GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF PERI-IMPLANT DISEASES

Miguel Padial-Molina, DDS, PhD[1,2], Fernando Suarez, DDS[3], Hector F. Rios, DDS, PhD[4], Pablo Galindo-Moreno, DDS, PhD[2,5,6], and Hom-Lay Wang, DDS, MSD, PhD[7,*].

[1] Research Fellow, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor (MI), USA.

[2] Co-investigator. Research Group CTS#583, University of Granada – Junta de Andalucia, Granada, Spain.

[3] Graduate Student in Periodontics, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan.

[4] Assistant Professor, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan.

[5] Associate Professor, Department of Oral Surgery and Implant Dentistry, School of Dentistry, University of Granada, Granada, Spain.

[6] Visiting Associate Professor, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan.

[7] Professor and Director of Graduate Periodontics, Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan.

*** Corresponding author:**

Hom-Lay Wang DDS, MSD, PhD.

Professor and Director of Graduate Periodontics–Department of Periodontics and Oral Medicine

University of Michigan, School of Dentistry

1101 N. University, Ann Arbor, MI 48109-1078

Tel: 734-763-3383; Fax: 734-936-0374

email: homlay@umich.edu

Tables and Figures: 1 figure Word count: 2981

Running title: Clinical management of peri-implant diseases

ABSTRACT

Introduction: Although some risk factors are well defined, the lack of efficient and predictable approaches to deal with peri-implantitis has created difficulty in the management of those complications. **Objective**: The aim of this review was to evaluate the reliability of the diagnosis methods and to provide a set of guidelines to treat these compromised cases. **Materials and Methods**: A search of PubMed and a hand search of articles related to peri-implant diseases were conducted up to August 2013. **Results/Conclusion**: A summary of the current methods for the diagnosis of peri-implantitis, potential risk factors and a flow chart to guide the clinical management of these conditions are presented.

Key Words: peri-implant disease, mucositis, peri-implantitis, treatment, peri-implant GBR.

INTRODUCTION

Implant therapy is a predominant and very useful armamentarium for patients suffering from missing teeth. Increased number of procedures with no clear etiology of complications has led to an increase in cases of peri-implant disease. Peri-implant diseases may occur in two forms, peri-implant mucositis and peri-implantitis (1). Peri-implant mucositis describes an inflammatory lesion that resides in the soft tissue surrounding a dental implant without signs of bone loss following the initial bone remodeling. On the other hand, peri-implantitis also affects the supporting bone causing progressive bone loss beyond the normal biological remodeling (2). Peri-implantitis appears in combination with marginal bone loss greater than 3mm, bleeding on probing (BOP) or purulence or both (3). It has been estimated that 12-43% of implants have bone loss in combination with BOP (4), being around 10% for implant-supported single crown (5).

Different cross-sectional studies have investigated potential risk indicators for peri-implant disease including poor oral hygiene, smoking, pre- or co-existing periodontitis, diabetes, genetic traits, alcohol consumption, absence of keratinized mucosa and implant surface. However, there is not enough evidence to establish these factors as true risk factors (6). Acknowledging that, it is important to remember that an appropriate implant therapy must always include an appropriate preventive approach to avoid future complications accompanied by professional maintenance protocols and patient personal oral hygiene procedures.

Implant survival, defined as the retention of the implant at the site, should not be the main goal of the clinician's practice. Instead, success should be the goal of our treatment. Implant success has been classically defined as a crestal bone loss lower than 1.5 mm during the first year after loading and 0.2 mm annually thereafter (7). A more recent definition describes implant success (or healthy implant) as the ideal clinical condition for implants serving as prosthetic abutments

for at least 12 months after prosthetic loading in the absence of pain, mobility, radiographic bone loss beyond 2mm from initial surgery and exudates around the implant (8). However, those definitions do not include esthetic success (9), patient satisfaction in terms of discomfort and paresthesia, satisfaction with appearance, and ability to chew/taste (10). Even though esthetic and patient satisfaction have to be considered in the treatment plan, they are not strictly the aim of this review.

Diagnosis of peri-implant diseases requires the measurement of probing depth (PD), BOP, clinical attachment level (CAL), and a radiographic examination to further analyze the characteristic and extent of bone loss, if present (6). Different treatment strategies, often combined, have been proposed including mechanical debridement, pharmaceutical therapy and surgical procedures (open flap debridement, smoothing the implant surface, and 'decontamination' or 'detoxification' of the implant surface followed by resective procedures and/or bone regenerative procedures to correct the anatomical conditions for improving plaque control and for eliminating the pathological peri-implant pockets) (11). While non-surgical treatments are recommended for mucositis lesions, its use has been proven not to be effective in peri-implantitis lesions (12). In such scenarios, open flap debridement including mechanical or chemical methods for decontamination (13), and guided bone regeneration (GBR) are recommended (14, 15).

