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CeraNews | TO THE POINT

HEALTH ECONOMICS & POLICY | OUTCOMES RESEARCH | IMPLANT MATERIAL

Combating Infection: The Role of Implant Materials in Orthopedics and Dentistry

In 1952, the Swedish anatomy professor Per-Ingvar Brånemark was investigating as young researcher the anatomy of blood flow. One of his experiments studying the microcirculation in rabbit bone tissue resulted in the discovery of osseointegration and the beginning of implantology. Our colleague's original intention was to apply this finding to joint replacement, but then he turned his back on orthopaedics and dedicated his research to dental implantology.
It took a while before his research allowed a breakthrough. Still in 1974, the American Dental Association suggested that dental implants should not be used for routine clinical practice! History taught us that perseverance would reward Prof. Brånemark's efforts. Today, dental implantology records excellent outcomes, similar to what we see in hip or knee replacement. Together with this success, though, we also share a common enemy: bacteria.
Whereas orthopaedic surgeons fight against periprosthetic joint infection in hip and knee arthroplasty, dental implantologists face peri-implantitis and oral mucositis. Both disciplines can learn from each other in the battle against infection and understand the association between implant materials and host response. (...)

Javad Parvizi MD, FRCS
Rothman Orthopaedic Institute at Thomas Jefferson University in Philadelphia, PA

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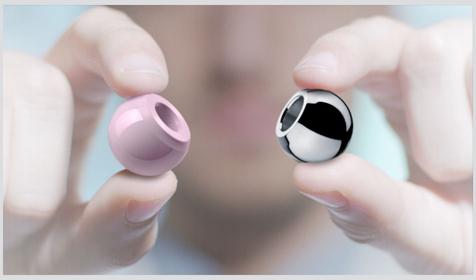
Reducing the Risk of Postoperative Infection with Ceramic in THA



Earlier studies suggest that metal heads are associated with an increased rate of revision for PJI. The causal relationships or mechanisms of infection with metal bearings surfaces are not yet fully understood. A recently published study by the research team led by J. Parvizi MD, FRCS, aimed to investigate this relationship, using prospectively collected data from Rothman Institute internal total hip replacement database.

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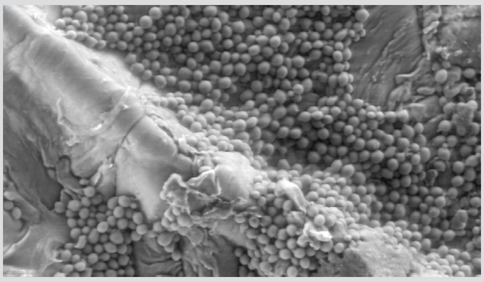
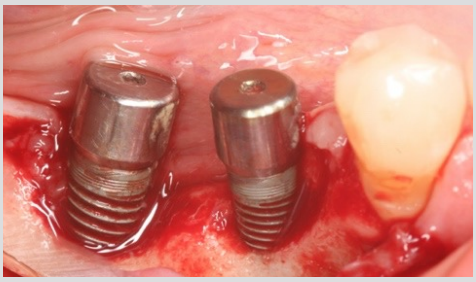
Bacteria and Biofilm Formation on Biomaterials



Fighting bacteria and infection is a concern that orthopedic surgeons and implantologists have in common. Bacteria strains and biofilm dynamics may differ, but the basic processes are the same. Microbial biofilm naturally adheres to implant surfaces. Research led by Prof. L. Rimondini at Università del Piemonte Orientale "A. Avogadro", brought a huge contribution to understand the mechanisms of interaction of bacteria with implant surfaces.

Understand the background

Peri-implantitis: Definition, Treatment and Implant Material-Associated Metallosis



Like orthopedic surgeons, dental implantologists fear the pathogenic bacteria, which lead to peri-prosthetic joint infection in orthopedics or in case of oral implants to an overreaction of the immune system leading to peri-implantitis. Prof. Dr. G. Romanos, periodontist at Stony Brook University, NY, shares more insights about this destructive inflammatory process in the oral cavity and possible association with the implant material.

