The Temporomandibular Joint, Components and Repair

The temporomandibular joint (TMJ), the jaw joint, is located between the mandible and temporal bones and has hinge, sliding and translational characteristics that allow for complex movements like chewing, swallowing, talking, yawning, breathing, and facial expressions. It is a joint containing soft fibrocartilaginous tissues essential for its normal functions; abnormalities in its structure or function may lead to painful, disabling TMJ disorders (TMD). These conditions afflict about 25% of the population, primarily women in their childbearing years. Most TMD patients experience mild, transient symptoms; however, a small percentage of patients go on to develop chronic, disabling TMDs. Initially, TMD patients may present with decreased jaw function and range of motion with pain and joint sounds. Treatments for these patients should be conservative, simple, and non-invasive. Surgical therapies such as arthrocentesis and arthroscopic surgeries are sometimes recommended. More invasive procedures such as open joint operations are indicated for TMD only if all other treatments have failed and a specific diagnosis suggests surgical care; for example, replacing or reconstructing degenerated or damaged TMJ discs with synthetic materials. However, most of these minimally or highly invasive treatment options for chronic TMDs currently lack strong scientific justification. Recent research results suggest that TMDs are complex, multisystem, biopsychosocial conditions, not localized to the joint itself, that require multiple, interdisciplinary clinical treatment approaches. However, traumatic injuries, arthritic conditions, other inflammatory and mechanical conditions, and iatrogenic procedures affecting the jaw joint are quite prevalent and may require treatments focused on the specific components involved in the pathology.

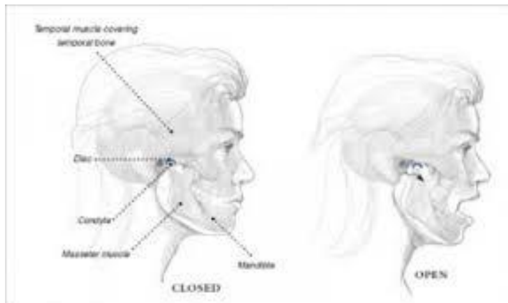
Alloplastic Repair and Reconstruction

Some early attempts in the 1980's at pathological disc and bone replacement with synthetic materials such as Dow Corning Silastic (based on Silicone) and the Vitek, Inc. Proplast-Teflon implants led to catastrophic consequences from material failures. There were reports of Silastic fragmentation and deterioration leading to localized and systemic adverse reactions. Similarly, the use of Proplast-Teflon based TMJ discs and Teflon-coated total joint devices led to biomechanical failure, giant cell reactions, skull perforations and bony changes. These failed attempts to repair components of the TMJ eventually led to efforts to develop successful TMJ implants. Current implant materials and reconstructive surgical procedures for TMD treatments are similar to those used in other diseased joints in the body. Several FDA-approved custom and stock TMJ replacement systems are available. They use titanium and cobalt-chromium-molybdenum alloy condyle components and ultra-high molecular weight polyethylene fossa components in total joint replacement systems. The clinical literature reports successful joint implants in several select cohorts. However, implant patient reports to FDA's MedWatch Reports for TMJ Devices and to the TMJ Association continue to describe sometimes severe consequences from these joint replacement surgeries including metal sensitivity, premature transplant resection, continued painful jaw function, and development of additional comorbid conditions. Currently, there are no formal clinical practice guidelines or standards of care for diagnosis and treatment of TMDs. A well-crafted guideline promotes quality treatments by reducing healthcare variations, providing diagnostic accuracy, promoting effective therapy, and discouraging ineffective or potentially harmful interventions.

Research in tissue engineering/regenerative medicine (TE/RM) approaches for tissues of the TMJ is ongoing but has not yet reached clinical applicability. This brief report describes the tissues of the TMJ and discusses some of the current experimental approaches for treating degenerative and pathological conditions of the TMJ. While these approaches are currently not available for use in TMD patients, they are likely to be at the forefront of sound TMD treatments in the future.

Tissues of the TMJ

The human TMJ is a complex, bilateral joint, functioning as one unit and comprised of numerous tissues working in unison to allow nominal operations essential to life.



It is surrounded by a fibrous membrane, called a capsule. There are three ligaments that help to stabilize the joint, the major one is the temporomandibular ligament. There are several important jaw opening and closing muscles including the temporalis, masseter, and lateral pterygoid. These bilateral muscles work together to allow joint movement in many directions including lateral, vertical, and cyclic motions. The articular disc is a fibrocartilaginous structure located within the capsule between the condyle of the mandible and the temporal bone of the skull and it cushions the movements of these two bones as they articulate. The trigeminal nerve controls sensory and motor functions to the joint. Several branches of the external carotid artery provide blood supply to the joint. A synovial membrane lines the capsule and produces fluids that help to lubricate the joint. Interestingly, the articular disc is mostly avascular and lacks innervation, but receives nutrients from synovial fluid surrounding the joint. The disc and other fibrocartilaginous tissues of the joint have limited regenerative properties and thus when this joint is subjected to trauma or repeated stresses, a degenerative process can produce painful, pathological TMDs. New replacement materials or implants for damaged joints will involve research in the areas of TE/RM and is presented below.

Tissue Engineering/Regenerative Medicine Research

Several excellent literature reviews detail the current status of treatment approaches for the repair and regeneration of structural and functional deficits in the TMJ (Donahue RP, Hu JC, Athanasiou KA: 2019; Acri TM, Shin K, Seol D, Laird NZ, Song I, Geary SM, Chakka JL, Martin JA, Salem AK: 2018; and Xavier Van Bellinghen, Ysia Idoux-Gillet, Marion Pugliano, Marion Strub, Fabien Bornert, Francois Clauss, Pascale Schwinté, Laetitia Keller, Nadia Benkirane-Jessel, Sabine Kuchler-Bopp, Jean Christophe Lutz and Florence Fioretti: 2018). In all, over 20 recent reviews on TE/RM approaches for treating defects in the TMJ tissues were examined as well as follow-up with selected primary source articles.

