

NEW TRENDS IN RISKS AND IMPLANT MATERIALS IDENTIFICATION AND DEVELOPMENT OF PERI-IMPLANTITIS THERAPY

Ioana BUNOIU¹, Ioana DEMETRESCU², Andreea DIDILESCU³

Abstract. *The goal of this paper is to present different aspects related to peri-implantitis disease, the destructive inflammatory process affecting the tissues surrounding dental implants. In the context of extended use of dental implants, this review identifies the risks factors to promote implant loss, the implant materials used and the development of therapy for solving problem. Being an infectious disease, the bacteria presence is discussed as well. The aspects of osseointegration and type and structure of the implant surface materials are parts of general consideration presented as strategy before introducing surgical and non-surgical therapies.*

Keywords: dental implants materials, risks of implant loss, peri-implantitis, therapy

1. Introduction

In the context of extended use of dental implants statistically it is an increase number of diseases affecting people after implantation, such as peri-implantitis, the destructive inflammatory process of the tissues surrounding dental implants. Due to prevalence rates up to 56%, peri-implantitis in the absence of prevention and therapy protocols may lead in shorter or longer time to the loss of the implant. [1].

Peri-implantitis disease affects a significant number of patients, and it is important to understand the difficulties in diagnosing it and the risk factors, which can be modified to reduce the potential for disease progression. Nowadays, unfortunately, available information on exact prevalence and the standard therapeutic protocol for diseases affecting the implant is inadequate.

Implant failure can be divided into early bone loss meaning prior to prosthetic treatment or late, after prosthetic rehabilitation, usually after a year. Early failure is generally due to interference in the healing process after implant placement.

2. Risks factors for the development of peri-implantitis

In Fig.1 it is presented the radiological aspect of peri-implantitis.

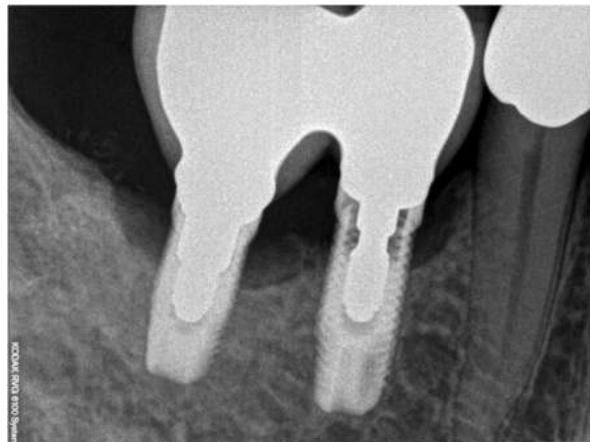


Fig. 1. Radiological aspect of peri-implantitis

The following factors have been reported as risk factors for the development of peri-implantitis [1-5]:

- Smoking, associated with a significantly complications increase
- Lack of compliance and limited oral hygiene
- Systemic diseases such as, poorly treated diabetes or cardiovascular disease
- Iatrogenic causes ("cementitis")
- History of periodontitis
- Soft tissue defects or soft tissues at the level of the implantation area.

The smoking is the most cited risk factor for peri-implant disease followed by a history of periodontitis in the etiology of one or more failures in osseointegration of implants [6]. The periodontitis existence or smoking increased the risk of peri-implantation up to 4.7 times [1]. In addition, smoking has been shown to be a predictor of implant failure [7]. In a recent meta-analysis, smoking, was found the main risk factor and the annual bone loss rate increased by 0.16 mm / year in association with this factor [8]. At the same time osseointegration is impaired, taking into account that generally in smokers oral hygiene is lower [1].

There are not bodies of evidence of predictors for implant success by sex or age, but in the area where are placed, maxillary/mandibular implants respectively [7], it was reported that jaw implants had an increased risk of peri-implantation bone loss as compared to mandibular implants [7].

For over 10-years investigation period in a group of patients with bacterial periodontitis involving *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, it was observed that these bacteria could be detected again in the oral mucosa [1]. Infection with *Prevotella intermedia* was still evident in microscopic examinations. This aspect indicates that bacteria survive for a long time, even after dental extraction. Therefore, particular care should be taken with periodontal teeth remaining in the oral cavity of the patient, which is a potential source of infection. Therefore, the type of edentation, partial *versus* total, may influence colonization of peri-implantation tissue with periodontal pathogens [9]. The impact of the keratinized gum on dental implants has been discussed, but most studies emphasize the importance of a suitable keratinization area around implants [10].

