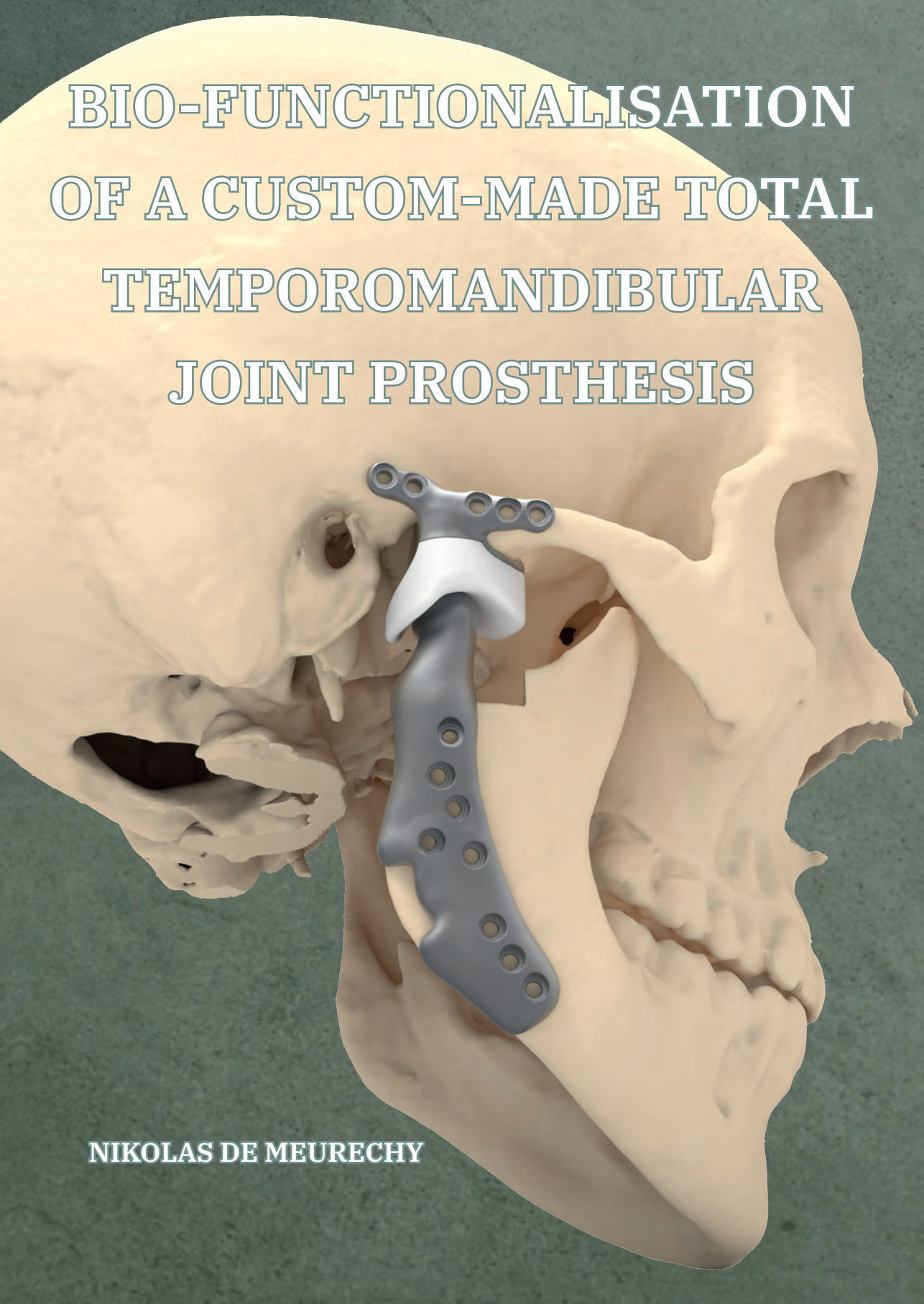
BIO-FUNCTIONALISATION OF A CUSTOM-MADE TOTAL TEMPOROMANDIBULAR JOINT PROSTHESIS



NIKOLAS DE MEURECHY

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BIO-FUNCTIONALISATION OF A CUSTOM-MADE TOTAL TEMPOROMANDIBULAR JOINT PROSTHESIS

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2023-2024

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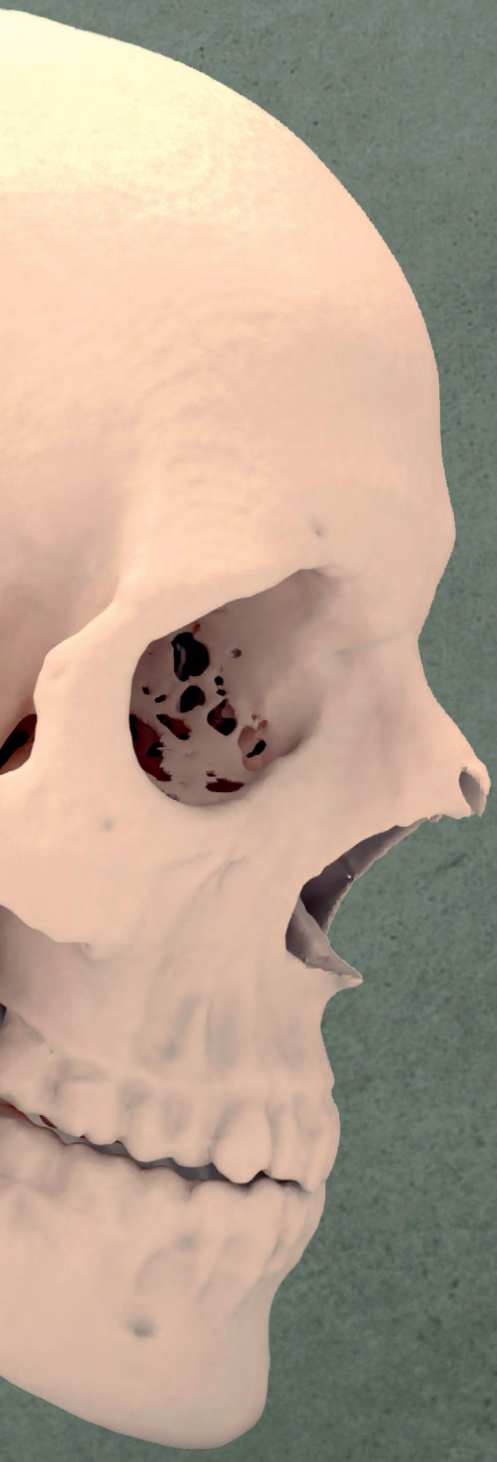


Chapter 1

General introduction and overview of the thesis

General introduction

The temporomandibular joint (TMJ) plays a role in many functions such as mastication, swallowing, talking, facial expressions, breathing, airway support and even maintaining the correct pressure of the middle ear. The joint can perform both translative and rotational movements and subjected to more cyclic loading and unloading than any other joint in the body. As a result, temporomandibular disorders (TMDs) are far from rare.(1) A 2008 study by the National Health Interview Survey concluded that up to 5% of all Americans deal with TMD-related pain(2), and a study conducted by Janal et al.(3) reported that up to 10% of all female patients examined had a TMD. Despite this high prevalence, in most cases conservative therapy such as physiotherapy and pharmacotherapy will suffice as treatment. Yet in about 5 to 10%, symptoms persist, demanding a more invasive approach.(4,5) which can range from a simple arthrocentesis to ultimately total joint replacement surgery. (1,6)

TMJ anatomy

To better understand the function of the temporomandibular joint, as well as the total joint replacement (TJR) (procedure), a comprehensive knowledge of this diarthrosis' anatomy is needed.

The TMJ is comprised of the head of the mandibular condyle and the temporal glenoid fossa. The condyle is an ovoid process at the superior part of the mandibular ramus. It has a convex form and is wider in the mediolateral sense (15-20 mm) than in the anteroposterior direction (8-10 mm), with the medial side of the condyle being directed more posteriorly compared to the lateral side. The articular surface of the condyle is located on the anterosuperior part of the condyle.(7)

Anteriorly of the tympanic plate, the articular temporal component can be found and shows several landmarks. Most anteriorly, the articular eminence and tubercle are located. The eminence has a strong incline, which becomes nearly horizontal towards the glenoid fossa, forming the preglenoid plane. The centrally located glenoid fossa is widest in the mediolateral direction, as the condyle is seated in this fossa. Posteriorly,

an elevation is seen, forming the posterior articular ridge. This ridge laterally further increases in height, forming the post-glenoid process, which forms the posterior border of the joint.(7)

The temporal and condylar component are both separated by an oval-shaped biconcave fibrocartilaginous articular disc. This disc divides the joint in an larger upper and smaller inferior compartment, allowing for a rotational/hinge movement to occur in the inferior compartment, whilst a translational/gliding movement occurs in the upper compartment. The anterior and posterior part of the disc are quite a bit thicker at respectively 2 and 3mm compared to the center, where the disc measures about 1 mm. The posterior part, known as the bilaminar region, has an upper elastin and a lower fibrous layer, separated by connective tissue. The upper layer is connected to the post-glenoid process, preventing anterior displacement of the disc. The inferior layer fuses with the joint capsule below the condyle as to prevent the disc rotating over the condyle. The disc is also fixed to the medial and lateral pole of the condyle, to allow it to move together with the latter. Anteriorly, the disc is fixed to the fibrous capsule of the joint. This fibrous capsule surrounding the whole of the TMJ is called the articular capsule. Anteriorly, an opening in the capsule is seen, allowing the lateral pterygoid muscle (LPM) to pass through and insert itself onto the condyle and the anterior part of the disc. The inside of the capsule is lined with a synovial membrane, thus making the TMJ a synovial joint.(7,8)

Besides the capsule, the movements of TMJ are restricted by three main ligaments. The lateral ligament forms a part of the capsule and limits both the forward and posterior translation of the condyle, as well as the maximal lateral movement. The fibers originate from the articular tubercle and insert in the lateral side of the condyle and the condylar neck, as well as into the articular disc. The stylomandibular ligament, which inserts onto the mandibular angle and the posterior border, limits to protrusive movement of the mandible in case of more extreme movements. Lastly, the sphenomandibular ligament remains passive during movement of the lower jaw.(9)

There are four true mastication muscles which make direct contact with the TMJ. Three of these muscles help to close the mouth. The masseter muscle is the 'main closer' of the mouth, and is further aided by the medial pterygoid muscle, which could be seen as the counterpart to the masseter muscle, yet on the medial side of the mandible. The third muscle to help close the mouth, is the temporal muscle, which inserts onto the coronoid process. However, as mastication is more than rather just opening and closing, the lateral pterygoid muscle can be seen as vital to proper masticatory function. Whereas the superior belly of the LPM inserts into the disc, allowing proper disc movement, the inferior belly inserts into the condyle and allows for protrusion of the condyles when both side contract simultaneously, leading to the mouth opening. Additionally to allowing proper disc movement, the superior belly also participates in contralateral and protrusive moment. Despite this involvement of the superior belly, the inferior one is the principal muscle for laterotrusive movement. In case of a unilateral contraction, a laterotrusive movement will occur, which is extremely important for being able to properly chew. Important to note is that, with current TMJ TJR, the LPM's function is not retained, thus losing the possibility of laterotrusive movement.(8–11)

Equally important for every surgeon to the structure of the joint are the main blood vessels and nerves surrounding the joint. The maxillary artery and superficial temporal artery provide the main vascularization to the joint. The superficial temporal artery is the terminal branch of the external carotid and can be found relatively superficially, posterolaterally to the condyle. It makes for a point of attention during a surgical exploration, especially when taking a pre-auricular approach. The maxillary artery branches from the external carotid as well, yet passes on the medial side of the mandible, between the ramus and the sphenomandibular ligament, below the sigmoid notch. This artery is important, as the arteria meningea media branches off at the level of the condyle and passes medially from it, risking being damaged when performing a condylectomy. Venous drainage is realized mainly through the pterygoid plexus and superficial temporal vein, as well as several other maxillary veins, forming the retromandibular vein.(12,13)

Although the masseteric and auriculotemporal nerve provide innervation to respectively the anterolateral and lateral area of the articular capsule, the main nerve to keep in mind during surgical treatment of the TMJ is the facial nerve. After exiting the skull, the seventh cranial nerve divides into the cervicofacial and temporofacial branch, with the latter being most at risk during a surgical procedure. As the superior limit of the nerve is situated below the line connecting the tragus and lateral palpebral commissure, this nerve could be easily damaged or even sectioned by a novice surgeon. (13–15) Secondly, when making use of a submandibular approach, the marginal ramus has to be kept in mind as well. (16)

Surgical indications and approach for a TMJ replacement

Keeping in mind that only 5-10% of patients with TMD need an invasive treatment, the amount of patients that needs to be subjected to a TMJ TJR is considerably less. (4,5) Indications for a TMJ TJR were well outlined by both the American Association of Oral and Maxillofacial Surgeons (AAOMS) (17) and the National Institute for Health and Care Excellence (NICE) (18) guideline. These indications include TMJ ankylosis and end-stage joint disease resulting from trauma, infection, degenerative arthrosis, cancer, developmental/inherited craniofacial anomalies affecting the mandible and TMJ, failed/failing temporomandibular joint replacement (TMJR) devices or failed prior invasive surgery.

When a surgical replacement of the TMJ is indicated, there are several surgical approaches to the joint, each with its own advantages and disadvantages. Firstly, an extraoral approach is preferred over an intraoral, arthroscopic, or endoscopy-assisted approach, as these techniques provides only limited access to the joint. When opting for an extraoral approach, a general distinction can be made between a preauricular, endaural and postauricular technique. The preauricular approach, developed by Blair and first reported on by Risdon, is relatively easy to use, allows for good exposure and can easily be modified to allow for larger exposure of the TMJ and the peri-articular area.(19) Since then, several popular modifications have found their way into the TMJ-surgeon's 'bag of tricks'.

The ‘standard’ preauricular approach that is often opted for, was designed by Dingman. The incision starts at the helix and runs in the preauricular crease, over the tragal margin to the attachment of the lobule. With time he modified his approach to include a temporal and anterior extension, following a more vertical pre-auricular path. (20) Rowe and Killey developed a similar approach to the first technique by Dingman, starting more superior at the helix and passing front of the preauricular crease. (21) Al Kayat and Bramley further extended the preauricular approach, using a 4 to 6 cm pre-tragal incision, running over the helical root and extending cranially, thus passing behind the superficial temporal artery and auriculotemporal nerve.(22) This incision can be temporally extended if needed, allowing for an easier deep subfascial approach to preserve the temporofacial branch with further exposure of the zygomatic arch and thus glenoid component, which can be needed for the placement of the fossa component of the prosthesis.

Whilst adding a Lazy ‘S’ modification to the preauricular approach, to allow for better access to the mandibular angle, could be considered when performing a TMJR, the submandibular approach as suggested by Risdon should be considered. Whilst the marginal ramus of the facial nerve has to be kept in mind during this approach, it allows for a better exposure of the lateral aspect of de mandible and the mandibular angle, thus making it easier to insert and fixate the ramal component of the prosthesis.(19)

Besides the preauricular approach, an endaural approach such as the modified Lempert technique by Rongetti could be considered it younger patients, for its cosmetic results, although the surgeon has to be weary not to damage the tragal cartilage.(23,24) The same can be said for the postauricular technique, in which a retro-auricular incision is made, followed by an anterior dissection to reach the TMJ. Taking this approach, the meatus acusticus externus needs to be transected. If this transection occurs too close to the bony auditory canal, risk of stenosis in the cartilaginous part significantly increases, making this technique less preferable for surgeon’s who are new to TMJ surgery. However, in patients prone to keloid formation, this technique should be considered.(19,25)

Aims and overview of the thesis

In 2019 Elledge et al.(26) reported on 27 different TMJ TJR being produced in over fifteen countries with only 2 of them being approved by the United States Food and Drug Administration (FDA). Twenty-two of these TJR applied a similar design to these 2 approved systems, yet still varied in the prosthetic materials that were used. Also, only 12 systems performed preclinical laboratory tests, yet none underwent in vivo testing before being implanted in human patients. The authors concluded that 'Not all systems are equal in terms of design, material composition, preclinical laboratory testing, manufacturing methods, regulatory status, and reports of clinical outcomes.'

Thus, this doctoral thesis set out to develop and properly investigate a personalized TMJ prosthesis. The hypothesis is that it would be possible to develop a prosthesis that meets orthopedic standards in both wear properties and adverse tissue reactions. We also hypothesized that is possible to reinsert the LPM onto the prothesis, allowing for lateral condylar movement. Also, we aimed to further improve the per-operative and post-operative protocols that are currently in place, by evaluating the available literature and developing new guidelines or protocols.

General introduction

The first chapter provides a general introduction on the anatomy of the joint, its surgical indications, and approaches. The outline of the thesis is presented as well.

Part 1 Literature analysis and development

By better understanding the historic development of temporomandibular joint prosthetic systems with attention for the different materials and designs that were used, significant insights can be obtained in developing a new TMJR. By analyzing the challenges and complications that were encountered not only by engineers, but also by surgeons, the design of a new TMJR can also be influenced from a clinical point of view. This second chapter provides an extensive systematic review of the historical evolution

of the prosthetic replacement of the joint, leading to several conclusions for future application.

Whereas the second chapter briefly touches the prosthetic materials that were used in both the past and present, the third chapter further elaborates on this topic by means of a narrative review. The importance of the use of biocompatible materials is evident, yet certain materials are clearly less suited for loading or articulation, compared to other materials, as their use nearly resulted in an abandonment of the prosthetic replacement of the TMJ. Thus, this chapter discusses the criteria that a biomaterial must meet, other than biocompatibility, to be considered suitable for implantation. An insight is also provided into both surface modification techniques to further improve on current materials, as well as potential future materials.

While at first, TMJ prostheses were stock implants, sometimes provided in different sizes, there was no possibility to deal with the patient's specific anatomy. Through the development of computer-assisted design/computer-assisted manufacturing (CAD-CAM) systems, patient-specific implants (PSI) were developed. In chapter four a meta-analysis is performed to compare both types of protheses, with special attention for functionality (maximal mouth opening), pain and diet, as well as possible confounders that might influence these results.

Part 2 Animal-model experiment

Using the data and conclusions from the literature analysis that was performed, a novel patient-specific implant was designed. To evaluate if the implant was suitable for human implantation and could meet orthopedic standards, an animal-model experiment using sheep was designed. The prosthesis was first implanted in one sheep, to evaluate the surgical procedure and to establish the standard procedure. Next, 6 sheep were implanted with a 'regular' prosthesis and 6 ewes were treated with a prosthesis that underwent surface modification on the condylar head. Ten months after implantation, the sheep were euthanized to evaluate the peri-articular tissues, as well as the implants themselves.

In the fifth chapter of this thesis the surface wear of both the condylar and fossa component are analyzed and discussed. Both a linear and volumetric wear analysis of the fossa was performed through optical scanning. The condylar surface was evaluated through scanning electron and confocal laser microscopy. The amount of wear between the two types of prosthetic systems was compared and the condylar surface smoothness was analyzed to determine the effect of the surface treatment. Lastly, the amount of wear that occurred was compared to the standards set in orthopedic surgery.

Following the wear analysis of the prosthetic components, the next chapter discusses a histological analysis of the peri-articular tissues that was performed to evaluate the amount of inflammation in the peri-articular tissues. The inflammatory response between both types of prostheses was also compared. The tissues were evaluated for the presence of chronic inflammation as well as 'synovial-like interface membrane' type I synovitis and type VI reactions.

Besides assuring suitability of implantation, based on wear properties, good osseointegration of the prosthetic system is needed as well. The last two chapters of the second part of this thesis discuss both the integration of the prosthetic system, as well as the integration of the reinserted LPM onto the condylar component. In chapter 7 a radiological analysis of the prosthetic system is performed, to first evaluate the integration of the LPM onto the condylar component. This led to the finding of four different radiological situations, based on which those sheep who showed (partial) bony integration were selected for further histological analysis in chapter 8, to determine if bony ingrowth within a scaffold at the condylar neck occurred. In both chapters the integration of the prosthetic components was also evaluated.

Part 3 Clinical application and protocols

Using the data and conclusions from the earlier chapters, the first chapter in the final part of this thesis discusses the development of the novel type of patient-specific, custom-made TMJ prosthesis, now applied for human implantation, using CAD-CAM, additive manufacturing and surface

treatment. Eleven patients and a total of sixteen joints were treated using the TMJR and its function was evaluated the analysis of the early in vivo results, with attention for the reported pain and dietary scores, as well as the measured movements. In chapter ten, the prosthetic system is further adapted to not only restore the function of the TMJ, but also to restore segmental mandibular defects with occlusal abnormalities. A total of five patients and six joints were treated using the extended TMJR (eTMJR) and evaluated for at least one year. The chapter also focusses on problems that can occur during the implantation of an eTMJR.

Both chapters eleven and twelve focus on further improving the per- and postoperative protocols for a total mandibular joint replacement. Through a systematic review, the first chapter discusses the usefulness of a periprosthetic autologous fat graft (AFG), to prevent postoperative heterotopic bone formation, leading to an ankylotic joint and necessity for a surgical revision. Besides per-operative measures to ensure proper joint function, post-operative physiotherapy is important as well to keep the joint mobile. By use of a systematic review, physiotherapeutic treatments are analyzed. This chapter seeks to develop a new postoperative physiotherapy protocol which is thorough yet comprehensible for practitioners and supported by scientific evidence.

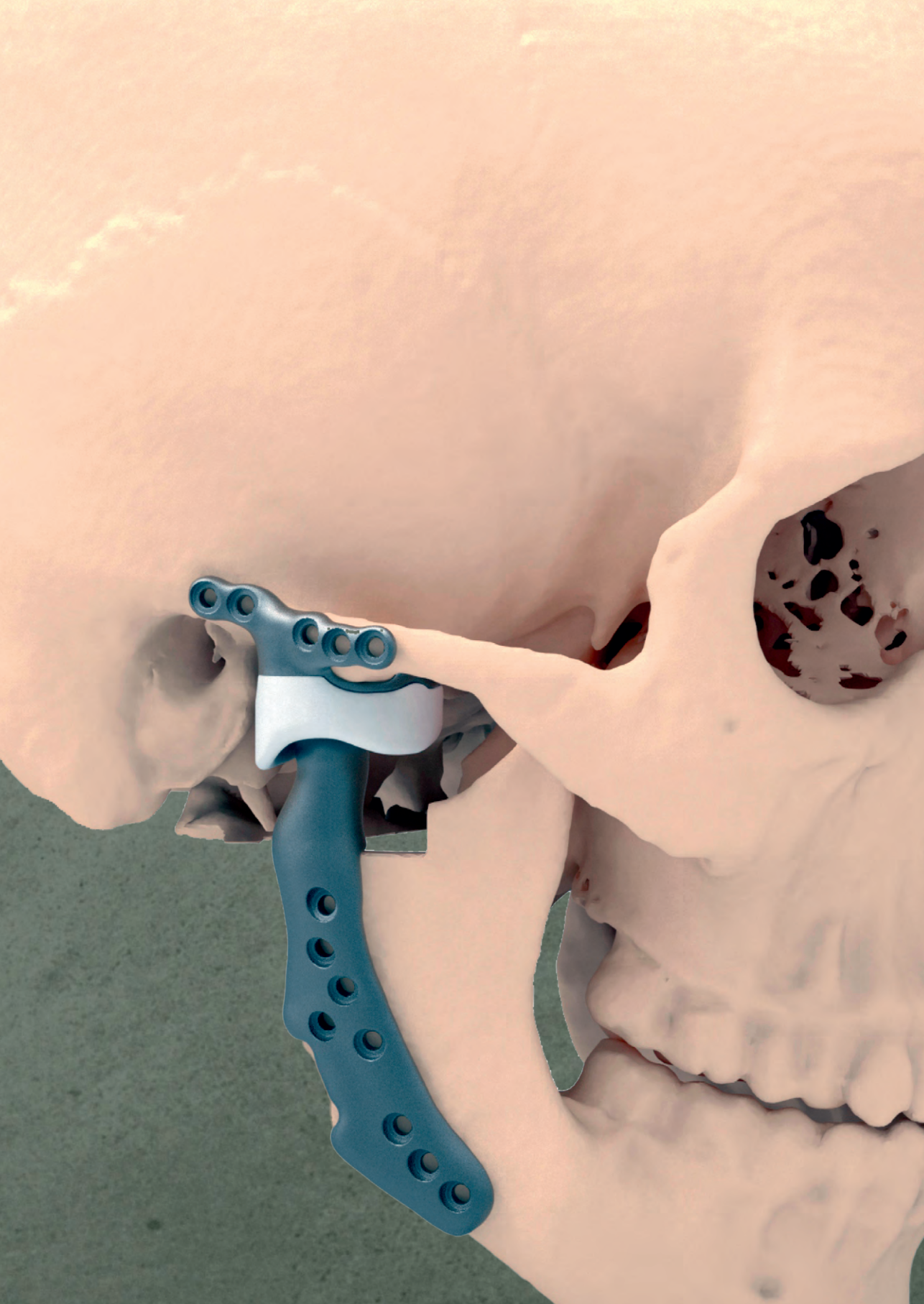
Discussion and summary

In Chapter 13 we discuss the general findings of the previous chapters and provide insight into future studies to further improve and support the developed TMJ prosthesis. The final chapter contains both Dutch and English summaries of this thesis.

References

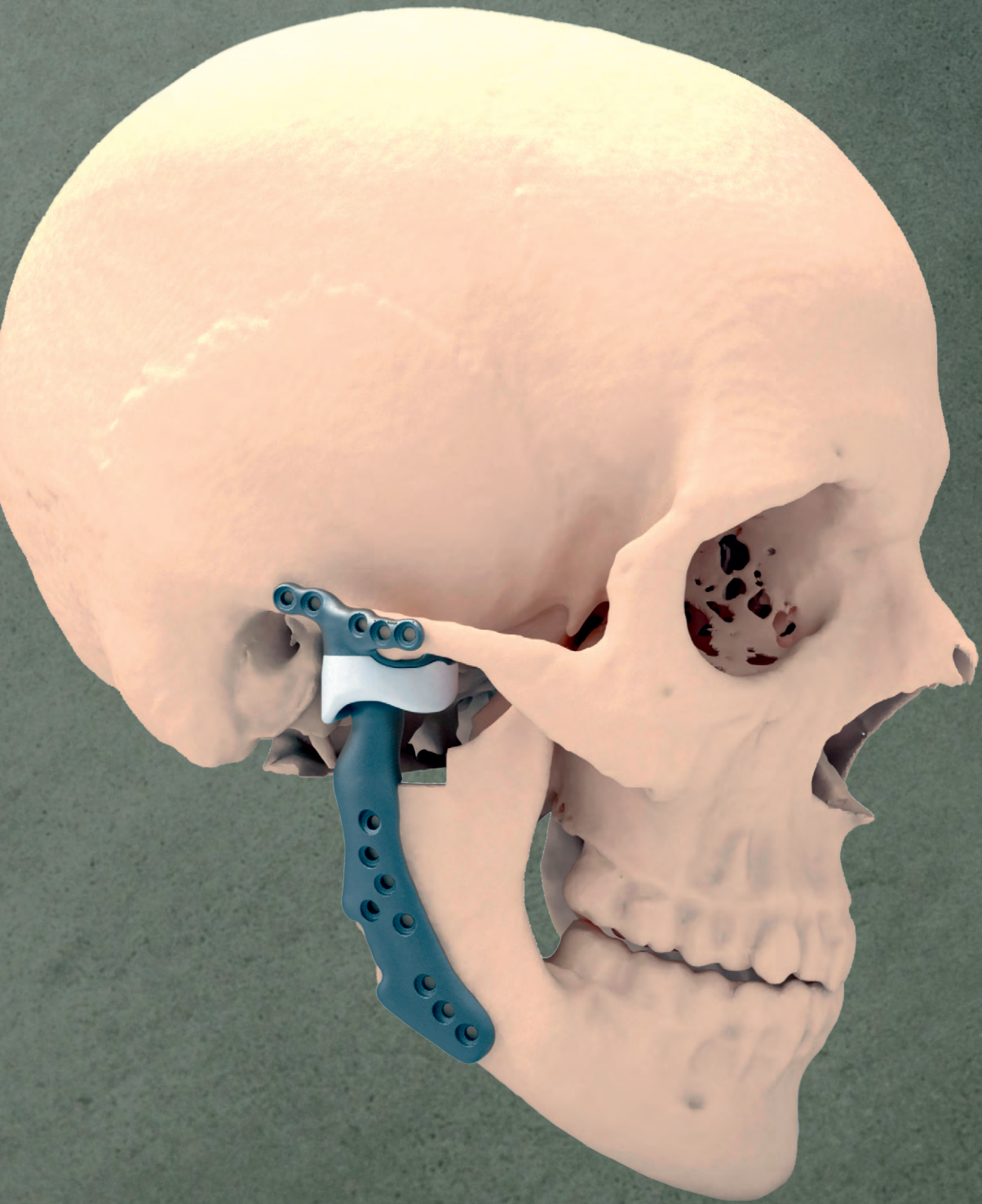
1. Guarda-Nardini L, Manfredini D, Ferronato G. Temporomandibular joint total replacement prosthesis: current knowledge and considerations for the future. Int J Oral Maxillofac Surg. 2008;37(2):103–10.
2. Isong U, Gansky SA, Plesh O. Temporomandibular joint and muscle disorder-type pain in U.S. adults: the National Health Interview Survey. J Orofac Pain [Internet]. 2008;22(4):317–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19090404%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4357589
3. Janal MN, Raphael KG, Nayak S, Klausner J. Prevalence of myofascial temporomandibular disorder in US community women. J Oral Rehabil. 2008;35(11):801–9.
4. Reston JT, Turkelson CM. Meta-analysis of surgical treatments for temporomandibular articular disorders. J Oral Maxillofac Surg [Internet]. 2003 Jan 1;61(1):3–10. Available from: https://doi.org/10.1053/joms.2003.50000
5. Dimitroulis G. The role of surgery in the management of disorders of the Temporomandibular Joint: a critical review of the literature. Part 1. Int J Oral Maxillofac Surg. 2005 Mar;34(2):107–13.
6. Dimitroulis G. Management of temporomandibular joint disorders: A surgeon's perspective. Aust Dent J [Internet]. 2018 Mar 1;63(S1):S79–90. Available from: https://doi.org/10.1111/adj.12593
7. Alomar X, Medrano J, Cabratosa J, Clavero JA, Lorente M, Serra I, et al. Anatomy of the Temporomandibular Joint. Semin Ultrasound, CT MRI [Internet]. 2007;28(3):170–83. Available from: https://www.sciencedirect.com/science/article/pii/S0887217107000297
8. Bravetti P, Membre H, El Haddioui A, Gérard H, Fyad JP, Mahler P, et al. Histological study of the human temporo-mandibular joint and its surrounding muscles. Surg Radiol Anat. 2004;26(5):371–8.
9. Iturriaga V, Bornhardt T, Velasquez N. Temporomandibular Joint: Review of Anatomy and Clinical Implications. Dent Clin North Am. 2023 Apr;67(2):199–209.
10. Huang BY, Whittle T, Murray GM. Activity of inferior head of human lateral pterygoid muscle during standardized lateral jaw movements. Arch Oral Biol. 2005;50(1):49–64.
11. Murray GM, Bhutada M, Peck CC, Phanachet I, Sae-Lee D, Whittle T. The human lateral pterygoid muscle. Arch Oral Biol. 2007;52(4):377–80.
12. Cuccia AM, Caradonna C, Caradonna D, Anastasi G, Milardi D, Favaloro A, et al. The arterial blood supply of the temporomandibular joint: an anatomical study and clinical implications. Imaging Sci Dent. 2013 Mar;43(1):37–44.
13. Yang H-M, Won S-Y, Kim H-J, Hu K-S. Neurovascular structures of the mandibular angle and condyle: a comprehensive anatomical review. Surg Radiol Anat. 2015 Nov;37(9):1109–18.
14. de Bonnecaze G, Chaput B, Filleron T, Al Hawat A, Vergez S, Chaynes P. The frontal branch of the facial nerve: can we define a safety zone? Surg Radiol Anat. 2015 Jul;37(5):499–506.
15. Kucukguven A, Demiryurek MD, Vargel I. Temporomandibular joint innervation: Anatomical study and clinical implications. Ann Anat = Anat Anzeiger Off organ Anat Gesellschaft. 2022 Feb;240:151882.
16. Saylam C, Ucerler H, Orhan M, Uckan A, Ozek C. Localization of the marginal mandibular branch of the facial nerve. J Craniofac Surg. 2007 Jan;18(1):137–42.
17. Koslin M, Indresano AT, Mercuri LG. Temporomandibular joint surgery. J Oral Maxillofac Surg. 2012;70:204–31.
18. NICE. Total prosthetic replacement of the temporomandibular joint Interventional procedures guidance. Natl Inst Heal Care Excell [Internet]. 2014;(August):2–8. Available from: www.nice.org.uk/guidance/ipg500
19. Anantanarayanan P, Elavenil P, Bhoj M. Surgical Approaches to the Temporomandibular Joint BT - Temporomandibular Joint Disorders: Principles and Current Practice. In: Bhargava D, editor. Singapore: Springer Singapore; 2021. p. 171–87. Available from: https://doi.org/10.1007/978-981-16-2754-5_14

20. Dingman RO, Grabb WC. Intracapsular temporomandibular joint arthroplasty. Plast Reconstr Surg. 1966 Sep;38(3):179–85.
21. Rowe NL. Surgery of the temporomandibular joint. Proc R Soc Med. 1972 Apr;65(4):383–8.
22. Al-Kayat A, Bramley P. A modified pre-auricular approach to the temporomandibular joint and malar arch. Br J Oral Surg. 1979 Nov;17(2):91–103.
23. Rongetti JR. Meniscectomy; a new approach to the temporomandibular joint. AMA Arch Otolaryngol. 1954 Nov;60(5):566–72.
24. Santos GS, Nogueira LM, Sonoda CK, de Melo WM. Using endaural approach for temporomandibular joint access. Vol. 25, The Journal of craniofacial surgery. United States; 2014. p. 1142–3.
25. Alexander RW, James RB. Postauricular approach for surgery of the temporomandibular articulation. J Oral Surg. 1975 May;33(5):346–50.
26. Elledge R, Mercuri LG, Attard A, Green J, Speculand B. Review of emerging temporomandibular joint total joint. Br J Oral Maxillofac Surg [Internet]. 2019; Available from: https://doi.org/10.1016/j.bjoms.2019.08.009



Part 1

Literature analysis and development



Chapter 2

Alloplastic temporomandibular joint replacement systems: a systematic review of their history

This chapter is based on:
The Alloplastic Temporomandibular Joint Replacement Systems: A Systematic Review of their History.

Nikolas De Meurechy
Maurice Y. Mommaerts

International Journal of Oral and Maxillofacial Surgery 2018 Jun;47(6):743-754

Introduction

The temporomandibular joint (TMJ) is subjected to more cyclic loading and unloading than any other joint in the body. As a result temporomandibular disorders (TMDs) are far from rare.(1) Early data from 1990 indicated a prevalence of TMD of about 12% in the general population, but more recent literature provides more conservative estimates.(1) A 2008 study by the National Health Interview Survey(2) concluded that up to 5% of all Americans deal with TMD-related pain, and a study conducted by Janal et al.(3) in 2008 noted an even higher prevalence, showing that up to 10% of all female patients examined had a TMD. The literature concurs, however, that a significantly higher proportion of TMDs manifest in women than in men (3:1 ratio). Furthermore, symptoms tend to first present themselves between the ages of 20-40 years, and tend to lessen as the patient ages. (1–3)

Despite the high prevalence of TMDs, the use of a surgical approach is only rarely needed. As such, the pre-requisites for TMJ replacement surgery are a combination of positive radiological imaging confirming pathology and structural changes within the TMJ, a significant history of pain, dysfunction, and failure of previous conservative and surgical treatments. The current indications for TMJ replacement surgery by the American Association of Oral and Maxillofacial Surgeons (AAOMS)(4) and the National Institute for Health and Care Excellence guidelines(5) are listed in Table 1.

Table 1: Indications for TMJ replacement surgery.(2,4,5)

Multiple-operated TMJ with insufficient result
Ongoing symptoms and severe functional limitation despite previous alloplastic implants
Connective tissue and autoimmune diseases
Inflammatory, infective, or reactive diseases
Ankylosis
Failed reconstruction with autogenous grafts
Neoplasia

At first, joint surgery largely consisted of surgical excision that was mainly performed for severely damaged joints, with the first documented hemi-

and total mandibular resections dating from the early 19th century.(6,7) The initial placement of alloplastic material as a treatment for TMD dates back to the mid-19th century. The surgical procedures performed in this first century of TMJ intervention can largely be classified as 'experimental", with concepts rarely gaining attention. By the mid-20th century, however, many different types of TMJ surgeries and TMJ replacements were being explored, ranging from disk prosthesis to total joint replacement (TJR). Despite promising short-term results, the long-term results of these systems often proved disappointing, and in some cases resulted in serious inflammation with destruction of the surrounding tissues. As a result, this era of development soon tapered off. Although many different systems were once conceived, only two main manufacturers of serial US Food and Drug Administration-approved, total TMJ prostheses remain globally. An overview of the different prosthetic systems is provided in Tables 2-4.

Materials and Methods

Information about the history and evolution of the TMJ prosthesis over time was gathered by performing a computerized literature search using several databases. This search was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.(8) The following databases were used: PubMed Central, Elsevier ScienceDirect Complete, Wiley Online Library Journals, Ovid Lippincott Williams & Wilkins, and Cochrane Library Plus. The following search terms were used: ("TMJ" OR "temporomandibular joint") AND ("replacement" OR "prosthesis") AND ("history" OR "evolution" OR "advancement"). The combination in which these terms were used varied slightly depending on the database, although the search terms themselves remained unchanged. To assess the methodological soundness of each article, a quality evaluation was performed using the 2011 Oxford Centre for Evidence-Based Medicine Levels of Evidence (OCEBM LOE) recommendations.(9) Quality was categorized from levels I to V. Articles written in a language other than English, Dutch, German, or French were not included.

The initial search returned 7122 published articles. Subsequently, the number of articles was reduced by removing all duplicates, after which titles and abstracts of the remaining articles were screened on their content and relevance to the search. In case of any uncertainty, a second reviewer was called on to evaluate the title or abstract as well. This process led to the exclusion of 7036 articles. After examining the final 86 articles and confirming the quality of these studies, excluding any level V studies, 20 articles were included in the systematic review. An additional 21 articles were identified by manually searching the reference lists of the included articles. These articles mainly concerned the original articles of the different prostheses reported over time. The search results are summarized in a PRISMA flow chart in Fig. 1. Considering the need for historical accuracy, a few original articles concerning early implant systems could not be excluded for obvious reasons, even when they attained only level V for quality; these studies are marked "H".

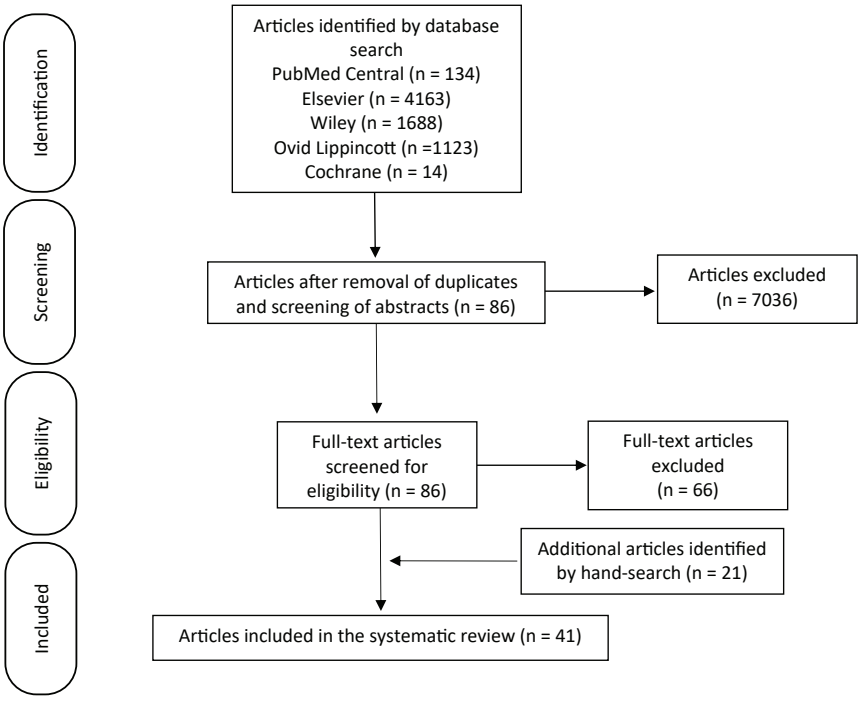


Fig. 1: PRISMA flow chart

Results

TMJ fossa-eminence prostheses and condylar prostheses used separately

Interpositioning materials and fossa prosthesis

John Carnochan(10) (H) was a pioneering neurosurgeon who first described the use of an interpositioning material in the 1840s as a treatment technique for the ankylosed TMJ. He carved a piece of wood for gap arthroplasty that was inserted between the glenoid fossa and condyle.(7,11,12) The literature then fell silent for decades until 1889, when Rosner introduced the use of gold as an interpositioning material after performing a condylectomy to prevent recurrent ankylosis.(6)

This design was further altered by Orlow(13) (OCEBM LOE IV) in 1903, who made use of gold-coated aluminum plates that were fixed to the resected bone.(6) As relatively good results were seen in two of the three patients treated by Orlow(13), the use of interpositioning materials to prevent recurring ankylosis after TMJ resection gained traction. Consequently, several different materials were used as interpositioning material placed below the fossa, with the aim of reducing the foreign body reaction. These include ivory by Partsch(14) (H) in 1932, gold foil by Risdon(15) (H) in 1934, and a metallic plate by Risdon(6) (H) in 1934. Later, tantalum foil was used as an interpositioning prosthesis by Eggers(16) (H) in 1946 and Goodsell(17) (H) in 1947.(11,12,18–20) However, tantalum foil had a tendency to be displaced, which Goodsell(17) attempted to prevent by fixing the foil using two stainless steel wires that ran through the foil and several drill holes made in the fossa.(18) Despite the improved anchorage, the tendency of tantalum to fragment remained, which caused inflammation and further ankylosis; therefore, the material was abandoned.

Although the use of interpositioning materials is a technique that is still relied upon, the early literature is mainly limited to sporadic case reports and letters of opinion. A notable step forward was made in the 1950s, which could be considered the dawn of customized TMJ biomaterials,

when Smith and Robinson (OCEBM LOE IV) developed stainless steel custom-made bent plates for gap arthroplasty.(11,12,19,21) Compared to the previous plethora of gap inserts, this new concept was revolutionary because their approach initially focused on joint dynamics. By bending the plate, a pivoting point for the mandible was created, allowing better movement of the lower jaw.(18,19) This concept brought a new stimulus to the field of TMJ prosthesis design, and 3 years later, Robinson developed a 'false' fossa implant out of stainless steel that covered the glenoid fossa and articular eminence and was fixed to the zygomatic arch using two screws. This design was meant to improve implant and joint stability, and as such, achieved success and longevity.(12,18,19) Due to the box-like design of the fossa, the posterior slope of the articular eminence was absent, allowing for increased forward movement of the mandible.(19)

In 1963, Christensen, inspired by Robinson's idea to create a fossa prosthesis, created a 0.5-mm Vitallium (a cobalt-chromium (CoCr) alloy) plate covering the fossa and articular eminence.(11,12,18,19) Christensen's plate incorporated screw holes over the zygomatic arch and lateral articular tubercle.(19) A portfolio of initially 20, and later 33 and 44, different templates was produced to assist the surgeon in selecting the 'best fit' stock implant. Not only was this the first approach that allowed the surgeon to select the best fitting prosthesis without having to worry about peri-operative reshaping of bony structures, it was also the first interpositioning prosthesis used on a more significant scale, and it is still used today.(18–20) In 1964, despite previously reported negative outcomes, Hellinger made use of tantalum foil. While results were not noteworthy, Hellinger left a mark on the history of the TMJ implantology by being the first to consider physical therapy as a keystone component of rehabilitation.(11) In 1965, Morgan made further modifications to Christensen's original design and limited coverage to the articular eminence, providing five different stock implants. As the implant was only meant to be used in cases of osteoarthrosis and arthritis, the risk of recurring ankylosis due to covering only the articular eminence instead of the entire fossa was minimal.(18,19)

Another milestone occurred in 1968, when the Silastic sponge (polysiloxane) was introduced to the field of prosthetic TMJ surgery by Robinson, as an alternative to stainless steel. While first being introduced as an interpositioning material in hand surgery, it quickly made its way into other prosthetic fields. (11,18) Despite Silastic's relatively short life span in the world of implantology, it can be considered as one of the materials with the biggest impact on TMJ implantology. As well as Robinson, Morgan also made use of Silastic, albeit as an addition to his previously developed Vitallium prosthesis. When a degenerative condyle was present, the use of a Silastic® block was recommended to seat the Vitallium prosthesis more caudally to compensate for the diminished condylar height.(18,19)

Two final important designs were the Vitek Teflon interpositional implant, first introduced in 1976(22), which will be discussed further on, and the Kriens(23) (OCEBM LOE IV) fossa prosthesis, which made use of Silastic® and was first used in 1973. This prosthesis was unique in that it abandoned the use of metallic parts altogether. It consisted of two Silastic strips that were implanted below the fossa and were then shaped by the pressure and movement of the condyle, which allowed for the prosthesis to achieve a well-adapted fit.(18,23)

Table 2: Interpositional materials and fossa prosthesis.(6,12,13,15-19,21,24-26)

Material	Surgeon	Year of introduction
Wood	Carnochan	1840
Gold	Rosner	1889
Gold-coated aluminum plate	Orlow	1903
Ivory	Partsch	1932
Gold foil	Risdon	1934
Metallic plate	Ridson	1934
Tantalum	Eggers	1946
Tantalum	Goodsell	1947
Stainless Steel	Smith and Robinson	1957
Stainless Steel	Robinson	1960
Co-Cr	Christensen	1963
Tantalum	Hellinger	1964
Co-Cr	Morgan	1965
Silastic®	Robinson	1968
Silastic®	Kriens	1973
Proplast-Teflon	Vitek	1976

Condylar prosthesis

The early days of the condylar prosthesis began with development of the immediate prosthesis, including the natural rubber prosthesis developed by Martin in 1878 and the hollowed-out hard rubber prosthesis by Schöder that was first used in 1901. These first two 'prototypes' served as a blueprint from which many alterations were made, such as the removable immediate tin prosthesis by Fritzsche in 1901 and the Partsch glass prosthesis in 1917. They were fitted to the non-resected part of the mandible and could be either screwed onto the resection stump or secured to adjacent teeth using several clips. Their main purpose was not to serve as a functional replacement but rather to prevent postoperative scar contraction and provide sufficient soft tissue support.(6)

The use of a functional condylar prosthesis was first mentioned in 1890, at the height of the ivory trade, by Gluck(24) (H). He described a partial joint arthroplasty with an ivory condylar prosthesis.(11) Gluck adapted his technique following previous success with this endo-prosthesis material in total wrist arthroplasty and developed one of the first implant prostheses that could be fixed to the residual jaw. About 20 years after development of the condylar prosthesis by Gluck, both König(25) (H) and Sudeck(26) (H) also implanted an ivory ramal prosthesis. These early designs were fixed by placing a spike situated at the corporal end into the spongious bone of the mandible. While initially retaining acceptable stability, an increase in mobility was seen over time, which made it necessary to remove the prosthesis.(6) 50 years later, in 1964, Hahn(27) (OCEBM LOE IV) introduced his 'ramus prosthesis' to reconstruct the vertical ramus and condyle following ablative surgery. Possibly inspired by the results of Christensen's fossa prosthesis, Hahn developed a Vitallium mesh prosthesis with an acrylic condyle. The idea behind the mesh design was that it would allow enhanced fibroblast penetration and scar tissue formation to improve prosthesis stability.(18)

During the 1970s, as the hip prosthesis was further developed, several of its principles and design aspects were clearly taken up by innovators who furthered the development of the TMJ prosthesis**.** The first, and probably most infamous in the history of the TMJ prosthesis, was the introduction

of polytetrafluoroethylene (PTFE), also known as Teflon, to the field of TMJ surgery by Kent(28,29) (OCEBM LOE IV, OCEBM LOE III) in 1972. The material was deemed of interest because it had a porous structure that allowed soft and hard tissue ingrowth and potentially allowed better fixation. Kent used Proplast, a mixture of carbon fibers and Teflon, which was used to coat the condylar head of a CoCr ramal prosthesis. (28,29) To further improve implant stability, the ramal component was redesigned with an L-shape 2 years after its introduction.(18,19) A second alteration to the design was made 11 years after its introduction due to a significant number of patients showing resorption of the glenoid fossa. As countermeasures, the condyle was flattened and elongated, and a fossa component was developed to be combined with the condyle.(18)

Keeping this complication in mind, Spiessl(30) (OCEBM LOE IV) developed a titanium condylar prosthesis in 1976, which also was known as the AO/ASIF prosthesis (Association for Osteosynthesis (AO)/Association for the Study of Internal Fixation (ASIF)). In addition to being influenced by the Kent prosthesis, he also applied the concept of intramedullary placement, which had become a favorable means of fixation in orthopedic surgery. Further stability and fixation were provided by seven transcortical screws. (18,19) Presently, the AO/ASIF prosthesis is still available, although it is used with certain alterations. Short and longer versions have been developed in addition to a condylar head 'add-on' option. Despite the manufacturer stating that the short condylar implant can still be used for certain indicated pathologies(18), a total TMJ replacement system should be preferred over the use of a condylar prosthesis, as discussed later.

In 1977, Silver et al.(31) (OCEBM LOE III), inspired by orthopedic prosthetic hip surgery, developed a condylar prosthesis which was fixated using both a rectangular intramedullary Vitallium pin and polymethylmethacrylate (PMMA) cement. However, due to the heat created during the polymerization process, causing risk of thermal damage to surrounding tissues, the prosthesis was abandoned.(18) Furthermore, two of the three implants that were placed showed mobility, which proved that the system was too unstable for implantation.(19) Raveh et al.(32) (OCEBM LOE IV) introduced a titanium-based system with a ball-joint

design in 1982, in which the position of the condyle could be adapted not only in the coronal plane but also in the axial and sagittal planes. The condyle was fixed with two screws in the correct position, after which the implant was fixed to the lower mandibular border using a reconstruction plate and four titanium-coated hollow screws.(18,19) While in theory a very interesting system, the prosthesis was only seldom used due to difficulty in positioning of the condyle.

Flot et al.(33) (OCEBM LOE IV) also found clear inspiration in orthopedic prosthetic surgery. In 1984 they developed a condyle prosthesis with a polyethylene domed 'cap' that covered a steel or titanium head. This cap however was not fixed to the fossa, allowing for forward and lateral movement, as the cap could move over the fossa. Furthermore, Flot et al.(33) claimed that additional rotational mandibular movement was made possible due to movements between the head and the cap. The prosthesis was fixated using a screw-shaped intramedullary stem.(19) In 1987, due fretting and fragmentation of polyethylene, the material of the cap was changed to Al_2O_3-ceramic.(18)

Table 3: Materials and TMJ condylar prosthesis.(6,13,20,21,26-35)

Material	Surgeon	Year of introduction
*Rubber	Martin	1878
*Rubber	Schöder	1901
Ivory	Gluck	1890
*Tin	Fritzsche	1901
Ivory	König	1908
Ivory	Sudeck	1909
*Glass	Partsch	1917
Co-Cr with acrylic condyle	Hahn	1964
Co-Cr with condylar Teflon coating	Kent	1972
Titanium	Spiessl	1976
Co-Cr with PMMA cement	Silver	1977
Titanium	Raveh	1982
Steel with polyethylene cap	Flot	1984
Titanium with Al_2O_3 cap		1987

*: It should be remarked that these prostheses were immediate prosthesis instead of implantation devices.

Total TMJ replacement

Having developed one of the first serial-produced fossa prosthesis in 1963, Christensen also created the first total TMJ prosthesis in 1965 by combining his Vitallium fossa-eminence implant, which was first reported in 1970, with a standardized cast Vitallium ramus component with a PMMA condylar head (11,12,18) Inspired by Christensen's fossa prosthesis and Hahn's ramus prosthesis, Kiehn et al. designed a total TMJ replacement consisting of a Vitallium mandibular fossa plate and a Vitallium ramus-condyle prosthesis in 1974.(11,18) Both components were fitted and fixed using PMMA cement. Burr holes in the mandibular ramus and the lateral part of the glenoid fossa increased the cement contact area between the prosthesis and bone, thus improving retention. However, as previously mentioned, the use of PMMA cement was abandoned, and thus the prosthesis as well. Two years later, Morgan designed a condylar prosthesis to be used in combination with his previously designed fossa-eminence prosthesis. The mandibular component consisted of a Vitallium plate that was screwed to the mandible and an acrylic condylar head to articulate with the fossa component.(12,19) In 1984 House, Morgan, et al. (34) (OCEBM LOE IV) published a follow-up study, discussing the results of the implant system. Although 41.7% of the responding patients reported excellent results, fair to poor results were reported by as many as 29.4% of the patients.

Momma was the first to make use of a metal-on-metal total TMJ replacement system, using screw fixation, in 1977. Both the mandibular component and fossa of the Protasul were made out of Vitallium. While anterior-posterior movement was possible, movement in other directions was limited.(19) During the same year Kummoona(35) (OCEBM LOE IV) introduced his CoCr metal-on-metal TJR. Similar to the condylar prosthesis of Silver et al.(31), Kummoona's condylar component was fixated using both an intramedullary stem and PMMA cement. A second significant difference between the prostheses of Momma and Kummoona, other than the materials used, was found in the fossa. The fossa component covered the glenoid fossa, zygomatic arch, and zygomatic process of the temporal bone and was fixed with screws. The key part of the design, a flattened condylar head, was to encourage fibrous tissue penetration across the head of the prosthesis from the joint capsule.(18,19) The idea was that

the 'fibrous cushion' would reduce wear and tear. Kummoona tested this prosthesis in primates and found that 50% failed after 9-10 months due to dislocation of the condylar component. (35) Post-euthanasia dissection together with microscopic and microradiographic examinations showed that the prosthesis had acceptable biological tolerance.

In 1983, the Vitek-Kent prosthesis was created.(12,20,36) This prosthesis has arguably shaped the history and evolution of the TMJ prosthesis more than any other design, albeit not in a positive way. As stated earlier, Kent noticed that the use of only a condylar prosthesis led to resorption of the fossa. In response to this problem, the condylar component was redesigned to have a more flattened and elongated head, and a fossa component was developed. Originally, the fossa component had a bilaminated structure. The articulating side consisted of a 2-mm high density PTFE coating (Teflon). The surface of the tissue-side consisted of a more porous carbon fibre-reinforced Teflon, also known as Proplast I. Later, this layer was altered to an aluminum oxide fiber-reinforced Teflon layer (Proplast II). Also the medial aspect of the ramus was coated with Proplast. The shape of the fossa prosthesis was pre-operatively based on lateral radiographic tracing and could be adapted further by carving, after which it was fixed to the zygomatic arch using three screws.(12,19,20)

However, it quickly became apparent that Teflon was not suitable as an articulating surface, as wear debris began accumulating only several years after implantation of both the implant system and the Teflon interpositional disc replacement. This led to foreign body giant cell reactions (FBGCR), bone resorption, and refractory pain syndromes. In response to these complaints the articulating Teflon layer of the fossa component was replaced with an ultra-high molecular weight polyethylene (UHMWPE) layer in 1986.(12,18,19,36) Despite this attempt to salvage both the TJR system and the disc prosthesis, Proplast then proved insufficiently strong, resulting in fragmentation of the material.

As both the Vitek disc implant and the Vitek-Kent system gained considerable popularity among maxillo-facial surgeons, leading to their implantation in several thousand patients, the backlash was equally

as impressive as its quick rise in popularity, and this resulted in many surgeons temporarily avoiding the use of alloplastic TMJ TJR. Within 10 years after its first use, the FDA recommended the recall of all patients treated with the Vitek disc prosthesis, following which the AAOMS and FDA recommended removal of the implant, as expanded on in the Discussion section.(12,18,37)

In 1983, Sonnenburg and Fethke developed the first version of their prosthesis. The titanium/palladium alloy condylar part had a spherical head connected to a base. This base was fixed on the mandible where the autologous condyle had originally been, using a plate with five screw holes. The fossa component was made from high-pressure polymerized polyethylene and was fixed to the articular tubercle with a single screw. To assure a precise fit and sufficient fixation, PMMA cement was used between the fossa component and the base of the skull. (11,18,19) The fossa for this first version was developed based on cephalometric tracings of the patient's fossa, making the system somewhat a patient-specific implant. With production in mind, Sonnenburg and Sonnenburg(38) (OCEBM LOE IV) then designed a new polyethylene fossa prosthesis with a reduced antero-posterior dimension, although fitting and fixation was still done using PMMA cement.(19)

In 1989, Techmedica developed a patient-specific total TMJ replacement system using data obtained from computed axial tomography scans of a patient's skull. The prosthetic joint was first designed on a computer-aided design/computer-aided manufacturing (CAD/CAM) system and fitted to a replica of the patient's skull. Differences in patient-specific occlusion, jaw position, and anatomy could be adjusted at the design level and then checked at the construction level. The fossa component consisted of titanium mesh coated with UHMWPE.(12,18,19,39,40) The titanium mesh allowed for bony and soft tissue ingrowth, furthering the fixation in addition to the three to four screws that were placed in the zygomatic arch. The condylar component of the prosthesis was composed of a titanium alloy shaft and a cobalt-chrome-molybdenum (CoCrMo) alloy head. It was fitted to the mandible using six screws, although this number was increased after reports of stability problems.(19) The

condylar head was designed to have the same geometry as the UHMWPE fossa to maximize contact while reducing the amount of wear.(18) Techmedica ceased production in 1993 after the FDA ordered a stop to the manufacturing of all TMJ prosthesis that were developed after 1976, as a direct effect of complications seen with the Vitek-Kent TMJ system. In 1997, TMJ Concepts took over manufacturing, after marketing was once more allowed by the FDA in 1996.(40) In 1999, the system received full FDA approval.(18) Mercuri et al.(39,41) and Wolford et al.(42) conducted several multi-center follow-up studies, evaluating patients treated between 1989 and 1993, with a TMJ concepts TJR device. The first study was conducted 1 year after implantation and the most recent study was published in 2015. All studies had similar conclusions, stating a significant decrease in pain, and a significant increase in mandibular function, mouth opening and quality of life. Furthermore, no failures were seen during long-term follow-up, although it should be noted that only 56 out of 111 patients were included in the most recent study.(39,41,42)

In 1992, Bütow et al. started developing a titanium/titanium nitride TMJ (TTN-TMJ), which was released in 1994. Both the condylar surface and fossa were treated with nitride to harden the material and create better wear properties.(18) Bütow et al.(43) (OCEBM LOE IV) released a clinical review of their system in 2001, evaluating 27 patients. It is unclear if the system was used afterwards. A year after the TTN-TMJ system was released, Hoffman and Pappas released a CAD/CAM system that resembled both the TMJ Concepts and TTN-TMJ system. While the fossa consisted of titanium mesh with a UHMWPE articulating surface, the condylar component was composed entirely of titanium, with the articulating surface coated with nitride. Unique to this system was the possibility of replacing the UHMWPE surface in case of deterioration, by sliding the UHMWPE block out of the titanium base. Furthermore, the system required fewer screws compared to other systems due to the use of micro-locking screws.(44) Tsang et al.(44) (OCEBM LOE IV) conducted a retrospective study in 2008 evaluating 113 implants placed between 1995 and 2006, and stated that the system produced good results. However, the Hoffman-Pappas TMJ system did not receive FDA approval and production was halted.

Walter Lorenz Surgical Inc. (now Biomet Microfixation, Jacksonville, FL, USA) also released a stock prosthesis. The glenoid fossa was made from UHMWPE (ArCom) and was provided in three different sizes ranging from small to large.(12,18) Although initially additional fixation of the fossa could be obtained using PMMA cement, this approach was abandoned due to the risk of thermal damage. Furthermore, fragmentation of PMMA under functional loading was observed.(18) The mandibular component consisted of a CoCr alloy and the ramal surface of the condylar implant was coated with titanium plasma spray, creating a rougher surface. Like the fossa, the ramal component was provided in three different lengths (45, 50, and 55 mm) and styles (standard, narrow, and offset).(12) All components were freely interchangeable and selection was made based on the patient's anatomy. The system received FDA approval ten years after its initial release in 1995 and has been used widely since then. A recently released 3-year follow-up by Giannakopoulos et al.(12) (OCEBM LOE IV), with over 442 implants, revealed satisfactory results. A significant decrease in pain intensity was found, while a significant improvement in mouth opening and jaw function were seen. Furthermore, no device-related mechanical failures were observed. A follow-up study by Lobo Leandro et al.(45) (OCEBM LOE IV), which included 300 patients, reported similar results.

In 1996, due to reports of fragmentation of PMMA under functional loading, Chase reinvented Christensen's prosthesis, now known as the Nexus CMF system, by replacing the PMMA condylar head with a CoCr condylar head. (7,11) This change was inspired by metal-on-metal systems that were used in orthopedic hip prostheses, although Chase and Christensen both failed to recognize the difference in loading between both the hip joint and the TMJ, which would have dire consequences for the system.(7) Two years later, Christensen developed a metal-on-metal all cast CoCr TJR system, which was designed and manufactured much like the TMJ Concepts system.(18) Initial short-term clinical studies were positive, boasting lower amounts of wear compared to metal-on-acrylic systems, as well as good clinical results. This led to FDA approval for the device in 2001.(46,47) However, long-term studies reported on patients with metallosis, prosthesis loosening, osteolysis, and implant failure. As a result, the approval was withdrawn in 2015 and production of the device has halted.(7)

Another recently introduced system is the Groningen TMJ prosthesis, which was released in 1999.(48) (OCEBM LOE IV) Both a stock implant and patient-specific implant were developed. The latter was used when the patient had an insufficient amount of bone to use the stock device. The system used a titanium fossa with a zirconia plate on the articulating side. The ramal component was also made of titanium, with the condyle being composed of a zirconia ball. A UHMWPE disc was placed between the zirconia fossa and condyle.(18,48) Adapting Falkenström's 1993 design, which placed the point of rotation more inferior to the middle of the natural condyle, creating a translation movement when the mouth was opened, the center of rotation was placed more inferiorly compared to other TMJ prostheses.(19,48) Falkenström also calculated that by lowering this point of rotation, the use of a unilateral prosthesis would no longer overload the contralateral healthy joint over time.(19) Evaluation after 8-year follow-up of the Groningen TMJ prosthesis showed that it was mechanically successful in 87.5% of patients, and patient satisfaction was scored high.(48) Due to a lack of perceived financial viability, however, “mainstream” manufacturing ceased.

Discussion

To understand the evolution of the alloplastic TMJ prosthesis, several different aspects of its development must be highlighted. Changes in materials and designs over time will be discussed in an attempt to explain why certain systems failed whereas other systems were successful and are still used today.

Materials

When evaluating the evolution of the TMJ prosthesis, be it a fossa prosthesis or a TJR device, it is apparent that each new design utilized the newest materials that were available at the time of its conception. (7) However, not all of these materials were suitable for implantation, as became abundantly clear through postoperative results. For a material to be suitable for implantation, it must meet several criteria. First, proper fixation of the implant system (to preventing micromotions)

Table 4: Materials and Total TMJ prosthesis. (13,20, 21, 36, 38-44,46-48)

Material	Surgeon	Year of introduction
Ramus: Co-Cr with PMMA condyle Fossa: Co-Cr	Christensen	1965
Ramus: Co-Cr Fossa: Co-Cr with PMMA cement	Kiehn	1974
Ramus: Co-Cr with acrylic condyle Fossa: Co-Cr	Morgan	1976
Ramus: Co-Cr Fossa: Co-Cr	Momma	1977
Ramus: Co-Cr with PMMA cement Fossa: Co-Cr	Kummoona	1977
Ramus: Co-Cr Fossa: Teflon® and Proplast® (I and II) Fossa: Proplast® and UHMWPE	Vitek-Kent	1983 1986
Ramus: Titanium and palladium Fossa: Polyethylene with PMMA cement	Sonnenburg and Fethke	1983
Ramus: Titanium and palladium Fossa: Polyethylene with PMMA cement	Sonnenburg and Sonnenburg	1983
Ramus: Titanium with Co-Cr-Mo condyle Fossa: Titanium and UHMWPE	Techmedia	1989
Ramus: Nitride coated titanium Fossa: Nitride coated titanium	TTN-TMJ	1992
Ramus: Titanium with nitride coated condyle Fossa: Titanium and UHMWPE	Hoffman and Pappas	1993
Ramus: Co-Cr Fossa: UHMWPE	Biomet	1993
Ramus: Co-Cr Fossa: Co-Cr	Nexus CMF	1996
Ramus: Titanium with zirconia condyle Fossa: Titanium and zirconia Interpositional disc: UHMWPE	Groningen TMJ	1999

and osseointegration of the ramal component of the TMJ TJR system are absolute necessities for treatment success.(49) The process of osseointegration is influenced by many different factors, including the properties of the material.(50) For instance, while the implant material must be stiff enough to prevent micromotions after implantation, which prevent good osseointegration, the elastic modulus must be comparable to that of bone to prevent the shielding of the underlying bone from forces on the implant, as the under-stimulation of bone can decrease bone density, leading to bone resorption and failure of osseointegration.(51,52) Second, the wear resistance of material properties is important. Considering that the prosthesis is subjected to repetitive force and movements, a material

with a lower wear resistance will undergo wear and develop wear debris. As a result, the implant will have a shortened total life span and the wear debris formed can possibly result in an inflammatory or allergic reaction.(52–54) Third, the materials must be biocompatible. When this is not the case, adverse reactions such as foreign body giant cell reactions (FBGCR) or metallosis can be seen.(53,55)

A more in-depth discussion of these critical biomaterial properties can be found several excellent articles.(56–59) This paper will focus on the more significant materials that have left their mark on the history of the TMJ prosthesis.

Earliest materials

Some of the earliest materials used for the TMJ prosthesis were wood (Carnochan(10)) in 1840, ivory (Gluck(24)) in 1890, and tantalum (Eggers(16) and Goodsell(17)) in 1946-1947. Although there are no other reports of wood being used in the TMJ, several animal studies evaluated wood as a potential biomaterial. Kristen et al.(60) implanted alcohol pre-treated ash wood into the dorsal part of the calcaneus of rabbits in 1979, and on explantation noticed soft tissue growth of the Achilles tendon as well as bony ingrowth into the pores, had occurred. Gross and Ezerietis implanted juniper wood femur prostheses into rabbits.(61) Juniper wood was chosen because of its stiffness that approaches that of bone and its porous structure allowing for bony ingrowth. It also releases a natural oil that prevents infection. Before implantation, the wood was treated by placement in boiling water for 10 minutes. During the 3 year follow-up no foreign body cell reaction was found, and no signs of hindrance due to the prosthesis were observed in the rabbits. The authors concluded that the bone showed ingrowth into the wood and that the implant was capable of withstanding functional forces. While these studies might indicate that certain types of wood could be suitable for implantation after being treated before implantation, no human *in vivo* studies have ever been undertaken, thus the possibility of success is impossible to predict. Furthermore, it would be safe to assume that Carnochan(10) was unaware of these essential factors. Since 1840, there have been no reports of the use of wood as an interpositioning material in the TMJ.

Ivory was first used as TMJ implant material by Gluck, yet its use was not exclusive to the TMJ. Ivory was also favored by many plastic surgeons after Joseph first used the material as nasal dorsum for rhinoplasty in 1918. Implantation continued until the middle of the 20th century; when a 40% rejection rate was observed, resulting in the material being abanded. (62–65) Pichler also described the need for explantation of the ivory condylar prosthesis by Köning due to loss of stability.(6) Despite these findings, Baw developed a femoral prosthesis that made use of an ivory head. He chose the material because of properties such as the friction coefficient, which was close to that of cartilage if the ivory was well polished, as well as strength, being nearly as strong as Vitallium when statically compressed. He placed more than 100 ivory hip replacements with a reported success rate of 88%.(66)

A third material worth mentioning is tantalum. Although the material was recently reintroduced in the field of knee and hip arthroplasty, it was first used in neurosurgery for cranioplasty, after Burke(67) and Pudenz(68) demonstrated that the material had high corrosion resistance.(69) Furthermore, Pudenz(68) noticed the formation of a tissue capsule around the material, which made surgeons believe that the implant was better fixed. Not much later, the material was used as an interpositional foil in the TMJ by Eggers(16) and Goodsell.(17) However, as it was very expensive to make, and was reported to fragment and result in inflammation, the use of tantalum was halted.(18,69)

Subsequent generation of materials

Silicone elastomers

The polydimethylsiloxane silicone elastomer Silastic was first produced by Dow Corning in 1948. After Wesolowski et al.(70) concluded that the material was biologically inert when used as joint replacement material in 1966, it quickly gained attention in the medical world because it was easily carved, did not allow tissue ingrowth, was flexible and was easily available.(71) The popularity of the elastomer followed in part after a misinterpretation of Brown's research by Braley.(72) While Brown et al.(73) concluded that the material was capable of preventing recurring ankylosis of the joint, as they noticed that a fibrous capsule had formed

around the implant, Braley[63] failed to mention that Brown et al.[64] explanted the discs at the end of their experiment. Silastic was first used for hand surgery in 1968 but was quickly adopted by maxillofacial surgeons. Robinson added a layer of Silastic to his fossa prosthesis in the same year, where it served as interpositioning material between the surface of the prosthesis and the bony fossa.(18) Morgan et al.(18) used Silastic to line the fossa prosthesis in cases of a degenerated condyle, while Kriens et al.(23) went one step further and removed the metal fossa, exchanging it for several layers of Silastic, which were then shaped by the pressure of the condylar component of the prosthesis.

While short-term results were very promising, positive reports of long-term results without complications were initially lacking. Mercuri stated that this could have been due to a reluctance to report, but by 1982 reports of the fragmentation of the material and FBGCR in humans and animals became more frequent, and the long-term instability of the material became clear.(74) Small Silastic particles were found in lymph nodes near the implant site, and severe reactive synovitis was reported.(71,74) In 1992, Eriksson et al.(75) compared patients who underwent a discectomy with patients who received a Silastic implant and concluded that all patients who showed less favorable results had received a Silastic implant. Mercuri and Giobbie-Hurder concluded that patients who were previously exposed to Silastic showed poorer long-term outcomes after alloplastic reconstruction compared with patients who had not come into contact with the material.(74) This resulted in the AAOMS advising against further use of the material in 1993, leading to a halt in the production of Silastic.(76)

Polytetrafluoroethylene

First developed in 1938, PTFE found its way into medical applications after Cook reported on its successful use as an interpositional material with an absence of inflammatory reaction in two animal studies and four human cases, which were followed for a period of 18 months.(77) Opposing these findings were studies conducted by Charnley(22,78) and Scales and Stinson(79), who noticed fragmentation of Teflon leading to FBGCR when the material was used in a hip prosthesis. Cook, however,

discarded these findings, claiming that the TMJ was subjected to lighter loads and would be less susceptible to fragmentation.(71) Influenced by Cook's findings, Kent coated the articulating surface of his condylar prosthesis with Proplast in 1972. By adding a fossa component to the ramal component in 1983, due to reports showing resorption of the fossa, the infamous Vitek-Kent prosthesis was created.(18,19,36,71,74) As with Silastic, the material was also used as a replacement for the TMJ disc, which was first devised in 1976. A survey conducted by Vitek(74) showed that over 5070 patients had been treated with the interpositional implant by 1986 and Spagnoli and Kent(80) estimated that up to 20,000 disc implants were placed before the production of the prosthesis was halted.

At the annual AAOMS meeting in 1986, there were several reports of implants showing biomechanical failure. Vitek, however, stated that the reported failures were due to operative technique of the surgeon rather than a flawed choice in materials.(80) As time went on, more reports were published showing far less promising results such as severe bony degeneration, FBGCR, material fragmentation, and particles found in lymph nodes near the implant site.(81–85) This led to the discontinuation of the Proplast disc replacement in 1988.(80) In the end, a study by Wagner and Mosby(22), as well as two master's theses from the University of Iowa, led the FDA to issue a safety alert in 1990 to US oral and maxillofacial surgeons, who were asked to re-examine all patients treated with Proplast or Teflon.(74) Wagner and Mosby found that 19 out of 20 patients treated with a Proplast-Teflon TMJ disc experienced severe pain, 14 patients showed a restricted maximum inter-incisal opening, and all patients showed radiological degeneration of the condyle. The authors concluded that this degeneration was caused by a FBGCR to the debris that was formed as the material wore down.(22)

In an attempt to salvage the TMJ TJR system, the outer Teflon layer was replaced by a UHMWPE layer, but Proplast also became recognized for its non-compatible properties and its accompanying signs of wear, fracture lines, and fractures.(54,71,80) A study by Spagnoli and Kent(80) concluded that up to 54% of all Vitek-Kent implants included in the study might fail, with the implant system having an average *in vivo* lifespan of

only 3 years. They also noted that while Vitek-Kent reported a 3% failure rate per year, most clinicians reported an annual failure rate of up to 18%. (22,80,82,86)

These findings resulted in the FDA recommendation to remove PTFE implants from all symptomatic patients and from asymptomatic patients showing radiological changes, as well as the discontinuation of the Vitek-Kent replacement system in 1992.(37)

Polymethyl methacrylate

PMMA was first used as an implantation material by Judet(87) in 1946, as a replacement for the femoral head. Although this system was far from a success, with significant breakage and tissue reaction to wear debris, the material still found its way into the field of TMJ surgery.(88) It was first introduced in 1954 by Healy(89), who used it to reconstruct the mandible after ablative surgery. Ten years later, in 1965, Christensen used it as the condylar head of his prosthesis. Several other surgeons such as Kiehn, Silver, and Kummoona used this acrylate as a cement to better fix the ramal or fossa component, and to achieve a better fit between the fossa and the base of the skull.(18,19,31,35) For PMMA to function as a cement, unpolymerized PMMA had to be combined with a catalyst, causing a polymerization reaction with heat being produced and dissipated to the surrounding tissues. Although a cadaver study by Mercuri et al.(90) confirmed that the amount of heat released was not sufficient to increase intracranial temperature, caution was strongly advised when using PMMA cement. Also, if the cement was unable to completely polymerize, it would not only result in a weakened state of the material, but residual monomers could also be washed out, leading to local and systemic reactions.(18) Furthermore, there were several reports that PMMA was not able to cope with normal functional loading, leading to fragmentation of the acrylate. As a result, the use of PMMA has been abandoned by all current implant systems.(18)

Current materials

Cobalt-chromium alloy

After first being introduced in orthopedic surgery, CoCr found its way to TMJ surgery in 1951, when Kleitsch and Castigliano used a Vitallium plate to prevent recurring ankylosis.(11,91) As it became clear that the material possessed several highly interesting properties such as high strength and fatigue resistance, high corrosion resistance, and good biocompatibility, it quickly became a favored implantation material. Due to its excellent wear resistance, it was even used as an articulating surface in total hip arthroplasty.(51) Although several systems made use of CoCr, such as the Biomet Lorenz and TMJ Concepts device, the system that most heavily relied on the use of a CoCr alloy was the metal-on-metal Christensen TJR system. While other systems articulated using metal-on-polyethylene communication, Christensen based his system on the early theoretical success of the metal-on-metal hip prosthesis and used a metal-on-metal articulation. This decision was based on the fact that the total wear volume in a metal-on-metal hip prosthesis is around a tenfold to even 100 times less than compared to a metal-on-UHMWPE implant.(46,52) What Christensen failed to notice, however, was that while the hip is a constrained joint, this is not the case for the TMJ, which is much more like the knee.(91) As a result, cyclic loading of the fossa could lead to micromotion, fretting corrosion, fatigue, and even fracturing of the fossa.(92) Also, although metal-on-metal TMJ devices produced less wear volume, the incidence of metal hypersensitivity was higher than with metal-on-UHMWPE prostheses, as was concluded by Wolford and Cassano after following up on 115 patients with a Christensen or TMJ Concepts system.(93) While only 3% of TMJ Concepts prostheses had to be removed due to metal hypersensitivity or device failure, 33% of Christensen prostheses had to be explanted. Similar findings were made by Sidebottom et al.,(94) who abandoned the Christensen system altogether.

Wolford et al.(53) reported that patients fitted with a metal-on-metal device exhibited significantly elevated body levels of Co and Cr. In comparison, patients fitted with a TMJ Concepts prosthesis showed no signs of UHMWPE or metallic debris, which indicated good wear

characteristics of the CoCrMo-UHMWPE combination in TMJ articulation. The same conclusion was reached by Westermark et al.(95) after histologic analysis of soft tissues surrounding Biomet and TMJ concept prostheses. These findings were further supported by several *in vitro* and *in vivo* studies showing that CoCr particles could exert toxic effects in exposed tissues. In animal studies, McGregor et al.(96) found sufficient evidence for the carcinogenicity of metallic Co and limited evidence for the carcinogenicity of Co alloys; thus, Co-containing implants were classified as possibly carcinogenic for humans. These findings led to withdrawal of FDA approval for the Nexus CMF system in 2015.

Design

Interpositional prosthesis

Between 1840 and 1980, the main purpose of the TMJ prosthesis was as a treatment for TMJ ankylosis.(7,97–99) The rationale behind the development of the intrapositional implant was that if something was placed between the fossa and condyle recurring ankylosis could be prevented, and this offered a less invasive alternative to procedures such as gap arthroplasty and condylectomy.(6,98) A recent meta-analysis by Ma et al.(98) concluded that interpositional arthroplasty could be considered a superior treatment to gap arthroplasty, as it resulted in a better maximal inter-incisal opening and lower rate of recurring ankylosis. Alternatively an autogenous interpositional graft, of which the temporalis flap is considered the most favorable, could also be used.(97,100) Yet these autogenous interpositional grafts are not without problems; the muscle may start to shrink and even develop fibrosis, cartilage could calcify or develop fibrosis and fascia might lack the necessary bulk.(101) In comparison, alloplastic materials are easy to use, do not incur donor site morbidity, and are abundantly available. When evaluating the evolution of interpositional materials, we can observe two distinct phases. First, different materials were tested, leading to the development of suitable materials for implantation. Second, from the middle of the 20th century onward, the volume of the prosthesis was reduced,(6) leading to the development of prostheses such as ultra-thin silicon sheets.(101)

From condylar to total TMJ replacement

While the interpositional and fossa prostheses were developed to treat ankylotic joints, the condylar and TJR prostheses aimed to restore mandibular function and form. Over time alloplastic TJR devices have become the gold standard treatment for irreparably damaged TMJs in adults and they have recently gained appreciation in older children.(102)

At first, most devices were of solitary focus, consisting of either a fossa or a ramal prosthesis. However, as it became clear that the solitary use of a condylar prosthesis led to resorption of the glenoid fossa, certainly in absence of an interpositional disc, total TMJ systems were developed.(18,19,103) In order to achieve good primary stability, reduce micromotions and allow good osseointegration, several techniques, such as the use of porous implants, PMMA cement, and intramedullary pins were conceived, yet none proved ideal.(18,19,49,51) A recent, more successful, option is the use of radiological imaging and CAD/CAM design. As the implant is developed to fit the patient's specific anatomy, optimal primary stability can be achieved. Current literature reviews have indicated that the use of patient-specific implants improves long-term outcomes over stock devices, with an increased quality of life.(49) As such, it is safe to assume that further individualization of TJR systems will be a driving force for future TMJ implants.

Future considerations

When evaluating the development of the alloplastic TMJ prosthesis, it is clear that its history was mainly a process of trial and error and that it has clearly been influenced by the development of new materials over time; such developments have often attracted the interest of the medical field. Principles in design as well as many materials were first tested in the field of orthopedic surgery, after which they found their way into the field of TMJ surgery. While some of these innovations proved suitable, such as the use of titanium or the metal-on-UHMWPE design, this was not always the case. The use of unsuitable materials such as Silastic and Teflon, as well as unsuitable design principles such as metal-on-metal systems or PMMA

cement, resulted in the need for explantation of the implant systems in several thousand patients, as well as a loss of confidence in the alloplastic TMJ TJR.

Although recent literature has shown satisfying results for these current systems, as well as a renewed interest in this field of prosthetic surgery, it is important to notice that further improvements can still be made. The continuing importance of CAD/CAM in the medical field will undoubtedly shape the development of the newer systems' designs, allowing for a better anatomical fit, improving fixation, and keeping the positions of various structures such as the inferior alveolar nerve in mind when designing the implant.(49) Also, advances can be made in the field of materials, such as new coatings and alloys (eg. β-titanium and alumina-toughened zirconia), allowing the development of implant systems with an elastic modulus closer to bone, with better wear properties, better biocompatibility, and so on.(52,104–107)

References

1. Guarda-Nardini L, Manfredini D, Ferronato G. Temporomandibular joint total replacement prosthesis: current knowledge and considerations for the future. Int J Oral Maxillofac Surg. 2008;37(2):103–10.
2. Isong U, Gansky SA, Plesh O. Temporomandibular joint and muscle disorder-type pain in U.S. adults: the National Health Interview Survey. J Orofac Pain [Internet]. 2008;22(4):317–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19090404%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4357589
3. Janal MN, Raphael KG, Nayak S, Klausner J. Prevalence of myofascial temporomandibular disorder in US community women. J Oral Rehabil. 2008;35(11):801–9.
4. Koslin M, Indresano AT, Mercuri LG. Temporomandibular joint surgery. J Oral Maxillofac Surg. 2012;70:204–31.
5. NICE. Total prosthetic replacement of the temporomandibular joint Interventional procedures guidance. Natl Inst Heal Care Excell [Internet]. 2014;(August):2–8. Available from: www.nice.org.uk/guidance/ipg500
6. Driemel O, Ach T, Müller-Richter UDA, Behr M, Reichert TE, Kunkel M, et al. Historical development of alloplastic temporomandibular joint replacement before 1945. Int J Oral Maxillofac Surg. 2009;38(4):301–7.
7. Mercuri LG, TMS. Temporomandibular Joint Replacement: Past, Present and Future Material Considerations. In: TMS 2014 Supplemental Proceedings [Internet]. John Wiley & Sons, Inc.; 2014. p. 181–90. Available from: http://dx.doi.org/10.1002/9781118889879.ch24
8. Moher D, Liberati A, Tetzlaff J, DG A, Group and the P. Preferred reporting items for systematic reviews and meta-analyses: The prisma statement. Ann Intern Med [Internet]. 2009 Aug 18;151(4):264–9. Available from: http://dx.doi.org/10.7326/0003-4819-151-4-200908180-00135
9. Howick J, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, et al. The 2011 Oxford CEBM Levels of Evidence: Introductory Document [Internet]. Oxford Centre for Evidence-Based Medicine. 2011. p. 1–3. Available from: http://www.cebm.net/index.aspx?o=5653
10. Carnochan JM. Mobilizing a patient's ankylosed jaw by placing a block of wood between the raw bony surfaces after resection. Arch Med. 1860;284.
11. Mercuri LG. Alloplastic temporomandibular joint reconstruction. Oral Surg Oral Med Oral Pathol. 1998;Volume 85,(July 1998):631–7.
12. Giannakopoulos HE, Sinn DP, Quinn PD. Biomet microfixation temporomandibular joint replacement system: A 3-year follow-up study of patients treated during 1995 to 2005. J Oral Maxillofac Surg [Internet]. 2012;70(4):787–94. Available from: http://dx.doi.org/10.1016/j.joms.2011.09.031
13. Orlow LW. Ankylosis mandibulae vera. Dtsch Zeitschrift f{ü}r Chir [Internet]. 1903;66(5):399–508. Available from: http://dx.doi.org/10.1007/BF02790915
14. Partsch C, Bruhn C, Kantorowicz A. Die chirurgischen Erkrankungen der Mundhöhle, der Zähne und Kiefere. In: Handbuch der Zahnheilkunde. München: Bergmann; 1932. p. 359–361.
15. Risdon F. Ankylosis of the Temporomaxillary Joint. J Am Dent Assoc [Internet]. 1934 Apr 26;21(11):1933–7. Available from: http://dx.doi.org/10.14219/jada.archive.1934.0286
16. Eggers GWN. Arthroplasty of the temporomandibular joint in children with interposition of tantalum foil. J Bone Joint Surg Am [Internet]. 1946 Jul 1 [cited 2016 Sep 2];28(3):603–6. Available from: http://jbjs.org/content/28/3/603.abstract
17. Goodsell JO. Tantalum in temporomandibular arthroplasty; report of case. J Oral Surg (Chic). 1947 Jan;5(1):41–5.
18. Driemel O, Braun S, Müller-Richter UDA, Behr M, Reichert TE, Kunkel M, et al. Historical development of alloplastic temporomandibular joint replacement after 1945 and state of the art. Int J Oral Maxillofac Surg. 2009;38(9):909–20.

19. van Loon JP, de Bont LGM, Boering G. Evaluation of temporomandibular joint prostheses. Review of the literature from 1946 to 1994 and implications for future prosthesis designs. J Oral Maxillofac Surg. 1995;53(9):984–96.
20. Indresano AT, Mobati DA. History of Temporomandibular Joint Surgery. Oral Maxillofac Surg Clin North Am. 2006;18(3):283–9.
21. Smith AE, Robinson M. A new surgical procedure for the creation of a false temporomandibular joint in cases of ankylosis by means of non-electrolytic metal. Am J Surg. 1957 Dec;94(6):837–45.
22. Wagner JD, Mosby EL. Assessment of Proplast-Teflon disc replacements. J Oral Maxillofac Surg. 1990;48(11):1140–4.
23. Kriens O. Indirect fossa arthroplasty in temporomandibular joint ankylosis. A preliminary report. Dtsch Zahnarztl Z. 1973 Mar;28(3):433–7.
24. Gluck T. Referat über sie durch das moderne chirurgische Experiment gewonnenen positiven Resultate, betreffend die Naht und den Ersatz von Defecten höherer Gewebe, sowie über die Verwerthung resorbirbarer und lebendiger Tampons in der Chirurgie. Arch Klin Chir. 1891;4:186–92.
25. König F. Weitere Erfahrungen über Kieferersatz bei Exartikulation des Unterkiefers. Dtsch Zeitschrift für Chir [Internet]. 1908;93(3):237–51. Available from: http://link.springer.com/10.1007/BF02791774
26. Sudeck P. Demonstration einer König-Roloff-schen Elfenbeinprothese als Ersatz einer exartikulierten Unterkieferhälfte. Zentralbl Chir. 1909;14:500.
27. Hahn G. Vitallium mesh mandibular prosthesis. J Prosthet Dent. 1957;14(4):1–4.
28. Kent JN, Misiek DJ, Akin RK, Hinds EC, Homsy CA. Temporomandubular Joint Condylar Prosthesis: A ten year report. J Oral Maxillofac Surg. 1983;41:245–54.
29. Kent JN, Homsy CA, Gross BD, Hinds EC. Pilot studies of a porous implant in dentistry and oral surgery. J Oral Surg. 1972 Aug;30(8):608–15.
30. Spiessl B. Erste Erfahrungen mit einer Kiefergelenkprothese. Fortschr Kiefer Gesichtschir. 1976;21:119–21.
31. Silver CM, Motamed M, Carlotti AEJ. Arthroplasty of the temporomandibular joint with use of a vitallium condyle prosthesis: report of three cases. J Oral Surg. 1977 Nov;35(11):909–14.
32. Raveh J, Geering A, Sutter F, Stich H. Erste Erfahrungen mit einer neuen Kiefergelenkprothese, vorläufige Resultate. Schweiz Mschr Zahnheilk. 1982;92:681–9.
33. Flot F, Stricker M, Chassange JF. Place de la prothèse intermédiaire à cupule non scellée dans la chirurgie reconstructive de l'articulation temporo-mandibulaire. Ann Chir Plast esthétique [Internet]. 1984 [cited 2016 Sep 2];29(3):253–5. Available from: http://cat.inist.fr/?aModele=afficheN&cpsidt=8892178
34. House LR, Morgan DH, Hall WP, Vamvas SJ. Temporomandibular joint surgery: Results of a 14-year joint implant study. Laryngoscope [Internet]. 1984;94(4):534–8. Available from: http:https://dx.doi.org/10.1288/00005537-198404000-00020
35. Kummoona R. Functional rehabilitation of ankylosed temporomandibular joints. Oral Surg Oral Med Oral Pathol. 1978 Oct;46(4):495–505.
36. Kent JN, Block MS, Halpern J, Fontenot MG. Update on the Vitek partial and total temporomandibular joint systems. J Oral Maxillofac Surg [Internet]. 1993;51(4):408–15. Available from: http://www.sciencedirect.com/science/article/pii/S0278239110803568
37. Recommendations for management of patients with temporomandibular joint implants. In: Journal of Oral and Maxillofacial Surgery [Internet]. Elsevier; 1993. p. 1164–72. Available from: http://dx.doi.org/10.1016/S0278-2391(10)80464-1
38. Sonnenburg I, Sonnenburg M. Total condylar prosthesisfor alloplastic jaw articulation replacement. J Maxillofac Surg. 1985;13(C):131–5.
39. Mercuri LG, Wolford LM, Sanders B, White RD, Hurder A, Henderson W. Custom CAD/CAM total temporomandibular joint reconstruction system. Preliminary multicenter report. J Oral Maxillofac Surg. 1995;53(2):106–15.

40. Wolford LM, Rodrigues DB, McPhillips A. Management of the infected temporomandibular joint total joint prosthesis. J Oral Maxillofac Surg [Internet]. 2010;68(11):2810–23. Available from: http://dx.doi.org/10.1016/j.joms.2010.05.089
41. Mercuri LG, Wolford LM, Giobbie-hurder A. Long-Term Follow-Up of the CAD / CAM Patient Fitted Total Temporomandibular Joint Reconstruction System. 2002;1440–8.
42. Wolford LM, Mercuri LG, Schneiderman ED, Movahed R, Allen W. Twenty-year follow-up study on a patient-fitted temporomandibular joint prosthesis: the Techmedica/TMJ Concepts device. J Oral Maxillofac Surg [Internet]. 2015;73(5):952–60. Available from: http://dx.doi.org/10.1016/j.joms.2014.10.032
43. Butow KW, Blackbeard GA, van der Merwe AE. Titanium/titanium nitride temporomandibular joint prosthesis: historical background and a six-year clinical review. SADJ. 2001 Aug;56(8):370–6.
44. Tsang DL, Pappas M. Poster 077: The Efficacy of Hoffman-Pappas Total Temporomandibular Joint Replacement System and the Use of the Severity of Impairment Scale as a Prognostic Indicator to Predict the Outcome of the Surgery. J Oral Maxillofac Surg [Internet]. 2008 Aug [cited 2017 Apr 30];66(8):114–5. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0278239108007519
45. Leandro LFL, Ono HY, Loureiro CC de S, Marinho K, Guevara HAG. A ten-year experience and follow-up of three hundred patients fitted with the Biomet/Lorenz Microfixation TMJ replacement system. Int J Oral Maxillofac Surg. 2013 Aug;42(8):1007–13.
46. Lippincott III A, Dowling J, Phil D, Medley J, Christensen RW. Temporomandibular Joint Arthroplasty Using Metal-on-Metal and Acrylic-on-Metal Configurations: Wear in Laboratory Tests and In Retrievals. Surg Technol Int. 1999;8:321–30.
47. Chase DC, Hudson J, Gerard DA, Russell R, Chambers K, Curry JR, et al. The Christensen prosthesis: A retrospective clinical study. Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology [Internet]. 1995;80(3):273–8. Available from: http://www.sciencedirect.com/science/article/pii/S1079210405803828
48. Schuurhuis JM, Dijkstra PU, Stegenga B, De Bont LGM, Spijkervet FKL. Groningen temporomandibular total joint prosthesis: An 8-year longitudinal follow-up on function and pain. J Cranio-Maxillofacial Surg [Internet]. 2012;40(8):815–20. Available from: http://dx.doi.org/10.1016/j.jcms.2012.03.001
49. Mercuri LG. Alloplastic temporomandibular joint replacement: Rationale for the use of custom devices. Int J Oral Maxillofac Surg [Internet]. 2012;41(9):1033–40. Available from: http://dx.doi.org/10.1016/j.ijom.2012.05.032
50. Parithimarkalaignan S, Padmanabhan T V. Osseointegration: An update. J Indian Prosthodont Soc. 2013;13(1):2–6.
51. Sinno H, Tahiri Y, Gilardino M, Bobyn D. Engineering alloplastic temporomandibular joint replacements. McGill J Med. 2010;13(1):63–72.
52. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants - A review. Prog Mater Sci [Internet]. 2009;54(3):397–425. Available from: http://dx.doi.org/10.1016/j.pmatsci.2008.06.004
53. Wolford LM. Factors to consider in joint prosthesis systems. Baylor Univ Med Cent Proc. 2006;19(3):232–8.
54. Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement – TMJ TJR - A Comprehensive Reference for Researchers, Material Scientists and Surgeons. 1st ed. New York: Springer International Publishing; 2016.
55. Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. Semin Immunol. 2008;20(2):86–100.
56. Royhman D, Radhakrishnan R, Yuan JC-C, Mathew MT, Mercuri LG, Sukotjo C. An electrochemical investigation of TMJ implant metal alloys in an artificial joint fluid environment: The influence of pH variation. J Cranio-Maxillofacial Surg [Internet]. 2014;42(7):1052–61. Available from: http://www.sciencedirect.com/science/article/pii/S1010518214000316

57. Kerwell S, Alfaro M, Pourzal R, Lundberg HJJ, Liao Y, Sukotjo C, et al. Examination of failed retrieved temporomandibular joint (TMJ) implants. Acta Biomater [Internet]. 2016;32:324–35. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1742706116300010

58. Mathew M, Kerwell S, Alfaro M, Royman D, Barao V, Cortino S. Tribocorrosion and TMJ TJR Devices. In: Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement -- TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons [Internet]. Cham: Springer International Publishing; 2016. p. 251–63. Available from: https://doi.org/10.1007/978-3-319-21389-7_10

59. Hallab N. Material Hypersensitivity. In: Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement - TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons. New York: Springer International Publishing; 2015. p. 227–50.

60. Kristen H, Bosch P, Bednar H, Plenk HJ. The effects of dynamic loading on intracalcaneal wood implants and on the tissues surrounding them. Arch Orthop Trauma Surg. 1979 Apr;93(4):287–92.

61. Gross K a, Ezerietis E. Juniper wood as a possible implant material. J Biomed Mater Res A [Internet]. 2003;64(4):672–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12601779

62. Maliniak J. Comparative study of ivory and organic transplants in rhinoplasty. Endonasal operative technic of some nasal deformities with report of cases. Laryngoscope [Internet]. 1924 Nov 1;34(11):882–900. Available from: http://dx.doi.org/10.1288/00005537-192411000-00005

63. Vilar-Sancho B. An old story: an ivory nasal implant. Aesthetic Plast Surg. 1987;11(1):157–61.

64. Staindl O, Hellmich S, Berghaus A. [Ivory as a nose implant performed by Jacques Joseph. Late results after more than 40 years]. Laryngorhinootologie. 1989 Oct;68(10):576–80.

65. Lupo G. The history of aesthetic rhinoplasty: Special emphasis on the saddle nose. Aesthetic Plast Surg. 1997;21(5):309–27.

66. Baw S. Proceedings: Ivory prostheses for ununited fractures of neck of femur. JBJS. 1970;52B:177.

67. Burke GL. The Corrosion of Metals in Tissues; and an Introduction To Tantalum. Can Med Assoc J. 1940;43(2):125–8.

68. Pudenz H. The repair of cranial defects with tantalum: An experimental study. J Am Med Assoc [Internet]. 1943 Feb 13;121(7):478–81. Available from: http://dx.doi.org/10.1001/jama.1943.02840070006002

69. Flanigan P, Kshettry VR, Benzel EC. World War II, tantalum, and the evolution of modern cranioplasty technique. Neurosurg Focus [Internet]. 2014;36(4):E22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24684335

70. Wesolowski S, Martinez A, McMahon J. Use of Artificial Materials in Surgery. Clin Probl Surg. 1966;

71. Ferreira JNAR, Ko CC, Myers S, Swift J, Fricton JR. Evaluation of Surgically Retrieved Temporomandibular Joint Alloplastic Implants: Pilot Study. J Oral Maxillofac Surg. 2008;66(6):1112–24.

72. Braley S. Symposium on synthetics in maxillofacial surgery. I. The silicones in maxillofacial surgery. Laryngoscope [Internet]. 1968;78(4):549–57. Available from: http://dx.doi.org/10.1288/00005537-196804000-00006

73. Brown JB, Fryer MP, Kollias P, Oohlwiler DA, Templeton JB. Silicone and Teflon Prostheses, Including Full Jaw Substitution: Laboratory and Clinical Studies of Etheron. Ann Surg [Internet]. 1963;157(6). Available from: http://journals.lww.com/annalsofsurgery/Fulltext/1963/06000/Silicone_and_Teflon_Prostheses,_Including_Full_Jaw.12.aspx

74. Mercuri LG, Giobbie-Hurder A. Long-term outcomes after total alloplastic temporomandibular joint reconstruction following exposure to failed materials. J Oral Maxillofac Surg. 2004;62(9):1088–96.

75. Eriksson L, Westesson PL. Temporomandibular joint diskectomy. No positive effect of temporary silicone implant in a 5-year follow-up. Oral Surg Oral Med Oral Pathol. 1992 Sep;74(3):259–72.

