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# Treatment of Peri-implant Diseases: A Review of the Literature and Protocol Proposal

**Abstract:** Over 100,000 implants were placed in the UK in 2010. As the numbers of patients with implant-retained prostheses increases, operators are encountering an increasing number of biological implant complications, most commonly peri-implant mucositis and peri-implantitis. The effective management of these complications is crucial to maintain patients' oral health. In particular, in contrast to common periodontal infections, some peri-implant infections may benefit from surgical intervention as a first line approach.

**Clinical Relevance:** This article reviews the literature on the treatment options for peri-implant mucositis and peri-implantitis and proposes a protocol for their treatment

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Over the last two decades, the use of dental implants has become a common treatment option for the replacement of missing teeth. Industry predictions suggest that over 200,000 implants will be placed in the UK in 2013. With the increasing utilization of this treatment option, the frequency with which operators can expect to encounter biological complications increases. Peri-implant disease is a collective term for

the inflammatory reactions of tissues surrounding implants, encompassing two main entities: peri-implant mucositis and peri-implantitis. Originally, up to 0.2 mm of bone loss around implants in the first year, then 0.1 mm per year subsequently, was deemed within acceptable limits.<sup>1</sup> However, as techniques improve, less bone loss is expected.<sup>2</sup> Bone loss exceeding acceptable limits threatens implant success and therefore requires intervention.

(SUP)(Figure 1b), loss of supporting bone, visible clinically on reflection of the soft tissue for surgical treatment (Figure 1c) but usually evidenced radiographically (Figure 1d) and, infrequently, implant mobility is clinically detectable.<sup>3</sup> The extent of peri-implant disease may be graded, grade 0, 1, 2 or 3 (Table 1). A more recently described, possibly different disease, 'retrograde peri-implantitis' is diagnosed as a symptomatic periapical lesion, which may demonstrate a draining sinus. Radiographically, a periapical radiolucency may be seen, with normal osseointegration of the coronal portion of the implant (Figure 2). This lesion often develops shortly after implant insertion and, in the majority of the cases, requires surgical treatment, the discussion of which is beyond the scope of this paper.<sup>4</sup>

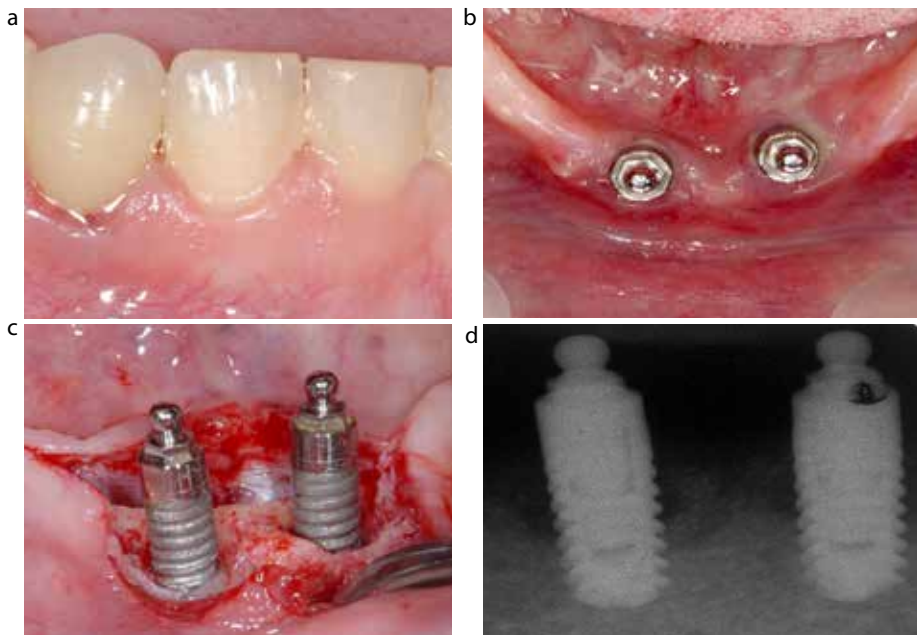
## Prevalence

In large studies, peri-implant mucositis has been shown to occur in 80% of subjects and in 50% of implant sites.<sup>3</sup> Prevalence rates for peri-implantitis of 28–56% of subjects and 12–43% of implant

