Regenerative treatment of peri-implantitis using bone substitutes and membrane: a systematic review

Sahrmann, P; Attin, T; Schmidlin, P R

Postprint available at:
http://www.zora.uzh.ch

Posted at the Zurich Open Repository and Archive, University of Zurich.
http://www.zora.uzh.ch

Originally published at:
Regenerative treatment of peri-implantitis using bone substitutes and membrane: a systematic review

Abstract

ABSTRACT Purpose: This systematic review aimed to assess the available literature for regenerative treatment of peri-implantitis using bone graft substitutes and membranes. Methods: A search in electronic databases was conducted to assess all types of clinical studies treating bone defects derived from peri-implantitis using guided bone regeneration (GBR) techniques. Results: During the first screening, 399 titles were identified. Finally, 17 articles reporting on 173 implants were included. The articles mainly focused on radiographic bone fill of the defect. Qualitative measures of "bone fill" were reported: 10.4% of the implants showed complete "bone fill," whereas 85.5% revealed incomplete defect closure. No bone fill was shown in 4.0%. Little information (in 53.2%) was provided regarding the probing depth before or after treatment. Data concerning the inflammatory status of soft tissues were also scarce and only reported in three studies. A large heterogeneity concerning disinfection protocols and regenerative materials used was found. The high percentage of low-quality studies rendered a meta-analysis impossible. Conclusion: Complete fill of the bony defect using GBR seems not to be a predictable outcome. The mucosal health status is left unconsidered in most studies. Well-controlled trials are needed to determine predictable treatment protocols for the successful regenerative treatment of peri-implantitis using GBR technique.
Regenerative treatment of peri-implantitis using bone substitutes and membrane: A systematic review

Philipp Sahrmann, Thomas Attin, Patrick R. Schmidlin*

Clinic of Preventive Dentistry, Periodontology and Cariology
Center for Dental and Oral Medicine, University of Zürich
Plattenstrasse 11, CH 8032 Zürich
Switzerland

* Correspondence:
PD Dr. Patrick Schmidlin
Clinic for Preventive Dentistry, Periodontology and Cariology

Phone +41 44 634 32 84
FAX: +41 44 634 43 08
E-mail patrick.schmidlin@zzmk.uzh.ch
Abstract

AIM: This systematic review aimed to assess the available literature for regenerative treatment of peri-implantitis using bone graft substitutes and membranes.

METHODS: A search in electronic databases was conducted to assess all types of clinical studies treating bone defects derived from peri-implantitis using GBR techniques.

RESULTS: During the first screening, 399 titles were identified. Finally, seventeen articles reporting on 173 implants were included. The articles mainly focused on radiographic bone fill of the defect. Qualitative measures of “bone fill” were reported: 10.4% of the implants showed complete “bone fill”, whereas 85.5% revealed incomplete defect closure. No bone fill was shown in 4.0%. Little information (in 53.2%) was provided regarding the probing depth before or after treatment. Data concerning the inflammatory status of soft tissues was also scarce and only reported in three studies. A large heterogeneity concerning disinfection protocols and regenerative materials used was found. The high percentage of low-quality studies rendered a meta-analysis impossible.

Conclusion: Complete fill of the bony defect using GBR seems not to be a predictable outcome. The mucosal health status is left unconsidered in most studies. Well-controlled trials are needed to determine predictable treatment protocols for the successful regenerative treatment of peri-implantitis using GBR-technique.
1. Introduction