76. Mercuri LG. Silicone elastomer implants in surgery of the temporomandibular joint. Br J Oral Maxillofac Surg. 2013;51(7):584–6.
77. Cook HP. Teflon implantation in temporomandibular arthroplasty. Oral Surg Oral Med Oral Pathol. 1972 May;33(5):706–16.
78. Ward C. History of Self-Experimentation in Orthopaedics. Iowa Orthop J [Internet]. 2009;29:127–9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2723708/
79. Scales J, Stinson N. Tissue reactions to polytetrafluorethylene. Lancet [Internet]. 2017 Aug 6;283(7325):169. Available from: http://dx.doi.org/10.1016/S0140-6736(64)92260-3
80. Spagnoli D, Kent JN. Multicenter evaluation of temporomandibular joint Proplast-Teflon disk implant. Oral Surgery, Oral Med Oral Pathol. 1992;74(4):411–21.
81. Ryan DE. Alloplastic implants in the temporomandibular joint. Oral Maxillofac Surg Clin North Am. 1989;1:427–41.
82. Timmis DP, Aragon SB, Van Sickels JE, Aufdemorte TB. Comparative study of alloplastic materials for temporomandibular joint disc replacement in rabbits. J Oral Maxillofac Surg. 1986 Jul;44(7):541–54.
83. Lagrotteria L, Scapino R, Granston AS, Felgenhauer D. Patient with lymphadenopathy following temporomandibular joint arthroplasty with Proplast. Cranio. 1986 Apr;4(2):172–8.
84. Heffez L, Mafee MF, Rosenberg H, Langer B. with a Proplast-Teflon Laminate. J Oral Maxillofac Surg. 1987;45:657–65.
85. Wade ML, Waite DE. Temporomandibular Joints Following Polytetrafluoroethylene Implants. 1984;71:183–8.
86. Bronstein SL. Retained alloplastic temporomandibular joint disk implants: a retrospective study. Oral Surg Oral Med Oral Pathol. 1987 Aug;64(2):135–45.
87. Judet J, Judet R. The use of an artificial femoral head for arthroplasty of the hip joint. J Bone Joint Surg Br [Internet]. 1950;32-B(2):166–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15422013
88. d'Aubigné RM, Postel M. The Classic: Functional Results of Hip Arthroplasty with Acrylic Prosthesis. Vol. 467, Clinical Orthopaedics and Related Research. New York; 2009. p. 7–27.
89. Healy MJJ, Sudbay JL, Niebel HH, Hoffman BM, Duval MK. The use of acrylic implants in one stage reconstruction of the mandible. Surg Gynecol Obstet. 1954 Apr;98(4):395–406.
90. Mercuri LG. Measurement of the heat of reaction transmitted intracranially during polymerization of methylmethacrylate cranial bone cement used in stabilization of the fossa component of an alloplastic temporomandibular joint prosthesis. Oral Surgery, Oral Med Oral Pathol. 1992;74(2):137–42.
91. Baier RE, Meyer AE. TMJ TJR Biomaterials. In: Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement - TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons [Internet]. Cham: Springer International Publishing; 2016. p. 29–39. Available from: http://dx.doi.org/10.1007/978-3-319-21389-7_2
92. Mercuri LG. The role of custom-made prosthesis for temporomandibular joint replacement. Rev Esp Cir Oral y Maxilofac [Internet]. 2013;35(1):1–10. Available from: http://dx.doi.org/10.1016/j.maxilo.2012.02.003
93. Wolford LM, Cassano DS. Autologous fat grafts placed around Temporomandibular Joint (TMJ) total joint prostheses to prevent heterotopic bone. Autologous Fat Transf Art, Sci Clin Pract. 2010;1893(1):361–82.
94. Sidebottom AJ, Speculand B, Hensher R. Foreign body response around total prosthetic metal-on-metal replacements of the temporomandibular joint in the UK. Br J Oral Maxillofac Surg. 2008;46(4):288–92.
95. Westermark A, Leiggener C, Aagaard E, Lindskog S. Histological findings in soft tissues around temporomandibular joint prostheses after up to eight years of function. Int J Oral Maxillofac Surg [Internet]. 2011;40(1):18–25. Available from: http://dx.doi.org/10.1016/j.ijom.2010.09.009

96. McGregor DB, Baan RA, Partensky C, Rice JM, Wilbourn JD. Evaluation of the carcinogenic risks to humans associated with surgical implants and other foreign bodies - A report of an IARC Monographs Programme Meeting. Eur J Cancer. 2000;36(3):307–13.

97. Movahed R, Mercuri LG. Management of Temporomandibular Joint Ankylosis. Oral Maxillofac Surg Clin North Am [Internet]. 2015;27(1):27–35. Available from: http://dx.doi.org/10.1016/j.coms.2014.09.003

98. Ma J, Liang L, Jiang H, Gu B. Gap arthroplasty versus interpositional arthroplasty for temporomandibular joint ankylosis: A meta-analysis. PLoS One. 2015;10(5):1–12.

99. Karaca C, Barutcu A, Baytekin C, Yilmaz M, Menderes A, Tan O. Modifications of the inverted T-shaped silicone implant for treatment of temporomandibular joint ankylosis. J Cranio-Maxillofacial Surg. 2004;32(4):243–6.

100. Al-Moraissi EA, El-Sharkawy TM, Mounair RM, El-Ghareeb TI. A systematic review and meta-analysis of the clinical outcomes for various surgical modalities in the management of temporomandibular joint ankylosis. Int J Oral Maxillofac Surg [Internet]. 2015;44(4):470–82. Available from: http://dx.doi.org/10.1016/j.ijom.2014.10.017

101. Kalra GS, Kakkar V. Temporomandibular joint ankylosis fixation technique with ultra thin silicon sheet. Indian J Plast Surg [Internet]. 2011;44(3):432–8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3263270/

102. Sidebottom AJ. Alloplastic or autogenous reconstruction of the TMJ. J oral Biol craniofacial Res [Internet]. 2013;3(3):135–9. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3942016&tool=pmcentrez&rendertype=abstract

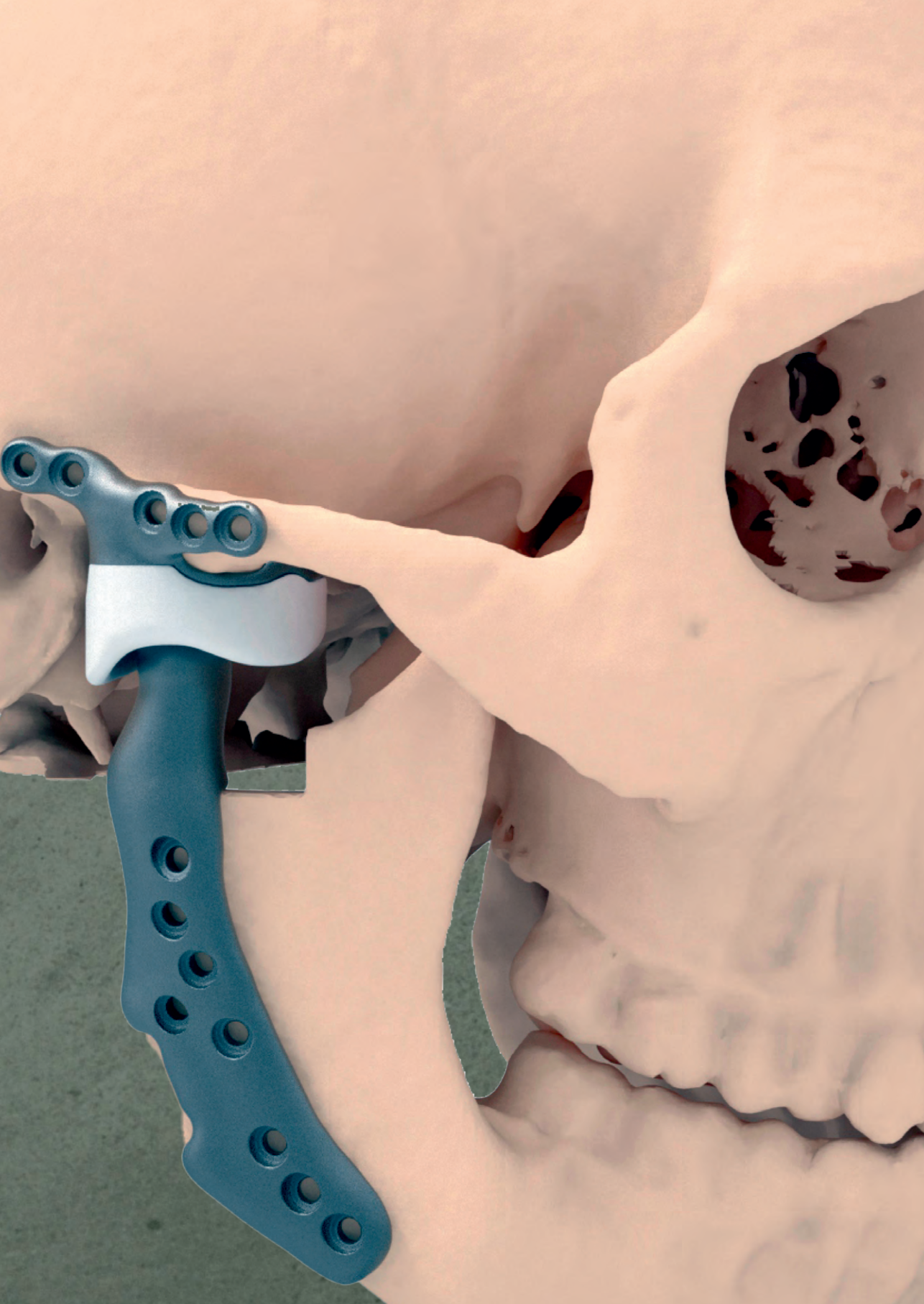
103. Lindqvist C, Soderholm AL, Hallikainen D, Sjövall L. Erosion and heterotopic bone formation after alloplastic temporomandibular joint reconstruction. J oral. 1992;50(9):942–9.

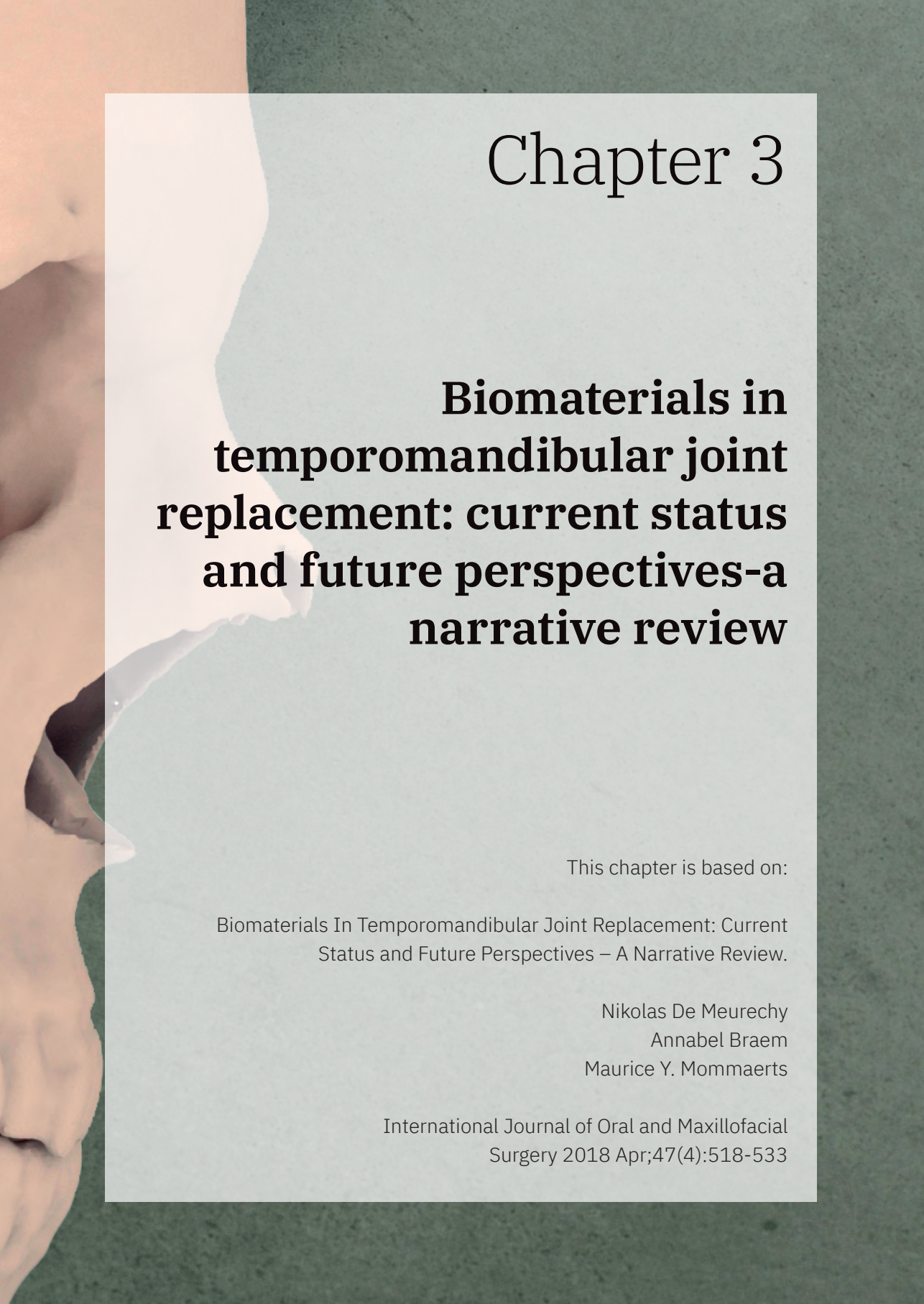
104. Chen Q, Thouas GA. Metallic implant biomaterials. Mater Sci Eng R Reports [Internet]. 2015;87:1–57. Available from: http://dx.doi.org/10.1016/j.mser.2014.10.001

105. Chan CW, Lee S, Smith G, Sarri G, Ng CH, Sharba A, et al. Enhancement of wear and corrosion resistance of beta titanium alloy by laser gas alloying with nitrogen. Appl Surf Sci [Internet]. 2016;367:80–90. Available from: http://dx.doi.org/10.1016/j.apsusc.2016.01.091

106. Kurtz SM, Kocagöz S, Arnholt C, Huet R, Ueno M, Walter WL. Advances in zirconia toughened alumina biomaterials for total joint replacement. J Mech Behav Biomed Mater. 2014;31:107–16.

107. Chevalier J. What future for zirconia as a biomaterial? Biomaterials. 2006;27(4):535–43.





Chapter 3

Biomaterials in temporomandibular joint replacement: current status and future perspectives-a narrative review

This chapter is based on:

Biomaterials In Temporomandibular Joint Replacement: Current Status and Future Perspectives – A Narrative Review.

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Introduction

The temporomandibular joint (TMJ), is a relatively complex joint, consisting of an upper and lower compartment, separated by a fibrocartilaginous disk. Both rotational and translational motions allow for the opening and closing of the mouth, mastication, talking, and other activities.

Although the prevalence of TMJ diseases is high, treatment using a TMJ prosthesis remains relatively rare.(1,2) According to Sidebottom et al. (3), up to 80% of all patients seen by a specialist can be treated with a more conservative approach, such as rest and anti-inflammatory medications. Less than 10% of all patients in a specialist center will present the need for arthroscopy or arthrocentesis, and even fewer patients will require open surgery. TMJ replacement is widely accepted as end-stage therapy, which should only be considered for certain well-specified indications when previous, more conservative (noninvasive) treatments have been proven unsatisfactory.(4) This widespread highly prudent approach is partly the result of overuse of surgery in the past, in combination with catastrophic experiences with early alloplastic TMJ replacements (e.g., the Vitek-Kent prosthesis). (5–11) Indications for total joint replacement include the following: inflammatory arthritis involving the TMJ, recurrent fibrosis or bony ankylosis after failed tissue grafts (bone and soft tissue), failed alloplastic joint reconstruction, or loss of vertical mandibular height or a proper occlusal relationship because of bony resorption, trauma, developmental abnormalities, or pathological lesions.(5–10)

For a TMJ prosthesis to be successful, it must achieve good imitation of the function of the joint, a close fit between the prostheses and host bone, and a reasonable lifetime, which should equal that of other prostheses. Furthermore the prosthesis should reduce the suffering and disability of the patient, not be unduly expensive, and not require excessive treatment. (5,10,12,13)

Although the problems with the Vitek-Kent prosthesis were later determined to be due to inappropriate material selection, leading to the formation of severe wear debris and subsequent osteolysis, the

alloplastic TMJ prosthesis was abandoned for many years, and autologous alternatives, such as sternoclavicular, costochondral and fibular grafting, became more prevalent.(5,14) However, the rapid evolution of biomaterial science during the last couple decades, providing a rational basis for the selection of materials, as well as the development of computer-aided design and computer-aided manufacturing (CAD/CAM) planning, allowing the production of patient-fitted components, has led to substantial progress in the construction of alloplastic TMJ prostheses. Consequently, alloplastic prostheses have steadily gained more acceptance by craniomaxillofacial (CMF) surgeons.

Appropriate material selection for the different components is key to successful implementation. However, while other fields of expertise, such as orthopedic surgery, have an extensive history of debating the advantages and disadvantages of various materials, literature and research concerning the selection of materials for TMJ prostheses is relatively scarce. Therefore, the aim of this review is to discuss several previously used biomaterials and the current state-of-the-art with respect to the different biomaterials used in alloplastic TMJ prostheses, as well as to consider the potential of future materials that address some of the current shortcomings.

Materials and Methods

Information about TMJ prostheses was gathered by a computerized literature search using multiple databases, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The following databases were used to conduct the search: Pubmed Central, Elsevier ScienceDirect Complete, Wiley Online Library Journals, Ovid Lippincot Williams & Wilkins, Cochrane Library Plus. The following heading was used to perform the search; (“Temporomandibular joint” OR “TMJ”) AND (“Material” OR “Biomaterial” OR “Biocompatible”) AND (“Prosthesis” OR “Prostheses” OR “Replacement” OR “Implant”). While the search terms remained unchanged, the combination in which they were used was database dependable. To assess the methodological

soundness of each article, a quality evaluation was performed using the 2011 Oxford Centre for Evidence-Based Medicine LOE65 (Level of Evidence) recommendations. The quality was categorized from levels I to IV; level V studies were not included.

The initial search returned 10,433 published articles. Subsequently the number of hits was reduced by removing all duplicates and reviewing the titles of these articles. This led to a total of 113 articles, which were evaluated by reading through the abstract. Articles not containing a reference to the temporomandibular joint in the abstract were excluded, leading to a further exclusion of 37 articles. By reading through the final 76 full-text articles, applying the inclusion criteria, a total of 37 articles were included in the systematic search. Reasons for exclusion were: Article written in other language than English, Dutch or French; Full text not accessible. Additionally 16 articles were included through hand searching reference lists of the included articles. Finally, in order to provide a sound biomaterial background, an additional 8 articles were handpicked by a biomaterial engineer from the specialized literature, to provide further unbiased details on material specifics and properties, while still maintaining the methodological soundness and objectivity of the systematic search results. The performed search has been summarized in the PRISMA-flow chart (Fig. 1).

History of materials used in temporomandibular joint reconstruction

The importance of appropriate selection of prosthetic materials has clearly marked the history of TMJ prosthesis design, as many designs have been conceived, yet only a few remain. The use of inadequate materials can, for instance, result in metal hypersensitivity, foreign body giant cell reaction, heterotopic ossification, and even implant loosening and failure. Below, a short summary of the history of the different types of prostheses, with their respective materials has been provided.(15–20)

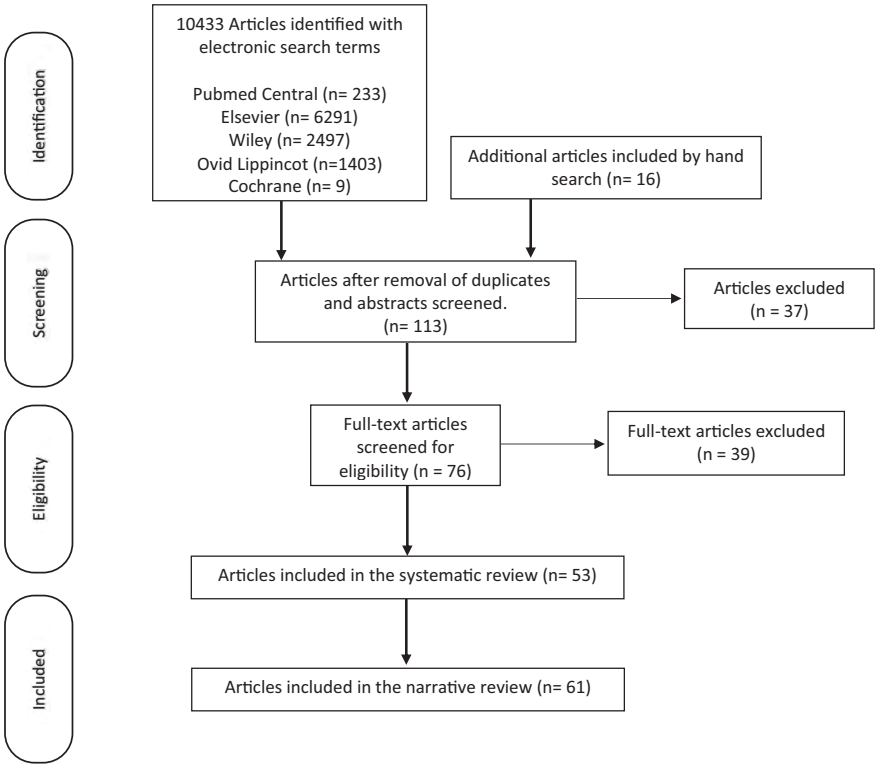


Fig. 1: PRISMA-flow chart

Early developments

Fossa prostheses

Nearly one century after Carnochan inserted a block of wood between the skull and mandible as a treatment for ankyloses in 1840(7), several surgeons such as Risdon, Eggers and Goodsell started using interpositional materials such as tantalum (TA) foil as a treatment for TMD. Smith and Robinson first introduced the use of stainless steel in 1950, to replace the fossa and during the 1960's cobalt-chromium (CoCr) alloys such as Vitallium made their way to the TMJ thanks to Christensen and Morgan. (6,12,21,22) Besides metals, also polymer materials, such as silicone and polytetrafluoroethylene (PTFE) were used as disc replacement materials. Two of these polymer fossa prosthesis worth mentioning are the Vitek Proplast-Teflon disc prosthesis and the Silastic disc prosthesis. The inner part of the Vitek disc implant contained a high denstity PTFE (Teflon), while

the outer layers consisted of a mixture of Teflon and carbon fibers, known as Proplast. While initially highly popular, it became apparent several years after the first placement, that the disc was not suited for *in vivo* functional loading, resulting in excessive wear, leading to debris accumulation in the fossa region, triggering a foreign body giant cell reaction and eventual bone resorption. As a result, production was halted in 1990 and in 1991 the USA Food and Drug Administration (FDA) recommended the removal of all Proplast/Teflon devices.(6,7,12,23,24) The Silastic disc underwent a similar fate, as functional loading led to fragmentation of the silicone elastomer, with abandonment of the disc prosthesis in 1993.(6,25)

Condylar prostheses

Polymer materials also came into use for condylar prostheses. The first polymer prosthesis was released in 1964 by Hahn et al.(26) , which consisted of an acrylic (polymethymethacrylate (PMMA)) caput and Vitallium mesh condylus. Shortly thereafter, several more prostheses followed, such as the vitreous carbon coated CoCr condylar prosthesis by Kent in 1972 and the titanium prosthesis by Raveh.(6,12) In 1992, however, Lindqvist et al.(27) concluded that use of a condylar replacement alone led to resorption of the fossa, indicating that using solely a condylar replacement is insufficient as treatment. Westermark et al.(28) also came to the same conclusion and advocated the use of a total TMJ prosthesis instead of replacing only the condyle.

Total temporomandibular joint prostheses

The total TMJ prosthesis was first reported in 1970 by Christensen et al.(12,29), who combined their previously developed CoCr fossa-eminence prosthesis with a new CoCr condylar prosthesis incorporating a PMMA condylar head.(21,22) Because of particulation of the PMMA, it was later replaced by CoCr.(7,30) Further development of the total TMJ prosthesis introduced several new designs using a wide variety of materials, such as the metal-only CoCr prosthesis by Kummoona(31) or the titanium-palladium (TiPd) alloy condyle and PE fossa prosthesis by Sonnenburg and Sonnenburg.(32) However, of the many total TMJ implant designs, the Vitek-Kent total joint prosthesis (Fig. 2) was the first system to be used extensively in the United States of America (USA), resulting

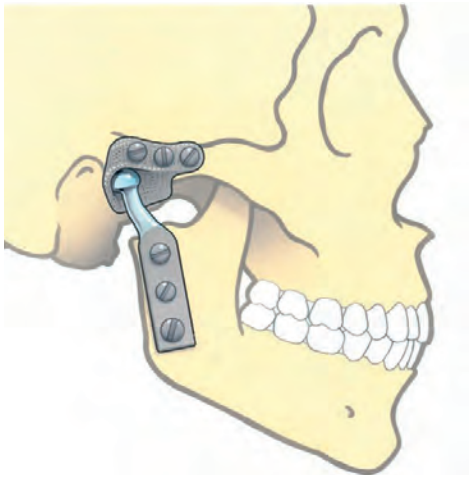


Fig. 2: Vitek-Kent Total Joint Prosthesis

in more than 26,000 patients who were treated with either the Vitek-Kent system or the Vitek Proplast-Teflon disc replacement before the production was halted. (6,7,12,24,33,34) The fossa component consisted of three (and later two) layers of porous Proplast and high density PTFE (Teflon). While the Proplast layer in contact with the fossa temporal bone could allow ingrowth of both soft and hard tissues, the Teflon layer articulating against the condyle was meant to withstand wear from the joint articulation. (6,12,23,34).

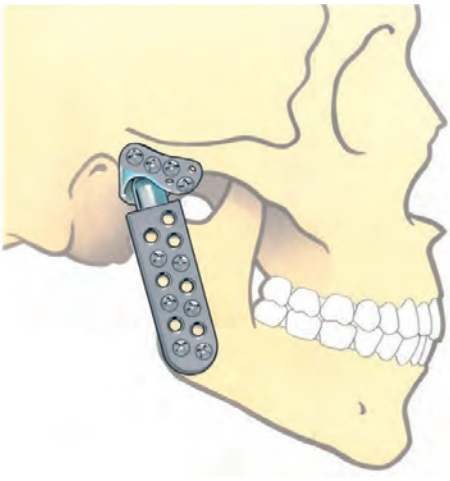


Fig. 3: Nexus CMF Total Joint Prosthesis

A final TMJ system to be highlighted is the Nexus CMF TMJ Total Joint Prosthesis (more commonly known as the Christensen TMJ System) (Fig. 3). This system different from the other recent (more traditional) metal-on-polymer bearing type of implants systems, in being a metal-on-metal joint replacement device. This meant both the fossa and condylar head were made of a cast cobalt-chromium-molybdenum (CoCrMo) alloy. Furthermore, the complete mandibular component and the fixation screws were also made of CoCrMo.(6,7,11,35–37) Due to reason explained further in this paper, the Christensen device recently had its FDA approval revoked and the system is no longer manufactured.

Current alloplastic total temporomandibular joint prostheses

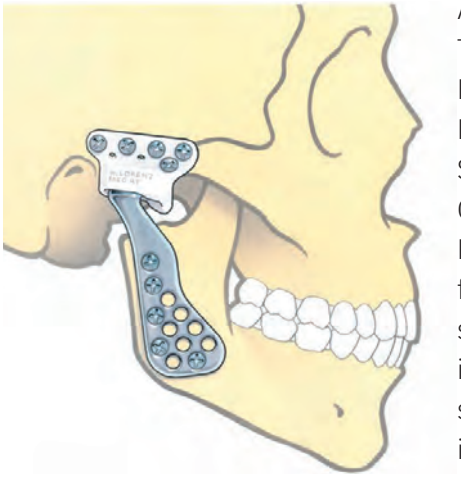


Fig. 4: Biomet/Lorenz Microfixation TMJ Replacement System

At the time of writing, two total TMJ devices have received US FDA-approval: The Biomet/Lorenz Microfixation TMJ Replacement System (Fig. 4), and the TMJ Concepts Patient-Fitted Total TMJ Replacement System. (Fig. 5). The first system, as the Christensen system, uses a stock prosthesis that is available in different standard sizes. During surgery, the best fit is selected based on the patient's anatomy, and after the necessary alterations are made to the host bone, the components are attached with screws.(5,7,8,35,38,39) By contrast, the TMJ Concepts system is a custom-made and patient-fitted prosthesis. First, the prosthesis is fabricated using CAD/CAM technology based on a maxillofacial computed tomography scan of the patient. Next, a stereolithographic model of the patient's skull is printed, from which the final components are designed and manufactured. Through this custom design, the prosthesis can be altered to the patient's specific anatomy, including jaw abnormalities and jaw position. Additionally, the fixation screw positions can be optimized, taking into account the patient's anatomical structures, such as the inferior alveolar nerve. As will be further discussed below, optimizing the positioning and contact with the bone can greatly improve the stability of the prosthesis.(6,9,35,38,40)

The two systems also differ with respect to the materials used for the various components, as shown in the overview of these materials presented in Table 1. The Biomet/Lorenz system , which received FDA approval as an investigational device in 1995 and full approval in 2005(7,41), employs a cast CoCrMo ramal component, in which the medial surface is coated with a plasma-sprayed Ti coating. This enables bone ingrowth to improve integration into the host bone (osseointegration). The fossa, on the other

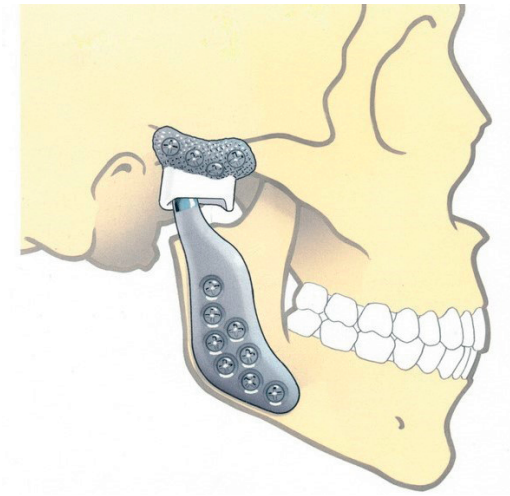


Figure 5: TMJ Concepts Patient-Fitted Total TMJ Replacement System

hand, consists solely of UHMWPE, without a metal support. For early implants, any surface roughness in the fossa was leveled using PMMA cement, but this was abandoned later because of the risk of fragmentation of PMMA under functional loading.(6) Both components are fixated using self-tapping screws made of Ti-6Al-4V.(7,8,36,39)

The TMJ Concepts system was introduced in 1989 as a Techmedica system, however the FDA halted the manufacturing of custom devices in 1993. In 1996, the new company TMJ Concepts, Inc., received FDA approval for their custom TMJ implant system as an investigational device, with the device becoming available for patient use in 1997. Finally in 1999 TMJ Concepts, Inc. received full FDA approval for their patient-fitted TMJ implant system. The fossa of the TMJ Concepts prosthesis is made from a commercially pure (cp) Ti mesh backing, which can be adapted to the patient's anatomy, and four layers of cp Ti mesh, which provide stability and allow for bony ingrowth to occur. On the caudal side of the mesh backing, a UHMWPE lining functions as the articulating surface. While the ramal shaft of the Techmedica implant was made of either cp Ti or a wrought Ti6Al4Valloy, the newer TMJ Concepts, Inc. system only uses Ti-6Al-4V. Both the fossa and mandibular parts are fixated with the help of Ti6Al4Vscrews. (6,9,37,40)

Considerations for temporomandibular joint total joint replacement materials

The previous paragraphs highlighted several difficulties encountered throughout the history of the (total) TMJ prosthesis, which could often be traced back to inappropriate material selection for a given implant design, such as the use of Proplast in the Vitek-Kent system or Silastic

Table 1: Materials used in (previously) United States Food and Drug Administration–approved implant systems* (6,11,37,41,55–57)

	Biomet System	Nexus CMF System	TMJ Concepts System
Design	Stock	Stock	Custom
Fossa	UHMWPE	Co-Cr-Mo	Cp Ti UHMWPE
Condyle	Co-Cr-Mo	Co-Cr-Mo	Co-Cr-Mo
Ramus	Co-Cr-Mo Ti-coating	Co-Cr-Mo	Cp Ti or Ti-6Al-4V
Screws	Ti-6Al-4V	Co-Cr-Mo	Ti-6Al-4V

Al, aluminum; Co, cobalt; Cp Ti, commercially pure titanium; Cr, chromium; Mo, molybdenum; Ti, titanium; UHMWPE, ultra-high-molecular-weight polyethylene; V, vanadium

*: The Nexus CMF system has recently lost its FDA-approval.

for the fossa-bearing surface. Nevertheless, these previous setbacks, in combination with the extensive expertise acquired in the field of orthopedic surgery for more than 5 decades, now provide us with the indispensable information required for the development of newer implant systems. When selecting the appropriate materials for TMJ prostheses, the following considerations should be taken in to account.

Biocompatibility

A prerequisite for any successful clinical application of an implant is biocompatibility, a concept originally conceived to refer to a material's ability to be in contact and interact with the tissues of the human body without eliciting any adverse effects at the implant site (locally) or in the patient as a whole. As such, a material and its degradation products should be non-cytotoxic—i.e., support cell survival and maintain specific cellular functions—and not cause inflammation or allergic reactions (hypersensitivity).(34,42) Advances in medical technology, such as the development of biodegradable implant materials and tissue engineering, have urged a re-evaluation of the biocompatibility edict to not only address biological safety but also the specific functionality aspect of a material. According to Williams, a biomaterial can also be expected to passively allow or actively generate the most appropriate beneficial cellular or tissue response in a given application site.(43) The relevant biological processes in TMJ TJR are osteogenesis and vascularization; as

such, TMJ materials should be able to support proper functioning of loco-specific cell types, such as osteoblasts.

Foreign body giant cell reactions
Implantation of a biomaterial in the body can lead to a cascade of inflammatory reactions, starting with blood-material interactions and provisional matrix formation, and followed by acute and chronic inflammation. Finally granulation tissue can develop, leading to fibrous capsule development, as well as a foreign body reaction. Foreign body reactions are known to lead to degradation of biomaterials through an oxidative chain cleavage reaction triggered by macrophages and foreign body giant cells, leading to subsequent device failure. Because of this chemical degradation, the surface of the implant becomes brittle and more susceptible to physical damage; as physical damage occurs, cracks open in the material exposing new surfaces to oxidants released by the macrophages and foreign body giant cells. (15)

Metal hypersensitivity
Metal hypersensitivity can develop at any age and has a much higher incidence in females.(44) It should also be noted that patients can develop metal hypersensitivity even after implantation. Induction of hypersensitivity to metals can be caused by chronic exposure to low concentrations of metals or sudden exposure to high concentrations of metals. Acute stressors, such as viral and bacterial infections, as well as psychological trauma, have also been described as possible induction mechanisms.(18,19,45) Current data suggest that about 10% to 15% of the population has an allergy to one or more of the metallic components currently used in the field of implantology. The incidence is even higher amongst patients with an implant: 23%. Up to 63% of patients with a failing prosthesis have been shown to test positive for metal hypersensitivity.(19,46) While nickel (Ni) is most often the responsible element, Co, Cr, vanadium (V), aluminum (Al), and even Ti can also cause an allergic reaction.

Ions and particles can be released from the implant by either dissolution, corrosion, or wear. These particles will act as haptens (initiators of an

immunological response), which can form organometallic complexes by binding to cells or proteins. These complexes can subsequently cause allergic sensitization by being processed by antigen-presenting cells (APCs), such as macrophages, B-cells, or dendritic cells. APCs present the processed allergen to T-helper cells, which in turn activate either B-cells or cytotoxic T-cells. B-cells are responsible for type I hypersensitivity reactions, which are characterized by the production of IgE antibodies and activation of mast cells and basophils. Cytotoxic T-cells cause type IV hypersensitivity, also known as the delayed-type hypersensitivity reactions. APCs cause sensitization of T_H1-cells, which release cytokines when stimulated; the cytokines, in turn, activate both macrophages and cytotoxic T-cells, resulting in cellular damage.(18,45,46)

It should be noted that the particle size of the debris plays an important role in the risk of hypersensitization. While UHMWPE-particles vary in size from <10 µm to >100 µm, most metal debris is around 1–4 µm. While the larger particles cannot be processed by APCs, the smaller metal wear debris can.(18) As a result, while metal-on-metal TMJ prostheses produce less wear, the incidence of metal hypersensitivity is higher than with metal-on-UHMWPE prostheses. This was clearly demonstrated by the results of a study by Wolford et al.(16), in which prosthesis removal because of metal hypersensitivity or device failure was required for 33% of Christensen prostheses but only 3% of TMJ Concepts prostheses.

As a result of hypersensitivity reactions to metals, patients can develop both local and systemic symptoms. Local symptoms vary from skin dermatitis, erythema, and urticaria to TMJ or myofascial pain, facial swelling, muscular spasms, headaches, earaches, tinnitus, and vertigo. Systemic reactions include depression, fibromyalgia/chronic fatigue, neurologic or gastrointestinal problems, vasculitis, cardiac instability, and even end-organ failure and death (in the most extreme cases). Furthermore, the local reaction can lead to loosening of the implant, resulting in failure.(18,45,46)

Both Sidebottom et al.(47) and Hussain et al.(46) advise performing a patch test in all patients who are scheduled for a TMJ TJR to prevent

allergic reactions and the risk of early rejection of the TMJ TJR. If patch testing is inconclusive, further assessment using lymphocyte transformation testing can be considered.(45)

Corrosion

With respect to metals, the physiological situation is an extremely aggressive environment. The presence of both salts, especially chloride [Cl^-] anions, and proteins significantly facilitates (electro)chemical reactions leading to dissolution of metal ions into the body. These released ions can accumulate around the implant, causing cytotoxicity and inflammation or be transported throughout the body, resulting in systemic effects, eliciting hypersensitivity, disturbing trace metal ion levels and their concomitant biochemical reactions, and even producing carcinogenic effects.(19,48) Metallic biomaterials, such as CoCr or Ti alloys, owe their biocompatibility to the formation of a thin, yet protective, oxide film during the early stages of corrosion (passivation). This layer is immediately rebuilt when damaged (re-passivation) because of its thermodynamic stability and acts as a barrier against the diffusion of metal ions from the bulk metal into the surroundings, effectively limiting the uniform corrosion rate. However, in addition to their main components, Cr_2O_3 (CoCr alloys) or TiO_2 (Ti alloys), these layers also incorporate small amounts of sub-oxides and oxides of other alloying elements present in the base metal. Such alterations in the passive film can make the implant more sensitive to corrosion, a concern that has initiated the development of new alloys.

Moreover, different forms of localized corrosion can still endanger the longevity of an implant and should be taken into account during the implant design process. Examples of these deteriorative processes are the accelerated corrosion in shielded sites, such as underneath screw heads (crevice corrosion); corrosion due to highly localized de-passivation of the protective oxide layer, especially in the presence of Cl^- ions (pitting corrosion); corrosion due to electrical contact between dissimilar metals, such as implants versus fixation screws (galvanic corrosion); and corrosion induced by micro-motions due to cyclic loading at the implant-bone interface (fretting corrosion).(19,48)

Osseointegration

For any type of alloplastic bony implant to be successful and achieve good longevity, osseointegration is required. Direct bone anchorage, without formation of an intervening fibrous tissue layer, is the key to establishing a rigid connection between the implant and the bone, which augments the load-bearing capacity of the prosthesis. Achieving good osseointegration relies on the interrelationship of a number of factors, such as the implant (biocompatibility, surface topography and chemistry), status of the bone bed (bone quantity and quality), surgical technique (primary stability, surgical trauma, aseptic environment), and loading conditions after implantation (immediate loading or not).(49,50)

Implant surface characteristics

The implant–tissue interaction (and therefore also osseointegration) is largely determined by a cascade of events at the implant surface, ranging from protein absorption to cellular adhesion, proliferation, and differentiation to tissue development. As indicated above, the surface chemistry governing a material's biocompatibility is a crucial parameter, but other surface characteristics, such as topography and surface energy, are important as well. It has been shown that micro-topography favors cellular adhesion, whereas macroscale roughness (e.g., porous coatings) offers the advantage of bone ingrowth, leading to mechanical interlocking of the implant with the host bone. A higher surface energy (hydrophilicity) is more favorable for cell attachment.(50)

Primary stability

To ensure osseointegration, the device must be well fixated at the moment of implantation (primary stability). This reduces micro-motions, allowing load transfer from the implant to the bone and vice versa without a risk of bone degeneration and fibrous tissue formation, leading to implant loosening and eventually even failure.(6,10,12,13,34,38,48) While in orthopedic surgery, fixation can be achieved by using cementation or press-fitting, this is not possible for TMJ implants. Current TMJ implants are fixated using screws,(6,12,13,34,38) which provide good primary stability.

Furthermore, a good fit is needed as well.(6,12,13,34,38) This, however, is quite difficult, as patients in need of a total TMJ prosthesis often have a deformed TMJ, caused either by prior surgical procedures or the nature of their joint pathology.(12,13) Several earlier designs made use of PMMA to both fixate the prosthesis and achieve a better fit, but this approach was abandoned because of the risks of thermal trauma to the surrounding tissue during *in situ* curing of the polymer, as well as fragmentation under functional loading.(6,12,13,38) Alternatively, more flexible materials that can be easily adapted to the form of the patient's skull will allow for a good fit, although micro-motions can occur because of their flexible nature.(12,34) Manufacturers of modern FDA-approved stock TMJ TJR devices have tried to overcome fit problems by providing their device components in different sizes and shapes, among which the surgeon can select the best fit for the individual patient. Despite these attempts, the surgeon will often be forced to 'make the components fit', as stated by Mercuri et al.(13), either by altering the patient's anatomy to the prosthesis via reshaping the bone; shimming the component with autogenous bone, bone substitute, or alloplastic cement; or bending the device components.(5,12,13,38) On the contrary, custom TMJ TJR devices, such as the TMJ Concepts system, are designed and manufactured to the patient's anatomy, so no or only very little alteration is needed during implantation.(9,13,37,38)

Stress shielding

Besides achieving good fixation and fit with primary stability, the elastic modulus (E value) also plays an important role in preventing micromotion and assuring good stability. Bone has an elastic modulus of 4–30 GPa, depending on the type of bone and direction of measurement.(34,48,51) Materials with a lower elastic modulus, such as titanium alloys (55–112 GPa), are more flexible, while the elastic modulus of Vitallium is 218 GPa, resulting in a less deformable material. The importance of the elastic modulus becomes clear in the process of stress shielding. As the elastic modulus of a material increases, it takes more force to deform the material and the underlying bone will be 'shielded' from stress. According to Wolff's law, which states that bone will remodel itself in accordance to the loads it is subjected to, this would lead to a loss in bone density and weakening of the bone. As a result, bone resorption and implant loosening can be seen.

This means that materials with an elastic modulus closer to that of bone are preferred over materials with a higher elastic modulus.(34,48,51) Also, as the size of an implant device becomes larger, it becomes stiffer, resulting in stress shielding. This problem can be overcome by making the device hollow or porous.(34,51) It should however be noted that up until this date, no issues concerning stress shielding with total TMJ implant devices have been reported, meaning that this should be considered rather a theoretical, than a practical consideration.

Functionality

In addition to the host response to the materials used, premature material breakdown can also significantly decrease the longevity of an implant. For load-bearing implant applications, the materials must be mechanically sound and should be able to withstand the forces they are subjected to over a long period of time. With respect to TJR, high strength, excellent fatigue and wear resistance, and fracture toughness, are desired qualities.(13,34,48)

Mechanical strength

It is important to realize that the distribution of loads is very different for a TMJ device, compared to a hip or knee TJR, for instance.(52) A hip prosthesis has a functional load varying from 3.5 to 6 times the body weight and a rather constrained functional anatomy. Determining the functional load for a TMJ prosthesis, however, is far more difficult, as the biting forces measured at the molars (estimated at 265 N) differ greatly from those at the incisors (estimated at 60 to 160 N), and the functional anatomy of a TMJ prosthesis is less constrained. Thus, the functional load is dependent on the position of the lower jaw at any given moment. Furthermore, patients who are in need of a TMJ TJR will most likely exhibit altered TMJ function, resulting in different and often reduced functional loads.(13,18) Apart from the altered function, in many cases there is also an alteration in the anatomy of the joint, resulting once more in great alterations in the load the joint is subjected to, depending on the position of the lower jaw.(5,13,38,40)

Fatigue

Besides the static mechanical strength, also the dynamic fatigue strength plays an essential role in determining the durability of an implant. Fatigue refers to the progressive structural damage resulting from repeated cyclic loading. It is important to realize that any material inherently contains small defects or can develop micro-cracks because of stress concentrations, which will enlarge if the applied load exceeds a certain threshold (fatigue strength, endurance limit). As a result, the implant material becomes weaker and can fracture unexpectedly, even when loading conditions remain well below its static mechanical strength. As stated earlier, the stiffness of an object can be reduced by increasing its porosity. While these surface irregularities allow for tissue ingrowth with better fixation of the implant, they also form stress zone hotspots where micro-cracks can form.(48)

Wear

Materials with low wear resistance promote the formation of wear debris, which can cause implant loosening and inflammatory or allergic reactions. Furthermore, a lower wear resistance limits the total life span of the implant, which must be taken into consideration when treating younger and more active patients.(48) The rate at which wear appears can be influenced by several factors, such as the surface roughness and the geometry of the articulating surfaces.(34)

In hip implants, the total wear volume is 20–100 times lower with metal-on-metal CoCr implants than with metal-on-UHMWPE implants.(48) However, several issues regarding these findings deserve comment. First, there is a clear difference in loading between the TMJ and the hip joint. Whereas the hip is a concentric, rotational joint in which the articulation is semi-constrained, the TMJ can perform both rotational and translational movements, with a total contact area smaller and less congruent than that found in the hip joint. The absence of foreign body giant cell reactions in metal-on-UHMWPE TMJ systems, which can be found in metal-on-UHMWPE hip prosthesis, is a clear indicator of this difference in loading.(18,34) Mercuri et al.(41) state that because of these anatomical differences, the TMJ is not suited for metal-on-metal TJR.

Second, it should be noted that while wrought CoCrMo has better wear properties than cast CoCrMo, the Christensen system made use of the latter.(18) However, CoCrMo-on-UHMWPE implants have shown excellent wear properties, and when used in articulation with UHMWPE during hip simulator testing, Ti6Al4V exhibits a 35% higher wear rate than CoCrMo.(41,48) As such, CoCrMo-on-UHMWPE is currently considered the gold standard for low friction articular components in orthopedic and TMJ TJR systems.(18,38,40,41)

In vitro and in vivo performance

When designing a prosthesis, it is important to rigorously test the selected materials for all the properties discussed above, not only by standard material characterization techniques but also by using both *in vitro* and *in vivo* tests, as the biological environment can have a significant impact on the material's performance. The importance of *in vivo* wear testing, for example, has been clearly established for hip joint prostheses, in which it has become clear that the wear rate can be much higher than that encountered during *in vitro* testing.(12) With respect to TMJ implants, the use of Proplast in the Vitek-Kent prosthesis serves as a clear example of how *in vitro* testing without thorough *in vivo* experimentation is insufficient to allow the appropriate choice of materials.(6,12,23,34,37,48)

Materials Currently Used in Total Temporomandibular Joint Prostheses

Although current implant devices make use of materials that have been thoroughly tested and evaluated in the field of orthopedic surgery, many different and much less well-suited materials have been used throughout the history of TMJ TJR. For example, some of the first screws or even prostheses, such as the condylar design by Flot et al., were made out of a stainless steel alloy.(6,34) While several stainless steel alloys, such as 316L, have low production costs, good availability, and good tensile strength and fatigue properties, they are not suitable TMJ implantation materials. This is at least partially because they are susceptible to corrosion and crevice formation, and they are biotolerant rather than

bioactive. Furthermore, stainless steel alloys have a high elastic modulus (E = 210 GPa), which promotes stress shielding.(34,48)

Also Proplast/Teflon, despite its beneficial properties such as its low elastic modulus (E = 0.5 GPa) and the occurrence of rapid soft and hard tissue ingrowth, had proven unsuitable as PTFE was found to be unable to withstand the compressive loads the TMJ is subjected to. As a result, perforations located mainly on the central aspects of the implants developed, and originating from these perforations, a great many fracture lines and fiber extrusions could be seen. A significant amount of layer tearing was also noted.(23) Spagnoli et al.(53) reached similar conclusions after removing 96 implants: 44% of implants showed signs of wear involving either the Teflon or both the Teflon and Proplast layers, and nearly 15% of removed implants exhibited fractures.(53) Furthermore, animal studies have shown an increase in the incidence of sarcomas associated with the use of implants containing PTFE. The incidence was significantly increased when the implant had a large PTFE surface area with a flat and smooth surface morphology. This led McGregor et al.(54) to conclude that PTFE implants, when used as thin smooth films, are possibly carcinogenic for humans.

Currently, Ti, Ti6Al4V, CoCrMo, and UHMWPE are considered the gold standards among the materials used for low-friction orthopedic total joint replacements.(13,18,38,40)

Cobalt-chromium alloys

CoCr alloys were one of the first materials used in load-bearing total joint implants because they combine high strength and fatigue resistance with good biocompatibility, owing to the passivating Cr-oxide layer.(41,42) Moreover, because of their relatively high hardness, CoCr alloys have excellent wear resistance and can be applied as the joint-bearing surface. All current FDA-approved TMJ devices still make use of more recently developed CoCrMo alloys for their condylar components.(6,34)

While the Nexus CMF (Christensen) system implemented a cast American Society for Testing and Materials (ASTM) F75 CoCrMo alloy containing

58.9–69.5 weight (wt) % Co, 27.0–30.0 wt % Cr, 5.0–7.0 wt % Mo, and up to 2.5 wt % Ni, the two FDA-approved systems make use of a newer wrought ASTM F1537 CoCrMo alloy with similar Co, Cr, and Mo content but a Ni content below 1 wt %.(7,9,55–57) Thermomechanical processing of these wrought alloys results in improved mechanical properties and wear resistance.(42) The elastic modulus remains equally high for both types of CoCrMo alloys and is around 210 GPa. As a result, CoCr and CoCrMo alloys are prone to stress shielding.(48)

As discussed earlier, the Nexus CMF (Christensen) system provided a metal-on-metal articulation, whereas in the two FDA-approved systems, a metal-on-polyethylene bearing is applied. However, clear concerns have been reported regarding the use of metal-on-metal systems in TMJ replacements. Multiple reports in the recent literature have described the need for explantation of the Christensen system because of reactions caused by metallic debris.(3,47). While the absolute wear volume might be lower in metal-on-metal systems, more reactions to the wear debris are seen. Wolford et al.(18) reported that patients fitted with a metal-on-metal system exhibited significantly elevated body levels of Co and Cr. In comparison, patients fitted with a TMJ Concepts prosthesis showed no signs of UHMWPE or metallic debris, indicating good wear characteristics of the CoCrMo–UHMWPE combination in TMJ articulation. The same conclusion was reached by Westermark et al.(58) after histologic analysis of soft tissues surrounding Biomet and TMJ concept prostheses. These findings are further supported by several *in vitro* and *in vivo* studies showing that CoCr particles can exert toxic effects in the exposed tissues. McGregor et al.(54) found through animal studies that there is sufficient evidence for the carcinogenicity of metallic Co and limited evidence for the carcinogenicity of Co alloys; they classified Co-containing implants as possibly carcinogenic for humans.

Titanium alloys

Growing concerns regarding the toxicity and stress shielding risks of CoCr alloys have stimulated the use of Ti alloys in TJR. Although the strength and fatigue resistance are somewhat lower than for CoCr, they are still sufficient for load-bearing implant applications and Ti alloys have

outstanding biocompatibility properties. The Ti-oxide layer limits metal ion release more than the passivating layers on stainless steel or CoCr alloys. As a result, the cell/tissue response is improved, resulting in very little adverse tissue reaction, and close apposition between the implant and bone is established.(38,48) Moreover, Ti alloys have a low density; hence, Ti outperforms any other implant material when considering the specific strength.(48) Ti was first used as a material for TMJ implants in 1976 in the AO/ASIF-TMJ prosthesis and has since been used in many different alloys.(6) Commercially pure (cp) Ti (98.8–99.6 wt % Ti) and Ti6Al4V(89.0–91.0 wt % Ti, 5.5–6.5 wt % Al, and 3.5–4.5 wt % V) are currently the most commonly used Ti materials for implant applications in orthopedic surgery, and they are used in the two FDA-approved TMJ implants.(48)

Ti can adopt two different crystal structures: a closely-packed hexagonal structure known as the α-phase, which is stable at low temperatures or in the presence of certain alloying elements such as Al, oxygen (O), and nitrogen (N); and a body-centered cubic structure knows as the β-phase, which is stable above 883°C but can also be preserved at lower temperatures depending on the presence of certain alloying elements, such as V, niobium (Nb), Mo, and Ta. Ti6Al4Vconsists of a mixture of both the α- and β-phase and, as such, can be subjected to thermomechanical processing, which improves its mechanical properties, such as tensile strength and fatigue strength.(48) However, the passive film of Ti6Al4Vis known to be more susceptible to corrosion, as the V_2O_5 in the film can dissolve, producing openings in the film and exposing the underlying Ti alloy.(19) The unalloyed cp Ti consists of α-Ti, which has a lower strength and fatigue resistance than the alloy, but because of the absence of alloying elements in the protective oxide layer, cp Ti is much more corrosion resistant and, hence, more biocompatible. This is most likely the rationale for the selection of materials for the Biomet/Lorenz and TMJ Concepts prostheses. For the fixation screws, a high strength and fatigue resistance is more critical than biocompatibility; therefore, Ti6Al4Vis used in both systems. For the ramal surface finish in the Biomet/Lorenz system and the backing of the UHMWPE fossa in the TMJ Concepts system, optimal osseointegration is the goal, so excellent biocompatibility

is prioritized over the load-bearing capacity of the material, resulting in the selection of cp Ti for these parts. Furthermore, cp Ti and Ti6Al4Vhave an elastic modulus of 105 GPa and 115 GPa, respectively. This reduces the risk of stress shielding, compared with stainless steel or CoCr alloys, although these modulus values are still clearly different from that of bone. (48,59)

It should be noted, however, that despite of its advantages, Ti is not a material without flaws. Ti and its alloys are rather soft and have a low wear resistance, meaning that the material is not suited for articulating surfaces.(48) A second potential problem of Ti6Al4Vrelates to its alloying components. The alloy contains both V and Al, which can be released over time because of corrosion. Release of these ions has been found to be associated with long-term health problems, such as osteomalacia and neuropathy, as they are respectively toxic and neurotoxic. McGregor et al.(54) found no reports of tumors in animal studies with either Ti or Ti alloys, except for one study with Ti-6Al-4V, in which the alloy was implanted in the femur of rats, resulting in an increased incidence of local tumors. Loosening of the implant resulted in a further increase in the incidence of tumors. However, no other study showed the occurrence of tumors with the use of Ti-6Al-4V. Based on both epidemiological evidence and animal experiments, these authors concluded that there is inadequate evidence to indicate that Ti or Ti alloys (Ti6Al4Vincluded) are carcinogenic for humans.

To overcome Ti's shortcomings both β-Ti alloys and surface modification are currently being developed and discussed further below in the "Future Directions for Temporomandibular Joint Materials" section.

Ultra-high-molecular-weight polyethylene

After UHMWPE was first used in orthopedic surgery in 1962(60), the Techmedica device was the first to make use of this material for TMJ purposes in 1990, using the material as the articulating surface of the fossa component. Not long after, the Biomet system followed suit. (6,38,60)

UHMWPE is a type of linear unbranched PE with a high molecular weight (>1×10^6 amu) and high degree of crystallinity, which can be found in various forms.(60) The polymer is relatively cheap to process and has many advantageous properties, such as high stiffness and high impact strength, low coefficient of friction, good impact load damping capability, and good resistance to body fluids.(38) Throughout 5 decades of use, further improvements have been made, resulting in the current high grade cross-linked UHMWPEs, which have significantly better wear resistance and lower wear rates and coefficients of friction, compared with other polymers, such as high density PE, PMMA, and PTFE.(38,61)

Because the material is used as an insert between load-bearing surfaces, the type of material and finish of the counter-element and the environment have a defining influence on the wear and friction of UHMWPE. When the opposing material has a smoother surface, the abrasive wear will be lower than when the opposing material is rougher. Body fluids that surround the implant help create an elastohydrodynamic lubrication between the two surfaces. The amount of pressure and kinematics also have a significant influence on the amount of wear to which UHMWPE is subjected.(60) (Table 2). Important to note is that, while the amount of wear between metal-on-UHMWPE implants is greater than with metal-on-metal implants using CoCrMo alloys, potential problems due to wear can be prevented by increasing the thickness of the articulating surface. As such, the UHMWPE fossa of the Biomet TMJ prosthesis has a minimal thickness of 4 mm.(8)

One problem that current stock TMJ implant devices using UHMWPE can still encounter is that of creep (also known as cold flow), which is a form of slow permanent deformation resulting from long-term exposure to loading. This phenomenon has been well documented in orthopedic hip TJR and was also observed in stock TMJ TJR with flange screw fixation.(60) Deformation of the UHMWPE components risks diminishing the fit of the prosthesis part, resulting in increased micromotions and potentially eventual device failure.(38)

Table 2: Influence of the opposing material on wear of polymer materials in hip prostheses[60]

Material	Amount of wear
Non-modified UHMWPE	Ceramic head: 0.098–0.03 mm/y Metallic head: 0.12–0.25 mm/y
Hylamer	Ceramic head: 0.15–0.33 mg/million cycles Metallic head: 0.13–0.4 mm/y
HDPE	Ceramic head: 0.072 mm/y Metallic head: 0.076 mm/y

HDPE, high density polyethylene; UHMWPE, ultra-high-molecular-weight polyethylene

A second problem with UHMWPE is shelf aging, a process of oxidative degradation (chain scission) that is initiated by reactive free radicals generated by common γ-irradiation sterilization procedures. As a result of chain scission, the mechanical properties change during storage and implantation with a loss of mechanical strength, and wear resistance is diminished. This problem has been partially solved by exposing the PE during sterilization to a neutral gas or vacuum atmosphere, resulting in significantly reduced oxidation of the surface layer. As a result, the effects of long term shelf aging after irradiation have been limited to a decrease in fracture and fatigue resistance.(62,63)

Another solution to this problem can be found in the use of antioxidants such as vitamin E, creating vitamin E-stabilized UHMWPE. By incorporating α-tocopherol in UHMWPE, the material's oxidation resistance is increased, as vitamin E is capable of interacting with free radicals, actively preventing oxidative degradation. This incorporation is possible by either blending α-tocopherol in UHMWPE powder, or by diffusing vitamin E into UHMWPE. (63) While vitamin E is added after radiation crosslinking in the latter, this is not the case for the mixed blend. As a result, as the concentration of α-tocopherol increases, the efficiency of crosslinking is diminished. As such both the concentration of α-tocopherol and radiation dosage have to be optimized to achieve both optimal wear- and oxidation-resistance. (63,64) Oral et al.(64) concluded that vitamin E should not exceed 0.3wt%, with 0.1wt% being more optimal to achieve a similar crosslink density compared to untreated UHMWPE.

Along with the addition of vitamin E, an increase in radiation dose is needed to achieve a crosslink density approaching that of a blend without

α-tocopherol. This is of course of great importance, as a lower degree of crosslink density results in lower wear resistance. When diffusing vitamin E into the crosslinked UHMWPE has no effect on the crosslinking density and thus higher concentrations can be achieved. Of course, as long as α-tocopherol has not been applied to the UHMWPE, oxidation degradation can occur.(63) Also Bracco et al.(63) found that vitamin E-stabilized UHMWPE had better mechanical strength and showed less deterioration compared to non-treated UHMWPE, as long as a correct dosage of both vitamin E and radiation was applied. Furthermore, Wolf et al.(65) have come to prove through animal studies that the addition of vitamin to UHMWPE has no cytotoxic or genotoxic effect. It should be noted that, although UHMWPE is very suitable as an interpositioning material between load-bearing surfaces, care should be taken when using UHMWPE as the sole component of the fossa because of the increased risk of creep, fracture and back-side wear, and poor surface fixation with bone and bone cement originating from the hydrophobic nature of UHMWPE, which can result in micromotion.(13,38)

Despite these potential drawbacks, the fossa of the Biomet system is made solely of UHMWPE, which is fixated with Ti6Al4Vscrews. To our knowledge, there have been no systematic findings of failure of the Biomet system's fossa. A 3-year follow-up study after placement of a Biomet prosthesis conducted by Sanovich et al.(39) reported four implant failures, only one of which was due to loosening of fossa screws. Giannakopoulos et al.(7) and Leandro et al.(8) performed follow-up studies of 288 and 300 patients, respectively. The authors of both studies concluded that the system produced satisfactory results, with a 3.2% failure rate in the study by Giannakopoulos et al.(7) and an absence of device-related failure in the other study. Despite high success rates, varying between 84% and 91%, it should be noted that only a limited number of studies are available in literature and most of these involved small numbers of patients and relatively short follow-up periods (3 to 10 years).(7,8)

Discussion: Future Directions for Temporomandibular Joint Materials

Although indications for alloplastic TMJ TJR have been clearly outlined, and vast advancements in TMJ TJR systems have been made over the last couple of decades, it is clear that there is still room for improvement, especially with respect to biocompatibility and wear resistance of the currently used materials. As recent research by Onoriobe et al.(66) has indicated that the demand for use of TMJ TJR devices in the management of end-stage TMD will only further increase up until 2030, it is important that research into future generations of TMJ materials will address these shortcomings.

As such, current research focusses on both the development of new materials, as well as surface modification strategies. Another important advance is undoubtedly the introduction of additive manufacturing, which allows the production of customized patient-fitted implants with tailored material characteristics. Furthermore, as in other fields, the implementation of tissue engineering approaches is gaining attention. The literature suggests that further development of TJR is currently at a crossroads between alloplastic design and tissue engineering. While tissue engineering has shown very promising results, more cost-effective 3 dimensional (3D)-printing and further developments in the field of biomaterials are showing promising results as well. Furthermore, tissue engineering is still far from being perfected; as such, it is not likely to be a reliable therapeutic solution in the immediate or near future.(33,67) Only advances in the field of biomaterials development are discussed below.

β-titanium alloys

As indicated earlier, although Ti alloys have proven to be highly corrosion-resistant and biocompatible, there are growing concerns regarding long-term implantation because of the release of potentially toxic alloying elements, such as Al and V, and the risk of stress shielding, as their elastic modulus values are still relatively high compared to the elastic modulus of bone. These limitations have triggered the development of more biocompatible, low-modulus β-Ti alloys that contain non-toxic

β-stabilizing alloying elements, such as Nb, zirconium (Zr), Mo, Ta, and iron (Fe), instead of Al and V.(48,59,68)

While β-Ti alloys have been used since the 1960s (mainly for aerospace applications), specialized biocompatible alloys were only first developed in the 1990s.(69) The quaternary Ti-Nb-Zr-Ta (TNZT) alloys are currently considered to be among the most promising alloys to replace cp Ti and Ti6Al4Vin implant applications.(68) These β-Ti alloys exhibit higher corrosion resistance than the older Ti alloys because of the presence of Nb, Zr, and Ta, which form more stable oxides (especially in comparison with V). The presence of Nb_2O_5, ZrO_2, or Ta_2O_5 strengthens the TiO_2 passive film, effectively reducing the release of metal ions.(48) Another important asset of these new alloys is their lower elastic modulus, compared with cp Ti and Ti-6Al-4V. The two most common TNZT alloys, Ti–29Nb–13Ta–4.6Zr and Ti–35Nb–7Zr–5Ta, have elastic modulus values of 65 GPa and 55 GPa, respectively, which are a closer match to the modulus of cortical bone.(48,59)

An important drawback of β-Ti alloys, however, is their lower fatigue strength, compared with that of Ti-6Al-4V. One possible strategy to improve fatigue strength uses thermal treatment to induce the formation of finely dispersed α and ω phases throughout the β matrix. Overall, β-Ti alloys have a good heat treatment response, meaning that, depending on the thermal processing, it is possible to fine-tune their mechanical properties. As such, a combination of enhanced strength (including fatigue strength) and fracture toughness can be obtained, yet at the expense of a low elastic modulus.(48,59,70) Alternatively, particles such as Y_2O_3, SiO_2/ZrO_2, SrO, and CeO_2 can be added to the alloy, as these cause dispersion strengthening of the material.(59,70)

Furthermore, although the friction wear characteristics of Nb-containing β-Ti alloys are superior to those of cp Ti or Ti6Al4Vbecause of the lubricating properties of Nb_2O_5, the total wear resistance is still too low for using these alloys in articulating joint surfaces.(48,68) It should also be noted that although *in vitro* studies have shown that phagocytic cells are stimulated more by Ti6Al4Vwear debris than by Ti-6Al-6Nb or Ti-13Nb-13Zr debris(19), further long-term research concerning

the biocompatibility and toxicity of these newer elements is needed.(48,59,68) To overcome the problem of wear, several approaches have been studied, such as reinforcing the matrix with hard precipitates, heat treatment, surface modifications, and laser 3D-printing. Yet increasing the wear resistance of Ti alloys remains a challenge. While Samuel et al.(71) found that the addition of hard ceramic phases, such as boride (B), might enhance wear resistance, research by Majumdar et al.(72) indicated that adding TiB to the matrix of a β-Ti alloy led to deterioration of the wear properties and less attachment of human osteoblast-like MG-63 cells to the material, compared with non-reinforced alloys.(73)

As of now, no perfect technique has been found to increase the wear resistance of β-Ti alloys. Studies conducted by Kopova et al.(69), reinforcing the β-Ti alloy matrix with Fe and Si, have shown positive results. These authors reported improvement in both mechanical and biological properties and concluded that Ti-35Nb-7Zr-6Ta-2Fe-0.5Si might be suitable for orthopedic implantation. However, they did not mention the wear resistance of this material. Recent research by Chan et al.(68) using laser surface treatment with a continuous wave fiber laser has also shown promising results, producing better wear resistance and corrosion resistance than untreated TNZT.

Surface modifications

While altering the alloy composition of Ti to prevent the release of potentially toxic metal ions, such as Al and V, is a valuable approach to improving its biocompatibility, an alternative method is to modify the implant's surface. As discussed earlier, a biomaterial's surface can be a decisive factor determining its long-term success. Extensive research efforts have been focused on surface modifications of Ti, either by triggering an appropriate cell response to improve osseointegration or by hindering bacterial attachment to limit infection rates. There are a wide variety of surface modification strategies described in the literature, including techniques to alter the surface topography, as well as the chemical composition, of the surface. For a comprehensive overview of the various surface modifications available and under investigation to date, the reader is referred to several outstanding review papers.(74–76)

The general consensus regarding surface roughness is that while surfaces directly in contact with bone are preferentially roughened to promote cell adhesion (micro-topography) or bone ingrowth (macro-topography), smooth surfaces are preferred wherever adhesion of bacteria should be avoided. With respect to wettability, hydrophilic surfaces are preferred, as these seem to have a beneficial effect on cell spreading, while limiting the attachment of bacteria.(77) In addition, introducing inorganic materials (such as hydroxyapatite) or biomolecules at the implant surface that mimic the natural bone interface can lead to improved osseointegration. In addition to triggering appropriate biological responses, surface modifications of Ti are also being considered to improve its wear resistance, thereby allowing its use in articulating surfaces.(19,48,59,76,78)

Application of a thin, hard, wearresistant protective coating material, such as titanium nitride (TiN), titanium carbide (TiC), or diamond-like carbon (DLC), can significantly improve the tribological properties of Ti-based implants. TiN has shown favorable effects with respect to biocompatibility, as well as wear and corrosion resistance.(19,48,79) It should be noted, however, that the strength and durability of the coating are very dependent on the coating process. Physical vapor deposition (PVD) is the most commonly used technique for creating a TiN coating, yet several studies in the field of orthopedic surgery have noted increased third body wear due to delamination of the TiN coating. This has been attributed to the lack of chemical reactions or diffusion phenomena between substrate and coating during PVD, resulting in adhesive failure.(78,79) Alternatively, plasma nitriding can be applied; however, it has been reported that as processing time increases, corrosion fatigue properties are diminished. With respect to corrosion, nitrogen-ion implantation has been shown to be the preferred technique over plasma nitriding, even if no differences are observed between both techniques in wear properties.(19) Very little research has been conducted regarding TiN coatings in the field of TMJ surgery. Kerwell et al.(80) reported delamination in two explanted TiN-coated TMJ TJR devices, which had resulted in wear and corrosion of the TiN coating; unfortunately, the authors provided no information regarding which technique was used for the coating process.

Another form of surface modification that can be used involves carbon. When carbon is applied to Ti's surface, both TiC and graphite (C-C) can be formed. The bonds that are formed depend on the amount of carbon applied to the metal's surface.(76) The use of carbon increases hardness and resistance to wear and corrosion, and it also improves adhesion, growth, and maturation of bone-derived cells.(19,48,76) However, if the concentration of carbon is too high, a decrease in hardness will occur.(76)

Another suitable coating material is DLC, a metastable form of amorphous carbon with both tetrahedrally bonded (sp^3) carbon atoms, as in diamond, and trigonal planar bonded (sp^2) carbon atoms, as in graphite. With increasing diamond-like bonds, DLC-coatings typically exhibit more diamond-like properties, such as a low friction coefficient and high hardness.(76,81–83) Moreover, DLC-coatings are chemically inert and exhibit high bio- and hemocompatibility, as well as corrosion resistance. (48,82–84) Besides a high hardness, a very smooth surface can also be obtained with DLC, resulting in excellent wear resistance. (83,84) Jiang et al.(82), Kim et al.(84), and Firkins et al.(85) reported that when in contact with UHMWPE, DLC-coated stainless steel and Ti produced less wear than the pristine substrate materials. Jiang et al.(82) noted that while UHMWPE initially forms more debris when combined with DLC-coated Ti6Al4V, the amount of debris decreased as the amount of total movement increased. As a result, after a total sliding distance of 500 m, a higher total amount of UHMWPE debris was formed when combined with untreated Ti6Al4V than with DLC-coated Ti6Al4V.

DLC-coating can be applied via several different techniques, such as magnetron sputtering, ion beam deposition, and plasma-enhanced chemical vapor deposition (CVD).(83) However, care must be taken when selecting the appropriate processing route. Because of the difference in the thermal expansion coefficient and structure between the coating and Ti, as well as a high intrinsic stress, adhesion between the two surfaces is relatively poor.(76,81–83,86) As a result, when a coated Ti implant is subjected to higher forces, plastic deformation of the softer Ti can occur, resulting in insufficient support of the harder DLC coating.(83,84,86) This can cause chipping, fractures, and even delamination of the coating,

leading to increased wear and eventual implant failure.(81,84) To overcome this problem, several techniques are under research. Jiang et al.(82) made use of a gradient coating in which the carbon concentration gradually increases towards the surface. While only C-C bonds can be found on the surface and Ti-C bonds can be found deeper in the Ti, a hybrid layer of Ti-C and C-C bonds can be seen between these two layers. This not only improved adhesion but also increased wear resistance. Yetim et al.(86) applied a duplex surface technique to Ti6Al4V, in which the surface of the Ti alloy was first treated with plasma nitriding, after which a DLC layer was applied using magnetron sputtering. This produces a diffusion layer below the DLC coating, which acts as a hardened case, giving more support to the DLC layer, while retaining a low friction coefficient. As a result, wear properties were superior to those seen with a single treated surface. Furthermore, adhesion of the DLC layer increased, although only by a moderate amount.(86)

Polyetheretherketone

Despite the recent advances in Ti alloy development, mismatch with the elastic modulus of bone remains a serious problem. Non-metallic fiber-reinforced composites are currently being considered as an alternative for load-bearing implant applications.(87) These materials can combine a low elastic modulus, characteristic of the polymer matrix, with some excellent mechanical properties, depending on the nature and volume fraction of the reinforcing fibers. One of the materials of interest is polyetheretherketone (PEEK), a semi-crystalline polyaromatic linear polymer and part of the polyaryletherketones (PAEKs).

Interest in polyaromatic polymers grew in the 1980s in an attempt to design hip stems and fracture plates with an elastic modulus close to that of bone.(88) After extensive studies of its biological and mechanical properties, PEEK was first used for implantation by Brantigan and Steffee in 1989.(89) This was a 2-year clinical study during which PEEK was used as spine cage for lumbar fusion. PEEK was commercialized as a biomaterial in 1998 and has been used since then in the field of spine surgery.(88)

PEEK has many advantageous biomaterial properties, such as good biocompatibility and bone formation capacity.(88,90) Furthermore, Sagomonyants et al.(90) reported good boney fusion around an implanted PEEK, equaling the *in vitro* bone formation capacity of Ti. Furthermore, PEEK is radiolucent, which is beneficial for x-ray imaging of an implant. PEEK is also highly resistant to gamma and electron beam radiation, processes used for sterilization; compared to UHMWPE, for example, the quantity of free radicals produced during irradiation is much less and the radicals that are generated will decay quickly.(88) As such, PEEK is less prone to oxidative degradation due to chain scission, which is initiated by free radicals.

While unaltered PEEK has an elastic modulus of 3–4 GPa, the addition of carbon fibers can increase its elastic modulus, so it matches that of both cortical and trabecular bone.(88,91) This carbon fiber-reinforced PEEK (CFR-PEEK) also exhibits improved mechanical properties. Compared to untreated PEEK, CFR-PEEK has greater tensile strength and a higher fatigue limit but similar bone formation capacity and biocompatibility.(88,90)

When considering PEEK and CFR-PEEK as an articulating bearing surface, data in the field of CMF surgery are extremely scarce, but data are available for orthopedic hip and knee TJR. A systematic review by Li et al.(92) included a total of 20 clinical and/or biochemical articles and 3 scientific reports, published between 1990 to 2013. Of 20 studies, 17 showed that wear resistance was superior for CFR-PEEK compared with UHMWPE, when used as a bearing surface in hip joint simulations, regardless of whether the opposite articulating material was a ceramic material or metal alloy. Less clear were the results concerning knee joint simulations. While Scholes and Unsworth(93) reported favorable results for using CFR-PEEK in knee TJR, Wang et al.(91) reported that UHMWPE was a more suitable bearing surface in the knee joint simulation and concluded that CFR-PEEK should not be used as a bearing surface in knee TJR. Grupp et al.(94) concluded that while CFR-PEEK reduced wear compared with PEEK, it is still unclear whether wear is considerably reduced compared with UHMWPE. Similar to Wang et al.(91), Brockett et al.(95) concluded that, despite better results for CFR-PEEK, both PEEK and CFR-PEEK

showed significantly higher wear rates compared to UHMWPE, when used in low-conformity designs such as a knee TJR device.

Despite the absence of cytotoxic effects observed with PEEK composite wear debris, the conclusions of Wang et al.(91), Grupp et al.(94) and Brockett et al.(95) are of extreme importance when considering the use of (CFR-) PEEK as a bearing material for a TMJ TJR device. As stated by Mercuri et al.(13), the functional anatomy of the knee is far less constrained than that of the hip joint. The same can be said for the TMJ, which in this aspect is far more comparable to the knee joint than to the hip joint. As such, based on the available orthopedic literature, CFR-PEEK should be considered unsuitable as a bearing surface for a TMJ TJR system, though research and simulations designed specifically for TMJ TJR are necessary to make more definite conclusions.

Alumina-zirconia composites

With respect to tribological properties, ceramic materials outperform metals and polymers. As such, the bioinert ceramics, alumina (Al_2O_3) and zirconia (ZrO_2), are widely applied as articulating surfaces in orthopedic joint replacements. While Al_2O_3 has been in use in hip joints since the 1970s, ZrO_2 was first introduced into the field of orthopedic surgery around 1980; its fracture toughness and flexural strength are superior to those of Al_2O_3.(96) Indeed, ZrO_2 displays a high resistance to crack propagation owing to stress-induced phase transformation at the crack tip, which is accompanied by a volumetric expansion that induces compressive stresses.(97) As a result of this exceptional balance of toughness and strength, ZrO_2 steadily gained popularity, and excellent success was reported (failure rates as low as 0.002%).(97) In 2001, however, because of deviations in thermal processing during manufacturing, particular batches of ZrO_2 femoral heads experienced accelerated aging, resulting in high fracture rates *in vivo*. The inevitable withdrawal of these batches from the market led to a loss of confidence in ZrO_2 and focus shifted to using metal-on-metal implants.(48,96,98)

The problem with thermal processing regretfully highlighted one of the main concerns about ZrO_2 ceramics, which is its high sensitivity to aging, also known as low temperature degradation (LTD), in the presence of

water. LTD results in surface roughening and micro-cracking, which in articulating joint bearings leads to increased wear and debris release into the surrounding tissue and eventual implant failure.(97,98) In an attempt to overcome the issues associated with ZrO_2, ceramic composites fabricated of mixtures of Al_2O_3 and ZrO_2 have recently been developed, combining the advantageous properties of both components. Composites with Al_2O_3 as the primary or continuous phase (70% to 95%) and ZrO_2 as the secondary phase (30% to 5%) are called zirconia-toughened alumina (ZTA). While the excellent wear characteristics and aging resistance of the Al_2O_3 matrix are maintained, ZrO_2 reinforcement increases the strength and fracture toughness.(96) Mixtures composed mainly of ZrO_2 (80%) with additions of Al_2O_3 (20%) are referred to as alumina-toughened zirconia (ATZ).(96) ATZ composites maintain the high flexural strength and fracture toughness of the ZrO_2 matrix, while the presence of Al_2O_3 significantly improves resistance to aging compared with pure ZrO_2, although aging resistance remains less than that seen with ZTA materials.(99)

Currently, two ZTA grades and one ATZ grade are commercially available: Biolox Delta (76.1 wt % Al_2O_3, 22.5 wt % ZrO_2, and 1.4 wt % other), Bioceram (79 wt % Al_2O_3, 19 wt % ZrO_2, and 2 wt % others), and Ceramys (80 wt % ZrO_2 and 20 wt % Al_2O_3).(96) To prevent a loss in hardness and to prevent crack propagation, Cr_2O_3 and SrO, respectively, were added in very low quantities to Biolox delta, composing about 1 wt % of the composition.(100) Several *in vitro* hip simulator wear studies have reported significantly reduced wear rates for ZTA-on-ZTA and ATZ-on-ATZ compared to Al_2O_3-on-Al_2O_3.(101) Furthermore, Chevalier et al. have shown that newly developed ZTA materials with carefully controlled nano-sized microstructure exhibit very limited wear damage in a hip simulator, while having a crack resistance well beyond that of all existing biomedical-grade ceramics.(98)

Overall, these data corroborate the hypothesis that the mechanical performance and durability of ZTAs are suitable for application as an articulating bearing surface, such as in TMJ TJR. However, it should be noted that *in vivo* research and clinical data for ZTA are currently limited, and longer implantation studies are required.(96)

Conclusion

While hip and knee TJR systems have widely been accepted as standard end-stage treatment options in orthopedic surgery, the TMJ TJR system is still seen as an obscurity in the field of maxillofacial surgery, partially due to previous negative experiences with systems using unsuitable materials or suffering from flawed biomechanical design. Nevertheless, a slow yet certain increased demand for TMJ TJR systems can be seen, urging for the development of more suitable and durable materials. The authors of this article believe that with the development of newer materials such as ZTA and surface modification techniques, as well as 3D-printing, allowing for customization, the TJR system may very well provide a long term satisfactory treatment to end-stage TMJ pathology, although further research into these newer materials is needed.

References

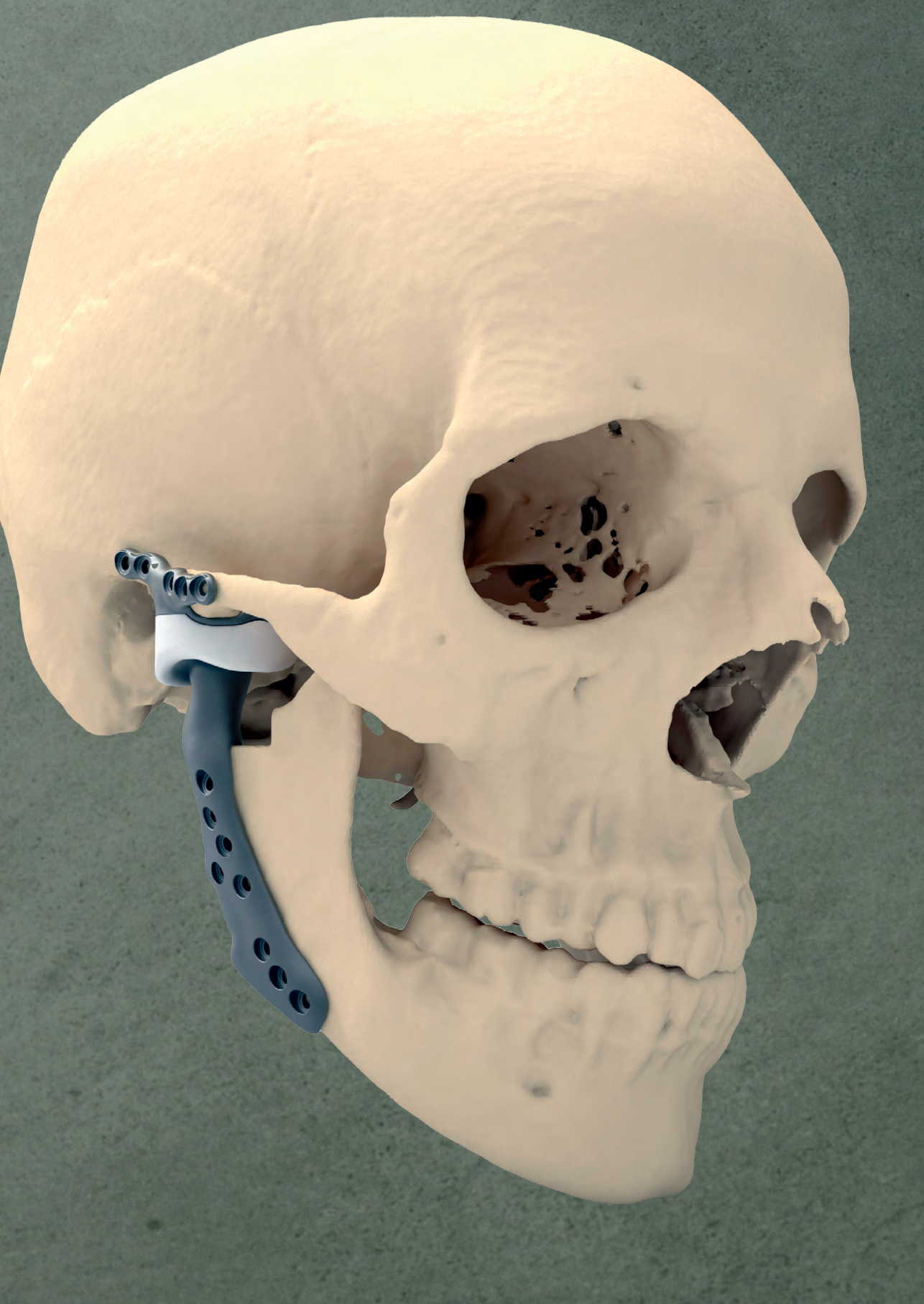
1. Isong U, Gansky SA, Plesh O. Temporomandibular joint and muscle disorder-type pain in U.S. adults: the National Health Interview Survey. J Orofac Pain [Internet]. 2008;22(4):317–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19090404%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4357589
2. Janal MN, Raphael KG, Nayak S, Klausner J. Prevalence of myofascial temporomandibular disorder in US community women. J Oral Rehabil. 2008;35(11):801–9.
3. Sidebottom AJ. Current thinking in temporomandibular joint management. Br J Oral Maxillofac Surg. 2009;47(2):91–4.
4. Mercuri L. End-Stage TMD and TMJ Reconstruction. In: Miloro M, Ghali G, Larsen P, Waite P, editors. Peterson's Principles of Oral & Maxillofacial Surgery. 3rd ed. PMPH, USA Ltd.; 2012. p. 1173–86.
5. Mercuri LG. Total Joint Reconstruction-Autologous or Alloplastic. Oral Maxillofac Surg Clin North Am. 2006;18(3):399–410.
6. Driemel O, Braun S, Müller-Richter UDA, Behr M, Reichert TE, Kunkel M, et al. Historical development of alloplastic temporomandibular joint replacement after 1945 and state of the art. Int J Oral Maxillofac Surg. 2009;38(9):909–20.
7. Giannakopoulos HE, Sinn DP, Quinn PD. Biomet microfixation temporomandibular joint replacement system: A 3-year follow-up study of patients treated during 1995 to 2005. J Oral Maxillofac Surg [Internet]. 2012;70(4):787–94. Available from: http://dx.doi.org/10.1016/j.joms.2011.09.031
8. Leandro LFL, Ono HY, Loureiro CC de S, Marinho K, Guevara HAG. A ten-year experience and follow-up of three hundred patients fitted with the Biomet/Lorenz Microfixation TMJ replacement system. Int J Oral Maxillofac Surg. 2013 Aug;42(8):1007–13.
9. Wolford LM, Pitta MC, Reiche-Fischel O, Franco PF. TMJ Concepts/Techmedica custom-made TMJ total joint prosthesis: 5-year follow-up study. Int J Oral Maxillofac Surg [Internet]. 2003;32(3):268–74. Available from: http://www.sciencedirect.com/science/article/pii/S0901502702903504
10. Mercuri LG. The Use of Alloplastic Prostheses for Temporomandibular Joint Reconstruction. J Oral Maxillofac Surg [Internet]. 2000;58(1):70–5. Available from: http://www.sciencedirect.com/science/article/pii/S0278239100800191
11. Guarda-Nardini L, Manfredini D, Ferronato G. Temporomandibular joint total replacement prosthesis: current knowledge and considerations for the future. Int J Oral Maxillofac Surg. 2008;37(2):103–10.
12. van Loon JP, de Bont LGM, Boering G. Evaluation of temporomandibular joint prostheses. Review of the literature from 1946 to 1994 and implications for future prosthesis designs. J Oral Maxillofac Surg. 1995;53(9):984–96.
13. Mercuri LG. The role of custom-made prosthesis for temporomandibular joint replacement. Rev Esp Cir Oral y Maxilofac [Internet]. 2013;35(1):1–10. Available from: http://dx.doi.org/10.1016/j.maxilo.2012.02.003
14. Sidebottom AJ. Alloplastic or autogenous reconstruction of the TMJ. J oral Biol craniofacial Res [Internet]. 2013;3(3):135–9. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3942016&tool=pmcentrez&rendertype=abstract
15. Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. Semin Immunol. 2008;20(2):86–100.
16. Wolford LM, Cassano DS. Autologous fat grafts placed around Temporomandibular Joint (TMJ) total joint prostheses to prevent heterotopic bone. Autologous Fat Transf Art, Sci Clin Pract. 2010;1893(1):361–82.
17. Shehab D, Elgazzar AH, Collier BD. Heterotopic ossification. J Nucl Med [Internet]. 2002;43(3):346–53. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11884494
18. Wolford LM. Factors to consider in joint prosthesis systems. Baylor Univ Med Cent Proc. 2006;19(3):232–8.
19. Singh R, Dahotre NB. Corrosion degradation and prevention by surface modification of biometallic materials. J Mater Sci Mater Med. 2007;18(5):725–51.

20. Kriens O. Indirect fossa arthroplasty in temporomandibular joint ankylosis. A preliminary report. Dtsch Zahnarztl Z. 1973 Mar;28(3):433–7.
21. Christensen RW. The correction of mandibular ankylosis by arthroplasty and the insertion of a cast vitallium glenoid fossa: a new technique. A preliminary report of three cases. Am J Orthop. 1963 Jan;5:16–24.
22. Christensen RW. Mandibular joint arthrosis corrected by the insertion of a cast-vitallium glenoid fossa prosthesis: A new technique. Oral Surgery, Oral Med Oral Pathol [Internet]. 1964;17(6):712–22. Available from: http://www.sciencedirect.com/science/article/pii/0030422064905225
23. Ferreira JNAR, Ko CC, Myers S, Swift J, Fricton JR. Evaluation of Surgically Retrieved Temporomandibular Joint Alloplastic Implants: Pilot Study. J Oral Maxillofac Surg. 2008;66(6):1112–24.
24. Recommendations for management of patients with temporomandibular joint implants. In: Journal of Oral and Maxillofacial Surgery [Internet]. Elsevier; 1993. p. 1164–72. Available from: http://dx.doi.org/10.1016/S0278-2391(10)80464-1
25. Mercuri LG. Silicone elastomer implants in surgery of the temporomandibular joint. Br J Oral Maxillofac Surg. 2013;51(7):584–6.
26. Hahn G. Vitallium mesh mandibular prosthesis. J Prosthet Dent. 1957;14(4):1–4.
27. Lindqvist C, Soderholm AL, Hallikainen D, Sjövall L. Erosion and heterotopic bone formation after alloplastic temporomandibular joint reconstruction. J oral. 1992;50(9):942–9.
28. Westermark A, Koppel D, Leiggener C. Condylar replacement alone is not sufficient for prosthetic reconstruction of the temporomandibular joint. Int J Oral Maxillofac Surg. 2006;35(6):488–92.
29. Christensen RW. Arthroplastic implantation of the TMJ. In: Thomas CC, editor. Oral Implantology. Springfield; 1970. p. 284–98.
30. Mercuri LG. The Christensen prosthesis. Oral Surg Oral Med Oral Pathol. 1996;81(February):1134–5.
31. Kummoona R. Functional rehabilitation of ankylosed temporomandibular joints. Oral Surg Oral Med Oral Pathol. 1978 Oct;46(4):495–505.
32. Sonnenburg I, Sonnenburg M. Total condylar prosthesisfor alloplastic jaw articulation replacement. J Maxillofac Surg. 1985;13(C):131–5.
33. Yuan K, Lee TM, Huang JS. Temporomandibular joint reconstruction: From alloplastic prosthesis to bioengineering tissue. J Med Biol Eng. 2010;30(2):65–72.
34. Sinno H, Tahiri Y, Gilardino M, Bobyn D. Engineering alloplastic temporomandibular joint replacements. McGill J Med. 2010;13(1):63–72.
35. Vega LG, González-García R, Louis PJ. Reconstruction of Acquired Temporomandibular Joint Defects. Oral Maxillofac Surg Clin North Am [Internet]. 2013;25(2):251–69. Available from: http://dx.doi.org/10.1016/j.coms.2013.02.008
36. Ramos A, Mesnard M. Christensen vs Biomet Microfixation alloplastic TMJ implant: Are there improvements? A numerical study. J Cranio-Maxillofacial Surg. 2015;43(8):1398–403.
37. Wolford LM, Dingwerth DJ, Talwar RM, Pitta MC. Comparison of 2 temporomandibular joint total joint prosthesis systems. J Oral Maxillofac Surg. 2003;61(6):685–90.
38. Mercuri LG. Alloplastic temporomandibular joint replacement: Rationale for the use of custom devices. Int J Oral Maxillofac Surg [Internet]. 2012;41(9):1033–40. Available from: http://dx.doi.org/10.1016/j.ijom.2012.05.032
39. Sanovich R, Mehta U, Abramowicz S, Widmer C, Dolwick MF. Total alloplastic temporomandibular joint reconstruction using Biomet stock prostheses: The University of Florida experience. Int J Oral Maxillofac Surg [Internet]. 2014;43(9):1091–5. Available from: http://dx.doi.org/10.1016/j.ijom.2014.04.008
40. Wolford LM, Mercuri LG, Schneiderman ED, Movahed R, Allen W. Twenty-year follow-up study on a patient-fitted temporomandibular joint prosthesis: the Techmedica/TMJ Concepts device. J Oral Maxillofac Surg [Internet]. 2015;73(5):952–60. Available from: http://dx.doi.org/10.1016/j.joms.2014.10.032
41. Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement – TMJ TJR - A Comprehensive Reference for Researchers, Material Scientists and Surgeons. 1st ed. New York: Springer International Publishing; 2016.

42. Peters K, Unger RE, Kirkpatrick CJ. Biomedical materials. In: Narayan R, editor. Biomedical Materials. 1st ed. New-York: Springer; 2009. p. 1–566.
43. Williams DF. On the mechanisms of biocompatibility. Biomaterials. 2008;29(20):2941–53.
44. Caicedo MS, Solver E, Coleman L, Jacobs JJ, Hallab NJ. Females with Unexplained Joint Pain Following Total Joint Arthroplasty Exhibit a Higher Rate and Severity of Hypersensitivity to Implant Metals Compared with Males: Implications of Sex-Based Bioreactivity Differences. J Bone Joint Surg Am. 2017 Apr;99(8):621–8.
45. Hallab N. Material Hypersensitivity. In: Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement - TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons. New York: Springer International Publishing; 2015. p. 227–50.
46. Hussain OT, Sah S, Sidebottom AJ. Prospective comparison study of one-year outcomes for all titanium total temporomandibular joint replacements in patients allergic to metal and cobalt-chromium replacement joints in patients not allergic to metal. Br J Oral Maxillofac Surg [Internet]. 2014;52(1):34–7. Available from: http://dx.doi.org/10.1016/j.bjoms.2013.02.014
47. Sidebottom AJ, Speculand B, Hensher R. Foreign body response around total prosthetic metal-on-metal replacements of the temporomandibular joint in the UK. Br J Oral Maxillofac Surg. 2008;46(4):288–92.
48. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants - A review. Prog Mater Sci [Internet]. 2009;54(3):397–425. Available from: http://dx.doi.org/10.1016/j.pmatsci.2008.06.004
49. Albrektsson T, Branemark PI, Hansson HA, Lindstrom J. Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. Acta Orthop Scand. 1981;52(2):155–70.
50. Parithimarkalaignan S, Padmanabhan T V. Osseointegration: An update. J Indian Prosthodont Soc. 2013;13(1):2–6.
51. Pruitt LA, Chakravartula AM. Mechanics of Biomaterials: Fundamental Principles for Implant Design [Internet]. Cambridge University Press; 2011. (Cambridge Texts in Biomedical Engineering). Available from: https://books.google.be/books?id=gD4gAwAAQBAJ
52. Lundberg H. TMJ Biomechanics. In: Mercuri LG, editor. Temporomandibular Joint Total Joint Replacement - TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons. New York: Springer International Publishing; 2015. p. 3–28.
53. Spagnoli D, Kent JN. Multicenter evaluation of temporomandibular joint Proplast-Teflon disk implant. Oral Surgery, Oral Med Oral Pathol. 1992;74(4):411–21.
54. McGregor DB, Baan RA, Partensky C, Rice JM, Wilbourn JD. Evaluation of the carcinogenic risks to humans associated with surgical implants and other foreign bodies - A report of an IARC Monographs Programme Meeting. Eur J Cancer. 2000;36(3):307–13.
55. Biomet. Biomet Total Joint Replacement System [Internet]. 2016. Available from: http://www.biomet.com
56. Nexus CMF. Nexus CMF Device Description [Internet]. 2016. Available from: http://www.nexuscmf.com/fossa-eminence-condylar-prosthesis-system-device-description.html
57. TMJ Concepts. TMJ Concepts Material description [Internet]. 2016. Available from: http://tmjconcepts.com/product-information/material-description/
58. Westermark A, Leiggener C, Aagaard E, Lindskog S. Histological findings in soft tissues around temporomandibular joint prostheses after up to eight years of function. Int J Oral Maxillofac Surg [Internet]. 2011;40(1):18–25. Available from: http://dx.doi.org/10.1016/j.ijom.2010.09.009
59. Chen Q, Thouas GA. Metallic implant biomaterials. Mater Sci Eng R Reports [Internet]. 2015;87:1–57. Available from: http://dx.doi.org/10.1016/j.mser.2014.10.001
60. Kowalewski P, Wieleba W. Sliding polymers in the joint alloplastic. Arch Civ Mech Eng. 2007;7(4):107–19.
61. Gupta A, Tripathi G, Lahiri D, Balani K. Compression Molded Ultra High Molecular Weight Polyethylene-Hydroxyapatite-Aluminum Oxide-Carbon Nanotube Hybrid Composites forHard Tissue Replacement. J Mater Sci Technol [Internet]. 2013;29(6):514–22. Available from: http://dx.doi.org/10.1016/j.jmst.2013.03.010
62. Li S. Ultra High Molecular Weight Polyethylene : From Charnley To Cross-Linked. Oper Tech Orthop. 2001;11(4):288–95.

63. Bracco P, Oral E. Vitamin E-stabilized UHMWPE for total joint implants: A review. Clin Orthop Relat Res. 2011;469(8):2286–93.
64. Oral E, Godleski Beckos C, Malhi AS, Muratoglu OK. The effects of high dose irradiation on the cross-linking of vitamin E-blended ultrahigh molecular weight polyethylene. Biomaterials. 2008;29(26):3557–60.
65. Wolf C, Lederer K, Muller U. Tests of biocompatibility of alpha-tocopherol with respect to the use as a stabilizer in ultrahigh molecular weight polyethylene for articulating surfaces in joint endoprostheses. J Mater Sci Mater Med. 2002 Jul;13(7):701–5.
66. Onoriobe U, Miloro M, Sukotjo C, Mercuri LG, Lotesto A, Eke R. How Many Temporomandibular Joint Total Joint Alloplastic Implants Will Be Placed in the United States in 2030 ? J Oral Maxillofac Surg [Internet]. 2016;74(8):1531–8. Available from: http://dx.doi.org/10.1016/j.joms.2016.04.011
67. Malik HH, Darwood ARJ, Shaunak S, Kulatilake P, El-Hilly AA, Mulki O, et al. Three-dimensional printing in surgery: a review of current surgical applications. J Surg Res [Internet]. 2015;199(2):512–22. Available from: http://dx.doi.org/10.1016/j.jss.2015.06.051
68. Chan CW, Lee S, Smith G, Sarri G, Ng CH, Sharba A, et al. Enhancement of wear and corrosion resistance of beta titanium alloy by laser gas alloying with nitrogen. Appl Surf Sci [Internet]. 2016;367:80–90. Available from: http://dx.doi.org/10.1016/j.apsusc.2016.01.091
69. Kopova I, Str??sk?? J, Harcuba P, Landa M, Jane??ek M, Ba????kova L. Newly developed Ti-Nb-Zr-Ta-Si-Fe biomedical beta titanium alloys with increased strength and enhanced biocompatibility. Mater Sci Eng C. 2016;60:230–8.
70. Song X, Wang L, Niinomi M, Nakai M, Liu Y, Zhu M. Microstructure and fatigue behaviors of a biomedical Ti-Nb-Ta-Zr alloy with trace CeO2 additions. Mater Sci Eng A [Internet]. 2014;619:112–8. Available from: http://dx.doi.org/10.1016/j.msea.2014.09.069
71. Samuel S, Nag S, Scharf TW, Banerjee R. Wear resistance of laser-deposited boride reinforced Ti-Nb-Zr-Ta alloy composites for orthopedic implants. Mater Sci Eng C. 2008;28(3):414–20.
72. Majumdar P, Singh SB, Chakraborty M. The influence of heat treatment and role of boron on sliding wear behaviour of ??-type Ti-35Nb-7.2Zr-5.7Ta alloy in dry condition and in simulated body fluids. J Mech Behav Biomed Mater [Internet]. 2011;4(3):284–97. Available from: http://dx.doi.org/10.1016/j.jmbbm.2010.10.007
73. Majumdar P, Singh SB, Dhara S, Chakraborty M. Influence of in situ TiB reinforcements and role of heat treatment on mechanical properties and biocompatibility of ?? Ti-alloys. J Mech Behav Biomed Mater [Internet]. 2012;10:1–12. Available from: http://dx.doi.org/10.1016/j.jmbbm.2012.02.014
74. Bagno A, Di Bello C. Surface treatments and roughness properties of Ti-based biomaterials. J Mater Sci Mater Med. 2004;15(9):935–49.
75. Le Guéhennec L, Soueidan A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. Dent Mater. 2007;23(7):844–54.
76. Liu X, Chu PK, Ding C. Surface modification of titanium, titanium alloys, and related materials for biomedical applications [Internet]. Vol. 47, Materials Science and Engineering R: Reports. 2004. p. 49–121. Available from: http://dx.doi.org/10.1016/j.mser.2014.10.001
77. Braem A, Van Mellaert L, Mattheys T, Hofmans D, De Waelheyns E, Geris L, et al. Staphylococcal biofilm growth on smooth and porous titanium coatings for biomedical applications. J Biomed Mater Res A. 2014;102(1):215–24.
78. Mishnaevsky L, Levashov E, Valiev RZ, Segurado J, Sabirov I, Enikeev N, et al. Nanostructured titanium-based materials for medical implants: Modeling and development. Mater Sci Eng R Reports. 2014;81(1):1–19.
79. Van Hove RP, Sierevelt IN, Van Royen BJ, Nolte PA. Titanium-Nitride Coating of Orthopaedic Implants: A Review of the Literature. Biomed Res Int. 2015;2015.
80. Kerwell S, Alfaro M, Pourzal R, Lundberg HJJ, Liao Y, Sukotjo C, et al. Examination of failed retrieved temporomandibular joint (TMJ) implants. Acta Biomater [Internet]. 2016;32:324–35. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1742706116300010
81. Ching HA, Choudhury D, Nine J, Abu Osman NA. Effects of surface coating on reducing friction and wear of orthopaedic implants. Sience Technol Adv Mater. 2014;014402(15).
82. Jiang SW, Jiang B, Li Y, Li YR, Yin GF, Zheng CQ. Friction and wear study of diamond-like carbon gradient coatings on Ti6Al4V substrate prepared by plasma source ion implant-ion beam enhanced deposition. Appl Surf Sci. 2004;236(1):285–91.

