Dental implants surface characteristics (modifications) as a risk factor for peri-implantitis.

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Preface

In this master`s thesis I wrote an article review about "Dental implants surface as a risk factor for peri-implantitis". I wanted to investigate a subject about dental implants, and my supervisor, professor Håvard J. Haugen helped me to narrow down this subject to the title of this study. I also want to thank him, and co-adviser, postdoctoral fellow Qianli Ma for their help and contributions in this work.

Porsgrunn, May 2023

Elena Mikalsen

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Abstract:

Background, Purpose:

This review paper aims to provide an overview of the impact of dental implant surfaces on the development of peri-implantitis.

Over the last decades, dental implantation has become a popular treatment for replacing missing teeth due to its good clinical results. Moraschini et al. revealed survival and success rates of implants of 94.6% ± 6% and 89.7% ± 10.2% after functional loading periods of 13.4 years and 15.7 years, respectively (Moraschini et al., 2015).

Now exist a significant diversity of endosseous dental implants with various surface characteristics (Smeets et al., 2016). Many methods and modifications of the implant surfaces have been developed to improve osseointegration, for reduction of bacteria-related infections that cause peri-implantitis, and extension of implants lifetime (Ogle, 2015), (Elias & Meirelles, 2010), (Albrektsson & Wennerberg, 2019), (Kligman et al., 2021).

While laboratory in vitro and in vivo research demonstrates promising results of implants with modified surfaces, long-term clinical observations are few and show controversial results (Albrektsson & Wennerberg, 2019). Experiments on animals show that the surface characteristics of modified implants negatively impact the progression of peri-implantitis.

However, clinical studies on humans do not show any significant difference in the development of peri-implantitis around implants with different surface modifications.

Methods: This study uses relevant full-text articles in the English language, reviewed in PubMed, and includes a systematic review and meta-analysis articles.

Conclusion: The result of this study indicates the necessity of long-term clinical observations of peri-implantitis to clarify implant surface role in this issue.

Keywords:

Peri-implantitis, risk factors for peri-implantitis, treatment of peri-implantitis, dental implant surface modification and meta-analysis.

Introduction:

A. Definition of peri-implantitis.

Peri-implantitis is a major complication of dental implant therapy that results in inflammation of the peri-implant soft tissues and loss of supporting bone (Schwarz et al., 2018). The etiology of peri-implantitis is multifactorial, with a variety of host- and implant-related factors contributing to its development.

B. Prevalence of peri-implantitis.

Studies have reported varied prevalence of peri-implantitis. The prevalence of peri-implantitis was 16.4% and 7.3% for patients and implants, respectively (Dalago et al., 2017). Wada et al. reported that the prevalence of peri-implantitis at the subject and implant levels were 15.8% and 9.2%, respectively after three years of function (Wada et al., 2021). Diaz et al. concluded that the prevalence of peri-implantitis was 12,53 % at the implant level and 19,53 % at the patient level. Studies with a follow-up period from 5 to 9 years and with more longevity did not show significant differences at implant and patient levels (Diaz et al., 2022). Renvert et al. determined peri-implantitis in 22.1% of cases after 20-26 years of titanium dental implants in function at the patient level (Renvert et al., 2018). In general, peri-implantitis is a common condition that represents an implantology issue.

C. Importance of the implant surface on the development of peri-implantitis.

Dental implants' success is affected by the formation of stable direct contact between the implant and surrounding living bone, or osseointegration (Albrektsson et al., 1981). The importance of the quality of titanium surfaces for cellular contact and osseointegration of dental implants was highlighted by Albrektsson in 1981 (Albrektsson et al., 1981). In addition, improved cellular contact and osteointegration have an important role in preventing biological complications of dental implantation, including peri-implant mucositis and peri-implantitis.

The surface characteristics of dental implants have been shown to play a crucial role in their clinical success, and several studies have investigated the relationship between implant surface modifications and the development of peri-implantitis. Understanding the impact of implant surface on the development of peri-implantitis is critical for designing implant surfaces that promote osseointegration while minimizing the risk of implant failure due to peri-implantitis.

The paper will also explore the factors affecting implant surface modifications, including manufacturing processes and surface treatments. Clinical relevance of implant surface modifications will be discussed, including clinical outcomes, long-term stability, and cost-effectiveness. Finally, the paper will discuss prevention and treatment options for peri-implantitis related to implant surfaces, as well as future directions in the field.

In conclusion, the impact of implant surface on the development of peri-implantitis is a complex issue that requires careful consideration. This review paper will provide a comprehensive overview of the literature on this topic and will be of interest to dental professionals, implant manufacturers, and researchers in the field.

Materials and methods:

An electronic literature search of the PubMed database was conducted for articles published between 1 January 1983 and 01 May 2023. Studies characterising the influence of dental implant surface characteristics on peri-implantitis include animal studies, in vitro experimentation, and clinical trials.

8926 studies were identified in the search strategy and 89 studies were included. Searching in PubMed, with keywords as "peri-implantitis+ risk factors+ implant surface ", shows 53 full-text articles about this subject, with a timespan from 1999 to 01 May 2023. 3513 full-text articles were found in PubMed with a search of "peri-implantitis " from 1991 to 2023. A search on "peri-implantitis+ risk factors " yielded results in 403 full text articles from 1996 to 2023. "Osseointegration + dental implant surface " gave results in 3329 full-text articles from 1983 to 2023, and "peri-implantitis+ dental implant surface " gave 919 results from 1994 to 2023. “Peri-implantitis+ treatment+ implant surface” results in 709 articles from 1994 to 2023 with significant increase in last decay.

Most of these articles represent a systematic review and meta-analysis of the subject.

89 articles were included in this study.

Literature search strategy:

The search strategy incorporated the examination of electronic databases PubMed, searches for articles published in English, with the timespan 1983- 2023. The following keywords were used: Peri-implantitis, risk factors for peri-implantitis, treatment of peri-implantitis, dental implant surface modification and meta-analysis. A screening of relevant publications' references improved the search's sensibility.

Inclusions and exclusions criteria:

The initial search resulted in 8926 articles. Inclusions criteria involved articles published in English, with access to the full text until May 2023, reporting clinical and laboratory implantation outcomes, with different implant surface modifications and possible influence of implant surface characteristics on peri-implantitis. Exclusion criteria: studies not published in English; studies not reporting details concerning characteristics of dental implants surface or peri-implantitis.

Implant surfaces and their impact on peri-implantitis:

A. Characteristics of implant surfaces.

Conventional implant systems consist of an implant and an abutment that fixed to the implant and connects implant with restoration. Integration of implant system with bone and soft tissues depends on implant design and such properties of implant surfaces as surface chemistry, topography, surface charge, thickness of oxide layer and wettability. Both implant and abutment surfaces should be unfavourable to attachment of bacteria and formation of biofilm, contribute tight adherence of peri-implant tissues in the transmucosal zone to prevent mucositis and peri-implantitis (Milleret et al., 2019). Properties of the dental implant surface can be divided into chemical, mechanical, topographical, and physical characteristics that interact with each other. Modification of one characteristic influence other implant surfaces properties (Albrektsson & Wennerberg, 2019). The goal of implant surface modification is to enhance osseointegration, reduce risk for peri-implantitis and increase implant-supported restoration's survival.

1. Roughness. Implant roughness, or porosity, encompass macroscopic, microscopic, and nano characteristics. The macroscopic level has the range of millimetres to tens of microns. Macro porous surface gives surface roughness of more than 10 µm. The high roughness of implant surface improves interlocking between implant and bone, and hence, mechanical stability of prosthetics. Increase in peri-implantitis and ionic leakage are major risk for implants with macroporous surface (Le Guéhennec et al., 2007).