During the last decades, the use of dental implants has become a routine procedure in dentistry to replace one or more missing teeth. Using implant survival as the indicator of successful clinical outcome, a majority of clinical studies have shown very positive results for dental implants. However, limited focus has been put on peri-implant mucosal health thus far. Recent studies reported a rate of 8.6% - 9.7% of chronic inflammation of soft and hard tissues neighbouring implants after five years. Lately, a comprehensive investigation concluded, that the peri-implant inflammation is a common clinical finding about ten years after implantation. The pathologic conditions termed mucositis and “peri-implantitis” are considered the major complication in dental implantology. Clinical manifestations like gingival bleeding, swelling and at a later state, bone loss highly resemble periodontal inflammation. Plenty of research has been conducted, proving that both diseases have a bacterial etiology with a similar spectrum of pathogens. In analogy to periodontitis and gingivitis, peri-implantitis can be distinguished from mucositis by the clinical finding of attachment loss to supporting tissues, i.e. to the supporting bone. Thus, increased peri-implant probing depth and radiographic bone loss around the implant’s neck are considered the most reliable parameters proving peri-implantitis. Additionally, bleeding on periodontal probing (BOP), though an indicator for mucositis and not peri-implantitis, is a relevant parameter for the risk assessment of peri-implantitis. A broad variety of different treatment modalities have been proposed for the treatment of peri-implantitis and there is still a lack of evidence concerning their indication and outcome. At the turn of the millennium a systematic treatment scheme called “Cumulative Interceptive Supportive Therapy” (CIST) was formulated. Based on clinical and radiographical findings, a peri-implant lesion was categorized into a maintenance classification system, which consistently lead to a specific treatment recommendation. In the CIST-protocol, regenerative surgery using Guided Tissue Regeneration (GTR) techniques is recommended to fill bony defects caused by peri-implantitis. Due to the fact that in peri-implantitis treatment regeneration is limited to bony tissue the term “Guided Bone Regeneration” (GBR) has obtained acceptance in the literature. There have numerous case reports, case series and clinical trials been published reporting on GBR-techniques in peri-implantitis treatment, in which a combination of both membranes and bone graft substitutes was used. However, there is limited evidence on success and reliability of that treatment protocol. The aim of the present review was to systematically evaluate the outcome of GBR using a bone graft substitute in combination with a membrane to treat bone
defects derived from peri-implantitis on the basis of the parameters peri-implant probing depth (PPD), bleeding-on-probing (BOP) and marginal bone loss (BL).

**Material and methods**

**Search method**

Using the *U.S. National Library of Medicine* (Medline), *EMBASE* and *OVID* a literature search was performed on articles published up to January 2008. The following synonyms and groups were included:

(periiplant*) OR (peri-implant*)  
AND  
(membrane) OR (gtr) OR (gbr)  
AND  
(clinical)

A manual search covered the reference lists of the included articles as well as of review articles concerning the topic. Furthermore the “related articles” option on the NCBI website was used as data source.

**Screening and Selection**

In a first step, titles and abstracts of the electronic search were independently screened by two reviewers (PS, PRS) and assessed for possible inclusion in the review.

- RCT studies comparing interventions using membrane and bone graft substitutes to control groups treated without GBR techniques.
- Non-randomized clinical trials and case reports and series.
- Only cases treating bone defects derived from marginal peri-implantitis were considered. Studies dealing with peri-apical peri-implantitis were not included due to its different etiology and therapeutic approaches.

With respect to a valid comparability of the treatment modalities, only publications reporting on a treatment protocol including application of both membrane (resorbable and non resorbable) and bone substitutes were included.

In a second step, the full texts of all possibly relevant studies, including manually retrieved articles, were then evaluated separately and independently by the same reviewers. Disagreement between the reviewers was resolved by discussion.
From the included articles the data for the assessment parameters probing depth around implants (PPD), bleeding-on-probing (BOP) and bone level (BL) were extracted if given. The difference of these values before and after treatment and their weighted means were calculated if possible. For publications providing only means and standard deviations for a collective of peri-implantitis cases, differences of the means were calculated. In some cases, more detailed data from the authors of the more comprehensive studies was requested.

Results

Initially 399 titles and abstracts from the electronic search were screened and assessed for possible inclusion in the review. Out of these, titles that obviously did not meet the inclusion criteria were excluded in a first step and 62 studies remained for further analysis. Four additional articles were included by manual search and two by the “related links function”. These 68 studies were then separately and independently evaluated by the reviewers. In this step, a further 51 articles were excluded. The main reasons for exclusion were: animal studies (12) 13-24, review articles (10) 6,8,25-32, missing peri-implantitis situation or peri-implantitis treatment (9) 31,33-40, treatment with only membrane or only bone graft substitute or none of both (8) 41-48, in-vitro studies (6) 49-54 or for further reason (5) 4,55-58 (figure 1).

Disagreement between the reviewers in 4.4 % of the cases was consequently resolved by discussion.

From finally remaining 17 original articles, including 173 treated implant cases, the data for the assessment parameters bleeding-on-probing (BOP), periodontal probing depth (PPD) and bone level (BL) was extracted if given.