The so-called "cementitis" may be considered the most important, iatrogenic risk factor [11]. In a group of patients undergoing a study it was shown that residual dental cement was present in 81% of the sites. After its removal, clinical signs disappeared in 74% of affected patients [12]. In another study [13], it was found that the removal of cement residues led to a decrease in the inflammatory response of nearly 60% [13]. Linkevicius et al. examined the manifestation of peri-implantitis in a group of patients with present residual cement. In those who had a history of periodontal disease, it was found that residual cement resulted in peri-implantitis in 100% of cases, while patients without a history of periodontal disease were affected by 65% [14].

Peri-implant probe examination is recommended to be performed carefully and with minimal probing force. However, the so-called platform switch (abutment is located horizontally between the implant and the crown) can complicate the research and thus hide other forms of the peri-implantitis [1-3]. However, studies have indicated that the platform may be an important protective factor against peri-implant disease [1].

Implant loss can be due according to certain criteria based on additional factors as following [4]:

- Prosthetic overload of the implant
- Material problems and wrong techniques
- Poor bone quality at the implant area
- Systemic disease and regular drug abuse, which inhibit bone remodeling according to Wolff's law.

Implants longer than 10 mm have a higher success rate than the shortest [1]. Also, implant surfaces that have more than 2 microns appear to have better osseointegration than smooth ones that are <0.5 microns, or moderate (1-2 microns) [1]. In addition, in order to prevent implant diseases, there is a need for

oral hygiene improvement in the frame of preventive and implant cleaning strategies in the dental clinic, as well as in the dental office and individually. The periodic examinations of the implant and surrounding tissues is mandatory, together with particular attention to reducing the risk factors mentioned above.

3. Implant materials

Regarding implant materials their selection is an important issue and nowadays is a challenge in materials research [15]. Titanium (Ti) a valve biocompatible metal has been the choice for long in oral cavity for implant purpose. During the years, to improve its performance not only the commercially pure Ti but also some binary and tertiary Ti alloys were used. The alloying aim was to enhance mechanical properties without compromising the biocompatibility and biological behaviour compare to cp-Ti. As a result, a large variety of Ti binary alloys, including Ti–Zr, Ti–In, Ti–Ag, Ti–Cu, Ti–Au, Ti–Pd, Ti–Nb, Ti–Mn, Ti–Mo, Ti–Cr, Ti–Co, Ti–Sn, Ti–Ge and Ti–Ga, were tested and processed ing for ‘dental implant’ and ‘medical implant’. During the processing, Ti exists as α phase, a hexagonal close-packed crystal lattice, and its passive oxide film on the surface [16] can absorb calcium and phosphate ions inducing protein and apatite formation as a step before osseointegration. This passive oxide layer being very thin, various method from a simple oxidation [17] to bioactive layer [18] and sophisticated coating at nanolevel were proposed[19] to thicken the oxide layer. It is to mention that is a need for Ti oxide to remain <10 nm) and to prevent Ti ions leakage which was identified as main cause the protein denaturation and tissue necrosis [16]. It is well known that TiO_2 predominant oxide, as a function of pH undergoes several steps of hydrolysis leading to negative or positive charge on surface depending on hydroxylated oxide form. The positive $[Ti-OH_2]^+$ form with hydrophilic character [20] has better chance for Ti-osteoblast bonding without the addition of growth factors or /proteins [21].For longer period of time due to the fact that Ti oxide become thicker to preserve hydrophilicity and nanostructure several strategies has been introduced such as developmmment of new surface treatments [22] and introducing new alloys [23,24]. Between the various Ti binary alloys TiZr probably gained the best position as an alternative for other possibilities [25]. Among TiZr alloys subjected to investigations, the alloys with higher Zr content [26] have a much larger passive range in the polarization curves and are found to be the most resistant to localized corrosion[27]. In 2009 Straumann introduced Roxolid ($TiZr13\text{--}17\%$) as an implant which was very thin, (3.3 mm in diameter), that could be used in molars and premolars restorations without any need for addition bone structure[28] and this implant become representative of a new smaller and safer implants generation for cases where is limited space between teeth

In contrast to titanium, zirconia, a ceramic material is a recent achievement [29], Ceramics were first introduced in implantology as coatings onto metal-based endosseous implants to improve osseointegration as both forms bioactive ceramics, (calcium phosphates and bioglasses), and inert ceramics, (aluminium oxide and zirconium oxide) Ceramics need improvement of their mechanical properties and only development of biomaterials technology which involves increasing of properties make them suitable substrates in oral implantology. In Table 1 a summary of common oral implant materials are presented.