Implant surfaces with moderately textured microtopographic profile has roughness of 1-10 µm that results in improved osseointegration because of maximized interlocking between implant device surface and peri-implant bone, advanced cell process and reduction of healings time (Civantos et al., 2017).

In vitro and animal studies demonstrates that dental implant surfaces with nanometre range have favourable adsorption of proteins, adhesion of osteoblasts, and improves osseointegration (Kligman et al., 2021). However, clinical studies are needed to investigate optimal nano surface topography (Le Guehennec et al., 2008).

Although the roughness of the implant surface was considered a factor which improves osseointegration, rough surface promotes plaque accumulation and results in peri-implantitis (Asensio et al., 2019).

Initially plaque forms on supragingival and transgingival part of implant that contacting with abutment. Bacterial colonization of exposed surfaces of implant and abutment leads to inflammation in peri-implant tissues, a common reason for implant failure (Barbour et al., 2007). Hence, roughness of abutments surface plays a role for develop of mucositis and peri-implantitis.

Zandim-Barcelos et al. conclude that implants with rough and moderately rough surfaces "might have a higher risk of peri-implantitis. Therefore, well-designed prospective clinical trials are needed to validate or refute these findings" (Zandim-Barcelos et al., 2019).

On the other hand, Saulacic and Schaller conclude that the roughness of the implant surface does not influence the incidence of peri-implantitis (Saulacic & Schaller, 2019).

The most of commercially available implant systems represent implants the moderate roughness of surface, or micro-level modification that provides biomechanical interlocking (Albrektsson & Wennerberg, 2004), (Jordana et al., 2018).

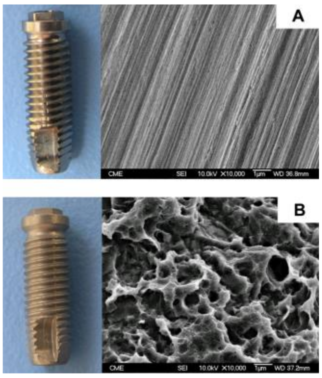

Figure 1. Surface treatment. Different roughness of micrometric surface structure of machined, turned implant (A) and sand-blasted and then acid-etched implant (B) (Civantos et al., 2017).

2. Chemical composition. Surface chemical composition is determined by properties of bulk implant material. Commercially pure Titanium, titanium-aluminium-vanadium and titanium-zirconium alloys have favourable mechanical and biological characteristics such as weight-to-strength ratio, biocompatibility and corrosion resistance due to formation of the passive thin oxide layer on the implants surface (Gittens et al., 2014).
Modulus and hardness properties of Titanium are like cortical bone tissue. Mechanical strength, resilience, maximum load, bending, fatigue strength, and stiffness are properties of Titanium that allows to simulate bone tissue, bear loading, regulate bone cell phenotypic specification (Civantos et al., 2017).

3. Wettability. Biological response of implant surface is affected by wetting behaviour, that meased by liquid-solid contact angle, or angle between "the tangent line to liquid drop`s surface at the three -phase boundary and the horizontal solid`s surface". Hydrophilic surface has liquid-solid surface angle lower than 90°. Surfaces with liquid-solid surface angle above 90° have hydrophobic properties. In vivo and in vitro studies show effect of surface wettability on adhesion of proteins, macromolecules onto the implant surface, interaction between implant surfaces and tissues around implant, bacterial adhesion, formation of biofilm, and osseointegration. Hydrophilicity allows close interaction between surface and biological fluids, cell receptors and support adsorption of proteins.
Hydrophobic surfaces are predisposed to contamination with hydrocarbon, that induce entrapment of air bubbles that interferer with adsorption of proteins and adhesion/activation of cell receptor (Gittens et al., 2014).

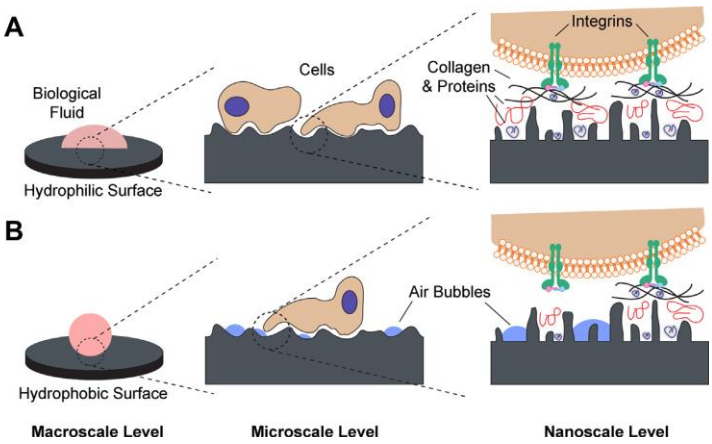

Figure 2. Possible interactions with (A) hydrophilic and (B)hydrophobic surfaces at different length scales (Gittens et al., 2014).

4. Topography. Importance of implant surface topography has been in focus for last decades. The original turned (smooth) Brånemark implant (Nobel Biocare) was the gold standard with good clinical results. However, experimental studies in mid-1990s showed that implants with moderately roughened surface have stronger bone response compared with turned and rough plasma-sprayed implants (Albrektsson & Wennerberg, 2004).
Porosity and roughness are topographic characteristics directly increase surface area, affecting adhesion, proliferation and differentiation of cells , promotes biomechanical interlocking between implant and bone (Civantos et al., 2017). Manufacturing processer of implant treatment encompasses machining technology, physical and chemical technics of implant surface topography modifying gained to improve tissue response and osseointegration (Civantos et al., 2017).

Mechanical characteristics of the implant surface, such as hardness and resistance to microcracks formation, are the least investigated properties because of the difficulties of quantitative measurement. Furthermore, mechanical properties are closely related to the other surface characteristics (Albrektsson & Wennerberg, 2019).

B. Impact of implant surfaces on peri-implantitis.

1. **Biofilm formation.**

Implant surface, as an important implant-related factor for peri-implantitis, can affect the ability of bacteria to adhere to the implant surface, form biofilm, and initiate an inflammatory response. Formation of microbial biofilm begins with adsorption of proteins, subsequent bacterial adhesion, maturation and dispersal, that influenced of exposure of different factors.

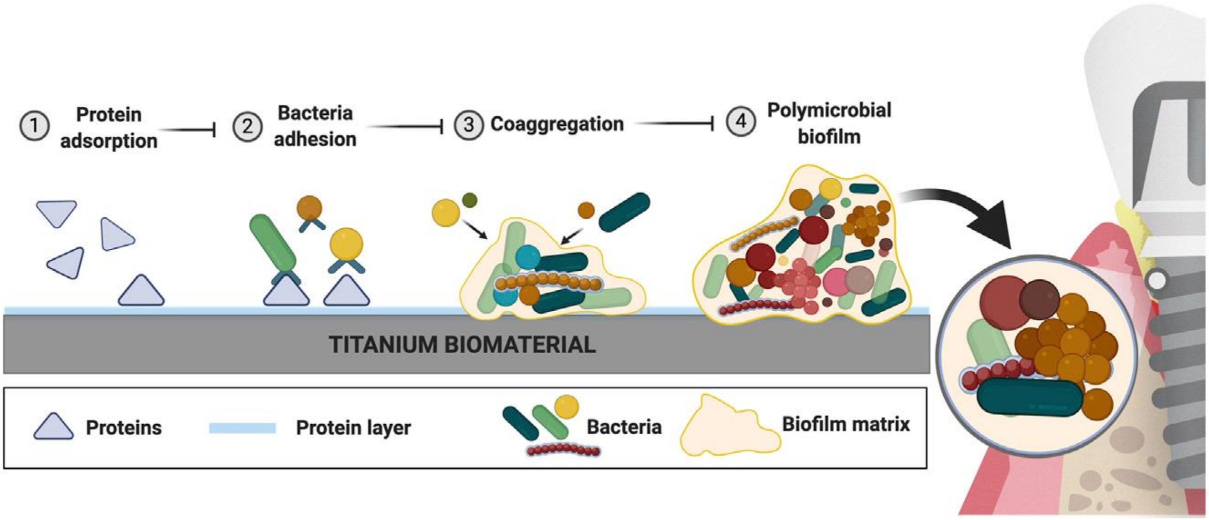

Figure 3. Formation of polymicrobial biofilm on Titanium surface (Souza et al., 2021).

