite element model of the mandible including the TMJ was developed for the analysis of TMJ stresses on hemi-joint TMJ fossa prosthesis is produced by Cr-Co-Mo, Ti-6Al-4V and PEEK. <u>Results:</u> Our results showed that the stress is critical around the contact with the condyle where it reaches respectively a maximum of 146MPa for the Cr-Co-Mo, 132MPa for the Ti-6Al-4V and 93MPa for the PEEK. The results also reviled that the maximum stress occurred at the location of the first screw hole of all different materials of prosthesis. <u>Conclusion:</u> This study demonstrated that there are load transfer on hemijoint fossa prosthesis which made of different type of materials and stress distribution on the screws. The results of our study have potential clinical benefits in usage of new materials on hemijoint fossa prosthesis.

6:45 PM CLOSE

7:30 PM DINNER

<u>DAY 3 – September 13, 2016</u>

8:30 AM BREAKFAST

9:00 AM KEYNOTE SPEAKER - Andrew Sidebottom, BDS, FDSRCS, MBChB, FRCS, OMFS

10:00 AM BREAK

CLINICAL STUDIES

10:30 AM Comparison of arthrocentesis and single intraarticulary injection of sodium hyaluronate or corticosteroids in patients with Wilkes classification II-III, IV-V. Prospectice 24 months long term study.

Vladimir M, Jitka L Charles University and Faculty Hospital Prague, Dept.of Oral and Maxillofacial Surgery, Prague, Czech Republic

Authors compared 3 methods for therapy of pain in patients with Wilkes classification II-III and IV-V. Study underwent 300 patients. 244 patients underwent evaluation 24 months after. All patients were divided in 3 groups, patients in group 1 underwent arthrocentesis (with 2 needles), patients in group 2 underwent single injection of sodium hyaluronate and patients in group 3 underwent single injection of corticosteroid (betamethason). Therapeutical effect (decreasing of pain) was in all 3 groups (1 month after) similar. Next control (3,6,12 and 24 months) were with statistically significant decreasing of therapeutical effect of corticosteroid. Therapeutical effect of arthrocenthesis and single injection of sodium hyaluronate was without statistical difference in next controls ((3,6,12 and 24 months)). Authors believe, that single injection of sodium hyaluronate could be an alternative arthrocentesis in therapy of pain of TMD.

10:45 AM Hydroxyapatite collagen scaffold with autologous bone marrow aspirate for condylar regeneration

Howlader D, Vignesh U, Bhutia DP, Mahajan N, Chandra T, Mehrotra D Department of Oral & Maxillofacial Surgery, King George's Medical University, Lucknow

<u>Objective</u>: The best reconstructive option is autogenous graft, but is fraught with donor site morbidity, necessity for a second surgical procedure and additional operating time. For the maxillofacial surgeon, this inadequacy can be more acutely appreciated in the field of TMJ reconstruction. Recently, there has been an elevated interest in the applicability of Bone Marrow Aspirate Concentrate (BMAC) as an osteoinductive agent. The objective of this study was to observe if delivered appropriately on a hydroxyapatite collagen (HA-Col) scaffold, BMAC could induce osteogenesis, potentially forming a functional neocondyle. <u>Material Methods</u>: Seven patients of Temporomandibular joint ankylosis underwent osteoarthrectomy followed by reconstruction with HA-Col condylar scaffold. A collagen sponge imbibed with autologous BMAC was placed at the junction of the scaffold to the ramal stump. The scaffold was fixated to the ramus by a trapezoidal miniplate. All patients were put on aggressive physiotherapy after 10 days, and were followed at one, three and six months. <u>Results</u>: The average inter-incisal mouth opening increased from 2.42mm to 29.1 mm at 6 months and there was no pain or swelling. Radiographs showed increased radio-opacity at the interface suggesting osteogenesis. <u>Conclusion</u>: BMAC impregnated HA-Col scaffold could serve as a promising new method of TMJ regeneration.

11:00 AM Hyaluronic acid injection vs. occlusal splint treatment of chronic temporomandibular joint disorders.