The lack of an agreement on etiology and a more precise disease classification leads to proposing random therapies. Hence, the aim of this review was to analyze the diagnosis and risk indicators for peri-implant diseases and to propose a clinically-based guide for the management of these conditions.

DIAGNOSIS OF PERI-IMPLANT DISEASES

Implant complications could be biological, technical and/or esthetic in origin. Prognosis, once disease is already present, will be determined by the ability to restore those characteristics.

Clinical parameters

In general, based on longitudinal clinical studies, the time of prosthesis installation should be chosen to establish baseline criteria both at a clinical and radiographical level representing homeostasis (1). It is evident that recorded baseline data will be the reference from which the development of peri-implant disease can be recognized and followed in subsequent examinations. Changes from implant placement to prosthesis delivery must also be considered. However, changes in that early phase should not be considered as peri-implant disease but physiological remodeling or early implant failure, none of which are the purpose of this review. During follow-up visits, if changes in the clinical parameters indicate pathology/disease (BOP, increased CAL / PD), the clinician is encouraged to take new radiographs to evaluate possible bone loss and accordingly treat the case depending on the criteria that will be discussed below.

Implant mobility

If the mobility is due to abutment loosening, occlusion should be checked and adjusted. Mobility of an implant clearly indicates the complete lack of osseointegration and the implant should be removed (6). Lack of clinical detection of implant mobility is a condition often used to describe implant integration (8). However, that does not mean an absolute absence of mobility, since a healthy implant may move up to 75µm (which cannot be clinically detected) (16).

Probing depth

A reliable reference point such as the implant shoulder or the implant–abutment junction should be used to determine the CAL / PD and repeat these measurements over time. This reference point to measure CAL can change by implant design, system and placement level. So, PD is most widely accepted. On the other hand, probing around an implant may be also influenced by different parameters, like the quality of the histological soft tissue seal, the type and surface of the implant and suprastructure (17), and probing force (0.2-0.3 N) (18-21). No data exists with regards to how probe material (metal versus plastic) or design influence peri-implant probing (6).

Generally, implant PD ranges from 3-4 mm and this can vary between implant systems, esthetic placement depths, bone levels to adjacent teeth, healing time, surgical protocol (1- or 2-stages), and loading protocol (22, 23). Although these studies did not include concepts such as platform switching, which may lead to lower measurements, it is widely accepted that this soft tissue thickness down to the crest of the bone is a constant in a healthy tissue with no more than 2mm of radiographic bone loss from the implant platform. A baseline PD measurement after the initial soft tissue healing after loading should be established and monitored since an increase in PD over time has been clearly associated with attachment and bone loss in experimental peri-implantitis studies (24, 25). Six millimeter peri-implant pocket has been suggested as the cut-off indicative of peri-implant disease if accompanied by other signs (e.g., radiographic radiolucencies, purulent exudate, bleeding) and/or symptoms (e.g., discomfort, pain) (26). Sulcus depths greater than 5 to 6 mm around implants have a greater incidence of anaerobic bacteria and may require intervention in the presence of inflammation or exudate (8). Therefore, PD must not be considered as an absolute and isolated diagnostic tool.

Bleeding on probing

Presence of bleeding on probing is a useful parameter for the diagnosis of mucosal inflammation. Lang et al. demonstrated that healthy peri-implant sites had absence of BOP while there was increased BOP at mucositis (67%) and peri-implantitis (91%) sites (18). Furthermore, BOP is considered a valuable parameter for diagnosing peri-implant disease with a high negative predictive value. Moreover, it also has a positive predictive value of 100% (27). Thus, absence of BOP is a good indicator of stable peri-implant conditions (6). In contrast, presence of BOP clearly suggests a diagnosis of peri-implant mucositis. Hence, the clinician must evaluate other clinical parameters, such as PD, exudates, and radiographic data to rule out the presence of peri-implantitis (1).

Suppuration

The presence of pus in the peri-implant sulcus, either spontaneously or after probing, indicates the presence of an infection and/or an inflammatory lesion (26, 28). This is a common finding in peri-implantitis sites (1).