Description of the studies

No RCT studies comparing peri-implantitis treatment by using membrane and bone graft substitutes to a non-GBR treatment were found.

Finally 17 clinical studies were included:
- 3 controlled clinical trials
- 2 cohort studies
- 8 case series
- 4 single case presentations (s. table 1)

Different types of membranes (diverse synthetic membrane products, resorbable bovine or porcine collagen) were used in combination with different bone substitutes (DFDBA, 59-66)
DFDBA in combination with PepGen and PRP, autogenous bone, hydroxyl apatite, bovine xenografts and algae-derived calciumcarbonate. Furthermore, a broad variety of different implant types were treated (table 5).

Treatment strategies varied between the studies in terms of the pre- or postsurgical use of antibiotics and the kind of disinfection protocol used for implant surface decontamination. In most of the studies plastic or carbon curettes were used for mechanical debridement. Single studies used an ultrasonic scaler, rotating instruments, air powder or soft laser treatment. As a supportive maintenance program, different strategies concerning appointment frequency and treatment were executed (table 5). The re-evaluation periods in the various publications varied from five to 36 months.

**Periodontal probing depth**

Seven studies comprising 92 (53.2%) of the total 173 included implants provided information concerning the values of the PPD before and after the treatment or PPD reduction. All articles except one assessing more than three cases reported on mean values and standard deviations or confidence intervals. Only one of the studies reported on individual values for every treated implant. In the studies, both parametric and non-parametric statistical tests were used indicating the same skewness of the data. Consequently, values for the single implant often remain unknown and uncalculable, impeding any attempt of interstudy comparison or even meta-analysis. The authors’ request for more detailed information in case of insufficient data did not yield any useful additional information. In studies, where values for PPD were given, no outliers could be identified. Consequently, mean values instead of medians were calculated and used for comparison. Two studies reported on „healthy and firm mucosa“ after treatment but were not included in the calculation of means. The weighted mean reduction of PPD for all implants was 3.29 mm (table 3). In most cases there was no data given for PPD after surgery, though in some cases it was possible to calculate it by subtracting probing depth reduction from the probing depth measured before treatment. This value served for estimating a mean value of the residual pocket depth of 3.23 mm post treatment. Search for Clinical Attachment Level (CAL) data provided no additional information.

**Bleeding on Probing**

Of the 17 included articles five studies reported on pre-treatment BOP values, but only three of these also reported on post-treatment data. It has to be noted, that most study designs included an immediate conservative treatment like rinsing of the peri-implant pockets prior to surgical
treatment, so BOP values at baseline might differ from those immediately before intervention. Two studies suggested absence of BOP after intervention when „healthy and firm mucosa“ was found \(^{70,71}\) (figure 2).

**Bone fill**

In all of the 17 included articles quantitative or qualitative data on the bone level around implant sites was given: seven studies (comprising 104 implants) reported a quantitative analysis of bone level values (table 1). In three studies mean values and standard deviations of bone level reduction were given.\(^{68,74,75}\) One study reported the values for every single implant.\(^{67}\)

Eighteen (10.4%) out of 173 implants investigated showed a complete fill of the intrabony defect. In 148 implant cases (85.5%) a gain of bone level was reported: ninety-eight implants (56.6%) showed incomplete bone-fill and 50 implants (28.9%) showed „bone win“ which was not further specified. Finally, seven implants (4.0%) failed to gain any new bone or showed bone loss, or the implant had to be removed (table 4).

A weighted mean value of bone win of 2.1 mm was calculated after GBR treatment (table 2). The residual mean bone defect depth at the time of reevaluation was 2.6 mm.

Twelve studies reported qualitative or semi-quantitative informations like „partial“ or not further specified „bone fill“ without providing any quantitative data (table 4, figure 3).

**Discussion**

This review aimed to assess the outcome of peri-implantitis treatment using membranes and bone graft substitutes. Unfortunately, there were no RCT studies comparing the results of peri-implantitis treatment with GBR-techniques using both membrane and bone graft substitute, to an adequate control group, i.e. scaling or non-regenerative surgery. Consequently, studies of a lower level of evidence, like case presentations and proportions of patient cohorts from RCT studies with a different aim, were included in order to benefit from the available data in literature and to investigate possible differences the quality of data presentation. The risk of including confounding factors was estimated low as with GBR techniques the plausibility of intervention–outcome affinity is high. Therefore, it was decided to enclose these non-controlled studies in the analysis.
Furthermore, there was a lack of studies with numerous implants: The majority of the studies presented data of single cases or small case series. Only six studies included more than 7 implants. These studies assessed clinical parameters like BOP and PPD more often. However, incomplete data presentation in these studies hampered comparability and rendered a meta-analysis impossible.