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Combating Infection: The Role of Implant Materials in Orthopedics and Dentistry

Javad Parvizi MD, FRCS
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Whereas orthopaedic surgeons fight against periprosthetic joint infection in hip and knee arthroplasty, dental implantologists face peri-implantitis and oral mucositis. Both disciplines can learn from each other in the battle against infection and understand the association between implant materials and host response.

Prof. Lia Rimondini is an expert in development and pre-clinical characterization of implantable biomaterials. As part of her research field, she explored the role of bacteria and biofilm formation on dental implant materials. She extended her research to orthopaedic implant materials and could confirm what she had discovered for oral implants: bacteria are generally more prone to adhere to metal than to ceramics. In other words, ceramics accumulate less biofilm than metal or even polymers. In her contribution Prof. Rimondini compares the behavior of bacteria and biofilm formation in both body regions.

Prof. Romanos is an implantologist and professor of dentistry. Routinely, he has long used titanium implants. Like many of his colleagues, he faces a high prevalence of inflammatory processes after implanting titanium implants. He has dedicated his life to investigating the mechanisms causing peri-implantitis and peri-implant mucositis. As in orthopaedics, the reasons are multifactorial. However, the advances in ceramic implantology and the improvement of ceramic materials convinced him that using ceramic could cause less plaque formation and less inflammation around zirconia implants. Current studies support his observations.

At Rothman, we routinely use ceramic heads in total hip replacement because our research has shown the impact of material on the risk of infection. At our institution, we compared the infection rates of our patients treated with metal-on-polyethylene (MoP) to those treated with ceramic-on-polyethylene (CoP) implants. Our findings, recently published in the Journal

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of Orthopaedic Research, show a significantly higher incidence of infection in patients with metal heads. We suspect that the reasons are multifactorial, but a specific mechanism related to leucocyte recruitment to metal implants can be an explanation.

More than ever, nurturing an interdisciplinary research culture with solid bonds between basic research and clinical research appears to be the key to understanding our patients and their comorbidities, and selecting adequate treatment for them.

Javad Parvizi MD, FRCS

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Reducing the Risk of Postoperative Infection with Ceramic in THA: A Comparative Study

By Emanuele Chisari MD and Javad Parvizi MD, FRCS

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Is there a difference in infection rates between MoP and CoP bearing couples? A study recently published by Rothman Institute shows significantly higher infection rates when metal femoral heads are involved.

Due to concerns regarding early revision and complications associated with the use of metal-on-metal (MoM) couplings[1], metal-on-polyethylene (MoP) and ceramic-on-polyethylene (CoP) have become the most commonly used bearing surfaces for total hip replacement in the USA. While MoP bearings have several advantages over MoM, they have also recently been shown to release metal particles and ions. Upon contact with host tissue and joint fluid, these ions and particles can enhance tribocorrosion mechanisms due to the combined action of mechanical loading and chemical corrosion.[2,3,4] Thus, similarly to MoM bearings, CoCr wear particles and cobalt and chromium ions can be found in the tissue surrounding the implant as well as in systemic circulation[5,6] in patients with MoP bearings. Ceramic has become the material of choice in the US[1] due to the proven low incidence of implant failure with CoP bearings[7,8] and the ceramic heads' ability to mitigate fretting corrosion.[9]

Earlier studies also suggested that metal heads are associated with an increased rate of revision for post-surgical infection, namely periprosthetic joint infection (PJI).[10-14] However, the studies were not without limitations and further research was needed.

MoP vs CoP cohort

In a recently published study[15], we aimed to investigate this relationship, using prospectively collected data from our internal total hip replacement database. Our primary endpoint was the risk of infection based on the 2018 International Consensus Meeting (ICM) definition of periprosthetic infection.[16] We reviewed a consecutive series of patients who underwent primary total hip arthroplasty (THA) between 2015 and 2019. 6,052 of them received a CoP and 4,550 a MoP bearing. Patients inconclusive for PJI were excluded based on the 2018 ICM definition. Both acute and chronic PJI were included.

