Geistlich
Biomaterials

major publications

Geistlich Bio-Gide®
Geistlich Bio-Oss®
Geistlich Bio-Oss® Collagen
Geistlich Mucograft®

Geistlich Pharma AG
Business Unit Biomaterials
Bahnhofstrasse 40
CH-6110 Wolhusen/Switzerland
phone +41/41/492 56 30
fax +41/41/492 56 39
biomaterials@geistlich.ch
www.geistlich-pharma.com

Version December 15

Overview

1. Meta-analyses/Reviews

A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation

Pjetursson BE, Tan WC, Zwahlen M, Lang NP
J Clin Periodontol, 2008; 35: 216-240.

OBJECTIVES: The objectives of this systematic review were to assess the survival rate of grafts and implants placed with sinus floor elevation. MATERIAL AND METHODS: An electronic search was conducted to identify studies on sinus floor elevation, with a mean follow-up time of at least 1 year after functional loading. RESULTS: The search provided 839 titles. Full-text analysis was performed for 175 articles resulting in 48 studies that met the inclusion criteria, reporting on 12,020 implants. Meta-analysis indicated an estimated annual failure rate of 3.48% [95% confidence interval (CI): 2.48%-4.88%] translating into a 3-year implant survival of 90.1% (95% CI: 86.4%-92.8%). However, when failure rates was analyzed on the subject level, the estimated annual failure was 6.04% (95% CI: 3.87%-9.43%) translating into 16.6% (95% CI: 10.9%-24.6%) of the subjects experiencing implant loss over 3 years. CONCLUSION: The insertion of dental implants in combination with maxillary sinus floor elevation is a predictable treatment method showing high implant survival rates and low incidences of surgical complications. The best results (98.3% implant survival after 3 years) were obtained using rough surface implants with membrane coverage of the lateral window.

Which Hard Tissue Augmentation Techniques Are the Most Successful in Furnishing Bony Support for Implant Placement?

Aghaloo TL, Moy PK
J Oral Maxillofac Implants 2007; 22 (Suppl): 49-7.

Purpose: A variety of techniques and materials have been used to establish the structural base of osseous tissue for supporting dental implants. The aim of this systematic review was to identify the most successful technique(s) to provide the necessary alveolar bone to place a dental implant and support long-term survival. Methods: A systematic online review of a main database and manual search of relevant articles from refereed journals were performed between 1980 and 2005. Updates and additions were made from September 2004 to May 2005. The hard tissue augmentation techniques were separated into 2 anatomic sites, the maxillary sinus and alveolar ridge. Within the alveolar ridge augmentation technique, different surgical approaches were identified and categorized, including guided bone regeneration (GBR), onlay/veneer grafting (OVG), combinations of onlay, veneer, interpositional inlay grafting (COG), distraction osteogenesis (DO), ridge splitting (RS), free and vascularized autografts for discontinuity defects (DD), mandibular interpositional grafting (MI), and socket preservation (SP). All identified articles were evaluated and screened by 2 independent reviewers to meet strict inclusion criteria. Articles meeting the inclusion criteria were further evaluated for data extraction. The initial search identified a total of 526 articles from the electronic database and manual search. Of these, 335 articles met the inclusion criteria after a review of the titles and abstracts. From the 335 articles, further review of the full text of the articles produced 90 articles that provided sufficient data for extraction and analysis. Results: For the maxillary sinus grafting (SG) technique, the results showed a total of 5,128 implants placed, with follow-up times ranging from 12 to 102 months. Implant survival was 92% for implants placed into autogenous and autogenous/composite grafts, 93.3% for implants placed into allogeneic/nonautogenous composite grafts, 81% for implants placed into alloplast and alloplast/xenograft materials, and 95.6% for implants placed into xenograft materials alone. For alveolar ridge augmentation, a total of 2,620 implants were placed, with follow-up ranging from 5 to 74 months. The implant survival rate was 95.5% for GBR, 90.4% for OVG, 94.7% for DO, and 83.8% for COG. Other techniques, such as DD, RS, SP, and MI, were difficult to analyze because of the small sample size and data heterogeneity within and across studies. Conclusions: The maxillary sinus augmentation procedure has been well documented, and the long-term clinical success/survival (> 5 years) of implants placed, regardless of graft material(s) used, compares favorably to implants placed conventionally, with no grafting procedure, as reported in other systematic reviews. Alveolar ridge augmentation techniques do not have detailed documentation or long-term follow-up studies, with the exception of GBR. However, studies that met the inclusion criteria seemed to be comparable and yielded

favorable results in supporting dental implants. The alveolar ridge augmentation procedures may be more technique- and operator-experience–sensitive, and implant survival may be a function of residual bone supporting the dental implant rather than grafted bone. More in-depth, long-term, multicenter studies are required to provide further insight into augmentation procedures to support dental implant survival.

Bone Augmentation Techniques.

Mc Allister B, Haghighat K
J Periodontol 2007, 78, 377-396

Background: The advent of osseointegration and advances in biomaterials and techniques have contributed to increased application of dental implants in the restoration of partial and completely edentulous patients. Often, in these patients, soft and hard tissue defects result from a variety of causes, such as infection, trauma, and tooth loss. These create an anatomically less favorable foundation for ideal implant placement. For prosthetic-driven dental implant therapy, reconstruction of the alveolar bone through a variety of regenerative surgical procedures has become predictable; it may be necessary prior to implant placement or simultaneously at the time of implant surgery to provide a restoration with a good long-term prognosis. Regenerative procedures are used for socket preservation, sinus augmentation, and horizontal and vertical ridge augmentation. Methods: A broad overview of the published findings in the English literature related to various bone augmentation techniques is outlined. A comprehensive computer-based search was performed using various databases that include Medline and PubMed. A total of 267 papers were considered, with non-peer-reviewed articles eliminated as much as possible. Results: The techniques for reconstruction of bony defects that are reviewed in this paper include the use of particulate bone grafts and bone graft substitutes, barrier membranes for guided bone regeneration, autogenous and allogenic block grafts, and the application of distraction osteogenesis. Conclusions: Many different techniques exist for effective bone augmentation. The approach is largely dependent on the extent of the defect and specific procedures to be performed for the implant reconstruction. It is most appropriate to use an evidenced-based approach when a treatment plan is being developed for bone augmentation cases.

Systematic review of survival rates for implants placed in the grafted maxillary sinus

Del Fabbro M, Testori T, Francetti L, Weinstein R
Int J Periodontics Restorative Dent. 2004; 24: 565-77.

Based on a systematic review of the literature from 1986 to 2002, this study sought to determine the survival rate of root-form dental implants placed in the grafted maxillary sinus. Secondary goals were to determine the effects of graft material, implant surface characteristics, and simultaneous versus delayed placement on survival rate. A search of the main electronic databases was performed in addition to a hand search of the most relevant journals. All relevant articles were screened according to specific inclusion criteria. Selected papers were reviewed for data extraction. The search yielded 252 articles applicable to sinus grafts associated with implant treatment. Of these, 39 met the inclusion criteria for qualitative data analysis. Only 3 of the articles were randomized controlled trials. The overall implant survival rate for the 39 included studies was 91.49%. The database included 6,913 implants placed in 2,046 subjects with loaded follow-up time ranging from 12 to 75 months. Implant survival was 87.70% with grafts of 100% autogenous bone, 94.88% when combining autogenous bone with various bone substitutes, and 95.98% with bone grafts consisting of bone substitutes alone. The survival rate for implants having smooth and rough surfaces was 85.64% and 95.98%, respectively. Simultaneous and delayed procedures displayed similar survival rates of 92.17% and 92.93%, respectively. When implants are placed in grafted maxillary sinuses, the performance of rough implants is superior to that of smooth implants. Bone-substitute materials are as effective as autogenous bone when used alone or in combination with autogenous bone. Studies using a split-mouth design with one variable are needed to further validate the findings.

Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review

Wallace SS, Froum SJ
Ann Periodontol 2003; 8: 328-343.

BACKGROUND: Grafting the floor of the maxillary sinus has become the most common surgical intervention for increasing alveolar bone height prior to the placement of endosseous dental implants in the posterior maxilla. Outcomes of this procedure may be affected by specific surgical techniques, simultaneous versus delayed implant placement, use of barrier membranes over the lateral window, selection of graft material, and the surface characteristics and the length and width of the implants. RATIONALE: The primary objective of this systematic review was to determine the efficacy of the sinus augmentation procedure and compare the results achieved with various surgical techniques, grafting materials, and implants. FOCUSED QUESTION: In patients requiring dental implant placement, what is the effect on implant survival of maxillary sinus augmentation versus implant placement in the non-grafted posterior maxilla? SEARCH PROTOCOL: MEDLINE, the Cochrane Oral Health Group Specialized Trials Register, and the Database of Abstracts and Reviews of Effectiveness were searched for articles published through April 2003. Hand searches were performed on Clinical Oral Implants Research, International Journal of Oral and Maxillofacial Implants, and the International Journal of Periodontics & Restorative Dentistry and the bibliographies of all relevant papers and review articles. In addition, researchers, journal editors, and industry sources were contacted to see if pertinent unpublished data that had been accepted for publication were available. SELECTION CRITERIA: INCLUSION CRITERIA: Human studies with a minimum of 20 interventions, a minimum follow-up period of 1-year loading, an outcome measurement of implant survival, and published in English, regardless of the evidence level, were considered. EXCLUSION CRITERIA: Studies involving multiple simultaneous interventions (e.g., simultaneous ridge augmentation) and studies with missing data that could not be supplied by the study authors were excluded. DATA COLLECTION AND ANALYSIS: Where adequate data were available, subgroups of dissimilar interventions (e.g., surgical techniques, graft materials, implant surfaces, membranes) were isolated and subjected to meta-regression, a form of meta-analysis. MAIN RESULTS: 1. Forty-three studies, 3 randomized controlled clinical trials (RCTs), 5 controlled trials (CTs), 12 case series (CS), and 23 retrospective analyses (RA) were identified. Thirty-four were lateral window interventions, 5 were osteotome interventions, 2 were localized management of the sinus floor, and 2 involved the crestal core technique. 2. Meta-regression was performed to determine the effect of the variables of block versus particulate grafting techniques, implant surface, graft material, and the use of a membrane over the lateral window. 3. The survival rate of implants placed in sinuses augmented with the lateral window technique varied between 61.7% and 100%, with an average survival rate of 91.8%. For lateral window technique: 4. Implant survival rates reported in this systematic review compare favorably to reported survival rates for implants placed in the non-grafted posterior maxilla. 5. Rough-surfaced implants have a higher survival rate than machine-surfaced implants when placed in grafted sinuses. 6. Implants placed in sinuses augmented with particulate grafts show a higher survival rate than those placed in sinuses augmented with block grafts. 7. Implant survival rates were higher when a membrane was placed over the lateral window. 8. The utilization of grafts consisting of 100% autogenous bone or the inclusion of autogenous bone as a component of a composite graft did not affect implant survival. 9. There was no statistical difference between the covariates of simultaneous versus delayed implant placement, types of rough-surfaced implants, length of follow-up, year of publication, and the evidence level of the study. REVIEWERS' CONCLUSIONS: Insufficient data were present to statistically evaluate the effects of smoking, residual crestal bone height, screw versus press-fit implant design, or the effect of implant surface micromorphology other than machined versus rough surfaces. There are insufficient data to recommend the use of platelet-rich plasma in sinus graft surgery.

Efficacy of Porous Bovine Bone Mineral in Various Types of Osseous Deficiencies: Clinical Observations and Literature Review

Z. Artzi, C. Nemcovsky, H. Tal
Int J Periodontics Restorative Dent, 21(4), 2001

Recent developments in osseous regenerative techniques have increased the demand for bone-substitute grafting materials. Porous deproteinized bovine bone mineral (Bio-Oss®), a biocompatibel xenograft, has been used in different osseous deficiencies prior to or in conjunction with the placement of titanium

implants. The different Bio-Oss® applications in fresh extraction sited, anatomic defects, and subantral floor elevation techniques are described. The use of an occlusive barrier membrane to regenerate bone via guided tissue regeneration principles was determined for each patient by clinical parameters. Bio-Oss® was well amalgamated and incorporated with the augmented hard tissue, but the transition between preexisting bone and the newly regenerated bone-like tissue was distinguishable by clinical examination even after 12 months. Grafted material was also identified using follow-up radiographs. In the presented cases, Bio-Oss® showed clinically satisfactory results as a biocompatible filler in bone augmentation procedures.

Regeneration of periodontal tissues: combinations of barrier membranes and grafting materials - biological foundation and preclinical evidence: a systematic review.

Sculean, A., D. Nikolidakis, et al.
J Clin Periodontol 2008; 35(8 Suppl): 106-16.

BACKGROUND: Regenerative periodontal therapy aims to predictably restore the tooth's supporting periodontal tissues and should result in formation of a new connective tissue attachment (i.e. new cementum with inserting periodontal ligament fibres) and new alveolar bone. Histologic evidence from preclinical models has demonstrated periodontal regeneration following treatment with barrier membranes, various types of grafting materials or a combination thereof. However, it is still not clear to what extent a combination of barrier membranes and grafting materials may additionally enhance the regeneration process compared with barrier membranes alone, grafting materials alone or open flap debridement. OBJECTIVES: To review with a systematic approach all preclinical (i.e. animal) studies presenting histologic support for periodontal regeneration using the combination of barrier membranes and grafting materials. MATERIAL AND METHODS: Based on a focused question, an electronic and manual search was conducted for animal studies presenting histological data for the effect of the combined use of barrier membranes and grafting materials on the treatment of periodontal defects. A systematic approach was followed by two independent reviewers including eligibility criotateria for study inclusion, outcome measures determination, screening method, data extraction, data synthesis and drawing of conclusions. RESULTS: Ten papers completely fulfilling the inclusion criteria were selected. All relevant data from the selected papers were extracted and recorded in separate tables according to the types of periodontal defects treated (i.e. supra-alveolar defects, intrabony defects, furcation defects and fenestration defects) with the combination of barrier membranes and grafting materials. Most studies have demonstrated periodontal regeneration following the combination approach. Most studies demonstrated superior histologic healing following the combination of barrier membranes and grafting materials than following open flap debridement. Histologically superior healing following the combination of barrier membranes and grafting materials when compared with barrier membranes alone or grafting materials alone were only obtained in non-contained two wall intrabony and supraalveolar defects. CONCLUSION: Within its limits the present analysis indicates that: (a) The combination of barrier membranes and grafting materials may result in histological evidence of periodontal regeneration, predominantly bone repair. (b) No additional benefits of combination treatments were detected in models of three wall intrabony, Class II furcation or fenestration defects. (c) In supra-alveolar and two wall intrabony (missing buccal wall) defect models of periodontal regeneration, the additional use of a grafting material gave superior histological results of bone repair to barrier membranes alone. (d) In one study using a supra-alveolar model, combined graft and barrier membrane gave a superior result to graft alone.

2. Post Extraction Socket

A methodological approach to assessing alveolar ridge preservation procedures in humans: hard tissue profile

Lambert F, Vincent K, Vanhoutte V, Seidel L, Lecloux G, Rompen E.
J Clin Periodontol 2012.

AIMS: Multiple surgical protocols using biomaterials have been proposed to limit the typical post-extraction bone resorption. However, because of the heterogeneity of the studies, particularly the differences in assessment methods, it is difficult to determine the superiority of one technique over

another. The objective of this study was to describe a new radiographic method to draw a map of alveolar bone remodelling after alveolar ridge preservation procedures to compare different surgical techniques more accurately. The newly developed measuring method was applied to a case series describing a specific preservation technique. MATERIALS AND METHODS: Fourteen extraction sites (in 14 patients) located in the upper anterior maxilla were treated with bovine hydroxyapatite (0.25- to 1-mm particles) and a saddled connective tissue graft. A radiographic three-dimensional assessment of the hard tissues was performed at baseline and 3 months after the procedure. Standardized horizontal measurements were taken at three corono-apical levels (-2, -5 and -9 mm) and at three mesio-distal levels (mesial, centre and distal) in the buccal and palatal aspects. Vertical measurements were also recorded in nine regions superior to the alveolar crest. The measurements were performed by two independent observers and intra- and inter-observer effects were evaluated. RESULTS: No inter- and intra-observer effects were found when analysing the measurements from these two observers. The horizontal dimension of the crest decreased by 1.6 mm (20%) in the cervical regions (-2 mm level), decreased moderately, by 1 mm (12%), at the -5 mm level and decreased very little, 0.5 mm (6%), at the apical (-8 mm) level. The losses were always significantly higher in the buccal than in the palatal aspect. Buccally, the maximal bone remodelling at the cervical level remained below 1 mm. Vertical bone resorption was homogeneous and<1 mm in the nine measured regions. DISCUSSION: The radiographic measuring methodology proved to be reproducible. It can be applied in other clinical settings. It successfully assessed the alveolar ridge preservation technique (BHA+saddle connective tissue graft).

Socket preservation using bovine bone mineral and collagen membrane: a randomized controlled clinical trial with histologic analysis

Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L, Cardaropoli G.
Int J Periodontics Restorative Dent 2012;32(4):421-430.

After tooth extraction, varying amounts of bone resorption occur because of qualitative and quantitative changes at the edentulous site of the alveolar process. The aims of this randomized controlled clinical trial were (1) to compare the postextraction changes in residual ridge dimensions during spontaneous healing with those during socket preservation, (2) to analyze the histologic and histomorphometric aspects of the grafted sockets, and (3) to compare probing procket depth (PPD) and clinical attachment level (CAL) changes at teeth adjacent to extraction sites. Forty-eight teeth were extracted from 41 patients referred for extraction of 1 or more maxillary or mandibular premolars or molars. The edentulous sites were randomly assigned to the control (EXT, extraction alone) or experimental groups (SP, extraction and socket preservation). In the SP group, the sockets were filled with bovine bone mineral and covered with porcine collagen membrane. At baseline and after 4 months, PPD, gingival recession (REC), and CAL were measured at teeth adjacent to the edentulous sites. The changes in ridge dimensions from baseline to 4 months were assessed on dental casts. At 4 months, bone was harvested from the grafted areas in the SP group and the edentulous areas in the EXT group. PPD, REC, and CAL were comparable between groups. However, from baseline to 4 months, the SP group showed significantly less reduction in ridge width (1.04 +/- 1.08 mm vs 4.48 +/- 0.65 mm, P < .001) and height (0.46 +/- 0.46 mm vs 1.54 +/- 0.33 mm, P < .001). Histologically, the grafted sockets exhibited various stages of bone maturation and formation without inflammatory responses. No significant difference in the mineralized and nonmineralized fractions was noted between the groups. Socket preservation using bovine bone mineral and porcine collagen membrane considerably limits the amount of horizontal and vertical bone resorption when compared with extraction alone.

Socket site preservation using bovine bone mineral with and without a bioresorbable collagen membrane

Perelman-Karmon M, Kozlovsky A, Liloy R, Artzi Z.
Int J Periodontics Restorative Dent 2012;32(4):459-465.

The purpose of this study was to compare extraction sites augmented with bovine bone mineral (BBM) with and without resorbable membrane coverage. BBM particles were grafted in fresh human extraction sockets of 23 patients; in 12 of these patients, a guided tissue regeneration (GTR) membrane was applied. After 9 months of histomorphometric evaluation, cylindric hard tissue specimens were obtained. Percent bone area fractions (BAFs) of the crestal, middle, and apical sections from each specimen were calculated using the point-counting technique. Changes in values were compared. In sites augmented with BBM, the mean BAF ranged from 22.8% (coronal) to 36.3% (apical) compared to sites augmented with BBM and collagen

membrane (35.2% [coronal] to 47% [apical]). Comparison between the different depths and the two groups showed a distinct increase in BAF from coronal to apical regions (P < .001). This pattern was observed in both groups (P < .001) and was significantly higher in the group augmented with BBM and collagen membrane (P < .05). In the immediate postextraction phase, BBM as a grafted biomaterial preserved the socket volume and enabled newly formed bone for future implant site preparation. The amount of the osseous fraction increased with GTR membrane.

Evidence-based knowledge on the biology and treatment of extraction sockets

Hämmerle CH, Araújo MG, Simion M, Osteology Consensus Group 2011.
Clin Oral Implants Res 2012;23 Suppl 5:80-2.

OBJECTIVES: The fresh extraction socket in the alveolar ridge represents a special challenge in everyday clinical practice. Maintenance of the hard and soft tissue envelope and a stable ridge volume were considered important aims to allow simplifying subsequent treatments and optimizing their outcomes in particular, when implants are planned to be placed. MATERIAL AND METHODS: Prior to the consensus meeting four comprehensive systematic reviews were written on two topics regarding ridge alteration and ridge preservation following tooth extraction and implant placement following tooth extraction. During the conference these manuscripts were discussed and accepted thereafter. Finally, consensus statements and recommendations were formulated. RESULTS: The systematic reviews demonstrated that the alveolar ridge undergoes a mean horizontal reduction in width of 3.8 mm and a mean vertical reduction in height of 1.24 mm within 6 months after tooth extraction. The techniques aimed at ridge preservation encompassed two different approaches: i) maintaining the ridge profile, ii) enlarging the ridge profile. Regarding timing of implant placement the literature showed that immediate implant placement leads to high implant survival rates. This procedure is primarily recommended in premolar sites with low esthetic importance and favorable anatomy. In the esthetic zone, however, a high risk for mucosal recession was reported. Hence, it should only be used in stringently selected situations with lower risks and only by experienced clinicians. In molar sites a high need for soft and hard tissue augmentation was identified. CONCLUSIONS: Future research should clearly identify the clinical and patient benefits resulting from ridge preservation compared with traditional procedures. In addition, future research should also aim at better identifying parameters critical for positive treatment outcomes with immediate implants. The result of this procedure should be compared to early and late implant placement.

Alveolar process preservation at implants installed immediately into extraction sockets using deproteinized bovine bone mineral - an experimental study in dogs

Caneva M, Botticelli D, Morelli F, Cesaretti G, Beolchini M, Lang NP.
Clin Oral Implants Res 2011;21.

AIM: To evaluate the soft tissue and the dimensional changes of the alveolar bony crest at sites where deproteinized bovine bone mineral (DBBM) particles, concomitantly with the placement of a collagen membrane, were used at implants installed into sockets immediately after tooth extraction. MATERIAL AND METHODS: The pulp tissue of the mesial roots of (3) P(3) was removed in six Labrador dogs, and the root canals were filled. Flaps were elevated bilaterally, the premolars hemi-sectioned, and the distal roots removed. Recipient sites were prepared in the distal alveolus, and implants were placed. At the test sites, DBBM particles were placed in the residual marginal defects concomitantly with the placement of a collagen membrane. No treatment augmentation was performed at the control sites. A non-submerged healing was allowed. Impressions were obtained at baseline and at the time of sacrifice performed 4 months after surgery. The cast models obtained were analyzed using an optical system to evaluate dimensional variations. Block sections of the implant sites were obtained for histological processing and soft tissue assessments. RESULTS: After 4 months of healing, no differences in soft tissue dimensions were found between the test and control sites based on the histological assessments. The location of the soft tissue at the buccal aspect was, however, more coronal at the test compared with the control sites (1.8 +/- 0.8 and 0.9 +/- 0.8 mm, respectively). At the three-dimensional evaluation, the margin of the soft tissues at the buccal aspect appeared to be located more apically and lingually. The vertical dislocation was 1 +/- 0.6 and 2.7 +/- 0.5 mm at the test and control sites, respectively. The area of the buccal shrinkage of the alveolar crest was significantly smaller at the test sites (5.9 +/- 2.4 mm(2)) compared with the control sites (11.5 +/- 1.7 mm(2)). CONCLUSION: The use of DBBM particles concomitantly with the application of a

collagen membrane used at implants placed into sockets immediately after tooth extraction contributed to the preservation of the alveolar process.

Stability of contour augmentation and esthetic outcomes of implant-supported single crowns in the esthetic zone: 3-year results of a prospective study with early implant placement postextraction

Buser D, Wittneben J, Bornstein MM, Grutter L, Chappuis V, Belser UC.
J Periodontol 2011;82(3):342-355.

Background: Early implant placement is one of the treatment options after tooth extraction. Implant surgery is performed after a healing period of 4 to 8 weeks and combined with a simultaneous contour augmentation using the guided bone regeneration technique to rebuild stable esthetic facial hard- and soft-tissue contours. Methods: In this prospective study, 20 patients were treated with an implant-born single crown and followed for 3 years. Clinical, radiologic, and esthetic parameters were recorded to assess treatment outcomes. Results: At the 3-year examination, all 20 implants were successfully integrated, demonstrating ankylotic stability and healthy peri-implant soft tissues as documented by standard clinical parameters. Esthetic outcomes were assessed by the pink esthetic score (PES) and white esthetic score (WES) and confirmed pleasing results overall. WES values were slightly superior to PES values. Periapical radiographs showed minimal crestal bone loss around used bone-level implants with a mean bone loss of 0.18 mm at 3 years. Only two implants revealed bone loss between 0.5 and 1.0 mm. One of these implants had minor mucosal recession <1.0 mm. Conclusions: This prospective study evaluates the concept of early implant placement and demonstrated successful tissue integration for all 20 implants and stable bone-crest levels around implant-abutment interfaces according to the platform-switching concept. The midterm 3-year follow-up revealed pleasing esthetic outcomes and stable facial soft tissues. The risk of mucosal recession was low, with only one patient showing minor recession of the facial mucosa. These encouraging results need to be confirmed with a 5-year follow-up examination.

Ridge preservation with the use of Bio-Oss® Collagen: A 6-month study in the dog

Araújo M, Lindhe J.
Clin.Oral Impl. Res. 20, 2009;433-440.

Background: In previous short-term studies, it was observed that while the placement of biomaterial in alveolar sockets may promote bone formation and ridge preservation, the graft may in fact also delay healing.
Aim: The objective of the present experiment was to evaluate the more long-term effect on hard tissue formation and the amount of ridge augmentation that can occur by the placement of a xenogeneic graft in extraction sockets of dogs.
Material and methods: Five beagle dogs were used. The third mandibular premolars were hemi-sected. The distal roots were carefully removed. A graft consisting of Bio-Osss collagen was placed in one socket while the contra-lateral site was left without grafting. After 6 months of healing, the dogs were euthanized and biopsies were sampled. From each experimental site, four ground sections – two from the mesial root and two from the healed socket – were prepared, stained and examined under a microscope.
Results: The placement of Bio-Osss collagen in the fresh extraction socket served as a scaffold for tissue modeling but did not enhance new bone formation. In comparison with the non-grafted sites, the dimension of the alveolar process as well as the profile of the ridge was better preserved in Bio-Osss-grafted sites.
Conclusion: The placement of a biomaterial in an extraction socket may modify modeling and counteract marginal ridge contraction that occurs following tooth removal.

Socket grafting in the posterior maxilla reduces the need for sinus augmentation.

Rasperini G, Canullo L, Dellavia C, Pellegrini G, Simion M.
Int J Periodontics Restorative Dent 2010;30(3):265-73.

This study compared the dimensional alterations, the need for sinus floor elevation, and the histologic wound healing of augmented and nonaugmented alveolar sockets. Sixteen human extraction sockets were either grafted or left untreated. At baseline and 3 and 6 months postextraction, alveolar ridge alterations were evaluated; at 3, 6, and 9 months, histologic analyses were conducted. Implant placement with or without sinus floor augmentation was decided at 6 months. Three of eight patients in the control group underwent sinus floor augmentation compared to one of six in the experimental group. The alveolar ridge augmentation procedure presented here increases the possibility of inserting implants without the need for a sinus augmentation procedure.

Dynamics of Bio-Oss Collagen incorporation in fresh extraction wounds: an experimental study in the dog.

Araujo, M. G., Liljenberg, B., Lindhe, J.
Clin Oral Implants Res 2010; 21(1):55-64.

AIM: The objective of this experiment was to analyze processes involved in the incorporation of Bio-Oss Collagen in host tissue during healing following tooth extraction and grafting. METHODS: Five beagle dogs were used. Four premolars in the mandible ((3)P(3), (4)P(4)) were hemi-sected, the distal roots were removed and the fresh extraction socket filled with Bio-Oss Collagen. The mucosa was mobilized and the extraction site was closed with interrupted sutures. The tooth extraction and grafting procedures were scheduled in such a way that biopsies representing 1 and 3 days, as well as 1, 2 and 4 weeks of healing could be obtained. The dogs were euthanized and perfused with a fixative. Each experimental site, including the distal socket area, was dissected. The sites were decalcified in EDTA, and serial sections representing the central part of the socket were prepared in the mesio-distal plane and parallel with the long axis of the extraction socket. Sections were stained in hematoxylin and eosin and were used for the overall characteristics of the tissues in the extraction socket. In specimens representing 1, 2 and 4 weeks of healing the various tissue elements were assessed using a morphometric point counting procedure. Tissue elements such as cells, fibers, vessels, leukocytes and mineralized bone were determined. In deparaffinized sections structures and cells positive for tartrate-resistant acid phosphatase activity (TRAP), alkaline phosphatase and osteopontin were identified. RESULTS: The biomaterial was first trapped in the fibrin network of the coagulum. Neutrophilic leukocytes [polymorphonuclear (PMN) cells] migrated to the surface of the foreign particles. In a second phase the PMN cells were replaced by multinuclear TRAP-positive cells (osteoclasts). The osteoclasts apparently removed material from the surface of the xenogeneic graft. When after 1-2 weeks the osteoclasts disappeared from the Bio-Oss granules they were followed by osteoblasts that laid down bone mineral in the collagen bundles of the provisional matrix. In this third phase the Bio-Oss particles became osseointegrated. CONCLUSIONS: It was demonstrated that the incorporation of Bio-Oss in the tissue that formed in an extraction wound involved a series of different processes.

Analysis of the socket bone wall dimensions in the upper maxilla in relation to immediate implant placement.

Huynh-Ba, G., Pjetursson, B. E., Sanz, M., Cecchinato, D., Ferrus, J., Lindhe, J., Lang, N. P.
Clin Oral Implants Res 2010; 21(1):37-42.

BACKGROUND: Animal and human researches have shown that immediate implant placement into extraction sockets failed to prevent socket dimensional changes following tooth extraction. It has been suggested that a minimal width of 1-2 mm of buccal bone is necessary to maintain a stable vertical dimension of the alveolar crest. AIM: To determine the dimensions of the bony wall at extraction sites in the esthetic zone (anterior teeth and premolars in the maxilla) and relate it to immediate implant placement. METHODS: As part of an ongoing prospective randomized-controlled multicenter clinical study on immediate implant placement, the width of the buccal and palatal bony walls was recorded at 93 extraction sites. RESULTS: The mean width of the buccal and palatal bony walls was 1 and 1.2 mm, respectively (P<0.05). For the anterior sites (canine to canine), the mean width of the buccal bony wall was 0.8 mm. For the posterior (premolar) sites, it was 1.1 mm (P<0.05). In the anterior sites, 87% of the buccal bony walls had a width < or = 1 mm and 3% of the walls were 2 mm wide. In the posterior sites, the corresponding values were 59% and 9%, respectively. CONCLUSIONS: If the criterion of a minimal buccal bone width of 2 mm to maintain a stable buccal bony wall is valid, only a limited number of sites in the anterior maxilla display such a clinical situation. The data suggested that in the majority of extraction sites in the anterior maxilla, thin (< or = 1 mm) buccal walls were present. This, in turn, means that in most clinical

situations encountered, augmentation procedures are needed to achieve adequate bony contours around the implant.

Aesthetic and patient preference using a bone substitute to preserve extraction sockets under pontics. A cross-sectional survey.

Schlee, M. and M. Esposito
Eur J Esthet Dent 2009;2(3):209-217.

Purpose: To evaluate aesthetic and patient satisfaction after tooth extraction using a bone substitute (and soft tissue grafting when tissue thickness was lacking) under a pontic to preserve the alveolar ridge for aesthetic purposes. The contralateral natural tooth acted as internal control.
Materials and methods: All patients with at least one site under a pontic augmented with Bio-Oss® or Bio-oss® Collagen with or without a concomitant connective tissue graft with at least a follow-up of 6 months after the ridge preservation procedure were eligible for the present retrospective study. Sites with a damaged buccal wall were excluded. Outcome measures were: aesthetics (pink esthetic score, PES) evaluated by an independent and blinded dental hygienist on the basis of clinical pictures, patient satisfaction, patient preference and complications.
Results: Twenty-six patients were consecutively treated, and 23 patients attended the evaluation visit. In seven patients, soft tissue grafts were performed in conjunction with Bio-Oss placement. Eight to 86 months after the ridge augmentation procedure (mean 38 months), there were no statistically significant differences observed in PES between preserved sites and control teeth. Patient satisfaction did not show any statistically significant difference between the two groups either. All patients declared they would undergo the same procedure again.
Conclusions: Bio-Oss placement in post-extractive sites with a remaining buccal bone plate lead to a good aesthetic result. Randomised clinical trials with suitable control groups are needed to identify the most effective techniques and/or materials to preserve ridges under pontics.

Extraction site management using a natural bone mineral containing collagen: rationale and retrospective case study.

Ackermann, K.L.
Int J Periodontics 2009; 29(5):489-97.

Socket or ridge preservation is performed to maintain the contour of the alveolar ridge prior to conventional or implant-based prosthetic therapy. In this retrospective analysis of consecutive subjects, a natural bone mineral containing collagen was grafted into 110 sockets in 62 patients. The sites were left open to heal. Based on external measurements with a periodontal probe, the soft tissue volume and contour were largely preserved at all sites, irrespective of the initial defect morphology. Clinical advantages of this protocol include predictable preservation of the soft tissues, favorable healing characteristics, and easy handling of the material.

Comparative histomorphometric analysisi of extraction sockets healing implanted with bovine xenografts, irradiated cancellous allografts, and solvent-dehydrated allografts in humans.

Lee, D. W., S. H. Pi, et al.
Int J Oral Maxillofac Implants 2009 ; 24(4): 609-615.

Purpose: Bovine-derived bone xenograft and mineralized cancellous bone allograft have been successfully used as bone substitutes in dental surgery, but few clinical studies in humans have been reported. The objective of this study was to compare the osteoconductive effects of deproteinized bovine bone mineral (DBBM), irradiated cancellous allograft (ICA), and solvent-dehydrated allograft (SDA) when used to preserve extraction sockets. Materials and Methods: Twenty patients received bone grafting in extraction sockets with DBBM (n = 7), ICA (n = 8), or SDA (n = 5). Core biopsies were taken from each graft site 4 to 6 months after grafting and were evaluated histomorphometrically. One-way analysis of variance was used to compare each variable. P values less than .05 were considered significant. Results: DBBM induced more new bone deposition in the periphery of the native bone particles than ICA or SDA, whereas ICA and SDA were

more frequently surrounded by fibrous tissue than DBBM. In addition, DBBM retained more residual graft bony particles than ICA or SDA. Conclusions: Based on these findings, the DBBM showed more of an osteoconductive effect than ICA or SDA, producing a more rigid bony structure. It is therefore suggested that DBBM may be more favorable for the preservation of extraction sockets than allogeneic graft materials.

Effect of a xenograft on early bone formation in extraction sockets: an experimental study in dog

Araujo, M., E. Linder, et al.
Clin Oral Implants Res 2009; 20(1): 1-6.

AIM: The aim of this study was to study the effect on early bone formation resulting from the placement of a xenograft in the fresh extraction socket in dogs. MATERIAL AND METHODS: Five beagle dogs were used. The distal roots of the third and fourth mandibular premolars were removed. In one quadrant, a graft consisting of Bio-Oss Collagen was placed in the fresh extraction wound, while the corresponding premolar sites in the contra-lateral jaw quadrant were left non-grafted. After 2 weeks of healing, the dogs were perfused with a fixative, the mandibles removed, the experimental sites dissected, demineralized, sectioned in the mesio-distal plane and stained in hematoxyline-eosine. RESULTS: The central portion of the non-grafted sockets was occupied by a provisional matrix comprised of densely packed connective tissue fibers and mesenchymal cells. Apical and lateral to the provisional matrix, newly formed woven bone was found to occupy most of the sockets. In the apical part of the grafted sockets, no particles of the xenograft could be observed but newly formed bone was present in this portion of the experimental site. In addition, limited numbers of woven bone trabeculae occurred along the lateral socket walls. The central and marginal segments of the grafted sockets, however, were occupied by a non-mineralized connective tissue that enclosed Bio-Oss particles that frequently were coated by multinucleated cells. CONCLUSIONS: The placement of Bio-Oss Collagen in the fresh extraction wound obviously delayed socket healing. Thus, after 2 weeks of tissue repair, only minute amounts of newly formed bone occurred in the apical and lateral borders of the grafted sockets, while large amounts of woven bone had formed in most parts of the non-grafted sites.

Early implant placement with simultaneous guided bone regeneration following single-tooth extraction in the esthetic zone: 12-month results of a prospective study with 20 consecutive patients.

Buser, D., S. Halbritter, et al.
J Periodontol 2009; 80(1): 152-62.

BACKGROUND: Early implant placement is one of the treatment options in postextraction sites in the anterior maxilla. Implant placement is performed after a soft tissue healing period of 4 to 8 weeks. Implant placement is combined with a simultaneous guided bone regeneration (GBR) procedure to rebuild esthetic facial hard and soft tissue contours. METHODS: In this prospective case-series study, 20 consecutive patients treated with an implant-borne single crown were prospectively followed for 12 months. Clinical, radiologic, and esthetic parameters were recorded to assess treatment outcomes. RESULTS: At the 12-month examination, all 20 implants were successfully integrated, demonstrating ankylotic stability and healthy peri-implant soft tissues as documented by standard parameters. The esthetic outcomes assessed by a pink esthetic score (PES) and a white esthetic score (WES) demonstrated pleasing results overall. The WES values were slightly superior to the PES values. The periapical radiographs showed minimal crestal bone loss around the used bone level implants, with mean bone loss of 0.18 mm at 12 months. Only one implant showed >0.5 mm bone loss, combined with minor mucosal recession of 0.5 to 1.0 mm. CONCLUSIONS: This prospective case series study evaluating the concept of early implant placement demonstrated successful tissue integration for all 20 implants. The short-term follow-up of 12 months revealed pleasing esthetic outcomes overall, as assessed by objective parameters. The risk for mucosal recession was low; only one patient showed minor recession of the facial mucosa. These encouraging results need to be confirmed with 3- and 5-year follow-up examinations.

Hard tissue alterations after socket preservation: an experimental study in the beagle dog

Fickl S, Zuhr O, Wachtel H, Bolz W, Hürzeler MB.
Clin Oral Implants Res, 2008; 19: 1111-1118.

OBJECTIVES: The aim of the following experimental study was to assess bone changes in the horizontal and vertical dimension when using different socket preservation procedures. MATERIAL AND METHODS: In five beagle dogs the distal roots of the 3rd and 4th premolar were extracted without elevation of a mucoperiosteal flap and the following treatments were assigned: Tx 1: The extraction socket was filled with BioOss Collagen (Geistlich Biomaterials, Wolhusen, Switzerland) and interrupted sutures were applied.: Tx 2: The extraction socket was filled with BioOss Collagen (Geistlich Biomaterials, Wolhusen, Switzerland) and a free gingival graft was sutured to cover the socket.: Tx 3: The extraction socket was left with its blood clot and interrupted sututes were applied.: Four month after surgery the dogs were sacrificed and from each extraction site two histological sections were selected for histometric analysis. The following parameters were evaluated: (1) the vertical dimension was determined by placing a horizontal line on the lingual bone wall. Then, the distance from this line to the buccal bone wall was measured. (2) The horizontal dimension was assessed at three different areas measured from the top of the lingual crest: 1 mm (Value 1), 3 mm (Value 3) and 5 mm (Value 5). RESULTS: The mean vertical loss of the buccal bone plate for the Tx 1 group was 2.8+/-0.2 mm. The Tx 2 group showed vertical loss of 3.3+/-0.2 mm. The Tx 3 group demonstrated 3.2+/-0.2 mm of mean vertical loss. The horizontal dimension of the alveolar process was 4.4+/-0.3/6.1+/-0.2/7.2+/-0.1 mm at the three different levels for the Tx 1 group. The Tx 2 group depicted bone dimensions of 4.8+/-0.2/6.0+/-0.2/7.1+/-0.1 mm. The horizontal dimension of the Tx 3 group was 3.7+/-0.3/6.2+/-0.2/7.0+/-0.1 mm. When the results from the horizontal measurements were tested with the analysis of variance (ANOVA), a clear significance could be found in particular for Value 1 mm between the test groups Tx 1 and Tx 2 and the control group (Tx 3) ($P<0.001$). Furthermore the mean of treatment 1 (Tx 1) was slightly significantly lower than of treatment 2 (Tx 2) ($P<0.05$). CONCLUSION: The findings from the present study disclose that incorporation of BioOss Collagen into the extraction socket has only limited impact on the subsequent biologic process with particular respect to the buccal bone plate. The horizontal measurement of the alveolar ridge depicted that the loss of the buccal bone plate was replaced to a certain amount by newly generated bone guided by the BioOss Collagen scaffold. It seems that the mechanical stability provided by BioOss Collagen and furthermore by a free gingival graft could act as a placeholder preventing the soft tissue from collapsing.

Dimensional changes of the alveolar ridge contour after different socket preservation techniques

Fickl S, Zuhr O, Wachtel H, Stappert CFJ, Stein JM, Hürzeler MB.
J Clin Periodontol, 2008; 35: 906-913.

OBJECTIVES: The aim of the following study was to assess contour changes after socket preservation techniques. MATERIAL AND METHODS: In five beagle dogs, the distal root of the third and fourth mandibular premolars was extracted. The following treatments (Tx) were randomly assigned for the extraction socket. Tx 1: BioOss Collagen. Tx 2: BioOss Collagen and a free soft tissue graft. Tx 3: No treatment. Tx 4: The internal buccal aspect was covered with an experimental collagen membrane, the extraction socket was filled with BioOss Collagen and the membrane folded on top of the graft. Impressions were obtained at baseline, 2 and 4 months after surgery. Bucco-lingual measurements were performed using digital imaging analysis. RESULTS: All groups displayed contour shrinkage at the buccal aspect. Only the differences between the two test groups (Tx 1, Tx 2) and the control group (Tx 3) were significant at the buccal aspect ($p< or =0.001$). No measurements of the Tx 4 group could be performed. CONCLUSION: Socket preservation techniques, used in the present experiment, were not able to entirely compensate for the alterations after tooth extraction. Yet, incorporation of BioOss Collagen seems to have the potential to limit but not avoid the post-operative contour shrinkage.

Tissue alterations after tooth extraction with and without surgical trauma: a volumetric study in the beagle dog

Fickl S, Zuhr O, et al.
J Clin Periodontol 2008; 35(4): 356-63.

OBJECTIVES: The aim of this study is to evaluate whether tooth extraction without the elevation of a muco-periosteal flap has advantageous effects on the resorption rate after tooth extraction. MATERIAL AND METHODS: In five beagle dogs polyether impressions were taken before the surgery. The roots of the first and second pre-molars (P(1) and P(2)) were extracted and the sites were assigned to one of the following treatments: treatment group (Tx) 1, no treatment; Tx 2, surgical trauma (flap elevation and repositioning); Tx 3, the extraction socket was filled with BioOss Collagen and closed with a free soft-tissue graft; Tx 4, after flap elevation and repositioning, the extraction socket was treated with BioOss Collagen and a free soft-tissue graft. Impressions were taken 2 and 4 months after surgery. The casts were scanned, matched together with baseline casts and evaluated with digital image analysis. RESULTS: The "flapless groups" demonstrated significant lower resorption rates both when using socket-preservation techniques and without. Furthermore, socket-preservation techniques yielded better results compared with not treating the socket. CONCLUSION: The results demonstrate that leaving the periosteum in place decreases the resorption rate of the extraction socket. Furthermore, the treatment of the extraction socket with BioOss Collagen and a free gingival graft seems beneficial in limiting the resorption process after tooth extraction.

The influence of Bio-Oss Collagen on healing of an extraction socket: an experimental study in the dog

Araujo M, Linder E, et al. (2008)
Int J Periodontics Restorative Dent 28(2): 123-35.

The objective of the present experiment was to evaluate the effect on hard tissue modeling and remodeling of the placement of a xenograft in fresh extraction sockets in dogs. Five mongrel dogs were used. Two mandibular premolars (4P4) were hemisected in each dog, and the distal roots were carefully removed. In one socket, a graft consisting of Bio-Oss Collagen (Geistlich) was placed, whereas the contralateral site was left without grafting. After 3 months of healing, the dogs were euthanized and biopsies sampled. From each experimental site, four ground sections (two from the mesial root and two from the healed socket) were prepared, stained, and examined under the microscope. The presence of Bio-Oss Collagen failed to inhibit the processes of modeling and remodeling that took place in the socket walls following tooth extraction. However, it apparently promoted de novo hard tissue formation, particularly in the cortical region of the extraction site. Thus, the dimension of the hard tissue was maintained and the profile of the ridge was better preserved. The placement of a biomaterial in an extraction socket may promote bone modeling and compensate, at least temporarily, for marginal ridge contraction.

A prospective clinical study of non-submerged immediate implants: clinical outcomes and esthetic results.

Chen ST, Darby IB, et al. (2007).
Clin Oral Implants Res 18(5): 552-62.