Immediately after insertion of implant, supra-mucosal del of Titanium implant surface coats by saliva proteins, and plasma in submucosal segment. Properties of protein layer that forms from absorption of proteins on titanium surface, are affected by both physical and chemical characteristics of implant surface. Initial colonizers, mainly Streptococcus species, binds to the protein layer. Coaggregation and cooperation of different species promotes formation of biofilm. Microbial colonies are embedded in the extracellular matrix, proteins and eDNA. Structure of biofilm promotes cooperation and interaction of bacteria, retention and diffusion of biomolecules and nutrients, biofilm virulence, and antimicrobial resistance (Souza et al., 2021), (Costa et al., 2021).

2. Inflammatory response.

Inadequate oral hygiene and lack of biofilm removal contribute to increasing of biofilm accumulation, that together with environmental factors as pH, nutrients, metabolites, level of oxygen, leads to bacterial dysbiosis (Costa et al., 2021). Soaza et al. identified carbohydrate exposure, particles of Titanium that released from dental implants, structure of extracellular matrix as factors contributing to dysbiosis condition of microbiota (Souza et al., 2021) .

Microbiological shift trigger local inflammation in peri-implant tissues with favouring proteolytic and Gram-negative bacteria (Souza et al., 2021). Clinical symptoms of inflammation in peri-implant tissue, or mucositis, are erythema, bleeding on probing, swelling, suppuration. Progressive loss of ben surrounding implant characterise peri-implantitis.

3. Bacterial adhesion and colonization.

Fürst et al. reported that colonisation of bacteria occurs within 30 minutes after implant insertion. Bacterial patterns that colonize dental implants differ from bacterial species on tooth sites. Streptococcus ,Fusobacterium, and Capnocytophaga species have been reported as prevalent in early colonizers of dental implant surfaces (Fürst et al., 2007).

Initial microbial adhesion leads to interaction of strains of different bacterial species. Co-aggregation of bacteria leads to formation of polymicrobial biofilm that represents stable structure, or “climax community”, with ideal physicochemical environment, developed virulence, and resistance to antibiotics (Marsh et al., 2011), (Souza et al., 2021).

A cross-arch controlled in vivo investigation of Schincalia et al. showed less accumulation of biofilm on smooth implant surfaces compared with teeth, and more heterogeneous bacterial dysbiosis during the lack of removal of biofilm, despite of similarity in biofilms that forms in healthy teeth and implants surfaces (Schincaglia et al., 2017).

Bacterial adhesion is influenced by surface roughness, hydrophilicity, surface free energy , configuration of implant-abutment configuration Increased roughness and free energy of implant surface promotes biofilm formation (Subramani et al., 2009).

4. **Bone apposition and integration.**

Immediately after insertion of implant occurs apposition, or cellular and molecular reactions between implant surface and host tissues. Initial apposition is a crucial factor for integration of implant into the bone structure (Pikos & Miron, 2019).

Absorption of serum proteins onto titanium surface after implantation modulate activity of immune system. Blood cells neutrophiles, lymphocytes, monocytes, and macrophages express biological factors in peri-implant tissue, recognize characteristics of surface material and send signals that polarize macrophage population. After polarization of macrophages to M1 proinflammatory phenotype associated with microbial infection, and M2 anti-inflammatory phenotype, fibrous encapsulation of implant device occurs as response for foreign body. Three scenarios of implant integration are possible (Figure 4): A. Failure. M1 macrophage polarization and fibrous encapsulation lead to inflammation in peri-implant tissue with formation of foreign giant cell, and rejection of implant device. B. and C. Integration. B. M2macrophage polarization is predominant. Implant surrounded by granulations tissue that transforms into bone tissue after deposition of matrix. C. favouring osseointegration occurs without adverse reactions, in presence of M2 macrophage -phenotype (Civantos et al., 2017).

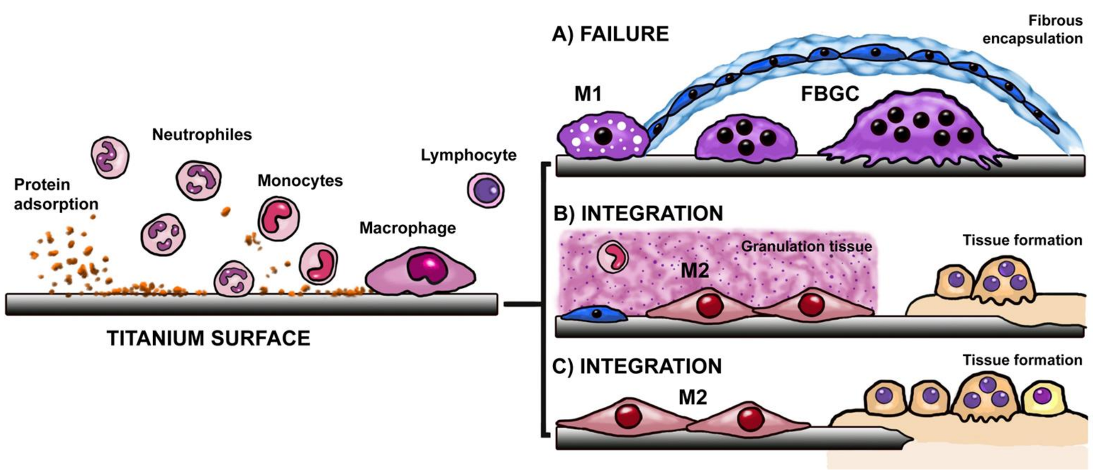

Figure 4. Biological response in Titanium implantation (Civantos et al., 2017).

Surface topography directly influences the bioactivity of the dental implant. Sandblasting, acid-etching, anodization, plasma spraying, and laser radiation are the main techniques to improve the bioactivity of dental implant surfaces and osseointegration. Changing of the implant surface's free surface energy, chemical composition, and roughness enhance osseointegration (Accioni et al., 2022).

Factors affecting implant surface modifications:

A. Manufacturing processes.

The roughness of implant surfaces creates by sandblasting, acid-etching, anodization, plasma-spraying, and laser radiation. These manufacturing technologies of surface treatment are widespread in commercial implants available on the market.

1. Machined implants are made by turned, milled, or polished manufacturing method, that increase surface area and roughness of material. In vitro studies evaluated that polishing methods prevent colonization with bacteria and fungi (Barbour et al., 2007). Results in vivo investigations shows improvement at the contact between bone and implant, and attachment of osteogenic cells to imperfections in the machined implant surface (Smeets et al., 2016).