83. Roy RK, Lee K-R. Biomedical applications of diamond-like carbon coatings: a review. J Biomed Mater Res B Appl Biomater. 2007 Oct;83(1):72–84.
84. Kim DH, Kim HE, Lee KR, Whang CN, Lee IS. Characterization of diamond-like carbon films deposited on commercially pure Ti and Ti-6Al-4V. Mater Sci Eng C. 2002;22(1):9–14.
85. Firkins P, Hailey JL, Fisher J, Lettington AH, Butter R. Wear of ultra-high molecular weight polyethylene against damaged and undamaged stainless steel and diamond-like carbon-coated counterfaces. J Mater Sci Mater Med. 1998;9(10):597–601.
86. Yetim AF, Celik A, Alsaran A. Improving tribological properties of Ti6Al4V alloy with duplex surface treatment. Surf Coatings Technol [Internet]. 2010;205(2):320–4. Available from: http://dx.doi.org/10.1016/j.surfcoat.2010.06.048
87. Lee WT, Koak JY, Lim YJ, Kim SK, Kwon HB, Kim MJ. Stress shielding and fatigue limits of poly-ether-ether-ketone dental implants. J Biomed Mater Res - Part B Appl Biomater. 2012;100 B(4):1044–52.
88. Kurtz SM, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. Biomaterials. 2007;28(32):4845–69.
89. Brantigan JW, Steffee AD. A carbon fiber implant to aid interbody lumbar fusion. Two-year clinical results in the first 26 patients. Spine (Phila Pa 1976). 1993 Oct;18(14):2106–7.
90. Sagomonyants KB, Jarman-Smith ML, Devine JN, Aronow MS, Gronowicz GA. The in vitro response of human osteoblasts to polyetheretherketone (PEEK) substrates compared to commercially pure titanium. Biomaterials. 2008;29(11):1563–72.
91. Wang A, Lin R, Stark C, Dumbleton J. Suitability and limitations of carbon fiber reinforced PEEK composites as bearing surfaces for total joint replacements. Wear. 1999;225–229:724–7.
92. Li CS, Vannabouathong C, Sprague S, Bhandari M. The use of carbon-fiber-reinforced (CFR) peek material in orthopedic implants: A systematic review. Clin Med Insights Arthritis Musculoskelet Disord. 2014;8:33–45.
93. Scholes SC, Unsworth A. Wear studies on the likely performance of CFR-PEEK/CoCrMo for use as artificial joint bearing materials. J Mater Sci Mater Med. 2009;20(1):163–70.
94. Grupp TM, Utzschneider S, Schr??der C, Schwiesau J, Fritz B, Maas A, et al. Biotribology of alternative bearing materials for unicompartmental knee arthroplasty. Acta Biomater [Internet]. 2010;6(9):3601–10. Available from: http://dx.doi.org/10.1016/j.actbio.2010.04.003
95. Brockett CL, Carbone S, Fisher J, Jennings LM. PEEK and CFR-PEEK as alternative bearing materials to UHMWPE in a fi xed bearing total knee replacement : An experimental wear study. Wear [Internet]. 2017;374–375:86–91. Available from: http://dx.doi.org/10.1016/j.wear.2016.12.010
96. Kurtz SM, Kocagöz S, Arnholt C, Huet R, Ueno M, Walter WL. Advances in zirconia toughened alumina biomaterials for total joint replacement. J Mech Behav Biomed Mater. 2014;31:107–16.
97. Chevalier J, Gremillard L, Deville S. Low-Temperature Degradation of Zirconia and Implications for Biomedical Implants. Annu Rev Mater Res [Internet]. 2007;37(1):1–32. Available from: http://www.annualreviews.org/doi/abs/10.1146/annurev.matsci.37.052506.084250%5Cnhttp://www.annualreviews.org/doi/pdf/10.1146/annurev.matsci.37.052506.084250
98. Chevalier J. What future for zirconia as a biomaterial? Biomaterials. 2006;27(4):535–43.
99. Sequeira S, Fernandes MH, Neves N, Almeida MM. Development and characterization of zirconia-alumina composites for orthopedic implants. Ceram Int [Internet]. 2016; Available from: http://dx.doi.org/10.1016/j.ceramint.2016.09.216
100. Affatato S, Modena E, Toni A, Taddei P. Retrieval analysis of three generations of Biolox?? femoral heads: Spectroscopic and SEM characterisation. J Mech Behav Biomed Mater [Internet]. 2012;13:118–28. Available from: http://dx.doi.org/10.1016/j.jmbbm.2012.04.003
101. Clarke IC, Green DD, Williams PA, Kubo K, Pezzotti G, Lombardi A, et al. Hip-simulator wear studies of an alumina-matrix composite (AMC) ceramic compared to retrieval studies of AMC balls with 1-7 years follow-up. Wear. 2009;267(5–8):702–9.



Chapter 4

Total Temporomandibular Joint Replacement: Stick to Stock or Optimization by Customization?

This chapter is based on:

Total Temporomandibular Joint Replacement: Stick to stock or optimization by customization?

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Introduction

Prosthetic treatment of the temporomandibular joint (TMJ) is far from new, with the first alloplastic interpositioning dating back to the mid-19th century and total joint replacement (TJR) first reported in 1965.(1) Since then, TJR has seen significant changes, using different designs and materials, as well as the development of both stock and computer-assisted design/computer-assisted manufacturing (CAD-CAM) systems. Most well-known current systems are the stock and patient-fitted Zimmer Biomet Microfixation TMJ Replacement System (Jacksonville, FL, USA) and the TMJ Concepts Patient-Fitted Total TMJ Replacement System (Ventura, CA, USA). While several other PSI are available on the market as well, these two systems are currently the only U.S. Food & Drug Administration (FDA)-approved TJR systems available.(1,2)

The stock Biomet system makes use of three differently sized mandibular and fossa components, requiring the surgeon to select a size and intra-operatively alter the recipient's bone to achieve a desirable fit.(2,3) In contrast, PSI joint replacements, such as the TMJ Concepts prosthesis, rely on CAD/CAM technology. A pre-operative computed tomographic scan of the region of interest is digitally converted to a dataset by which the TJR components are designed, considering any anatomical abnormalities and the need for occlusal correction. As such, the surgeon is not forced to adapt the anatomical structures to achieve a tight fit, and operating time is reduced. Fixation screw placement can be optimized, minimizing the risk of inferior alveolar nerve damage.(2,4,5) As stated by Mercuri et al.(5,6), it is expected that PSI, also known as custom(ized) systems, provide significantly better results compared to stock prostheses. Reimbursement stakeholders worry if the results outweigh the higher production cost. Keeping in mind that the number of TMJ TJRs is increasing over time and is projected to exceed 1000 procedures within 15 years in the U.S. alone(7), we set out to evaluate both systems by means of a meta-analysis, as to guide craniomaxillofacial (CMF) surgeons and reimbursement stakeholders.

Objective

To the best of our knowledge, two published meta-analyses compared the results of stock and PSI TMJ TJR systems.(8,9) Whereas the meta-analysis by Zou et al.(9) evaluated both the short- (≤3 years) and long-term results (> 3 years), Johnson et al.(8) did not make this distinction and evaluated the Biomet Lorenz, TMJ Concepts, and Nexus CMF systems over the entire follow-up period as a whole. As a result, both types of prosthetic systems are compared to one another without clearly defined endpoints in time. This resulted in the inclusion of articles with a 6-month follow-up being compared with those with a 60-month follow-up. This increases the risk of skewing the post-operative results.

This systematic review and meta-analysis aims to evaluate and compare post-operative results in patients who were treated with either a PSI or stock prosthesis, at well-defined moments in time, to determine if there are significant differences in post-operative results between these two approaches. We hypothesized that the use of a CAD/CAM approach with the development of a PSI would lead to better post-operative results.

Materials and methods

Study design

We performed a systematic review by conducting a computerized literature search. The search was performed up to August 15, 2018, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The following databases were used: PubMed Central, Web of Science, Cochrane Library Plus, and EMBASE. The following heading was used to define the search string: ("Temporomandibular Joint" OR TMJ) AND ("Prosthesis" OR "Prostheses" OR "Implant" OR "Total Joint Replacement"). The search was conducted using both medical subject headings (MeSH) and free text words. The exact combination in which these search terms were used depended on the database and can be found in Table 1. A manual search of reference lists of the included articles was also performed.

Table 1: Database search terms

Database	Search terms	Hits
PubMed Central	("Temporomandibular Joint"[MeSH] OR "Temporomandibular Joint"[tiab] OR TMJ[tiab]) AND ("Prosthesis"[tiab] OR "Joint Prosthesis"[MeSH] OR "Joint Prosthesis"[tiab] OR "Total joint replacement"[tiab])	657
Web of Science	("Temporomandibular Joint" OR TMJ) AND (Prosthes* OR "joint prosthes*" OR "total joint replacement")	511
Cochrane	("Temporomandibular Joint" OR TMJ) AND (Prosthes* OR "joint prosthes*" OR "total joint replacement")	16
EMBASE	("Temporomandibular Joint" OR TMJ) AND (Prosthes* OR "joint prosthes*" OR "total joint replacement")	397

For an article to be included, the patient sample had to consist of humans who received either unilateral or bilateral stock or custom(ized) TMJ TJR systems. Both pre-operative maximal mouth opening (MMO) and pain scores needed to be available, as well as those of at least 1 year post-operatively. These data had to be available at well-defined endpoints in time (e.g., 1, 2, and/or 3 years after surgery). If any information on diet was provided, these data were also included. There were no boundaries set for age or sex, and the minimal patient population was set to 5. Articles evaluating post-operative results of the Vitek-Kent prosthesis were not considered for inclusion, due to the negative long-term results following the use of incompatible materials.(2)

Randomized controlled trials (RCTs), non-RCTs, comparative and prospective studies, retrospective studies, and case series were included. Case reports and expert opinions were excluded to maintain scientific soundness. Systematic reviews and meta-analyses concerning the use of a stock or patient-specific TJR were reviewed to identify possible eligible studies. Only articles written in English, Dutch, French, or German were included, and the full text had to be accessible.

Study bias

All included studies were assessed for risk of bias. For non-RCTs and other observational studies, both prospective and retrospective, bias was assessed using the Methodological Index for Non-Randomized Studies (MINORS) scale, first introduced in 2003 by Slim et al.(10) The items were scored 0 if not reported; 1 when reported, but inadequately;

and 2 when reported adequately. As an unbiased assessment of study endpoints was not possible in the non-comparative studies due to the nature of the subject, this criterion was left out of the analysis. While the item “adequate statistical analysis” is normally only used for comparative trials, it was also used for the included articles to evaluate the quality of analysis between pre- and post-operative results.

Study variables and data collection

After assessing the eligibility of all studies retrieved, the following data were extracted when available: authors, year of publication, number of patients included, sex, mean age of patients (in years), type of TMJ TJR, time of follow-up (in months), MMO (in mm), and pain and diet measurements using a Visual Analog Scale (VAS) measurement. All VAS scores were based on the patients’ subjective evaluation and ranged from 0 to 10. For pain, a score of 0 meant a total absence of pain, while a score of 10 was considered the worst imaginable pain someone could experience. A dietary VAS score of 0 indicated that the patient could only eat liquids, while a score of 10 reflected solid foods.

The use of a TMJ prosthesis was considered the predictor variable, and the MMO and VAS pain score were the main outcome variables. The diet VAS score was considered the secondary outcome variable, which was further analyzed to determine the effect of physiotherapy.

Several authors were contacted to determine if there was any duplication within their patient groups. As a result, not all data provided by Mercuri et al.(11–13) were included. Also the articles by Gruber et al.(14) and Sidebottom et al.(15) used the same patient population. We decided to use the data provided by Sidebottom et al.(15) at 1 year and at 3 years post-operatively by Gruber et al.(14) to obtain as many patients as possible. Gonzalez-Perez et al.(16) reported on the same patient group twice, albeit one article discussed the stock TMJ TJR, while the other evaluated both the stock and custom(ized) TJR systems.(17) Only the data obtained from the article discussing both patient groups were included.

Statistical analysis

The outcomes between the stock and PSI systems were based on the weighted mean gain of the MMO, and the weighted mean gain or reduction in VAS scores for pain and diet, and their seWMD. Weighted mean difference (WMD) and standard error of WMD (seWMD) between pre- and postoperative MMO, pain, and diet scores were calculated using the following formulas:

$$\mathrm{WMD} = \overline{X_{post-operative}} - \overline{X_{pre-operative}}$$

$$\mathrm{se(WMD)} = \sqrt{\frac{s^2_{pre-operative}}{n_{pre-operative}} + \frac{s^2_{post-operative}}{n_{post-operative}}}$$

Forest plots were constructed for both primary and secondary outcomes, showing the summary and 95% CI estimated in the meta-analyses. Mean difference were pooled using the generic inverse variance method. A random effect model (DerSimonian-Laird method) was used, variation in effects due to differences in study populations and methods were expected. Heterogeneity between subgroups was evaluated using the χ^2 test and I^2 metrics, where $P < 0.1$ or $I^2 > 50\%$ indicated significant heterogeneity.(18) The meta-analysis was performed using Review Manager 5.3 (Cochrane IMS, Copenhagen, Denmark).

Ethics approval

Internal ethical committee approval and confirmation of adherence to the Helsinki Declaration were not necessary for this literature review.

Results

Study inclusions

The initial search and selection was independently performed by two of the authors. Their results were then compared, and a third reviewer was asked to evaluate the reference in case of conflict. This search returned 1581 published articles. After removing the duplicates, 1078 articles were screened, and 1026 were excluded based on the contents of the title (n =

907) and abstract (n = 119). By reading the final 52 articles and applying the inclusion criteria, a total of 13 articles were analyzed. Two additional articles were identified by manually searching the reference list of one of the meta-analyses. The performed search is summarized in the PRISMA flow diagram (Fig. 1). Five articles met the inclusion criteria for stock prostheses(3,16,19–21), while eight were included for patient-specific TMJ TJR.(11–15,22–24) Both Machon et al.(25) and Gonzalez-Perez et al.(17) evaluated both a stock system and PSI. The basic characteristics of the included articles are in Tables 2 to 5. As stated earlier, not all articles that were included in the systematic review were included in the meta-analysis, as to prevent duplication of patient population.

In total, 12 of the 15 included articles provided data that were included in the meta-analysis.(3,13,24,25,14–16,19–23) A total of 413 patients were treated with either a uni- or bilateral patient-matched implant, while 691 patients were treated with a stock implant. While not all articles reported on sex, a clear female dominance with 411 female patients versus 220 male patients for stock implants.(3,20,21,25) This was more so the case for the PSI, with 308 and 36 female and male patients, respectively. (13,15,23–25) Both groups were also relatively similar in age. A more detailed overview of the study populations for stock and custom(ized) TMJ TJR can be found in Tables 2 and 3.

We chose not to divide the included prosthetic systems on basis of brand for this meta-analysis. As a result, a direct comparison was made between both stock and patient-fitted systems. While not intentional, all stock TMJ TJRs consisted of the Biomet system, with less heterogeneity in the PSI group.

Risk of bias

All 15 studies were assessed using the MINORS scale. Only those by Machon et al.(25) and Gonzalez-Perez et al.(17) were of comparative nature. Overall, the risk of bias was relatively low for articles dealing with stock and custom(ized) systems, with respective mean scores of 12/16 and 12.2/16 for the non-comparative articles. It should be noted that all included articles either did not report on or did not prospectively calculate

the necessary study size. A second point on which many studies scored poorly was the loss in follow-up, frequently exceeding over 50% of the initially included patient population. Both comparative articles scored a low risk of bias with scores of 15/18(17) and 14/18(25), with points lost for not calculating the necessary patient population. (Tables 6 and 7).

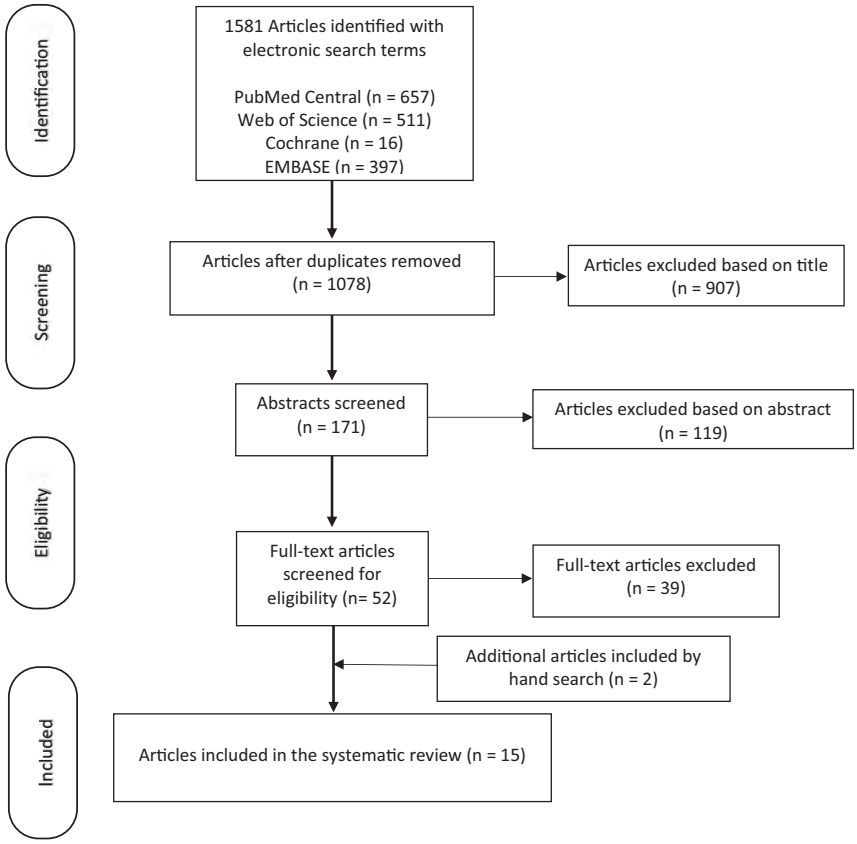


Fig 1: PRISMA-flow diagram

Table 2: Study characteristics for custom(ized) TMJ TJR.

Author, year	Type of TMJ TJR	Patients, n	TMJ TJR, n	Male	Female	Mean age (SD)	Follow-up
Mercuri(13) (1995)	TMJ Concepts	215	363	13	202	40.9 (± 10.3)	1 y 2 y 3 y
Mercuri(11) (2002)	TMJ Concepts	58	97	6	52	M: 39.8 (± 11.9) F: 39.9 (± 9.7)	1 y 2 y 3 y
Mercuri(12) (2007)	TMJ Concepts	60	102	/	/	/	1 y 2 y 3 y
Mercuri(23) (2008)	TMJ Concepts	20	33	4	16	44 (± 11.3)	1 y 2 y 3 y
Kanatas(24) (2011)	Christensen custom	31	44	9	22	45	1 y
Machon(25) (2012)	Biomet custom	4	4	1	3	33 (± 12.9)	1 y
Sidebottom(15) (2013)	TMJ Concepts	74	103	9	65	47	1 y
Aagaard(22) (2014)	Biomet custom	64	81	/	/	41 (± 16)	1 y 2 y 3 y
Gruber(14) (2015)	TMJ Concepts	58	84	52	6	47	1 y 3 y
Gonzalez-Perez(17) (2016)	Biomet custom	5	7	/	/	51.8 (± 11.7)	1 y 2 y 3 y

Abbreviations: TJR: total joint replacement, TMJ: temporomandibular joint, SD: standard deviation, y: years.

Table 3: Study characteristics for stock TMJ TJR.

Author, year	Type of TMJ TJR	Patients, n	TMJ TJR, n	Male	Female	Age, years (SD)	Follow-up
Westermark(19) (2010)	Biomet	12	19	/	/	29	1 y
Giannakopoulos(3) (2012)	Biomet	288	422	32	256	41.1 (± 11.1)	1 y 3 y
Machon(25) (2012)	Biomet	23	34	6	21	35.6 (± 11.04)	2 y
Lobo Leandro(20) (2013)	Biomet	300	399	180	120	20-60	1 y 3 y
Dimitroulis(21) (2014)	Biomet	16	17	2	14	55.3 (± 7.7)	2 y
Gonzalez-Perez(16) (2016)	Biomet	52	68	/	/	52.6 (± 11.5)	1 y 2 y
Gonzalez-Perez(17) (2016)	Biomet	52	68	/	/	52.6 (± 11.5)	1 y 2 y 3 y

Abbreviations: TJR: total joint replacement, TMJ: temporomandibular joint,
SD: standard deviation, y: years.

Study results

A total of 686 stock prosthesis were included in the 1-year follow-up results. This number significantly dropped to 122 for the 2-year follow-up, and then increased to 468 for the 3-year follow-up. In comparison, 252 PSIs were available at the 1-year mark, 85 at 2 years, and 124 at 3 years. Both stock and patient-fitted systems achieved significant increases in post-operative MMO, with a mean increase of 17.32 mm (95% confidence interval [CI], 6.39 to 28.25) for stock implants and 13.27 mm (95% CI, 8.47 to 18.08) for custom(ized) implants (Figure 2). However, the difference between the implant systems quickly decreased after 2 years. The difference between both groups was non-significant at both 1 (P = 0.51), 2 (P= 0.84) and 3 (P = 0.63) years.

In total, 268 sides in patients treated with stock implants were evaluated for pain both pre- and post-operatively (Figure 3). At 2 and 3 years, 103 and 256 sides were evaluated, respectively. A significant decrease in the VAS pain score was noted, with a 5.02 (95% CI, -5.42 to -4.62) decrease on a 0 to 10 scale. While this decrease was higher for the 252 sides treated with a patient-fitted implant at the 1-year post-operative assessment at 5.34 (95% CI, -6.15 to -4.53), this difference was non-significant (P = 0.49). This lack of significance persisted at 2 (P = 0.81) and 3 years (P = 0.76).

Only Lobo-Leandro et al.(20) provided information on patient dietary capabilities, with 300 included patients at the 1-year mark and 212 patients at the 3-year mark (Figure 4). A significant increase for both time points was seen for the dietary VAS score: 7.60 (95% CI, 7.45 to 7.75) and 7.62 (95% CI 7.47 to 7.77) at 2 and 3 years, respectively. Patients treated with a PSI showed a significant increase in their dietary VAS score (5.45 [95% CI, 4.95 to 5.96] and 4.82 [95% CI, 2.98 to 6.67])(13–15,17,22–25), albeit less significantly compared to the 1-year (P < 0.001) and 3-year results (P <0.01) results published by Lobo-Leandro et al.(20)

Table 4: Primary and secondary outcome variables for custom(ized) TMJ TJR.

Author, year	Follow-up	MMO mm (SD)		Pain (VAS 0-10)		Diet (VAS 0-10)	
		Pre	Post	Pre	Post	Pre	Post
Mercuri(13) (1995)	Pre	24.2 (± 10.6)		8.44 (± 2.32)		3.3 (± 2.3)	
	1 y		30.7 (± 8.2)		3.58 (±2.94)		7.3 (± 2.55)
	2 y		31.6 (± 9.1)		4.3 (± 3.2)		
	3 y		32.4 (± 8.7)		4.18 (± 3.22)		6.45 (± 2.6)
Mercuri(11) (2002)	Pre	25.5 (± 11.4)		7.4 (± 1.98)		3.55 (± 2.7)	
	1 y		33.0 (± 6.6)		2.84 (± 2.29)		7.2 (± 2.07)
	2 y		31.6 (± 9.2)		3.03 (± 2.8)		
	3 y		35 (± 8.7)		2.89 (± 2.32)		7.3 (± 2.29)
Mercuri(12) (2007)	Pre	24.9 (± 10.5)		7.25 (± 2.6)		3.8 (± 2.71)	
	1 y		31.6 (± 7.8)		3.11 (± 2.56)		7.11 (± 2.25)
	2 y		32.9 (± 7.1)		3.34 (± 2.8)		
	3 y		33.6 (± 6.5)		3.41 (± 2.96)		6.79 (± 2.71)
Mercuri(23) (2008)	Pre	14.0 (± 9.2)		6.69 (± 3.18)		2.42 (± 2.25)	
	1 y		33.8 (± 7.9)		3.18 (± 3.2)		7.87 (± 2.84)
	2 y		27.4 (± 6.8)		3.75 (± 3.95)		
	3 y		29.0 (± 7.9)		3.82 (± 3.44)		8.36 (± 1.71)
Kanatas(24) (2011)	Pre	19.7 (± 10.8)		7.4 (± 3.1)		/	/
	1 y		28.2 (± 7.3)		1.6 (± 2.4)		
Machon(25) (2012)	Pre	27.5 (± 6.24)		1.7 (± 2.5)		/	/
	2 y		37.8 (± 11.62)		0.5 (± 1)		
Sidebottom(15) (2013)	Pre	22.4 (± 9.7)		7.2 (± 2.5)	0.8 (± 1.7)	3.8 (± 2.3)	9.3 (± 1.6)
	1 y		33.7 (± 6.2)				
Aagaard(22) (2014)	Pre	29.5 (± 11.3)		7.2 (± 2.6)		/	/
	1 y		38.7 (± 7.0)		1.8 (± 2.7)		
	2 y		35.8 (± 5.6)		1.3 (± 1.5)		
	3 y		31.8 (± 11.1)		1.6 (± 3.1)		
Gruber(14) (2015)	Pre	21.0 (± 10)		7.4 (± 2)		4.1 (± 2)	
	1 y		34 (± 6)		0.9 (± 1)		9.1 (± 2)
	3 y		35.5 (± 7)		0.6 (± 2)		9.7 (± 1)

Table 4: continued.

Author, year	Follow-up	MMO mm (SD)		Pain (VAS 0-10)		Diet (VAS 0-10)	
		Pre	Post	Pre	Post	Pre	Post
Gonzalez-Perez(17) (2016)	Pre	15.2 (± 4.8)		6.0 (± 1.58)		/	/
	1 y		42 (± 4.9)		2.2 (± 0.44)		
	2 y		41.6 (± 0.48)		2.2 (± 0.44)		
	3 y		43.2 (± 5.6)		2.2 (± 0.44)		

Abbreviations: TJR: total joint replacement, TMJ: temporomandibular joint, MMO: Maximal mouth opening, SD: standard deviation, VAS: visual analogue scale, y: years.

Table 5: Primary and secondary outcome variables for Stock TMJ-TJR

Author, year	Follow-up	MMO mm (SD)		Pain (VAS 0-10)		Diet (VAS 0-10)	
		Pre	Post	Pre	Post	Pre	Post
Westermark(19) (2010)	Pre	16.3 (± 13.3)		/		/	
	1 y		33.3 (± 6.23)		/		/
	2 y		34.5 (± 7.24)				
Giannakopoulos(3) (2012)	Pre	20.4 (± 10.12)		8 (± 2.65)		/	
	1 y		30.9 (± 6.05)		2.8 (± 2.44)		/
	3 y		29.5 (± 6.55)		2.6 (± 2.3)		
Machon(25) (2012)	Pre	15.87 (± 8.16)		5.48 (± 3.34)		/	
	2 y		30.91 (± 6.02)		2.78 (± 2.64)		/
Lobo Leandro(20) (2003)	Pre	11.3 (± 4.2)		2.36 (± 2.02)		2.32 (± 1.44)	
	1 y		38.9 (± 6)		0 (± 0)		9.92 (± 0.38)
	3 y		41.8 (± 4.5)		0 (± 0)		9.94 (± 0.3)
Dimitroulis(21) (2014)	Pre	32.53 (± 6.85)		7.52 (± 1.6)		/	/
	2 y		34.57 (± 5.19)		1.6 (± 2.4)		
Gonzalez-Perez(16) (2016)	Pre	27 (± 9.7)		6.44 (± 1.43)		/	/
	1 y		41.1 (± 0.6)		1.65 (± 1.29)		
	2 y		41.7 (± 0.66)		1.57 (± 1.22)		
Gonzalez-Perez(17) (2016)	Pre	27 (± 9.7)		6.44 (± 1.43)		/	/
	1 y		41.1 (± 0.6)		1.65 (± 1.29)		
	2 y		41.7 (± 0.66)		1.57 (± 1.22)		
	3 y		41.7 (± 0.66)		1.57 (± 1.22)		

Abbreviations: MMO: Maximal mouth opening, TJR: total joint replacement, TMJ: temporomandibular joint, SD: standard deviation, VAS: visual analogue scale, y: years.

Table 6: Risk of bias assessment of non-randomized controlled trials of PSIs using the MINORS scale(10).

Study (year)	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of the study endpoint	Follow-up period appropriate to study aim	<5% Lost to follow-up	Prospective calculation of study size	Adequate statistical analyses	Total
Mercuri(13) (1995)	2	2	2	2	/	2	0	0	2	12/16
Mercuri(11) (2002)	2	2	1	2	/	2	0	0	2	11/16
Mercuri(12) (2007)	2	2	1	2	/	2	0	0	2	11/16
Mercuri(23) (2008)	2	2	2	2	/	2	0	0	2	12/16
Kanatas(24) (2011)	2	2	2	2	/	2	0	0	2	12/16
Machon(25) (2012)	2	2	2	2	0	2	2	0	2	14/18
Sidebottom(15) (2013)	2	2	2	2	/	2	1	0	2	13/16
Aagaard(22) (2014)	2	2	2	2	/	1	0	0	2	11/16
Gruber(14) (2015)	2	2	2	2	/	2	2	0	2	14/16
Gonzalez-Perez(16) (2016)	2	2	2	2	/	2	2	0	2	14/16
Gonzalez-Perez(17) (2016)	2	2	2	2	1	2	2	0	2	15/18

Abbreviations: MINORS: Methodological Index for Non-Randomized Studies, PSI: patient-specific implant.

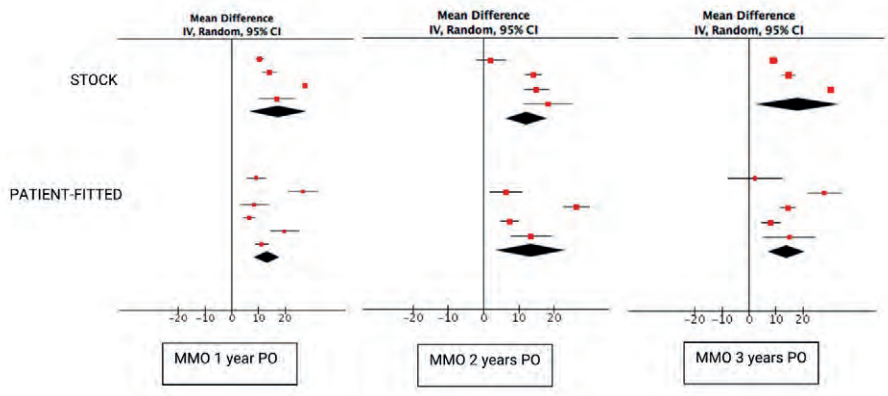


Fig 2: Forrest-plot Maximal mouth-opening at 1, 2 and 3 years after surgery

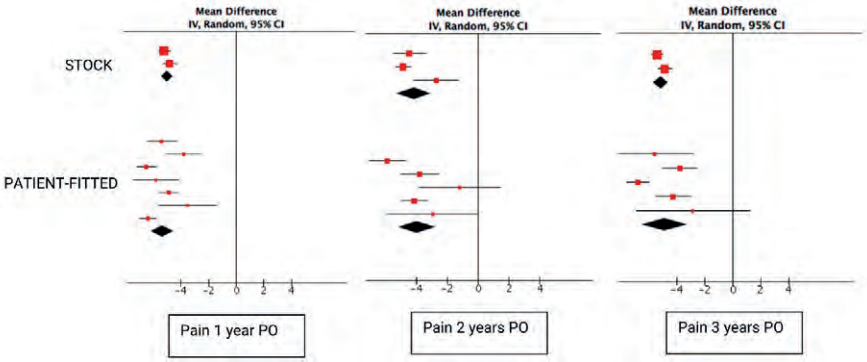


Fig 3: Forrest-plot Pain VAS score at 1, 2 and 3 years after surgery

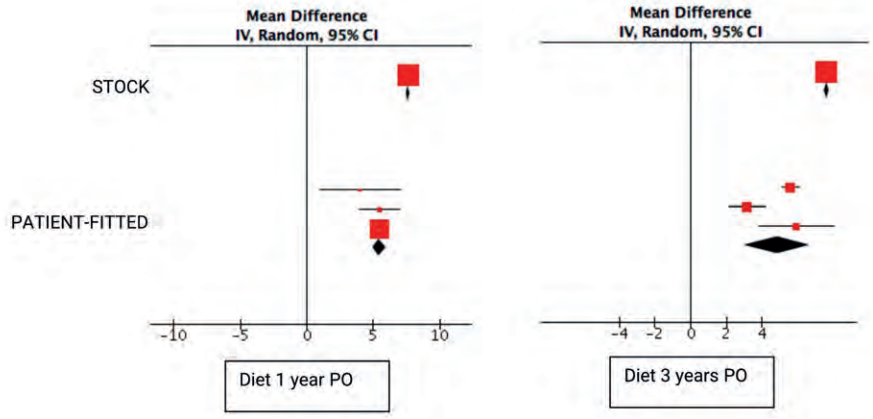


Fig 4: Forrest-plot Dietary VAS score at 1 and 3 years after surgery.

Table 7. Risk of bias assessment of non-randomized controlled trials of stock prosthesis using the MINORS scale(10).

Study (year)	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of the study endpoint	Follow-up period appropriate to study aim	<5% Lost to follow-up	Prospective calculation of study size	Adequate statistical analyses	Total
Westermark(19) (2010)	2	2	2	2	/	2	2	0	2	14/16
Giannakopoulos(3) (2012)	2	2	2	2	/	2	0	0	2	12/16
Machon(25) (2012)	2	2	2	2	0	2	2	0	2	14/18
Lobo-Leandro(20) (2013)	2	2	2	2	/	2	0	0	2	12/16
Dimitroulis(21) (2014)	2	2	0	2	/	2	0	0	2	10/16
Gonzalez-Perez(17) (2016)	2	2	2	2	1	2	2	0	2	15/18

Abbreviation: MINORS: Methodological Index for Non-Randomized Studies.

Discussion

While our approach was different from that of Zou et al.(9) and Johnson et al.(8), the statistical findings were similar for the three meta-analyses. Despite the conviction of Mercuri et al.(5) and many other surgeons, the current available data do not seem to indicate a clear advantage of patient-fitted implant systems over their stock counterparts. However, several significant remarks must be made before reaching this conclusion, and several confounders should be mentioned.

Bias of pooled data

While Lobo Leandro et al.(20) noted similar post-operative MMO results compared to the other included articles, both their mean pre-operative mouth opening at 11.3 mm and mean post-operative dietary VAS scores of 9.92 and 9.94 at 1 and 3 years post-operatively are significantly lower

or higher compared to the other included articles. Furthermore, only Lobo Leandro et al.(20) provided dietary VAS scores for the stock prosthesis, significantly weakening the conclusion of these findings. Due to the large population size(20), these data have a significant effect on the meta-analysis results, heavily "benefitting" the overall results for the stock prosthesis. This remark was also made by Johnson et al.(8) in their meta-analysis. Excluding the data provided by Lobo Leandro et al.(20) had a significant effect on the effect size for MMO, leading to a smaller increase in MMO from 17.32 to 13 mm (95% CI, 9.60 to 16.39) and from 18.11 to 11.82 mm (95% CI, 6.33 to 17.30), and a smaller increase in MMO compared to patients treated with a patient-fitted implant. While the data of Lobo Leandro et al.(20) cannot simply be discarded, this demonstrates the sensitivity of the pooled data to bias.

Lack of pathology grading

Pathology grading was lacking in the included studies. While it is well known that TJR should be considered the last resort for patients with end-stage joint disease, the studies had great variability in the clinical severity of the pathologies and indications for surgery.(26,27) For example, one of the indications was joint ankylosis. Sawhney et al.(28) made clear distinctions among four different types, whereas Turlington and Durr(29) identified three types (Tables 8, 9). While all four types of Sawhney et al.(28) come into consideration for TJR surgery, it is evident that differences in severity and type of ankylosis (osseous, fibrous, mixed, or extended) can affect results. Post-operative results obtained in the ankylosis group of one study were negatively influenced by the presence of more severe cases, even if they are diagnosed as being of the same type.(28)

Table 8. Grading of ankyloses of the TMJ by Sawhney et al.(28)

Type I	The head of the condylar process is visible but significantly deformed, with fibroadhesions making TMJ movement impossible
Type II	Consolidation of the deformed head of the condylar process and articular surface occurs mostly at the edges and in the anterior and posterior parts of the structures, and the medial part of the surface of the condylar head remain undamaged
Type III	The ankylotic mass involves the mandibular ramus and zygomatic arch; an atrophic and displaced fragment of the anterior part of the condylar head is in a medial location
Type IV	The TMJ is completely obliterated by a bony ankylotic mass growing between the mandibular ramus and cranial base

Abbreviation: TMJ: temporomandibular joint.

Two scales often used to evaluate TMD severity and joint degeneration are the Wilkes' staging classification for internal derangement of the TMJ and the Helkimo index.(30,31) Whereas the Helkimo index has three subindexes (anamnestic, clinical, and occlusal dysfunction), the Wilkes classification is based on both clinical and radiological properties. Both indexes have wide ranges, with the final stage coming into consideration for TMJ TJR surgery.(30,31) As such, while two patients might have a similar score on the Helkimo index(31), the amount of bony destruction can be significantly different. However, surgeons are currently unable to report this distinction in severity due to the lack of diagnostic tools for end-stage TMD. Nevertheless, anatomical abnormality affects both the choice of implant system and one- versus two-stage surgery, as well as the post-operative results. When comparing MMO, pain and diet, the relative numbers of patients with ankylosis and severe inflammatory/degenerative joint disease in the study group can affect the post-operative improvements.(5,27,32)

Table 9. Grading of ankyloses of the TMJ by Turlington and Durr.(29)

Grade 0	No bone islands visible
Grade 1	Islands of bone visible within the soft tissue around the joint
Grade 2	Periarticular bone formation
Grade 3	Apparent bony ankylosis

Abbreviation: TMJ: temporomandibular joint.

Many surgeons prefer the use of a patient-fitted system in case of more severe anatomical abnormalities.(5,8,33,34) This was illustrated by Gonzalez-Perez et al.(17) who opted for a PSI system in patients with large and complex defects. The amounts of subjective and objective improvement diminish as the severity of anatomical abnormalities and number of previous treatments increases, due to compromised (neuro) muscular anatomy and function.(13,35,36) When a patient-fitted system is preferred in case of severe TMJ degeneration or in revision surgery, it is obvious that its potential for post-operative improvement is more limited compared to a stock implant system that is usually indicated in less severe or primary cases. This is a major contributor to bias in the meta-analysis.

Surgical risks and operation time

The immediate advantage of a patient-fitted prosthesis is that it requires no alteration of the patient's anatomy. The total contact surface between the mandibular component and the mandible is optimal for improved osseointegration and stability.(2) In contrast, when using a stock implant, either the bony surface has to be fitted to the implant, or the implant must be bent or grinded down. This increases the total operation time and puts the materials at risk for fatigue and micromotions, which can lead to implant failure.(2,11,12,24,37)

Zhoa et al.(37) set out to evaluate the amount of bone that needed to be removed or grafted to achieve a good fit for the stock Biomet system in 63 joints they had treated between 2010 and 2016. Computer simulation revealed that a medium amount of bone trimming was needed (150-300 mm^3 bone) in 46% of skull bases, and in 33% a large volume (>300 mm^3) of bone trimming was necessary. The mandibular bone required medium and large amounts of trimming in 27% and 29% of all cases, respectively. Furthermore, in 44% of all cases a medium bone graft was needed elsewhere on the fossa to achieve a good fit, while in 35% a large amount was needed. They concluded that a patient-fitted implant required less adaptation, which decreases surgery time and the risk of injury to the skull base and alveolar nerve.(37)

Similarly, Abramowicz et al.(38) set out to evaluate the necessity of the use of a patient-fitted implant in 22 cases by evaluating if a stock Biomet implant could be fitted to the stereolithographic models of patients who were treated with an TMJ Concepts device. They found that in 23% of all sites, no fit could be achieved by means of a stock implant. In an additional 27% of all sites, significant alterations had to be performed to either the skull base or condylar bone with a minimum of 3 mm of bone that needed to be removed. They concluded that in more complex cases, such as patients who underwent multiple operations or who have more severe anatomical abnormalities, the use of a patient-fitted solution should be preferred over a stock implant. However, for more straightforward and simple cases, they found that a stock implant was a more cost-effective solution.(38)

Extra advantages of patient-fitted prostheses

Custom(ized) prostheses allow for controlled occlusal correction and proper mastication without having to opt for (simultaneous) orthognathic surgery.(11) In case of congenital anomalies with severe hypoplasia (e.g., hemifacial microsomia), the extended mandibular and fossa components also substitute missing bone and allow for proper facial rotation in conjunction with other facial osteotomies.(39) For defects due to trauma, osteomyelitis, or oncological resection, an extended TJR can substitute both the affected TMJ and the additional bony defect in the mandible or skull base, once again making further surgery (e.g., microvascular bone flaps) unnecessary.(39,40) One of the distinct advantages of CAD/CAM-designed implants for these cases is the optimal aesthetic outcome (and consequent psychosocial integration), which would not be possible through the combination of a stock TMJ TJR and a second implant or autologous graft.(39)

Screw position and length can be determined using a patient-fitted approach to prevent damage to the inferior alveolar nerve.(5,38) For simple TJR, the patient-fitted mandibular component can be inserted via a mini-retromandibular incision, diminishing the risk of lesioning the mandibular branch of the facial nerve, in a similar fashion as described by Biglioli et al.(41) for condylar fractures.

Both FDA-approved systems (Zimmer Biomet and TMJ Concepts) manufacture at least parts (condylar head) in cobalt-chromium-molybdenum (CoCrMo) alloy. It should be noted that Zimmer Biomet also has a version of their stock prosthesis fully in Ti, yet this version is not FDA-approved, nor are there, as far as we are aware of, any post-operative results discussed in current literature.

In a meta-analysis on orthopedic prostheses, about 10% of the population was found to be allergic to one or more components of the implants, usually nickel, of which they contain 1%. Other components are cobalt (62%–67%), chromium (27%–30%), and molybdenum (5%–7%).(42) In patients with a functioning prosthesis, the proportion of allergies rose to 23%, and in those with a failing prosthesis to 63%. It may be that the

symptoms are disguised either because of the depth of the implant in the tissues or because the pain has been ascribed to another cause.(42) Given the huge impact on outcome, it seems at least advisable to select a titanium prosthesis, which currently are only available in the custom(ized) version (3D-printed titanium). The prevalence of Ti allergy is not known but is estimated to be very low, and a patch test with titanium salt or the actual titanium alloy is recommended.(43)

Surgical techniques do not easily lend themselves to scrutiny via randomized clinical trials.(44) Observational cohort studies and comparisons with historical controls may take decades when the indications are so limited as for TMJ TJR. On the other hand, surgeons are quickly convinced of techniques that are more promising from a physiological point of view. To switch back from a customized TMJ to a stock prosthesis may seem like switching from open reduction and (semi) rigid osteosynthesis to closed reduction and intermaxillary fixation in CMF trauma repair. Luckily, in Europe, the costs for some animal-tested customized TMJ TJRs have become similar to those of FDA-approved systems.

Conclusion

This meta-analysis evaluated the MMO and VAS scores for pain and diet to provide pooled estimates for both patient-fitted and stock TMJ-TJR systems. While no significant differences were found between the implant systems, the provided data do not consider pathology severity, which can heavily influence post-operative outcomes and is prone to bias of pooled data. By means of a prospective randomized trial, this bias could be overcome, yet this forces the use of a certain implant system even if not deemed suited by the performing surgeon, posing an important ethical dilemma.

There is need for a detailed diagnostic evaluation tool to better describe the degree of joint degeneration, as well as pre-operative testing for allergies to the implant components to prevent the need for explantation

due to soft tissue inflammation. Also, post-operative follow-up should give more attention to functionality and quality of life, rather than only MMO and pain.

Using a patient-fitted implant in more straightforward cases decreases risk of damage to the alveolar and facial nerves by optimization of screw positioning and using a smaller approach during placement. In more complex cases, the need for secondary surgery can be prevented (e.g., by using an extended TJR), thus compensating for the initial higher cost of a patient-fitted implant.

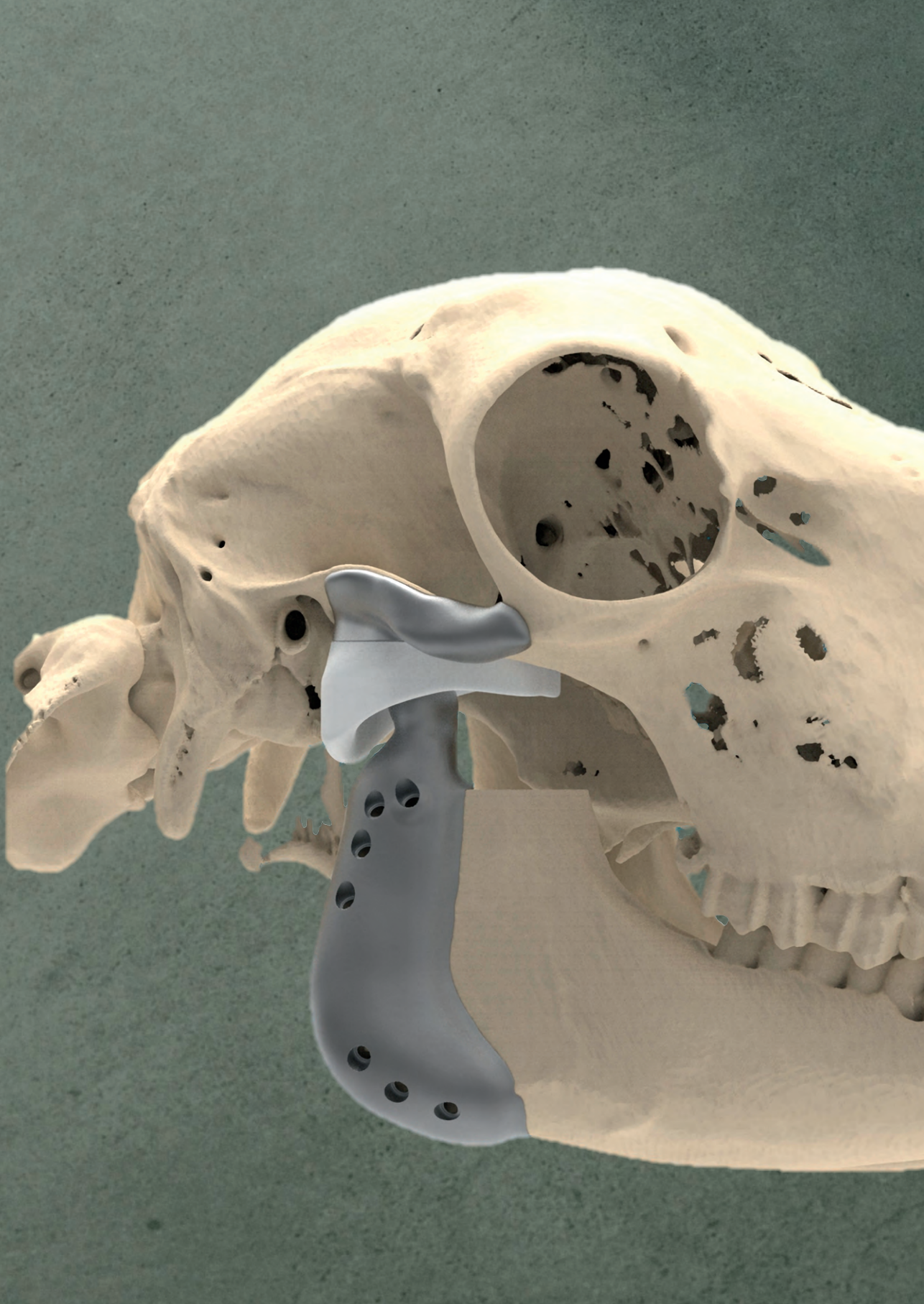
Lastly, while FDA-approved stock implants contain CoCrMo, to which 10% of the population is allergic, PSI can be completely manufactured out of Ti, significantly diminishing the risk of an allergic reaction and implant failure.

References

1. De Meurechy N, Mommaerts MY. Alloplastic temporomandibular joint replacement systems: a systematic review of their history. Int J Oral Maxillofac Surg. 2018 Feb;
2. De Meurechy N, Braem A, Mommaerts MY. Biomaterials in temporomandibular joint replacement: current status and future perspectives-a narrative review. Int J Oral Maxillofac Surg. 2017 Nov;
3. Giannakopoulos HE, Sinn DP, Quinn PD. Biomet microfixation temporomandibular joint replacement system: A 3-year follow-up study of patients treated during 1995 to 2005. J Oral Maxillofac Surg [Internet]. 2012;70(4):787–94. Available from: http://dx.doi.org/10.1016/j.joms.2011.09.031
4. Wolford LM, Pitta MC, Reiche-Fischel O, Franco PF. TMJ Concepts/Techmedica custom-made TMJ total joint prosthesis: 5-year follow-up study. Int J Oral Maxillofac Surg [Internet]. 2003;32(3):268–74. Available from: http://www.sciencedirect.com/science/article/pii/S0901502702903504
5. Mercuri LG. Alloplastic temporomandibular joint replacement: Rationale for the use of custom devices. Int J Oral Maxillofac Surg [Internet]. 2012;41(9):1033–40. Available from: http://dx.doi.org/10.1016/j.ijom.2012.05.032
6. Mercuri LG. Patient-Fitted (“ Custom”) Alloplastic Temporomandibular Joint Replacement Technique. Atlas Oral Maxillofac Surg Clin North Am [Internet]. 2011;19(2):233–42. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L362440617
7. Onoriobe U, Miloro M, Sukotjo C, Mercuri LG, Lotesto A, Eke R. How Many Temporomandibular Joint Total Joint Alloplastic Implants Will Be Placed in the United States in 2030 ? J Oral Maxillofac Surg [Internet]. 2016;74(8):1531–8. Available from: http://dx.doi.org/10.1016/j.joms.2016.04.011
8. Johnson NR, Roberts MJ, Doi SA, Batstone MD. Total temporomandibular joint replacement prostheses: a systematic review and bias-adjusted meta-analysis. Int J Oral Maxillofac Surg [Internet]. 2016;46(1):1–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0901502716302132
9. Zou L, He D, Ellis E. A Comparison of Clinical Follow-Up of Different Total Temporomandibular Joint Replacement Prostheses: A Systematic Review and Meta-Analysis. J Oral Maxillofac Surg [Internet]. 2018;76(2):294–303. Available from: https://doi.org/10.1016/j.joms.2017.08.022
10. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ J Surg. 2003 Sep;73(9):712–6.
11. Mercuri LG, Wolford LM, Giobbie-hurder A. Long-Term Follow-Up of the CAD / CAM Patient Fitted Total Temporomandibular Joint Reconstruction System. 2002;1440–8.
12. Mercuri LG, Edibam NR, Giobbie-Hurder A. Fourteen-year follow-up of a patient-fitted total temporomandibular joint reconstruction system. J Oral Maxillofac Surg. 2007 Jun;65(6):1140–8.
13. Mercuri LG, Wolford LM, Sanders B, White RD, Hurder A, Henderson W. Custom CAD/CAM total temporomandibular joint reconstruction system. Preliminary multicenter report. J Oral Maxillofac Surg. 1995;53(2):106–15.
14. Gruber EA, McCullough J, Sidebottom AJ. Medium-term outcomes and complications after total replacement of the temporomandibular joint. Prospective outcome analysis after 3 and 5 years. Br J Oral Maxillofac Surg [Internet]. 2015 May;53(5):412–5. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L603254794
15. Sidebottom AJ, Gruber E. One-year prospective outcome analysis and complications following total replacement of the temporomandibular joint with the TMJ Concepts system. Br J Oral Maxillofac Surg [Internet]. 2013 Oct;51(7):620–4. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L369792272

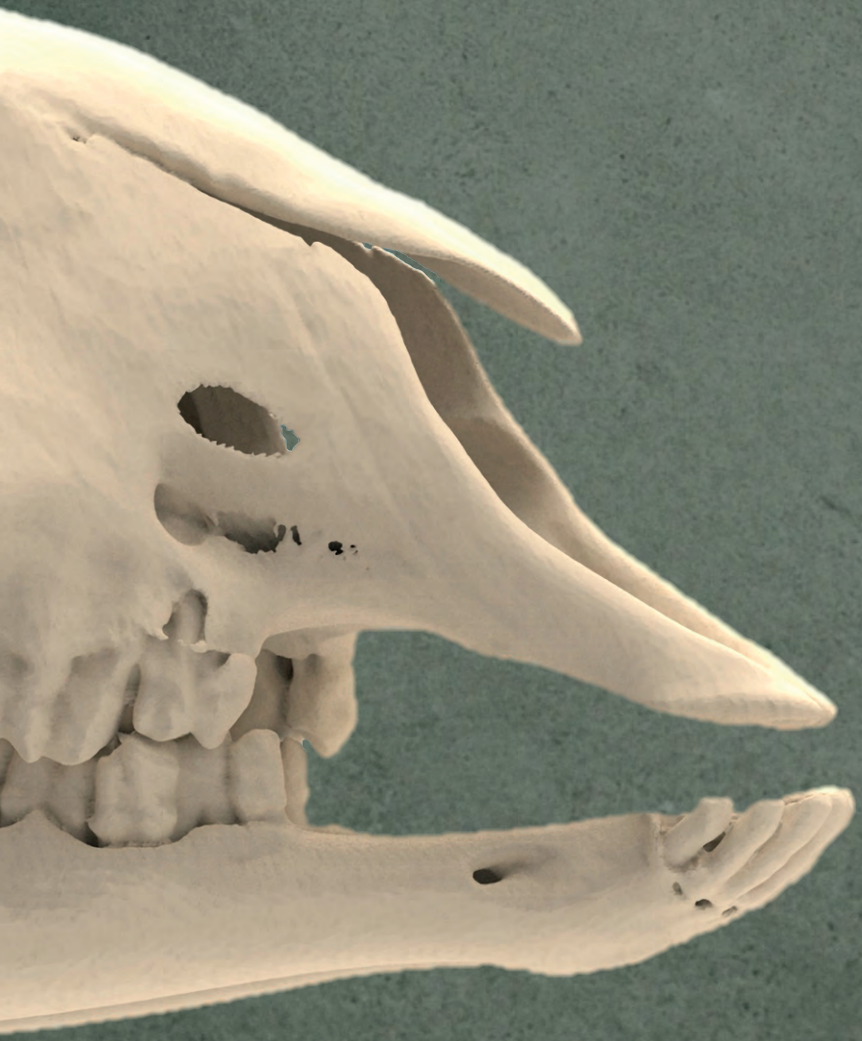
16. Gonzalez-Perez LM, Fakih-Gomez N, Gonzalez-Perez-Somarriba B, Centeno G, Montes-Carmona JF. Two-year prospective study of outcomes following total temporomandibular joint replacement. Int J Oral Maxillofac Surg [Internet]. 2016;45(1):78–84. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L606041533
17. Gonzalez-Perez LM, Gonzalez-Perez-Somarriba B, Centeno G, Vallellano C, Montes-Carmona JF. Evaluation of total alloplastic temporo-mandibular joint replacement with two different types of prostheses: A three-year prospective study. Med Oral Patol Oral Cir Bucal. 2016;21(6):e766–75.
18. Higgins J, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. Version 5. Chichester, West Sussex ; Hoboken NJ : John Wiley & Sons, [2008] ©2008; 2011. Available from: http://handbook.cochrane.org
19. Westermark A. Total reconstruction of the temporomandibular joint. Up to 8 years of follow-up of patients treated with Biomet (R) total joint prostheses. Int J Oral Maxillofac Surg. 2010;39(10):951–5.
20. LoboLeandro LF, Ono HY, de Souza Loureiro CC, Marinho K, Garcia Guevara HA. A ten-year experience and follow-up of three hundred patients fitted with the Biomet/Lorenz Microfixation TMJ replacement system. Int J Oral Maxillofac Surg [Internet]. 2013;42(8):1007–13. Available from: http://dx.doi.org/10.1016/j.ijom.2013.04.018
21. Dimitroulis G. Comparison of the outcomes of three surgical treatments for end-stage temporomandibular joint disease. Int J Oral Maxillofac Surg. 2014 Aug;43(8):980–9.
22. Aagaard E, Thygesen T. A prospective, single-center study on patient outcomes following temporomandibular joint replacement using a custom-made biomet TMJ prosthesis. J Oral Maxillofac Surg [Internet]. 2014 Oct;69(9):e-46. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L53200004
23. Mercuri LG, Ali FA, Woolson R. Outcomes of total alloplastic replacement with periarticular autogenous fat grafting for management of reankylosis of the temporomandibular joint. J Oral Maxillofac Surg. 2008 Sep;66(9):1794–803.
24. Kanatas AN, Needs C, Smith AB, Moran A, Jenkins G, Worrall SF. Short-term outcomes using the Christensen patient-specific temporomandibular joint implant system: A prospective study. Br J Oral Maxillofac Surg [Internet]. 2011 Mar;50(2):149–53. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L51345875
25. Machon V, Hirjak D, Beno M, Foltan R. Total alloplastic temporomandibular joint replacement: the Czech-Slovak initial experience. Int J Oral Maxillofac Surg. 2012 Apr;41(4):514–7.
26. Sidebottom AJ. Guidelines for the replacement of temporomandibular joints in the United Kingdom. Br J Oral Maxillofac Surg. 2008;46(2):146–7.
27. NICE. National Institute for Health and Care Excellence Scope. Natl Inst Heal Care Excell [Internet]. 2014;(May):1–9. Available from: https://www.nice.org.uk/guidance/gid-cgwave0704/resources/multimorbidity-final-scope2
28. Sawhney CP. Bony ankylosis of the temporomandibular joint: follow-up of 70 patients treated with arthroplasty and acrylic spacer interposition. Plast Reconstr Surg. 1986 Jan;77(1):29–40.
29. Durr ED, Turlington EG, Foote RL. Radiation treatment of heterotopic bone formation in the temporomandibular joint articulation. Int J Radiat Oncol Biol Phys. 1993 Nov;27(4):863–9.
30. Wilkes C. Internal derangements of the temporomandibular joint: pathological variations. Arch Otolaryngol Neck Surg [Internet]. 1989 Apr 1;115(4):469–77. Available from: http://dx.doi.org/10.1001/archotol.1989.01860280067019
31. Helkimo M. Studies on function and dysfunction of the masticatory system. II. Index for anamnestic and clinical dysfunction and occlusal state. Sven Tandlak Tidskr. 1974 Mar;67(2):101–21.
32. Guarda-Nardini L, Manfredini D, Ferronato G. Total temporomandibular joint replacement: a clinical case with a proposal for post-surgical rehabilitation. J Craniomaxillofac Surg. 2008 Oct;36(7):403–9.
33. Saeed NR, Hensher R, McLeod NMH, Kent JN. Reconstruction of the temporomandibular joint autogenous compared with alloplastic. Br J Oral Maxillofac Surg. 2002;40(4):296–9.

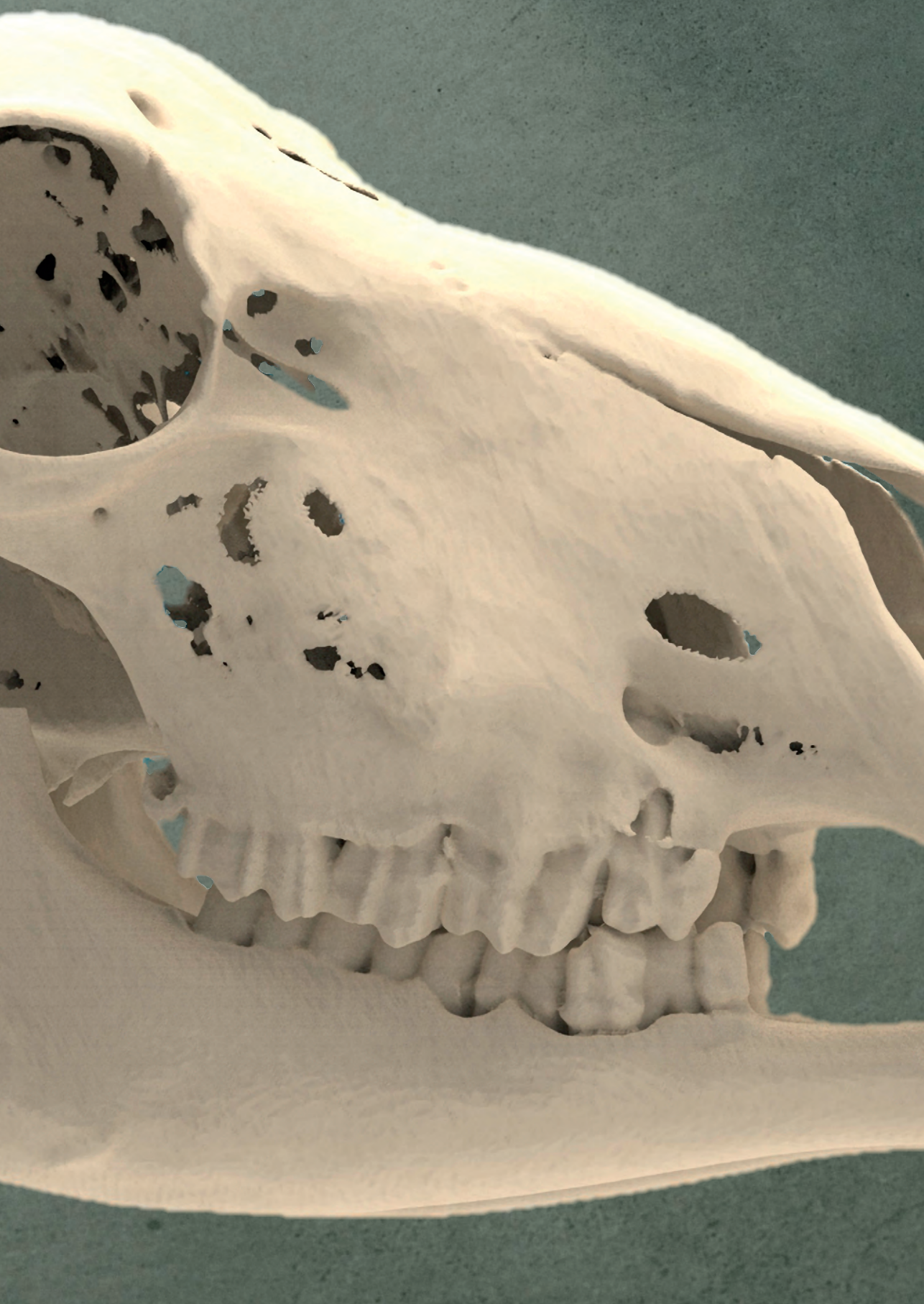
34. Elledge R, Attard A, Green J, Lowe D, Rogers SN, Sidebottom AJ, et al. UK temporomandibular joint replacement database: a report on one-year outcomes. Br J Oral Maxillofac Surg. 2017;55(9):927–31.
35. Garrett WR, Abbey PA, Christensen R. Temporomandibular joint reconstruction with a custom total temporomandibular joint prosthesis: use in the multiply operated patient. Surg Technol Int. 1997;6:347–54.
36. Henry CH, Wolford LM. Treatment outcomes for temporomandibular joint reconstruction after Proplast-Teflon implant failure. J Oral Maxillofac Surg. 1993 Apr;51(4):352–60.
37. Zhao J, Zou L, He D, Ellis E. Comparison of bone adaptation after modi fi cation in biomet standard alloplastic temporomandibular joint prostheses. J Cranio-Maxillofacial Surg [Internet]. 2018;46(10):1707–11. Available from: https://doi.org/10.1016/j.jcms.2018.07.024
38. Abramowicz S, Barbick M, Rose SP, Dolwick MF. Adaptability of stock TMJ prosthesis to joints that were previously treated with custom joint prosthesis. Int J Oral Maxillofac Surg [Internet]. 2012 Apr;41(4):518–20. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L51762392
39. Westermark A, Heden P, Aagaard E, Cornelius CP. The use of TMJ Concepts prostheses to reconstruct patients with major temporomandibular joint and mandibular defects. Int J Oral Maxillofac Surg. 2011;40(5):487–96.
40. Elledge R, Mercuri L, Speculand B. Extended total temporomandibular joint replacements: a classification system. Br J Oral Maxillofac Surg [Internet]. 2018;56(7):578–81. Available from: http://dx.doi.org/10.1016/j.bjoms.2018.06.002
41. Biglioli F, Colletti G. Mini-retromandibular approach to condylar fractures. J Craniomaxillofac Surg. 2008 Oct;36(7):378–83.
42. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. J Bone Joint Surg Am. 2001 Mar;83-A(3):428–36.
43. de Graaf NPJ, Feilzer AJ, Kleverlaan CJ, Bontkes H, Gibbs S, Rustemeyer T. A retrospective study on titanium sensitivity: Patch test materials and manifestations. Contact Dermatitis. 2018 May;
44. Mommaerts MY, Foster ME, Gundlach KKH. How to do clinical research in cranio-maxillo-facial surgery. J Craniomaxillofac Surg. 2012 Feb;40(2):97–102.



Part 2

Animal-model experiment





Chapter 5

Surface wear in a custom manufactured temporomandibular joint prosthesis

This chapter is based on:

Surface wear in a custom manufactured temporomandibular joint prosthesis

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Introduction

Since the first implantation of alloplastic material as a means to treat temporomandibular joint (TMJ) disease, many different prosthetic concepts have been developed, including a total joint replacement (TJR) with both condylar and fossa component. Although the indications for TMJ TJR remain limited, an increase in case numbers has been observed in recent years–including younger patients (1–3)–raising concerns about the lifespan of the used prostheses. A recent meta-analysis on total knee prostheses reported 95% and 92% survival of the implant at 15 and 20 years, respectively. They concluded that, when the patient is first treated at a young age, at least one replacement surgery in a patient's lifetime might be necessary.(4) This is of significant importance, as the expected lifespan of a TJR decrease is inversely correlated to the number of revision surgeries.(5) The rate at which wear appears, can be influenced by both material-related factors such as material choice, surface roughness, and the geometry of the articulating surfaces, as well as patient related factors such as the amount of force that is generated and the amount of activity and movement(6). Wear debris also can lead to foreign-body giant cell reactions, bone resorption, and aseptic implant loosening, contributing to long-term implant failure.(2,7–9)

Despite several TMJ systems being available on the market, there is a clear lack of both proper *in vivo* and *in vitro* wear analysis. (10,11) This lack of testing is a significant shortcoming, as mechanical properties and wear resistance play a pivotal role in determining the long term outcomes of TJR and, therefore, the need for revision or replacement surgery (2,7). As far as the authors are aware of, Van Loon et al.(12,13) are the only group to publish their *in vitro* TMJ TJR wear results, prior to commercial release of their prosthesis. They designed a wear testing machine, which simulated the articulation of the mandibular head against the UHMWPE disc, while the implant was submerged in bovine fetal calf serum, diluted with distilled water. The UHMWPE disc was weighed both before and after a 7 million cycle-run, which corresponds to ten years *in vivo* functioning, resulting in a wear rate of 0.65mm^3 per year or linear wear of less than 0.01mm/year (13). While they afterwards also conducted an *in vivo* sheep

experiment, reporting on histological findings of the peri-articular tissues, no evaluation of the amount of wear was reported on (12). Several more studies evaluated either the histological reaction of the peri-articular tissues or wear pattern in explanted TMJ TJR after, yet as far as we are aware of, this is the first study to report on TMJR wear results through an *in vivo* experiment (9,14).

While wear can be evaluated via either *in vitro* or *in vivo* testing, *in vivo* testing is preferred for TMJ replacements for at least three reasons. Firstly, there is evidence from hip joint prostheses that *in vivo* wear rates are much higher than those evaluated by *in vitro* testing, risking underestimation of the total wear rate (15). Secondly, the TMJ makes rotational and anteroposterior as well as mediolateral translative movements. Mimicking *in vivo* scenarios in an *in vitro* testing environment that captures the specific degrees of freedom in movement that occur during mastication would be extremely difficult. Thirdly, the amount of force to which the TMJ is subjected remains uncertain (14,16), which limits the ability to create a reliable *in vitro* experimental environment. When evaluating potential *in vivo* animal models, the primate TMJ is most similar to a human's, yet their daily mastication rate is rather low. In addition, several major ethical issues and cost of care prohibit the use of primates for this type of research. It is for said reason that several different animal models, such as the pig, goat and sheep model, have been investigated and proven to be reliable and relatable *in vivo* experimental models for TMJ investigations. While having both their advantages (the anatomically and biomechanical resemblance to the human TMJ) and limitations (the more outspoken laterotrusive movements) both the goat and sheep model are considered the 'gold standard' in large animals (17,18). Further, sheep spend on average 4 hours per day eating at a rate of 128 mastication cycles per minute and an average of 8 to 9 hours per day ruminating at a rate of 100 cycles per minute (19). Due to this high daily mastication rate, exceeding that of goats, the total duration of an *in vivo* evaluation of implant wear can be conducted over a shorter time frame than in humans or other species.

After developing a novel patient-specific additively manufactured (AM, also referred to as 3D-printed) titanium (Ti) alloy TMJ replacement

system, which aims to restore laterotrusive movement through reinsertion and integration of the lateral pterygoid muscle (LPM), a sheep model animal experiment was designed to further investigation (2,20–23). Whereas the proper implant integration and LPM insertion was previously evaluated (24), this paper aims to evaluate the *in vivo* wear rate in the condylar and fossa components. Furthermore, the difference in wear between the polished condylar head, coated with a HadSat' diamond-like carbon (H-DLC) layer, was investigated and compared to that of the non-coated condylar head. Also the amount of wear of the fossa composed of a machined Vitamin E-enriched and ɣ-irradiated ultra-high molecular weight polyethylene (UHMWPE) component articulating with either type of condylar surface was evaluated. The total evaluation period in the present study was 288 days, which is equivalent to 22 years of human masticatory function (25).

Materials and Methods

In vivo test subjects

This study was approved by the ethical committee at Medanex Clinic (license number LA 1210576 - code of approval EC MxCl 2018-090). Fourteen ewes (Swifter crossbreed) aged 2-5 years, with an average weight of 73.4 kg (range: 52-86 kg) and without any missing teeth were enrolled in the study. They were allowed to roam freely in the meadow until the operation.

First, a pilot surgery was performed on two sheep, consisting of a sham surgery with surgical TMJ approach, including opening of the joint capsule, but without condylectomy or prosthesis implantation in one sheep. The second sheep received a TMJ TJR to establish standard procedures before the following twelve sheep were operated.

During the first post-operative week, the sheep were kept in solitary confinement, after which they were put together in a larger indoor pen.

Implant manufacturing

Six weeks before surgery, each sheep was subjected to a computed tomography (CT) scan of the head. This data was provided to the engineers of CADskills BV (Ghent, Belgium) in DICOM format. Using the derived standard template library (STL) files, a virtual condylectomy was performed on the left side, from which a total joint prosthesis was designed using Geomagic Freeform Plus (3D Systems, Rock Hill, SC, USA). The overall design of the prosthesis was slightly enhanced for animal use after examining a 3D-printed plastic model of the first sheep's skull (Makerbot, MakerBot Industries, Brooklyn, NY, USA and Formlabs II, Formlabs, Somerville, MA, USA). However, the actual prosthetic design, including the number of screws and screw diameters, was devised to be similar to those used in humans. The specific course of the inferior alveolar nerve in the sheep was taken into account for screw length and position in the mandibular stump.

The ramal component was produced in a medical-grade Ti alloy (Ti6Al4V ELI grade 23) by AM, more specifically selective laser melting (SLM 125 HL, SLM Solutions Group AG, Lübeck, Germany). A scaffold structure (500 mm interconnected pores with a diamond unit cell structure) was provided both at the boney interface with the mandible as well as at the condylar neck to provide optimal conditions for boney union and enthesis reconstruction of LPM respectively. A narrow tunnel with a diameter of 2.4-2.5 mm, to accommodate a size 0 suture, was designed in the neck of the condyle (Fig.1). After printing, all condylar heads were first milled to achieve a 0.02mm accuracy to the 'design-STL', after which they are polished using a chalk-based polishing paste. Six of the 13 condylar heads were further treated with a H-DLC coating using the non-disclosed HadSat protocol, whereas the other seven condylar heads were left untreated after polishing. The identity of the supplier, as well as the means for applying the H-DLC-coating onto the condylar head surface are proprietary information. The surface roughness of one, non-implanted, coated condyle was determined using a confocal laser microscope (Ra = 0.09 µm , Rt = 0.53 µm) to serve as a comparison for the explanted condyles. Ti alloy screws (Ti6Al4V grade 5, 2.3 mm diameter; Surgi-Tec NV, Ghent, Belgium) were used for fixation of the ramal component.

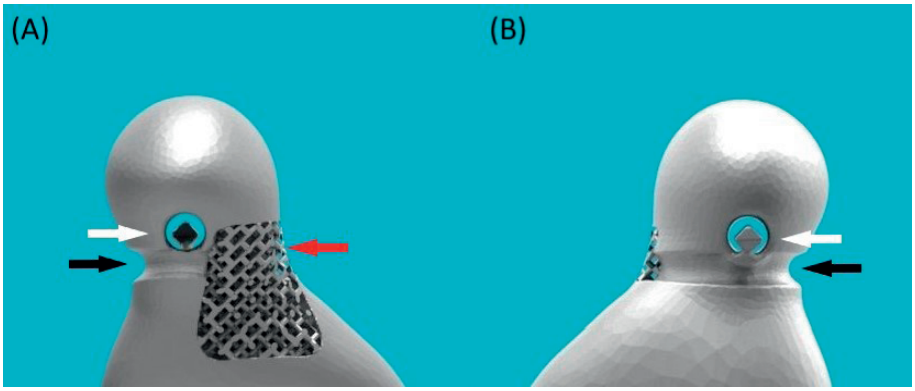


Fig. 1: Condylar head with suture threading tunnel and hook for fixation of the lateral pterygoid muscle enthesis. (A) Mesial side. Black arrow: subcondylar groove to guide enthesis' sutures. White arrow: 2.4 mm subcondylar tunnel and hook-like extension for fixation of the enthesis. Red arrow: lattice structure for enthesis' bony ingrowth. (B) Lateral side. Black arrow: subcondylar groove to guide enthesis' sutures. White arrow: 2.4 mm subcondylar tunnel and hook-like extension for fixation of the enthesis

The fossa component (Fig. 2) consisted of an AM Ti6Al4V part (procedure as described above), which fits on the glenoid fossa and articular eminence, as well as a computer numerical controlled (CNC) milled Vitamin E-enriched UHMWPE part facing the artificial condyle. Details concerning the grade and manufacturing of the UHMWPE are proprietary information. Both parts were joined together by hot pressing a Ti6Al4V scaffold structure onto the UHMWPE.

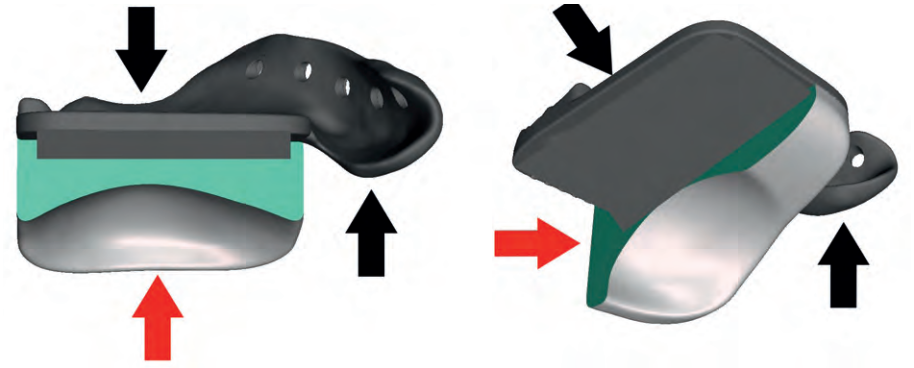


Fig. 2: Fossa component with sagittal and transversal sectional view. The titanium mesh connecting the UHWMPE to the titanium component has been removed for proprietary reasons.
(A) Frontal view. Black arrow: titanium component. Red arrow: UHMWPE component.
(B) Inferior view. Black arrow: titanium component. Red arrow: UHMWPE component

The fossa component was ɣ-irradiated (100 kGy, Gammatom s.r.l. Como, Italy) to increase the number of crosslinks in the UHMWPE and for sterilization purposes. Ti alloy screws (Ti6Al4V grade 5, 2.0-mm diameter; Surgi-Tec NV) were used for fixation of the fossa component. Both the screws and condylar component were 40 minutes autoclaved in a 134° C - 5 minutes cycle.

Surgical protocol

The left side of the face was aseptically prepared after orotracheal intubation and antibiotics (Enrofloxacin 5 mg/kg (Floxadil, EMDOKA BVBA, Hoogstraten, Belgium)) were administered at the start of surgery, up until 5 days post-operatively. The joint was accessed through both an incision over the posterior lower border of the mandible and a pre-auricular S-shaped incision inferior to the zygomatic arch. Once proper access was obtained, a patient/prosthesis specific Ti alloy (Ti6Al4V ELI, grade 23, CADskills BV, Ghent, Belgium) cutting guide was fixed onto the vertical ramus and a condylectomy with preservation of the LPM insertion was performed. This LPM insertion was isolated and a PDS 0 suture (Ethicon, Somerville, NJ, USA) was threaded through the tendon of the LPM. After fitting a dummy version of the fossa component and adapting the soft tissues if needed, the fossa component was fixed to the zygomatic arch with five screws between 5 and 13 mm in length. Next, the PDS suture was run through the condylar tunnel and the ramal component was positioned and fixated onto the mandibular stump using seven screws between 13 and 17 mm in length. Important to remark were the difficulties faced to properly attach the LPM onto the scaffold, due to an obstructive edge at the anteromedial side of the UHMWPE part of the fossa component. Consequently, all UHMWPE parts were scalpel-reduced at their non-articulating anteromedial side. A multi-layer closure was then performed, after which a compressive bandage was applied. A more detailed description of the surgery protocol can be found in one of our earlier published papers (24).

Euthanasia and implant retrieval

Ten months after surgery, after being kept in an indoor pen, all 14 sheep were euthanized. All sheep were then decapitated and the left half of the

skull was retained. The rest of the sheep was disposed of. Next, the left side of the skull was skinned, and the neurocranium, left eye, and anterior maxillary and mandibular halves were removed. After three months of immersion in formalin 4%, the peri-articular tissues were resected for histological evaluation. The condyle was transected at the condylar neck by means of an Exakt 300 diamond band saw (EXAKT Technologies, Inc., Oklahoma, USA) at Morphisto Gmbh (Frankfurt, Germany). The fossa component was first clinically evaluated for its bony integration (e.g. if any macro-motions were seen or if a fibrous layer had formed between the implant and the bone) after which the screws were removed and the fossa was removed from the skull.

With respect to the fossa, both linear and volumetric wear analysis of the articulating UHMWPE surface was performed by means of optical scanning. Linear wear, expressed in mm/year, is used in orthopedic surgery to determine the lifecycle of an implant. However, as it does not determine the total amount of UHWMPE volume that is lost, the volumetric wear, reported as mm^3 per year, was evaluated as well. This is of importance, as it evaluates the total amount of debris that is formed and does not just evaluate the deepest point of material loss on the bearing surface.

To determine the amount of linear wear, first a 3D scanner applying blue-light technology (ATOS CORE 135, GOM GmbH, Braunschweig, Germany) was used. The scanner was first calibrated according to the company prescribed calibration procedure, using a type CP40/170 calibration plate. This glass plate has circular markers with several markers having a larger diameter compared to the rest of the markers. These larger markers define the coordinate origin of the panel coordinate system. The 3D coordinates of the central points of each circular marker are measured, as well as distances between certain defined markers. This calibration process was performed and certified by a GOM-employed specialist, resulting in a 13µm accuracy. However, because this 3D scanner does not allow for evaluation beyond a depth of 1 mm, the linear wear of these samples was recalculated and confirmed using a LC60Dx laser line scanner (LLS) (Nikon Metrology NV, Leuven, Belgium) mounted onto an MC16 Coordinate Measuring Machine (CMM) (Coord3 S.r.l., Bruzolo, Italy)

through an indexable PH10M rotary head (Renishaw Benelux B.V., Breda, Netherlands). This LLS system was also used to assess the volumetric wear of the UHMWPE fossa part. To this end, Focus Inspection version 9.4 (Nikon Metrology NV) was used to create an STL file of the point cloud generated through scanning the fossa with the LLS.

Prior to scanning the fossa, all of the 21 kinematic error sources (the axes' translational, rotational and squareness error components) of the MC16 CMM were calibrated, to identify and compensate for any geometrical errors. This calibration was performed by a manufacturer technician, following a standardized method, reaching a micron level of precision for each individual axis. Furthermore, as to eliminate any environmental changes, all measurements were performed in a climate and humidity controlled room with air pressure monitoring. Lastly, prior to performing the CMM, qualification of the combined system of CMM and LLS was performed. This was done by use of a reference sphere, which was measured from all orientations used within the scanning sequence. The margin of error of this entire measurement technique is estimated to range from 0.01 mm to 0.1 mm. This generated STL was then overlapped with the STL of the design of the fossa component by means of a 'best fit' iterative closest-point algorithm using GOM Inspect (GOM GmbH). This method does not allow for closed loop information, as would be the case when reference points were marked before implantation ensuring a 100% fit. Instead up to hundreds of matching points are calculated by the program's algorithm, in order to provide a reliable and reproduceable overlap. For cooperative surfaces, this technique results in the same accuracy and error margin as provided by the scanner.

The 'explanted-STL' was then subtracted from the 'design-STL' to quantify the volume lost due to wear. Next, the articulating areas of the UHWMPE were isolated and evaluated rather than the entire UHMWPE fossa part. This was done to prevent overestimation of the wear volume, due to the scalpel reduction that was performed during implantation. Wear volume was calculated using VGSTUDIO MAX Version 3.3.2 (Volume Graphics GmbH, Heidelberg, Germany).

The linear and volumetric UHMWPE wear of one fossa could not be analyzed because the software was not able to retrieve a 'best fit' between the design and the scan of the explanted fossa. The error margin in the overlap between the two STL models was too large to provide reliable results due to the intraoperative trimming of UHMWPE in non-load-bearing regions, as well as the posterior UHMWPE ridge being erroneously trimmed down during the post-euthanasia implant retrieval as well as the titanium part for fixation onto the zygoma. (Fig. 3) While this does not affect the articulating surface, the difference between the 'design-STL' and 'explanted-STL' was too significant for the best-fit algorithm, thus resulting in non-cooperative surfaces. One additional fossa could not be analyzed for volumetric wear because the software was unable to provide a 'best fit' between both explanted fossa and their 'design-STL', within the margin of error. As a result, a reliable volumetric wear volume could not be determined.

Both the non-coated and coated Ti6Al4V condylar surfaces were evaluated using a 3D scanner (ATOS CORE 135, GOM GmbH, Braunschweig, Germany) to determine the linear wear of the condylar articulating surface, in similar fashion to the UHMWPE fossa part.

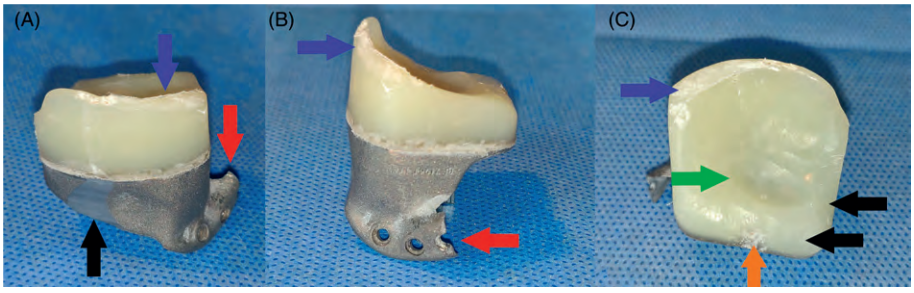


Fig. 3: Macroscopic images of explanted fossa components of sheep #4473, with additional damage, having occurred during the explantation. This severe additional damage, occurred during retrieval, no longer allowed for reliable overlapping with the 'design'-STL. No linear, or volumetric wear could be analyzed of this fossa.

(A) Posterior view. Blue arrow: damage to posterior UHMWPE ridge. Black arrow: damage to titanium part. Red arrow: damage to titanium extension for fixation onto the zygomatic arch.

(B) Lateral view. Blue arrow: damage to posterior UHMWPE ridge. Red arrow: damage to titanium extension for fixation onto the zygomatic arch.

(C) Inferior view. Blue arrow: damage to posterior UHMWPE ridge. Black arrow: scalpel-reduced non-articulating UHMWPE. Green arrow: worn out UHMWPE due to articulating with the condylar surface. Orange arrow: anteriorly worn out UHMWPE volume due to contact with the coronoid process

The surface roughness was determined by 3D non-contact profilometry using a confocal laser microscope (µSurf Explorer, NanoFocus AG, Oberhausen, Germany). For each sample, a 4.5 x 1.5 mm^2 worn area of the condylar surface was selected and polynomial filters were applied to remove form of the condyles. 3D surface roughness amplitude parameters (average roughness *Sa*, arithmetic mean of the absolute values of the surface departures from the mean plane, and root mean square height *Sq*, the root mean square value of the surface departures) were determined. In addition, a 2D profile was generated along the long direction of the scanned area (multiple profiles were extracted and averaged) and 2D surface roughness amplitude parameters were defined (average roughness *Ra*, the arithmetic average of the absolute values of the profile heights, and maximum height of the profile, *Rt*, the vertical distance between the highest and lowest points of the profile). One pristine (i.e. not implanted) coated condyle was assessed. It served as a reference for both the non-coated and coated condyles as the application of the DLC coating does not alter the surface smoothness. In addition, the surface of both types of condyles was also investigated using a light microscope (Vertex 251UC, Micro-Vu, Windsor, CA, USA) at magnifications of 19x, 37x, 204x, and 425x. Furthermore, the surfaces of the DLC-coated condyles were visualized using scanning electron microscopy (SEM, Nova NanoSEM 450, FEI Company, Hillsboro, OR, USA) operated at standard high-vacuum settings at 5 mm working distance and 10 keV accelerating voltage.

Results

Analysis of the UHMWPE fossa component

Macroscopically, all fossae exhibited UHMWPE wear in the center as well as in the middle of the anterior border, where the polyethylene came into contact with the coronoid process (Fig. 4 A and B). No macroscopically visible signs of UHMWPE delamination, warping, or fracturing were seen. There was some soft tissue adhesion on the medial and lateral side of the fossa, where the UHMWPE was pressed against the titanium, however upon closer inspection, this soft tissue adhesion remained strictly

superficial and no dehiscence between the two components was seen macroscopically, nor during probing and removal of the soft tissue.

3D scanning of the fossa surface, articulating either with an uncoated (Fig. 5A) or coated condyle (Fig. 5B) was conducted and in most samples the wear volume clearly corresponded with the form of the condyle, with the articulation taking place in the center of the fossa. However, in sheep # 5158 the center of the wear volume was located slightly more laterally, whereas the mediolateral direction was slightly more diagonal compared to the other samples (Fig. 5 B).

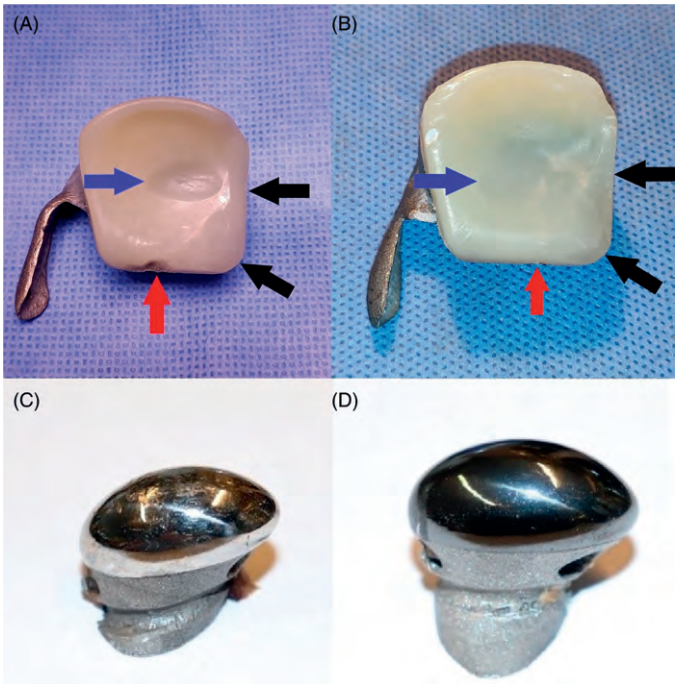


Fig. 4: Representative macroscopic images of explanted components of the custom temporomandibular joint total joint replacement after 9 months of mastication and rumination in a sheep model. (A) Ultra-high molecular weight polyethylene (UHMWPE) fossa of sheep #1724 that articulated with a non-coated condyle. Blue arrow: worn out UHMWPE due to articulating with the condylar surface. Black arrow: scalpel-reduced nonarticulating UHMWPE. Red arrow: anteriorly worn out UHMWPE volume due to contact with the coronoid process. (B) UHMWPE fossa of sheep #5158 that articulated with an HadSat® (H-DLC) diamond-like carbon coated condyle. Blue arrow: worn out UHMWPE due to articulating with the condylar surface. Black arrow: scalpel-reduced nonarticulating UHMWPE. Red arrow: anteriorly worn out UHMWPE volume due to contact with the coronoid process. (C) Non-coated Ti6Al4V condyle. (D) H-DLC coated condyle

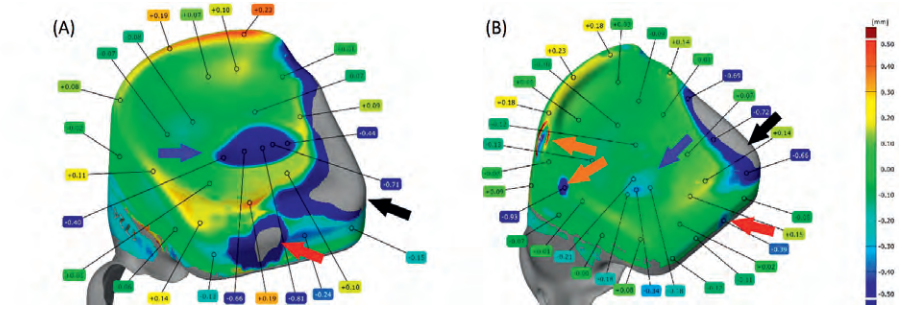


Fig. 5: Representative 3D scans of explanted components of the custom temporomandibular joint total joint replacement after 9 months of mastication and rumination in a sheep model. (A) Ultra-high molecular weight polyethylene (UHMWPE) fossa of sheep #1724 that articulated with a non-coated condyle. The maximal wear depth measures 0.81 mm. Blue arrow: worn out UHMWPE due to articulating with the condylar surface. Black arrow: scalpel-reduced non-articulating UHMWPE. Red arrow: anteriorly worn out UHMWPE volume due to contact with the coronoid process. (B) UHMWPE fossa of sheep #5158 that articulated with an HadSat diamond-like carbon coated condyle. The maximal wear depth measures 0.34 mm. Blue arrow: worn out UHMWPE due to articulating with the condylar surface. Black arrow: scalpel-reduced nonarticulating UHMWPE. Red arrow: anteriorly worn out UHMWPE volume due to contact with the coronoid process. Orange arrow: worn out sections due to post-mortem dissection of the overlaying soft tissues.

In 4 sheep, more apparent deviant wear patterns were found. (Fig. 6 A-D) The edges of the worn volume of ewe # 2177 were far less clearly marked compared to the other samples (Fig.6 A). The fossa in sheep #4246 not only showed this distinct wear volume in the center, but also a slight additional posteriorly orientated wear track (Fig. 6 B). The fossa of ewe # 8087 showed one main wear volume, which was also more diagonally orientated and additionally three more anteriorly positioned wear 'bodies' (Fig. 6 C). While no clear macroscopic signs of creep were seen, 3D surface analysis revealed some warping anteriorly of these additional wear bodies. Lastly, ewe # 7998 not only developed only little wear near the center of the fossa, but there also occurred wear near the posterior lateral border of the implant, as well as some warping, anteriorly from the center wear volume. (Fig. 6 D). Thus in both cases showing warping, this occurred in non-articulating locations.

While 3D scanning of the fossa surface seemed to indicate more extensive wear for UHMWPE components in contact with a non-coated Ti6Al4V condyle as compared to a coated condyle (Fig. 5 A and B), no significant

difference in the amount of linear, nor volumetric wear, was seen between both groups of fossa.

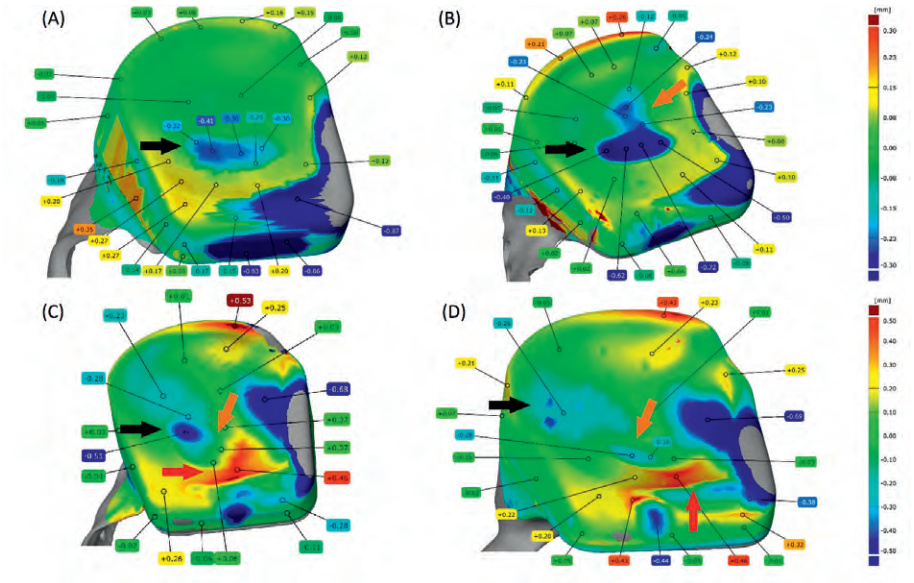


Fig. 6: 3D scans of explanted fossa component of the custom temporomandibular joint total joint replacement after 9 months of mastication and rumination in a sheep model with deviant wear patterns. (A) Ultra-high molecular weight polyethylene (UHMWPE) fossa of sheep #2177 that articulated with a non-coated condyle. Black arrow: worn out UHMWPE due to articulating with the condylar surface, with uneven edges. (B) UHMWPE fossa of sheep #4246 that articulated with an H-DLC coated condyle. Black arrow: main worn out UHMWPE volume due to articulating with the condylar surface. Orange arrow: posteriorly orientated UHMWPE wear track. (C) UHMWPE fossa of sheep #8087 that articulated with an H-DLC coated condyle. Black arrow: main worn out UHMWPE volume due to articulating with the condylar surface. Orange arrow: three additional condylar-shaped UHMWPE wear tracks. Red arrow: UHMWPE creep deformation, in non-articulating region. (D) UHMWPE fossa of sheep #7998 that articulated with a non-coated condyle. Black arrow: main worn out UHMWPE volume due to articulating with the condylar surface. Orange arrow: initial, centered, UHMWPE wear volume due to articulating with the condylar surface. Red arrow: UHMWPE creep deformation, in non-articulating region.

As already mentioned previously, due to not being able to determine the linear wear by means of 3D scanning for all the fossa, the amount of linear wear was determined by means of LLS. However, in one sample (ewe # 4473, Fig 4) no proper alignment of the explanted model and the STL file was possible and thus no (correct) measurement was possible. The average linear wear of the UHMWPE surface in contact with the non-coated condyle was 0.88 ± 0.41 mm, while for the UHMWPE surface in contact

with the coated condyle it was 0.67 ± 0.28 mm. The difference between these two groups was not statistically significant (p = 0.3765, t-test). When converted to human mastication habits, these values are equivalent to 0.04 ± 0.02 mm respectively 0.03 ± 0.01 mm per year (Tables 1-3).

An average volume loss of 45.85 ± 22.01mm³ could be observed for the UHMWPE articulated with the non-coated Ti6Al4V condyle surface as compared to 25.29 ± 11.43 mm³ when articulated with the coated condyles. The difference was not statistically significant (p = 0.1448; t-test). Based on these results, the amount of volumetric wear translates to 2.08 ± 1.00 resp. 1.15 ± 0.52 mm³/year of human mastication.

Table 1: Quantitative results of the damage analysis on explanted components of the custom TMJ TJR. For the UHMWPE fossa component, linear and volumetric wear were determined by 3D scanning and laser line scanning. For the Ti6Al4V condylar surface, surface roughness was assessed using 3D non-contact profilometry. Prostheses incorporating a non-coated Ti6Al4V condyle or a H-DLC-coated Ti6Al4V condyle are compared. Values represent mean ± standard deviation.