## Diagnosis and classification

Peri-implant mucositis describes inflammation in the mucosa at an implant area with no signs of loss of supporting bone.<sup>3</sup> Diagnosis of peri-implant mucositis is usually by detection of bleeding on probing (BOP), though redness and swelling may also occur (Figure 1a). Peri-implantitis, on the other hand, describes the presence of inflammation in the mucosa at an (osseointegrated) implant with loss of supporting bone after one year in function. Diagnosis of peri-implantitis is based on increased probing pocket depths (BOP), suppuration

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**Figure 1.** Peri-implant mucositis and implantitis. **(a)** Peri-implant mucositis at the cervical gingival aspect of implant-retained single crown. **(b)** Clinical and **(c)** surgical views of erythema and suppuration from mandibular implants for implant-retained removable prosthesis. **(d)** Periapical radiograph showing evidence of loss of supporting bone up to two-thirds of implant height.

sites have been reported. Risk indicators, such as poor oral hygiene, previous history of periodontitis, diabetes and tobacco smoking have all been linked with increased prevalence of peri-implant diseases.<sup>5</sup>

### Aetiology

There are broadly three theories currently proposed to explain the aetiopathogenesis of peri-implantitis:

1. A pathogenic microbial plaque is a necessary, albeit insufficient, cause;
2. The disease is the result of micro-movement of the implant; and
3. A compromise in the host healing and adaptation predisposes to peri-implantitis.

The microbial biofilm associated with peri-implant disease is mixed and variable, although generally dominated by Gram-negative anaerobic bacteria. Several studies have indicated that peri-implantitis may be associated with an increased proportion of *P. gingivalis*, *T. denticola*, *F. nucleatum*, and *A. actinomycetemcomitans*.

	Signs of Disease	Advised Treatment Regimen
<b>Peri-implant Mucositis</b>	<ul style="list-style-type: none"> <li>■ Inflammation</li> <li>■ BOP</li> <li>■ PPD &lt;4 mm</li> <li>■ No bone loss</li> </ul>	Non-surgical instrumentation and disinfection with chlorhexidine
<b>Peri-implantitis Grade 0</b>	<ul style="list-style-type: none"> <li>■ Failure of osseointegration</li> <li>■ Implant fracture</li> <li>■ Implant mobility &gt;1 mm horizontal movability</li> </ul>	Explant
<b>Peri-implantitis Grade 1 (mild)</b>	<ul style="list-style-type: none"> <li>■ BOP +/- SUP</li> <li>■ PPD &lt;4 mm</li> <li>■ Bone loss &lt;2 mm</li> <li>■ Foreign body in peri-implant sulcus (commonly cement)</li> </ul>	Removal of abutment Non-surgical instrumentation and disinfection
<b>Peri-implantitis Grade 2 (moderate)</b>	<ul style="list-style-type: none"> <li>■ BOP +/- SUP</li> <li>■ PPD 4–6 mm</li> <li>■ Bone loss &lt;2 mm</li> </ul>	Removal of abutment Non-surgical instrumentation and disinfection
<b>Peri-implantitis Grade 3 (severe)</b>	<ul style="list-style-type: none"> <li>■ BOP +/- SUP</li> <li>■ PPD &gt;6 mm</li> <li>■ Bone loss &gt;2 mm</li> </ul>	Removal of abutment Surgical access Instrumentation and Disinfection Systemic antibiotics ? Resective/regenerative surgery

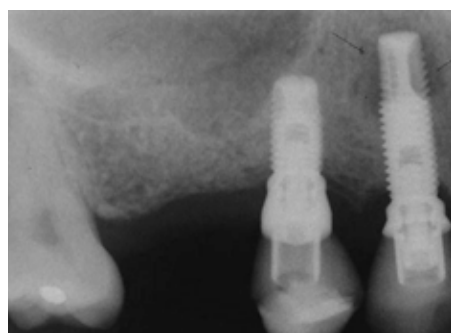
**Table 1.** Classification of peri-implant diseases and advised treatment regimen Renvert and Claffey.<sup>48</sup>

However, other studies identify a diverse spectrum of bacteria, including indigenous oral commensals and bacteria associated with infections of implanted medical devices (eg *S. aureus* and *S. epidermidis*). Therefore, the microbes associated with all cases of peri-implantitis may not simply be identical to those in periodontal disease.<sup>5</sup> Although biofilm removal is associated with clinical improvement, this does not prove that the biofilm causes the diseases.