OBJECTIVES: To evaluate healing of marginal defects in immediate transmucosal implants grafted with anorganic bovine bone, and to assess mucosal and radiographic outcomes 3-4 years following restoration. MATERIAL AND METHODS: Thirty immediate transmucosal implants in maxillary anterior extraction sites of 30 patients randomly received BioOss (N=10; BG), BioOss and resorbable collagen membrane (N=10; BG+M) or no graft (N=10; control). RESULTS: Vertical defect height (VDH) reductions of 81.2+/-5%, 70.5+/-17.4% and 68.2+/-16.6%, and horizontal defect depth (HDD) reductions of 71.7+/-34.3%, 81.7+/-33.7% and 55+/-28.4% were observed for BG, BG+M and control groups, respectively, with no significant inter-group differences. Horizontal resorption was significantly greater in control group (48.3+/-9.5%) when compared with BG (15.8+/-16.9%) and BG+M (20+/-21.9%) groups (P=0.000). Ten sites (33.3%) exhibited recession of the mucosa after 6 months; eight (26.7%) had an unsatisfactory esthetic result post-restoration due to recession. Mucosal recession was significantly associated (P=0.032) with buccally positioned implants (HDD 1.1+/-0.3 mm) when compared with lingually positioned implants (HDD 2.3+/-0.6 mm). In 19 patients followed for a mean of 4.0+/-0.7 years, marginal mucosa and bone levels remained stable following restoration. CONCLUSION: BioOss significantly reduced horizontal resorption of buccal bone. There is a risk of mucosal recession and adverse soft tissue esthetics with immediate implant placement. However, this risk may be reduced by avoiding a buccal position of the implant in the extraction socket.

Effect of bone mineral with or without collagen membrane in ridge dehiscence defects following premolar extraction.

Kim M. et al.
In Vivo 2008. 22(2): 231-236.

BACKGROUND: The purpose of this investigation was to evaluate the regenerative response to deproteinized porous bovine bone mineral (BM) when used alone or in combination with a bioresorbable porcine-derived bilayer collagen membrane (CM) for alveolar ridge augmentation in dogs. MATERIALS AND METHODS: The mandibular premolars were extracted unilaterally and three ridge defects were induced in six mongrel dogs. Each defect site was randomly assigned to one of the following treatment groups: BM alone (group A), BM in combination with CM (group B), or neither membrane nor bone graft, which served as a control (group C). No adverse events occurred during the experimental period. Dental computed tomography (CT) scans were taken after postoperative periods of 8 and 16 weeks. RESULTS: The percentage of CT-derived bone density in groups A and B was significantly different from that of group C ($p < 0.01$) at 8 and 16 weeks. The percentage of CT-derived bone density of the dogs in Group B was significantly higher than that of those in group A at 8 and 16 weeks ($p < 0.01$). Gross evaluation of the 3-dimensional CT reconstruction image of the canine mandibles after 16 weeks of implantation showed that group B had the greatest amount of bone augmentation and excellent thickness of the buccal aspect of the alveolar ridge. CONCLUSION: These results suggest that BM leads to more successful bone regeneration for guided bone regeneration procedures, especially in conjunction with the use of a CM as a barrier in order to promote the regeneration of canine alveolar ridge defects.

Immediate implant placement with transmucosal healing in areas of aesthetic priority. A mulitcentre randomized –controlled clinical trial I. Surgical outcomes.

Lang N., Tonetti M.S., Suvan J.E:, Bernard J.P., Botticelli D., Fournousis I, Hallund M., Jung R., Laurell L., Salvi G., Shafer D, Weber H.P
Clin Oral Impl Res 2007; 18: 188–196.

Objectives: To compare the clinical outcomes of standard, cylindrical, screw-shaped to novel tapered, transmucosal (Straumann Dental((R))) implants immediately placed into extraction sockets. Material and methods: In this randomized-controlled clinical trial, outcomes were evaluated over a 3-year observation period. This report deals with the need for bone augmentation, healing events, implant stability and patient-centred outcomes up to 3 months only. Nine centres contributed a total of 208 immediate implant placements. All surgical and post-surgical procedures and the evaluation parameters were discussed with representatives of all centres during a calibration meeting. Following careful luxation of the designated tooth, allocation of the devices was randomly performed by a central study registrar. The allocated SLA titanium implant was installed at the bottom or in the palatal wall of the extraction socket until primary stability was reached. If the extraction socket was >/=1 mm larger than the implant, guided bone regeneration was performed simultaneously (Bio Oss((R)) and BioGide((R))). The flaps were then sutured. During non-submerged transmucosal healing, everything was done to prevent infection. At surgery, the need for augmentation and the degree of wound closure was verified. Implant stability was assessed clinically and by means of resonance frequency analysis (RFA) at surgery and after 3 months. Wound healing was evaluated after 1, 2, 6 and 12 weeks post-operatively. Results: The demographic data did not show any differences between the patients receiving either standard cylindrical or tapered implants. All implants yielded uneventful healing with 15% wound dehiscences after 1 week. After 2 weeks, 93%, after 6 weeks 96%, and after 12 weeks 100% of the flaps were closed. Ninety percent of both implant designs required bone augmentation. Immediately after implantation, RFA values were 55.8 and 56.7 and at 3 months 59.4 and 61.1 for cylindrical and tapered implants, respectively. Patient-centred outcomes did not differ between the two implant designs. However, a clear preference of the surgeon's perception for the appropriateness of the novel-tapered implant was evident. Conclusions: This RCT has demonstrated that tapered or standard cylindrical implants yielded clinically equivalent short-term outcomes after immediate implant placement into the extraction socket.

Effect of Bio-Oss on osseointegration of dental implants surrounded by circumferential bone defects of different dimensions: an experimental study in the dog.

Polyzois I, Renvert S, Bosshardt DD, Lang NP, Claffey N.
Clin Oral Implants Res 2007

Objectives: This study was designed to evaluate the effect of gap width and graft placement on bone healing around implants placed in simulated extraction sockets of various widths in four Labrador dogs. Materials and Methods: Five Osseotite((R)) implants per dog were placed in the mandible of four dogs. Two implants were inserted into sites with a 2.37 mm and two with a 1 mm gap present between the implants and bone around the coronal 6 mm of the implants in each dog. For one of each gap sizes, the gap was filled with Bio-Oss((R)), and the other two with blood alone. A fifth implant was inserted without a gap and used as a control. Ground sections were prepared from biopsies taken at 4 months and histometric measurements of osseointegration and bone between the threads made for the coronal 6 mm. Results: The medians for osseointegration ranged from 5.2 mm for control to 1-2.6 mm for the test modalities. There were significant differences for linear measurements of osseointegration (chi(2) 18.27; df 4; P=0.0011) and bone area within threads (chi(2) 23.4; df 4; P=0.0001) between test modalities. Conclusions: The results suggest that the wider the gap around the implants, the less favourable the histological outcome at short time intervals following treatment. They also infer that bone grafting with anorganic bovine bone xenograft seems to lead to a more favourable histological outcome for wider circumferential defects but not for narrower defects. To cite this article: Polyzois I, Renvert S, Bosshardt DD, Lang NP, Claffey N. The effect of Bio-Oss((R)) on osseointegration of dental implants surrounded by circumferential bone defects of different dimensions: an experimental study in the dog.

A study of the fate of the buccal wall of extraction sockets of teeth with prominent roots.

Nevins M, Camelo M, et al.
Int J Periodontics Restorative Dent 2006; 26(1): 19-29

The objective of this investigation was to determine the fate of thin buccal bone encasing the prominent roots of maxillary anterior teeth following extraction. Resorption of the buccal plate compromises the morphology of the localized edentulous ridge and makes it challenging to place an implant in the optimal position for prosthetic restoration. In addition, the use of Bio-Oss as a bone filler to maintain the form of the edentulous ridge was evaluated. Nine patients were selected for the extraction of 36 maxillary anterior teeth. Nineteen extraction sockets received Bio-Oss, and seventeen sockets received no osteogenic material. All sites were completely covered with soft tissue at the conclusion of surgery. Computerized tomographic scans were made immediately following extraction and then at 30 to 90 days after healing so as to assess the fate of the buccal plates and resultant form of the edentulous sites. The results were assessed by an independent radiologist, with a crest width of 6 mm regarded as sufficient to place an implant. Those sockets treated with Bio-Oss demonstrated a loss of less than 20% of the buccal plate in 15 of 19 test sites (79%). In contrast, 12 of 17 control sockets (71%) demonstrated a loss of more than 20% of the buccal plate. In conclusion, the Bio-Oss test sites outperformed the control sites by a significant margin. No investigator was able to predict which site would be successful without the grafting material even though all were experienced clinicians. This leads to the conclusion that a patient has a significant benefit from receiving grafting materials at the time of extraction.

Healing of extraction sockets and surgically produced - augmented and non-augmented - defects in the alveolar ridge. An experimental study in the dog

Cardaropoli G, Araujo M, Hayacibara R, Sukekava F, Lindhe J.
J Clin Periodontol 2005; 32: 435-440.

OBJECTIVES: The current experiments had three aims (i) to determine whether the absence of the periodontal ligament (PDL) may alter features of the healing of an extraction socket, (ii) to examine if there were differences in the proportion of different tissues in resolved extraction sockets and surgically produced defects after 3 months of healing, (iii) to study the influence of different biomaterials on the healing of surgically produced bone defects. MATERIAL AND METHODS: Extraction sites: In five dogs, the

4th mandibular pre-molars were hemi-sected and the distal roots were removed. The extraction socket of one of the pre-molars was instrumented to eliminate all remnants of the PDL tissue. The socket of the contra-lateral pre-molar was left without instrumentation. The dogs were sacrificed after 3 months of healing. Defect sites: In five dogs, the pre-molars and 1st molars on both sides of the mandible were first removed and 3 months of healing allowed. After this interval three standardized cylindrical defects were prepared in each side of the mandible. The defects were 3.5 mm in diameter and 8 mm deep. In each quadrant one defect was grafted with Bio-Oss Collagen, one with Collagen Sponge and one defect was left non-grafted. The dogs were sacrificed 3 months after the grafting procedure. RESULTS: Extraction sites: The two categories of extraction sockets did not differ with respect to gross morphological features. The tissue of the extraction sites, apical of a newly formed bone bridge, was dominated by bone marrow. Few trabeculae of lamellar bone were also present. Defect sites: The non-augmented defect was sealed by a hard-tissue bridge. In the central and apical portions of the defect bone marrow made up about 61%, and mineralized bone 39% of the tissues. The invagination of the surface of this crestal bone was 0.8+/-0.3 mm. The defect augmented with Collagen Sponge was covered by a hard-tissue bridge 38% of the tissue within the defect was made up of bone marrow while the remaining 62% was occupied by mineralized bone. The invagination of the hard-tissue bridge was on the average 0.6+/-0.1 mm. In defects augmented with Bio-Oss Collagen the biomaterial occupied a substantial portion of the tissue volume. Eighty-five percent of the periphery of the Bio-Oss particles were found to be in direct contact with newly formed mineralized bone. Woven bone and bone marrow made up 47% and 26% of the newly formed tissue. The invagination of the most coronal part of the bone defect was 0.1+/-0.1 mm. CONCLUSION: Sockets that following tooth removal had their PDL tissue removed exhibited similar features of healing after 3 months as sockets which had the PDL retained. The tissues present in an extraction site appeared to be more mature than those present in a surgically produced defect of similar dimension. The Bio-Oss Collagen augmented defect exhibited less wound shrinkage than the non-augmented defect.

Postextraction Tissue Management: A Soft Tissue Punch Technique

Jung R, Siegenthaler D, Hämmerle CH.
Int J Periodontics Restorative Dent 2004 ;24: 545-553.

The aim of this prospective clinical study was to analyze graft-enhanced soft tissue healing during the initial phases after tooth extraction. Twenty patients in need of tooth extraction (incisors, canines, and premolars) and implant replacement were included. In patients with multiple extractions, one tooth was randomly selected for treatment. After administration of antibiotics, the selected tooth was gently removed. The socket was completely filled with deproteinized bovine bone mineral integrated in a 10% collagen matrix to fill out the space of the alveolus and support the soft tissue. A biopsy punch with a diameter corresponding to the socket orifice was chosen to harvest a free gingival graft of 2- to 3-mm thickness from the palate. The punched graft was carefully sutured to the deepithelialized soft tissue margins of the socket. One week after graft insertion, 64.3% of the mean graft area was fully integrated, 35.6% was fibrinoid, and 0.1% showed necrotic parts. Three and 6 weeks postsurgery, the mean integrated graft surface increased to 92.3% and 99.7%, respectively. After 6 weeks, a mean of 0.3% of the surface in four grafts showed incomplete wound closure, and no fibrin or necrosis was present. Colorimetry of the graft and adjacent tissue revealed a mean color match of deltaE = 2.91, lower than the critical threshold of 3.7 for intraoral visibility of different colors. This soft tissue punch technique led to successful biologic and esthetic integration of the transplanted graft into the local host tissues.

Efficacy of bovine bone mineral for alveolar augmentation: a human histologic study

Norton M, Odell E, Thompson I, Cook R
Clin Oral Implants Res. 2003; 14: 775-783

The purpose of this study was to evaluate the osteoconductivity of bovine bone mineral in humans. Fifteen patients referred to a private specialist surgical practice were treated consecutively for the repair of alveolar defects, and/or ridge maintenance at the site of extraction sockets, prior to implantation. Bio-Oss xenograft was utilized as the principal grafting material. Bone cores were trephined out at the time of implant placement and processed and examined to evaluate the tissue response under the light microscope. A total of 22 trephines were processed for histomorphometric evaluation to calculate the mean percentage of bone, residual graft and connective tissue by area. In addition, the mean percentage bone-to-graft contact was also calculated. The mean percentage area of new bone formation was 26.9% and the

percentage contact length between bone and residual graft was 34%. One implant placed into a site, which was histologically identified as having little new bone and, unusually, an inflammatory infiltrate, failed with mobility at abutment connection. All other implants were restored into function, with a survival rate at baseline of 97%.

The clinical use of deproteinized bovine bone mineral on bone regeneration in conjunction with immediate implant installation

Van Steenberghe D., Callens A., Geers L., Jacobs R.
Clin Oral Impl Res 200; 11: 210-16.

Twenty-one c.p. titanium screw-shaped implants were immediately installed after extraction and thorough curettage of the alveoli in 15 patients. Granules of natural bovine bone of 0.25-1.0 mm diameter were used to fill the remaining defect when the distance of the defect wall to the implant surface was >3 mm. Dimensional measurements of the defect height and width were made with a pocket probe. Fourteen sites in the upper jaw and 7 sites in the lower jaw were thus treated. The mean defect depth varied between 7 mm vestibularly and 10 mm mesially. The mucoperiosteal flaps were hermetically closed. At re-entry, the particles were packed and firmly attached but still distinguishable from the surrounding bone. Of the 21 sites treated, 5 sites had an exposure of the implant cover screw during the healing period. An exposure of the granular material occurred in 4 sites, but loss of granules in only 3. Even in these sites no signs of infection or inflammation of the soft tissues were observed. At re-entry after 6 months, 10 sites were completely and 9 partially filled. For the partial fills, the mean remaining defect height was 1.6 mm (range: 0.6-3.0 mm). Two sites showed an increased defect of respectively 2.4 and 4.8 mm. No fixtures were lost. The present results indicate that natural bovine bone is a safe filling material to fill remaining defects around implants installed in fresh extraction sockets.

Healing around implants placed in bone defects treated with Bio-Oss®
An experimental study in the dog

Berglundh T., Lindhe J.
Clin. Oral Impl Res 1997; 8: 117-124.

The aim of the present experiment was to study the healing after 3 and 7 months of bone defects filled with cancellous bovine bone mineral and compare the healing around implants placed in normal bone and in defects filled with bovine bone mineral. 5 beagle dogs, about 1-year-old, were used. At baseline, extractions of all mandibular left and right premolars were performed. Bone defects were prepared in the left mandibular quadrant. The defects was immediately filled with natural bovine cancellous bone mineral particles (Bio-Oss®). No resective surgery was performed in the right jaw quadrant. In both quadrants the flaps were adjusted to allow full coverage of the edentulous ridge and sutured. 3 months later, 2 dogs (group I) were euthanized and biopsies from the premolar regions obtained and prepared for histologic analysis. The 3 remaining dogs (group II) were at this time interval (3 months) subjected to implant installation in the premolar region of both the right and left mandibular jaw quadrants. 2 fixtures of the ITI Dental Implant System (solid-screw) were installed in each side. The fixtures in the test side were placed within the previously grafted defect area. while the fixtures in the control side were placed in normally healed extraction sites. A 4 month period of plaque control was initiated. At the end of this period, a clinical examination including assessment of plaque and soft tissue inflammation was performed and radiographs obtained from the implant sites. Biopsies were harvested and 4 tissue samples were yielded per dog, each including the implant and the surrounding soft and hard peri-implant tissues. The biopsies were processed for ground sectioning or ”fracture technique ” and the sections produced were subjected to histological examination. The volume of the hard tissue that was occupied by clearly identified Bio-Oss® particles was reduced between the 3- and 7-month intervals. This indicates that with time, Bio-Oss® becomes integrated and subsequently replaced by newly formed bone. In other words, this xenograft fulfills the criteria of an osteoconductive material. It was also observed that 4 months after implant installation, the titanium/hard tissue interface at test and control sites exhibited, from both a quantitative and qualitative aspect, a similar degree of ”implant osseointegration”.

Healing Response to Anorganic Bone Implantation in Periodontal Intrabony Defects in Dogs. Part I: Bone Regeneration. A Microradiographic Study.

Clérgeau L.P., Danan M., Clergeau-Guérithault S., Brion M.
J Periodontol 1996; 67(2): 140-149.

The purpose of the present study was to explore the regenerative potential of natural bone mineral plus collagen (Bio-Oss® COLLAGEN) in experimental intrabony defects. Eight healthy female beagle dogs were used. After extraction of the mandibular third premolars (P3), surgical defects were created and inflammation induced by placement of cotton and steel braids. Eight weeks later, the braids were removed. The experimental lesions thus obtained were either treated by plain flap curettage (group 1: control) or implanted with Bio-Oss® COLLAGEN (group 2: experimental). The results show that the surface of the implanted particles have the characteristics of a bone tissue. These particles are gathered together with a fibrillar network. 6, 18, and 36 weeks postoperative (PO), non-decalcified specimens from both groups were examined histologically by contact microradiography. In the control group, no significant bone regeneration was observed at 6, 18, or 36 weeks PO. In group 2, trabeculae undergoing mineralization and circumscribing dense particles above the reference notch were seen at 6 weeks PO; 18 and 36 week specimens showed significant bone regeneration with more or less dense remaining particles. The periodontal ligament space was always clear and the only signs of ankylosis noticed were deep in the notch on one 18 week test specimen and on one 36 week control specimen

Ridge alterations following grafting of fresh extraction sockets in man. A randomized clinical trial.

Araújo MG1, da Silva JC, de Mendonça AF, Lindhe J.
Clin Oral Implants Res. 2015 Apr;26(4):407-12. doi: 10.1111/clr.12366. Epub 2014 Mar 12.

OBJECTIVE: To evaluate dimensional alterations of the alveolar ridge that occurred following tooth extraction at sites grafted with Bio-Oss(®) Collagen.

MATERIAL AND METHODS: Twenty-eight subjects with maxillary incisors, canines, and premolars scheduled for extraction were included. The tooth was carefully removed. The patients were randomly assigned to a test or a control group. In the test group patients, Bio-Oss(®) Collagen was placed in the fresh extraction socket while in the controls no grafting was performed. Radiographic examination (cone beam computed tomograms, CBCT) was performed immediately after tooth extraction and socket treatment. Four months later, a new CBCT was obtained. In the radiographs, (i) the distance (mm) between base of the alveolar process (apex) and the buccal and palatal crests was determined, (ii) the outer profile of alveolar process of the experimental sites was outlined, and the cross section of the area (mm(2)) determined.

RESULTS: After 4 months of healing, the buccal and to a less extent also the palatal bone plate had become markedly reduced in height. The placement of a biomaterial in the socket failed to prevent resorption of the buccal and palatal bone walls. The cross-sectional area of the control ridge was reduced about 25% and of the test ridge with 3%.

CONCLUSION: The placement of a xenograft in fresh extraction sockets markedly counteracted the reduction in the hard tissue component of the edentulous sites.

Surgical techniques for alveolar socket preservation: a systematic review.

Vittorini Orgeas G1, Clementini M, De Risi V, de Sanctis M.
Int J Oral Maxillofac Implants. 2013 Jul-Aug;28(4):1049-61. doi: 10.11607/jomi.2670.

PURPOSE: To evaluate, through a systematic review of the literature, the efficacy of different surgical techniques in maintaining residual bone in the alveolar process following tooth extractions.

MATERIALS AND METHODS: MEDLINE/PubMed was searched through January 2010 and papers were selected according to the CONSORT statement and an independent three-stage screening process. The selected outcome variables were clinical width and height changes of the socket, and means and standard deviations were calculated from the included studies. For those studies that were randomized controlled

trials, six meta-analyses were performed by dividing studies into three groups with regard to the use of barriers and grafting (barriers alone, graft alone, or both).

RESULTS: Thirteen papers met the eligibility criteria and were included in the analyses. Statistically significant ridge preservation was found for studies that used barriers alone; the pooled weighted mean was 0.909 mm (95% confidence interval, 0.497554 to 1.320732 mm) for bone height, while the mean for bone width was 2.966 mm (95% confidence interval, 2.334770 to 3.598300 mm).

CONCLUSIONS: Socket preservation procedures are effective in limiting horizontal and vertical ridge alterations in postextraction sites. The meta-analysis indicates that the use of barrier membranes alone might improve normal wound healing in extraction sites.

Soft tissue healing in alveolar socket preservation technique: histologic evaluations.

Pellegrini G, Rasperini G, Obot G, Farronato D, Dellavia C.
Int J Periodontics Restorative Dent. 2014 Jul-Aug;34(4):531-9. doi: 10.11607/prd.1857.

After tooth extraction, 14 alveolar sockets were grafted with porous bovine bone mineral particles and covered with non-cross-linked collagen membrane (test group), and 14 alveolar sockets were left uncovered. At 5 and 12 weeks, microvascular density (MVD), collagen content, and amount of lymphocytes (Lym) T and B were analyzed in soft tissue. At 5 weeks, MVD was significantly lower and Lym T was significantly higher in tests than in controls ($P < .05$). At 12 weeks no differences were found. Placement of resorbable membrane seems to induce an initial and transient modification of the normal wound healing process of the soft tissue.

Soft tissue contour changes at immediate implants: a randomized controlled clinical study.

Cardaropoli D, Gaveglio L, Gherlone E, Cardaropoli G.
Int J Periodontics Restorative Dent. 2014 Sep-Oct;34(5):631-7. doi: 10.11607/prd.1845.

In 52 patients, single anterior teeth were extracted and replaced by immediate implants. The peri-implant gap was left either untreated (control) or was grafted and covered with a membrane (test group). After 12 months the horizontal bone resorption was significantly lower in the test group (test sites: 0.69 ± 0.68 mm, 8.13%; control sites: 1.92 ± 1.02 mm, 21.62%; P = .001), and there was less reduction in ridge height (test sites: 0.58 ± 0.77 mm; control sites: 1.69 ± 1.74 mm;P = .004). Ridge preservation considerably limited the amount of horizontal and vertical soft tissue alterations when compared with implant placement alone.

Alveolar ridge preservation. A systematic review.

Horváth A1, Mardas N, Mezzomo LA, Needleman IG, Donos N.
Clin Oral Investig. 2013 Mar;17(2):341-63. doi: 10.1007/s00784-012-0758-5. Epub 2012 Jul 20.

OBJECTIVE: The objective of this paper is to examine the effect of alveolar ridge preservation (ARP) compared to unassisted socket healing.

METHODS: Systematic review with electronic and hand search was performed. Randomised controlled trials (RCT), controlled clinical trials (CCT) and prospective cohort studies were eligible.

RESULTS: Eight RCTs and six CCTs were identified. Clinical heterogeneity did not allow for meta-analysis. Average change in clinical alveolar ridge (AR) width varied between -1.0 and -3.5 ± 2.7 mm in ARP groups and between -2.5 and -4.6 ± 0.3 mm in the controls, resulting in statistically significantly smaller reduction in the ARP groups in five out of seven studies. Mean change in clinical AR height varied between +1.3 ± 2.0 and -0.7 ± 1.4 mm in the ARP groups and between -0.8 ± 1.6 and -3.6 ± 1.5 mm in the controls. Height reduction in the ARP groups was statistically significantly less in six out of eight studies. Histological analysis indicated various degrees of new bone formation in both groups. Some graft interfered with the healing. Two out of eight studies reported statistically significantly more trabecular bone formation in the

ARP group. No superiority of one technique for ARP could be identified; however, in certain cases guided bone regeneration was most effective. Statistically, significantly less augmentation at implant placement was needed in the ARP group in three out of four studies. The strength of evidence was moderate to low.

CONCLUSIONS: Post-extraction resorption of the AR might be limited, but cannot be eliminated by ARP, which at histological level does not always promote new bone formation. RCTs with unassisted socket healing and implant placement in the ARP studies are needed to support clinical decision making.

CLINICAL RELEVANCE: This systematic review reports not only on the clinical and radiographic outcomes, but also evaluates the histological appearance of the socket, along with site specific factors, patient-reported outcomes, feasibility of implant placement and strength of evidence, which will facilitate the decision making process in the clinical practice.

Soft tissue contour changes at immediate postextraction single-tooth implants with immediate restoration: a 12-month prospective cohort study.

Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L.
Int J Periodontics Restorative Dent. 2015 Mar-Apr;35(2):191-8. doi: 10.11607/prd.2326.

In the maxillary arch from premolar to premolar, 26 single dental implants were inserted in fresh extraction sockets and immediately provisionalized. The bone-to-implant gap was grafted with a bovine bone mineral. After 3 months, definitive ceramic crowns were placed. At baseline and after 1 year, the soft tissue horizontal width, mesiodistal papillary level, midfacial gingival level, and pink esthetic score were evaluated. No statistical differences were found between baseline and 1 year for all parameters. Immediate single-tooth implants, with immediate restoration, are capable of maintaining the soft tissue contour and esthetics compared to the pretreatment status.

Postextraction socket preservation using epithelial connective tissue graft vs porcine collagen matrix. 1-year results of a randomised controlled trial.

Meloni SM, Tallarico M, Lolli FM, Deledda A, Pisano M, Jovanovic SA.
Eur J Oral Implantol. 2015 Spring;8(1):39-48.

PURPOSE: To compare epithelial connective tissue graft vs porcine collagen matrix for sealing postextraction sockets grafted with deproteinised bovine bone.

MATERIALS AND METHODS: A total of 30 patients, who needed a maxillary tooth to be extracted between their premolars and required a delayed, fixed, single implant-supported restoration, had their teeth atraumatically extracted and their sockets grafted with deproteinised bovine bone. Patients were randomised according to a parallel group design into two arms: socket sealing with epithelial connective tissue graft (group A) vs porcine collagen matrix (group B). Outcome measures were: implant success and survival rate, complications, horizontal and vertical alveolar bone dimensional changes measured on Cone Beam computed tomography (CBCT) scans at three levels localised 1, 3, and 5 mm below the most coronal aspect of the bone crest (levels A, B, and C); and between the palatal and buccal wall peaks (level D); and peri-implant marginal bone level changes measured on periapical radiographs.

RESULTS: 15 patients were randomised to group A and 15 to group B. No patients dropped out. No failed implants or complications were reported 1 year after implant placement. Five months after tooth extraction there were no statistically significant differences between the 2 groups for both horizontal and vertical alveolar bone dimensional changes. At level A the difference was 0.13 ± 0.18; 95% CI 0.04 to 0.26 mm (P = 0.34), at level B it was 0.08 ± 0.23; 95% CI -0.14 to 0.14 (P = 0.61), at level C it was 0.05 ± 0.25; 95% CI -0.01 to 0.31 mm (P = 0.55) and at level D it was 0.13 ± 0.27; 95% CI -0.02 to 0.32 mm (P = 0.67). One year after implant placement there were no statistically significant differences between the 2 groups for peri-implant marginal bone level changes (difference: 0.07 ± 0.11 mm; 95% CI -0.02 to 0.16; P = 0.41).

CONCLUSIONS: When teeth extractions were performed atraumatically and sockets were filled with deproteinised bovine bone, sealing the socket with a porcine collagen matrix or a epithelial connective

tissue graft showed similar outcomes. The use of porcine collagen matrix allowed simplification of treatment because no palatal donor site was involved.

Clinical and histologic outcomes of socket grafting after flapless tooth extraction: a systematic review of randomized controlled clinical trials.

Jambhekar S1, Kernen F2, Bidra AS3.
J Prosthet Dent. 2015 May;113(5):371-82. doi: 10.1016/j.prosdent.2014.12.009. Epub 2015 Mar 4.

STATEMENT OF PROBLEM: Several biomaterials and techniques have been reported for socket grafting and alveolar ridge preservation. However, the evidence for clinical and histologic outcomes for socket grafting with different types of materials in flapless extraction is not clear.

PURPOSE: The purpose of this systematic review was to analyze the outcomes of a socket grafting procedure performed with flapless extraction of teeth in order to determine which graft material results in the least loss of socket dimensions, the maximum amount of vital bone, the least remnant graft material, and the least amount of connective tissue after a minimum of 12 weeks of healing. Secondary outcomes, including the predictability of regenerating deficient buccal bone, necessity of barrier membranes, and coverage with autogenous soft tissue graft, were also evaluated.

MATERIAL AND METHODS: An electronic search for articles in the English-language literature was performed independently by multiple investigators using a systematic search process with the PubMed search engine. After applying predetermined inclusion and exclusion criteria, the final list of randomized controlled clinical trials (RCTs) for flapless extraction and socket grafting was analyzed to derive results for the various objectives of the study.

RESULTS: The initial electronic search resulted in 2898 titles. The systematic application of inclusion and exclusion criteria resulted in 32 RCTs studying 1354 sockets, which addressed the clinical and histologic outcomes of flapless extraction with socket grafting and provided dimensional and histologic information at or beyond the 12-week reentry period. From these RCTs, the mean loss of buccolingual width at the ridge crest was lowest for xenografts (1.3 mm), followed by allografts (1.63 mm), alloplasts (2.13 mm), and sockets without any socket grafting (2.79 mm). Only 3 studies reported on loss of width at 3 mm below the ridge crest. The mean loss of buccal wall height from the ridge crest was lowest for xenografts (0.57 mm) and allografts (0.58 mm), followed by alloplasts (0.77 mm) and sockets without any grafting (1.74 mm). The mean histologic outcomes at or beyond the 12-week reentry period revealed the highest vital bone content for sockets grafted with alloplasts (45.53%), followed by sockets with no graft material (41.07%), xenografts (35.72%), and allografts (29.93%). The amount of remnant graft material was highest for sockets grafted with allografts (21.75%), followed by xenografts (19.3%) and alloplasts (13.67%). The highest connective tissue content at the time of reentry was seen for sockets with no grafting (52.53%), followed by allografts (51.03%), xenografts (44.42%), and alloplast (38.39%). Data for new and emerging biomaterials such as cell therapy and tissue regenerative materials were not amenable to calculations because of biomaterial heterogeneity and small sample sizes.

CONCLUSIONS: After flapless extraction of teeth, and using a minimum healing period of 12 weeks as a temporal measure, xenografts and allografts resulted in the least loss of socket dimensions compared to alloplasts or sockets with no grafting. Histologic outcomes after a minimum of 12 weeks of healing showed that sockets grafted with alloplasts had the maximum amount of vital bone and the least amount of remnant graft material and remnant connective tissue. There is a limited but emerging body of evidence for the predictable regeneration of deficient buccal bone with socket grafting materials, need for barrier membranes, use of tissue engineering, and use of autogenous soft tissue grafts from the palate to cover the socket.

3. Minor Bone Augmentation

Ridge augmentation by applying bioresorbable membranes and deproteinized bovine bone mineral: a report of twelve consecutive cases.

Hämmerle CHF, Jung RE, Yaman D, Lang NP.
Clin Oral Implants Res 2008; 19(1) :19-25.

OBJECTIVE: Lateral ridge augmentations are traditionally performed using autogenous bone grafts to support membranes for guided bone regeneration (GBR). The bone-harvesting procedure, however, is accompanied by considerable patient morbidity. AIM: The aim of the present study was to test whether or not resorbable membranes and bone substitutes will lead to successful horizontal ridge augmentation allowing implant installation under standard conditions. MATERIAL AND METHODS: Twelve patients in need of implant therapy participated in this study. They revealed bone deficits in the areas intended for implant placement. Soft tissue flaps were carefully raised and blocks or particles of deproteinized bovine bone mineral (DBBM) (Bio-Oss) were placed in the defect area. A collagenous membrane (Bio-Gide) was applied to cover the DBBM and was fixed to the surrounding bone using poly-lactic acid pins. The flaps were sutured to allow for healing by primary intention. RESULTS: All sites in the 12 patients healed uneventfully. No flap dehiscences and no exposures of membranes were observed. Nine to 10 months following augmentation surgery, flaps were raised in order to visualize the outcomes of the augmentation. An integration of the DBBM particles into the newly formed bone was consistently observed. Merely on the surface of the new bone, some pieces of the grafting material were only partly integrated into bone. However, these were not encapsulated by connective tissue but rather anchored into the newly regenerated bone. In all of the cases, but one, the bone volume following regeneration was adequate to place implants in a prosthetically ideal position and according to the standard protocol with complete bone coverage of the surface intended for osseointegration. Before the regenerative procedure, the average crestal bone width was 3.2 mm and to 6.9 mm at the time of implant placement. This difference was statistically significant (P<0.05, Wilcoxon's matched pairs signed-rank test). CONCLUSION: After a healing period of 9-10 months, the combination of DBBM and a collagen membrane is an effective treatment option for horizontal bone augmentation before implant placement.

Horizontal ridge augmentation using autogenous block grafts and the guided bone regeneration technique with collagen membranes: a clinical study with 42 patients.

von Arx T, Buser D.
Clin Oral Implants Res 2006; 17(4): 359-366

To analyze the clinical outcome of horizontal ridge augmentation using autogenous block grafts covered with anorganic bovine bone mineral (ABBM) and a bioabsorbable collagen membrane. In 42 patients with severe horizontal bone atrophy, a staged approach was chosen for implant placement following horizontal ridge augmentation. A block graft was harvested from the symphysis or retromolar area, and secured to the recipient site with fixation screws. The width of the ridge was measured before and after horizontal ridge augmentation. The block graft was subsequently covered with ABBM and a collagen membrane. Following a tension-free primary wound closure and a mean healing period of 5.8 months, the sites were re-entered, and the crest width was re-assessed prior to implant placement. Fifty-eight sites were augmented, including 41 sites located in the anterior maxilla. The mean initial crest width measured 3.06 mm. At re-entry, the mean width of the ridge was 7.66 mm, with a calculated mean gain of horizontal bone thickness of 4.6 mm (range 2-7 mm). Only minor surface resorption of 0.36 mm was observed from augmentation to re-entry. The presented technique of ridge augmentation using autogenous block grafts with ABBM filler and collagen membrane coverage demonstrated successful horizontal ridge augmentation with high predictability. The surgical method has been further simplified by using a resorbable membrane. The hydrophilic membrane was easy to apply, and did not cause wound infection in the rare instance of membrane exposure. To cite this article: von Arx T, Buser D. Horizontal ridge augmentation using autogenous block grafts and the guided bone regeneration technique with collagen membranes: a clinical study with 42 patients.

Vertical ridge augmentation of the atrophic posterior mandible with interpositional bloc grafts: bone from the iliac crest vs. bovine anorganic bone. Clinical and histological results up to one year after loading from a randomized-controlled clinical trial.

Felice, P., C. Marchetti, et al.
Clin Oral Implants Res 2009 Dec;20(12):1386-93

Abstract Objectives: To compare two different techniques for vertical bone augmentation of the posterior mandible: bone blocs from the iliac crest vs. anorganic bovine bone blocs used as inlays. Materials and methods: Ten partially edentulous patients having 5-7 mm of residual crestal height above the mandibular canal had their posterior mandibles randomly allocated to both interventions. After 4 months implants were inserted, and after 4 months, provisional prostheses were placed. Definitive prostheses were delivered after 4 months. Histomorphometry of samples trephined at implant placement, prosthesis and implant failures, any complication after loading and peri-implant marginal bone-level changes were assessed by masked assessors. All patients were followed up to 1 year after loading. Results: Four months after bone augmentation, there was statistically significant more residual graft (between 10% and 13%) in the Bio-Oss group. There were no statistically significant differences in failures and complications. Two implants could not be placed in one patient augmented with autogenous bone because the graft failed whereas one implant and its prosthesis of the Bio-Oss group failed after loading. After implant loading only one complication (peri-implantitis) occurred at one implant of the autogenous bone group. In 16 months (from implant placement to 1 year after loading), both groups lost statistically significant amounts of peri-implant marginal bone: 0.82 mm in the autogenous bone group and 0.59 mm in the Bio-Oss group; however, there were no statistically significant differences between the groups. Conclusions: Both procedures achieved good results, but the use of bovine blocs was less invasive and may be preferable than harvesting bone from the iliac crest. To cite this article: Felice P, Marchetti C, Iezzi G, Piattelli A, Worthington H, Pellegrino G, Esposito M. Vertical ridge augmentation of the atrophic posterior mandible with interpositional bloc grafts: bone from the iliac crest vs. bovine anorganic bone. Clinical and histological results up to one year after loading from a randomized-controlled clinical trial.

Vertical ridge augmentation using xenogenous bone blocks: a histomorphometric study in dogs

Rothamel, D., F. Schwarz, et al.
Int J Oral Maxillofac Implants 2009; 24(2): 243-50.

PURPOSE: Because vertical ridge augmentation with autogenous bone blocks carries with it a risk of graft resorption and donor site morbidity, the aim of the present study was to compare histologically the healing following vertical ridge augmentation using screwable, xenogenous deproteinized blocks or autologous bone blocks in dogs. MATERIALS AND METHODS: Standardized vertical mandibular defects were surgically created in edentulous ridges of six foxhounds. Two bone blocks (6 x 10 x 15 mm) were inserted on each mandibular side and fixed with both a titanium implant and an osteosynthetic screw. Three different therapies were tested: (1) xenogenous block alone; (2) xenogenous block, covered with a chemically cross-linked collagen membrane; and (3) autologous blocks, harvested during defect preparation. After 3 months of submerged healing, the miniscrews were removed and replaced by dental implants. Following an additional healing period of 3 months, the animals were sacrificed, and dissected blocks were prepared for histomorphometric analysis. RESULTS: During the primary healing period, three of 12 hemimandibles (six blocks) had to be removed because of severe inflammatory reactions (two xenogenous block sites with collagen membrane, one autologous block site). In general, histologic analysis revealed that xenogenous blocks, used alone or combined with a collagen membrane, exhibited osteoconductive properties on a level equivalent to that of autologous blocks, resulting in means of 50% to 60% of ossification of the blocks. Some parts of the xenograft were encased in soft tissue, partly surrounded by multinuclear giant cells. However, all groups showed obvious signs of bone/graft resorption. CONCLUSIONS: Within the limits of the present study, it was concluded that the examined screwable xenogenous bone block might be a useful scaffold for ridge augmentation procedures. However, the combination of xenogenous blocks with a cross-linked collagen membrane did not appear to improve outcomes.

Vertical ridge augmentation around implants by e-PTFE titanium-reinforced membrane and bovine bone matrix: a 24- to 54-month study of 10 consecutive cases.

Canullo, L. and V. A. Malagnino
Int J Oral Maxillofac Implants 2008; 23(5): 858-66.

PURPOSE: The objective of the present study was to clinically and histologically evaluate the effectiveness of deproteinized bovine bone as the augmentation material in vertical ridge augmentation of the inserted implants. MATERIALS AND METHODS: This retrospective study was performed on 10 vertically augmented ridges in which 24 dental implants were inserted. Deproteinized bovine bone (Bio-Oss) was used as the only

augmentation material and was covered with a titanium-reinforced expanded polytetrafluoroethylene (e-PTFE) membrane (Gore-Tex). For 3 augmented areas, bone samples were retrieved for histologic and histomorphometric examination. RESULTS: Clinical evaluations showed bone defects around the implants of 2 to 9 mm (average -5.1 mm; SD = 2.1). Bone height gain at 6 to 8 months after augmentation was 3 to 9 mm (average 5.3 mm; SD = 1.7). Differences between pre- and postaugmentation were statistically significant, for a mean value of > 4 mm (P < .005). The obtained bone biopsy specimens showed significant new bone formation and remodeling of the deproteinized bovine bone material. The radiographic data and the clinical stability showed that all implants were successfully osseointegrated. The radiographic and clinical follow-up indicated that the generated bone crest levels were stable. CONCLUSION: This clinical study suggests that vertical ridge augmentation with an e-PTFE membrane and deproteinized bovine bone is predictable and can lead to long-term success.

Vertical ridge augmentation with autogenous bone grafts: resorbable barriers supported by osteosynthesis plates versus titanium-reinforced barriers. A preliminary report of a blinded, randomized controlled clinical trial.

Merli M, Migani M, Esposito M.
J Oral Maxillofac Implants 2007; 22(3): 373-382.

PURPOSE: To compare the efficacy and complications of 2 different techniques for vertical bone augmentation at implant placement: particulated autogenous bone grafts covered either by resorbable collagen barriers supported by osteosynthesis plates (test) or by nonresorbable titanium-reinforced e-polytetrafluoroethylene (e-PTFE) barrier (control). MATERIALS AND METHODS: Twenty-two partially edentulous patients requiring vertical bone augmentation were randomly allocated to 2 treatment groups of 11 patients each. Early implant failures, the amount of vertically regenerated bone measured intrasurgically, and biologic complications were recorded by an independent assessor blinded to the group allocation. The implant site requiring the most vertical bone regeneration was selected in each patient for the bone gain assessment. Patients were followed from implant insertion with simultaneous augmentation procedure to insertion of the provisional restoration. Paired and independent t tests and Fisher exact tests were conducted to compare means and proportions at the .05 level of significance. RESULTS: No patient dropped out or was excluded. Both procedures obtained significant bone gain and achieved the desired results, 2.2 mm (SD 1.5; P < .001) on average for resorbable barriers and 2.5 mm (SD 1.1) for nonresorbable barriers (P < .001). There was no statistically significant difference in bone gain between the 2 procedures (P = .58). Complications occurred in 40% of the patients. There was no difference in occurrence of complications between the procedures (P > .99). Three major complications occurred, 2 in the resorbable group and 1 in the nonresorbable group, which determined the complete failure of the augmentation procedure. CONCLUSIONS: Both techniques were effective in augmenting bone; however, both were associated with complications. Clinicians and patients must carefully weigh risks and benefits when considering the use of vertical guided bone regeneration.

Vertical ridge augmentation by expanded-polytetrafluoroethylene membrane and a combination of intraoral autogenous bone graft and deproteinized anorganic bovine bone (Bio Oss).

Simion M, Fontana F, Raspereini G, Maiorana C.
Clin Oral Implants Res 2007; 18(5): 620-629.

OBJECTIVE: To evaluate, from a histological and histomorphometrical perspective, the efficacy of a 1 : 1 mixture of deproteinized bovine bone mineral (DBBM) and autogenous bone graft associated with an expanded-polytetrafluoroethylene (e-PTFE) membrane for vertical ridge augmentation in the human. MATERIAL AND METHODS: Seven patients with 10 surgical sites requiring vertical ridge augmentation of partially edentulous lower jaws were included in the study. The vertical augmentation procedure was performed combining a titanium-reinforced e-PTFE Gore-Tex membrane with a composite graft consisting of a 1 : 1 ratio of DBBM (Bio-Oss) and autogenous bone. Twenty-seven Branemark implants have been inserted. Eleven biopsies from the regenerated area were analyzed histologically and histomorphometrically. RESULTS: The healing period was uneventful in nine surgical sites. In one site the membrane showed an exposure after 3 months. At the abutment connection, all implants appeared stable and submerged by a hard regenerated tissue clinically similar to bone. The histological analysis showed new bone formation and ongoing remodelling of the autogenous bone and the DBBM particles. CONCLUSIONS:

The findings from the present clinical and histological study support the use of a 1 : 1 combination of DBBM and autogenous bone chips for vertical ridge augmentation by means of guided bone regeneration techniques. The regenerated bone may lead to proper osseointegration of a dental implant inserted at the time of the regenerative procedure or after a healing period of at least 6 months. DBBM undergoes very slow resorption and substitution with new bone. Furthermore, long-term clinical studies are needed to confirm the positive effect of DBBM in enhancing the lasting stability of the vertically augmented bone

Vertical Ridge Augmentation Around Implants Using e-PTFE Titanium-Reinforced Membrane and Deproteinized Bovine Bone Mineral (Bio-Oss): A Case Report.

Canullo L, Trisi P, Simion M.
Int J Periodontics Restorative Dent, 2006; 26(4): 355-361

The aim of this case report was to evaluate the ability of Bio-Oss used together with an expanded polytetrafluoroethylene, titanium-reinforced membrane to restore a vertical bone defect. Bio-Oss served as a filler material. After the membrane was removed, screw-type implants were placed. During this phase, cylindric bone samples were retrieved from the augmented area for histologic examination. The biopsy samples were composed of low-density trabecular bone with numerous interspersed graft particles. Clinical and histologic results demonstrated that this surgical technique could be a successful and predictable procedure for rebuilding a resorbed ridge to place implants.