Tartaglia GM, Connelly ST, Silva R, Gizdulich A University of California San Francisco

Visco-supplementation with hyaluronic acid (HA) has been used to treat inflammatory-degenerative joint disorders. We compared the effectiveness of HA with a stabilization oral appliance (OA) versus an OA alone, in the management of chronic TMJ degenerative disorders. Twenty-one patients were divided into two treatment groups: 10 received HA plus an OA, 11 received an OA alone. They were examined before and 3.6 months after treatment. Pain levels on a 10-point VAS scale and patient-reported outcome satisfaction were used to rate treatment effectiveness. EMG analysis of the stomatognathic neuromuscular system was also performed. Both groups reported a significant decline in VAS scores (HA group, from 8 to 4.8; OA group, from 7.6 to 4.7; p<0.001), without between-groups differences (p=0.907). Patient satisfaction was higher in the HA group (90%) than in the OA group (73%), but not significantly (p=0.586). No significant variations of the EMG parameters were found. In the present prospective study, the post-treatment findings support the effectiveness of both treatment protocols in terms of neuromuscular equilibrium and pain perception. A slight advantage of HA treatment was observed in terms of patient satisfaction. Visco-supplementation can be a useful treatment for pain relief in patients with chronic TMJ pain.

11:15 AM BREAK

ORTHODONTIC TREATMENTS

11:30 AM TMJ from an Orthodontic Point of View

Martin D

There is much research being conducted all over the world with respect to TMJ cell biology, bone physiology, biomaterials and tissue engineering. However, in many instances, researchers are not aware of the clinical presentation and complications faced by clinicians. Researchers and clinicians need to collaborate and take full advantage of the information that exists in order for the field to advance. It is often difficult for clinicians to keep up with the scientific advances and thus do not incorporate them into their treatment plans. On the other hand, some researchers do not have a full understanding of the treatments modalities being practiced and therefore cannot visualize how their research information can translate to clinical practice. This presentation will explain the practice of a TMJ -centered orthodontist that improves the conditions (signs and symptoms) of TMD patients. The goal is to facilitate the dialogue between clinicians and researchers to encourage collaboration between both parties and reach the ultimate goal: understanding and treating the TMJ.

11:45 AM Meridian AM: Novel Orthotic for TMD Treatment

Cress SE

Background: TMD patients present with functionally restricted mandibular movements due to retruded mandibular position and disc displacement with arthralgia. This abstract describes a novel maxillary occlusal appliance for these complex patients. Materials/Methods: Dental models are set in centric relation and then opened to ideal facial height. Anterior teeth are sectioned and repositioned into more ideal arch form. An expansion screw is placed in the pallet of the appliance for horizontal expansion. This design allows for resting disc position and minor orthodontic tooth movement. Bite force and range of motion are recorded before and after appliance delivery, and intermittently during treatment. The appliance guides the lower jaw into an occlusal index, creating an anterior/posterior and a vertical space for the disc to rest, as well as decreasing mandibular restriction by maxillary anterior dental expansion. Trauma to the disc is relieved, decreasing inflammation and pain. Results: Patients wear the appliance continually during the day and report varying degrees of relief 24 hours after delivery. Patients are seen every 4 weeks, and occlusal adjustments are made until occlusion is corrected and the patient has minimal functional impairment. Treatment may take up to 9 months. Conclusion: This novel orthotic is a conservative, non-surgical approach to TMD treatment. The appliance allows the disc of the TMJ to be placed in a new functional environment, diminishing TMD symptoms.

12:00 PM Effects of Tooth Clenching on Pain Tolerance

BrüggerM^{1,2}, Waech T¹, Gallo LM¹, Ettlin D¹

¹Center of Dental Medicine, University of Zurich, Zurich, Switzerland; ²Institute for Biomedical Engineering, University of Zurich and ETH Zurich, Zurich, Switzerland