In addition to the microbiological theory for implant bone loss, there is also experimental evidence that excessive or adverse loading may cause advancing bone resorption. Clinically applicable evidence is, however, currently somewhat lacking.<sup>6</sup> A further postulated theory is that of 'the compromised healing/adaptation theory'.<sup>7</sup> In this theory, implant anchorage is disturbed by poor surgical technique, killing cells needed for repair. Alternatively, a poor host bed response, or excessive strain due to implant misfit or prosthodontic errors, or disturbance of bone cells and their vascular supply, may create an environment predisposing to colonization with pathogenic biofilm, leading to peri-implantitis. The theory of a poor host response is perhaps reinforced by evidence that there are subtle differences in the host response and lesion development in periodontal disease and peri-implantitis.<sup>8</sup>

### Treatment of peri-implant diseases

In spite of the confusion around the aetiology of bone loss around implants,



**Figure 2.** Retrograde peri-implantitis. Periapical radiograph showing evidence of periapical bone loss surrounding the implant in the right maxillary premolar region.

and whether it is a primary or secondary infective process, it is universally accepted that the microbial biofilm plays a central role in the disease<sup>9</sup> and its disruption is required for successful treatment. Prior to commencing treatment, iatrogenic factors that may promote peri-implantitis or mucositis should be identified and, if possible, addressed; for example, excess cement, over-contoured restorations or poorly positioned implants.<sup>10</sup>

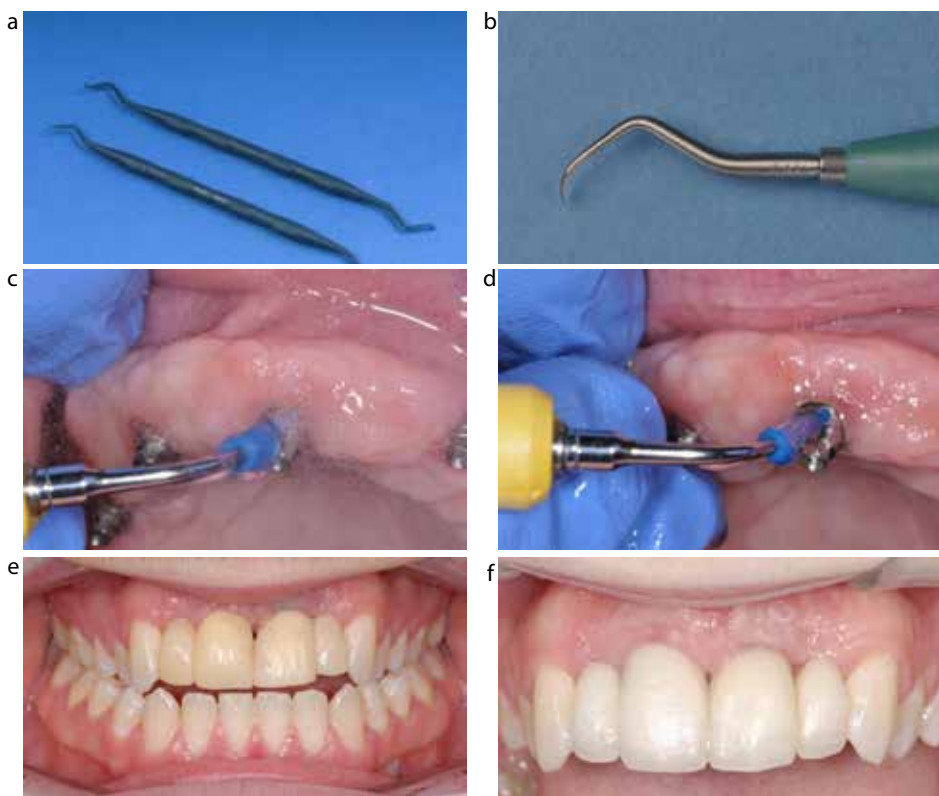
### Treatment of peri-implant mucositis

Peri-implant mucositis is usually treated by non-surgical mechanical therapy, using carbon fibre (Figure 3a) or titanium instruments (Figure 3b), or plastic insert ultrasonics (Figure 3c, d) to minimize damage to the implant surface and superstructure. Adequate access for professional debridement for the treatment of peri-implant mucositis may require removal and if

necessary adjustment of the superstructure (Figure 3e, f). Whether mechanical therapy alone is effective, or requires adjunctive anti-microbial therapy, has been extensively investigated. Human studies have employed non-surgical mechanical therapies with adjunctive abrasive carbonate air powder, or phosphoric acid gel, and demonstrate that peri-implant mucositis can be successfully treated mechanically, with or without these adjuncts. Similarly, there is limited evidence for the adjunctive use of chlorhexidine irrigation and home use mouthwash. However, these are routinely used in practice.<sup>11-14</sup>