Vertical ridge augmentation using xenogenic material supported by a configured titanium mesh: clinicohistopathologic and histochemical study.

Artzi Z, Dayan D, Alpern Y, Nemcovsky CE.
Int J Oral Maxillofac Implants 2003; 18(3): 440-446.

PURPOSE: The aim of this study was to evaluate the capability of a configured titanium mesh (CTM) to serve as a mechanical and biologic device for restoring a vertically defected/resorbed alveolar ridge. MATERIALS AND METHODS: The study comprised 10 severely resorbed sites in 10 patients. Pre- and post-operative ridge measurements were taken with reference to the neighboring teeth and supporting screw head base of the CTM. Bio-Oss® served as the augmentation filler material. The metal mesh was removed after 9 months. Subsequently, root-form, screw-type implants were placed. During the implant placement phase, cylindric bone samples were retrieved from the augmented area for histopathologic and histochemical examination. RESULTS: Upon soft tissue reflection and before augmentation, defect height, as recorded by a periodontal probe along the main threads exposed on the support screw, was between 5 and 8 mm (average 6.4 mm; SD +/- 1.17). At 9 months after augmentation, during the implant placement phase, the defect height was between 0 and 2 mm (average 1.2 mm; SD +/- 0.63). Differences were statistically significant ($P < .001$). Bone height gain was between 4 and 6 mm (average 5.2 mm, SD +/- 0.79), which gave an average bone fill of 81.2% (SD +/- 7.98). Polarizing microscopic examination of sections stained with Picrosirius red showed a gradual increase in new lamellar bone from coronal to apical cuts, reaching the highest area percentage in the deep apical zone. DISCUSSION: At 9 months postaugmentation using the CTM surgical technique, the quality and quantity of the newly established hard tissue appeared to be different in the coronal versus apical areas of the restored alveolar ridge. CONCLUSION: Although at 9 months postoperatively, the augmented alveolar ridge had different bone content, clinicohistochemical results demonstrated that this surgical technique could be a successful and predictable procedure for rebuilding a resorbed/defected ridge to accommodate endosseous implants.

Vertical ridge augmentation using xenogenous bone blocks: a comparison between the flap and tunneling procedures.

Xuan F1, Lee CU1, Son JS1, Fang Y1, Jeong SM2, Choi BH3.
J Oral Maxillofac Surg. 2014 Sep;72(9):1660-70. doi: 10.1016/j.joms.2014.04.003. Epub 2014 Apr 13.

PURPOSE: Previous studies have shown that the subperiosteal tunneling procedure in vertical ridge augmentation accelerates healing after grafting and prevents graft exposure, with minor postoperative complications. It is conceivable that new bone formation would be greater with the tunneling procedure than with the flap procedure, because the former is minimally invasive. This hypothesis was tested in this

study by comparing new bone formation between the flap and tunneling procedures after vertical ridge augmentation using xenogenous bone blocks in a canine mandible model.

MATERIALS AND METHODS: Two Bio-Oss blocks were placed on the edentulous ridge in each side of the mandibles of 6 mongrel dogs. The blocks in each side were randomly assigned to grafting with a flap procedure (flap group) or grafting with a tunneling procedure (tunneling group).

RESULTS: The mean percentage of newly formed bone within the block was 15.3 ± 6.6% in the flap group and 46.6 ± 23.4% in the tunneling group.

CONCLUSION: Based on data presented in this study, when a tunneling procedure is used to place xenogenous bone blocks for vertical ridge augmentation, bone formation in the graft sites is significantly greater than when a flap procedure is used.

Clinical and radiographic comparison of implants in regenerated or native bone: 5-year results.

Benic, G. I., R. E. Jung, et al.
Clin Oral Implants Res 2009 May;20(5):507-13

Abstract Purpose: The aim of this study was to test whether or not implants associated with bone regeneration show the same survival and success rates as implants placed in native bone in patients requiring both forms of therapy. Material and methods: Thirty-four patients (median age of 60.3 years, range 18-77.7 years) had been treated 5 years before the follow-up examination. Machined screw-type implants were inserted following one of two surgical procedures: (1) simultaneously with a guided bone regeneration (GBR) procedure, which involved grafting with xenogenic bone substitute material, autogenous bone or a mixture of the two and defect covering with a bio-absorbable collagen membrane (test) and (2) standard implantation procedure without bone regeneration (control). For data recording, one test and one control implant from each patient were assessed. Examination included measurements of plaque control record (PCR), probing pocket depth (PPD), bleeding on probing (BOP), width of keratinized mucosa (KM), frequency of situations with supra-mucosal location of the crown margin, implant survival assessment and radiographic examination. Radiographs were digitized to assess the marginal bone level (MBL). Differences between groups were tested using the one-sample t-test. The estimation of survival rate was based on Kaplan-Meier analysis. Results: The follow-up period of the 34 GBR and 34 control implants ranged from 49 to 70 months (median time 57 months). Cumulative survival rates reached 100% for the GBR group and 94.1% for the control group without statistical significance. No statistically significant differences for clinical and radiographic parameters were found between the two groups regarding PCR, BOP, PPD, KM and MBL. Conclusion: The present study showed that, clinically, implants placed with concomitant bone regeneration did not performed differently from implants placed into native bone with respect to implant survival, marginal bone height and peri-implant soft tissue parameters.

Reduction of autogenous bone graft resorption by means of Bio-Oss coverage: a prospective study

Maiorana C, Beretta M, Salina S, Santoro F.
Int J Periodontics Restorative Dent 2005; 25: 19-25.

Bone grafting may be required prior to implant placement, at the time of implant placement, or subsequent to it. The aim of this study was to compare the healing of onlay block grafts when deproteinized bovine bone coverage was used with the healing of the grafts without such coverage. The purpose was a clinical evaluation of deproteinized bovine bone's ability to reduce grafted bone resorption. The results indicated that bovine bone can be placed over grafted areas, taking advantage of its osteoconductive properties and compensating for the natural bone resorption caused by remodeling.

Alveolar Ridge Augmentation with Bio-Oss: A Histologic Study in Humans

N. Zitzmann, P. Schärer, C. Marinello, P. Schüpbach, T. Berglundh
Int J Periodontics Restorative Dent 2001;21: 288-95.

The aim of the present study was to investigate the healing of alveolar ridge defects augmented with cancellous bovine bone mineral. In six partially edentulous patients, bone augmentation was necessary prior to implant placement because of severe alveolar ridge resorption. The defect sites, all located in the maxilla, were filled with Bio-Oss and covered with the resorbable collagen membrane Bio-Gide. Biopsies were obtained from the defect sites 6 to 7 months following grafting and were processed for ground sectioning. The histologic analysis revealed that the Bio-Oss particles occupied 31% of the total biopsy area. An intimate contact between woven bone and Bio-Oss was detected along 37% of the particle surfaces A mixed type of bone was found; it contained woven bone and parallel-fibered bone, which demonstrates features of remodeling activity. Signs of resorption of the grafting material were observed in the histologic sections, which indicates that the material takes part in the remodeling process. It is suggested that Bio-Oss may be a very suitable material for staged localized ridge augmentation in humans.

Long-term stability of contour augmentation in the esthetic zone: histologic and histomorphometric evaluation of 12 human biopsies 14 to 80 months after augmentation.

Jensen SS1, Bosshardt DD, Gruber R, Buser D.
J Periodontol. 2014 Nov;85(11):1549-56. doi: 10.1902/jop.2014.140182. Epub 2014 Jul 10.

BACKGROUND: Contour augmentation around early-placed implants (Type 2 placement) using autogenous bone chips combined with deproteinized bovine bone mineral (DBBM) and a collagen barrier membrane has been documented to predictably provide esthetically satisfactory clinical outcomes. In addition, recent data from cone beam computed tomography studies have shown the augmented volume to be stable long-term. However, no human histologic data are available to document the tissue reactions to this bone augmentation procedure.
METHODS: Over an 8-year period, 12 biopsies were harvested 14 to 80 months after implant placement with simultaneous contour augmentation in 10 patients. The biopsies were subjected to histologic and histomorphometric analysis.
RESULTS: The biopsies consisted of 32.0% ± 9.6% DBBM particles and 40.6% ± 14.6% mature bone. 70.3% ± 14.5% of the DBBM particle surfaces were covered with bone. On the remaining surface, multinucleated giant cells with varying intensity of tartrate-resistant acid phosphatase staining were regularly present. No signs of inflammation were visible, and no tendency toward a decreasing volume fraction of DBBM over time was observed.
CONCLUSIONS: The present study confirms previous findings that osseointegrated DBBM particles do not tend to undergo substitution over time. This low substitution rate may be the reason behind the clinically and radiographically documented long-term stability of contour augmentation using a combination of autogenous bone chips, DBBM particles, and a collagen membrane.

Long-term stability of contour augmentation with early implant placement following single tooth extraction in the esthetic zone: a prospective, cross-sectional study in 41 patients with a 5- to 9-year follow-up.

Buser D1, Chappuis V, Bornstein MM, Wittneben JG, Frei M, Belser UC.
J Periodontol. 2013 Nov;84(11):1517-27. doi: 10.1902/jop.2013.120635. Epub 2013 Jan 24.

BACKGROUND: Early implant placement with simultaneous contour augmentation is documented with short- and medium-term studies. The long-term stability of contour augmentation is uncertain.
METHODS: In this prospective, cross-sectional study, 41 patients with an implant-borne single crown were examined twice, in 2006 and 2010. Clinical, radiologic, and esthetic parameters were assessed at both examinations. In addition, a cone beam computed tomographic (CBCT) image was obtained during the second examination to assess the dimensions of the facial bone wall.
RESULTS: All 41 implants demonstrated ankylotic stability without signs of peri-implant infection at both examinations. The clinical parameters remained stable over time. Satisfactory esthetic outcomes were noted, as assessed by the pink and white esthetic score (PES/WES) indices. Overall, the PES scores were slightly higher than the WES scores. None of the implants developed mucosal recession over time, as confirmed by values of the distance between implant shoulder and mucosal margin and cast measurements. The periapical radiographs yielded stable peri-implant bone levels, with a mean distance between implant shoulder and first visible bone-implant contact value of 2.18 mm. The CBCT analysis demonstrated a mean

thickness of the facial bone wall ≈2.2 mm. In two implants (4.9%) no facial bone wall was detectable radiographically.
CONCLUSIONS: This prospective cross-sectional study demonstrates stable peri-implant hard and soft tissues for all 41 implants examined and satisfactory esthetic outcomes overall. The follow-up of 5 to 9 years confirmed again that the risk for mucosal recession is low with early implant placement. In addition, contour augmentation with guided bone regeneration was able to establish and maintain a facial bone wall in 95% of patients.

Bone dimensions in the posterior mandible: a retrospective radiographic study using cone beam computed tomography. Part 2--analysis of edentulous sites.

Braut V, Bornstein MM, Kuchler U, Buser D.
Int J Periodontics Restorative Dent. 2014 Sep-Oct;34(5):639-47. doi: 10.11607/prd.1895.

A precise radiographic evaluation of the local bone dimensions and morphology is important for preoperative planning of implant placement. The purpose of this retrospective study was to analyze dimensions and morphology of edentulous sites in the posterior mandible using cone beam computed tomography (CBCT) images. This retrospective radiographic study measured the bone width (BW) of the mandible at three locations on CBCT scans for premolars (PM1, PM2) and molars (M1, M2): at 1 mm and 4 mm below the most cranial point of the alveolar crest (BW1, BW2) and at the superior border of the mandibular canal (BW3). Furthermore, the height (H) of the alveolar process (distance between the measuring points BW1 and BW3), as well as the presence of lingual undercuts, were analyzed. A total of 56 CBCTs met the inclusion criteria, resulting in a sample size of 127 cross sections. There was a statistically significant increase from PM1 to M2 for the BW2 ($P < .001$), which was not present for BW1 and BW3 values. For the height of the alveolar process, the values exhibited a decrease from PM1 to M2 sites. Sex was a statistically significant parameter for H ($P = .001$) and for BW1 ($P = .03$). Age was not a statistically significant parameter for bone width (BW1: $P = .37$; BW2: $P = .31$; BW3: $P = .51$) or for the height of the alveolar process ($P = .41$) in the posterior mandible. Overall, 73 (57.5%) edentulous sites were evaluated to be without visible lingual undercuts; 13 (10.2%) sites exhibited lingual undercuts classified as influential for implant placement. Precise evaluation of the alveolar crest by cross-sectional imaging is of great value to analyze vertical and buccolingual bone dimensions in different locations in the posterior mandible. In addition, CBCTs are valuable to diagnosing the presence of and potential problems caused by lingual undercuts prior to implant placement.

[Clinical and radiological study on tissue regeneration after alveolar bone augmentation with various osteoplastic materials and membranes].

[Article in Russian]
Mikhalovski AA, Kulakov AA, Korolev VM, Vinnichenko OIu.
Stomatologiia (Mosk). 2014;93(4):37-40

The aim of the study was to compare the efficiency of alveolar bone augmentation using a variety of osteoplastic materials and collagen membrane and healing under a clot. The study included patients undergoing the extraction of symmetric teeth. After extraction one of the sockets were filled with osteoplastic materials while symmetrically located socket with no bone grafting served as a control. In group 1 augmentation was performed using Bio-Oss Collagen Bio-Gide membrane, in group 2 - Osteodent-M and Collost membranes, in group 3 - BIOPLAST-dent and BIOPLAST-dent-MK membranes. Clinical and radiological evaluation revealed positive impact of bioplastic materials on the bone tissue healing and recovery rates. The best results showed Bio-Oss Collagen with barrier bioresorbable membrane Bio-Gide allowing the creation of the most favorable conditions for delayed implantation.

4. Sinus Floor Augmentation

Guided bone regeneration using collagen membranes for sinus augmentation

Li X, Chen SL, Zhu SX, Zha GQ
Br J Oral Maxillofac Surg 2012;50(1):69-73.

We investigated the effect of guided bony regeneration using collagen membranes for sinus augmentation in the first maxillary molars of 18 adult female beagle dogs. The teeth were extracted bilaterally and the sinus floors were lifted with simultaneous implantation. The grafted material composed of a combination of autografts and Bio-oss in a 2:1 ratio. On the experimental side in each dog, collagen membrane was folded at the lateral osteotomy window, at the apex of the implants, and at a certain part of the palatal bone. On the opposite (control) side, the collagen membrane covered the osteotomy window. Six animals were killed at each of 4, 12, and 24 weeks postoperatively. Gross observation, biomechanical testing, and histological examinations were made. On the experimental side, grafted materials showed no obvious resorption or subsidence, and a new bone had formed at the apex of the implants. On the control side, the grafted materials had been shifted and absorbed. Histological examination showed increased formation of a new bone in the experimental group, which matured over time. At 4 weeks, inflammatory cells were present in the control group, which showed less maturation of the new bone. The pull-out force increased with time and, at week 24, there was a significant difference in pull-out force between the two groups ($p<0.01$). Guided bony regeneration with the enfolded coverage of membrane can effectively reduce resorption of grafted bone on the apical surface of implants and stimulate formation of the new bone in sinus augmentation.

Influence of space-filling materials in subantral bone augmentation: blood clot vs. autogenous bone chips vs. bovine hydroxyapatite

Lambert F, Léonard A, Drion P, Sourice S, Layrolle P, Rompen E.
Clin Oral Implants Res 2011;22(5):538-545.

AIM: The first objective of the present study was to compare the short- and long-term 3D volume stability of sub-sinusal bone regeneration in rabbits using different space fillers. The second objective was to assess qualitatively and quantitatively the early bone formation process and long-term behavior of the regenerated bone. MATERIALS AND METHODS: Fifteen rabbits underwent a double sinus lift procedure using: blood clot (Clot), autogenous bone chips (Auto) and bovine hydroxyapatite (BHA). Animals were euthanized at 1 week, 5 weeks and 6 months. Samples were subjected to X-ray microtomography and histology. Variations in the volume of bone augmentations were calculated at different time points. Qualitative analysis was performed using 7 mum sections and quantitative histomorphometric analyses were carried out using scanning electron microscopy. RESULTS: From baseline (100%) to 5 weeks, the augmented volumes declined to 17.3% (Clot), 57.6% (Auto) and 90.6% (BHA). After 6 months, only 19.4% (Clot) and 31.4% (Auto) of initial volumes were found, while it remained more stable in the BHA group (84%). At 1 week, an initial osteogenesis process could be observed in the three groups along the bone walls. At 5 weeks, despite a significant decline in the volume, newly formed bone density was higher with Clot and Auto than with BHA. At 6 months, bone densities were statistically similar in the three groups. However, after 6 months, the surface invaded by newly formed bone (regenerated area) was significantly higher when BHA was used as space filler. In the BHA group, the biomaterial area slightly decreased from 42.7% (1 week) to 40% (5 weeks) and 34.9% (6 months) and the density of the composite regenerated tissue (bone+BHA) reached >50% at 6 months. CONCLUSIONS AND CLINICAL IMPLICATIONS: The three space fillers allowed bone formation to occur. Nevertheless, augmented volumes declined in the Clot and Auto groups, while they remained stable with BHA. A slowly resorbable biomaterial might be suitable in sub-sinusal bone augmentation for preventing the re-expansion process and for augmenting the density of the regenerated tissues.

A prospective study of implants placed in augmented sinuses with minimal and moderate residual crestal bone: results after 1 to 5 years

Urban IA, Lozada JL.
Int J Oral Maxillofac Implants 2010;25:1203-1212

Purpose: The aims of this prospective study were to: (1) determine clinical and radiographic success and survival rates of implants placed in a staged procedure after sinus augmentation; and (2) compare the success and survival rate of implants in two patient groups with different ridge height prior to treatment (those with minimal residual crestal bone [=/< 3.5 mm] below the sinus and those with moderate residual crestal bone [> 3.5 mm]). Materials and Methods: The study used anorganic bovine bone-derived mineral and autogenous bone for the sagittal sandwich bone augmentation technique, a collagen membrane to protect the sinus window, and a staged approach for implant placement; all implants featured an anodized surface. Results: Two hundred forty-five implants were placed in 100 sinus sites (79 patients), and 244 have survived to date. The cumulative success and survival rates of all implants overall at 5 years were 96.5% (SE 2.0%) and 99.6% (SE 0.4%), respectively. The overall success and survival rates at 5 years for implants placed into minimal residual crestal bone were 94.1% (SE 3.4%) and 99.4% (SE 0.6%), respectively. For implants placed into moderate crestal bone, overall success and survival rates were both 100.0% (SE 0.0%). Conclusions: Success of implants placed after sinus augmentation appears similar to implants placed in native bone when a classical submerged implant healing time of 6 months is used. The success and survival rates and crestal bone remodeling of implants placed in minimal residual crestal bone were comparable to those of implants placed in moderate residual crestal bone.

Effect of anorganic bovine bone to autogenous cortical bone ratio upon bone remodeling patterns following maxillary sinus augmentation

Galindo-Moreno P, Moreno-Riestra I, Avila G, Padial-Molina M, Paya JA, Wang HL, O'Valle F.
Clin Oral Implants Res 2011

Introduction: Maxillary sinus augmentation is a predictable implant site development technique, although several local and systemic factors may influence outcomes. The aim of this study was to evaluate healing patterns and bone remodeling activity following the use of two different graft mixtures for maxillary sinus augmentation. Materials and methods: Patients in need of maxillary sinus augmentation were randomly assigned to two different groups. A graft mixture using a 50% autologous bone (AB) to 50% anorganic bovine bone (ABB) ratio was used in group 1, while a 20% AB to 80% ABB ratio was utilized for group 2. After a 6-month healing period, bone core biopsies were harvested for histological, histomorphometrical, and immunohistochemical analyses. Results: Twenty-eight subjects participated in this study. No statistically significant differences were found between groups in regards to vital bone and non-mineralized tissue proportions. Higher number of osteoid lines (18.05 +/- 10.06 in group 1 vs. 9.01 +/- 7.53 in group 2; P=0.023) and higher cellularity, particularly regarding the number of osteocytes (631.85 +/- 607.98 in group 1 vs. 219.08 +/- 103.26 in group 2; P=0.002), were observed in specimens from group 1. Differences in expression patterns of osteopontin and tartrate-resistant acid phosphatase were also detected between groups. Conclusion: AB to ABB ratio appears to influence bone remodeling patterns and cell content following maxillary sinus augmentation procedures. Similar proportion of vital bone was found in specimens obtained from both groups. More cellular presence was observed in samples containing higher proportions of AB.

Retrospective cohort study of the predictors of implant failure in the posterior maxilla

Conrad HJ, Jung J, Barczak M, Basu S, Seong WJ.
Int J Oral Maxillofac Implants 2011;26(1):154-162.

PURPOSE: The purpose of this study was to retrospectively analyze a cohort of patients who had implants placed in the posterior maxilla and assess and identify the predictors of implant failure. MATERIALS AND METHODS: With institutional review board approval, dental records from a population of patients who had maxillary posterior implants placed were used to create a database. Independent variables were divided into continuous (age of the patient at stage-one implant surgery [S1], time between extraction and S1, time between extraction and sinus augmentation, time between sinus augmentation and S1, time between S1 and stage-two implant surgery [S2], and the time between S2 and restoration of the implant) and categorical (gender, American Society of Anesthesiologists [ASA] status, current smoking status, implant position, implant proximity, residual crestal bone height, implant length and diameter, and sinus augmentation technique and materials). The dependent variable was implant failure, which was defined as complete removal of the implant. Simple logistic regression was used to assess the influence of each of the predictors

on implant failure (P < .05). RESULTS: The final database included 504 maxillary posterior implants with an overall survival rate of 93.2% over a mean follow-up period of 35.7 months. For the continuous variables, the age of the patient at S1 was statistically associated with implant failure (P = .028), as was the time between extraction and S1 (P = .014). For the categorical variables, ASA status (P < .001), implant proximity (P = .043), residual crestal bone height (P < .001), implant diameter (P = .050), sinus augmentation technique (P = .002), and sinus graft materials (P < .001) were statistically associated with implant failure. CONCLUSION: Within the limitations of this retrospective study, the results suggest that there are risk factors associated with maxillary posterior implant failure. Implants placed in areas with inadequate residual crestal bone height that required sinus augmentation were statistically associated with implant failure.

Sinus floor augmentation using large (1-2 mm) or small (0.25-1 mm) bovine bone mineral particles: a prospective, intra-individual controlled clinical, micro-computerized tomography and histomorphometric study.

Chackartchi T, Iezzi G, Goldstein M, Klinger A, Soskolne A, Piattelli A, Shapira L.
Clin Oral Implants Res. 2011 May;22(5):473-80.

OBJECTIVES: To compare the amount of newly formed bone after sinus floor augmentation with two different particle sizes of bovine bone mineral (BBM) using clinical, micro-computerized tomography (CT) and histological techniques.
METHODS: Bilateral sinus floor augmentations were performed in 10 patients. Six to 9 months later, bone samples were retrieved and analyzed.
RESULTS: Results: Both groups were not different in vertical bone height achieved after augmentation, post-operative complications and maximal torque for the insertion of implants. Micro-CT measurements could not detect a statistically significant difference in bone volume between the groups (with a tendency for new more bone in the small granules group). Histomorphometric analysis revealed that both granule sizes produced the same pattern of bone formation, surrounding the graft granules, and producing a shape of a network, "bridging" between the BBM particles. Multi-nucleated giant cells, probably osteoclasts, were observed directly on the BBM particle surface in both groups. The osteoclast-like cells preferred the small-size BBM particles and not the large particles both in the small-size and the large-size granules group.
CONCLUSION: Both sizes of BBM granules preformed equally and achieved the aim of the sinus floor augmentation procedure clinically and histologically.

Histological and histomorphometrical analyses of biopsies harvested 11 years after maxillary sinus floor augmentation with deproteinized bovine and autogenous bone.

A. Mordenfeld, M. Hallmann, CB Johansson, T. Albrektsson
Clin Oral Implants Res. 2010 May 24

Objective: The purpose of the present study was to histologically and histomorphometrically evaluate the long-term tissue response to deproteinized bovine bone (DPBB) particles used in association with autogenous bone and to compare particle size after 6 months and 11 years, in the same patients, in order to determine possible resorption. Material and methods: Twenty consecutive patients (14 women and six men) with a mean age of 62 years (range 48-69 years) with severe atrophy of the posterior maxilla were included in this study. Thirty maxillary sinuses with <5 mm subantral alveolar bone were augmented with a mixture of 80% DPBB and 20% autogenous bone. Eleven years (mean 11.5 years) after augmentation, biopsies were taken from the grafted areas of the 11 patients who volunteered to participate in this new surgical intervention. The following histomorphometrical measurements were performed in these specimens: total bone area in percentage, total area of the DPBB, total area of marrow space, the degree of DPBB-bone contact (percentage of the total surface length for each particle), the length of all DPBB particles and the area of all DPBB particles. The length and the area of the particles were compared with samples harvested from the same patients at 6 months (nine samples) and pristine particles from the manufacturer. Results: The biopsies consisted of 44.7+/-16.9% lamellar bone, 38+/-16.9% marrow space and 17.3+/-13.2% DPBB. The degree of DPBB to bone contact was 61.5+/-34%. There were no statistically significant differences between the length and area of the particles after 11 years compared with those measured after 6 months in the same patients or to pristine particles from the manufacturer. Conclusion: DPBB particles were found to be well integrated in lamellar bone, after sinus floor augmentation in humans, showing no significant changes in particle size after 11 years.

Optimal microvessel density from composite graft of autogenous maxillary cortical bone and anorganic bovine bone in sinus augmentation: influence of clinical variables.

Galindo-Moreno, P., Padial-Molina, M., Fernandez-Barbero, J. E., Mesa, F., Rodriguez-Martinez, D., O'Valle, F.
Clin Oral Implants Res 2010; 21(2):221-7.

OBJECTIVES: The objectives of this study were to assess the microvessel density (MVD) of intra-sinus grafts after 6 months of wound healing and to study the relationship between revascularization processes and patient clinical variables and habits. MATERIAL AND METHODS: We performed 45 maxillary sinus augmentations with different implant placements in 25 consecutive patients, obtaining bone cores of the grafted area for histological, histomorphometric and immunohistochemical study. Biopsies were also taken from pristine bone in the posterior maxilla (control). RESULTS: All implants survived at 24 months. Biopsies of sinus augmentation areas showed significantly greater remodeling activity vs. pristine bone, with significantly more osteoid lines. The morphometry study revealed 34.88+/-15.2% vital bone, 32.02+/-15.1% non-mineralized tissue and 33.08+/-25.4% remnant anorganic bovine bone particles. The number of CD34-positive vessels was 86.28+/-55.52/mm(2) in graft tissue vs. 31.52+/-13.69/mm(2) in native tissue (P=0.002, Mann-Whitney U=46). The larger amount of non-mineralized tissue in grafts was directly correlated with a higher MVD (r=0.482, P=0.0001, Pearson's test). MVD was affected by the presence of periodontitis or tobacco and alcohol consumption. CONCLUSION: The angiogenesis and revascularization obtained by this type of graft achieve adequate tissue remodeling for osseointegration and are influenced by periodontal disease and tobacco or alcohol consumption.

Ridge preservation with the use of Bio-Oss® collagen: A 6-month study in the dog.

Araújo MG, Lindhe J.
Clin. Oral Impl. Res. 2009;433-440.

Background: In previous short-term studies, it was observed that while the placement of biomaterial in alveolar sockets may promote bone formation and ridge preservation, the graft may in fact also delay healing.
Aim: The objective of the present experiment was to evaluate the more long-term effect on hard tissue formation and the amount of ridge augmentation that can occur by the placement of a xenogeneic graft in extraction sockets of dogs.
Material and methods: Five beagle dogs were used. The third mandibular premolars were hemi-sected. The distal roots were carefully removed. A graft consisting of Bio-Osss collagen was placed in one socket while the contra-lateral site was left without grafting. After 6 months of healing, the dogs were euthanized and biopsies were sampled. From each experimental site, four ground sections – two from the mesial root and two from the healed socket – were prepared, stained and examined under a microscope.
Results: The placement of Bio-Osss collagen in the fresh extraction socket served as a scaffold for tissue modeling but did not enhance new bone formation. In comparison with the non-grafted sites, the dimension of the alveolar process as well as the profile of the ridge was better preserved in Bio-Osss-grafted sites.
Conclusion: The placement of a biomaterial in an extraction socket may modify modeling and counteract marginal ridge contraction that occurs following tooth removal.

A clinical study of 406 sinus augmentations with 100% anorganic bovine bone.

Ferreira CE, Novaes AB, Haraszthy VI, Bittencourt M, Martinelli CB, Luczyszyn SM.
J Periodontol. 2009 Dec;80(12):1920-7.

BACKGROUND: The aim of the present study is to evaluate the use of anorganic bovine bone (ABB) associated with a collagen membrane (CM) for a sinus graft by means of clinical, histologic, and radiographic parameters in cases with bone availability < or =7 mm. A preliminary evaluation consisted of a clinical examination, computed tomography (CT), and a panoramic x-ray. METHODS: Ninety-two patients requiring bilateral sinus grafts and 222 requiring unilateral procedures (total: 406 sinuses) participated in

this study. A total of 1,025 implants were placed in the grafted sinuses. A total of 118 implants were placed simultaneously with the sinus graft (one stage), and 907 implants were placed in a subsequent surgery (two stages), 6 to 12 months after the graft was performed. In seven cases, a biopsy was harvested for histomorphometric analysis. Recall appointments were scheduled every 6 months, and panoramic and periapical x-rays were required every year for 3 years. RESULTS: Among 1,025 implants, 19 were lost (survival rate: 98.1%). The difference in survival rates for implants placed in native bone < or =3 mm (98.1%), >3 to < or =5 mm (98.6%), and >5 to < or =7 mm (97.0%) was not statistically significant (P = 0.3408). The survival rates for implants with rough and machined surfaces (98.6% and 97.0%, respectively) were not statistically significant (P = 0.0840). The histomorphometric analysis showed new bone formation (39.0% +/- 12%), marrow space (52.9% +/- 9.3%), and residual ABB (8% +/- 2.7%). CONCLUSION: Our results indicated that 1,025 implants placed in sinuses grafted exclusively with ABB combined with CM led to an excellent and predictable survival rate of 98.1%.

Retrospective radiographic investigation of the long-term stability of xenografts (Geistlich Bio-Oss) in the sinus.

Ruoff, H. and H. Terheyden
Z Zahnärztl Impl 2009; 25(2): 160-169.

The Bio-Oss graft proved to be very stable over a 10-year investigation period. The height reduction over the apex of the implant averaged 0.1 mm per year. Six of the 364 implants in Bio-Oss grafts were lost (two before and four after loading) during the observation period of 0 to 12 years. Therefore, the cumulative survival rate was 98.4 %. Marginal bone loss was monitored for almost six years. Crestal bone resorption in the mesial aspect averaged 0.235 mm per year with a standard error of 0.021 mm per year. In the distal aspect, the resorption rate was 0.211+/-0.018 mm per year. Since the implants were still completely osseointegrated within the follow-up period, even in the case of low preoperative bone levels, it can be concluded that the Bio-Oss graft contributed to the stabilization of the implants.

Prospective observation of 41 perforations of the Schneiderian membrane during sinus floor elevation

Becker, S. T., H. Terheyden, et al.
Clin Oral Implants Res 2008; 19(12): 1285-9.

OBJECTIVES: The aim of this study was to follow 41 intraoperative perforations of the Schneiderian membrane during sinus floor elevation and to identify potential differences from patients without perforations. MATERIAL AND METHODS: Two hundred and one sinus floor elevations were performed at the department of oral and maxillofacial surgery of the University Hospital of Schleswig-Holstein in the years 2005 and 2006. Forty-one intraoperative perforations (20.4%) were documented and treated according to the following scheme: defects smaller than 5 mm were covered with a collagen membrane. Larger defects were additionally sutured. Particulated jawbone mixed 50 : 50 with bone substitute (25 cases) and a 50 : 50 mix of particulated iliac crest bone and BioOss (six cases) mainly served as graft material in the perforation group. In 12 cases, implants were installed at the time of sinus grafting, and in 27 cases, a second operation was performed. RESULTS: Four sinus lift procedures had to be discontinued intraoperatively. Over a mean control interval of 162 days, one implant of the 93 inserted had to be replaced in the perforation group. After 1 year, the implant survival rate was 14 out of 14 in the perforation group vs. 81/92 in the control group. CONCLUSIONS: With appropriate treatment, intraoperative sinus membrane perforations did not represent an elevated risk for implant loss, infectious complications or displacement of graft material in the investigated population.

RFA Values of Implants Placed in Sinus Grafted and Nongrafted Sites after 6 and 12 Months

Degidi M, Daprile G, Piattelli A.
Clin Implant Dent Relat 2008 ; Res. Sep 9

Background: Maxillary sinus floor elevation surgery is widely used as a preimplantology method to permit implant insertion. Nevertheless, very few data are available about long-term stability of dental implants

inserted in grafted sites. Purpose: The aims of the present study were to evaluate the evolution of resonance frequency analysis (RFA) values at 6 and 12 months from the implant insertion in sinus grafted sites and nongrafted sites. Materials and Methods: In 14 patients, 80 Xive implants (Dentsply Friadent GmbH, Mannheim, Germany) were inserted. Sixty-three implants were inserted in a site previously treated with a sinus lift; 17 implants were inserted in healed or postextraction sites. For each implant diameter, length, bone density, insertion torque, and percentage of implant fixed to a nongrafted bone were recorded. RFA values at implant insertion after 6 and 12 months were recorded. Results: After 6 and 12 months, grafted sites showed higher RFA values than the control sites; after 12 months, the difference was statistically significant (.007). A statistically significant positive correlation was found between resonance frequency values and bone quality after 12 months (.05). No statistically significant correlation between RFA values and all the other variables considered was found. Conclusions: Sites treated with sinus lift can offer good long-term stability. After 6 and 12 months, the geometric characteristics of the implant are no longer important to obtain high RFA values, and the bone-implant interface seems to be determinant.

A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation

Pietursson BE, Tan WC, Zwahlen M, Lang NP.
J Clin Periodontol, 2008; 35: 216-240.

OBJECTIVES: The objectives of this systematic review were to assess the survival rate of grafts and implants placed with sinus floor elevation. MATERIAL AND METHODS: An electronic search was conducted to identify studies on sinus floor elevation, with a mean follow-up time of at least 1 year after functional loading. RESULTS: The search provided 839 titles. Full-text analysis was performed for 175 articles resulting in 48 studies that met the inclusion criteria, reporting on 12,020 implants. Meta-analysis indicated an estimated annual failure rate of 3.48% [95% confidence interval (CI): 2.48%-4.88%] translating into a 3-year implant survival of 90.1% (95% CI: 86.4%-92.8%). However, when failure rates was analyzed on the subject level, the estimated annual failure was 6.04% (95% CI: 3.87%-9.43%) translating into 16.6% (95% CI: 10.9%-24.6%) of the subjects experiencing implant loss over 3 years. CONCLUSION: The insertion of dental implants in combination with maxillary sinus floor elevation is a predictable treatment method showing high implant survival rates and low incidences of surgical complications. The best results (98.3% implant survival after 3 years) were obtained using rough surface implants with membrane coverage of the lateral window.

Impact of implant surface and grafting protocol on clinical outcomes of endosseous implants

Marchetti C, Pieri F, et al.
Int J Oral Maxillofac Implants 2007; 22(3): 399-407.

PURPOSE: The objectives of this study were to (1) evaluate the survival of implants placed in maxillary sinuses augmented with a 70:30 mixture of autogenous bone and anorganic bovine hydroxyapatite (Bio-Oss) at 1 and 5 years, (2) observe the difference in survival rate between 1-stage and 2-stage procedures, and (3) compare the survival rate of rough-surfaced implants with that of machined implants. MATERIALS AND METHODS: A total of 30 consecutively patients (48 sinuses) with Cawood and Howell Class V and VI atrophy were evaluated. Lateral osteotomy techniques were used in all cases. Implants were placed either simultaneous with grafting (1-stage procedure) or after a delay (2-stage procedure), depending on the amount of residual bone. A 70:30 mixture of autogenous bone and anorganic bovine hydroxyapatite was used as the graft material. All patients were followed up at 1 year after prosthetic loading, while a limited group of these patients was followed up to 5 years. RESULTS: In 8 patients where the residual crestal bone under the sinus floor assessed by computed tomography was at least 4.5 mm (mean, 5.3 mm), the 1-stage procedure was used for 11 sinus elevations and 32 implants. In 22 patients where the residual crestal bone was less than 4.5 mm (mean, 2.5 mm), the 2-stage procedure was used for 37 sinus elevations and 108 implants. For the 140 implants placed, the overall survival rate was 95.7% at the healing abutment surgery, and the cumulative survival rate was 94.9% at 1 and 5 years. The type of surgical technique was significantly associated with implant failure ($P < .05$); implants placed using the 1-stage procedure showed a failure rate of 12.5%, while implants placed with the 2-stage procedure had a failure rate of 2.8%. No significant difference in survival rate was observed with respect to implant surface. CONCLUSIONS: A high survival rate was achieved when sinus elevation was performed with a combination of autogenous bone and

anorganic bovine hydroxyapatite, even where a minimal amount of residual crestal bone was present. The survival rate was improved when implants were placed after a healing period.

Repair of large sinus membrane perforations using stabilized collagen barrier membranes: surgical techniques with histologic and radiographic evidence of success."

Testori T, Wallace SS, et al.
Int J Periodontics Restorative Dent 2008; 28(1): 9-17.

The most frequent intraoperative complication with sinus elevation is perforation of the schneiderian membrane. In most instances, the repair of this perforation is necessary to contain particulate grafting material and complete the procedure. New techniques are presented here for the management of large perforations of the schneiderian membrane. A bioabsorbable collagen membrane is stabilized outside the antrostomy and then folded inward to create either a new superior wall that can obliterate a large perforation or a "pouch" that can completely contain the particulate material. This can make it possible to complete a procedure that otherwise may have had to be aborted by preventing dispersion of the particulate graft within the sinus cavity. Clinical cases are shown, along with follow-up at 6 to 9 months, demonstrating histologic and/or radiographic evidence of success, continued sinus health, and superior vital bone formation. The authors have used this technique on 20 consecutive patients without experiencing any procedural failures.

Sinus elevation with alloplasts or xenogenic materials and implants: an up-to-4-year clinical and radiologic follow-up.

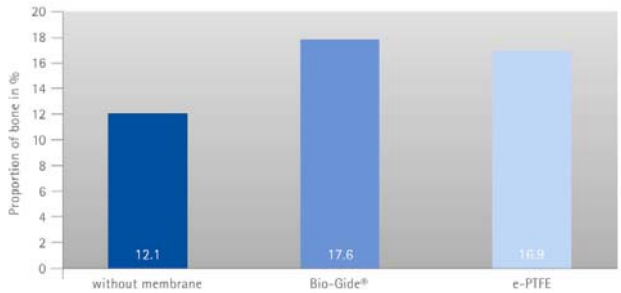
Maiorana C, Sigurta D, Miranda A, Garlini G, Santoro F.
Int J Oral Maxillofac Implants 2006; 21(3): 426-432.

PURPOSE: The clinical and radiologic results of bone substitute application in the sinus elevation procedure were evaluated for up to 4 years after a grafting procedure followed by implant placement. MATERIALS AND METHODS: Between 1997 and 2001, augmentation of the maxillary sinus floor with alloplastic or xenogenic materials was performed in 34 nonsmoking patients with generally good health. However, only 18 patients attended all of the required annual clinical and radiographic examinations and thus were included in the study. Mean follow-up after implantation was 29 months. RESULTS: At the second-stage surgery all the implants were osseointegrated, except for 1 Frialit-2, which was removed. Following prosthetic rehabilitation no implant was lost after 4 years of function, for a prosthetic success rate of 100%. The cumulative implants survival rate after 48 months was 97% (36 of 37 implants). DISCUSSION: Osseointegrated implants are a reliable treatment option for restoring the posterior maxilla, and final predictability was not influenced by their placement in augmented areas after sinus elevation with bone substitutes. CONCLUSIONS: The survival rate obtained with this study is similar to that expected for implants placed in nongrafted areas. This study showed that alloplasts and xenogenic materials are reliable for bone regeneration in the subantral cavities, as they showed very low resorption in the present study.

Sinus augmentation utilizing anorganic bovine bone (Bio-Oss) with absorbable and nonabsorbable membranes placed over the lateral window: histomorphometric and clinical analyses.

Wallace SS, Froum SJ, Cho SC, Elian N, Monteiro D, Kim BS, Tarnow DP.
Int J Periodotics Restorative Dent 2005; 25: 551-559.

The purpose of the present study, which used anorganic bovine bone (Bio-Oss) with and without autogenous bone as the augmentation material, was to compare the results of sinus elevation performed without a membrane (control) with the results of sinus elevation performed with either a short-term bioabsorbable membrane (Bio-Gide) or a nonabsorbable membrane (Gore-Tex) with regard to both vital bone formation and implant survival. Sinus lifts were performed on 51 patients (38 unilateral, 13 bilateral) with the



delayed placement of 135 implants. Histomorphometric data were obtained at the time of implant placement, 6 to 10 months following the grafting procedure. Vital bone formation was 17.6%, 16.9%, and 12.1%, respectively, for the Bio-Gide, Gore-Tex, and no membrane groups. Of the 135 implants placed there were 3 failures (2 Bio-Gide, 1 Gore-Tex). There was no significant difference between the membrane groups as to vital bone formation and implant survival.

Systematic review of survival rates for implants placed in the grafted maxillary sinus

Del Fabbro M, Testori T, Francetti L, Weinstein R.
Int J Periodontics Restorative Dent. 2004; 24: 565-77.

Based on a systematic review of the literature from 1986 to 2002, this study sought to determine the survival rate of root-form dental implants placed in the grafted maxillary sinus. Secondary goals were to determine the effects of graft material, implant surface characteristics, and simultaneous versus delayed placement on survival rate. A search of the main electronic databases was performed in addition to a hand search of the most relevant journals. All relevant articles were screened according to specific inclusion criteria. Selected papers were reviewed for data extraction. The search yielded 252 articles applicable to sinus grafts associated with implant treatment. Of these, 39 met the inclusion criteria for qualitative data analysis. Only 3 of the articles were randomized controlled trials. The overall implant survival rate for the 39 included studies was 91.49%. The database included 6,913 implants placed in 2,046 subjects with loaded follow-up time ranging from 12 to 75 months. Implant survival was 87.70% with grafts of 100% autogenous bone, 94.88% when combining autogenous bone with various bone substitutes, and 95.98% with bone grafts consisting of bone substitutes alone. The survival rate for implants having smooth and rough surfaces was 85.64% and 95.98%, respectively. Simultaneous and delayed procedures displayed similar survival rates of 92.17% and 92.93%, respectively. When implants are placed in grafted maxillary sinuses, the performance of rough implants is superior to that of smooth implants. Bone-substitute materials are as effective as autogenous bone when used alone or in combination with autogenous bone. Studies using a split-mouth design with one variable are needed to further validate the findings.

Histomorphometric analysis of natural bone mineral for maxillary sinus augmentation

John HD, Wenz B.
Int J Oral Maxillofac Implants 2004; 19: 199-207

PURPOSE: Lack of bone height in the posterior maxilla often necessitates augmentation prior to or simultaneously with dental implant placement. The purpose of this clinical study was to evaluate the use of the natural bone mineral Bio-Oss alone or in combination with autogenous bone in sinus floor elevations performed as 1- or 2-step procedures. MATERIALS AND METHODS: Thirty-eight patients required sinus augmentation. Natural bone mineral alone was used in sinus floor augmentation in 21 patients. In 13 patients, a mixture of the bone substitute and autogenous bone was used, and in 4 patients autogenous bone alone was used. In all of the patients, samples were taken for biopsy 3 to 8 months postoperatively, and bone regeneration was evaluated histologically and histomorphometrically. RESULTS: In all patients, the amount of new bone significantly increased over the observation time, while marrow areas decreased. There was no statistically significant difference in the amount of new bone formation between the Bio-Oss group (new bone 29.52% +/- 7.43%) and the Bio-Oss/autogenous bone group (new bone 32.23% +/- 6.86%). In the 4 patients treated with autogenous bone alone, a greater amount of newly formed bone was found; however, in these cases the area volume filled was smaller than in the other 2 groups. DISCUSSION: The data showed that new bone formation takes place up to 8 months after sinus floor elevation and that there is no difference in the amount of bone formation between procedures done with the bone substitute alone or with the mixture of the substitute and autogenous bone. CONCLUSION: These data suggest that predictable bone formation can be achieved with the use of Bio-Oss.

Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review

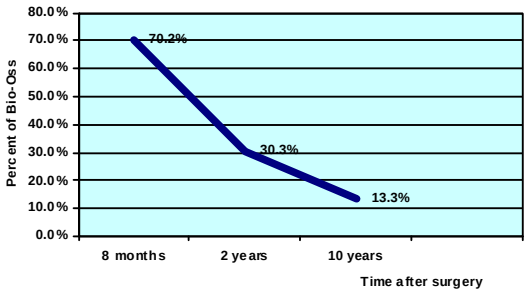
Wallace SS, Froum SJ
Ann Periodontol 2003; 8:328-343.