Radiographic evaluation

It is assumed that an initial bone loss due to adaptive remodeling and creation of biologic width at the marginal level of implant is normal. Platform switching may reduce/eliminate that marginal bone loss (29). It is required, however, to periodically evaluate (every 6 months to 1 year) both clinical and radiographic data during the maintenance phase to determine changes over time in the distance from a fixed reference point (e.g. implant shoulder or implant–abutment junction) to the inter-proximal bone level as recorded at baseline (6). Although bone loss in

buccal and lingual sides is difficult to detect radiographically, standardized and high quality radiographs should always be performed for the early detection of peri-implantitis (8).

Several different radiographic techniques can be used to evaluate the peri-implant structures, such as intraoral radiography, panoramic tomography, computer tomography (CT), cone beam computed tomography (CBCT) and volume imaging (30).

Conventional radiography

Conventional radiography includes intraoral and panoramic techniques. Both techniques are widely used for peri-implant diagnosis and both are reliable to assess bone levels around dental implants (31). While panoramic radiographs offer a view of both jaws, intraoral radiographs provide less magnification/distortion, a more detailed picture and higher resolution (32). Nonetheless, both methods underestimate the marginal bone loss, are unable to monitor facial and lingual bone levels, and have low sensitivity in the detection of early bone loss (33). Hence, a thorough clinical examination is mandatory for complete diagnosis.

Subtraction radiography

Subtraction radiography allows the clinician to digitally compare periapical intraoral (34) as well as panoramic radiographs (35) from different time points in order to obtain information on marginal bone levels and minor variations in bone density that would be more challenging to detect with conventional radiograph analysis.

Computer tomography

Due to the limitations of conventional radiography, the use of 3-Dimensional images to diagnose the peri-implant surrounding architecture has arisen during the past few years. The accuracy and quality of such techniques have been documented (36), which make them a promising useful set

of technology for assessing bone levels on implants. However, the application of these new technologies needs to be further studied. In addition to the possibility of measuring the bone defects in three planes, CT and digital volume tomography (DVT) showed minimal deviation compared to direct peri-implant defect measurements, while the DVT scans were found to offer the best imaging quality with less scattering, which may help to overcome this technical limitation (36).

Risk indicators

Oral hygiene

Poor oral hygiene and peri-implant alveolar bone loss have been correlated (37) with an increased OR of 14.3 (95% CI: 2.0–4.1) (38). So, in all cases, plaque detection and oral hygiene instructions should be performed at every follow-up visit, including teeth cleaning as needed.

History of periodontitis

Patients with history of periodontitis are more susceptible to peri-implant diseases (39) and peri-implant marginal bone loss (40). Therefore, before placing dental implants, the existing periodontitis condition must be adequately treated. If not, those infected sites (PPD > 5mm) may act as reservoirs of pathogens to colonize implant surfaces, which represent a significant risk for the development of peri-implantitis and implant loss (41). However, it is important to mention that, despite similarities in clinical features, etiology and host response to biofilms (42), histopathological differences exist between peri-implantitis and periodontitis lesions (43).

Smoking and alcohol consumption

The negative effect of cigarette smoking on the peri-implant tissues is well-documented, not only at peri-implant mucositis but also noted at marginal bone loss and peri-implantitis (40, 44-46).

Regarding alcohol consumption, it has been reported that peri-implant marginal bone loss can be significantly related to a daily consumption of >10g of alcohol. In that study, marginal bone loss was even greater in patients taking alcohol compared with tobacco users (40).

Prosthetic rehabilitation

Peri-implant disease may be also initiated by prosthodontic/iatrogenic factors such as cement remnants, inadequate restoration-abutments seating, overcontoured restorations, presence of cantilevers and technical complications (1). Implant mal-positioning, other than esthetic complications, may also increase the risk to peri-implant disease development. Clinicians must consider on an individual basis the influence of that mal-positioning to determine whether or not is a true peri-implant disease or an expected consequence of the malposition (e.g., fenestration, dehiscences). When the implant mal-position is so severe that the implant cannot be adequately restored, implant removal and placement of a new one in a position closer to ideal should be considered as the best long-term treatment option.

Occlusal overloading seems to play a role as a co-factor in the initiation and progression of peri-implant diseases as well (47). Miyata et al. in a monkey study found that traumatic occlusion plays a role in bone breakdown around the implant. The authors proposed a threshold of excessive height of the superstructures at which peri-implant tissue breakdown may start at approximately 180 μm, even when there was no inflammation in peri-implant tissue (48). On the contrary, a recent study in Labrador dogs concluded that, in the presence of peri-implant mucosal health, excessive occlusal load did not result in loss of osseointegration or marginal bone loss when compared with non-loaded implants. However, no force measurements were performed in this study (49).