2. Acid-etched implants. Acid-etching strategies are used in Osseotite, Steri-Oss Etched implants. Acid treatment of implant surface, with different concentrations of HCl, HNO_3, HF, H_2SO_4, expositions time and working temperature, increases roughness and influences osteogenic cell properties (Accioni et al., 2022).

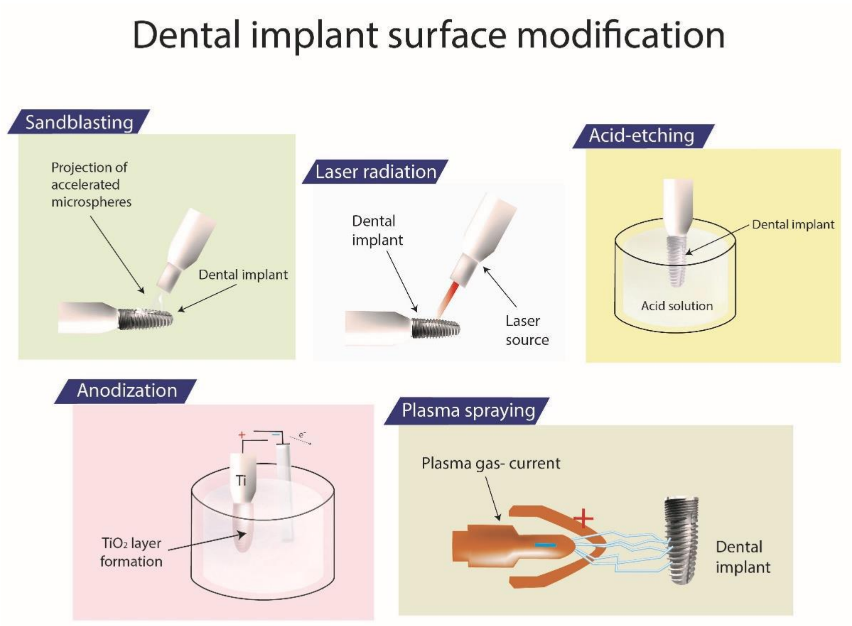

Figure 5. Mainstream engineering strategies in dental implantology (Accioni et al., 2022).

3. Laser-treated implants. The laser ablation technique modifies the nano-topography of the implant surface. This technology increases corrosion resistance and hardness and uses in Laser-Lok (BioHorizons, Birmingham, AL, USA) implants. In addition, generating micro and nanochannels on the implant surface increases the connection between implant surface and tissues around the implant, preventing epithelial ingrowth (Nevins et al., 2008).

4. Sandblasted and acid-etched implants. Sandblasting with microspheres of TiO_2, Al_2O_3, SiO_2 or HA by pressured air steam influences the macro-roughness of the implant surface. Incorporated in the implant surface particles of Al, Si, and HA, improves the adsorption of osteoblasts and osteointegration. Sandblasting technology combines frequently with finishing acid etching. For instance, SLA surface is made by sandblasting the turned Titanium surface with large-grit particles and etching of the blasted surface with hydrochloric, nitric, and sulfuric acids. Osteogenic cells migrate to irregularities on SLA surface, secrete a bone matrix, and contact osteogenesis takes place. Osseointegration accelerates compared to the turned surface (Yeo, 2019).

5. Hydrophilic implants. The Titanium surface have hydrophobic properties (Yeo, 2019). Rupp et al. highlight a change from focusing on topographical properties and surface roughness to a new paradigm that includes the role of wetting features of the implant surface. Wetting and micro- and nano roughness of implant surface influence bacteria retention and biofilm formation on the implants and cell behaviour at the material interface. Implants with hydrophilic surfaces have been proven to achieve initial blood contact for improved wound healing and osseointegration (Rupp et al., 2018).

Hydrophilic implant that being clinically used is SLActive (Institute Straumann AG, Basel, Switzerland). Hydrophilic SLA surface produces by a water rinse of the original SLA implant in a nitrogen chamber and packing with storing the implant in an isotonic sodium chloride solution without contact with atmosphere (Yeo, 2019).
However, it remains unclear what the optimal degree of hydrophilicity is for the best biological and clinical results. While several recent hydrophilic implant systems favour super hydrophilicity, it is unclear if more moderate hydrophilicity would further optimise interfacial reactions (Gittens et al., 2014).

B. Surface treatments:

1. Chemical treatments. Chemical modifications encourage osseointegration and decrease formation of biofilm by providing hydrophilic surface, discrete crystalline deposition, anodic oxidation, ultraviolet treatment , fluoride, hydroxyapatite, calcium chloride treatment, plasma oxidation, atmospheric pressure plasma processing (Kligman et al., 2021).

Hydrophilic implant surface enhances cell attachment and migration, neoangiogenesis, bone density, improves contact between implant and bone, especially in the earlier osteointegration stages. Hydrophilic implants have hydroxylated, rinsed under nitrogen protection surface, and are stored in isotonic saline solution (Buser et al., 2004), (Kligman et al., 2021) .

Discrete crystalline deposition is a sol-gel process of modification of double acid-etched surface. 50% of surface treated by discrete crystalline deposition contain particles of Calcium phosphate of 20-100 nm. This modification improves osteoconduction, osseointegration, reduce adhesion of bacteria to the implant surface(Mendes et al., 2009),(Kligman et al., 2021).

Anodization, anodic electrochemical oxidation of titanium surfaces, increases the titan dioxide layers, roughness and surface area. This surfaces microstructure increases blood clot retention, improving cell adhesion and proliferation of osteoblasts, deposition of gingival fibroblast (Accioni et al., 2022).

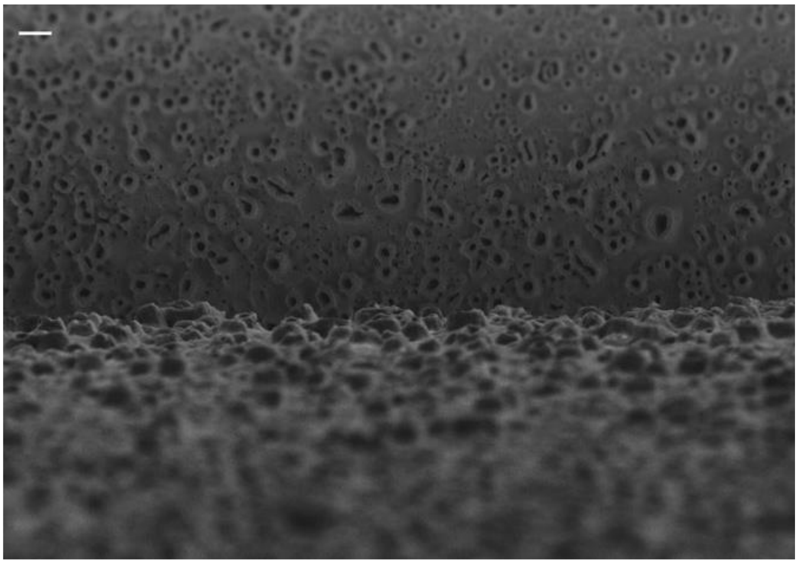

Figure 6. The anodized TiUnite Implant is made by micro-arc oxidation. The scale bar indicates 10 µm (Albrektsson & Wennerberg, 2019).

Fluoride treatment produces by cathodic reduction reaction resulting in application of fluoride to implant surface. Fluoride modification stimulates proliferation of undifferentiated osteoblasts, beneficial for bone-to-implant contact. Alkaline phosphatase activity increases. Disruption and detachment of biofilm promotes (Yeo, 2019), (Kligman et al., 2021).

