REFERENCES


ABSTRACT

Attempts to augment osseointegration led to the development of porous surface coatings that allowed a limited amount of bone ingrowth for additional mechanical stability. Trabecular Metal Dental Implants represent a significant paradigm shift from the traditional osseointegrated implant model with or without additional surface porosity. They retain the benefits of tapered, threaded implant designs while featuring a biomimetic porous section that approximates the structure and mechanical characteristics of natural bone. After placement, the implant is not just biologically anchored through conventional bone-to-implant contact, but actually becomes incorporated into living, vascularized bone that enters the internal pores of the implant. This process is called osseoincorporation. The design rationale of Trabecular Metal Material is thus to enhance secondary stability through a high volume of ingrowth into the pores and onto the struts of the material. This article reports on recent research studies that have documented clinical use of Trabecular Metal Dental Implants.

INTRODUCTION

Porous surface coatings were originally developed to enhance implant osseointegration by permitting bone ingrowth into the pores of the coating,\(^1\)\(^-\)\(^3\) however, the volume and quality of achievable bone ingrowth was limited by the number and size of the pores that the coating provided (Figure 1). For example, while a pore size of 100 μm was adequate for bone ingrowth, it was found that pores 150 μm in size were necessary for osteon formation inside porous materials, and pores greater than 300 μm were necessary to support the ingrowth of vascularized tissue.\(^4\)\(^-\)\(^6\) To address these issues, Zimmer introduced highly porous Trabecular Metal Material (Zimmer TMT, Parsippany, NJ), which has a structure similar to trabecular bone (Figure 2).\(^7\)\(^-\)\(^14\) With up to 80% porosity, Trabecular Metal Material more closely approximates the elastic characteristics of natural bone than titanium and other surgical metals used in orthopedics.\(^14\)\(^-\)\(^21\)\(^-\)\(^22\) It is fabricated by coating a vitreous carbon skeleton (~2%) with elemental tantalum (~98%) through a chemical vapor deposition process.\(^7\)\(^-\)\(^8\),\(^10\) The finished biomaterial is a nanotextured, osteoconductive framework of three-dimensional, interconnected pores.\(^10\)\(^-\)\(^11\),\(^19\)\(^-\)\(^20\) The pores of Trabecular Metal Material are adequately sized to accommodate the ingrowth of bone and blood vessels, and the formation of osteons inside the pores.\(^5\)\(^-\)\(^6\) The biocompatibility and corrosion resistance of the 3 combined constituent materials (titanium, vitreous carbon, tantalum) used in the implant design have been extensively documented\(^15\)\(^-\)\(^17\) and clinically evaluated through corrosion testing and more than 15 years of orthopedic implant use.\(^9\)\(^-\)\(^11\),\(^13\)\(^-\)\(^14\),\(^21\)

They have also been used individually at various times as dental implant materials.\(^15\)\(^-\)\(^18\)

![Trabecular Metal Material struts intersect at nodes to create dodecahedron-shaped cells with 12 interconnecting pores. Average pore size is approximately 440 μm with approximately 80% interconnected porosity.](image1)

![Examples of surface coatings with limited porosity and irregular pore sizes: commercially pure titanium bead (A); CSTi™ cancellous structured titanium (B); hydroxyapatite (C); titanium plasma spray (TPS) (D).](image2)

![Trabecular Metal Dental Implant](image3)
More recently, Trabecular Metal Material has been applied to the midsection of root-form, threaded, titanium alloy dental implants to create a three-dimensional, peri-implant bone ingrowth scaffold (Figure 3). Preclinical mechanical and animal studies on Trabecular Metal Dental Implants have been previously reported. This paper will provide an update on continuing Trabecular Metal Dental Implant research.

### BASIC SCIENCE AND CLINICAL APPLICATIONS

In a review of the basic science and clinical uses of Trabecular Metal Material, Bencharit et al. reported that tantalum is biocompatible, nontoxic to surrounding cells and was found to enhance osteoblastic differentiation processes in comparison to titanium and chromium in an in vitro study. The structure of Trabecular Metal Material presents a high surface area available for bone-implant contact (Figure 4) and allow angiogenesis and new bone formation inside the porous material (Figure 5). This combination of bone ingrowth into the porous material and conventional bone-to-implant contact (osseointegration/bone ongrowth) with the porous and solid implant surfaces is called osseointegration. Trabecular Metal Material’s average pore size is ~550 μm, which is thought to be an effective dimension for allowing osseointegration. As a biomimetic surgical metal, Trabecular Metal Material has an elastic modulus that is closer to that of both cortical and cancellous bone than other alloys used for dental implants. The latter allows for elastic deformation and load distribution throughout the structure to the surrounding bone, which may help to prevent stress shielding and its associated long-term bone loss.