	Non-coated Ti6Al4V condyle	H-DLC-coated Ti6Al4V condyle
Linear wear of UHMWPE fossa		
Max wear (mm)	0.88 ± 0.41	0.67 ± 0.28
Maximal wear/year in sheep (mm/year)	1.11 ± 0.53	0.85 ± 0.35
Maximal wear/year in humans (mm/year)	0.04 ± 0.02	0.03 ± 0.01
Volumetric wear of UHMWPE fossa		
Total wear (mm³)	45.85 ± 22.01	25.29 ± 11.43
Wear/year in sheep (mm³/y)	58.17 ± 27.95	32.04 ± 14.49
Wear/year in humans (mm³/y)	2.08 ± 1.00	1.15 ± 0.52
Roughness of Ti6Al4V condyle		
Sa (µm)	2.40 ± 2.08 *	0.69 ± 0.07 *
Sq (µm)	3.47 ± 3.01 *	0.90 ± 0.08 *
Ra (µm)	0.28 ± 0.17 *	0.12 ± 0.04 *
Rt (µm)	1.91 ± 1.23 *	0.65 ± 0.27 *

Sa = average roughness, the arithmetic mean of the absolute values of the surface departures from the mean plane within the sampling area
Sq = root mean square height, the root mean square value of the surface departures within the sampling areaRa = average roughness, the arithmetic average of the absolute values of the heights of the assessed profiles
Rt = maximum height of the profile, the vertical distance between the highest and lowest points of the assessed profiles
* Statistically significant difference between coated and non-coated condyles

Analysis of the Ti6Al4V condylar component

Macroscopically, the non-coated condyles exhibited a significant amount of surface damage, ranging from superficial scratches to deep pits, whereas on the coated condyles no obvious damage could be observed (Fig. 4 C and D). This was again confirmed by 3D scans of the condylar surfaces where pits and scratches could be observed in the center of the non-coated condyles while the surface of the coated condyles appeared smooth. Microscopic investigation of the surface revealed multi-directional surface scratches on both types of condyles, yet the scratches appeared remarkably deeper and more densely concentrated on the non-coated Ti6Al4V condylar surfaces than on the H-DLC-coated surfaces (Fig. 7 B and C). For both types, the surface damage was limited to the load-bearing surface of the condyle. In comparison to the pristine condyle, similar multi-directional scratches were seen on the retrieved coated condyles, indicating that these scratches are due to the polishing protocol that is applied before coating the condyle (Fig. 7 A). The amount of surface marks found on the explanted non-coated condyles was markedly higher, indicating that some abrasion had occurred during usage. For a more detailed investigation of the coated surfaces, scanning electron microscopy (SEM) analysis was performed. This analysis confirmed that in five out of six condyles, multi-directional scratches were present without significant damage to the articular surface (Fig. 8 A and B). The condylar surface of ewe #2177 presented deeper marks, for which an additional surface topography analysis using MeX (Alicona Imaging GmbH, Raaba, Austria) was performed, revealing that the surface damage penetrated through the DLC coating (Fig. 8 C and D).

The surface roughness of the condylar bearing surface was analyzed using a confocal laser microscope. The 3D as well as 2D surface roughness amplitude parameters are presented in Table 1 and 4. Overall, these quantitative results indicate that the roughness for the non-coated Ti6Al4V condylar surface was higher than for the DLC-coated Ti6Al4V condylar surface and analysis showed a statistically significant difference between both the coated and non-coated average surface roughness for both *Sa* ($p = 0.0083$; Mann-Whitney U test) and *Ra* ($p = 0.0182$; Mann-Whitney U test).

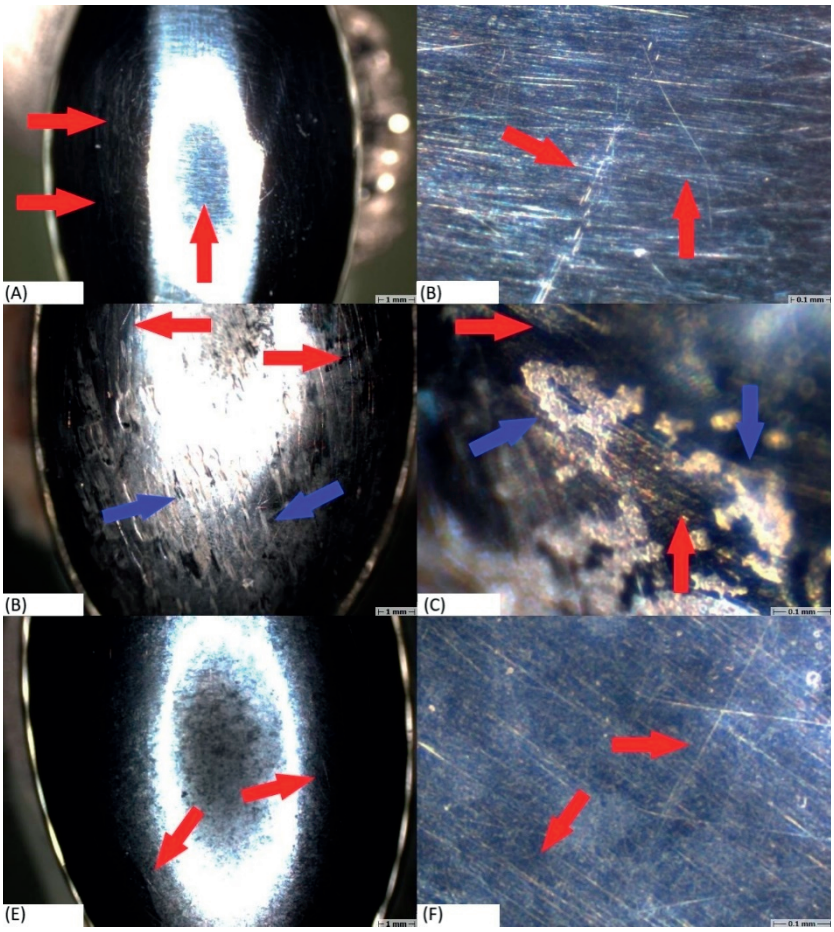


Fig. 7: Representative light microscopy images of the condylar surface of the custom temporomandibular joint total joint replacement. (A,B) Condylar surface of a pristine, non-coated condyle. Red arrow: superficial, multidirectional scratches. (C,D) Condylar surface of the non-coated condyle of sheep #8787, explanted after 9 months of mastication and rumination in a sheep model. Red arrow: superficial, multidirectional scratches. Blue arrow: deeper abrasive wear. (E,F) Condylar surface of the HadSat diamond-like carbon-coated Ti6Al4V condyle of sheep #5158, explanted after 9 months of mastication and rumination in a sheep model. Red arrow: superficial, multi-directional scratches.

Moreover, comparison with the pristine DLC-coated condyle demonstrates a similar surface roughness for DLC-coated surface before and after 22 months of implantation in the sheep model. These results are also supported by a qualitative assessment of the 3 types of condylar surfaces, with their representative 3D roughness profiles shown in Fig. 9.

Table 2: Amount of linear ultra-high molecular weight polyethylene wear

	Sample	Max wear (mm)	Maximal wear/ year (mm/year) (Sheep)	Maximal wear/ year (mm/year) (Human)
H-DLC-coated TMJR	3520	0.81 mm	1.03 mm / y	0.037 mm / y
	8087	0.51 mm	0.65 mm / y	0.023 mm / y
	2177	0.41 mm	0.52 mm / y	0.019 mm / y
	5158	0.34 mm	0.43 mm / y	0.014 mm / y
	2549	0.81 mm	1.03 mm / y	0.015 mm / y
	4249	1.15 mm	1.46 mm / y	0.052mm / y
Non-coated TMJR	0032	0.64 mm	0.81 mm / y	0.029 mm / y
	7998	0.28 mm	0.35 mm / y	0.013 mm / y
	4246	0.72 mm	0.91 mm / y	0.033 mm / y
	1724	0.81 mm	1.03 mm / y	0.036 mm / y
	8787	1.35 mm	1.71 mm / y	0.061 mm / y
	4248	1.48 mm	1.88 mm / y	0.067 mm / y
	4473	>1 mm	> 1.27 mm / y	> 0.045 mm / y

For sample 4473, the error margin in the overlap between the two STL models was too large for the 'best fit' iterative closest-point algorithm to provide reliable results. Based on the 3D scanner analysis, the linear wear was found exceed one millimeter, yet no specific result was determined.

Abbreviation: TMJR: Temporomandibular joint replacement

Discussion

The present study evaluated a novel model of TMJ TJR in a sheep model and set out to identify the wear patterns of both the condylar and fossa components of the prosthetic device implanted over a period of 288 days. This theoretically equals an estimated lifespan of 22 years in human implantation, based on the number of mastication movements.

While being an *in vivo* experiment, we were not constricted to the use of *in vivo* wear evaluation techniques such as the radiostereometric analysis introduced by Selvik et al. (26) as the sheep were sacrificed and the TMJR were explanted. Thus optical scanning was used to determine linear UHMWPE wear, while CMM laser scanning was used to determine volumetric UHMWPE wear and reconfirm the results on linear wear. The articulating Ti condylar surface was analyzed as well, by means of scanning electron and confocal laser microscopy surface.

UHMWPE wear analysis

Linear wear, expressed in mm/year, is used in orthopedic surgery to determine the lifecycle of an implant. It does not however determine the total amount of UHWMPE volume that is lost. This is of importance as, along with particle size and shape, the wear volume is a significant determinant for the occurrence of periprosthetic osteolysis (8). Dumbleton et al. (27) concluded that the risk of osteolysis occuring is rare as long as the total amount of linear wear remains under 0.1 mm/year. Similar findings were reported by Oparaugo et al. (28), who found that the risk of osteolysis was rare if the total amount of wear was limited to 80 mm^3 per year.

Both the coated and non-coated TMJR systems exhibited linear wear equivalent to less than 0.1 mm and volumetric wear equivalent of far less than 80 mm^3 per year of human functioning (Tables 1-3). In comparison to the average linear wear of 0.08 to 0.2mm per year and 48-155mm^3 volumetric wear per year in total hip implants and 0.05 to 0.23mm linear wear per year for a total knee implant, our results can be considered excellent (29). Important to notice is that, while upon inspection, there was a qualitative difference observed between the fossa articulating with either a coated or non-coated condyle, no statistically significant difference was observed between these samples. A Shapiro-Wilk test confirmed the Gaussian distribution of both the linear and volumetric wear data, supporting the use of a *t-test*, yet *post hoc* power calculations indicated that this study would have needed 15 sheep per group to achieve adequate power to detect a significant difference between these two groups of fossa. While the sample size of this study was chosen to minimize the number of animals subjected to the invasive procedures required for this study it is highly likely that the non-statistical difference that was found was due to the small group sizes.

Secondly, a displacement of the fossa was found in several ewes. While a 3-month post-operative CT scan revealed a good positioning of the fossa in ewe #7998, during the post-mortem CT scan and dissection a significant caudodorsal displacement of the fossa was seen. This was also reflected by the wear pattern that was found through 3D scanning

of the fossa component. Also, sheep #5158 showed a normal positioning of the TMJR at three months after surgery, yet a limited latero-inferior displacement of the fossa was found during the post-operative dissection. A similar displacement was found in sheep #2177 at both the 6-month post-operative CT scan that was made as an exception, for a study analyzing the LPM insertion to the TMJR, as well as during explantation. However, as the displacement of the fossa was rather limited, this only led to a slightly more laterally positioned wear volume in case of ewe #5158 and the edges of the wear volume were less sharply marked in case of sheep #2177 (Fig. 6). In addition to these three displaced fossa, also the fossa of ewe #4246 showed a deviant wear pattern, with a slight latero-medial extension of the wear track. This could potentially be caused due to laterotrusive movements of the contralateral joint, with the implanted side functioning as stabilizing joint.

Table 3: Amount of volumetric ultra-high molecular weight polyethylene wear

	Sample	Total volumetric wear (mm^3)	Volumetric wear/ year (mm^3/y) (Sheep)	Volumetric wear/ year (mm^3/y) (Human)
H-DLC-coated TMJR	4249	42.70 mm^3	54.12 mm^3 / y	1.94 mm^3 / y
	2177	16.45 mm^3	20.85 mm^3 / y	0.75 mm^3 / y
	3520	31.79 mm^3	40.29 mm^3 / y	1.45 mm^3 / y
	2549	32.92 mm^3	41.7 mm^3 / y	1.5 mm^3 / y
	5185	9.18 mm^3	11.63 mm^3 / y	0.42 mm^3 / y
	8087	18.68 mm^3	23.67 mm^3 / y	0.85 mm^3 / y
Non-coated TMJR	1724	32.61 mm^3	41.33 mm^3 / y	1.48 mm^3 / y
	4246	27.77 mm^3	35.19 mm^3 / y	1.26 mm^3 / y
	8787	59.45 mm^3	75.34 mm^3 / y	2.7 mm^3 / y
	0032	26.47mm^3	33.84 mm^3 / y	1.20 mm^3 / y
	4248	82.96 mm^3	105.15 mm^3 / y	3.77 mm^3 / y
	7998	-	-	-
	4473	-	-	-

For both sample 7998 and 4473, the error margin in the overlap between the two STL models was too large for the 'best fit' iterative closest-point algorithm to provide reliable results.

Abbreviation: TMJR: Temporomandibular joint replacement

The displacement of these three fossa was most likely due to the use of 2mm diameter screws for the fixation of the fossa component, as is done

in human TMJ TJR. Keeping the higher mastication rate and laterotrusive movement in mind, the force the fossa is subjected to is higher compared to that in humans. This might have led to excessive stress in the bone surrounding the screws, resulting in bone resorption and micromovements between the fossa and the underlying bone, causing aseptic loosening of the implant component (30–32). In order to ascertain the effect of the altered wear patterns and volumes, the results of either only sheep # 7998 or all 3 sheep were removed from the results and a renewed statistical evaluation was made. However the difference in linear and volumetric wear between both groups remained non-significant, and in both cases the human equivalent for the measured linear and volumetric wear remained well within the acceptable range. Despite the deviant wear pattern for the fourth fossa, we kept these results included, as there was no displacement that occurred.

Condylar wear analysis

In knee and hip arthroplasty, there is an industry standard for surface smoothness (American Society for Testing and Materials F 2083-12, American Society for Testing and Materials F 2033-12), which does not exist for TMJ replacements. This is of importance because earlier studies have proven that a high surface roughness (Ra 0.2–0.63 μm) will also increase the amount of wear that can occur in the opposing articular surface (33–35) and can lead to the formation of larger wear particles, which can cause third body wear. (14,36).

In this study, the industry standard for total knee prostheses was applied to the TMJ implant surfaces. These surfaces were polished to obtain a *Ra* below 0.1 μm, which was confirmed by the surface roughness parameters determined here for DLC-coated condyle prior to implantation (*Ra* =0.09). The non-coated implants exhibited a significant increase in wear after implantation, resulting in an *Ra* (0.28 ± 0.17) well above the orthopedic industry standard. The *Ra* of the DLC-coated condyles (0.12 ± 0.04) however, remained well within the industry standard (Tables 1 and 4). Furthermore, the difference in both *Sa* and *Ra* was found to be significant by means of Mann-Whitney *U* test, as a non-Gaussian distribution was found for the non-coated condyles.

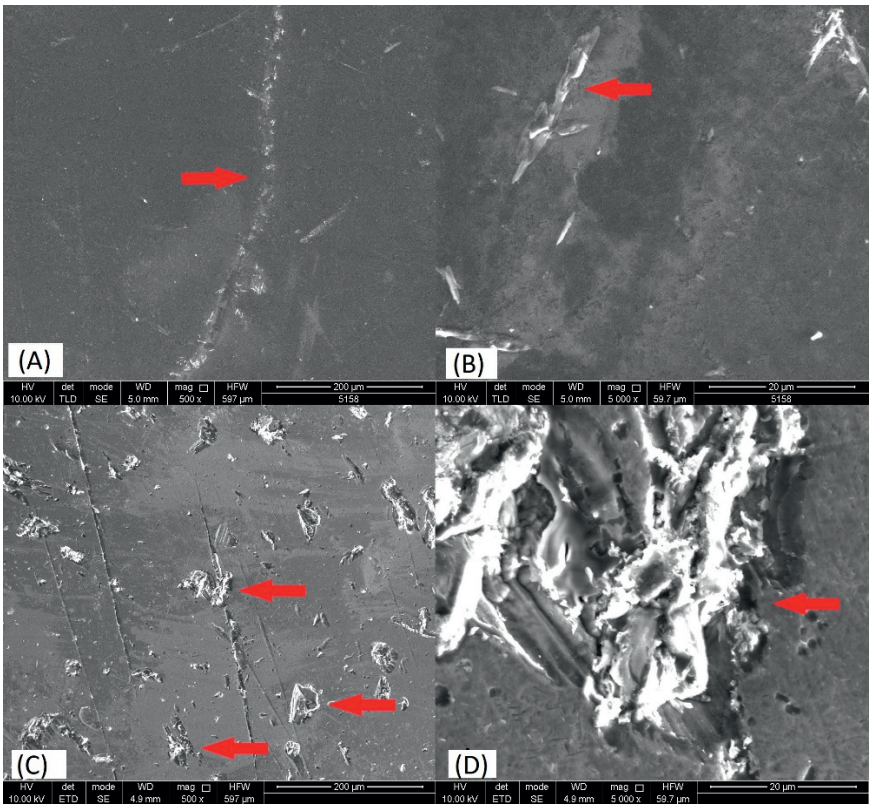


Fig. 8: Scanning electron microscopy images of the coated condylar surfaces after explantation. A: Sheep #5158 Intact, smooth, condylar surface without significant damage (Magnification 500x) Red arrow: Superficial scratch with intact coating B: Sheep #5158 Intact, smooth, condylar surface without significant damage (Magnification 5000x) Red arrow: Superficial scratch with intact coating C: Sheep #2177 Damaged condylar surface (Magnification 500x) Red arrow: Deep abrasive wear, penetrating the condylar coating

D: Sheep #2177 Damaged condylar surface (Magnification 5000x) Red arrow: Deep abrasive scratches penetrating the condylar coating

This non-Gaussian distribution was due to the high *Ra* and *Sa* (6.59) that were measured for the condylar surface of ewe #8787. Despite the fossa being in its proper position, as well as the mandibular component, and although upon explantation no macroscopically visible third bodies were found inside the joint, the wear pattern on the condyle indicates third body abrasive wear occurred with the surface damage being mediolateral oriented. This is confirmational to the expected mastication pattern, as sheep mainly perform laterotrusive movements. Due to this increased surface roughness, a high amount of linear (1.35 mm) and volumetric wear

(59.45 mm³) was found in the fossa as well, supporting our statement for the importance of a low *Ra* and *Sa* in order to limit surface wear (14,36). In order to evaluate the effect of this finding, a new Shapiro-Wilk test without this sample was performed, finding a Gaussian distribution for the other samples. However, a significant difference in both the *Sa* (p = 0.0692) and *Ra* (p= 0.0565) was still found when using an unpaired two sample *t*-test, indicating a significant increase in *Sa* and *Ra* in the uncoated condyles, compared to the coated condylar surface.

Table 4: Condylar surface roughness analysis

Sample	***Sa* (µm)**	Sq (µm)	***Ra* (µm)**	Rt (µm)
2177	0.77	0.98	0.16	0.78
2549	0.61	0.81	0.10	0.81
3520	0.64	0.83	0.10	0.59
4249	0.70	0.91	0.10	0.69
5158	0.64	0.83	0.07	0.09
8087	0.78	1.02	0.18	0.91
Non-implanted DLC	0.58	0.76	0.09	0.53
1724	2.30	3.38	0.20	1.52
4246	1.27	1.81	0.20	1.22
8787	6.91	10.1	0.63	4.65
0032	0.72	0.91	0.14	0.66
4248	1.05	1.80	0.26	2.01
7998	0.86	1.27	0.12	1.03
4473	3.72	5.05	0.44	2.31

Sa = average roughness, the arithmetic mean of the absolute values of the surface departures from the mean plane within the sampling area.
Sq = root mean square height, the root mean square value of the surface departures within the sampling area.iles.
Ra = average roughness, the arithmetic average of the absolute values of the heights of the assessed profiles.
Rt = maximum height of the profile, the vertical distance between the highest and lowest points of the assessed profiles.

Ti surface modification

Our in vivo results were also in line with several in vitro experiments, evaluating the amount of wear between DLC-coated Ti as compared to non-coated Ti articulating with UHMWPE, finding a decreased amount of wear in the former group (37–39). While these findings highlight the importance of Ti surface modification in load-bearing surfaces, potential disadvantages have to be evaluated as well. A significant potential

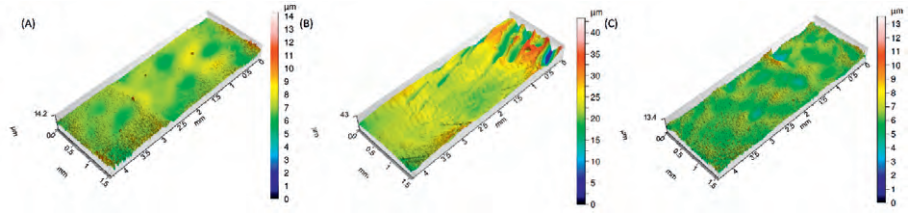


Fig. 9: Representative 3D roughness profiles of the condylar surface of the custom TMJ TJR.

A: Condylar surface of pristine, non-implanted, coated condyle.

B: Condylar surface of a non-coated condyle of sheep #1724, explanted after 9 months of mastication and rumination in a sheep model.

C: Condylar surface of a H-DLC coated condyle of sheep #5185, explanted after 9 months of mastication and rumination in a sheep model

disadvantage to the use of a DLC coating is the relatively poor adhesion between the DLC layer and the Ti surface (37,40–43). This can lead to plastic deformation of the softer Ti when the implant is subjected to high forces. This in turn can lead to chipping or delamination of the DLC coating (38,41,43), which may result in a significant increase in *Ra* and subsequent wear. Other surface modification techniques, such as titanium nitride (TiN) coatings, also have this limitation, as delamination and third body wear can occur after physical vapor deposition (PVD) of the TiN coating (14,44,45). Several techniques have been developed to overcome this problem. One technique involves the use of a gradient coating in which the carbon concentration increases towards the surface. Another technique is to use plasma nitriding on the Ti first, and then apply the DLC coating through magnetron sputtering (37,41). In this study, this limitation was addressed by using the patented HadSat-coating; no delamination was observed on the surfaces of any of the coated condyles.

Limitations

In total hip prostheses, the unworn volume of the acetabular component can be reconstructed when conducting a CMM measurement, out of an unworn surface, no such application exists at this moment for reconstruction of the fossa (7). Thus it would have been preferable to scan the pre-wear UHMWPE component of the fossa before implantation, to limit any error margin. However due to sterilization issues, it was not

achievable to scan the fossa after production. However, this error margin did not significantly affect the UHWMPE fossa part under investigation, as they were oversized 3D-printed and consequently milled down to the original STL file boundaries with a precision of 0.02 mm, as was also the case for the titanium condylar component. In addition, as we were not able to scan the implants prior to implantation, we were unable to predetermine reference points as to use a closed loop information system to overlap the 'pre-implantation' STL and 'explanted-STL' and instead relied on the 'best-fit' method using GOM Inspect (GOM GmbH).

A second limitation we faced, were the fitting difficulties of the UHMWPE fossa during implantation, resulting in the trimming down of the non-load-bearing UHMWPE surfaces. While this allowed for easier implantation, this did result in problems determining the both linear and volumetric wear in one sample and volumetric wear in one additional sample. This was due to the 'best-fit' algorithm no longer being able to find a sufficient amount of matching surface points between the design-STL and the explanted fossa.

A significant limitation we were confronted with as well, was the lack of prior research into both *in vitro* and *in vivo* wear analysis in TMJ TJR. Thus we were forced to compare our results to wear evaluation in TKR.

Conclusion

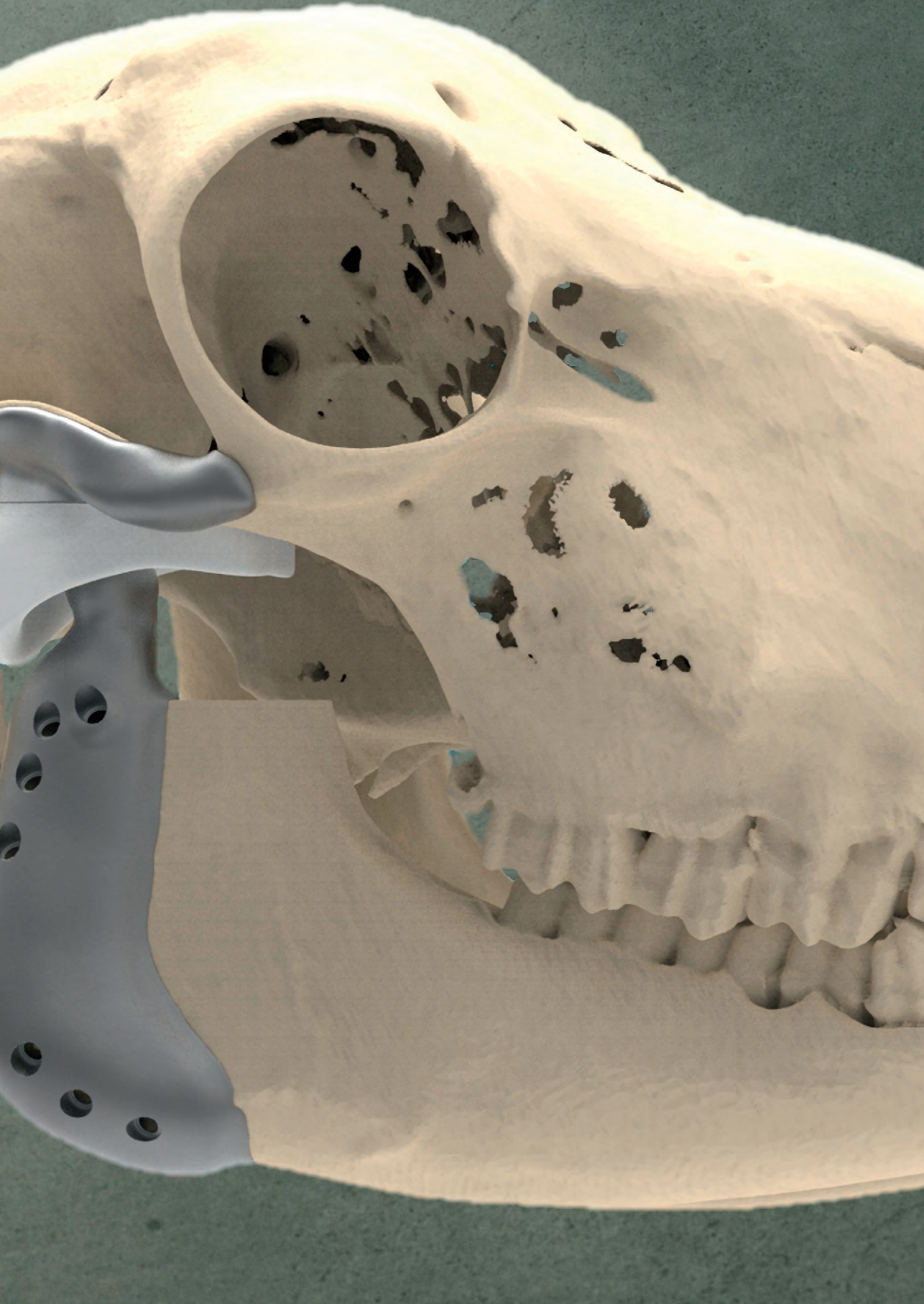
Our custom additively manufactured TMJ replacement system is well-suited for implantation, with an average linear and volumetric UHMWPE wear well below the maximum allowed per year in TKR, for both the non-coated and H-DLC-coated Ti6Al4V condyles. Furthermore, the use of the H-DLC coating significantly improved the surface roughness of the condylar surface. Based on these findings, the combined use of the condylar H-DLC-coating with Vitamin E-stabilized UHMWPE should be considered the preferable TMJ implant option.

References

1. Onoriobe U, Miloro M, Sukotjo C, Mercuri LG, Lotesto A, Eke R. How Many Temporomandibular Joint Total Joint Alloplastic Implants Will Be Placed in the United States in 2030 ? J Oral Maxillofac Surg [Internet]. 2016;74(8):1531–8. Available from: http://dx.doi.org/10.1016/j.joms.2016.04.011
2. De Meurechy N, Braem A, Mommaerts MY. Biomaterials in temporomandibular joint replacement : current status and future perspectives — a narrative review. Int J Oral Maxillofac Surg [Internet]. 2018;47(4):518–33. Available from: http://dx.doi.org/10.1016/j.ijom.2017.10.001
3. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants - A review. Prog Mater Sci [Internet]. 2009;54(3):397–425. Available from: http://dx.doi.org/10.1016/j.pmatsci.2008.06.004
4. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR. How long does a knee replacement last ? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. Lancet [Internet]. 2016;393(10172):655–63. Available from: http://dx.doi.org/10.1016/S0140-6736(18)32531-5
5. van Loon JP, de Bont LGM, Stegenga B, Spijkervet FKL, Verkerke GJ. Groningen temporomandibular joint prosthesis. Development and first clinical application. Int J Oral Maxillofac Surg. 2002;31(1):44–52.
6. Sinno H, Tahiri Y, Gilardino M, Bobyn D. Engineering alloplastic temporomandibular joint replacements. McGill J Med [Internet]. 2010;13(1):63–72. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L362021455
7. Sagbas B, Durakbasa MN. Measurement of Wear in Orthopedic Prosthesis. In: Proceedings of the International Congress on Advances in Applied Physics and Materials Science,. 2012. p. 131–4.
8. Jacobs JJ, Roebuck KA, Archibeck M, Hallab NJ, Glant TT. Osteolysis: basic science. Clin Orthop Relat Res. 2001 Dec;(393):71–7.
9. Alonso A, Kaimal S, Look J, Swift J, Fricton J, Myers S, et al. A quantitative evaluation of inflammatory cells in human temporomandibular joint tissues from patients with and without implants. J Oral Maxillofac Surg. 2009 Apr;67(4):788–96.
10. De Meurechy N, Mommaerts MY. Alloplastic temporomandibular joint replacement systems: a systematic review of their history. Int J Oral Maxillofac Surg. 2018 Feb;
11. Elledge R, Mercuri LG, Attard A, Green J, Speculand B. Review of emerging temporomandibular joint total joint. Br J Oral Maxillofac Surg [Internet]. 2019; Available from: https://doi.org/10.1016/j.bjoms.2019.08.009
12. van Loon JP, de Bont LGM, Spijkervet FKL, Verkerke GJ, Liem RSB. A short-term study in sheep with the Groningen temporomandibular joint prosthesis. Int J Oral Maxillofac Surg. 2000;29(5):315–24.
13. Van Loon JP, Verkerke GJ, de Bont LGM, Liem RSB. Wear-testing of a temporomandibular joint prosthesis: UHMWPE and PTFE against a metal ball, in water and in serum. Biomaterials. 1999;20(16):1471–8.
14. Kerwell S, Alfaro M, Pourzal R, Lundberg HJJ, Liao Y, Sukotjo C, et al. Examination of failed retrieved temporomandibular joint (TMJ) implants. Acta Biomater [Internet]. 2016;32:324–35. Available from: http://dx.doi.org/10.1016/j.actbio.2016.01.001
15. van Loon JP, de Bont LGM, Boering G. Evaluation of temporomandibular joint prostheses. Review of the literature from 1946 to 1994 and implications for future prosthesis designs. J Oral Maxillofac Surg. 1995;53(9):984–96.
16. Ingawalé SM, Goswami T, Ingawale S, Goswami T. Biomechanics of the Temporomandibular Joint. In 2012.
17. Angelo DF, Morouço P, Alves N, Viana T, Santos F, González R, et al. Choosing sheep (Ovis aries) as animal model for temporomandibular joint research: Morphological, histological and biomechanical characterization of the joint disc. Morphologie. 2016;100(331):223–33.

18. Almarza AJ, Brown BN, Arzi B, Ângelo DF, Chung W, Badylak SF, et al. Preclinical Animal Models for Temporomandibular Joint Tissue Engineering. Tissue Eng Part B Rev. 2018 Jun;24(3):171–8.
19. Domingue BM, Dellow DW, Barry TN. The efficiency of chewing during eating and ruminating in goats and sheep. Br J Nutr. 1991 May;65(3):355–63.
20. Mommaerts MY. On the reinsertion of the lateral pterygoid tendon in total temporomandibular joint replacement surgery. J Cranio-Maxillo-Facial Surg [Internet]. 2019;47(12):1913–7. Available from: https://doi.org/10.1016/j.jcms.2019.11.018
21. Singh R, Dahotre NB. Corrosion degradation and prevention by surface modification of biometallic materials. J Mater Sci Mater Med. 2007;18(5):725–51.
22. Bracco P, Oral E. Vitamin E-stabilized UHMWPE for total joint implants: A review. Clin Orthop Relat Res. 2011;469(8):2286–93.
23. Wolf C, Lederer K, Muller U. Tests of biocompatibility of alpha-tocopherol with respect to the use as a stabilizer in ultrahigh molecular weight polyethylene for articulating surfaces in joint endoprostheses. J Mater Sci Mater Med. 2002 Jul;13(7):701–5.
24. De Meurechy N, Verwilghen D, De Brucker Y, Van Thielen B, Mommaerts MY. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation. J Cranio-Maxillofacial Surg. 2021 Feb;49(4):256–68.
25. Verplancke K, De Waele W, De Bruyn H. Dental implants, what should be known before starting an in vitro study. Conf Sustain Constr Des [Internet]. 2011;2(3):360–9. Available from: https://biblio.ugent.be/publication/1177030
26. Selvik G. Roentgen stereophotogrammetric analysis. Acta Radiol. 1990 Mar;31(2):113–26.
27. Dumbleton JH, Manley MT, Edidin AA. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. J Arthroplasty. 2002 Aug;17(5):649–61.
28. Oparaugo PC, Clarke IC, Malchau H, Herberts P. Correlation of wear debris-induced osteolysis and revision with volumetric wear-rates of polyethylene: a survey of 8 reports in the literature. Acta Orthop Scand. 2001 Feb;72(1):22–8.
29. Benjamin J, Szivek J, Dersam G, Persselin S, Johnson R. Linear and Volumetric Wear of Tibial Inserts in Posterior Cruciate-Retaining Knee Arthroplasties. 2001;(392):131–8.
30. Chaudhary N, Lovald ST, Wagner J, Khraishi T, Baack B. Experimental and Numerical Modeling of Screws Used for Rigid Internal Fixation of Mandibular Fractures. Model Simul Eng [Internet]. 2008 Jan;2008. Available from: https://doi.org/10.1155/2008/628120
31. Tada S, Stegaroiu R, Kitamura E, Miyakawa O, Kusakari H. Influence of implant design and bone quality on stress/strain distribution in bone around implants: a 3-dimensional finite element analysis. Int J Oral Maxillofac Implants. 2003;18(3):357–68.
32. Skinner R, Maybee J, Transfeldt E, Venter R, Chalmers W. Experimental pullout testing and comparison of variables in transpedicular screw fixation. A biomechanical study. Spine (Phila Pa 1976). 1990 Mar;15(3):195–201.
33. Wang A, Polineni VK, Stark C, Dumbleton JH. Effect of femoral head surface roughness on the wear of ultrahigh molecular weight polyethylene acetabular cups. J Arthroplasty [Internet]. 1998;13(6):615–20. Available from: http://www.sciencedirect.com/science/article/pii/S0883540398800028
34. Jedenmalm A, Affatato S, Taddei P, Leardini W, Gedde UW, Fagnano C, et al. Effect of head surface roughness and sterilization on wear of UHMWPE acetabular cups. J Biomed Mater Res A. 2009 Sep;90(4):1032–42.
35. Tubb CC, Longaray JA, Herrera L, Essner AP, Molloy RM. The Effect of Femoral Component Roughness on the Wear of Total Knee Implants. Orthop Res Soc. 2011;36.
36. McGloughlin TM, Kavanagh AG. Wear of ultra-high molecular weight polyethylene (UHMWPE) in total knee prostheses: a review of key influences. Proc Inst Mech Eng Part H, J Eng Med. 2000;214(4):349–59.
37. Jiang SW, Jiang B, Li Y, Li YR, Yin GF, Zheng CQ. Friction and wear study of diamond-like carbon gradient coatings on Ti6Al4V substrate prepared by plasma source ion implant-ion beam enhanced deposition. Appl Surf Sci. 2004;236(1):285–91.

38. Kim DH, Kim HE, Lee KR, Whang CN, Lee IS. Characterization of diamond-like carbon films deposited on commercially pure Ti and Ti-6Al-4V. Mater Sci Eng C. 2002;22(1):9–14.
39. Firkins P, Hailey JL, Fisher J, Lettington AH, Butter R. Wear of ultra-high molecular weight polyethylene against damaged and undamaged stainless steel and diamond-like carbon-coated counterfaces. J Mater Sci Mater Med. 1998;9(10):597–601.
40. Ching HA, Choudhury D, Nine J, Abu Osman NA. Effects of surface coating on reducing friction and wear of orthopaedic implants. Sience Technol Adv Mater. 2014;014402(15).
41. Yetim AF, Celik A, Alsaran A. Improving tribological properties of Ti6Al4V alloy with duplex surface treatment. Surf Coatings Technol [Internet]. 2010;205(2):320–4. Available from: http://dx.doi.org/10.1016/j.surfcoat.2010.06.048
42. Liu X, Chu PK, Ding C. Surface modification of titanium, titanium alloys, and related materials for biomedical applications [Internet]. Vol. 47, Materials Science and Engineering R: Reports. 2004. p. 49–121. Available from: http://dx.doi.org/10.1016/j.mser.2014.10.001
43. Roy RK, Lee K-R. Biomedical applications of diamond-like carbon coatings: a review. J Biomed Mater Res B Appl Biomater. 2007 Oct;83(1):72–84.
44. Van Hove RP, Sierevelt IN, Van Royen BJ, Nolte PA. Titanium-Nitride Coating of Orthopaedic Implants: A Review of the Literature. Biomed Res Int. 2015;2015.
45. Mishnaevsky L, Levashov E, Valiev RZ, Segurado J, Sabirov I, Enikeev N, et al. Nanostructured titanium-based materials for medical implants: Modeling and development. Mater Sci Eng R Reports. 2014;81(1):1–19.



Chapter 6

Inflammatory cell response evaluation after total temporomandibular joint replacement in an animal experiment

This chapter is based on:

Inflammatory cell response evaluation after total temporomandibular joint replacement in an animal experiment

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Introduction

Since total temporomandibular joint replacement (TMJR) was first introduced in modern medicine, many different systems have been developed.(1,2) Whilst the indications for the prosthetic replacement have become well-defined (3,4), the quality standards these systems need to meet, remain poorly regulated. Often proper in vivo and in vitro testing of TMJR prostheses is lacking, (5) with implantation of unsuited materials potentially leading to significant, detrimental, patient side effects such as synovitis, foreign body giant cell reactions (FBGCR), bone resorption and implant failure. (1,6–9) One such example is the Vitek-Kent. Although the system seemed promising at first, the 2mm thick articulating Teflon coating was found to be an unsuitable articulating surface. This resulted in the accumulation of wear debris several years after implantation, leading to severe local reactions and finally a recommendation of removal by both the US Food and Drug Administration (FDA) and the American Association of Oral and Maxillofacial Surgeons.(1,8,9)

This illustrates the absolute importance of proper TJR evaluation, before human application. Thus, in order to properly evaluate a novel patient-specific additively titanium (Ti) alloy TMJ replacement system developed by CADskills BV (Ghent, Belgium), an *in vivo* animal experiment, using a sheep model, was designed. Three focal points were selected for investigation: Wear, lateral pterygoid muscle (LPM) enthesis integration and adverse tissue reactions.(5,10)

Previously published papers evaluated and discussed the development of the TMJR, implant integration, LPM enthesis reconstruction, wear rates of both the fossa and condylar components.(5,10,11) This paper aims to evaluate the amount of inflammation of the peri-articular tissues, whilst also comparing the inflammatory response in TMJR with and without a condylar diamond-like carbon (DLC) coating.(6) For more information concerning this coating and its effect on wear, we refer to two of our previous papers that discuss this at length, as this is beyond the scope of this paper.(5,11)

Materials and Methods

Following approval by the Medanex Clinic Ethics Committee (license number LA 1210576 - code of approval EC MxCl 2018-090), an *in vivo* experimental animal study using fourteen ewes (Swifter crossbreed), was performed. A total of thirteen sheep were randomly divided into two groups. Both groups were implanted with a novel custom titanium 6-aluminum 4-vanadium (Ti6Al4V) TMJR system, of which six had a DLC-coated condyle. The other seven prosthesis had an uncoated condylar surface. One sheep functioned as a control group. In this case, the TMJ was surgically approached, yet no condylectomy or prosthesis implantation was performed. We refer to our previously published research for an extensive description of the surgery protocol and post-operative follow-up, and will only focus on the histological evaluation in this paper.(5,10)

Sample processing and coloring

288 days after implantation of the custom TMJR, all sheep were euthanized and decapitated. The skull was cut in half midsagitally. All the bodies and right half of the skulls were properly disposed of. The left half was further dissected by systematically removing the neurocranium, the anterior half of the mandible and maxilla, the upper half of the orbit and the orbital contents. The remaining tissue was then fixated for three months by immersion in 4% formaldehyde. Once properly fixated, all samples were rinsed for 3 days to remove the excess formalin. The peri-articular 'neo-synovial' tissues were then excised, taking care not to contain scar tissue from the implant surgery. During dissection of the neo-synovial tissues, several samples revealed an intracapsular brownish material, which appeared to be amorphous. This material was preserved and embedded in paraffin as well, to allow for further analysis. The 'neo-synovial' tissues were prepared, before staining, according to the following protocol; All specimen were put into sample cassettes and put into a 4% buffered Formalin solution. The samples were then washed out with running tap water to remove excess fixative from the tissues and prevent interaction of glutaraldehyde with the staining. The samples then were manually dehydrated in an ascending row of ethanol (30%, 50%, 60%, 70%) before further dehydration (90%, 96% ethanol and 100%

isopropanol) and infiltration with xylene and paraffin in a Leica Peloris 3 infiltration automaton (Deer Park, IL, USA). After processing all tissues were embedded in paraffin and stored at 4°C. All fixed and paraffin-embedded (FFPE) specimen were cut on a Leica RM 2255 rotation microtome (Deer Park, IL, USA), including a cooling unit and a water basin. Five µm thin sections were put onto special adhesive microscopic SuperFrost Plus slides (VWR Collection, Darmstadt, Germany) dried overnight and then stored at 4°C until histologic processing.

A hematoxylin-eosin coloring was then applied to these tissues.(Table 1) While hematoxylin is a nuclear stain that results in a purple to blue color after processing, eosin is a cytoplasmic stain. It results in a bright pinkish-red color in red blood cells; muscle fibers; collagen fibers and was used to evaluate the tissue, including the inflammatory cells present. Analysis of the slides was performed using a light microscope (BX40 (Olympus Belgium N.V., Antwerp, Belgium)) at a magnification of 4x, 10x, 20x and 100x.

Table 1: Hematoxylin & Eosin staining protocol

Step	Reagent/solution	Time	
1	Xylene	0:05:00	Deparaffinization
2	Xylene	0:05:00	Deparaffinization
3	Ethanol 96%	0:05:00	Rehydration
4	Ethanol 80%	0:05:00	Rehydration
5	Ethanol 70%	0:05:00	Rehydration
6	Aqua dest	0:01:30	Rehydration
7	Hematoxylin	0:05:00	Staining cell nuclei
8	Aqua dest	0:00:30	Wash/removal of excess staining solution
9	Running water	0:05:00	Wash/Blueing of hematoxylin (with fixation of the hematein molecules)
10	Eosin 1%, aqueous, pH 6	0:05:00	Staining of cytoplasm and other components
11	Running water	0:04:00	Wash
12	Ethanol 96%	0:01:30	Dehydration
13	Ethanol 96%	0:02:00	Dehydration
14	Isopropanolol	0:05:00	Dehydration
15	Xylene	0:05:00	De-alcoholization
16	Xylene	0:05:00	De-alcoholization

Histological analysis

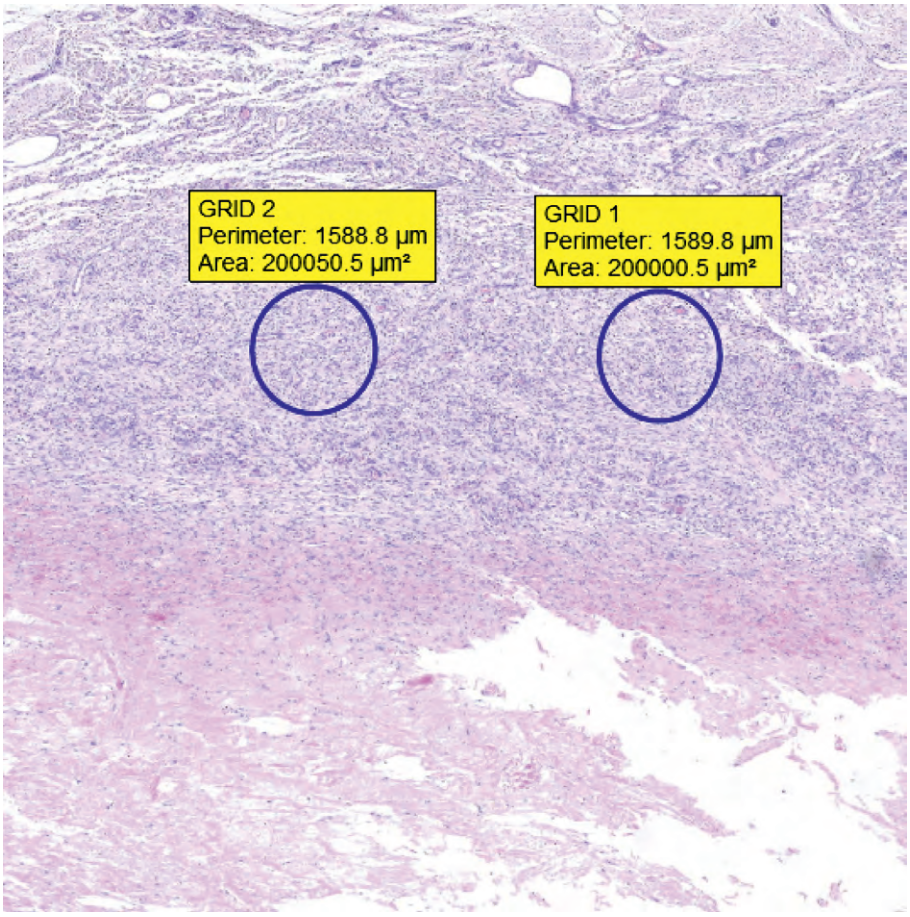


Fig. 1: A tissue sample, HE colored, with two 0.20mm² digital grids applied.

A total of two stained samples of the peri-prosthetic 'neo-synovial' tissue were randomly selected per sample. Next, in order to obtain an unbiased tissue evaluation, a 0.20mm² digital grid was projected on the tissue sample at five random locations. (Fig. 1) This was achieved by first obscuring the view of the sample and only then revealing the sample. In the event that a grid was either only partially filled with tissue, or if the grid view was (partially) obstructed by, for example, the presence of a blood vessel, a new random grid projection was generated.

A distinction was made between acute and chronic inflammatory response by light microscopic evaluation with manual cell counting. Lymphocytes were identified based on cell morphology. To be counted as a lymphocyte, cells had to be mononuclear with a solitary round and dark blue nucleus (no multiple lobes as in neutrophils) and have minimal surrounding cytoplasm. Macrophages had to be round to oval in shape (10-30 µm in diameter), with an eccentrically placed, oval or indented nucleus. Although the cytoplasm is usually "foamy", this need not be the case and was not used as an exclusion criterium.

Statistical analysis

Per TMJR, two stained samples were evaluated. A total of five grids were applies per sample. This resulted in a total of 60 grids for the sheep implanted with a DLC-coated condyle (n=6) and 70 grids for those with an uncoated condyle (n=7). A total of ten randomly selected grids were examined on the ewe that underwent sham surgery. For each grid, the number of macrophages and lymphocytes was counted, as well as polymorphonuclear leukocytes if present. The normality macrophage and lymphocyte counts was assessed by a Kolmogorov-Smirnov and Shapiro-Wilk test, which revealed non-normal distributions ($P < 0.001$). Thus, a Kruskal-Wallis non-parametric ANOVA test was used to test for differences in numbers of macrophages and lymphocytes between treatment groups, with a Bonferroni correction. The mean number of cells per group was calculated. All data are expressed as mean ± SD.

Results

No signs of acute infection, marked by the presence of neutrophiles, were found in any of the samples. There were signs of chronic inflammation and presence of macrophages in all samples. (Figs. 2 & 3)

Analysis of the distribution plot for lymphocytes (Fig. 4) in the DLC-coated and uncoated samples, reveals higher outliers in the uncoated (140), compared to the coated group (91), as well as a larger mean and larger distribution in the uncoated group (34.51 ± 28.58) compared

to the coated samples (24.6 ± 18.45). In comparison, a relatively low amount of lymphocytes was found in the sham peri-articular tissue (9.5 ± 5.2). In addition, analysis using the Bonferroni correction found a statistically significant difference in both groups, compared to the sham-group. This significantly higher lymphocyte count was more pronounced in the uncoated tissues (p = 0.001), compared to the coated samples (p = 0.018). No significant difference was found between the uncoated and coated peri-articular tissue with respect to the concentration of lymphocytes.

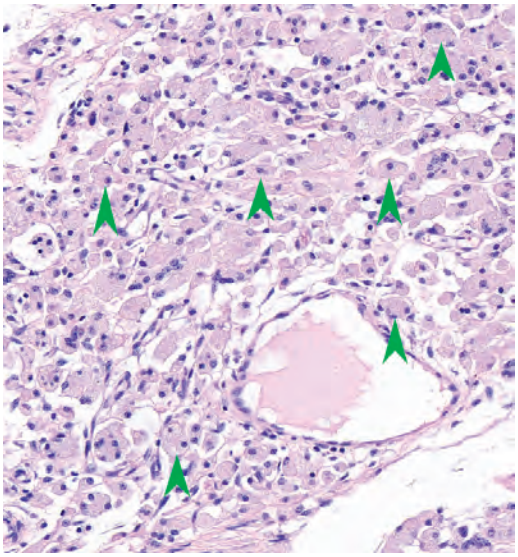


Fig. 2: Peri-articular tissue of the specimen revealing a high macrophage count. (hematoxylin-eosin stain, original magnification X 100). Green arrow: Macrophages

When evaluating the presence of macrophages in the samples (Fig. 5), the sham tissues again show the least amount of macrophages (7.4 ± 10.36). The coated system's tissues have a higher number of macrophages (22.15 ± 25.31) compared to the uncoated samples (17.76 ± 21.16), but this difference was not significant (p = 0.405). However, the coated group showed a significantly higher number of macrophages compared to the sham-group (p = 0.019), while the uncoated group did not (p = 0.141). The amorphous material that was found during dissection revealed to contain large amounts of hemosiderin (Fig. 3) and clusters of erythrocytes.

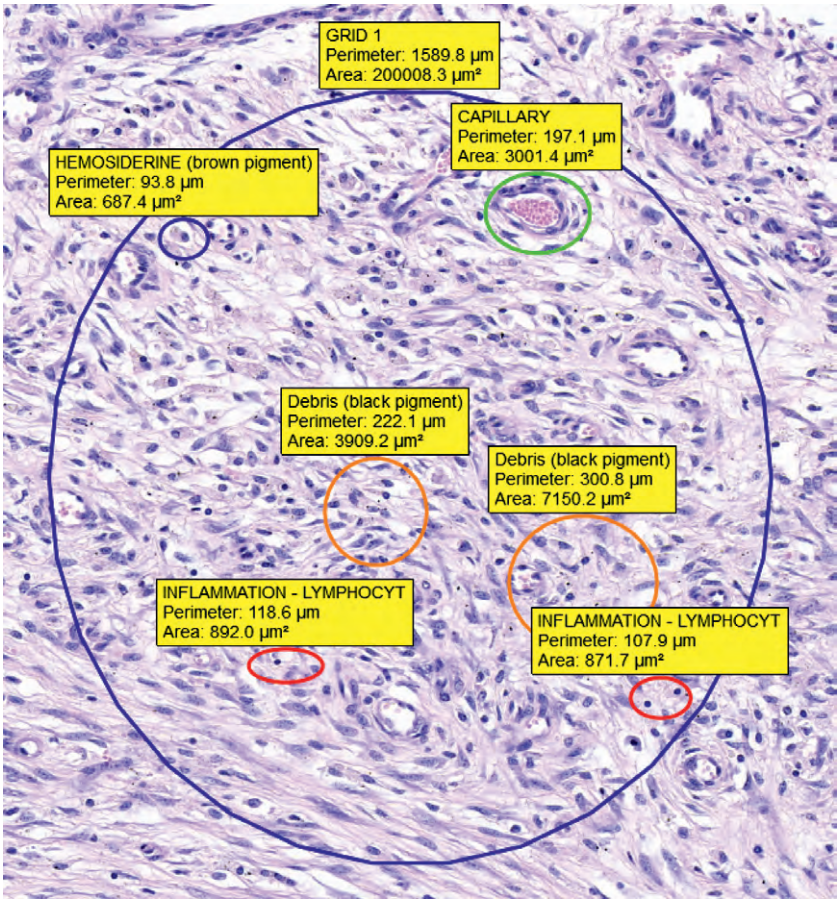


Fig. 3: Peri-articular tissue showing lymphocytes, debris, hemosiderin and a capillary present. (hematoxylin-eosin stain, original magnification X 100). Green circle: Capillary Red Circle: Lymphocytes Orange Circle: Debris Blue Circle: Hemosiderin

Discussion

Given the severe adverse inflammatory reaction observed in patients treated with the Vitek-Kent replacement system (1,6,8), which had a significant impact on the use of TMJR with a near abandonment of the treatment method during several years, we aimed to provide a quantitative analysis of the inflammatory cell types found in sheep treated with a novel TMJR system, developed by CADskills BV (Ghent, Belgium), to determine its suitability for human implantation.

Table 2: SLIM consensus classification

Type I	Wear-induced synovitis/SLIM
Type II	Infection-induced synovitis/SLIM
Type III	Mixed synovitis/SLIM
Type IV	Indifferent (not wear-induced, not infection-induced) synovitis/SLIM
Type V	Prosthesis-associated arthrofibrosis
Type VI	Adverse local tissue reactions to implant wear particles
Type VII	Local osseous pathologies

To properly assess periprosthetic tissue responses, the 'synovial-like interface membrane' (SLIM) consensus classification (Table 2) has proven to be an extremely useful system. For a 'neo-synovitis' to be classified as being wear-induced (Type I), more than 20% of the sample must be filled in with macrophages. In addition, multinucleated foreign-body giant cells can be found as well. In addition to these inflammatory cells, wear particles are present within the macrophages.(12–14)

Evaluation of peri-articular tissues from both the DLC-coated and uncoated systems revealed an increase in macrophagic cells compared to the control group. However, in all samples, the total wear volume and linear wear were well below the gold standard and well below the rate of 1mm/year and 80mm^3 volume at which osteolysis can occur. (5,15) This was also reflected in the low macrophage response, which averaged 3.8% of the total surface area in case of the DLC-coated system and 3.1% in the case of the uncoated system. The authors concluded that no wear induced 'neo-synovitis' was found in any of the samples. (Tables 3 and 4)

Evaluation of peri-articular tissues from both the DLC-coated and uncoated systems revealed an increase in macrophagic cells compared to the tissues from the control group. On further analysis, Important to note is that the significantly increased number of macrophages in the coated system was influenced by one sheep, showing a significantly higher number of macrophages compared to the other samples. When the recorded data for this sheep was omitted, both mean (17) and SD (16.08) dropped sharply. In fact, there was no longer a significant difference ($p = 0.71$) in the amount of macrophages found between the two groups and the average infiltration rate dropped to 2.9%. Post-operative clinical

records and a previously performed radiological (10) and wear-analysis (5) were reviewed to determine a cause for the increased macrophage count, yet no abnormalities were found in the bloodwork, weight and diet, or clinical presentation. No significant radiological findings were observed either, nor were there abnormalities in the amount of wear.

Table 3: Surface area (in mm²) covered per 1mm² with macrophages, in the uncoated tissue samples.

Sheep number	Sample 1	Sample 2
Sheep 1	0,059	0.018
Sheep 2	0.021	0.065
Sheep 3	0.013	0.009
Sheep 4	0.020	0.012
Sheep 5	0.059	0.052
Sheep 6	0.032	0.053
Sheep 7	0.012	0.007

Table 4: Surface area (in mm²) covered per 1mm² with macrophages, in the DLC-coated tissue samples.

Sheep number	Sample 1	Sample 2
Sheep 1	0.028	0.007
Sheep 2	0.052	0.035
Sheep 3	0.072	0.094
Sheep 4	0.019	0.023
Sheep 5	0.042	0.026
Sheep 6	0.017	0.045

In addition to this Type I-reaction, wear particles can also lead to local toxicity, resulting in adverse local tissue reactions (Type VI-reaction), as observed with the Vitek-Kent replacement system.(6,7) This Type VI-reaction can be divided into three different groups. Firstly, a mainly macrophagic pattern with absent or minimal lymphocytic response is seen (2); a mixed inflammatory pattern, with both macrophagic and lymphocytic cells, with variable presence of plasma cells, eosinophils, and mast cells and (3) a granulomatous pattern, predominant or associated with the mixed inflammatory pattern. (12,13) Again, none of our samples met these criteria.

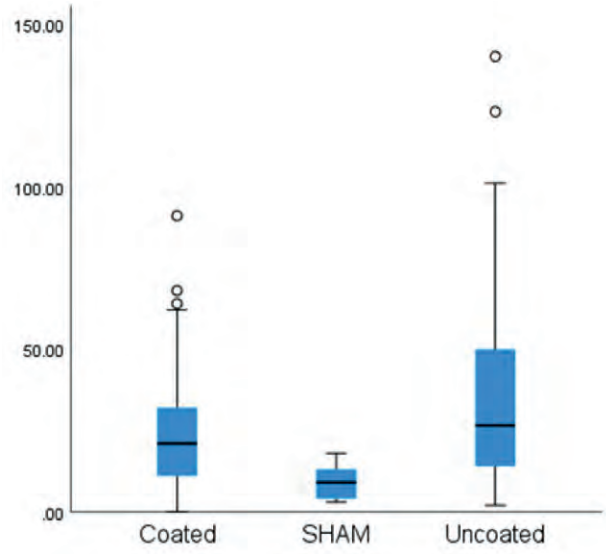


Fig. 4: Box plot for lymphocyte distribution

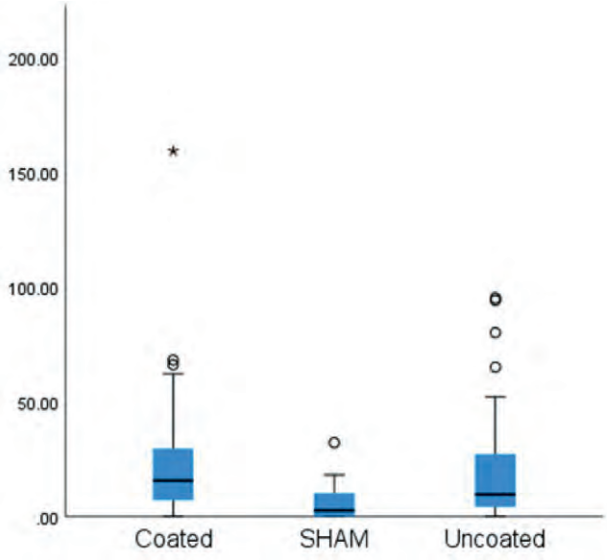


Fig. 5: Box plot for macrophage distribution

While one sheep developed a peri-articular swelling 2 months prior to euthanasia, possibly indicative of an infection-induced 'neo-synovitis' (Type II-reaction) , drainage revealed the swelling to be hemorrhagic in nature. A blood sample showed no leukocytosis and a bacterial culture of

the drained fluid yielded no results. Histopathological evaluation revealed the presence of both macrophage and a lymphocytic response (limited to less than 20% of the sample surface), but no polymorphonuclear leukocytes were found. Given the negative microbiological diagnosis, together with the absence of polymorphonuclear leukocytes, as well as the absence of abscess formation, we concluded no prosthetic joint infection or Type II reaction occurred.(12,16) Instead, post-mortem radiological evaluation revealed that the fossa component had been luxated. This was probably caused by the chosen screw diameter. This was similar to that in humans, whilst a larger diameter would have provided better fixation. The event of the luxation of the fossa component may well have led to the hematoma formed.

Although no wear-induced 'neo-synovitis' was found, we did find a significantly increased amount of lymphocytes in the uncoated TMJR tissue samples compared to both the coated TMJR and the control tissues. This suggests that a chronic inflammatory response, or at least more chronic inflammation, was present in the uncoated TMJR group. This is important, as studies by both Hobza et al.(17) and Lohmann et al.(18) have shown that higher tissue concentrations of metals resulted in a higher lymphocytic infiltration. Their findings are consistent with ours, as less wear was found in the coated system compared to the uncoated system. Whilst we have not focused on implant integration and the interface between implant and bone in this paper, previously published studies have shown good histological results regarding bone ingrowth into the implant surface, thus no type V or VI-reactions were seen.

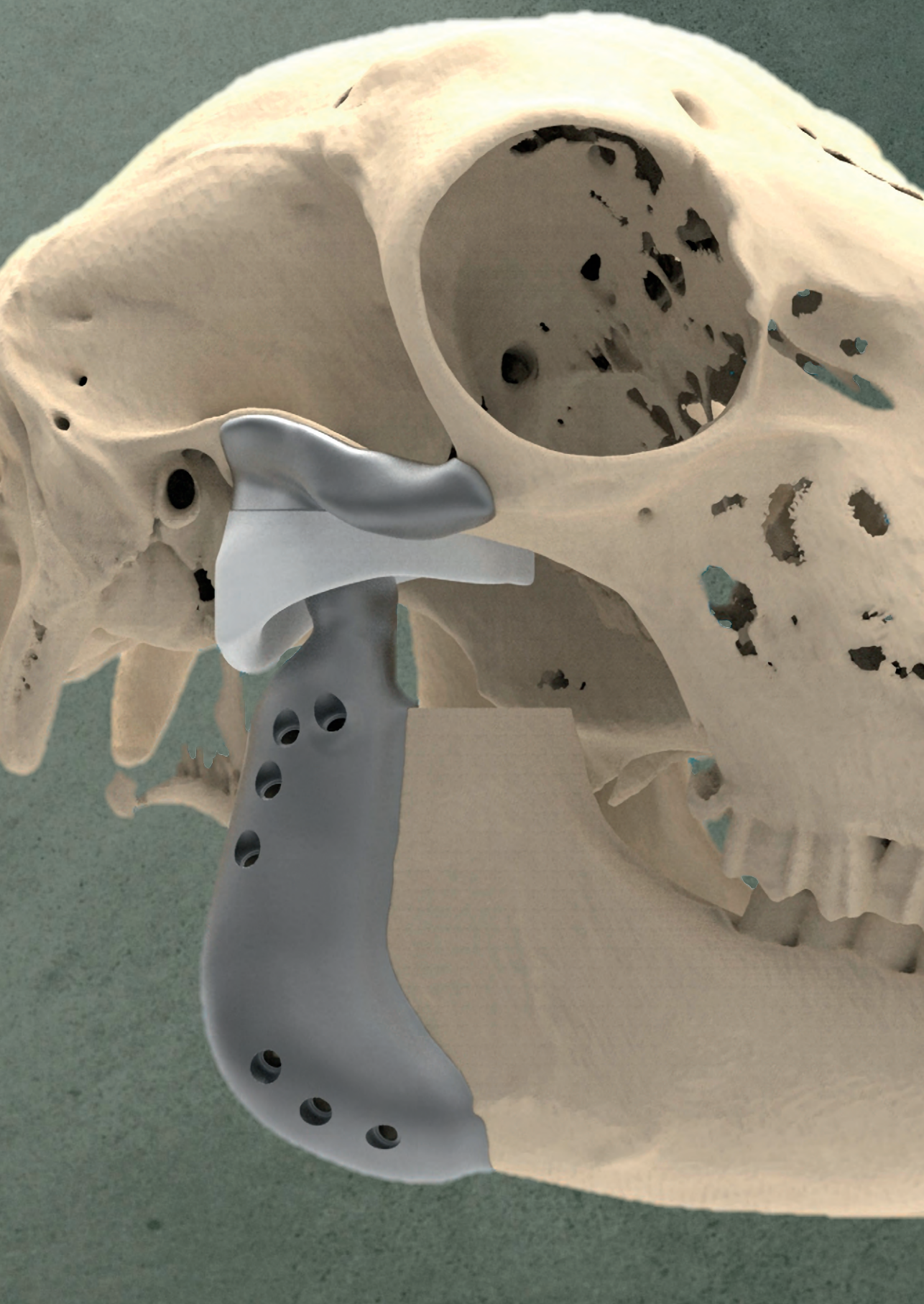
The intracapsular material that was encountered during the dissection, was similar to the discovery by Van Loon et al.(19), during their sheep experiment. Although they hypothesized this were clusters of degenerated erythrocytes, we hypothesized that this brown material was a remnant of the hemostatic gelatin sponge (Spongostan, Ethicon, New Jersey, USA) placed in each of the intracapsular spaces during implantation.

Conclusion

A significant increase in lymphocyte counts was seen in both samples treated with the DLC-coated and the uncoated condyle, although this increase was more significant in the uncoated system. A significant increase in macrophages was also observed in the tissue samples from the coated system, but none of the samples examined, showed any sign of 'neo-synovitis' caused by wear or infection. No adverse local tissue reactions were observed. We can conclude that these results are satisfying and warrant further investigation through human application, as we do not expect any adverse reactions based on these results.

References

1. De Meurechy N, Mommaerts MY. Alloplastic temporomandibular joint replacement systems: A systematic review of their history. Int J Oral Maxillofac Surg [Internet]. 2018;47(6):743–54. Available from: https://doi.org/10.1016/j.ijom.2018.01.014
2. Elledge R, Mercuri LG, Attard A, Green J, Speculand B. Review of emerging temporomandibular joint total joint. Br J Oral Maxillofac Surg [Internet]. 2019; Available from: https://doi.org/10.1016/j.bjoms.2019.08.009
3. Koslin M, Indresano AT, Mercuri LG. Temporomandibular joint surgery. J Oral Maxillofac Surg. 2012;70:204–31.
4. NICE. National Institute for Health and Care Excellence Scope. Natl Inst Heal Care Excell [Internet]. 2014;(May):1–9. Available from: https://www.nice.org.uk/guidance/gid-cgwave0704/resources/multimorbidity-final-scope2
5. De Meurechy N, Aktan MK, Boeckmans B, Huys S, Verwilghen DR, Braem A, et al. Surface wear in a custom manufactured temporomandibular joint prosthesis. J Biomed Mater Res B Appl Biomater. 2022 Jun;110(6):1425–38.
6. De Meurechy N, Braem A, Mommaerts MY. Biomaterials in temporomandibular joint replacement : current status and future perspectives — a narrative review. Int J Oral Maxillofac Surg [Internet]. 2018;47(4):518–33. Available from: http://dx.doi.org/10.1016/j.ijom.2017.10.001
7. Alonso A, Kaimal S, Look J, Swift J, Fricton J, Myers S, et al. A quantitative evaluation of inflammatory cells in human temporomandibular joint tissues from patients with and without implants. J Oral Maxillofac Surg. 2009 Apr;67(4):788–96.
8. Trumpy IG, Roald B, Lyberg T. Morphologic and immunohistochemical observation of explanted Proplast-Teflon temporomandibular joint interpositional implants. J Oral Maxillofac Surg. 1996 Jan;54(1):63–70.
9. Trumpy IG, Lyberg T. In vivo deterioration of proplast-teflon temporomandibular joint interpositional implants: a scanning electron microscopic and energy-dispersive X-ray analysis. J Oral Maxillofac Surg. 1993 Jun;51(6):624–9.
10. De Meurechy N, Verwilghen D, De Brucker Y, Van Thielen B, Mommaerts MY. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation. J Cranio-Maxillofacial Surg. 2021 Feb;49(4):256–68.
11. Huys SEF, Braem A, De Meurechy N, Van de Sande R, Vander Sloten J, Mommaerts MY. Evolutionary Steps in the Development of a Patient-specific Temporomandibular Joint Prosthesis. Craniomaxillofacial Res Innov [Internet]. 2022 Aug 1;7:27528464221118784. Available from: https://doi.org/10.1177/27528464221118784
12. Krenn V, Perino G. Histological Diagnosis of Implant-Associated Pathologies. Springer, Berlin, Heidelberg; 2017. 44 p.
13. Krenn V, Morawietz L, Perino G, Kienapfel H, Ascherl R, Hassenpflug GJ, et al. Pathology – Research and Practice Revised histopathological consensus classification of joint implant related pathology. Pathol -- Res Pract [Internet]. 2014;210(12):779–86. Available from: http://dx.doi.org/10.1016/j.prp.2014.09.017
14. Morawietz L, Classen R-A, Schroder JH, Dynybil C, Perka C, Skwara A, et al. Proposal for a histopathological consensus classification of the periprosthetic interface membrane. J Clin Pathol. 2006 Jun;59(6):591–7.
15. Dumbleton JH, Manley MT, Edidin AA. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. J Arthroplasty. 2002 Aug;17(5):649–61.
16. Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. J Orthop Res. 2014 Jan;32 Suppl 1:98–107.
17. Hobza M, Milde D, Slobodova Z, Gallo J. The number of lymphocytes increases in the periprosthetic tissues with increasing time of implant service in non-metal-on-metal total joint arthroplasties: A role of metallic particles? Biomed Pap Med Fac Univ Palacky, Olomouc, Czechoslov. 2021 Nov;165(4):416–27.
18. Lohmann CH, Meyer H, Nuechtern J V, Singh G, Junk-Jantsch S, Schmotzer H, et al. Periprosthetic tissue metal content but not serum metal content predicts the type of tissue response in failed small-diameter metal-on-metal total hip arthroplasties. J Bone Joint Surg Am. 2013 Sep;95(17):1561–8.
19. Van Loon JP, De Bont LGM, Spijkervet FKL, Verkerke GJ, Liem RSB. A short-term study in sheep with the Groningen temporomandibular joint prosthesis. Int J Oral Maxillofac Surg. 2000;29(5):315–24.



Chapter 7

Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation

This chapter is based on:

Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation

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Maurice Y. Mommaerts

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Introduction

Since the first total temporomandibular joint replacement (TMJR) method was conceived in 1965 by Christensen, many more systems have been devised. Twenty-seven different TMJR systems are currently in use. (1,2) However, none provides for reinsertion of the lateral pterygoid muscle (LPM), which is surgically detached during the condylar resection phase.

The importance of the LPM is apparent when examining the different phases of mastication. The incisor and canine teeth first cut and tear the food, respectively. The premolars and molars then crush and chew the food, which is ground to the point where it can easily be swallowed and further improve digestion. Mastication efficiency is the number of chews necessary to grind down the food. It is dependent on good articular and muscular function and on the individual's dental condition. (3,4)

The lateral pterygoid muscle participates in the cutting and tearing phases of mastication by performing protrusion. It also performs laterotrusive motions during the chewing and grinding phase. Laterotrusive motions occur via unilateral contraction of the LPM. Protrusion results from bilateral contraction of the lateral pterygoid muscle. Loss of the lateral pterygoid muscle results in impaired laterotrusive and protrusive functions. For example, the average laterotrusion in humans is 10 mm, but Mercuri's et al. (5) long-term follow-up study found that significant post-operative decreases in laterotrusion occur after TMJR procedures. They reported an average laterotrusion of 3.07 mm (95%, 2.09 to 4.04) to the contralateral side after unilateral, right TMJR and 3.04 mm (95% CI, 1.98 to 4.10) after unilateral, left TMJR procedures. Similar findings were reported by Dimitroulis et al. (6). They found that laterotrusion can be limited to a mean value of 1.6 mm (range 0 - 2.9 mm). Correct mastication occurs bilaterally. During unilateral mastication, the TMJs are subjected to an uneven load, and further deterioration of the TMJ that experiences most of the load can result.(7)

In an attempt to reinstall laterotrusive movement after joint replacement, Mommaerts reconstructed the LPM enthesis using direct reinsertion

of the muscle onto the TMJR in three patients.(7) He proposed the use of a condylar lattice structure in the pterygoid fovea of the mandibular component of the TMJR to which the enthesis can be reattached. This structure is first filled with crushed autologous bone and concentrated bone marrow aspirate, to promote the formation of bone and collagenous tissue after reattachment of the LPM. Three patients were treated using this 'reattachment' technique. The study findings indicated that under the correct conditions, use of a condylar lattice structure resulted in a good outcome.

With these findings serving as clinical proof of concept, we optimized this patient-specific TMJR and designed an animal model to further investigate the possibility of reconstruction of the lateral pterygoid muscle enthesis without addition of bone marrow aspirate as well as to evaluate overall TMJR performance.

Materials and Methods

In vivo test subjects

There are biomechanical and morphological differences between the TMJ's of different species. Therefore, compared with other species, some are more suitable for use as experimental animal models.(8) Primates such as monkeys are very similar to humans in both morphological and biomechanical TMJ characteristics, but their use is severely limited by ethics. While both sheep and goat TMJs show morphological similarities to the human TMJ, the total amount of daily mastication of goats is relatively limited compared with sheep. The latter spend an average of 4 hours per day eating at 128 mastication cycles per minute and 8 to 9 hours ruminating at 100 cycles per minute.(9) This high number of mastication cycles per day allows for reductions in the total period of in vivo evaluation, especially in terms of wear and overall performance (i.e., except for materials ageing), making them more suitable for this experiment. The total duration for the experiment was set at 288 days, which is equivalent to 22 years of human function. (10)

Fourteen sheep (Swifter crossbreed) were acquired after gaining ethical committee approval (License nr. LA 1210576) for the study (code of approval EC MxCl 2018-090). All ewes were between 2 and 5 years of age, weighed between 52 and 86 kg (average weight, 73.4 kg), and had no teeth missing (Table 1). The ewes were allowed to move freely in a meadow up until the day of surgery. After the surgery, they were kept in solitary confinement for 1 week. After this first week, they were put together in a larger indoor confinement area.

In the first series of surgeries, two sheep were operated upon in April 2018. An animal-specific unilateral TMJR was placed in one sheep. The other sheep was used for the sham surgery. The sham surgery consisted of the same surgical approach with dissection of the joint, but no implant was placed nor was a condylectomy performed. We did not include the sham in this article, as the LPM was left intact. The 12 other sheep were operated upon 2 months later, after the surgical technique was optimized based on the experience with the first two sheep.

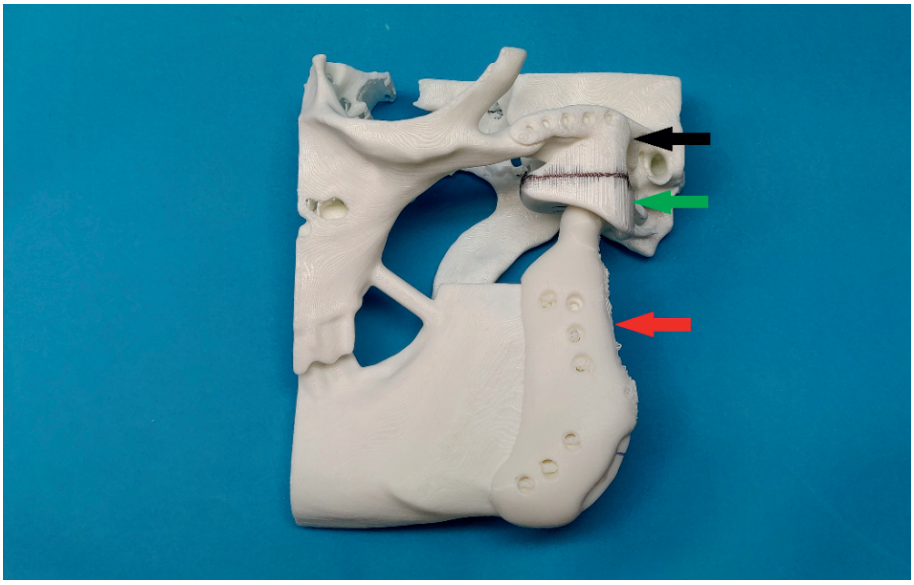


Fig. 1: Fused deposit three-dimensional model of a partial sheep's skull with the total temporomandibular joint replacement (TMJR). Red arrow: Mandibular component of the TMJR; green arrow: ultra-high-molecular weight polyethylene component of the TMJR fossa component; black arrow: titanium component of the TMJR fossa component.

Table 1: Sheep number and weight (kg) at pre-op, 1 week post-op, 1-3-6-9-10 months post-op.

Sheep #	Pre-op	1w post-op	3m post-op	6m post-op	9m post-op	10m post-op
3520	86.6	78.8	73.5	76.6	71.4	74.2
8087	61.4	53.8	52.1	53.9	59.8	59.6
2177	79.4	71.2	67.5	72.3	78.2	79.9
5158	72.3	63.3	66.8	70.9	77.6	80.1
2549	63.3	55.8	55.9	61.3	63.2	63.9
4249	75.8	65.5	61.5	62.5	64	63.6
0032	64.2	55.9	51.9	58.7	59.1	60.4
7998	83.9	76.2	68.7	70.8	75.8	77.2
4246	74.6	66.3	66.2	71.8	77.3	76.1
1724	83.9	76.3	75.8	84.3	90	91.9
4248	69.2	62.4	65.1	68.6	72.4	72.9
8787	52.3	50	45.6	47.3	48.6	47.7
4473	86	77.2	75.2	78.4	81.7	83.2
0075	74.3	68.3	78	80.2	86.9	87.6

Implant

To design the implants, a computerized tomography (CT) scan was made of each sheep 6 weeks before the surgery date. The CT data was provided in Digital Imaging and Communications in Medicine (DICOM)-format to CADskills BV engineers (Ghent, Belgium). They reconstructed the images to a standard template library (STL)-file, performed the resections virtually, and then designed the implants using Geomagic Freeform Plus (3D Systems, Rock Hill, SC, USA). All implants were designed for the left TMJ, and the implant design, number of screws, and screw diameters were as similar to the human design as possible. The lengths and positions of the screws were predetermined during implant design and were based on the amounts of bone and the adjacent anatomical structures (e.g. the inferior alveolar nerve). Subsequently, both the skull and the implant associated with the first sheep were 3D-printed using a fused deposit model 3D-printer (Makerbot, MakerBot Industries, Brooklyn, NY, USA) and a stereolithographic resin 3D-printer (Formlabs II, Formlabs, Sommerville, MA, USA), respectively (Fig 1). The resulting prints were used to make further implant design improvements.

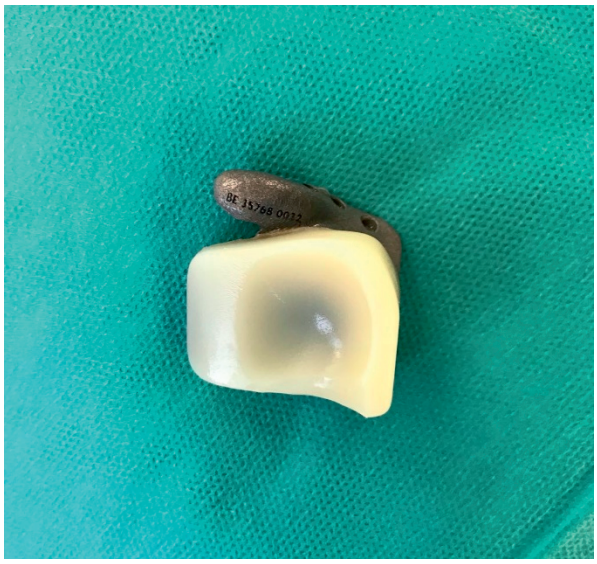


Fig. 2: Fossa component

The skull base component consisted of two parts. One part was printed from a medical grade titanium alloy grade 23 extra low interstitials (ELI-23), which fit over the glenoid fossa and articular eminence and was screw-fixed to the zygomatic arch. The other part faced the condyle and was made out of a concave computer numeric controlled milled vitamin-E enriched ultra-high molecular weight polyethylene (UHMWPE), which was then ɣ-radiated to increase the amount of crosslinks within the polyethylene. Both parts were connected via non-disclosed pressure, time, and temperature settings in a scaffold layer at the condyle-facing side of the titanium component. The titanium was alumina (550-m grit) micro-shot-peened and oxalic acid etched to promote osseointegration. Fixation was performed using five titanium screws (Gr 5, diameter 2.0 mm, length 5 mm to 13 mm; Surgi-Tec NV, Ghent, Belgium) (Fig 2).

In addition to a lattice structure at the bony interface, the ELI-23 titanium alloy ramal component had a large connecting lattice structure in the condylar neck and a tunnel through the condylar neck with a small hook-like extension on the lateral side. The tunnel and hook were used to thread PDS 0 suture material, which was passed through the preserved bony or fibrocartilaginous enthesis of the LPM and fixed to the ‘hook-like’

extension. The lattice structure interior (500-m interconnected pores with a diamond unit cell structure) provided an optimal region for bony union of the enthesis with the transplanted bone particles (Fig. 3). Six of the ramal components' condylar heads were treated using a HadSat diamond-like carbon coating; seven remained untreated. Fixation of the ramal component was performed using an average of six titanium Gr 5 screws (Surgi-Tec, Ghent, Belgium; diameter 2.3 mm, length 13 to 17 mm).

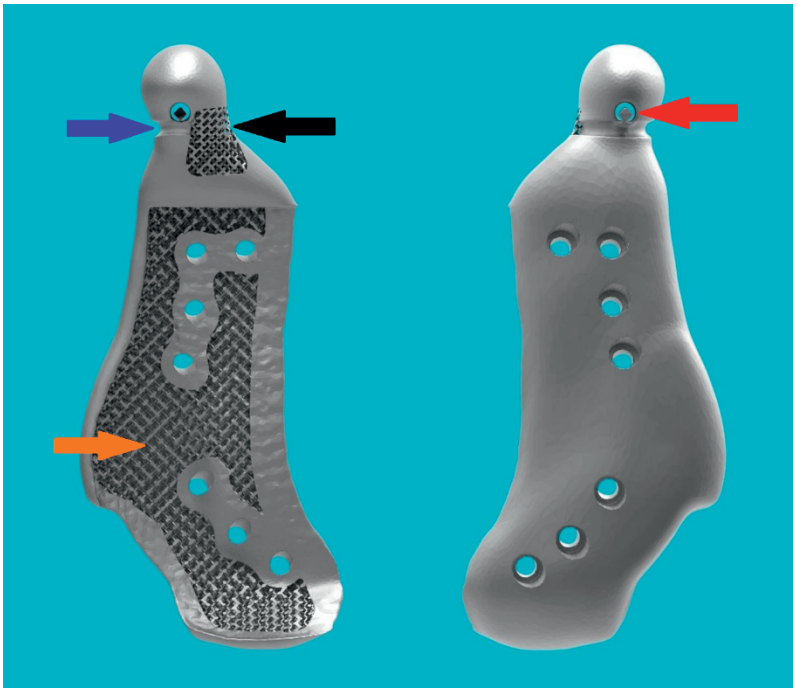


Fig. 3: Three-dimensional rendering of the ramal component with lattice structure and tunnel for fixation of the enthesis. Red arrow: subcondylar tunnel and hook-like extension for fixation of the enthesis; blue arrow: subcondylar groove to guide enthesis' sutures; black arrow: lattice structure for enthesis' bony ingrowth; orange arrow: lattice structure for mandibular bony ingrowth into the ramal component.

Surgical protocol

Each ewe was first sedated using xylazine (0.1 mg/kg) and then shaved over the left mandible. Anesthesia was subsequently given using ketamine (4 mg/kg) and midazolam (0.2 mg/kg) for induction. The sheep was then intubated with a cuffed tube and anesthesia was maintained using mechanical ventilation with an oxygen-isoflurane mixture. Surgical site

was aseptically prepared. Xylocaine (1%) with 1/80.000 epinephrine was locally infiltrated at the jaw angle and over the zygomatic arch to achieve local vasoconstriction and anesthesia.

A 4-cm incision was made over the posterior lower border of the mandible. The lateral surface and the angle of the mandible were exposed. A pre-auricular, s-shaped incision inferior to the zygomatic arch was used to expose the TMJ, and a subperiosteal connection was made with the previously prepared lateral side of the vertical ramus. An ELI-23 titanium cutting guide was screw-fixed to the vertical ramus to aid in performing the condylectomy. The joint space was then opened and the temporomandibular disc was removed. The condylectomy was then performed. The bony attachment of the lateral pterygoid muscle to the condyle was preserved in six sheep. In seven sheep, only the fibrocartilaginous part of the muscle insertion was unintentionally preserved. In two sheep, it was unclear whether either or both could be preserved. Compared with humans, it was difficult to keep the tendon inserted in the pterygoid fovea during dissection and removal of the rest of the condylar process. In our experience, in humans there is a larger bony insertion for the LPM to attach to the condyle. Sheep have a mostly fibrotic insertion into both the intra-articular disc and condyle. A PDS 0 suture (Ethicon, Sommverville, NJ, USA) was threaded through either the bony part of the enthesis or the fibrocartilaginous insertion.

The fossa component was first placed using a dummy version and was fixed using five screws. Bone from the resected condyle was harvested, crushed, and mixed with fibrin sealant (Tisseel, Baxter, Deerfield, IL, USA). It was then manually pressed into the pterygoid fovea scaffold (Fig 4a, b). The ramal component was then fit in place while the PDS 0 was threaded through the subcondylar tunnel and then tied to the small hook as soon as the ramal component was fixed to the mandible (Fig 5). Using the suture to pull the bony enthesis to the bone in the scaffold proved difficult because the UHMWPE of the fossa component was interfering in a caudal direction. All UHMWPE parts were scalpel-reduced at the anteromedial side to facilitate routing the enthesis or tendon/fibrocartilaginous part of the disc.

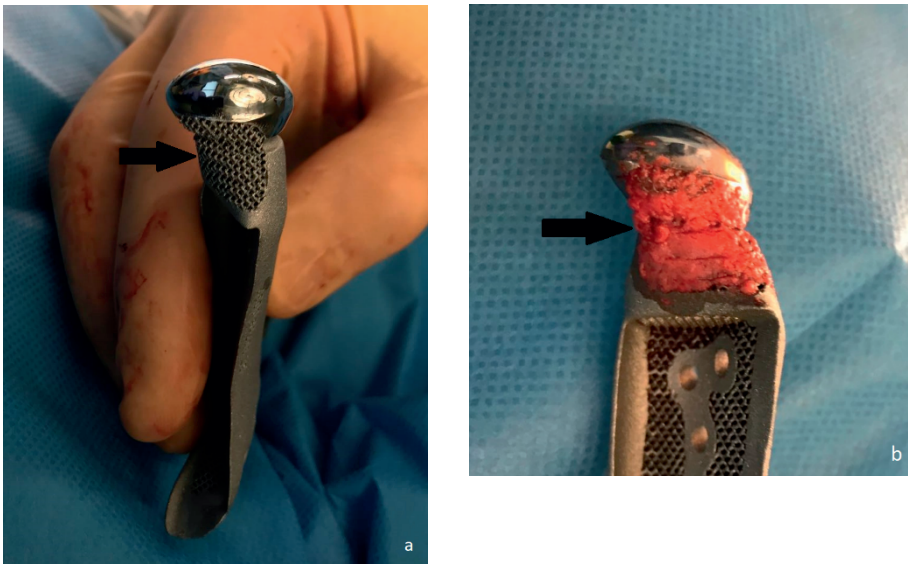


Fig. 4: (a) Lattice structure before bone application (black arrow).
(b) Lattice structure with mixture of bone and fibrin sealant (black arrow).

This excess volume of UHMWPE resulted from using the human type of fossa UHMWPE design, in which there is to reckon with a lower total muscle mass of the lateral pterygoid muscle, resulting in less spherical obstruction. As we were not able to completely segment the LPM during the design process of the implant, this led to a slight underestimation of the total muscle volume. All UHMWPE parts were altered in such a fashion that it did not affect the articulating surface, nor that the LPM experienced any obstruction after correction.

The articular capsule and soft tissues were closed in multiple layers and a compressive bandage was placed for one week. Per-operative pain control was achieved using buprenorphine (6 µg/kg) administered via the intravenous route.

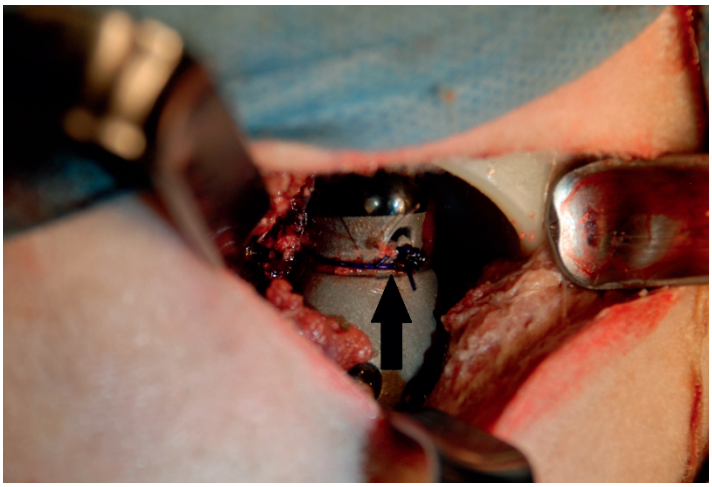


Fig. 5: Mandibular component fixed with enthesis fixed through the subcondylar tunnel. Black arrow: PDS 0 suture (Ethicon, Sommverville, NJ, USA) threaded through the subcondylar tunnel, run around the subcondylar groove, and fixed to the hook-like extension.

Post-operative protocol and euthanasia

Each ewe was kept alone during the first post-operative week. Heart rate, respiratory rate, body temperature, dietary status (appetite, whether water consumed), and excretions were recorded daily. The compressive bandage was replaced daily, and the wound was examined for swelling and signs of infection. Blood samples were taken on a daily basis during the first postoperative week to check the white cell count and formula. Ionogram and inflammatory parameters were checked twice the first week. If necessary, meloxicam (0.5 mg/kg) was used for pain management. Buprenorphine (5 µg/kg) was added if meloxicam was insufficient for proper pain control. During the first week, only soft, moistened food was given to the ewes. After 1 week, they were confined together in a large indoor pen, and blood samples were taken and a clinical examination was performed once per week.

In one sheep, submentovertical and lateral post-operative radiographic images were acquired shortly after implantation to investigate some observed mandibular asymmetry. Both images showed correct placement of the implant. At 1 month, 3 months, and 6 months after surgery, CT images were taken of two randomly selected sheep to evaluate implant position and condition, bony ingrowth into the scaffolds, and attachment of the enthesis.

The 14 animals were euthanized 9.5 months after implantation. A clinical evaluation was done and blood samples were taken before euthanasia. Xylazine (0.1 mg/kg) was administered for induction and heparin (300 IU/kg) was given to prevent coagulation. Induction was done using a combination of ketamine (4 mg/kg) and midazolam (0.2 mg/kg). The product administered to achieve euthanasia cannot be disclosed per agreement with the animal laboratory. After euthanasia, each ewe was decapitated, the skull was cut in half, and the right side was disposed of, except for three randomly selected sheep. In these sheep, specimens were kept for comparative analysis. Further decomposition of the left side of the skull was performed by skinning the specimen, removing the neurocranium, and removing the anterior half of the mandible and maxilla. The eye and upper half of the orbit were also removed.

Specimens were fixed using immersion in formaldehyde (4%) for 2 months. A post-mortem CT-scan of each specimen was then performed (slice thickness 0.7 mm, 500 mAs, 120 kV, reconstruction thickness <1 mm; Revolution, General Electric, Fairfield, CT, USA). The images were analyzed using Agfa IMPAX 6, Agfa-Gevaert NV, Mortsel, Belgium) and were reconstructed into STL-files and 3D-renders using Mimics inPrint 3.0 (Materialise, Haasrode, Belgium). The goal of the imaging analysis was to determine the presence or absence of enthesis reconstruction.

The peri-articular tissues were resected, stained using hematoxylin-eosin, and embedded in paraffin. The goal was to examine local adverse tissue reaction to the implant materials, infection, and wear-induced synovitis, which will be reported separately. The CT scan and 3D-reconstruction were used to determine where and how sections should be made through the lateral pterygoid muscle and its enthesis, and through the implant, to allow for histological analysis of the enthesis and its connection to the scaffold. Masson-Goldner (M-G) trichrome stain was used for the histology. (11)

Results

Weight and cinematics

During the post-operative period, each sheep was weighed and evaluated weekly. The average preoperative weight was 73.4 kg, and an average loss of 8.4 kg occurred during the first post-operative week. The average weight then declined even more by 3 months after implantation, but then increased and was 72.7 kg at the end of the observation period (Table 1).

Sheep have a preferred side for rumination, but they will switch sides.(12) To ascertain that the ewes did not perform only left-sided laterotrusion, video recordings of the right-sided rumination movements of two randomly selected sheep were made before surgery. Videos of 2 sheep that pre-operatively randomly selected, were also made at 1 week, 3 months, and 9 months after surgery. They revealed the presence of laterotrusive movement to the right side, which indicated unilateral contraction of the LPM on the operated side. The LPM was still attached to the implant and allowed for laterotrusive movement to the contralateral side (Video 1-3).

Radiology

The CT scans were evaluated for the presence of a bony insertion of the LPM that was in contact with the subcondylar lattice structure. The operative notes described whether a bony piece of the enthesis or whether fibrocartilaginous tissue was re-attached to the implant (Table 2).

The follow-up scans at 1 month after surgery revealed good positioning of the fossa component in ewe 1724. The ramal component was not yet well-integrated with the mandible. However, as expected, there was callus formation between the mandible and the ramal component. There was also a soft tissue connection with a thickness of 3mm between the implant and the enthesis. In comparison, the post-mortem scan showed both bony and soft tissue connections between the implant and the scaffold. This result can be explained by formation of heterotopic bone surrounding the ramal component, which provided additional support and stability and allowed for better integration. The results for the second sheep that was scanned, ewe 8087, also indicated there was good positioning of both

Table 2: Per-operative reconstruction and post-operative CT evaluation connection between the lateral pterygoid muscle (LPM) and the implant scaffold.

Sheep #	Per-operative	1m post-op	3m post-op	6m post-op	Post-mortem
3520	Bony				Soft tissue
8087	Unclear	Bone			Bone
2177	Bony			Absent	Absent
5158	Unclear		Bone		Bone + Soft tissue
2549	Fibrocartilaginous			Absent	Absent
4249	Fibrocartilaginous				Bone
0032	Fibrocartilaginous				Soft tissue
7998	Bony		Absent		Absent
4246	Bony				Bone + Soft tissue
1724	Bony	Soft tissue			Soft tissue
4248	Bony				Bone + Soft tissue
8787	Fibrocartilaginous				Absent
4473	Fibrocartilaginous				*Absent
0075	SHAM	SHAM	SHAM	SHAM	SHAM

* Due to dissection

components and initial osseointegration of the ramal component. There was a good attachment of the enthesis onto the scaffold, and there were several centers of early, non-mineralized bone between the enthesis and scaffold and the enthesis and the mandible. Early heterotopic osseous centers lateral to the mandibular implant were also found (Table 3).

The 3-month in vivo CT scans of the sheep marked 7998 revealed that despite the intra-operative bony connection that was achieved, the enthesis was no longer connected to the implant. Instead, there was an osseous connection between the mandible and the enthesis of the LPM. Both the fossa and ramal component were well positioned, and there was good integration of the ramal component. The second sheep that was scanned at 3 months after surgery, ewe 5158, had good positioning of both the fossa and ramal component, good integration of the ramal component, and a bony connection between the attached enthesis and the implant. As with the other sheep, there was also a bony connection between the mandible and the enthesis. Although both TMJR components were well-positioned and integrated, heterotopic bone was formed

Table 3: Type of connection formed post-mortem between the mandible and lateral pterygoid muscle (LPM), based on CT evaluation

Sheep #	Connection type
3520	Soft tissue connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
8087	Bony connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
2177	Boney connection between the mandible and reattached enthesis
5158	Partial bony and soft tissue connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
2549	Absent
4249	Bony connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
0032	Soft tissue connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
7998	Bony connection between the mandible and reattached enthesis
4246	Partial bony and soft tissue connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
1724	Soft tissue connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
4248	Partial bony and soft tissue connection between the implant scaffold and reattached enthesis Bony connection between the mandible and reattached enthesis
8787	Absent
4473	*Absent
0075	SHAM

* Due to dissection

laterally from the implant and appeared to connect the mandible to the skull base. A fracture of this heterotopic bone prevented joint ankylosis. This fracture was likely due to continued movement of the mandible.

One of the two sheep scanned at 6 months after surgery, # 2177, had a bony connection between the enthesis and the mandible, as was found in the previous two sheep. However, there was no bony connection between the enthesis and the scaffold. There was heterotopic bone formation around the lateral side of both the ramal and the fossa components. There was also a slight latero-inferior displacement of the fossa component, showing non-integration onto the articular tubercle. The scan of the second sheep, ewe 2549, revealed good positioning of both TMJR components, but there was no enthesis reconstruction with osseous or fibrotic characteristics.

The post-mortem CT scans revealed four different conditions (Table 3). In four of the ewes, there was no reconstruction between the implant and the LPM, with complete absence or a large distance between the LPM and the implant. In one case, the post-operative specimen was poorly dissected and there was destruction of the enthesis reconstruction as a result of this. In two of the sheep, the ostectomized bony enthesis was sutured to the scaffold in the condylar neck during the implantation surgery. In the other two cases, the fibrocartilaginous tissue was re-attached.

Three sheep had purely soft tissue connections between the ostectomized bony insertion of the LPM and the lattice structure of the implant. Two of these three sheep had a per-operative bony reattachment, and in one sheep the fibrocartilaginous tissue was re-attached to the subcondylar scaffold (Fig. 6).

Three sheep had a combination of partial bony and partial soft tissue enthesis attachment to the scaffold (Fig. 7). The average thickness of the soft tissue attachment was significantly less compared with that of the sheep who only had a soft tissue connection (i.e., 0.3 to 0.5 mm (average 0.4 mm) and 0.5 to 0.9 mm (average 0.7mm), respectively) (Table 4). In one of these three sheep, the type of tissue that was preserved on the LPM stump during per-operative fixation was unclear; the bony enthesis was preserved in the other two sheep.