Other indicators of occlusal overloading such as lost or loosening screws, prosthesis detachment, porcelain fractures, etc. help the clinician in identifying the presence of a problem before the supporting bone is affected.

Implant surface

Many different implant surfaces and new modifications of them are commercially available (50, 51). Interestingly, according to recent evidence, there is not enough data to assure that implant surface characteristics can have a significant effect on the initiation of peri-implantitis (52). However, rough surfaces tend to accumulate more biofilm and are more difficult to clean. Therefore, it has been suggested that, once exposed to the oral environment, rough surfaces are more likely to develop peri-implantitis. They are also more susceptible to disease progression than smooth or minimally rough surfaces (53, 54).

Keratinized mucosa

Regarding the role of keratinized mucosa (KM) or attached mucosa (AM) in maintaining healthy tissues around dental implants, no clear evidence is available yet. Some studies have reported no association between the absence of an adequate width of KM (i.e., $\geq$2mm) or AM (i.e., $\geq$1mm) and peri-implant diseases (28). However, evidence for the opposite is also available (55-57). In this sense, the 3rd EAO Consensus Conference concluded that evidence in support of the need for keratinized tissues around implants to maintain health and tissue stability is limited (58), similarly to a more recent systematic review that was unable to draw a definitive conclusion (59). Nonetheless, it seems to be well-established that the absence of adequate KM promotes higher gingival inflammation and plaque accumulation, especially in posterior implants (60), which

would lead to more susceptibility to tissue inflammation, and, therefore, increase the risk for peri-implant disease. Similar results have been reported in a 5 year multicenter study (61).

Biological markers

In recent years, microbiological tests and peri-implant crevicular fluid and saliva analyses to detect different biological markers (such as cytokines, enzymes or matrix metalloproteinases) have been introduced. They could enhance the prognostic characteristics of other parameters, orient for an early diagnosis and therefore allow prompt treatment of peri-implant infections (27, 62). However, even though current evidence shows promising results, prospective longitudinal studies are needed, and consequently, the search for markers predicting peri-implant diseases continues (6).

TREATMENT OF PERI-IMPLANT DISEASES

Continuing with the proposed diagnosis flow chart (Figure 1), several clinical and radiographic parameters must be considered before proposing any treatment. Every single one of them will provide valuable information about the etiology, risk factors and severity of the disease and, therefore, will guide the clinicians in the decision process to provide the most reliable treatment. No single parameter (except mobility) is intended to substitute the others; all have to be studied as key constituents of the whole process.

First of all, a clinically detectable mobile implant after prosthesis delivery must be removed, since there is no chance for the implant to be osseointegrated again. It is very important to be sure that the mobility is due to the implant itself and not to the prosthesis or abutments. Any co-existing periodontitis lesion must be treated before or simultaneously to the peri-implant lesions. In all cases, plaque detection and oral hygiene instructions should be discussed with the patient.

Similarly, smoking and/or alcohol consumption cessation counseling is always recommended. Occlusal overloading, premature contacts and other prosthodontic issues, such as inadequate restoration-abutment seating, should be analyzed and corrected at every follow-up visit.

According to the Pisa Consensus Conference on Implant success, survival, and failure, optimum health is defined as an implant with no BOP nor radiographic bone changes higher than 2mm from baseline, no mobility, and no pain upon function (8). However, sometimes a healthy implant might be a treatment failure if it does not allow for a functional and esthetic reconstruction, and therefore it should not be considered as a successful treatment. Different approaches can be designed to deal with such cases, from changes in prosthetic design to use of pink porcelain, soft tissue strategies and even implant removal.

Diagnosis of mucositis considering positive BOP with increased or normal PD but no radiographic bone changes leads to a conservative treatment. Peri-implant mucositis is usually a reversible condition that can be successfully treated with non-surgical therapy and the adjunctive use of antimicrobial mouth rinses (12, 63). Food impaction, cement retention, overcontoured restorations and any kind of irritative agents should be explored and removed.

When PD lower than 5 mm and positive BOP (with or without purulent exudates) are detected, a radiographic examination is also required. Presence of radiographic bone defects can be hardly detectable at this point. So, the initial therapy should be as a mucositis problem followed by closely monitoring. If radiographic bone loss is obvious (≥2mm), an open flap debridement is needed. This procedure should always be accompanied by a proper surface decontamination and detoxification (13). Such decontamination/detoxification can be performed by either mechanical or chemical methods. Its aims are to remove all bacteria deposits, to facilitate soft tissue re-accommodation and to limit and minimize future plaque deposition that would reinitiate the

disease episode. Grafting procedures at this time may be indicated in cases of retentive bone defects while bone re-contouring is indicated in irregular bone defects. If prosthesis replacement is required, prosthesis removal, closed bone grafting procedure and delivery of the new prosthesis after 6 months is of choice when the crest of the bone is near to the implant shoulder.