Hydroxyapatite layer created by plasma spraying have antibacterial effect against S.aureus, P.gingivalis, and improves rapid contact between bone and implant (Kulkarni Aranya et al., 2017), (Kligman et al., 2021).

Applying thermally melted plasma-condition hydroxyapatite and titanium alloys to the implant's titanium surface produce a rough, irregular porous surface. The implant surface treatment with plasma spraying is used in ITI-TPS (Straumann Institute, Waldenburg, Germany).

Changing of hydrophilicity of Titanium oxide achieves by UV treatment. Photofunctionalization results in enhanced proliferation and adsorption of plasma proteins, attachment of osteogenic cells. It has been found reduction in the attachment of S.mutans, S.salivarius, S.sanguis (Yeo, 2019), (Kligman et al., 2021).

Atmospheric pressure plasma processing increase hydrophilicity of implant surface ,adhesion of cells , activity of alkaline phosphatase ,and reduce Gram-negative bacteria (Lee et al., 2019), (Kligman et al., 2021).

Plasma oxidation of implant surface combines high wettability effect and micro/nano-structures, notable increasing early apposition of bone (Jiang et al., 2018).

2.Physical treatments:

Physical treatments of implant surfaces include modification on the macro, micro and nano levels (Yeo, 2019). Macro-level treatment defined as visual geometry, shape of implant, thread pattern, and macro-level irregularities. Parallel or tapered implant design, diameter ang length of fixture have impact on implant stability. Threading allows to achieve optimal primary contact, stress distribution in the bone, and improve stability (Kligman et al., 2021).

Micro-level modifications include machining, grit-blasting, and combination of acid etching and sandblasting, improving bone growth, turnover, remodelling, interlocking of implant-bone interface (Barfeie et al., 2015).

Implant surface treatment in nano-level increase surfaces wettability, free energy, enhance growth of cells and differentiation of osteogenic cells. Laser ablation, nanocomposite coatings treatment resulting in protein absorption and adhesion of osteoblasts on the implant surface (Kligman et al., 2021).

3.Combinational treatments:

Both physical and chemical techniques can be used for addition of various nanoparticles, bioactive materials, drugs to Titanium (Kligman et al., 2021), (Accioni et al., 2022).
Novel coatings have been divided into organic and inorganic coatings (Accioni et al., 2022).
Inorganic coatings, or ceramics, improve osseointegration. The most used inorganic coatings are nanostructured calcium, calcium phosphate and hydroxyapatite, applied on the Titanium surface by plasma spraying or hydrothermal deposition. Releasing of Calcium and phosphate-ions encourage the mineralisation of bone-implant interface and bone healing process (Accioni et al., 2022), (Civantos et al., 2017). The ceramic coating technique have been used for delivery of molecules that help in activation of bone formation, modulating inflammation, prevent infections, resorption of bone, foreign body reaction (Civantos et al., 2017).
Bioactive molecules aimed to induce bone formation, prevent bone resorption, molekules with antibiotic and immunomodulation properties, incorporate in inorganic coatings (Civantos et al., 2017).
Nano-engineering allows using organic and inorganic coatings combined with the controlled release of proteins or antibiotics (Accioni et al., 2022).

Different methods have been used for incorporation of silver nanoparticles in titanium implants surfaces. Embedment of silver particles in implant coating with polymeric materials, soda-lime glass coating, attachment of silver particles on nano/micro titanium surfaces and penetration of nanotubular structures of titanium resulting in release of silver particles in surrounding tissues. Duration of maximal antibacterial effect was 15 days with gradual decline after that and possible providing of adverse effects. Lack of clinical studies and concerns about biocompatibility limits clinical application (Haugen et al., 2022).

Synthetic polymers, polysaccharides, proteins, growth factors, peptides are used as organic surface modifications to improve cell response at the tissue-bone contact.

Synthetic polymeric coatings such as polylactic-co-glycolic acid, polyethylene glycol, poly-caprolactone, polymethylmethacrylate, are used frequently in metallic implants providing biocompatibility, biodegradation, and good mechanical properties. Environment friendly properties combines with prevention od bacterial adhesion to the implant surface (Civantos et al., 2017).

Polysaccharides, peptides, and extracellular matrix proteins occurs naturally, and have shown low toxicity and cost, are biodegradable and osteoconductive, induce cell adhesion (Civantos et al., 2017).

Clinical relevance of implant surface modifications:

A. Clinical outcomes. Clinical results of use commercially available implants have been evaluated in clinical trials. Comparation of Titanium implants with machined surface and implants with surface treated by anodization shows increased bone-to-implant contact. 100% implant success followed the implants with oxidized surface (Nobel Biocare TiUnite) compared success rate of 96,4% with turned implants Nobel Biocare Mark III (Jungner et al., 2005).

A 10 years retrospective study in 303 partially edentulous patients with 511 Titanium implants with sandblasted and acid-etched surfaces showed implants survival rate of 98,8% and success 97%, with peri-implantitis prevalence 1,8% (Buser et al., 2012).

SLA Active (Straumann Institute, Basel, Switzerland) implants have nano surface with increased hydrophilicity, biological response, and cell recruiting, obtained by blasting, acid etching and flushing with nitrogen. This surface treatment technology provides fast bone healing with a rate of success of 91.7% (Accioni et al., 2022). Van Velzen et al. investigated ten years of survival rate and incidence of peri-implantitis of 374 implants with SLA surface. The implant and patient-level survival rates were 99.7% and 99.4%, respectively. Peri-implantitis was diagnosed in 7% of dental implants (van Velzen et al., 2015).

Clinical studies of TiOblast® (Astra Tech, Mölndal, Sweden) implants show high osteointegration success with peri-implantitis complication in 3.5% of implants (Al-Nawas et al., 2012). On the other hand, a 20-year follow-up of 25 patients with 64 implants, compared a non-modified turned surface device and TiOblast®, suggested these topographies did not improve bone healing. A moderate increase in surface roughness did not affect the level of peri-implant bone (Donati et al., 2018).

Long-term studies of the clinical use of Osseotite report success in more than 96% of cases. The acid-etched surface showed the highest cell proliferation rate of the implant surface and triggered osteogenic cell responses in vitro studies (Blatt et al., 2018). Velasco-Ortega et al. report a survival and success rate of 92.9% of implants with TSA acid-etched surfaces. Implants were loaded early, and prosthodontic clinical findings were followed for 17 years. The most frequent complication was prosthetic technical complications (14.2%, followed by peri-implantitis (10.6%). Peri-implantitis appeared mostly in smokers and patients with periodontitis (Velasco-Ortega et al., 2020).

Despite the effective biological response, researchers underline that the mechanical stability of anodised implants is a challenge (Alipal et al., 2021).

Only 8.23% of TiUnite (Nobel Biocare, Gothenburg, Sweden) implants made by micro-arc oxidation, were involved in peri-implantitis, with signs of infection, pus and bone loss on radiographs, at first 10-years follow-up after surgery using immediate loading implants (Degidi et al., 2012).

Becker et al. re-evaluated 388 TPS dental implants, with titanium-sprayed surfaces inserted in 92 patients, with observation time from 12.2 to 23.5 years. The survival rate was 88.03%, while peri-implantitis was diagnosed in 9.7% of the implants (Becker et al., 2016).