Patients who did not meet either of these criteria for infection at the time of most recent follow-up were considered uninfected. For patients undergoing revision for reasons connected to infection, culture results and causative pathogens were identified. Evidence of adverse local tissue reaction (ALTR) noted in the operative report based on macroscopic observation or patient record was also recorded.

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The statistical analysis consisted of descriptive statistics, univariate analysis, and regression modeling. Compared to the CoP patient cohort, the MoP cohort was older, included more females, had a higher body mass index, and was more commonly affected by comorbidities.

Four times more reinfections with MoP

The most important finding was the significantly higher rate of PJI in patients receiving MoP implants compared to CoP (2.40% vs 1.64%). This association remained significant when adjusted for confounders including age, sex, BMI, and Charlson Comorbidity Index. While we did not find a significantly higher rate of reinfection within one year of revision, after the first year, patients initially treated with MoP showed reinfection rates that were almost four times higher than those seen in CoP patients (12.6% vs 3.6%, p=0.031). This finding is consistent with basic science studies suggesting permanent pro-inflammatory changes promoting leukocyte recruitment to the environment surrounding prosthetic joint implants. This may be a result of the hypothesized "trojan horse" mechanism.[17-19]

Total revision-free survivorship (p=0.017) and infection-free survivorship (p=0.006) were both significantly higher in the CoP group. While rates of ALTR were similar between the groups, these findings provide strong clinical evidence that MoP implants present a higher risk for PJI than CoP implants.

Chemotaxis

The causal relationships or mechanisms of infection with metal bearings surfaces remain unclear. It is well established that the local toxicity of these metal ions is associated with ALTR, adverse reactions to metal debris (ARMD), inflammatory pseudotumors and local osteolysis.[20,21] Based on alterations in native host tissues and increased T-lymphocyte migration, the local and systemic toxicity of these metal ions has also been increasingly taken into focus.[22-24] One of the possible mechanisms considered describes that CoCr wear particles and ions released by the implant induce a pro-inflammatory response that ultimately chemoattracts leukocytes, including macrophages and neutrophils, to the surgical site. In other words, there is a "trojan horse" mechanism: the neutrophils and macrophages transport intracellular pathogens from a remote site and bring them to the prosthetic joint via chemotaxis because of specific cytokines at the site of ALTR.[17-19]

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Despite the lack of a definitive description of the biological mechanisms involved, all clinical evidence to date shows an increased risk of biological complications with metal bearings. These findings may also lead the orthopaedic community to further consider ceramic bearing surfaces for other joint replacements such as total knee arthroplasty or dual mobility hip implants. Previous data have shown that modular junctions for each of these implant types create cobalt and chromium ions.

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Bacteria and Biofilm Formation on Biomaterials

By Prof. Lia Rimondini

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While both deal with inserting foreign bodies into bone, there are many fundamental differences between arthroplasty and dental implantology. However, with peri-implant infection they have one major complication in common. Bacteria strains and biofilm dynamics may differ, but the basic processes are the same. The studies show that the role of implant material regarding infection is similar in both fields.

Nowadays, implants used in joint replacement and in oral implantology are common devices used to treat different diseases and impairments with different aims. Arthroplasty intends to reduce pain and to restore function; oral implantology is meant to replace teeth lost because of injury, periodontal disease or agenesia. The fight against bacteria and infection is one thing orthopedic surgeons and implantologists have in common.

Differences between joint and dental implants

Periprosthetic joint infection, mucositis and peri-implantitis all lead to the failure of the implant but differ in several aspects:

1. Whereas periprosthetic joint infection (PJI) can lead to a significant incidence of mortality, an infection of the oral implant is not life-threatening. Peri-implantitis is rather uncomfortable for the patients and costly due to the necessity of implant replacement.
2. Infection is more frequent in dentistry than in orthopedics. The 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions extensively reviewed the incidence and the comorbidity of oral mucositis and peri-implantitis concluding that both conditions are very frequent especially in patients with a medical history of periodontitis.[1]
3. In joint replacement, periprosthetic joint infection is involved in 14-29% of the implant failures.[2] While artificial joints do not pass the sterile barrier, dental implants are transmucosal devices. The part below the soft tissue sealing must be sterile while the part above it naturally hosts the oral microbiota. Thanks to the soft tissue sealing at the implant's neck microbiota does not invade the bone below.
4. Microbial biofilm naturally adheres to oral implant surfaces coronally to the epithelium attachment. The infection disease is not due to the presence of bacteria itself but to an unbalanced microbiota ecosystem with prevalence of Gram-negative anaerobic bacteria that trigger and boost inflammation and then invade the tissues. Bacteria adhesion and biofilm formation differ between biomaterial surfaces used in orthopedic implants. Significantly less biofilm is formed on ceramic surfaces compared to polyethylene and metal.[3]

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5. The presence of an orthopedic implant reduces the bacterial concentration required to induce infection by 100,000 times[2], since bacteria can survive in the periprosthetic environment by adhering to the implant. While in arthroplasty periprosthetic joint infections are due to a small number of bacteria species, mainly nosocomial, in oral implantology the infection is caused by a complex biofilm composed of many different species.[4]

Biofilm formation and development

The formation and composition of a biofilm strongly depends on the substrate surface on which it grows. The surface properties play a more important role in dentistry than in orthopedics, even if the formation of the biofilm is very similar (Fig. 1). In the oral cavity, the formation starts when planktonic bacteria coming from saliva approach the implant surface and initially interact with it by electrostatic forces. Once adherent, bacteria improve the adhesion on the surface via receptor-ligand interaction. They proliferate and secrete different kinds of macromolecules, principally polysaccharides and glycolipids, known as extracellular polymeric substances, which embed and protect the newly formed bacteria community.

In joint replacement, biofilm formation begins when planktonic bacteria, mostly coming from the surgical incision site or from independent infection sources, escape immunological surveillance and adhere to the implant surface.[5] In peri-implant joint infection, the bacteria

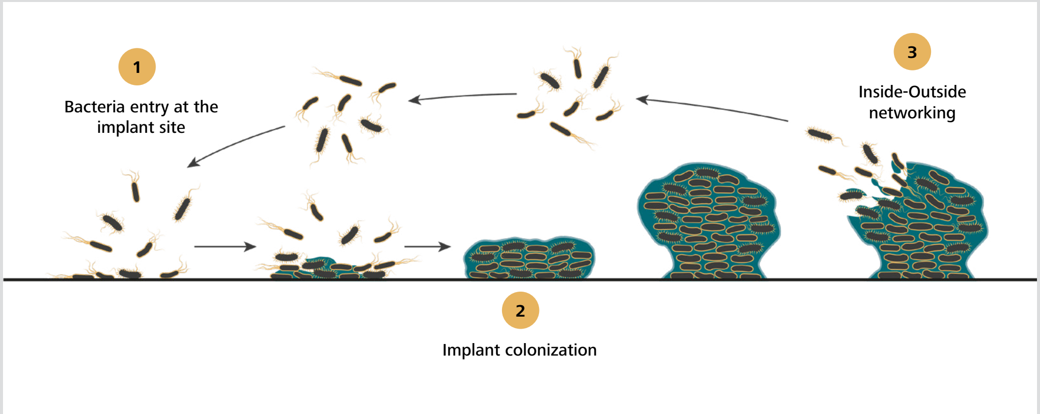

Fig. 1: Scheme of the bacteria-biofilm formation on implants: 1) bacteria approaching and attaching on the surface; 2) biofilm growth; 3) bacteria detachment and infection propagation.

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community is formed by few species. The most common bacteria involved are nosocomial strains, often antibiotic-resistant, including the so-called ESKAPE bacteria (*S. aureus, S.epidermidis, Enterococcus faecium, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp.*).[6]

In the oral cavity, the composition of the biofilm which grows on natural surfaces and on devices is made up by commensals and changes from the early to the late stages. In the first phases aerobic and Gram-positive commensals bacteria are predominant; during maturation the community is enriched by pathobiontic Gram-negative anaerobic bacteria. Therefore, the easy strategy to maintain the oral peri-implant tissue in a healthy condition is to keep the colonization of the implant surfaces at the level of the early stages rather than to avoid any colonization.

