Annals of Biomedical Engineering, Vol. 35, No. 8, August 2007 (© 2007) pp. 1301–1311
DOI: 10.1007/s10439-007-9298-6

A Call to Action for Bioengineers and Dental Professionals: Directives for the Future of TMJ Bioengineering

MICHAEL S. DETAMORE,[1] KYRIACOS A. ATHANASIOU,[2] and JEREMY MAO[3]

[1]Department of Chemical & Petroleum Engineering, University of Kansas, 1530 W. 15th St., Room 4132, Lawrence, KS 66045-7609, USA; [2]Department of Bioengineering, Rice University, Houston, TX 77251, USA; and [3]College of Dental Medicine and Department of Biomedical Engineering, Columbia University, 630 W. 168 St. – PH7E, New York, NY 10032, USA

(*Received 6 November 2006; accepted 13 March 2007; published online 29 March 2007*)

Abstract—The world's first TMJ Bioengineering Conference was held May 25–27, 2006, in Broomfield, Colorado. Presentations were given by 34 invited speakers representing industry, academics, government agencies such as NIH, and private practice, which included surgeons, engineers, biomedical scientists, and patient advocacy leaders. Other attendees included documentary film makers and FDA officials. The impetus for the conference was that the field of TMJ research has been lacking continuity, with no open forum available for surgeons, scientists, and bioengineers to exchange scientific and clinical ideas and identify common goals, strengths, and capabilities. The goal was thus to plant the seeds for establishing a forum for multidisciplinary and interdisciplinary interactions. The collective wisdom and interactions brought about by a melting pot of these diverse individuals has been pooled and is disseminated in this article, which offers specific directives to bioengineers, basic scientists, and medical and dental professionals including oral and maxillofacial surgeons, pain specialists, orthodontists, prosthodontists, endocrinologists, rheumatologists, immunologists, radiologists, neurologists, and orthopaedic surgeons. A primary goal of this article was to attract researchers across a breadth of research areas to lend their expertise to a significant clinical problem with a dire need for new talent. For example, researchers with expertise in finite element modeling will find an extensive list of clinically significant problems. Specific suggestions for TMJ research were presented by the leading organizations for TMJ surgeons and TMJ patients, and further research needs were identified in a series of group discussions. The specific needs identified at the conference and presented here will be essential for those who endeavor to engage in TMJ research, especially in the areas of tissue engineering and biomechanics. Collectively, it is our hope that many of the questions and directives presented here find their way into the proposals of multidisciplinary teams across the world with new and promising approaches to diagnose, prevent and treat TMJ disorders.

Address correspondence to Michael S. Detamore, Department of Chemical & Petroleum Engineering, University of Kansas, 1530 W. 15th St., Room 4132, Lawrence, KS 66045-7609, USA. Electronic mail: detamore@ku.edu

Keywords—Temporomandibular joint, Tissue engineering, Biomechanics, Biology, Genomics, Proteomics, Finite element modeling.

INTRODUCTION

The temporomandibular joint (TMJ), or jaw joint, is one of the least studied joints in the body, despite the large patient population and the significant morbidity related to a plethora of TMJ disorders. Epidemiological surveys have reported that 20–25% of the population exhibit symptoms of temporomandibular joint disorders,[85] while patient studies show that 3–4% of the population seek treatment.[38] The most common TMJ disorders are pain dysfunction syndrome, internal derangement, arthritis and traumas.[38,72] Collectively, current treatments are not able to fully address severe TMJ disorders.[27,66,67]

The field of TMJ research has not been explored by the orthopaedic community, and most orthopaedic researchers are unfamiliar with the TMJ as an anatomical structure. The orthopaedic community has the Orthopaedic Research Society, where interaction of engineers, scientists and clinicians is commonplace. However, there has been no forum for those who are interested in TMJ bioengineering, and significant gaps have been evident between different groups within the field of TMJ research.[27] Accordingly, our objective was to organize a scientific conference, exclusively dedicated to the TMJ, by bringing together bioengineers, clinicians, and biomedical scientists to communicate with each other and with patients, patient advocacy groups, and government agencies.

The objectives of this conference were to (1) establish the needs and requirements of TMJ bioengineering with guidance from the clinical community, (2) obtain TMJ bioengineering suggestions from the patient population and patient advocacy leaders, (3) set a benchmark for current state-of-the-art treatments and scientific knowledge of the TMJ, and (4) explore ground breaking pathways for TMJ bioengineering. Bioengineering directives from the clinical community were offered in a keynote lecture by William Kirk, D.D.S., immediate past-president of the American Society of TMJ Surgeons (ASTMJS). In preparation for Dr. Kirk's address, the ASTMJS held a session at their annual meeting two months earlier where key areas of need from bioengineers were collectively identified. Directives from the patient community were presented by Terrie Cowley in a keynote lecture, drawn from her 20 years as president and co-founder of the TMJ Association (TMJA), the premiere TMJ patient advocacy organization in the country, and from three previous scientific meetings of the TMJA. As a TMJ patient herself, and with decades of first-hand experience with other TMJ patients, Ms. Cowley has a unique perspective of the challenges faced by severely afflicted TMJ patients. Dr. Kirk and Ms. Cowley are listed in Table 1 for their special lectures, along with Eleni Kousvelari, D.D.S., D.Sc., of the National Institute of Dental and Craniofacial Research (NIDCR), who provided an overview of TMJ research supported by the NIDCR, with an emphasis on tissue engineering research.

The TMJ Bioengineering Conference was divided into four separate sections: Tissue Engineering, Biomechanics, Clinical, and Biology. Following the invited lectures (Table 2) in each session, a discussion period led by the session co-chairs was held to identify the major issues in each area. These discussions, along with keynote directives, were arguably the most valuable aspect of the conference, with stimulating interchanges between surgeons, scientists, engineers, and others feeding off each other's ideas and energy, filling in many gaps with the depth and breadth of collective expertise in the room, and identifying the biggest and most urgent challenges ahead.

The purpose of this article is to disseminate the major findings of these sessions, and to forward on the directives from the clinical and patient communities, with the objective of attracting new talent to an area of medicine in dire need. The time is ripe for researchers in a plethora of disciplines to apply their *existing* research strengths to the burgeoning arena of TMJ research. The following sections, which outline specific needs as identified at the conference in each of the sessions, can be viewed as a "call to arms" for the bioengineering community.

DIRECTIVES FROM THE PATIENT COMMUNITY

Ms. Cowley opened the conference with a poignant presentation that reminded all in attendance of the reason for the need to advance TMJ research: the TMJ patients. Severely afflicted patients often endure feelings of hopelessness and despair, suffering from agonizing pain in every day activities most people take for granted such as eating, yawning, and talking; even acts of affection such as caressing the face and kissing can be painful and interfere with relationships.