Table 1. Common oral implant materials

Implant Material	Composition
Metals	
Stainless Steel 316L	Cr –Ni – Mo (austenitic)
Cobalt Chromium Alloy	CoCr
Titanium different grade	Ti-6Al-4V extra low interstitial (ELI)
Titanium alloys	Ti-15 Zr-4Nb-2Ta-0.2Pd TixZr, Roxolid (83%–87%Ti-13%–17%Zr) Gold Alloys (Au alloy) Zirconia ZrO ₂
Ceramic materials	

4. Diseases prevention and bacterial inflammation

The disease prevention for the affected tissues around the implant begins with a sufficient period of planning, including understanding and assessment of risk factors, optimal tissue establishment, and best implant design. The periodic clinical examinations of the periodontal condition are mandatory as a part of prevention.

The various degrees of damage due to inflammation and ulceration of soft and hard tissues at the level of implants are similar to gingivitis and periodontitis and represent mucositis and peri-implantitis [12]. Often are different stages unclear to be clinically separable [1].

Mucositis represents bacterial-induced inflammation of the soft tissue around the implant, which is reversible, including redness, swelling and bleeding of the tissues during periodontal examination [12]. Such typical signs are not clearly visible always and, an indicator as bleeding could be a peri-implantitis indication as well.

The peri-implantitis is progressive and the disease involves bone resorption, decreased osseointegration, and increase of periodontal pockets depth [12]. The type of the implant and its connections, the structure material, and the prosthetic superstructure, or too deep insertion of the implant, could be the reasons for bone

loss as well.

Based on clinical data collected from literature, the prevalence of peri-implantitis seems to affect around 10% of the implants and 20% of the patients within 5-10 years after implant insertion [13].

It is to mention other factors that should be considered to affect prevalence figures such as differential diagnosis, thresholds for the bone loss, differences in treatment methods and differences in selection of patients in target groups. Of course, general health, oral health status and bad habits are used criteria for selection but each of them has different importance. As examples several studies indicated the smoking and history of periodontal status more closely related to the occurrence of peri-implantitis than other factors. Due to difference in building target groups for study, the prevalence of peri-implant diseases varied in various studies.

Most investigations have reported that the prevalence of mucositis and peri-implantitis is up to 25%, and that up to 10% of implants have to be removed due to peri-implantitis. There is an agreement on the etiological factors as following [30]:

- 1) bacterial plaque;
- 2) smoking;
- 3) incorrect occlusal adaptation;
- 4) poor oral hygiene;
- 5) use of excess gel/mouthwash;
- 6) debridement of the affected area (non-surgical);
- 7) the use of systemic antibiotics;

The dental clinics' current practice indicates that implantation diseases are common problems and that the absence of a standard therapeutic protocol led to the empirical use of therapeutic approaches, not always satisfactory.

The pathognomonic characteristics of the peri-implantitis have been the subject of repeated consensus meetings[1]. Thus, for peri-implantitis, the following signs and symptoms are mandatory:

- Inflammation causes bleeding and /or suppuration in gentle examination with a dull instrument;
- The periodontal pocket depth is more than 4 mm around the implant in the case of a non-obstructed access to the lesion;
- The bony defect around the implant is limited with a characteristic of crater shape;
- Osseointegration is maintained beyond the defect when the implant does not show mobility

The optional signs and symptoms of peri-implantitis are:

- The lining mucosa may be swollen;
-

- The bone craters may be confused with a large defect bone form when adjacent implants are affected;
- The contour of the crater can be interrupted if an implant is located near the edge of the crest. For narrow crest, the lesion takes an "u" shape;
- The pain is not always present.