This study focussed on GBR techniques using both, bone graft substitute and membrane: this treatment modality represents the major part of published GBR cases. Hence, studies using solely one of both materials, were excluded in order not to further jeopardize the validity of comparison.

There are a multitude of different implant systems with varying fixture design and different surfaces combined with a diversity of bone graft substitutes and barrier membranes. Therefore, comparison among the different peri-implant surgery cases is also problematic.

Observation periods in the included studies ranged from five months to three years, and re-examination intervals varied greatly. Thus, a comparison after the same period for all studies was impossible. Moreover, short observation times strongly limit the clinical relevance of the treatment outcome. Long-term follow-up examinations are required for a more valid assessment. Not surprisingly, all studies investigated radiographic bone morphology. However, less attention was paid to crucial clinical parameters like BOP and PPD. These parameters were rarely reported. This conflicts with the recommendations of the American Academy of Periodontology and the European Workshop on Periodontology which explicitly call for the data collection of BOP and PPD in the examination of peri-implantitis cases. This finding indicates a shortcoming in soft tissue evaluation and is in accordance with a lately published review on peri-implantitis therapy.

Still, the etiology of marginal bone defects around implants is a topic of debate: Reasons for marginal peri-implant bone loss like adverse occlusal loading effects from hyper-contacts unfavourable healing and the effect of position and adaption of the microgap are common topics of the discussion about peri-implant bone loss. However, studies in periodontology prove a pivotal role of the soft tissues in the inflammation process.

The authors concluded a mean probing depth reduction of 3.29 mm and a residual probing depth of 3.23 mm. It is thereby estimated that a peri-implant probe penetrates approximately 3 mm in a healthy situation and according to the CIST protocol no further invasive intervention is indicated. Therefore, these results seem to suggest peri-implant health. However, it must be
considered that the calculated PPD mean value was derived from a broad range of PPD values varying from study to study and even from case to case.

There is clear evidence that peri-implantitis processes start as a peri-mucosal inflammation from the most external contact of implant and tissues, i.e. from the mucosal seal around the implant neck. 7,29,85 Analog to the transition from gingivitis to periodontitis the drawdown of attachment level is the crucial symptom to distinguish peri-mucositis from peri-implantitis. As early as in the 1980s, it was shown that the PPD differs from the histological pocket depth in periodontal sites. 86 In inflamed periodontal situations probes tend to penetrate deeper into the tissues because of the decreased tenseness of the soft tissues. The same effect, though more pronounced, has been shown for peri-implant situations. 87,88 This finding underlines that PPD assessment is an even more sensitive instrument for the detection of attachment loss in potentially inflamed situations. The inaccuracies of deeper probe penetration should not restrain practitioners from using this diagnostic tool: as inflammation fades in the course of treatment the difference between clinical and histological pocket depth will decrease and in the same way the accuracy of the parameter PPD will increase. Contrary to sporadically expressed assumptions, there is no evidence that careful peri-implant probing could damage the implant surface or create persistant injury to the tissues. 9,89

Noteworthy, only three of 17 studies reported on BOP measurements. With regard to BOP assessment it has been shown in periodontal sites that absence of bleeding after probing is a reliable predictor for periodontal stability. 89-91 Consequently, BOP assessment is most reasonable for both peri-implantitis screening and evaluation of a peri-implantitis treatment.

With regard to bone fill most of the studies provided only qualitative or semi-quantitative data for the amount of fill of the intrabony defect. For better comparability improved parameters for the defect size characterization would be helpful. For this purpose, reliable and quick methods have been published. 92,93 In this review, 10.4% of the included implant collective showed a complete and 85.5% at least a partial defect fill. This amounts to 96% of all analyzed cases where a bonefill of whatsoever extent was achieved by GBR technique. In this respect, GBR treatment can be assumed to lead to rather safe success. The interpolated 2.6 mm of residual bone defect after surgery should be interpreted with caution: both the reference level, i.e. implant benchmarks or neighbouring bone level, and the calculation might lead to inadequate conclusions. Anyhow, it should be kept in mind that there is no evidence for the need of either complete or incomplete defect fill.