In case of dental implants, daily hygiene procedures contribute to remove the biofilm mechanically. In arthroplasty, apart from clinical protocol optimizations, the use and design of "low contamination devices" such as highly polished or modified metallic surfaces and ceramics could be an alternative strategy.

Biofilm viability of different materials

In a multicentric and interdisciplinary study[7], we compared the bacteria adhesion mechanisms on CoCr, XLPE, alumina (BIOLOX®*forte*) and zirconia-toughened alumina (ZTA) ceramic (BIOLOX®*delta*). The MTT evaluation of the biofilm formed on the surface of the investigated orthopedic materials indicated the highest biofilm viability for XLPE and CoCrMo surfaces after 24 hours (Fig. 2).

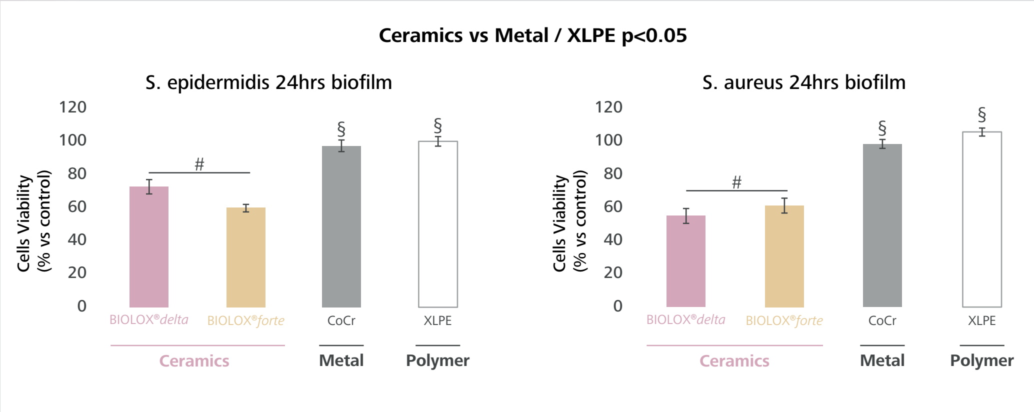

Fig. 2: Both ZTA (BIOLOX®delta) and alumina (BIOLOX®forte) resulted to be significantly less contaminated ($p < 0.05$, indicated by §) than XLPE and CoCrMo, after 24 hours infection, with both bacteria strains, S. aureus and S. epidermidis, respectively.

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In comparison, ceramic samples showed reduced bacterial adhesion and slower biofilm development with both bacteria strains tested (*S. aureus* and *S. epidermidis*).

In-vitro and *in-vivo*, ceramic materials have shown their ability to accumulate thinner biofilm in the short term compared to metal and polymers (Fig. 3).[8] These observations suggest that ceramic surfaces may contribute to the prevention of prosthetic joint infection and oral peri-implant mucositis (if associated with proper daily biofilm removal). The arthroplasty registries demonstrated the lower risk of revision for deep infection in hip replacement at long term with ceramic bearings. In contrast, there is no clear long-term information available in dental implantology, mainly due to the limited available literature and the absence of broad-based national registers. The risk factors for the incidence of infection are manyfold and – just as in arthroplasty – only observational studies including the analysis of granular and robust registry data will allow to detect the independent factors associated with implant infection in dental implantology, too.