The primary directive offered by Ms. Cowley was to engage in multidisciplinary efforts. She emphasized the need to bring together bioengineers with clinicians and scientists, to collaborate and thereby expedite solutions. She echoed a concern shared by many, which was that TMJ research should not be restricted to the dental community alone. Although the majority of TMJ disorders are clearly medical conditions, it is a grave concern that they are treated instead as dental problems, an error that is readily apparent even in health insurance policies. More specifically, TMJ research will require a more global analysis, with collaborative input from branches of medicine including pain, endocrinology, rheumatology, immunology, radiology, neurology, and orthopaedics.

A high priority directive from patients was understanding the basis of the gender paradox. It is widely known that more women are treated for TMDs than men, with reports of the female to male patient prevalence varying from 3:1 to 8:1,[23,38,85] if not higher. Is this an issue of estrogen receptors,[1,11,23,68] or female sex hormones playing a role in pain transmission?[62,105] Additional basic science research is warranted to investigate etiology in general and the role of gender in etiology in particular. Beyond the important issue of gender, the patient community offered specific

TABLE 1. Special invited lectures at the TMJ Bioengineering Conference.

Lecturer	Position*	Presentation Title
Terrie Cowley	President, TMJ Association	Directives from the TMJ Association (Keynote)
William Kirk, DDS	Immediate Past President, American Society of TMJ Surgeons	Directives from the American Society of TMJ Surgeons (Keynote)
Eleni Kousvelari, DDS, DSc	Acting Director, Center for Biotechnology and Innovation, NIDCR	NIDCR-supported TMJ tissue engineering

*In May, 2006.

TABLE 2. The four sessions of the TMJ Bioengineering Conference and invited lecturers for each session.

Tissue Engineering	Biomechanics	Clinical	Biology
Kristi Anseth, PhD	Mark Beatty, DDS, MS	Robert Christensen, DDS	Barry Berkovitz, FDS, PhD
Kyriacos Athanasiou, PhD	Ken Fischer, PhD	James Fricton, DDS, MS	Edward Guo, PhD
Michael Detamore, PhD	Luigi Gallo, PhD	Alan Glaros, PhD	Regina Landesberg, DMD, PhD
Julie Glowacki, PhD	Sue Herring, PhD	Louis Mercuri, DDS, MS	Richard LeBaron, PhD
Scott Hollister, PhD	Michael Liebschner, PhD	Peter Quinn, DMD, MD	Stephen Milam, DDS, PhD
Ching-Chang Ko, DDS, PhD	Lori Setton, PhD	Mark Wong, DDS	Dorrit Nitzan, DMD
Helen Lu, PhD	Eiji Tanaka, DDS, PhD		Paulette Spencer, DDS, PhD
Jeremy Mao, DDS, PhD			
David Mills, PhD			
Anthony Ratcliffe, PhD			
Charles Vacanti, MD			

directives for TMJ implant design. An emphasis was placed on biomaterial selection, given the fiasco with alloplastic TMJ disc implants that still haunts patients today.[84,109]

The TMJ literature is replete with evidence of the detrimental effects of these implants, namely Proplast-Teflon (Vitek Inc, Houston, TX) and Silastic (Dow Corning Corp, Midland, MI), summarized well in a recent report by Mercuri and Giobbie-Hurder.[66] In brief, TMJ disc replacement implants enjoyed popularity in the 1970s and 1980s, but by the early 1990s, numerous publications had surfaced with reports of complications,[81,84,103] leading to a safety alert and a public health advisory from the FDA urging surgeons to discontinue using these implants.[18,36,39] In 1992, it was argued by participants of an American Association of Oral and Maxillofacial Surgeons (AAOMS) workshop that use of Proplast-Teflon implants should be discontinued.[80] Although these devices are no longer used, a population of patients affected by the failure of these implants continues to suffer. The problem with these particular implants was that they were prone to tears, cracks, perforation, and fragmentation,[100] leading to foreign body giant cell reactions, pain, osteoarthritis, bone resorption, cranial perforation, and/or immunologic dysfunction.[109] Understandably, it is very important to the TMJ patient community that the TMJ research community understands how and why this happened so that something like this never happens again.

In addition, a concern pertaining to heat transfer was addressed, which was that some patients have complained of a painfully cold feeling with alloplastic devices in extremely cold weather. Mathematical heat transfer models or empirical approximations could quantify the degree to which a biomaterial selection would affect the temperature of adjacent tissues. Three additional directives from the patient community were to develop computer models of the joint to better understand joint motion and forces (also the primary directive from surgeons, below), to find ways to reduce or eliminate pain, and to determine whether drilling and pounding during surgery has any effect on the brain.

DIRECTIVES FROM THE CLINICAL COMMUNITY

The TMJ Bioengineering Conference was a landmark event in the extent to which bioengineers and basic scientists were able to interact with leaders in TMJ surgery. Moreover, the authoritative body in TMJ surgery, the ASTMJS, was able to directly communicate for the first time their clinical needs to engineers and scientists. The significance here is that a major stride in achieving continuity in TMJ research was made, and hopefully we are now starting to row in the same direction, which is to the overall benefit of TMJ research progress, which ultimately will translate to new hope and better technology for the millions of TMJ patients.

Dr. Kirk emphasized a historical understanding of TMJ disorders, referring to when Gysi[40] in 1921 proposed a model of TMJ forces in a time where it was generally taught that there was no loading in the TMJ. It was not until Hylander's[47,48] work, published in the 1970s, that loading in the TMJ became more generally accepted. Of course, it is now commonly known that the TMJ is a loaded joint, and it was no surprise to see that the ASTMJS put a heavy emphasis on biomechanics, particularly with modeling forces in the joint. There was little interest in tracking jaw motion in and of itself, except as a necessary ingredient in force models. In fact, the TMJ surgeons collectively expressed great interest in quantifying forces associated with translation, chewing, and clenching. They would like to see distinctions made in the *locations* of various forces, which may be correlated to clinical observations, with one key example being the observation of pathology affecting the lateral region of the disc to a greater extent.[107] Patient-specific force models would be highly valuable for comparing pre- and post-operative conditions, and to obtain data from people with healthy TMJs as a baseline group. It was offered that biomechanical models should include muscle forces, pressure distribution in the synovial fluid, and the dentition. Moreover, the disc should be viewed as part of a larger whole, including all peripheral attachments (retrodiscal tissue, joint capsule, etc.). Specific comparisons desired by TMJ surgeons include pathological vs. normal anatomy, comparisons of facial types,[12,21,26,69,77] and comparisons of various dentitions. Moreover, force models are needed to address the following specific clinical questions: How do dental appliances (e.g., all types of splints in various situations) affect TMJ biomechanics? Is an osteophyte a cause or effect in pathogenesis, or both? Are lateral impingements the result of lateral fossa rim hyperplasias, osteophytes of the lateral condyle, or both, and how does this happen? How do the lateral disc/capsule attachments affect TMJ biomechanics?[17] More specifically, does internal derangement begin with rupture of the lateral capsular attachments L1 and L2? Given that slight deviations from ''normal'' anatomy do not necessarily indicate a pathology,[71] does the disruption of anatomical congruity necessarily imply a problem? Assuming the emphasis is indeed on establishing functional congruency, what are the biomechanics associated with the process of heterotopic bone moving the mandible out of position? Referring to the age-old question of the relationship between whiplash and TMDs,[33,50,64,70] can bioengineers shed new light on the actual forces experienced in whiplash? More specifically, what is the significance of extension/flexion injuries of the neck and TMJ and the magnitude of condylar acceleration in these instances? More generally speaking, what threshold forces in various situations are required to detach, break, or permanently deform tissues?