Jordana et al. evaluated the impact of implant roughness on peri-implantitis in humans. Surface roughness of implant and peri-implantitis are associated. "The higher the surface roughness, the higher the mean periimplantitis rate. There are little peri-implantitis up to an arithmetic mean surface roughness (S_a) of 1 mm. Peri-implantitis appears for S_a values greater than 1.2 mm”. Therefore, it was recommended that clinicians use machined or sandblasted surfaces (Jordana et al., 2018).

Ossean (Intra-Lock, Boca Raton, FL, USA) implants surface, produces with a combination of grit-blasting and acid-etching technology, with impregnation of calcium phosphate nanoparticles. In Nanolite (Zimmer Biomet, Palm Beach Gardens, FL, USA) implants, the surface is treated by discrete crystalline deposition of CaP nanoparticles (Asensio et al., 2019). Hydroxyapatite-based biomimetic coatings of Osstem GS-HA III and Osstem TS III-HA (Osstem Implant Co., Busan, Korea) trigger the activity of osteoblasts for the formation of bone.

Peri-implantitis was registered in 2.2% of Osstem and TS III-HA implants and 1.4% of TSV-HA (Jung et al., 2018). Magnesium-based biomimetic coatings - phosphate salts of magnesium have a better promotion of osteoblasts function and higher formation of bone than calcium phosphate surfaces. Nanoparticles of magnesium have a high antibacterial activity against biofilm formation (Accioni et al., 2022).

Dalago et al. studied titan implants, with the body blasted with titanium particles and the implant neck with low roughness. Implants with the same surface characteristics from one manufacturer were evaluated. Results of a cross-sectional study with 916 implants showed that implant-related factors, such as implant location in the jaw, shape, diameter, length of the implant, implant connection, type of antagonist and use of a block graft at the surgery, were not related to the presence of peri-implantitis. Therefore, implant surface characteristics were not evaluated as risk factors. Risk indicators of peri-implantitis were identified with periodontitis, cemented crowns, occlusal dysfunction, and full-mouth implant restorations (Dalago et al., 2017).

Lopez-Valverde et al. assessed effectiveness of antibacterial Ti implant surfaces with incorporation of Tantalum, Strontium, Doxycycline, Bacitracin, and human bone morphogenetic protein, on osseointegration in preclinical animal studies. Improved antibacterial capacity and osseointegration of implants with antibacterial coatings of surfaces was proved with relative caution because of bias in methodological aspects and experimental models (López-Valverde et al., 2021). However, commercially available implants with antibacterial capacity are limited. Promising research includes the investigation of coatings based on growth-factor, extracellular matrix proteins and polysaccharides, antibacterial coatings, drug-releasing coatings, "No-releasing" coatings and antifouling coatings (Asensio et al., 2019).

However, Albrektsson concluded in a review that there is a lack of clinical evidence that any particular type of implant surface with nano-structure or hydrophilic implants have improved clinical outcome, despite positive results from animal studies (Albrektsson & Wennerberg, 2019).

Stavropoulos et al. analysed the incidence, severity, and progression of peri-implantitis on pre-clinical in vivo peri-implantitis experiments on dogs and clinical trials with more than five years of follow-up of more than two different types of implant materials or surface characteristics. Clinical studies did not reveal the incidence of peri-implantitis among implants with various surface characteristics, while pre-clinical in vivo animal experiments reported the significant influence of implant surface modifications on the progression of peri-implantitis. Limited information does not allow to make conclusions about the possible influence of implant surface characteristics on the incidence or progression of peri-implantitis (Stavropoulos et al., 2021).

B. Long- term stability. Simones reported 10-16 -year follow-up of Straumann Dental Implant with implant success and survival parameters as long-term results. Survival implant and fixed prothesis presented in mouth independent of complications. Definition of success includes implants free from complications over follow-up period. The cumulative survival rate up to 16 years was 82,94%. Whereas biological complications occur in 16,94%, technical complications rate was 31,09%. Despite relatively high survival rate, complications occurred frequently (Simonis et al., 2010). Yan et al. studied treatment of pure Titanium with nitrogen plasma for improvement of surface characteristics facilitating osseointegration and prevent material aging. It suggested that surface implant characteristics influence significantly osseointegration and long-term stability after insertion. Aging is a reason of biodegradation of Titanium biologically from active material to biologically inert (Yan et al., 2022). However, aging, and long-term stability of Titanium implants needs further investigations.

C. Cost-effectiveness. Cost -effectiveness of implants with different surface modifications evaluates clinical outcomes in relation to cost. Parameters for assessment are success rate, long-term stability, and patients' satisfaction.

The evaluation encompasses the clinical benefits of varying surface modifications concerning their costs, considering the success rate, longevity, and patient satisfaction. Previous literature has demonstrated that various surface modifications, including topographical and chemical alterations, can influence osseointegration, enhance implant stability, and potentially reduce the risk of periimplantitis (Wennerberg & Albrektsson, 2009). However, the cost-effectiveness of these modifications must be weighed against the potential benefits to determine their clinical relevance. In implant dentistry, cost-effectiveness refers to the optimal balance between the costs and benefits of a particular treatment modality, considering both clinical outcomes and economic implications. Several studies have investigated the cost-effectiveness of implants with different surface modifications. For example, Buser et al. conducted a retrospective study on 511 titanium implants with a sandblasted and acid-etched surface, demonstrating high survival and success rates over ten years in partially edentulous patients (Buser et al., 2012). The study highlights the potential long-term benefits of specific surface modifications regarding clinical outcomes and cost-effectiveness.
Furthermore, Roccuzzo et al. examined the long-term results of a three-arm prospective cohort study on implants in periodontally compromised patients, focusing on the sandblasted and acid-etched (SLA) surface. The findings of this study revealed favourable outcomes for SLA surfaces in terms of success rate, longevity, and patient satisfaction, suggesting that this surface modification could be a cost-effective option in specific clinical scenarios (Roccuzzo et al., 2014).

Evaluating the cost-effectiveness of different implant surface modifications is an essential aspect of determining the clinical relevance of these modifications. While various surface modifications have been shown to improve clinical outcomes, it is necessary to consider factors such as success rate, longevity, and patient satisfaction with their costs. Further research is needed to understand better the cost-effectiveness of different implant surface modifications in diverse patient populations and clinical situations, ultimately enabling clinicians to make informed decisions regarding the most appropriate treatment options for patients at risk of peri-implantitis.