Objectives: 'Bite your teeth', 'grit your teeth' or 'clench your jaw' are idioms that universally exist in diverse languages and cultures and reflect a wisdom of crowds. The verbal advice refers to a stopgap measure that is supposed to suppress acute pain. If true, this maneuver would be a simple and cheap analgesic. Yet, to our knowledge, no scientific evidence exists regarding the validity of this popular wisdom. This pilot study aimed at investigating the analgesic effect of clenching using an easy applicable standardized sensory testing device. Methods: 59 healthy pain-free subjects (33 females, aged 22 - 61) participated. All research procedures were approved by the local ethics committee. Constant current stimuli were generated by Pain Matcher (Cefar Medical AB, Lund, Sweden). It delivers rectangular, 0 -396µs wide pulses of 10Hz frequency and 15mA amplitude. Slight pressure applied by subjects to the sensors between left index finger and thumb instantly started the stimulation. Over time, the current strength increases linearly until subjects release one finger. Following familiarization with the device, a first experimental run started with participants randomly assigned to pain tolerance threshold determination while clenching (Cle) or without clenching (Con). Three additional runs followed with interrun intervals of 5 minutes.

Results:

Gender	Pain Tolerance Perception, PTT [mean/SD]			
	Con ₁	Cle1	Con ₂	Cle ₂
Total	36.10[29.9]	46.10[34.18]	39.02[32.04]	49.93[36.72]
Female	22.85[20.54]	31.73[28.55]	25.45[23.32]	34.00[31.93]
Male	52.92[31.94]	64.35[32.36]	56.23[33.68]	70.15[32.6]

Whereas no significant difference were detected within clenching conditions, PTT was significantly increased during clenching compared to control (p<0.05). Females and males differed significantly in all experimental conditions (p<0.05). Conclusions: This is the first study revealing that clenching results in increased pain tolerance, thus providing scientific evidence for a popular wisdom of crowds

12:15 PM Efficacy of Modified Twin-Block Splint Treatment on Temporomandibular Joint Disc Displacement

with Reduction

Zhu Y, Gu Y, Hu X, He L, Liang Z Department of Oral and Maxillofacial Surgery, Shenzhen Second People; Hospital, the First Affilliated Hospital, University of Shenzhen,

<u>Aims</u>: The aim of this randomized, controlled trial study was to assess the efficacy of modified Twin-Block splint treatment on temporomandibular joint anterior disc displacement with reduction (ADDWR). <u>Methods</u>: The sample consisted of 120 consecutive referred patients who had stage I and II internal derangement(ID), according to the classification of Wilkes were randomly assigned to the splint group (n = 66) and the control group (n =54). Subjects in the splint group were treated with a modified Twin-Block splint, whereas subjects in the control group did not receive. MRIs were used before and after splint treatment. The disk position was judged according to the success criteria with sagittal planes after treatment. Outcomes were opening click and the disk position of MRI which were measured at baseline and after 2-month follow-up. <u>Results</u>: 93.8% patients (61/65) in the splint group and 20.4% patients (11/54) in the control group, whose disk of TMJ was in normal position with opening click disappeared were evaluated to be excellent. <u>Conclusions</u>: The evidence supporting the use of modified Twin-Block splint in the treatment of temporomandibular disorders (TMD) is effective and fast.

12:30 PM LUNCH ON YOUR OWN

TMJ TISSUE ENGINEERING –PART 2

1:30 PM Properties of Remodeled ECM Scaffolds in the Porcine Temporomandibular Joint

Lowe J, Chung W, Brown B, Johnson S, Badylak S, Almarza A University of Pittsburgh, Department of Bioengineering, Department of Oral and Maxillofacial Surgery, Department of Oral Biology, McGowan Institute for Regenerative Medicine, Center for Craniofacial Regeneration

There are no current long term graft replacements for the TMJ following discectomy. Extracellular matrix (ECM) scaffolds have shown potential as a graft replacement in the canine TMJ model. In this study, we evaluated the biochemical and biomechanical remodeling of ECM scaffolds implanted in a porcine model following discectomy at 1, 3, and 6 months post implantation. Three month old female pigs received unilateral implantation of an ECM scaffold following discectomy. Scaffolds were resected at 1, 3, and 6 months post implantation and compared to age-matched native controls. Hydroxyproline, glycosaminoglycan (GAG), and DNA assays were performed to determine biochemical content. Unconfined stress relaxation compressive testing and uniaxial tensile testing were performed to determine the compressive stress, compressive tangent modulus, tensile peak stress, and tensile between groups in collagen, GAG, and DNA content after 1 month post-implantation. No statistical differences between remodeled scaffolds and native were seen for compressive stress and tangent modulus. There were no statistical differences for tensile properties past 3 months post implantation. These results suggest the potential efficacy of ECM scaffolds as a TMJ disc graft replacement.