### CERVICAL MICROGROOVES AND MICROTEXTURE

During the early years of modern implant dentistry, a 2-stage, delayed loading technique was considered a prerequisite for preventing any implant micromovements that could result in fibrous tissue encapsulation and clinical failure of the implant. More recent cellular animal studies have suggested that implant cervical regions with microgrooves, microthreads, microtextured surfaces or a combination of these features might help to foster bone attachment to the cervical region of the implant surface and bone formation inside the microgrooves to impede epithelial tissue downgrowth. The shapes and dimensions of the microgrooves themselves have also been reported to influence the behavior of epithelial and connective-tissue cells differently in vivo. Extending cervical microtexture to the top of the implant in the canine model has also been reported to reduce the amount of peri-implant crestal bone loss without adversely affecting soft tissue health; however, concern about the possibility of increased bacterial attachment to microtextured implant surfaces as compared to machined (turned) surfaces exposed to the gingival crevice in humans has been expressed in the dental literature. After 6 months of plaque accumulation in dogs, the roughened surfaces of acid-etched implants, which have been previously reported to be slightly rougher than Zimmer Dental’s MTX® Microtextured Surface Treatment, failed to influence any greater plaque formation or establishment of inflammatory cell lesions in the peri-implant mucosa than control implants with machined surfaces. Based on these findings and limited use in human subjects, Trabecular Metal and Tapered Screw-Vent Dental Implants with cervical microgrooves and surface microtexture extended to the top of the implant are available as new surgical options for the clinician (Figure 6).

### OSSEONCIRPORATION IN CANINES

Kim et al. conducted a randomized, prospective study in canin study to determine if Trabecular Metal and Tapered Screw-Vent Dental Implants would exhibit comparable levels of primary and secondary stability, and whether bone would grow into the porous section during 0-12 weeks of healing. A total of 24 Trabecular Metal Dental Implants (experimental group) and 24 Tapered Screw-Vent Dental Implants (control group) were placed in the healed mandibular extraction sites of 8 dogs. Each animal received 3 experimental and 3 control implants in a randomized sequence. Two dogs were sacrificed at each time interval of 2, 4, 8 and 12 weeks post implantation. Resonance frequency analysis was conducted at implant placement (Figure 7) and after animal sacrifice, and values were recorded in the unit’s (Ostell ISQ, Ostell AB, Gothenburg, Sweden) implant stability quotient (ISQ) values, which ranged from 1 (least stable) to 100 (most stable). Prior to
necropsy, calcein was injected to label newly mineralizing bone tissue.\textsuperscript{46} Histological sections from each dog were prepared and analyzed using (1) bright field, (2) calcein labeling and (3) Goldner’s trichrome stain to identify osteoid and mature bone (Figure 8).\textsuperscript{46-48} The effects of (1) implant type and (2) healing time on the histomorphometric and ISQ measurements were statistically analyzed.\textsuperscript{46-48}

The average cortical bone-to-implant contact ratio (CBIC) exceeded 70\% for both implant types and average ISQ values were $\geq 60$ for Tapered Screw-Vent and $\geq 65$ for Trabecular Metal Dental Implants at all time periods.\textsuperscript{46-48} There was no statistically significant difference in stability or CBIC between the two study groups. Inside the Trabecular Metal Material pores, new bone formation was first observed at 2 weeks, and in some pores new bone was observed to have grown across the full thickness (approximately 0.25 mm) at 4 weeks.\textsuperscript{46-47} It is important to note, however, that bone growth in dogs is approximately three times faster than bone growth in humans.\textsuperscript{49}

Histomorphometric analyses demonstrated that the highest percentage of newly mineralizing tissue occurred at week 2 (36.08\%) inside the pores of the Trabecular Metal Material, which was significantly lower at weeks 4 (17.69\%), 8 (22.40\%) and 12 (19.95\%) (p<.05).\textsuperscript{46-48} Similarly, the percentage of osteoid, the unmineralized, organic portion of the bone matrix that forms prior to the mineralization of bone tissue, was highest at week 2 (35.97\%) and significantly lower as weeks 8 (35.97\%) and 12 (41.94\%) (p<.05).\textsuperscript{46-48} Conversely, matured bone significantly increased at week 2 (3.32\%), 8 (9.01\%) and 12 (18.69\%) (p<.05).\textsuperscript{46-48} The authors\textsuperscript{46-48} concluded that the levels of osseointegration and implant stability were comparable for both the experimental and control implants in this study.