The assessment of the crestal bone level on conventional radiographs has been proven to be a highly specific testing method. 94 Thus, an initial peri-implant defect is not easily detected on the
radiograph: Studies show that on conventional radiographs the sensitivity for identification of smaller defects, as expected for the onset peri-implant defect, is low. \textsuperscript{94,95} Considerable improvements with CT and DVT technique have recently been reported. \textsuperscript{96} Of course, the radiographs provide no information about the nature of bone and interface. It is indeterminable in an augmented site with an apparently dense bone formation at the implant’s neck, whether osseointegration on a histological level has actually occurred. \textsuperscript{94} Putting the main focus on radiographic bone fill relies on a phenomenon of doubtful nature; there is still no evidence showing what kind of structure actually fills the bone defect. Furthermore, there is disagreement in research about the amount of remaining bone substitute and regenerated genuine bone, which can be expected depending on resorption time of the various bone graft materials. \textsuperscript{94} \textsuperscript{97-99} Autogenous bone, defined as the gold standard in bone augmentation, shows a volume loss of approximately 40% during healing time. On the other hand, synthetic bone graft substitutes show a high stability in volume, but remain nearly or completely unresorbed even several years after surgery. \textsuperscript{100} In clinical practice, this implies that visual bone fill on the x-ray \textit{per se} is not sufficient to claim a successful biological outcome after peri-implantitis treatment, \textsuperscript{101} especially in the long-term.

**Conclusion**

Complete fill of bony defects caused by peri-implantitis using a GBR-protocol with membrane and bone graft substitutes does not seem to be a predictable outcome, although a partial defect fill can be expected.

Published peri-implantitis literature lacks comprehensive studies with high number of cases that would enable a sound statistical analysis. The mucosal health status as a reliable indicator for peri-implant inflammation, reflected by the parameters BOP and PPD, is not reported in the majority of the studies.

RCT studies comparing GBR treatment to non-invasive debridement in peri-implantitis cases are needed in order to provide evidence for an additional benefit of the use of bone graft substitutes and membranes. In these studies, assessment of quantitative values for bone loss, PPD and BOP would be desirable.
Reference list:


47. 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

48. Schuckert KH, Jopp S, Muller U. De novo grown bone on exposed implant surfaces using
photodynamic therapy and recombinant human bone morphogenetic protein-2: case report.

49. Giannelli M, Chellini F, Margheri M, Tonelli P, Tani A. Effect of chlorhexidine
digluconate on different cell types: a molecular and ultrastructural investigation. Toxicol In

(matrilysin-1) and MMP-8 (collagenase-2) in diseased human peri-implant sulcular fluid. J

metalloproteinase-25 and -26 expression in chronic and aggressive periodontitis and in

52. Lang NP, Wetzel AC, Stich H, Caffesse RG. Histologic probe penetration in healthy and

titanium implants with or without a clinical diagnosis of inflammation. Clin Oral Implants

54. Talarico GM, Neiders ME, Comeau RL, Cohen RE. Phenotypic characterization of
mononuclear cells from gingiva associated with periodontitis and peri-implantitis. J Oral
Implantol 1997; 23:5-11.


Figure 1
Flow-chart of the screening procedure and included/excluded articles

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Screening step</th>
</tr>
</thead>
<tbody>
<tr>
<td>399 titles</td>
<td>Search on MEDLINE and OVID for „peri-implantitis”/“periimplantitis” and „membrane”/“gtf”</td>
</tr>
<tr>
<td></td>
<td>Title screening</td>
</tr>
<tr>
<td></td>
<td>Independently by 2 reviewers</td>
</tr>
<tr>
<td>61 abstracts</td>
<td>Abstract reevaluation</td>
</tr>
<tr>
<td></td>
<td>Titles found by manual search</td>
</tr>
<tr>
<td></td>
<td>in bibliography/reference lists</td>
</tr>
<tr>
<td></td>
<td>…in „related links“ on NBCI-site</td>
</tr>
<tr>
<td>67 full texts</td>
<td>Full text reevaluation</td>
</tr>
<tr>
<td></td>
<td>Exclusion for</td>
</tr>
<tr>
<td>95.6% agreement</td>
<td>• 12 animal studies</td>
</tr>
<tr>
<td>prior to discussion</td>
<td>• 10 review articles</td>
</tr>
<tr>
<td></td>
<td>• 9 missing peri-implantitis situation</td>
</tr>
<tr>
<td></td>
<td>• 8 treatment without either membrane or bone fillers</td>
</tr>
<tr>
<td></td>
<td>• 6 in-vitro studies</td>
</tr>
<tr>
<td></td>
<td>• 5 for further reason</td>
</tr>
<tr>
<td>50 articles</td>
<td>Reviewed full texts</td>
</tr>
<tr>
<td>17 included articles</td>
<td></td>
</tr>
</tbody>
</table>
Figure 2.