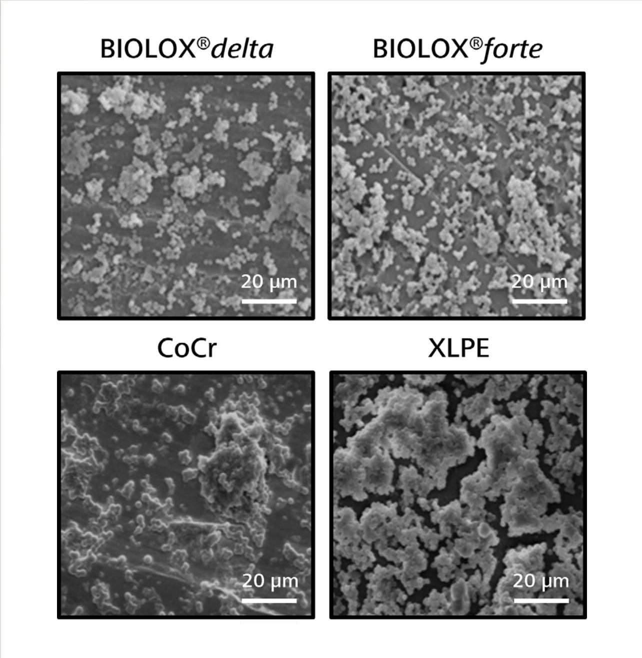

Fig.3: ZTA (BIOLOX®delta) and alumina (BIOLOX®forte) showed less colonization by Staphylococcus aureus than metal surfaces (p<0.005) and XLPE (p<0.005).

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Peri-implantitis: Definition, Treatment and Implant Material-Associated Metallosis

By Prof. Dr. Georgios E. Romanos

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Stony Brook University, School of Dental Medicine in Stony Brook, New York, NY

In arthroplasty and in dental implantology, implants are identified as foreign bodies by the immune system. A mild immune reaction combined with an appropriate inflammation around the implant serve to protect implants from bacterial attacks for decades. What all orthopedic surgeons and implantologists fear are the pathogenic bacteria, which lead to peri-prosthetic joint infection in orthopedics or in case of oral implants to destructive inflammatory processes known as peri-implant mucositis and peri-implantitis.

Introduction

The clinical success of dental implantology and titanium implants in particular is indisputable. There is evidence of oral implants with a follow-up of 30 years and case reports of survival of over 50 years. This success is intimately linked to the discovery of the osseointegration concept by P.I. Brånemark in 1952 and his following breakthrough research on implants made of biocompatible titanium. Titanium - which is also used in orthopedics - is considered in dental implantology as the gold standard today. Despite these excellent results, implantologists have all been facing cases in which bone and soft tissues surrounding dental implants become inflamed, seemingly infected and in some instances, leading to peri-implant diseases and implant loss. In implantology, we differentiate between peri-implant mucositis and peri-implantitis.

Definition

Peri-implant mucositis can be defined as an inflammatory lesion of the soft tissues (mucosa) surrounding the dental implant. Peri-implantitis is an inflammatory lesion of the mucosa affecting the supporting bone (crestal bone) with crestal bone loss and loss of osseointegration. Derks et al. report a prevalence of 43% for peri-implant mucositis and Jepsen et al. estimate that the prevalence of peri-implantitis could reach 22% (Figs. 1, 2).[2,3] Peri-implantitis is usually accompanied by crestal bone loss (Fig. 3) and soft tissue changes in the peri-implant sulcus, which can be diagnosed by an increase in bleeding on probing (BOP) more than 5mm over previous examinations and/or suppuration[8] (Fig. 4). Also excess of residual cement might contribute to crestal bone loss (Fig. 5).[7]

The underlying inflammatory processes are still not completely understood. However, increasing evidence shows that the host and the peri-implant conditions might play a pivotal role in the development of peri-implantitis (Figs. 1, 2).[2,3]

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Oral biofilm, oral hygiene, poorly controlled diabetes, smoking and peri-implant plaque have been identified as independent risk factors enabling the development and progression of peri-implantitis. Also, the routinely usage of screw-retained implant-supported restorations seem to be associated with a higher prevalence of peri-implantitis. Having said that, the exact etiology remains often unknown.[4-6] And patients with titanium implants and with a good oral hygiene can also develop peri-implantitis.[5]