Bioengineers worldwide have made major strides in modeling the TMJ, with major contributions from groups in Japan,[78,89–98] the Netherlands,[14–16,53–60,102] Spain,[73–76] and Switzerland.[34,35,61] An excellent review of TMJ biomechanical models was provided by Koolstra[53] in 2003, and significant progress has been made since then by the aforementioned groups and others.[22,30,31,46,51,52] Now, with clinical directives specifically delineated above, and the computational tools in place, these groups and other bioengineers with modeling capabilities are poised to answer these questions of considerable clinical significance.

In addition to biomechanics, there were a handful of areas where TMJ surgeons requested further research. Among these were hypersensitivity to implant materials, neuromuscular control, and the pathophysiology and genomics behind the etiology of TMJ disorders. With regard to tissue engineering, the general feeling among surgeons was that an engineered disc would probably be the most important tissue, followed by the condyle.

TISSUE ENGINEERING SESSION

Although TMJ tissue engineering[27,37,104] is a relatively new field with only a handful of tissue engineering studies available for the TMJ disc[6–10,13,28,29,41,79,86,99] and mandibular condyle,[2–5,24,25,32,44,45,63,82,83,101,106,108] the number of researchers in the field is growing exponentially as investigators in related fields are discovering a new application for their existing orthopaedic tissue engineering strengths. With more researchers joining the TMJ tissue engineering effort, it is crucial that they are aware of TMJ-specific concerns and understand the pressing questions that exist today. The tissue engineering session, co-chaired by Anthony Ratcliffe, Ph.D. and Louis Mercuri, D.D.S., M.S., identified several important challenges and questions in the discussion.

Among concerns raised were attachment, integration, metaplasia, angiogenesis, patient age, developing a marketable product, and creating a condyle-disc composite scaffold. Due to the practical difficulty (or impossibility, depending on individual opinions) of surgically implanting and attaching a TMJ disc alone, it was proposed that attaching an engineered disc-condyle composite would be the most logical approach for implanting an engineered disc. However, the issue of attaching the condyle to the ascending ramus and assimilating with surrounding attachment tissues still remains. Moreover, the attachment will need to resist early shear and torque during loading, given that TMJ surgeons advocate mobilizing the jaw early after surgery. Metaplasia and angiogenesis were viewed by some as being bigger clinical concerns than attachments, as even if the attachment issue is solved, it will be imperative to ensure that the cartilage does not convert to bone *in vivo* and that the bone is infiltrated with a vascular supply. Marketing is a realistic limitation, as the number of patients requiring engineered TMJ implants will likely not match the numbers of joints in the orthopaedic community such as the hip and knee, a challenge currently faced by manufacturers of alloplastic reconstruction devices. Eventually, surrounding tissues will also become the focus of future tissue engineering efforts. Basic characterization (biochemical, cellular, and biomechanical) tests will first be required to understand the functions of these tissues.

Perhaps the foremost example is the retrodiscal tissue, which sustains tremendous damage in advanced cases of internal derangement,[49] although the fossa-eminence and joint capsule may also likely be candidates in the future.

The session left the research world with the following questions: What are the best factors to use for chondrogenic and osteogenic differentiation of stem cells? Would it help to have osteoinductive factors on the surface of the implant? How can we facilitate early osteointegration? Is there anything we can do about heterotopic bone formation? And finally, what is the best animal model?

The invited speakers (Tables 1 and 2) pooled together their ideas for TMJ research needs prior to the conference, which were organized into each of the four session areas for conference participants. Several additional questions in TMJ tissue engineering not mentioned above were gleaned from the invited speakers. Many of these questions were based on comparisons between TMJ and orthopaedic applications. For example, which advances in orthopedic biomaterials can be applied to the TMJ? More specifically, can we adapt tissue engineering knowledge from hyaline cartilage to TMJ fibrocartilage? As a follow-up, do we even want autologous cells obtained from the TMJ, or would mature autologous cells from other locations or stem cells be more desirable? Other questions were more general; for example, what are the best combination of bioactive signals, scaffold material and scaffold design to replicate the bone/cartilage interface of the mandibular condyle? Which goal should we target first, developing tissues for TMJ repair or replacement? Finally, what are the biological and biomechanical constraints that we will need to identify and understand before we can produce functional TMJ tissues?

BIOMECHANICS SESSION

Co-chairs William Kirk, D.D.S. and Luigi Gallo, Ph.D. led this session, which provided a basis for contemporary knowledge of tissue properties and mechanical models for the TMJ. The clinical directives above identified several excellent points for the future of biomechanics research. As with the tissue engineering session, valuable input was provided by invited speakers to identify needs for TMJ biomechanics research, which will be the focus of this section. For the sake of brevity, and given the thorough analysis of biomechanics above, only salient input not already presented will be offered here.

Research needs identified include basic mechanical property data for TMJ tissues (ideally, human *in vivo* data), a better understanding of dynamic loading of the TMJ, computational models to predict thresholds for TMJ injury (plastic deformation and failure of tissues) in specific situations and to establish design requirements for tissue engineered constructs, calculations of TMJ disc loads with finite element models, and functional testing of tissue-engineered TMJ cartilage. In addition, a need was identified for more comprehensive models of the TMJ that use kinematic activation to examine pathological development.

CLINICAL SESSION

Peter Quinn, D.M.D., M.D. and James Fricton, D.D.S., M.S. chaired the clinical session and discussion. The number one concern raised in this discussion was the lack of TMJ clinical specialists.[65] One suggestion was to encourage the American Association of Oral and Maxillofacial Surgeons (AAOMS) to require TMJ surgery in oral and maxillofacial surgery (OMS) residency programs, or for the National Institutes of Health (NIH) or the Oral and Maxillofacial Surgery Foundation (OMSF) to offer residency stipends for OMS residents performing TMJ research and learning TMJ surgery. Certainly a new crop of skilled surgeons will be needed to implant engineered tissues as they become available in the decades ahead. If we could identify a single message to federal funding agencies, it would be to establish fellowships in TMJ surgery. Other salient points from this discussion were a need for a better understanding for approaching the problem of heterotopic bone formation, for better science to enable surgeons to not only repair but also to treat the underlying condition, and for breaking down barriers to bring in orthopaedic surgeons. Perhaps a large-scale effort to coordinate with orthopaedic surgeons could be to encourage TMJ surgeons and researchers to attend and present at meetings of the Orthopaedic Research Society.