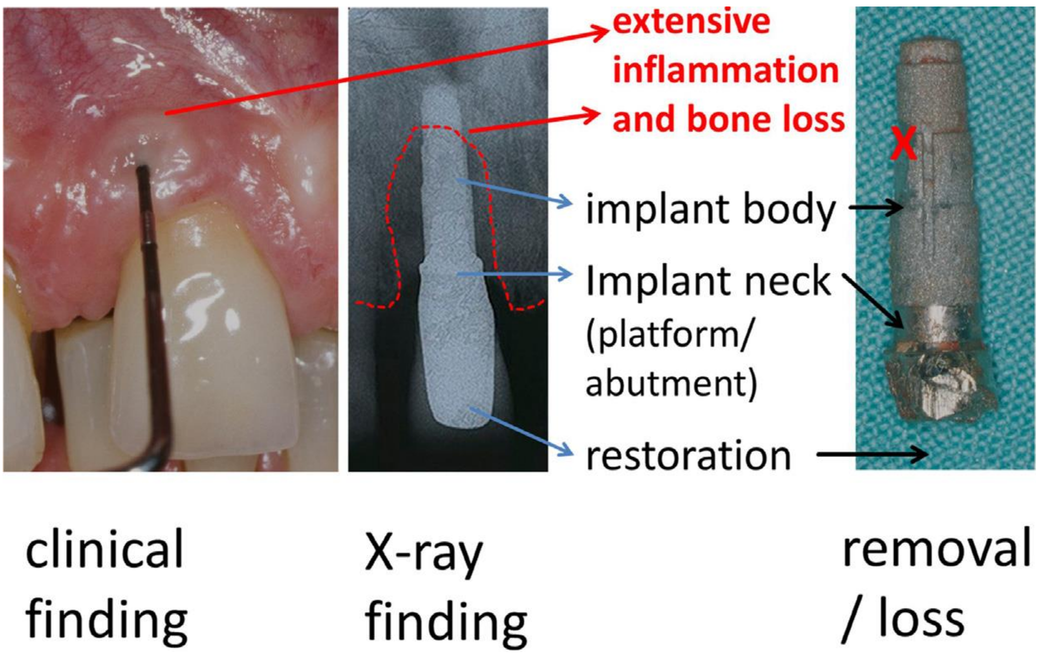

Figure 7. Clinical example of peri-implantitis with extensive loss of bone and osseointegration. Clinical findings were swelling, suppuration and bleeding on probing. Pain-free probing evaluated up to 6 mm pockets depth (Rupp et al., 2018).

Prevention and treatment of peri-implantitis related to implant surfaces:

A. Preventions strategies. Although it is accepted that peri-implantitis is a multifactorial disease with bacterial plaque and microbial dysbiosis as primary etiology, factors related to patients, implants and long-term factors contribute to development of peri-implantitis (Sun et al., 2023).

Fu et al. determine risk factors in developing peri-implantitis as patient-related factors, implant design, prosthesis, and clinician-related factors. All these factors influence the host's response to the bacterial plaque at the implant's surface. Patient-related factors are poor plaque control (Serino & Ström, 2009), lack of regular periodontal maintenance care of patients with dental implants, history of active periodontitis (Ferreira et al., 2018), smoking (Chrcanovic, Albrektsson, et al., 2015) and diabetes (Dreyer et al., 2018).

Bornstein et al. evaluated systemic diseases with and without systemic medication as risk factor for dental implant failure. Human studies reporting survival rates of osseointegrated dental implants at patients with at least one of 12 systemic diseases such as scleroderma, Sjøgren`s syndrome, neuropsychiatric disorders, lichen planus, AIDS, HIV,ectodermal dysplasia, Crohn, transplantation, cardiovascular, diabetesor insulin therapy, or glucose intolerance, osteoporosis, oral bisphosphonates, radiotherapy.

Despite of many systemic conditions have been suggested as potential risk factors, it was concluded that evidence level for absolute and relative contraindications for dental implant therapy is low. For patients with bisphosphonates therapy are type, duration and dosage of medication crucial in risk for bisphosphonate-related osteonecrosis. Osteoradionecrosis after insertion of dental implants before and after radiotherapy with failure rates from 0% to 12,6% for 12 years follow-up period was reported (Bornstein et al., 2009).

Implant site-related factors are tissue phenotype (Isler et al., 2019) and residual infection (Chrcanovic, Martins, et al., 2015). Excess cement (Wilson, 2009), over-contoured superstructures (Katafuchi et al., 2018), and occlusal overloading (Canullo et al., 2016),(Fu et al., 2012) / interproximal opening (Jeong & Chang, 2015) are prothesis-related factors. The spatial malposition of implants is a clinician-related factor (Fu & Wang, 2020).

Zandim-Barcelos et al. identify implant-based risk factors for peri-implantitis, such as implant surface topography; location of the implant; occlusal overload; time in function; prosthesis-associated, such as rehabilitation extension, excess of cement and implant-abutment connection; and metal particle release (Zandim-Barcelos et al., 2019).

One important implant-related factor is the implant surface, which can affect the ability of bacteria to adhere to the implant surface, form biofilm, and initiate an inflammatory response.

Long-term factors identified as lack of supportive therapy and poor control of plaque (Sun et al., 2023).

Sun et al. concludes that the best strategy for prevention of peri-implantitis and mucositis is a treatment planning including properly validation of potential factors of risk both before and after treatment, and maintenance program. Effective plaque control, compliance, quit smoking, control of glycemic level are important patient-related factors for successful outcome of implant therapy (Sun et al., 2023).

Prevention and treatment of peri-implantitis related to implant surfaces include maintenance protocols, antibacterial coatings, photodynamic therapy, implant surface decontamination, surgical and nonsurgical treatments, and implant removal and replacement. The choice of prevention and treatment options depends on the severity of the disease, patient factors, and the expertise of the clinician.

1. Maintenance protocols. There is established evidence that implant treatment should not be limited to the surgical insertion of implant with final prothesis. Supportive treatment , or maintenance therapy has to be performed regularly to control indicators of peri-implant inflammation, and risk factors (Fu & Wang, 2020), (Cortellini et al., 2019).

Soares et al. identified available oral care instruments and hygiene instructions for home hygiene procedures, protocols and intervals for professional supportive therapy for patients with implant-supported prothesis (Soares et al., 2022). Relevant advises was drown based on findings:

1. Qualified personnel must give understandable instructions in a form, so every individual patient know how to use the hygiene instruments. Motivate and make the patients able to evaluate the effectiveness of the procedure when they are home. Besides that, repeated recalls for professional hygiene evaluation and instructions are important, according to the individual need of every patient.

2. Adequate advice for home oral care is cleaning with ordinary toothbrushes and low-abrasive toothpastes and interproximal hygiene devices, such as dental floss or interdental brushes.

3. Use of antiseptic solutions and irrigators may also be indicated, although these do not replace mechanical instruments for biofilm removal.

4. Professionals must evaluate the restoration condition and adjacent tissues at each professional recall for preserving, in addition to performing instructions for hygiene and for cleaning the prostheses and implants, using instruments that make no damage on the implant or the abutment surface (Soares et al., 2022).

2. Antibacterial coatings. Bacterial biofilm in peri-implant tissues represents risk for mucositis and peri-implantitis. Antibacterial coating of the internal chamber implant PIXIT (Edierre srl, Genova Italy) with an alcoholic solution containing polysiloxane oligomers and chlorhexidine gluconate at 1% was investigated in clinical studies by Carinci et al (Carinci et al., 2019). Results demonstrated ability of antibacterial coating to decrease bacterial loading and influence quality of microbiota in the peri-implant tissues, especially species related to the peri-implantitis (Carinci et al., 2019).

Rahmati et al. investigated effect of doxycycline coating on titanium-zirconium implants osseointegration in animal rabbits and dogs' models. Doxycycline presented physically and released on the surface of titanium-zirconium implants after 4 weeks in dogs' models and 8 weeks for rabbits. Biocompatibility and osseointegration effects were not reduced. Authors concluded that coating of implant surface with doxycycline indicated no negative effect on implants osseointegration. A local doxycycline delivery system have suggested for administration after implant surgery to reduce infection complications in risk patients (Rahmati et al., 2020).

Håvard J. Haugen et al. investigated potential of dental implants with silver nanoparticles-treated surface to reduce peri-implantitis (Haugen et al., 2022). A prolonged antibacterial effect of silver nanoparticles was revealed both in vitro and in vivo studies.

3. Photodynamic therapy. Photodynamic therapy uses for detoxification of implant surface. Diode soft laser uses with photosensitizer toluidine blue O that binds to target cells. Laser light activates photosensitizer, and toxic for bacteria singlet oxygen and free radicals produces (Dörtbudak et al., 2001).