A final correct diagnosis of peri-implantitis requires simultaneously the presence of several signs. Bleeding or bone loss around the implant is not sufficient for a peri-implantitis diagnosis. Authors, such as Zitzmann, support the idea that depositing bacterial biofilms on the surface of the implant can cause local inflammation of the mucosa around it [8]. As long as it has not yet reached the bone level, this stage is reversible and is called mucositis. A peri-implantitis diagnosis therefore requires evidence of bone loss caused by the infection.

There are some situations where the bone is lost for reasons other than infection, such as implant placement too close to each other, and this can cause bone loss without infection [30]. In the case of two-piece implants, the bone loss was frequently associated with subsequent remodeling of the bone within the first few weeks after prosthetic loading [31]. The deep insertion of the implant can induce similar bone loss around [32]. In the case of peri-implantitis suspicion, long-term implant monitoring is required, based firstly on the documents obtained once tissue homeostasis has been established and secondly on the radiographs taken immediately after implant placement

It is accepted that not every pocket depth of over 3 mm represents clearly a sign of the peri-implantitis, being important, according to Gallucci et al., [33] the implant type and shape, the connecting parts and the prosthetic suprastructure, or the aesthetic observation of the 5 mm distance to create the illusion of an interdental papilla.

The role of biofilms in implant diseases, highlighted in literature [34], emphasize the occasional development of peri-implant infections as a consequence of events favoring the pathogenic microbial flora. For example, persistence under the mucosa of the cement may give rise to an infectious process that can not be controlled without the application of anti-infectious measures together with the removal of the initial cause. Differential diagnosis of peri-implantitis should include the identification of a specific cause even if the biofilm's presence indicates a bacterial infection.

Although the formation of periodontal pockets, bleeding on probing, and bone loss are clinical signs, the prevalence or incidence of the disease can not be estimated solely based on their frequency. Some authors overestimated the prevalence of peri-implantitis. Depending on the bone defect configuration, Schwarz et al. introduced intraosseous class I defects, and supra-alveolar defects of class II in the crestal area of the inserted implant [35]. Spiekermann

characterized the type of bone resorption as horizontal (Class I), hey-shaped (class II), funnel shaped (class IIIa), gap-like (class IIIb), as well as a horizontal-circular form (class IV) [36].

At the microscopic and molecular level there are clearly differences between the peri-implant affected tissue and the intact periodontium, allowing determination of the transition between zones. The tissues surrounding the implant are more susceptible to inflammatory disease compared to periodontal tissues due to both factors such as reduced vascularization and parallel orientation of collagen fibers. This phenomenon has been verified immunohistochemically [36]. Also the level of metalloproteinases (MMPs), such as MMP-8, was increased to 71% in peri-implant tissue lesions, recommending metalloproteinases use in diagnosis [11-13]. A differentiation of the peri-implantitis from other periodontal inflammatory processes can be performed on human saliva using markers such as osteocalcin, tartrate-resistant acid phosphatase (TRAP), protein-1 dickkopf-1 (DKK-1), osteoprotegerin (OPG) and cathepsin K (CatK) [9,14].

Most strategies accepted for the treatment of peri-implantitis are mainly based on the same steps used in periodontal therapy. The reason is that the bacterial colonization of dental surfaces and implant has similar principles, and it is accepted that microbial biofilm plays an analogous role in the development of peri-implantation tissue inflammation [1].

5. Therapy

As part of a holistic therapy, procedures evaluation should be performed following a defined control, with appropriate documentation and taking into account the reference parameters. The information about the place of inflammation in implantation area will be identified by aids of radiographs performed in the area with increased bone resorption [1].

Treatment of an early failing implant by guided bone regeneration using resorbable collagen membrane barrier in combination with bioactive glass [4] indicated complete resolution of the osseous defect, thus suggesting that this technique may hold promise in the treatment of implants undergoing early failure. The treatment of peri-implant infections comprises conservative (non-surgical) and surgical approaches. Depending on the level severity of the peri-implant disease (mucositis, moderate or severe peri-implantitis), only a non-surgical therapy might be sufficient. When the problems persist, such step needs to be completed by a surgical treatment.

One of the main aims of peri-implant therapy is disinfection of the contaminated implant surface. In the presence of peri-implant mucositis, non-surgical methods are appropriate and sufficient for such process, which includes implant mechanical cleaning with titanium or plastic curettes, ultrasonics or air polishing.