**OSSEOINCORPORATION IN HUMANS**

Clemente de Arriba et al.\textsuperscript{50} evaluated bone ingrowth and ongrowth (osseoincorporation) into Trabecular Metal Material cylinders (3 mm x 5 mm) implanted in the jaws of human volunteers. This prospective clinical study was performed in Spain at the University of Léon with oversight provided by the university’s institutional review board (phase I: patient recruitment and surgeries), and at the University of Alcalá (phase II: histological processing and analyses).\textsuperscript{50} A total of 23 healthy subjects with available bone of at least 7mm in width to accommodate 1 or more Trabecular Metal Material cylinders between or distal to preexisting dental implants were enrolled in the study.\textsuperscript{50} Study subjects were assigned to 1 of 4 groups (6 cylinders per group) designated for cylinder explantation at specific times.\textsuperscript{50} After signed patient consent, osteotomies were prepared and cylinders were placed flush with the mandibular or maxillary ridge and covered by the soft tissues without a barrier membrane.\textsuperscript{50} At the designated retrieval time of 2, 3, 6 or 12 weeks, the Trabecular Metal Material cylinders were explanted with 5.0 mm trephines and marked to indicate orientation at placement.\textsuperscript{50} The cylinders were buffered in 10\% formaldehyde and processed histologically.\textsuperscript{50} Slides were stained to identify cells (hematoxylin-eosin), osteoid tissue (Masson trichrome) and markers of developing and existing trabecular bone (toluidine blue).\textsuperscript{50}
After 12 weeks, ongoing osseoincorporation was observed, as evidenced by new bone formation inside the pores (ingrowth) and in direct contact with the external surfaces (ongrowth) of all samples (Figure 9).50 The mean percentage of bone fill inside the cylinders, as measured longitudinally from their outside surfaces, was 22.7% at a depth of 0.5mm (measurement field = ~0.5x5mm), 16.8% at a depth of 1 mm (measurement field = ~1x5mm), and 14.4% for the entire 3 mm x 5 mm cylinders.50 While very little osteoclastic activity or bone resorption was observed, bone was still in the maturation process.50 Although mucosal epithelium penetrated one sample, the presence of mesenchymal cells, bone formation activity and angiogenesis in all samples indicated developing osseoincorporation with no adverse tissue responses.50 Inside and on the outside surfaces of most samples, newly formed trabeculae with osteoid borders surrounded by osteoblasts were evident.50 Bone ingrowth into the Trabecular Metal Material cylinders primarily occurred along the lingual-buccal or -palatal surfaces.50 Implants exhibited the progressive formation of bone trabeculae alternating with vascularized tissue inside the samples in all but 1 sample, which had poor tissue formation inside the pores and some evidence of foreign body reaction.50

The earliest evidence of conventional osseointegration (bone ongrowth) reportedly occurs after a few weeks of early healing, and then progressively forms on the implant surface over a period of months or years.51 In the present study, bone ingrowth was both observable and quantifiable after 12 weeks of early healing.50 The presence of maturing and developing bone and blood vessels inside and outside the porous Trabecular Metal Material after 12 weeks of healing demonstrated that osseoincorporation was a progressive process.50 Additional information on the development and progression of osseoincorporation will be reported after the conclusion of this study.

Figure 10. Immediate Loading Proof-of-Principle Study: (A) Preoperative view of the edentulous space; (B) abutment in place at suture removal; (C) 2 weeks after definitive restoration; (D) 1 year after definitive restoration.