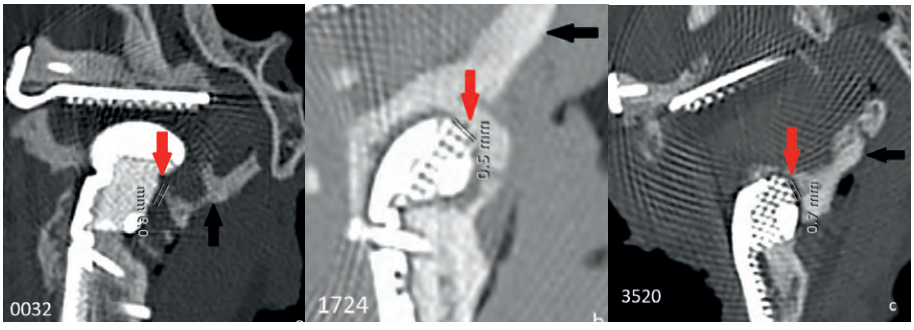


Fig. 6: Soft tissue connection between lateral pterygoid muscle (LPM) and the implant scaffold with measurement. (a) Sheep no. 0032; (b) Sheep no. 1724; (c) sheep no. 3520. Red arrow: soft tissue connection between the LPM enthesis and scaffold. (a) 0.9 mm; (b) 0.5 mm; (c) 0.7 mm. Black arrow: partial calcification of the LPM.

In two sheep, there was uniquely bony ingrowth of the enthesis into the scaffold (Fig. 8). In one of these ewes, per-operative reconstruction of the enthesis was performed using fibrocartilaginous tissue. In the other ewe, it was unclear whether a bony or fibrocartilaginous reconstruction had been achieved.

No significant difference could be found between those sheep whom had a boney part of the enthesis attached to the scaffold and those sheep in whom an approximation of fibrocartilaginous tissue was achieved, with concern to the formation of either a new boney or soft tissue connection ($p>0.05$).

In 10 out of 13 sheep, an additional bony connection between the mandible and the reattached LPM was found below the ostectomy line (Fig. 9). In one of the remaining three sheep this connection could not be found due to postmortem dissection too close to the implant that resulted in loss of tissue medial to the implant.

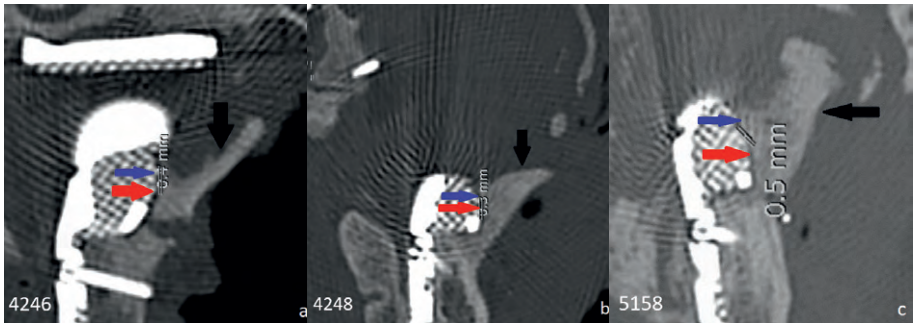


Fig. 7: Partially soft tissue connection between lateral pterygoid muscle (LPM) and the implant scaffold with measurement. (a) Sheep no. 4246; (b) sheep no. 4248; (c) sheep no. 5158. Red arrow: partial soft tissue connection between the LPM enthesis and scaffold. (a) 0.4 mm; (b) 0.3 mm; (c) 0.5 mm. Blue arrow: bony connection between the LPM and the implant scaffold. Black arrow: partial calcification of the LPM.

In four sheep, an aseptic loosening and subsequent displacement of the fossa was found (Table 5). In three out of four sheep, a latero-inferior displacement occurred, while in one ewe, an infero-dorsal displacement was seen. All four sheep developed heterotopic ossification surrounding the displaced fossa component, reaching towards the mandibular component. Nevertheless, the bearing surface as well as function of the TMJ remained intact in these sheep.

Table 4 Radiological distance between implant scaffold and boney attachment of the lateral pterygoid muscle (LPM).

Sheep #	Distance implant - bony insertion
3520	0.7mm
0032	0.9mm
1724	0.5mm
5158	0.5mm
4246	0.4mm
4248	0.3mm

Discussion

Food particles need to be broken down to pieces smaller than 1 millimeter, in order to be swallowed. The first breakdown of these food particles occurs during initial chewing, followed by chewing during rumination.(9) Sheep spend about 4 hours per day eating and about 8 hours ruminating .(9) This masticatory movement is heavily dependent on laterotrusive movement, which is generated through what Allouch calls 'the unilateral group'.(13,14) This group of masticatory muscles includes the medial and lateral pterygoid muscle. These structures are also referred to as the internal and external pterygoid muscle, respectively. The latter inserts onto the medial surface of the mandible (above the mandibular foramen) and onto the condyle and disc.(14). While the internal/medial pterygoid muscle brings the mandible into a medial and upward position, the external/LPM creates a protrusive movement, as in humans. This muscle and its insertion were dissected intraoperatively and reattached onto the prosthesis.

When placing a TMJR with loss of the LPM, a test subject could lose a significant amount of weight due to reduced laterotrusive function that results in a loss of masticatory efficiency. This outcome did not occur in this group of sheep.

In humans, the lateral pterygoid muscle consists of a superior and inferior belly. It is the only masticatory muscle with horizontally oriented fibers.

(15) Murray et al.(16) suggested that the inferior part can be further divided into four zones. They used fine-wire electrodes to measure LPM activity and found a total of 374 single motor units. The superomedial part initiates protrusive and contralateral movements, and the superolateral and inferomedial parts follow through with these movements. The specific function of the inferolateral part has not been determined. The generally accepted hypothesis is that the superior belly has a role in retrusive movements and closing of the jaw, but Murray et al.(16) found this hypothesis to be false. They found that the superior belly also participates in contralateral and protrusive movements. The medial part does not display any additional activity, but the lateral part also activates during retrusion and closure of the mouth. Using EMG-based research, Huang et al.(17) also found that the inferior belly is the principal muscle for laterotrusive movement when the teeth are in contact; the other masticatory muscles have at most a facilitatory role.

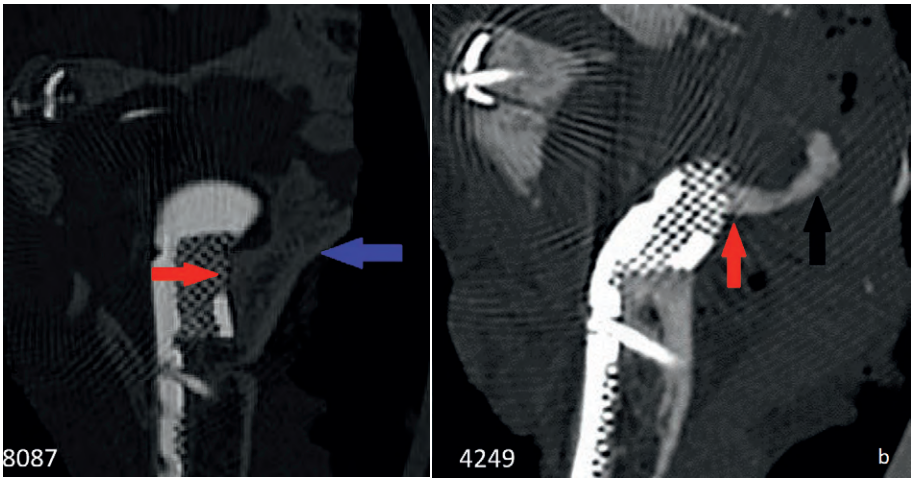


Fig. 8: Bony connection between lateral pterygoid muscle (LPM) and the implant scaffold. (a) Sheep no. 8087; (b) sheep no. 4249. Red arrow: bony connection between the LPM and the implant scaffold; black arrow: partial calcification of the LPM; Blue arrow: significant calcification of the LPM.

To our knowledge, there are only two articles that discuss the reinsertion of the lateral pterygoid muscle when placing a TMJR. Collins et al.(18) attempted to reattach the lateral pterygoid muscle below the point of the condylectomy in 20 joints. They then compared functionality to

four joints in which no reconstruction was performed. They performed a condylectomy and dissected the LPM from the anterior aspect of the condyle, then fixed the muscle to the anterior aspect of the condylar neck in the sigmoid notch region using 2 No 0 polyglactine 910 (Vicryl Ethicon, Sommverville, NJ, USA) sutures. They found significant differences in both laterotrusive and protrusive movements between the two patient groups; the patients who had a reconstruction had a better outcome. Despite these positive results, this research group did not publish more studies on this topic.(18) When Mommaerts examined the reconstruction of the LPM enthesis, on which this experiment was based, he found that a reinsertion of the LPM was possible, given the use of a titanium lattice structure in the condylar neck to allow for boney ingrowth.(7)

When attempting to create bony ingrowth into a scaffold, specific conditions must be met to achieve a good outcome. The implant and scaffold surfaces need to be sufficiently osteoconductive to stimulate bone cell growth. The environment also needs to be osteoinductive to promote differentiation of mesenchymal stem cells (MSCs) into (pre)osteoblasts. Good osteogenesis also must also be achieved (i.e., sufficient MSCs, osteoblasts, and osteocytes need to be present). In a natural situation, the mandible is covered by periosteum, however when performing a resection and placing an implant, the periosteum can be lost. This difference is important because the inner layer of the periosteum (i.e., the cambium) includes differentiated osteogenic progenitor cells, fibroblasts, and osteoblasts.(19,20) The cambium has significant osteoblastic potential, which has a role during fracture healing. However, not all bones are covered by periosteum. Sesamoid bones (e.g., the patella) are not covered by periosteum, but are capable of osseous healing after a fracture.(21)

As described by both Shapiro and Colnot, several types of bone repair can occur after a fracture.(22,23) The first and primary type is endochondral; a hematoma forms around the fracture, which is stabilized by the periosteum and the surrounding soft tissues. Cells from the cambium start proliferating and differentiating, and membranous ossification starts at the periphery of the fracture. Meanwhile, a central mass of cartilage is also formed. This mass ossifies via endochondral ossification. A clear

periosteal reaction can be observed on radiographs. This type of repair can still occur during conditions of macro- or micromotion. In the case of absence of periosteum and absence of motion, osteoprogenitor cells are derived directly from the Haversian canals when there is direct contact between the two bony pieces. This type of healing is “contact repair”. If there is a gap between the two pieces, lamellar bone is formed directly or woven bone is formed first and then transformed into lamellar bone if the gap is larger. This type of bone repair is also known as (direct) transformational bone repair.(22)

Periosteum was not preserved in our sheep surgeries, and there were no Haversian canals on the prosthetic side. Therefore, only transformational bone repair can occur as a possible form of repair with associated osseointegration of the LPM tendon. This means that the material to which the LPM attaches must be osteoinductive and osteoconductive. Compared with cobalt-chromium-molybdenum alloy, the elasticity of titanium alloy Gr 23 is closer to that of bone. Its roughened surface has good biocompatibility and is osteoconductive.(24) Titanium is considered a bio-inert material that does not possess any osteoinductive properties. However, Tamaddon et al.(25) performed in vitro and in vivo experiments and found that even untreated porous titanium scaffolds can be osteoinductive. Many studies have found that as surface roughness increases, the connection between the implant and the adjacent bone becomes stronger. Yeniyol et al.(26) found that oxalic acid etching improves surface roughness by creating micro-pitting. It also improves cell adhesion, which allows for better osteogenesis. The use of ELI-23 titanium allowed for both an osteoinductive and osteoconductive environment, which also allows cementless fixation of titanium implants in orthopedic surgery.(27,28)

Sufficient numbers of MSCs, osteoblasts, and osteocytes needed to be present after the periosteum was stripped during the resection. Therefore, part of the resected bone was ground, mixed with a fibrin sealant and applied to the scaffold to provide high concentrations of osteoinductive cells. Spalthoff et al.(29) found that bone marrow aspirate (BMA) provides an abundant and reliable source of growth factors and osteogenic cells.

They examined the use of β-tricalcium phosphate (β-TCP) as a matrix material for seeding and which specific osteogenic cells can improve osteoinductivity. They found that in the group where the β-TCP cylinders were mixed with BMA mixed with crushed bone, the β-TCP is largely replaced with osseous tissue and the cylinder becomes hard and inflexible. The use of venous blood or solely BMA results in significantly less or even no bone formation. They concluded that the combined use of cancellous bone and BMA provides the best results for in vivo heterotopic bone regeneration.(30) Mommaerts applied this technique in humans but one of the downsides to BMA usage is that it is an expensive procedure.(7) One of our goals was to exclude the use of MSCs and bone marrow aspirate (BMA) at the scaffold site, to evaluate if it has any merit over only using autologous grounded bone, to establish a reconnection of the enthesis.

While all three factors for bone regeneration and integration were mostly provided, only two of the sheep had radiological bone formation that was up against the scaffold. There was no formation of soft tissue in between the scaffold and the enthesis. Three sheep had a connection that was both soft tissue and bony. A first remark that has to be made concerning these findings, is the spherical hindrance by the UHMWPE part of the fossa during surgery. While the height was reduced, there was still some difficulty as to achieve proper positioning of the LPM enthesis. Due to the height and width, other than in its human counterpart, it was not always possible to evaluate if the fixation of the enthesis was directly against the scaffold, forming a potential cause for non-integration.

Furthermore, in addition to creating an optimal environment for osteogenesis, implant stability is also important. Pilliar et al.(31) and Burke et al.(32) found that movement between the bone and the implant should be less than 28 μm for bone ingrowth to occur. Fibrous tissue can form if movement is more than 150 μm, especially when repetitive micromotion occurs. During orthopedic surgery, large compressive forces are applied to achieve good fixation to prevent the forces to which the implant is exposed to during post-operative loading from exceeding the forces necessary to dislodge the implant. The amount of stability can be increased by increasing surface roughness and the total contact surface

between the implant and the bony surface (limited in our experiment). In the absence of good initial stability, successful osseointegration between the implant and its bony contact surface will be severely limited.(33)

This was a significant limitation of our experiment, because it was impossible to prevent the sheep from performing laterotrusive movements using their LPMs. Activation of this muscle can create micromovements between the enthesis attachment and the implant scaffold and result in insufficient stability. This relationship seems relevant to three out of five of the sheep. Interconnecting heterotopic ossification (HO) was found around the lateral sides of both the fossa and mandible, which possibly resulted in additional stabilization between the LPM and implant. However, this finding was not present for the other two sheep that had (partial) bony reattachment of the LPM enthesis, no displacement of the fossa, nor any heterotopic bone formation (Table 5).

Table 5: Fossa and ramal component positioning

Sheep #	Ramal component	Fossa component
3520	Normal	Normal
8087	Normal with lateral incapsulation	Normal with heterotopic bone formation
2177	Normal	Latero-inferior displacement with heterotopic bone incapsulation
5158	Normal with lateral incapsulation	Infero-dorsal displacement with heterotopic bone incapsulation
2549	Normal	Normal
4249	Normal	Normal
0032	Normal	Normal
7998	Normal	Latero-inferior displacement with heterotopic bone incapsulation
4246	Normal	Normal
1724	Normal	Normal
4248	Normal with lateral incapsulation	Latero-inferior displacement with heterotopic bone incapsulation
8787	Normal	Normal
4473	Normal	Normal
0075	SHAM	SHAM

Unlike sheep, humans can be asked to consume a liquid to soft diet and only perform depression and elevation of the mandible during the first 6 weeks after surgery. This restriction can prevent LPM micromovements and maximize the chances of good ingrowth. However, restoration of the maximal 'range of motion' during the post-operative recovery period could be delayed.(34) While a limitation in movement might lead to concerns with regard to HO and possible ankylosis, several remarks have to be made. Firstly, none of the patients that were included in the study by Mommaerts that were treated with LPM reinsertion, showed heterotopic bone formation.(7) Secondly, with consideration of the per-operative difficulties that were experienced as to evaluate if the enthesis came in direct contact with the subcondylar lattice structure, sometimes residual bone chips were added to the assumed gap. This in turn might have led to a hyperostotic reaction in some sheep. Thirdly, evidence seems to indicate that by filling out the negative space around the joint, by means of an autologous fat graft for instance, the risk of heterotopic ossification can be reduced as well.(35)

Lastly, while five ewes developed heterotopic bone formation, four of these sheep presented themselves with an aseptic loosening and subsequent displacement of the fossa (Table 5). Despite the fossa being designed to achieve a perfect anatomical fit, the aseptic loosening most likely occurred due to micromovements between the fossa and the underlying bone. This resulted in bone resorption underneath the titanium surface of the fossa.(36) A possible cause was the use of 2mm diameter screws for fixation of the zygomatic component. Considering the higher mastication rate and mainly laterotrusive movement, the fossa is subjected to higher forces compared to its human counterpart. While a higher screw diameter increases the fatigue resistance and lessens the risk of failure as excessive stress in the bone surrounding the screw, the opposite is true for screws with a smaller diameter.(37,38) This excessive stress can lead to bone resorption and implant failure.(36,39) As a result, using 2mm diameter screws under this higher load compared to its human counterpart, can very well have resulted in insufficient fixation of the fossa in four out of 13 ewes. Furthermore, in humans a soft diet can be maintained during the period of osseointegration, limiting the amount of force the TMJ is

subjected to. While no loosening or displacement of the fossa component was seen in humans, further trails in humans are needed to support this statement.(7)

Although no evidence is available concerning HO following TMJ implant displacement, a significant effect was found between the occurrence of HO and the displacement of the fossa component. ($p < 0.01$). As trauma and fractures have been validated as causes for HO in orthopedic literature, as well as TMJ ankylosis, we would advise not to apply this technique of enthesis reconstruction in young patients, nor in patients suffering from an ankylotic joint.(40,41) This to avoid any risk of (re-)ankylosis, until further trials in humans are done.

The effects of imaging artifacts should also be considered. Because the TMJR was completely made of titanium, artifacts that caused decreases in image quality might have affected the results. Titanium has a high density, so low-energy photons are more absorbed than high-energy photons, leading to beam hardening.(42) This effect is even more apparent between an implant and other high density materials or tissue such as bone.(43) When photons change direction they can end up in the wrong detector, which results in dark streaks in the areas of photon loss.(42) These artifacts can lead to blurred inaccurate images.(42,44) Limiting these artifacts was attempted by decreasing the reconstruction thickness, as proposed by Moon et al.(45) However, the kilovoltage was 120 kV, and an increase to 140kV might have resulted in further reduction of metal artifacts.(45) A metal artifact-reducing sequence (MARS algorithm) was used as to improve the image during processing. Nevertheless, due to the high density and possibly due to the irregular shape of the scaffold, current artifact removal software is unable to completely remove artifacts.(42) The darkened areas can reduce the accuracy of the evaluation between the reconstructed enthesis and the implant, and increase the need for histological analysis of the scaffold and enthesis insertion.

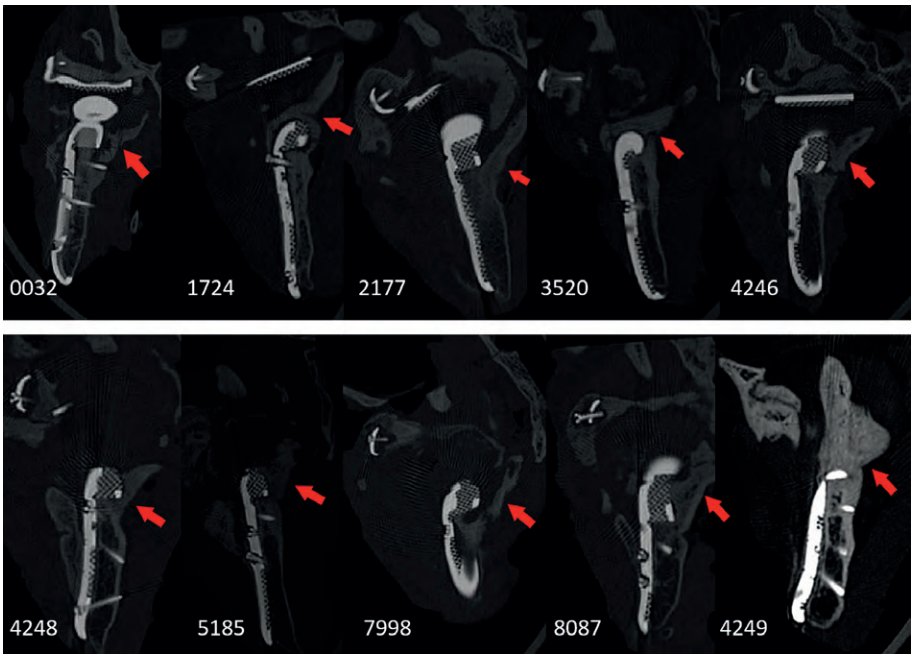


Fig. 9: Bony connection between the enthesis and mandible. Red arrow: bony connection between the lateral pterygoid muscle (LPM) and the mandible.

Despite only five sheep showing ingrowth of the bone into the scaffold, the LPM remained well-connected in 10 out of 13 sheep, either through the formation of an attachment to the scaffold, and/or due to the lateral pterygoid muscle reinserting on the mandibular bone below the osteotomy. These sheep had good laterotrusive movement and clinical function. The typology of the enthesis provides one explanation for these findings. According to Benjamin et al.(46) there are two types of enthesis (i.e., fibrous and fibrocartilaginous). Fibrous entheses are present in several large muscles (e.g., the deltoid muscle) and are less prone to overuse compared to fibrocartilaginous entheses. This group is then further divided into the periosteal and the bony types, which attach to the periosteum or directly into the bone. Based on the cinematic imaging results, weights, and radiological findings, the findings for our sheep might have been affected by this type of enthesis. Further histological analysis of enthesis reconstruction is needed.

In sheep, the masseteric muscle can be dissected into three distinct layers. The most extensive layer also exerts a protrusive force.(14) This characteristic suggests that the laterotrusive movements seen during the clinical analysis were due to these fibers rather than the LPM. However, the previously discussed evidence negates this argument.

When using larger and more complex scaffolds, sufficient blood supply is needed to provide adequate nutrition to the osteogenic cells.(47,48) The outer layer of the periosteum mainly consists of collagen and fibroblasts, but it also contains the highest density of blood vessels and provides vascularization to adjacent bone and muscle.(49) The use of periosteal flaps and free periosteal grafts to provide vascularization and an osteoinductive and conductive environment to bone grafts is not new.(20,50) In 10 out of 13 sheep, a bony connection was formed between the osseous mandible and the enthesis. Important to notice is that the distance from the insertion of the muscle to the bony mandibular margin was much smaller in the TMJR that were placed, compared to the design for human use. This was due to a reduced height of the condylar neck in the implants that were placed. As such it is possible that this boney connection was formed due to the periosteal sleeve still being intact, providing not only the necessary environment for bone formation to occur, but also the necessary vascularity, which might have been absent near the scaffold.

Gallardo-Calero et al.(51) found that intramembranous ossification occurs in areas where a bony defect is covered with a vascularized periosteal flap. However, Leucht et al.(52) found that intramembranous ossification occurs when mandibular periosteum is transplanted onto a tibial bony defect. Endochondral ossification occurs when tibial periosteum is transplanted onto a mandibular defect. These findings indicate that the origin of the periosteum affects the repair. Leucht et al.(52) concluded that in craniomaxillofacial and orthopedic surgeries, regardless of the origin of the periosteum, it allows for bone regeneration independent of the type of repair that occurs. Therefore, the preservation of periosteal tissue could be considered to maximize the possibility of bony integration of the enthesis into the scaffold. However, because a soft diet and restriction

in movement can be applied in humans, inclusion of a surgically-difficult vascularized periosteal flap might not be necessary, urging the need for trial in humans with strict limitations on laterotrusion during the first six post-operative weeks.

A first limitation we encountered in this study were the difficulties with concern to the reattachment of the LPM. While these were mainly due to the anatomical differences of the sheep's TMJ compared to its human counterpart, these could be facilitated by providing muscle relaxant medication during surgery, when performing the condylectomy. A second solution could be to alter the design of the condylar component, by adding an extension at the level of the neck with a lattice structure. This can help reduce the distance between the scaffold and the tendon, allowing for an easier fixation.

A second significant limitation we encountered during our research, was the impossibility to limit immediate post-operative laterotrusive movement, as previously discussed. While in human patients, besides prohibiting laterotrusive movements for purpose of rehabilitation, a liquid to soft diet is indicated for at least three weeks' time in the post-operative phase. In the present study a similar dietary program could not be implemented considering the particular ruminant digestive anatomy and physiology that cannot sustain longer periods of lack of roughage due to risk of dysbacteriosis.(53) This limited the duration of dietary restrictions to only one week after implantation.

Lastly the exact typology of the enthesis reconstruction (i.e., fibrous and fibrocartilaginous) could not be determined by means of radiological imaging. In order to gain a more complete insight into this matter, further histological analysis will be conducted.

Conclusion

The study shows great promise for improvements upon the current approach to TMJR in terms of replacing the joint itself and reconstruction

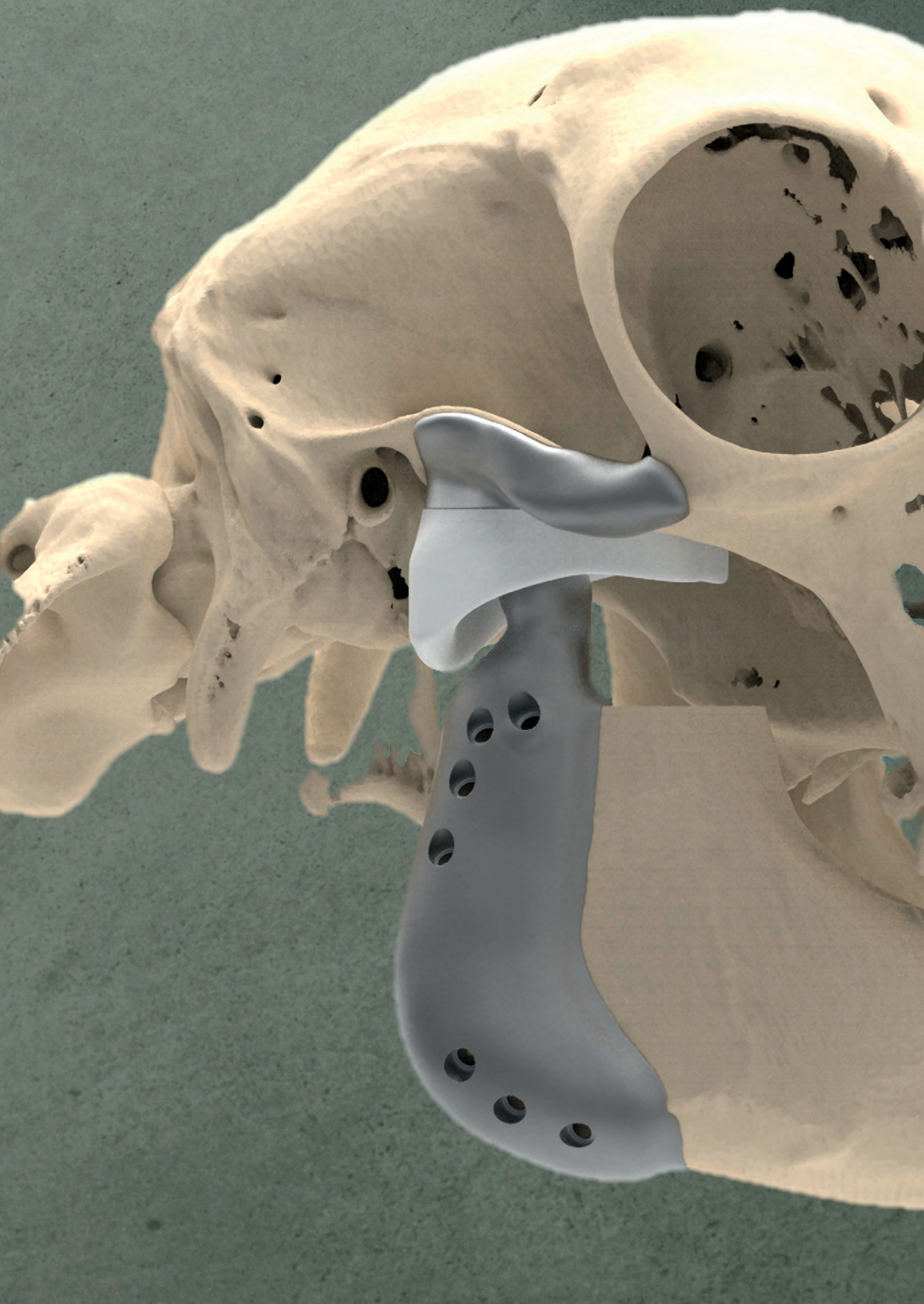
of the lateral pterygoid muscle's insertion and function. However, enthesis reconstruction is most likely not warranted in young children, nor in cases of TMJ ankylosis, because of risk of (re)ankylosis. Further optimization of the reattachment technique and scaffold position and surface area should be done, as well as trials in humans as to evaluate the effect of proper revalidation.

References

1. De Meurechy N, Mommaerts MY. Alloplastic temporomandibular joint replacement systems: A systematic review of their history. Int J Oral Maxillofac Surg [Internet]. 2018;47(6):743–54. Available from: https://doi.org/10.1016/j.ijom.2018.01.014
2. Elledge R, Mercuri LG, Attard A, Green J, Speculand B. Review of emerging temporomandibular joint total joint. Br J Oral Maxillofac Surg [Internet]. 2019; Available from: https://doi.org/10.1016/j.bjoms.2019.08.009
3. Bates JF, Stafford GD, Harisson A. Masticatory function — a review of the literature. Jourtial Oral Rehabil. 1976;3:57–67.
4. Kijak E, Margielewicz J, Lietz-Kijak D, Wilemska-Kucharzewska K, Kucharzewski M, Śliwiński Z. Model identification of stomatognathic muscle system activity during mastication. Exp Ther Med. 2017;13(1):136–45.
5. Mercuri LG, Wolford LM, Giobbie-hurder A. Long-Term Follow-Up of the CAD / CAM Patient Fitted Total Temporomandibular Joint Reconstruction System. 2002;1440–8.
6. Dimitroulis G. Comparison of the outcomes of three surgical treatments for end-stage temporomandibular joint disease. Int J Oral Maxillofac Surg. 2014 Aug;43(8):980–9.
7. Mommaerts MY. On the reinsertion of the lateral pterygoid tendon in total temporomandibular joint replacement surgery. J Cranio-Maxillofacial Surg [Internet]. 2019;47(12):1913–7. Available from: https://doi.org/10.1016/j.jcms.2019.11.018
8. Angelo DF, Morouço P, Alves N, Viana T, Santos F, González R, et al. Choosing sheep (Ovis aries) as animal model for temporomandibular joint research: Morphological, histological and biomechanical characterization of the joint disc. Morphologie. 2016;100(331):223–33.
9. Domingue BM, Dellow DW, Barry TN. The efficiency of chewing during eating and ruminating in goats and sheep. Br J Nutr. 1991 May;65(3):355–63.
10. Verplancke K, De Waele W, De Bruyn H. Dental implants, what should be known before starting an in vitro study. Conf Sustain Constr Des [Internet]. 2011;2(3):360–9. Available from: https://biblio.ugent.be/publication/1177030
11. Rentsch C, Schneiders W, Manthey S, Rentsch B, Rammelt SS. Comprehensive histological evaluation of bone implants. Biomatter. 2014;4:1–11.
12. Ângelo DF, Gil FM, González-García R, Mónico L, Sousa R, Neto L, et al. Effects of bilateral discectomy and bilateral discopexy on black Merino sheep rumination kinematics: TEMPOJIMS – phase 1 – pilot blinded, randomized preclinical study. J Cranio-Maxillofacial Surg. 2018;46(2):346–55.
13. Allouch MG. Functional anatomy of the masticatory mechanism: A comparative study of physical characteristics of jaw- unilateral muscles in sheep. Int J Vet Sci. 2018;7(3):134–9.
14. Parker WS. The comparative anatomy of the internal and external pterygoid muscles. Functional variations among species. Angle Orthod. 1983 Jan;53(1):9–18.
15. Stöckle M, Fanghänel J, Knüttel H, Alamanos C, Behr M. The morphological variations of the lateral pterygoid muscle: A systematic review. Ann Anat [Internet]. 2019;222:79–87. Available from: https://doi.org/10.1016/j.aanat.2018.10.006
16. Murray GM, Bhutada M, Peck CC, Phanachet I, Sae-Lee D, Whittle T. The human lateral pterygoid muscle. Arch Oral Biol. 2007;52(4):377–80.
17. Huang BY, Whittle T, Murray GM. Activity of inferior head of human lateral pterygoid muscle during standardized lateral jaw movements. Arch Oral Biol. 2005;50(1):49–64.
18. Collins CP, Wilson KJ, Collins PC. Lateral pterygoid myotomy with reattachment to the condylar neck: an adjunct to restore function after total joint reconstruction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003 Jun;95(6):672–3.
19. Dwek JR. The periosteum: What is it, where is it, and what mimics it in its absence? Skeletal Radiol. 2010;39(4):319–23.
20. Lin Z, Fateh A, Salem DM, Intini G. Periosteum: Biology and applications in craniofacial bone regeneration. J Dent Res. 2014;93(2):109–16.

21. Andersen H. Histochemical studies on the histogenesis of the knee joint and superior tibio-fibular joint in human foetuses. Acta Anat (Basel). 1961;46:279–303.
22. Shapiro F. Bone development and its relation to fracture repair. The role of mesenchymal osteoblasts and surface osteoblasts. Eur Cells Mater. 2008;15:53–76.
23. Colnot C. Skeletal cell fate decisions within periosteum and bone marrow during bone regeneration. J Bone Miner Res. 2009 Feb;24(2):274–82.
24. Polo-Corrales L, Latorre-Esteves M, Ramirez-Vick JE. Scaffold design for bone regeneration. Journal of nanoscience and nanotechnology. 2014;14(1):15–56.
25. Tamaddon M, Samizadeh S, Wang L, Blunn G, Liu C. Intrinsic Osteoinductivity of Porous Titanium Scaffold for Bone Tissue Engineering. Int J Biomater. 2017;2017.
26. Yeniyol S, Bölükbaşi N, Çakir AF, Bilir A, Ozdemir T. Effects of surface modifications with oxalic acid etching and sandblasting on surface topography and biocompatibility of cpTi surfaces. Biotechnol Biotechnol Equip. 2013;27(4):3995–4001.
27. Cross MJ, Roger GJ, Spycher J. 7 - Cementless fixation techniques and challenges in joint replacement. In: Revell PABT-JRT, editor. Woodhead Publishing; 2014. p. 186–211. Available from: http://www.sciencedirect.com/science/article/pii/B9780857098412500072
28. Konttinen YT, Milošev I, Trebše R, van der Linden R, Pieper J, Sillat T, et al. 4 - Metals for joint replacement. In: Revell PABT-JRT, editor. Woodhead Publishing; 2014. p. 81–151. Available from: http://www.sciencedirect.com/science/article/pii/B9780857098412500047
29. Spalthoff S, Jehn P, Zimmerer R, Mollmann U, Gellrich N-C, Kokemueller H. Heterotopic bone formation in the musculus latissimus dorsi of sheep using beta-tricalcium phosphate scaffolds: evaluation of an extended prefabrication time on bone formation and matrix degeneration. Int J Oral Maxillofac Surg. 2015 Jun;44(6):791–7.
30. Spalthoff S, Zimmerer R, Dittmann J, Kokemüller H, Tiede M, Flohr L, et al. Heterotopic bone formation in the musculus latissimus dorsi of sheep using β-tricalcium phosphate scaffolds: Evaluation of different seeding techniques. Regen Biomater. 2018;5(2):77–84.
31. Pilliar RM, Lee JM, Maniatopoulos C. Observations on the effect of movement on bone ingrowth into porous-surfaced implants. Clin Orthop Relat Res. 1986 Jul;(208):108–13.
32. Burke D, CR B, Jasty M, Haire T, Harris W. Dynamic measurement of interface mechanics in vivo and the effect of micromotion on bone ingrowth into a porous surface device under controlled loads in vivo. In: 37th Annual Meeting of Orthopaedic Research Society. Anaheim; 1991. p. 103.
33. Karrholm J, Herberts P, Hultmark P, Malchau H, Nivbrant B, Thanner J. Radiostereometry of hip prostheses. Review of methodology and clinical results. Clin Orthop Relat Res. 1997 Nov;(344):94–110.
34. De Meurechy NKG, Loos P-J, Mommaerts MY, Meurechy NKG De, Loos P-J, Mommaerts MY. Postoperative Physiotherapy After Open Temporomandibular Joint Surgery: A Three-Step Program. J Oral Maxillofac Surg [Internet]. 2018; Available from: https://doi.org/10.1016/j.joms.2018.12.027
35. Van Bogaert W, De Meurechy N, Mommaerts MY. Autologous Fat Grafting in Total Temporomandibular Joint Replacement Surgery. Ann Maxillofac Surg [Internet]. 2018;8(2):299–302. Available from: https://pubmed.ncbi.nlm.nih.gov/30693249
36. Shen P, Zhang S, Yang C, Huang D. The mandibular symmetry evaluation of total temporomandibular joint replacement on developing sheep. J Cranio-Maxillofacial Surg [Internet]. 2014 Apr;42(3):201–5. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L52620255
37. Skinner R, Maybee J, Transfeldt E, Venter R, Chalmers W. Experimental pullout testing and comparison of variables in transpedicular screw fixation. A biomechanical study. Spine (Phila Pa 1976). 1990 Mar;15(3):195–201.
38. Chaudhary N, Lovald ST, Wagner J, Khraishi T, Baack B. Experimental and Numerical Modeling of Screws Used for Rigid Internal Fixation of Mandibular Fractures. Model Simul Eng [Internet]. 2008 Jan;2008. Available from: https://doi.org/10.1155/2008/628120
39. Tada S, Stegaroiu R, Kitamura E, Miyakawa O, Kusakari H. Influence of implant design and bone quality on stress/strain distribution in bone around implants: a 3-dimensional finite element analysis. Int J Oral Maxillofac Implants. 2003;18(3):357–68.

40. Yan Y-B, Liang S-X, Shen J, Zhang J-C, Zhang Y. Current concepts in the pathogenesis of traumatic temporomandibular joint ankylosis. Head Face Med [Internet]. 2014 Sep 4;10:35. Available from: https://pubmed.ncbi.nlm.nih.gov/25189735
41. Nauth A, Giles E, Potter BK, Nesti LJ, O ' brien FP, Bosse MJ, et al. Heterotopic ossification in orthopaedic trauma. J Orthop Trauma [Internet]. 2012 Dec;26(12):684–8. Available from: https://pubmed.ncbi.nlm.nih.gov/23010648
42. Wellenberg RHH, Hakvoort ET, Slump CH, Boomsma MF, Maas M, Streekstra GJ. Metal artifact reduction techniques in musculoskeletal CT-imaging. Eur J Radiol [Internet]. 2018;107:60–9. Available from: https://doi.org/10.1016/j.ejrad.2018.08.010
43. Zhao S, Robertson DD, Wang G, Whiting B, Bae KT. X-ray CT metal artifact reduction using wavelets: An application for imaging total hip prostheses. IEEE Trans Med Imaging. 2000;19(12):1238–47.
44. Zhang X, Wang J, Xing L. Metal artifact reduction in x-ray computed tomography (CT) by constrained optimization. Med Phys [Internet]. 2011 Feb;38(2):701–11. Available from: https://pubmed.ncbi.nlm.nih.gov/21452707
45. Moon SG, Hong SH, Choi J-Y, Jun WS, Kang H-G, Kim H-S, et al. Metal artifact reduction by the alteration of technical factors in multidetector computed tomography: a 3-dimensional quantitative assessment. J Comput Assist Tomogr. 2008;32(4):630–3.
46. Benjamin M, Kumai T, Milz S, Boszczyk BM, Boszczyk AA, Ralphs JR. The skeletal attachment of tendons - Tendon "entheses." Comp Biochem Physiol - A Mol Integr Physiol [Internet]. 2002 Dec;133(4):931–45. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L35463154%0Ahttp://dx.doi.org/10.1016/S1095-6433(02)00138-1%0Ahttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=10956433&id=doi:10.1016/S1095-6433(02)00138-1&atitle=The+skeletal+att
47. Kokemueller H, Spalthoff S, Nolff M, Tavassol F, Essig H, Stuehmer C, et al. Prefabrication of vascularized bioartificial bone grafts in vivo for segmental mandibular reconstruction: experimental pilot study in sheep and first clinical application. Int J Oral Maxillofac Surg. 2010;39(4):379–87.
48. Laschke MW, Rucker M, Jensen G, Carvalho C, Mulhaupt R, Gellrich N-C, et al. Improvement of vascularization of PLGA scaffolds by inosculation of in situ-preformed functional blood vessels with the host microvasculature. Ann Surg. 2008 Dec;248(6):939–48.
49. Allen MR, Hock JM, Burr DB. Periosteum: biology, regulation, and response to osteoporosis therapies. Bone. 2004 Nov;35(5):1003–12.
50. Hernigou P. Bone transplantation and tissue engineering. Part II: bone graft and osteogenesis in the seventeenth, eighteenth and nineteenth centuries (Duhamel, Haller, Ollier and MacEwen). Int Orthop. 2015 Jan;39(1):193–204.
51. Gallardo-Calero I, Barrera-Ochoa S, Manzanares MC, Sallent A, Vicente M, López-Fernández A, et al. Vascularized Periosteal Flaps Accelerate Osteointegration and Revascularization of Allografts in Rats. Clin Orthop Relat Res [Internet]. 2019;477(4). Available from: https://journals.lww.com/clinorthop/Fulltext/2019/04000/Vascularized_Periosteal_Flaps_Accelerate.16.aspx
52. Leucht P, Kim J-B, Amasha R, James AW, Girod S, Helms JA. Embryonic origin and Hox status determine progenitor cell fate during adult bone regeneration. Development. 2008 Sep;135(17):2845–54.
53. Hoover WH, Miller TK. Rumen digestive physiology and microbial ecology. Vet Clin North Am Food Anim Pract. 1991 Jul;7(2):311–25.



Chapter 8

Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: an animal experiment with histological verification

This chapter is based on:

Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with histological verification

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Introduction

Total temporomandibular joint replacement (TMJR) is an uncommon treatment that, is considered the final option in cases of end-stage temporomandibular disorders. Its indications are well described by both the American Association of Oral and Maxillofacial Surgeons (AAOMS)(1) and British National Institute for Health and Care Excellence guidelines.(2) The main purpose of joint replacement is to restore proper temporomandibular joint (TMJ) function, as well as to relieve the patient of pain and improve the overall quality of life. Current TMJRs can reduce pain and improve mouth opening. However, they lack the ability to restore proper masticatory function, due to the loss of protrusive and laterotrusive movements for tearing and grinding of food.

In humans, the lateral pterygoid muscle (LPM) plays a crucial role in this process. It allows for protrusion through bilateral contraction and by unilateral contraction for laterotrusive movement.(3,4) The LPM can be divided into a superior and inferior muscle belly, of which the latter is subdivided into four components. Each of these parts play a role in either initiating or continuing through with protrusive and laterotrusive movements.(5,6) However, despite the distinct muscle bellies, their fibers variously insert into the muscle tendon, fovea, capsular ligament and disc, resulting in a 'uniform' insertion or attachment in the mandibular condylar area.(7) Because both the intra-articular disc and condyle are resected during the placement of a total TMJ prosthesis, the LPM insertion is effectively lost. This situation results in impaired laterotrusive and protrusive jaw function as shown by both Mercuri et al.(8) and Dimitroulis et al.(9). Additionally, because correct mastication occurs bilaterally, unilateral mastication results in an uneven load distribution over the two TMJs. This increased load can lead to further joint deterioration – for example, through articular disc damage and cartilage destruction – resulting in pain and limited function.(10–12)

To prevent an increased load in the contralateral joint, as well as to retain LPM function in patients treated with a TMJR, Mommaerts(13) aimed to develop a new patient-specific additively manufactured TMJR, together

with CADskills BV (Ghent, Belgium), that allowed for the reinsertion and reintegration of the LPM, onto the TMJR. The aim was to dissect the LPM and preserve all components of the muscle enthesis together with the condylar bony fragment onto which the muscle inserts itself. This (fibrous) enthesis consists of the muscle belly, the myotendinous junction (MTJ), the tendon and the bone-tendon junction (BTJ))(14,15). He aimed to reattach the both the enthesis and adjacent condylar bone to a scaffold in the condylar neck of the TMJR, to allow for LPM reconstruction and possible osseointegration.

Following a promising human case series that served as a clinical proof of concept, an animal model was designed for further systematic investigation.(16) A first radiological analysis of the LPM reconstruction revealed a direct connection between the condylar scaffold and the LPM enthesis, be it either soft tissue, bony or a combination of the two, with close (less than 1mm) or direct approximation of the LPM's bony enthesis against the condylar scaffold.(16) The aim of the current study was to further evaluate the histological aspects of the (osseous) integration of the enthesis into the TMJR scaffold, based on these radiological results, in a selected sample of five sheep. In two of these sheep, a fully bony connection was achieved, in three a partially soft tissue and bony connection was found.(16) Based on these results, we hypothesized that proper reinsertion had occurred in all five samples, at the level of the scaffold.

Materials and Methods

In vivo test subjects

Although several species of animals show similarities to the human TMJ and can be considered for experimental purposes, an animal model using sheep was selected for several reasons.(17) In addition to encountering fewer ethical concerns than those using of primates, sheep show significantly higher daily mastication activity than goats, allowing reduction of the total experiment duration.(18) The experiment duration was set at 288 days, equaling 22 years of human function.(19)

A total of 14 ewes (Swifter crossbreed) were enrolled after approval by the ethics committee at Medanex Clinic (license number LA 1210576 - code of approval EC MxCl 2018-090) was acquired. All the animals were in good health before surgery, weighed 73.4 kg on average (range: 52-86 kg) and were aged between 2 and 5 years. None had missing teeth. The sheep were allowed to roam freely in the meadow until the day of surgery. During the first week after surgery, they were kept in solitary confinement, followed by indoor confinement in a large stable for remaining duration of the study.

Implant

Mandibular component

The mandibular component was additively manufactured from grade 23 extra-low interstitial (ELI) Titanium 6-Aluminum 4-Vanadium (Ti6Al4V). A large connecting lattice structure at the bony interface was provided, to allow osseous mandibular integration. In order to allow for LPM reattachment, a subcondylar a tunnel with a small 'hook-like' extension on the lateral side was designed. By running a PDS 0 suture through the preserved bony or fibrocartilaginous enthesis of the LPM, this suture could then be threaded through the subcondylar tunnel and be fixed to the extension. Additionally, a large subcondylar lattice structure was designed to allow for osseous integration of the enthesis.

Through the process of computer-assisted design (CAD), the TMJR bone interface contained interconnecting pores with a 500 μm diameter and a 80% porosity, as improved bone ingrowth and stability are found in a porosity of up to at least 70%.(20) By micro-shot peening using alumina grit with a 550 μm diameter and etching using 2 wt% oxalic acid at 85 °C for 10 min, a sandblasted, large-grit, and acid-etched (SLA) surface at the bony interface of the implant was achieved. To remove any remaining alumina residue, which can reduce corrosion resistance and interfere with proper osseointegration, acidic etching with 2 wt% oxalic acid was applied.(21–23) This process also further increases the surface roughness through micro-pitting.(21,24,25)

Finally, although all condylar articulating surfaces were polished after printing, 6 of 13 condylar heads were resurfaced using a diamond-like carbon coating to increase surface hardness and reduce wear.(26) Application of the coating was achieved using the nondisclosed HadSat protocol with a Vickers hardness (HV0.05) of 3,500 ± 500 and a friction coefficient of 0.1. The biocompatibility of the coating was tested under the International Standard ISO 10993-1 by the North American Science Associates (Northwood, OH, USA).

Fossa component

The fossa component consisted of both a titanium and polyethylene component. The titanium component was additively manufactured from ELI Ti6Al4V and the as with the mandibular component, the bony interface was subjected to a SLA treatment to improve the bony ingrowth at the temporal fossa. Fixation was achieved using 5 titanium Gr 5, 2.0 mm diameter screws (Surgi-Tec NV, Ghent, Belgium) with lengths ranging from 5 to 13 mm, which were screwed into the zygomatic arch. At its condylar-facing side, a scaffold was designed, onto which a concave computer numeric controlled milled ɣ-radiated (100 kGy; Gammatom s.r.l. Como, Italy) Vitamin-E enriched highly-crosslinked ultra-high molecular weight polyethylene (HXLPE) component was hot pressed. The parameters for this process, such as pressure, temperature, and time, are proprietary information.

Design adaptation

Although the TMJR was to be implanted in sheep, the design was kept as close as possible to its human counterpart. Similar to the design and development for humans, a computed tomography (CT) scan was performed 6 weeks before the date of surgery. The CT data were provided in the Digital Imaging and Communications in Medicine (DICOM)-format to the engineers of CADskills BV (Ghent, Belgium), who processed the DICOM files into a standard template library (STL) file. Next, virtual resection of the left condyle was performed and a cutting guide was designed using Geomagic Freeform Plus (3D Systems, Rock Hill, SC, USA), allowing the surgeon to achieve the same ostectomy. Based on the performed ostectomy, an individual implant was then designed. The

length and position of each screw was predetermined during the design of the implant, based on the amount of bone and adjacent anatomical structures, such as the inferior alveolar nerve. Additionally, 6 prostheses were randomly selected for additional HadSat-treatment of the condyle.

Surgical protocol

An initial series of two sheep were treated to evaluate the surgical technique. One was treated using a TMJR, the other was subjected to sham surgery (the same surgical approach without condylectomy or prosthetic treatment). After further optimization of the surgical approach following these two sheep, 12 additional sheep were subjected to surgery using the established protocol.

All the sheep were first pre-medicated using xylazine 0.1 mg/kg (Xyl M, V.M.D. nv, Arendonk, Belgium). Next, induction was achieved using ketamine 4 mg/kg (Nimatek; Dechra Pharmaceuticals PLC, Northwich, United Kingdom) and midazolam 0.2 mg/kg (Dormazolam; Le Vet Pharma BV, Oudewater, Netherlands), followed by orotracheal intubation. A mixture of O_2-isoflurane was used to maintain anesthesia and intravenous administration of buprenorphine 6 µg/kg (Vetergesic; Ceva Santé Animale BV, Naaldwijk, Netherlands) was applied for an analgesic effect. Enrofloxacin 5 mg/kg (Floxadil; EMDOKA BVBA, Hoogstraten, Belgium) was administered both during surgery and for the first 5 post-operative days to prevent infection.

After aseptic preparation (i.e., clipping, washing and disinfecting) and draping of the operative site, a 4-cm long mark was made over the posterior lower border of the mandible as well as a pre-auricular S-shaped mark inferior to the zygomatic arch. Local infiltration with xylocaine 1% containing 1/80,000 epinephrine (Dentsply Sirona, Charlotte, NC, USA) was administered to achieve local vasoconstriction and anesthesia, after which an incision through both marks was made. The masseter muscle was cut at the lower mandibular border, and subperiosteal elevation was achieved to allow insertion of the patient/prosthesis specific ELI-Ti cutting guide (CADskills BV, Ghent, Belgium) over the vertical ramus.

The incision below the zygomatic arch was used to dissect the joint space and insert the cutting guide to ensure that the condylectomy identical to the virtual planning. During the condylectomy, an attempt was made minimally preserve the BTJ of the LPM (i.e., the enthesis), as well as some of the adjacent condylar bone by partially resecting the condyle and then threading a PDS 0 suture (Ethicon, Somerville, NJ, USA) through the tendon of the LPM, after which the remainder of the condyle, apart from the BTJ and adjacent bone, was resected. This step proved challenging. Humans have a larger bony insertion area of the LPM, whereas sheep have a small and mostly fibrotic insertion into both the intra-articular disc and condyle. Thus, the condylar bone and BTJ could only be preserved in six cases. In seven cases, only the BTJ or fibrocartilaginous part of the muscle insertion could be preserved. In two cases, it was unclear whether either the BTJ or even MTJ was preserved (Table 1).

Table 1: Per-operative reconstruction and post-mortem radiological analysis between the lateral pterygoid muscle (LPM) and the implant scaffold.

Sheep nr	Per-operative	Post-mortem
3520	Bony	Fibrotic
8087	Unclear	Bone
2177	Bony	Absent
5158	Unclear	Bone + Fibrotic
2549	Fibrocartilaginous	Absent
4249	Fibrocartilaginous	Bone
0032	Fibrocartilaginous	Fibrotic
7998	Bony	Absent
4246	Bony	Bone + Fibrotic
1724	Bony	Fibrotic
4248	Bony	Bone + Fibrotic
8787	Fibrocartilaginous	Absent
4473	Fibrocartilaginous	Absent
0075	SHAM	SHAM

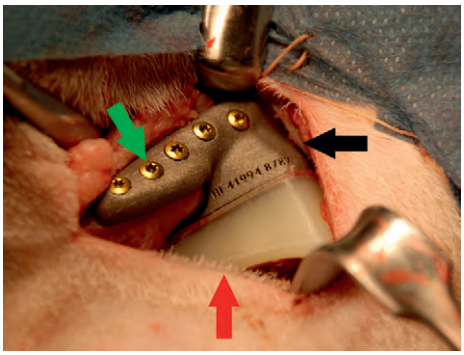


Fig. 1: Fixated Zygoma component. Red arrow: HXLPE articulating part. Black arrow: ELI23Ti6Al4V part. Green arrow: Grade 5-Ti screws

After performing the condylectomy, a dummy of the fossa component was applied to confirm whether the soft tissues were sufficiently dissected. Next, the Ti-HXLPE fossa component was placed and fixed to the zygomatic arch with five grade 5-Ti screws.(Fig. 1) During the placement of the fossa component, the assistant surgeon crushed bone that was harvested from the resected condyle, which was then mixed with fibrin sealant (Tisseel; Baxter, Deerfield, IL, USA) and applied to the subcondylar scaffold of the ramal component. The PDS 0 suture that was previously threaded through the LPM enthesis was then threaded through the tunnel in the condylar neck, and the ramal component was positioned onto the mandibular stump. Fixation of the ramal component was achieved using seven grade 5 Ti screws.

Next, by pulling the PDS 0 suture further through the subcondylar tunnel and tying it to the 'hook-like' extension on the lateral side of the tunnel, a stable fixation of the enthesis against the subcondylar scaffold was attempted.(Fig. 2) Because of an obstructive caudal edge at the anteromedial side of the HXLPE part of the fossa component, proper approximation and visualization of the LPM enthesis against the subcondylar scaffold proved challenging. Consequently, all the HXLPE parts were scalpel-reduced at their non-articulating anteromedial side. However, proper approximation still could not be visualized, making it difficult to determine the intraoperative success of the LPM reattachment against the subcondylar scaffold.

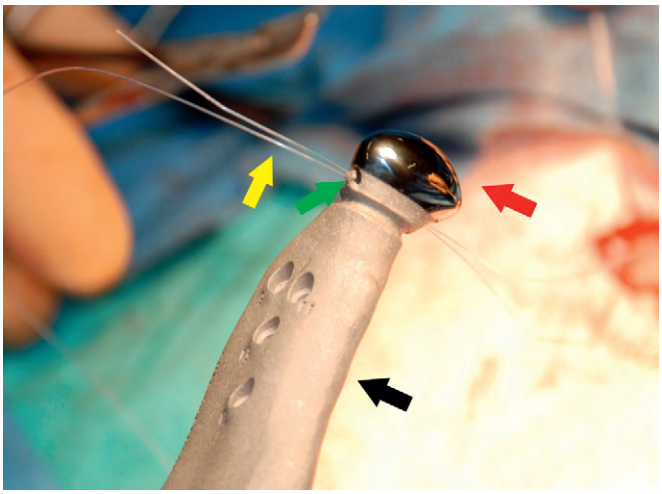


Fig. 2: ELI23 Ti6Al4V Ramal component of the TMJR. Black arrow: Ramal component. Green arrow: subcondylar tunnel with 'hook-like' extension. Yellow arrow: PDS 0 suture. Red arrow: HadSat coated condyle.

The surgery site was then rinsed thoroughly with aqueous chlorohexidine, after which the articular capsule and soft tissues were closed in multiple layers using polyglyconate 910 2-0 (Vicryl; Ethicon J&J, Somerville, NY, USA) for the deeper layers and poliglecaprone 25 2-0 (Monocryl; Ethicon J&J, Somerville NY, USA) for the intra-dermal closure. A 10-ml subdermal deposit of ropivacaine 7.5 mg/ml (Naropin; AstraZeneca, Wilmington DE, USA) was administered for an additive local analgesic effect. Finally, the wound was sprayed with chlorotetracycline hydrochloride (Cyclospray; Dechra Pharmaceuticals PLC, Northwich, United Kingdom) and the incisions were covered with a sterile primary layer and a compressive head bandage for seven days.

Post-operative protocol and Euthanasia

All the sheep were kept in solitary confinement during the first week, while their vital parameters (heart rate, respiratory rate, and body temperature), dietary status (appetite and fluids intake), and excretions were evaluated and recorded daily. Renewal of the compressive bandaging was performed daily, during which the wounds were evaluated for possible signs of infection. Blood samples were also taken daily during the first post-operative week checking the white cell count and formula, as well as the ionogram and inflammatory parameters twice. Post-operative pain

control was managed using meloxicam 0.5 mg/kg (Metacam; Boehringer Ingelheim, Ingelheim am Rhein, Germany) and buprenorphine 5 µg/kg (Vetergesic; Ceva Santé Animale BV, Naaldwijk, Netherlands) if needed.

During this first week only, moistened food was administered to the ewes to limit the stress on the TMJ and LPM. After one week, all the sheep were housed together in a large indoor confinement, where they stayed for the remainder of the study. After the first post-operative week, blood samples were taken once per week, during which a clinical examination was also performed.

Two hundred eighty-eight days after implantation, all 14 animals were euthanized. Before euthanasia a final clinical evaluation and blood sampling were performed, after which xylazine 0.1mg/kg (Xyl M; V.M.D. nv, Arendonk, Belgium) was administered for induction, as well as heparine 300 IU/kg to prevent coagulation. Induction was performed using a combination of ketamine 4mg/kg (Nimatek; Dechra Pharmaceuticals PLC, Northwich, United Kingdom) and midazolam 0.2 mg/kg (Dormazolam; Le Vet Pharma BV, Oudewater, Netherlands). The product that was administered to achieve euthanasia remains undisclosed per agreement with Medanex Clinic (Diest, Belgium)

Sample processing and selection

After euthanasia was performed, all the sheep were decapitated. The skull was then cut in half midsagitally and the implanted left side of the skull was skinned and further trimmed down by removing the neurocranium, the anterior half of the mandible and maxilla, the upper half of the orbit and the eye.

After fixation of the specimen by immersion in formaldehyde 4% for three months, a post-mortem CT scan of each specimen was performed (slice thickness 0.7mm, 500mAs, 120kV, reconstruction thickness <1mm; Revolution, General Electric, Fairfield, CT, USA). Next, all samples were rinsed for 3 days as to remove the excess formalin, after which the peri-articular 'neo-synovial' tissues were resected and stored for further debris analysis, which will be discussed in a separate paper.

By using prosthetic landmarks (ramal screw holes, the subcondylar tunnel), anatomical landmarks (infra-orbital rim, teeth) and the reconstructed STL files of the post-mortem CT scans using Mimics inPrint 3.0 (Materialise, Haasrode, Belgium), section planes were determined in order to further trim the samples while retaining both the LPM and its attempted enthesis reconstruction. After marking these planes onto the samples, sections were made using the cutting and grinding technique with an Exakt 300 diamond band saw (EXAKT Advanced Technologies GmbH, Norderstedt, Germany) at Morphisto GmbH (Frankfurt, Germany). Next, the condylar head was resected to allow for wear evaluation.(27)

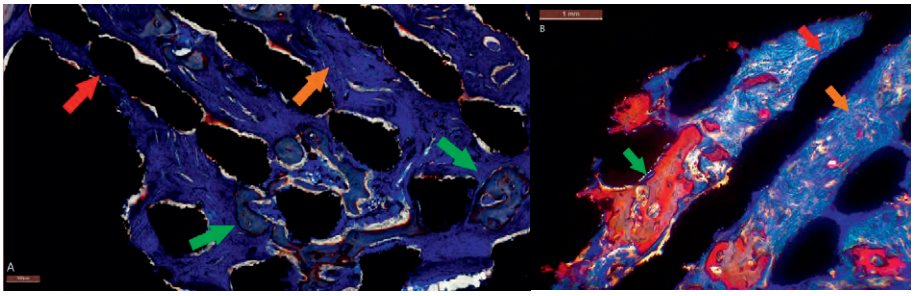
After performing a radiological analysis of the attempted enthesis reconstruction(16) five specimens showing radiographic signs of osteointegration were selected for further histological evaluation. On imaging a unique bony contact of the enthesis against the scaffold was seen in two of these sheep, whereas in the other three samples a partial bony and soft tissue reattachment of the enthesis against the scaffold was revealed.(16) These selected samples were slowly dehydrated for seven days by immersion in baths with an increasing concentration of alcohol. The samples were pre-infiltrated during 3 weeks and then infiltrated over a period of 20 days, using Technovit 9100 (Kulzer GmbH, Wehrheim, Germany). Several sections were made using the cutting and grinding technique with an Exakt 300 diamond band saw and 400 CS Micro Grinder machine (EXAKT Advanced Technologies GmbH, Norderstedt, Germany), until the correct height (e.g. enthesis' scaffold) was obtained. Through the use of Technovit 9100-embedding, a relatively limited thickness of 40-42 µm was achieved. Next, a Masson-Goldner (M-G) trichrome staining was applied, allowing to differentiate tissues such as collagen, bone and muscle by means of light microscopic analysis. (28) In addition, a section was made at the level of the ramal scaffold in two randomly selected specimen, in order to evaluate the bony ingrowth of the mandible into the ramal component.

Results

Enthesis integration

In all samples, storiform collagen was found within the non-translucent implant scaffold. Overall little to no osteogenic activity was found inside the scaffold of the unique section plane per condylar scaffold, apart from a number of isolated bony islands being formed in two samples. (Figs. 3a, b) In both samples bony islands were antero-posteriorly dispersed throughout the scaffold. Both osteocytes and active remodellation were observed in these bony islands. This was indicative of vital tissue activity. Many iron-loaded macrophages were observed in several samples, suggesting the resorption of the bone chips that were inserted during surgery, yet were no longer present.

Despite the close approximation of the enthesis to the scaffold in all samples, only two samples were found with bony extension of the enthesis into the implant scaffolding albeit limited.(Fig. 4) No osseous connection was found between the bony enthesis and bony islands in either sample. However, apart from these osseous extensions, all samples were found to have a thin lamellar layer of collagenous tissue between the implant and the bone, ranging from 20 to 150µm, except for one sample where a maximal thickness of 500µm was found. (Fig. 5)



Figs. 3a and b: Detailed view of the scaffold interior. Red arrow: Titanium scaffold Green arrow: Osteogenic activity inside of scaffold with active remodellation. Orange arrow: Storiformly organized, dense connective tissues

The BTJ and adjacent bone of the enthesis were viable in all samples, with a multitude of Haversian canals with osteocytes, osteoblasts and erythrocytes. Active bone remodellation was seen throughout all the

analyzed enthesis and was most apparent near the implant scaffold site. (Fig. 5) Despite this bone remodeling, no or very limited ingrowth into the scaffold was seen. Important to notice is that in all 5 samples, the enthesis evaluated was considerably larger in width and length compared to the intraoperatively dissected bony enthesis, suggesting active growth of the bony enthesis, mainly in anteromedial direction. Furthermore, in 2 samples some heterotopic ossification was found surrounding the implant. Lastly, in all samples a dense well-organized layer of collagenous tissue was present anteromedially of the enthesis, transitioning into muscle fibers of the LPM. (Fig. 6)

Besides these general findings, a 1190μm thick cartilaginous structure was identified in one sample. This cartilage was located near the anterior edge of the implant and was flanked by an osseous structure, suggesting a possible incomplete resection of the articular disc. The LPM tendon was found inserting onto this cartilaginous tissue as well.

Important to remark is that in one sample, following to tissue loss occurring during the cutting and grinding of the sample, part of the implant became dislodged out of the Technovit 9100 block. As such it was no longer possible to obtain sections at a similar height to the other samples, resulting in a section that is several millimeters below the preferred section height. As a result, the opening of the scaffold towards the bony enthesis is not included in the sample.

Ramal integration

Both samples showed good osseointegration of the ramal component onto the mandible, with bone having formed in between the non-translucent scaffolds (Fig. 7). One sample partially contained two Ti screws, with bone surrounding the screw threads. In one sample a layer of storiformly organized connective tissue was observed near the anterior border of the ramal component. At the anterior border, the connective tissue becomes a 320-580μm thick lamellar layer reverting to the exterior side. This layer of connective tissue was likely due to improper antero-posterior positioning of the implant. In the second sample, a layer of storiformly organized collagen is seen at the rear edge of the implant,

again indicating a possible improper antero-posterior positioning of the implant, resulting in a 500-1900µm gap between the mandible and the implant. Throughout the rest of the sample, dense cortical bone is found in between the several scaffolds.

Both samples show multitude of haversian canals and osteocytes, with bone remodelation, indicating viable osseous tissue. Whereas the first sample centrally contains hematopoetic tissue, the second is far more cortically organized, with only 2 small central fields with hematopoetic tissue. This can be explained due to the section being obtained just below the level where the ostectomy was performed and thus corticalization has occurred since.

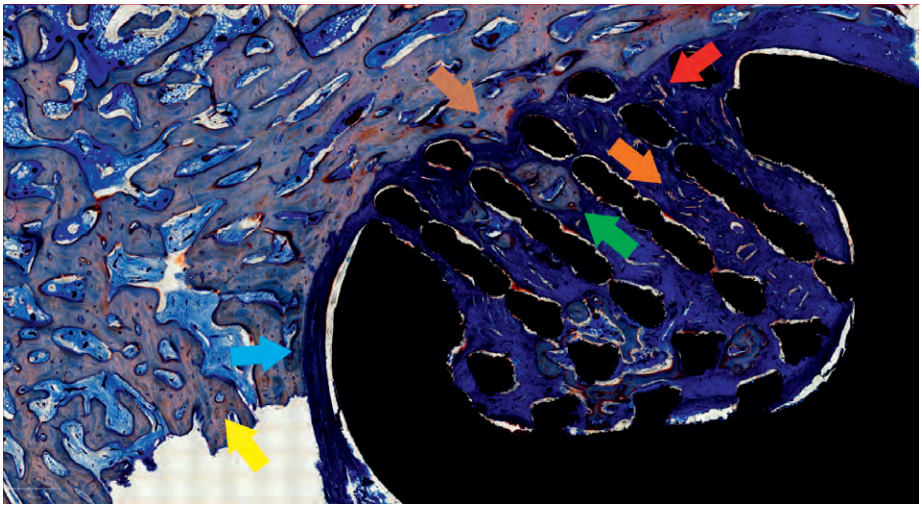


Fig. 4: Overview of the implant scaffold with enthesis. Red arrow: Implant scaffold Yellow arrow: Bony enthesis Green arrow: osteogenic activity inside of the scaffold Orange arrow: Storiform connective tissue Brown arrow: Osseous extension towards the implant scaffold Blue arrow: Connective tissue layer in-between implant and enthesis

Discussion

Collins et al.(29) were the first to attempt reattachment of the LPM on the sigmoidal notch or condylar stump, just below the point of the condylectomy. They claimed significantly better laterotrusive and

protrusive function in patients with a restored LPM. However, their study was not supported by any radiographical, histological or kinematic results. Furthermore, no information was provided as to which component of the LPM was reinserted onto the mandibular stump is unclear.(29) This is of importance, as a distinction between two different types of enthesis, the fibrous and the fibrocartilaginous enthesis, can be made. The first consist of dense fibrous connective tissue with mineralized collagen fibers connecting to the periosteum or directly inserting into the bone, whereas the latter contains four zones, with increasing amounts of calcified tissues to transition into bone, allowing for a strong insertion and the force that is generated to be transitioned to the bone.(15,30,31)

The entheses found in masticatory muscles are unique as they boast both types of entheses.(15,30,32) This is also the case for the lateral pterygoid muscles' insertion. The LPM enthesis transitions from a fibrocartilaginous one immediately below the attachment of the mandibular joint capsule to a fibrous one more caudally, which first inserts directly into the bone and below that with the periosteum. (15,30,32) Whilst the fibrous enthesis is less prone to injury, both the MTJ and BTJ in the fibrocartilaginous enthesis are highly specialized tissues, with only limited healing capacities. Notably, after injury of either the BTJ or MTJ, scar tissue formation often occurs, leading to both a decreased function and an increased risk of recurrent injury.(14,15) While research into enthesis healing and reconstruction is currently very active, pursuing several different approaches (mesenchymal stem cells, growth factors,...) results for broad clinical application remain scarce at this point.(14,15) Therefor, the surgery protocol was devised in such a fashion that the risk of the tendon failing at either of these levels was overcome by not only preserving the enthesis as a whole, but also dissection part of the adjacent bone. In addition to preserving the enthesis' integrity, we hypothesized this could allow for osseointegration onto and into the TMJR, providing further long-term stability to the LPM reinsertion. However, to allow for proper osseointegration, several important factors come into play.

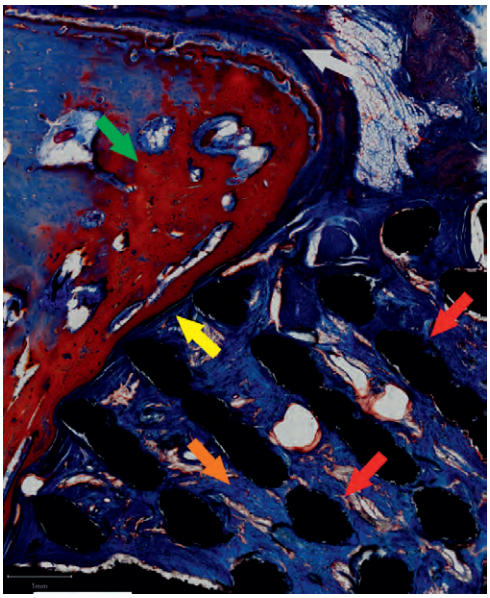


Fig. 5: Detailed view of the enthesis approximation against the scaffold. Red arrow: Titanium scaffold Green arrow: Bony enthesis with active osteogenic remodellation Orange arrow: Storiformly organized, dense connective tissues Yellow arrow: Thin layer of dense lamellar collagen between the implant scaffold and enthesis

Both the TMJR design and production were optimized to allow for the possibility of local osseointegration. The scaffold's porous design not only allows for bone to grow inside of these void areas, but also allows for higher calcium deposition and osteocalcin and alkaline phosphate concentrations to be achieved within these pores. This phenomenon leads to better (mesenchymal) cell adhesion and elicitation of cell differentiation into osteocytes, thus improving bone formation and osseointegration.(20,33–38) Although of lesser significance for the LPM reconstruction, by increasing the amount of porosities in the surface through CAD and SLA-treatment(28–30), not only is the elastic modulus further reduced, limiting the risk of bone resorption and implant loosening due to stress shielding (23,31,32), but the surface roughness is also further increased.(30,40–43) This higher surface roughness in turn leads to an increased total surface area and improved osseointegration with increased interface strength thanks to improved interlocking.(44–46)

The formation of viable osseous tissue within the ramal scaffold that was seen during the histological analysis, as well as the ramal integration that was seen during the radiological analysis(16), proved that a good osteoconductive, -inductive and biocompatible environment was achieved. Despite these good ramal results, we found or only a limited amount of osteogenesis within the subcondylar scaffold and an absence of proper osseointegration of the LPM. Several possible reasons can be found as to why a fibrous, rather than osseous reinsertion of the LPM enthesis occurred.

In order for osseointegration to occur, not only implant properties have to be considered. The implant environment needs to be both sufficiently osteogenic (i.e. sufficient mesenchymal stem cells, osteoblasts and osteocytes) and osteoinductive (promoting the differentiation of stem cells).(39,40)

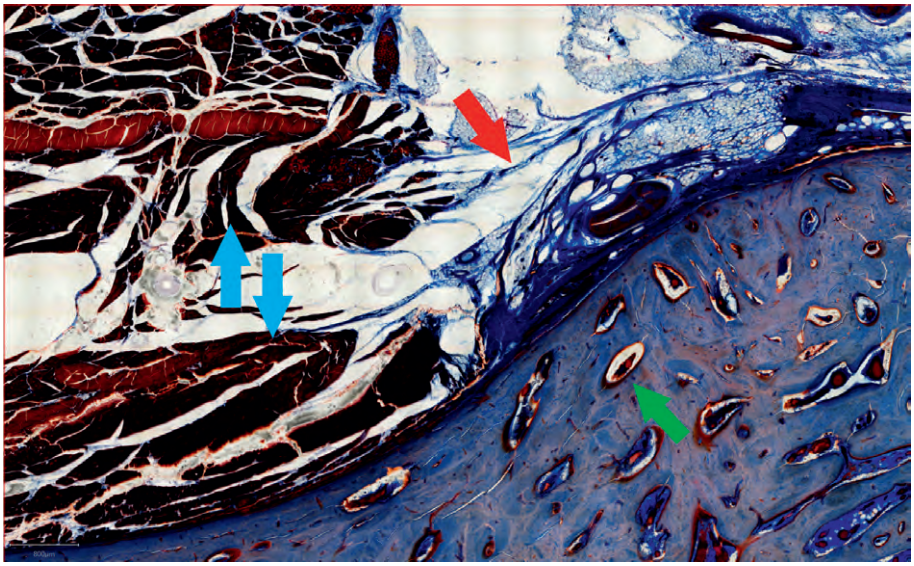


Fig. 6: Lateral pterygoid muscle (LPM) insertion. Blue arrow: LPM fibers Red arrow: Muscle tendon Green arrow: Haversian canals within enthesis

Considering the periosteum and bone marrow near the enthesis-scaffold junction were removed during the ostectomy, a reduced amount of mesenchymal cells has likely been present in this area. Those cells are essential to differentiate into (pre)osteoblasts(39,40), and therefor

contribute to better osteointegration. While part of the resected bone was ground down and applied into the scaffold, providing a local high concentration of osseoinductive cells, no local MSC's were added to the construct, thus limiting the osteogenic properties. The occurrence of heterotopic ossification adjacent to the ramal component of the implant, where the periosteum was retained,(16) seems to further support the importance of the presence of mesenchymal cells. This limitation at the scaffold site could be overcome through the use of either mesenchymal stem cells or bone marrow aspirate (BMA), preferably combined with β-tricalcium phosphate (β-TCP), as proven by Spalthoff et al.(41,42)

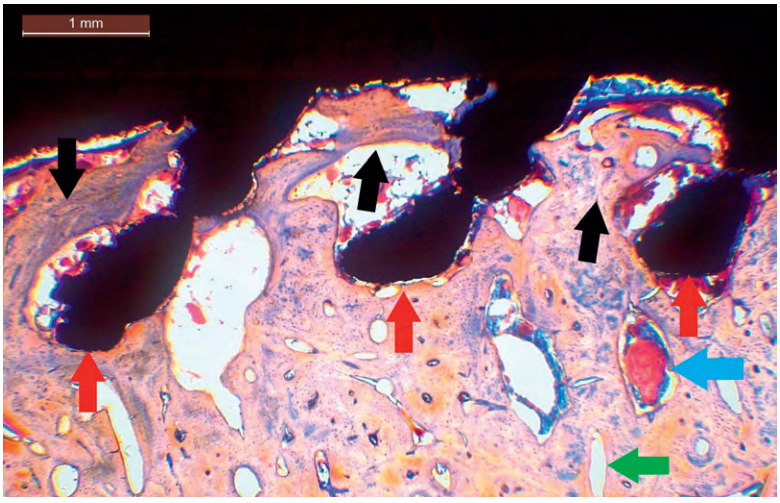


Fig. 7: Detailed view of osseous ingrowth of the mandibular ramus into the implant scaffold Red arrow: Titanium scaffold. Black arrow: Ramal cortical bone Green arrow: Haversian canals Blue arrow: Vascular lumen with blood

Besides providing a suitable environment for osseous healing to occur, direct contact between the implant and the bony tissue is needed for contact repair to occur. This direct contact between the scaffold and the bony fragment allows for osteoprogenitor cells to be derived directly from the Haversian canals. (43,44) While there were no significant difficulties to properly dissect and fixate the bony condylar segment in the patients treated by Mommaerts(13), this was less so the case for the operated sheep. Both difficult dissection and ostectomy due to anatomical differences compared to its human counterpart, as well as difficulties with proper fixation onto the scaffold, were significant

hindrances that were encountered during the sheep interventions. The importance thereof became clear during the radiological analysis of the reconstructed enthesis, as 8 out of 13 cases did not show proper approximation of the bony enthesis against the implant scaffold.(16) Obviously contact osteogenesis could not occur in these 8 ewes without proper approximation of the enthesis.

A second prerequisite that is necessary for contact repair, is the absence of motion. Pilliar et al.(45) found that in case of repetitive micromotions of 150µm or more, fibrous tissue is formed between the implant and the adjacent bone. Further research concluded that micromotions between the implant and the adjacent bone should be limited to 28 µm or less in order to promote osteogenesis.(45–48) In absence of this stability, successful osseointegration between the implant and its bony contact surface will be severely limited, with the risk of development of pseudoarthrosis.(49) While both the ramal and fossa component were properly fixated through the use of titanium screws, achieving similar stability in the LPM enthesis was far more difficult, as fixation of the LPM onto the scaffold was limited to a PDS 0 suture.

Thus it is very likely that an insufficient amount of stability between the LPM and scaffold was obtained in our experiment, with repetitive micromotions of more than 150µm having occurred in the LPM reconstruction during both chewing and rumination. We believe this to be the reason why no osseointegration, yet rather fibrous integration, occurred in the five selected samples, despite the radiological bony contact that was observed.(16) In order to attempt to prevent micromovements on the level of the LPM in humans, a liquid diet and restriction of movement could be maintained during the first six postoperative weeks. It should be remarked however, that this could in turn delay or even limit the restauration of the maximal ‘range of motion’ during the post-operative recovery.(50)

It should be remarked that, despite this the absence of osseointegration, a good approximation of the enthesis against the scaffold was achieved in all samples, with the formation of dense storiform to lamellar fibrous

connective tissue, keeping the enthesis well in place during the duration of our experiment. Furthermore, clinical evaluation showed that the sheep's pre-operative weight was regained and kinematic analysis proved that restoration of proper laterotrusive function was achieved, despite the absence of full osseointegration of the enthesis into the scaffold.(16) Thus while it would have been preferable to achieve proper osseointegration, being more predictable and stable compared to the soft tissue connection formed between the LPM and the TMJR, a functional reattachment was achieved nevertheless.

Conclusion

An *in vivo* sheep experiment was conducted to investigate a novel patient-specific TMRJ. Both a subcondylar scaffold and tunnel were designed for the reinsertion of the LPM (enthesis). Histological analysis of the enthesis reconstruction in preselected samples revealed an uninterrupted, functional, fibrotic reinsertion of the LPM onto the TMJR, restoring the muscle's function. Multiple osteogenic islands within the enthesis scaffold. Further research should include application of bone marrow aspirate and growth factors, intra-operative monitoring the approximation of the bony part of the enthesis to the scaffolded area and minimizing mobilization during healing, to attempt osseous integration. Such experiment may only be possible in human subjects

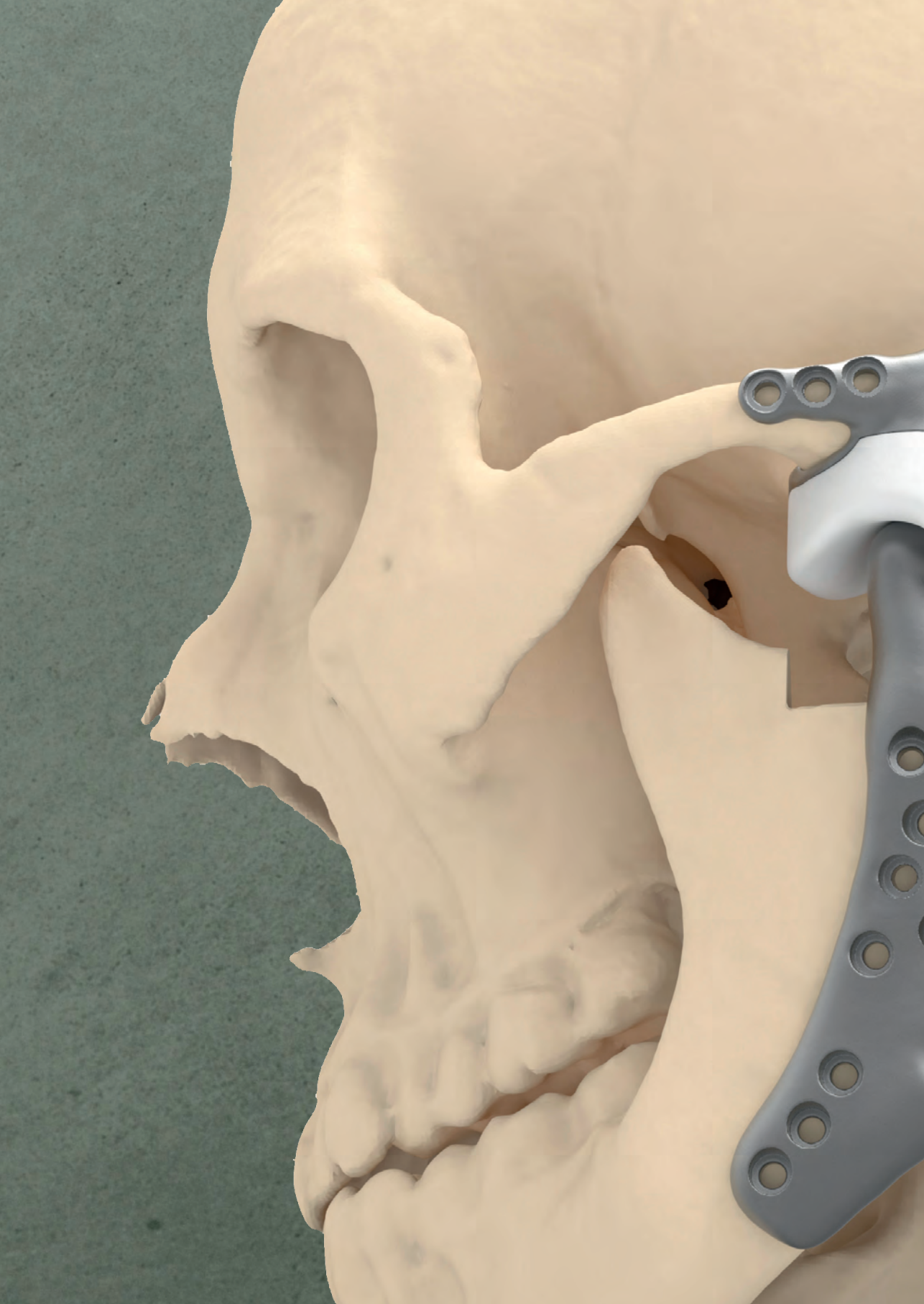
References

1. Koslin M, Indresano AT, Mercuri LG. Temporomandibular joint surgery. J Oral Maxillofac Surg. 2012;70:204–31.
2. NICE. Total prosthetic replacement of the temporomandibular joint Interventional procedures guidance. Natl Inst Heal Care Excell [Internet]. 2014;(August):2–8. Available from: www.nice.org.uk/guidance/ipg500
3. Bates JF, Stafford GD, Harisson A. Masticatory function — a review of the literature. Jourtial Oral Rehabil. 1976;3:57–67.
4. Kijak E, Margielewicz J, Lietz-Kijak D, Wilemska-Kucharzewska K, Kucharzewski M, Śliwiński Z. Model identification of stomatognathic muscle system activity during mastication. Exp Ther Med. 2017;13(1):136–45.
5. Murray GM, Bhutada M, Peck CC, Phanachet I, Sae-Lee D, Whittle T. The human lateral pterygoid muscle. Arch Oral Biol. 2007;52(4):377–80.
6. Huang BY, Whittle T, Murray GM. Activity of inferior head of human lateral pterygoid muscle during standardized lateral jaw movements. Arch Oral Biol. 2005;50(1):49–64.
7. Hannam AG, McMillan AS. Internal organization in the human jaw muscles. Crit Rev oral Biol Med an Off Publ Am Assoc Oral Biol. 1994;5(1):55–89.
8. Mercuri LG, Wolford LM, Giobbie-hurder A. Long-Term Follow-Up of the CAD / CAM Patient Fitted Total Temporomandibular Joint Reconstruction System. 2002;1440–8.
9. Dimitroulis G. Comparison of the outcomes of three surgical treatments for end-stage temporomandibular joint disease. Int J Oral Maxillofac Surg. 2014 Aug;43(8):980–9.
10. Commisso MS, Martínez-Reina J, Ojeda J, Mayo J. Finite element analysis of the human mastication cycle. J Mech Behav Biomed Mater. 2015 Jan;41:23–35.
11. Ramos AM, Mesnard M. The stock alloplastic temporomandibular joint implant can influence the behavior of the opposite native joint: A numerical study. J Craniomaxillofac Surg. 2015 Oct;43(8):1384–91.
12. Mommaerts M. On the reinsertion of the lateral pterygoid tendon in total temporomandibular joint replacement surgery. J Cranio-Maxillofacial Surg. 2019;47(12):1913–7.
13. Mommaerts MY. On the reinsertion of the lateral pterygoid tendon in total temporomandibular joint replacement surgery. J Cranio-Maxillofacial Surg [Internet]. 2019;47(12):1913–7. Available from: https://doi.org/10.1016/j.jcms.2019.11.018
14. Baldino L, Cardea S, Maffulli N, Reverchon E. Regeneration techniques for bone-To-Tendon and muscle-To-Tendon interfaces reconstruction. Br Med Bull. 2016;117(1):25–37.
15. Apostolakos J, Durant TJS, Dwyer CR, Russell RP, Weinreb JH, Alaee F, et al. The enthesis: A review of the tendon-to-bone insertion. Muscles Ligaments Tendons J. 2014;4(3):333–42.
16. De Meurechy N, Verwilghen D, De Brucker Y, Van Thielen B, Mommaerts MY. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation. J Cranio-Maxillofacial Surg. 2021 Feb;49(4):256–68.
17. Angelo DF, Morouço P, Alves N, Viana T, Santos F, González R, et al. Choosing sheep (Ovis aries) as animal model for temporomandibular joint research: Morphological, histological and biomechanical characterization of the joint disc. Morphologie. 2016;100(331):223–33.
18. Domingue BM, Dellow DW, Barry TN. The efficiency of chewing during eating and ruminating in goats and sheep. Br J Nutr. 1991 May;65(3):355–63.
19. Verplancke K, De Waele W, De Bruyn H. Dental implants, what should be known before starting an in vitro study. Conf Sustain Constr Des [Internet]. 2011;2(3):360–9. Available from: https://biblio.ugent.be/publication/1177030
20. Wang Z, Wang C, Li C, Qin Y, Zhong L, Chen B, et al. Analysis of factors influencing bone ingrowth into three-dimensional printed porous metal scaffolds: A review. J Alloys Compd [Internet]. 2017;717(May 2018):271–85. Available from: http://dx.doi.org/10.1016/j.jallcom.2017.05.079

21. Bagno A, Di Bello C. Surface treatments and roughness properties of Ti-based biomaterials. J Mater Sci Mater Med. 2004;15(9):935–49.
22. Aparicio C, Gil FJ, Fonseca C, Barbosa M, Planell JA. Corrosion behaviour of commercially pure titanium shot blasted with different materials and sizes of shot particles for dental implant applications. Biomaterials. 2003 Jan;24(2):263–73.
23. Wang Q, Zhou P, Liu S, Attarilar S, Ma RL-W, Zhong Y, et al. Multi-Scale Surface Treatments of Titanium Implants for Rapid Osseointegration: A Review. Nanomater (Basel, Switzerland). 2020 Jun;10(6).
24. Li D, Ferguson SJ, Beutler T, Cochran DL, Sittig C, Hirt HP, et al. Biomechanical comparison of the sandblasted and acid-etched and the machined and acid-etched titanium surface for dental implants. J Biomed Mater Res. 2002 May;60(2):325–32.
25. Yeniyol S, Bölükbaşi N, Çakir AF, Bilir A, Ozdemir T. Effects of surface modifications with oxalic acid etching and sandblasting on surface topography and biocompatibility of cpTi surfaces. Biotechnol Biotechnol Equip. 2013;27(4):3995–4001.
26. De Meurechy N, Braem A, Mommaerts MY. Biomaterials in temporomandibular joint replacement : current status and future perspectives — a narrative review. Int J Oral Maxillofac Surg [Internet]. 2018;47(4):518–33. Available from: http://dx.doi.org/10.1016/j.ijom.2017.10.001
27. De Meurechy N, Aktan MK, Boeckmans B, Huys S, Verwilghen DR, Braem A, et al. Surface wear in a custom manufactured temporomandibular joint prosthesis. J Biomed Mater Res B Appl Biomater. 2022 Jun;110(6):1425–38.
28. Rentsch C, Schneiders W, Manthey S, Rentsch B, Rammelt S. Comprehensive histological evaluation of bone implants. Biomatter. 2014;4.
29. Collins CP, Wilson KJ, Collins PC. Lateral pterygoid myotomy with reattachment to the condylar neck: an adjunct to restore function after total joint reconstruction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003 Jun;95(6):672–3.
30. Bravetti P, Membre H, El Haddioui A, Gérard H, Fyad JP, Mahler P, et al. Histological study of the human temporo-mandibular joint and its surrounding muscles. Surg Radiol Anat. 2004;26(5):371–8.
31. Benjamin M, Kumai T, Milz S, Boszczyk BM, Boszczyk AA, Ralphs JR. The skeletal attachment of tendons - Tendon "entheses." Comp Biochem Physiol - A Mol Integr Physiol [Internet]. 2002 Dec;133(4):931–45. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L35463154%0Ahttp://dx.doi.org/10.1016/S1095-6433(02)00138-1%0Ahttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=10956433&id=doi:10.1016/S1095-6433(02)00138-1&atitle=The+skeletal+att
32. Hems T, Tillmann B. Tendon entheses of the masticatory muscles. Anat Embryol (Berl). 2000;202(3):201–8.
33. Tamaddon M, Samizadeh S, Wang L, Blunn G, Liu C. Intrinsic Osteoinductivity of Porous Titanium Scaffold for Bone Tissue Engineering. Int J Biomater. 2017;2017.
34. Xue W, Krishna BV, Bandyopadhyay A, Bose S. Processing and biocompatibility evaluation of laser processed porous titanium. Acta Biomater [Internet]. 2007;3(6):1007–18. Available from: https://www.sciencedirect.com/science/article/pii/S1742706107000852
35. Karageorgiou V, Kaplan D. Porosity of 3D biomaterial scaffolds and osteogenesis. Biomaterials [Internet]. 2005;26(27):5474–91. Available from: https://www.sciencedirect.com/science/article/pii/S0142961205001511
36. Markhoff J, Wieding J, Weissmann V, Pasold J, Jonitz-Heincke A, Bader R. Influence of Different Three-Dimensional Open Porous Titanium Scaffold Designs on Human Osteoblasts Behavior in Static and Dynamic Cell Investigations. Vol. 8, Materials . 2015.
37. Cheng A, Humayun A, Cohen DJ, Boyan BD, Schwartz Z. Additively manufactured 3D porous Ti-6Al-4V constructs mimic trabecular bone structure and regulate osteoblast proliferation, differentiation and local factor production in a porosity and surface roughness dependent manner. Biofabrication [Internet]. 2014;6(4):45007. Available from: http://dx.doi.org/10.1088/1758-5082/6/4/045007
38. Taniguchi N, Fujibayashi S, Takemoto M, Sasaki K, Otsuki B, Nakamura T, et al. Effect of pore size on bone ingrowth into porous titanium implants fabricated by additive manufacturing:

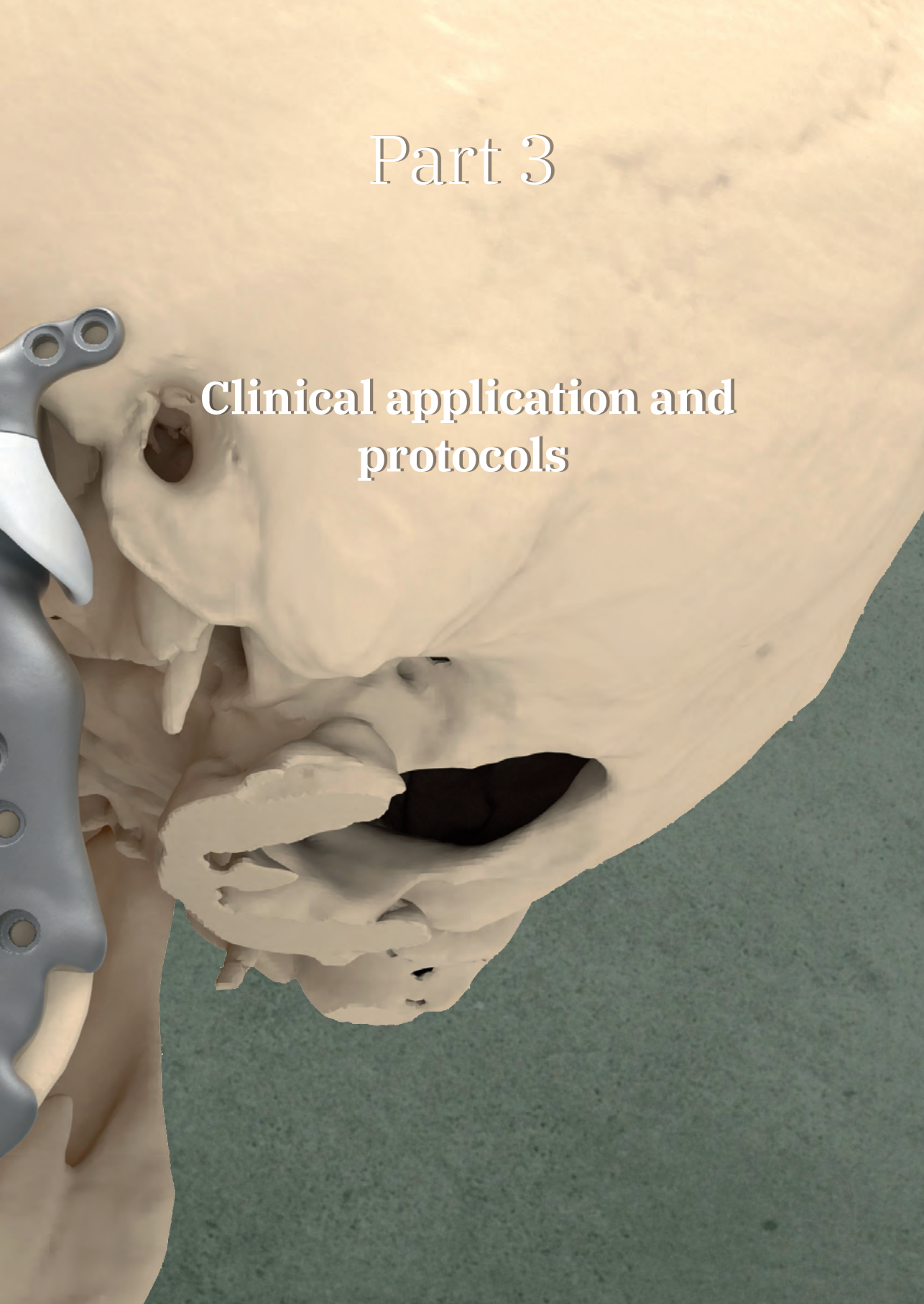
An in vivo experiment. Mater Sci Eng C [Internet]. 2016;59:690–701. Available from: https://www.sciencedirect.com/science/article/pii/S0928493115305002

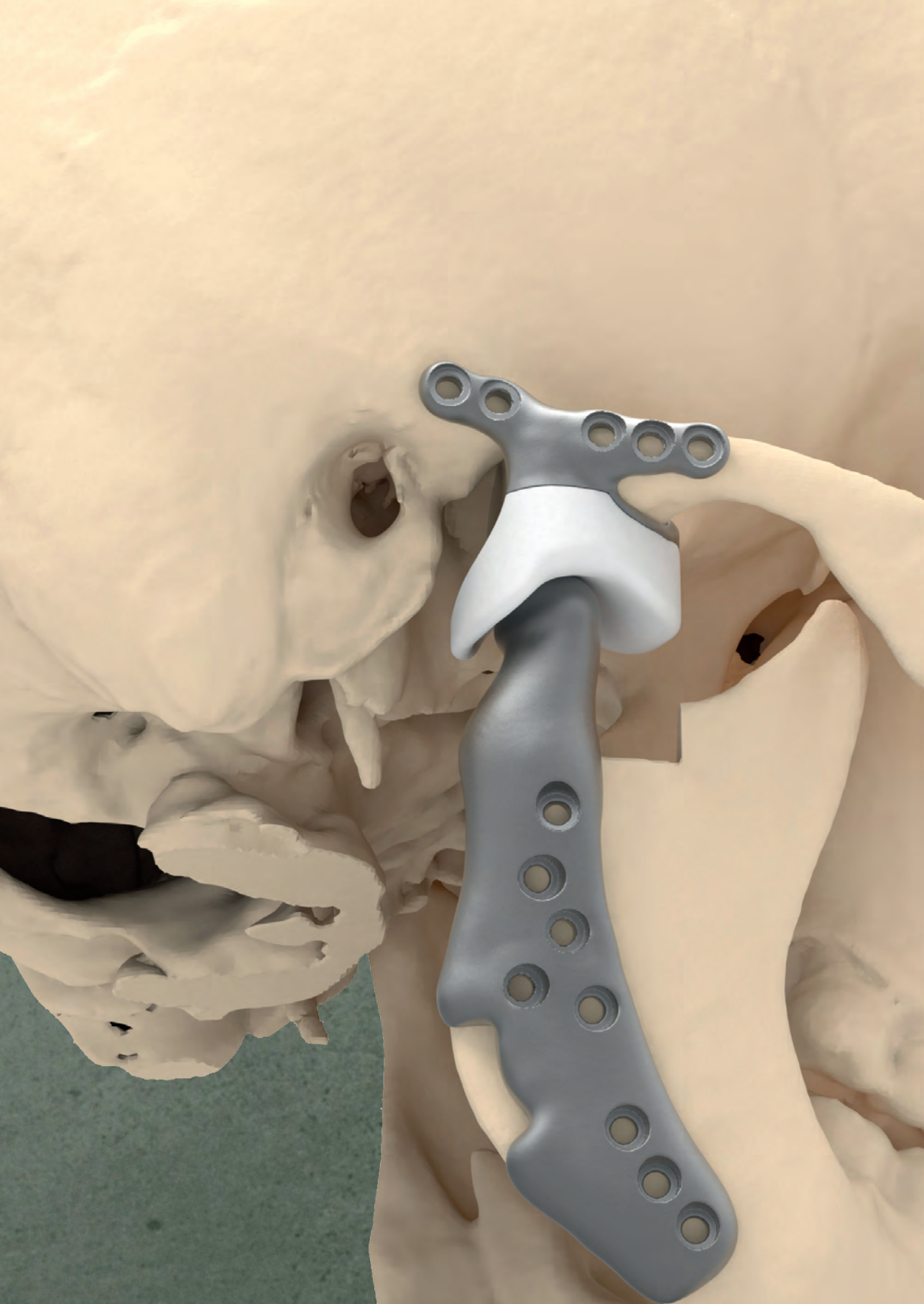
39. Dwek JR. The periosteum: What is it, where is it, and what mimics it in its absence? Skeletal Radiol. 2010;39(4):319–23.
40. Lin Z, Fateh A, Salem DM, Intini G. Periosteum: Biology and applications in craniofacial bone regeneration. J Dent Res. 2014;93(2):109–16.
41. Spalthoff S, Jehn P, Zimmerer R, Mollmann U, Gellrich N-C, Kokemueller H. Heterotopic bone formation in the musculus latissimus dorsi of sheep using beta-tricalcium phosphate scaffolds: evaluation of an extended prefabrication time on bone formation and matrix degeneration. Int J Oral Maxillofac Surg. 2015 Jun;44(6):791–7.
42. Spalthoff S, Zimmerer R, Dittmann J, Kokemüller H, Tiede M, Flohr L, et al. Heterotopic bone formation in the musculus latissimus dorsi of sheep using β-tricalcium phosphate scaffolds: Evaluation of different seeding techniques. Regen Biomater. 2018;5(2):77–84.
43. Shapiro F. Bone development and its relation to fracture repair. The role of mesenchymal osteoblasts and surface osteoblasts. Eur Cells Mater. 2008;15:53–76.
44. Colnot C. Skeletal cell fate decisions within periosteum and bone marrow during bone regeneration. J Bone Miner Res. 2009 Feb;24(2):274–82.
45. Pilliar RM, Lee JM, Maniatopoulos C. Observations on the effect of movement on bone ingrowth into porous-surfaced implants. Clin Orthop Relat Res. 1986 Jul;(208):108–13.
46. Goodman S, Aspenberg P. Effects of mechanical stimulation on the differentiation of hard tissues. Biomaterials. 1993;14(8):563–9.
47. Burke D, CR B, Jasty M, Haire T, Harris W. Dynamic measurement of interface mechanics in vivo and the effect of micromotion on bone ingrowth into a porous surface device under controlled loads in vivo. In: 37th Annual Meeting of Orthopaedic Research Society. Anaheim; 1991. p. 103.
48. Franchi M, Fini M, Martini D, Orsini E, Leonardi L, Ruggeri A, et al. Biological fixation of endosseous implants. Micron. 2005;36(7–8):665–71.
49. Karrholm J, Herberts P, Hultmark P, Malchau H, Nivbrant B, Thanner J. Radiostereometry of hip prostheses. Review of methodology and clinical results. Clin Orthop Relat Res. 1997 Nov;(344):94–110.
50. De Meurechy NKG, Loos P-J, Mommaerts MY. Postoperative Physiotherapy After Open Temporomandibular Joint Surgery: A 3-Step Program. J Oral Maxillofac Surg. 2019 May;77(5):932–50.