Special consideration should be given to cases of implants with a PD ≥ 8mm or more than 50% of the implant length. According to a recent systematic review, re-osseointegration is unpredictable, and is not achieved for the entire previously contaminated implant surface (64). Therefore, if a deep circumferential defect is present, although GBR could be performed, extraction of the problematic implant followed by GBR to reconstruct the lost bone and placement of a new implant in the regenerated bone is a good, safer and more predictable alternative. Vertical bone defects are a risk that may be overcome by early implant explantation. Otherwise, clinical scenarios with vertical bone defects can be more challenging to treat. In contrast, cases with non-retentive bone defects should be treated by open flap debridement followed by mechanical and/or chemical decontamination/detoxification. Prosthesis removal followed by a closed bone grafting procedure and delivery of the new prosthesis after 6 months can benefit GBR procedure.

According to the literature, no single method of surface decontamination is superior (13, 65). Similarly, regenerative procedures such as bone graft techniques with or without the use of barrier membranes result in various degrees of success, although these techniques are not aimed to resolve the disease but to restore the osseous defect (65).

In any of the above-mentioned cases, if KM is deficient (<2mm), a corrective soft tissue grafting procedure could be performed. Free gingival grafts (66), allografts (67) or collagen membranes (68) can be used.

Finally, we should remark once again that every implant patient, healthy or not, should be carefully instructed in oral hygiene techniques, counseled on the risk factors for peri-implant disease development such as use of tobacco and alcohol or the presence of co-existing or previously treated periodontitis, and strongly encouraged to adhere closely to the maintenance regimen. Of course, this also requires from clinicians a careful peri-implant diagnosis, treatment planning, and maintenance protocols, all of which are key to achieving successful implant therapy.

CONCLUSIONS

With the limitations of lacking an agreement on etiology and a more precise disease classification, a flow-chart based on current evidence and daily clinical practice is proposed for the treatment of peri-implant diseases. Based on 3 probing depth ranges (i.e., ≤5mm, 6-7mm, and ≥8mm), bleeding on probing and radiographic bone loss (i.e., ≤2mm; >2mm), different diagnosis are depicted and treatment modalities proposed. Those include non-surgical therapy, open flap debridement, decontamination/detoxification, and GBR. In some particular cases, such as implant mobility, extreme mal-positioning or extensive but retentive bone loss, implant removal is recommended. Bone defect shape and KM should also be considered and corrected. Plaque index, oral hygiene, periodontal status, smoking/alcohol intake, esthetic, occlusion and prosthesis must be checked and corrected if needed.

ACKNOWLEDGEMENTS AND SOURCE OF FUNDING

Authors were supported in part by the Talentia Scholarship Program (*Junta de Andalucía*, Spain) (MPM), the Research Group #CTS-583 (*Junta de Andalucía*) (MPM, PGM), and the University of

Michigan Periodontal Graduate Student Research Fund (FS). The authors do not have any financial interests, either directly or indirectly, in the products listed in the study.

REFERENCES

1. Lang NP, Berglundh T. Periimplant diseases: where are we now?--Consensus of the Seventh European Workshop on Periodontology. J Clin Periodontol 2011;38 Suppl 11:178-181.

2. AAP-Academy-Report. Peri-implant mucositis and peri-implantitis: a current understanding of their diagnoses and clinical implications. J Periodontol 2013;84:436-443.

3. Roos-Jansaker AM, Renvert S, Egelberg J. Treatment of peri-implant infections: a literature review. J Clin Periodontol 2003;30:467-485.

4. Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases. J Clin Periodontol 2008;35:286-291.

5. Jung RE, Pjetursson BE, Glauser R, Zembic A, Zwahlen M, Lang NP. A systematic review of the 5-year survival and complication rates of implant-supported single crowns. Clin Oral Implants Res 2008;19:119-130.

6. Heitz-Mayfield LJ. Peri-implant diseases: diagnosis and risk indicators. J Clin Periodontol 2008;35:292-304.

7. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: a review and proposed criteria of success. Int J Oral Maxillofac Implants 1986;1:11-25.