Data distribution for different reported parameters Bleeding on Probing, Peri-implant Probing Depth and Bone Loss.
Table 1.
Data extraction of the included studies reporting on differences in Bleeding on Probing (ΔBOP), Periodontal Probing Depth (ΔPPD) and depth of the bony defect (ΔBL)

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year of publication</th>
<th>n</th>
<th>Study design</th>
<th>ΔBOP (%)</th>
<th>ΔPPD (mm)</th>
<th>ΔBL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artzi et al.</td>
<td>1998</td>
<td>2</td>
<td>cs</td>
<td>n.d.</td>
<td>n.d.</td>
<td>100%</td>
</tr>
<tr>
<td>Bell et al.</td>
<td>1994</td>
<td>1</td>
<td>scp</td>
<td>n.d.</td>
<td>n.d.</td>
<td>+</td>
</tr>
<tr>
<td>Deporter &amp; Todescan</td>
<td>2001</td>
<td>1</td>
<td>scp</td>
<td>n.d.</td>
<td>n.d.</td>
<td>40%</td>
</tr>
<tr>
<td>Haas et al.</td>
<td>2000</td>
<td>24</td>
<td>ct</td>
<td>n.d.</td>
<td>n.d.</td>
<td>2.00±1.90</td>
</tr>
<tr>
<td>Khoury &amp; Buchmann</td>
<td>2001</td>
<td>20</td>
<td>cct</td>
<td>n.d.</td>
<td>2.6±1.6</td>
<td>2.8±3.1</td>
</tr>
<tr>
<td>Kraut &amp; Judy</td>
<td>1991</td>
<td>4</td>
<td>cs</td>
<td>n.d.</td>
<td>n.d.</td>
<td>100%</td>
</tr>
<tr>
<td>Mellonig &amp; Triplett</td>
<td>1993</td>
<td>10</td>
<td>cs</td>
<td>n.d.</td>
<td>n.d.</td>
<td>100%</td>
</tr>
<tr>
<td>Mellonig et al.</td>
<td>1995</td>
<td>1</td>
<td>cs</td>
<td>n.d.</td>
<td>8mm</td>
<td>9.0mm</td>
</tr>
<tr>
<td>Petrungaro</td>
<td>2002</td>
<td>1</td>
<td>scp</td>
<td>n.d.</td>
<td>n.d.</td>
<td>100%</td>
</tr>
<tr>
<td>Roos-Jansäker et al.</td>
<td>2007a</td>
<td>16</td>
<td>ct</td>
<td>68,7</td>
<td>4.2±1.5</td>
<td>2.3±1.2</td>
</tr>
<tr>
<td>Roos-Jansäker et al.</td>
<td>2007b</td>
<td>29</td>
<td>cct</td>
<td>57,7</td>
<td>2.86±2.0</td>
<td>1.52±1.16</td>
</tr>
<tr>
<td>Schwarz et al.</td>
<td>2008</td>
<td>11</td>
<td>cct</td>
<td>36</td>
<td>1.5±0.6</td>
<td>+</td>
</tr>
<tr>
<td>Suh et al.</td>
<td>2003</td>
<td>1</td>
<td>cs</td>
<td>n.d.</td>
<td>n.d.</td>
<td>100%</td>
</tr>
<tr>
<td>Tinti &amp; Parma-Benfanti</td>
<td>2001</td>
<td>3</td>
<td>cs</td>
<td>(reestablishment of healthy and firm mukosa)</td>
<td>3.5</td>
<td>2.7</td>
</tr>
<tr>
<td>von Arx et al.</td>
<td>1997</td>
<td>1</td>
<td>scp</td>
<td>(reestablishment of healthy and firm mukosa)</td>
<td>(reestablishment of healthy and firm mukosa)</td>
<td>5.0</td>
</tr>
</tbody>
</table>

n – number of implants  scp – single case presentation further specified bone win cs – case series  ct – clinical trial  cct – controlled clinical trial  + - no grey fields indicate: no data (n.d.) provided