Moreover, photodynamic therapy as well as local antiseptic drugs, such as chlorhexidenglukonate, hydrogen peroxide, sodium percarbonate, povidone-iodine support the antimicrobial therapy. However, most of the published strategies for peri-implantitis therapy are mainly based on the treatments used for periodontitis.

Conclusions

Taking into account the extended use of dental implants nowadays, it is important to have more knowledge about the actual stage of the art regarding the role of the materials and the risks of diseases appearance after implantation in order to use preventive measures required to minimize the complications.

To achieve this, a good control of the risk factors and risk indicators of peri-implantation inflammation is required.

R E F E R E N C E S

1. R. Smeets, A. Henningsen, O. Jung, M. Heiland, C. Hammächer, J.M. Stein, Definition, etiology, prevention and treatment of peri-implantitis – review. *Head & Face Medicine*, **10**, 34, 2014
2. O. Charyeva, K. Altynbekov, R. Zhartybaev, A. Sabdanaliev. Long-term dental implant success and survival—a clinical study after an observation period up to 6 years. *Swed Dent J*, **36**, 1–6. 2012
3. Heitz-Mayfield LJA: Peri-implant diseases: diagnosis and risk indicators. *J Clin Periodontol*, **35**: 292–304, 2008
4. Prakash S, Talreja, G. V. Gayathri, and D. S. Mehta Treatment of an early failing implant by guided bone regeneration using resorbable collagen membrane and bioactive glass *J Indian Soc Periodontol*. 17(1): 131–136, 2013
5. Huynh-Ba G, Lang NP, Tonetti MS, Zwahlen M, Salvi GE. Association of the composite IL-1 genotype with peri-implantitis: a systematic review. *Clin Oral Implants Res* 2008, 19:1154–1162.
6. Mombelli A, Muller N, Cionca N. The epidemiology of peri-implantitis. *Clin Oral Implants Res* 2012, 23: 67–76.
7. Vervaeke S, Collaert B, Cosyn J, Deschepper E, De Bruyn H. A multifactorial analysis to identify predictors of implant failure and peri-implant bone loss. *Clin Implant Dent Relat Res* 2013, 2:10.
8. Zitzmann NU, Berglundh T: Definition and prevalence of peri-implant diseases. *J Clin Periodontol* 2008, 35: 286–291.

9. Karbach J, Callaway A, Kwon YD, d'Hoedt B, Al-Nawas B. Comparison of five parameters as risk factors for peri-mucositis. *Int J Oral Maxillofac Implants* 2009, 24:491–496.
 10. Malo P, Rigolizzo M, Nobre M, Lopes A, Agliardi E. Clinical outcomes in the presence and absence of keratinized mucosa in mandibular guided implant surgeries: a pilot study with a proposal for the modification of the technique. *Quintessence Int* 2013, 44:149–157.
 11. Wilson TG Jr. The positive relationship between excess cement and peri-implant disease: a prospective clinical endoscopic study. *J Periodontol* 2009, 80:1388–1392.
 12. Clementini M, Rossetti PH, Penarrocha D, Micarelli C, Bonachela WC, Canullo L. Systemic risk factors for peri-implant bone loss: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg* 2014, 43:323–334.
 13. Korsch M, Obst U, Walther W. Cement-associated peri-implantitis: a retrospective clinical observational study of fixed implant-supported restorations using a methacrylate cement. *Clin Oral Implants Res* 2014, 25:797–802.
 14. Linkevicius T, Puisys A, Vindasiute E, Linkeviciene L, Apse P.: Does residual cement around implant-supported restorations cause peri-implant disease? A retrospective case analysis. *Clin Oral Implants Res* 2012, 24:1179–1184.
 15. Xiaotian Liu Shuyang Chen James K.H. Tsoi and Jukka Pekka Matinlinna: Binary titanium alloys as dental implant materials—a review. *Regenerative Biomaterials* 2017, 315–323
 16. James RA. : Subperiosteal implant design based on peri-implant tissue behavior. *N Y J Dent* 1983;53: 407–14.
 17. Sul YT, Johansson CB, Kang Y. et al.: Bone reactions to oxidized titanium implants with electrochemical anion sulphuric acid and phosphoric acid incorporation. *Clin Implant Dent Relat Res* 2002;4:78–87
 18. Hamouda IM, Enan ET, Al-Wakeel EE et al. : Alkali and heat treatment of titanium implant material for bioactivity. *Int J Oral Maxillofac Implant* 2012; 27:776–84
 19. Luiza Ichim, Cristina Dumitriu, Alina Surugiu, Georgeta Totea, Ioana Demetrescu : Elaboration and characterization of a complex coating on Ti with TiO₂ nanotubes functionalized, carbon single carbon nanotubes hydroxyapatite and iron Annals AOSR Series on Physics and Chemistry vol.2 nr 2 pag 7-22
 20. Zinelis S, Silikas N, Thomas A et al. : Surface characterization of SLActive dental implants. *Eur J Esthetic Dent* 2012;7:72–92
-