Part 3

Clinical application and protocols





Chapter 9

Evolutionary Steps in the Development of a Patient-specific Temporomandibular Joint Prosthesis

This chapter is based on:

Evolutionary Steps in the Development of a Patient-specific Temporomandibular Joint Prosthesis

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Introduction

The temporomandibular joint (TMJ) has multiple supportive functions (breathing, chewing, supporting the upper airway, sucking, swallowing, making facial expressions, vocalizing, and sustaining correct pressure in the middle ear) which are all derived from protrusion, retrusion, and lateralization of the mandible and opening of the mouth. Indications for prosthetic replacement include TMJ ankylosis and end-stage joint disease resulting from trauma, infection, degenerative arthrosis, cancer, developmental/inherited craniofacial anomalies affecting the mandible and TMJ, failed/failing TMJR devices or failed prior invasive surgery.(1–4) The decision to replace the affected joint is based on the severity of the reduced quality of life, mainly related to mandibular function, food intake and pain.

While stock prostheses may reduce pain and aid mouth opening, they do not naturally function in alignment with the healthy, contralateral joint because they have not been adapted based on the patient's anatomy nor do they allow for proper grinding movements. This is because the lateral pterygoid muscle was sacrificed during condylectomy and not re-attached. Optimal biological integration and acceptable wear of alloplastic components are prerequisites for any TMJ prosthesis. Moreover, for optimal success, the TMJ prosthesis should be made of biocompatible materials, should be able to withstand the loads delivered over the full range of function of the joint, must be stable in situ and the surgery to implant the prosthesis must be performed for the proper indications, and it must be performed aseptically.(5)

Regardless of whether the TMJ is reconstructed with alloplastic, allogeneic, or autogenous material, it should improve mandibular function and form, reduce suffering and disability, contain excessive treatment and cost and prevent morbidity.(6)

According to a review performed by De Meurechy et al.(7) no extensive research has been conducted (over the last 20 years) to improve TMJ prostheses regarding both materials and functionality. To optimize and

improve these existing TMJ stock prosthesis concepts, all physiological movements that are required for the abovementioned functions of a normal TMJ should be restored on both the replaced and contralateral (healthy or replaced) sides. The objective of this article is to discuss the development of such an improved TMJ prosthesis, called the TMJ Parametro (Figs. 1a, b; Video 1) (CADskills BV, Ghent, Belgium).

Materials and Methods

All the procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee (Centraal Studieloket, UZ Brussel, Code of approval: EC-2022-075) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The authors certify that they have obtained all appropriate patient consent forms. On the form, the patients have given their consent for their images and other clinical information to be reported in this journal. This study encloses a descriptive technical review/report, a summary of the early results and two case studies.

Implant Design

Metallic component.

The mandibular component and the skull base segment of the fossa component are additively manufactured using a Ti6Al4V ELI. The condyle is resurfaced using a diamond-like carbon (DLC) coating (Figs. 1c, 2), which is applied using the nondisclosed HadSat protocol with a Vickers hardness (HV0.05) of 3500 ± 500 and a friction coefficient of 0.1. The HadSat coating is a nontoxic, carbon-based coating that meets the Food and Drug Administration guidelines. The biocompatibility of this coating was tested under the International Standard ISO 10993-1 by the North American Science Associates. The test results are summarized in Table 1.

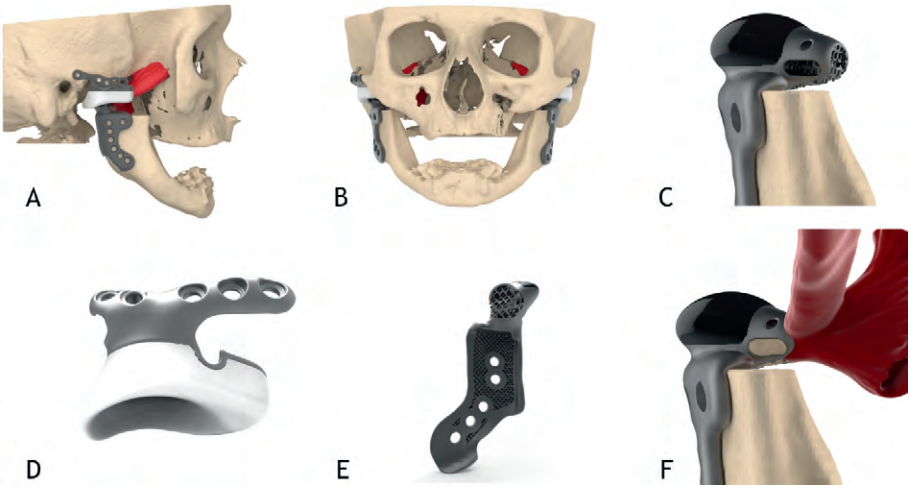

Fig 1: Renders of a TMJ Parametro with pterygoid muscle reattachment. (a) Lateral view of a TMJ Parametro total joint. (b) Frontal view of a bilateral TMJ Parametro total joint. (c) Frontal view of the Ti6Al4V mandibular component with the HadSat® coating. (d) The fossa component consisting of highly cross-linked polyethylene and a grade 23 Ti6Al4V extra-low interstitial. (e) The bone-implant interface, which shows the 3D-printed lattice structure used to induce osseointegration as a secondary fixation method. (f) Lateral pterygoid muscle reattachment using bone chips and the corresponding enthesis.

Table 1: Overview of Biocompatibility Tests Performed on the HadSat Coating by the North American Science Associates.

Test	Result
Cytotoxicity – ISO Elution	Nontoxic (Cytotoxicity grade was 0)
ISO Maximization Sensitization	No evidence of delayed dermal contact sensitization
Intracutaneous Reactivity Study	No evidence of significant irritation
Acute Systemic Toxicity	No mortality or evidence of significant systemic toxicity
Rabbit Pyrogen Test	Nonpyrogenic
In Vitro Hemolysis	Nonhemolytic (Mean hemolytic index was 0%)
Bacterial Reverse Mutation Study	Nonmutagenic
Muscle Implantation Study (1 week)	Nonirritating

Polymeric component.

The articulating part of the fossa component, which is in contact with the condyle, is made of γ-irradiated tocopherol-enriched highly cross-linked UHMWPE (HXLPE) (Fig. 1d). This HXLPE component is hot pressed onto the scaffold of a Ti6Al4V component, which in turn is fitted onto the glenoid fossa. Processing parameters as temperature, time, and pressure settings are confidential.

Surface Finishing

A sandblasted, large-grit, and acid-etched (SLA) surface at the bony interface of the mandibular component and the skull base of the fossa component of the TMJ Parametro is achieved by both micro-shot peening with alumina grit (ø =550 µm) and etching using 2 wt% oxalic acid at 85°C for 10 min. This enhanced surface roughness allows for bone ingrowth which reduces the stress on the screw-bone interface quite rapidly, allowing a reduction in the number screws required for primary stability from seven to five. (Fig. 1e)

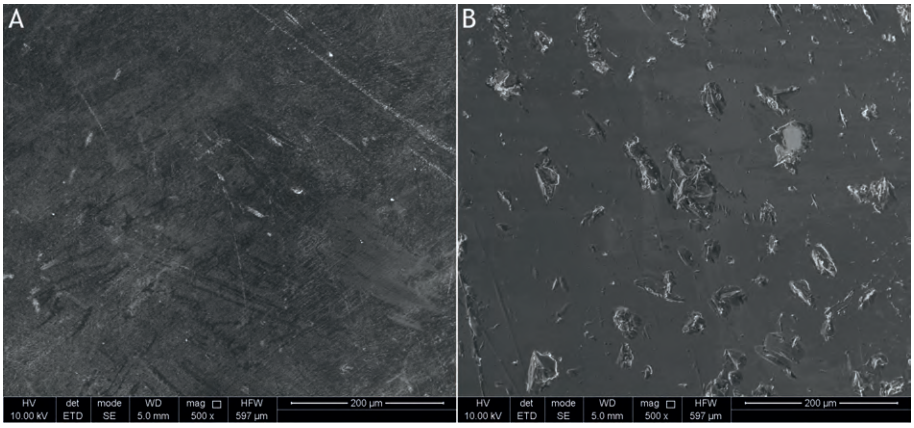

Fig 2: Microscopic views (Magnification 500x) of the condylar surfaces of two different TMJ Parametro implants using scanning electron microscopy. (a) A condyle that was coated with HadSat showing few irregularities. (b) An uncoated, polished condyle showing multiple grooves.

Functionality

Kinematics of the prosthetic joint.

When comparing the load on the contralateral side of a mandible that has undergone total TMJ replacement with the load on the condyle of a healthy mandible, the load increase is approximately 15% when using a stock prosthesis.(8–13) Increases in mechanical loads have been shown to stimulate cartilage production and articular disc damage which can negatively affect the patient (e.g., pain) and should thus be avoided.(14,15)

In order to prevent disease development in the unaffected joint, an attempt was made to prevent an increase in load in the untreated joint.

This was done by allowing the replaced side to move synchronously with the other joint during both rotational movements with the other joint and vice versa, as well as during translative movements (e.g., when performing movements of opening and closing, both the healthy and replaced condyle should move without causing interferences in each other's joint space). In comparison with the Groningen TMJ prosthesis, where a more bulky fossa component with a low rotational point is used, the articular surface of the TMJ is placed more cranial, to allow for a more natural movement.(16) The same study, concerning the Groningen TMJ prosthesis, did indicate that a more accurate planning and prediction was feasible thanks to the patient-specific fit.

Furthermore, mastication involves laterotrusion, which is only possible with intact lateral pterygoid muscle function since occasional recruitment of the medial pterygoid muscle and minimal support by the masseter muscle cannot be predicted. Reattachment of the lateral pterygoid muscle is one of the main (innovative) features of the discussed joint. (17) In order to realize this reattachment, a scaffold in the condylar neck area (optionally, with a tunnel for temporary fixation with bioresorbable sutures) was provided, to form a bony union with the enthesis that has been carefully chiseled from the pterygoid fovea prior to condylar resection. (Figs. 1c, f) Therefore, both the condylar axis angle, the Bennett shift and free excursion at the anteromedial joint space should be integrated into the design of the prosthesis.

Prosthetic joint design.

The occurrence of material wear is unavoidable, due to constant friction during mastication and other jaw movements. Also, to keep the center of rotation as high as possible, so as to mimic the original TMJ position, the HXLPE has a central thickness of only 2 mm. Despite the possible occurrence of a more uneven wear pattern caused by the more natural movements of the TMJ Parametro artificial condyle when compared to regular stock implants, the replacement of the fossa component may be required. This exchange could be facilitated by applying a tongue-and-groove fixation between the HXLPE and titanium parts as to minimize the invasiveness of the revision surgery. However, the use of such a fixation

would also increase the surface area available for bacterial colonization by pumping actions, potentially resulting in the formation of a biofilm and in turn an acute infection.

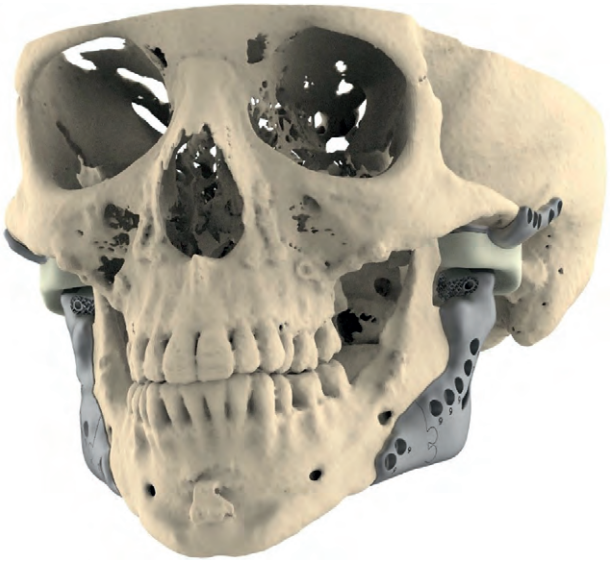

Fig. 3: A more prominent jaw angle can be used in the mandibular component to avoid or compensate for asymmetries.

As previously discussed, a rigid fixation is achieved by compressing the HXLPE onto a thin titanium scaffold (Figure 1d). Tests performed in sheep have demonstrated that this type of fixation is protective against infection, while at the same time counteracting undue deformation over time.(18) In order to allow for replacement of the fossa component (typically after 20 years or more) no residual scaffold was provided at the interface between the fossa component and the skull base, which is likely thin at the middle cranial fossa and easily out-fractured, as to prevent excessive force during replacement.

Because the design of the joint is specific to the patient, care should be taken when extending the fixation plate of the fossa component anteriorly (not surpassing the midtubercular level to protect the frontal branch of the facial nerve) and posteriorly (making use of the non-pneumatized part of the temporal squama).

The size of the anterior extension of the fossa component depends on whether the coronoid process was resected or maintained. With the origin and insertion of the temporalis muscle intact, the anterior shift of the condyle is limited and anterior dislocation of the condyle is not anticipated. The more limited space and less anterior shift are likely to shorten the extension of the condylar path of the fossa component. The reverse situation applies when the coronoid process is resected.

If no undercuts are present or when they can be eliminated, a saddle-like design can be used to fit over the resection stump. This physically prevents any potential downward, medial and lateral movements. In doing so, a minimal set of screws are sufficient to counteract upward movements, which by themselves are minimized by the action of the masseter and medial pterygoid muscles.

Finally, the design of an improved joint prosthesis should also consider psychosocial functions. Asymmetries in the lower face, which can lead to a compromised self-image, can be addressed by using design software that has mirroring tools (e.g., Geomagic Freeform Plus, 3DSystems, Rock Hill, SC, USA) to achieve correct aesthetic outcomes postoperatively. By correcting side differences in the gonial angle and mandibular border using the mirrored side as a reference and whilst taking into consideration the quantity and quality of overlying soft tissue, the TMJ prosthesis act as a facial contouring implant as well.(Fig. 3) Thus alleviating stigmata of pathological deformations.

Patients and Methodology

After thoroughly evaluating the proposed implants in sheep experiments,(18,19) eleven patients (2 men, 9 women; mean age at surgery of 49 years, 1 months) received all together 16 customized total TMJ Parametro prostheses. The surgery was performed by one surgeon in the same hospital. Follow-up ranged between 1 month and 4.5 years. Four patients suffered from end-stage degenerative arthrosis/arthritis due to disc pathology. Three had conservatively treated subcondylar fractures with subsequent degenerative joint disease. One patient had osteomyelitis in the ascending ramus after a ballistic trauma. One

showed bilateral condylar resorption after orthognathic surgery. There was one female adolescent with unilateral craniofacial microsomia and one with TMJ ankylosis as a result of radiotherapy in childhood for a rhabdomyosarcoma. The indications for surgery varied between severe pain, refractory to conservative treatment and/or tissue sparing surgery, and severe trismus with severe dietary restrictions. Results were recorded in the electronic medical files, using Helkimo's index and a patient-reported outcome measure questionnaire.(20) The criteria and indications for these TMJ replacements are as described by Sidebottom and as mentioned in CADskills BV's TMJ manual.(21)

Results

The main aim of the paper is to present technical evolutionary steps, not to analyze clinical end-results. However, in order to demonstrate the clinical behavior of the novel prosthesis, early results of this first small group of patients are described here for completeness.

Group Results

Because the heterogeneity of indications, descriptive statistics about pain relief, increased mandibular movements, and dietary improvements are not representative for individual changes in wellbeing. The ankylosis and hemifacial microsomia caused no pain, whereas a maximal mouth opening of 28 mm was present in the patient with bilateral condylar resorption, who scored 10 in the Visual Analogue Scale (VAS, 0–10) before joint replacement. Therefore, the following results should be interpreted with caution. Two cases are described in detail to complement the group results.

One patient was excluded from the descriptive statistics because she twice received joint replacements within a year interval, once on the right-hand side and once on the lefthand side, leading to a disrupted follow-up. The total number of patients that were included in the descriptive analysis was 11, including one patient with a major component of neuropathic facial pain, whose pain score remained 8.

Important to remark is that the reattachment of the lateral pterygoid muscle was not always achievable, nor favorable. In cases with too much osteogenic capacity (young, ankylotic joint) or in absence of the lateral pterygoid muscle altogether (hemifacial microsomia, Pruzansky type III), no reconstruction of the muscle enthesis was attempted. In 25% of the discussed joint replacements, an enthesis reconstruction could not be performed, otherwise, the lateral pterygoid reattachment was carried out as described in the work of Prof Mommaerts.(17)

Post-operative maximal mouth opening increased from 25.9 (SD 4.3) mm to 32.5 (SD 1.3) mm. The preoperative average pain score of 8.1 (SD 1.2) dropped to 1.4 (SD 1.3), whilst the mean preoperative diet score of 1.7 (1= liquid, 2 = soft, 3 = solid; SD 0.4) increased to 2.8 (SD 0.3). The average follow-up period was 23.3 months.

Case Studies

To illustrate the functionality of the TMJ Parametro, unilateral and bilateral replacement cases are discussed.

Case study #1: unilateral total joint replacement.

In the early 1990s, a male patient was treated using intermaxillary fixation for 11 months (according to the patient, unverified) following a facial trauma. Since that time, the patient has experienced progressive worsening of joint function and increasing pain. This persistent pain became unbearable in 2017, forcing the patient to sleep upright. The majority of the pain was located on the right side, both at rest and while medicated. While speaking, the patient had to push the right ascending ramus into protrusion using his index finger. In 2018, a maximal mouth opening of 40 mm was measured, and laterotrusive motions of 10 mm and 5 mm to the left and right, respectively, were observed. Both at rest and during movement, capsulitis arthralgia was noticeable, which limited the patient's diet to only liquid and very soft foods. A visual analogue scale (VAS) pain score of 10/10 was obtained, which led to an overall Wilkes Stage 5 classification(22) and a clinical dysfunction degree (Helkimo Index) of III.(20) CT scans showed bilateral, degenerative changes of both TMJs, narrowing of both joint spaces, and bilateral formation of

osteophytes with flattening of the condyles (Figure 4). Since the clinical symptomatology was worse on the right side, the surgeons opted for a unilateral (right) joint replacement.

Fig. 4: A 3D model of the TMJ on the right side of the first patient, showing formation of osteophytes and flattening of the condyle (red arrow).

In 2018, at the age of 55 years, he received a TMJ Parametro prosthesis on the right side. The lateral pterygoid tendon was fixed to the scaffold in the condylar neck of the mandibular component. The postoperative maximal mouth opening progressed from 21 mm (1 month postoperatively) to 49 mm (3 years postoperatively) (Fig. 5a), while the laterotrusive motion to the left (towards the unoperated side) increased from 6 mm to 14 mm during the same time period (Fig. 5b). Meanwhile, the laterotrusive motion towards the operated side increased from 5 mm to 13 mm. The results from the follow-up of his maximal mandibular movements during this 3-year period are shown in Figure 6a. His VAS pain scores (on a scale of 10) decreased from 10 (preoperatively) to 3 (1 month postoperatively), 2 (3 months postoperatively), and 0 during his next three check-ups (6 months, 1 year and 3 years postoperatively) (Fig. 6a). After 3 months, the patient was able to eat solid food again (Fig. 6a).

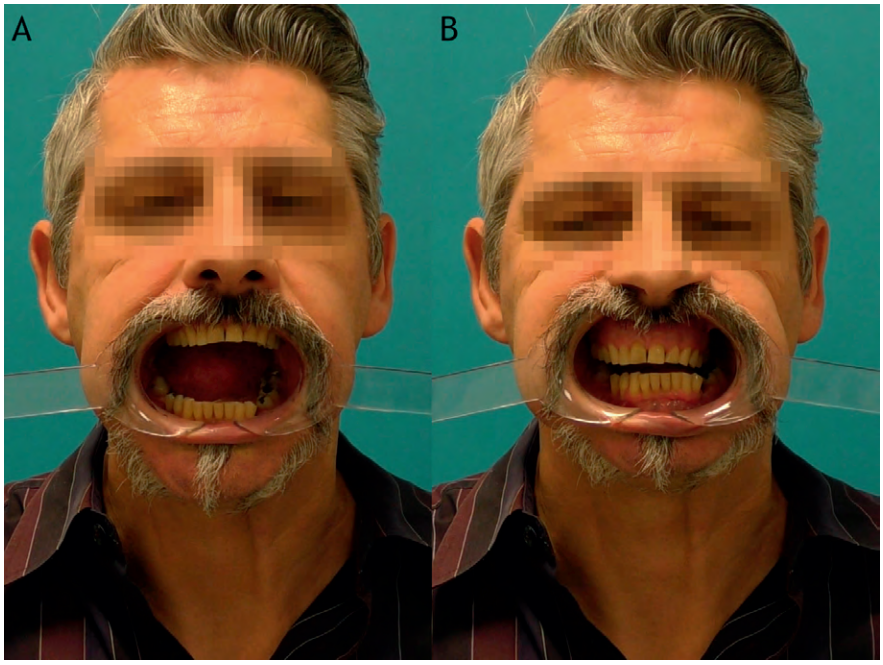

Fig. 5: Clinical visualization of the patient's maximal mouth opening (a) and lateral movement towards the unoperated side. (b) after unilateral temporomandibular joint replacement.

Case study #2: bilateral total joint replacement.

A 77-year-old female patient underwent conservative treatment for bilateral arthrogenic TMJ pain that had persisted since 1986. In 2007, a CT scan showed an extensive degenerative process in both joints. In 2011, a CT scan showed extreme narrowing of the joint spaces and a dysmorphic appearance of the condyles, including osteophytic and resorptive processes. In 2017, she visited multiple hospitals with pain in both TMJs which, at rest, radiated temporally and worsened during movement. Her maximal mouth opening was restricted to 25 mm. VAS pain scores of 8/10 (right) and 6/10 (left) were obtained, which led to a VAS dietary score of 4 (where 0 is a liquid diet and 10 is a normal diet) and an overall Wilkes Stage 5 classification with variable pain at rest and crepitations and pain during movement.(22)

In 2019, she underwent bilateral total joint replacement with a customized TMJ Parametro prosthesis at the Universitair Ziekenhuis Brussel. Both left and right lateral pterygoid tendons were reinserted into the scaffold in the condylar neck of the corresponding mandibular components.(17) (Fig. 7) Her postoperative maximal mouth opening progressed from 15 mm (1 month postoperatively) to 32 mm (3 years postoperatively), while her laterotrusive motion to the right increased from 1.5 mm to 5 mm during the same period. Meanwhile, the opposing laterotrusive motion increased from 1.5 mm to 3 mm. The results from her current follow-up of her maximal mandibular movements during this 3-year period are shown in Figure 6b. At the 1-month postoperative check-up, her pain had already completely disappeared (VAS pain score of 0, Fig. 6b), and after the 6-month mark, she was finally able to eat solid food again. (Fig. 6b)

Discussion

Abovementioned post-operative results, which mimic healthy biomechanical movements of the mandible, were achieved by extensive research and careful selection of the most suited biomaterials and features, which are being discussed here. The main limitation of this study is the currently small sample group and short follow-up. Moreover, the electromyographic results of lateral pterygoid muscle activity could not be monitored. It would be interesting to correlate such findings with various lateral pterygoid muscle enthesis reconstructions.

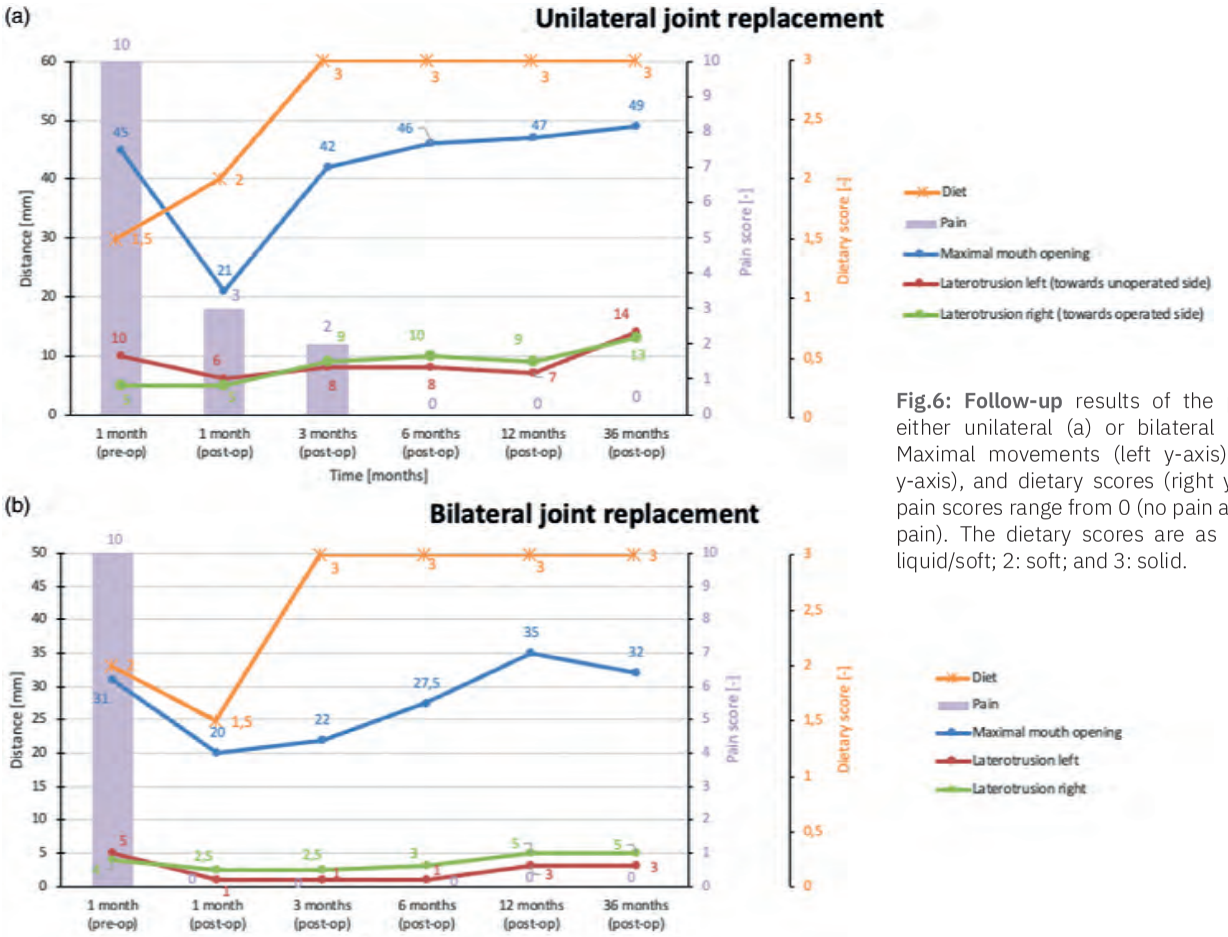

Fig.6: Follow-up results of the patients who received either unilateral (a) or bilateral (b) joint replacement. Maximal movements (left y-axis), pain scores (middle y-axis), and dietary scores (right y-axis) are shown. The pain scores range from 0 (no pain at all) to 10 (unbearable pain). The dietary scores are as follows: 1: liquid; 1.5: liquid/soft; 2: soft; and 3: solid.

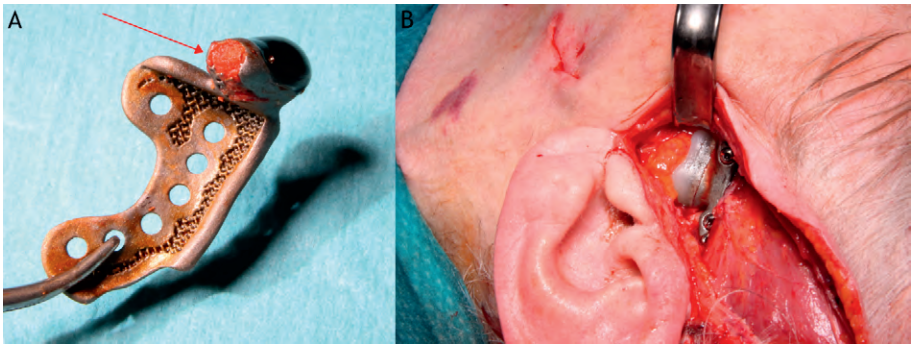

Fig. 7: Intra-operative pictures of case 2. (a) Condensed bone chips in the scaffold in the condylar neck for lateral pterygoid muscle attachment (red arrow). (b) The implanted fossa component.

Metals

A meta-analysis of implant-related metal sensitivity showed that 10% of the general population is allergic to at least one or more alloy components (usually nickel) found in orthopedic implants. In patients with a functioning prosthesis, this number increased to 23%, while for patients with a failing prosthesis, it was as high as 63%.(23) A more recent study reported that nickel, chromium, and cobalt induce allergic skin reactions in 20%, 4%, and 7%, respectively, of the general population in Europe and in 14%, 4%, and 9%, respectively, of the population in the United States.(24) The prevalence of metal sensitivity appears to be rising and is most pronounced in nickel-containing implants.(25) In contrast, only occasional sensitivity has been reported for titanium.(23) In a recent review, only two studies presented strong evidence of sensitization to commercially pure titanium.(26) In contrast to chromium-cobalt particles, titanium-aluminum-vanadium-containing particles of a similar size to those found in the surrounding tissues of failed prostheses in humans showed little toxicity in an in vitro study using rat macrophages, even at high concentrations.(27)

These findings result in Ti6Al4V being the preferred titanium alloy in small load-bearing implant applications. Important to remark is that the use of grade 23 Ti6Al4V extra-low interstitial (ELI) is preferred for long-term implants, such as in joint applications. Because of the reduced oxygen, nitrogen, and iron content, this grade shows enhanced biocompatibility

compared to industrial grade 5 Ti6Al4V. Grade 23 is also most frequently used as a starting powder during the additive manufacturing of titanium implants.

Besides Ti's excellent strength and manufacturability, it also boasts a high corrosion resistance. This is thanks to the presence of a thin (1.5 – 10 nm in thickness) but stable oxide film on the surface which minimizes the release of metal ions from the bulk.(28,29) This layer is mainly composed of amorphous TiO2 with small amounts of suboxides TiO and Ti2O3 near the metal/oxide interface, and depending on the alloying elements, traces of Al2O3, V2O3 or V2O5, ...(30,31) The nearly-stoichiometric structure of TiO2 with few ionic defects/vacancies makes this compound an excellent barrier for ionic migration from the bulk metal to the environment.(32) As a result and in contrast to other bioinert implant materials, Ti alloy implants are not encapsulated by fibrous tissue. Even in particulate form, tissue activation remains weak because of this protective layer.(33)

However, the presence of other metal oxides in the passive film on the Ti6Al4Valloy does raise some concerns. Although Al2O3 has never been associated with toxicity or allergy after orthopedic biomaterial degradation,(34) vanadium oxide can cause allergic reactions,(35) as well as toxicity at low concentrations and with continuous exposure.(36) Moreover, the presence of alloying metal ions (Al, V) having a different valence than the host metal (Ti) can alter the ionic transport across the oxide layer. Whereas the stable Al2O3 decreases the anion vacancies thereby enhancing the barrier function of TiO2, vanadium oxide dissolves from the passive film creating vacancies that enable ionic transport and therefore increase metal ion release.(32)

Despite the limited Ti ion release from Ti based implants, it can still be a problem for certain percentage of the patient population. Prospective skin patch testing of orthodontic patients who wear titanium- and nickelcontaining appliances demonstrated a nickel allergy prevalence of 14% and a titanium allergy prevalence of 4%.(37) It is thus imperative to subject potential candidates for TMJ replacement to skin patch testing for titanium hypersensitivity. However, a standardized patch test is not

yet available. An important aspect to testing is sensitization. Should allergy or sensitization susceptibility be tested? Specific immunoglobulin E (IgE) antibodies are produced after prior exposure to a substance that consequently becomes an allergen. Hence, should patch testing be repeated after 3 months to ensure that the original test has not sensitized the candidate to that substance? Is epicutaneous sensitization possible, or is intradermal testing mandatory? T-lymphocytes are constantly observed surrounding titanium debris in tissues. Titania microparticles can act as adjuvants to drive antigenic T helper 2 cell differentiation and the IgE response. Should titania microparticles be injected intradermally to rule out hypersensitivity?

A second remark that has to be made with concern to the use of titanium alloys is the material's poor abrasion/wear resistance. While compression forces are on average 66 N/cm2 in a TMJ, shear forces do play a greater role.(12,38) Even more so by restoring the lateral pterygoid muscle (LPM) function, as all movements, including protrusion and lateralization, remain simultaneously present. Despite the low forces generated, low friction and a hard coating are advised for the condylar head to prevent wear of the opposing fossa component, which usually consists of softer polyethylene. The latter can be achieved by using a diamond-like carbon coating (DLC). (39) DLC is an amorphous carbon composed of a mixture of sp3 and sp2 carbon bonds with various levels of hydrogen. Coatings of materials within the DLC family can be fabricated based on hydrogen content, the addition of metallic and nonmetallic doping elements, the presence of interlayers, and the choice of bonding and deposition methods. These parameters can be controlled for the engineering of a broad range of thin (1–5 μm) coatings with a hardness of 8–80 GPa or higher. Diamond is the hardest known material to date, with 70–150 GPa Vickers hardness. The coefficient of friction, surface finish, and application temperature can also be manipulated. After the application of the coating, a polishing process can be used to increase the tribological properties of the prosthesis.(40)

Delayed delamination from its substrate because of corrosion poses a serious issue for implant stability. Delamination occurs because of the dissolution of the silicon-adhesion-promoting interlayer and has been

observed in noncemented hip prostheses.(41) Consequently, excessive wear of the polyethylene counterpart occurs. Interfacial and interlayer properties should, therefore, be carefully monitored.

HXLPE

Medical-grade, ultra-high molecular weight polyethylene (UHMWPE) wear debris (ie, small particles generated from articular surfaces in joint prostheses) often triggers an inflammatory response.(42) The infiltration of monocytes and the activation of fibroblasts and histiocytes into the pseudo-synovial membrane lead to the production of chemokines, cytokines, and osteoclastogenic factors. Monocytes and macrophages differentiate into osteoclasts, which are responsible for osteolysis and loosening of the implant. The formation of submicron-size particles (<1.0 mm) leads to a higher proinflammatory cytokines production compared to particles that are larger than 1 mm, which induce giant cell formation.(42)

In order to limit the amount of UHMWPE wear, crosslinking can be achieved using ionizing irradiation. This leads to the production of free radicals that can recombine and form the cross-links.(43) While highly cross-linked UHMWPE (HXLPE) exhibits decreased volumetric wear, the immune reaction to these HXLPE particles is higher than to conventional UHMWPE particles.(44) Nevertheless, as there is a significant decrease in total particle volume, less inflammation and foreign body reaction occurs when using HXLPE, making it for instance preferrable to conventional polyethylene for hip prostheses.(45) HXLPE bearings exhibit a reduced incidence of aseptic loosening and osteolysis.

As previously discussed, the HXLPE-component has also been treated with tocopherol. Vitamin E, which acts as an antioxidant will prevent oxidation during compression molding, radiation cross-linking (due to γ-irradiation), and shelf storage. Furthermore, it will also protect the HXLPE from oxidation after implantation, and implantation as free radicals are generated in vivo by both cyclic loading and the reactions of lipids absorbed from the synovial fluid. (43,46) As a result, HXLPE blended with vitamin E exhibits good resistance to fatigue wear.(47) However, important to remark is that, clinically, the addition of tocopherol has not been proven

to be an asset, even when reduced total femoral head penetration was observed at a 3-year follow-up.(48)

Tissue Integration

Another important aspect of an implant (endoprosthesis) besides biocompatibility is tissue integration. Osseous integration is the apparent direct attachment of bone to a biocompatible material without intervening tissue. A recent study(49) found that there is a direct relationship between the roughness of the titanium surface and the stimulation of bone formation, with pores measuring 600 μm (macroroughness) show greater bone ingrowth compared to a smaller (100–300 μm) pore diameter.(50–53) Secondly, sandblasted, large-grit, and acid-etched (SLA) surfaces (micro roughness) show increased osseointegration compared to smooth surfaces.(50) It is believed that these mechanical and chemical abrasions induce the adsorption of fibronectin and other proteins that, in turn, trigger osteoblasts to form focal adhesions via an integrin-mediated mechanism.(54,55) Removing surface contaminants while imparting wettability is equally useful and may trigger hard tissue formation as well.(56–58) Further, plasma activation induces the initial adhesion of proteins and bone marrow cells. Unfortunately, steam sterilization after plasma activation completely removes this increase in wettability.

In comparison to osseointegration, soft tissue integration is less precisely defined. It is rather described as “a strong soft tissue-implant seal … with a thin capsule containing few inflammatory cells and fibroblasts… and collagen fiber orientation preferably oblique to the implant surface or randomly oriented”.(59) A surface roughness Ra value between 0.5 and 1 μm has been shown to induce soft tissue adhesion. Smoother surfaces, with the exception of acidpolished and anodized titanium (Ra = 0.2 μm), prevent adhesion. Micro-arc oxidation (also known as plasma electrolytic oxidation) significantly increases the percentage of soft tissue adhesion.(60) Similarly, a fibroblast growth factor-2/apatite composite coating applied by immersion (for 48 h) induced significantly less inflammation and yielded promising skin-screw interfaces.(61) Both processes have a low cost-effectiveness.(59)

Heterotopic Ossification

A last point of discussion that has to be touched upon in light of reattachment of the LPM's enthesis, is the occurrence of heterotopic ossification (HE).(62) HE is defined as 'a heterogeneous disorder characterized by pathologic endochondral ossification with hematopoietic bone marrow in soft tissues, such as subcutaneous tissue, skeletal muscle, or fibrous tissue adjacent to joints'.(63) About 10% of HE cases result in limitations in range of motion. Once it develops, surgical removal is the only effective treatment, followed by local irradiation, which in turn may induce malignancy, and/or nonsteroidal anti-inflammatory agents to prevent recurrence.(64) A strong relationship between trauma (e.g., arthroplasty) and the involvement of multiple organ systems seems to exclude the influence of the type of material or its surface characteristics.(63) An important question is whether the pores of the titanium scaffold must be filled with particulate bone, calcium phosphate, stem cells, or growth factors to enhance bone formation and guarantee bony union with the reattached enthesis. In a sheep model of TMJ replacement, postoperative function suggested that filling the scaffold with autologous bone chips was sufficient.(19) The addition of calcium phosphate may hinder reattachment, even if more bone will be formed within the pores, and the addition of bone marrow-derived mesenchymal stem cells has not been clinically proven to enhance bony fusion.(65–67)

Even though an increase in movement capabilities can be seen by using this method, longstanding limitations of lateral movements cannot be undone by lateral pterygoid reattachment. Disuse atrophy of the lateral pterygoid muscle does not appear to be reversed by exercise. Supplementation with branched-chain amino acids and anabolic steroids was not investigated in that respect.

Conclusion

A careful analysis of the requirements for a successful TMJ replacement has led to the development of a new type of individualized, artificial joint that mimics both normal joint anatomy and function. Even though various

features contribute greatly to optimal functionality and biocompatibility, the final outcome of the replacement will not only depend on these added features but also on the underlying disease and its duration, as well as on compliance with postoperative physiotherapy. Even though a larger sample size (potentially with division between indications) is needed to have sufficient evidence on the added values of this prosthesis, the case series still supports further investigations on the use of the prosthesis. Early clinical results are promising. Results in a sheep experiment and a small study series indicate that further clinical use is justified. Further long-term follow-up in a larger sample is planned for.

References

1. Brennan PA, Ilankovan V. Arthrocentesis for temporomandibular joint pain dysfunction syndrome. J oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg. 2006 Jun;64(6):949–51.
2. Carvajal WA, Laskin DM. Long-term evaluation of arthrocentesis for the treatment of internal derangements of the temporomandibular joint. J oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg. 2000 Aug;58(8):852–7.
3. Quinn P, Granquist EJ. Stock Prostheses for Total Reconstruction of the Temporomandibular Joint BT - Temporomandibular Joint Total Joint Replacement – TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons. In: Mercuri LG, editor. Cham: Springer International Publishing; 2016. p. 69–90. Available from: https://doi.org/10.1007/978-3-319-21389-7_4
4. Mercuri LG. Temporomandibular Joint Total Joint Replacement -- TMJ TJR: A Comprehensive Reference for Researchers, Materials Scientists, and Surgeons [Internet]. Springer International Publishing; 2015. Available from: https://books.google.be/books?id=lKUvCwAAQBAJ
5. Mercuri LG. The Use of Alloplastic Prostheses for Temporomandibular Joint Reconstruction. J Oral Maxillofac Surg [Internet]. 2000;58(1):70–5. Available from: http://www.sciencedirect.com/science/article/pii/S0278239100800191
6. Mercuri LG. The TMJ Concepts Patient Fitted Total Temporomandibular Joint Reconstruction Prosthesis. Oral Maxillofac Surg Clin North Am [Internet]. 2000;12(1):73–91. Available from: https://www.sciencedirect.com/science/article/pii/S104236992030234X
7. De Meurechy N, Mommaerts MY. Alloplastic temporomandibular joint replacement systems: A systematic review of their history. Int J Oral Maxillofac Surg [Internet]. 2018;47(6):743–54. Available from: https://doi.org/10.1016/j.ijom.2018.01.014
8. Bekcioglu B, Bulut E, Bas B. The Effects of Unilateral Alloplastic Temporomandibular Joint Replacement on the Opposite-Side Natural Joint: A Finite-Element Analysis. J Oral Maxillofac Surg [Internet]. 2017;75(11):2316–22. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L617021633
9. Linsen SS, Schön A, Teschke M, Mercuri LG. Does Maximum Voluntary Clenching Force Pose a Risk to Overloading Alloplastic Temporomandibular Joint Replacement?-A Prospective Cohort Study. J oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg. 2021 Dec;79(12):2433–43.
10. Linsen SS, Schön A, Mercuri LG, Teschke M. How Does a Unilateral Temporomandibular Joint Replacement Affect Bilateral Masseter and Temporalis Muscle Activity?-A Prospective Study. J oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg. 2021 Feb;79(2):314–23.
11. Linsen SS, Schön A, Mercuri LG, Teschke M. Unilateral, Alloplastic Temporomandibular Joint Reconstruction, Biomechanically What Happens to the Contralateral Temporomandibular Joint?-A Prospective Cohort Study. J oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg. 2021 Oct;79(10):2016–29.
12. Linsen SS, Reich RH, Teschke M. Maximum voluntary bite force in patients with alloplastic total TMJ replacement - A prospective study. J Cranio-Maxillofacial Surg. 2013;41(5):423–8.
13. Linsen SS, Reich RH, Teschke M. Mandibular Kinematics in Patients With Alloplastic Total Temporomandibular Joint Replacement-A Prospective Study. J Oral Maxillofac Surg. 2012;70(9):2057–64.
14. Commisso MS, Martínez-Reina J, Ojeda J, Mayo J. Finite element analysis of the human mastication cycle. J Mech Behav Biomed Mater. 2015 Jan;41:23–35.
15. Ramos AM, Mesnard M. The stock alloplastic temporomandibular joint implant can influence the behavior of the opposite native joint: A numerical study. J Craniomaxillofac Surg. 2015 Oct;43(8):1384–91.
16. Merema BJ, Kraeima J, Witjes MJH, van Bakelen NB, Spijkervet FKL. Accuracy of fit analysis of the patient-specific Groningen temporomandibular joint prosthesis. Int J Oral Maxillofac

Surg [Internet]. 2021;50(4):538–45. Available from: https://www.sciencedirect.com/science/article/pii/S0901502720303283

17. Mommaerts MY. On the reinsertion of the lateral pterygoid tendon in total temporomandibular joint replacement surgery. J Cranio-Maxillo-Facial Surg [Internet]. 2019;47(12):1913–7. Available from: https://doi.org/10.1016/j.jcms.2019.11.018
18. De Meurechy N, Aktan MK, Boeckmans B, Huys S, Verwilghen DR, Braem A, et al. Surface wear in a custom manufactured temporomandibular joint prosthesis. J Biomed Mater Res B Appl Biomater. 2022 Jun;110(6):1425–38.
19. De Meurechy N, Verwilghen D, De Brucker Y, Van Thielen B, Mommaerts MY. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation. J Cranio-Maxillofacial Surg. 2021 Feb;49(4):256–68.
20. Helkimo M. Studies on function and dysfunction of the masticatory system. II. Index for anamnestic and clinical dysfunction and occlusal state. Sven Tandlak Tidskr. 1974 Mar;67(2):101–21.
21. Sidebottom AJ. Guidelines for the replacement of temporomandibular joints in the United Kingdom. Br J Oral Maxillofac Surg. 2008;46(2):146–7.
22. Wilkes C. Internal derangements of the temporomandibular joint: pathological variations. Arch Otolaryngol Neck Surg [Internet]. 1989 Apr 1;115(4):469–77. Available from: http://dx.doi.org/10.1001/archotol.1989.01860280067019
23. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. JBJS. 2001;83(3):428.
24. Kounis NG, Koniari I. Hypersensitivity to metallic implants: pathophysiologic and diagnostic considerations. Acta Biomed. 2018 Oct;89(3):428–9.
25. Ort MJ, Geissler S, Rakow A, Schoon J. The Allergic Bone Marrow? The Immuno-Capacity of the Human Bone Marrow in Context of Metal-Associated Hypersensitivity Reactions. Front Immunol. 2019;10:2232.
26. Albrektsson T, Chrcanovic B, Mölne J, Wennerberg A. Foreign body reactions, marginal bone loss and allergies in relation to titanium implants. Eur J Oral Implantol. 2018;11:S37–46.
27. Haynes DR, Rogers SD, Hay S, Pearcy MJ, Howie DW. The differences in toxicity and release of bone-resorbing mediators induced by titanium and cobalt-chromium-alloy wear particles. J Bone Joint Surg Am. 1993 Jun;75(6):825–34.
28. Lausmaa J, Kasemo B, Mattsson H. Surface spectroscopic characterization of titanium implant materials. Appl Surf Sci [Internet]. 1990;44(2):133–46. Available from: https://www.sciencedirect.com/science/article/pii/016943329090100E
29. Sul YT, Johansson CB, Jeong Y, Albrektsson T ri. The electrochemical oxide growth behaviour on titanium in acid and alkaline electrolytes. Med Eng Phys. 2001 Jun;23(5):329–46.
30. Milosev I, Metikos-Huković M, Strehblow HH. Passive film on orthopaedic TiAlV alloy formed in physiological solution investigated by X-ray photoelectron spectroscopy. Biomaterials. 2000 Oct;21(20):2103–13.
31. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants - A review. Prog Mater Sci [Internet]. 2009;54(3):397–425. Available from: http://dx.doi.org/10.1016/j.pmatsci.2008.06.004
32. Hallab NJ, Jacobs JJ. 2.5.4 - Orthopedic Applications. In: Wagner WR, Sakiyama-Elbert SE, Zhang G, Yaszemski MJBT-BS (Fourth E, editors. Academic Press; 2020. p. 1079–118. Available from: https://www.sciencedirect.com/science/article/pii/B9780128161371000702
33. Rae T. The biological response to titanium and titanium-aluminium-vanadium alloy particles: II. Long-term animal studies. Biomaterials [Internet]. 1986;7(1):37–40. Available from: https://www.sciencedirect.com/science/article/pii/0142961286900864
34. Sansone V, Pagani D, Melato M. The effects on bone cells of metal ions released from orthopaedic implants. A review. Clin cases Miner bone Metab Off J Ital Soc Osteoporosis, Miner Metab Skelet Dis. 2013 Jan;10(1):34–40.

35. Engelhart S, Segal RJ. Allergic reaction to vanadium causes a diffuse eczematous eruption and titanium alloy orthopedic implant failure. Cutis. 2017 Apr;99(4):245–9.
36. Costa BC, Tokuhara CK, Rocha LA, Oliveira RC, Lisboa-Filho PN, Costa Pessoa J. Vanadium ionic species from degradation of Ti-6Al-4V metallic implants: In vitro cytotoxicity and speciation evaluation. Mater Sci Eng C [Internet]. 2019;96:730–9. Available from: https://www.sciencedirect.com/science/article/pii/S0928493118317193
37. Zigante M, Rincic Mlinaric M, Kastelan M, Perkovic V, Trinajstic Zrinski M, Spalj S. Symptoms of titanium and nickel allergic sensitization in orthodontic treatment. Prog Orthod. 2020 Jul;21(1):17.
38. Tanaka E, Tanne K, Sakuda M. 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. 1994 Jul;16(4):316–22.
39. Silva A de M, Figueiredo VMG de, Prado RF do, Santanta-Melo G de F, Ankha MDVEA, de Vasconcellos LMR, et al. Diamond-like carbon films over reconstructive TMJ prosthetic materials: Effects in the cytotoxicity, chemical and mechanical properties. J oral Biol craniofacial Res. 2019;9(3):201–7.
40. Döring J, Crackau M, Nestler C, Welzel F, Bertrand J, Lohmann CH. Characteristics of different cathodic arc deposition coatings on CoCrMo for biomedical applications. J Mech Behav Biomed Mater [Internet]. 2019;97:212–21. Available from: https://www.sciencedirect.com/science/article/pii/S1751616118316977
41. Hauert R, Falub C V, Thorwarth G, Thorwarth K, Affolter C, Stiefel M, et al. Retrospective lifetime estimation of failed and explanted diamond-like carbon coated hip joint balls. Acta Biomater. 2012 Aug;8(8):3170–6.
42. Steinbeck MJ, Baxter RM, Freeman TA. Chapter 23 - Pathophysiologic Reactions to UHMWPE Wear Particles. In: Kurtz SMBT-UBH (Second E, editor. Boston: Academic Press; 2009. p. 341–53. Available from: https://www.sciencedirect.com/science/article/pii/B9780123747211000237
43. Oral E, Ghali BW, Neils A, Muratoglu OK. A new mechanism of oxidation in ultrahigh molecular weight polyethylene caused by squalene absorption. J Biomed Mater Res B Appl Biomater. 2012 Apr;100(3):742–51.
44. Engh CAJ, Hopper RHJ, Huynh C, Ho H, Sritulanondha S, Engh CAS. A prospective, randomized study of cross-linked and non-cross-linked polyethylene for total hip arthroplasty at 10-year follow-up. J Arthroplasty. 2012 Sep;27(8 Suppl):2-7.e1.
45. Prock-Gibbs H, Pumilia CA, Meckmongkol T, Lovejoy J, Mumith A, Coathup M. Incidence of Osteolysis and Aseptic Loosening Following Metal-on-Highly Cross-Linked Polyethylene Hip Arthroplasty: A Systematic Review of Studies with Up to 15-Year Follow-up. J Bone Joint Surg Am. 2021 Apr;103(8):728–40.
46. Regis M, Bracco P, Giorgini L, Fusi S, Dalla Pria P, Costa L, et al. Correlation between in vivo stresses and oxidation of UHMWPE in total hip arthroplasty. J Mater Sci Mater Med. 2014 Sep;25(9):2185–92.
47. SHIBATA N, KURTZ SM, TOMITA N. Recent Advances of Mechanical Performance and Oxidation Stability in Ultrahigh Molecular Weight Polyethylene for Total Joint Replacement: Highly Crosslinked and α-Tocopherol Doped. J Biomech Sci Eng. 2006;1(1):107–23.
48. Wyatt MC, Roberton A, Foxall-Smi M, Beswick AD, Kunutsor SK, Whitehouse MR. Does vitamin E highly-crosslinked polyethylene convey an advantage in primary total hip replacement? A systematic review and meta-analysis. Hip Int J Clin Exp Res hip Pathol Ther. 2020 Sep;30(5):598–608.
49. Gehrke SA, Dedavid BA, Aramburú JS, Pérez-Díaz L, Guirado JLC, Canales PM, et al. Effect of Different Morphology of Titanium Surface on the Bone Healing in Defects Filled only with Blood Clot: A New Animal Study Design. Biomed Res Int. 2018;2018.
50. Yeo I-SL. Modifications of Dental Implant Surfaces at the Micro- and Nano-Level for Enhanced Osseointegration. Mater (Basel, Switzerland). 2019 Dec;13(1).
51. Prananingrum W, Naito Y, Galli S, Bae J, Sekine K, Hamada K, et al. Bone ingrowth of various porous titanium scaffolds produced by a moldless and space holder technique: an in vivo study in rabbits. Biomed Mater. 2016 Feb;11(1):15012.

52. Taniguchi N, Fujibayashi S, Takemoto M, Sasaki K, Otsuki B, Nakamura T, et al. Effect of pore size on bone ingrowth into porous titanium implants fabricated by additive manufacturing: An in vivo experiment. Mater Sci Eng C [Internet]. 2016;59:690–701. Available from: https://www.sciencedirect.com/science/article/pii/S0928493115305002
53. Zhao L, Pei X, Jiang L, Hu C, Sun J, Xing F, et al. Bionic design and 3D printing of porous titanium alloy scaffolds for bone tissue repair. Compos Part B Eng [Internet]. 2019;162:154–61. Available from: https://www.sciencedirect.com/science/article/pii/S1359836818325794
54. Schneider G, Burridge K. Formation of focal adhesions by osteoblasts adhering to different substrata. Exp Cell Res. 1994 Sep;214(1):264–9.
55. Kilpadi KL, Chang PL, Bellis SL. Hydroxylapatite binds more serum proteins, purified integrins, and osteoblast precursor cells than titanium or steel. J Biomed Mater Res. 2001 Nov;57(2):258–67.
56. Jimbo R, Sawase T, Baba K, Kurogi T, Shibata Y, Atsuta M. Enhanced initial cell responses to chemically modified anodized titanium. Clin Implant Dent Relat Res. 2008 Mar;10(1):55–61.
57. Kieswetter K, Schwartz Z, Hummert TW, Cochran DL, Simpson J, Dean DD, et al. Surface roughness modulates the local production of growth factors and cytokines by osteoblast-like MG-63 cells. J Biomed Mater Res. 1996 Sep;32(1):55–63.
58. Foest R, Kindel E, Ohl A, Stieber M, Weltmann K-D. Non-thermal atmospheric pressure discharges for surface modification. Plasma Phys Control Fusion [Internet]. 2005;47(12B):B525–36. Available from: http://stacks.iop.org/0741-3335/47/B525/ppcf5_12B_S38.pdf LK - http://dx.doi.org/10.1088/0741-3335/47/12B/S38
59. Zigterman BGR, Van den Borre C, Braem A, Mommaerts MY. Titanium surface modifications and their soft-tissue interface on nonkeratinized soft tissues-A systematic review (Review). Biointerphases. 2019 Aug;14(4):40802.
60. Chen GJ, Wang Z, Bai H, Li JM, Cai H. A preliminary study on investigating the attachment of soft tissue onto micro-arc oxidized titanium alloy implants. Biomed Mater. 2009 Feb;4(1):15017.
61. Mutsuzaki H, Ito A, Sogo Y, Sakane M, Oyane A, Ochiai N. Enhanced wound healing associated with Sharpey's fiber-like tissue formation around FGF-2-apatite composite layers on percutaneous titanium screws in rabbits. Arch Orthop Trauma Surg. 2012 Jan;132(1):113–21.
62. Mercuri LG, Saltzman BM. Acquired heterotopic ossification of the temporomandibular joint. Int J Oral Maxillofac Surg. 2017 Dec;46(12):1562–8.
63. Kan L, Kessler JA. Animal models of typical heterotopic ossification. J Biomed Biotechnol. 2011;2011:309287.
64. Cullen N, Perera J. Heterotopic Ossification: Pharmacologic Options. J Head Trauma Rehabil [Internet]. 2009;24(1). Available from: https://journals.lww.com/headtraumarehab/fulltext/2009/01000/heterotopic_ossification__pharmacologic_options.10.aspx
65. Yin B, Xue B, Wu Z, Ma J, Wang K. A novel hybrid 3D-printed titanium scaffold for osteogenesis in a rabbit calvarial defect model. Am J Transl Res. 2018;10(2):474–82.
66. Imam MA, Holton J, Ernstbrunner L, Pepke W, Grubhofer F, Narvani A, et al. A systematic review of the clinical applications and complications of bone marrow aspirate concentrate in management of bone defects and nonunions. Int Orthop. 2017 Nov;41(11):2213–20.
67. Hsieh PC, Chung AS, Brodke D, Park J-B, Skelly AC, Brodt ED, et al. Autologous Stem Cells in Cervical Spine Fusion. Glob spine J. 2021 Jul;11(6):950–65.

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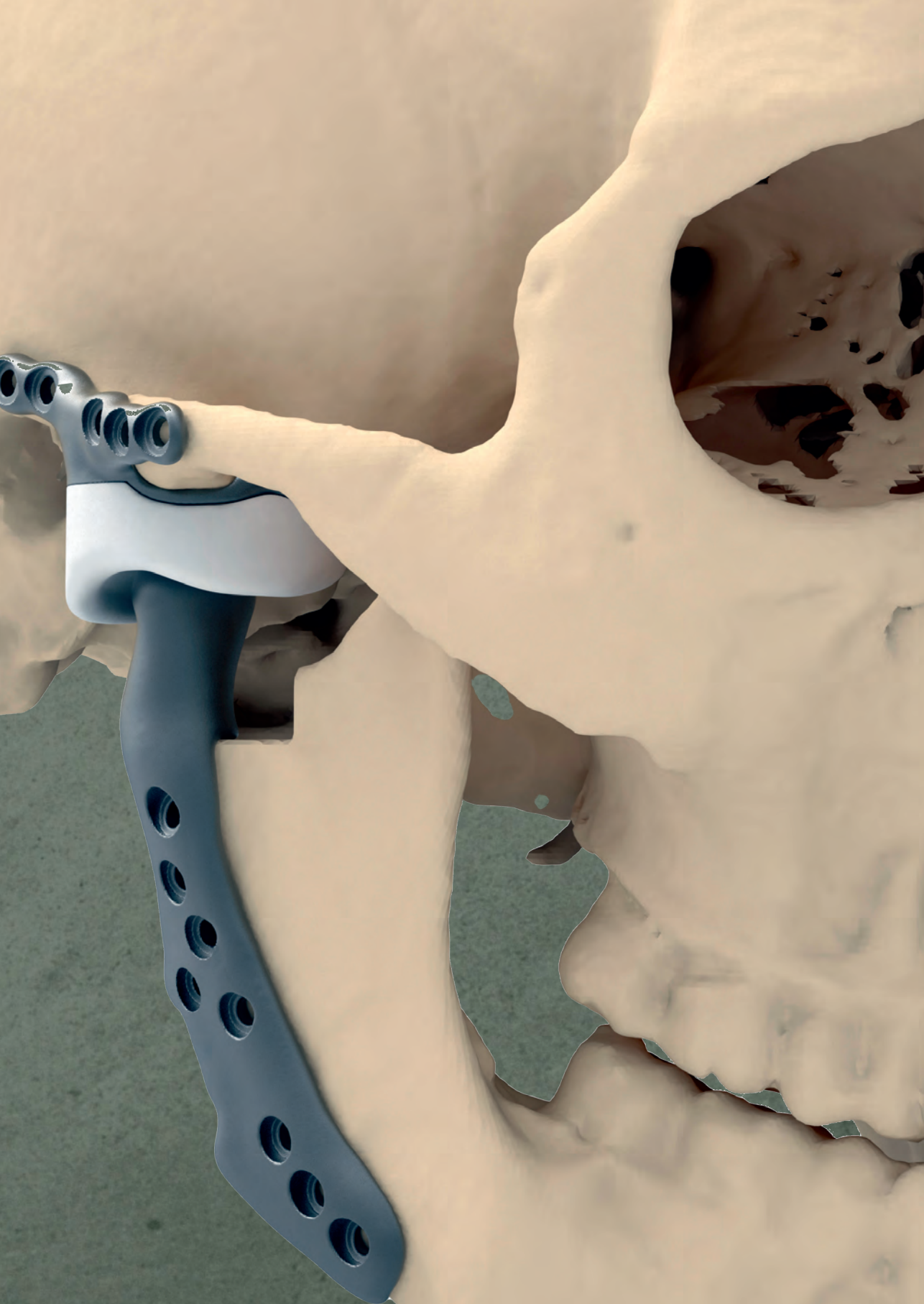

Chapter 10

Extended Total Temporomandibular Joint Replacement with Occlusal Adjustments: Pitfalls, Patient-reported Outcomes, Subclassification, and a New Paradigm

This chapter is based on:

Extended Total Temporomandibular Joint Replacement with Occlusal Adjustments: Pitfalls, Patient-reported Outcomes, Subclassification, and a New Paradigm

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Introduction

Extended temporomandibular joint (TMJ) prostheses replace not only joint components but also adjacent mandibular and/or temporal bone defects.(1) We recently shifted from autologous to alloplastic replacement for a number of segmental mandibular defects, considering autologous replacement as a salvage procedure for implant failure. A similar strategy was advocated in 1999 by Peckitt in oncological cases.(2) It was heavily criticized and did not become popular in the pre-three-dimensional (3D) printing era. We herein review our experience with total alloplastic extended TMJ replacement (eTMJR), describing intraoperative obstacles and deficiencies in occlusal and esthetic outcomes. Our experience may guide future reconstructive surgeries.

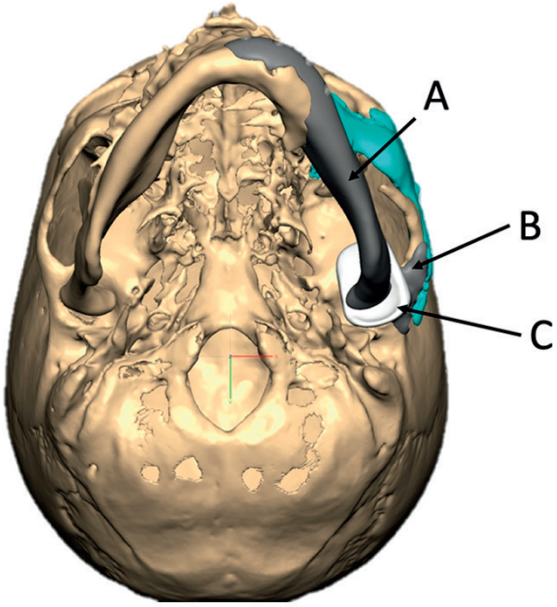

Fig. 1: Rendered basilar view of the eTMJR of Case #2 showing its components. (A) Mandibular component three-dimensional printed out of Titanium Grade 23. (B) Cranial base part of the fossa component, three-dimensional printed out of Titanium Grade 23. (C) Caudal part of the fossa component, CNC-milled out of UHMWPE enriched with alpha-tocopherol and crosslinked using 100 Gy gamma irradiation. Note the posterior lip extending caudally. CNC=Computer numerical controlled; UHMWPE = Ultra-high-molecular-weight polyethylene

Materials and Methods

We analyzed the records of all patients who received an additively manufactured eTMJR (CADSkills BV, Gent, Belgium) implant in 2017 and 2018.(Fig. 1) All operations were performed by the same surgeon (MYM). The following information was extracted from the records: age, sex, diagnosis, Elledge classification(3), simultaneous corrections of occlusion and facial contours, intraoperative obstacles, and postoperative complications.

To evaluate patient satisfaction with their results, independent of the clinician's perception, all patients completed the standardized FACE-Q 'Satisfaction with Outcome' questionnaire at the latest follow-up consultation.(4) Both the sum scores (maximum of 24) and corresponding transformed Rasch scores (maximum of 100) were determined. Statistical analysis was limited to descriptive statistics, with calculation of the mean Rasch score.

Results

All patients were followed up for at least 1 year after their eTMJR surgery. In all patients, healing occurred without any complications, such as infection, dehiscence, or implant exposure.

Case #1

This patient had Pruzansky-Kaban Type IIb hemifacial microsomia. The planned position of the mandibular component at the lateral mandibular surface required changing intraoperatively because of severe lateral deviation of the occlusion, despite resection of the coronoid process. The vertical ramus compartment probably lacked neuromuscular support because of the underlying microsomia. Although neutral occlusion and midline correction were obtained during surgery, they were not fully maintained postoperatively.(Figs. 2, 3) Subsequent elastic traction and orthodontic treatment resulted in functional occlusion but with midline deviation.

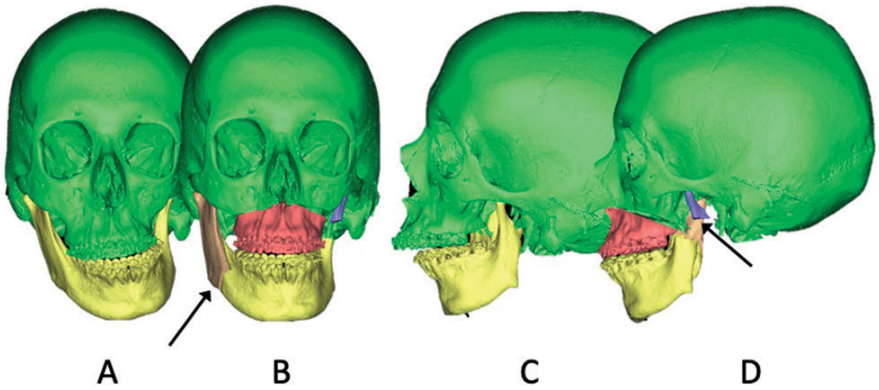

Fig. 2: Case #1. Planning in ProPlan CMF (Materialize, Leuven, Belgium). (A) Frontal view. (B) Frontal view. Planned maxillary and mandibular rotation repositioning osteotomy. The arrow indicates the sagittal split osteotomy on the side contralateral to the extended temporomandibular joint replacement. (C) Left profile view. (D) Left profile view. Planned maxillary and mandibular rotation repositioning osteotomy planned. The arrow indicates the coronoidotomy

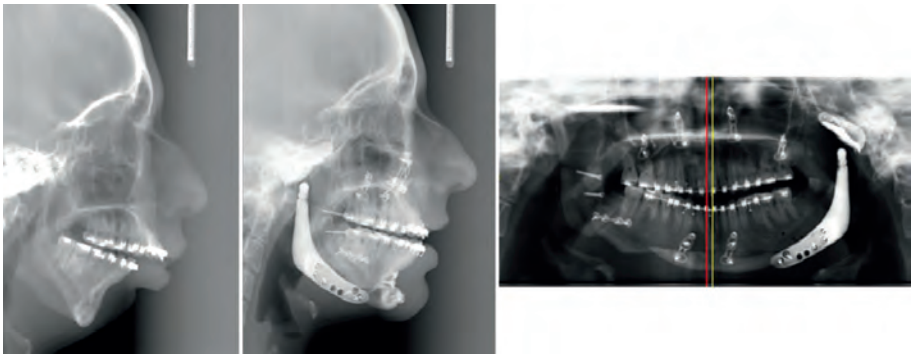

Fig. 3: Case #1 continued. (a) Preoperative profile cephalogram. (b) Postoperative profile cephalogram. (c) Orthopantomogram. The red line indicates the upper dental midline, and the yellow line indicates the lower dental midline

Case #2

This patient sustained traumatic facial injuries when her village was bombed in 2007. She initially underwent reconstruction surgery in Germany, including polyether ether ketone zygoma replacement and placement of an artificial eye. The mandibular reconstruction subsequently failed, and she presented to our institution with a chronic plate infection, malunion, a mandibular defect, and fibrous TMJ ankylosis on the affected side.(Fig. 4) During eTMJR, it was extremely difficult to seat the prosthetic condyle in the fossa component. The mandibular component was pushed inwardly by the scarred soft tissues at the mandibular angle. The

reconstruction plate had been segmented out and was removed during implant insertion. The residual bony and titanium irregularities were difficult to match in the parasymphyseal region.(Fig. 4) Finally, the bony surface was smoothened, and extreme force was required to guide the condyle into a proper position mediolaterally. Intraoperative 3D Pulsera imaging (Phillips, Eindhoven, The Netherlands) was repeated three times. Stable occlusion and articulation were achieved, with full occlusal contact at both sides checked with thin double-sided articulating paper and a spontaneous maximal mouth opening of 31 mm. Still, the alloplastic condyle seemed caudally positioned in relationship to the fossa on the computed tomography (CT) scan, even taking into account, the ultra-high-molecular-weight polyethylene part of the fossa component being radiolucent.

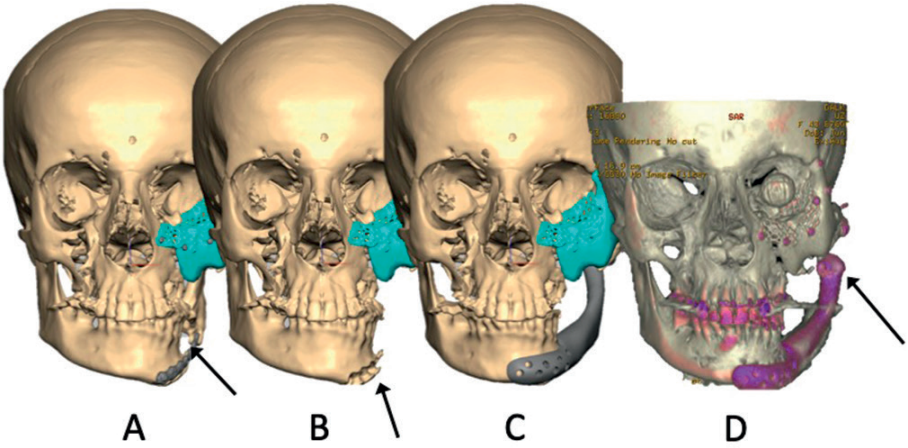

Fig. 4: Case # 2. Planning and postoperative result. (A) Surface tesselation language render with arrow indicating the mandibular defect. The left zygoma was replaced with a polyether ether ketone implant (blue). (B) Surface tesselation language render with the arrow indicating bony irregularities at the mandibular border after virtual removal of the titanium reconstruction plate using segmentalization. (C) Surface tessellation language render with the extended temporomandibular joint replacement indicated in gray. (D) Postoperative frontal view of the computerized scan of the cranium showing the condylar sag (arrow)

Case #3

This patient initially had pericoronitis of the lower right third molar, and subsequently developed osteomyelitis after the tooth was extracted. The infection did not resolve with antibiotics and decortication, so the patient

underwent resection with microvascular fibula flap reconstruction of the mandibular defect and this also had failed. By the time we saw the patient, there was extra bony ankylosis of the TMJ and extra- and intra-oral fistulization. Intravenous and prolonged peroral antibiotic treatment eradicated the infection.

Segmentation of the CT DICOM dataset was performed using Mimics inPrint 3.0 (Materialise, Leuven, Belgium), with repositioning of the residual mandible using ProPlan CMF (Materialise, Leuven, Belgium). The latter needed a repositioning osteotomy on the left.(Fig. 5) eTMJR and unilateral sagittal osteotomy were thereby performed simultaneously. Malunion, plate fracture, and cranial rotation of the left-sided proximal segment necessitated revision surgery using an iliac bone graft and comprehensive intraoral plating during a second surgical session, at which time root implants were placed in the anterior mandible. Blood analysis did not show any abnormalities of bone metabolism. The patient received an additively manufactured subperiosteal jaw implant under general anesthesia during a third operation and is currently undergoing prosthetic rehabilitation.

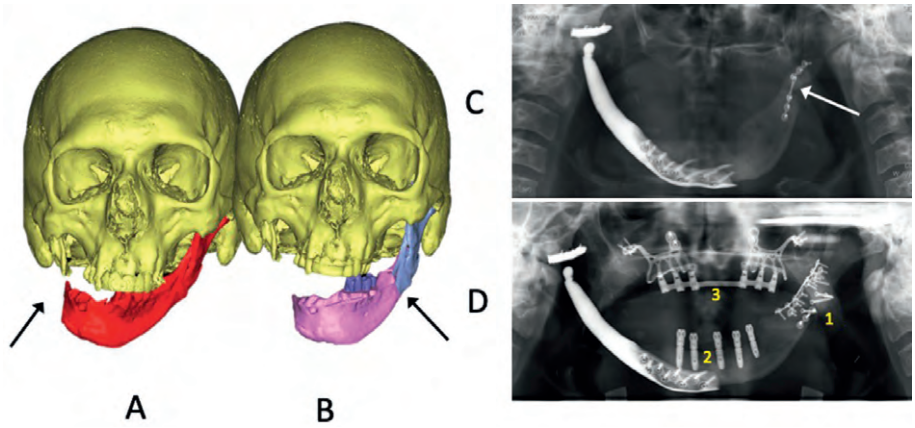

Fig. 5: Case # 3. (A) Surface tesselation language render with the arrow indicating the defect. (B) Surface tesselation language render with planned rotational repositioning of the mandible. The arrow indicates the sagittal split osteotomy contralateral to the extended temporomandibular joint replacement. (C) Orthopantomogram demonstrating an osteosynthesis plate fracture (arrow). (D) Orthopantomogram demonstrating extensive osteosynthesis and iliac bone grafting (1), root-shaped dental implants (2), and an additively manufactured subperiosteal jaw implant (3) one has the impression that mandible was splitted at a higher position than indicated in B. This is due to the fact that the proximal segment rotated anterocranially because of the malunion and because of the projective geometry of orthopantomogram technology

Case #4

This patient previously underwent bimaxillary surgery *alio loco* for Class II, open bite occlusion.(Fig. 6) She presented with bilateral condylar resorption and extreme pain (10 on a 0–10 visual analog scale).

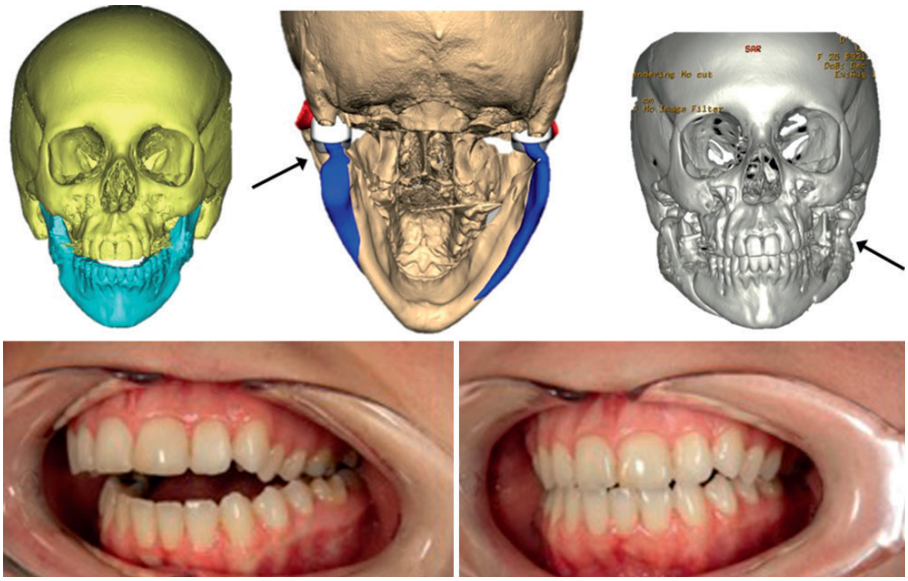

Fig. 6: Case # 4. (a) Surface tesselation language render before planning demonstrating the anterior open bite. (b) Surface tessellation language render after planning for bilateral extended temporomandibular joint replacement and mandibular repositioning. The arrow indicates the concavity in the subcondylar area secondary to postoperative maintenance of the yaw position of the mandible and the attempt to symmetrize the mandibular angle area by augmentation. (c) Postimplantation CT scan, frontal view. The arrow indicates the mid-cheek concavity. (d) Left — profile view of the preoperative occlusion. (e) Left— profile view of the post-eTMJR occlusion

Conservative measures, including bite splint, physiotherapy, pain medications, and steroid injections, over 1 year did not help. The patient developed mental depression, at which time, it was decided that she should undergo bilateral eTMJR, together with surgically-assisted maxillary expansion using a transpalatal distraction device (Surgi-Tec, Gent, Belgium), to replace the missing bone, correct the mandibular position, and remove the source of pain. Asymmetry at the gonial angles was managed with augmentation of the eTMJR. We planned to not fully correct the left side for two reasons. One reason was that the patient would have required an extended period of treatment, beginning with surgery to correct the

transverse relapse of the upper dental arch, followed by orthodontic treatment, and then, the eTMJR operation after a considerable amount of time. Because of her pain, depression, and marital relationship, such prolonged treatment was deemed inappropriate. The second reason was that with her rotated mandible, the subcondylar area on the left would show a concavity if the angle were symmetrically augmented.

Case #5

This patient was initially treated for fibrous dysplasia with continuity resection at her left mandibular angle.(Fig. 7) The defect was reconstructed using a free iliac bone graft, which failed. She was left with a dangling mandible for 2.5 years. During the eTMJR surgery, optimal occlusion could not be achieved. Manipulation at the resection stump was difficult because of the resistance to upward rotation and our decision to not lengthen the submandibular incision. Orthodontic treatment was resumed 1 year after the surgery. Prosthetic rehabilitation is planned for.

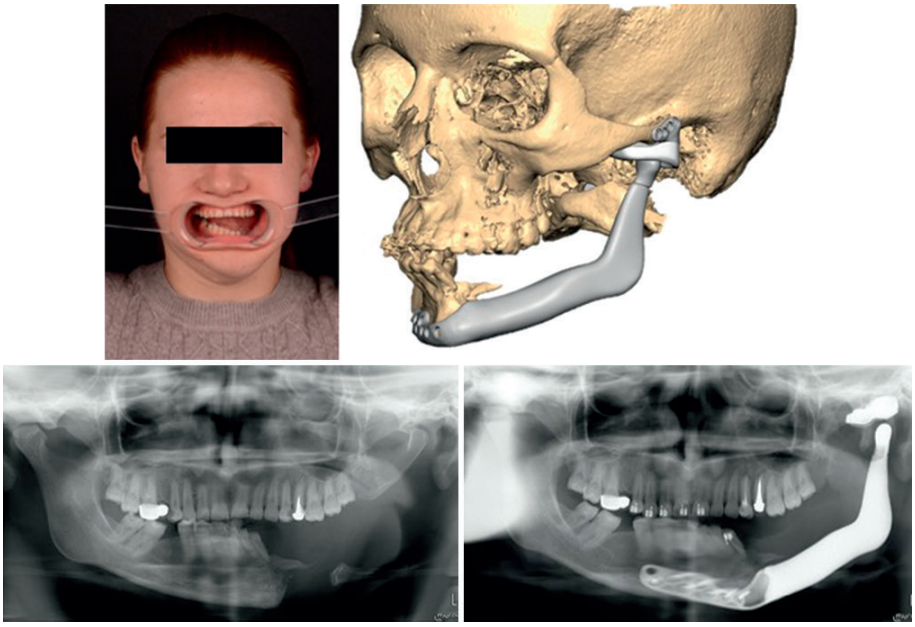

Fig. 7: Case # 5. (a) Preoperative facial frontal view with open mouth. (b) Surface tesselation language render of the planned extended temporomandibular joint replacement. (c) Orthopantomogram showing the preoperative occlusion and left-sided mandibular defect. (d) Orthopantomogram showing the postoperative occlusion and extended temporomandibular joint replacement *in situ*

The results of the FACE-Q questionnaire are presented in Tables 1 and 2. While one patient reported a lower Rasch score (59/100), all other patients evaluated their satisfaction with the implant between 87/100 and 100/100, representing excellent results. The mean Rasch score was 89.2/100.

Table 1: FACE-Q Satisfaction with outcome

	Very Dissatisfied	Somewhat Dissatisfied	Somewhat Satisfied	Very Satisfied
I am pleased with the result.	0	0	1	4
The result turned out great.	0	0	1	4
The result was just as I expected.	0	0	1	4
I am surprised at how good I look in the mirror.	0	0	1	4
The result is fantastic.	0	0	1	4
The result is miraculous.	0	0	2	3

Discussion

During eTMJR surgery, we encountered a number of obstacles. Adjustment at both sides of the implant was the most frequent (Cases #1, #4, and #5). Neuromuscular deficiency of the pterygomasseteric sling was likely the reason for the occlusal deviation observed in case #1.(Fig. 3) Lack of manual control over the vertical position of the condyle in the fossa before the screw fixation was likely the reason in case #2.(Fig. 4) The difficulty in retrieving the proper position at the symphysis, necessitating modification of the contact surfaces, probably contributed to the slight malpositioning as well. Both of these patients also had facial paresis on the affected side, but that was probably a coincidence. The solution could involve suture suspension of the prosthetic condyle to the prosthetic fossa and proper fixation of the pterygomasseteric sling through holes in the gonial region.(5)(Fig. 8) Case #3 had a diminutive and mostly cortical area on the contralateral osteotomy side, with rotation of the segments in three planes; there was considerable space between the segments but no space for bicortical screw osteosynthesis. Delayed union was also observed after revision surgery, involving extensive osteosynthesis plus addition of a cancellous bone block and particulate cancellous bone between the repositioned segments.(Fig. 5)

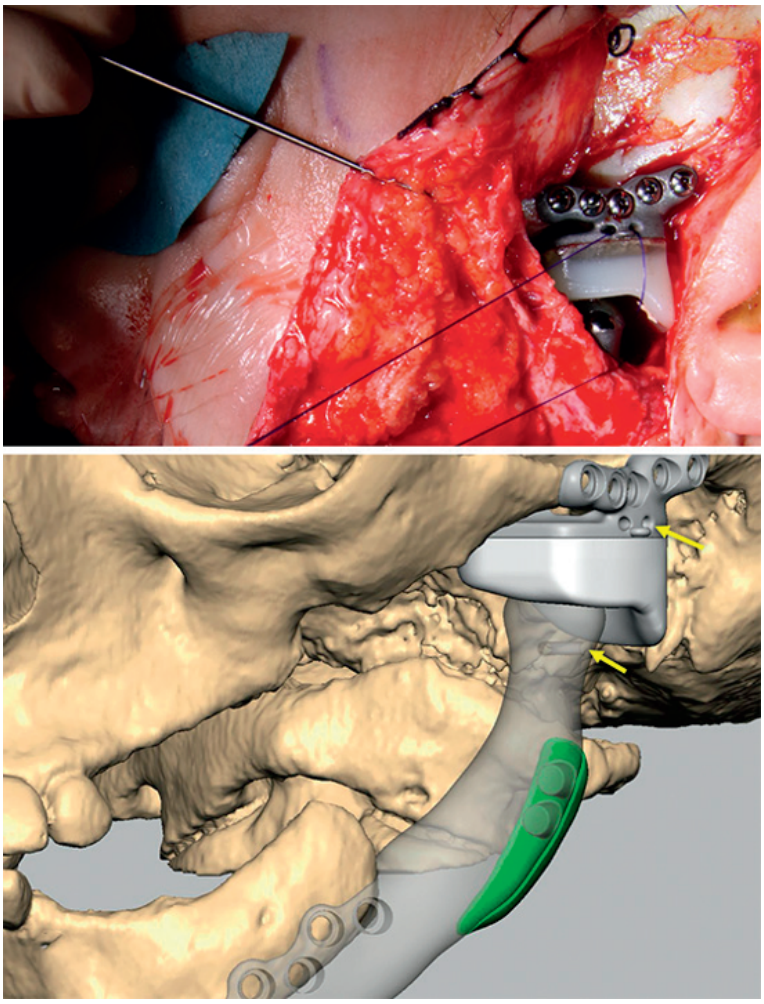

Fig. 8: The condyle is sutured suspended to the fossa. (a) Intraoperative view of a case not presented in this article. (b) Render of the eTMJ of the case in A, demonstrating the tunnels in the fossa and the condyle (yellow arrows) meant for suture suspension

Table 2: FACE-Q™ Satisfaction with outcome (Score per patient):

Case	Sum Score (maximum, 24)	Equivalent Rasch Transformed Score (maximum, 100)
# 1	18	59
# 2	22	79
# 3	24	100
# 4	24	100
# 5	24	100

Facial contouring can be performed with eTMJR. The less than ideal outcome in case #4 was related to the decision to not delay the eTMJR surgery. The importance of facial contouring and correct anatomical reconstruction of the face was clear when evaluating patient-reported outcomes with the FACE-Q 'Satisfaction with outcome' questionnaire. While four of our five patients reported a perfect or excellent score, case #1 reported a considerably lower score (59/100). It should, however, be noted that this patient had hemifacial microsomia and underwent several other treatments (e.g., autologous ear reconstruction and free gluteal fat grafting) before and after eTMJR and facial rotation surgery to improve her facial appearance. As such, only partial esthetic facial reconstruction could be achieved by eTMJR, which likely explained the reported esthetic result. Elledge et al.(3) stated that any classification system for eTMJR must be "unambiguous and easy to use; exhaustive and mutually exclusive so that each possibility exists in only one class; clinically relevant and appropriate; and flexible enough to accommodate any advances or changes in technology." Considering our (albeit limited) experience, it appeared that unidimensional extension was not the only factor affecting technical difficulties and outcomes. Indeed, we found no difference between M1 and M2 eTMJR with respect to surgical difficulties or clinical outcomes. In contrast, mandibular repositioning in three dimensions to deal with dental occlusion, with or without contralateral mandibular osteotomies, posed major obstacles and complications. Contour corrections increased the difficulty of implantation and resulted in compromised esthetic outcomes. Elledge et al.(3) agreed that other subclassifications can be considered when autogenous tissue transfer is used in conjunction with eTMJR. We, therefore, suggest adding the aforementioned potential obstacles (contour corrections, occlusal adjustments, and simultaneous contralateral mandibular osteotomy) as a subclassification system. (Table 3) Identification and anticipation of these obstacles may lead to facilitating actions.

Bredell et al.(6) described 15 patients requiring ablative surgery of the mandible (including the condyles), mainly for oncological reasons. Two patients received a reconstruction plate with a metallic condyle, whereas the others underwent autologous replacement, primarily with a free fibula

flap. The authors focused on complications and concluded that "free vascularized grafts, specifically fibula, appear to be the option with the lowest surgical complication rate and good function that must be weighed against donor-site morbidity in high-risk cases." However, additive manufacturing was not yet an option between 2001 and 2012, when that study was conducted. Our indications for surgery differed from those in the Bredell et al.(6) study, and we consider autologous reconstruction to be a second-choice option when dealing with nonmalignant tumors or other conditions. In addition to the advantage of more anatomically accurate reconstruction of the mandible with alloplastic eTMJR, the durations of both surgery and hospital stay are shorter with alloplastic reconstruction than with free vascularized grafts. Although the costs of materials may be relatively high with alloplastic eTMJR, the shorter durations not only lower morbidity risks but also reduce total costs, compared to autologous treatment options.(7,8) Furthermore, graft resorption, fracturing, malunion, nonvascularization, and donor-site morbidity are all potential complications of autologous flaps, which have not been observed with eTMJR.(9,10) A literature research conducted by Kearns et al.(11) evaluated donor-site morbidity according to patient-reported outcomes and showed that all frequently used autologous flaps, except the scapular flap, are susceptible to chronic pain, scarring, and sensory abnormalities at the donor site. Furthermore, during the early postoperative period after a free vascularized graft, surgeons often opt for intermaxillary fixation to improve the likelihood of flap healing, but this reduces total joint mobility, and thereby increased the risk of (recurrent) ankylosis. In contrast, eTMJR permits early mobilization, which has been shown to improve functional outcomes, when compared with immobilization after surgery.(12,13)

When comparing outcomes between eTMJR and autologous reconstruction, an objective measure of functionality is required. This can involve evaluating parameters such as maximal mouth opening or lateral excursion, as well as postoperative pain and dietary function. These data are readily available for alloplastic TMJ reconstruction but not for autologous reconstruction of the TMJ and mandible. Saeed et al.(13) compared 49 patients who underwent autologous treatment with a costochondral graft with 50 patients who underwent TMJR. Patients

undergoing alloplastic TMJR exhibited better results for all outcomes, including dietary function, pain, and maximal mouth opening. However, it should be noted that no patient in the study had a mandibular defect other than the condylar abnormality. One disadvantage of using eTMJR is that in Elledge M3 and M4 cases, occlusal rehabilitation would not be feasible, whereas an osseous flap would offer the possibility for root-shaped implants. Elledge M2 cases could, however, still be helped with an extended wrap around the bridge, based on root-shaped implants in the symphyseal region. Further comparative studies are necessary to determine the patient groups, for which eTMJR is most appropriate and accompanied by the highest patient satisfaction.

Table 3. Patient demographics, pathology, surgery classification and subclassification, and additional treatments

Case#, sex	Pathology	Age at eTMJR (years)	Laterality	Cl	Div	Other corrective osteotomies	Other procedures at a later date
1, female	Hemifacial microsomia	22	Left	M0	O, C, A	Le Fort I-type osteotomy, sliding genioplasty	Free gluteal fat transplantation
2, female	Posttraumatic angle defect and malunion	43	Left	M2	O,	-	-
3, male	TMJ ankylosis and osteomyelitis with failed microvascular fibula replacement	46	Right	M2	O, C	-	AMSJI, root implants
4, female	Condylar resorption after bimaxillary surgery	25	Left and right	M0	O, A	TPD	-
5, female	Resection of fibrous dysplasia and loss of subsequent iliac bone graft	25	Left	M2-3	O	-	-

Abbreviations: AMSJI=Additively manufactured subperiosteal jaw implant; Cl=Classification according to Elledge et al.(3); Div=Suggested subclassification according to occlusal correction (O), C=Contralateral mandibular osteotomy; A=Extra contour correction by augmentation (A); eTMJR=Extended alloplastic TMJ Replacement; TMJ=Temporomandibular joint; TPD=Transpalatal distraction osteogenesis

Conclusion

Obstacles during unilateral alloplastic eTMJR surgery relate to 3D rotations of the remaining mandible. Sagging of the prosthesis was noted in patients with neuromuscular deficiency, for which suspension techniques are proposed. Patients reported high satisfaction with the procedure. We suggest a treatment paradigm shift, with consideration of alloplastic eTMJR as the primary surgical approach, instead of reconstruction through microvascular osseous transplantation, in patients not requiring radiotherapy. This will avoid donor-site morbidity and lengthy reconstructive surgery while leaving autologous osseous transplantation available as a future possibility in case of implant failure. A subclassification system of eTMJR is proposed that takes into account three potential obstacles: contour corrections, occlusal adjustments, and simultaneous contralateral mandibular osteotomy.

References

1. Vega LG, Meara D. Mandibular Replacement Utilizing TMJ TJR Devices. In: Mercuri LG, editor. emporomandibular Joint Total Joint Replacement – TMJ TJR. Springer, Cham; 2016. p. 165–83.
2. Peckitt NS. Stereoscopic lithography: customized titanium implants in orofacial reconstruction. A new surgical technique without flap cover. Br J Oral Maxillofac Surg. 1999 Oct;37(5):353–69.
3. Elledge R, Mercuri L, Speculand B. Extended total temporomandibular joint replacements: a classification system. Br J Oral Maxillofac Surg [Internet]. 2018;56(7):578–81. Available from: http://dx.doi.org/10.1016/j.bjoms.2018.06.002
4. Klassen AF, Cano SJ, Schwitzer JA, Scott AM, Pusic AL. FACE-Q Scales for Health-Related Quality of Life, Early Life Impact, Satisfaction with Outcomes, and Decision to Have Treatment: Development and Validation. Plast Reconstr Surg. 2015;135(2).
5. Farzad P. Reconstruction of nongrowing hemifacial microsomia patient with custom-made unilateral temporomandibular joint total joint prosthesis and orthognathic surgery. J oral Biol craniofacial Res. 2017;7(1):62–6.
6. Bredell M, Gratz K, Obwegeser J, Gujer AK. Management of the temporomandibular joint after ablative surgery. Craniomaxillofac Trauma Reconstr. 2014 Dec;7(4):271–9.
7. Al-Moraissi EA, El-Sharkawy TM, Mounair RM, El-Ghareeb TI. A systematic review and meta-analysis of the clinical outcomes for various surgical modalities in the management of temporomandibular joint ankylosis. Int J Oral Maxillofac Surg. 2015 Apr;44(4):470–82.
8. Sidebottom AJ. Alloplastic or autogenous reconstruction of the TMJ. J oral Biol craniofacial Res. 2013;3(3):135–9.
9. Vega LG, Gonzalez-Garcia R, Louis PJ. Reconstruction of Acquired Temporomandibular Joint Defects. Oral Maxillofac Surg Clin North Am. 2013;25(2):251-+.
10. De Meurechy NKG, Loos P-J, Mommaerts MY, Meurechy NKG De, Loos P-J, Mommaerts MY. Postoperative Physiotherapy After Open Temporomandibular Joint Surgery: A Three-Step Program. J Oral Maxillofac Surg. 2018;
11. Kearns M, Ermogenous P, Myers S, Ghanem AM. Osteocutaneous flaps for head and neck reconstruction: A focused evaluation of donor site morbidity and patient reported outcome measures in different reconstruction options. Arch Plast Surg. 2018 Nov;45(6):495–503.
12. Mercuri LG. Total Joint Reconstruction-Autologous or Alloplastic. Oral Maxillofac Surg Clin North Am. 2006;18(3):399–410.
13. Saeed NR, Hensher R, McLeod NMH, Kent JN. Reconstruction of the temporomandibular joint autogenous compared with alloplastic. Br J Oral Maxillofac Surg. 2002;40(4):296–9.

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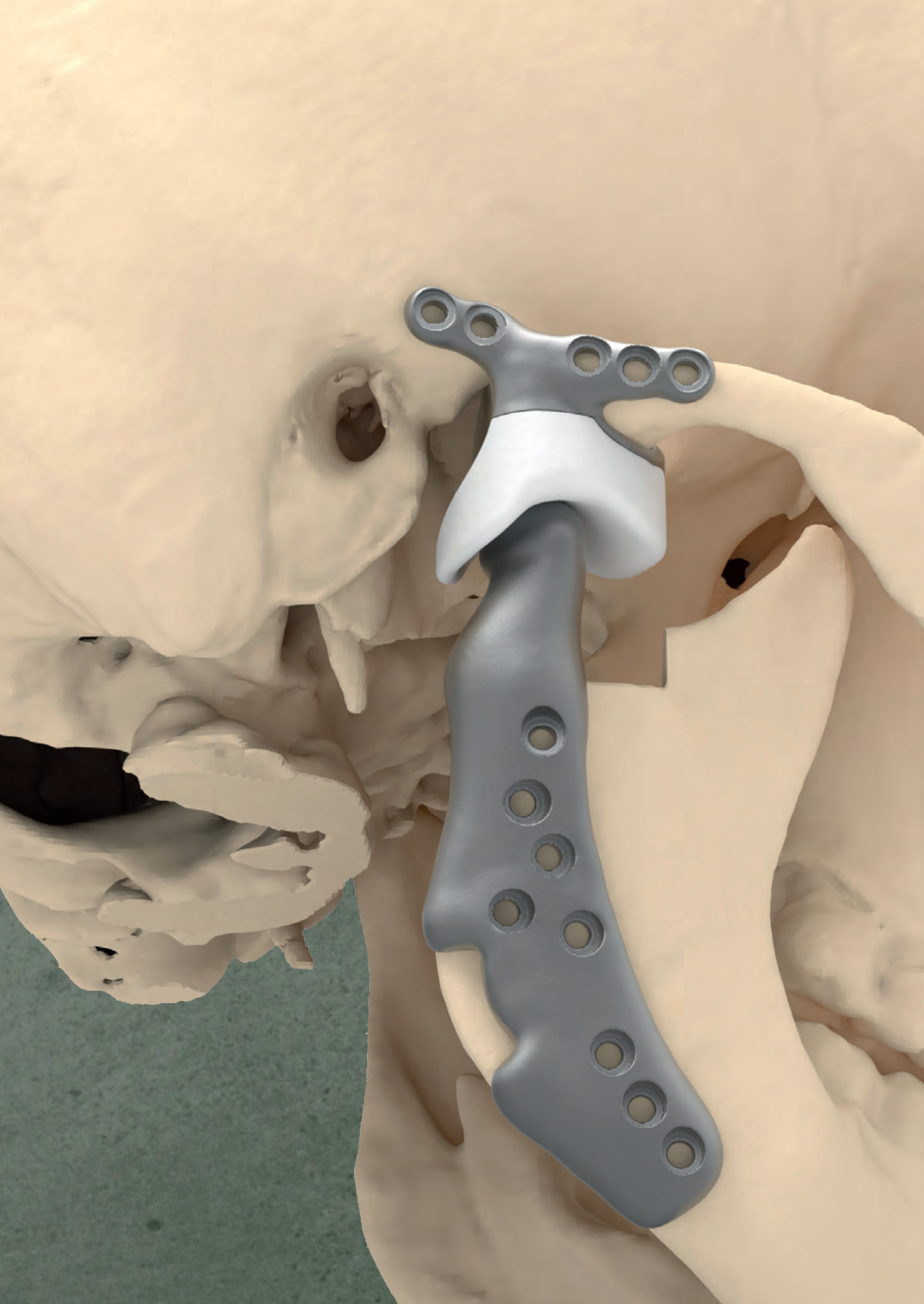

Chapter 11

Autologous Fat Grafting in Total Temporomandibular Joint Replacement Surgery

This chapter is based on:

Autologous Fat Grafting in Total Temporomandibular Joint Replacement Surgery

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Maurice Y Mommaerts

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Introduction

Calcifications and reankylosis are potential complications after alloplastic temporomandibular joint (TMJ) replacement. This process can occur through the formation of a hematoma after joint debridement, in which cells can differentiate to osteoblasts, which can deposit bone.(1) By wrapping the joint space with autologous fat grafts (AFGs), the dead space can be filled out, preventing the formation of a hematoma and as such has been advocated to counteract the occurrence of calcifications.(Fig. 1) The aim of this narrative review was to find evidence for this rationale.