Table 2.
Result of bone fill reported in the included studies

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year of publication</th>
<th>Number of implants</th>
<th>Mean ΔBL (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haas et al.</td>
<td>2000</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>Khoury &amp; Buchmann</td>
<td>2001</td>
<td>9</td>
<td>1.9</td>
</tr>
<tr>
<td>Mellonig et al.</td>
<td>1995</td>
<td>1</td>
<td>9.0</td>
</tr>
<tr>
<td>Roos-Jansäker et al.</td>
<td>2007a</td>
<td>16</td>
<td>2.3</td>
</tr>
<tr>
<td>Roos-Jansäker et al.</td>
<td>2007b</td>
<td>29</td>
<td>1.52</td>
</tr>
<tr>
<td>Tinti &amp; Parma-Benfanti</td>
<td>2001</td>
<td>3</td>
<td>2.0</td>
</tr>
<tr>
<td>Von Arx et al.</td>
<td>1997</td>
<td>1</td>
<td>5.0</td>
</tr>
<tr>
<td>Sum/mean</td>
<td></td>
<td>104</td>
<td>2.2</td>
</tr>
</tbody>
</table>
Table 3.
Studies reporting PPD reductions

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year of publication</th>
<th>Number of implants</th>
<th>Mean ΔPPD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khoury &amp; Buchmann</td>
<td>2001</td>
<td>9</td>
<td>5.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>2.6</td>
</tr>
<tr>
<td>Mellonig et al.</td>
<td>1995</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Roos-Jansäker et al.</td>
<td>2007a</td>
<td>16</td>
<td>4.2</td>
</tr>
<tr>
<td>Roos-Jansäker et al.</td>
<td>2007b</td>
<td>29</td>
<td>2.86</td>
</tr>
<tr>
<td>Schwarz et al</td>
<td>2008</td>
<td>11</td>
<td>1.5</td>
</tr>
<tr>
<td>Tinti &amp; Parma-Benfeanti</td>
<td>2001</td>
<td>3</td>
<td>3.5</td>
</tr>
<tr>
<td>Sum</td>
<td></td>
<td>91</td>
<td>299.7</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>3.29</td>
</tr>
</tbody>
</table>
Table 4.