24 weeks of follow-up in the group of patients with peri-implantitis that was treated with photodynamic therapy showed decrease of proinflammatory index. However, reduction of anaerobic bacteria on the implants rough surfaces after treatment of peri-implantitis was not so significant as after surgery (Bombeccari et al., 2013).

4. Implant surface decontamination. Treatment strategy aims in arrest of peri-implantitis and influenced of severity of peri-implant lesion. Reduction of peri-implant pocket depth, bleeding on probing and bone consolidation revealed radiographically are the goals of nonsurgical and surgical interventions (Ephros et al., 2020). Pocket depth less 3 mm with presence of plaque, calculus, and bleeding on probing is indication for nonsurgical methods of decontamination of implant surfaces. Plastic, carbon – fiber and titanium- coated curettes, ultrasonic non-metallic tips, and lasers uses for mechanical removal of bacterial biofilm from implant surfaces. Decontamination of rough implants surface is a challenge because of promoted adhesion of bacterial plaque (Ephros et al., 2020).

B. Treatment options:

1. Surgical treatment. If signs of inflammation remains after nonsurgical treatment, is surgical intervention indicated (Figuero et al., 2014). Surgical treatment includes pocket elimination using resective techniques in patients with pockets depth greater than 5 mm in combination with suppuration, bleeding on probing and lose of peri-implant bone.

Roccuzzo et al. describes surgical treatment of peri-implantitis following procedure of periodontal surgery, with initial elevation of a full-thickness flap for access to the contaminated implant surface. Decontamination of implant surface with titanium and Teflon curettes and ultrasonics, titanium and chitosan brushes, glycine powder performs gained to optimal removal of biofilm. Soft tissue granulations remove. Both mechanical and chemical decontamination combines before assessment of bone defect. The main surgical operations of treatment of peri-implantitis described in literature are open flap with and without resective procedures, reconstructive surgery, combined resective and reconstructive procedures (Roccuzzo et al., 2021).

Carcuac et al. revealed that success of surgical treatment of peri-implantitis for implants with modified surface was significantly lower than result for implants with machined surfaces (Carcuac et al., 2016). Less inflammation was registered around implants with smooth nonmodified surface after surgical peri-implantitis treatment by Koldsland et al. (Koldsland et al., 2018).

2. Nonsurgical treatment. Systemic antibiotics and antiseptic agent supplements both nonsurgical and surgical implant surface decontamination. Despite of temporary reduction of bleeding on probing in treatment of peri-implantitis , “there is no generally accepted recommendations for the use of antimicrobials “ for treatment of peri-implantitis (Hussain et al., 2021).

Studies of Carcuac et al. have shown limited effect of use of systemic antibiotics in surgical treatment of peri-implantitis of implants with modified surface (Carcuac et al., 2017).

Besides, there is a general concern among experts about increased risk of development of antibiotic resistance in bacteria when systemic antibiotic uses in therapy of peri-implantitis. Benefits of antibacterial therapy in management of peri-implantitis have to be pondered to consequences of antibiotic resistance for health of population (Ardila & Vivares-Builes, 2022), (Hussain et al., 2021).

3. Laser therapy. Laser therapy with use of erbium-doped yttrium aluminium garnet laser and diode laser was proposed for remove of subgingival calculus without damage of implant surface (Figuero et al., 2014). Ablation and anti-infective properties of laser allows achieve effective debridement and decontamination of implant surface (Figuero et al., 2014). However, no significant advantage was evaluated in terms of bleeding on probing and level of clinical attachment when laser was used for debridement compared with conventional resective surgical intervention (Schwarz et al., 2011).

4. Implant removal and replacement. Severe vertical and horizontal bone lose around implants because of progressive peri-implantitis is indication for removal of implant. Block resection, buccal bone osteotomi and trephine osteotomy, resective methods using of piezosurgery, electrosurgical probe and laser have been reported to remove fail dental implants (Winnen et al., 2021).

Anitua et al. studied effect of implant surface characteristics on the reason of fail and technique of removal of failed nonmobile implants (Anitua et al., 2016). Acid-etched, particle-blasted, oxidized, titanium plasma-sprayed, hydroxyapatite coated, and turned implants was removed caused peri-implantitis and malpositioning of implants. Most of the explanted implants were acid etched (47.5%) and oxidized (19.6%).

Minimally invasive method of application of counter torque at implant-bone interface was used for explantation of implants. Removal torque was significant higher for acid-etched, particle-blasted, and oxidized implants. Authors concludes that occurrence of peri-implantitis and value of removal torque are influences by the type of implants surface (Anitua et al., 2016).

Future perspective:

Looking towards the future, the influence of implant surface properties as risk factors for peri-implantitis will continue to be an essential topic of research and clinical interest. There are several areas where further investigation is needed to improve our understanding of the impact of implant surface on the development of peri-implantitis. One area of future research is the development of personalised implant surface modifications. Technological advances may make it possible to tailor implant surface characteristics to the individual patient's needs and risk factors for peri-implantitis. This approach can potentially improve the long-term success of dental implant therapy and minimise the risk of complications.

Another area of future research is the development of precision medicine for peri-implantitis treatment. By using molecular and genetic markers, it may be possible to identify the specific bacteria responsible for peri-implantitis in individual patients and develop targeted treatments to eliminate them. This approach can potentially improve the effectiveness of peri-implantitis treatment and reduce the risk of antibiotic resistance. Furthermore, developing novel implant surface modifications and coatings will continue to be an important area of research. New materials, such as nanomaterials and bioactive ceramics, may offer advantages over traditional implant materials in their ability to enhance osseointegration and minimise the risk of peri-implantitis. Finally, it will be important to continue to evaluate the long-term clinical outcomes of implant surface modifications and to refine maintenance protocols and treatment options as new technologies and approaches become available.

Conclusions:

Peri-implantitis is an actual issue in implantology, therefore, prevention of peri-implantitis is essential for long-term oral rehabilitation with implants. Implant surface characteristic is one of the factors that influence the osseointegration of implants. However, clinical use does not exhibit significant improvement between machine-turned and modified implant surfaces. Information about the association between implant surface treatment and the incidence and progression of peri-implantitis is limited and controversial. Long-term clinical investigations are required to support promising laboratory in vitro and in vivo results.

The literature suggests that implant surface properties play a crucial role in the development of peri-implantitis. The roughness, chemical composition, wettability, and topography of the implant surface affect biofilm formation, inflammatory response, bacterial adhesion and colonization, and bone apposition and integration.

Implant surface modifications, such as manufacturing processes and surface treatments, have been developed to enhance osseointegration and minimize the risk of implant failure due to peri-implantitis. These modifications have shown promising results in terms of clinical outcomes, long-term stability, and cost-effectiveness.

Prevention and treatment options for peri-implantitis related to implant surfaces include maintenance protocols, antibacterial coatings, photodynamic therapy, implant surface decontamination, surgical and nonsurgical treatments, and implant removal and replacement. The choice of prevention and treatment options depends on the severity of the disease, patient factors, and the expertise of the clinician.

Future directions in the field of implant surface modifications include the development of novel implant surfaces and coatings, personalized implant surface modifications, and precision medicine for peri-implantitis treatment. These advances in technology have the potential to improve the long-term success of dental implant therapy and minimize the risk of complications such as peri-implantitis.

In conclusion, the literature supports the idea that implant surface properties are important risk factors for peri-implantitis. Further research is needed to develop effective prevention and treatment strategies and to explore the potential of novel implant surface modifications. Dental professionals and implant manufacturers should carefully consider the impact of implant surface on the development of peri-implantitis when selecting and designing implant systems.

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