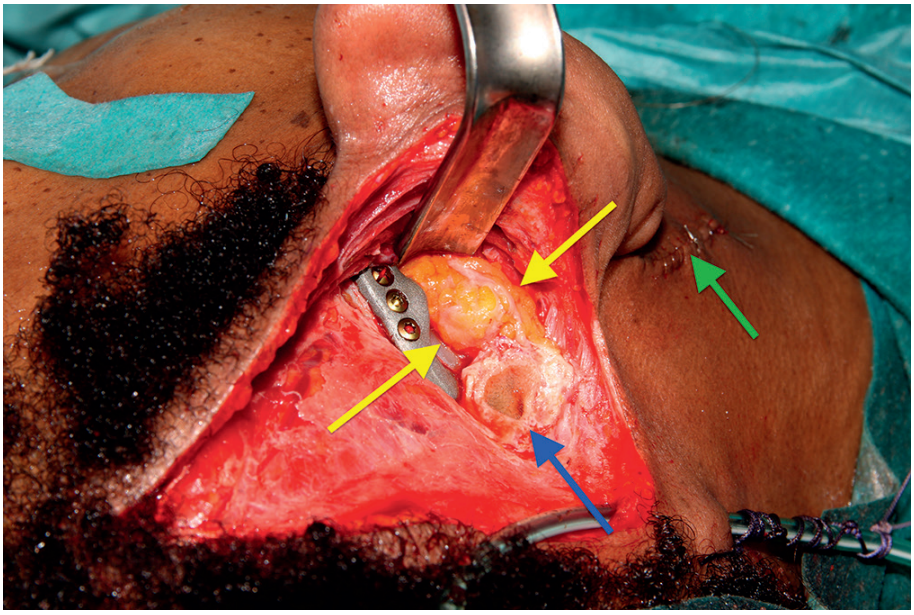

Fig. 1: Abdominal fat transplant surrounding the condylar head and neck (yellow arrows). A transparotid Biglioli approach (green arrow) was chosen for fixing the mandibular part and a retroauricular approach (blue arrow) for fixing the fossa part

Materials and Methods

A computerized literature search was performed up to April 2018, following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The following databases were used

when conducting this search: PubMed Central, Elsevier ScienceDirect Complete, Wiley Online Library Journals, Ovid Lippincott Williams and Wilkins, and Cochrane Library Plus. The following search terms were used: ("TMJ" OR "TMJ") AND ("replacement"OR "prosthesis") AND ("fat"). No time or language limitations were imposed. The inclusion criteria used in this study were TMJ ankylosis, therapy involving surgery, and the use of AFG. The patient sample had to consist of human patients, with no boundary set for age or sex. The exclusion criteria were articles not involving the TMJ, not involving a prosthetically treated TMJ, and articles with a main focus on medical imaging.

The initial search returned 8011 articles. After removal of duplicates, this number was reduced to 6607. Screening of both the title and abstract led to a further reduction to 43 and 8 articles, respectively. These articles were then fully read, and by applying the inclusion and exclusion criteria, a total of 7 articles were selected. No additional articles were included through handsearching the reference list of the included articles. A summary of this search can be found in the PRISMA flowchart.(Fig. 2)

The quality assessment of the included studies was described with the effective public health practice project (EPHPP) quality assessment tool. (2) (Table 1) This tool evaluates eight different domains: selection bias, study design, confounders, blinding, data collection methods, withdrawal and dropouts, intervention integrity, and analysis. Each of these domains is given a rating of strong, moderate, or weak, yet only the first six domains make up for the global rating. If an article has no weak ratings and at least four strong ratings, it is considered strong. A moderate article has <4 strong ratings and no weak ratings, whereas an article is weak if it has at least two weak ratings. Normally, only strong and moderate articles are included in a review, yet as described in Table 1, all included articles have a weak quality based on the EPHPP instrument. Apart from the global rating, the overall intervention integrity of the studies included was considered strong regarding the number of patients receiving the intervention of interest, except a study by Wolford et al.(1), with a weak assessment due to <60% of all patients included receiving the intervention.

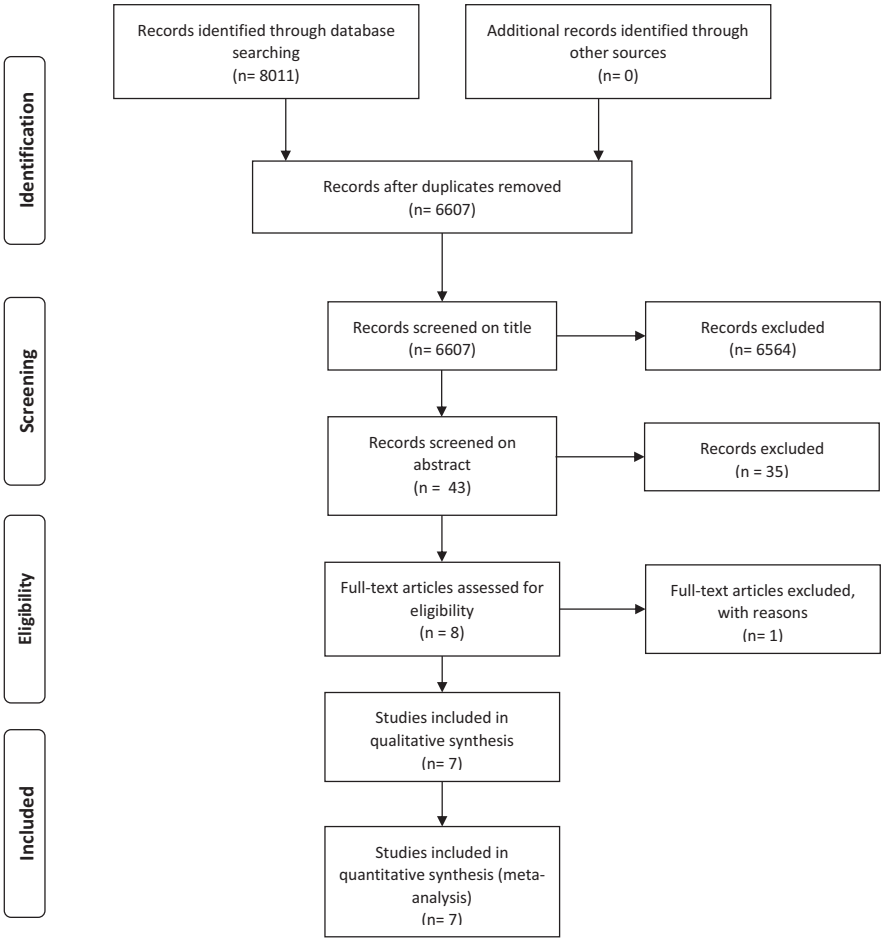

Fig. 2: PRISMA chart

Measurement of consistency ranged from strong(3–5) to moderate assessment(6) or even weak. (1,7,8) In the studies conducted by Roychoudhury et al.(8), Selbong et al.(6), and Wolford et al.(3,5), it is possible that the patients received an unintended intervention that might influence the results. All studies performed a statistical analysis of their results, which was deemed sufficient, based on the evaluation criteria in the EPHPP instrument.(1,3–8) Due to the paucity of data, we chose not to abandon this review based on this limitation and included these articles despite their weak rating. One case report was also included.

Table 1. Quality assessment using the EPHPP tool.

	Selection bias	Design	Con-founders	Blinding	Data collection methods	With-drawals and drop-outs	Overall score
Wolford et al., 1997	Moderate	Moderate	Weak	Moderate	Strong	Weak	Weak
Wolford et al., 2008	Strong	Moderate	Weak	Moderate	Strong	Weak	Weak
Shanyong et al., 2015	Moderate	Moderate	Weak	Moderate	Moderate	Weak	Weak
Wolford et al., 2016	Strong	Moderate	Weak	Moderate	Moderate	Weak	Weak
Selbong et al., 2016	Moderate	Weak	Weak	Moderate	Moderate	Weak	Weak
Mercuri et al., 2008	Strong	Moderate	Weak	Moderate	Moderate	Weak	Weak
Roychoudhury et al., 2017	Moderate	Moderate	Weak	Moderate	Strong	Weak	Weak

Results

A computerized literature search was performed up to April 2018, following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The following databases were used when The pilot study published by Wolford et al.(1) in 1997 included 15 patients who received AFG, providing a total of 22 treated joints. The control group consisted of twenty patients. All patients had the same type of prosthesis made by TMJ Concepts (Ventura, CA, USA). The authors described an increase of maximal incisal opening (MIO) of 11.8 mm at the 12 months of follow-up consultation next to an increase of 6.3 mm in the control group. There was no difference in the decrease of pain level. While 35% of the control group had heterotopic bone formation which required reoperation, none of the patients in the fat-grafted group were diagnosed with heterotopic calcifications or fibrosis.

In 2008, Wolford et al.(3) published a second study with a larger patient sample to substantiate their results. One hundred fifteen patients were included in this study, and 5–20 cc of autologous fat from the abdominal wall was placed around the articulating portion of either the Christensen

or TMJ Concepts total joint prosthesis. While the increase in MIO with 3.5 mm was somewhat disappointing for the Christensen system, the TMJ Concepts system showed an increase of 6.8 mm in MIO. Neither of the prostheses developed heterotopic bone formation that could be seen on radiographic images, nor did they report any donor site-specific complications such as the development of a seroma or infection.

The treatment efficacy of TMJ total joint replacement (TJR) with periarticular AFG in patients who had recurrent TMJ ankylosis was studied by Mercuri et al.(7) in 2008. They included a total of 20 patients, totaling 33 joint replacements, with a mean follow-up of 50.4 ± 28.8 months. While they found a significant reduction in pain, an improvement in quality of life (QoL), and an increase in MIO, no report on the recurrence of heterotopic bone formation was made.

Shanyong et al.(4) performed a retrospective single-center study involving 15 patients and 19 TMJ, to evaluate three modifications to the TMJ replacement technique. Among them was the use of an AFG harvested from the subcutaneous fat, to prevent fibrosis and heterotopic bone formation, by filling up the periprosthetic dead spaces. They concluded that in patients where AFG was used, there was no clinical nor radiographic sign of periprosthetic bone formation, while the two joints which were not treated with AFG showed the formation of heterotopic bone.

Wolford et al.(5) published another study in 2016 to address the treatment of TMJ ankylosis by placement of a TMJ TJR combined with AFG in 32 patients. This treatment proved to be successful, resulting in a significant increase in QoL, MIO, lateral extrusion, and jaw function, as well as decrease in pain. Furthermore, only 2 of 32 patients developed heterotopic bone formation. It is interesting to remark that both patients had been previously treated with a Vitek–Kent system.

In 2016, Selbong et al.(6) described three cases with heterotopic bone formation around a TMJ TJR. They removed the prosthesis, resected the heterotopic bone, and replaced the prosthesis, packing the articulating surface with AFG. No reoccurrence of heterotopic bone was reported.

In 2017, Roychoudhury et al.(8) published a prospective study evaluating the outcomes of TJR surgery along with the placement of AFG transplantation in 11 patients who suffered of TMJ ankylosis. They found a significant increase in MIO without adverse effects regarding the occlusion nor the QoL.

Discussion

The technique of AFG transplantation in the TMJ was first documented by Blair(1,3) in 1913 as a treatment of ankylosis and in 1992 Thomas et al.(9) first described the use of AFG transplantation as a means of prevention of fibrosis and heterotopic calcification in hip prosthesis surgery. Heterotopic bone formation can be defined as the pathological formation of osseous tissue in nonskeletal tissues. While this process is not yet fully understood, it is currently presumed that trauma, such as surgery, resulting in the activation of the inflammatory system, as well as the innate immune system and the nervous system can lead to heterotopic bone formation. Through one of these systems, the production of several osteoinductive cytokines and growth factors such as skeletal growth factor can be promoted, leading to the differentiation and proliferation of mesenchymal stem cells into osteogenic cells. This can then lead to an overactivation of the bone morphogenetic proteins cascade, which, in a permissive environment, will result in heterotopic bone formation.(7,10)

While several preventive techniques such as the use of nonsteroidal anti-inflammatory drugs (NSAIDs), bisphosphonates, and extracorporeal shock-wave therapy have been described, the preferential technique for prevention of fibrosis and calcification after prosthesis placement in orthopedic surgery is postoperative low-dose radiation.(7,10) However, due to the various side effects of radiation, the increased incidence of radiation-induced sarcomas as reported by several authors, and the important anatomical structures of head and neck, this option is best avoided.(7) The use of bisphosphonates is an unattractive option for obvious reasons as well and the use of NSAIDs can lead to gastrointestinal side effects, limiting the duration of application.(10)

A more invasive approach, which was first described by Thomas et al.(9) in 1992, is the use AFGs around a hip prosthesis, thereby filling out any negative space around the joint. There are only four research groups who published their findings regarding the use of AFG in TMJ TJR surgery, with Wolford et al.(1) being the first to step into the tracks of Thomas et al.(9) in 1997. All four reported positive results, yet it is not common practice to place AFG during TMJ TJR surgery. All three studies by Wolford et al.(1,3,5) were based on accumulating but overlapping data, gathered since 1992. There is room for external validation of these results with a study involving multiple centers, multiple surgeons, and a wider variety of patients.

Besides the obvious need for randomized controlled trials evaluating the effectiveness of AFG in TMJ TJR, it is of interest as to why this technique does not seem to have been widely implemented yet, despite its beneficial results. A possible explanation could be that the use of TMJ TJR remains relatively limited, resulting in the limited amount of literature dealing on the topic of heterotopic bone formation and AFG transplantation. However, another explanation might be that surgeons find results in daily practice not as good as they are depicted in the studies mentioned above.

Conclusion

Despite all the positive results regarding the use of AFG in TMJ TJR, scientific evidence remains limited. Further evaluation by means of a prospective multicenter randomized controlled trial is needed to achieve more definitive results of this seemingly promising technique.

References

1. Wolford LM, Karras SC. Autologous fat transplantation around temporomandibular joint total joint prostheses: Preliminary treatment outcomes. J Oral Maxillofac Surg. 1997;55(3):245–51.
2. Thomas BH, Ciliska D, Dobbins M, Micucci S. A process for systematically reviewing the literature: providing the research evidence for public health nursing interventions. Worldviews evidence-based Nurs. 2004;1(3):176–84.
3. Wolford LM, Morales-Ryan CA, Morales PG, Cassano DS. Autologous fat grafts placed around temporomandibular joint prostheses to prevent heterotopic bone formation. Autologous Fat Transf. 2008;21(3):248–54.
4. ShanYong Z, Liu H, Yang C, Zhang X, Abdelrehem A, Zheng J, et al. Modified surgical techniques for total alloplastic temporomandibular joint replacement: One institution's experience. J Craniomaxillofac Surg. 2015 Jul;43(6):934–9.
5. Wolford L, Movahed R, Teschke M, Fimmers R, Havard D, Schneiderman E. Temporomandibular Joint Ankylosis Can Be Successfully Treated With TMJ Concepts Patient-Fitted Total Joint Prosthesis and Autogenous Fat Grafts. J Oral Maxillofac Surg. 2016 Jun;74(6):1215–27.
6. Selbong U, Rashidi R, Sidebottom A. Management of recurrent heterotopic ossification around total alloplastic temporomandibular joint replacement. Int J Oral Maxillofac Surg [Internet]. 2016;45(10):1234–6. Available from: http://dx.doi.org/10.1016/j.ijom.2016.02.017
7. Mercuri LG, Ali FA, Woolson R. Outcomes of total alloplastic replacement with periarticular autogenous fat grafting for management of reankylosis of the temporomandibular joint. J Oral Maxillofac Surg. 2008 Sep;66(9):1794–803.
8. Roychoudhury A, Yadav R, Bhutia O, Aggrawal B, Soni B, Gowswami D, et al. Is total joint replacement along with fat grafts a new protocol for adult temporomandibular joint ankylosis treatment? Int J Oral Maxillofac Surg. 2017;46:236.
9. Thomas BJ. Heterotopic bone formation after total hip arthroplasty. Orthop Clin North Am. 1992 Apr;23(2):347–58.
10. Mercuri LG, Saltzman BM. Acquired heterotopic ossification of the temporomandibular joint. Int J Oral Maxillofac Surg. 2017 Dec;46(12):1562–8.

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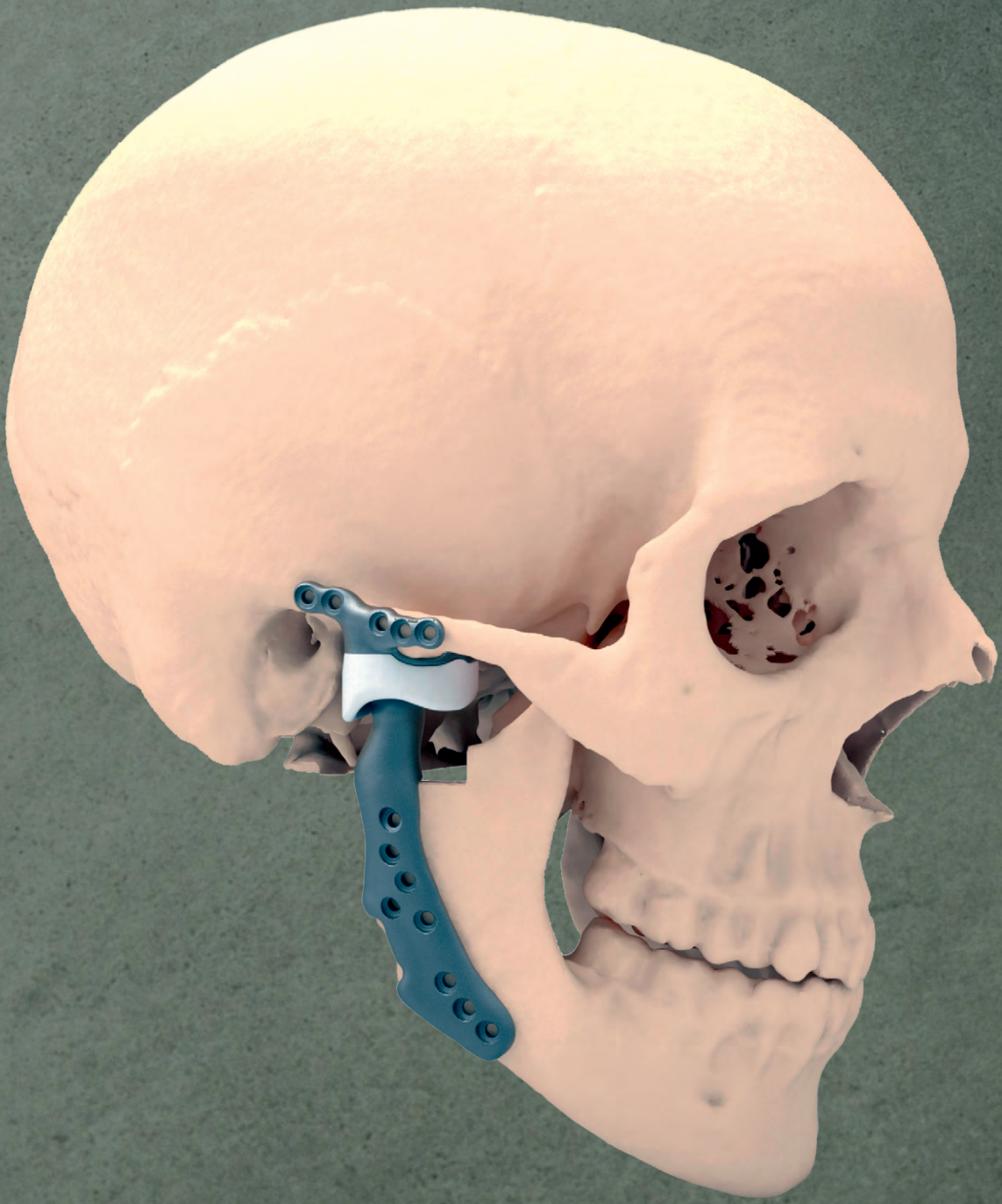

Chapter 12

Postoperative Physiotherapy After Open Temporomandibular Joint Surgery: A 3-Step Program

This chapter is based on:

Postoperative Physiotherapy After Open Temporomandibular Joint Surgery: A 3-Step Program

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Introduction

Well-defined indications for temporomandibular surgery exist. Arthroscopy and arthrocentesis can be considered in patients with osteoarthritis and patients with a displaced disk leading to pain or impaired mouth opening. When these indications are properly met, an efficacy of up to 83.5% can be achieved.(1,2) Open surgery, such as a discectomy, can be considered in cases of severe disk perforation or perseverance of disk displacement symptoms without reduction despite previous discopexy. It can even be considered for partial or total joint replacement (TJR) using an autogenous transplant. Alloplastic replacement can also be considered, although this should be seen as the last resort out of a poor condition.(3,4) Although temporomandibular joint (TMJ) surgery aims to improve joint movement and reduce joint pain, surgery induced disuse muscle atrophy of the masticatory muscles can occur. Furthermore, immobilization can lead to capsular changes and adhesion formation, as abnormal scar tissue formation can occur.(5,6)

The use of physiotherapy after surgical treatment aims to relieve pain and inflammation and decrease swelling. It also aims to prevent joint contracture and adhesion formation from occurring.(7,8) Physiotherapy can be active or passive in nature. Passive therapy can entail heat or cold application to relax the muscles or decrease inflammation, respectively. Exercises including passive opening of the mouth with the aid of an apparatus, such as the TheraBite system (Atos Medical, Malmö, Sweden), also can be used. Continuous passive motion (CPM) has been used in the field of orthopedic surgery for quite some time, mainly in the immediate postoperative phase as a means to lessen the detrimental effects of immobilization and to increase range of motion (ROM).(9) In contrast, active exercises, rely on muscle and joint activation, such as electrostimulation of the muscle and opening and closing of the joint by the patient without any assistance.

Despite the important role postoperative physiotherapy plays in other orthopedic articular surgeries, such as total knee or hip replacements, and although physiotherapy as a nonsurgical treatment for temporomandibular

disorders (TMDs) has been "better" explored, there has been far less exploration of the use of postoperative TMJ physiotherapy. As a result, the literature and research on this topic remain scarce.

This systematic review aimed to provide an overview of the postoperative physiotherapeutic schedules used after open TMJ surgery to assess their effect on postoperative results. The authors hypothesized that the use of a more elaborate physiotherapeutic approach would lead to better postoperative results. Furthermore, this paper aims to achieve an "up-to-date" and scientifically grounded physiotherapeutic approach for surgeons to provide to their patients after surgery.

Material and methods

Study design

The investigators performed a systematic review by conducting a computerized literature search. This search was performed up to April, 1, 2018, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The following databases were used: PubMed Central, Web of Science, Cochrane Library Plus, CINAHL, and EMBASE. The following heading was used to define the search string; ("Temporomandibular Joint" OR TMJ) AND ("Postoperative Care" OR "Physical Therapy" OR "Physical Therapy Modality" OR Exercise OR Revalidation OR Rehabilitation) AND (Arthroplasty OR Prosthesis OR "Total Joint Replacement"). Although these search terms remained largely unchanged (with the exception of the EMBASE search), the combination in which they were used was dependent on the database. Table 1 lists the specific search terms used for each database. In addition, a manual search of reference lists of the included articles and systematic reviews was performed.

For an article to be included in the study sample, the patient sample had to consist of humans who underwent unilateral or bilateral open TMJ surgery. These patients had to have had postoperative physiotherapy with the aim of improving rehabilitation of the patient and TMJ function

and an elaboration of this therapy had to be provided. Although the use of physiotherapy did not have to be the main subject of the study, a comparative approach had to be provided. This could be by a comparative study concept or by providing comparative results. There was no boundary set for age or gender. Because of the relatively scarce amount of literature available, the minimal patient population was set to 2 patients.

Table 1: Search terms used per database.

Database	Search terms	Hits
PubMed Central	((("Temporomandibular Joint"[MeSH] OR "Temporomandibular Joint"[tiab] OR TMJ[tiab])) AND ("Mandibular Prosthesis"[MeSH] OR "Mandibular Prosthesis"[tiab] OR "Joint Prosthesis"[MeSH] OR "Joint Prosthesis"[tiab] OR "Arthroplasty"[MeSH] OR Arthroplasty[tiab] OR "Total joint replacement"[tiab])) AND ("Postoperative Care"[MeSH] OR "Postoperative Care"[tiab] OR "Physical Therapy Modalities"[MeSH] OR "Physical Therapy Modalities"[tiab] OR "Rehabilitation"[MeSH] OR "Rehabilitation"[tiab] OR "Revalidation"[tiab])	102
Web of Science	TOPIC: ("Postoperative Care" OR "Physical Therap*" OR "Physical Therapy Modalit*" OR Exercis* OR Revalidation OR Rehabilitation) AND TOPIC: (Arthroplast* OR prosthes* OR "Total joint replacement*") AND TOPIC: ("Temporomandibular Joint" OR TMJ)	272
Cochrane	("Temporomandibular Joint" OR TMJ) AND ("Postoperative Care" OR "Physical Therapy" OR "Physical Therapy Modality" OR Exercise OR Revalidation OR Rehabilitation) AND (Arthroplasty OR Prosthesis OR "Total Joint Replacement")	21
CINAHL	("Temporomandibular Joint" OR TMJ) AND ("Postoperative Care" OR "Physical Therapy" OR "Physical Therapy Modality" OR Exercise OR Revalidation OR Rehabilitation) AND (Arthroplasty OR Prosthesis OR "Total Joint Replacement")	60
EMBASE	("Temporomandibular Joint" OR TMJ) AND ("Postoperative Care" OR "Physiotherapy" OR Exercise OR Rehabilitation) AND ("Total Arthroplasty" OR Prosthesis OR Arthroplasty)	345

Randomized controlled trials (RCTs); non-RCTs; comparative, prospective, and retrospective studies; and case series were included. Case reports were excluded to provide scientific soundness. Systematic reviews concerning postoperative physiotherapy and rehabilitation after TMJ surgery were reviewed to identify possible eligible studies. Only articles written in Dutch, English, German, or French were included and the full text had to be accessible.

Study Bias

All included studies were assessed for risk of bias. The risk of bias of non-RCTs and other observational studies, prospective and retrospective, was

assessed using the Methodological Index for Non-Randomized Studies (MINORS) scale, first introduced in 2003 by Slim et al.(10) The items were scored 0 if not reported; 1 when reported but inadequately, and 2 when reported adequately.

Risk of bias for an RCT was assessed using the Cochrane Collaboration tool,(11) for which 6 different domains were evaluated: (1) random sequence generation (selection bias), (2) allocation concealment (selection bias), (3) blinding of outcome assessment (detection bias), (4) incomplete outcome data (attrition bias), (5) selective reporting (reporting bias), and (6) other bias. Blinding of participants and personnel was not included, as the nature of the study did not allow for participant blinding. The risk of bias was unclear if 1 or more of the 6 domains were indicated as unclear. A low risk of bias was determined if all domains showed a low risk. A high risk of bias was assessed if one or more domains were deemed to have a high risk of bias.

Study Variables and Data Collection

After assessing the eligibility of all studies retrieved, the following data were extracted when available: author(s), year of publication, number of patients included, gender distribution, mean age of patients (in years), type of surgery, physiotherapy protocol, onset and end of physiotherapy, maximal mouth opening (MMO) in mm, laterotrusion in mm, pain measurement using a Visual Analog Scale (VAS), quality-of-life (QoL) measurement, and the conclusion of the included study (Tables 2 and 3). The use of physiotherapy was considered the predictor variable and the MMO was the main outcome variable (Table 4). Laterotrusion and the VAS pain score, if provided, were considered the secondary outcome variables (Table 5), which were further analyzed to determine the effect of physiotherapy.

Results

Study Inclusion

The initial search returned 675 published articles. After removing all duplicates, the number was reduced to 523 articles. A further 482 articles were excluded by screening the title (n=83) and abstract (n=41). By reading through the final 41 articles and applying the inclusion criteria, a total of 6 articles were included for analysis. No additional articles were included through manual searching reference lists of the included articles. The performed search is summarized in the PRISMA flow diagram (Fig. 1). Because of to the lack of sufficient data and impossibility to achieve the raw study data, the authors could not conduct a meta-analysis of the included articles. Instead the statistical results of each study included in this systematic review were analyzed and compared where possible.

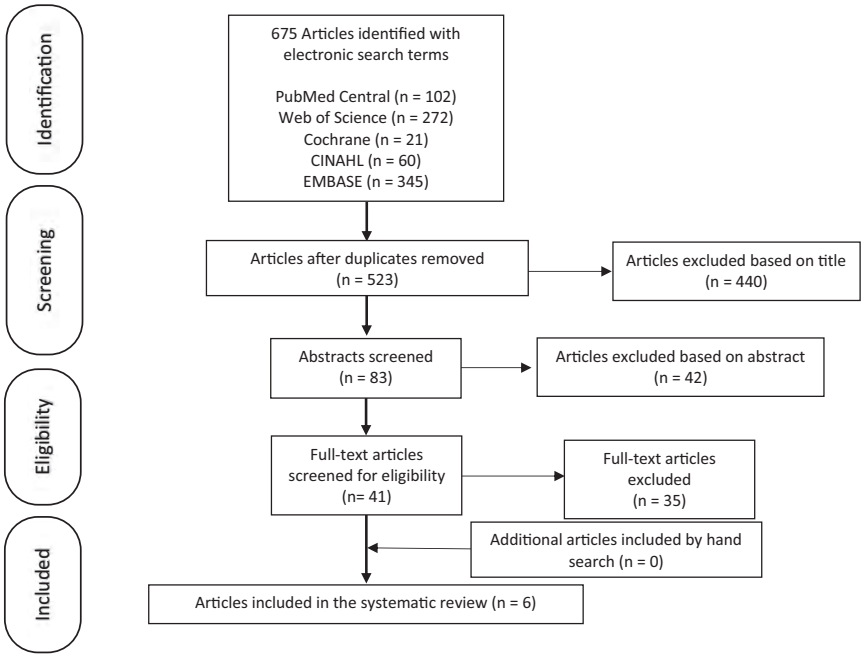


Fig. 1: PRISMA flow diagram

Table 2. Study characteristics, type of surgery, evaluation, and outcome. (n = 6)

Study (year)	Study population	Type of surgery
Austin & Shupe (1993) (12)	Control group: 22 female, 4 male	Unilateral arthroscopy (n=1), unilateral arthroplasty (n=9), bilateral arthroscopy (n=2), bilateral arthroplasty (n=11), bilateral arthroscopy-arthroplasty (n=0), bilateral arthroscopy-arthroplasty with implant (n=4)
	Treatment group: 23 female, 1 male	Unilateral arthroscopy (n=1), unilateral arthroplasty (n=10), bilateral arthroscopy (n=5), bilateral arthroplasty (n=5), bilateral arthroscopy-arthroplasty (n=3), bilateral arthroscopy-arthroplasty with implant (n=0)
Braun (1987) (13)	Control group: 29 female	Unilateral disk repair procedures (n=11), unilateral meniscectomy with disk implantation (n=6), bilateral disk repair procedures (n=4), bilateral meniscectomy with disk implantation (n=8)
	Treatment group: 25 female, 4 male	Unilateral disk repair procedures (n=5), unilateral meniscectomy with disk implantation (n=14), bilateral disk repair procedures (n=3), bilateral meniscectomy with disk implantation (n=7)
Capan et al. (2017) (14)	Control group: 15 female; mean age: 32.2 ± 6.0 years	TMJ condylar discopexy
	Treatment group: 15 female, 1 male; mean age: 31 ± 5.9 years	TMJ condylar discopexy
Leandro et al. (2013) (15)	Treatment group: 120 female, 180 male; age: range 20-60 years	TMJ TJR with Biomet/Lorenz system
Oh et al. (2002) (7)	Control group: 19 female, 3 male; mean age: 22.95 years	N/A
	Treatment group: 20 female, 2 male; mean age: 22.09 years	N/A
Robiony (2011) (16)	Treatment group: 2 female, 3 male	TMJ TJR with Biomet/Lorenz system

Abbreviations: BTX-A, botulin toxin A; MIO, maximal interincisal opening; MO, mouth opening; MMO, maximal mouth opening; ROM, range of motion; TJR, total joint replacement; TMJ, temporomandibular joint.

Outcome	Conclusion
3 of 26 patients reached a minimum ROM of 40 mm after 8 weeks	A significant difference in maximal ROM between both groups was found; however, no significant difference in lateral movement was seen
20 of 24 patients in treatment group reached a minimum of 40 mm ROM after 8 weeks	
Mean increase of 8.8 mm in ROM; nonsignificant chi-square value for patients with initial MO of ≤30 mm	Postoperative physical therapy can lead to a significantly improved ROM compared to patients without this therapy; physical therapy should be applied on a consistent and regular basis to achieve optimal results
Mean increase of 11.8 mm in ROM; significant chi-square value for patients with initial MO of ≤30mm; significant reduction in headache pain reported by all patients	
Both groups showed significant improvement in MMO, protrusion, and lateral movements, but a significantly larger evolution in MMO and protrusion was seen in the patient group that received professional physiotherapy; however, no significant difference in lateral movement was found	
13 patients showed MMO <25 mm after 6 months; all these patients did not undertake physical therapy; mandibular function showed significant improvement over time, the rate of which was determined by the compliance to the physiotherapy exercises; low function of speech was seen in patients who skipped their jaw opening exercises	Achieving significant improvements in jaw function, speech, and MIO are not only related to the surgical procedure, but also to intense physical therapy
	Physiotherapy has a positive effect on relieving pain and restoring TMJ function after surgery
Significantly less pain and significantly improved CMI in the treatment group, compared to the control group	
Significant reduction in pain after 1 month, yet MMO <30 mm after injection + physiotherapy: significant improvement MMO + stable result throughout time	Physical therapy performed during the action period of BTX-A allows for elongation of the muscle fibers; BTX-A can help in improving the joint function

Table 3. Physiotherapy protocol, start and stop, and evaluation.

Study (year)	Physiotherapy protocol
Austin & Shupe(1993) (12)	Control group: No protocol was used
	Treatment group: 3 phases Phase 1 (days 7-14 after surgery): mobilization–gentle distraction; forced opening 3 times/day with scissor exercises (3×5 reps with 10-sec holding); oral education Phase 2 (days 14-21 after surgery): previous exercises; mobilization–distraction and (pain-free) translation; forced lateral movement exercises (1×5 reps with 10-sec holding, 3 times/day); isometric exercises–passive stretch (1×5 reps with lateral and opening contractions with 10-sec holding, 3 times/day); oral education Phase 3 (days 21-28 after surgery): previous exercises; mobilization–distraction, lateral, and anterior; forced opening exercises (2-3 min, 3 times/day); jetting exercise (1×15 reps, 3 times/day); oral education
Braun (1987) (13)	Control group: No protocol was used
	Treatment group: superficial heat; ultrasound; ROM and mobilization techniques
Capan et al. (2017) (14)	Control group: 30-min sessions at home, 7 days/week for 8 weeks
	Treatment group: 4 phases with 30-min session, 3 days/week for 8 weeks, supervised by a physiotherapist + 30-min session at home 4 days/week Phase 1 (days 1-7 after surgery): posture exercises; active rotation exercises (1×20 reps, 3 times/day); mouth-opening exercises (1×20 reps, 3 times/day); oral education, liquid diet, cold application Phase 2 (days 7-30 after surgery): posture exercises; controlled rotational movement exercises; opening and closing exercises; active assistive self-stretching (stimulating MMO); self-mobilization; soft diet, heat application, massage Phase 3 (weeks 4-6 after surgery): forced, fully active exercise (MMO stimulation with spatula); strengthening and endurance exercise; active resistance exercise to opposite side; soft diet, massage Phase 4 (weeks 6-8 after surgery): coordination exercises by opening and closing in front of mirror; all of the above

Start of physiotherapy	Stop of physiotherapy	Evaluation
		ROM measured at 1 and 8 weeks after surgery
5 - 7 days after surgery	8 weeks after surgery	As above
		ROM, pain relief, swelling
		ROM, pain relief, swelling
		ROM
		MIO and pain measured within 1 month after surgery and during the last follow-up appointment, within 1 year after surgery
1 week after surgery	(Minimum of 6 months of home therapy) ROM of at least 35 mm; significant reduction in pain; no change in pain and ROM for 4 treatments	MIO and pain measured at first physical therapy appointment and last follow-up appointment, within 1 year after surgery
Within 24 hours after surgery	8 weeks after surgery	MMO, protrusion, and right and left lateral movement were measured before surgery and 2 m after surgery; pain was evaluated using a VAS score (1-10) and QoL was measured using several parameters, such as feelings of depression and quality of sleep
Within 24 hours after surgery	8 weeks after surgery	As above

Table 3. continued

Study (year)	Physiotherapy protocol
Leandro et al. (2013) (15)	2 phases
	Phase 1 (days 3-14 after surgery): opening and closing exercises; MMO stimulation keeping mouth open at wider range; 3-5 times/day
	Phase 2 (day 15-2 months after surgery): opening and closing exercises; forced, fully active exercise (MMO stimulation with spatula); 3-5 times/day
Oh et al. (2002) (7)	Control group: no protocol
	Treatment group: 3 phases
	Phase 1 (until week 3 after surgery): ice pack 1×20 min, 5 times/day; postural correction; resting tongue position instructions; active controlled condylar rotation; active therapeutic exercises with tongue
	Phase 2 (weeks 3-6 after surgery): hot pack; ultrasound; postural correction 1×20 min, 3 times/day; active vertical and lateral mandibular movement 1×20 min, 3 times/day; stretching exercises 1×20 min, 3 times/day; isometric exercises 1×20 min, 3 times/day
	Phase 3 (from 7 weeks after surgery): all of the above; release technique for masticatory and neck muscles; intrinsic condylar mobilization
Robiony (2011) (16)	4 months after surgery: bilateral BTX-A injections in masseteric muscles; physiotherapy 1×3-5 min, 4 times/day, including lateral excursion, active hinge opening, manual finger stretching, and TheraBite System 1×2 min, 10 times/day

Abbreviations: BTX-A, botulin toxin A; MIO, maximal interincisal opening; MMO, maximal mouth opening; QoL, quality of life; ROM, range of motion; VAS, Visual Analog Scale.

Start of physiotherapy	Stop of physiotherapy	Evaluation
48 hours after surgery	Minimum duration of 12 weeks	Pain and mandibular function through VAS score + measurement of MMO; weekly for first 2 months; monthly for months 3-12; yearly after 12 months
N/A	N/A	Pain through VAS and craniomandibular index (dysfunction index, palpation index) before surgery, 6 weeks after surgery, and 7 months after surgery
Within 1 week after surgery	N/A	As above
BTX-A infiltration 4 months after surgery; physiotherapy 7 days after injection	Minimum duration of 1 year after surgery	MMO and pain and jaw function using VAS scores before surgery and 1, 2, and 4 months after surgery

Table 4. Effect of physiotherapy on the primary outcome variable (Maximal Mouth Opening)

Study (year)	Study population	Primary outcome variable (MMO)
Austin & Shupe (1993) (12)	Control group: 22 female, 4 male	MMO ≥40 mm by 8 weeks: n = 3
	Treatment group: 23 female, 1 male	MMO ≥40 mm by 8 weeks: n = 20
Braun (1987) (13)	Control group: 29 female	MMO ≤ 35 mm after1 year: n = 8 MMO 35-39 mm after 1 year: n = 6 MMO ≥40 mm after 1 year: n = 15 Mean MMO after 1 year: 39 mm
	Treatment group: 25 female, 4 male	MMO ≤ 35mm after 1 year: n = 4 MMO 35-39mm after 1 year: n = 13 MMO ≥40mm after 1 year: n = 12 Mean MMO after 1 year: 38.9 mm
Capan et al. (2017) (14)	Control group: 15 female; mean age: 32.2 ± 6.0 years	Mean MMO by 8 weeks: 27.6 ±3.0 mm
	Treatment group: 15 female, 1 male; mean age: 31 ± 5.9 years	Mean MMO by 8 weeks: 32.8 ±1.6 mm

Abbreviations: MMO: maximal mouth opening

Table 5. Effect of physiotherapy on the secondary outcome variables (Laterotrusion and the Visual Analog Scale pain score)

Study (year)	Study population
Austin & Shupe (1993)[12]	Control group: 22 female, 4 male
	Treatment group: 23 female, 1 male
Capan et al. (2017)[14]	Control group: 15 female; mean age: 32.2 ± 6.0 years
	Treatment group: 15 female, 1 male; mean age: 31 ± 5.9 years
Oh et al. (2002)[7]	Control group: 19 female, 3 male; mean age: 22.95 years
	Treatment group: 20 female, 2 male; mean age: 22.09 years

Abbreviations: VAS: Visual Analog Scale

Mean increase in MMO	Analysis
8.5 ±4.45 mm	Increase MMO: χ^2 = 23.0874; *df*= 1; *P* = .0004
11.04 ±4.56 mm	Mean MMO: *t*(48) = 1.99383, *P* = .0259
8.8 mm	Increase MMO with initial MMO≤30mm: control group χ^2 = 1.0 (*P* > .05)
11.8 mm	Increase MMO with initial MMO≤30mm treatment group: χ^2 = 6.2 (*P* < .05) Mean MMO: Independent *t* test: significantly larger increase in treatment group (*P* = ?)
9.56 mm	
5 mm	Independent *t* test: *P* = .001

Secondary outcome variable	Analysis
Laterotrusion ≥ 8 mm by 8 weeks: n = 13	
Laterotrusion ≥ 8 mm by 8 weeks: n = 18	Independent χ^2 test: χ^2 = 2.33460; *df*= 1; *P* = .1265
Mean laterotrusion (L) by 8 weeks: 4.7 ±0.8 mm	Independent *t* test: *P* = .241
Mean laterotrusion (R) by 8 weeks: 4.8 ±0.9 mm	Independent *t* test: *P* = .462
Mean pain at rest (VAS) after 8 weeks: 1.6 ±1.2	Mann-Whitney *U* test: *P* = .017
Mean pain with activity (VAS) after 8 weeks: 3.4 ±0.9	Mann-Whitney *U* test: *P* = .004
Mean laterotrusion (L) by 8 weeks: 2.8 ± 0.8 mm	
Mean laterotrusion (R) by 8 weeks: 5.2 ± 1.0 mm	
Mean pain at rest (VAS) after 8 weeks: 0.8 ±1.1	
Mean pain with activity (VAS) after 8 weeks: 1.6 ±1.3	
Mean pain (VAS) 6 weeks after surgery: 29.09 ±4.37	Independent *t* test: *P* = .80
Mean pain (VAS) 7 months after surgery: 16.36 ±8.38	Independent *t* test: *P* = .05
Mean pain (VAS) 6 weeks after surgery: 28.50 ±9.67	
Mean pain (VAS) 7 months after surgery: 11.77 ±6.44	

Risk of Bias

4 studies were assessed using the MINORS scale, of which 1 was noncomparative and 3 were comparative. Due to the retrospective nature and lack of blinding of the results in several studies, the overall score of both the comparative and noncomparative studies was rather low, indicating a high risk of bias. (Table 6). One RCT was screened for bias using the Cochrane Collaboration tool. An overview of this assessment is included in Table 7. This study scored an unclear risk of bias due to not mentioning if blinding of personnel and blinding of outcome assessment had occurred. In the other fields evaluated, this study scored a low risk of bias. One case series was not evaluated for bias because it was—per definition—more susceptible to bias and selection bias in particular. As such, it was considered "high" in risk for bias.

Table 6. Risk of bias assessment of nonrandomized controlled trial using the MINORS scale.(10)

Study (Year)	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of the study endpoint	Follow-up period appropriate to study aim	<5% lost to follow-up	Prospective calculation of study size	Adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Total
Austin & Shupe (1993) (12)	2	2	2	2	0	1	2	0	0	1	2	2	16/24
Braun (1987) (13)	2	0	0	2	0	2	2	0	2	0	2	2	14/24
Oh et al. (2002) (7)	2	2	1	2	2	0	2	0	2	2	2	2	19/24
Leandro et al. (2013) (15)	2	2	0	2	2	2	2	0	N/A	N/A	N/A	N/A	12/16

Abbreviations: N/A, not applicable

Table 7: Risk of bias assessment of randomized controlled trials using the Cochrane Collaboration's Tool.

Study (year)	Random sequence generation	Allocation concealment	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other
Capan et al. (2017) (14)	+	+	?	+	+	+

Abbreviations: +, low risk of bias; –, high risk of bias; ?, unclear risk of bias.

Study Results

Austin and Shupe(12) treated a total of 50 patients, who were divided into a treatment group of 24 patients and a control group of 26 patients. The surgical treatment varied from arthroscopy to arthroplasty and, in 4 cases, placement of a disk implant. Although the control group did not receive a specific schedule for physical therapy, the treatment group underwent 3 different phases of physiotherapy, each of which only started if the preset requirements in ROM, pain relief, and decrease in swelling were met. These different phases are further elaborated on in Table 3. With 20 of 24 patients in the treatment group having a ROM of at least 40 mm at 8 weeks after surgery compared to 3 of 26 for the control group, they concluded that the importance of physical therapy after surgery was obvious, resulting in a significantly larger than predicted increase in MMO (P = .0004) and a significantly larger MMO (*P* = .03). However, no significant difference in increase of lateral movement was found between groups (*P* = 0.13). Three patients in the control group and 6 patients in the treatment group underwent unilateral or bilateral arthroscopy rather than open surgery, which in turn could lead to a bias in the mentioned results. However, because of the paucity of data available, the authors chose not to exclude this article from the results.

Braun(13) used a similar set-up, dividing 58 patients into a treatment group (n= 29) that received postoperative physiotherapy and a control group (n = 29) that did not. Although the 2 groups showed comparable end results, the treatment group had less initial jaw mobility and more complaints of headaches and severe pain in the TMJ region. More importantly, in addition to the markedly larger increase in maximal interincisal opening (MIO) in the treatment group, Braun(13) found a significant chi-square value ($P < .05$) for patients with an initial mouth opening of 30 mm or less within this group, meaning that patients who received postoperative physical therapy showed a greater increase in MIO than would be expected in a normal distribution. They also found that there was a greater tendency to achieve an MMO of more than 40 mm in patients who had a preoperative MMO of more than 30 mm if they were subjected to physiotherapy. However, no statistical analysis was provided to support this claim. Although Braun(13) also found a markedly larger increase in mean MMO in the treatment group compared with the control group by independent t test, no P value was provided.

The authors decided against inclusion of the pain results of this article because the evaluation was mainly dependent on the clinical notes, rather than a VAS pain score, for example; as such, the study was possibly subject to incomplete documentation.

Capan et al(14) advocated the use of physiotherapy as soon as within the first 24 hours after discopexy because it prevents the formation of abnormal fibrous tissue. Furthermore, physical therapy can help improve muscle vascularity and muscle mass, while decreasing fatigability. To that end, they performed an RCT comparing a group of patients who performed postoperative physiotherapy exercises at home with a group of patients who underwent the same program, but were supervised by a physiotherapist 3 times per week. The 2 groups showed significant improvement in MMO, protrusion, and lateral movements; however as measured by independent t test a significantly larger change in MMO (P = .01) and protrusion (P = .01) were seen in the patient group that received professional guidance. In comparison no significant difference in lateral movement to the left (P = .24), nor right (P = .46) was found. Furthermore,

as measured by a Mann-Whitney U test, a more significant decrease in pain was seen in the treatment group after two months at rest (P = .02) and during activities (P = .004).(14)

Oh et al(7) surgically treated 44 patients, of which 22 received an elaborate postoperative physiotherapy schedule, whereas the control group did not receive any physiotherapy after discharge from the hospital. As measured by an independent t test, they concluded that both groups showed a similar improvement in the VAS pain score 6 weeks after surgery (P = .80). They attributed this to the fact that the surgery rather than the physiotherapy brought initial pain relief. However, 7 months after surgery, the treatment group scored significantly better (P = .05), showing the importance of physiotherapy over the long-term.(7)

Leandro et al(15) conducted a 10-year follow-up study of patients who underwent TMJ TJR using a Biomet total TMJ replacement system (Zimmer Biomet, Warsaw, IN, USA). 300 patients were treated after being diagnosed with severe joint or articular changes or condylar resorption. Patients underwent rigorous physical therapy from 48 hours after surgery for a minimum of 12 weeks. During follow-up, it became apparent that those patients (n = 13) who showed a final MMO of less than 25 mm had not properly conducted their physiotherapy. Also, impaired function of speech was seen in those patients who did not follow their physiotherapy schedule. Despite not having been set up as a comparative trial, it was clear that not performing postoperative physiotherapy had an obvious negative effect on the restoration of mandibular function.

Robiony(16) treated 5 patients with the Biomet/Lorenz TJR system for TMJ ankylosis. Although patients quickly showed a significant decrease in their VAS score for pain, despite “vigorous physiotherapy”, the MMO remained less than 30 mm after 4 months. In an attempt to improve the MMO, 5 injections of botulin toxin A (BTX-A) were given in the masseter muscle. These injections allowed for muscle relaxation and, with an additional physiotherapy schedule with manual finger stretching, TheraBite system exercises, active hinge opening, and lateral excursions, elongation of the muscle fibers occurred, allowing for a significant improvement in MMO.

Robiony(16) concluded that the use of BTX-A should be included in the physiotherapeutic treatment of patients who have had an ankylosed joint for a longer period because the temporalis and masseter muscles often have degenerated and shortened. By using BTX-A, relaxation of the masticatory muscles could be achieved together with an analgesic effect which, through physiotherapy, allowed for an elongation of the masticatory muscles.

Discussion

The TMJ and masticatory muscles can be affected by a wide array of disorders. As a result, this heterogeneous group of pathologies, better known as TMDs, is the most frequent cause of nonodontogenic orofacial pain. With many different epidemiological studies being conducted with different patient groups, the current literature estimates that 10% to 25% of the general population is subject to a TMD at any given point in time, with a 3:1 ratio of women to men and an onset of symptoms occurring mainly between the ages of 20 and 40 years.(17–21) Although most TMD are self-limiting, a meta-analysis by Al-Jundi et al(21) concluded that approximately 15.6% to 16.2% of all TMD patients are in need of professional treatment.

To evaluate the severity of the TMD and the indicated therapy based on this diagnosis, several tools can be used, such as the staging classification for internal derangement of the TMJ by Wilkes and the Helkimo index.(22,23) The Helkimo index can be broken down into 3 sub-indices: anamnestic, clinical, and occlusal dysfunction. The anamnestic and occlusal subindexes have 3 different levels ranging from none to moderate or severe occlusal dysfunction or symptoms; the clinical dysfunction ranges from no dysfunction symptoms to mild, moderate or severe symptoms.(23) The Wilkes' classification is based on clinical and radiological properties, as well as the anatomical appearance of the TMJ. The scale ranges from early stage internal derangement, recognizable by a click during opening of the mouth and a slight forward displacement of the disk, to early intermediate, intermediate, late intermediate, and late-stage internal derangement. In case of the latter, perforations of the disk

or its attachment can be seen as well as degenerative changes to the hard tissues. The patient will also complain of a limitation in joint mobility and articular pain.(22) Another tool that can be used to assess the severity of a TMD is the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD). This tool was first presented in 1992 and has been frequently updated since. The most recent improvements were presented in 2014.(24) The Axis I protocol can be used to evaluate the pain and joint, through a questionnaire for the patient's pain history and diagnostic criteria for differentiating the most-common TMD, whereas the Axis II protocol can be used to determine psychosocial factors such as distress and pain disability.(24,25) Depending on how the patient scores on these tools, treatment options will vary from less to more invasive. In more than 80% of all TMDs, a more conservative approach, such as a combination of anti-inflammatory therapy, an occlusal splint, and physiotherapy, combined with oral reeducation will suffice.(14,26–28) However, when these noninvasive treatments fail to provide resolution, a more invasive approach might be needed, ranging from minimally invasive intra-articular injections to open joint surgery.(27)

The importance of physiotherapy after TMJ surgery is not a recent discovery. Studies included in this systematic review date from 1987 when Braun(13) first conducted a retrospective study of patients who were surgically treated due to internal derangement of the TMJ. Despite her conclusion that patients could greatly benefit from early onset of physiotherapy, only a few objective studies assessing the effects of physiotherapy on postoperative patients are available to this day.(12) Furthermore, although nearly all the included studies concluded that early onset and rigorous physiotherapy over a prolonged is needed to achieve optimal postoperative results, these studies failed to highlight the importance of individual exercises.(7,12–16) In this systematic review, the authors aimed to provide the reader with an overview and analysis of the available qualitative literature on postoperative physiotherapy after open TMJ surgery and to ascertain its value. Although the amount of comparative literature on this topic is clearly insufficient, it was concluded that postoperative physiotherapy plays an important role in achieving a good MMO and decreasing pain.

These findings were also supported by several other articles, such as a study conducted by Singh et al,(29) who treated 10 patients with an ankylotic TMJ by placement of a sternoclavicular graft with buccal fat pad lining, after which an intense physiotherapeutic program was set up. Physiotherapy started within 1 day after surgery with both passive and active exercises, which increased over time. Although follow-up was limited to 6 months, a marked improvement in MIO, laterotrusion, and protrusion were seen. Furthermore, all patients claimed to be pain-free after 6 months. They found that the improvements in mobility were greater compared with similar studies and attributed this to the use of the buccal fat pad (instead of temporalis muscle) and the aggressive physiotherapy. They also stressed that neglecting postoperative physiotherapy can negate a potentially successful reconstruction. In a prospective trial by Lo et al(30) 5 patients with an ankylotic TMJ (unilateral or bilateral), had a surgical release performed. Unlike most studies, Lo et al(30) allowed their patients to halt their postoperative physiotherapy with a TheraBite-like exerciser as soon as they deemed it was no longer necessary. Moreover, the physiotherapeutic schedule was very limited compared with the studies included in this systematic review. In allowing the patients to determine when to stop, the mean treatment time was only 40 days and the minimum duration was as short as 14 days. Lo et al(30) found that although results at the end of the physiotherapy treatment period had significantly improved to a mean MMO of 29.6 ± 4 mm, a notable relapse occurred in the posttreatment period, with the mean MMO decreasing to 23.8 ± 8.3 mm. In comparison, other patients who underwent orthognathic or trauma surgery did not show a similar relapse. In addition, they concluded that, for treatment of an ankylotic TMJ, more rigorous, prolonged, and frequent physiotherapy is needed.

Physiotherapeutic Phases

When researching different physiotherapeutic techniques and trying to provide a potential postoperative treatment plan (included in Table 8), it is important to understand the different postoperative phases the joint goes through and why certain techniques are more suited for a phase than others. As stated by Dijkstra et al(9), even the insertion of fine arthroscopic instruments into the TMJ will lead to the development of

transient traumatic arthritis, independent of the type of joint pathology. As a result, irritation of the synovial membrane will occur, which will lead to joint effusion and result in reflex muscle splinting as a mechanism to protect the joint. In response, the patient will tend to immobilize the joint to avoid any painful movement.(16,31) However, as has clearly been shown by the studies included in this review and many other studies, this immobilization has been found to be detrimental to the joint, resulting in degenerative changes to the joint and changes in the fibrous structure with the formation of scar and adhesion as the connective tissue starts to heal. Due to the ensuing immobilization, synovial fluid dynamics become impaired with the resulting decreased intra-articular lubrication.(5,32,33)

Table 8. Proposed revalidation schedule.

Phase	Timing	Therapy
1	Within 24 hours after surgery to 7 days after surgery	Nonchewing diet Cold therapy over joint 1×20 minutes, (minimally) 5 times per day Condylar rotational exercises (passive opening and closing, 20 repetitions, 3 times per day; active opening and closing, 20 repetitions, 3 times per day) Grade I joint distraction Grade II joint distraction toward end of phase 1 Oral reeducation with avoidance of parafunctions
2	From 1 to 3 weeks after surgery	Soft diet Moist heat application over muscles 20 minutes before exercises, cold application over joint after exercises Coordination exercise using a mirror 1. Condylar rotational exercises as in phase 1 2. Active mouth opening and closing 3. "Mandibular snake": protrusion, depression, retrusion, elevation, return to neutral position Range of motion exercises (until pain limit, not over pain limit) 1. Insertion of tongue spatula or TheraBite system 7x7 seconds, 7 times per day 2. Active assisted opening: 10 repetitions, keeping the maximal mouth opening for 30 seconds, 3 times per day 3. Active lateral movement: 10 repetitions keeping the maximum lateral deviation for 30 seconds, 3 times per day 4. Active protrusive and retrusive movement: 10 repetitions, keeping the pro/retrusive deviation for 30 seconds, 3 times per day Grade II joint distraction Use of chewing gum

Table 8. continued.

Phase	Timing	Therapy
3	From 4 weeks on after surgery	Transition to solid diet Stabilization exercises 1. Lower jaw maintained in a neutral, slightly open position (lateral manual pressure: 1x6 repetitions, 5 times per day; upward manual pressure: 6 repetitions, 5 times per day) Lower jaw maintained in a closed position (attempting to open the during upward manual pressure: 6 repetitions, 5 times/day) Range of motion exercises 1. Maximum opening (insertion of tongue spatula or TheraBite system: 5x30 seconds, 5 times per day; active assisted opening: 5 repetitions, keeping the maximum mouth opening for 30 seconds - 1 minute, 3 times per day; active opening: 5 repetitions, keeping the maximum mouth opening for 30 seconds -1 minute, 3 times per day) 2. Lateral deviation: 10 repetitions, 3 times per day per side Grade III & IV joint distraction Massage of masticatory muscles Use of chewing gum

First Phase (Days Postoperatively)

Fig. 2: Goldfish exercise: Condylar rotation. The mouth is opened and closed while the tongue pressed against the palate.

First, the immediate postoperative phase of physiotherapy should be aimed at decreasing joint inflammation and pain and maintaining mandibular mobility to prevent the formation of abnormal adhesions.(7,9,34) The total number of exercises should be limited to 3 to 5 daily to avoid overexertion of the capsular tissue and muscles. The number of repetitions is kept high and the intensity is kept low during this phase because the main goals are to maintain mobility within a restricted range, prevent muscular inhibition, and decrease pain and inflammation without putting too much stress on the joint and muscles.(35,36) Frequent application of cold against the joint helps relieve pain by numbing the area and decreasing swelling and inflammation through vasoconstriction.(37) In the current mindset of fast-track surgery, some might believe that opting for cryotherapy might prove more useful, but a recent RCT by Thienpont(38) concluded that there was no clinical advantage to the use of cryotherapy over conventional cold packs in patients who underwent a knee arthroplasty. In addition, sufficient pain medication should be prescribed as well because pain reduction will lead to more patient confidence and an improved ROM.(9)

Second, ROM exercises should be incorporated, with limitation to condylar rotation. This is to prevent TMJ stretching, which could increase the inflammatory response or TMJ luxation in case of a TJR.(34) Movement also should be limited to within the pain-free zone. A possible exercise that can be performed is active vertical mandibular movement while the tongue maintains contact with the palate, because this limits the movements in such a way that only condylar rotation will occur.(7) These exercises are also known as 'goldfish' exercises. (Fig 2) The mandible can be passively opened and closed again using a finger, or also slowly actively opened and closed, while looking in a mirror to maintain good symmetric movement. The simple insertion of several tongue blades, or even the TheraBite system mouthpiece, without further activation, can also be used.

Third, some mild joint mobilization can be performed by the physiotherapist, such as grade I and II joint distraction.(9) To prevent possible muscle overexertion, a 'no chew diet' is advised and detrimental parafunctions should obviously be avoided at all times.(9)

Second Phase (1-3 weeks postoperatively)

Fig. 3: Cross-fingered exercise: The thumb and index finger are used to assist mouth opening.

With the immediate inflammatory response subsiding after the first postoperative week, this second phase aims at further increasing the ROM, while increasing the muscle control and coordination and performance to achieve functional mobility. The number of exercises can gradually be increased to 5 to 10 daily and the number of repetitions can be decreased. This allows for a more 'high-intensity endurance' shift in rehabilitation. Pain therapy still plays an important role in this phase. (9,35,36) Cold application can be continued as a means to lessen joint pain (e.g., after certain exercises), and local moist heat application should be used as well. Heat application not only relieves muscle tension and pain, but also improves the extendibility of collagen fibers and decreases tissue viscosity, which can help when performing stretching exercises. (39,40) Furthermore, because local blood flow and metabolism are increased, tissue healing can become facilitated. The aim of this heat therapy is to achieve muscle relaxation; therefore, heat should be applied directly on the muscle - instead of on the joint - and should be used

20 minutes before the exercise program to allow the muscles to be as relaxed as possible.(9,14,41) One could also consider the use of cold therapy immediately after the physical exercises; Lin(41) found that the combination of pretreatment heat application and posttreatment cold application yielded better results in total ROM compared with the use of only heat application. It should be noted though that this study evaluated knee motion, so results for the TMJ may be different.

Previously performed condylar rotational exercises can be continued because they considerably aid in achieving a symmetrical mouth opening, as was indicated by Oh et al(42) in patients with TMD. Furthermore, performing coordination exercises in front of a mirror can further aid muscle coordination. After drawing a straight vertical line on the mirror, the patient should attempt to keep the midline of the lower jaw on this line when performing exercises with vertical movement. This use of a mirror can also be combined with other exercises, such as active opening and closing or protrusive and retrusive exercises.(43)

Fig. 4: Hook-pull exercise: The index finger is hooked in the lower jaw, after which the jaw is opened and gently pulled farther open using the hooked finger.

Exercises to begin stretching the joint, with rotational and translative movement, also can be started in this phase. By no longer keeping the tongue pressed against the palate, translational movement becomes possible. Active horizontal mandibular movements can be aided by placing dental cotton rolls or a pen between the molars (for protrusion and retrusion) or between the incisors (for active lateral movement). Active vertical mandibular movement can be assisted by using tongue blades or by active assisted exercises such as the cross-fingered exercise, in which the mouth is actively opened while being aided by both thumb and index finger, and the 'hook-pull' in which the index finger hooks in the floor of the mouth, aiding the downward mandibular movement during opening. (Figs. 3,4) Placement of the index fingers over the condyles allows the patient to perceive the translative movement of the condyles, aiding in guidance when opening and closing. Passive exercises, such as manual finger stretching or using a passive motion apparatus such as the TheraBite system, also can be considered. The pace at which the mouth opening evolves should not be set per day, but rather be determined by the pain-free zone to prevent inflammation from overexertion and to avoid slower progression than potentially possible. The joint distraction can be continued and massaging of the muscles can be performed.(7,9,14,43,44)

The use of chewing gum can also be considered toward the end of this phase when inflammation has been subdued because this promotes active movement in the horizontal and vertical planes and reinforces the masticatory muscles. However, the total amount of gum chewing should remain limited to avoid overexertion of the muscles and the joint. (9,29,34,45)

Third Phase (>4 Weeks)

The third phase should aim to achieve smooth and symmetrical movements of the lower jaw. Any imbalances and asymmetry still present should be resolved in this phase and the ROM should be further increased leading to restoration of normal joint kinematics. As in the previous phase, exercises can be performed in front of a mirror to aid with muscle coordination and symmetry.(Fig. 5)

Fig. 5: Guidance exercise: maximal mouth opening with index finger. For maximal mouth opening, the index finger rests on the midline to indicate the center of the lower jaw. During opening and closing, the patient should attempt to keep the index finger moving in a straight line while standing in front of a mirror.

Depending on the type and focus of the exercise, the number of repetitions can be similar to the second phase or be decreased while increasing the total load, with the focus further shifting toward muscular strength. (35,43)

Isometric contractions of the jaw in a neutral position can be used to gain better stability. This can be accomplished by attempting to open the mouth from an occlusal position while performing upward manual pressure against the mandible, by preventing movement of the lower jaw, or by applying upward/lateral manual pressure against the mandible, while the lower jaw maintains its position through muscle activity.(Fig. 6) Further strengthening and loading of the muscles through active and passive exercises and increasing muscle endurance are central in this phase. Continued previous exercises and forced opening exercises and strengthening exercises, such as active resistance exercises, can be

added in this phase. Joint mobilization also can increase in intensity to grade III or even IV. The diet can now evolve from a soft to solid diet. (12,14,15,29,34,35)

Fig. 6: Isometric exercise: attempting mouth opening from closed position. Opening the mouth is attempted while applying manual pressure against the lower jaw.

Other Treatment Options

The effect of low-intensity pulsed ultrasound (LIPUS) was first highlighted in an animal trial by Byl et al.(46) who found that LIPUS application during the first postoperative week significantly improved tissue healing compared with animals who did not receive this therapy. Since this finding, many studies have reported the notable influence LIPUS exerts on soft tissue wound healing. A recent meta-analysis by Lou et al(47) concluded that LIPUS shortens the time to fracture union.(48,49) Tehranchi et al(50) came to a similar conclusion after conducting a comparative prospective study in which 9 patients who underwent orthognathic surgery were treated with LIPUS. They found that the use of this technique led to a significant increase in bone density and significantly decreased pain during the first 3 postoperative weeks. As such, the use of LIPUS can be

considered an additional analgesic tool to further aid a well-balanced schedule of pain medication, which promotes tissue healing and further decreases inflammation during the first phase.

Although several studies(51–53) have reported good results using a CPM apparatus such as the TheraPacer (Denver, Co, USA), current up-to-date literature is lacking. Furthermore, current systematic reviews of the use of CPM after total knee arthroplasty are quite divided on the matter. A recent RCT by Lenssen et al.(54) stated that prolonged CPM can have a short-term effect on the ROM, but that no beneficial long-term effects were found compared with physiotherapy alone.(54) A similar conclusion was stated in the meta-analysis by Milne et al.(55) As such, the authors cannot advise the use of CPM as a treatment modality, because of the cost versus limited benefit. Further research is needed for a sounder conclusion.

Guarda-Nardini et al(56) and Sidebottom et al(57) found that the use of BTX-A in patients with masticatory muscle aches led to a significant improvement in pain and an increase in MMO and laterotrusion. Although both articles noted that further research is needed, the use of BTX-A on patients with myogenic complaints seemed relevant. As such, the use of BTX-A can be considered a postoperative treatment modality in patients with significant myogenic pain complaints. This was also clearly highlighted by Robiony(16), who used the muscle relaxant in 5 patients who were treated with TJR of the TMJ, yet showed rather poor postoperative results because of reactive muscle splinting of the masseter muscle. However, after administration of BTX-A, a significant increase in MMO was achieved, stressing the usefulness of BTX-A in a postoperative setting. However, because of the lack of research on the use of BTX-A for temporomandibular surgery, there is no clear consensus about what dosage should be used, resulting in dosages ranging between 25 and 150 units.(58) Further research is needed to provide a more standardized approach of BTX-A within TMJ surgery.

Conclusion

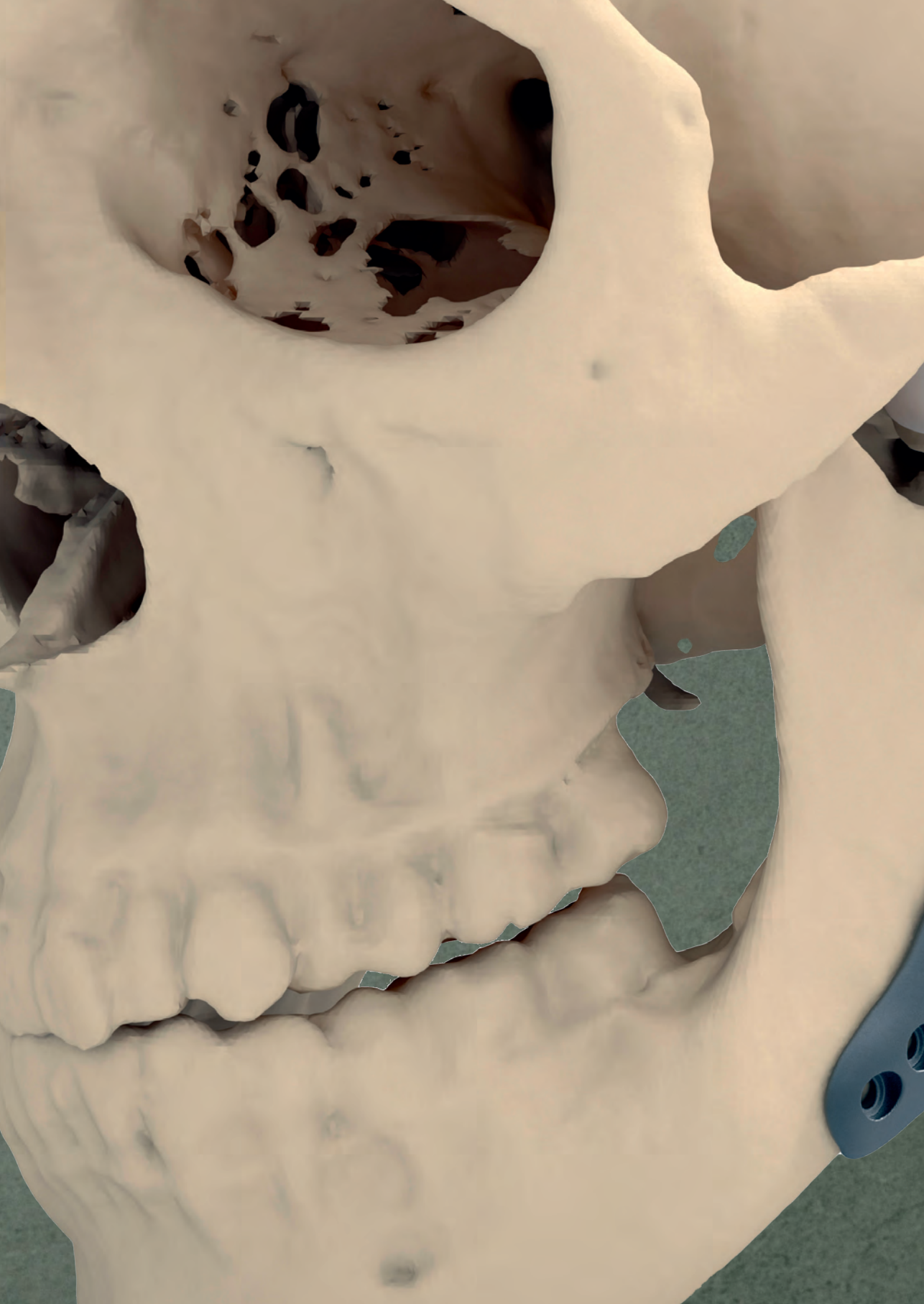
Based on the current, albeit limited, scientific literature included in this systematic review, it can be concluded that physiotherapy after open TMJ surgery plays a significant role in achieving good long-term postoperative results. A physiotherapeutic scheme, divided into 3 phases, is proposed. Further prospective evaluation, comparing this treatment to no approach and a more limited approach, is necessary to determine its efficacy.

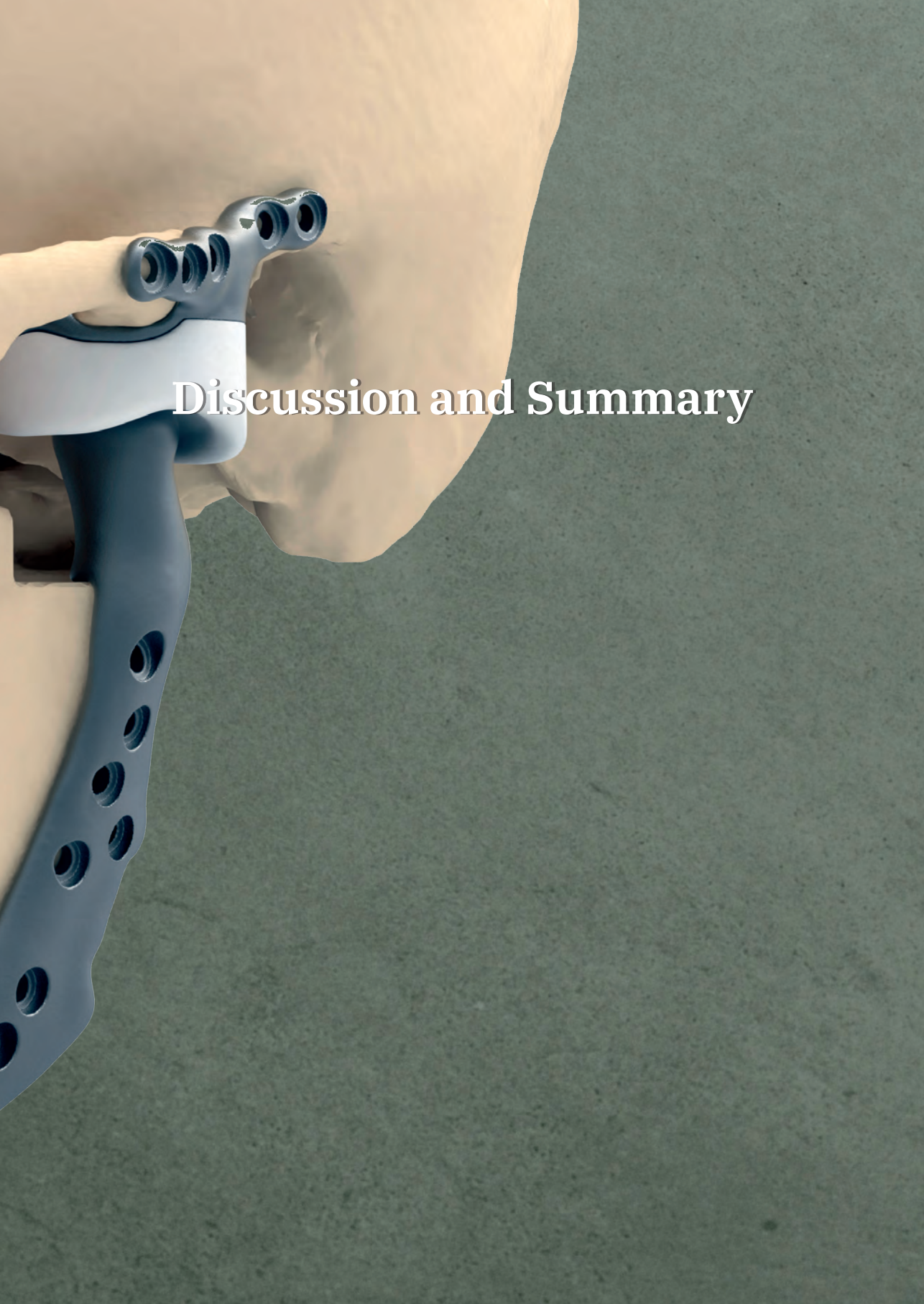
References

1. Monje-Gil F, Nitzan D, González-Garcia R. Temporomandibular joint arthrocentesis . Review of the literature. Med Oral Patol Oral Cir Bucal. 2012;17:e575(4).
2. Liu F, Steinkeler A. Epidemiology, diagnosis, and treatment of temporomandibular disorders. Dent Clin North Am [Internet]. 2013 Jul;57(3):465–2004. Available from: http://dx.doi.org/10.1016/j.cden.2013.04.006
3. NICE. National Institute for Health and Care Excellence Scope. Natl Inst Heal Care Excell [Internet]. 2014;(May):1–9. Available from: https://www.nice.org.uk/guidance/gid-cgwave0704/resources/multimorbidity-final-scope2
4. Koslin M, Indresano AT, Mercuri LG. Temporomandibular joint surgery. J Oral Maxillofac Surg. 2012;70:204–31.
5. Bell WH, Gonyea W, Finn RA, Storum KA, Johnston C, Throckmorton GS. Muscular rehabilitation after orthognathic surgery. Oral Surg Oral Med Oral Pathol. 1983 Sep;56(3):229–35.
6. Osborne JJ. A physical therapy protocol for orthognathic surgery. Cranio. 1989 Apr;7(2):132–6.
7. Oh DW, Kim KS, Lee GW. The effect of physiotherapy on post-temporomandibular joint surgery patients. J Oral Rehabil. 2002;29(5):441–6.
8. Uriell P, Bertolucci L, Swaffer C. Physical therapy in the postoperative management of temporomandibular joint arthroscopic surgery. Cranio. 1989 Jan;7(1):27–32.
9. Dijkstra PU. Post-operative physical therapy of the temporomandibular joint. Stegenga B, de Bont LGM, editors. Management of Temporomandibular Joint Degenerative Diseases. Switzerland: Birkhäuser Basel; 1996. 177–189 p.
10. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ J Surg. 2003 Sep;73(9):712–6.
11. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct;343:d5928.
12. Austin BD, Shupe SM. The role of physical therapy in recovery after temporomandibular joint surgery. J Oral Maxillofac Surg [Internet]. 1993;51(5):495–8. Available from: http://dx.doi.org/10.1016/S0278-2391(10)80503-8
13. Braun BL. The effect of physical therapy intervention on incisal opening after temporomandibular joint surgery. Oral Surg Oral Med Oral Pathol [Internet]. 1987;64(5):544–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3478638
14. Capan N, Esmaeilzadeh S, Karan A, Dıracoglu D, Emekli U, Yıldız A, et al. Effect of an early supervised rehabilitation programme compared with home-based exercise after temporomandibular joint condylar discopexy: a randomized controlled trial. Int J Oral Maxillofac Surg [Internet]. 2017;46(3):314–21. Available from: http://dx.doi.org/10.1016/j.ijom.2016.07.010
15. Leandro LF, Ono HY, De Souza Loureiro CC, Marinho K, Garcia Guevara HA. A ten-year experience and follow-up of three hundred patients fitted with the Biomet/Lorenz Microfixation TMJ replacement system. Int J Oral Maxillofac Surg [Internet]. 2013;42(8):1007–13. Available from: http://dx.doi.org/10.1016/j.ijom.2013.04.018
16. Robiony M. Intramuscular injection of botulinum toxin as an adjunct to total joint replacement in temporomandibular joint ankylosis: preliminary reports. J Oral Maxillofac Surg [Internet]. 2011 Jan;69(1):280–4. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L51137502
17. Karthik R, Hafila MI, Saravanan C, Vivek N, Priyadarsini P, Ashwath B. Assessing prevalence of temporomandibular disorders among university students: a questionnaire study. Vol. 7, Journal of International Society of Preventive & Community Dentistry. India; 2017. p. S24-9.
18. Macfarlane T V, Blinkhorn AS, Davies RM, Kincey J, Worthington H V. Oro-facial pain in the community: prevalence and associated impact. Community Dent Oral Epidemiol. 2002 Feb;30(1):52–60.

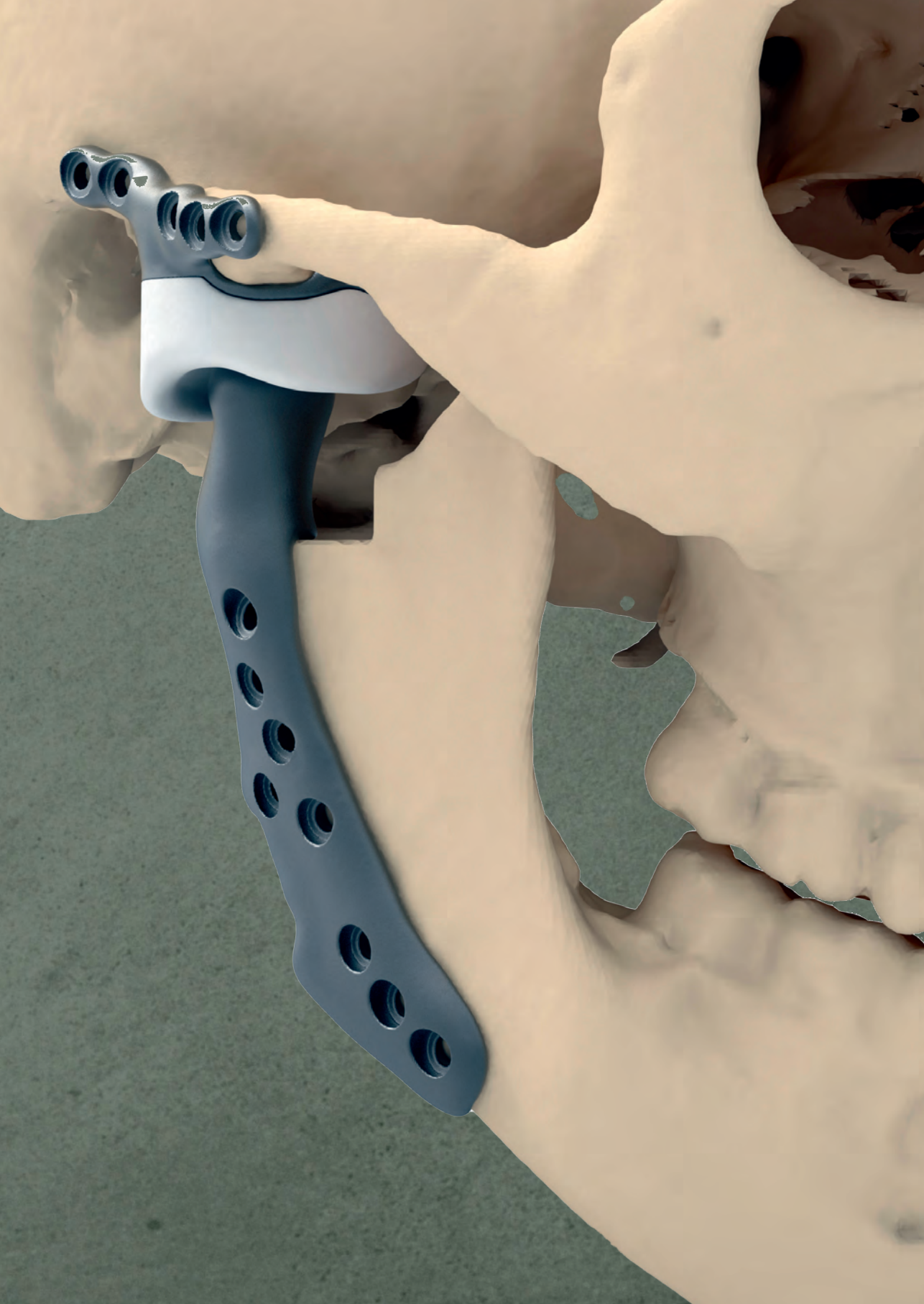
19. LeResche L. Epidemiology of temporomandibular disorders: implications for the investigation of etiologic factors. Crit Rev Oral Biol Med. 1997;8(3):291–305.
20. Paço M, Peleteiro B, Duarte J, Pinho T. The Effectiveness of Physiotherapy in the Management of Temporomandibular Disorders: A Systematic Review and Meta-analysis. J Oral Facial Pain Headache. 2016;30(3):210–20.
21. Al-Jundi MA, John MT, Setz JM, Szentpetery A, Kuss O. Meta-analysis of treatment need for temporomandibular disorders in adult nonpatients. J Orofac Pain. 2008;22(2):97–107.
22. Wilkes C. Internal derangements of the temporomandibular joint: pathological variations. Arch Otolaryngol Neck Surg [Internet]. 1989 Apr 1;115(4):469–77. Available from: http://dx.doi.org/10.1001/archotol.1989.01860280067019
23. Helkimo M. Studies on function and dysfunction of the masticatory system. II. Index for anamnestic and clinical dysfunction and occlusal state. Sven Tandlak Tidskr. 1974 Mar;67(2):101–21.
24. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet J-P, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. Vol. 28, Journal of Oral & Facial Pain and Headache. 2014. p. 6–27.
25. Schiffman E, Ohrbach R. Executive summary of the Diagnostic Criteria for Temporomandibular Disorders for clinical and research applications. J Am Dent Assoc. 2016 Jun;147(6):438–45.
26. Truelove E, Huggins KH, Mancl L, Dworkin SF. The efficacy of traditional, low-cost and nonsplint therapies for temporomandibular disorder: a randomized controlled trial. J Am Dent Assoc. 2006 Aug;137(8):1099–107; quiz 1169.
27. Rossi SS De, Greenberg MS, Rcsd FDS, Liu F, Steinkeler A. Temporomandibular Disorders Evaluation and Management. Med Clin North Am. 2014;98(6):1353–84.
28. Fricton J. Myogenous Temporomandibular Disorders : Diagnostic and Management Considerations. 2007;51:61–83.
29. Singh V, Dhingra R, Bhagol A. Prospective analysis of temporomandibular joint reconstruction in ankylosis with sternoclavicular graft and buccal fat pad lining. J Oral Maxillofac Surg [Internet]. 2012 Apr;70(4):997–1006. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L51526536
30. Lo L-J, Lin C-L, Chen Y-R. A device for temporomandibular joint exercise and trismus correction: design and clinical application. J Plast Reconstr Aesthetic Surg. 2008;61(3):297–301.
31. Pinals R. Traumatic arthritis and allied conditions. In: McCarty D, Koopman W, editors. Arthritis and allied conditions. 12th ed. Philadelphia: Lea & Febiger; 1993. p. 1521.
32. Kuwahara T, Bessette RW, Maruyama T. Effect of continuous passive motion on the results of TMJ meniscectomy. Part I: Comparison of chewing movement. Cranio. 1996 Jul;14(3):190–9.
33. Ellis E 3rd, Carlson DS. The effects of mandibular immobilization on the masticatory system. A review. Clin Plast Surg. 1989 Jan;16(1):133–46.
34. Wilk BR, Stenback JT, McCain JP. Postarthroscopy physical therapy management of a patient with temporomandibular joint dysfunction. J Orthop Sports Phys Ther. 1993;18(3):473–8.
35. Reiman MP, Lorenz DS. Integration of strength and conditioning principles into a rehabilitation program. Int J Sports Phys Ther [Internet]. 2011;6(3):241–53. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3164002&tool=pmcentrez&rendertype=abstract
36. Grimsby O, Rivard J. Science, theory and clinical application in orthopaedic manual physical therapy. Vol. 3. Taylorsville, UT: Academy of Graduate Physical Therapy; 2009.
37. Kullenberg B, Ylipaa S, Soderlund K, Resch S. Postoperative cryotherapy after total knee arthroplasty: a prospective study of 86 patients. J Arthroplasty. 2006 Dec;21(8):1175–9.
38. Thienpont E. Does advanced cryotherapy reduce pain and narcotic consumption after knee arthroplasty? Clin Orthop Relat Res [Internet]. 2014 Nov 25;472(11):3417–23. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4182365/
39. Rigby BJ. The effect of mechanical extension upon the thermal stability of collagen. Biochim Biophys Acta [Internet]. 1964;79(3):634–6. Available from: http://www.sciencedirect.com/science/article/pii/0926657764902347

40. Mason P, Rigby BJ. Thermal transitions in collagen. Biochim biophys Acta. 1963;66:448–50.
41. Lin YH. Effects of thermal therapy in improving the passive range of knee motion: Comparison of cold and superficial heat applications. Clin Rehabil. 2003;17(6):618–23.
42. Oh J-S, Kim S-H, Park K-N. Effects of controlled condylar rotation exercise on symmetrical mouth opening in patients with temporomandibular disorder. J Phys Ther Sci. 2015;27(5):1319–21.
43. Sayson J, Rivard J, Grimsby O, Wong W. Exercise rehabilitation of the temporomandibular joint. In: Hossain A, Grant D, editors. Science, theory and clinical application in orthopaedic manual physical therapy: Scientific Therapeutic Exercise Progressions (STEP) The neck and upper extremity. 1st ed. Taylorsville, UT: The Academy of Graduate Physical Therapy; 2008. p. 245.
44. Singh V, Bhagol A, Dhingra R, Kumar P, Sharma N, Singhal R. Management of temporomandibular joint ankylosis type III: Lateral arthroplasty as a treatment of choice. Int J Oral Maxillofac Surg [Internet]. 2014;43(4):460–4. Available from: http://dx.doi.org/10.1016/j.ijom.2013.08.013
45. Roychoudhury A, Parkash H, Trikha A. Functional restoration by gap arthroplasty in temporomandibular joint ankylosis - A report of 50 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;87(2):166–9.
46. Byl NN, McKenzie AL, West JM, Whitney JD, Hunt TK, Scheuenstuhl HA. Low-dose ultrasound effects on wound healing: a controlled study with Yucatan pigs. Arch Phys Med Rehabil. 1992 Jul;73(7):656–64.
47. Lou S, Lv H, Li Z, Zhang L, Tang P. The effects of low-intensity pulsed ultrasound on fresh fracture: a meta-analysis. Med. 2017;96:e8181(39).
48. Iwanabe Y, Masaki C, Tamura A, Tsuka S, Mukaibo T, Kondo Y, et al. The effect of low-intensity pulsed ultrasound on wound healing using scratch assay in epithelial cells. J Prosthodont Res. 2016 Oct;60(4):308–14.
49. Khanna A, Nelmes RT, Gougoulias N, Maffulli N, Gray J. The effects of LIPUS on soft-tissue healing: a review of literature. Br Med Bull. 2009;89:169–82.
50. Tehranchi A, Badiee M, Younessian F, Badiei M, Haddadpour S. Effect of low-intensity pulsed ultrasound on postorthognathic surgery healing process. Ann Maxillofac Surg [Internet]. 2017;7(1):25–9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5502510/
51. McCarty WL, Darnell MW. Rehabilitation of the temporomandibular joint through the application of motion. Cranio. 1993 Oct;11(4):298–307.
52. Fontenot MG. Continuous passive motion following total temporomandibular joint arthroplasty. J Oral Maxillofac Surg [Internet]. 1989;47(8, Supplement 1):138–9. Available from: http://www.sciencedirect.com/science/article/pii/0278239189906824
53. Sebastian MH, Moffett BC. Appliance improvement, normal subject evaluation, pilot clinical trial. Oral Surgery, Oral Med Oral Pathol [Internet]. 1989;67(6):644–53. Available from: http://www.sciencedirect.com/science/article/pii/0030422089900029
54. Lenssen TA, van Steyn MJ, Crijns YH, Waltje EM, Roox GM, Geesink RJT, et al. Effectiveness of prolonged use of continuous passive motion (CPM), as an adjunct to physiotherapy, after total knee arthroplasty. BMC Musculoskelet Disord. 2008 Apr;9:60.
55. Milne S, Brosseau L, Robinson V, Noel MJ, Davis J, Drouin H, et al. Continuous passive motion following total knee arthroplasty. Cochrane database Syst Rev. 2003;(2):CD004260.
56. Guarda Nardini L, Manfredini D, Salamone M, Salmaso L, Tonello S, Ferronato G. Efficacy of botulinum toxin in treating myofascial pain in bruxers : a controlled placebo pilot study. Cranio. 2008;26:126.
57. Sidebottom AJ, Patel AA, Amin J. Botulinum injection for the management of myofascial pain in the masticatory muscles . A prospective outcome study. Br J Oral Maxillofac Surg [Internet]. 2013;51(3):199–205. Available from: http://dx.doi.org/10.1016/j.bjoms.2012.07.002
58. Srivastava S, Kharbanda S, Pal US, Shah V. Applications of botulinum toxin in dentistry: A comprehensive review. Natl J Maxillofac Surg [Internet]. 2015;6(2):152–9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4922224/





Discussion and Summary



Chapter 13

General discussion and future perspectives

General discussion

Of the 27 different total TMJ prostheses that have been distributed in over fifteen countries in 2019, only two had an FDA approval.(1) Many of the new implant brands seem to copy the design of these two 'tested and tried' systems, without providing any significant clinical improvements. They also fail to be properly tested, with only 12 of them having gone through preclinical laboratory tests. None of these systems has gone through in vivo testing before being applied in humans. This is of significant importance, as in vivo wear rates might be higher compared to those measured in vitro.(2) Although several in vitro laboratory and in silico models have been developed, there remains uncertainty concerning the amount of force the TMJ is subjected to.(3,4) During mastication, both rotational and translational movements occur, which is difficult to properly mimic in a laboratory model.

The aim of this thesis was threefold. Firstly, by performing several literature analyses, we aimed to determine an evidence-based proper implant design and material choice. This design was tested in silico regarding stress and strain.(5) Secondly, said design was in vivo tested by means of an animal-model experiment, to determine if the TMJR met orthopedic standards in terms of wear, adverse tissue reactions and tissue integration. Lastly, by both human application and literature analysis, we aimed to improve upon the implant replacement procedure, its revalidation and perform an, albeit short-term, functional evaluation.

Implant development – Material choice

When developing a new joint prosthesis several main issues must be regarded. Through literature analysis, we found that for a material to be suitable for implantation, it needs to meet several criteria. Firstly, the materials used must be biocompatible. While this may seem obvious, these materials are subjected to loading and wear, during which they must remain biocompatible. This means that the material used should be able to be in contact and interact with the human tissues without eliciting any adverse effects such as inflammation or allergic reactions.(6–9) Otherwise, such could lead to severe reactions, such as fragmentation of

the material and FBGCR, as was the case for both Silastic® and Proplast® implants.(10–15) In addition, the materials should have high strength, excellent fatigue and wear resistance, and fracture toughness, for the implant to have proper longevity.(7,16,17) The materials need to be stiff enough so that no micromotions of the implant components can occur, yet at the same time show a sufficiently high elastic modulus, preferably as close as possible to bone, to prevent stress shielding and underlying bone resorption.(7,16,18) If these criteria are not met, proper osseointegration and implant longevity will not result.

When evaluating the 27 TMJR that were being developed or available for placement in 2019, three TMJR had a stainless steel (SS) ramal component.(1) While SS alloys such as 316L have good fatigue and tensile strength properties and are significantly cheaper and easier to manufacture compared to titanium, allowing for a lower production cost, our literature analysis revealed that SS has the lowest corrosion resistance amongst the most common biomaterials. This makes it susceptible to stress corrosion, cracking, and crevice corrosion, rendering it unsuitable as a bearing prosthetic material. While the corrosion resistance can be improved through passivation, the elastic modulus of 190-210 GPa is significantly higher than that of human bone, making the material significantly prone to stress shielding, making it an unsuitable material for prosthetic use.(19) The TMJR developed by Genovesi (20) used a polyether ether ketone (PEEK) ramal component. Our narrative literature analysis revealed this to be an interesting material with good biocompatibility and bone formation capacity.(21,22) Through reinforcement with carbon fibers, the elastic modules can be increased to mimic that of bone and the tensile strength can be improved as well. However, as an articulating material, both PEEK and carbon-reinforced PEEK showed significantly worse wear resistance compared to UHMWPE in knee TJR, making it unsuitable as an articulating prosthetic TMJR material.(23,24)

Seven out of 27 systems used a cobalt chrome (CoCr) or cobalt chrome molybdenum (CoCrMo) condylar head and three systems used a complete CoCr ramal component.(1) While CoCr and CoCr alloys have excellent wear resistance, high strength and fatigue resistance, there are 2 main

concerns when opting for Co or Cr. (7,25) Firstly, due to a high elastic modulus, stress shielding might occur in CoCr prostheses. Secondly, animal studies indicate that CoCr particles can exert toxic effects in the exposed tissues, with Co-containing implants being classified as possibly carcinogenic for humans and metal hypersensitivity occurring significantly more in the metal-on-metal CoCrMo prosthesis (like the Nexus CMF).(26–28) Furthermore, a meta-analysis investigating implant-related metal sensitivity revealed that 10% to 15% of the population has an allergy to one or several alloy components, with nickel, chromium and cobalt leading to allergic skin reactions in respectively 20%, 7% and 4% of Europeans and 14%, 9% and 4% in Americans.(29,30) In comparison, an allergy for titanium remains very rare.(31)

Titanium alloy has an even better biocompatibility compared to CoCr prostheses, thanks to the Ti-Oxide layer that is formed. By combining Ti with aluminum and vanadium, the strength and fatigue resistance are improved. (16,32,33) In addition, both commercially pure Ti and Ti-6Al-4V boast an elastic modulus of respectively 105 and 115 GPa, which is closer to that of bone, compared to Co-Cr alloys. For said reasons, we found titanium alloys to be preferable over cobalt-chromium alloys. Important to notice is that the biocompatibility of commercially pure Ti is higher, compared to that of Ti-6Al-4V, due to the more stable Ti-oxide layer and thus higher corrosion resistance. In comparison, Ti-6Al-4V has both a higher tensile strength and fatigue strength.(16) By opting for grade 23 Ti-6Al-4V extra-low interstitials, the amounts of oxygen, nitrogen and iron are reduced, resulting in an enhanced biocompatibility compared to industrial Ti-6Al-4V.(34) Despite these properties making Ti (alloys) the more interesting option for implantation, Ti is a softer material compared to CoCr, thus resulting in a lower wear resistance and making it less suitable as an articulating surface.(16) This might also explain why 19 of the discussed TMJR by Elledge et al.(1) used a Ti ramal component, though altered the material for the condylar head in 9 systems. To overcome this flaw, two possible solutions were discussed.

The use of β-Ti alloys such as Titanium-Niobium-Zirconium-Tantalum alloys could be considered. Not only do these alloys have an elastic modulus that is close to that of bone, they also have a higher corrosion resistance and better friction wear resistance.(16,33,35) However, this increased friction wear resistance is still too little to serve as an articulation surface.(16,35) Although research is being done to further improve wear resistance, by for instance adding boride to the alloy or using laser surface treatment, this research remains experimental, with unclear results.(35–38) Thus, this approach was not opted for.