1:45 PM Chondrocyte Phenotype Progression is Sensitive to Hydrogel Composition in Engineered Physis Microtissues

Chen J, Donius AE, and Taboas JM University of Pittsburgh, Pittsburgh, PA



Figure 1: Von Kossa at 8 weeks (black: mineral, red: fast red counterstain. Scale bar=0.5mm.

(A, B) Effects of hydrogel formulation on chick sternal chondrocytes. (A) PGH. (B) GEL.

(C, D) Effects of hydrogel formulation on hMSCs. (C) PGH. (D) GEL

Introduction: Mandibular condular fibrocartilage shares morphologic features and signaling mechanisms with physical cartilage. Both exhibit a stratified architecture with chondrocytes in zones of distinct differentiation states, including polymorphic, proliferative and hypertrophic zones. To successfully regenerate this structure and promote function of regenerate condular and growth plate cartilage, a regenerative approach is needed that supports the several physeal chondrocyte states and proper interzonal signaling. In this work, we evaluated the effect of two hydrogel formulations on chondrogenesis and terminal differentiation of progenitor cells (human mesenchymal stem cells, hMSCs) and chondrocytes already at different states of differentiation (isolated from distinct regions of chick sternae). We used a murine subcutaneous implant model to evaluate methacrylated gelatin hydrogels (GEL, 10% w/v) compared to a composite hydrogel (PGH, 10% w/v) composed of GEL, methacrylated poly (ethylene glycol) (PEG), and methacrylated heparin. Results: The PGH hydrogel favored chondrogenic differentiation of hMSCs under the presence of TGF-B3, and augmented maintenance of chick sternal chondrocytes in glycosaminoglycan (GAG) producing state while delayed development of the hypertrophic phenotype. The GEL hydrogel favored osteogenic differentiation of hMSCs under the presence of TGF- β 3, and led to decreased GAG synthesis, accelerated hypertrophy, and ECM mineralization in chick sternal chondrocytes.

2:00 PM Role of BMP signaling mediated by ACVR1 During Chondrogenic Induction of Neural Crest Cells

Stephens C¹, Carrion R¹, Yang J², Mishina Y², Coleman RM^{1,3} ¹Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI; ²Department, of Biologic and Materials Sciences, School of Dentistry, University of Michigan, Ann Arbor, MI; ³Department of Mechanical Engineering, University of Michigan, Ann Arbor, MI

Normal craniofacial development requires a combination of environmental cues (matrix stiffness and composition) and biochemical cues (growth factor signaling) to promote chondrogenic differentiation and control chondrocyte maturation of ectodermal-derived neural crest cells (NCCs), which eventually give rise to craniofacial tissues. Key regulators of this process are the bone morphogenetic proteins (BMPs). Mutations in the type I BMP receptor, Acvr1 (Alk2), in mesenchymal progenitor cells can lead to heterotopic bone formation in soft tissues, but its role in NCC chondrogenesis is largely unknown. In the present study, chondrogenesis and chondrocyte maturation was investigated in NCCs derived from mutant mice harboring a gain- of-function mutation in Acvr1 (ca-Acvr1) and control littermates in the presence of BMP2. Exogenous BMP2 supplementation in hydrogel culture induced chondrogenesis of both NCC lines, as was demonstrated by Col2a1, Agcn, and Sox9 gene expression and production of a glycosaminoglycan (GAG)-rich matrix. Matrix content was lower and progression to hypertrophy faster in ca-Acvr1 NCCs, as we evinced by higher Col10a1 expression in these cells. These results indicate that ACVR1 has a role in the initiation and maturation of craniofacial cartilage and our next steps will be to determine how modulation of matrix stiffness and composition further modulates this process.