Clinical research needs identified by the invited speakers focused on pain and implants. With regard to pain, a need was identified for objectively evaluating the efficacy of surgical and non-surgical treatments for TMJ pain. It was also advised that the most likely sources of clinically observed TMJ pain should be clearly identified. With regard to implants, clinicians have identified several current challenges that tissue engineers are highly advised to consider in their design, including biocompatibility, integration, immediate mobility, wear, longevity, hypersensitivity, biofilm infections, cost, insurance reimbursement, market demand, and replacing failed implants from a previous operation.[66] Another current concern among the three available total joint replacement options is the use of both stock and custom implants with predictable success rates. More generally, we must understand the outcomes of all TMJ implants in a controlled comparative manner, and to evaluate the biological characteristics of failed implants compared to controls to determine mechanism of implant failure. Fortunately, with the advent of the TMJ Implant Registry and Repository (TIRR), these outcomes and evaluations may soon become a reality. The final note for needs in clinical research pertains to imaging, where improved resolution of dynamic imaging is needed to permit the study of changes in human tissue microstructure and joint function in TMJ disorders.

BIOLOGY SESSION

The biology session was co-chaired by Stephen Milam, D.D.S., Ph.D. and Paulette Spencer, D.D.S., Ph.D. The important topic of animal model selection was addressed, with the general consensus being that the pig is probably the best animal model for biomechanics, given the high cost of primate research. The literature supports this contention, based on pigs and humans having the same components and a similar gross morphology, and the same size and shape of each structure, including the disc.[19,20,42,43,87,88] The primary differences between pig and human TMJs are the retrodiscal tissue, which is fibrous in the pig and vascular in the human, and the zygomatic arch, which extends inferiorly over the lateral pole of the condyle in pigs, making pig TMJs less accessible in surgery. With regard to mechanistic studies, the use of smaller animals was supported, e.g., rats and mice for pain studies. The animal model for tissue engineering studies was less clear, although pigs in the long-term will likely be the best models.

Creative thinking led to some interesting ideas, such as the possibility of a biomaterial construct or cell therapy that could release factors to directly modify the source of the TMJ disorder, the notion of looking for answers in the synovial fluid, and the notion of a genetically engineered "smart" tissue with genes that are activated only when the appropriate signals such as disease or inflammation are detected. The need for genomics and proteomics was emphasized, as was improving biological approaches to diagnostics. The need for a systems approach was reiterated, emphasizing the need for experts from a breadth of medical specialties in addition to experts in dental sciences such as orthodontics and oral and maxillofacial surgery. Finally, the need for understanding and improving joint lubrication was emphasized, further supporting the need for interaction with the orthopaedic community.

The invited speakers identified two additional research needs. The first was a directive for immunology research, which was to identify what pre-operative immunologic tests can assist in predicting foreign body reactions to implant materials. The other was a directive for bone biologists, which was to identify how the mechanobiology of bone influences TMJ disorders.

DISCUSSION

The overall feeling at the conclusion of the world's first TMJ Bioengineering Conference was very positive. For many, this was the first opportunity to meet directly with bioengineers or surgeons to discuss TMJ research, and for some others, this was their first exposure to the TMJ. Together, this diverse group collectively offered a tremendous depth and breadth of TMJ knowledge, which ultimately led to the enormous productivity of the group discussions and the identification of the biggest concerns and needs in contemporary TMJ research. Several details were presented in the preceding sections, and here we consolidate these research initiatives into the most salient points, the highest priority needs for the future of TMJ research (Table 3).

In tissue engineering, attaching tissues was a major concern. At this stage, it appears that a composite condyle plus disc will be the best route to a long-term solution. In the long-term, an industrial vision must also be taken into account, including marketing, profit,

TABLE 3. The highest priority needs for TMJ research identified at the TMJ Bioengineering Conference.

Tissue Engineering	Biomechanics	Clinical	Biology
Attachment of engineered tissues (condyle + disc?)	Comparing normal vs. pathological cases	More TMJ specialists, especially from oral & maxillofacial surgery	Understanding etiology
Commercial success	Effects of osteophytes, whiplash	Collaborations with orthopaedic surgeons (ORS)	Understanding gender paradox
Identification of tissue function	Patient specific data		Incorporating genomics and proteomics
Angiogenesis and preventing metaplasia	Correlating macroscopic forces to tissue failure		

ORS = Orthopaedic Research Society.

and regulatory compliance, as well as avoiding complications that TMJ surgeons have identified with current alloplastic TMJ replacements. Other major concerns were identifying the functions of related tissues, their mechanical properties, and ultimately incorporating them in some capacity in the overall approach, either as an anchor for the structures of the tissue engineered joint or as part of these structures themselves. TMJ surgeons emphasized that for rheumatoid arthritis and heterotopic bone patients, tissue engineering will not be a feasible treatment alternative until those underlying diseases are treated and cured, which is also a concern for orthopaedic surgeons. Finally, metaplasia and vascularization of engineered constructs are important considerations, and given that these concerns are also shared by the orthopaedic tissue engineering community, this is a great example for the need for cross-pollination of ideas between the orthopaedic and craniofacial tissue engineers.

Biomechanical modeling was a clear priority for TMJ surgeons, which would allow investigation of specific occurrences such as the effect of an osteophyte on the condyle or the forces associated with and ramifications emanating from whiplash in car accidents. Computer models are needed specifically for comparing normal vs. pathological cases, determining what conditions and forces lead to tissue failure, and providing patient-specific data. For these goals to be realized, it is imperative that reliable material property data continue to be obtained for TMJ tissues, including time-dependent data.

The clinical side of managing TMJ disorders is suffering from a considerable man-power problem—there is a dire need for TMJ specialists. Not only are oral and maxillofacial surgeons trained in TMJ surgery needed to work together closely with tissue engineers and to implant engineered joints, they are needed to improve upon and pass on the wealth of knowledge possessed by a large number of seasoned TMJ surgeons that are approaching retirement in the coming decade. Moreover, the new generation of TMJ surgeons will be expected to have a profound appreciation for scientific methods to assist bioengineers and to help develop more rigorous treatment regimens for TMJ disorders by building on the momentum of groups such as the American Society of TMJ Surgeons (ASTMJS). As alluded to earlier, there is something of a disconnect between oral surgeons and orthopaedic surgeons. All other joints fall under the umbrella of orthopaedic research, so why has the TMJ been excluded? It is time for the TMJ to be included on the orthopaedic radar, for the exchange of ideas not only between TMJ surgeons and orthopaedic surgeons, but also between surgeons and bioengineers and basic scientists. It is our hope that the Orthopaedic Research Society will be supportive in this endeavor by expanding the content of TMJ research at its meetings, which in turn TMJ researchers should support by staying up to date with the orthopaedic research at the conference. Lastly, improved imaging capabilities will be of tremendous value to practicing clinicians in diagnosing and treating TMJ disorders.

TABLE 4. Interconnectedness of the four major categories.