BACKGROUND: Grafting the floor of the maxillary sinus has become the most common surgical intervention for increasing alveolar bone height prior to the placement of endosseous dental implants in the posterior maxilla. Outcomes of this procedure may be affected by specific surgical techniques, simultaneous versus delayed implant placement, use of barrier membranes over the lateral window, selection of graft material, and the surface characteristics and the length and width of the implants. RATIONALE: The primary objective of this systematic review was to determine the efficacy of the sinus augmentation procedure and compare the results achieved with various surgical techniques, grafting materials, and implants. FOCUSED QUESTION: In patients requiring dental implant placement, what is the effect on implant survival of maxillary sinus augmentation versus implant placement in the non-grafted posterior maxilla? SEARCH PROTOCOL: MEDLINE, the Cochrane Oral Health Group Specialized Trials Register, and the Database of Abstracts and Reviews of Effectiveness were searched for articles published through April 2003. Hand searches were performed on Clinical Oral Implants Research, International Journal of Oral and Maxillofacial Implants, and the International Journal of Periodontics & Restorative Dentistry and the bibliographies of all relevant papers and review articles. In addition, researchers, journal editors, and industry sources were contacted to see if pertinent unpublished data that had been accepted for publication were available. SELECTION CRITERIA: INCLUSION CRITERIA: Human studies with a minimum of 20 interventions, a minimum follow-up period of 1-year loading, an outcome measurement of implant survival, and published in English, regardless of the evidence level, were considered. EXCLUSION CRITERIA: Studies involving multiple simultaneous interventions (e.g., simultaneous ridge augmentation) and studies with missing data that could not be supplied by the study authors were excluded. DATA COLLECTION AND ANALYSIS: Where adequate data were available, subgroups of dissimilar interventions (e.g., surgical techniques, graft materials, implant surfaces, membranes) were isolated and subjected to meta-regression, a form of meta-analysis. MAIN RESULTS: 1. Forty-three studies, 3 randomized controlled clinical trials (RCTs), 5 controlled trials (CTs), 12 case series (CS), and 23 retrospective analyses (RA) were identified. Thirty-four were lateral window interventions, 5 were osteotome interventions, 2 were localized management of the sinus floor, and 2 involved the crestal core technique. 2. Meta-regression was performed to determine the effect of the variables of block versus particulate grafting techniques, implant surface, graft material, and the use of a membrane over the lateral window. 3. The survival rate of implants placed in sinuses augmented with the lateral window technique varied between 61.7% and 100%, with an average survival rate of 91.8%. For lateral window technique: 4. Implant survival rates reported in this systematic review compare favorably to reported survival rates for implants placed in the non-grafted posterior maxilla. 5. Rough-surfaced implants have a higher survival rate than machine-surfaced implants when placed in grafted sinuses. 6. Implants placed in sinuses augmented with particulate grafts show a higher survival rate than those placed in sinuses augmented with block grafts. 7. Implant survival rates were higher when a membrane was placed over the lateral window. 8. The utilization of grafts consisting of 100% autogenous bone or the inclusion of autogenous bone as a component of a composite graft did not affect implant survival. 9. There was no statistical difference between the covariates of simultaneous versus delayed implant placement, types of rough-surfaced implants, length of follow-up, year of publication, and the evidence level of the study. REVIEWERS' CONCLUSIONS: Insufficient data were present to statistically evaluate the effects of smoking, residual crestal bone height, screw versus press-fit implant design, or the effect of implant surface micromorphology other than machined versus rough surfaces. There are insufficient data to recommend the use of platelet-rich plasma in sinus graft surgery.

Ten-year follow-up in a maxillary sinus augmentation using anorganic bovine bone (Bio-Oss). A case report with histomorphometric evaluation.

Sartori S, Silvestri M, Forni F, Icaro Cornaglia A, Tesei P, Cattaneo V.
Clin Oral Impl Res 2003; 14(3): 369-372

Several bone grafting materials have been used in sinus augmentation procedures. Bio-Oss (deproteinized and sterilized bovine bone) has shown to have osteoconductive properties and no inflammatory or adverse responses have been published. In spite of these successful results, histologic data regarding bone augmentation using Bio-Oss in humans is scarce. The purpose of this study was to



analyse the amount of Bio-Oss ossification in a case of maxillary sinus augmentation, recording and comparing histomorphometric data 8 months, 2 and 10 years after surgery. This long-term histologic evaluation of retrieved specimens has been performed, comparing histomorfometric measures at different times. Eight months after surgery we observed in 20 different thin sections of the specimen a mean amount of bone tissue (including medullar spaces) of 29.8% (and 70.2% of Bio-Oss) +/- 2.6. At 2 years the bone tissue increased to 69.7% + 2.7 and 10 years after surgery it was 86.7% +/- 2.8. The comparison of the means for each time has shown a highly significant increasing trend in bone formation associated with Bio-oss resorption: at 8 months, 2 and 10 years.

Maxillary sinus grafting with anorganic bovine bone: a clinical report of long-term results

Valentini P, Abensur DJ.
Int J Oral Maxillofac Implants 2003; 18(4): 556-60.

PURPOSE: The aim of the present retrospective study was to evaluate the survival rate of titanium plasma spray-coated cylindric and machined screw-type implants placed in sinuses grafted with Bio-Oss® mixed with demineralized freeze-dried bone allograft (DFDBA) or with Bio-Oss® alone. MATERIALS AND METHODS: The patients included in this study were treated with a 1- or 2-stage technique, according to the volume of residual bone. This determined the possibility of primary stabilization and the duration of the treatment, which was 9 or 12 months, respectively. RESULTS: The overall implant survival rate was 94.5% after a mean functioning period of 6.5 +/- 1.9 years. The Implant survival rate was better in sinuses grafted with Bio-Oss® alone than with a mixture of Bio-Oss® with DFDBA (96.8% versus 90%). The implant survival rate was similar for cylindric and screw-type implants in sinuses grafted with Bio-Oss® alone. DISCUSSION: Because of the good bone quality, the implant survival rate was similar for cylindric and screw-type implants in sinuses grafted with Bio-Oss®. CONCLUSION: Bio-Oss® used alone appears to be a suitable material for sinus floor augmentation.

Deproteinized cancellous bovine bone (Bio-Oss) as bone substitute for sinus floor elevation

Tadjoedin ES, de Lange GL, Bronckers ALJJ, Lyaruu DM, Burger EH
J Clin Periodontol 2003; 30: 261-270.

OBJECTIVES: To study in detail the performance of deproteinized cancellous bovine bone (DPBB, Bio-Oss) granules as a bone substitute, a histomorphometric was performed on five patients treated with Bio-Oss® for reconstruction of the severely atrophic maxilla. MATERIAL AND METHODS: DPBB was used as mixture with autogenous bone particles, in concentrations that increased from 20% to 100% BIO-OSS®, with the time of healing increasing accordingly from 5 to 8 months. A total of 20 vertical biopsies was taken at the time of fixture installation and used for histomorphometry as undecalcified Goldner stained sections. RESULTS: The results show that in all cases, the BIO-OSS® granules had been interconnected by bridges of vital newly formed bone. The volume of bone in the grafted area correlated inversely with the concentration of BIO-OSS® grafted, and varied between 37% and 23%. However, the total volume of mineralized material (bone plus DPI3B granules) remained within the same range in all five patients (between 53% and 59%). The high values for osteoid and resorption surface, and the presence of tartrate-resistant acid phosphatase-positive multinucleated osteoclasts in resorption lacunae, indicated that bone remodeling was very active in all grafts. Osteoclasts were also observed in shallow resorption pits on BIO-OSS® surfaces. The percentage BIO-OSS® surface in contact with bone remained stable at about 35% and could not be related to the proportion of BIO-OSS® grafted. CONCLUSION: Although the number of patients examined was limited, the data suggest that Bio-Oss®, preferably combined with autogenous bone particles, is a suitable material for sinus floor elevation in the severely atrophic human maxilla.

A Clinical and Histologic Evaluation of Implant Integration in the Posterior Maxilla After Sinus Floor Augmentation with Autogenous Bone, Bovine Hydroxyapatite, or a 20:80 Mixture

Hallmann M, Sennerby L, Lundgren S
Int J Oral Maxillofac Implants 2002; 17: 635-643.

Purpose: This study was designed to clinically and histologically evaluate the integration of titanium implants in different grafting materials used for maxillary sinus augmentation procedures. Materials and Methods: A total of 21 patients and 36 maxillary sinuses were augmented with (1) autogenous particulated bone from the mandibular ramus, (2) bovine hydroxyapatite (BH) with membrane coverage, or (3) an 80/20 mixture of BH and autogenous bone. The grafts were allowed to heal for 6 to 9 months prior to placement of microimplants for histology and standard implants for prosthetic rehabilitation. After another 6 months of healing, when abutments were connected, the microimplants were retrieved for histologic and morphometric analyses. The outcome of the standard implants was clinically evaluated after 1 ear of loading. Results: The mean bone-implant contact was 34.6 ± 9.5%, 54.3 ± 33.1%, and 31.6 ± 19.1% for autogenous bone, mixture of 20% autogenous bone/80% BH, and 100% BH, respectively. The corresponding values for the bone area parameter were 37.7 ± 31.3%, 39.9 ± 8%, and 41.7 ± 26.6%. The BH area was found to be 12.3 ± 8.5% and 11.8 ± 3.6% for 20% autogenous bone/80% BH and 100% BH, respectively. There were no statistically significant differences for any parameter between any of the groups. After 1 year of loading, 6 of the 33 implants placed in autogenous bone grafts, 2 of the 35 implants placed in the BH/autogenous bone mixture, and 2 of 43 implants placed in BH were lost. There were no statistically significant differences between any of the groups. Discussion: The histomorphometric analysis showed no differences between the 3 groups indicating that autogenous bone graft can be substituted with bovine hydroxyapatite to 80% or 100% when used for maxillary sinus floor augmentation. The effect of adding autogenous bone remains unclear but may allow for a reduction of the healing time. Conclusion: The results from this clinical and histologic study indicate that similar short-term results can be expected when using autogenous bone, Bio-Oss, or a mixture of them for maxillary sinus floor augmentation and delayed placement of dental implants

A Prospective 1-Year Clinical and Radiographic Study of Implants Placed After maxillary Sinus Floor Augmentation With Bovine Hydroxyapatite and Autogenous Bone

Hallmann M., Hedin M., Sennerby L., Lundgren S.
J Oral Maxillofac Surg 2002; 60: 277-284.

Purpose: The purposes of this study were 1) to evaluate the survival rate of implants placed in maxillary sinuses augmented with bovine hydroxyapatite (Bio-Oss) and autogenous bone 6 months before implant surgery and 2) to estimate dimensional changes of the bone graft with time using a new radiographic method.
Patients and Methods: Thirty maxillary sinuses in 20 consecutive patients with severe resorption (mean, 3.8mm of remaining alveolar bone) were augmented with a mixture of 80% Bio-Oss and 20% autogenous bone mixed with fibrin glue to enable the placement of screw-shaped dental implants. After 6 months of primary healing, 108 implants were placed and followed with clinical and radiographic examinations during the first year of loading. Measurements of changes in height, width, and length of the grafted material were made on tomographic Scanora and panoramic radiographs taken 3 and 12 months after grafting and after 1 year of bridge loading.
Results: Ten implants in 6 patients were lost during the study (9 before loading and 1 after 1 year of functional loading), for a survival rate of 90.7%. All patients received fixed restorations, and the bridge survival rate was 100% after 1 year of loading. Small (<10%) but statistically significant dimensional changes in the grafted material were seen during the study period.
Conclusions: Acceptable short-term results can be obtained with implants placed after the use of Bio-Oss and autogenous bone for maxillary sinus floor augmentation. These grafts show good resistance to resorption.

Sinus Floor Elevation Using a Bovine Bone Mineral (Bio-Oss) With or Without the Concomitant Use of a Bilayered Collagen Barrier (Bio-Gide): A Clinical Report of Immediate and Delayed Implant Placement

G. Tawil, M. Mawla
Int J Oral Maxillofac Impl 2001; 16: 13-21

Xenografts have been used extensively, either alone or in combination with autogenous bone, in sinus floor elevation techniques. However, controversy exists regarding the need to cover the lateral osteotomy site with a membrane. Also, the healing period before loading remains undefined when machined-surface implants are placed. Twenty-nine patients showing reduced bone volume in the posterior maxilla had 61 Brånemark System implants placed in 30 sinuses augmented with a lateral osteotomy approach. Sinuses grafted with Bio-Oss® and covered with a collagen membrane Bio-Gide® (M+) received 29 implants, while grafted but uncovered sites (M-) received 32 implants. An immediate procedure was followed to place 41 implants and a staged procedure was used for 20 implants. Abutment connection was made in 2 distinct postoperative periods: 6 to 9 months and over 9 months. The patients were followed for an average of 22.4 months. The survival rate of the implants was dependent on the postoperative healing time and membrane presence. In case of the immediate procedure and in M- sites, when residual bone height was less than 5 mm, more failures occurred when the loading was done at 6 to 9 months than after 9 months. No failures occurred in the M- series when a staged approach was followed. The overall survival rate was 78.1% for the M- sites and 93.1% for the M+ sites. No failures occurred (0/35) in the control implants placed in adjacent native bone. Implant survival rate was related to the quality of the reconstructed cortical plate and to implant length. The concomitant use of a collagen barrier to cover the osteotomy site, when machined-surface implants were used in sinus grafting, seemed to improve the quality of the graft healing and survival rate of the implants loaded between 6 and 9 months after placement.

Treatment of Maxillary Ridge Resorption by Sinus Augmentation with Iliac Cancellous Bone, Anorganic Bovine Bone, and Endosseous Implants: A Clinical and Histologic Report

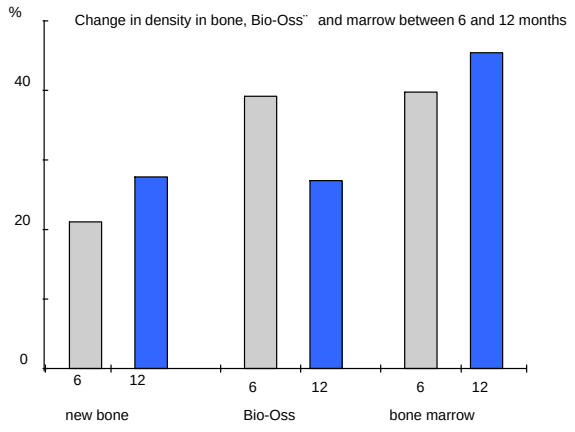
C. Maiorana, M. Redemagni, M. Rabagliati, S. Salina
Int J Oral Maxillofac Implants 2000 : 15 : 873–78.

In this clinical study, a 1:1 mix of particulate cancellous bone and marrow (PCBM) and bovine deproteinized bone (Bio-Oss) was used to fill cavities after elevating the sinus mucosa for major sinus dehiscences. Ten patients with edentulous posterior maxillae were treated with 12 sinus augmentation procedures according to a 2-stage technique, and 30 Frialit-2 endosseous implants were used to complete the implant-prosthetic rehabilitation. Bone cylinders were removed at second-stage surgery immediately prior to implant placement (5 to 7 months after grafting), and histologic evaluation was performed. The results showed that Bio-Oss is a reliable osteoconductive material and its association with PCBM leads to the formation of new bone with an increased overall density.

Sinus grafting with porous bone mineral (Bio-Oss®) for implant placement: A study on 15 patients

P. Valentini, D. Abensur, B. Wenz, M. Peetz, R. Schenk
Int J Periodontics Restorative Dent 2000; 20: 245-53.

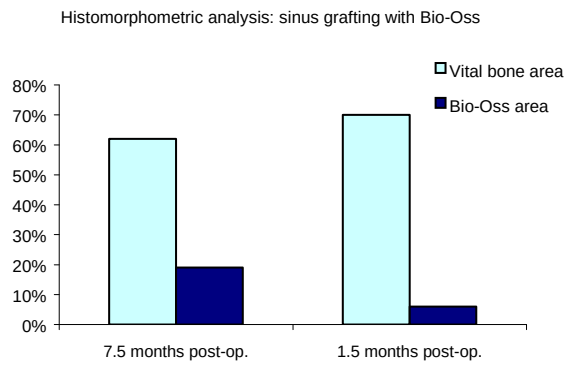
In 15 patients the efficacy of Bio-Oss® as graft material for sinus floor elevation was studied. Twenty sinus lift were performed, 57 implants were placed 6 months later. New bone formation was confirmed in biopsies of 3 patients (see Fig.).
The histomorphometry which was performed on it revealed no contact between Bio-Oss® remnants and the implant surface. The osseointegrated surface was 73% in the grafted area vs. 63% in the non grafted area. The overall survival rate for the implants placed was 98.2% after a mean period of loading of 31.7 ± 6.1 months (range 24-42). The excellent osteoconductive properties of Bio-Oss® were confirmed.



Eighteen-Month Radiographic and Histologic Evaluation of Sinus Grafting with Anorganic Bovine Bone in the Chimpanzee

B. McAllister, M. Margolin, A. Cogan, D. Buck, J. Hollinger, S.E. Lynch
Int J Oral Maxillofac Implants: 1999 ; 14.

The purpose of this in vivo study was to determine the bone mineral density (BMD) of the sinus grafts, the vertical height stability, the vital bone area, and the extent of anorganic bovine bone replacement 18 months postoperatively in 4 maxillary sinuses from 4 different animals. Radiographic analysis of computed tomographic scans taken at 1.5 years revealed an average BMD of 658 mg/mL, which was not significantly different from the values found at 6.5 months. The radiographic vertical height was maintained between the 6.5- and 18-month time points. On average, the grafts were found to have a height of 14 mm. Lateral wall biopsy specimens at 7.5 months were compared to those at 18 months (see Fig.).



The results demonstrate that sinus grafting with natural bone mineral maintains radiographic evidence of density and height stability to 1.5 years. In addition, histologic evidence supports the hypothesis that natural bone mineral is replaced by vital bone.

Bovine hydroxyapatite for maxillary sinus augmentation: analysis of interfacial bond strength of dental implants using pull-out tests

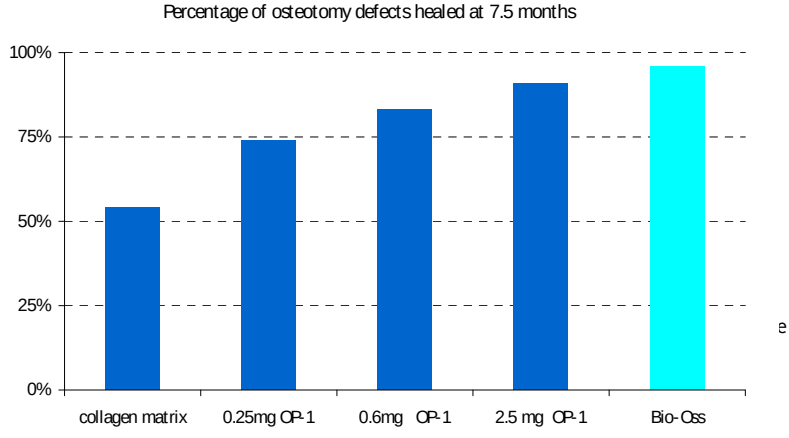
Haas R., Mailath G., Dörtbudak O., Watzek G.
Clin Oral Impl Res 1998; 9: 117-122.

This study examines the effect of sinus lift surgery using Bio-Oss® on the bone anchorage of titanium plasma flame-spray-coated cylindrical implants. A total of 54 implants were placed n the lateral bony antral walls of 27 mountain sheep. Host site augmentation was done simultaneously using Bio-Oss® and autogenous cancellous bone from the iliac crest in 18 sinuses each. The bone walls of the remaining 18 sinuses received no augmentation. Pull-out tests were carried out at 12, 16 and 26 weeks, revealing a significant influence of the implants resident time on pull-out strength (P=0.004). The implants of the non-augmented group and those of the group augmented using cancellous bone showed a linear increase in pull-out strength to 169.8 N and 523.7 N, respectively, until the 26th week. The implants of the group augmented with Bio-Oss® exhibited the highest initial pull-out strength (325.1 N) that further increased to 521.8 N until the 26th week. All in all, this group showed a significantly greater pull-out strength than did the negative control group (P=0.03).

Residual Lateral Wall Defects Following Sinus Grafting With Recombinant Human Osteogenic Protein-1 or Bio-Oss® in the Chimpanzee

B. McAllister, M. Margolin, A. Cogan, M. Taylor, J. Wollins
Int J Periodontics Restorative Dent 1998; 18(3).

Sinus grafting procedures area viable means of ensuring adequate bone for the placement of dental implants



in the posterior maxilla. In the quest to improve predictability and accelerate the time line toward receiving a final prosthesis, researchers have turned to recombinant human proteins like osteogenic protein-1 for the potential to therapeutically enhance bone formation. Bilateral sinus augmentations were performed in 15 adult chimpanzees to evaluate treatment with different doses of the osteogenic protein-1 device or natural bone mineral (Bio-Oss®). Methods of evaluation included soft tissue healing, radiography (computed tomographic scan), histology, residual lateral wall defect surface area at 7,5 months, and the extent of soft tissue encleftation at 7,5 months. Findings revealed radiographic and histologic evidence of bone formation with all treatment groups and a statistically significant reduction in the depth of soft tissue encleftation and the residual lateral wall defect surface area for both the Bio-Oss® and the 2.5-mg osteogenic protein-1 per gram collagen matrix treatments when compared to collagen matrix alone (see Fig.). These results suggest that Bio-Oss® and the 2.5-mg osteogenic protein-1 per gram collagen matrix effectively stimulate bone formation in the maxillary sinus.

Maxillary sinus augmentation using different grafting materials and dental implants in monkeys- Part I. Evaluation of anorganic bovine-derived bone matrix

Hürzeler M.B., Quiñones C.R., Kirsch A., Gloker C., Schüpbach P., Strub J.R., Caffesse R.G.
Clin Oral Impl Res 1997; 8: 476-486.

The aim of this study was to evaluate clinically, histologically and histometrically the use of natural bovine bone matrix (i.e. Bio-Oss®) as a grafting material for maxillary sinus augmentation procedures. In 4 adult male rhesus monkeys (i.e. Macaca mulatta) the 1st, 2nd and 3rd maxillary molars on one side of the jaws were extracted. The remaining bone between the alveolar crest and the bottom of the sinus was then reduced to 3-4 mm. After 3 months, maxillary sinus augmentation procedures were performed on one side of the jaws in each monkey and the sinuses were grafted with the bovine bone matrix. At that time, 2 IMZ pure titanium plasma coated implants were immediately placed into the augmented sinuses (i.e. simultaneous implants-loaded group). After 4 months, 2 additional similar implants were placed into these previously augmented sinuses (i.e. delayed implants-loaded group). Four months later, the abutment connection was performed and all 4 implants were loaded with a gold-alloy bridge for 6 months (i.e. until sacrifice of the animals). The contralateral side of each monkey received the same treatment with the exception that the extractions were performed 7 months after those in the opposite side and that the implants in this side were not loaded. Thus, 2 additional study groups (i.e. simultaneous implants-unloaded group and delayed implants-unloaded group) were obtained. Clinically, all loaded implants were stable at the day of sacrifice. Histologically, the grafted sinuses exhibited significant bone formation with integration of the bovine bone matrix particles to the new bone. Direct mineralized bone-to-implant contact was greater for the delayed implant placement groups than for the implants installed simultaneously with the sinus augmentation. Furthermore, the percentage of direct mineralized bone-to-implant contact was greater in the residual bone than in the augmented area. It was concluded that the natural bovine bone matrix facilitated bone formation and implant osseointegration in the augmented sinuses and that the delayed implant placement in combination with the sinus augmentation procedure seemed to be preferable.

Maxillary Sinus Floor Elevation for Implant Placement With Demineralized Freeze-Dried Bone and Bovine Bone (Bio-Oss®): A clinical study of 20 patients

P. Valentini, D. Abensur
Int J Periodontics Restorative Dent 1997; 17.

The objective of this study was to determine the predictability of endosseous implants placed in a maxillary sinus grafted with a mixture of porous bone mineral (Bio-Oss®) and demineralized freeze-dried bone. Sixty implants were placed in 20 patients representing 28 sinuses using either a one- or two-stage technique. After an implant loading period of more than 2 years, the survival rate (eg. a clinically functioning implant without signs of mobility or infection) varied from 90% to 96%. No infections or other complications were encountered. The data suggest that this treatment regimen can result in a high rate of survival.
Conclusion: The results of this human study suggest that composite grafts represent an important alternative to autografts in sinus floor lift procedures, especially when cylindrical implants are used. Autogenous bone still remains the most predictable material for the sinus lift procedure, especially in cases of large sinuses with only a thin cortical layer of bone bordering the inferior aspect of the sinus cavity. On the other hand, the porous natural bone mineral (Bio-Oss®) showed excellent osseoconductive properties

and could be indicated alone in case of sufficient remaining bone around the sinus. The histologic findings suggest that the osseoinductive effect of DFDBA is insufficient and that promotion of new bone is a result of the osseoconductive properties of the bone mineral matrix (Bio-Oss®).

Bone apposition onto oral implants in the sinus area filled with different grafting materials

Wetzel A.C., Stich H., Caffesse R.G.
Clin Oral Impl Res 1995; 6: 155-163.

The aim of this study was to evaluate histologically the simultaneous placement of endosseous implants into the sinus cavity and the surgical elevation of the sinus floor including filling the cavity with different grafting materials. In 9 sinus areas of 5 beagle dogs, 9 titanium implants (ITI® Dental Implant System) were placed, and the void space of the sinus cavity was filled simultaneously with either demineralized freeze-dried human cortical bone, a resorbable hydroxyapatite or natural cancellous bone mineral (Bio-Oss®). To study bone formation, fluorochrome markers (tetracycline-HCI and calcein green) were used at 2 and 8 weeks.
Clinically, all implants healed uneventfully, and 5 months after implant placement the dogs were killed for histologic evaluation. The implants surrounded by freeze-dried human bone yielded no formation of new bone, whereas the sites with hydroxyapatite or natural bovine bone mineral demonstrated newly formed bone with direct contact at the implant surface. The average extent of bone to implant contact was 25 % (SD = 10.6 %) and 27% (SD = 8.8 %), respectively in relation to the length of the originally denuded implant surface. In addition, the bone markers revealed a rapid bone formation and remodeling, especially around Bio-Oss® particles. This study yields new bone formation with direct contact to the implants surfaces in the sinus cavity into which suitable grafting materials were placed simultaneously.

1-stage versus 2-stage lateral sinus lift procedures: 1-year post-loading results of a multicentre randomised controlled trial.

Felice P, Pistilli R, Piattelli M, Soardi E, Barausse C, Esposito M.
Eur J Oral Implantol. 2014 Spring;7(1):65-75

PURPOSE: To compare the efficacy of 1-stage versus 2-stage lateral maxillary sinus lift procedures.
MATERIALS AND METHODS: Sixty partially edentulous patients requiring 1 to 3 implants and having 1 to 3 mm of residual bone height and at least 5 mm bone width below the maxillary sinus, as measured on CT scans were selected. They were randomised according to a parallel group study design into two equal arms to receive either a 1-stage lateral window sinus lift with simultaneous implant placement or a 2-stage procedure with implant placement delayed by 4 months, using a bone substitute in three different centres. Implants were submerged for 4 months, loaded with reinforced provisional prostheses, which were replaced, after 4 months, by definitive prostheses. Outcome measures, assessed by masked assessors, were: augmentation procedure failures; prosthesis failures and implant failures; complications; and marginal peri-implant bone level changes. Patients were followed up to 1 year after loading. Only data of implants placed in 1 to 3 mm of bone height were reported.
RESULTS: Two patients dropped out from the 1-stage group and none from the 2-stage group. No sinus lift procedure failed in the 1-stage group but one failed in the 2-stage group, the difference being not statistically significant (P = 1.00). Two prostheses failed or could not be placed in the planned time in the 1-stage group and one in the 2-stage group, the difference being not statistically significant (P = 0.51). Three implants failed in three patients of the 1-stage group, versus one implant in the 2-stage group, the difference being not statistically significant (P = 0.28). Two complications occurred in the 1-stage group and one in the 2-stage group, the difference being not statistically significant (P = 0.61). One year after loading, 1-stage treated patients lost an average of -1.01 mm (SD: 0.56) of peri-implant bone and 2-stage sites about -0.93 mm (SD: 0.40). There were no statistically significant differences in bone level change between groups 1 year after loading (-0.08 mm 95%CI: -0.33 to 0.18 P = 0.56).
CONCLUSION: No statistically significant differences were observed between implants placed according to 1- or 2-stage sinus lift procedures. However this study may suggest that in patients having residual bone height between 1 to 3 mm below the maxillary sinus, there might be a slightly higher risk for implant failures when performing a 1-stage lateral sinus lift procedure.

Effect of xenograft (ABBM) particle size on vital bone formation following maxillary sinus augmentation: a multicenter, randomized, controlled, clinical histomorphometric trial.

Testori T1, Wallace SS, Trisi P, Capelli M, Zuffetti F, Del Fabbro M.
Int J Periodontics Restorative Dent. 2013 Jul-Aug;33(4):467-75. doi: 10.11607/prd.1423.

The purpose of this study was a histomorphometric comparison of vital bone formation following maxillary sinus augmentation with two different particle sizes of anorganic bovine bone matrix (ABBM). Bilateral sinus floor augmentations were performed in 13 patients. Trephine bone cores were taken from the lateral window areas of 11 patients 6 to 8 months after augmentation for histologic and histomorphometric analysis. Bone samples from both the large and small particle size groups showed evidence of vital bone formation similar to that seen in previous studies, confirming the osteoconductivity of ABBM. Significant bone bridging was seen creating new trabeculae composed of the newly formed bone and residual ABBM particles. Histologic evaluation revealed the newly formed bone to be mostly woven bone with some remodeling to lamellar bone. Osteocytes were seen within the newly formed bone as well as osteoblast seams with recently formed osteoid. Isolated osteoclasts were observed on the ABBM surfaces. Vital bone formation (primary outcome measure) was more extensive in the large particle grafts compared with the small particle grafts (26.77% ± 9.63% vs 18.77% ± 4.74%, respectively). The histologic results reaffirm the osteoconductive ability of ABBM when used as the sole grafting material in maxillary sinus augmentation. The histomorphometric results at 6 to 8 months revealed a statistically significant increase (P = .02) in vital bone formation when the larger particle size was used. Additional studies should be performed to confirm these results.

Prospective randomized, controlled trial of sinus grafting using Escherichia-coli-produced rhBMP-2 with a biphasic calcium phosphate carrier compared to deproteinized bovine bone.

Kim MS1, Lee JS, Shin HK, Kim JS, Yun JH, Cho KS.
Clin Oral Implants Res. 2015 Dec;26(12):1361-8. doi: 10.1111/clr.12471. Epub 2014 Sep 3.

AIM: This study compared the effects of Escherichia-coli-produced recombinant human bone morphogenetic protein 2 (ErhBMP-2) with a biphasic calcium phosphate (BCP) carrier to those of deproteinized bovine bone in human maxillary sinus floor augmentation.

MATERIAL AND METHODS: Screening for this clinical trial selected 56 sites that provided informed consent to participate, of which 46 were ultimately enrolled and 41 were finally included in the study. The sites were divided into two groups using a random-number table, and the material was applied. A trephine biopsy was performed after 24 weeks, and implants wider than the biopsy site were inserted. Computed tomography and plain panoramic images were obtained immediately and then again at 24 weeks after the surgery. Radiographic images were reconstructed to allow measurement of the linear and volumetric changes. The biopsy samples were processed for histologic and histometric analyzes.

RESULTS: All sites healed uneventfully with no complications. Radiographic analysis revealed a tendency for the volume to increase, but the difference was not statistically significant in either group. Comparison of volumetric changes between the two groups also revealed no significant difference. Moreover, none of the histometric parameters differed significantly between the groups, although different healing patterns were observed on histologic analysis.

CONCLUSIONS AND CLINICAL IMPLICATIONS: It can be concluded that sinus augmentation with ErhBMP-2 carrying BCP carrier did not enhance bone regeneration compared to the conventional treatment using deproteinized bovine bone at 24 weeks after the surgery.

Sinus floor augmentation with autogenous bone vs. a bovine-derived xenograft - a 5-year retrospective study.

Lutz R1, Berger-Fink S, Stockmann P, Neukam FW, Schlegel KA.
Clin Oral Implants Res. 2015 Jun;26(6):644-8. doi: 10.1111/clr.12352. Epub 2014 Feb 20.

OBJECTIVES: The long-term outcome after sinus augmentation with autogenous bone or a bovine xenograft (Bio-Oss(®)) was assessed in 47 patients. Inclusion criterion was a vertical dimension of the maxilla of <4 mm. After a functional loading period of 60 months, implant survival and reduction in the augmentation height were compared between the two groups evaluated.

MATERIAL AND METHODS: Sinus augmentation was performed using mandibular bone grafts or Bio-Oss(®). In the autogenous bone group, 70 implants were placed in 23 patients, while in the Bio-Oss(®) group, 24 patients received 98 implants. Fisher's exact test and equivalence testing were used to compare implant survival rates.

RESULTS: The overall survival rate of the implants was 95.8% 5 years after implant insertion. In the autogenous bone group, the implants had a survival rate of 97.1%, while in the Bio-Oss(®) group, 94.9% of the implants survived. The difference was not statistically significant (P > 0.05); both treatments are equivalent (confidence interval 90%) for the equivalence interval [-0.1; 0.1]. 43.5% of the cases showed no reduction in the augmentation height 5 years after implant insertion, when augmentation was performed with autogenous bone, while in the Bio-Oss(®) group, no resorption was found in 50% of the augmented areas. Up to 25% reduction in augmentation height was found in 47.8% in the autogenous and in 45.8% in the Bio-Oss(®) group. In 8.7% of all cases in the autogenous bone group and in 4.2 % in the Bio-Oss(®) group, up to 50% of the augmented height was resorbed.

CONCLUSION: After a 5 years evaluation period, Bio-Oss(®) as material for the indication maxillary sinus augmentation shows to be equivalent to autogenous bone grafting.

Fate of a Bovine-Derived Xenograft in Maxillary Sinus Floor Elevation After 14 Years: Histologic and Radiologic Analysis.

Ayna M, Açil Y, Gulses A.
Int J Periodontics Restorative Dent. 2015 Jul-Aug;35(4):541-7. doi: 10.11607/prd.2135.

This report assesses the results following sinus floor augmentation performed 14 years previously in which bovine bone xenograft material was used without implant insertion. After sinus floor augmentation, using a 20:80 mixture of autogenous bone and inorganic bovine bone material (Bio-Oss), bone biopsy specimens were taken from the grafted site, processed with Donath's sawing and grinding technique, stained with toluidine blue, and mounted on high-sensitivity plates for histology and microradiography. Histologic and microradiographic analysis showed the ingrowth of newly formed bone into the graft with interspersed residual Bio-Oss granules. The percentage of Bio- Oss and newly formed bone was 10.18% and 9.32%, respectively, within a total surface area of 70.61 mm^2 at the site of the corresponding missing first molar, and the percentage of Bio-Oss and newly formed bone was 11.47% and 14.96%, respectively, within a total surface area of 63.92 mm^2 at the corresponding missing second molar. The newly formed bone was vital without signs of resorption. This study produced strong evidence that newly formed bone was distributed throughout the bone substitute material around all of its granules and that the grafted site consisted of vital bone even in its central parts. The differences in degradation rate and/or whether the effect of bone graft substitutes alone and/ or in combination with other types, shapes, and sizes of graft materials needs further clinical investigation, especially in regard to long-term changes.

5. GTR and GBR – Benefit of Membrane

a Intra-bony defects

Five-year results of a prospective, randomized, controlled study evaluating treatment of intrabony defects with a natural bone mineral and GTR.

Sculean A, Schwarz F, Chiantella GC, Donos N, Arweiler NB, Brecx M, Becker J. J Clin Periodontol 2007, 34, 72 –77.

Background: Treatment with a natural bone mineral (NBM) and a guided tissue regeneration (GTR) has been shown to promote periodontal regeneration. However, until now there are only very limited data on the long-term clinical results following this regenerative technique. Aim: To present the 5-year results of a prospective, randomized, controlled clinical study evaluating the treatment of deep intra-bony defects either with open flap debridement (OFD) and a combination of an NBM and GTR (test) or OFD alone (control). Methods: Nineteen patients diagnosed with advanced chronic periodontitis, and each of whom displayed one intra-bony defect, received randomly the test or the control treatment. Results were evaluated at baseline, at 1 and at 5 years following therapy. Results: No statistically significant differences in any of the investigated prameters were observed at baseline between the two groups. At 1 aear after therapy, the test group showed a reduction in mean probing depth (PD) from 9.1± 1.1 to 3.7 ± 0.8 mm (P<0.001) and a change in mean clinical attachment level (CAL) from 10.4 ± 1.3 to 6.4 ± 1.2 mm (p<0.001). At 5 years, mean PD and CAL measured 4.3 ± 0.8 and 6.7 ± 1.6 mm, respectively. At 5 years, both PD and CAL were statistically significantly improved compared with baseline (p<0.001) without statistically significant differences between the 1- and 5-year results. In the control group, mean PD was reduced from 8.9 ± 1.3 to 4.9 ± 1.2 (p<0.001 and mean CAL changed from 10.6 ± 1.4 to 8.8 ± 1.5 mm (p<0.01). At 5 years, mean PD and CAL measured 5.6 ± 1.1 and 9.1 ± 1.3 mm, respectively, and were still statistically significantly improved compared with baseline (p<0.01). No statistically significant differences were found between the 1- and 5-year results. The test treatment, at both 1 and 5 years, yielded statistically signigficantly higher CAL gains than the control one (p<0.01). Compared with baseline, at 5 years a CAL gain of 3>mm was found in nine defects (90%) of the test group but in none of the defects treated with OFD alone. Conclusions: It was concluded that (i) treatment of intra-bony defects with OFD + NBM + GTR may result in significantly higher CAL gains than treatment with OFD, and (ii) the clinical results obtained after both treatments can be maintained over a period of 5 years.

Effects of combined treatment with porous bovine inorganic bone grafts and bilayer porcine collagen membrane on refractory one-wall intrabony defects.

Sakata J, Abe H, Ohazama A, Okubo K, Nagashima C, Suzuki M, Hasegawa K.
Int J Periodontics Restorative Dent 2006; 26: 161-169

The aim of this study was to investigate the effects of a combination of porous bovine inorganic bone graft (Bio-Oss) and bilayer porcine collagen membrane (Bio-Gide) on refractory one-wall intrabony defects in dogs. Bio-Oss and Bio-Gide were applied into the refractory one-wall intrabony defect. The contralateral sites were used as controls (without the application of Bio-Oss and Bio-Gide). At 24 weeks after surgery, similar pocket depths were found in both groups. However, histologic observation revealed an infiltration of inflammatory cells in the control group caused by poor gingival architecture, whereas only a few of the experimental sites showed inflammatory infiltration. In addition to the healthy gingival tissue, periodontal tissue regeneration was observed in the experimental group. The combination of Bio-Oss and Bio-Gide was an effective treatment for refractory one-wall intrabony defects in dogs.

Healing of intra-bony defects following treatment with a composite bovine-derived xenograft (Bio-Oss Collagen) in combination with a collagen membrane (Bio-Gide Perio)

Sculean A, Chiantella GC, Windisch P, Arweiler NB, Brecx M, Gera I.

J Clin Periodontol 2005; 32: 720-724.

AIM: The purpose of the present study was to compare clinically the treatment of deep intra-bony defects with a combination of a composite bovine-derived xenograft (BDX Coll) and a bioresorbable collagen membrane [guided tissue regeneration (GTR)] to access flap surgery only. METHODS: Thirty-two patients, each of whom displayed one intra-bony defect, were treated either with BDX Coll+GTR (test) or with access flap surgery (control). The results were evaluated at 1 year following therapy. RESULTS: No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the test group showed a reduction in the mean probing depth (PD) from 8.3+/-1.5 to 2.9+/-1.3 mm (p<0.001) and a change in the mean clinical attachment level (CAL) from 9.4+/-1.3 to 5.3+/-1.5 mm (p<0.0001). In the control group, the mean PD was reduced from 8.0+/-1.2 to 4.4+/-1.7 mm (p<0.001) and the mean CAL changed from 9.6+/-1.3 to 7.9+/-1.6 mm (p<0.01). The test treatment resulted in statistically higher PD reductions (p< or =0.05) and CAL gains (p<0.001) than the control one. In the test group, all sites (100%) gained at least 3 mm of CAL. In this group, a CAL gain of 3 or 4 mm was measured at 10 sites (62%), whereas at six sites (38%), the CAL gain was 5 or 6 mm. In the control group, no CAL gain occurred at three sites (19%), whereas at 10 sites (62%), the CAL gain was only 1 or 2 mm. A CAL gain of 3 mm was measured in three defects (19%). CONCLUSIONS: Within the limits of the present study, it can be concluded that the combination of BDX Coll+GTR resulted in significantly higher CAL gains than treatment with access flap surgery alone, and thus appears to be a suitable alternative for treating intra-bony periodontal defects

Clinical outcomes following treatment of human intrabony defects with GTR/bone replacement material or access flap alone.

Tonetti MS, Cortellini P, Lang NP, Suvan JE, Adriaens P, Dubravec D, Fonzar A, Fourmousis I, Rasperini G, Rossi R, Silvestri M, Topoll H, Wallkamm B, Zybutz M.
J Clin Periodontol 2004; 31(9): 770-6.

Aim: This prospective multicenter randomized controlled clinical trial was designed to compare the clinical outcomes of papilla preservation flap surgery with or without the application of a guided tissue regeneration (GTR)/bone replacement material. Materials and Methods: One hundred and twenty-four patients with advanced chronic periodontitis were recruited in 10 centers in seven countries. All patients had at least one intrabony defect of >/=3 mm. The surgical procedures included access for root instrumentation using either the simplified or the modified papilla preservation flap in order to obtain optimal tissue adaptation and primary closure. After debridement, the regenerative material was applied in the test subjects, and omitted in the controls. At baseline and 1 year following the interventions, clinical attachment levels (CALs), probing pocket depths (PPDs), recession, full-mouth plaque scores and full-mouth bleeding scores (FMBS) were assessed. Results: One year after treatment, the test defects gained 3.3+/-1.7 mm of CAL, while the control defects yielded a significantly lower CAL gain of 2.5+/-1.5 mm. Pocket reduction was also significantly higher in the test group (3.7+/-1.8 mm) when compared with the controls (3.2+/-1.5 mm). A multivariate analysis indicated that the treatment, the clinical centers, baseline PPD and baseline FMBS significantly influenced CAL gains. Odds ratios (ORs) of achieving above-median CAL gains were significantly improved by the test procedure (OR=2.6, 95% CI 1.2-5.4) and by starting with deeper PPD (OR=1.7, 1.3-2.2) but were decreased by receiving treatment at the worst-performing clinical center (OR=0.9, 0.76-0.99). Conclusions: The results of this trial indicated that regenerative periodontal surgery with a GTR/bone replacement material offers an additional benefit in terms of CAL gains, PPD reductions and predictability of outcomes with respect to papilla preservation flaps alone.

Healing of intrabony defects following treatment with a bovine-derived xenograft and collagen membrane

Sculean A, Berakdar M, Chiantella GC, Donos N, Arweiler NB, Brecx M.
J Clin Periodontol 2003; 30:73-80

AIM: The purpose of the present study was to compare clinically the treatment of deep intrabony defects with a combination of a bovine-derived xenograft (Bio-Oss®) and a bioresorbable collagen membrane (Bio-Gide®) to access flap surgery. METHODS: Twenty-eight patients suffering from chronic periodontitis, and each of whom displayed one intrabony defect, were randomly treated with Bio-Oss®+ collagen membrane (test) or with access flap surgery (control). Soft tissue measurements were made at baseline and at 1 year

following therapy. RESULTS: No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the test group showed a reduction in mean probing depth (PD) from 9.2+/-1.3 to 3.9+/-0.7 mm (p<0.001) and a change in mean clinical attachment level (CAL) from 10.2+/-1.5 to 6.2+/-0.5 mm (p<0.0001). In the control group, the mean PD was reduced from 9.0+/-1.2 to 5.2+/-1.8 mm (p<0.001) and the mean CAL changed from 10.5+/-1.5 to 8.4+/-2.1 mm (p<0.01). The test treatment resulted in statistically higher PD reductions (p<or=0.05) and CAL gains (p<0.001) than the control one. In the test group all sites (100%) gained at least 3 mm of CAL. In the control group no CAL gain occurred in four sites (29%), whereas at six sites (43%) the CAL gain was 2 mm. A CAL gain of 3 mm or more was measured in four defects (29%). CONCLUSION: Within the limits of the present study, it can be concluded that: (i) at 1 year after surgery both therapies resulted in significant PD reductions and CAL gains, and (ii) treatment with Bio-Oss®+collagen membrane resulted in significantly higher CAL gains than treatment with access flap surgery

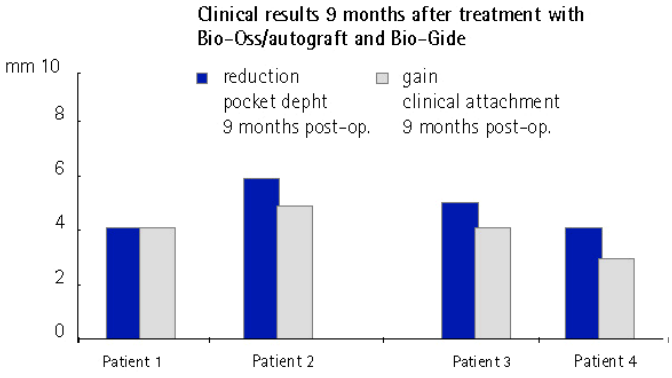
Effect of Porous Xenographic Bone Graft with Collagen Barrier Membrane on Periodontal Regeneration

Yamada S., Shima N., Kitamura H., Sugito H.
Int J Periodontics Restorative Dent 2002; 22(4):389-397.