21. Han A, Tsoi JK, Rodrigues FP et al.: Bacterial adhesion mechanisms on dental implant surfaces and the influencing factors. *Int J Adhesion Adhesives* 2016;69:58–71
22. Hwang M-J, Park E-J, Moon W-J et al.: Characterization of passive layers formed on Ti–10wt% (Ag, Au, Pd, or Pt) binary alloys and their effects on galvanic corrosion. *Corros Sci* 2015;96:152–9
23. Wang QY, Wang YB, Lin J et al.: Development and properties of Ti–In binary alloys as dental biomaterials. *Mater Sci Eng C* 2013;33:1601–6.
24. Sista S, Nouri A, Li Yet al.: Cell biological responses of osteoblasts on anodized nanotubular surface of a titanium-zirconium alloy. *J Biomed Mater Res A* 2013;101:3416–30.
25. Chelariu, R.; Mareci, D.; Munteanu, C.: Preliminary electrochemical testing of some Zr–Ti alloys in 0.9% NaCl solution. *Mater. Corros.* 2013, 64, 585–591.
26. Akimoto, T. et al.: Evaluation of corrosion resistance of implant-use Ti-Zr binary alloys with a range of compositions. *Biomed. Mater. Res. B* 2018,106B, 73–79
27. Gottlow, et al.: Evaluation of a new titanium-zirconium dental implant: a biomechanical and histological comparative study in the mini pig. *Clin Implant Dent Relat Res.*2012, 14, 538–545
28. Straumann: Roxolid vs. Titanium Implants Clinical Review 2014. (https://www.straumann.com/content/dam/internet/straumann_xy/resources/clinical-reviews/Roxolid%20vs.%20Titanium%20Implants%20Clinical%20Review%202014.pdf)
29. Reham B. Osman and Michael V. Swain A Critical Review of Dental Implant Materials with an Emphasis on Titanium *versus* Zirconia Materials . 2015, 8(3): 932–958.
30. Tarnow, D. P., Cho, S. C. & Wallace, S. S. : The effect of inter-implant distance on the height of inter-implant bone crest. *Journal of Periodontology* 2000, 71: 546–549.
31. Adell R, Lekholm U, Rockler B, Branemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. *Int J Oral Surg* 1981, 10: 387-416
32. Hammerle, C. H., Bragger, U., Burgin, W. & Lang, N. P. The effect of subcrestal placement of the polished surface of ITI implants on marginal soft and hard tissues. *Clinical Oral Implants Research* 1996, 7:111–119.
33. Gallucci, G. O., Grutter, L., Chuang, S. K. & Belser, U. C. Dimensional changes of peri-implant soft tissue over 2 years with single-implant crowns in the anterior maxilla. *Journal of Clinical Periodontology* 2011, 38: 293–299.

34. Mombelli, A. & Decaillet, F. The characteristics of biofilms in peri-implant disease. *Journal of Clinical Periodontology* 2011, 38: 203–213.
35. Schwarz F, Sahm N, Becker J: Aktuelle Aspekte zur Therapie periimplantärer Entzündungen. *Quintessenz* 2008, 59:10.
36. Nickenig HJ, Spiekermann H, Wichmann M, Andreas SK, Eitner S: Survival and complication rates of combined tooth-implant-supported fixed and removable partial dentures. *Int J Prosthodont* 2008, 21(2): 131-7.