Category	Biomechanics	Clinical	Biology
Tissue engineering	Tissue engineers must understand the TMJ biomechanical environment and the function of specific tissues, and perform appropriate biomechanical evaluation. Biomechanical models can predict implant performance.	Tissue engineers must be cognizant of prior success and failures with TMJ implants, borrow from orthopaedic tissue engineering, and consider clinical needs and market demands. Clinicians will need new and improved treatment options for severely afflicted TMJ patients.	Tissue engineered products may be doomed to failure in certain cases unless underlying degenerative processes are identified and remedied.
Biomechanics		Researchers in biomechanics must understand the needs of the clinical community to design models of clinical significance. Clinicians require an understanding of biomechanical implications of treatments and traumas.	Identifying structure-function relationships of TMJ tissues and elucidating biological responses to mechanical forces will be invaluable to tissue engineers and important to clinical application.
Clinical			A better understanding of etiology, the gender paradox, and disease mechanisms will enable clinicians to better prevent, diagnose, and treat TMJ disorders.

One of the most crucial needs from the biological sciences is the understanding of the etiology of TMJ disorder pathogenesis. Although colleagues in biomechanics can shed light on traumatic events, a large fraction of TMJ disorder causes are currently unexplained. Not only will understanding the etiology of TMJ disorders help to prevent them from occurring, it will also help to prevent an engineered joint from befalling the same fate as the joint it replaced. Another major concern is understanding why women are predominately affected. Unlocking this mystery may lend to new insights into strategies for treating TMJ disorders.

One cannot overemphasize the importance of highlighting the interconnectedness of the major categories presented heretofore: tissue engineering, biomechanics, clinical practice, and biology (Table 4). In the past, gaps were evident between these communities,[27] and there is new hope that breaking down these barriers will be a catalyst in accelerating the progress of TMJ research in the coming years, especially as new talent in drawn to the field. Continuing the cross-talk between specialties and forming interdisciplinary and multidisciplinary partnerships will be essential in moving the field to unparalleled new heights.

Undoubtedly, the TMJ Bioengineering Conference posed more questions than it answered, but as all researchers understand, identifying the right questions is arguably the most important ingredient in scientific progress. Some of these questions have now been identified here, and can serve as a guide for TMJ researchers for many years to come. It is a sincere hope that continued TMJ Bioengineering Conferences will be held to monitor progress and to ensure that surgeons, scientists, and bioengineers continue working as a united community of researchers for the ultimate benefit of the TMJ patient.

ACKNOWLEDGMENTS

First and foremost, we thank the invited speakers (Tables 1 and 2) for their contributions, which in addition to presentations include identifying research needs, issuing directives to bioengineers and scientists, and leading the discussions. We gratefully acknowledge funding from the National Institutes of Health (NIDCR and NIBIB), grant number #1 R13 DE017286-01, which made the TMJ Bioengineering Conference possible. In particular, we thank Dr. Eleni Kousvelari at the NIDCR for her support throughout the entire process, from concept to conclusion. We extend a special thanks to our platinum level sponsors: Bose-EnduraTEC, Rice University, the University of Kansas Center for Research, Inc., and the University of Kansas School of Engineering. We also acknowledge our gold level sponsors: the NIDCR's TMJ Implant Registry and Repository (TIRR), Instron, and Walter Lorenz Surgical, Inc.; and our silver level sponsors: TMJ Concepts and Synthasome. We acknowledge and appreciate endorsements from the Biomedical Engineering Society (BMES), the American Society of TMJ Surgeons (ASTMJS), and the American Society of Biomechanics (ASB). Finally, we appreciate the assistance in publicity provided by the TMJ Association, the International Association for Dental Research (IADR), American Academy of Orofacial Pain (AAOP), American Association of Oral and Maxillofacial Surgeons (AAOMS), and Cranio: The Journal of Craniomandibular Practice.

REFERENCES

[1]Abubaker, A. O., W. Arslan, and G. C. Sotereanos. Estrogen and progesterone receptors in the temporomandibular joint disc of symptomatic and asymptomatic patients. *J. Oral. Maxillofac. Surg*. 49:111–112, 1991.

[2]Abukawa, H., H. Terai, D. Hannouche, J. P. Vacanti, L. B. Kaban, and M. J. Troulis. Formation of a mandibular condyle in vitro by tissue engineering. *J. Oral. Maxillofac. Surg*. 61:94–100, 2003.

[3]Alhadlaq, A., J. H. Elisseeff, L. Hong, C. G. Williams, A. I. Caplan, B. Sharma, R. A. Kopher, S. Tomkoria, D. P. Lennon, A. Lopez, and J. J. Mao. Adult stem cell driven genesis of human-shaped articular condyle. *Ann. Biomed. Eng*. 32:911–923, 2004.

[4]Alhadlaq, A., and J. J. Mao. Tissue-engineered neogenesis of human-shaped mandibular condyle from rat mesenchymal stem cells. *J. Dent. Res*. 82:951–956, 2003.

[5]Alhadlaq, A., and J. J. Mao. Tissue-engineered osteochondral constructs in the shape of an articular condyle. *J. Bone. Joint. Surg. Am*. 87:936–944, 2005.

[6]Allen, K. D., and K. A. Athanasiou. Growth factor effects on passaged TMJ disk cells in monolayer and pellet cultures. *Orthod. Craniofac. Res*. 9:143–152, 2006.

[7]Allen, K. D., and K. A. Athanasiou. Tissue engineering of the TMJ disc: a review. *Tissue Eng*. 12:1183–1196, 2006.

[8]Almarza, A. J., and K. A. Athanasiou. Seeding techniques and scaffolding choice for tissue engineering of the temporomandibular joint disk. *Tissue Eng*. 10:1787–1795, 2004.

[9]Almarza, A. J., and K. A. Athanasiou. Effects of initial cell seeding density for the tissue engineering of the temporomandibular joint disc. *Ann. Biomed. Eng*. 33:943–950, 2005.

[10]Almarza, A. J., and K. A. Athanasiou. Evaluation of three growth factors in combinations of two for temporomandibular joint disc tissue engineering. *Arch. Oral. Biol*. 51:215–221, 2006.

[11]Aufdemorte, T. B., J. E. Van Sickels, M. F. Dolwick, P. J. Sheridan, G. R. Holt, S. B. Aragon, and G. A. Gates. Estrogen receptors in the temporomandibular joint of the baboon (Papio cynocephalus): an autoradiographic study. *Oral. Surg. Oral. Med. Oral. Pathol*. 61:307–314, 1986.