Instead of altering the alloy composition, we choose to modify the implant's surface, allowing for several intended effects such as improved wear resistance, improved or reduced cellular adhesion, as well as the promotion of biological responses such as osteosynthesis.(16,33,39–41) Through application of a hard, wear-resistant protective coating such as titanium nitride (N) or diamond-like carbon (DLC) on the articulating surfaces of the implant, it is possible to significantly improve the tribological properties. Bütow was the first to release a TiN TMJR in 1994.(1,42) Since then, a second Nitride-coated TMJR has been released by OrthoTin (Whippany, NJ, USA). Whilst nitriding the titanium surface leads to better wear and corrosion resistance, as well as biocompatibility, our literature analysis revealed that the process in which the coating is applied is highly significant.(39,40,43) Physical vapour deposition is most often used to coat the implant surface, yet delamination due to adhesive failure has been seen in orthopedic implants. This was also seen by Kerwell et al.(44) during the explantation of 2 Bütow TMJR. Alternatively, plasma nitriding can be used, yet corrosion fatigue properties diminish with increased processing time.

In comparison, DLC-coatings are chemically inert and boast high bio- and hemocompatibility and corrosion resistance, as well as a low friction coefficient and high hardness.(16,41,45–48) Besides a high hardness, a very smooth surface can also be obtained with DLC, resulting in excellent wear resistance.(47,48) Due to the high hardness of the DLC layer however, as well as the difference in thermal expansion coefficient between the DLC-coating and the underlying Ti, deformation of the underlying Ti could occur under higher loads, resulting in insufficient support of the DLC-

coating, which could then chip, fracture or even delaminate.(47,49) This problem can however be overcome by applying a gradient in the DLC-layer with more Ti-C bonds near the underlying Ti surface and C-C bonds near the implant surface. Which even further increases the wear resistance. (46) Thus, in the development of the TMJR, a proprietary protocol using a DLC-coating (HadSat®) was developed for the condylar articulating surface.(50) A second surface modification technique that was applied, was large-grit sandblasting and acid-etching (SLA) of the bony interface of the mandibular component. By increasing the surface roughness, both cell adhesion and bone ingrowth are promoted, thus reducing stress on the screw-bone interface.(50,51)

Our literature analysis revealed that the risk of developing metal hypersensitivity is higher in metal-on-metal TMJR than in metal-on-UHMWPE combinations.(9,26,27) Several researchers found that although the total wear volume was considerably less in the CoCr metal-on-metal Christensen prosthesis compared to for instance the TMJ Concepts CoCr-on-UHMWPE prosthesis, a significantly higher amount of metal ions such as Co and Cr were found in the first group. Whereas only 3% metalosis was seen in the metal-on-UHMWPE group, 33% of all patients with a metal-on-metal system needed explantation of the TMJR.(52,53) Interestingly, five systems discussed by Elledge et al.(1) still rely on a metal-on-metal articulation. All but one other TMJR rely on a UHMWPE articulating surface for the fossa.(1) UHMWPE is a well-researched material with high stiffness and high impact strength, low coefficient of friction, good impact load damping capability, and good resistance to body fluids.(32) Over time, these properties have even been improved upon through high-grade crosslinking (also called highly cross-linked polyethylene or HXLPE).(32) However, UHMWPE, and HXLPE, are not without flaw, as oxidative degradation over time due to reactive free radicals formed by common γ-irradiation sterilization procedures, also known as “shelf aging”, leads to loss of mechanical strength and wear resistance. This issue can be overcome by incorporating α-tocopherol (vitamin E) in UHMWPE, greatly increasing oxidation resistance. As a result, an increase in mechanical strength and less deterioration occurs, compared to non-treated UHMWPE.(54)

Roughly half of the fossa components discussed by Elledge et al.(1) are metal-backed, whereas 10 are fully made out of UHMWPE. The latter poses a risk however, as deformation of UHMWPE can occur due to long term exposure to loading, called creep. The risk of creep occurring is increased when opting for a solely UHMWPE fossa. This deformation can result in a diminished fit, possibly leading to micromovements and in turn loosening of the fossa component, thus resulting in implant failure. Furthermore, due to the hydrophobic nature of UHMWPE, poor surface fixation between the UHMWPE fossa and bone/bone cement can occur, once again leading to the increased risk of micromovements.(17,55–57) Thus a Vitamin E-enriched articulating surface for the fossa component was opted for, which was then hot pressed onto a custom designed Ti-6Al-4V scaffold to be fitted onto the cranial base.

Implant development – Design

Equally important to the material choice is the design of the prosthesis. By performing a systematic historical review, a better understanding was gained of the design flaws in the past. Whereas the first alloplastic TMJ replacements were interpositional materials that were used after a condylectomy, just to prevent reankylosis, Smith and Robinson were the first to focus on restoring joint dynamics.(2,25,58) This led to the development of the fossa component, which aimed to further improve joint function and stability.(2) Hoping to further improve mandibular form and function, condylar prostheses were developed. However, as it became clear that the solitary use of a condylar prosthesis led to resorption of the glenoid fossa, total alloplastic TMJ replacements were developed. (2,25,59) These TMJR were designed as stock implants at first. Thus, the patient's anatomy needed to be adapted to achieve a good fit of the implant. With the development of CAD-CAM, patient-specific custom made TMJR came to the market as well. These systems were developed to fit the patient's anatomy specifically, thus needing no alterations during placement.(19,60) Also, these patient specific implants (PSI) allow for optimization of the fixation screws, thus minimizing the risk of damaging the inferior alveolar nerve.(19,32,61)

A comparative meta-analysis was done to evaluate and compare both stock and custom-made TMJR, to help determine the design approach. Although no significantly better post-operative results were found for either system, the remark was made that a potential bias of pooled data had occurred, which benefitted the stock implants.(62) This seems to follow suit with the recent findings by Kanatsios et al.(63), who compared a stock and custom TMJR via a retrospective cohort study. Whereas the included patient did not have a significantly different preoperative maximal mouth opening, the post-operative increase was significantly greater for the custom group compared to those patients treated with a stock prosthesis. Additionally, systematic literature analysis revealed that many surgeons prefer the use of a patient-fitted system in case of more severe anatomical abnormalities, thus leading to additional bias in the meta-analysis.(32,64–66)

We found that the use of a PSI has several additional benefits over a stock implant. The custom implant does not require any adaptation of the patient's anatomy. Surgical time and risk can be reduced. The total contact surface between the implant and the fossa/mandible is improved and no alterations need to be made to the implant itself.(19,67–70) Secondly, several additional corrections can be 'worked into' the custom made TMJR, such as an occlusal correction, a substitution of missing bone in cases with a mandibular defect (e.g. hemifacial microsomia, traumatic loss, oncological resection or osteomyelitis defects), thus preventing the need for additional surgery.(68,71,72) Importantly, a load increase in the contralateral healthy TMJ of 15% is seen, when a stock prosthesis is fitted. Over time, this increase in load can result in articular disc damage. (73–75) These advantages were of such significant nature, that it was concluded that the prosthesis we set out to develop, needed to be a custom-made TMJR.

To limit the increase in load on the healthy/untreated joint, the center of rotation was kept as close to the axis of its anatomical counterpart rotation as possible, as to allow both joints to move synchronously. This was achieved by keeping the central thickness of the UHMWPE fossa as thin as 2mm. This might mean that a replacement of the fossa-component

could be indicated over time, due to the thinner UHMWPE part. For such reason no scaffold was provided at the interface between the skull and fossa component.(50)

The mandibular component was designed in such fashion that it fitted over the resection stump of the mandible, thus preventing any potential downward, medial or lateral movement of the implant. Besides roughening the implant surface through SLA, which also improves cell attachment and proliferation,(76–80) interconnecting pores with a diameter of 600µm pores and a 80% porosity were computer-assisted designed on the bony interface of the mandibular component. The porous design allows for bone to grow inside of these void areas, improving the implant stability.(81) This extra stability, allowed for only needing 5, rather than 7, fixation screws. The position of these 5 screws is in turn dictated by the position of the inferior alveolar nerve. Also, a higher calcium deposition and higher osteocalcin and alkaline phosphate concentrations can be achieved within these pores. This phenomenon leads to better (mesenchymal) cell adhesion and elicitation of cell differentiation into osteocytes, thus improving bone formation and osseointegration.(76,82–87)

As to further improve upon currently available TMJR, we aimed to retain the function of the LPM, thus allowing for laterotrusive movement. For said reason, a scaffold was designed in the condylar neck, allowing the reattachment of the LPM. By retaining the bony enthesis, together with the LPM, when performing the condylectomy, this enthesis could be threaded through a tunnel in the condylar neck and fixed against this scaffold. Lastly, as the prosthesis is custom-made, corrections for mandibular asymmetries and for jaw angle improvements could be implemented in the design immediately as well.(50) Both the ramal component and the Ti fossa component were additively manufactured using selective laser melting. This approach is not only more ecological than milling, but it also offers greater design flexibility. As a result, the intricate, patient-specific porous implant design was achievable.

In *vivo* analysis – Tribological results

Having implemented the data that was gathered during the literature analysis in the design of a novel custom-made total TMJ prosthesis, an animal model experiment was conducted to evaluate its suitability for human implantation. A sheep model was opted for, as they are considered the gold standard in large animals.(88,89) As they spend 4 hours per day eating, and 8 to 9 hours per day ruminating at rate of 128 and 100 mastication cycles per minute on average respectively, an evaluation period of 288 days equals 22 human years of masticatory function, thus allowing for a proper tribological evaluation.(90,91)

Both a linear and volumetric analysis of the amount of wear of the UHMWPE-component of the fossa was performed. Linear wear (mm/year) is used in orthopedic surgery to determine the lifecycle of an implant and thus providing information within how much time after implantation, the fossa component needs to be replaced. With an average linear wear of 0.67 ± 0.28mm days for the coated system and 0.88 ± 0.41mm for the uncoated prosthesis, which converts to respectively 0.03 ± 0.01mm/year and 0.04 ± 0.02mm/year, the custom-made TMJ prosthesis outperformed both total hip implants (0.08-0.2mm/year) and total knee prostheses (0.05-0.23mm/year).(92) This is of significant importance, as the risk of periprosthetic osteolysis increases if the amount of linear wear is higher than 0.1mm/year.(93) In addition, a volumetric wear analysis was performed to determine the total amount of lost UHMWPE volume. This is of importance as the risk of periprosthetic osteolysis remains rare if the wear volume remains below 80mm^3 per year. (94) With an average volumetric wear of 25.29 mm^3 ± 11.43mm^3 and 45.85mm^3 ± 22.01mm^3, which converts to 1.15 ±0.52mm^3/year for the coated TMJR and 2.08 ±1.00mm^3/year for the uncoated system, the TMJR outperformed both the total hip and knee replacement in this field as well.(95)

One of the shortcomings in our research on the wear analysis of the UHMWPE component was the inability to register the fossa component prior to implantation. Due to logistical constraints and the need to maintain the implant's sterility, we used the implant design render instead of the actual printed component. In future analyses, whether in

human or animal trials, this issue should be corrected. This correction would also enable improvements to the best-fit algorithm by preselecting a series of reference points for each fossa component, thereby enhancing the accuracy of the analysis data. Additionally, although no significant difference in wear was observed between the coated and uncoated systems, a post hoc power analysis revealed that this was due to an insufficient sample size. While financial and ethical considerations limited our total sample size, this must be taken into account in future research.

Important to remark is that a displacement of the fossa component was seen in 3 of the sheep. This displacement was most likely due to the use of 2mm diameter fixation screws for the fossa component, as determined for human subjects, despite the fossa being subjected to more laterotrusive movement in the sheep. This might have led to excessive stress in the bone surrounding the screws, with gradual bone resorption and thus micromovement of the fossa component, resulting in this displacement. (96–98) However, after removal of these three results, both the average linear and volumetric wear remained well within the acceptable range. (95)

A high surface roughness (Ra 0.2-0.63 µm) can increase the amount of wear of the opposing articular surface and lead to larger wear particles. For this reason, an industry standard for the surface smoothness of metallic and ceramic articulating surfaces in both knee (ISO 7207-2) and hip prostheses (ISO 7206-2) at the point of implantation (Ra ≤0.1 µm, Ra 0.05-0.02 µm) has been established. This is not the case for TMJR. (4,99–102) In order for this custom-made total TMJR to meet orthopedic standards, a polishing protocol was established within the HadSat®-protocol, to obtain a Ra ≤0.1 µm, as is the standard for a total knee prosthesis. A pristine DLC-coated sample was analyzed using confocal laser microscopy analysis, revealing a surface roughness (Ra) of 0.09 µm. A confocal laser microscopy analysis of the uncoated condyles after explantation revealed a mean Ra of 0.28 µm ± 0.17 µm (Sa of 2.40 µm ± 2.08 µm), thus risking an increase in amount of wear of the opposing articulating surface. In comparison, the coated condyles revealed a mean Ra of 0.12 µm ± 0.04 µm (Sa of 0.69 µm ± 0.07 µm) which was not only

well below the threshold, but also did not differ significantly from the surface roughness of the pristine condyle, thus proving the value of the HadSat®-protocol.(95)

Besides the wear analysis of the prosthesis, a histological evaluation of the peri-articular tissues was performed as well, which was then applied to the 'synovial-like interface membrane'-classification (SLIM), to determine the presence of neo-synovitis (Type I), infection-induced synovitis (Type II) and adverse local tissue reactions to implant wear particles (Type VI). In addition, during the histological evaluation of the enthesis, the osseous integration was evaluated as well, thus evaluating a Type V-reaction (prosthesis-associated arthrofibrosis).(103–105)

To be able to classify a reaction as a SLIM Type I reaction, a wear-induced neosynovitis, 20% of the tissue sample needs to be infiltrated with macrophages, containing wear debris usually smaller than 1 µm in diameter. In addition, multinucleated foreign-body giant cells can be found as well. These cells mostly contain wear debris particles larger than 5 µm.(103–105) Although an increased amount of macrophages was seen in both the coated TMJR tissues (22.15 ± 25.31) and uncoated tissues (17.76 ± 21.16) compared to the control samples (7.4 ± 10.36), the maximal amount of macrophagic surface infiltration remained well below the threshold with an average infiltration of 3.8% for the coated and 3.1% for the uncoated system tissues.

A SLIM type II reaction, a synovitis due to infection, can either be low- or high-grade. Whereas in case of the first granulation tissue with fibroblasts, vascular proliferation, chronic edema and neutrophil granulocytes, plasma cells and lymphocytes are found, a high-grade infection boasts a larger amount of neutrophil granulocytes.(103–105) In none of evaluated samples were signs of an infectious synovitis, nor did any of the trail animals develop clinical signs of an infectious joint.

A SLIM-type VI reaction is an adverse inflammatory tissue reaction, being caused by particle toxicity and/or host allergy, with three types of histological reactions having been described. A mainly macrophagic

infiltration with minimal lymphatic response, a mixed macrophagic and lymphocytic response with the presence of mast cells, plasma cells and eosinophils, a granulomatous pattern.(103–105) The risk of a type VI reaction increases significantly, in case of a volumetric wear volume of more than 80mm³ or when linear wear is exceeds 0.1mm/year. In neither of the prosthetic groups was this amount of wear found and no type VI-reaction was found.

Although no SLIM-reactions were found, there was a significant increase in the amount of lymphocytes in the peri-articular tissues of both the coated (24.6 ± 18.45) and uncoated prostheses (34.51 ± 28.58) compared to the control group (9.5 ± 5.2). Although the role of lymphocytes in the periarticular tissues is not yet fully understood, it is believed that higher tissue concentrations of metals resulted in a higher lymphocytic infiltration. Our findings were consistent with these studies, showing a stronger lymphocytic reaction in the peri-articular tissues of the uncoated TMJR, which also developed more condylar wear. (106,107) In turn, if this exposure becomes high enough, it is believed this lymphocyte response could lead to metal hypersensitivity and in turn aseptic loosening of the implant.(108) Although no clear threshold has been reported on, the increase in lymphocytes was relatively limited in the coated samples, nor was any aseptic loosening of the implant seen in any of the sheep, thus we concluded that the custom-made prosthesis was not at risk of aseptic loosening. It should be noted that both the uncoated and coated groups exhibited a large standard deviation during statistical analysis, presumably due to the relatively small sample sizes in the animal experiment.

The tribological evaluation of the custom made total TMJR revealed that the prosthesis answered to all the wear-related standards that have been set in orthopedic surgery.

In *vivo* analysis – LPM reconstruction

With the development of this novel custom-made total TMJR, one of the objectives that was aimed for, was to achieve functional improvement compared to current total joint replacements, by means of reattachment of the lateral pterygoid muscle's enthesis. To achieve this, a scaffold in

the condylar neck and a tunnel to allow for reattachment and fixation of the enthesis were provided. By preserving the enthesis of the LPM with its bony attachment during the condylectomy, a wire could be threaded through the subcondylar tunnel, allow for fixation of the bony enthesis against the scaffold, which was intraoperatively filled with harvested, particulated bone. This was done as we hypothesized that it would allow for better promotion of osteosynthesis.

Important to remark is that we experienced several difficulties concerning the reattachment of the LPM during surgery of the sheep. Proper dissection and retainment of the bony enthesis of the LPM was found to be more difficult in sheep compared to humans. As the fossa design was only adapted minimally from the human design, a spherical obstruction in the anteromedial side was experienced to properly reattach the LPM. This was most likely due to the inability to completely segment the LPM during the design process of the implant, leading to a slight underestimation of the total muscle volume. The enthesis of the LPM is also more caudally reattached than its original position, because of the thickness of the fossa component, which does not replace the glenoid fossa but is posed caudally to it. The arc of rotation with the origin as center displaces the enthesis medially. All UHMWPE parts were altered in such a way that nor did it affect the articulating surface, nor that the LPM experienced any obstruction anymore during its reconstruction. In the human application, the scaffold is foreseen on a extension in the condylar neck into the direction of the enthesis. Lastly, it was not always possible to properly evaluate if the bony part of the enthesis was directly touching the scaffold, because the mandibular component and the depth of the surgical cavity medially to it hindered vision.

Clinical evaluation revealed nearly no weight loss of the included sheep, as well as laterotrusive movements to the healthy side of several randomly selected sheep, indicating a successful reattachment of the LPM. A radiological and subsequently histological evaluation substantiated this finding. Post-mortem radiological evaluation revealed 4 different conditions, however. In four of the sheep, there was no proper reconstruction of the LPM, with a large distance between the scaffold and the muscle. However it is

important to note that in one case, the post-mortem dissection was poorly executed, resulting in the loss of the LPM enthesis. In two other samples, the bony enthesis was not retained yet instead the fibrocartilaginous enthesis was fixated onto the scaffold. Three sheep showed a purely fibrous tissue connection between the bony enthesis and the condylar scaffold. Again, in one sheep, the fibrocartilaginous enthesis was reinserted rather than the bony enthesis. Three sheep displayed both a partial bony and partial soft tissue reattachment. The total thickness of this soft tissue attachment was with an average thickness of 0.4mm markable thinner compared to the specimen that only showed a soft tissue connection. Lastly, two sheep showed a uniquely bony ingrowth of the enthesis into the scaffold. Interestingly, in one of these samples, only the fibrocartilaginous enthesis was preserved and reattached. The five specimens with a (partial) bony reattachment of the LPM were selected for further histological analysis. Despite our radiological findings, in only two samples an actual boney extension, albeit limited, into the condylar scaffold was objectified. These samples revealed several vital, isolated, bony islands within the scaffold, with the presence of osteocytes and active remodeling. However, these bony islands were not in contact with the bony LPM enthesis in the section plane that was analyzed. All samples had developed dense, storiform collagen within the scaffold, as well as a thin lamellar layer of collagenous tissue between the implant and the bone, ranging from 20 to 150µm, except for one sample where a maximal thickness of 500µm was found. The enthesis itself were found to be viable in all samples with active bone remodeling which was most apparent near the implant scaffold site. Despite this bone remodeling, no or very limited ingrowth into the scaffold was seen.

For osseointegration to be possible, a good osteoconductive, -inductive and biocompatible environment needs to be provided. The implant and scaffold surfaces need to be sufficiently osteoconductive to stimulate bone cell growth. The environment also needs to be osteoinductive to promote differentiation of mesenchymal stem cells (MSCs) into (pre)osteoblasts. Good osteogenesis also must also be achieved (i.e., sufficient MSCs, osteoblasts, and osteocytes need to be present). As discussed previously, both the material choice and surface modifications aimed to achieve and improve upon both osteoconductivity and -inductivity. We concluded this

was successful, as a proper integration of the ramal component was seen in both the radiological analysis, as well as the histological analysis of the two ramal samples, showing bone formation within the lattice structure. (109)

However, for proper osseous integration of the LPM enthesis, several other requirements must be met as well. Firstly, the enthesis needs to be in direct contact with the condylar scaffold. As stated earlier, several intraoperative difficulties were encountered, hindering proper fixation onto the scaffold. Furthermore, once fixated, proper stability is needed for osseous integration to occur. Micromotions between an implant and the adjacent bone should not only be limited to 28µm in order to promote osteogenesis, but in case of the occurrence of repetitive micromotions of 150µm or more, formation of fibrous tissue between the implant and adjacent bone can be seen.(110–113) In absence of this stability, successful osseointegration between the implant and its boney contact surface will be severely limited, leading to the formation of a soft tissue connection. Because the fixation of the LPM is limited to the use of a polydioxanone (PDS) suture, in addition to the sheep being highly dependent on the LPM during chewing and rumination, it is very likely that an insufficient amount of stability between the LPM and scaffold was obtained in our experiment.

Sufficient MSC, osteoblasts and osteocytes need to be present at the implant site. However, when performing the condylectomy, the periosteum is removed. This can have an additional negative effect, as the periosteal inner layer, containing osteogenic progenitor cells, has significant osteoblastic potential.(114,115) In case of absence of the periosteum, these progenitor cells can be derived directly from the Haversian canals, as is the case for the ramal and fossa component. However, this contact repair can only occur in case of direct contact between the implant and when micromotions between the implant and adjacent bone are limited to 28µm.(110–113,116) While a local increase in osteoblasts and osteocytes was attempted by grinding down the resected condyles and applying this bone into the scaffold, mixed with a fibrin sealant, no MSC were applied, thus limiting the possibility of osteogenesis as well.

Although no osseous ingrowth was found, clinical, radiological, as well as the histological analysis of the treated sheep and the selected samples revealed that the specific scaffold design allowed for the enthesis of the lateral pterygoid muscle to produce a strong and functional fibrous reattachment to the implant, allowing for lateral mandibular movement, thus improving functionality compared to currently available TMJR.

In vivo analysis – Implant integration

Besides the reattachment of the LPM, both the condylar and fossa components were also radiologically evaluated for proper integration. All condylar components revealed good radiological integration. In addition, 2 ramal components were histologically evaluated, revealing bony ingrowth into the porous structure. In both samples, a multitude of haversian canals and osteocytes, with bone remodeling was seen, indicating viable osseous tissue and thus a successful osteointegration of the ramal component.

As stated earlier, a latero-inferior displacement of the fossa component was seen in 3 sheep. We hypothesized this was due to the use of 2mm diameter fixation screws for the fossa component, as determined for human subjects, despite the fossa being subjected to more laterotrusive movement. This might have led to excessive stress in the bone surrounding the screws, with gradual bone resorption and thus micromovement of the fossa component, resulting in this displacement.(96–98) Nevertheless, the bearing surface as well as function of the TMJ remained intact in these sheep. One sheep showed a slight infero-dorsal displacement, yet the fixation screws remained intact, thus this displacement is likely due to improper placement and fixation.

Clinical application and future considerations

Following the successful animal trail, 11 patients and 16 joints were treated with a 'regular' custom designed TMJR. Five patients, equaling six TMJ were treated with an 'extended' TMJR (eTMJR). As stated earlier, the use of a custom designed TMJR allows for several additional corrections to be 'worked into' the prosthesis, thus preventing the need for additional surgery.(68,71,72) Whilst little difficulties were encountered in the first

group of patients, those treated with an extended TMJR proved more challenging. Elledge et al.(117) have suggested a classification system for these patients, based on the extension of both the fossa and condylar component, thus focusing on the eTMJR itself. We found however that this classification could be misleading, as the difficulty of surgery is not only determined by the extensiveness of the TMJR, but by the need of other secondary corrections as well. Thus, an improvement on the existing classification was suggested by including the need for contour correction, occlusal adjustment and simultaneous contralateral mandibular osteotomy as additional factors to keep in consideration when planning these patients. This improved classification allows for surgeons to better determine the complexity and feasibility of the surgery. This classification will need further evaluation and fine-tuning, as potential new obstacles are met.(50)

Having extensively researched the pre- and intra-operative conditions to allow for the treatment to be successful, a final systematic literature analysis was performed to improve upon the post-operative phase. While we found that postoperative physiotherapy over a prolonged period of time is needed to achieve optimal results, no clear schedule had been described in the available literature.(118–120) Thus a physiotherapy protocol was designed, based on the different post-operative phases, with the first phase aiming to reduce joint inflammation and preventing abnormal adhesions. As the inflammatory response subsides, the second phase is aimed at further improving the range of motion, muscle control and coordination, to regain functional mobility. The third phase aims to deal with any remaining imbalances and asymmetrical movements, while also regaining muscle strength. A difficulty we encountered while developing this scheme, was the osseous integration of the LPM. Whilst immobilization during the first six weeks might greatly improve the possibility of the osseous integration, this would significantly increase the risk of adhesions being formed, lessened mobility and increased pain, as well as heterotopic ossification.(118,119,121,122) Whereas the results of one of our systematic reviews indicated that the use of autologous fat grafting to eliminate any periarticular negative space proved useful to prevent heterotopic ossification(123), this postoperative physiotherapy schedule will need to be further applied and reviewed, to allow for proper revalidation while not interfering with the LPM integration.

References

1. Elledge R, Mercuri LG, Attard A, Green J, Speculand B. Review of emerging temporomandibular joint total joint. Br J Oral Maxillofac Surg [Internet]. 2019; Available from: https://doi.org/10.1016/j.bjoms.2019.08.009
2. van Loon JP, de Bont LGM, Boering G. Evaluation of temporomandibular joint prostheses. Review of the literature from 1946 to 1994 and implications for future prosthesis designs. J Oral Maxillofac Surg. 1995;53(9):984–96.
3. Ingawalé SM, Goswami T, Ingawale S, Goswami T. Biomechanics of the Temporomandibular Joint. In 2012.
4. Kerwell S, Alfaro M, Pourzal R, Lundberg HJJ, Liao Y, Sukotjo C, et al. Examination of failed retrieved temporomandibular joint (TMJ) implants. Acta Biomater [Internet]. 2016;32:324–35. Available from: http://dx.doi.org/10.1016/j.actbio.2016.01.001
5. Huys SEF, Pastor-Alonso D, Theuns P, van Lenthe GH, Vander Sloten J, Mommaerts MY. A novel 3D-printed, patient-specific alloplastic temporomandibular joint replacement allowing enthesis reconstruction: A finite element analysis. Ann 3D Print Med [Internet]. 2022;6:100058. Available from: https://www.sciencedirect.com/science/article/pii/S2666964122000145
6. Peters K, Unger RE, Kirkpatrick CJ. Biomedical materials. In: Narayan R, editor. Biomedical Materials. 1st ed. New-York: Springer; 2009. p. 1–566.
7. Sinno H, Tahiri Y, Gilardino M, Bobyn D. Engineering alloplastic temporomandibular joint replacements. McGill J Med. 2010;13(1):63–72.
8. Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. Semin Immunol. 2008;20(2):86–100.
9. Wolford LM. Factors to consider in joint prosthesis systems. Baylor Univ Med Cent Proc. 2006;19(3):232–8.
10. Mercuri LG, Giobbie-Hurder A. Long-term outcomes after total alloplastic temporomandibular joint reconstruction following exposure to failed materials. J Oral Maxillofac Surg. 2004;62(9):1088–96.
11. Ferreira JNAR, Ko CC, Myers S, Swift J, Fricton JR. Evaluation of Surgically Retrieved Temporomandibular Joint Alloplastic Implants: Pilot Study. J Oral Maxillofac Surg. 2008;66(6):1112–24.
12. Ward C. History of Self-Experimentation in Orthopaedics. Iowa Orthop J [Internet]. 2009;29:127–9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2723708/
13. Wagner JD, Mosby EL. Assessment of Proplast-Teflon disc replacements. J Oral Maxillofac Surg. 1990;48(11):1140–4.
14. Scales J, Stinson N. Tissue reactions to polytetrafluorethylene. Lancet [Internet]. 2017 Aug 6;283(7325):169. Available from: http://dx.doi.org/10.1016/S0140-6736(64)92260-3
15. Spagnoli D, Kent JN. Multicenter evaluation of temporomandibular joint Proplast-Teflon disk implant. Oral Surgery, Oral Med Oral Pathol. 1992;74(4):411–21.
16. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants - A review. Prog Mater Sci [Internet]. 2009;54(3):397–425. Available from: http://dx.doi.org/10.1016/j.pmatsci.2008.06.004
17. Mercuri LG. The role of custom-made prosthesis for temporomandibular joint replacement. Rev Esp Cir Oral y Maxilofac [Internet]. 2013;35(1):1–10. Available from: http://dx.doi.org/10.1016/j.maxilo.2012.02.003
18. Pruitt LA, Chakravartula AM. Mechanics of Biomaterials: Fundamental Principles for Implant Design [Internet]. Cambridge University Press; 2011. (Cambridge Texts in Biomedical Engineering). Available from: https://books.google.be/books?id=gD4gAwAAQBAJ
19. De Meurechy N, Braem A, Mommaerts MY. Biomaterials in temporomandibular joint replacement: current status and future perspectives-a narrative review. Int J Oral Maxillofac Surg. 2017 Nov;

20. Genovesi W. A New Concept and Design for an Alloplastic TOTAL TMJ Prosthesis Using PEEK LT1 20% BA. J Oral Maxillofac Surg [Internet]. 2018 Oct 1;76(10):e75–6. Available from: https://doi.org/10.1016/j.joms.2018.06.159
21. Kurtz SM, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. Biomaterials. 2007;28(32):4845–69.
22. Sagomonyants KB, Jarman-Smith ML, Devine JN, Aronow MS, Gronowicz GA. The in vitro response of human osteoblasts to polyetheretherketone (PEEK) substrates compared to commercially pure titanium. Biomaterials. 2008;29(11):1563–72.
23. Wang A, Lin R, Stark C, Dumbleton J. Suitability and limitations of carbon fiber reinforced PEEK composites as bearing surfaces for total joint replacements. Wear. 1999;225–229:724–7.
24. Grupp TM, Utzschneider S, Schr??der C, Schwiesau J, Fritz B, Maas A, et al. Biotribology of alternative bearing materials for unicompartmental knee arthroplasty. Acta Biomater [Internet]. 2010;6(9):3601–10. Available from: http://dx.doi.org/10.1016/j.actbio.2010.04.003
25. Driemel O, Braun S, Müller-Richter UDA, Behr M, Reichert TE, Kunkel M, et al. Historical development of alloplastic temporomandibular joint replacement after 1945 and state of the art. Int J Oral Maxillofac Surg. 2009;38(9):909–20.
26. Sidebottom AJ, Speculand B, Hensher R. Foreign body response around total prosthetic metal-on-metal replacements of the temporomandibular joint in the UK. Br J Oral Maxillofac Surg. 2008;46(4):288–92.
27. Sidebottom AJ. Current thinking in temporomandibular joint management. Br J Oral Maxillofac Surg. 2009;47(2):91–4.
28. McGregor DB, Baan RA, Partensky C, Rice JM, Wilbourn JD. Evaluation of the carcinogenic risks to humans associated with surgical implants and other foreign bodies - A report of an IARC Monographs Programme Meeting. Eur J Cancer. 2000;36(3):307–13.
29. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. J Bone Joint Surg Am. 2001 Mar;83-A(3):428–36.
30. Kounis NG, Koniari I. Hypersensitivity to metallic implants: pathophysiologic and diagnostic considerations. Acta Biomed. 2018 Oct;89(3):428–9.
31. Albrektsson T, Chrcanovic B, Mölne J, Wennerberg A. Foreign body reactions, marginal bone loss and allergies in relation to titanium implants. Eur J Oral Implantol. 2018;11:S37–46.
32. Mercuri LG. Alloplastic temporomandibular joint replacement: Rationale for the use of custom devices. Int J Oral Maxillofac Surg [Internet]. 2012;41(9):1033–40. Available from: http://dx.doi.org/10.1016/j.ijom.2012.05.032
33. Chen Q, Thouas GA. Metallic implant biomaterials. Mater Sci Eng R Reports [Internet]. 2015;87:1–57. Available from: http://dx.doi.org/10.1016/j.mser.2014.10.001
34. Huys S, Pastor Alonso D, Theuns P, van Lenthe H, Braem A, Mommaerts M, et al. Mechanical evaluation of a patient-specific temporomandibular joint replacement implant with enthesis reconstruction using finite element analysis. Unpublished.
35. Chan CW, Lee S, Smith G, Sarri G, Ng CH, Sharba A, et al. Enhancement of wear and corrosion resistance of beta titanium alloy by laser gas alloying with nitrogen. Appl Surf Sci [Internet]. 2016;367:80–90. Available from: http://dx.doi.org/10.1016/j.apsusc.2016.01.091
36. Samuel S, Nag S, Scharf TW, Banerjee R. Wear resistance of laser-deposited boride reinforced Ti-Nb-Zr-Ta alloy composites for orthopedic implants. Mater Sci Eng C. 2008;28(3):414–20.
37. Majumdar P, Singh SB, Dhara S, Chakraborty M. Influence of in situ TiB reinforcements and role of heat treatment on mechanical properties and biocompatibility of ?? Ti-alloys. J Mech Behav Biomed Mater [Internet]. 2012;10:1–12. Available from: http://dx.doi.org/10.1016/j.jmbbm.2012.02.014
38. Majumdar P, Singh SB, Chakraborty M. The influence of heat treatment and role of boron on sliding wear behaviour of ??-type Ti-35Nb-7.2Zr-5.7Ta alloy in dry condition and in simulated body fluids. J Mech Behav Biomed Mater [Internet]. 2011;4(3):284–97. Available from: http://dx.doi.org/10.1016/j.jmbbm.2010.10.007

39. Mishnaevsky L, Levashov E, Valiev RZ, Segurado J, Sabirov I, Enikeev N, et al. Nanostructured titanium-based materials for medical implants: Modeling and development. Mater Sci Eng R Reports. 2014;81(1):1–19.
40. Singh R, Dahotre NB. Corrosion degradation and prevention by surface modification of biometallic materials. J Mater Sci Mater Med. 2007;18(5):725–51.
41. Liu X, Chu PK, Ding C. Surface modification of titanium, titanium alloys, and related materials for biomedical applications [Internet]. Vol. 47, Materials Science and Engineering R: Reports. 2004. p. 49–121. Available from: http://dx.doi.org/10.1016/j.mser.2014.10.001
42. De Meurechy N, Mommaerts MY. Alloplastic temporomandibular joint replacement systems: A systematic review of their history. Int J Oral Maxillofac Surg [Internet]. 2018;47(6):743–54. Available from: https://doi.org/10.1016/j.ijom.2018.01.014
43. Van Hove RP, Sierevelt IN, Van Royen BJ, Nolte PA. Titanium-Nitride Coating of Orthopaedic Implants: A Review of the Literature. Biomed Res Int. 2015;2015.
44. Kerwell S, Alfaro M, Pourzal R, Lundberg HJJ, Liao Y, Sukotjo C, et al. Examination of failed retrieved temporomandibular joint (TMJ) implants. Acta Biomater [Internet]. 2016;32:324–35. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1742706116300010
45. Ching HA, Choudhury D, Nine J, Abu Osman NA. Effects of surface coating on reducing friction and wear of orthopaedic implants. Sience Technol Adv Mater. 2014;014402(15).
46. Jiang SW, Jiang B, Li Y, Li YR, Yin GF, Zheng CQ. Friction and wear study of diamond-like carbon gradient coatings on Ti6Al4V substrate prepared by plasma source ion implant-ion beam enhanced deposition. Appl Surf Sci. 2004;236(1):285–91.
47. Roy RK, Lee K-R. Biomedical applications of diamond-like carbon coatings: a review. J Biomed Mater Res B Appl Biomater. 2007 Oct;83(1):72–84.
48. Kim DH, Kim HE, Lee KR, Whang CN, Lee IS. Characterization of diamond-like carbon films deposited on commercially pure Ti and Ti-6Al-4V. Mater Sci Eng C. 2002;22(1):9–14.
49. Yetim AF, Celik A, Alsaran A. Improving tribological properties of Ti6Al4V alloy with duplex surface treatment. Surf Coatings Technol [Internet]. 2010;205(2):320–4. Available from: http://dx.doi.org/10.1016/j.surfcoat.2010.06.048
50. Huys SEF, Braem A, De Meurechy N, Van de Sande R, Vander Sloten J, Mommaerts MY. Evolutionary Steps in the Development of a Patient-specific Temporomandibular Joint Prosthesis. Craniomaxillofacial Res Innov [Internet]. 2022 Aug 1;7:27528464221118784. Available from: https://doi.org/10.1177/27528464221118784
51. Braem A, Van Mellaert L, Mattheys T, Hofmans D, De Waelheyns E, Geris L, et al. Staphylococcal biofilm growth on smooth and porous titanium coatings for biomedical applications. J Biomed Mater Res A. 2014;102(1):215–24.
52. Wolford LM, Morales-Ryan CA, Morales PG, Cassano DS. Autologous fat grafts placed around temporomandibular joint prostheses to prevent heterotopic bone formation. Autologous Fat Transf. 2008;21(3):248–54.
53. Sidebottom AJ, Speculand B, Hensher R. Foreign body response around total prosthetic metal-on-metal replacements of the temporomandibular joint in the UK. Br J Oral Maxillofac Surg [Internet]. 2008;46(4):288–92. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L351635753
54. Bracco P, Oral E. Vitamin E-stabilized UHMWPE for total joint implants: A review. Clin Orthop Relat Res. 2011;469(8):2286–93.
55. Wolford LM. Factors to consider in joint prosthesis systems. Proc (Bayl Univ Med Cent). 2006 Jul;19(3):232–8.
56. Mercuri LG, L.G. M. Alloplastic temporomandibular joint replacement: Rationale for the use of custom devices. Int J Oral Maxillofac Surg [Internet]. 2012 Sep;41(9):1033–40. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L52096544
57. Kowalewski P, Wieleba W. Sliding polymers in the joint alloplastic. Arch Civ Mech Eng. 2007;7(4):107–19.

58. Driemel O, Ach T, Müller-Richter UDA, Behr M, Reichert TE, Kunkel M, et al. Historical development of alloplastic temporomandibular joint replacement before 1945. Int J Oral Maxillofac Surg. 2009;38(4):301–7.
59. Lindqvist C, Soderholm AL, Hallikainen D, Sjövall L. Erosion and heterotopic bone formation after alloplastic temporomandibular joint reconstruction. J oral. 1992;50(9):942–9.
60. Giannakopoulos HE, Sinn DP, Quinn PD. Biomet microfixation temporomandibular joint replacement system: A 3-year follow-up study of patients treated during 1995 to 2005. J Oral Maxillofac Surg [Internet]. 2012;70(4):787–94. Available from: http://dx.doi.org/10.1016/j.joms.2011.09.031
61. Wolford LM, Pitta MC, Reiche-Fischel O, Franco PF. TMJ Concepts/Techmedica custom-made TMJ total joint prosthesis: 5-year follow-up study. Int J Oral Maxillofac Surg [Internet]. 2003;32(3):268–74. Available from: http://www.sciencedirect.com/science/article/pii/S0901502702903504
62. De Meurechy NKG, Zaror CE, Mommaerts MY. Total Temporomandibular Joint Replacement: Stick to Stock or Optimization by Customization? Craniomaxillofac Trauma Reconstr. 2020 Mar;13(1):59–70.
63. Kanatsios S, Thomas AM, Tocaciu S. Comparative clinical outcomes between stock vs custom temporomandibular total joint replacement systems. J Cranio-Maxillofacial Surg [Internet]. 2022;50(4):322–7. Available from: https://www.sciencedirect.com/science/article/pii/S1010518222000117
64. Johnson NR, Roberts MJ, Doi SA, Batstone MD. Total temporomandibular joint replacement prostheses: a systematic review and bias-adjusted meta-analysis. Int J Oral Maxillofac Surg [Internet]. 2016;46(1):1–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0901502716302132
65. Saeed NR, Hensher R, McLeod NMH, Kent JN. Reconstruction of the temporomandibular joint autogenous compared with alloplastic. Br J Oral Maxillofac Surg. 2002;40(4):296–9.
66. Elledge R, Attard A, Green J, Lowe D, Rogers SN, Sidebottom AJ, et al. UK temporomandibular joint replacement database: a report on one-year outcomes. Br J Oral Maxillofac Surg. 2017;55(9):927–31.
67. Mercuri LG, Edibam NR, Giobbie-Hurder A. Fourteen-year follow-up of a patient-fitted total temporomandibular joint reconstruction system. J Oral Maxillofac Surg. 2007 Jun;65(6):1140–8.
68. Mercuri LG, Wolford LM, Giobbie-hurder A. Long-Term Follow-Up of the CAD / CAM Patient Fitted Total Temporomandibular Joint Reconstruction System. 2002;1440–8.
69. Zhao J, Zou L, He D, Ellis E. Comparison of bone adaptation after modi fi cation in biomet standard alloplastic temporomandibular joint prostheses. J Cranio-Maxillofacial Surg [Internet]. 2018;46(10):1707–11. Available from: https://doi.org/10.1016/j.jcms.2018.07.024
70. Kanatas AN, Needs C, Smith AB, Moran A, Jenkins G, Worrall SF. Short-term outcomes using the Christensen patient-specific temporomandibular joint implant system: A prospective study. Br J Oral Maxillofac Surg [Internet]. 2011 Mar;50(2):149–53. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L51345875
71. Elledge R, Mercuri L, Speculand B. Extended total temporomandibular joint replacements: a classification system. Br J Oral Maxillofac Surg [Internet]. 2018;56(7):578–81. Available from: http://dx.doi.org/10.1016/j.bjoms.2018.06.002
72. Westermark A, Heden P, Aagaard E, Cornelius CP. The use of TMJ Concepts prostheses to reconstruct patients with major temporomandibular joint and mandibular defects. Int J Oral Maxillofac Surg. 2011;40(5):487–96.
73. Ramos AM, Mesnard M. The stock alloplastic temporomandibular joint implant can influence the behavior of the opposite native joint: A numerical study. J Craniomaxillofac Surg. 2015 Oct;43(8):1384–91.
74. Linsen SS, Reich RH, Teschke M. Mandibular Kinematics in Patients With Alloplastic Total Temporomandibular Joint Replacement-A Prospective Study. J Oral Maxillofac Surg. 2012;70(9):2057–64.

75. Bekcioglu B, Bulut E, Bas B. The Effects of Unilateral Alloplastic Temporomandibular Joint Replacement on the Opposite-Side Natural Joint: A Finite-Element Analysis. J Oral Maxillofac Surg. 2017;75(11):2316–22.
76. Wang Z, Wang C, Li C, Qin Y, Zhong L, Chen B, et al. Analysis of factors influencing bone ingrowth into three-dimensional printed porous metal scaffolds: A review. J Alloys Compd [Internet]. 2017;717(May 2018):271–85. Available from: http://dx.doi.org/10.1016/j.jallcom.2017.05.079
77. Bagno A, Di Bello C. Surface treatments and roughness properties of Ti-based biomaterials. J Mater Sci Mater Med. 2004;15(9):935–49.
78. Park JY, Davies JE. Red blood cell and platelet interactions with titanium implant surfaces. Clin Oral Implants Res. 2000 Dec;11(6):530–9.
79. Buser D, Broggini N, Wieland M, Schenk RK, Denzer AJ, Cochran DL, et al. Enhanced bone apposition to a chemically modified SLA titanium surface. J Dent Res. 2004 Jul;83(7):529–33.
80. Wang Q, Zhou P, Liu S, Attarilar S, Ma RL-W, Zhong Y, et al. Multi-Scale Surface Treatments of Titanium Implants for Rapid Osseointegration: A Review. Nanomater (Basel, Switzerland). 2020 Jun;10(6).
81. Loh QL, Choong C. Three-Dimensional Scaffolds for Tissue Engineering Applications: Role of Porosity and Pore Size. Tissue Eng Part B Rev [Internet]. 2013 May 14;19(6):485–502. Available from: https://doi.org/10.1089/ten.teb.2012.0437
82. Tamaddon M, Samizadeh S, Wang L, Blunn G, Liu C. Intrinsic Osteoinductivity of Porous Titanium Scaffold for Bone Tissue Engineering. Int J Biomater. 2017;2017.
83. Xue W, Krishna BV, Bandyopadhyay A, Bose S. Processing and biocompatibility evaluation of laser processed porous titanium. Acta Biomater [Internet]. 2007;3(6):1007–18. Available from: https://www.sciencedirect.com/science/article/pii/S1742706107000852
84. Karageorgiou V, Kaplan D. Porosity of 3D biomaterial scaffolds and osteogenesis. Biomaterials [Internet]. 2005;26(27):5474–91. Available from: https://www.sciencedirect.com/science/article/pii/S0142961205001511
85. Markhoff J, Wieding J, Weissmann V, Pasold J, Jonitz-Heincke A, Bader R. Influence of Different Three-Dimensional Open Porous Titanium Scaffold Designs on Human Osteoblasts Behavior in Static and Dynamic Cell Investigations. Vol. 8, Materials . 2015.
86. Cheng A, Humayun A, Cohen DJ, Boyan BD, Schwartz Z. Additively manufactured 3D porous Ti-6Al-4V constructs mimic trabecular bone structure and regulate osteoblast proliferation, differentiation and local factor production in a porosity and surface roughness dependent manner. Biofabrication [Internet]. 2014;6(4):45007. Available from: http://dx.doi.org/10.1088/1758-5082/6/4/045007
87. Taniguchi N, Fujibayashi S, Takemoto M, Sasaki K, Otsuki B, Nakamura T, et al. Effect of pore size on bone ingrowth into porous titanium implants fabricated by additive manufacturing: An in vivo experiment. Mater Sci Eng C [Internet]. 2016;59:690–701. Available from: https://www.sciencedirect.com/science/article/pii/S0928493115305002
88. Angelo DF, Morouço P, Alves N, Viana T, Santos F, González R, et al. Choosing sheep (Ovis aries) as animal model for temporomandibular joint research: Morphological, histological and biomechanical characterization of the joint disc. Morphologie. 2016;100(331):223–33.
89. Almarza AJ, Brown BN, Arzi B, Ângelo DF, Chung W, Badylak SF, et al. Preclinical Animal Models for Temporomandibular Joint Tissue Engineering. Tissue Eng Part B Rev. 2018 Jun;24(3):171–8.
90. Domingue BM, Dellow DW, Barry TN. The efficiency of chewing during eating and ruminating in goats and sheep. Br J Nutr. 1991 May;65(3):355–63.
91. Verplancke K, De Waele W, De Bruyn H. Dental implants, what should be known before starting an in vitro study. Conf Sustain Constr Des [Internet]. 2011;2(3):360–9. Available from: https://biblio.ugent.be/publication/1177030
92. Benjamin J, Szivek J, Dersam G, Persselin S, Johnson R. Linear and Volumetric Wear of Tibial Inserts in Posterior Cruciate-Retaining Knee Arthroplasties. 2001;(392):131–8.
93. Dumbleton JH, Manley MT, Edidin AA. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. J Arthroplasty. 2002 Aug;17(5):649–61.

94. Oparaugo PC, Clarke IC, Malchau H, Herberts P. Correlation of wear debris-induced osteolysis and revision with volumetric wear-rates of polyethylene: a survey of 8 reports in the literature. Acta Orthop Scand. 2001 Feb;72(1):22–8.

95. De Meurechy N, Aktan MK, Boeckmans B, Huys S, Verwilghen DR, Braem A, et al. Surface wear in a custom manufactured temporomandibular joint prosthesis. J Biomed Mater Res B Appl Biomater. 2022 Jun;110(6):1425–38.

96. Chaudhary N, Lovald ST, Wagner J, Khraishi T, Baack B. Experimental and Numerical Modeling of Screws Used for Rigid Internal Fixation of Mandibular Fractures. Model Simul Eng [Internet]. 2008 Jan;2008. Available from: https://doi.org/10.1155/2008/628120

97. Tada S, Stegaroiu R, Kitamura E, Miyakawa O, Kusakari H. Influence of implant design and bone quality on stress/strain distribution in bone around implants: a 3-dimensional finite element analysis. Int J Oral Maxillofac Implants. 2003;18(3):357–68.

98. Skinner R, Maybee J, Transfeldt E, Venter R, Chalmers W. Experimental pullout testing and comparison of variables in transpedicular screw fixation. A biomechanical study. Spine (Phila Pa 1976). 1990 Mar;15(3):195–201.

99. Wang A, Polineni VK, Stark C, Dumbleton JH. Effect of femoral head surface roughness on the wear of ultrahigh molecular weight polyethylene acetabular cups. J Arthroplasty [Internet]. 1998;13(6):615–20. Available from: http://www.sciencedirect.com/science/article/pii/S0883540398800028

100. Jedenmalm A, Affatato S, Taddei P, Leardini W, Gedde UW, Fagnano C, et al. Effect of head surface roughness and sterilization on wear of UHMWPE acetabular cups. J Biomed Mater Res A. 2009 Sep;90(4):1032–42.

101. Tubb CC, Longaray JA, Herrera L, Essner AP, Molloy RM. The Effect of Femoral Component Roughness on the Wear of Total Knee Implants. Orthop Res Soc. 2011;36.

102. McGloughlin TM, Kavanagh AG. Wear of ultra-high molecular weight polyethylene (UHMWPE) in total knee prostheses: a review of key influences. Proc Inst Mech Eng Part H, J Eng Med. 2000;214(4):349–59.

103. Krenn V, Perino G. Histological Diagnosis of Implant-Associated Pathologies. Springer, Berlin, Heidelberg; 2017. 44 p.

104. Krenn V, Morawietz L, Perino G, Kienapfel H, Ascherl R, Hassenpflug GJ, et al. Pathology – Research and Practice Revised histopathological consensus classification of joint implant related pathology. Pathol -- Res Pract [Internet]. 2014;210(12):779–86. Available from: http://dx.doi.org/10.1016/j.prp.2014.09.017

105. Morawietz L, Classen R-A, Schroder JH, Dynybil C, Perka C, Skwara A, et al. Proposal for a histopathological consensus classification of the periprosthetic interface membrane. J Clin Pathol. 2006 Jun;59(6):591–7.

106. Hobza M, Milde D, Slobodova Z, Gallo J. The number of lymphocytes increases in the periprosthetic tissues with increasing time of implant service in non-metal-on-metal total joint arthroplasties: A role of metallic particles? Biomed Pap Med Fac Univ Palacky, Olomouc, Czechoslov. 2021 Nov;165(4):416–27.

107. Lohmann CH, Meyer H, Nuechtern J V, Singh G, Junk-Jantsch S, Schmotzer H, et al. Periprosthetic tissue metal content but not serum metal content predicts the type of tissue response in failed small-diameter metal-on-metal total hip arthroplasties. J Bone Joint Surg Am. 2013 Sep;95(17):1561–8.

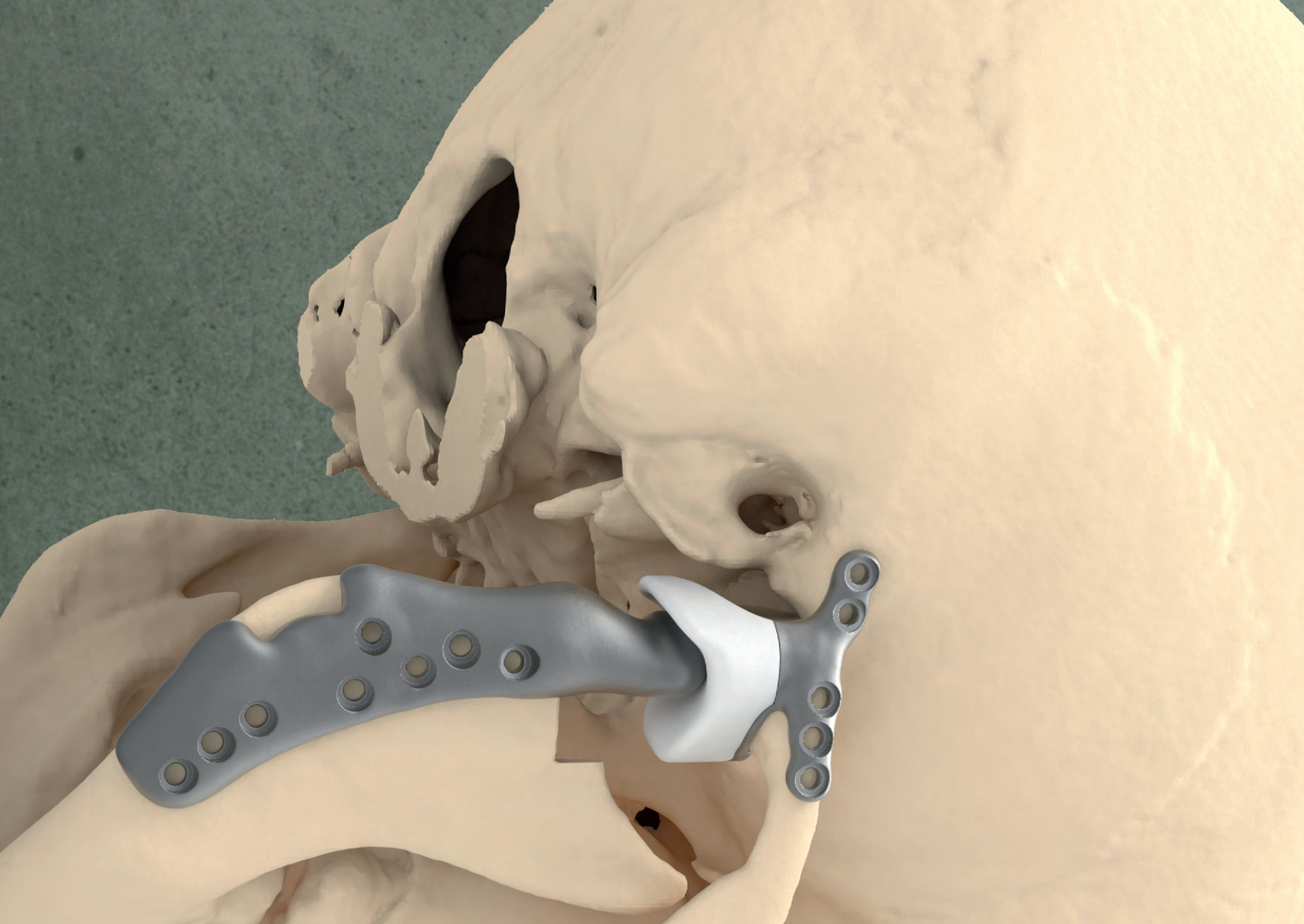
108. Revell PA. The combined role of wear particles, macrophages and lymphocytes in the loosening of total joint prostheses. J R Soc Interface. 2008;5(28):1263–78.

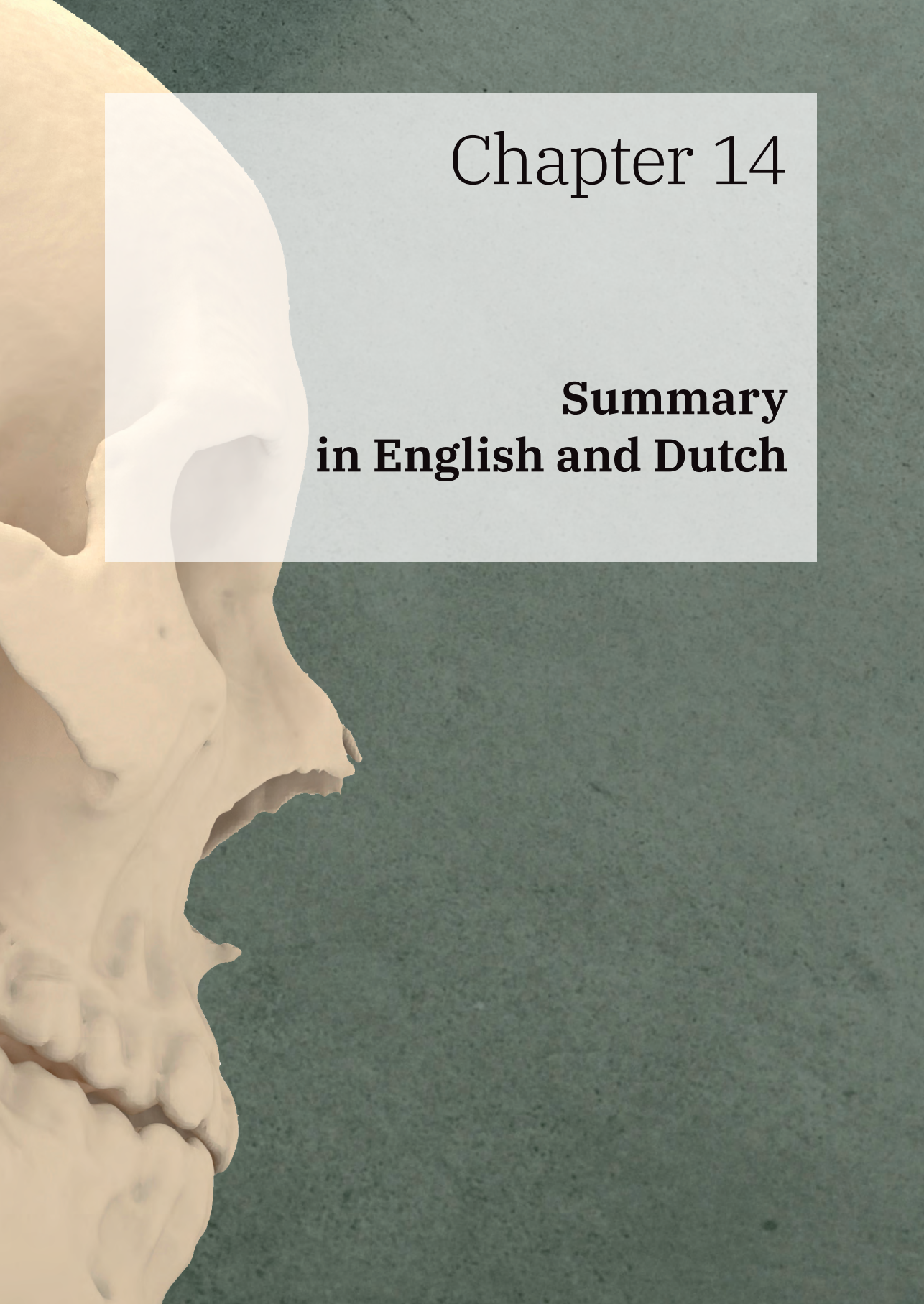
109. De Meurechy N, Verwilghen D, De Brucker Y, Van Thielen B, Mommaerts MY. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation. J Cranio-Maxillofacial Surg. 2021 Feb;49(4):256–68.

110. Pilliar RM, Lee JM, Maniatopoulos C. Observations on the effect of movement on bone ingrowth into porous-surfaced implants. Clin Orthop Relat Res. 1986 Jul;(208):108–13.

111. Goodman S, Aspenberg P. Effects of mechanical stimulation on the differentiation of hard tissues. Biomaterials. 1993;14(8):563–9.

112. Burke D, CR B, Jasty M, Haire T, Harris W. Dynamic measurement of interface mechanics in vivo and the effect of micromotion on bone ingrowth into a porous surface device under controlled loads in vivo. In: 37th Annual Meeting of Orthopaedic Research Society. Anaheim; 1991. p. 103.
113. Franchi M, Fini M, Martini D, Orsini E, Leonardi L, Ruggeri A, et al. Biological fixation of endosseous implants. Micron. 2005;36(7–8):665–71.
114. Dwek JR. The periosteum: What is it, where is it, and what mimics it in its absence? Skeletal Radiol. 2010;39(4):319–23.
115. Lin Z, Fateh A, Salem DM, Intini G. Periosteum: Biology and applications in craniofacial bone regeneration. J Dent Res. 2014;93(2):109–16.
116. Shapiro F. Bone development and its relation to fracture repair. The role of mesenchymal osteoblasts and surface osteoblasts. Eur Cells Mater. 2008;15:53–76.
117. Elledge R, Mercuri LG, Speculand B. Extended total temporomandibular joint replacements : Br J Oral Maxillofac Surg [Internet]. 2018;56(7):578–81. Available from: https://doi.org/10.1016/j.bjoms.2018.06.002
118. Austin BD, Shupe SM. The role of physical therapy in recovery after temporomandibular joint surgery. J Oral Maxillofac Surg [Internet]. 1993;51(5):495–8. Available from: http://dx.doi.org/10.1016/S0278-2391(10)80503-8
119. Singh V, Dhingra R, Bhagol A. Prospective analysis of temporomandibular joint reconstruction in ankylosis with sternoclavicular graft and buccal fat pad lining. J Oral Maxillofac Surg [Internet]. 2012 Apr;70(4):997–1006. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L51526536
120. Lo L-J, Lin C-L, Chen Y-R. A device for temporomandibular joint exercise and trismus correction: design and clinical application. J Plast Reconstr Aesthetic Surg. 2008;61(3):297–301.
121. Kuwahara T, Bessette RW, Maruyama T. Effect of continuous passive motion on the results of TMJ meniscectomy. Part I: Comparison of chewing movement. Cranio. 1996 Jul;14(3):190–9.
122. Ellis E 3rd, Carlson DS. The effects of mandibular immobilization on the masticatory system. A review. Clin Plast Surg. 1989 Jan;16(1):133–46.
123. Van Bogaert W, De Meurechy N, Mommaerts MY. Autologous Fat Grafting in Total Temporomandibular Joint Replacement Surgery. Ann Maxillofac Surg [Internet]. 2018;8(2):299–302. Available from: https://pubmed.ncbi.nlm.nih.gov/30693249





Chapter 14

Summary in English and Dutch

Summary

This thesis aimed to develop and research a patient-specific total temporomandibular joint prosthesis, which would not only meet the orthopedic standards set for both wear properties and adverse tissue reactions but would also provide improved functionality through the reattachment of the lateral pterygoid muscle. In addition, we hypothesized that the experience and knowledge gained through this research would also lead to the development of new, improved, per- and post-operative protocols.

The **1st chapter** discussed the complex anatomy of the TMJ with attention to the peri-articular surgical and anatomical landmarks. The indications for a total joint replacement were highlighted and the surgical approaches used to access the joint were elaborated upon. The TMJ is a highly complex diarthrosis, that is comprised of the head of the mandibular condyle and the temporal glenoid fossa, which are enveloped by a fibrous capsule with a synovial lining. The joint is divided into a superior and inferior compartment by a fibrocartilaginous disc, allow rotational movement in the inferior compartment and translational movement in the upper compartment. Four muscles insert directly onto the joint, three of which are responsible for closing of the mouth, whereas the lateral pterygoid muscle allows for laterotrusive and protrusive movement. These movements are limited by both the capsular tissue and the articular ligaments.

When the indications for a surgical replacement are met, an extraoral approach is considered as the preferred approach. Whilst a retro- or endaural approach can be considered, the preauricular approach is usually opted for. Several modifications to this approach have been described, all aiming for better exposure of the joint. During this procedure, one must not neglect the presence of the facial nerve and its temporofacial branch, nor the auriculotemporal nerve, when gaining access to the joint. In addition, when performing the condylectomy, the surgeon must be mindful of the medial meningeal artery. In addition to the auricular approach, a submandibular approach is used for proper exposure of the mandibular angle and ramus. Attention to the cervical facial branch must be given when performing this dissection.

Chapter 2 provided an insight in the historical evolution of the prosthetic treatment of the TMJ, by means of a systematic review. Forty-one articles were included and discussed. The evolution in different materials and implant designs, starting from a simple interpositional wooden block to a CAD-CAM 3D-printed PSI, were discussed. This led to the conclusion that the historic development of the alloplastic TMJR was mainly a process of trial and error. Principles in design as well as materials that were applied in orthopedic surgery were transferred into the field of TMJ surgery, despite not always being suitable. This led to the use of both unsuited implant design, such as the solitary use of a condylar prosthesis, as well as the implantation of incompatible materials. Although this resulted in the need to explant several thousand prosthesis and a near loss of confidence in the TMJ TJR, it also led to further insights in the development of modern, successful TMJR.

The **3rd chapter** further focused on the materials that were and are being used in past and current prosthetic systems, through a narrative review. A total of 53 articles were included by means of a systematic review, with 8 more articles being handpicked from specialized literature. The properties a material needs to meet as a prosthetic material were highlighted, ranging from its biocompatibility, to its potential for osseointegration, as well as its functionality. The materials used in current TMJR were evaluated for these properties, to determine their advantages and shortcomings. Future materials, as well as surface modification techniques were then discussed to determine if current materials can be improved upon. We concluded that the use of titanium should be preferred over cobalt-chromium alloys and the use of metal-on-UHMWPE is superior to metal-on-metal articulations. We also concluded that the properties of titanium can be further improved upon through the use of surface modification techniques.

This **4th chapter** aimed to determine the efficacy between a patient-specific and a stock TMJ TJR. A systematic review and meta-analysis were performed, in which the maximal mouth opening, pain and diet were analyzed. Although no significant difference was found between the two types of implants, several confounding factors such as the lack

of pathology grading, bias of pooled data and lessened surgery time were discovered and discussed. In addition, advantages to the use of PSI were not taken into consideration during the statistical analysis. We concluded that, despite the initial higher cost of a custom-made TMJR, its use allows for optimal positioning of the screws thus decreasing the risk of damage to the alveolar and facial nerve, which can prevent for the need of a second corrective surgery.

After determining the proper materials to be used for implantation, as well as the fact that the prosthetic design needs to consist of two components and is best designed as a patient-specific implant, the next 4 chapters discussed the development and findings of an animal-model experiment, using a total of fourteen sheep. One sheep served as a control group, whereas seven sheep were implanted with a sheep-specific TMJ TJR that did not receive any surface modification. This group was then compared to six sheep that were implanted with a TMJR, of which the condylar component underwent a surface modification, by means of a H-DLC-coating. Two-hundred and eighty-eight days after implantation, equaling 22 years of human masticatory function, the sheep were euthanized, and the tissues and prosthetic components were analyzed to determine the suitability of the novel implant for human application.

In **chapter 5** the amount of wear that occurred in the fossa component, using optical scanning, was evaluated. The average linear wear when combined with a coated condyle did not differ significantly from the non-coated combination average. The same was true for the volumetric analysis. In both cases, the amount of wear that occurred was well below the maximum that is allowed in a TKR. In addition, the condylar surfaces were assessed as well, using scanning electron and confocal laser microscopy. SEM-analysis revealed that the coated condyles had developed multi-directional scratches, which were also present on a pristine sample, indicating these were due to the polishing protocol (HadSat®)that is applied prior to implantation. One coated condyle developed deeper marks, penetrating through the H-DLC coating, potentially due to the fossa having become slightly displaced over time. In comparison, the uncoated condyles showed significantly more surface

damage and the confocal laser microscope analysis revealed that the uncoated condyles had a significantly higher surface roughness. In comparison, the coated condyles performed so well that their surface roughness did not differ significantly from a pristine condyle.

Whereas chapter 5 evaluated the prosthetic wear, in **chapter 6** a quantitative analysis of the inflammatory cell types in the peri-articular tissues was performed, to determine if a SLIM Type I synovitis, SLIM Type VI reaction or chronic inflammation occurred. A comparison was made between both the coated and uncoated system's tissue samples. To prevent any bias, each tissue sample was blinded and a 20mm^2 digital grid was projected at five random locations per tissue sample. These five grids were then manually analyzed. A significantly higher number of lymphocytes was found in the peri-articular tissues of both sample groups compared to the control group. This increased number of lymphocytes was more pronounced in the uncoated sample, yet no significant difference was seen between both prosthetic sample groups. Although the coated sample group revealed more macrophages, the difference between both implant types was once again not significant. The criteria for a SLIM Type I synovitis or SLIM Type VI reaction were not met and although there was a higher lymphocyte count, this was still within acceptable bounds and more outspoken in the uncoated samples.

Both next chapters focused on the insertion and reattachment of the LPM. In **chapter 7,** we performed a radiological evaluation of the LPM's enthesis using a CT scan. Four types of outcomes were found. In four sheep, there was no reconstruction between the implant and the LPM. Three sheep revealed a purely soft tissue connection of 0.5-0.9 mm between the ostectomized bony LPM insertion and the implant's lattice structure. A combination of partial bony and partial soft tissue enthesis attachment (0.3-0.5 mm) was found in three sheep. A bony ingrowth of the enthesis into the scaffold occurred in two sheep. A secondary bony connection between the mandible and the insertion of the LPM was found in 10 out of 13 sheep. A displacement of the fossa component was seen in 4 sheep, yet no loss of TMJ function was noted in these ewes.

Chapter 8 further analyzed the 5 previously mentioned sheep which showed either a purely bony or partially bony and partially soft tissue attachment to the condylar scaffold. To do so, a detailed anatomical analysis was made to determine how the samples needed to be sectioned, after which histological analysis of the condylar scaffold and LPM was performed. This analysis revealed multiple osteogenic islands within the enthesis scaffold, yet no apparent bony ingrowth had occurred. Nevertheless, all specimens had developed an uninterrupted fibrotic connection between the enthesis and scaffold, allowing for a proper functional restoration of the LPM. Analysis of the ramal component revealed proper osseous integration onto the mandible. Further investigation of the reattachment technique in human subjects was proposed, to improve upon the osseous integration and to evaluate the effectiveness of a possible fibrotic connection.

With the animal-model experiment proved successful, **chapter 9** discussed the development of the novel patient-specific TMJ prosthesis, while staying true to the general design as previously evaluated, mimicking both normal joint anatomy and function, for human implantation. This chapter served as a summary and clinical application of the previous 8 chapters. In addition, early clinical results for pain, diet, maximal mouth opening and laterotrusion were included, which were all promising. We concluded that further human clinical use was justified.

The **10th chapter** continued and expanded where the previous chapter left off. As stated in chapter four, one of the advantages of a PSI over a stock implant is the possibility to treat larger defects, by means of an alloplastic eTMJR. In this chapter we developed 6 eTMJRs to treat 5 patients with severe defects. Each case was elaborated upon and asked to fill out a questionnaire, determining the patient-reported outcomes. We reported on the surgical difficulties that were encountered and suggested the use of a new subclassification system of eTMJR. This new system further elaborated on the classification according to Elledge et al., taking in account the need for contour corrections, occlusal adjustments and a simultaneous contralateral mandibular osteotomy.

In **Chapter 11** we aimed to further improve the operative protocol that was used, as to reduce the potential need for revisory surgery due to reankylosis, since heterotopic bone formation was seen in multiple sheep. Several papers had previously mentioned the use of an AFG, thus a narrative review was performed to confirm its usefulness. Out of 8011 initial articles, a total of 7 articles were selected. We found that the use of AFG has not yet been widely implemented in TMJ TJR, yet positive results were seen in the studies that were included. Further evaluation by means of a prospective multicenter randomized controlled trial was suggested.

Chapter 12 focused on the post-operative treatment, to develop an evidence-based physiotherapy protocol which was thorough yet comprehensible and applicable for practitioners. To do so, a systematic review was performed with 675 initial hits. After screening, six papers were included. Not only did we conclude, based on the analysis of these papers, that the use of proper post-operative physiotherapy led to an increase in MMO, but also to significantly lower pain scores. A detailed and thorough 3-phase post-operative rehabilitation schedule, ranging from 24 hours after surgery until more than 4 weeks after surgery, was developed using the literature analysis, to further improve the post-operative results. A comparative randomized trial was proposed to determine its effectiveness.

Chapter 13 combined all the previous findings, which were then evaluated in the general discussion. A perspective for the future is provided, with further development of the novel prosthesis. The results of this thesis have shown that the developed PSI not only met the standards that have been set by the field of orthopedic surgery, but also improved upon the current TMJ TJR, thus being suited for human implantation and even improving clinical care. Further optimization of the reattachment technique and scaffold, as well as post-operative follow-up and revalidation, was needed to further improve the possibility of proper osseointegration of the bony enthesis. The per- and post-operative protocols could further add to improved clinical outcome but should be further investigated as well.

Samenvatting

Dit proefschrift had tot doel een patiënt-specifieke totale temporomandibulaire gewrichtsprothese te ontwikkelen en te onderzoeken, die niet alleen zou voldoen aan de orthopedische normen voor zowel slijtage-eigenschappen als ongunstige weefselreacties, maar ook een verbeterde functionaliteit zou bieden door de herbevestiging van de laterale pterygoideus-spier. Daarnaast veronderstelden we dat de ervaring en kennis die door dit onderzoek werden opgedaan, zou leiden tot de ontwikkeling van nieuwe, verbeterde, per- en postoperatieve protocollen.

In het **1e hoofdstuk** wordt de complexe anatomie van het kaakgewricht met aandacht voor de peri-articulaire chirurgische en anatomische oriëntatiepunten besproken. De indicaties voor een totale gewrichtsvervanging worden belicht en de chirurgische benaderingen die worden gebruikt om toegang te krijgen tot het gewricht worden uitgewerkt. Het kaakgewricht is een zeer complexe diarthrose, bestaande uit de mandibulaire condylus en de temporale fossa glenoidalis. Deze worden afgelijnd door een fibreus, synoviaal gewrichtkapsel. Het gewricht wordt opgedeeld in een superieur en inferieur compartiment dankzij een fibrocartilageneuze discus. Hierdoor kunnen er rotatiebewegingen in het inferieure compartiment optreden en translatiebeweging in het bovenste compartiment. Vier spieren insereren rechtstreeks op het gewricht. Drie van deze spieren zijn verantwoordelijk voor het sluiten van de mond, terwijl de laterale pterygoideus-spier laterotrusieve en protrusieve bewegingen mogelijk maakt. Deze bewegingen worden beperkt door zowel het gewrichtskapsel alsook door de ligamenten.

Indien er een indicatie is tot een prothetische vervanging van het kaakgewricht, wordt er in de eerste plaats geopteerd voor een extraorale benadering. Hoewel een retro- of endaurale benadering overwogen kunnen worden, wordt er meestal gekozen voor een preauriculaire benadering. Deze chirurgische benadering kent verschillende modificaties, die allemaal gericht zijn op een betere visualisatie van het gewricht. Tijdens chirurgische benadering van het kaakgewricht, mag men de aanwezigheid van de n. facialis en zijn temporofaciale tak, noch de n. auriculotemporalis, niet uit het oog verliezen. Bovendien dient een

chirurg bij het uitvoeren van een condylectomie rekening houden met de a. meningea media. Bijkomend aan auriculaire benadering wordt een submandibulaire benadering gebruikt voor een betere visualisatie van de angulus en ramus ascendens. Bij het uitvoeren van deze dissectie moet aandacht worden besteed aan de r. marginalis.

Hoofdstuk 2 geeft inzicht in de historische evolutie van de prothetische behandeling van het kaakgewricht aan de hand van een systematisch literatuuronderzoek. Eenenveertig publicaties worden geïncludeerd en besproken. De evolutie van verschillende materialen en prothetische ontwerpen, gaande van een eenvoudig interpositioneel houten blok tot een CAD-CAM 3D-geprint patiënt-specifiek implantaat wordt besproken. Dit leidt tot de conclusie dat de historische ontwikkeling van de alloplastische kaakgewrichtsvervangingen vooral een proces van trail and error was. Materialen die werden gebruikt in de orthopedische chirurgie, alsook principes van prothetische ontwerpen, werden rechtstreeks overgebracht naar het gebied van kaagewrichtschirurgie, ondanks dat ze niet altijd geschikt waren. Dit leidde tot het gebruik van zowel ongeschikt implantaatontwerp, zoals de solitaire condylaire prothese, alsook de implantatie van incompatibele materialen. Hoewel dit resulteerde in de explantatie van duizenden prothesen, waarbij het toepassen van een alloplastische kaakgewrichtsvervanging bijna verlaten werd, leidde het ook tot verdere inzichten waaruit de moderne, succesvolle alloplastische kaakgewrichtsprothesen zijn ontstaan.

Het **3e hoofdstuk** richt zich verder op de materialen die werden en worden gebruikt in vroegere en huidige prothetische systemen, aan de hand van een narratief literatuuronderzoek. In totaal worden 53 publicaties opgenomen door middel van een systematisch literatuuronderzoek, waarbij nog eens 8 publicaties met de hand worden geselecteerd uit gespecialiseerde literatuur. De eigenschappen waaraan een prothetisch materiaal moet voldoen, worden toegelicht, met aandacht voor de biocompatibiliteit, het potentieel voor osseointegratie en diens functionaliteit. De materialen die in de huidige alloplastiche kaakgewrichtsvervanging worden gebruikt, worden geëvalueerd op deze eigenschappen om hun voor- en nadelen te bepalen. Daarnaast worden toekomstige materialen en

oppervlaktebehandelingstechnieken besproken om te bepalen of de huidige materialen kunnen worden verbeterd. We concluderen dat het gebruik van titanium de voorkeur verdient boven kobalt-chroomlegeringen en dat bij de articulerende oppervlakken het gebruik van metaal-UHMWPE superieur is aan metaal -metaal . We concluderen ook dat de eigenschappen van titanium verder kunnen worden verbeterd door het gebruik van oppervlaktemodificatietechnieken.

Het **4e hoofdstuk** vergelijkt de werkzaamheid van een patiënt-specifieke kaakgewrichtsprothese, met deze van een standaard prothese. Er worden een systematisch literatuuronderzoek en meta-analyse uitgevoerd, waarbij de maximale mondopening, pijn en dieet geanalyseerd worden. Hoewel er geen significant verschil tussen de twee types implantaten aangetoond kan worden, worden er wel verschillende verstorende factoren gevonden en besproken. Het gebrek aan beoordeling van ernst van de pathologie, vertekening van gepoolde gegevens en verminderde operatietijd worden waargenomen en toegelicht. Bovendien wordt bij de statistische analyse geen rekening gehouden met bepaalde voordelen van het gebruik van patiënt-specifieke implantaten. We concluderen dat, ondanks de hogere kosten van een op maat gemaakte gewrichtsprothese, het gebruik van dit type prothese toelaat om een optimale positionering van de schroeven te bekomen. Hierdoor wordt het risico op schade aan de n. alveolaris inferior en n. facialis verminderd, wat de noodzaak van een tweede corrigerende operatie kan voorkomen.

Na het bepalen van de juiste materialen die voor implantatie moeten worden gebruikt, evenals het feit dat het prothetische ontwerp uit twee componenten moet bestaan en het beste kan worden ontworpen als een patiënt-specifiek implantaat, bespreken de volgende 4 hoofdstukken de ontwikkeling en bevindingen van een diermodelexperiment, waarbij in totaal veertien schapen werden gebruikt. Hiervan trad 1 proefdier op als controle, terwijl zeven schapen werden geïmplanteerd met een schaapspecifiek alloplastisch kaakgewricht dat geen oppervlaktemodificatie onderging. Deze groep werd vervolgens vergeleken met zes schapen die werden geïmplanteerd met een prothese waarvan de condylaire component een oppervlaktemodificatie onderging,

door middel van een H-DLC-coating. Tweehonderdachtentachtig dagen na implantatie, gelijk aan 22 jaar menselijke kauwfunctie, werden de schapen geëuthanaseerd en werden de weefsels en prothetische componenten geanalyseerd om de geschiktheid van het nieuwe implantaat voor menselijke toepassing te bepalen.

In **hoofdstuk 5** wordt de hoeveelheid slijtage die is opgetreden in de fossa-component geëvalueerd met behulp van een optisch scanner. Er is geen significant verschil in de gemiddelde lineaire slijtage van de fossa-component tussen beide gecoate en de niet-gecoate groep. Eenzelfde bevinding wordt gemaakt voor de volumetrische analyse. In beide gevallen ligt de hoeveelheid slijtage die optrad ruim onder het maximum dat is toegestaan in voor een totale knieprothese . Daarnaast worden ook de condylaire oppervlakken geanalyseerd, door middel van scanning-elektronen- en confocale lasermicroscopie. SEM-analyse toont aan dat de gecoate condylen multidirectionele krassen vertonen, die ook aanwezig zijn op een ongerept monster, wat aangeeft dat deze te wijten zijn aan het polijstprotocol (HadSat®) dat voorafgaand aan implantatie wordt toegepast. Eén gecoate condylus vertoont diepere markeringen, waarbij deze doorheen de H-DLC-coating heen gaan, mogelijks ten gevolge van een kleine verplaatsing van de fossa-component na implantatie. Ter vergelijking: De ongecoate condyli vertonen significant meer oppervlakteschade en de confocale lasermicroscoopanalyse toont aan dat de ongecoate condyli een significant hogere oppervlakteruwheid hebben. De gecoate condyli daarentegen vertonen geen significante toename in het oppervlakteruwheid tegenover deze van de ongerepte condylus.

Terwijl in hoofdstuk 5 de slijtage van de prothese wordt geëvalueerd, wordt in **hoofdstuk 6** een kwantitatieve analyse van de ontstekingscellen in de peri-articulaire weefsels uitgevoerd om te bepalen of er een SLIM Type I synovitis, SLIM Type VI reactie of chronische ontsteking optreedt. Hierbij wordt ook een vergelijking tussen het gecoate en het niet-gecoate systeem gemaakt. Om vertekening te voorkomen, wordt elk weefselmonster geblindeerd en wordt een digitaal rooster van 20 mm^2 geprojecteerd op vijf willekeurige locaties per weefselmonster. Deze vijf roosters worden vervolgens handmatig geanalyseerd. Er wordt

een significant hoger aantal lymfocyten gevonden in de peri-articulaire weefsels van beide monstergroepen in vergelijking met de controlegroep. Hoewel het verhoogde aantal lymfocyten meer uitgesproken is in de niet-gecoate monsters, is er geen significant verschil tussen beide prothetische groepen. Hoewel het gecoate systeem meer macrofagen laat optekenen, is ook dit verschil tussen beide implantaattypen niet significant. Aan de criteria voor een SLIM Type I synovitis of SLIM Type VI reactie wordt niet voldaan en hoewel er een hoger aantal lymfocyten is, is dit nog steeds binnen aanvaardbare grenzen.

Beide volgende hoofdstukken richten zich op de reïnsertie van de m. pterygoideus lateralis. In **hoofdstuk 7** wordt een radiologische evaluatie van de enthese van de LPM uitgevoerd met behulp van een CT-scan. Hierbij worden vier mogelijke uitkomsten waargenomen. Bij vier schapen is er geen reïnsertie tussen het implantaat en de LPM. Drie schapen vertonen enkel een wekedelen-verbinding van 0,5-0,9mm tussen de afgezaagde (condylaire) benige LPM-insertie en de scaffold-structuur van het implantaat. Bij drie schapen wordt een combinatie gevonden van een gedeeltelijke benige en gedeeltelijke weke delen aanhechting (0,3-0,5 mm). Bij twee schapen wordt een benige ingroei van de enthesis in de scaffold waargenomen. Bij 10 van de 13 schapen is er ook sprake van een secundaire benige verbinding tussen de onderkaak en de insertie van de LPM. Hoewel vier fossa-componenten verplaatst bleken te zijn, bleef de kaakgewrichtsfunctie in deze ooien behouden.

In **hoofdstuk 8** worden de 5 eerder genoemde schapen die ofwel een puur benige of gedeeltelijk benige en gedeeltelijk weke delen aanhechting vertoonden, verder geanalyseerd. Om dit mogelijk te maken, wordt een gedetailleerde anatomische analyse gemaakt ter bepaling hoe de monsters moeten worden doorgesneden, waarna histologische analyse van de condylaire scaffold en LPM kan worden uitgevoerd. Deze analyse onthult meerdere osteogene eilanden binnenin de scaffold, maar er is geen sprake van een duidelijke benige ingroei. Niettemin hebben alle specimens een ononderbroken fibrotische verbinding tussen de LPM-enthese en de scaffold ontwikkelt, waardoor een goed functioneel herstel van de LPM mogelijk is. Analyse van de ramuscomponent toont

een goede osteointegratie aan de onderkaak. Verder onderzoek naar de herbevestigingstechniek bij menselijke proefpersonen is nodig om de osteointegratie van de LPM-enthesis te verbeteren en om de effectiviteit van een mogelijke fibrotische verbinding verder te evalueren.

Nu het experiment met het diermodel succesvol is gebleken**,** bespreekt **hoofdstuk 9** de ontwikkeling van de nieuwe custom-made kaakgewrichtsprothese voor menselijke implantatie, terwijl het trouw blijft aan het algemene ontwerp zoals eerder geëvalueerd, dat zowel de normale anatomie als functie van het gewricht nabootst. Dit hoofdstuk dient als een samenvatting en klinische toepassing van de vorige 8 hoofdstukken. Daarnaast worden vroege klinische resultaten voor pijn, dieet, maximale mondopening en laterotrusie opgenomen, die allemaal veelbelovend zijn. We concluderen dat verdere klinisch applicatie bij mensen gerechtvaardigd is.

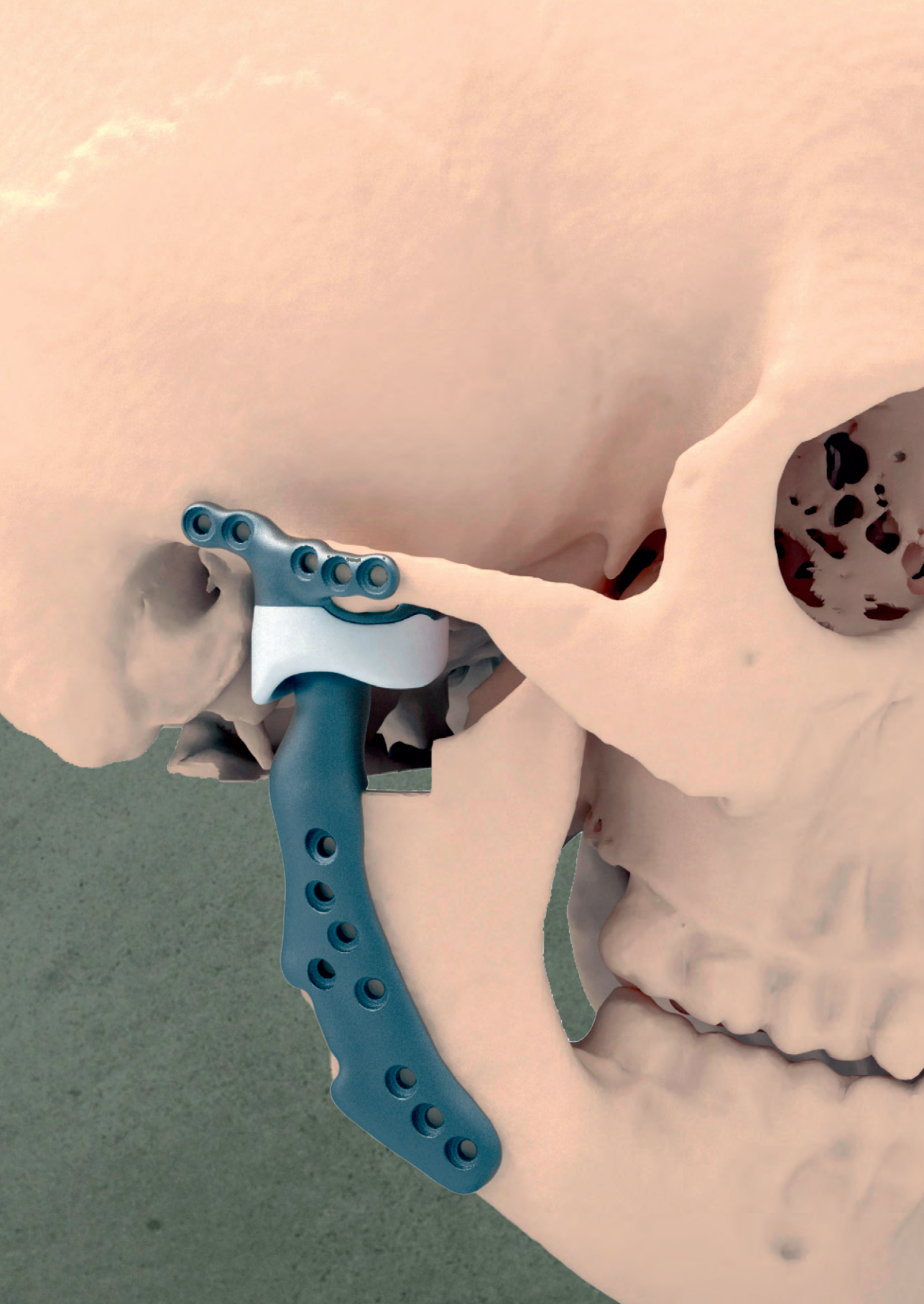
Het **10e hoofdstuk** gaat verder waar het vorige hoofdstuk ophield. Zoals vermeld in hoofdstuk vier, is een van de voordelen van een PSI ten opzichte van een stockimplantaat de mogelijkheid om grotere defecten te behandelen door middel van een alloplastisch eTMJR. In dit hoofdstuk hebben we 6 eTMJR's ontwikkeld voor de behandeling van 5 patiënten met ernstige afwijkingen. Elke casus wordt uitgewerkt en gevraagd om een vragenlijst in te vullen om de door de patiënt-gerapporteerde uitkomsten te bepalen. We rapporteren over de chirurgische moeilijkheden die zich voordoen en stellen het gebruik voor van een nieuw subclassificatiesysteem van eTMJR. Dit systeem werkt verder, op de classificatie volgens Elledge et al., rekening houdend met de noodzaak van contourcorrecties, occlusale aanpassingen en een gelijktijdige contralaterale mandibulaire osteotomie.

In **hoofdstuk 11** willen we het operatieve protocol dat werd gebruikt verder verbeteren, om de mogelijke noodzaak van revisiechirurgie als gevolg van reankylose te verminderen, aangezien heterotope botvorming werd gezien bij meerdere schapen. Verschillende artikels hadden eerder melding gemaakt van het gebruik van een vrije vetgreffe, dus werd een narratieve literatuurstudie uitgevoerd om het nut ervan

te bevestigen. Uit de 8011 oorspronkelijke artikelen worden in totaal 7 artikelen geselecteerd. We ontdekken dat het gebruik van een vrije vetgreffe nog niet op grote schaal is geïmplementeerd in alloplastiche kaakgewrichtsvervanging, maar toch werden positieve resultaten gezien in de onderzoeken die werden opgenomen. Verdere evaluatie door middel van een prospectieve multicenter gerandomiseerde gecontroleerde studie wordt voorgesteld.

Hoofdstuk 12 richt zich op de postoperatieve behandeling, om een evidence-based fysiotherapieprotocol te ontwikkelen dat grondig maar begrijpelijk en toepasbaar is voor behandelaars. Hiertoe wordt een systematisch literatuuronderzoek uitgevoerd met 675 eerste treffers. Na de screening worden zes papers opgenomen. Niet alleen concluderen we, op basis van de analyse van deze papers, dat het gebruik van de juiste postoperatieve fysiotherapie leidt tot een toename van MMO, maar ook tot significant lagere pijnscores. Aan de hand van de literatuuranalyse wordt een gedetailleerd en grondig postoperatief revalidatieschema in 3 fasen ontwikkeld, lopende van 24 uur na de operatie tot meer dan 4 weken na de operatie, om de postoperatieve resultaten verder te verbeteren. Er wordt een vergelijkende gerandomiseerde studie voorgesteld om de effectiviteit ervan te bepalen.

Hoofdstuk 13 bundelt alle voorafgaande bevindingen, die vervolgens in de algemene bespreking worden geëvalueerd. Er wordt een toekomstperspectief geboden, met de verdere ontwikkeling van de nieuwe prothese. De resultaten van dit proefschrift tonen aan dat de ontwikkelde prothese niet alleen voldoet aan de normen gesteld voor prothesen binnen de orthopedische chirurgie, maar ook een verbetering is ten opzichte van de huidige alloplastische kaagewrichtsvervanging. Hierdoor is de prothese geschikt voor menselijke implantatie en een verbetering van de klinische zorg tegenover de huidige kaakgewrichtsprothesen. Verdere optimalisatie van de herbevestigingstechniek van de m. pterygoideus lateralis, evenals postoperatieve follow-up en revalidatie, is nodig om de mogelijkheid van een goede osteointegratie van de benige enthese verder te verbeteren. De per- en postoperatieve protocollen kunnen verder bijdragen aan een beter klinisch resultaat, maar moeten ook verder worden onderzocht.



Appendices

List Of Abbreviations

AAOMS	American Association of Oral and Maxillofacial Surgeons
AFG	Autologous fat graft
BTJ	Bone-tendon junction
CAD/CAM	Computer-assisted design/computer-assisted manufacturing
Co	Cobalt
Cr	Chromium
CT	Computed tomography
DICOM	Digital Imaging and Communications in Medicine
DLC	Diamond-like carbon
eTMJR	Extended Temporomandibular joint replacement
FBGCR	Foreign body giant cell reaction
FDA	Food and Drug administration
LPM	Lateral Pterygoid muscle
MINORS	Methodological Index for Non-Randomized Studies
MTJ	Muscle-tendon junction
MIO	Maximal interincisal opening
MMO	Maximal mouth opening
Mo	Molybdenum
MSC	Mesenchymal stem cell
NICE	National Institute for Health and Care Excellence
OCEBM	Oxford Centre for Evidence-Based
LOE	Medicine Levels of Evidence
PEEK	Polyether ether ketone
PDS	Polydioxanone
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSI	Patient-specific implant
PTFE	Polytetrafluoroethylene
QoL	Quality of life
RCT	Randomized controlled trail
ROM	Range of motion
SLA	Large-grit sandblasting and acid-etching
SLIM	Synovial-like interface membrane

SS	Stainless steel
STL	Standard template library
Ti	Titanium
TJR	Total joint replacement
TKR	Total knee replacement
TMD	Temporomandibular disorder
TMJ	Temporomandibular joint
TMJR	Temporomandibular joint replacement
UHMWPE	Ultra-High Molecular Weight Polyethylene
VAS	Visual Analog Scale

List Of Publications

Included in Dissertation

De Meurechy N, Braem A, Mommaerts, M. Biomaterials In Temporomandibular Joint Replacement: Current Trends and Future Perspectives. Int J Oral Maxillofac Surg. 2018 Apr;47(4):518-533 2018

De Meurechy N, Mommaerts M. Alloplastic Temporomandibular Joint Replacement Systems: An Historical Overview – A Systematic Review. Int J Oral Maxillofac Surg. 2018 Jun;47(6):743-754

Van Bogaert W, De Meurechy N, Mommaerts M. Autologous Fat Grafting in Total Temporomandibular Joint Replacement Surgery. Ann Maxillofac Surg. 2018 Jul-Dec;8(2):299-302

De Meurechy N, Loos PJ, Mommaerts M. Postoperative Physiotherapy After Open Temporomandibular Joint Surgery: A 3-Step Program. J Oral Maxillofac Sur. 2019 May;77(5):932-950

De Meurechy N, Zaror C, Mommaerts M. Total Temporomandibular Joint Replacement: Stick to stock or optimization by customization? Craniomaxillofac Trauma Reconstr. 2020 Mar;13(1):59-70.

Mommaerts M, Nicolescu I, Dorobantu M, De Meurechy N. Extended total temporomandibular joint replacement with occlusal adjustments: pitfalls, patient-reported outcomes, subclassification, and a new paradigm. Ann Maxillofac Surg. 2020 Jan-Jun;10(1):73-79.

De Meurechy N, Verwilghen D, De Brucker Y, Van Thielen B, Mommaerts M. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: An animal experiment with radiological correlation. J Craniomaxillofac Surg. 2021 Apr;492 (4):256-268.

De Meurechy N, Aktan MK, Boeckmans B, Huys S, Verwilghen DR, Braem A, Mommaerts MY. Surface wear in a custom manufactured temporomandibular joint prosthesis. J Biomed Mater Res B Appl Biomater. 2022 Jun;110(6):1425-1438

Huys S, Braem A, De Meurechy N, Van De Sande R, Vander Sloten J, Mommaerts MY. Evolutionary Steps in the Development of a Patient-specific Temporomandibular Joint Prosthesis. Craniomaxillofacial Research & Innovation. 2022;7

De Meurechy N, Deman F, Verwilghen D, Mommaerts MY. Lateral pterygoid muscle enthesis reconstruction in total temporomandibular joint replacement: an animal experiment with histological verification. J Craniomaxillofac Surg.- SUBMITTED

De Meurechy N, Cras L, Verwilghen D, Ward MP, Mommaerts MY. Inflammatory cell response evaluation after total temporomandibular joint replacement in an animal experiment. Int J Oral Maxillofac Surg.- SUBMITTED

Other publications

De Meurechy N. Re: Review of emerging temporomandibular joint total joint replacements. Br J Oral Maxillofac Surg. 2020 Apr;58(3):379

De Meurechy N, Decoste C, Mommaerts MY. On the use of intraoperative 3D-RX C-arm imaging in orthognathic surgery: a prospective non-consecutive case series study. Oral Maxillofac Surg. 2022 Oct 24

Curriculum Vitae

Nikolas De Meurechy was born on the 21st of February 1989 in Sint-Niklaas, Belgium. He attended boarding school at the Sint-Jozef College Turnhout, completing his studies there in 2007. Following this, in the same year, he gained admission at the faculty of Medicine and Life Sciences at Hasselt University.

Upon completing his bachelor's degree, Nikolas commenced his master's studies in Medicine at the Catholic University of Louvain. It was during one of his internships that his interest in Oral and Maxillofacial Surgery was first sparked, prompting him to pursue further studies in Dentistry during his final year of Medicine. In 2015 he obtained his master's degree in Medicine followed by his graduation from Dentistry in 2018.

Between 2015 and 2018, Nikolas undertook a post-graduate training program in Oral Surgery, Oral Pathology and Oral Implantology at the Vrije Universteit Brussel, under the guidance of professor Maurice Mommaerts. It was during this period that his PhD-topic was conceptualized.

After obtaining both his degrees in Medicine and Dentistry, Nikolas continued his specialization at the European Face Centre, at the University Hospital Brussels. Under the guidance of Professor Maurice Mommaerts and Dr. Michael Büttner, he honed his skills. Additionally, he spent a year at the Elisabeth-TweeSteden Hospital Tilburg, where he was mentored by dr. Erik Nout. During this time Nikolas organized a multitude of congresses, as well as fundraising events for children with congenital maxillofacial malformations.

Upon obtaining his national certification as a specialist in Stomatology in 2020 and his board certification as Oral and Maxillofacial Surgeon in 2022, Nikolas joined the department of Oro-Maxillo-Facial Surgery at the Imelda Hospital and AZ Jan Portaels Hospital. The current department heads are Edward Swenden and Luc Van den Wouwer.

Nikolas currently resides in Bonheiden with his wife, Isabelle Smeets.

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