### Treatment of peri-implantitis

While non-surgical periodontal therapy is almost always the first line of treatment for periodontitis, regardless of severity. By contrast, Renvert *et al*<sup>21,32</sup> conclude that non-surgical therapy alone is not effective in the treatment of peri-



**Figure 3.** Non-surgical treatment of peri-implantitis. (a) Carbon fibre and (b) titanium curettes for debridement of titanium implant surfaces. (c, d) Ultrasonic scaler with plastic insert in use, after removal of maxillary implant superstructure. (e) Peri-implant mucositis around implant in position UL1 before and (f) after non-surgical debridement and oral hygiene instruction.

implantitis. Peri-implantitis treatment is further complicated by the design and the surface of the implants. Turned (smoother) implant surfaces demonstrated a 20% reduction in risk of being affected by peri-implantitis over a 3-year period, compared with rougher surface implants.<sup>15,16</sup> Moreover, implant geometry and different surface characteristics may also predispose to peri-implantitis.<sup>17</sup> The ultimate aim of treatment of peri-implantitis, similar to that of periodontitis, is regeneration of bone around the fixture, termed re-osseointegration. This has been shown to occur. Again, however, the implant surface exerts an effect. Although smoother surfaces may be slightly less susceptible to peri-implantitis, if affected by bone loss, these surfaces are also less amenable to re-osseointegration (22% re-osseointegration after treatment at turned sites compared with 84% at rougher, SLA™ sites). Biofilm removal is essential to re-osseointegration and this presents a significant challenge to successful treatment, as removing biofilm from rough surface implants is more difficult than its removal from smooth surfaces.<sup>18,19</sup> This is a complex situation, as even different rough surfaces show differences in their ability to re-osseointegrate in beagle dog studies.<sup>20</sup> Treatment options for peri-implant diseases are discussed below.

**Non-surgical treatment of peri-implant disease**

Similar to treatment of peri-implant mucositis, peri-implantitis treatment may be attempted by the use of hand instruments and/or ultrasonics. In addition, the use of Er:YAG lasers has been investigated. For non-surgical treatment of peri-implantitis, some studies describe removal of superstructure to improve access. However, none of these methods has been found to be consistently effective in the treatment of peri-implantitis.<sup>21,22</sup> Early re-assessment at 1–2 months post non-surgical treatment is recommended.<sup>10</sup>

**Surgical treatment**

There is sufficient evidence demonstrating that non-surgical treatment fails to eliminate or reduce

the bacterial counts at sites with peri-implantitis, and that non-surgical treatment alone may not be sufficient to treat peri-implantitis effectively.<sup>23</sup> Overall, a recent review of 26 studies estimated that surgical treatment for peri-implantitis eliminated symptoms of peri-implantitis and arrested progression of bone loss over a 5-year period, in 58% of the sites treated. The basis of this surgical treatment is access flap, removal of granulation tissue and implant surface decontamination.<sup>24</sup> However, within this framework, there is a wide variety of different surgical approaches to the treatment of peri-implantitis, making analysis of the most successful difficult. The essence of treatment remains to debride the implant surface and the majority of non-surgical mechanical debridement techniques described above have found application in surgical debridement (Figure 4 a–d). More recently, in addition to the titanium scalers described above, a rotating titanium bristle brush has been described for use when surgically debriding implants.<sup>25</sup> The options for surface decontamination, antimicrobials, resective vs regenerative and closed vs open healing are discussed in more detail.