[12]Baccetti, T., A. Antonini, L. Franchi, M. Tonti, and I. Tollaro. Glenoid fossa position in different facial types: a cephalometric study. *Br. J. Orthod.* 24:55–59, 1997.
[13]Bean, A. C., A. J. Almarza, and K. A. Athanasiou. Effects of ascorbic acid concentration on the tissue engineering of the temporomandibular joint disc. *Proc. Inst. Mech. Eng. [H]* 220:439–447, 2006.
[14]Beek, M., J. H. Koolstra, and T. M. van Eijden. Human temporomandibular joint disc cartilage as a poroelastic material. *Clin. Biomech. (Bristol, Avon)*. 18:69–76, 2003.
[15]Beek, M., J. H. Koolstra, L. J. van Ruijven, and T. M. van Eijden. Three-dimensional finite element analysis of the human temporomandibular joint disc. *J. Biomech.* 33:307–316, 2000.
[16]Beek, M., J. H. Koolstra, L. J. van Ruijven, and T. M. van Eijden. Three-dimensional finite element analysis of the cartilaginous structures in the human temporomandibular joint. *J. Dent. Res.* 80:1913–1918, 2001.
[17]Ben Amor, F., P. Carpentier, J. M. Foucart, and A. Meunier. Anatomic and mechanical properties of the lateral disc attachment of the temporomandibular joint. *J. Oral. Maxillofac. Surg.* 56:1164–1167, 1998.
[18]Benson, J. S. Public health advisory on Vitek Proplast temporomandibular joint implants. 1991: Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health.
[19]Berg, R. Contribution to the applied and topographical anatomy of the temporomandibular joint of some domestic mammals with particular reference to the partial resp. total resection of the articular disc. *Folia Morphol.* 21:202–204, 1973.
[20]Bermejo, A., O. Gonzalez, and J. M. Gonzalez. The pig as an animal model for experimentation on the temporomandibular articular complex. *Oral. Surg. Oral. Med. Oral. Pathol.* 75:18–23, 1993.
[21]Bishara, S. E., and J. R. Jakobsen. Longitudinal changes in three normal facial types. *Am. J. Orthod.* 88:466–502, 1985.
[22]Buranastidporn, B., M. Hisano, and K. Soma. Effect of biomechanical disturbance of the temporomandibular joint on the prevalence of internal derangement in mandibular asymmetry. *Eur. J. Orthod.* 28:199–205, 2006.
[23]Campbell, J. H., M. S. Courey, P. Bourne, and C. Odziemiec. Estrogen receptor analysis of human temporomandibular disc. *J. Oral. Maxillofac. Surg.* 51:1101–1105, 1993.
[24]Chen, F., S. Chen, K. Tao, X. Feng, Y. Liu, D. Lei, and T. Mao. Marrow-derived osteoblasts seeded into porous natural coral to prefabricate a vascularised bone graft in the shape of a human mandibular ramus: experimental study in rabbits. *Br. J. Oral. Maxillofac. Surg.* 42:532–537, 2004.
[25]Chen, F., T. Mao, K. Tao, S. Chen, G. Ding, and X. Gu. Bone graft in the shape of human mandibular condyle reconstruction via seeding marrow-derived osteoblasts into porous coral in a nude mice model. *J. Oral. Maxillofac. Surg.* 60:1155–1159, 2002.
[26]Collett, A. R., and V. C. West. Terminology of facial morphology in the vertical dimension. *Aust. Dent. J.* 38:204–209, 1993.
[27]Detamore, M. S., and K. A. Athanasiou. Motivation, characterization, and strategy for tissue engineering the temporomandibular joint disc. *Tissue Eng.* 9:1065–1087, 2003.
[28]Detamore, M. S., and K. A. Athanasiou. Evaluation of three growth factors for TMJ disc tissue engineering. *Ann. Biomed. Eng.* 33:383–390, 2005.
[29]Detamore, M. S., and K. A. Athanasiou. Use of a rotating bioreactor toward tissue engineering the temporomandibular joint disc. *Tissue Eng.* 11:1188–1197, 2005.
[30]Donzelli, P. S., L. M. Gallo, R. L. Spilker, and S. Palla. Biphasic finite element simulation of the TMJ disc from in vivo kinematic and geometric measurements. *J. Biomech.* 37:1787–1791, 2004.
[31]van Essen, N. L., I. A. Anderson, P. J. Hunter, J. Carman, R. D. Clarke, and A. J. Pullan. Anatomically based modelling of the human skull and jaw. *Cells Tissues Organs.* 180:44–53, 2005.
[32]Feinberg, S. E., S. J. Hollister, J. W. Halloran, T. M. Chu, and P. H. Krebsbach. Image-based biomimetic approach to reconstruction of the temporomandibular joint. *Cells Tissu. Organs.* 169:309–321, 2001.
[33]Ferrari, R., and M. S. Leonard. Whiplash and temporomandibular disorders: a critical review. *J. Am. Dent. Assoc.* 129:1739–1745, 1998.
[34]Gallo, L. M. Modeling of temporomandibular joint function using MRI and jaw-tracking technologies–mechanics. *Cells Tissues Organs.* 180:54–68, 2005.
[35]Gallo, L. M., J. C. Nickel, L. R. Iwasaki, and S. Palla. Stress-field translation in the healthy human temporomandibular joint. *J. Dent. Res.* 79:1740–1746, 2000.
[36]Gelb, L. N. FDA notifies physicians and patients about risks of TMJ implants. *FDA Med. Bull.* 21:2–3, 1991.
[37]Glowacki, J. Engineered cartilage, bone, joints, and menisci. Potential for temporomandibular joint reconstruction. *Cells Tissues Organs.* 169:302–308, 2001.
[38]Gray, R. J. M., S. J. Davies, and A. A. Quayle. Temporomandibular Disorders: A Clinical Approach. London: British Dental Association, 1995.
[39]Gundaker, W. E. FDA safety alert: Serious problems with Proplast-coated TMJ implant. Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, 1990.
[40]Gysi, A. Studies on the leverage problem of the mandible. Dent Digest. 27:74–84, 144–150, 203–208, 1921.
[41]Hanaoka, K., E. Tanaka, T. Takata, M. Miyauchi, J. Aoyama, N. Kawai, D. A. Dalla-Bona, E. Yamano, and K. Tanne. Platelet-derived growth factor enhances proliferation and matrix synthesis of temporomandibular joint disc-derived cells. *Angle Orthod.* 76:486–492, 2006.
[42]Herring, S. W. Animal models of temporomandibular disorders: how to choose. In: Temporomandibular Disorders and Related Pain Conditions, edited by B. J. Sessle, P. S. Bryant, and R. A. Dionne . Seattle: IASP Press, 1995, pp. 323–328.
[43]Herring, S. W., J. D. Decker, Z. J. Liu, and T. Ma. Temporomandibular joint in miniature pigs: anatomy, cell replication, and relation to loading. *Anat. Rec.* 266:152–166, 2002.
[44]Hollister, S. J., R. A. Levy, T. M. Chu, J. W. Halloran, and S. E. Feinberg. An image-based approach for designing and manufacturing craniofacial scaffolds. *Int. J. Oral. Maxillofac. Surg.* 29:67–71, 2000.
[45]Hollister, S. J., C. Y. Lin, E. Saito, C. Y. Lin, R. D. Schek, J. M. Taboas, J. M. Williams, B. Partee, C. L. Flanagan, A. Diggs, E. N. Wilke, G. H. Van Lenthe, R. Muller, T. Wirtz, S. Das, S. E. Feinberg, and P. H. Krebsbach. Engineering craniofacial scaffolds. *Orthod. Craniofac. Res.* 8:162–173, 2005.