The purpose of this study was to investigate the effect of porous xenographic bone graft (Bio-Oss) with a collagen barrier membrane (Bio-Gide) on formation of new cementum and new bone in experimental intrabony defects of dogs. The intrabony defects were treated by either guided tissue regeneration with the collagen membrane (control group) or the collagen membrane with the porous bone mineral graft (experimental group). After 8 weeks, the animals were sacrificed and the tissues were histologically examined. New cementum with inserting collagen fibers was observed on the exposed surfaces in both groups. The amount of new bone was significantly greater in the group using the bone graft with the membrane than in the control group. The use of the collagen barrier membrane in combination with the porous bone graft material may enhance new bone and cementum formation.

Periodontal Regeneration with an Autogenous Bone-Bio-Oss Composite Graft and a Bio-Gide Membrane

M. Camelo, M. Nevins, S. Lynch, R. Schenk, M. Simion, Myron Nevins
Int J of Periodontics & Restorative Dentistry 2001; 21.



This study evaluated the clinical, radiographic, and histologic response to the composite use of Bio-Oss® porous bone mineral and autogenous bone in combination with a Bio-Gide® bilayer collagen membrane to achieve regeneration when treating human periodontal bone defects. Preoperative recordings for four treatment areas included radiographs, clinical probing depths, and attachment levels; cementum with inserting collagen fibers and new bone formation on the surface of both types of grafts materials. This grafting combination not only compared favorably with the previous use of Bio-Oss® and Bio-Gide®, but exceeded that result with almost complete periodontal regeneration. This human histologic study demonstrated that autogenous bone in combination with porous bone mineral matrix, together with the Bio-Gide® collagen membrane, has the capacity to stimulate substantial new bone and cementum formation with Sharpey's fiber attachment.

A controlled re-entry study on the effectiveness of bovine porous bone mineral used in combination with a collagen membrane of porcine origin in the treatment of intrabony defects in humans.

PM Camargo, V. Lekovic, M. Weinländer, M. Nedic, N. Vasilic, LE Wolinsky, EB Kenney
J Clin Periodontol 2000; 27.

The purpose of this study was to evaluate the clinical effectiveness of a bovine porous bone mineral used in combination with a porcine derived collagen membrane as a barrier in promoting periodontal regeneration in intrabony defects in humans. The study employed a split-mouth design. 22 paired intrabony defects were treated and surgically re-entered 6 months after treatment. Experimental sites were grafted with bovine porous bone mineral and received a collagen membrane for guided tissue regeneration. Control sites were treated with an open flap debridement.
Preoperative pocket depths, attachment levels and trans-operative bone measurements were similar for control and experimental sites. Post surgical measurements revealed a significantly greater reduction in pocket depth (differences of 1.89±0.31 mm on buccal 0.88±0.27 mm on lingual measurements) and more gain in clinical attachment (differences of 1.51±0.33 mm on buccal and 1.50±0.35 mm on lingual measurements) in experimental sites. Surgical reentry of the treated defects revealed a significantly greater amount of defect fill in favor of experimental sites (differences of 2.67±0.91 mm on buccal and 2.54±0.87 mm on lingual measurement). The result of this study indicate that clinical resolution of intrabony defects can be achieved using a combination of bovine porous bone mineral and an absorbable, porcine derived collagen membrane when employing a technique based on the principles of guided tissue regeneration. The nature of the attachment between the newly regenerated tissue and the root surfaces needs to be evaluated histologically to confirm the presence of new attachment.

The Clinical Evaluation of Periodontal Surgery with Porous Bone Graft Material (Bio-Oss®) and Collagen Membrane (Bio-Gide®)

A. Ohazama, H. Kitamura, M. Suzuki, S. Yamada, K. Hasegawa
Journal of the Japanese Society of Periodontology, 41, 1999.

The purpose of this study was to assess the clinical efficacy of the periodontal surgery with porous bone graft material (Bio-Oss®) and collagen membrane (Bio-Gide®). Sixtyseven adult periodontitis patients each having a Class II furcation defects or vertical defects, participated in the study. Mucoperiosteal flaps were elevated and granulation tissue in the defects were debrided with hand instruments. After each defect was filled with Bio-Oss®, Bio-Gide® was positioned over graft material and the defects. The flaps were replaced coronary to cover the membrane ensuring primary closure.
The clinical examination were taken before surgery, at 1, 3 weeks, 3 and 6 months after surgery. Postoperatively, clinical healing generally progressed uneventfully in all patients. The significant differences were found in probing depth and clinical attachment level between pre-surgery and 6 months post-surgery measurements. Mean probing depth was reduced from 6.74±1.17 mm to 3.08±1.17 mm with a mean reduction of 3.67±1.21 mm. Mean clinical attachment level was reduced from 8.39±1.99 mm to 5.60±2.11 mm with a mean clinical attachment gain of 2.79±1.38 mm. The improvement of radioluency at defect area was noted in 48 of 66 patients. The side effect was not observed in any cases. This study revealed that the periodontal surgery with Bio-Oss® and Bio-Gide® is safety and clinical usefulness.

Reconstruction of anatomically complicated periodontal defects using a bioresorbable GTR barrier supported by bone mineral. A 6-month follow-up study of 6 cases

D. Lundgren, C. Slotte
J Clinical Periodontol 1999; 26.

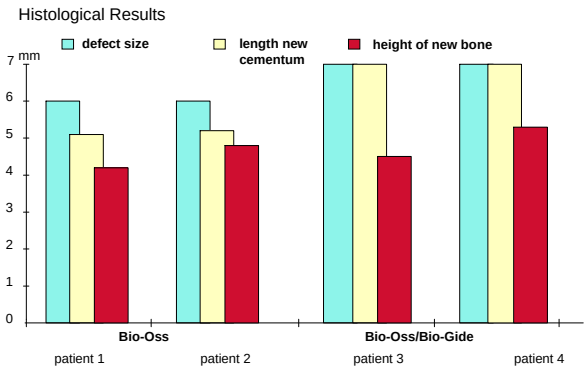
6 anatomically complicated periodontal intrabony defects in 6 patients were surgically reconstructed using a bioresorbable GTR barrier supported by cancellous bovine bone mineral. Following cause-related periodontal treatment open-flap surgery was performed to expose the defects. After debridement, the defects were filled with the bone mineral and covered with the barrier. All patients were advised to rinse 2x daily with an 0.2% chlorhexidine digluconate solution and to avoid brushing in the operated area for 6 weeks. The treatment results were evaluated clinically and radiographically 6 months after surgery. All defects healed uneventfully and all patients maintained a high standard of plaque control throughout the study. Probing assessments during surgery showed a bone defect depth and width of an average 7.2 and 2.8 mm. The corresponding measures on presurgical intra-oral radiographs were 7.9 and 2.6 mm respectively. Clinical attachment level (CAL) gain averaged 5.3 mm, corresponding to 73% of the original bone defect depth. Radiographically, the defect fill averaged 6.2 mm or 80% of the original radiographic bone defect. It was concluded that the placement of bovine bone mineral beneath bioresorbable GTR barriers facilitates

the clinical handling of the barrier and cahances the space for potential periodontal reconstruction of anatomically complicated defects. It remains, however, to be ascertained to what degree the achieved clinical and radiographic results reflect a gain in new connective tissue attachment and alveolar bone.

Clinical, Radiographic, and Histologic Evaluation of Human Periodontal Defects Treated with Bio-Oss® and Bio-Gide®

M. Camelo, M.L. Nevins, R.K. Schenk, M. Simion, G. Rasperini, S.E. Lynch, M. Nevins
Int J Periodontics Restorative Dent 1998; 18(4).

This study evaluated the clinical, radiographic, and histologic response to Bio-Oss® porous bone mineral when used alone or in combination with Bio-Gide® bilayer collagen membrane in human periodontal defects were treated: two received Bio-Oss® alone and two were treated with a combination of Bio-Oss® and Bio-Gide®. Radiographs, clinical probing depths, and attachment levels were obtained preoperatively and 6 to 9 months postoperative, and teeth and surrounding tissues were biopsied. Both treatments significantly improved clinical probing depths and attachment levels, and the radiographic appearance suggested osseous fill.



Histologic evaluation revealed that both treatments produced new cementum with inserting collagen fibers and new bone formation on the surface of the graft particle; this regenerative effect was more pronounced using the Bio-Oss®/Bio-Gide® combination, which resulted in 7 mm of new cementum and periodontal ligament and extensive new bone incorporating the graft (see Fig.). The membrane was intact at 7 months and partially degraded by 9 months after treatment. This human histologic study demonstrates that the porous bone mineral matrix used has the capacity to stimulate substantial new bone and cementum formation and that this capacity is further increased when the graft is used with a slowly resorbing collagen membrane.

b Furcation

Treatment of Class II molar furcation involvement: meta-analyses of reentry results.

Kinaia BM, Steiger J, Neely AL, Shah M, Bhola M.
Periodontol. 2011 Mar;82(3):413-28. Epub 2010 Nov 23.

BACKGROUND: Predictable regeneration of lost periodontal tissues in furcations is difficult to achieve. This paper investigates the efficacy of different treatment modalities for Class II molar furcations. METHODS: Publications in English were searched using PubMed, Medline, and Cochrane Library databases combined with hand searching from January 1, 1966 to October 1, 2007. The search included randomized controlled human trials in molar Class II furcations with over 6 months of surgical reentry follow-up. Changes in vertical probing depths, vertical attachment levels, and vertical and horizontal bone levels were compared. RESULTS: The search identified 801 articles of which 34 of 108 randomized clinical trials met the criteria. Thirteen trials had test and control arms allowing three meta-analyses: 1) five comparing non-resorbable versus resorbable membranes, 2) five comparing non-resorbable membranes versus open flap debridement and 3) three comparing resorbable membranes versus open flap debridement. There was significant improvement for resorbable versus non-resorbable membranes mainly in vertical bone fill (0.77 ± 0.33 mm; [95% CI; 0.13, 1.41]). Non-resorbable membranes showed significant improvement in vertical probing reduction (0.75 ± 0.31 mm; [95% CI; 0.14, 1.35]), attachment gain (1.41 ± 0.46 mm; [95% CI; 0.50, 2.31]), horizontal bone fill (1.16 ± 0.29 mm; [95% CI; 0.59, 1.73]), and vertical bone fill (0.58 ± 0.11 mm; [95% CI; 0.35, 0.80]) over open flap debridement. Resorbable membranes showed significant improvement in vertical probing reduction (0.73 ± 0.16 mm; [95% CI; 0.42, 1.05]), attachment gain (0.88 ± 0.16 mm; [95% CI; 0.55, 1.20]), horizontal bone fill (0.98 ± 0.12 mm; [95% CI; 0.74, 1.21]) and vertical bone fill (0.78 ± 0.19 mm; [95% CI; 0.42, 1.15]) over open flap debridement. CONCLUSIONS: Guided tissue regeneration with the use of resorbable membranes was superior to non-resorbable membranes in vertical bone fill. Both types of membranes were more effective than open flap debridement in reducing vertical probing depths and gaining vertical attachment levels and in gaining vertical and horizontal bone.

A clinical evaluation of anorganic bovine bone graft plus 10% collagen with or without a barrier in the treatment of class II furcation defects.

Reddy KP, Nayak DG, Uppoor AS
J Contemp Dent Pract. 2006 ,7: 60-70

The use of bone replacement grafts with barrier membranes in class II furcation defects are aimed at improving the outcome of the regenerative technique. In this regard, however, there is a paucity of studies comparing the results obtained with bone grafts alone or in combination with barrier membranes. The aim of this study was to clinically compare an anorganic bovine bone graft plus 10% collagen (BO) with or without a bioresorbable collagen barrier (BG) in human mandibular molar class II furcation defects. METHODS AND MATERIALS: Twenty mandibular class II furcation defects (ten patients with bilateral defects) were treated either with BO (group I) or a combination of BO/BG (group II). Each defect was randomly assigned to either group I or group II. The soft tissue and hard tissue measurements including vertical probing depth (VPD), horizontal probing depth (HPD), clinical attachment level (CAL), gingival recession (GR), vertical depth of furcation defect (VDF), and horizontal depth of furcation defect (HDF) were recorded at baseline and six months after surgery. RESULTS: Both treatment procedures resulted in statistically significant reduction in VPD and HPD, gain in CAL, and reduction in VDF and HDF. There was a statistically significant difference between group I and group II in all soft and hard tissue parameters with the exception of VPD reduction and gingival recession. CONCLUSION: The findings of this study suggest superior clinical results with BO/BG treatment when compared to BO treatment in mandibular class II furcation defects.

c *Peri-implant defects*

Long-term outcome of implants placed with guided bone regeneration (GBR) using resorbable and non-resorbable membranes after 12-14 years

Jung RE, Fenner N, Hämmerle CH, Zitzmann NU.
Clin Oral Implants Res 2012

AIM: The aim of the present prospective study was to evaluate the long-term outcome of implants placed simultaneously with guided bone regeneration (GBR) using resorbable and non-resorbable membranes. MATERIALS AND METHODS: The original study population consisted of 72 patients receiving a total of 265 implants. In all GBR-treated sites, demineralized bovine bone mineral (DBBM) was used in combination either with a collagen (CM) or an Expanded polytetrafluoroethylene (e-PTFE) membrane. A total of 112 implants was treated with CM, 41 implants were treated with e-PTFE membranes, and 112 served as a control group because implants were entirely surrounded by bone and did not need any GBR procedures. Clinical and radiographic analyses were performed after a period of 12-14 years. RESULTS: The median follow-up time was 12.5 years (range 12-14 years). A total of 58 patients participated in the present investigation, corresponding to 80.5% of the original study population. The cumulative implant survival rate at the follow-up examination was 93.2%. For the control group the cumulative survival rate was 94.6%, for the CM 91.9%, and for the e-PTFE 92.6%. Differences among the groups were not statistically significant. The radiographically determined marginal bone level (MBL) amounted to: CM 2.36 mm (SD), e-PTFE 2.4 mm (SD), control 2.53 mm (SD). There is no evidence ($P < 0.2$) that the slope of bone level over time is different for the three treatment groups. CONCLUSION: It is concluded that implants placed simultaneously with GBR procedures using resorbable or non-resorbable membranes reveal a high survival rate ranging from 91.9% to 92.6%, therefore it is considered to be a safe and predictable therapy.

Use of a new cross-linked collagen membrane for the treatment of peri-implant dehiscence defects: a randomised controlled double-blinded clinical trial

Annen BM, Ramel CF, Hämmerle CH, Jung RE.
Eur J Oral Implantol 2011;4(2):87-100.

PURPOSE: The aim of this randomised controlled double-blinded clinical trial was to determine the efficacy of a new cross-linked membrane (VN) in guided bone regeneration (GBR) around exposed dental implants compared to a native collagen membrane (BG). MATERIAL AND METHODS: A total of 16 patients in need of implant treatment at two different sites with osseous defects were planned for this split-mouth study. After inserting the dental implants, peri-implant defects were treated according to the GBR technique using a VN membrane with prolonged resorption time in the randomised test site and a BG membrane in the control site. After a healing time of 6 months, mucoperiosteal flaps were elevated for the evaluation of the primary (vertical bone fill [DeltaDL] and quality of newly formed tissue [QT]) and secondary outcome variables (infrabony defect height [DH], defect width [DW], defect depth [DD] and augmentation depth [AD]) and the sampling of biopsies apical to the implant shoulder. RESULTS: A total of 16 patients fulfilled the initial non-surgical inclusion and exclusion criteria. However, the study was discontinued early after 9 surgically treated patients because unacceptable safety issues arose and severe infection related to the VN membranes. The VN membrane revealed statistically significantly more soft tissue dehiscence than the BG membrane (56% and 11%, respectively, $P = 0.0455$). In 3 of these 9 patients the VN membrane had to be removed due to infection early after the first follow-up visit. For the statistical analyses these sites were designated as the value of the baseline. The mean DeltaDL values were 1.8 +/- 1.6 mm at the VN site and 4.7 +/- 3.3 mm at the BG site. The DeltaDD values were 0.6 +/- 1.0 mm and 1.1 +/- 1.2 mm, respectively, and reached statistical significance ($P = 0.0208$, CI 95% = -2.9 [-5.2;-0.6]). The corresponding linear defect fill (DF) values were 44% and 78%, respectively. The clinical assessment of QT showed comparable median values at sites treated with VN (3, interquartile range: 0; 3.5) and BG (3, interquartile range: 3; 4) without statistical significance. The histomorphometric analysis showed an average area density of 24.4% (SD 10.3, range 8-35%) newly formed bone at the test sites and of 35.0% (SD 20.6, range 8-60%) at the control sites. The histological data showed only some trends and did not reach statistical significance. CONCLUSION: In the present study, the VN membranes with prolonged resorption time demonstrated significantly more adverse events and insufficient bone regeneration compared to the native BG membranes and no advantages in favour of the VN membranes were detectable.

Long-term follow-up on soft and hard tissue levels following guided bone regeneration treatment in combination with a xenogeneic filling material: a 5-year prospective clinical study

Dahlin C, Simion M, Hatano N.
Clin Implant Dent Relat Res 2010;12(4):263-70.

PURPOSE: In the present prospective study, bone augmentation by guided bone regeneration (GBR) in combination with bovine hydroxyapatite (BHA) as filling material was evaluated with regard to soft and hard tissue stability over time. MATERIALS AND METHODS: Implant survival, radiologic bone level (marginal bone level [MBL]), and clinical soft tissue parameters (marginal soft tissue level [MSTL]) were observed. Twenty patients received a total of 41 implants (Branemark System, Nobel Biocare, Goteborg, Sweden) in conjunction with GBR treatment. The end point of the study was after 5 years following implant placement. RESULTS: The cumulative implant survival rate was 97.5% corresponding to one implant failure. The radiologic evaluation of the MBL demonstrated a crestal bone height above the level of the fixture head. The bone height decreased from -3.51 to -2.38 mm ($p < .001$). The MSTL was -1.52 mm at baseline and -1.15 mm at the 5-year follow-up ($p < .04$) demonstrating a stable submucosal crown margin throughout the study period. CONCLUSION: GBR treatment in combination with a xenogeneic filling material (BHA) is a viable treatment option in order to maintain stable hard and soft tissue levels in conjunction with augmentative procedure related to oral implant treatment.

Use of a new cross-linked collagen membrane for the treatment of dehiscence-type defects at titanium implants: a prospective, randomized-controlled double-blinded clinical multicenter study

Becker, J., B. Al-Nawas, et al.
Clin Oral Implants Res. 2009; doi: 10.1111/j.1600-0501.2008.01689.x

Abstract Objectives: The aim of the present randomized-controlled double-blinded clinical multicenter study was to assess the use of either a new cross-linked (VN) or a native collagen membrane (BG) for the treatment of dehiscence-type defects at titanium implants. Material and methods: A total of n=54 patients were recruited in four German university clinics. According to a parallel-groups design, dehiscence-type defects at titanium implants were filled with a natural bone mineral and randomly assigned to either VN or BG. Submerged sites were allowed to heal for 4 months. Primary (e.g., changes in defect length -DeltaDL, quality of newly formed tissue [0-4] - TQ) and secondary parameters (e.g., membrane exposure, tissue conditions at dehisced sites) were consecutively recorded. Results: Four patients were excluded due to an early wound infection (VN:3; BG:1), and one patient was lost during follow-up (VN). The mean DeltaDL was 3.0 +/- 2.5 mm in the VN, and 1.94 +/- 2.13 mm in the BG group. The assessment of TQ revealed comparable mean values in both groups (VN: 3.05 +/- 1.66, BG: 3.46 +/- 1.48). A significant correlation between membrane exposure and inflammation of the adjacent soft tissue was observed in the VN group. In both groups, the mean DL and TQ values were not significantly different at either non-exposed or exposed implant sites. Conclusion: The results of the present study have indicated that VN supported bone regeneration on a level non-inferior to BG. However, in case of a premature membrane exposure, cross-linking might impair soft-tissue healing or may even cause wound infections.

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

Schwarz F, Sculean A, et al.
J Clin Periodontol, 2008; 35(1): 80-7.

Objectives: The aim of the present case series was to evaluate the 2-year results obtained following treatment of peri-implantitis lesions using either a nanocrystalline hydroxyapatite (NHA) or a natural bone mineral in combination with a collagen membrane (NBM+CM). Material and Methods: Twenty-two patients suffering from moderate peri-implantitis (n=22 intra-bony defects) were randomly treated with (i) access flap surgery (AFS) and the application of NHA, or with AFS and the application of NBM+CM. Clinical parameters were recorded at baseline and after 12, 18, and 24 months of non-submerged healing. Results: Two patients from the NHA group were excluded from the study due to severe pus formation at 12 months.

At 24 months, both groups revealed clinically important probing depth (PD) reductions (NHA: 1.5+/-0.6 mm; NBM+CM: 2.4+/-0.8 mm) and clinical attachment level (CAL) gains (NHA: 1.0+/-0.4 mm; NBM+CM: 2.0+/-0.8 mm). However, these clinical improvements seemed to be better in the NBM+CM group (difference between groups: PD reduction: 0.9+/-0.2 mm; CAL gain: 1.0+/-0.3 mm). Conclusion: Both treatment procedures have shown efficacy over a period of 24 months, however, the application of NBM+CM may result in an improved outcome of healing.

Healing of intrabony peri-implantitis defects following application of a nanocrysalline hydroxyapatite (Ostim) or a bovine-derived xenograft (Bio-Oss) in combination with a collagen membrane (Bio-Gide). A case series.

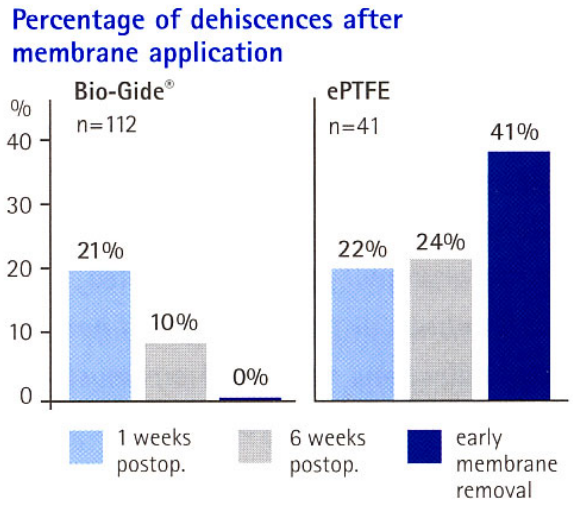
Schwarz F, Bieling K, Latz T, Nuesry E, Becker J.
J Clin Periodontol, 2006; 33(7): 491-499

OBJECTIVES: The aim of the present case series was to evaluate the healing of intrabony peri-implantitis defects following application of a nanocrystalline hydroxyapatite (NHA) or a bovine-derived xenograft in combination with a collagen membrane (BDX+BG). MATERIAL AND METHODS: Twenty-two patients having moderate peri-implantitis (n=22 intrabony defects) were randomly treated with (i) access flap surgery (AFS) and the application of NHA, or with AFS and the application of BDX+BG. Clinical parameters were recorded at baseline and after 6 months of non-submerged healing. RESULTS: Post-operative wound healing revealed that NHA compromized initial adhesion of the mucoperiosteal flaps in all patients. At 6 months after therapy, NHA showed a reduction in the mean PD from 7.0+/-0.6 to 4.9+/-0.6 mm and a change in the mean clinical attachment loss (CAL) from 7.5+/-0.8 to 5.7+/-1.0 mm. In the BDX+BC group, the mean PD was reduced from 7.1+/-0.8 to 4.5+/-0.7 mm and the mean CAL changed from 7.5+/-1.0 to 5.2+/-0.8 mm. CONCLUSION: Within the limits of the present case series, it can be concluded that at 6 months after surgery both therapies resulted in clinically important PD reductions and CAL gains.

Long-term Results of Implants Treated with Guided Bone Regeneration: A 5-year Prospective Study

N. Zitzmann, P. Schärer, C. Marinello
Int J of Oral & Maxillofac Implants 2001; 16(3).

The aim of this prospective 5-year longitudinal study was to follow endosteal implants in which guided bone regeneration (GBR) was applied during implant placement. In 75 patients, defects around implants (Branemark System) were treated with Bio-Oss® and Bio-Gide® (112 implants). In split-mouth patients in this group, Bio-Oss® and Gore-Tex were used in the second defect site (41 implants). All 75 patients had at least 1 implant that was entirely surrounded by bone and served as the control (112 implants). After placement of the definitive prostheses (single-tooth, fixed, or removable implant prostheses), patients were recalled after 6 months and then every 12 months during a 5-year observation period. The following variables were investigated: implant survival, marginal bone level (MBL), presence of plaque, peri-implant mucosal conditions, height of keratinized mucosa (KM), and marginal soft tissue level (MSTL). The cumulative implant survival rate after 5 years varied between 93% and 97% for implants treated with or without GBR. The mean MBL after 60 months was 1.83 mm for sites treated with Bio-Oss® and Bio-Gide®, 2.21 mm for sites treated with Bio-Oss® and Gore-Tex, and 1.73 mm for the control sites. The MBL values were found to increase significantly with time and differed significantly among the treatment groups. During the observation period, KM varied between 3.16 and 3.02 mm. A slight recession of 0.1 mm was observed, and plaque was found in 15% of all sites and was associated with inflammatory symptoms of the peri-implant mucosa. It was observed that such symptoms and recession correlated more strongly with the type of restoration than with the type of treatment. This study demonstrated that implants placed with or without GBR techniques had similar survival rates after 5 years, but that bone resorption was more pronounced in sites with GBR treatment. It was assumed that the use of GBR is indeed indicated when the initial defect size is larger than 2 mm in the vertical dimension.



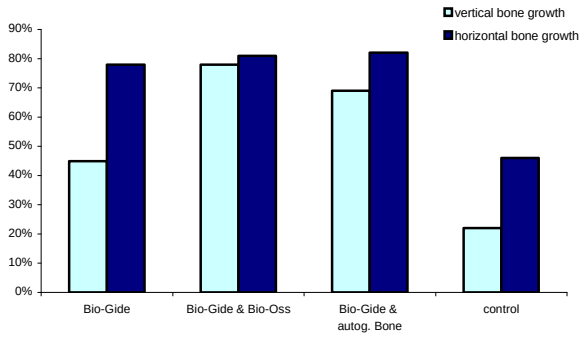
Single stage surgery combining transmucosal implant placement with guided bone regeneration and bioresorbable materials

Hämmerle CH, Lang NP
Clin Impl Res 2001; 21.

The aim of the present clinical study was to test whether peri-implant bone defects can successfully be filled with bone by applying bioresorbable materials for guided bone regeneration (GBR) procedures in conjunction with implants in the transmucosal healing position. Three women and 7 men ranging in age from 32 to 68 years (median 54.5) needed tooth replacement with dental implants. Eight to 14 weeks following careful tooth extraction, implants of the ITI Dental Implant System were placed at the extraction sites. At this time, all implants presented dehiscence defects of the alveolar bone partly exposing the rough titanium plasma sprayed (TPS) surfaces. GBR procedures were performed using deproteinized bovine bone mineral (Bio-Oss) as a membrane-supporting material and a bioresorbable collagen membrane (Bio-Gide) as a barrier. The membranes and the flaps were adjusted to fit around the necks of the implants, thus leaving the implants extending transmucosally into the oral cavity. Clinical measurements were taken at 6 sites around each implant (mesio-buccal, buccal, disto-buccal, disto-lingual, lingual, mesio-lingual) using a calibrated periodontal probe. These included: i) defect depth measured from the shoulder of the implant to the first bone-to-implant contact, ii) infrabony defect component measured from the bone crest to the first bone-to-implant contact, iii) defect width measured from the crest to the implant body in a direction perpendicular to the long axis of the implant. The Wilcoxon Matched Pairs Signed Rank Test was applied to detect differences over time. At baseline, the mean defect depth per patient amounted to 3.6 mm (Standard Deviation 1.6 mm, range 1.8-6.8 mm). The deepest extensions of the defects were located at the buccal aspects (mean 7.8 mm, SD 1.9 mm). At re-entry, the mean defect had decreased to 2.5 mm (SD 0.6 mm). This difference was statistically significant ($P < 0.01$). Initially, in 62% of sites the depth ranged from 0-3 mm, in 23% it ranged from 2-4 mm, and in 15% it amounted to more than 6 mm. Six to 7 months later, at re-entry, 95% of sites were 3 mm and less in depth and 5% ranged from 4-6 mm. Defect resolution, as assessed by the amount of coverage of the initially exposed rough implant surface, reached a mean value of 86% (SD 33%). One hundred percent resolution was accomplished at 8 out of 10 implants, 60% at one and 0% at another implant. The tissue at the latter implant showed signs of infection and inflammation during the healing phase. It is concluded that bioresorbable materials in GBR procedures at transmucosal implants can lead to successful bone regeneration into peri-implant defects.

The combined use of bioresorbable membranes and xenografts or autografts in the treatment of bone defects around implants - A study in beagle dogs

Hockers T, Abensur D, Valentini P, Legrand R, Hämmerle CHF
Clin Oral Impl Res 1999; 10.



The aim of the present investigation was to test the effect of a bioresorbable membrane supported by xenografts or autografts in regenerating bone into peri-implant defects. In 3 dogs, the mandibular premolars P_2, P_3, P_4 and M_1 were extracted bilaterally. After 4 months of healing, 3 standardized bone defects were prepared on each side of the mandible and 2 implant per defect was placed. The 6 sites in

each dog were distributed into 4 different treatment groups: 2 sites received a Bio-Gide® membrane alone 2 sites received a Bio-Gide® membrane supported by Bio-Oss®; 1 site received the Bio-Gide® membrane supported by autogenic bone harvested from the prepared defects; 1 site received neither membrane nor bone graft and served as control (C). The soft tissue flaps were adapted and sutured for primary healing. No adverse events occurred during the experimental period. After 16 weeks, the dogs were sacrificed and histomorphometric examinations on non-decalcified ground sections were carried out (see Fig.2). The surface fraction of the graft in direct bone contact measured 89% (SD±9%) in the Bio-Gide® + Bio-Oss® group and 93% (SD±3%) in the Bio-Gide® + Aut group. It is concluded that the bioresorbable membrane tested enhances bone regeneration, in particular in conjunction with the use of a supporting graft material. In addition, deproteinized bovine bone mineral and autogenic bone grafts appeared to be equally well integrated into regenerating bone. Finally, no additional effects in the bone growth was observed with the autogenous bone in comparison with the hydroxyapatite.

The effect of a deproteinized bovine bone mineral (Bio-Oss®) on bone regeneration around titanium dental implants

Hämmerle CHF, Chiantella GC, Karring T., Lang NP
Clin Oral Impl Res 1998; 9.

The aim of the present experiment was to test the effect of a bovine bone mineral (Bio-Oss®) on guided bone regeneration (GBR) in dehiscence defects around implants. The first 2 molars and all premolars were extracted on both sides of the mandible of 3 monkeys (Macaca fascicularis). Three months later, 2 titanium plasma-coated cylindrical implants were placed in all quadrants of each monkey. During the surgical procedure, standardized dehiscence defects were produced buccally and lingually, measuring 2.5 mm in with and 3 mm in height. Four different experimental situations were created: 2 sites in each monkey were covered with an ePTFE membrane (M), 2 were filled with the graft material (Bio-Oss®), 2 were filled with the graft material and also covered with a membrane (M+Bio-Oss®), and 2 control sites were neither grafted nor covered (C). The flaps were sutured to allow for primary healing. Linear measurements of bone height and width were calculated on histological specimens obtained 6 months following surgery. In addition, values for bone density and for surface fraction of graft to new bone contact were measured. Vertical bone growth along the implant surface of 100% (SD 0%) for M+Bio-Oss® , 91% (SD 9%) for M, 52% (SD 24%) for Bio-Oss®, and 42% (SD 35%) for C was measured. The width of the regenerated bone 1.5 mm above the bottom of the original defect, i.e. at the 50% mark of the vertical extension of the defect, in relation to the width at the bottom of the defect amounted to 97% (SD 2%) for M+Bio-Oss®, 85% (SD 9%) for M, 42% (SD 41%) for Bio-Oss®, and 23% (SD 31%) for C. Assessment of bone density within the confinement of the regenerated bone resulted in an increase of 30% (SD 11%) for M+Bio-Oss®, 45% (SD 20%) for M, 33% (SD 20%) for Bio-Oss®, and 22% (SD 23%) for C. The values for graft to new bone contact within this compartment amounted to 80% (SD 15%) for M+Bio-Oss® and 89% (SD 14%) for Bio-Oss®. In conclusion, Bio-Oss® exhibited osteoconductive properties and hence can be recommended for GBR procedures in dehiscence defects with respect to vertical and horizontal growth of bone.

Evaluation of a new bioresorbable barrier to facilitate guided bone regeneration around exposed implant threads . An experimental study in the monkey.

M.B. Hürzeler, R.J. Kohal, J. Naghshbandi, L.F. Mota, J. Conradt, D. Hutmacher, R.G. Caffesse
Int J Oral Maxillofac Surg 1998 ; 27.

The aim of this study was to evaluate the effectiveness of a new bioresorbable barrier (Bio-Gide®) alone or in combination with Bio-Oss® for guided bone regeneration around dental implants with exposed implant threads. Five adult Macaca fascicularis monkeys were used in this investigation. After extraction of all premolars and first molars, two endosteal oral implants were installed in each quadrant and the bony defects were randomly treated with either: 1) placement of the new bioresorbable device alone (group 1); 2) placement of the new bioresorbable barrier in combination with Bio-Oss® (group 2); 3) placement of an ePTFE barrier in combination with Bio-Oss® (group 3); or (4) control (group 4). After a period of six months the animals were killed and the histological processing was performed. There was a significant difference in the amount of new bone regeneration around the implants between the four groups (i.e. groups 1, 2, 3 and 4) (P=0.0122). There was no difference, however, between group 2 and group 3. It can be concluded that the new bioresorbable barrier (Bio-Gide®) in combination with Bio-Oss® appears to obtain the same results in this type of bony defects as the grafting material in combination with an ePTFE barrier.

Resorbable Versus Nonresorbable Membranes in Combination with Bio-Oss for Guided Bone Regeneration

N. Zitzmann, R. Naef, P. Schärer
Int J Oral Maxillofac Implants 1997 ; 12.

The purpose of this clinical investigation was to compare the new resorbable collagen membrane, Bio-Gide®, to the conventional expanded polytetrafluoroethylene material (Gore-Tex®) for guided bone regeneration in situations involving exposed implant surfaces. Over a 2-year period, 25 split-mouth patients were treated randomly: one defect site was treated with Bio-Gide® and the other defect site with Gore-Tex®; all 84 defects were filled with Bio-Oss® and covered with the respective membrane. The defect types, their dimensions, and their morphology were measured in detail initially and at re-entry to allow for calculation of the exposed implant surface. Changes in defect surface for both types of membranes were statistically significant (P< .0001); however, no statistical significance (P> .94) could be detected between the two membranes (see Fig.). The mean average percentage of bone fill was 92% for Bio-Gide® and 78% for Gore-Tex® sites. In the latter group, 44% wound dehiscences and/or premature membrane removal occurred. The resorbable membrane, Bio-Gide®, in combination with a bone graft, can be a useful alternative to the well-established expanded polytetrafluoroethylene membranes.

Awarded the 1st prize in Research Competitions of the Academy of Osseointegration, New York, Feb. 1996

Bone Regeneration around Implants: a Clinical Study with a New Resorbable Membrane

Hürzeler M.B., Weng D., Hutmacher D.
Deutsche Zahnärztliche Zeitschrift, 1996; 51(5).

The aim of this clinical study was to evaluate the bone regeneration potential of a new bioresorbable barrier (Bio-Gide®) in combination with a bone grafting material (Bio-Oss®) at dehiscent implant sites. In addition, new bioresorbable pins were used for the barrier fixation. 35 titanium dental implants with exposed threads in 15 patients were studied. After defect measurements the space was filled with Bio-Oss® and covered with a Bio-Gide® barrier. The barrier was fixed with three to four bioresorbable pins. Six months after installation of the implants the second stage surgery was performed and the remaining defects were clinically measured. In four patients biopsies were taken. After eight weeks one barrier became exposed and was removed. The regenerated areas were reentered after an uneventful healing period of 24 to 28 weeks. The percentage of bone fill at reentry showed complete regeneration in 22 out of 35 implants. The histologic examination of the specimens indicated a significant amount of new bone growth around the Bio-Oss® particles underneath the barriers. Within the limits of this clinical study the new bioresorbable barrier (Bio-Gide®) in combination with Bio-Oss® seems to enhance bone formation around dehisced dental implants.

Immediate or delayed immediate implantation versus late implantation when using the principles of guided bone regeneration

N. Zitzmann, R. Naef, P. Schüpbach, P. Schärer
Acta Med Dent Helv 1996; 1(10).

The aim of the present clinical study is to investigate the influence of the time of implantation on the guided bone regeneration of implant defects. 79 implants of the Brånemark type were inserted in 50 patients, and after detailed measurement their bone defects were filled with Bio-Oss® and covered with Bio-Gide® membranes. After a mean average increase in bone of 83% (p=0.0001), the immediate and delayed immediate implants offered a better result (89% and 86% respectively) than late implantation (76%). The difference was not, however, significant. The earlier time is associated with a better defect morphology for GBR and permits the insertion of longer fixtures, since the resorption process is not yet advanced. The appearance of wound dehiscence did not significantly influence the reduction of defects. The barrier function of the Bio-Gide® membrane could be verified; and the bone substitute material Bio-Oss® was shown histologically to be osseoconductive.

d others

Periosteal Distraction Osteogenesis and Barrier Membrane Application: An Experimental Study in the Rat Calvaria

Saulacic N, Schaller B, Bosshardt DD, Buser D, Jaun P, Haeniwa H, Iizuka T.
J Periodontol 2011

Background: Distraction of the periosteum results in the formation of new bone in the gap between the periosteum and the original bone. We postulate that the use of a barrier membrane would be beneficial for new bone formation in periosteal distraction. Method: To selectively influence the contribution of the periosteum, a distraction plate with perforations was used alone or covered by a collagen barrier membrane. All animals were subjected to a 7-day latency period and a 10-day distraction period with a rate of 0.1 mm per day. Four animals per group without or with a barrier membrane were sacrificed at 2, 4 and 6 weeks after the end of the distraction. The height of new bone generated relative to the areas bound by the parent bone and the periosteum was determined histomorphometrically. Results: New bone was found in all groups. At the periphery of the distraction plate, significant differences in bone height were found between the hinge and the distraction screw for the group without barrier membrane at 2 weeks (0.39?0.19 mm) compared to 4 weeks (0.84?0.44 mm, p=0.002) and 6 weeks (1.06?0.39 mm; p=0.004). Differences in maximum bone height with and without a barrier membrane were observed laterally to the distraction plate at 2-week (1.22?0.64 mm versus 0.55?0.14 mm; p=0.019) and 6-week of consolidation period (1.61?0.56 mm versus 0.73?0.33 mm; p=0.003). Conclusion: Within the limitations of the present study, the application of a barrier membrane may be considered beneficial for new bone formation induced by periosteal distraction.

Effect of bovine bone and collagen membranes on healing of mandibular bone blocks: a prospective randomized controlled study

Cordaro L, Torsello F, Morcavallo S, di Torresanto VM.
Clin Oral Implants Res 2011

Aim: The aim of the present study was to evaluate if the use of deprotenized bovine bone mineral (DBBM) and collagen barrier membranes (CM) in combination with mandibular bone block grafts could reduce bone block graft resorption during healing. Methods: A prospective randomized controlled study has been designed. Twenty-two ridges presenting horizontal alveolar deficiency (crest width <4 mm) and at least two adjacent missing teeth were included in the study. In the control group, one or multiple mandibular blocks were used to gain horizontal augmentation of the ridge. In the test group, DBBM granules were added at the periphery and over the graft. The reconstructions were covered by two layers of CM. Implants were placed 4 months after grafting. Direct measurements of crest width were performed before and immediately after bone augmentation, and immediately before implant placement. Results: Statistical analysis showed no significant differences in crest width between test and control groups at baseline and immediately after grafting. Mean augmentation at first surgery in the test group was 4.18 vs. 4.57 mm in the control group. Final gain obtained at the time of implant placement was 3.93 mm in the test and 3.67 mm in the control groups. The difference in mean graft resorption between test and control sites was statistically significant (0.25 mm in the test group vs. 0.89 mm in the control group, P=0.03). Complications seem to occur more often in the test group (complications recorded in three cases in the test group vs. one complication recorded in the control group). In all cases, implants could be placed in the planned sites and a total of 55 implants were placed (28 in the test group and 27 in the control group). All implants could be considered successfully integrated at the 24-month follow-up visit. Conclusion: The results from this study showed that the addition of bovine bone mineral and a CM around and over a mandibular bone block graft could minimize graft resorption during healing. On the other hand, the use of bone substitutes and barrier membranes in combination with block grafts increased the frequency of complications and the difficulty of their management.

The effect of enamel matrix derivative (Emdogain) on bone formation: a systematic review

Rathe F, Junker R, Chesnutt BM, Jansen JA.

Tissue Eng Part B Rev. 2009;15(3):215-24.

This systematic review focused on the question, if and to what extent enamel matrix derivative (Emdogain) [EMD]) promotes the regeneration of bone. The influence of combinations with other biomaterials was additionally evaluated. Twenty histomorphometric studies were included in this systematic review. Main results of the reviewed articles were (i) guide tissue regeneration (GTR) of infrabony defects seems to result in a higher degree of bone regeneration compared to treatment with EMD; (ii) combined therapy (GTR + EMD) of infrabony defects might not lead to better results than GTR therapy alone; (iii) there seems to be no additional benefit of combined therapy (GTR + EMD) in furcation defects over GTR therapy alone; (iv) EMD seems to lead to more bone regeneration of infrabony defects compared to open flap debridement; (v) however, EMD application might result in more bone formation when applied in supporting defects compared to nonsupporting defects; and (vi) EMD does not seem to promote external jaw/parietal bone formation in the titanium capsule model. The results of one study that suggest that EMD increases the initial growth of trabecular bone around endosseous implants by new bone induction need to be confirmed by additional research.

Efficacy of guided tissue regeneration in the management of through-and-through lesions following surgical endodontics: a preliminary study

Taschieri S, Del Fabbro M, Testori T, Saita M, Weinstein R.
Int J Periodontics Restorative Dent, 2008; 28(3): 265-271.

The purpose of this prospective study was to assess the outcome of periradicular surgery with or without guided tissue regeneration (GTR) for the treatment of through-and-through lesions. Thirty-four teeth were included according to specific selection criteria. In the test group (using GTR), after root-end filling, the defects were filled with anorganic bovine bone and covered with a resorbable collagen membrane. Healing was assessed according to specific criteria and graded as successful, doubtful, or failed. In the control group, neither grafts nor membranes were used. After 1 year, 31 teeth were evaluated. Of these, 22 (71%) healed successfully, 6 (19%) showed doubtful healing, and 2 were recorded as failures. The outcomes of the defects treated with GTR (88% successful) were significantly better than those of the control group (57% successful). The present study showed that the use of GTR associated with anorganic bovine bone in the treatment of through-and-through lesions may positively affect the healing process.

Treatment of Angular Bone Defects with a Composite Bone Grafting Material in Combination with a Collagen Membrane

Zitzmann N, Rateitschak-Plüss E, Marinello C.
J Periodontol 2003; 74: 687-694,

BACKGROUND: The purpose of this study was to evaluate the effect of a bioabsorbable collagen barrier (CB) in combination with a composite bone substitute (deproteinized bovine bone mineral with collagen, DBBM + C) in periodontal regeneration of angular bone defects in humans using a new application technique. METHODS: Twelve patients participated, each contributing at least 1 defect site, which exhibited a probing depth (PD) of > or = 5 mm, a clinical attachment level (CAL) of > or = 6 mm, and was positive for bleeding on probing (BOP) following initial therapy. Twenty-two angular bone defects were filled with DBBM + C. A hole was placed in the membrane, which was then pulled over the tooth. The observation period was 2 years and included measurements of plaque, gingivitis, tooth mobility, PD, CAL, soft tissue recession, and bone level as assessed from standardized radiographs. RESULTS: The residual PD and CAL were reduced to 3.3 mm (PD) and 5.6 mm (CAL) with a CAL gain of 3.2 mm at 24 months. The radiographic defect reduction (bone fill) was 4.0 mm after surgery and 2.2 mm at 24 months. The changes measured clinically and radiographically were more pronounced in sites with a deep intrabony defect component than in sites with shallow ones. CONCLUSIONS: These findings indicate that angular bone defects can be successfully treated with DBBM + C in combination with CB. A degradation of the filler material seems to occur particularly during the first 6 months, but without affecting the clinical parameters, which improved consistently

6. Peri-Implantitis

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.