Osteo-arthritic and other degenerative conditions of the TMJ are ideal target disorders for these TE/RM approaches for treatment and represent alternatives to major invasive, surgical repairs.
Several novel approaches for repair, reconstruction, and replacement of joint tissues in TMDs mainly focus on the fibrocartilaginous tissues of the joint. These approaches are in their infancy and researchers are examining proof of concept and assessing safety in vitro and in both small and large animal models

of TMD. Research teams are exploring various types of scaffolds upon which to develop replacement tissues of the TMJ; testing various stem and other cell types for use in growing cartilage, bone, and muscle structures on these scaffolds; and identifying and employing bioactive molecules to stimulate, modulate, or inhibit specific cell growth and functions. Before some of these new approaches are tested in a clinical setting, many safety and efficacy studies will need to be conducted in small and, more importantly, large animal models of TMDs. Large animal usage will be critical, since the TMJ spatial and functional characteristics of these models more closely mimic human jaw structure and function. Ultimately, human trials will need to be carried out to assess efficacy and safety of any new approach.

Tissue engineering for the repair, reconstruction, or replacement of damaged TMJ structures generally requires scaffolds as templates to mimic the shape and function of these tissues. Current scaffold designs focus on the use of ceramic or composite materials as well as the use of naturally occurring materials such as fibrin, chitosan and hyaluronic acid. Also, de-cellularized TMJ discs and bone have been used as scaffolds. The use of 3-D printing technology and nanolayering to fabricate new scaffolds allows for the precise addition of bioactive materials to prepare functionalized scaffolds. Scaffolds should be designed to resemble the original structures, be compatible with functionalization and have degradation rates that parallel the development of new tissues. Scaffold-free approaches for musculoskeletal cartilage tissue engineering include cell sheet engineering, aggregation, and self-assembling processes. Interestingly scaffold-free, self-assembling approaches together with mechanical compression are finding success in mimicking collagenous structures with high tensile strength approaching that of native tissues.

The selection of cell types to use in regenerative medicine is critical. Many options are available, depending upon the application. Autologous cells – cells from the same individual - are ideal for use in repairing or replacing TMJ tissues. However, because of the lack of healthy autologous cells from TMD patients, various allogeneic cells have been sought including tissue-specific stem/progenitor cells and dental pulp stem cells. These stem/progenitor cells have the ability to differentiate into multiple cell lineages, including chondrogenic and osteogenic cells. Stem cell isolation followed by rapid cell expansion, application to scaffolds, and differentiation into osteogenic and chondrogenic lineages is then induced. Other allogeneic cells, such as terminally differentiated costal chondrocytes, which can be expanded in culture while retaining their phenotype, have been used in scaffold-free constructs of TMJ discs.

In order to obtain functional similarity of new tissues, these scaffolds and cellular components will require appropriate stimulation. Many bioactive molecules (IGF-1, bFGF, TGF-β1, TGF-β3, CTGF, and EGF) have been utilized. Growth factors help tissue regeneration at several levels. They can promote the differentiation and proliferation of cells. They can support extracellular matrix synthesis. Trophic modulation of stem/progenitor cells by these bioactive compounds has been hypothesized to exert anti-inflammatory and immunomodulatory effects, possibly aiding in tissue repair. They can also modulate tissue regeneration in order for these engineered constructs to be self-limited and prevent ossification and fibrous adhesions.

Since the TMJ is subject to large compressive and tensile forces during normal functioning, various mechanical stimuli during tissue regeneration have been utilized to improve the mechanical/functional properties of the engineered disc and other components. Tension, compression and dynamic loading, deformational loading, low-intensity pulsing ultrasound, and hydrostatic pressure have been used as mechanical stimuli in TMJ engineering. In some instances, compressive and tensile stiffness and strength closely approaching those measures observed in vivo have been attained with engineered constructs.

Animal models are crucial to the development of new TE/RM treatments for TMDs. Both small and large animal models are being used, each with their own advantages. Small animal models including rodents and rabbits are useful because of their relatively low economic upkeep and husbandry and detailed genetic information. Long-term use of these animals has led to the development of several degenerative joint models for TMJ. Large animal models more closely resemble the spatial characteristics of the human TMJ and in some cases the jaw movements are more in line with human motions. These animals include pigs (both mini and farm pigs), goats, dogs, and sheep. Ducks and quail have also been used. Although large animals are more costly to use, their similarity to human jaw structure and function is important for assessing regenerative and repair properties, as well as safety concerns, in larger constructs that will be necessary for human treatment.

There are many TE/RM human studies of the knee, vertebrae, and ankle, mostly phase I and II clinical trials. At this point, very few human clinical trials in the TMJ have been performed with TE/RM approaches. Only one trial, carried out in Brazil, is registered in ClinicalTrials.gov. and involves the use of autologous nasal chondrocytes in degenerative lesions of the TMJ. The trial involves injection of cells into the capsule and follow-up for one year. Preliminary results show regeneration of cartilage after 6 months and this was maintained after one year as measured by functional assays and advanced imaging techniques.

Although in early stages, TE/RM approaches show much promise as scientifically sound treatment options for degenerative TMDs. The future use of bioengineered constructs to treat TMDs will require a multidisciplinary scientific research community, working together with regulatory agencies and TMD patients to rapidly bring to the market TE/RM TMJ components. These implants will need to meet the highest criteria for safety and efficacy, and precisely target patients who will be most likely to benefit from these treatments without untoward side effects and complications.