**Surface decontamination and conditioning**

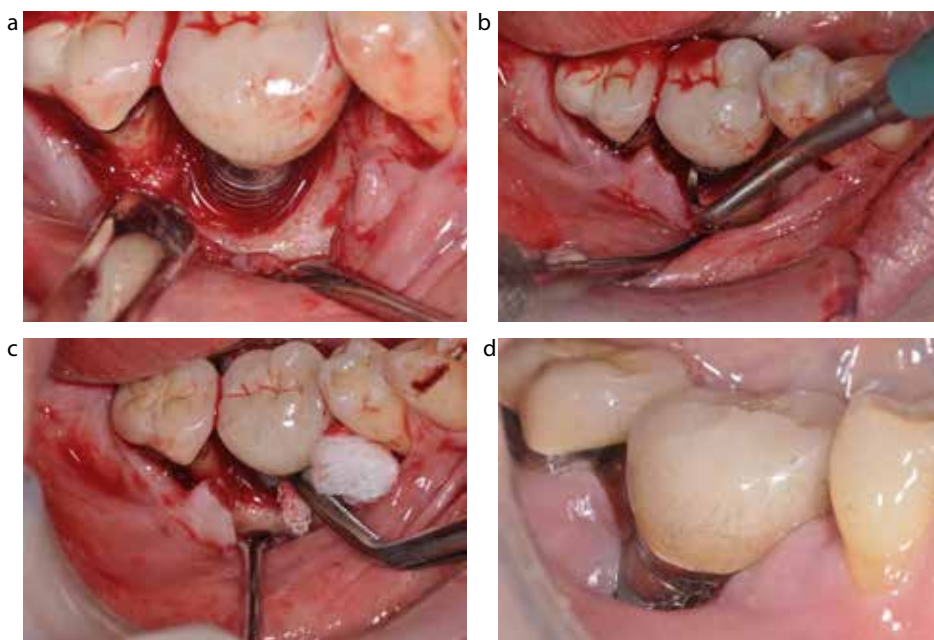
Rough surface implants may promote osseointegration.<sup>26</sup> However, these surfaces complicate the removal of plaque biofilms, therefore adjuncts and alternatives to mechanical debridement have been investigated. Er:YAG laser<sup>22,27</sup> subgingival irrigation with chlorhexidine<sup>28</sup> or air-powder abrasive unit, with or without citric acid, are no more effective than gauze soaked alternately in chlorhexidine and saline.<sup>29</sup>

**Adjunctive antimicrobial therapy**

Used in conjunction with surgical access, adjunctive local or systemic antibiotics<sup>11</sup> may reduce BOP and probing depths.<sup>30–36</sup> For example, successful results have been achieved with the use of tetracycline 50 mg/mL slurry over the debrided implant surface, in conjunction with systemic amoxicillin and metronidazole, incorporated into a six-step protocol to disinfect the implant surface.<sup>37</sup>

**Regenerative and resective**

Numerous studies have been undertaken to investigate the effectiveness of various regenerative procedures. All



**Figure 4.** Surgical treatment of peri-implantitis (a) Soft tissue flap reflected to expose remaining peri-implant bone. (b) Debridement of implant surface with titanium scaler. (c) Disinfection of implant surface with 2% chlorhexidine soaked gauze. (d) Soft tissue closure and recession resulting in stable peri-implant soft tissue with probing pocket depth less than 4 mm in all sites.



regenerative procedures for treating peri-implantitis remain somewhat unpredictable. However, the use of autogenous bone graft, with or without xenograft, with a resorbable membrane, appears to provide the best results for treatment of full or partial bony defects.<sup>37-42</sup> Romeo *et al*<sup>43</sup> concluded that implantoplasty, creating a smooth implant surface of the exposed threads, in conjunction with resective surgery of the bone defect, represents a reliable surgical procedure for arresting and controlling the peri-implant chronic infection, when compared with resective surgery only.

**Submerged versus non-submerged healing**

Schwarz *et al*<sup>44</sup> demonstrated that open flap debridement and submerged healing, in which the implant is fully covered by the gingival tissue and not exposed to the oral environment, was superior to open flap debridement and non-submerged healing. Although effective, submerged healing is not always an option when treating implants in aesthetic areas or implants that are required as bridge abutments.

On the basis of the studies discussed above, the surgical approach suggested by the authors is outlined in Table 2.

There is limited data regarding patient-centred outcomes for treatment of peri-implantitis. Patients should be advised of the likely soft tissue recession following treatment for peri-implantitis, the potential need for further treatment and implications of treatment failure.<sup>10</sup>

**Prevention of peri-implantitis**

**Pre-installation**

All risk factors for periodontal diseases should be assessed and controlled as far as is possible.<sup>10</sup> Periodontal treatment should be completed and there should have been a sufficient period of supportive therapy in order to assume stability.

**Post implant placement**

A follow-up programme for early detection of peri-implant diseases should include:

- Periodontal status, including OH and BOP and risk factors;
- Peri-implant pocket depths (using