2:15 PM BREAK

DIAGNOSTICS

2:45 PM

Correlation between computed tomographic and pathologic evidence of temporomandibular joint osteoarthritis in horses

> Tanner JC. Leale D. Arzi B. and Cissell DD Dept. of Surgical & Radiologic Sciences, University of California, Davis

Naturally occurring temporomandibular joint (TMJ) disease, and specifically TMJ osteoarthritis, is apparent in as

many as 25% of adult horses on skull CT exams. Although TMJ osteoarthritis has been implicated as a cause of reduced performance in isolated horses, the clinical significance of TMJ disease in horses is not well understood. Furthermore, pathologic changes of the equine TMJ associated with CT abnormalities have never been reported. The purpose of this study is to identify CT findings that correlate with gross and histopathologic evidence of TMJ osteoarthritis in horses. The skulls of normal horses and horses with TMJ osteoarthritis underwent CT examination followed by dissection of the

TMJs. The mandibular condyles were fixed in formalin, decalcified, and embedded in paraffin for histologic evaluation. Each TMJ was scored for the presence or absence of CT findings consistent with osteoarthritis and for gross abnormalities of the articular cartilage, TMJ disc, and subchondral bone. Results indicate that total CT scores correlate with gross pathology scores (p=0.002). Subchondral cystic lesions and subchondral erosions involving the mandibular condyle are significantly associated with greater gross pathology of the TMJ



Figure 1. CT images of equine temporomandibular joints (A,B) and gross pathology of matching mandibular condyles (C,D). Little or no pathology is observed on CT images of an equine TMJ with mild osteoarthritis (A,C). The most common gross pathologic finding was cartilage erosion and/or eburnation (^^) at the caudomedial aspect of the mandibular condyles (C,D). Subchondral bone erosions and cystic lesions apparent on CT (black arrows) correspond to severe cartilage damage and pitting of the subchondral bone (white arrows) in joints with severe

(p<0.05). No other individual CT abnormality is predictive of gross evidence of TMJ osteoarthritis in the horse.

3:00 PM Bouguila and Khochtali's technique for the treatment of recurrent temporomandibular dislocation

Bouguila J^{1,2,3}, Khochtali H¹ ¹Sahloul Hospital, Sousse, Tunisia, ²Tunis Medical School. Tunis-El Manar University. Tunisia, ³La Rabta Hospital, Tunis, Tunisia

Background: Many methods have been reported for the surgical treatment of recurrent anterior temporomandibular dislocation. Most of these techniques are designed to limit the forward migration of the condylar head. The great number of surgical techniques experimented illustrates the difficulty to find a satisfactory method for the treatment of these recurrent dislocations. Objectives: We present a modification of Gosserez and Dautrey's surgical technique for the treatment of recurrent anterior temporomandibular joint dislocation. Methods: The surgical technique is described and its indications are discussed. Findings: With an impressive success rate, we believe that Bouguila and Khochtali's technique offers the best chance for long-term resolution of recurrent temporomandibular dislocation. Conclusions: Dislocation of the temporomandibular joint occurs when the mandibular condyle is displaced anteriorly beyond the articular eminence. There are multiple causes for its occurrence, and treatments range from relatively conservative methods to complex surgical intervention. Although <u>Reference</u>: 1. Bouguila J, <u>Khochtali</u> H. Treatment of recurrent temporomandibular dislocation by displacement of the zygomatic arch: A modification of Gosserez and Dautrey's technique. Rev Stomatol Chir Maxillofac Chir Orale. 2014 Dec;115(6):374-6.; 2. Bouguila J, Khochtali H. Treatment of recurrent temporomandibular dislocation by displacement of the zygomatic arch: Bouguila and Khochtali's technique. International Journal of Oral and Maxillofacial Surgery, Volume 44, Supplement 1, October 2015, Pages e192-e193

3:15 PM BREAK

TREATMENTS AND MODELS

4:00 PM Arthrocentesis followed by intraarticular autologous blood injection for the treatment of recurrent temporomandibular joint dislocation