Schwarz, F., N. Sahm, et al.
J Clin Periodontol 2009; 36(9): 807-14.

OBJECTIVES: The present case series aimed at investigating the 4-year clinical outcomes following surgical regenerative therapy of peri-implantitis lesions using either a nanocrystalline hydroxyapatite (NHA) or a natural bone mineral in combination with a collagen membrane (NBM+CM). MATERIALS AND METHODS: Twenty patients suffering from moderate peri-implantitis (n=20 intrabony defects) were randomly treated with (1) access flap surgery (AFS) and the application of NHA (n=9), or with AFS and the application of NBM+CM (n=11). Clinical and radiographic (R) parameters were recorded at baseline (R) and after 36 and 48 (R) months of non-submerged healing. RESULTS: One patient from the NBM+CM group was discontinued from the study due to severe pus formation at 36 months. Compared with NHA, the application of NBM+CM resulted in higher mean PD reductions (NBM+CM: 2.5 +/- 0.9 mm versus NHA: 1.1 +/- 0.3 mm) and clinical attachment-level gains (NBM+CM: 2.0 +/- 1.0 mm versus NHA: 0.6 +/- 0.5 mm) at 48 months. A radiographic bone fill was observed for five sites in the NHA group, and eight sites in the NBM+CM group. CONCLUSION: While the application of NBM+CM resulted in clinical improvements over a period of 4 years, the long-term outcome obtained with NHA without barrier membrane must be considered as poor.

The efficacy of interventions to treat peri-implantitis: a Cochrane systematic review of randomised controlled clinical trials

Esposito M, Grusovin MG, Coulthard P, Worthington HV.
Eur J Oral Implantol 2008; 1(2): 111-125.

Objectives: To identify the most effective interventions for treating peri-implantitis around osseointegrated dental implants. Data sources: The Cochrane Oral Health Group's Trials Register, CENTRAL, MEDLINE and EMBASE were searched and several journals were handsearched with no language restriction up to January 2008. Review methods: Randomised controlled trials (RCTs) comparing interventions for treating peri-implantitis were eligible. Screening of studies, quality assessment and data extraction were conducted in duplicate. Missing information was requested. Outcome measures were: implant failure; complications; changes in radiographic marginal bone level, probing 'attachment' level (PAL), probing pocket depth (PPD), and recession; aesthetics evaluated by patients and dentists; cost and treatment time. Results: Ten eligible trials were identified, and seven were included (148 patients). They tested: (1) local antibiotics vs ultrasonic debridement; (2) adjunctive local antibiotics to debridement; (3) different techniques of subgingival debridement; (4) laser vs manual debridement and chlorhexidine irrigation/ gel; (5) systemic antibiotics plus resective surgery plus two local antibiotics with and without implant surface smoothening; and (6) nanocrystalline hydroxyapatite vs Bio-Oss and resorbable barriers. Follow up ranged from 3 months to 2 years. After 4 months, adjunctive local antibiotics to manual debridement in patients who lost at least 50% of peri-implant bone showed improved PAL and PPD (0.6 mm). After 6 months, peri-implant infrabony defects > 3 mm treated with Bio-Oss and barriers gained 0.5 mm more PAL and PPD than those treated with hydroxyapatite. In four trials subgingival mechanical debridement seemed to achieve results similar to more complex therapies. Conclusions: There is very little reliable evidence suggesting which could be the most effective interventions for peri-implantitis. Sample sizes were too small and follow up too short. This is not to say that currently used interventions are ineffective. Larger well-designed RCTs are needed.

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

Schwarz F, Sculean A, et al.
J Clin Periodontol 2008; 35(1): 80-7.

Objectives: The aim of the present case series was to evaluate the 2-year results obtained following treatment of peri-implantitis lesions using either a nanocrystalline hydroxyapatite (NHA) or a natural bone mineral in combination with a collagen membrane (NBM+CM). Material and Methods: Twenty-two patients suffering from moderate peri-implantitis (n=22 intra-bony defects) were randomly treated with (i) access flap surgery (AFS) and the application of NHA, or with AFS and the application of NBM+CM. Clinical parameters were recorded at baseline and after 12, 18, and 24 months of non-submerged healing. Results: Two patients from the NHA group were excluded from the study due to severe pus formation at 12 months. At 24 months, both groups revealed clinically important probing depth (PD) reductions (NHA: 1.5+/-0.6 mm; NBM+CM: 2.4+/-0.8 mm) and clinical attachment level (CAL) gains (NHA: 1.0+/-0.4 mm; NBM+CM: 2.0+/-0.8 mm). However, these clinical improvements seemed to be better in the NBM+CM group (difference between groups: PD reduction: 0.9+/-0.2 mm; CAL gain: 1.0+/-0.3 mm). Conclusion: Both treatment procedures have shown efficacy over a period of 24 months, however, the application of NBM+CM may result in an improved outcome of healing.

Healing of intrabony peri-implantitis defects following application of a nanocrysalline hydroxyapatite (Ostim) or a bovine-derived xenograft (Bio-Oss) in combination with a collagen membrane (Bio-Gide). A case series.

Schwarz F, Bieling K, Latz T, Nuesry E, Becker J.
J Clin Periodontol 2006; 33(7): 491-499.

OBJECTIVES: The aim of the present case series was to evaluate the healing of intrabony peri-implantitis defects following application of a nanocrystalline hydroxyapatite (NHA) or a bovine-derived xenograft in combination with a collagen membrane (BDX+BG). MATERIAL AND METHODS: Twenty-two patients having moderate peri-implantitis (n=22 intrabony defects) were randomly treated with (i) access flap surgery (AFS) and the application of NHA, or with AFS and the application of BDX+BG. Clinical parameters were recorded at baseline and after 6 months of non-submerged healing. RESULTS: Post-operative wound healing revealed that NHA compromized initial adhesion of the mucoperiosteal flaps in all patients. At 6 months after therapy, NHA showed a reduction in the mean PD from 7.0+/-0.6 to 4.9+/-0.6 mm and a change in the mean clinical attachment loss (CAL) from 7.5+/-0.8 to 5.7+/-1.0 mm. In the BDX+BC group, the mean PD was reduced from 7.1+/-0.8 to 4.5+/-0.7 mm and the mean CAL changed from 7.5+/-1.0 to 5.2+/-0.8 mm. CONCLUSION: Within the limits of the present case series, it can be concluded that at 6 months after surgery both therapies resulted in clinically important PD reductions and CAL gains.

10-year survival rate and the incidence of peri-implant disease of 374 titanium dental implants with a SLA surface: a prospective cohort study in 177 fully and partially edentulous patients.

van Velzen FJ1,2, Ofec R3, Schulten EA2, Ten Bruggenkate CM1,2.
Clin Oral Implants Res. 2015 Oct;26(10):1121-8. doi: 10.1111/clr.12499. Epub 2014 Nov 5.

PURPOSE: This prospective cohort study evaluates the 10-year survival and incidence of peri-implant disease at implant and patient level of sandblasted, large grid, and acid-etched titanium dental implants (Straumann, soft tissue level, SLA surface) in fully and partially edentulous patients.
MATERIAL AND METHODS: Patients who had dental implant surgery in the period between November 1997 and June 2001, with a follow-up of at least 10 years, were investigated for clinical and radiological examination. Among the 506 inserted dental implants in 250 patients, 10-year data regarding the outcome of implants were available for 374 dental implants in 177 patients. In the current study, peri-implantitis was defined as advanced bone loss (≥ mm. postloading) in combination with bleeding on probing.

RESULTS: At 10-year follow-up, only one implant was lost (0.3%) 2 months after implant surgery due to insufficient osseointegration. The average bone loss at 10 year postloading was 0.52 mm. Advanced bone loss at 10-year follow-up was present in 35 dental implants (9.8%). Seven percent of the observed dental implants showed bleeding on probing in combination with advanced bone loss and 4.2% when setting the threshold for advanced bone loss at 2.0 mm. Advanced bone loss without bleeding on probing was present in 2.8% of all implants.
CONCLUSION: In this prospective study, the 10-year survival rate at implant and patient level was 99.7% and 99.4%, respectively. Peri-implantitis was present in 7% of the observed dental implants according to the above-mentioned definition of peri-implantitis. This study shows that SLA implants offer predictable long-term results as support in the treatment of fully and partially edentulous patients.

Primary and secondary prevention of periodontal and peri-implant diseases: Introduction to, and objectives of the 11th European Workshop on Periodontology consensus conference.

Tonetti MS1, Chapple IL, Jepsen S, Sanz M.

BACKGROUND: Periodontitis prevalence remains high. Peri-implantitis is an emerging public health issue. Such a high burden of disease and its social, oral and systemic consequences are compelling reasons for increased attention towards prevention for individuals, professionals and public health officials.

METHODS: Sixteen systematic reviews and meta-reviews formed the basis for workshop discussions. Deliberations resulted in four consensus reports.

RESULTS: This workshop calls for renewed emphasis on the prevention of periodontitis and peri-implantitis. A critical element is the recognition that prevention needs to be tailored to the individual's needs through diagnosis and risk profiling. Discussions identified critical aspects that may help in the large-scale implementation of preventive programs: (i) a need to communicate to the public the critical importance of gingival bleeding as an early sign of disease, (ii) the need for universal implementation of periodontal screening by the oral health care team, (iii) the role of the oral health team in health promotion and primary and secondary prevention, (iv) understanding the limitations of self-medication with oral health care products without a diagnosis of the underlying condition, and (v) access to appropriate and effective professional preventive care.

CONCLUSIONS: The workshop provided specific recommendations for individuals, the oral health team and public health officials. Their implementation in different countries requires adaptation to respective specific national oral health care models.

7. Periodontitis

Prevention of mandibular third molar extraction-associated periodontal defects: a comparative study

Sammartino, G., M. Tia, et al.
J Periodontol 2009; 80(3): 389-96.

Background: Extraction of deep-impacted mandibular third molars may lead to periodontal defects at the distal surface of the adjacent second molar. The purpose of this study was to compare the ability of three regenerative approaches to prevent third molar extraction-related periodontal defects. Methods: Forty-five patients with bilateral osseous or soft tissue-impacted lower third molars were selected to participate in the study. Inclusion criteria were the presence of a pocket that was located distally to the mandibular second molar with a probing depth (PD) >/=7 mm and with a probing clinical attachment level (CAL) >/=6 mm. Ninety third molar impactions were used and were randomly assigned to three equal treatment groups (30 each): bovine porous bone mineral (BPBM) alone, BPBM plus collagen membrane (CM), and an untreated control group. Clinical and radiographic measurements were recorded at 3, 6, 9, 12, 18, 24, 36, 48, 60, and 72 months after the surgery. Results: BPBM or BPBM + CM resulted in a significant reduction in PD and gain in

CAL compared to the control group at all time points. BPBM + CM had the best outcome for the prevention of a second-molar periodontal defect. Conclusion: The application of BPBM, with or without a collagen membrane, can be a viable and stable treatment to alleviate the periodontal defects that are often associated with impacted mandibular third molar extractions.

Long-term Clinical Outcome after Reconstruction of Periodontal Defects using a Bovine-Derived Xenograft: a Retrospective Cohort Study

Tietmann C, Bröseler F.
Perio 2006; 3: 79–86.

The present retrospective study evaluates the long-term results of reconstructive periodontal surgery using a bovine-derived bone mineral with or without a bio-resorbable collagen membrane. Teeth (f241) in 54 patients were treated. Treatment was performed regardless of the patients genetic predisposition, medical status or social habits. The patients had to follow a strict oral hygiene program prior to periodontal surgery. One year after treatment, an overall reduction of the mean pocket probing depth (PPD) of 2.69 mm on average (from 6.88 ± 1.89 mm to 4.19 ± 1.40 mm) and an increase in clinical attachment level (CAL) of 3.14 mm on average (from 8.56 ± 2.39 mm to 5.42 ± 1.50 mm) could be shown. At two years from baseline, no statistical differences in PPD reduction were found compared to the one year's data.
Within the limits of the present study, it can be concluded that periodontal surgical therapy by the use of bovine-derived bone mineral with or without a bio-resorbable collagen membrane in combination with a strict oral hygiene program results in significantly high PPD reduction and CAL gain. Thus this treatment appears to be a suitable treatment for severe periodontal defects, leading to predictable and stable results.

Enamel matrix proteins and bovine porous bone mineral in the treatment of intrabony defects: a comparative controlled clinical trial

Zucchelli G, Amore C, Montebugnoli L, De Sanctis M.
J Periodontol 2003; 74: 1725-1735.

BACKGROUND: Various clinical studies have demonstrated that applying commercially available enamel matrix proteins (EMP) on the instrumented root surface during access flap surgery promotes clinically significant gains of clinical attachment and bone in intrabony defects. The aim of the present controlled clinical trial was to evaluate the adjunctive effect of filling the intrabony lesion with bovine porous bone mineral (Bio-Oss®) to a simplified papilla preservation (SPP) flap and EMP surgical procedure. METHODS: Sixty deep interproximal intrabony lesions in 60 patients with chronic periodontitis were treated with the SPP flap and EMP. In the 30 test defects, the intrabony component was filled with Bio-Oss® particles previously reconstituted with the EMP gel. A stringent infection control program was adopted for 1 year. The clinical and radiographical reevaluation was made 1 year after surgery. RESULTS: Both techniques resulted in clinically and statistically significant improvements between baseline and 1 year, in terms of clinical attachment level (CAL) gain, probing depth (PD) reduction, and radiographic bone fill; however, the Bio-Oss® test treatment showed statistically significantly greater CAL (5.8 +/- 1.1 versus 4.9 +/- 1.0) and radiographic bone (DEPTH) level gains (5.3 +/- 1.1 versus 4.3 +/- 1.5), and less increase in gingival recession (0.4 +/- 0.6 versus 0.9 +/- 0.5) than the control surgical procedure. CONCLUSION: The present study data supported the hypothesis that the adjunctive use of Bio-Oss® in grafting intrabony defects has the ability to improve clinical and radiographical outcomes achievable with EMP alone.

Treatment of Angular Bone Defects with a Composite Bone Grafting Material in Combination with a Collagen Membrane

Zitzmann N, Rateitschak-Plüss E, Marinello C.
J Periodontol 2003; 74: 687-694.

BACKGROUND: The purpose of this study was to evaluate the effect of a bioabsorbable collagen barrier (CB) in combination with a composite bone substitute (deproteinized bovine bone mineral with collagen, DBBM + C) in periodontal regeneration of angular bone defects in humans using a new application technique. METHODS: Twelve patients participated, each contributing at least 1 defect site, which exhibited a probing depth (PD) of > or = 5 mm, a clinical attachment level (CAL) of > or = 6 mm, and was positive for

bleeding on probing (BOP) following initial therapy. Twenty-two angular bone defects were filled with DBBM + C. A hole was placed in the membrane, which was then pulled over the tooth. The observation period was 2 years and included measurements of plaque, gingivitis, tooth mobility, PD, CAL, soft tissue recession, and bone level as assessed from standardized radiographs. RESULTS: The residual PD and CAL were reduced to 3.3 mm (PD) and 5.6 mm (CAL) with a CAL gain of 3.2 mm at 24 months. The radiographic defect reduction (bone fill) was 4.0 mm after surgery and 2.2 mm at 24 months. The changes measured clinically and radiographically were more pronounced in sites with a deep intrabony defect component than in sites with shallow ones. CONCLUSIONS: These findings indicate that angular bone defects can be successfully treated with DBBM + C in combination with CB. A degradation of the filler material seems to occur particularly during the first 6 months, but without affecting the clinical parameters, which improved consistently

Clinical and histologic evaluation of human intrabony defects treated with an enamel matrix protein derivative combined with a bovine-derived xenograft.

Sculean A, Windisch P, Keglevich T, Chiantella GC, Gera I, Donos N.
Int J Periodontics Restorative Dent 2003; 23: 47-55.

The purpose of the present case report study was to clinically and histologically evaluate the healing of deep intrabony defects following treatment with either a combination of an enamel matrix protein derivative (EMD) and a bovine-derived xenograft (Bio-Oss®) or with Bio-Oss® alone. Three female patients with generalized marginal periodontitis and presenting one advanced intrabony defect each were treated with either a combination of EMD + Bio-Oss® (two defects) or with Bio-Oss® alone (one defect). The postoperative healing was uneventful in all three cases. Six months after surgery, a gain of clinical attachment was measured at all treated sites. The histologic examination revealed that all three defects healed with a new connective tissue attachment (ie, new cellular cementum with inserting collagen fibers) and new bone. Most of the Bio-Oss® particles were surrounded by a bone-like tissue. No direct contact between Bio-Oss® particles and the root surface (cementum or dentin) was observed. Within their limits, the present data indicate that treatment with either EMD + Bio-Oss® or with Bio-Oss® alone may enhance the formation of new connective tissue attachment and new bone in human intrabony defects.

Evaluation of Periodontal Regeneration Following Grafting Intrabony Defects with Bio-Oss Collagen: A Human Histologic Report

Nevins ML, Camelo M, Lynch SE, Schenk RK, Nevins M
Int J Periodontics Restorative Dent 2003; 23:9-17.

This study evaluated the clinical, radiographic, and histologic response to Bio-Oss® Collagen when used alone or in combination with Bio-Gide® bilayer collagen membrane for the treatment of four intrabony defects (5 to 7 mm) around single-rooted teeth. After reflecting a full–thickness flap, thorough degranulation and root planning were accomplished. In all cases, Bio-Oss® Collagen was then used to fill the defects, and in tow cases a Bio-Gide® membrane was placed over the filled defect. Radiographs, clinical probing depths, and attachment levels were obtained before treatment and immediately preceding an bloc resection of teeth and surrounding tissues 9 months later. Reduction in pocket depth and gain in clinical attachment level were observed for both treatment protocols. The histologic evaluation demonstrated the formation of a complete new attachment apparatus, evidencing periodontal regeneration that varied with defect morphology. This human histologic study demonstrated that Bio-Oss® Collagen has the capacity to induce regeneration of the periodontal attachment apparatus when placed in intrabony defects.

Clinical Comparison of an Enamel Matrix Derivative Used Alone or in Combination With a Bovine-Derived Xenograft for the Treatment of Periodontal Osseous Defects in Humans

Velasquez-Plata D, Scheyer E, Mellonig JT
J Periodontol 2002; 73: 433–440.

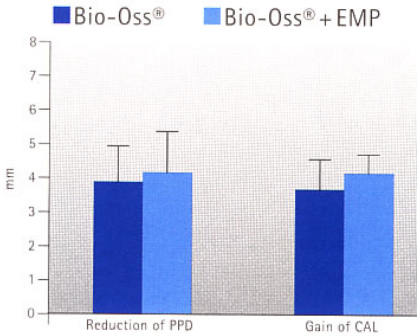
Background: The combination of bone replacement graft materials has been suggested for the treatment of periodontal osseous defects. The purpose of this study was to evaluate the effectiveness of enamel matrix derivative (EMD) combined with a bovine-derived xenograft (Bio-Oss®) as compared to EMD alone in the

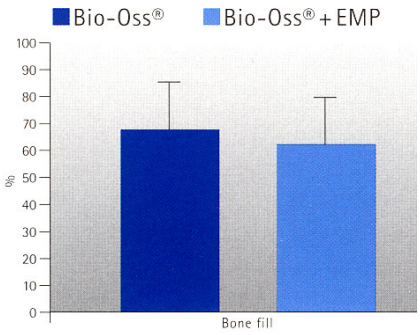
treatment of intraosseous defects in patients with moderate to advanced periodontitis. Methods: Sixteen adult patients with aat least 2 intrabony defects were entered in this split-mouth design study. Defects were treated with EMD alone or EMD + Bio-Oss®. Reentries were performed 6 to 8 months after initial surgery. The following soft and hard tissue measurements were recorded prior to initial surgery and at reentry: probing depth (D), gingival margin location, clinical attachment level (CAL), depth of defect, and crestal bone level. Statistical analyses were performed to determine changes in PD, CAL, fill of osseous defect, and crestal resorption. Percentages of bone fill (%BF) and defect resolution (%DR) were also calculated. Results: The most significant results were that gingival recession was greater for the groups treated with EMD alone (0.8 ± 0.8mm) compared to EMD + Bio-Oss® (0.3 ± 0.6mm) (P=0.04) and bone fill was greater for EMD + Bio-Oss® (4.0 ± 0.8mm) compared to EMD alone (3.1 ± 1.0mm) (P=0.02). The measures for PD reduction, attachment level gain, crestal resorption, %BF, and %DR did not present a statistically significant difference (P>0.10). Conclusions: This evaluated the performance of EMD + Bio-Oss® and EMD alone. The results demonstrated that a significant improvement in clinical parameters was observed. When comparing both modalities, a statistically significant difference was only found for gingival recession and bone fill, yielding a more favourable outcome towards the combined approach.

A clinical comparison of a bovine-derived xenograft used alone and in combination with enamel matrix derivative for the treatment of periodontal osseous defects in humans.

Scheyer ET, Velasquez-Plata D, Brunsvold MA, Lasho DJ, Mellonig JT.
J Periodontol 2002; 73(4): 423-432.

BACKGROUND: Enamel matrix protein derivative (EMD) and particulate anorganic cancellous bovine-derived bone xenograft (BDX) have both shown favorable clinical results in reducing intrabony periodontal defects as compared to open flap debridement alone. These materials have shown results comparable to those obtained with guided tissue regeneration. The primary aim of the present study was to evaluate the effectiveness of EMD combined with BDX as compared to BDX alone, with a secondary aim to compare the treatment outcomes of the 2 modalities. METHODS: Seventeen patients with paired intrabony defects and probing depths measuring > or = 5 mm who were being treated for chronic periodontitis were selected for this controlled, blinded, split-mouth study. Following non-surgical periodontal therapy, sites were randomly selected to receive either a combination of EMD and BDX (test group) or BDX alone (positive control group). Baseline and 6-month surgical reentry measurements were taken by a calibrated examiner blinded to the treatment. A paired Student t test was utilized to evaluate differences between baseline and post-treatment and between the treatment groups. RESULTS: Favorable clinical outcomes for both hard and soft tissue measurements were achieved for both treatment groups when compared to baseline (P < 0.001). There was no statistically significant difference for any of the measured clinical parameters. Probing depth reduction for the test group and control group was 4.2 +/- 1.1 mm and 3.9 +/- 1.3 mm, respectively (P > 0.8). Mean gain in clinical attachment levels for the test and control groups was 3.8 +/- 0.9 mm and 3.7 +/- 1.5 mm, respectively (P > 0.6). Hard tissue measurements obtained at surgical reentry were used to calculate the bone fill (BF) and percent bone fill (%BF). The BF was 3.2 +/- 1.4 mm and 3.0 +/- 1.2 mm (P > 0.6), and the %BF was 63.3 +/- 16.3% and 67.0 +/- 19.0% (P > 0.4) for the EMD + BDX and BDX groups, respectively. CONCLUSIONS: In summary, both the particulate anorganic cancellous bovine-derived bone xenograft used alone and in combination with enamel matrix derivative are effective for the treatment of human intrabony periodontal lesions.

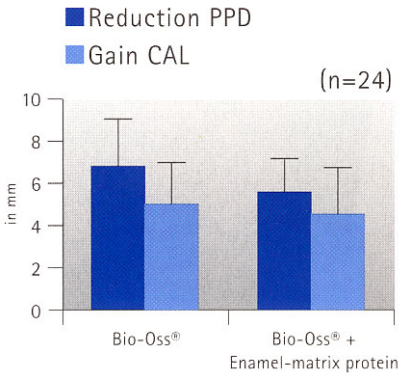




Clinical Evaluation of an Enamel Matrix Protein Derivative (Emdogain) Combined with a Bovine-Derived Xenograft (Bio-Oss) for the Treatment of Intrabony Periodontal Defects in Humans

Sculean A., Chiantella G., Windisch P., Gera I., Reich E.
Int J Periodontics Restorative Dent 2002; 22(3): 259-267.

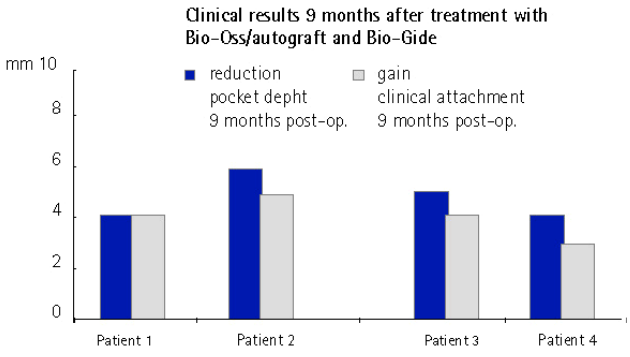
The purpose of the present study was to compare the treatment of deep intrabony defects with a combination of an enamel matrix protein derivative (EMD; Emdogain) and a bovine-derived xenograft (Bio-Oss) to Bio-Oss alone. Twenty-four healthy patients, each of whom displayed one intrabony defect, were randomly treated with a combination of EMD + Bio-Oss (test) or with Bio-Oss alone (control). Soft tissue measurements were made at baseline and 1 year following the therapy. No differences in any of the investigated parameters were observed at baseline between the two groups. No adverse healing response was observed in any of the patients. At 1 year after therapy, the sites treated with EMD + Bio-Oss showed a reduction in probing pocket depth (PPD) from 10.0 ± 1.5 mm to 4.3 ± 1.4 mm and a change in clinical attachment level (CAL) from 10.9 ± 2.00 mm to 6.2 ± 1.9 mm (P<.0001). In the group treated with Bio-Oss, the PPD was reduced from 9.7 ± 2.4 mm to 3.2 ± 0.7 mm and the CAL changed from 10.1 ± 2.3 mm to 5.2 ± 1.2 mm (P <.0001). Hard tissue fill was observed radiographically in all defects. Both treatments resulted in significant improvements of PPD and CAL. However, no statistically significant differences in any of the investigated parameters were observed between the test and control groups. Both therapies led to significant improvements of the investigated clinical parameters.



Periodontal Regeneration with an Autogenous Bone-Bio-Oss Composite Graft and a Bio-Gide Membrane

M. Camelo, M. Nevins, S. Lynch, R. Schenk, M. Simion, Myron Nevins
Int J of Periodontics & Restorative Dentistry 2001;21.

This study evaluated the clinical, radiographic, and histologic response to the composite use of Bio-Oss® porous bone mineral and autogenous bone in combination with a Bio-Gide® bilayer collagen membrane to achieve regeneration when treating human periodontal bone defects. Preoperative recordings for four treatment areas included radiographs, clinical probing depths, and attachment levels; cementum with inserting collagen fibers and new bone formation on the surface of both types of grafts materials. This grafting combination not only compared favorably with the previous use of Bio-Oss® and Bio-Gide®, but exceeded that result with almost complete periodontal regeneration. This human histologic study demonstrated that autogenous bone in combination with porous bone mineral matrix, together with the Bio-Gide® collagen membrane, has the capacity to stimulate substantial new bone and cementum formation with Sharpey's fiber attachment.



A Comparison Between Enamel Matrix Proteins Used Alone or in Combination With bovine Porous Bone Mineral in the Treatment of Intrabony Periodontal Defects in Humans

V. Lekovic, P. Camargo, M. Weinländer, M. Nedic,, Z. Aleksic, EB Kenney
J Periodontol 2000; 71.

It has been shown that clinical improvement of intrabony periodontal defects can be achieved with the use of enamel matrix proteins (Emdogain®) or by grafting with bovine porous bone mineral (Bio-Oss®). There is no report on the potential synergistic effect of Emdogain® and Bio-Oss® in periodontal regenerative therapy. The purpose of this study was to compare the clinical effectiveness of Emdogain® used alone or in combination with Bio-Oss® in the treatment of periodontal intrabony defects in humans.
Twenty-one paired intrabony defects were surgically treated using a split-mouth design. Intrabony defects were treated either with enamel matrix proteins (Emdogain® group) or with enamel matrix proteins combined with bovine porous bone mineral (Emdogain®/Bio-Oss® group). Re-entry surgeries were performed at 6 months. Preoperative probing depths, attachment levels, and transoperative bone measurements were similar for the Emdogain® and Emdogain®/Bio-Oss® groups. Postsurgical measurements taken at 6 months revealed a sigigicantly greater reduction in probing depth in the Emdogain®/Bio-Oss® group (3,43 ± 1.32 mm on buccal sites and 3.36 ± 1.35 mm on lingual sites) when compared to the Emdogain® grouon buccal sites and 1.85 ± 1.38 mm on lingual sites). The Emdogain®/Bio-Oss® group also presentedwith significantly more attachment gain (3.13 ± 1.41 mm on buccal sites and 3.11 ± 1.39 mm on lingual sites) than the Emdogain® group (1.72 ± 1.33 mm on buccal sites and 1.75 ± 1.37 mm on lingual sites). Surgical re-entry of the treated defects revealed a significantly greater amount of defect fill in favor of the Emdogain®/Bio-Oss® group (3.82 ± 1.43 mm on buccal sites and 3.74 ± 1.38 mm on lingual sites) as compared to the Emdogain® group (1.33 ± 1.17 mm on buccal sites and 1.41 ± 1.19 mm on lingual sites).
The results of this study indicate that Bio-Oss® has the ability to augment the effects of Emdogain® in reducing probing depth, improving clinical attachment levels, and promoting defect fill when compared to presurgical levels.

Human Histologic Evaluation of a Bovine-Derived Bone Xenograft in the Treatment of Periodontal Osseous Defects

J.T. Mellonig
Int J Periodontics Restorative Dent 2000; 20.

This study evaluated a bovine-derived bone xenograft (Bio-Oss®) in the treatment of human periodontal osseous defects. Four patients with at least one tooth that had been recommended for extraction because of interproximal advanced periodontal disease volunteered to participate. The surgical procedure consisted of flap reflection, soft tissue debridement, placing a notch in calculus as a histologic reference point, root planing, placement of the bovine-derived xenograft and a bioresorbable physical barrier (Bio-Gide®) and flap closure. Patients were seen every 2 weeks for plaque control and any necessary adjunctive treatment. At 4 to 6 months postsurgery, 6 teeth, along with the adjacent graft site, were removed en bloc. Histologic observations demonstrated new bone, new cementum, and new periodontal ligament coronal to the reference notch in 3 of the 4 specimens. This study indicates that periodontal regeneration is possible following grafting with a bovine-derived xenograft.

The Clinical Evaluation of Periodontal Surgery with Porous Bone Graft Material (Bio-Oss®) and Collagen Membrane (Bio-Gide®)

A. Ohazama, H. Kitamura, M. Suzuki, S. Yamada, K. Hasegawa
Journal of the Japanese Society of Periodontology 1999; 41.

The purpose of this study was to assess the clinical efficacy of the periodontal surgery with porous bone graft material (Bio-Oss®) and collagen membrane (Bio-Gide®). Sixtyseven adult periodontitis patients each having a Class II furcation defects or vertical defects, participated in the study. Mucoperiosteal flaps were elevated and granulation tissue in the defects were debrided with hand instruments. After each defect was filled with Bio-Oss®, Bio-Gide® was positioned over graft material and the defects. The flaps were replaced coronary to cover the membrane ensuring primary closure.
The clinical examination were taken before surgery, at 1, 3 weeks, 3 and 6 months after surgery. Postoperatively, clinical healing generally progressed uneventfully in all patients. The significant differences were found in probing depth and clinical attachment level between pre-surgery and 6 months post-surgery measurements. Mean probing depth was reduced from 6.74±1.17 mm to 3.08±1.17 mm with a mean reduction of 3.67±1.21 mm. Mean clinical attachment level was reduced from 8.39±1.99 mm to 5.60±2.11 mm with a mean clinical attachment gain of 2.79±1.38 mm. The improvement of radioluency at defect area was

noted in 48 of 66 patients. The side effects was not observed in any cases. This study revealed that the periodontal surgery with Bio-Oss® and Bio-Gide® is safety and clinical usefulness.

Clinical evaluation of Bio-Oss®: a bovine-derived xenograft for the treatment of periodontal osseous defects in humans

CR Richardson, JT Mellonig, MA Brunsvold, HAT MdDonnell, DL Cochran
J Clinical Periodontol, 1999; 26.

The purpose of this study was to compare Bio-Oss® to demineralized freeze dried bone allograft (DFDBA) in human intrabony defects. 17 healthy patients with no systemic disease with moderate-severe periodontitis (7 males, 10 females: aged 34-67), were treated. Surgically, defects were included only if the intraosseous defect depth was >3.0mm. Final selection included 30 defects. The sites were randomly assigned treatment with DFDBA or Bio-Oss®. Soft tissue and osseous defect measurements were taken the day of surgery and 6 months post-operatively at re-entry. Average baseline PD, CAL, and surgical defect depth for the DFDBA group were not statistically different from the Bio-Oss® group. No adverse healing response occurred. The results showed a statistically significant improvement in PD and AL for both materials at 6 months in 26 defects (4 defects did not respond to therapy). Soft tissue measurements for the DFDBA group included PD reduction of 2.0 ± 1.3mm, and AL gain of 2.6 ± 1.6 mm, while the Bio-Oss® group showed a PD reduction of 3.0 ± 1.7 mm, and AL gain of 3.6 ± 1.8 mm. Osseous measurements showed bone fill of 2.4 mm (46.8%) for the DFDBA group and 3.0 mm (55.8%) for the Bio-Oss® group. Defect resolution was 59.4% for the DFDBA group and 77.6% for the Bio-Oss® group. The defects were treated with the bovine derived xenograft, although not statistically different, did show and average of 1.0 mm more PD reduction, and 1.2 mm more AL gain. With regard to hard tissue results, the Bio-Oss® treatment group exhibited an average of 9.0% greater bone fill and an average defect resolution 19% greater than that demonstrated by the DFDBA treatment group.

Effects of Collagen Resorbable Membrane Placement After the Surgical Extraction of Impacted Lower Third Molars.

Cortell-Ballester I1, Figueiredo R2, Valmaseda-Castellón E3, Gay-Escoda C4.
J Oral Maxillofac Surg. 2015 Aug;73(8):1457-64. doi: 10.1016/j.joms.2015.02.015. Epub 2015 Feb 26.

PURPOSE: The use of resorbable collagen membranes (RMs) in the treatment of intraosseous defects and deep periodontal pockets on the distal side of a lower second molar (L2M) after surgical extraction of an impacted lower third molar (L3M) has shown contradictory results. This study evaluated the effects of RM placement on the healing of a bone defect distal to an L2M after surgical extraction of a horizontal or mesioangular impacted L3M.
PATIENTS AND METHODS: A parallel-group randomized controlled trial with 2 independent groups of 30 patients requiring surgical extraction of an L3M was carried out. After extraction, patients received an RM (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) or only suture. At the initial checkup and during postoperative monitoring at 1, 3, and 6 months, the distal vestibular, distal, and distolingual probing depths and distal vestibular attachment level of the L2M were measured.
RESULTS: Age (control group, 33.8 ± 6.9 yr; guided tissue regeneration group, 35.6 ± 6.3 yr; P = .322) and the number of women (control group, 15 of 29; guided tissue regeneration group, 14 of 27; P = .992) were similar in the 2 groups. The distal vestibular, distal, and distolingual probing depths of the L2M, distal vestibular attachment level, distance from the cementoenamel junction, and distance from the alveolar crest to the base of the defect showed greater improvement 6 months after surgical extraction in the RM group (P < .05).
CONCLUSIONS: The use of RMs after surgical extraction of mesioangular or horizontally impacted L3Ms stimulates bone regeneration, improving the attachment level and bone fill distal to the L2M. Likewise, it decreases the distal probing depth and results in faster recovery. RM placement after surgical extraction of an impacted L3M is recommended because it prevents periodontal defects after L3M surgery.

Deproteinized bovine bone in association with guided tissue regeneration or enamel matrix derivatives procedures in aggressive periodontitis patients: a 1-year retrospective study.

Artzi Z1, Tal H1, Platner O1, Wasersprung N1, Weinberg E1, Slutzkey S1, Gozali N2, Carmeli G3, Herzberg R4, Kozlovsky A1.

OBJECTIVES: To retrospectively evaluate and compare two regenerative periodontal procedures in young individuals with aggressive periodontitis (AgP).

METHODS: Thirty-two patients aged 14-25 years (mean ± SD 19.3 ± 5.7) were diagnosed as having AgP with multiple intra-bony defects (IBDs) and treated by one of two regenerative modalities of periodontal therapy: guided tissue regeneration (GTR) using deproteinized bone xenograft (DBX) particles and a resorbable membrane (the GTR group), or an application of enamel matrix derivatives (EMD) combined with DBX (the EMD/DBX group). Periodic monitoring of treated sites included recording of probing depth (PD), clinical attachment level (CAL) and gingival recession. Pre-treatment and 1-year post-operative findings were statistically analysed within and between groups.

RESULTS: The PD and CAL values decreased significantly with time, but not those between study groups. The mean pre-treatment and 1-year post-treatment PDs of the IBDs of the GTR group (n = 16; sites = 67) were 8.93 ± 1.14 mm and 3.58 ± 0.50 mm, respectively, and the mean CALs were 9.03 ± 1.03 mm and 4.16 ± 0.53 mm respectively. The mean PDs of the EMD/DBX group (n = 16; sites = 73) were 8.77 ± 1.04 mm and 3.61 ± 0.36 mm, respectively, and the mean CALS were 8.79 ± 1.04 mm and 3.77 ± 0.22 mm respectively ($p < 0.001$ for all).

CONCLUSION: Surgical treatment of AgP patients by either GTR or by application of EMD/DBX yielded similarly successful clinical results at 1-year post-treatment.

8. Soft-tissue regeneration

Impact of a collagen matrix on early healing, aesthetics and patient morbidity in oral mucosal wounds - a randomized study in humans

Thoma DS, Sancho M, Ettlin DA, Hämmerle CH, Jun RE.
J Clin Periodontol 2012

AIM: To test whether a collagen matrix (CM) can improve early wound healing and aesthetics, and decrease wound sensitivity compared with spontaneous healing. METHODS: In 15 volunteers, 6-mm punch biopsies were harvested at both palatal sites. A CM was sutured in one site; the other one was left untreated (control). Measurements included the remaining defect area, the colour match to surrounding tissue and somatosensory parameters at various time-points (pre-operative, post-operative, 4, 8, 15, 29 days). RESULTS: The defect area decreased over time for both treatments. Re-epithelization was completed in all subjects by day 15. The defect area was significantly smaller for CM (mean +/- SD: 19.3 +/- 3.4 mm(2)) compared with control (21.3 +/- 3.3 mm(2)) at day 4 ($p < 0.05$), and at day 8 (CM: 11.7 +/- 2.5 mm(2) ; control: 13.6 +/- 2.9 mm(2) ; $p < 0.01$). The colour match was more favourable for CM at day 4, 8 and 29 ($p > 0.05$). Somatosensory measurements revealed slightly lower wound sensitivity at day 4 for CM compared with control. CONCLUSIONS: The use of CM can enhance wound healing compared with spontaneous healing during the first week. This was mainly documented by a faster re-epithelization. Colour match and wound sensitivity measurements did not reach statistical significance between CM and control sites.

Soft tissue integration of a porcine collagen membrane: an experimental study in pigs

Rocchietta I, Schupbach P, Ghezzi C, Maschera E, Simion M.
Int J Periodontics Restorative Dent 2012:32(1):34-40.

Autogenous soft tissue augmentation procedures around natural teeth and dental implants are performed daily by clinicians. However, patient morbidity is often associated with the second surgical site; hence, research is moving toward an era where matrices may substitute autogenous grafts. The aim of this study was to assess the soft tissue response to a collagen matrix in an animal model. Nine pigs were included in this study. Each animal received four collagen matrices, two for each mandible. Three cohorts were included in the study: group A, where the matrix was applied as an onlay on a partial-thickness flap; group B, where the matrix was inserted under a partial-thickness flap; and group C, where the matrix was inserted in an inverted position under a full-thickness flap. Sacrifice occurred at 7, 15, and 30 days postoperatively for histologic assessment. The collagen matrix was seen in place for the first 2 weeks, and it was completely replaced by healthy connective tissue within 30 days in the inlay cohorts. No inflammatory adverse reactions were noticed in any specimen, resulting in optimal integration of the device. This study showed an optimal integration within 30 days postoperative of the placement of experimental collagen matrix in the soft tissues of an animal model. Its proven safety in this model provides an optimal starting point for further research projects considering its clinical applications.

Use of a new collagen matrix (mucograft) for the treatment of multiple gingival recessions: case reports

Rotundo R, Pini-Prato G.
Int J Periodontics Restorative Dent 2012;32(4):413-9.

The aim of this case report study was to demonstrate the use of a new collagen matrix as an alternative to the connective tissue graft for the treatment of multiple gingival recessions. Three women showing 11 maxillary gingival recessions were treated by means of the envelope flap technique associated with a novel collagen matrix as a substitute for the connective tissue graft. At 1 year, complete root coverage was achieved in 9 treated sites, with a mean keratinized tissue width of 3.1 mm, complete resolution of dental hypersensitivity, and a high level of esthetic satisfaction.

Evaluation of a resorbable collagen matrix infused with rhPDGF-BB in peri-implant soft tissue augmentation: a preliminary report with 3.5 years of observation

Simion M, Rocchietta I, Fontana F, Dellavia C.
Int J Periodontics Restorative Dent 2012;32(3):273-82.

Soft tissue augmentation around dental implants in the esthetic region remains a challenging and unpredictable procedure. The ideal surgical technique would include of an off-the-shelf product to minimize morbidity after autogenous grafting procedures. The aim of this study was to use a resorbable collagen matrix (Mucograft) to serve as a scaffold to recombinant human platelet-derived growth factor BB (rhPDGF-BB) to increase peri-implant soft tissue volume in anterior maxillary sites. A total of six patients who had previously undergone a bone regeneration procedure were included in this study. The collagen matrix was applied during stage-two surgery (expanded polytetrafluoroethylene membrane removal and implant placement). Measurements were performed through customized stents by means of endodontic files, and at abutment connection, a soft tissue biopsy specimen was harvested for histologic examination. The healing period was uneventful in all six patients. Measurements were taken apically, centrally, and occlusally for each site. The mean gains in volume from baseline to the 4-month measurement at the apical, central, and occlusal aspects were 0.87 +/- 2.13 mm, 2.14 +/- 3.27 mm, and 0.35 +/- 3.20 mm, respectively. The results showed a moderate increase in the soft tissue volume in esthetic peri-implant sites when applying a collagen matrix infused with rhPDGF-BB. However, the measuring techniques available need to be further improved to record exact changes in the soft tissue volume.

New collagen matrix to avoid the reduction of keratinized tissue during guided bone regeneration in postextraction sites

De Santis D, Cucchi A, de Gemmis A, Nocicni PF.
J Craniofac Surg 2012;23(3):186-9.

For decades, there has been an ongoing controversy regarding the need for an "adequate" width of keratinized gingiva/mucosa to preserve periodontal and implant health. Today, the presence of a certain width of keratinized tissue is recommended for achieving long-term periodontal and implant success, and therefore, a new collagen matrix has been developed to enhance the width of keratinized gingiva/mucosa. During postextraction socket preservation, guided bone regeneration techniques require complete coverage of the barrier membrane to reduce the risk of infection, occasionally causing a reduction of the width of keratinized tissue. Using the new collagen matrix, it is possible to leave the membrane intentionally uncovered, without suturing the surgical flap above it, to avoid the reduction of such tissue.

Clinical efficacy of a xenogeneic collagen matrix in augmenting keratinized mucosa around implants: a randomized controlled prospective clinical trial.

Lorenzo R, García V, Orsini M, Martin C, Sanz M.
Clin Oral Implants Res. 2012 Mar;23(3):316-24.

AIM: The aim of this controlled randomized clinical trial was to evaluate the efficacy of a xenogeneic collagen matrix (CM) to augment the keratinized tissue around implants supporting prosthetic restorations at 6 months when compared with the standard treatment, the connective tissue autograft, CTG). MATERIALS AND METHODS: This randomized longitudinal parallel controlled clinical trial studied 24 patients with at least one location with minimal keratinized tissue (≤1 mm). MAIN OUTCOME MEASURE: The 6-month width of keratinized tissue. As secondary outcomes the esthetic outlook, the maintenance of peri-implant mucosal health and the patient morbidity were assessed pre-operatively and 1, 3, and 6 months post-operatively. RESULTS: At 6 months, Group CTG attained a mean width of keratinized tissue of 2.75 (1.5) mm, while the corresponding figure in Group CM was 2.8 (0.4) mm, the inter-group differences not being statistically significant. The surgical procedure in both groups did not alter significantly the mucosal health in the affected abutments. There was a similar esthetic result and significant increase in the vestibular depth in both groups as a result of the surgery. In the CM group it changed from 2.2 (3.3) to 5.1 (2.5) mm at 6 months. The patients treated with the CM referred less pain, needed less pain medication, and the surgical time was

shorter, although these differences were not statistically significant when compared with the CTG group. CONCLUSIONS: These results prove that this new CM was as effective and predictable as the CTG for attaining a band of keratinized tissue.