PROOF-OF-PRINCIPLE STUDY ON IMMEDIATE LOADING

Schlee et al.52-53 reported preliminary, 1-year results from an international, 3-year, prospective, proof-of-principle study conducted to evaluate the clinical efficacy of immediately loading Trabecular Metal Dental Implants in human subjects (Figure 10). Partially edentulous patients were enrolled after providing signed, informed consent.52-53 Based on the findings of earlier studies,54-56 the research protocol mandated that an implant insertion torque value of 35 Ncm or greater was required as a preliminary indicator of adequate primary stability for immediate loading.52-53 Study subjects with Type IV50 bone and/or implants with less than 35 Ncm of insertion torque were excluded from the study.52-53 After 6, 12, 24 and 36 months of functioning, each study subject was reappraised for evaluation.52-53 Study endpoints included implant survival rates, changes in marginal bone levels on standardized periapical radiographs evaluated by an independent clinician, and changes in oral health status.52-53

Thirty patients (full study group) were treated per protocol (minimum insertion torque less than 35Ncm) with a total of 37 implants placed in 1 or 2 premolar or molar locations in either jaw.52-53 Provisional single acrylic crowns were immediately delivered to the implants and placed out of occlusion.52-53 Soft tissues were allowed to heal for 7-14 days, then the provisional restoration was removed and the implants were definitively restored in occlusion with porcelain-fused-to-metal crowns.52-53 Since 54.1% (n=20) of the study implants had less than 1 year of clinical follow-up, the present interim analysis was limited to the first 22 consecutively placed implants in 17 subjects (10 women, 7 men) that completed 1 year of clinical follow-up to date (focus group).52-53 One implant failed to integrate, which left the full study group with a cumulative survival rate of 97.3% (n=36/37) to date.52-53 In the focus group, cumulative implant survival was 100% (n=22/22) with mean marginal bone loss of 0.43 ± 0.41 mm.52-53 There were no irresolvable problems or serious complications.52-53 The combination of Trabecular Metal Material’s high coefficient of friction58 against bone with the triple lead threads of the implant have demonstrated suitable stability and strength for withstanding immediate loading in humans under the controlled study conditions.

TRABECULAR METAL DENTAL IMPLANT LONGITUDINAL DATA COLLECTION PROGRAM

Schlee et al.52 reported interim data on a prospective, 5-year, Longitudinal Data Collection Program currently being conducted in 23 clinical sites across Europe. The program was designed to evaluate the clinical outcomes of Trabecular Metal Dental Implants placed in normal, uncontrolled populations that presented in routine clinical practices.52 Investigators are required to follow the implant’s Instructions for Use, and to use their own clinical judgments in patient selection and treatment.52 Of the enrolled subjects, 110 patients treated with 150 implants have completed 1-year follow-up at the time of this first interim report.53 Within this group, five implants failed to integrate, which resulted in a preliminary cumulative implant survival rate of 96.7% (n=145/150) at one year.52 In the continuing interim group,
five additional subjects with nine implants were excluded for violations to the product’s Instructions for Use: uncontrolled diabetes, substance abuse, mental instability, and smoking of more than 20 cigarettes per day.\textsuperscript{52} The remaining 141 implants in 105 subjects exhibited 97.9% survival at 1 year. In this uncontrolled population, 41% (n=43/105) of the subjects with 41% (n=58/141) of all implants placed had risk factors that could adversely influence implant survival and/or bone loss rates: smoking, osteoporosis, bruxism, acute dental or periodontal infections, and chronic corticosteroid use.\textsuperscript{52} Implant survival rates were 100% for implants placed in fresh extraction sites (n=19/19) and Type IV\textsuperscript{56} bone (n=20/20), respectively.\textsuperscript{52} Implants placed in association with bone augmentation achieved 98.4% (n=60/61) survival.\textsuperscript{52} The potential effects of design and surface treatment in the cervical regions of the implants as well as other local and systemic risk factors on crestal bone maintenance are currently undergoing analysis.\textsuperscript{52}

The Longitudinal Data Collection Program anticipated that subjects still harboring risk factors that led to their edentulous state may likely constitute a high percentage of implant candidates that clinicians encounter in daily practice.\textsuperscript{52} Diseases and lifestyle choices are often the leading causes of tooth loss.\textsuperscript{52} The root cause for the three implant failures in the Longitudinal Data Collection Program were not directly related to the study device: preexisting infection, systemic infection induced sinusitis, and iatrogenic disruption of implant healing in a site with simultaneous bone augmentation by a non-sterile probe.\textsuperscript{52} In the event of implant failure, the presence of porous Trabecular Metal Material did not impede implant removal for grafting.\textsuperscript{52} In this interim analysis, Trabecular Metal Dental Implants routinely achieved stable prosthetic restorations.\textsuperscript{52}