Bayoumi AM, Al-Sebaei MO, Mohamed KM, Al-Yamani AO, Makrami AM

Temporomandibular joint (TMJ) dislocation is an excessive forward movement of the condyle beyond the articular eminence with complete separation of the articular surfaces and fixation in that position. This study was conducted to assess autologous blood injection to the TMJ for the treatment of chronic recurrent TMJ dislocation. Fifteen patients with bilateral chronic recurrent condylar dislocation were included in the study. Bilateral TMJ arthrocentesis was performed on each patient, followed by the injection of 2 ml of autologous blood into the superior joint compartment and 1 ml onto the outer surface of the joint capsule. Preoperative and postoperative assessment included a thorough history and physical examination to determine the maximal mouth opening, presence of pain and sounds, frequency of luxation, recurrence rate, and presence of facial nerve paralysis. Eighty percent of the subjects (12 patients) had a successful outcome with no further episodes of dislocation and required no further treatment at their 1-year follow-up, whereas three patients had recurrent dislocation as early as 2 weeks after treatment. Autologous blood injection is a safe, simple, and cost-effective treatment for chronic recurrent TMJ

dislocation.

4:15 PM Comparative Analysis of Histological & Radiological Findings in TMJ Ankylosis

Chandra S, Mehrotra D, Pandey R Department of Oral Pathology & Dept of Oral & Maxillofacial Surgery, King George's Medical University, Lucknow

Introduction: Classification of TMJ ankylosis by Sawhney, although widely accepted, does not incorporate histological characteristics. The objective of this study was to compare and correlate the histological findings with radiological ones across different grades of TMJ Ankylosis. <u>Materials & Methods</u>: 10 consenting patients visiting our outpatient clinic with a diagnosis of TMJ ankylosis were incorporated in this study. All had history of trauma and their mean age was 27.20±10.11. Panoramic radiographs and coronal section CT scans were obtained and used for Sawhney's Classification. The ankylosed mass was removed via Al-Kayat-Bramley incision and fixed in 10% buffered formalin and subsequently decalcified with 20% buffered EDTA. The specimens were then paraffin embedded and sectioned to 4 um thickness. Such processed sections were put to HE, Alcian blue/periodic acid –Schiff, Alizarin red, Mason trichrome staining and CD34 immunohistochemical staining. All sections were assessed using light microscopy. <u>Results</u>: Mucopolysaccharide content decreased, calcifications increased, osteogenic activity increased with increasing grades of TMJ ankylosis. The fibrous content decreased with increasing grade of TMJ ankylosis. Conclusion: CT imaging correlated well with histopathological characteristics. Integrating histo- pathogical findings into Sawhney's classification can help in better diagnosis and treatment planning.

4:30 PM Study protocol for bioengineered disc implants in Temporomandibular Joint (TMJ): experimental protocol of two exploratory Black Merino Sheep randomized controlled trials

Angelo DF, Salvado , Morouço P, Alves N, Gonzalez R, Monje F, Fernandes R, Ferreira J Faculty of Medicine of Lisbon

Background: There is no consensus concerning the therapeutic management of TMJ disc diseases. The appraisal of TMJ trials is hampered by differences in patients' characteristics and studied surgical procedures. No standard or predictive animal models for therapeutic studies in TMJ are available. Disc implants can be an efficacious complement in bioengineered joint reconstruction and animal models may offer the possibility to conduct informative preclinical studies. The main goal of these trials is to evaluate the feasibility of Black Merino Sheep as animal model for TMJ disc implant studies and to evaluate the histological and biomechanical articular changes induced by TMJ implant surgery. Methods/Design: The authors propose two sequential RCT in the Black Merino Sheep with blind outcome basement. In the first trial, 9 sheep will be randomized to three surgical bilateral procedures: discectomy group, discopexy group and sham surgery. In the second trial, 9 sheep will be randomized to three different TMJ discs implants. The primary outcome is the histological gradation of TMJ degeneration. Secondary outcomes are absolute masticatory time, rate masticatory time/masticatory cycle. masticatory kinetics, masticatory area and sheep weight. Conclusions: These will be the first trials using the Black Merino Sheep as the animal model to study the efficacy of disc implants in TMJ. Study design is innovative and will include a sham surgery group. Exploratory outcomes include histological analysis and new functional masticatory parameters. The proposed study methodology and the validation of such a large animal model for TMJ disorders may add important information for the development program of new therapeutic interventions for TMJ disc diseases.