Treatment of Gingival Recession Defects Using Coronally Advanced Flap With a Porcine Collagen Matrix Compared to Coronally Advanced Flap With Connective Tissue Graft: A Randomized Controlled Clinical Trial

Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L.
J Periodontol 2011.

Background: Connective tissue graft (CTG) plus coronally advanced flap (CAF) is the reference therapy for root coverage. The aim of the present study is to evaluate the use of a porcine collagen matrix (PCM) plus CAF as an alternative to CTG+CAF for the treatment of gingival recessions, in a prospective randomized ccontrolled clinical trial. Methods: Eighteen adult patients participated in this study. The patients presented 22 single Miller's class I or II gingival recessions, randomly assigned to the test (PCM+CAF) or control (CTG+CAF) group. Recession depth (REC), pocket depth, clinical attachment level (CAL) and width of keratinized tissue (KG) were evaluated at 12 months. In addition, the gingival thickness (GT) was measured 1 mm apical to the bottom of the sulcus. Results: At 12 months, mean REC was 0.23 mm for test sites and 0.09 mm for control sites ($p<0.01$), while percentage of root coverage was 94.32% and 96.97% respectively. CAL gain was 2.41 mm in test sites and 2.95 mm in control sites ($p<0.01$). KG gain was 1.23 mm in test group and 1.27 mm in control group ($p<0.01$). In test sites GT changed from 0.82 to 1.82 mm and in control sites GT changed from 0.86 to 2.09 mm ($p<0.01$). Conclusions: Within the limits of the study, both treatment procedures resulted in significant reduction in gingival recession at 12-months. No statistically significant differences were found between PCM+CAF and CTG+CAF with regard to any clinical parameter. The collagen matrix represents a possible alternative to CTG.

The use of mucograft collagen matrix to augment the zone of keratinized tissue around teeth: a pilot study

Nevins M, Nevins ML, Kim SW, Schüpbach P, Kim DM.
Int J Periodontics Restorative Dent 2011;31(4):367-73.

This prospective split-mouth pilot case series compared the use of a bilayer collagen matrix (CM) to an autogenous gingival graft (AGG) in the ability to increase the zone of keratinized attached gingiva. Five patients with inadequate amounts of keratinized attached gingiva bilaterally in the posterior mandible were enrolled using a split-mouth design. There were statistically significant increases in attached gingiva at all test (CM) and control (AGG) sites. The CM sites at 12 months blended well with surrounding tissues, while the AGG sites were morphologically dissimilar to the adjacent areas. Biopsy results showed intrapatient histologic similarity between CM and AGG treatments, with all sites exhibiting mature connective tissue covered by keratinized epithelium. Thus, the obtained data support further investigations in evaluating the role of CM as a viable alternative to AGG in augmenting areas deficient in keratinized gingiva.

Clinical and histological healing of a new collagen matrix in combination with the coronally advanced flap for the treatment of Miller class-I recession defects: an experimental study in the minipig

Vignoletti F, Nunez J, Discepoli N, De Sanctis F, Caffesse R, Munoz F, Lopez M, Sanz M.
J Clin Periodontol 2011;38(9):847-55.

Aim: To describe the histological and clinical outcomes of the use of a xenogeneic collagen matrix (CM) in combination with the coronally advanced flap (CAF) in the treatment of localized Miller class-I gingival recessions. Material and Methods: Gingival recession defects were surgically created on 12 minipigs. The defects were randomly treated with either the CAF procedure and the interposition of a CM (test) or the CAF alone (control). Clinical and histological outcomes at 1, 4 and 12 weeks were evaluated. Results: Histometrically, in the test group, there was a shorter junctional epithelial dimension [2.26 (SD 0.23) mm] compared with the control [2.79 (SD 0.77) mm]. On the contrary, the amount of newly formed cementum was larger in the test group [1.08 (SD 0.41) mm] than in the control group [0.75 (SD 0.25) mm], although the

differences were not statistically significant. Conclusions: Both techniques rendered similar clinical outcomes, achieving complete root coverage at the end of the study. Nevertheless, the CM graft attained more tissue regeneration, characterized by a shorter epithelium and a larger new cementum formation. The use of a xenogeneic CM resulted in the incorporation of the xenograft within the adjacent host connective tissues in the absence of significant inflammation.

Evaluation of the tissue reaction to a new bilayered collagen matrix in vivo and its translation to the clinic

Ghanaati S, Schlee M, Weber MJ, Willershausen I, Barbeck M, Balic E, Görlach C, Stupp SI, Sader RA, Kirkpatrick CJ. Biomed Mater 2011;6(1)

This study evaluates a new collagen matrix that is designed with a bilayered structure in order to promote guided tissue regeneration and integration within the host tissue. This material induced a mild tissue reaction when assessed in a murine model and was well integrated within the host tissue, persisting in the implantation bed throughout the in vivo study. A more porous layer was rapidly infiltrated by host mesenchymal cells, while a layer designed to be a barrier allowed cell attachment and host tissue integration, but at the same time remained impermeable to invading cells for the first 30 days of the study. The tissue reaction was favorable, and unlike a typical foreign body response, did not include the presence of multinucleated giant cells, lymphocytes, or granulation tissue. In the context of translation, we show preliminary results from the clinical use of this biomaterial applied to soft tissue regeneration in the treatment of gingival tissue recession and exposed roots of human teeth. Such a condition would greatly benefit from guided tissue regeneration strategies. Our findings demonstrate that this material successfully promoted the ingrowth of gingival tissue and reversed gingival tissue recession. Of particular importance is the fact that the histological evidence from these human studies corroborates our findings in the murine model, with the barrier layer preventing unspecific tissue ingrowth, as the scaffold becomes infiltrated by mesenchymal cells from adjacent tissue into the porous layer. Also in the clinical situation no multinucleated giant cells, no granulation tissue and no evidence of a marked inflammatory response were observed. In conclusion, this bilayered matrix elicits a favorable tissue reaction, demonstrates potential as a barrier for preferential tissue ingrowth, and achieves a desirable therapeutic result when applied in humans for soft tissue regeneration.

Xenogeneic Collagen Matrix with Coronally Advanced Flap compared to Connective Tissue with Coronally Advanced Flap for the Treatment of Dehiscence-Type Recession Defects.

MK McGuire, ET Scheyer.
J Periodontol 2010 Mar 29.

Background: For root coverage therapy, the connective tissue graft plus coronally advanced flap (CTG+CAF) is considered the "gold standard" therapy against which alternative therapies are generally compared. When evaluating these therapies, in addition to traditional measures of root coverage, patient-reported, qualitative measures of esthetics, pain and overall preferences for alternative procedures should also be considered. The purpose of this study was to determine if a xenogeneic collagen matrix (CM) with a coronally advanced flap might be as effective as CTG+CAF in the treatment of recession defects. Methods: This study was a single-blind, randomized, controlled, split-mouth study of dehiscence-type recession defects in contralateral sites - one defect receiving CTG+CAF and the other defect receiving CM+CAF. 25 subjects were evaluated at 6-months and 1-year. The primary efficacy endpoint was recession depth at six months. Secondary endpoints included traditional periodontal measures, such as width of keratinized tissue (KT) and percentage of Root Coverage (%RC). Patient reported values of pain, discomfort and esthetic satisfaction were also recorded. Results: At 6-months, recession depth was, on average, 0.52 mm for test sites and 0.10 mm for control sites, Recession depth change from baseline was statistically significant between test and control, with an average of 2.62 mm gained at test sites and 3.10 m gained at control sites for a difference of 0.4 mm (P = 0.0062). At one year, test %RC averaged 88.5%, and controls averaged 99.3%, P = 0.0313. KT width gains were equivalent for both therapies and averaged 1.34 mm for test sites and 1.26 mm for control sites, P = 0.9061. There were no statistically significant differences between patient reported values for esthetic satisfaction and subjects' assessments of pain/ discomfort were also equivalent. Conclusions: When balanced with patient reported esthetic values and compared with historical

root coverage outcomes reported by other investigators, CM+CAF presents a viable alternative to CTG+CAF, without the morbidity of soft tissue graft harvest.

Use of a Porcine Collagen Matrix as an Alternative to Autogenous Tissue for Grafting Oral Soft Tissue Defects.

A.S. Herford, L. Akin, M. Cicciu, C. Maiorana, PJ Boyne
J Oral Maxillofac Surg. 2010 Jul;68(7):1463-70.

PURPOSE: Soft tissue grafting is often required to correct intraoral mucosal deficiencies. Autogenous grafts have disadvantages including an additional harvest site with its associated pain and morbidity and, sometimes, poor quality and limited amount of the graft. Porcine collagen matrices have the potential to be helpful for grafting of soft tissue defects. PATIENTS AND METHODS: Thirty consecutive patients underwent intraoral grafting to re-create missing soft tissue. Defects ranged in size from 50 to 900 mm(2). Porcine collagen matrices were used to reconstruct missing tissue. Indications included preprosthetic (22), followed by tumor removal (5), trauma (2), and release of cheek ankylosis (1). RESULTS: The primary efficacy parameters evaluated were the degree of lateral and/or alveolar extension and the evaluation of re-epithelialization and shrinkage of the grafted area. Overall, the percentage of shrinkage of the graft was 14% (range, 5%-20%). The amount of soft tissue extension averaged 3.4 mm (range, 2-10 mm). The secondary efficacy parameters included hemostatic effect, pain evaluation, pain and discomfort, and clinical evaluation of the grafted site. All patients reported minimal pain and swelling associated with the grafted area. No infections were noted. CONCLUSION: This porcine collagen matrix provides a biocompatible surgical material as an alternative to an autogenous transplant, thus obviating the need to harvest soft tissue autogenous grafts from other areas of the oral cavity.

Clinical evaluation of a new collagen matrix (Mucograft prototype) to enhance the width of keratinized tissue in patients with fixed prosthetic restorations: a randomized prospective clinical trial.

Sanz, M., R. Lorenzo, et al.
J Clin Periodontol 2009; 36(10): 868-76.

AIM: The aim of this study was to test a new collagen matrix (CM) aimed to increase keratinized gingiva/mucosa when compared with the free connective tissue graft (CTG). MATERIAL AND METHODS: This randomized longitudinal parallel controlled clinical trial studied 20 patients with at least one location with minimal keratinized tissue (<or=1 mm). Main Outcome Measure: The 6-month width of keratinized tissue. As secondary outcomes, the aesthetic outlook, the maintenance of periodontal health and the patient morbidity were assessed pre-operatively at 1, 3 and 6 months. RESULTS: At 6 months, the CTG attained a mean width of keratinized tissue of 2.6 (0.9) mm, while the CM was 2.5 (0.9) mm, these differences being insignificant. In both groups, there was a marked contraction (60% and 67%, respectively) although the periodontal parameters were not affected. The CM group had a significantly lower patient morbidity (pain and medication intake) as well as reduced surgery time. CONCLUSIONS: These results prove that this new CM was as effective and predictable as the CTG for attaining a band of keratinized tissue, but its use was associated with a significantly lower patient morbidity.

Treatment of gingival recession with coronally advanced flap procedures: a systematic review

Cairo, F., U. Pagliaro, et al.
J Clin Periodontol 2008; 35(8 Suppl): 136-62.

BACKGROUND: The treatment of buccal gingival recessions is a common requirement due to aesthetic concern or root sensitivity. The aim of this manuscript was to systematically review the literature on coronally advanced flap (CAF) alone or in combination with tissue grafts, barrier membranes (BM), enamel matrix derivative (EMD) or other material for treating gingival recession. MATERIAL AND METHODS: Randomized clinical trials on treatment of Miller Class I and II gingival recessions with at least 6 months of follow-up were identified. Data sources included electronic databases and hand-searched journals. The primary outcome variable was complete root coverage (CRC). The secondary outcome variables were

recession reduction, clinical attachment gain, keratinized tissue gain, aesthetic satisfaction, root sensitivity, post-operative patient pain and complications. RESULTS: A total of 794 Miller Class I and II gingival recessions in 530 patients from 25 RCTs were evaluated in this systematic review. CAF was associated with mean recession reduction and CRC. The addition of connective tissue graft (CTG) or EMD enhanced the clinical outcomes of CAF in terms of CRC, while BM did not. The results with respect to the adjunctive use of acellular dermal matrix were controversial. CONCLUSIONS: CTG or EMD in conjunction with CAF enhances the probability of obtaining CRC in Miller Class I and II single gingival recessions.

Randomized, controlled clinical trial to evaluate a xenogeneic collagen matrix as an alternative to free gingival grafting for oral soft tissue augmentation.

McGuire MK1, Scheyer ET.
J Periodontol. 2014 Oct;85(10):1333-41. doi: 10.1902/jop.2014.130692. Epub 2014 Mar 5.

BACKGROUND: The standard of care for increasing keratinized tissue (KT) and vestibular area is an autogenous free gingival graft (FGG) and vestibuloplasty; however, there is morbidity associated with the harvest of autogenous tissue, and supply is limited. The purpose of this study is to determine if a xenogeneic collagen matrix (CM) might be as effective as FGG.

METHODS: This study is a single-masked, randomized, controlled, split-mouth study of 30 patients with insufficient zones of KT (<2 mm). It uses a within-patient treatment-comparison design to establish non-inferiority of the test (CM) versus control (FGG) therapy. The primary efficacy endpoint was change in KT width (ΔKT) from surgery to 6 months post-surgery. Secondary endpoints included traditional periodontal measures, such as clinical attachment level, recession, and bleeding on probing. Patient-reported pain, discomfort, and esthetic satisfaction were also recorded. Biopsies were obtained at 6 months.

RESULTS: Surgery and postoperative sequelae were uneventful, with normal healing observed at both test and control sites. The primary outcome, ΔKT width at 6 months, did not establish non-inferiority of CM compared to FGG (P = 0.9992), with the FGG sites averaging 1.5 mm more KT width than CM sites. However, the amount of new KT generated for both therapies averaged ≥2 mm. Secondary outcomes were not significantly different between test and control sites. All site biopsies appeared as normal mucoperiosteum with keratinized epithelium. CM sites achieved better texture and color matches, and more than two-thirds of patients preferred the appearance of their CM sites.

CONCLUSION: With the proviso of sufficient KT (≈2 mm in width) and study goals of lower morbidity, unlimited supply, and patient satisfaction, CM appears to be a suitable substitute for FGG in vestibuloplasty procedures designed to increase KT around teeth.

Coronally advanced flap with and without a xenogenic collagen matrix in the treatment of multiple recessions: a randomized controlled clinical study.

Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L.
Int J Periodontics Restorative Dent. 2014;34 Suppl 3:s97-102. doi: 10.11607/prd.1605.

Abstract Multiple adjacent recession defects were treated in 32 patients using a coronally advanced flap (CAF) with or without a collagen matrix (CM). The percentage of root coverage was 81.49% ± 23.45% (58% complete root coverage) for CAF sites (control) and 93.25% ± 10.01% root coverage (72% complete root coverage) for CM plus CAF sites (test). The results achieved in the test group were significantly greater than in the control group, indicating that CM plus CAF is a suitable option for the treatment of multiple adjacent gingival recessions.

Critical soft-tissue dimensions with dental implants and treatment concepts.

Thoma DS, Mühlemann S, Jung RE.
Periodontol 2000. 2014 Oct;66(1):106-18. doi: 10.1111/prd.12045.

Dental implants have proven to be a successful treatment option in fully and partially edentulous patients, rendering long-term functional and esthetic outcomes. Various factors are crucial for predictable long-term peri-implant tissue stability, including the biologic width; the papilla height and the mucosal soft-tissue level; the amounts of soft-tissue volume and keratinized tissue; and the biotype of the mucosa. The biotype of the mucosa is congenitally set, whereas many other parameters can, to some extent, be influenced by the treatment itself. Clinically, the choice of the dental implant and the position in a vertical and horizontal direction can substantially influence the establishment of the biologic width and subsequently the location of the buccal mucosa and the papilla height. Current treatment concepts predominantly focus on providing optimized peri-implant soft-tissue conditions before the start of the prosthetic phase and insertion of the final reconstruction. These include refined surgical techniques and the use of materials from autogenous and xenogenic origins to augment soft-tissue volume and keratinized tissue around dental implants, thereby mimicking the appearance of natural teeth.

Evidence-based alternatives for autogenous grafts around teeth: outcomes, attachment, and stability.

McGuire MK1.
Compend Contin Educ Dent. 2014 Jun;35(1 Suppl):1-7; quiz 8.

Although the use of autogenous harvested tissues has proven to be the gold standard for soft tissue augmentation procedures involving root coverage or generation of keratinized tissue, harvest site morbidity and limited supply have prompted clinicians to seek graft alternatives. Using a hierarchy of evidence, the author reviews both clinical and patient-reported results for harvest graft substitutes and, considering his own research experience, reviews autogenous graft substitute outcomes, attachment, and stability over time. Overall, when the goal is keratinized-tissue generation, living cellular constructs and xenogeneic collagen matrices have provided acceptable clinical results, but with better esthetics and patient preference than autogenous free gingival grafts. For root coverage therapy, enamel matrix derivatives, platelet-derived growth factors, and xenogeneic collagen matrices have provided acceptable results with equivalent esthetics to autogenous connective tissue grafts, while also being preferred by patients. Longterm results for enamel matrix derivatives, platelet-derived growth factors, and xenogeneic collagen matrices indicate root coverage can be maintained over time. In the author's hands, xenogeneic collagen matrices have been the only harvest graft alternatives that can be used either covered or uncovered by soft tissue.

Biology of soft tissue wound healing and regeneration--consensus report of Group 1 of the 10th European Workshop on Periodontology.

Hämmerle CH1, Giannobile WV; Working Group 1 of the European Workshop on Periodontology.
J Clin Periodontol. 2014 Apr;41 Suppl 15:S1-5. doi: 10.1111/jcpe.12221.

BACKGROUND: The scope of this consensus was to review the biological processes of soft tissue wound healing in the oral cavity and to histologically evaluate soft tissue healing in clinical and pre-clinical models.

AIMS: To review the current knowledge regarding the biological processes of soft tissue wound healing at teeth, implants and on the edentulous ridge. Furthermore, to review soft tissue wound healing at these sites, when using barrier membranes, growth and differentiation factors and soft tissue substitutes.

COLLECTION OF DATA: Searches of the literature with respect to recessions at teeth and soft tissue deficiencies at implants, augmentation of the area of keratinized tissue and soft tissue volume were conducted. The available evidence was collected, categorized and summarized.

FUNDAMENTAL PRINCIPLES OF ORAL SOFT TISSUE WOUND HEALING: Oral mucosal and skin wound healing follow a similar pattern of the four phases of haemostasis, inflammation, proliferation and maturation/matrix remodelling. The soft connective tissue determines the characteristics of the overlaying oral epithelium. Within 7-14 days, epithelial healing of surgical wounds at teeth is completed. Soft tissue healing following surgery at implants requires 6-8 weeks for maturation. The resulting tissue resembles scar tissue. Well-designed pre-clinical studies providing histological data have been reported describing soft tissue wound healing, when using barrier membranes, growth and differentiation factors and soft tissue

substitutes. Few controlled clinical studies with low numbers of patients are available for some of the treatments reviewed at teeth. Whereas, histological new attachment has been demonstrated in pre-clinical studies resulting from some of the treatments reviewed, human histological data commonly report a lack of new attachment but rather long junctional epithelial attachment and connective tissue adhesion. Regarding soft tissue healing at implants human data are very scarce.

CONCLUSIONS: Oral soft tissue healing at teeth, implants and the edentulous ridge follows the same phases as skin wound healing. Histological studies in humans have not reported new attachment formation at teeth for the indications studied. Human histological data of soft tissue wound healing at implants are limited.

CLINICAL RECOMMENDATIONS: The use of barriers membranes, growth and differentiation factors and soft tissue substitutes for the treatment of localized gingival/mucosal recessions, insufficient amount of keratinized tissue and insufficient soft tissue volume is at a developing stage.

Biology of soft tissue wound healing and regeneration--consensus report of Group 1 of the 10th European Workshop on Periodontology.

Hämmerle CH1, Giannobile WV; Working Group 1 of the European Workshop on Periodontology.
J Clin Periodontol. 2014 Apr;41 Suppl 15:S1-5. doi: 10.1111/jcpe.12221.

BACKGROUND: The scope of this consensus was to review the biological processes of soft tissue wound healing in the oral cavity and to histologically evaluate soft tissue healing in clinical and pre-clinical models.
AIMS: To review the current knowledge regarding the biological processes of soft tissue wound healing at teeth, implants and on the edentulous ridge. Furthermore, to review soft tissue wound healing at these sites, when using barrier membranes, growth and differentiation factors and soft tissue substitutes.
COLLECTION OF DATA: Searches of the literature with respect to recessions at teeth and soft tissue deficiencies at implants, augmentation of the area of keratinized tissue and soft tissue volume were conducted. The available evidence was collected, categorized and summarized.
FUNDAMENTAL PRINCIPLES OF ORAL SOFT TISSUE WOUND HEALING: Oral mucosal and skin wound healing follow a similar pattern of the four phases of haemostasis, inflammation, proliferation and maturation/matrix remodelling. The soft connective tissue determines the characteristics of the overlaying oral epithelium. Within 7-14 days, epithelial healing of surgical wounds at teeth is completed. Soft tissue healing following surgery at implants requires 6-8 weeks for maturation. The resulting tissue resembles scar tissue. Well-designed pre-clinical studies providing histological data have been reported describing soft tissue wound healing, when using barrier membranes, growth and differentiation factors and soft tissue substitutes. Few controlled clinical studies with low numbers of patients are available for some of the treatments reviewed at teeth. Whereas, histological new attachment has been demonstrated in pre-clinical studies resulting from some of the treatments reviewed, human histological data commonly report a lack of new attachment but rather long junctional epithelial attachment and connective tissue adhesion. Regarding soft tissue healing at implants human data are very scarce.
CONCLUSIONS: Oral soft tissue healing at teeth, implants and the edentulous ridge follows the same phases as skin wound healing. Histological studies in humans have not reported new attachment formation at teeth for the indications studied. Human histological data of soft tissue wound healing at implants are limited.
CLINICAL RECOMMENDATIONS: The use of barriers membranes, growth and differentiation factors and soft tissue substitutes for the treatment of localized gingival/mucosal recessions, insufficient amount of keratinized tissue and insufficient soft tissue volume is at a developing stage.

Periodontal soft tissue root coverage procedures: a systematic review from the AAP Regeneration Workshop.

Chambrone L1, Tatakis DN.
J Periodontol. 2015 Feb;86(2 Suppl):S8-51. doi: 10.1902/jop.2015.130674.

BACKGROUND: This paper aims to create a "bridge" between research and practice by developing a practical, extensive, and clinically relevant study that translates evidence-based findings on soft tissue root coverage (RC) of recession-type defects to daily clinical practice.

METHODS: This review is prepared in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement based on the proposed focused questions. A literature search with no restrictions regarding status or the language of publication was performed for MEDLINE and EMBASE databases up to and including June 2013. Systematic reviews (SRs), randomized clinical trials, controlled clinical trials, case series, and case reports evaluating recession areas that were treated by means of RC procedures were considered eligible for inclusion through the three parts of the study (part I, an overview of the base of SRs; part II, an alternative random-effects meta-analyses on mean percentage of RC and sites exhibiting complete RC; and part III, an SR of non-randomized trials exploring other conditions not extensively evaluated by previous SRs). Data on Class I, II, III, and IV recessions, type of histologic attachment achieved with treatment, recipient- and donor-site anatomic characteristics, smoking-related outcomes, root surface conditions, tooth type and location, long-term effectiveness outcomes, unusual conditions that may be reported during conventional daily practice, and patient-centered outcomes were assessed as well.

RESULTS: Of the 2,456 potentially eligible trials, 234 were included. Data on Class I, II, III, and IV gingival recessions, histologic attachment achieved after treatment, recipient- and donor-site anatomic characteristics, smoking-related outcomes, root surface conditions/biomodification, tooth type and location, long-term effectiveness outcomes and unusual conditions that may be reported during conventional daily practice, and patient-centered outcomes (i.e., esthetic, visual analog scale, complications, hypersensitivity, patients perceptions) were assessed. Subepithelial connective tissue (CT)-based procedures and coronally advanced flap plus acellular dermal matrix grafts, enamel matrx derivative, or collagen matrix led to the best improvements of recession depth, clinical attachment level (CAL) gain, and keratinized tissue (KT). Some conditions, such as smoking and use of magnification, may affect RC outcomes.

CONCLUSIONS: All RC procedures can provide significant reduction in recession depth and CAL gain for Miller Class I and II recession-type defects. Subepithelial CT graft-based procedures provided the best outcomes for clinical practice because of their superior percentages of mean and complete RC, as well as significant increase of KT.

Periodontal soft tissue non-root coverage procedures: a systematic review from the AAP Regeneration Workshop.

Kim DM1, Neiva R.
J Periodontol. 2015 Feb;86(2 Suppl):S8-51. doi: 10.1902/jop.2015.130674.

BACKGROUND: Gingival augmentation procedures around natural teeth and dental implants are performed to facilitate plaque control, to improve patient comfort, to prevent future recession, and in conjunction with restorative, orthodontic, or prosthetic dentistry. The aim of this study is to answer the most common questions related to this treatment modality based on the most relevant and current knowledge in the field.

METHODS: Two reviewers worked to answer the five most common and clinically relevant questions with supporting literature to understand the role of gingiva around teeth. 1) What circumstances require an increased zone of keratinized tissue (KT), or is KT important? 2) What is the ideal thickness of an autogenous gingival graft? Is a thick autogenous gingival graft more effective than a thin autogenous gingival graft? 3) What are the alternatives to autogenous gingival grafting to increase the zone of attached gingiva? 4) Does orthodontic intervention affect soft tissue health and dimensions? 5) What is the patient-reported patient outcome for minimal KT compared with that for an enhanced zone of KT? An extensive literature search was performed using PubMed, the Cochrane Oral Health Group Specialized Trials Registry (the Cochrane Library), and the most respected journals in the field.

RESULTS: Although gingival augmentation procedures were first introduced in 1960s, there have not been in-depth comparative studies examining the five questions that have been proposed by the authors. Lack of relevant systematic reviews and randomized clinical trials (RCTs) on this topic do not allow authors to answer those questions with a strong level of evidence. However, the following can be recommended after

reviewing case reports and case series on these topics. 1) There is enough clinical evidence to support maintaining an adequate band of gingiva for intracrevicular margin restoration. 2) Thick grafts do not appear to result in better clinical outcomes than thin grafts. Thick grafts are likely to result in more primary contraction, whereas thin grafts tend to be prone to secondary contraction. 3) Viable alternative treatment modalities are currently available that are capable of providing KT augmentation without the need for palatal donor tissue. 4) Appropriately applied orthodontic forces do not cause permanent damage to a healthy periodontium. The probability of recession during tooth movement in thin biotype is high to justify gingival augmentation when the dimension of gingiva is inadequate. In addition, cases in which there will be a facial tooth movement outside of the alveolar process need to be considered for a gingival augmentation procedure. 5) Although the articles that have been published on this topic did not consider patient-reported outcomes and esthetics as part of the overall treatment success assessment, patients who have received alternative treatment modalities that did not depend on palatal tissue harvesting appear to have reported more satisfaction and less discomfort after treatment.

CONCLUSIONS: Autogenous gingival grafts are still considered to be the "gold standard" procedure with unmatched success rates and clinical success when gingival augmentation procedures are required. However, tissue-engineered materials may offer viable options to palatal tissue harvesting for gingival augmentation. KT augmentation may prevent the development and progression of gingival recession, especially when restorative margins may interact with the periodontium and/or orthodontic treatment is indicated. Patient-reported outcomes should be considered for future studies on this topic. Additional RCTs and systematic reviews are needed to support these conclusions.

Long-term outcomes after vestibuloplasty with a porcine collagen matrix (Mucograft®) versus the free gingival graft: a comparative prospective clinical trial.

Schmitt CM1, Moest T, Lutz R, Wehrhan F, Neukam FW, Schlegel KA.
Clin Oral Implants Res. 2015 Feb 27. doi: 10.1111/clr.12575. [Epub ahead of print]

OBJECTIVES: Porcine collagen matrices are proclaimed being a sufficient alternative to autologous free gingival grafts (FGG) in terms of augmenting the keratinized mucosa. The collagen matrix Mucograft® (CM) already showed a comparable clinical performance in the early healing phase, similar histological appearance, and even a more natural appearance of augmented regions. Predictability for long-term stability does not yet exist due to missing studies reporting of a follow-up >6 months.

MATERIAL AND METHODS: The study included 48 patients with atrophic edentulous or partially edentulous lower jaw situations that had undergone an implant treatment. In the context of implant exposure, a vestibuloplasty was either performed with two FGGs from the palate (n = 21 patients) or with the CM (n = 27 patients). Surgery time was recorded from the first incision to the last suture. Follow-up examinations were performed at the following time points: 10, 30, 90, and 180 days and 1, 2, 3, 4, and 5 years after surgery. The width of keratinized mucosa was measured at the buccal aspect of each implant, and augmented sites were evaluated in terms of their clinical appearances (texture and color).

RESULTS: The groups showed similar healing with increased peri-implant keratinized mucosa after surgery (FGG: 13.06 mm ± 2.26 mm and CM: 12.96 mm ± 2.86 mm). The maximum follow-up was 5 years (5 patients per group). After 180 days, the width of keratinized mucosa had decreased to 67.08 ± 13.85% in the FGG group and 58.88 ± 14.62% in the CM group with no statistically significant difference. The total loss of the width of keratinized mucosa after 5 years was significant between the FGG (40.65%) and the CM group (52.89%). The CM group had significantly shorter operation times than the FGG group. Augmented soft tissues had a comparable clinical appearance to adjacent native gingiva in the CM group. FGGs could still be defined after 5 years.

CONCLUSIONS: The FGG and the CM are both suitable for the regeneration of the peri-implant keratinized mucosa with a sufficient long-term stability. With the CM, tissue harvesting procedures are invalid, surgery time can be reduced, and regenerated tissues have a more esthetic appearance.

Evaluation of a porcine collagen matrix used to augment keratinized tissue and increase soft tissue thickness around existing dental implants.

Schallhorn RA, McClain PK, Charles A, Clem D, Newman MG
Int J Periodontics Restorative Dent. 2015 Jan-Feb;35(1):99-103. doi: 10.11607/prd.1888.

Implant-supported prostheses often present with mucogingival deficiencies that may cause esthetic or hygienic issues. These issues may present as limited or no keratinized tissue, irregular soft tissue contour or concavity, and gray "showthrough" of the implant abutment and root forms. An interpositional soft tissue graft substitute that generates keratinized tissue and increases soft tissue thickness would be beneficial, as it would reduce donor site morbidity and be available in unlimited, off-the-shelf supply. Thirty patients were assessed as part of a multicenter, practice-based evaluation of the material. A xenogeneic collagen matrix was placed as an interpositional graft on the buccal aspect of implant sites; sites were reassessed at 6 months posttreatment. Results indicated that the collagen matrix increased tissue thickness and keratinized tissue around existing dental implants.

9. Geistlich Bio-Oss® Characteristics

The effect of deproteinized bovine bone on osteoblast growth factors and proinflammatory cytokine production.

Amerio P, Vianale G, Reale M, Muraro R, Tulli A, Piattelli A.
Clin Oral Implants Res 2010;21(6):650-5.

OBJECTIVE: To test the ability of Bio-Oss in inducing growth factors and proinflammatory cytokines that may have a role in inflammation after grafting, bone resorption, remodeling and in the homeostasis of osteoblasts. MATERIAL AND METHODS: Normal human osteoblasts were seeded in Petri dishes containing granules of Bio-Oss, cells were harvested after confluency and RNA was extracted. Reverse transcriptase polymerase chain reaction was performed using specific primers for osteonectin, bone sialoprotein (BSP), bone morphogenetic protein (BMP)-2 and BMP-7, platelet-derived growth factor (PDGF), interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-alpha) and integrin beta1. Glycerol-3-phosphate dehydrogenase was used as the housekeeping gene and normal human osteoblasts grown on Petri dishes without Bio-Oss granules were used as negative controls. RESULTS: Osteoblast grown on Bio-Oss showed a normal RNA expression of osteonectin, integrin beta1 and PDGF. However, compared with control osteoblasts it showed a reduced expression of BSP, BMP-2 and BMP-7, IL-6 and TNF-alpha. CONCLUSIONS: Our findings further support the evidence that Bio-Oss is an excellent biomaterial that does not enhance the production of proinflammatory cytokines.

Human osteoclast formation and activity on a xenogenous bone mineral.

Perrotti, V., B. M. Nicholls, et al.
J Biomed Mater Res A 2009; 90(1): 238-46.

To date, the majority of studies on bone substitute materials have investigated their regenerative properties; however, little is known about their resorption processes, forasmuch as it is believed that the ideal biomaterial for bone regeneration must be completely resorbable. This study is aimed at defining the in vitro resorption potential of human osteoclasts (OCLs) on a xenogenous bone mineral (XBM). Peripheral blood mononuclear cells from healthy volunteers were used to generate OCLs in vitro in the presence of macrophage colony stimulating factor and receptor activator of NF-kappaB ligand on bovine bone slices and XBM. By using morphologic and biochemical methods, we observed that OCL formation occurred on XBM and these cells were positive for the major OCL markers. Regarding OCL activity, resorption pits were detected on XBM by reflection and confocal microscopy. However, biochemical analysis revealed that collagen degradation at day 14 and 21 was significantly lower in XBM supernatants when compared to bovine bone, suggesting that XBM underwent a much slower resorption over time. These findings demonstrate that OCLs are generated on, attach to, and resorb XBM though more slowly than native bone, and suggest that cultured human OCLs could be used as a model for comparing resorption rates of bone substitute materials.

Histologic and elemental microanalytical study of anorganic bovine bone substitution following sinus floor augmentation in humans

Traini T, Degidi M, Sammons R, Stanley P, Piattelli A.

J Periodontol, 2008; 79(7): 232-240.

Background: Histologic data regarding the use of anorganic bovine bone (ABB) in humans are scarce. This study was a histologic evaluation and an examination of the elemental composition of ABB particles and adjacent bone in humans. Methods: Ten biopsies were retrieved 20 months after maxillary sinus augmentation in five patients. The investigation was carried out using light microscopy in brightfield, fluorescence, and circularly polarized light and scanning electron microscopy (SEM) with energy-dispersive x-ray spectroscopy. Results: The regenerated tissue consisted of 38% +/- 2.1% newly formed bone, 36% +/- 1.3% marrow spaces, and 29% +/- 1.8% residual ABB particles. Under polarized light, the newly formed bone was characterized by randomly oriented collagen fibers. Under fluorescence, the biomaterial showed close apposition to bone; under SEM, several projections of newly formed bone were seen penetrating the ABB particles. ABB and bone were distinguished by the lighter gray color of the biomaterial in back-scattered electron images; ABB particles were surrounded and linked by newly formed bone. Elemental analysis gave average calcium/phosphorus ratios (atomic %) approximately 1.9 for ABB and 1.4 for bone. Relatively high concentrations of calcium and phosphorus in the biomaterial decreased gradually toward the interface with bone. Conclusion: The persistence of ABB in the human tissue after 20 months might have been related to the relatively high calcium content of the biomaterial as well as the absence of proteins.

A histological and histomorphometric evaluation of inorganic bovine bone retrieved 9 years after a sinus augmentation procedure.

Traini T, Valentini P, Iezzi G, Piattelli A.
J. Periodontol 2007, 78, 955 – 961.

Background: Anorganic bovine bone (ABB) has been shown to have osteoconductive properties and no inflammatory or adverse responses as grafting materials used in sinus augmentation procedures. Despite these successful results, histologic data in humans over the long-term period are scarce. The purpose of this study was to analyze the histomorphometric data 9 years after surgery in a case of maxillary sinus augmentation using ABB. Methods: The histologic evaluation was performed in five different thin sections of the specimen, comparing histomorphometric measures for newly formed bone, marrow spaces, biomaterial particles remnants, and number of osteocytes embedded in both trabecular bone and bone tissue near the ABB. The investigation was carried out by means of scanning electron microscopy and brightfield and circularly polarized light microscopy. Results: We observed a mean amount of newly formed bone of 46.0% +/- 4.67%, ABB remnants of 16.0% +/- 5.89%, and marrow spaces of 38.0% +/- 8.93%. The osteocyte index was 4.43 for bone around ABB and 3.27 in the trabecular bone at a distance from the particles. Conclusions: After 9 years, the tissue pattern appeared composed by residual ABB particles in close contact to the newly formed bone. The bone mineralized matrix around the ABB had collagen fibers randomly oriented and more osteocytes embedded. The results demonstrate both a high level of osteoconductivity and a "biomimetic" behavior over the long term.

Acceleration of de novo bone formation following application of autogenous bone to particulated anorganic bovine material in vivo.

Thorwarth M, Schlegel KA, Wehrhan F, Srour S, Schultze-Mosgau S.
Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 101(3): 309-316

OBJECTIVE: This prospective animal study examined the de novo bone formation following application of deproteinized bovine bone matrix (DBBM) with or without autogenous bone (AB) to osseous defects. STUDY DESIGN: Defects of defined size were created in the frontal skull of domestic pigs and filled with DBBM alone (group A) and DBBM+25%AB (group B). De novo bone formation was analyzed qualitatively and quantitatively at 9 different times (0.5, 1, 2, 3, 4, 6, 8, 12, 26 weeks) by means of light microscopy, microradiography, and statistical analysis. RESULTS: Histological analysis indicated sufficient osseointegration of DBBM in both groups. Microradiography demonstrated a significant increase of bone formation in group B after 6 weeks (P = .0159) and 8 weeks (P = .0317). CONCLUSION: The addition of 25%AB to DBBM results in accelerated de novo bone formation in osseous defects. This effect is likely caused by osteoinductive properties of cellular elements transplanted with the autogenous bone.

Microvessel density and vascular endothelial growth factor expression in sinus augmentation using Bio-Oss.

Degidi M, Artese L, Rubini C, Perrotti V, Iezzi G, Piatelli A.
Oral Dis 2006; 12(5): 469-475.

The aim of this study was to evaluate microvessel density (MVD) and vascular endothelial growth factor (VEGF) expression in sinus augmentation with Bio-Oss((R)). Twenty patients participated in this study. The sinuses were filled with 100% Bio-Oss((R)). Implants were inserted after 3 months in group A, and 6 months in group B. A trephine was used to harvest bone cores. As control, the pre-existing subantral bone was used. The mean MVD in control bone was 23.6 +/- 1.8. In the sites augmented with Bio-Oss((R)), at 3 months, the MVD was 23.3 +/- 2.1, while in the sites retrieved at 6 months the MVD was 29.5 +/- 2.4. The difference in MVD between the control bone and group A was not statistically significant. The difference between the control bone and group B was statistically significant ($P < 0.05$). The statistical analysis showed that the difference in MVD between group A and group B was statistically significant ($P < 0.05$). Bio-Oss((R)) seemed to induce an increase in MVD that reached a higher value after 6 months. The percentage of vessels positive to VEGF was higher in group A than in group B. Our data also showed a higher percentage of vessel and stromal cells positive to VEGF and higher MVD values in areas where there was newly formed bone compared with areas where maturation processes were occuring, and this fact could point to a close spatial relationship between angiogenesis and osteogenesis.

Genetic effects of anorganic bovine bone (Bio-Oss) on osteoblast-like MG63 cells.

Carinci F, Piatelli A, Degidi M, Palmieri A, Perrotti V, Scapoli L, Martinelli M, Laino G, Pezzetti F.
Arch Oral Biol, 2006; 51: 154-163.

Bio-Oss (Geistlich, Wolhusen, Switzerland) is composed by anorganic bovine bone and is widely used in several bone regeneration procedures in oral surgery. How this biomaterial alters osteoblast gene expression to promote bone formation is poorly understood. We therefore attempted to address this question by using microarray techniques to identify genes that are differentially regulated in osteoblasts exposed to Bio-Oss. By using DNA microarrays containing 20,000 genes, we identified in osteoblast-like cells line (MG-63) cultured with Bio-Oss several genes which expression was significantly up- and down-regulated. The differentially expressed genes cover a broad range of functional activities: (a) signaling transduction, (b) transcription, (c) cell cycle regulation, (d) vesicular transport, (e) apoptosis, and (f) immunity. These results could explain the reported bioaffinity of Bio-Oss to host animals, its biological affinity to osteogenic cells and its capability to stimulate osteoblastic differentiation. The data reported are, to our knowledge, the first genetic portrait of Bio-Oss effects. They can be relevant to our improved understanding of the molecular mechanism underlying bone regenerative procedures and as a model for comparing other materials with similar clinical effects.

Maxillary Sinus Augmentation with Bio-Oss particles: A Light, Scanning, and Transmission Electron Microscopy Study in Man

Orsini G, Traini T, Scarano A, Degidi M, Perrotti V, Piccirilli M, Piattelli A.
J Biomed Mater Res 2005 Part B : Appl Biomater 74B :448-457.

Abstract: Biological interactions occurring at the bone–biomaterial interface are critical for long-term clinical success. Bio-Oss is a deproteinized, sterilized bovine bone that has been extensively used in bone regeneration procedures. The aim of the present study was a comparative light, scanning, and electron microscopy evaluation of the interface between Bio-Oss and bone in specimens retrieved after sinus augmentation procedures. Under light microscopy, most of the particles were surrounded by newly formed bone, while in a few cases, at the interface of some particles it was possible to observe marrow spaces and biological fluids. Under scanning electron microscopy, in most cases, the particle perimeter appeared lined by bone that was tightly adherent to the biomaterial surface. Transmission electron microscopy showed that the bone tissue around the biomaterial showed all the phases of the bone healing process. In some areas, randomly organized collagen fibers were present, while in other areas, newly formed compact bone was present. In the first bone lamella collagen fibers contacting the Bio-Oss surface were oriented at 243.73 ± 7.12° (mean ± SD), while in the rest of the lamella they were oriented at 288.05 ± 4.86° (mean ± SD) with a statistically significant difference of 44.32° ($p < 0.001$). In the same areas the intensity of gray value was 172.56 ± 18.15 (mean ± SD) near the biomaterial surface and 158.71 ± 21.95 (mean ± SD) in the other part of

the lamella with an unstatistically significant difference of 13.79 (p ±0.071). At the bone–biomaterial interface there was also an electron-dense layer similar to cement lines. This layer had a variable morphology being, in some areas, a thin line, and in other areas, a thick irregular band. The analyses showed that Bio-Oss particles do not interfere with the normal osseous healing process after sinus lift procedures and promote new bone formation. In conclusion, this study serves as a better understanding of the morphologic characteristics of Bio-Oss and its interaction with the surrounding tissues.

Histomorphometric analysis of natural bone mineral for maxillary sinus augmentation

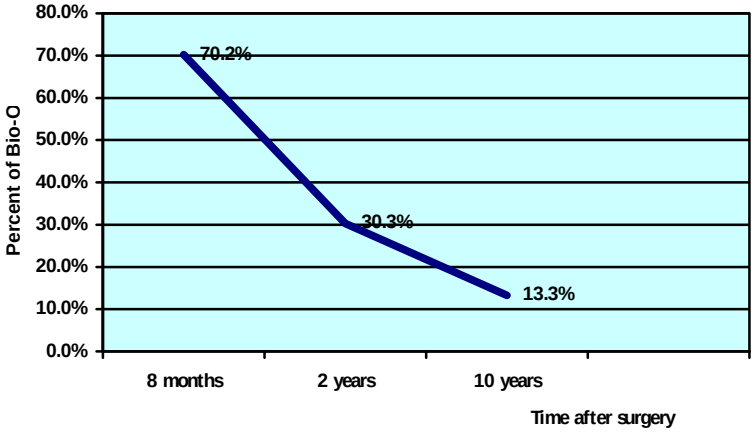
John HD, Wenz B
Int J Oral Maxillofac Implants 2004; 19: 199-207.

PURPOSE: Lack of bone height in the posterior maxilla often necessitates augmentation prior to or simultaneously with dental implant placement. The purpose of this clinical study was to evaluate the use of the natural bone mineral Bio-Oss alone or in combination with autogenous bone in sinus floor elevations performed as 1- or 2-step procedures. MATERIALS AND METHODS: Thirty-eight patients required sinus augmentation. Natural bone mineral alone was used in sinus floor augmentation in 21 patients. In 13 patients, a mixture of the bone substitute and autogenous bone was used, and in 4 patients autogenous bone alone was used. In all of the patients, samples were taken for biopsy 3 to 8 months postoperatively, and bone regeneration was evaluated histologically and histomorphometrically. RESULTS: In all patients, the amount of new bone significantly increased over the observation time, while marrow areas decreased. There was no statistically significant difference in the amount of new bone formation between the Bio-Oss group (new bone 29.52% +/- 7.43%) and the Bio-Oss/autogenous bone group (new bone 32.23% +/- 6.86%). In the 4 patients treated with autogenous bone alone, a greater amount of newly formed bone was found; however, in these cases the area volume filled was smaller than in the other 2 groups. DISCUSSION: The data showed that new bone formation takes place up to 8 months after sinus floor elevation and that there is no difference in the amount of bone formation between procedures done with the bone substitute alone or with the mixture of the substitute and autogenous bone. CONCLUSION: These data suggest that predictable bone formation can be achieved with the use of Bio-Oss.