8. Misch CE, Perel ML, Wang HL, Sammartino G, Galindo-Moreno P, Trisi P, et al. Implant success, survival, and failure: the International Congress of Oral Implantologists (ICOI) Pisa Consensus Conference. Implant Dent 2008;17:5-15.

9. Cooper LF. Objective criteria: guiding and evaluating dental implant esthetics. J Esthet Restor Dent 2008;20:195-205.

10. Papaspyridakos P, Chen CJ, Singh M, Weber HP, Gallucci GO. Success criteria in implant dentistry: a systematic review. J Dent Res 2012;91:242-248.

11. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: treatment of peri-implantitis. Cochrane Database Syst Rev 2012;1:CD004970.

12. Renvert S, Roos-Jansaker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. J Clin Periodontol 2008;35:305-315.

13. Suarez F, Monje A, Galindo-Moreno P, Wang HL. Implant surface detoxification: a comprehensive review. Implant Dent 2013;22:465-473.

14. Romeo E, Ghisolfi M, Murgolo N, Chiapasco M, Lops D, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part I: clinical outcome. Clin Oral Implants Res 2005;16:9-18.

15. Romeo E, Lops D, Chiapasco M, Ghisolfi M, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part II: radiographic outcome. Clin Oral Implants Res 2007;18:179-187.

16. Sekine H, Komiyama Y, Hotta H. Mobility characteristics and tactile sensitivity of osseointegrated fixture-supporting systems. In: van Steenberghe D (ed). Tissue Integration in Oral Maxillofacial Reconstruction. Amsterdam: Excerpta Medica, 1986.

17. Salvi GE, Lang NP. Diagnostic parameters for monitoring peri-implant conditions. Int J Oral Maxillofac Implants 2004;19 Suppl:116-127.

18. Lang NP, Wetzel AC, Stich H, Caffesse RG. Histologic probe penetration in healthy and inflamed peri-implant tissues. Clin Oral Implants Res 1994;5:191-201.

19. Schou S, Holmstrup P, Stoltze K, Hjorting-Hansen E, Fiehn NE, Skovgaard LT. Probing around implants and teeth with healthy or inflamed peri-implant mucosa/gingiva. A histologic comparison in cynomolgus monkeys (Macaca fascicularis). Clin Oral Implants Res 2002;13:113-126.

20. Mombelli A, Muhle T, Bragger U, Lang NP, Burgin WB. Comparison of periodontal and peri-implant probing by depth-force pattern analysis. Clin Oral Implants Res 1997;8:448-454.

21. Etter TH, Hakanson I, Lang NP, Trejo PM, Caffesse RG. Healing after standardized clinical probing of the perlimplant soft tissue seal: a histomorphometric study in dogs. Clin Oral Implants Res 2002;13:571-580.

22. Berglundh T, Lindhe J. Dimension of the periimplant mucosa. Biological width revisited. J Clin Periodontol 1996;23:971-973.

23. Cochran DL, Hermann JS, Schenk RK, Higginbottom FL, Buser D. Biologic width around titanium implants. A histometric analysis of the implanto-gingival junction around unloaded and loaded nonsubmerged implants in the canine mandible. J Periodontol 1997;68:186-198.

24. Lang NP, Bragger U, Walther D, Beamer B, Kornman KS. Ligature-induced peri-implant infection in cynomolgus monkeys. I. Clinical and radiographic findings. Clin Oral Implants Res 1993;4:2-11.

25. Schou S, Holmstrup P, Stoltze K, Hjorting-Hansen E, Kornman KS. Ligature-induced marginal inflammation around osseointegrated implants and ankylosed teeth. Clin Oral Implants Res 1993;4:12-22.

26. Fransson C, Wennstrom J, Berglundh T. Clinical characteristics at implants with a history of progressive bone loss. Clin Oral Implants Res 2008;19:142-147.

27. Luterbacher S, Mayfield L, Bragger U, Lang NP. Diagnostic characteristics of clinical and microbiological tests for monitoring periodontal and peri-implant mucosal tissue conditions during supportive periodontal therapy (SPT). Clin Oral Implants Res 2000;11:521-529.

28. Roos-Jansaker AM, Renvert H, Lindahl C, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. J Clin Periodontol 2006;33:296-301.

29. Nevins M, Gobbato L, Lee HJ, Wang CW, Kim DM. Maintaining interimplant crestal bone height via a combined platform-switched, Laser-Lok implant/abutment system: a proof-of-principle canine study. Int J Periodontics Restorative Dent 2013;33:261-267.