<b>Risk assessment</b> (prior to surgery)	<ul style="list-style-type: none"> <li>■ Smoking habits</li> <li>■ OH status</li> <li>■ Diabetes</li> <li>■ Previous periodontal disease experience</li> <li>■ Excess cement, design of prosthesis</li> <li>■ Implant surface properties</li> </ul>
<b>Surgical technique for access for treatment of peri-implantitis</b>	<ul style="list-style-type: none"> <li>■ Removal of superstructure, if possible, to attain good access to implant</li> <li>■ ± Recontouring of superstructure to allow self-performed plaque control</li> <li>■ Aim for pocket elimination in posterior segments</li> <li>■ Aim for Guided Bone Regeneration (GBR) in anterior segments (aesthetics)</li> <li>■ Reverse bevel incision to remove pocket epithelium</li> <li>■ Mechanical debridement titanium curettes/ultrasonic implant tips with plastic cover (Figures 3, 4)</li> <li>■ Adjunctive implant surface treatments such as tetracycline slurry 50 mg/mL with cotton pellets or a brush (or other antiseptic agents), water washes between antiseptic washes</li> <li>■ Apical reposition of flap ± osseous resection of bone peaks</li> <li>■ Submerge healing if possible</li> <li>■ Peri- or post-operative systemic antibiotics guided by culture and sensitivity testing if available</li> </ul>

**Table 2.** Authors' suggested treatment options.

stainless steel or plastic periodontal probes);

- Radiographic findings (first at the year review appointment and thereafter, if there is a clinical indication).

**Conclusions**

This review aims to present evidence from the most recent studies and systematic reviews<sup>24,45-47</sup> of the various treatment options for peri-implant diseases.

In conclusion:

- Preventive measures should be initiated prior to implant installation, in particular completion of active periodontal therapy aiming to eliminate residual pockets with BOP.
- Post placement for every implant patient a preventive programme should be tailored to each individual patient's risks, with

regular maintenance and close monitoring to detect early disease.

- Following diagnosis of peri-implantitis, risk factors should be identified and, if possible, eliminated; for example, excess cement, poor OH, smoking and diabetes, prior to active treatment of peri-implant disease.
- Non-surgical treatment alone is sufficient to treat peri-implant mucositis, but is often not sufficient for the treatment of peri-implantitis.
- The various adjuncts to surgical decontamination procedures seem similarly effective at removing the biofilm.
- Regenerative procedures may result in bony infill; this is unpredictable.
- Submerged healing yields better results than non-submerged healing.

■ Following treatment, frequent, regular follow-up visits and supportive therapy are essential.

■ Excessive marginal bone loss around implants is most likely a complex problem caused by many different healing and adaptation factors.

Further research regarding the long-term outcomes of the myriad proposed treatment options for peri-implantitis would be useful to clinicians. Ultimately, further advances are required to achieve predictable outcomes.