Number of implants with different levels of bone fill

<table>
<thead>
<tr>
<th>Number of implants</th>
<th>Complete bone fill</th>
<th>Partial bone fill</th>
<th>Bone fill (not further specified)</th>
<th>No bone fill/bone loss/failure</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18</td>
<td>98</td>
<td></td>
<td>(166)</td>
<td>173</td>
</tr>
<tr>
<td>%</td>
<td>10.4</td>
<td>56.6</td>
<td></td>
<td>(96.0)</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 5. Characteristics of the included studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number/ type of implants</th>
<th>Treatment protocol(1)</th>
<th>Bone substitute/membrane</th>
<th>Systematical antibiotic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artzi et al.</td>
<td>1998</td>
<td>2/ int, omn</td>
<td>ultrasound instrumentation</td>
<td>(DFDBA+agb+tcycl) / lamellar bone sheet</td>
<td>-</td>
</tr>
<tr>
<td>Bell et al.</td>
<td>1994</td>
<td>1/ nd</td>
<td>citric acid + tcycl</td>
<td>DFDBA / ePTFE</td>
<td>-</td>
</tr>
<tr>
<td>Deporter &amp; Todescan</td>
<td>2001</td>
<td>1/ edp</td>
<td>citric acid</td>
<td>(DFDBA+tcycl) / CaSO(_4)</td>
<td>amx 2g 1h pre 0,5g/d for 7d post</td>
</tr>
<tr>
<td>El Chaar &amp; Jalbout</td>
<td>2002</td>
<td>2/ bv (bx)</td>
<td>rotating instrumentation + citric acid</td>
<td>DFDBA / resorbable bovine membrane</td>
<td>amx 0,5g/d for 10d</td>
</tr>
<tr>
<td>Haas et al.</td>
<td>2000</td>
<td>24/ imz</td>
<td>toluidine blue + soft laser (906nm)</td>
<td>agb / ePTFE</td>
<td>Augmentine for 5d</td>
</tr>
<tr>
<td>Khoury et al.</td>
<td>2001</td>
<td>20/ imz f2 / imz f2</td>
<td>0,2% CHX + citric acid + H(_2)(_2) O(_2) rinsing</td>
<td>agb / ePTFE / agb / resorbable porcine collagen</td>
<td>div. 4w pre for 7d, post</td>
</tr>
<tr>
<td>Kraut &amp; Judy</td>
<td>1991</td>
<td>4/ nd (bx)</td>
<td>hyper tonic saline</td>
<td>DFDBA+HA / ePTFE</td>
<td>650mg/d clindamycin (t) in 600mg/d clindamycin, amx 2g 1h post</td>
</tr>
<tr>
<td>Mellonig &amp; Triplett</td>
<td>1993</td>
<td>59/ brm (tt)</td>
<td>-</td>
<td>DFDBA / ePTFE</td>
<td>broad band antibiotics i exposure for 14-21d</td>
</tr>
<tr>
<td>Mellonig et al.</td>
<td>1995</td>
<td>3/ (tpc hc)</td>
<td>tcycl</td>
<td>DFDBA / ePTFE</td>
<td>Doxycycline 0,1g/d for 4w post</td>
</tr>
<tr>
<td>Petrungho</td>
<td>2002</td>
<td>1/ nd</td>
<td>citric acid + EDTA</td>
<td>(DFDBA+PRP+PepGen) / resorbable bovine collagen</td>
<td>10d pre mnz 1g/d=amx</td>
</tr>
<tr>
<td>Romanos &amp; Nentwig</td>
<td>2006</td>
<td>27/ nd</td>
<td>bdx / resorbable porcine collagen</td>
<td>-</td>
<td>nd</td>
</tr>
<tr>
<td>Roos-Jansaker et al.</td>
<td>2007a</td>
<td>16/ brm</td>
<td>H(_2)(_2)O(_2) rinsing</td>
<td>CaCO(_3)/ Resorbable synthetic polymer</td>
<td>amx 3x375mg/clindam 800mg mnz for 10d</td>
</tr>
<tr>
<td>Roos-Jansaker et al.</td>
<td>2007b</td>
<td>29/ brm</td>
<td>H(_2)(_2)O(_2) rinsing</td>
<td>CaCO(_3)/ Resorbable synthetic polymer</td>
<td>amx 3x375mg/clindam 800mg mnz for 10d</td>
</tr>
<tr>
<td>Schwarz et al.</td>
<td>2008</td>
<td>1/ brm, clo, sla (2), tps, ksi, mtx (3), tsv, zld</td>
<td>sterile physiological saline</td>
<td>bdx / resorbable porcine collagen</td>
<td>nd</td>
</tr>
<tr>
<td>Suh et al.</td>
<td>2003</td>
<td>1/ itt (ss) / 2/ itt (hc)</td>
<td>mechanical smoothing</td>
<td>agb / ePTFE</td>
<td>amx 1,5g for 7d</td>
</tr>
<tr>
<td>Tinti &amp; Parma-Benfenati</td>
<td>2001</td>
<td>3/ brm</td>
<td>air powder NaCO(_3) tcycl-solution</td>
<td>agb=DFDBA/ePTFE</td>
<td>amx 2g 2h pre, 1g/d as</td>
</tr>
<tr>
<td>von Arx et al.</td>
<td>1997</td>
<td>1/ int (b)</td>
<td>chlx 0.5%</td>
<td>agb = resorbable polylactide</td>
<td>amx/cl 1,875g/d for 7d</td>
</tr>
</tbody>
</table>

\(1\)additional to instrumental debridement, full thickness flap and degranulation tcycl – Tetracyclin solution CHX – chlorhexidine DFDBA – demineralized fra ePTFE – expanded polytetrafluorethylene HA – Hydroxile apatite tTCP - β- Tricalcium phosphate bdx – bovine derived xenograft amx – amoxycillin m