[46]Hu, K., R. Qiguo, J. Fang, and J. J. Mao. Effects of condylar fibrocartilage on the biomechanical loading of the human temporomandibular joint in a three-dimensional, nonlinear finite element model. *Med. Eng. Phys.* 25:107–113, 2003.
[47]Hylander, W. L. The human mandible: lever or link?. *Am. J. Phys. Anthropol.* 43:227–242, 1975.
[48]Hylander, W. L. Experimental analysis of temporomandibular joint reaction force in macaques. *Am. J. Phys. Anthropol.* 51:433–456, 1979.
[49]Isacsson, G., A. Isberg, A. S. Johansson, and O. Larson. Internal derangement of the temporomandibular joint: radiographic and histologic changes associated with severe pain. *J. Oral. Maxillofac. Surg.* 44:771–778, 1986.
[50]Kirk, W. S. Jr. Whiplash as a basis for TMJ dysfunction. *J. Oral. Maxillofac. Surg.* 50:427–428, 1992.
[51]Kofod, T., P. M. Cattaneo, M. Dalstra, and B. Melsen. Three-dimensional finite element analysis of the mandible and temporomandibular joint during vertical ramus elongation by distraction osteogenesis. *J. Craniofac. Surg.* 16:586–593, 2005.
[52]Kofod, T., P. M. Cattaneo, and B. Melsen. Three-dimensional finite element analysis of the mandible and temporomandibular joint on simulated occlusal forces before and after vertical ramus elongation by distraction osteogenesis. *J. Craniofac. Surg.* 16:421–429, 2005.
[53]Koolstra, J. H. Number crunching with the human masticatory system. *J. Dent. Res.* 82:672–676, 2003.
[54]Koolstra, J. H., and T. M. van Eijden. Application and validation of a three-dimensional mathematical model of the human masticatory system in vivo. *J. Biomech.* 25:175–187, 1992.
[55]Koolstra, J. H., and T. M. van Eijden. Biomechanical analysis of jaw-closing movements. *J. Dent. Res.* 74:1564–1570, 1995.
[56]Koolstra, J. H., and T. M. van Eijden. The jaw open-close movements predicted by biomechanical modelling. *J. Biomech.* 30:943–950, 1997.
[57]Koolstra, J. H., and T. M. van Eijden. Three-dimensional dynamical capabilities of the human masticatory muscles. *J. Biomech.* 32:145–152, 1999.
[58]Koolstra, J. H., and T. M. van Eijden. Combined finite-element and rigid-body analysis of human jaw joint dynamics. *J. Biomech.* 38:2431–2439, 2005.
[59]Koolstra, J. H., and T. M. van Eijden. Prediction of volumetric strain in the human temporomandibular joint cartilage during jaw movement. *J. Anat.* 209:369–380, 2006.
[60]Koolstra, J. H., M. Naeije, and T. M. van Eijden. The three-dimensional active envelope of jaw border movement and its determinants. *J. Dent. Res.* 80:1908–1912, 2001.
[61]Krebs, M., L. M. Gallo, R. L. Airoldi, and S. Palla. A new method for three-dimensional reconstruction and animation of the temporomandibular joint. *Ann. Acad. Med. Singapore* 24:11–16, 1995.
[62]Loughner, B., J. Miller, V. Broumand, and B. Cooper. The development of strains, forces and nociceptor activity in retrodiscal tissues of the temporomandibular joint of male and female goats. *Exp. Brain Res.* 113:311–326, 1997.
[63]Mao, J. J. Stem-cell-driven regeneration of synovial joints. *Biol. Cell.* 97:289–301, 2005.
[64]McKay, D. C., and L. V. Christensen. Whiplash injuries of the temporomandibular joint in motor vehicle accidents: speculations and facts. *J. Oral. Rehabil.* 25:731–746, 1998.
[65]Mercuri, L. G. Are we getting out of TMJ surgery?. *J. Oral. Maxillofac. Surg.* 64:996, 2006.
[66]Mercuri, L. G., and A. Giobbie-Hurder. Long-term outcomes after total alloplastic temporomandibular joint reconstruction following exposure to failed materials. *J. Oral. Maxillofac. Surg.* 62:1088–1096, 2004.
[67]Mercuri, L. G., L. M. Wolford, B. Sanders, R. D. White, and A. Giobbie-Hurder. Long-term follow-up of the CAD/CAM patient fitted total temporomandibular joint reconstruction system. *J. Oral. Maxillofac. Surg.* 60:1440–1448, 2002.
[68]Milam, S. B., T. B. Aufdemorte, P. J. Sheridan, R. G. Triplett, J. E. Van Sickels, and G. R. Holt. Sexual dimorphism in the distribution of estrogen receptors in the temporomandibular joint complex of the baboon. *Oral. Surg. Oral. Med. Oral. Pathol.* 64:527–532, 1987.
[69]Miralles, R., R. Hevia, L. Contreras, R. Carvajal, R. Bull, and A. Manns. Patterns of electromyographic activity in subjects with different skeletal facial types. *Angle Orthod.* 61:277–284, 1991.
[70]Moses, A. J., and G. S. Skoog. Cervical whiplash and TMJ. *Basal Facts.* 8:61–63, 1986.
[71]Moses, J. J., and D. C. Topper. A functional approach to the treatment of temporomandibular joint internal derangement. *J. Craniomandib. Disord.* 5:19–27, 1991.
[72]Ogus, H. D., and P. A. Toller. Common Disorders of the Temporomandibular Joint 2nd ed. Bristol: John Wright & Sons Ltd, 1986.
[73]del Perez Palomar, A., and M. Doblare. 3D finite element simulation of the opening movement of the mandible in healthy and pathologic situations. *J. Biomech. Eng.* 128:242–249, 2006.
[74]del Perez Palomar, A., and M. Doblare. The effect of collagen reinforcement in the behaviour of the temporomandibular joint disc. *J. Biomech.* 39:1075–1085, 2006.
[75]del Perez Palomar, A., and M. Doblare. Finite element analysis of the temporomandibular joint during lateral excursions of the mandible. *J. Biomech.* 39:2153–2163, 2006.
[76]del Perez Palomar, A., and M. Doblare. An accurate simulation model of anteriorly displaced TMJ discs with and without reduction. *Med. Eng. Phys.* 29:216–226, 2007.
[77]Pertes, R. A. A review of vertical facial types and craniomandibular disorders. *N Y State Dent. J.* 51:570, 572, 575–578, 1985.
[78]del Pozo, R., E. Tanaka, M. Tanaka, M. Kato, T. Iwabe, M. Hirose, and K. Tanne. Influence of friction at articular surfaces of the temporomandibular joint on stresses in the articular disk: a theoretical approach with the finite element method. *Angle Orthod.* 73:319–327, 2003.
[79]Puelacher, W. C., J. Wisser, C. A. Vacanti, N. F. Ferraro, D. Jaramillo, and J. P. Vacanti. Temporomandibular joint disc replacement made by tissue-engineered growth of cartilage. *J. Oral. Maxillofac. Surg.* 52:1172–1177, 1994.
[80]Recommendations for management of patients with temporomandibular joint implants. Temporomandibular Joint Implant Surgery Workshop. *J. Oral. Maxillofac. Surg.* 51:1164–1172, 1993.
[81]Ryan, D. E. The Proplast/Teflon dilemma. *J. Oral. Maxillofac. Surg.* 47:222, 319–320, 1989.
[82]Schek, R. M., J. M. Taboas, S. J. Hollister, and P. H. Krebsbach. Tissue engineering osteochondral implants for

temporomandibular joint repair. *Orthod. Craniofac. Res.* 8:313–319, 2005.