## References

- 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**(1): 11–25. Epub 1986/01/01.
- Laurell L, Lundgren D. Marginal bone level changes at dental implants after 5 years in function: a meta-analysis. *Clin Implant Dent Relat Res* 2010; **13**(1): 19–28. Epub 2009/08/18.
- Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases. *J Clin Periodontol* 2008; **35**(8 Suppl): 286–291. Epub 2008/09/09.
- Quirynen M, Vogels R, Alsaadi G, Naert I, Jacobs R, van Steenberghe D. Predisposing conditions for retrograde peri-implantitis, and treatment suggestions. *Clin Oral Implants Res* 2005; **16**(5): 599–608. Epub 2005/09/17.
- Leonhardt A, Dahlen G, Renvert S. Five-year clinical, microbiological, and radiological outcome following treatment of peri-implantitis in man. *J Periodontol* 2003; **74**(10): 1415–1422. Epub 2003/12/05.
- Wennerberg A, Albrektsson T. Current challenges in successful rehabilitation with oral implants. *J Oral Rehabil* 2011; **38**(4): 286–294. Epub 2010/10/26.
- Chvartzaid K, Zarb GA. Osseointegration Failure. In: *Osseointegration: On Continuing Synergies in Surgery, Prosthodontics, and Biomaterials*. Zarb GA, Albrektsson T, Baker G, Eckert SE, Stanford C, Tarnow DP, Wennerberg A, eds. Chicago: Quintessence Publishing Co, 2008: pp. 157–164.
- Berglundh T, Zitzmann NU, Donati M. Are peri-implantitis lesions different from periodontitis lesions? *J Clin Periodontol* 2011; **38**: 188–202.
- Mattheos N, Collier S, Walmsley AD. Specialists' management decisions and attitudes towards mucositis and peri-implantitis. *Br Dent J* 2012; **212**(1): E1–E.
- Heitz-Mayfield GLL. *ITI Annual Conference 2013*. Bern, Switzerland, 2013. Clinical Recommendations: Prevention and management of technical and biologic complications <http://www.iti.org2013> [cited June 2013].
- Trejo PM, Bonaventura G, Weng D, Caffesse RG, Bragger U, Lang NP. Effect of mechanical and antiseptic therapy on peri-implant mucositis: an experimental study in monkeys. *Clin Oral Implants Res* 2006; **17**(3): 294–304. Epub 2006/05/05.
- Porras R, Anderson GB, Caffesse R, Narendran S, Trejo PM. Clinical response to 2 different therapeutic regimens to treat peri-implant mucositis. *J Periodontol* 2002; **73**(10): 1118–1125. Epub 2002/11/06.
- Maximo MB, de Mendonca AC, Renata Santos V, Figueiredo LC, Feres M, Duarte PM. Short-term clinical and microbiological evaluations of peri-implant diseases before and after mechanical anti-infective therapies. *Clin Oral Implants Res* 2009; **20**(1): 99–108. Epub 2009/01/08.
- Strooker H, Rohn S, Van Winkelhoff AJ. Clinical and microbiologic effects of chemical versus mechanical cleansing in professional supportive implant therapy. *Int J Oral Maxillofac Implants* 1998; **13**(6): 845–850. Epub 1998/12/19.
- Esposito MA, Koukoulopoulou A, Coulthard P, Worthington HV. Interventions for replacing missing teeth: dental implants in fresh extraction sockets (immediate, immediate-delayed and delayed implants). *Cochrane Database Syst Rev* 2006(4): CD005968. Epub 2006/10/21.
- Berglundh T, Gotfredsen K, Zitzmann NU, Lang NP, Lindhe J. Spontaneous progression of ligature induced peri-implantitis at implants with different surface roughness: an experimental study in dogs. *Clin Oral Implants Res* 2007; **18**(5): 655–661. Epub 2007/07/05.
- 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**(10): 997–1002. Epub 2008/10/03.
- Persson LG, Berglundh T, Lindhe J, Sennerby L. Re-osseointegration after treatment of peri-implantitis at different implant surfaces. An experimental study in the dog. *Clin Oral Implants Res* 2001; **12**(6): 595–603. Epub 2001/12/12.
- Alhag M, Renvert S, Polyzois I, Claffey N. Re-osseointegration on rough implant surfaces previously coated with bacterial biofilm: an experimental study in the dog. *Clin Oral Implants Res* 2008; **19**(2): 182–187. Epub 2007/11/28.
- 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**(1): 58–64. Epub 2010/11/26.
- Schwarz F, Bieling K, Bonsmann M, Latz T, Becker J. Nonsurgical treatment of moderate and advanced periimplantitis lesions: a controlled clinical study. *Clin Oral Investig* 2006; **10**(4): 279–288. Epub 2006/09/14.
- Schwarz F, Sahm N, Iglhaut G, Becker J. Impact of the method of surface debridement and decontamination on the clinical outcome following combined surgical therapy of peri-implantitis: a randomized controlled clinical study. *J Clin Periodontol* 2011; **38**(3): 276–284. Epub 2011/01/12.
- Karring ES, Stavropoulos A, Ellegaard B, Karring T. Treatment of peri-implantitis by the Vector system. *Clin Oral Implants Res* 2005; **16**(3): 288–293. Epub 2005/05/10.
- Renvert S, Polyzois I, Claffey N. Surgical therapy for the control of peri-implantitis. *Clin Oral Implants Res* 2012; **23**(Suppl 6): 84–94. Epub