30. Benavides E, Rios HF, Ganz SD, An CH, Resnik R, Reardon GT, et al. Use of cone beam computed tomography in implant dentistry: the International Congress of Oral Implantologists consensus report. Implant Dent 2012;21:78-86.

31. Kullman L, Al-Asfour A, Zetterqvist L, Andersson L. Comparison of radiographic bone height assessments in panoramic and intraoral radiographs of implant patients. Int J Oral Maxillofac Implants 2007;22:96-100.

32. Akesson L, Hakansson J, Rohlin M, zöguer B. An evaluation of image quality for the assessment of the marginal bone level in panoramic radiography. Swed Dent J 1992;17:9-21.

33. De Smet E, Jacobs R, Gijbels F, Naert I. The accuracy and reliability of radiographic methods for the assessment of marginal bone level around oral implants. Dentomaxillofac Radiol 2002;31:176-181.

34. Carneiro LS, da Cunha HA, Leles CR, Mendonca EF. Digital subtraction radiography evaluation of longitudinal bone density changes around immediate loading implants: a pilot study. Dentomaxillofac Radiol 2012;41:241-247.

35. Geraets WG, Verheij HG, Wismeijer D, van der Stelt PF. Detecting bone loss along dental implants by subtraction of panoramic radiographs. Clin Oral Implants Res 2012;23:861-865.

36. Mengel R, Kruse B, Flores-de-Jacoby L. Digital volume tomography in the diagnosis of peri-implant defects: an in vitro study on native pig mandibles. J Periodontol 2006;77:1234-1241.

37. Lindquist LW, Carlsson GE, Jemt T. Association between marginal bone loss around osseointegrated mandibular implants and smoking habits: a 10-year follow-up study. J Dent Res 1997;76:1667-1674.

38. Ferreira SD, Silva GL, Cortelli JR, Costa JE, Costa FO. Prevalence and risk variables for peri-implant disease in Brazilian subjects. J Clin Periodontol 2006;33:929-935.

39. Schou S, Holmstrup P, Worthington HV, Esposito M. Outcome of implant therapy in patients with previous tooth loss due to periodontitis. Clin Oral Implants Res 2006;17 Suppl 2:104-123.

40. Galindo-Moreno P, Fauri M, Avila-Ortiz G, Fernandez-Barbero JE, Cabrera-Leon A, Sanchez-Fernandez E. Influence of alcohol and tobacco habits on peri-implant marginal bone loss: a prospective study. Clin Oral Implants Res 2005;16:579-586.

41. Pjetursson BE, Helbling C, Weber HP, Matuliene G, Salvi GE, Bragger U, et al. Peri-implantitis susceptibility as it relates to periodontal therapy and supportive care. Clin Oral Implants Res 2012;23:888-894.

42. Lang NP, Bosshardt DD, Lulic M. Do mucositis lesions around implants differ from gingivitis lesions around teeth? J Clin Periodontol 2011;38 Suppl 11:182-187.

43. Berglundh T, Zitzmann NU, Donati M. Are peri-implantitis lesions different from periodontitis lesions? J Clin Periodontol 2011;38 Suppl 11:188-202.

44. Haas R, Haimbock W, Mailath G, Watzek G. The relationship of smoking on peri-implant tissue: a retrospective study. J Prosthet Dent 1996;76:592-596.

45. Levin L, Hertzberg R, Har-Nes S, Schwartz-Arad D. Long-term marginal bone loss around single dental implants affected by current and past smoking habits. Implant Dent 2008;17:422-429.

46. Strietzel FP, Reichart PA, Kale A, Kulkarni M, Wegner B, Kuchler I. Smoking interferes with the prognosis of dental implant treatment: a systematic review and meta-analysis. J Clin Periodontol 2007;34:523-544.

47. Misch CE, Suzuki JB, Misch-Dietsh FM, Bidez MW. A positive correlation between occlusal trauma and peri-implant bone loss: literature support. Implant Dent 2005;14:108-116.

48. Miyata T, Kobayashi Y, Araki H, Ohto T, Shin K. The influence of controlled occlusal overload on peri-implant tissue. Part 3: A histologic study in monkeys. Int J Oral Maxillofac Implants 2000;15:425-431.

49. Heitz-Mayfield LJ, Schmid B, Weigel C, Gerber S, Bosshardt DD, Jonsson J, et al. Does excessive occlusal load affect osseointegration? An experimental study in the dog. Clin Oral Implants Res 2004;15:259-268.

50. Padial-Molina M, Galindo-Moreno P, Avila-Ortiz G. Biomimetic ceramics in implant dentistry. Minerva Biotecnol 2009;21:173-186.