**PERI-IMPLANTITIS STUDIES**

Trabecular Metal Material is positioned approximately 4.25 mm below the prosthetic platform of the implant (Figure 3), which means that significant crestal bone loss would have to occur before the Trabecular Metal Material would be exposed. The most likely cause of such extensive crestal bone loss would be peri-implantitis, which is an infection of the supporting tissues adjacent to the surface of the implant. Peri-implantitis is caused by the same anaerobic microbes and follows a similar progression of tissue destruction as periodontitis around natural teeth.\textsuperscript{59} Because implants lack the same biologic seal that helps to protect natural dentition, the progressive tissue destruction caused by peri-implantitis tends to occur more rapidly than the tissue destruction that occurs with periodontitis.\textsuperscript{59} All dental implants are susceptible to peri-implantitis under certain adverse clinical situations. Any dental implant with peri-implantitis and 4.0 mm of crestal bone loss would have to be removed if clinical interventions could not alleviate the infection and pathologic progression of bone loss.

In an unpublished canine study\textsuperscript{60} (#1918-001) sponsored by Zimmer Dental, three groups of four or eight male mixed-breed hound dogs were surgically implanted with control (Tapered Screw-Vent Implants) and test (Trabecular Metal Dental Implants) devices into osteotomies created by drilling into the remaining bone immediately after tooth extraction. All implant sites were located in circular defects in the right and left mandible (P3, P4, M1, and M2 region).\textsuperscript{60} Each animal was implanted with four control or test devices (one per region) in the left side and four control or test devices in the right side.\textsuperscript{60} The devices were implanted on Day 0 and two animals per time point in Group 1 (Phase I) were allowed a 14, 28, 56, or 84 day recovery period.\textsuperscript{60} For Phase II, on Day 84, one group of four animals underwent a surgical procedure in which peri-implantitis was induced, and the other group of four animals underwent a sham peri-implantitis procedure.\textsuperscript{60} Animals in Phase II remained on study for a 168 (+1) or 266 (+1) -day recovery period (post-extraction/implantation procedure).\textsuperscript{60} Histopathological and histomorphometric findings showed that the Trabecular Metal Dental Implants performed similarly to the Tapered Screw-Vent Dental Implants in the presence of experimentally induced peri-implantitis, but no bacteria was found inside the pores of the Trabecular Metal Material itself.\textsuperscript{60}

In one case report\textsuperscript{61}, the authors concluded that Trabecular Metal Material not only promoted bone ingrowth for secondary implant stability, but may also possess a capacity to resist peri-implant inflammation. A Trabecular Metal Dental Implant reported\textsuperscript{61} to have failed as a result of peri-implantitis in humans was placed in a 54-year-old female exhibiting moderate chronic periodontitis after clinically successful treatment for the disease.\textsuperscript{61} After placement, the patient was not seen for 4 months because of unrelated medical issues.\textsuperscript{51} At the surgical re-opening 4 months after implant placement, peri-implant inflammation affecting one-third of the implant was observed.\textsuperscript{61} With patient consent, the implant was removed for histologic analysis.\textsuperscript{61} Histology highlighted a greater amount of peri-implant bone apposed to tantalum Trabecular Metal Material than to the titanium surfaces.\textsuperscript{61} The veracity of this finding cannot be determined without additional long-term studies.

**DISCUSSION**

Brånemark\textsuperscript{62} defined osseointegration as “a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant.” The direct connection at the bone-implant interface has been further described as a partially calcified proteoglycan layer with a minimal thickness of 200 Å.\textsuperscript{60} At a resolution of 30-50 Å, calcified tissue was observed in direct contact with the titanium implant surface without an intervening tissue layer.\textsuperscript{60} Bone cells and collagen bundles were separated from the implant surface by the proteoglycan layer.\textsuperscript{53} In contrast, the design rationale of Trabecular Metal Material is to enhance secondary stability through a high volume of ingrowth into the pores and onto the struts of the material. Some of the benefits provided by this new form of anchorage have been highlighted in this paper. Further research with long-term follow-up will better elucidate the outcome provided by Trabecular Metal Dental implants and the osseointegration mechanism.