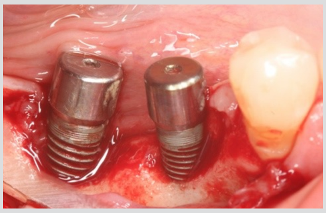

Fig. 1:
Severe peri-implant bone loss leading to unfavorable implant prognosis

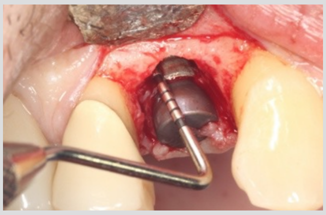

Fig. 2:
Peri-implant bony defect of 9mm due to peri-implantitis

Fig. 3:
Soft tissue complication around a dental implant with crestal bone loss

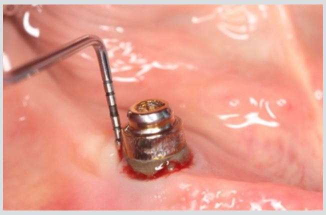

Fig. 4:
Bleeding on probing at the peri-implant tissues (peri-implantitis)

Fig. 5:
Peri-implant defect due to excess of cement

Metallosis

When comparing implantology and joint replacement, we can observe similarities in foreign body reaction and failure pattern.[9] The release of wear particles and metal ions from a CoCr femoral head in hip replacement can trigger fretting corrosion mechanisms and lead to what surgeons call "taperosis" or "trunnionosis". In oral implantology, several studies have shown that the release of titanium particles and ions into the surrounding tissue can lead to bone loss around some dental implants.[10-14] This process has been named "metallosis".

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Treatment

There are several conservative and surgical approaches available for the treatment of peri-implantitis. Non-surgical therapies are always the preferred treatment, while it is important to maintain implant cleanliness and oral hygiene. However, it is necessary to select approved oral hygiene instruments and to prevent surface damage with consequent generation of titanium particles and release of titanium ions.[19-21] Surgical non-regenerative approaches include implant surface decontamination, degranulation of the defect, bone grafting and implantoplasty which can also lead to good clinical outcome.[22] There is still ongoing research on methods for the decontamination of dental implants.[23] The use of lasers was shown to be potentially beneficial in the treatment of peri-implantitis.[24]

Ceramic implants as a prevention strategy?

Recently, ceramic implants were introduced as alternative strategy with the aim of preventing the development of peri-implantitis and bone loss (Fig. 6). Compared to titanium implants, studies show that zirconia implants are associated with lower plaque and bleeding scores.[15-17] Ceramic implants offer high resistance to corrosion, better peri-implant soft tissue conditions and less inflammation as well as lower oral biofilm adhesion. Apart from the excellent mid-term clinical outcomes, such as a high cumulative survival rate and a low level of average crestal bone loss, zirconia implants contribute to the aesthetics of dental restoration. The white color of zirconia comes close to that of natural teeth.[15,18] If the long-term clinical results of ceramic

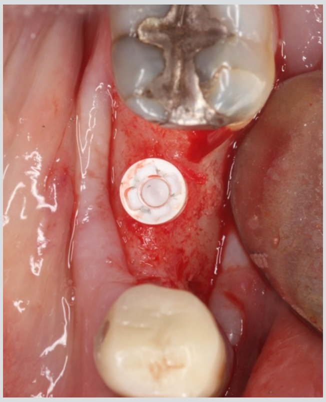

Fig. 6:
Ceramic implant for the replacement of the missing mandibular molar

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implants are confirmed to be equal to or better than the metal alternative, there is potential for a general switch to ceramics in the future.

Conclusion

Based on current evidence and studies suggesting that zirconia dental implants are associated with less peri-implant inflammatory reactions and less crestal bone loss (Fig. 7), we decided to investigate the behavior, the mechanical stability and the clinical outcomes of ceramic implants at our institution. The first patient implantations look promising. But long-term studies will be required to develop strong evidence and convince the large majority of dental implant surgeons to use zirconia dental implants as routinely as orthopedic surgeons do in hip replacement.

Fig. 7:
Characteristic crestal bone stability in an 82-year-old patient with ceramic implants in areas [24, 25] (10 years after placement) showing no crestal bone loss compared to the adjacent periodontally involved teeth

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