4:45 PM BREAK

BIOMECHANICS - PART III

5:15 PM Finite element modeling of temporomandibular joint mechanics utilizing a proportional integral derivative feedback controller

Coogan J., Eliason T, Nicolella D Southwest Research Institute The masticatory system is a functionally complex system, where multiple muscle groups, the temporomandibular joint, jaw, and teeth interact in order to control essential functions of the mouth. The objective of this work was to develop a dynamic finite element simulation of the TMJ that utilizes a proportional-integral-derivative (PID)-based muscle controller to determine the muscle activations required for mastication of a food bolus. The finite element model was constructed from medical imaging data, and a food bolus was introduced between the teeth. Since the material properties of the food bolus are known, chewing force is directly related to the stress within the bolus. The PID feedback controller uses the stress within the food bolus as a target and modifies the muscle activations in order to achieve the desired target. The PID controller functions in real time, so that the muscle activations can react quickly to



changes in the desired target. This allows a relationship between the stresses within the temporomandibular joint soft tissues (disc and ligaments) and the chewing force to be determined. Differences between bilateral and unilateral chewing were also determined. This study utilized a PID feedback controller to simulate chewing in a finite element model of the TMJ.

5:30 PM

Loading of the TMJ while wearing a Mandibular Advancement Device (MAD)

Koolstra JH, Heidsieck DSP Academic Centre for Dentistry Amsterdam (ACTA)

Obstructive Sleep Apnea (OSA) is characterized by repetitive collapse of the upper airway during sleep, resulting in repeated arousals, fragmented sleep and excessive daytime sleepiness. If left untreated OSA can lead to serious complications including increased risk of cardiovascular disease, stroke, diabetes and depression. Mandibular Advancement Devices (MAD) are intraoral splints designed to force the mandible in a forward position during the sleep, resulting in an increased upper airway volume and thereby maintaining the airway patency during sleep. Although MADs are considered effective in the treatment of mild and moderate OSA, patients may complain of pain in the area of the TMJ depending on the degree of mandibular protrusion. Since the impact of wearing a MAD on TMJ function is disregarded, the present study analyses TMJ loading as a function of the amount of advancement. The analysis was performed by biomechanical analysis of the deformations and tensions in the cartilaginous structures of the TMJ during closing of the jaw. During closing the mandible was guided forward by structures mimicking a SomnoDent® type MAD. Furthermore, the amount of mandibular advancement was increased in steps of 1 mm. For analysis of the tensions both shear and principal stresses were taken into account.

5:45 PM Mandibular instantaneous axis of rotation after alloplastic total TMJ replacement

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<u>Objective</u>: The main goal of alloplastic total temporomandibular joint replacements (TJR) is the restoration of normal mandibular function. The helical axis (HA) is a mathematical model used to describe the motion of a rigid body, in particular its instantaneous rotation. Mandibular kinematics can be represented comprehensively by this method, clearly visualizing the irregularity of functional movements. Aim of this study was to analyze the HA pathways of subjects with alloplastic TJR. <u>Methods</u>: Mouth opening/closing cycles (n=3) of 15 patients (7 operated unilaterally, 8 bilaterally, 11 F, age 24-72) were tracked with an optoelectronic system. Following HA parameters were calculated for each opening phase and for each session: dCP_{max} : mandibular maximum rotation around the HA and the central points (CP) within the condyles on both sides; Φ_{max} : mandibular maximum rotation around the HA; $\Sigma \Theta_{ei/i}$ the mean global fluctuation of the HA spatial orientation. <u>Results</u>: dCP_{max} was 42.1 ± 23.3 mm in joints of unilaterally operated subjects, whereas in bilaterally operated subjects, it was 30.8 ± 8.6 mm. Overall value $0^{\circ} m_{max}$ and $\Sigma \Theta_{ei/i}$ for unilaterally operated patients were $25.0^{\circ}\pm8.1^{\circ}$ and $18.5^{\circ}\pm7.4^{\circ}$ respectively, and $19.0^{\circ}\pm4.8^{\circ}$ and $9.4^{\circ}\pm2.5^{\circ}$ for bilaterally operated patients. <u>Conclusion</u>: In subjects with alloplastic TJR, mandibular helical axis pathways show a large variability. In particular the global fluctuation of the HA differs considerably from the values found in literature for asymptomatic subjects.

6:00 PM CLOSING REMARKS