51. Padial-Molina M, Galindo-Moreno P, Fernandez-Barbero JE, O'Valle F, Jodar-Reyes AB, Ortega-Vinuesa JL, et al. Role of wettability and nanoroughness on interactions between osteoblast and modified silicon surfaces. Acta Biomater 2011;7:771-778.

52. Renvert S, Polyzois I, Claffey N. How do implant surface characteristics influence peri-implant disease? J Clin Periodontol 2011;38 Suppl 11:214-222.

53. Albouy JP, Abrahamsson I, Persson LG, Berglundh T. Spontaneous progression of peri-implantitis at different types of implants. An experimental study in dogs. I: clinical and radiographic observations. Clin Oral Implants Res 2008;19:997-1002.

54. Albouy JP, Abrahamsson I, Persson LG, Berglundh T. Implant surface characteristics influence the outcome of treatment of peri-implantitis: an experimental study in dogs. J Clin Periodontol 2011;38:58-64.

55. Linkevicius T, Apse P, Grybauskas S, Puisys A. The influence of soft tissue thickness on crestal bone changes around implants: a 1-year prospective controlled clinical trial. Int J Oral Maxillofac Implants 2009;24:712-719.

56. Bouri A, Jr., Bissada N, Al-Zahrani MS, Faddoul F, Nouneh I. Width of keratinized gingiva and the health status of the supporting tissues around dental implants. Int J Oral Maxillofac Implants 2008;23:323-326.

57. Zigdon H, Machtei EE. The dimensions of keratinized mucosa around implants affect clinical and immunological parameters. Clin Oral Implants Res 2008;19:387-392.

58. Wennstrom JL, Derks J. Is there a need for keratinized mucosa around implants to maintain health and tissue stability? Clin Oral Implants Res 2012;23 Suppl 6:136-146.

59. Brito C, Tenenbaum HC, Wong BK, Schmitt C, Nogueira-Filho G. Is keratinized mucosa indispensable to maintain peri-implant health? A systematic review of the literature. J Biomed Mater Res B Appl Biomater 2013.

60. Chung DM, Oh TJ, Shotwell JL, Misch CE, Wang HL. Significance of keratinized mucosa in maintenance of dental implants with different surfaces. J Periodontol 2006;77:1410-1420.

61. Schrott AR, Jimenez M, Hwang JW, Fiorellini J, Weber HP. Five-year evaluation of the influence of keratinized mucosa on peri-implant soft-tissue health and stability around implants supporting full-arch mandibular fixed prostheses. Clin Oral Implants Res 2009;20:1170-1177.

62. Candel-Marti ME, Flichy-Fernandez AJ, Alegre-Domingo T, Ata-Ali J, Penarrocha-Diago MA. Interleukins IL-6, IL-8, IL-10, IL-12 and periimplant disease. An update. Med Oral Patol Oral Cir Bucal 2011.

63. Heitz-Mayfield LJ, Salvi GE, Botticelli D, Mombelli A, Faddy M, Lang NP. Anti-infective treatment of peri-implant mucositis: a randomised controlled clinical trial. Clin Oral Implants Res 2011;22:237-241.

64. Renvert S, Polyzois I, Maguire R. Re-osseointegration on previously contaminated surfaces: a systematic review. Clin Oral Implants Res 2009;20 Suppl 4:216-227.

65. Claffey N, Clarke E, Polyzois I, Renvert S. Surgical treatment of peri-implantitis. J Clin Periodontol 2008;35:316-332.

66. Simons AM, Darany DG, Giordano JR. The use of free gingival grafts in the treatment of peri-implant soft tissue complications: clinical report. Implant Dent 1993;2:27-30.

67. Park JB. Increasing the width of keratinized mucosa around endosseous implant using acellular dermal matrix allograft. Implant Dent 2006;15:275-281.

68. Lee KH, Kim BO, Jang HS. Clinical evaluation of a collagen matrix to enhance the width of keratinized gingiva around dental implants. J Periodontal Implant Sci 2010;40:96-101.

FIGURE LEGENDS

Figure 1: Guideline for the treatment of peri-implant diseases.

PD: probing depth; BOP: bleeding on probing; NST: non-surgical therapy; AMR: antimicrobial mouth rinse; RBL: radiographic bone loss; OFD: open flap debridement; DD: detoxification/decontamination; RBD: retentive bone defect; GBR: guided bone regeneration; KM: keratinazed mucosa; PI: plaque index; OHI: oral hygiene instructions.