[83]Schek, R. M., J. M. Taboas, S. J. Segvich, S. J. Hollister, and P. H. Krebsbach. Engineered osteochondral grafts using biphasic composite solid free-form fabricated scaffolds. *Tissue Eng.* 10:1376–1385, 2004.

[84]Schellhas, K. P., C. H. Wilkes, M. el Deeb, L. B. Lagrotteria, and M. R. Omlie. Permanent Proplast temporomandibular joint implants: MR imaging of destructive complications. *AJR Am. J. Roentgenol.* 151:731–735, 1988.

[85]Solberg, W. K., M. W. Woo, and J. B. Houston. Prevalence of mandibular dysfunction in young adults. *J. Am. Dent. Assoc.* 98:25–34, 1979.

[86]Springer, I. N., B. Fleiner, S. Jepsen, and Y. Acil. Culture of cells gained from temporomandibular joint cartilage on non-absorbable scaffolds. *Biomaterials* 22:2569–2577, 2001.

[87]Ström, D., S. Holm, E. Clemensson, T. Haraldson, and G. E. Carlsson. Gross anatomy of the mandibular joint and masticatory muscles in the domestic pig (Sus scrofa). *Arch. Oral. Biol.* 31:763–768, 1986.

[88]Sun, Z., Z. J. Liu, and S. W. Herring. Movement of temporomandibular joint tissues during mastication and passive manipulation in miniature pigs. *Arch. Oral. Biol.* 47:293–305, 2002.

[89]Tanaka, E., and T. van Eijden. Biomechanical behavior of the temporomandibular joint disc. *Crit. Rev. Oral. Biol. Med.* 14:138–150, 2003.

[90]Tanaka, E., R. del Pozo, M. Tanaka, D. Asai, M. Hirose, T. Iwabe, and K. Tanne. Three-dimensional finite element analysis of human temporomandibular joint with and without disc displacement during jaw opening. *Med. Eng. Phys.* 26:503–511, 2004.

[91]Tanaka, E., D. P. Rodrigo, Y. Miyawaki, K. Lee, K. Yamaguchi, and K. Tanne. Stress distribution in the temporomandibular joint affected by anterior disc displacement: a three-dimensional analytic approach with the finite-element method. *J. Oral. Rehabil.* 27:754–759, 2000.

[92]Tanaka, E., D. P. Rodrigo, M. Tanaka, A. Kawaguchi, T. Shibazaki, and K. Tanne. Stress analysis in the TMJ during jaw opening by use of a three-dimensional finite element model based on magnetic resonance images. *Int. J. Oral. Maxillofac. Surg.* 30:421–430, 2001.

[93]Tanaka, E., A. Sasaki, K. Tahmina, K. Yamaguchi, Y. Mori, and K. Tanne. Mechanical properties of human articular disk and its influence on TMJ loading studied with the finite element method. *J. Oral. Rehabil.* 28:273–279, 2001.

[94]Tanaka, E., K. Tanne, and M. Sakuda. A three-dimensional finite element model of the mandible including the TMJ and its application to stress analysis in the TMJ during clenching. *Med. Eng. Phys.* 16:316–322, 1994.

[95]Tanaka, E., K. Tanne, and M. Sakuda. A three-dimensional finite element model of the mandible including the TMJ and its application to stress analysis in the TMJ during clenching. *Med. Eng. Phys.* 16:316–322, 1994.

[96]Tanne, K., Y. C. Lu, E. Tanaka, and M. Sakuda. Biomechanical changes of the mandible from orthopaedic chin cup force studied in a three-dimensional finite element model. *Eur. J. Orthod.* 15:527–533, 1993.

[97]Tanne, K., E. Tanaka, and M. Sakuda. Stress distributions in the TMJ during clenching in patients with vertical discrepancies of the craniofacial complex. *J. Orofac. Pain.* 9:153–160, 1995.

[98]Tanne, K., E. Tanaka, and M. Sakuda. Stress distribution in the temporomandibular joint produced by orthopedic chincup forces applied in varying directions: a three-dimensional analytic approach with the finite element method. *Am. J. Orthod. Dentofacial. Orthop.* 110:502–507, 1996.

[99]Thomas, M., D. Grande, and R. H. Haug. Development of an in vitro temporomandibular joint cartilage analog. *J. Oral. Maxillofac. Surg.* 49:854–856, 1991: discussion 857.

[100]Trumpy, I. G., B. Roald, and T. Lyberg. Morphologic and immunohistochemical observation of explanted Proplast-Teflon temporomandibular joint interpositional implants. *J. Oral. Maxillofac. Surg.* 54:63–68, 1996.

[101]Ueki, K., D. Takazakura, K. Marukawa, M. Shimada, K. Nakagawa, S. Takatsuka, and E. Yamamoto. The use of polylactic acid/polyglycolic acid copolymer and gelatin sponge complex containing human recombinant bone morphogenetic protein-2 following condylectomy in rabbits. *J. Craniomaxillofac. Surg.* 31:107–114, 2003.

[102]Van Eijden, T. M., E. M. Klok, W. A. Weijs, and J. H. Koolstra. Mechanical capabilities of the human jaw muscles studied with a mathematical model. *Arch. Oral. Biol.* 33:819–826, 1988.

[103]Wagner, J. D., and E. L. Mosby. Assessment of Proplast-Teflon disc replacements. *J. Oral. Maxillofac. Surg.* 48:1140–1144, 1990.

[104]Wang L. and M. S. Detamore. Tissue engineering the TMJ condyle. *Tissue Eng.* 13, 2007.

[105]Warren, M. P., and J. L. Fried. Temporomandibular disorders and hormones in women. *Cells Tissues Organs.* 169:187–192, 2001.

[106]Weng, Y., Y. Cao, C. A. Silva, M. P. Vacanti, and C. A. Vacanti. Tissue-engineered composites of bone and cartilage for mandible condylar reconstruction. *J. Oral. Maxillofac. Surg.* 59:185–190, 2001.

[107]Werner, J. A., B. Tillmann, and A. Schleicher. Functional anatomy of the temporomandibular joint. A morphologic study on human autopsy material. *Anat. Embryol.* 183:89–95, 1991.

[108]Williams, J. M., A. Adewunmi, R. M. Schek, C. L. Flanagan, P. H. Krebsbach, S. E. Feinberg, S. J. Hollister, and S. Das. Bone tissue engineering using polycaprolactone scaffolds fabricated via selective laser sintering. *Biomaterials* 26:4817–4827, 2005.

[109]Wolford, L. M. Temporomandibular joint devices: treatment factors and outcomes. *Oral. Surg. Oral. Med. Oral. Pathol. Oral. Radiol. Endod.* 83:143–149, 1997.