- 2012/10/25.
25. Duddeck DU, Rothamel D, Zöller JE. Effects of rotating titanium debridement brushes on the surface structure of dental implants. *Clin Oral Implants Res* 2011; **22**(9): 882–1104.
  26. Albrektsson T, Wennerberg A. Oral implant surfaces: Part 1 – review focusing on topographic and chemical properties of different surfaces and *in vivo* responses to them. *Int J Prosthodont* 2004; **17**(5): 536–543. Epub 2004/11/17.
  27. Schwarz F, Bieling K, Nuesry E, Sculean A, Becker J. Clinical and histological healing pattern of peri-implantitis lesions following non-surgical treatment with an Er:YAG laser. *Lasers Surg Med* 2006; **38**(7): 663–671. Epub 2006/04/25.
  28. Lavigne SE, Krust-Bray KS, Williams KB, Killoy WJ, Theisen F. Effects of subgingival irrigation with chlorhexidine on the periodontal status of patients with HA-coated integral dental implants. *Int J Oral Maxillofac Implants* 1994; **9**(2): 156–162. Epub 1994/03/01.
  29. Schou S, Holmstrup P, Jorgensen T, Skovgaard LT, Stoltze K, Hjorting-Hansen E *et al*. Implant surface preparation in the surgical treatment of experimental peri-implantitis with autogenous bone graft and ePTFE membrane in cynomolgus monkeys. *Clin Oral Implants Res* 2003; **14**(4): 412–422. Epub 2003/07/19.
  30. Renvert S, Samuelsson E, Lindahl C, Persson GR. Mechanical non-surgical treatment of peri-implantitis: a double-blind randomized longitudinal clinical study. I: Clinical results. *J Clin Periodontol* 2009; **36**(7): 604–609. Epub 2009/06/23.
  31. 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**(8 Suppl): 305–315. Epub 2008/09/09.
  32. Lindhe J, Meyle J. Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. *J Clin Periodontol* 2008; **35**(8 Suppl): 282–285. Epub 2008/09/09.
  33. Mombelli A, Lang NP. Antimicrobial treatment of peri-implant infections. *Clin Oral Implants Res* 1992; **3**(4): 162–168. Epub 1992/12/01.
  34. Renvert S, Lessem J, Dahlen G, Lindahl C, Svensson M. Topical minocycline microspheres versus topical chlorhexidine gel as an adjunct to mechanical debridement of incipient peri-implant infections: a randomized clinical trial. *J Clin Periodontol* 2006; **33**(5): 362–369. Epub 2006/04/26.
  35. Buchter A, Meyer U, Kruse-Losler B, Joos U, Kleinheinz J. Sustained release of doxycycline for the treatment of peri-implantitis: randomised controlled trial. *Br J Oral Maxillofac Surg* 2004; **42**(5): 439–444. Epub 2004/09/01.
  36. Mombelli A, Feloutzis A, Bragger U, Lang NP. Treatment of peri-implantitis by local delivery of tetracycline. Clinical, microbiological and radiological results. *Clin Oral Implants Res* 2001; **12**(4): 287–294. Epub 2001/08/08.
  37. Froum SJ, Froum SH, Rosen PS. Successful management of peri-implantitis with a regenerative approach: a consecutive series of 51 treated implants with 3- to 7.5-year follow-up. *Int J Periodont Rest Dent* 2012; **32**(1): 11–20. Epub 2012/01/19.
  38. Roos-Jansaker AM, Renvert H, Lindahl C, Renvert S. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a prospective cohort study. *J Clin Periodontol* 2007; **34**(7): 625–632. Epub 2007/06/09.
  39. Schwarz F, Bieling K, Latz T, Nuesry E, Becker J. Healing of intrabony peri-implantitis defects following application of a nanocrystalline hydroxyapatite (Ostim) or a bovine-derived xenograft (Bio-Oss) in combination with a collagen membrane (Bio-Gide). A case series. *J Clin Periodontol* 2006; **33**(7): 491–499. Epub 2006/07/06.
  40. Schwarz F, Sculean A, Bieling K, Ferrari D, Rothamel D, Becker J. Two-year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane. *J Clin Periodontol* 2008; **35**(1): 80–87. Epub 2008/01/05.
  41. Schwarz F, Sahm N, Bieling K, Becker J. Surgical regenerative treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane: a four-year clinical follow-up report. *J Clin Periodontol* 2009; **36**(9): 807–814. Epub 2009/07/30.
  42. Sahrman P, Attin T, Schmidlin PR. Regenerative treatment of peri-implantitis using bone substitutes and membrane: a systematic review. *Clin Implant Dent Relat Res* 2010; **13**(1): 46–57. Epub 2009/08/18.
  43. 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**(2): 179–187. Epub 2007/03/14.
  44. Schwarz F, Jepsen S, Herten M, Sager M, Rothamel D, Becker J. Influence of different treatment approaches on non-submerged and submerged healing of ligature induced peri-implantitis lesions: an experimental study in dogs. *J Clin Periodontol* 2006; **33**(8): 584–595. Epub 2006/08/11.
  45. Claffey N, Clarke E, Polyzois I, Renvert S. Surgical treatment of peri-implantitis. *J Clin Periodontol* 2008; **35**(8 Suppl): 316–332. Epub 2008/09/09.
  46. Esposito M, Grusovin MG, Tzanetza E, Piattelli A, Worthington HV. Interventions for replacing missing teeth: treatment of perimplantitis. *Cochrane Database Syst Rev* 2010(6): CD004970. Epub 2010/06/18.
  47. Kotsovilis S, Karoussis IK, Trianti M, Fourmousis I. Therapy of peri-implantitis: a systematic review. *J Clin Periodontol* 2008; **35**(7): 621–629. Epub 2008/05/15.
  48. Renvert S, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. *J Clin Periodontol* 2008; **35**(s8): 305–315.