Ten-year follow-up in a maxillary sinus augmentation using anorganic bovine bone (Bio-Oss). A case report with histomorphometric evaluation.

Sartori S, Silvestri M, Forni F, Icaro Cornaglia A, Tesei P, Cattaneo V.
Clin Oral Impl Res 2003; 14(3): 369-372

Several bone grafting materials have been used in sinus augmentation procedures. Bio-Oss (deproteinized and sterilized bovine bone) has shown to have osteoconductive properties and no inflammatory or adverse responses have been published. In spite of these successful results, histologic data regarding bone augmentation using Bio-Oss in humans is scarce. The purpose of this study was to analyse the amount of Bio-Oss ossification in a case of maxillary sinus augmentation, recording and comparing histomorphometric data 8 months, 2 and 10 years after surgery. This long-term histologic evaluation of retrieved specimens has been performed, comparing histomorfometric measures at different times. Eight months after surgery we



observed in 20 different thin sections of the specimen a mean amount of bone tissue (including medullar spaces) of 29.8% (and 70.2% of Bio-Oss) +/- 2.6. At 2 years the bone tissue increased to 69.7% + 2.7 and 10 years after surgery it was 86.7% +/- 2.8. The comparison of the means for each time has shown a highly significant increasing trend in bone formation associated with Bio-oss resorption: at 8 months, 2 and 10 years.

The ultrastructure of anorganic bovine bone and selected synthetic hyroxyapatite used as bone graft substitute materials

Benezra Rosen V., Hobbs L.W., Spector M.
Biomaterials 2002; 22: 921-928.

The objective of this study was to investigate the morphology and organization of apatite crystallites in mature mammalian bone. Anorganic bovine bone was studied in this investigation to allow for the examination of the mineral crystallites after removal of the organic phase. Field-emission low-voltage scanning electron microscopy (FE-LVSEM) was employed to obtain images at nanometer resolution without the application of a conductive coating. Transmission electron microscopy (TEM) of the samples was also performed to confirm the identification of features observed in the SEM and to allow for comparison with earlier studies of bone mineral architecture. For comparison, in order to demonstrate how the interaction of collagen and apatite results in the architecture and crystal structure of bone mineral, two synthetic hydroxyapatite materials were also analyzed: OsteoGen and OsteoGraf/LD300. FE-LVSEM revealed distinctive features of bone mineral: a fibrillar organization of crystallites, a periodic spacing of crystallites along the fibrils consistent with the banding pattern of collagen, inter-fibrillar bridging crystallites, and a plate-like habit of the crystallites. These findings supported the hypothesis, derived from the earlier TEM data of others, that the mineralization of collagen comprising osteoid proceeds by the formation of apatite crystallites within the fibers at selected periodic sites along their length. Moreover, the very presence in this anorganic material of distinct fibers comprised of the crystallites is demonstration of inter-crystallite bonding. The crystallites of the synthetic hydroxyapatite materials did not display any of these ultrastructural features.

Orthodontic movement in bone defects augmented with Bio-Oss® - An experimental study in dogs

MG Araujo, D. Carmagnola, T. Berglundh, B. Lindhe
J Clin Periodontol 2001; 28.

Objective: To study if it was possible to move, by orthodontic means, a tooth into an area of the jaw that had been augmented with Bio-Oss®. *Material and Methods*: 5 beagle dogs were used. The 1st, 2nd, and 4th mandibular premolars on each side were removed. The defect at the left 4th premolar site was filled with a biomaterial (Bio-Oss®) while the corresponding defect in the right side was left for spontaneous healing. 3 months later, an orthodontic device was inserted in each side of the mandible. The device was designed to allow distal, bodily movement of the 3rd premolars. When the experimental teeth had been moved into the extraction sites of the 4th premolars, the animals were sacrificed and biopsies of the premolar-molar regions of the mandible sampled. The tissues were prepared for histological analysis using standard procedure. In the sections, 3 zone were identified: zone A=the bone tissue within the distal portion of the previous extraction site (4th premolar), zone B=the pressure side of the 3rd premolar, zone C=the tension side of the 3rd premolar. The area occupied by mineralized bone, Bio-Oss® particles and bone marrow was determined by a point counting procedure. The width of the periodontal ligament as well as the percentage of the root surface (in zone B) that exhibited resorption was determined. *Results*: The findings demonstrated that it was possible to move a tooth into an area of an alveolar ridge that 3 monbts previously had been augmented with a biomaterial. It was also demonstrated that 12 months after grafting, Bio-Oss® particles remained as inactive filler material in the not utilized part of zone A. The biomaterial was not present in zone C but present in small amounts in zone B. *Conclusion*: During the orthodontic tooth movement the graft material (Bio-Oss®) was degraded and eliminated from the part of the alveolar ridge that was utilized for the experiment. In the non-utilized part of the ridge the biomaterial, however, remained as a seemingly inactive filler material.

Three-dimensional cultivation of human osteoblast-like cells on highly porous natural bone mineral

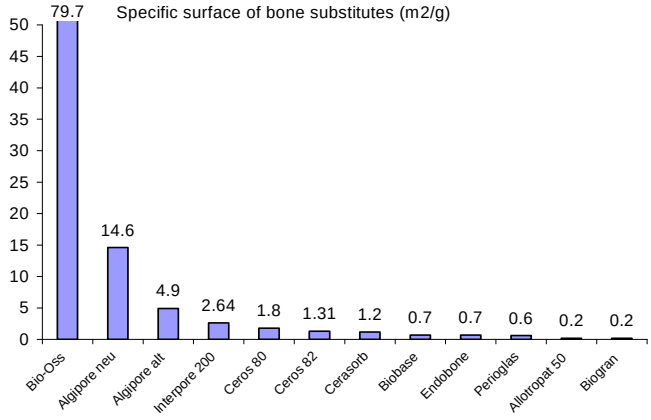
Y. Açil, H. Terheyden, A. Dunsche, B. Fleiner, S. Jepsen
J Biomed Mater Res 2000; 52.

In this study was investigated the growth and extracellular matrix synthesis of human osteoblast-like cells on highly porous natural bone mineral. Human bone cells were isolated from trabecular bone during routine iliac cresh biopsies. Under conventional culture conditions, trabecular bone cells were able to assume the organization of a three-dimensional structure on a porous natural bone mineral (Bio-Oss® Block). Scanning electron microscopy examination after 6 weeks revealed multiple cell layers on the trabecular block. Transmission electron microscopy examination after 6 weeks revealed the accumulation of mature collagen fibrils in the intracellular and extracellular spaces, and showed multilayered, rough endoplasmic reticulum as well as mitochondria-rich cells surrounded by dense extracellular matrix. These morphological observations suggest that the cell layer may resemble the natural three-dimensional structure. Biochemical analysis revealed that the hydroxylysylpyridinoline, lysylpyridinoline, and hydroxyproline content of the cell layer increased in a time-dependent manner, whereas in monolayer culture without natural bone mineral, no measurable amounts of hydroxylysylpyridinoline or lysylpyridinoline, and a barely measurable amount of hydrosyproline, were noted. Mature collagen extracted by ethylenediaminetetraacelic acid-demineralization from the cell layer on natural bone mineral showed an identical electrophoretic pattern to that observed in human bone, as evaluated by sodium dodecyl sulphate-polyacrylamide gel electrophoresis. The present study demonstrated an excellent biocompatibility of the highly porous natural bone mineral in a three-dimensional bone cell culture system, and thus its potential for tissue-engineered growth of human bone.

Analysis of the size of the specific surface area of bone regeneration materials by gas adsorption

G. Weibrich, R. Trettin, S.H. Gnoth, H. Götz, H. Duschner, W. Wagner
Mund Kiefer Gesichts Chir 2000; 156.

The surface area and the microporosity of bone regeneration materials influence their chemical and biological properties. Therefore, the size of the specific surface area (see Fig.) and the distribution of the pore diameters (pore<1 µm) of bone regeneration materials were analyzed within this study. The analyzed hydroxyapatites were of synthetic, bovine, and phytotroph origin. The tricalcium phosphates and the bioglasses included only synthetic materials.



Bone Reactions to Anorganic Bovine Bone (Bio-Oss®) Used in Sinus Augmentation Procedures: A Histologic Long-Term Report of 20 Cases in Humans

M. Piatelli, GA Favero, A. Scarano, G. Orsini, A. Piatelli
Int J Oral Maxillofac Implants 1999 ; 14(6).

The aim of the present study was to conduct a long-term histologic analysis of retrieved specimens in humans where Bio-Oss® was used in sinus augmentation procedures. Specimens were retrieved from 20 patients after varying periods from 6 months to 4 years and were processed to obtain thin ground sections. Bio-Oss® particles were surrounded for the most part by mature, compact bone. In some Haversian canals it was possible to observe small capillaries, mesenchymal cells, and osteoblasts in conjunction with new bone. No gaps were present at the interface between the Bio-Oss® particles and newly formed bone. In specimens retrieved after 18 months and 4 years, it was also possible to observe the presence of osteoclasts in the process of resorbing the Bio-Oss® particles and neighboring newly formed bone. Bio-Oss® appears to be highly biocompatible and osteoconductive, is slowly resorbed in humans, and can be used with success as a bone substitute in maxillary sinus augmentation procedures.

Tissue Reaction and Material Characteristics of four Bone Substitutes

Jensen S.S., Merete A., Pinholt E.M., Hjørting-Hansen E., Melsen F., Ruyter E.
Int J Oral Maxillofac Implants 1996 ; 11: 55-66.

The aim of the present study was qualitatively and quantitatively to compare the tissue reaction around four different bone substitutes used in orthopedic and craniofacial surgery. Cylinders of two bovine bone substitutes (Endobon® and Bio-Oss®) and two coral derived bone substitutes (Pro Osteon 500® and Interpore 500 HA/CC®) were implanted into 5 mm burr holes in rabbit tibia. Interpore 500 HA/CC® resorbed completely, whereas the other three biomaterials did not undergo any detectable biodegradation. Pro Osteon 500® and Endobon® showed no signs of resorption Bio-Oss® was osseointegrated to a high degree and became included in the natural remodeling process of bone.

10. Geistlich Bio-Gide® Characteristics

Functional assay, expression of growth factors and proteins modulating bone-arrangement in human osteoblasts seeded on an anorganic bovine bone biomaterial.

Trubiani O, Fulle S, Traini T, Paludi M, la Rovere R, Orciani M, Caputi S, Piattelli A.
Eur Cell Mater. 2010 Jul 21;20:72-83.

The basic aspects of bone tissue engineering include chemical composition and geometry of the scaffold design, because it is very important to improve not only cell attachment and growth but especially osteodifferentiation, bone tissue formation, and vascularization. Geistlich Bio-Oss (GBO) is a xenograft consisting of deproteinized, sterilized bovine bone, chemically and physically identical to the mineral phase of human bone. In this study, we investigated the growth behaviour and the ability to form focal adhesions on the substrate, using vinculin, a cytoskeletal protein, as a marker. Moreover, the expression of bone specific proteins and growth factors such as type I collagen, osteopontin, bone sialoprotein, bone morphogenetic protein-2 (BMP-2), BMP-7 and de novo synthesis of osteocalcin in normal human osteoblasts (NHOst) seeded on xenogenic GBO were evaluated. Our observations suggest that after four weeks of culture in differentiation medium, the NHOst showed a high affinity for the three dimensional biomaterial; in fact, cellular proliferation, migration and colonization were clearly evident. The osteogenic differentiation process, as demonstrated by morphological, histochemical, energy dispersive X-ray microanalysis and biochemical analysis was mostly obvious in the NHOst grown on three-dimensional inorganic bovine bone biomaterial. Functional studies displayed a clear and significant response to calcitonin when the cells were differentiated. In addition, the presence of the biomaterial improved the response, suggesting that it could drive the differentiation of these cells towards a more differentiated osteogenic phenotype. These results encourage us to consider GBO an adequate biocompatible three-dimensional biomaterial, indicating its potential use for the development of tissue-engineering techniques.

Effect of two bioabsorbable barrier membranes on bone regeneration of standardized defects in calvarial bone: a comparative histomorphometric study in pigs.

Bornstein, M. M., G. Heynen, et al.
J Periodontol 2009; 80(8): 1289-99.

BACKGROUND: The effect of two different bioabsorbable collagen membranes on bone regeneration was assessed in standardized, membrane-protected calvarial defects in pigs. METHODS: Two standardized defect types (6 x 6 x 6 mm and 9 x 9 x 9 mm) were produced in the calvaria of pigs: empty defects without a membrane (group 1; eight defects per size); defects filled with deproteinized bovine bone mineral (DBBM) without a membrane (group 2; eight defects per size); defects filled with DBBM and covered by a collagen membrane (group 3; eight defects per size); and defects filled with DBBM and covered by a cross-linked collagen membrane (CCM) (group 4; eight defects per size). Sacrifice took place 16 weeks after surgery, and

the following parameters were analyzed: descriptive histology; semiquantitative histology (SQH), assessing bone regeneration in the whole defect area; and histomorphometric analysis of the percentage of bone and DBBM in the regenerated area at three different depth levels of the defect. RESULTS: Using SQH, both membrane types resulted in significantly better bone regeneration compared to groups 1 and 2, irrespective of the defect size (P <0.005), with no difference between the two membranes. In the histomorphometric analysis, the layer immediately below the surface exhibited a significantly higher percentage of bone in groups 3 (27%) and 4 (36%) versus the two other groups for the 9 x 9 x 9-mm defects. No such differences were apparent for the 6 x 6 x 6-mm defects or the other two depth levels (bottom and middle layer) for either defect size. CONCLUSIONS: The two collagen membranes tested significantly enhanced bone regeneration, especially in the superficial level of the calvarial bone defects. The prototype CCM did not provide any further advantage in the present animal model.

Immunohistochemical characterization of guided bone regeneration at a dehiscence-type defect using different barrier membranes: an experimental study in dogs.

Schwarz, F., D. Rothamel, et al.
Clin Oral Implants Res 2008; 19(4): 402-15.

Objectives: The aim of the present study was to evaluate immunohistochemically the pattern of guided bone regeneration (GBR) using different types of barrier membranes. Material and methods: Standardized buccal dehiscence defects were surgically created following implant bed preparation in 12 beagle dogs. Defects were randomly assigned to six different GBR procedures: a collagen-coated bone grafting material (BOC) in combination with either a native, three cross-linked, a titanium-reinforced collagen membrane, or expanded polytetrafluorethylene (ePTFE), or BOC alone. After 1, 2, 4, 6, 9, and 12 weeks of submerged healing, dissected blocks were processed for immunohistochemical (osteocalcin - OC, transglutaminase II - angiogenesis) and histomorphometrical analysis [e.g., bone-to-implant contact (BIC), area of new bone fill (BF)]. Results: In general, angiogenesis, OC antigen reactivity, and new bone formation mainly arose from open bone marrow spaces at the bottom of the defect and invaded the dehiscence areas along the implant surface and BOC. At 4 weeks, membranes supporting an early transmembraneous angiogenesis also exhibited some localized peripheral areas of new bone formation. However, significantly increasing BIC and BF values over time were observed in all groups. Membrane exposure after 10-12 weeks was associated with a loss of the supporting alveolar bone in the ePTFE group. Conclusion: Within the limits of the present study, it was concluded that (i) angiogenesis plays a crucial role in GBR and (ii) all membranes investigated supported bone regeneration on an equivalent level.

Cross-linked and non-cross-linked collagen barrier membranes disintegrate following surgical exposure to the oral environment: a histological study in the cat

Tal H, Kozlovsky A, Artzi Z, Nemcovsky CE, Moses O.
Clin Oral Implants Res 2008; 19: 760-766.

BACKGROUND: Early barrier membrane degradation may result in decreased bone formation in guided bone regeneration (GBR) procedures. The aim of this study was to evaluate the bio-degradation of cross-linked (CLM) and non-cross-linked (NCLM) collagen membranes experimentally exposed to the oral environment of study animals. METHODS: In eight cats, 48 surgical procedures were performed, three along each side of the palate: 24 full-thickness soft tissue perforations were made and 24 full-thickness mini-flaps were raised. CLM or NCLM discs were placed either under the perforations and peripheral mucosa and left exposed (experimental) or covered by the flaps (controls). The four treatment modalities were equally distributed among the eight animals. Block sections were retrieved at 7 and 28 days post-operatively, providing histological specimens (6 each) at 7 and 28 days for each treatment modality. RESULTS: Histological observation revealed that CLM and NCLM remained intact in the control sites during the 28 days. At 7 and 28 days, CLM appeared interrupted in three and two experimental sites, respectively, and were undetected in the remaining sites. NCLM were interrupted in two sites each at 7 and 28 days, and were undetected in the other sites. There was no statistical difference between control specimens and between CLM and NCLM of the different treatment modalities at 7 or 28 days. CONCLUSIONS: Both cross-linked and non-cross-linked membranes were resistant to tissue degradation and maintained continuity throughout the study. However, none of the membranes was resistant to degradation when exposed to the oral environment

Angiogenesis pattern of native and cross-linked collagen membranes: an immunohistochemical study in the rat.

Schwarz, F., D. Rothamel, et al.
Clin Oral Implants Res 2006; 17(4): 403-9.

The aim of the present study was to immunohistochemically evaluate angiogenesis pattern of native and cross-linked collagen membranes after subcutaneous implantation in rats. Five commercially available and three experimental membranes (VN) were included: (1) BioGide (BG), (2) BioMend (BM), (3) BioMend Extend (BME), (4) Ossix (OS), (5) TutoDent (TD), and (6-8) VN(1-3). Specimens were randomly allocated in unconnected subcutaneous pouches (n=4) separated surgically on the back of 40 wistar rats, which were divided into five groups (2, 4, 8, 16, and 24 weeks), including eight animals each. Pattern of angiogenesis was labelled using primary mouse monoclonal antibody to transglutaminase II. For each membrane, the period of time, needed for a complete and homogeneous transmembraneous vascularization, was assessed immunohistomorhometrically. Differences between the membranes were found regarding the initial pattern of transmembraneous angiogenesis, as evaluated 2 weeks following implantation. Mean cross- and longitudinal-sectional area of blood vessels (%) was highest for VN(3) (5.27+/-2.73), followed by BG (2.45+/-0.88), VN(1) (2.07+/-0.29), VN(2) (1.91+/-0.55), TD (1.44+/-0.53), BME (0.35+/-0.29) and BM (0.25+/-0.4). In contrast to BG and VN(1-3), BM, BME and TD exhibited a homogeneous transmembraneous formation of blood vessels merely 4-8 weeks following implantation. OS, however, exhibited no signs of angiogenesis throughout the whole study period. Within the limits of the present study, it may be concluded that pattern of transmembraneous angiogenesis markedly differs among the membranes investigated.

Membrane durability and tissue response of different bioresorbable barrier membranes: a histologic study in the rabbit calvarium

Von Arx T, Broggini N, Storgard S, Bornstein M, Schenk R, Buser D
Int J Oral & Maxillofacial Impl 2005; 20: 843-853

PURPOSE: The objective of the present study was to histologically evaluate barrier durability and host tissue response of new prototype collagen membranes in comparison to clinically available collagen and synthetic polymer membranes. MATERIALS AND METHODS: The experimental study was conducted in 20 rabbits with 4 different healing periods of 2, 6, 12, and 28 weeks. Following surgical exposure of the calvarium, 6 circular bone defects (diameter 4 mm, depth 1.5 mm) were drilled into the outer cortex. After the bone had been removed, each defect was covered with 1 of 6 different membranes: 3 collagen prototype membranes, a Bio-Gide collagen membrane (BG), a glycolide-lactide-trimethylene carbonate Osseoquest membrane (OQ), and a polylactide Atrisorb membrane (AS). Histological analysis was performed following staining with toluidine blue and transversal sectioning of the calvarial bone. RESULTS: All collagen membranes showed similar tissue integration characterized by fibrous encapsulation with differentiation of a periosteumlike tissue upon the external bony surface. One prototype collagen membrane displayed clearly longer membrane integrity. The evaluated synthetic membranes demonstrated extended barrier durability but also exhibited inflammatory foreign-body reactions. DISCUSSION: Recent experimental investigations have shown that degradation of collagen membranes may begin within days to weeks of membrane placement. This was confirmed in the present study. However, 1 of the chemically modified collagen prototype membranes exhibited prolonged membrane integrity in the absence of an inflammatory tissue response. CONCLUSION: Further investigation of the prototype membrane that showed prolonged membrane integrity to evaluate its potential in GBR procedures is needed.

Biodegradation of differently cross-linked collagen membranes: an experimental study in the rat

Rothamel D, Schwarz F, Sager M, herten M, Sculean A, Becker J.
Clin Oral Impl Res 2005; 16: 369-378.

The aim of the present study was to compare the biodegradation of differently cross-linked collagen membranes in rats. Five commercially available and three experimental membranes (BN) were included: (1) Bio-Gide® (BG) (non-cross-linked porcine type I and III collagens), (2) BioMend® (BM), (3) BioMendExtend® (BME) (glutaraldehyde cross-linked bovine type I collagen), (4) Ossix® (OS) (enzymatic-cross-linked bovine

type I collagen), (5) TutoDent® (TD) (non-cross-linked bovine type I collagen, and (6-8) VN (1-3) (chemical cross-linked porcine type I and III collagens). Specimens were randomly allocated in unconnected subcutaneous pouches separated surgically on the back of 40 wistar rats, which were divided into five groups (2, 4, 8, 16, and 24 weeks), including eight animals each. After 2, 4, 8, 16, and 24 weeks of healing, the rats were sacrificed and explanted specimens were prepared for histologic and histometric analysis. The following parameters were evaluated: biodegradation over time, vascularization, tissue integration, and foreign body reaction. Highest vascularization and tissue integration was noted for BG followed by BM, BME, and VN(1); TD, VN(2), and VN(3) showed prolongated, while OS exhibited no vascularization. Subsequently, biodegradation of BG, BM, BME and VN(1) was faster than TD, VN(2), and VN(3). OS showed only a minute amount of superficial biodegradation 24 weeks following implantation. Biodegradation of TD, BM, BME, VN(2), and VN(3) was associated with the presence of inflammatory cells. Within the limits of the present study, it was concluded that cross-linking of bovine and porcine-derived collagen types I and III was associated with (i) prolonged biodegradation, (ii) decreased tissue integration and vascularization, and (iii) in case of TD, BM, BME, VN(2), and VN(3) foreign body reactions.

Biocompatibility of various collagen membranes in cultures of human PDL fibroblasts and human osteoblast-like cells

Rothamel D, Schwarz F, Sculean A, Herten M, Scherbaum W, Becker J.
Clin Oral Impl Res 2004; 15: 443-449.

The aim of the present study was to evaluate the biocompatibility of differently cross-linked collagen membranes in cultures of human PDL fibroblasts and human osteoblast-like cells. Four collagen membranes (Bio-Gide(BG), BioMend (BM), Ossix (OS) and TutoDent (TD)] were tested. Cells plated on culture dishes served as positive controls. Six specimens of each membrane were incubated with (1) human PDL fibroblasts ($2x10^4$ cells) (n=24), and (2) human osteoblast-like cells) (SaOs-2) ($2x10^4$ cells) (n=24) under standardized conditions. After 7 days, adherent cells were stained with hematoxylin and counted using a reflected light microscope and the cell density per square millimeter was calculated. Additionally, cell morphology was investigated using scanning electron microscopy (SEM). Cell counts were presented as means and standard deviations (cell/mm^2) and analyzed for statistical difference using the Wilcoxon test: (1) CD (434 ± 76)›BG (64 ± 19)=OS (61 ± 8)›TD (44 ± 4)›BM (12 ± 5); (2) CD (453 ± 92)›BG (94 ± 46)=TD (84 ± 49)›OS (41 ± 23)›BM (0). SEM examination revealed that PDL fibroblasts adherent on BG, TD and OS appeared spindle-shaped and flat, like cells on CD. SaOs-2 osteoblasts adherent on CD were star shaped and flat, but mostly round in shape on BG, OS and TD. BM appeared to be incompatible with the attachment and proliferation of SaOs-2 cells; however, a few PDL fibroblasts were found in a round shape. Within the limits of the present study, it was concluded that (i) BG, TD and OS promoted, and (ii) BM inhibited the attachment and proliferation of human PDL fibroblasts and human SaOs-2 osteoblasts.

Compatibility of resorbable and nonresorbable guided tissue regeneration membranes in cultures of primary human periodontal ligament fibroblasts and human osteoblast-like cells

B. Alpar, G. Leyhausen, H. Günay, W. Geurtsen
Clin Oral Invest 2000, 4:219-225

The purpose of this study was (a) to evaluate the cytocompatibility of three resorbable and nonresorbable membranes in fibroblast and osteoblast-like cell cultures and (b) to observe the growth of those cells on the various barriers by scanning electron microscopy (SEM). Primary human periodontal ligament fibroblasts (HPLF) and human osteoblast-like cells (SAOS-2) were incubated with nonresorbable polytetrafluoroethylene (ePTFE) barriers and resorbable polylactic acid as well as collagen membranes. Cytotoxic effects were determined by XTT (mitochondrial metabolic activity) and sulforhodamine B assays (cellular protein content). In addition, HPLF and SAOS-2 grown for 21 days on the investigated barriers were evaluated by SEM. Data were analyzed statistically by ANOVA using the Wilcoxon-Mann-Whitney test ($P<0.05$). No changes were established in the periodontal fibroblasts and human osteoblast-like cells after incubation with collagen membrane. Cytotoxic effects, however, were induced by the polylactic acid barrier which slightly inhibited cell metabolism of the periodontal fibroblasts (XTT:90.1%_+ 3.6of control value). Moderate cytotoxic reactions were caused by the nonresorbable ePTFE membrane in HPLF-cultures (XTT: 82.7%±3.5) and osteoblast-like cell monolayers (XTT: 80.0%±0.6%). Mitochondrial activity in both cell cultures was significantly reduced by ePTFE barriers in comparison to nonincubated control cells ($P=0.028$).

SEM analysis of cell behavior on barriers demonstrated the differences between these materials: collagen barriers were densely populated with HPLF and SASP-2, whereas only few or no cells were seen to adhere to the ePTFE and polylactic acid mambranes. Our findings indicate that the collagen barrier investigated is very cytocompatible and may be integrated into connective tissue well. On the contrary, the HPLF and SAOS-2, whereas only few or no cells were seen to adhere to the ePTFE and polylactic acid membranes. Our findings indicate that the collagen barrier investigated is very cytocompatible and may be integrated into connective tissue well. On the contrary, the ePTFE and polylactic acid membranes induced slight to moderate cytotoxic reactions which may reduce cellular adhesion. Thus, gap formation between the barrier surface and connective tissue may by promoted which may facilitate epithelial downgrowth and microbial accumulation. Consequently, these effects may reduce the potential gain in periodontal attachment.

11. Safety

Analysis of the risk of transmitting bovine spongiform encephalopathy through bone grafts derived from bovine bone

B. Wenz, B. Oesch, M. Horst
Biomaterials 2001; 22.

Bone substitutes of bovine origin are widely used for treatment of bone defects in dental and orthopedic surgery. Due to the occurrence of BSE and the new variant of Creutzfeldt Jakob Disease risks of transmitting diseases through the use of such materials need to be carefully evaluated. Risk analysis can either be based on theoretical assessments or experimental evidence. Here we present a comparative study on two bovine bone substitutes (Bio-Oss® and Osteograf/N) which is based on theoretical values. Furthermore, for one of these materials, i.e. Bio-Oss®, the prion inactivation capacity of one of the production steps was experimentally evaluated. Theoretical and experimental data indicate that the use of these materials does not carry a risk of transmitting BSE to patients.

12. Comparisons with other...

a ... bone substitute materials

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.

Schwarz, F., N. Sahm, et al.
J Clin Periodontol 2009; 36(9): 807-14.

OBJECTIVES: The present case series aimed at investigating the 4-year clinical outcomes following surgical regenerative therapy of peri-implantitis lesions using either a nanocrystalline hydroxyapatite (NHA) or a natural bone mineral in combination with a collagen membrane (NBM+CM). MATERIALS AND METHODS: Twenty patients suffering from moderate peri-implantitis (n=20 intrabony defects) were randomly treated with (1) access flap surgery (AFS) and the application of NHA (n=9), or with AFS and the application of NBM+CM (n=11). Clinical and radiographic (R) parameters were recorded at baseline (R) and after 36 and 48 (R) months of non-submerged healing. RESULTS: One patient from the NBM+CM group was discontinued from the study due to severe pus formation at 36 months. Compared with NHA, the application of NBM+CM resulted in higher mean PD reductions (NBM+CM: 2.5 +/- 0.9 mm versus NHA: 1.1 +/- 0.3 mm) and clinical attachment-level gains (NBM+CM: 2.0 +/- 1.0 mm versus NHA: 0.6 +/- 0.5 mm) at 48 months. A radiographic bone fill was observed for five sites in the NHA group, and eight sites in the NBM+CM group. CONCLUSION: While the application of NBM+CM resulted in clinical improvements over a period of 4 years, the long-term outcome obtained with NHA without barrier membrane must be considered as poor.

Comparative study of biphasic calcium phosphates with different HA/TCP ratios in mandibular bone defects. A long-term histomorphometric study in minipigs

Jensen SS, Bornstein MM, Dard M, Bosshardt DD, Buser D.
J Biomed Mater Res B Appl Biomater 2009; 90(1):171-81

Three biphasic calcium phosphate (BCP) bone substitute materials with hydroxyapatite (HA)/tricalcium phosphate (TCP) ratios of 20/80, 60/40, and 80/20 were compared to coagulum, particulated autogenous bone, and deproteinized bovine bone mineral (DBBM) in membrane-protected bone defects. The defects were prepared in the mandibles of 24 minipigs that were divided into four groups of six with healing times of 4, 13, 26, and 52 weeks, respectively. The histologic and histomorphometric evaluation focused on differences in amount and pattern of bone formation, filler degradation, and the interface between bone and filler. Collapse of the expanded polytetrafluoroethylene barrier membrane into the coagulum defects underlined the necessity of a filler material to maintain the augmented volume. Quantitatively, BCP 20/80 showed bone formation and degradation of the filler material similar to autografts, whereas BCP 60/40 and BCP 80/20 rather equaled DBBM. Among the three BCP's, the amount of bone formation and degradation of filler material seemed to be inversely proportional to the HA/TCP ratio. The fraction of filler surface covered with bone was highest for autografts at all time points and was higher for DBBM than BCP 80/20 and 60/40 at the early healing phase. TRAP-positive multinucleated cells were identified on BCP and DBBM surfaces without showing typical signs of resorption lacunae.

Histologic and histomorphometric evaluation of two bone substitute materials for bone regeneration: an experimental study in sheep.

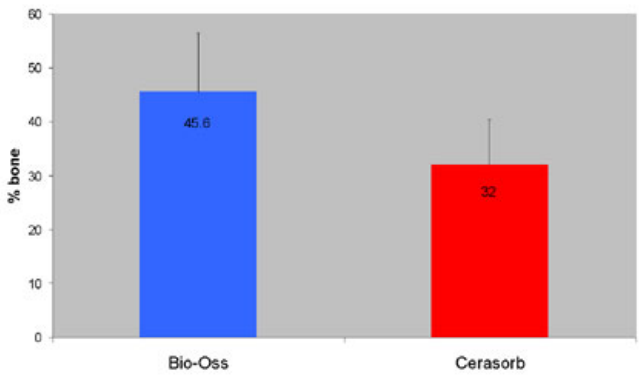
Paknejad, M., S. Emtiaz, et al.
Implant Dent 2008 17(4): 471-9.

INTRODUCTION: In the past decade, there has been an increase focus on regeneration approaches as related to periodontics and implant therapies. The main objective of the present study is the evaluation of quality, density, and thickness of the newly formed bone in experimental defects treated with deproteinized bovine bone mineral (DBBM) and bioapatite-collagen. MATERIALS: Fifteen identical cuboidal defects were prepared in the alveolar edentulous mandibular ridges in 10 male sheep. Defects were randomly assigned to be treated either with DBBM, Bioapatite-collagen or remained unfilled as the control group. Defects of these 3 groups were histologically examined after 6 months. RESULTS: The mean percentages of bone regeneration with DBBM, Bioapatite-collagen, and control group were 51.40% +/- 3.57%, 27.66% +/- 4.18%, and 19% +/- 1%, respectively ($P < 0.05$). Defects filled with Bio-Oss and control defects did not show foreign body reaction, whereas Biostite particles had a reaction in 40% of the specimens. Trabecular thickness and type of new regenerated bone were also significantly different between Bio-Oss and Biostite ($P < 0.05$) and control group ($P < 0.05$). CONCLUSION: The results of the present study suggest that using of DBBM particles can promote bone regeneration more effectively than Bioapatite-collagen, and both materials were more promising than the control group.

The amount of newly formed bone in sinus grafting procedures depends on tissue depth as well as the type and residual amount of the grafted material

Artzi Z, Kozlovsky A, Nemcovsky CE, Weinreb M.
J Clin Periodontol. 2005; 32: 193-199.

Objectives: Bone replacement substitutes are almost unavoidable in augmentation procedures such as sinus grafting. The objective of the present study was to evaluate the osteoconductive capability of two different scaffold fillers in inducing newly formed bone in this procedure. Material and Methods: Sinus floor augmentation and implant placement were carried out bilaterally in 12 patients. Bovine bone mineral (BBM) was grafted on one side and beta-tricalcium phosphate (beta-TCP) on the contralateral side. Both were mixed (1:1 ratio) with autogenous cortical bone chips harvested from the mandible by a scraper. Hard tissue specimen cores were retrieved from the augmented sites (at the previous



window area) at 12 months. Decalcified sections were stained with haematoxylin-eosin and the fraction area of new bone and filler particles was measured. In addition to the effect of the filler on new bone formation, the latter was tested to determine whether it correlated with the tissue depth and residual amount of the grafted material. Results: Bone area fraction increased significantly from peripheral to deeper areas at both grafted sites in all cores: from 26.0% to 37.7% at the beta-TCP sites and from 33.5% to 53.7% at the BBM-grafted sites. At each depth the amount of new bone in BBM sites was significantly greater than that in TCP sites. However, the average area fraction of grafted material particles was similar in both fillers and all depth levels (beta-TCP=27.9-23.2% and BBM=29.2-22.6%, NS). A significant negative correlation was found between bone area fraction and particle area fraction at the middle (p=0.009) and deep (p=0.014) depths in the beta-TCP sites, but not at the BBM sites. Conclusion: At 12 months post-augmentation, the two examined bone fillers, beta-TCP and BBM, promoted new bone formation in sinus grafting but the amount of newly formed bone was significantly greater in BBM-grafted sites. However, both exhibited similar residual grafted material area fraction at this healing period. This could imply that BBM possesses better osteoconductive properties.

Comparison of Porous Bone Mineral and Biologically Active Glass in Critical-Sized Defects

J.M. Schmitt, D.C. Buck, S.Joh, S.E. Lynch, J.O. Hollinger
J Periodontology 1997; 68(11): 1043-53.

Several materials have been proposed as therapies to augment alveolar bone and to promote periodontal regeneration. However, there are an insufficient number of studies that effectively evaluated these therapies. Consequently, the purpose of this study was to compare bone regeneration promoted by porous bone mineral (Bio-Oss®) and biologically active glass (PerioGlas®). Unilateral critical-sized defects (CSDs) were prepared in the radii of 24 rabbits, divided evenly between 2 time periods (4 and 8 weeks) and between 2 treatment groups (porous bone mineral and biologically active glass). Evaluations consisted of clinical examination, standardized radiography at baseline and every 2 weeks thereafter, as well as histology and histomorphometry. Data were analyzed by an unpaired Student *t*-test with significance established at $P \leq 0.05$. We determined that CSDs treated with porous bone mineral were significantly more radiopaque than biologically active glass-treated sites at both 4 and 8 weeks. Moreover, the amount of new bone was significantly greater at both 4 and 8 weeks in the porous bone mineral groups than in the biologically active glass groups. The authors concluded that in the rabbit radius CSD wound model, porous bone mineral appears to be more effective than biologically active glass in regenerating bone.

b ... membranes

Effect of a Collagen Membrane Combined with a Porous Titanium Membrane on Exophytic New Bone Formation in a Rabbit Calvarial Model

Shin SI, Herr Y, Kwon YH, Chung JH.
J Periodontol 2012.

Background: Previous studies showed that the use of a porous titanium membrane (TM) for exophytic bone regeneration does not effectively inhibit the infiltration of undesired tissue. Therefore, this study examined the effect of resorbable collagen membranes, such as cross-linked type I collagen membrane (BA) and double layered porcine collagen membrane (BG), on the promotion of exophytic bone formation in guided bone regeneration when used in conjunction with a porous titanium membrane. Methods: Thirty six male New Zealand white rabbits were used in this study. Six rabbits were allotted to each test group. After decorticating the parietal bone, with or without filling the inner space with a freeze-dried cortical bone allograft (OG), the collagen membranes were fixed with metal pins. The experimental groups were divided into the following 6 groups: TM only, TM+OG, TM+BA, TM+BG, TM+OG+BA, and TM+OG+BG. The experimental animals were sacrificed at 8 and 16 weeks after surgery. Non-decalcified specimens were prepared and processed for histological observations. The newly formed bone (%) was measured histomorphometrically. Results: BG combined with TM promoted new bone formation and maturation by inhibiting the infiltration of connective tissue. However, BA had no significant effect on new bone

formation. The amount of new bone formation was higher at 16 weeks than at 8 weeks but the difference was not significant. At 16 weeks the best result for newly formed bone was with TM+OG+BG with a significant difference from TM alone. Conclusions: Regardless of the use of graft materials, BG combined with TM promoted more bone formation than BA combined with TM or TM alone. Thus, using a commercial collagen membrane to cover a TM can promote new exophytic bone formation.

Cellular inflammatory response to porcine collagen membranes.

Patino MG, Neiders ME, Andreana S, Noble B, Cohen RE.
Periodontal Res. 2003 Oct;38(5):458-64

OBJECTIVES:The purpose of this study was to assess local inflammatory changes associated with the implantation of three different porcine collagen membranes having potential use in periodontal regeneration.
METHODS: Materials were implanted subcutaneously into prepared sites along the dorsal skin surface of 60 female Wistar rats. Saline and turpentine were used as negative and positive controls, respectively. Animals were killed and biopsies obtained after 3 d, and at 1, 2, 4, 6, and 8 weeks after membrane implantation. A panel of six monoclonal antibodies was used to identify circulating monocytes (ED1), resident tissue macrophages (ED2), lymphoid macrophages (ED3), Ia-antigen expression (OX6), T-lymphocytes (OX19), and B-lymphocytes (OX33). Cells identified by each antibody were subjected to quantitative immunocytochemistry to compare any differences present among groups. Sera obtained 8 weeks after grafting were used in immunoblotting assays to detect the presence of systemic antiporcine antibodies.
RESULTS: We found that the mononuclear cell subsets associated with implantation of porcine collagen membranes were similar to those obtained with saline administration. On the other hand, the use of turpentine resulted in an inflammatory infiltrate characterized by significantly higher numbers of all six monoclonal cell subsets at all time periods evaluated, compared to either saline or any of the membranes ($P < 0.001$).CONCLUSIONS: The collagen membranes do not appear to be associated with a significant local inflammatory response, nor a systemic immune response, and thus appear to be well tolerated, rendering them useful in periodontal regeneration.

Vivosorb((R)) as a barrier membrane in rat mandibular defects. An evaluation with transversal microradiography

Hoogeveen, E. J., P. F. Gielkens, et al.
Int J Oral Maxillofac Surg 2009 ; doi:10.1016/j.ijom.2009.04.002

Vivosorb((R)) is a new degradable membrane composed of poly(DL-lactide-varepsilon-caprolactone) (PDLLCL). The aim of this study was to appraise its performance in guided bone regeneration procedures. In 192 rats a 5.0mm defect was drilled in the mandibular angle. The defects were covered with a membrane (PDLLCL, collagen, or expanded polytetrafluoroethylene (ePTFE)) or left uncovered (control). Defect closure, mineralization and thickness of the new bone were assessed by means of transversal microradiography at three different time intervals (2, 4 and 12 weeks). The data were analysed using multiple regression analyses. The regression analyses showed significant effect modification between time and collagen and time and ePTFE for mineralization of the newly formed bone. For defect closure and bone thickness all membrane-treated groups showed effect modification between time and membrane; these effects were more significant and larger in the collagen and ePTFE groups. In the non-treated controls no effect modification was observed. The membrane groups showed significantly better results than the control groups. The ePTFE and collagen membranes performed equally well and better than the PDLLCL membrane during this experiment. It was concluded that a PDLLCL membrane is not suitable for clinical application in its current form.

Vivosorb, Bio-Gide, and Gore-Tex as barrier membranes in rat mandibular defects: an evaluation by microradiography and micro-CT

Gielkens PF, Schortinghuis J, et al.
Clin Oral Implants Res; 2008 19(5): 516-21.

OBJECTIVES: The objectives of this study were to determine whether a new degradable synthetic barrier membrane (Vivosorb) composed of poly(dl-lactide-epsilon-caprolactone) (PDLLCL) can be useful in implant dentistry and to compare it with collagen and expanded polytetrafluoroethylene (ePTFE) membranes. MATERIAL AND METHODS: In 192 male Sprague-Dawley rats, a standardized 5 mm circular defect was created through the right angle of the mandible. New bone formation was evaluated by post-mortem microradiography and micro-CT (muCT) imaging. Four groups (control, PDLLCL, collagen, ePTFE) were evaluated at three time intervals (2, 4, and 12 weeks). In the membrane groups the defects were covered; in the control group the defects were left uncovered. Data were analysed using a multiple regression model. RESULTS: New bone formation could be detected by post-mortem microradiography in 130 samples and by muCT imaging in 112 samples. Bone formation was progressive in 12 weeks, when the mandibular defect was covered with a membrane. Overall, more bone formation was observed underneath the collagen and ePTFE membranes than the PDLLCL membranes. CONCLUSIONS: In contrast to uncovered mandibular defects, substantial bone healing was observed in defects covered with a PDLLCL membrane. However, bone formation in PDLLCL-covered defects tended to be less than in the defects covered with collagen or ePTFE. The high variation in the PDLLCL samples at 12 weeks may be caused by the moderate adherence of this membrane to bone compared with collagen. These results indicate that further study is needed to optimize the properties of PDLLCL membranes.

Long-term bio-degradation of cross-linked and non-cross-linked collagen barriers in human guided bone regeneration

Tal H, Kozlovsky A, et al.
Clin Oral Implants Res, 2008; 19(3): 295-302.

Objective: This double-blind study clinically and histologically evaluated long-term barrier bio-durability of cross-linked and non-cross-linked collagen membranes (CLM and NCLM) in sites treated by guided bone regeneration procedures. Materials and methods: In 52 patients, 52 bony defects were randomly assigned to treatment with either a CLM or a NCLM. Post-surgical spontaneous membrane exposures were recorded. Before implant placement, full-thickness standard soft tissue discs were retrieved wherever suitable for histologic examination. Results: Spontaneous membrane exposure was observed in 13 (50%) CLM sites and in six (23.1%) NCLM sites ($P<0.05$). Clinical healing at exposed sites lasted 2-4 weeks. CLM were histologically intact in all non-perforated sites, were interrupted in five perforated sites, and undetected in four. NCLMs were undetected in all 18 specimens examined. In three non-perforated CLM sites, bone apposition and ossification at or within the membrane was observed. Conclusions: CLMs were more resistant to tissue degradation than NCLMs, and maintained integrity during the study. Neither membrane was resistant to degradation when exposed to the oral environment. CLMs were associated with a higher incidence of tissue perforations. In non-perforated sites, CLM ossification at or within the membrane was occasionally observed.

Ossification of a novel crosslinked porcine collagen barrier in guided bone regeneration in dogs.

Zubery Y, Goldlust A, Alves A, Nir E.
J Periodontol 2007, 78, 112–121.

Background: Collagen membranes for guided bone regeneration (GBR) and guided tissue regeneration (GTR) are used extensively as bioabsorbable barriers. Cross-linking of collagen increases its biodurability and enables the control of its degradation kinetics and barrier function. A novel cross-linking technology was used to produce a porcine type I collagen membrane (GLYM). The purpose of this study was to evaluate the safety, efficacy, and degradation kinetics of GLYM compared to a non-cross-linked bilayer type I and III porcine collagen membrane (BCM) in surgically created defects in dogs. Methods: After tooth extraction, two mandibular bilateral critical size defects were created in 12 beagle dogs that were randomly assigned to one of five groups: GLYM + bovine bone mineral (BBM), BCM + BBM, BBM alone, sham-operated, or GLYM alone. Dogs were euthanized after 8, 16, and 24 weeks, and sites were prepared for qualitative, semiquantitative, and quantitative light microscopy analyses. Results: Membrane-protected sites displayed bone filling between the BBM particles with almost complete restoration of the original ridge morphology that increased with time up to 16 weeks and remained unchanged at 24 weeks. Both membranes showed marked degradation within 16 to 24 weeks, with BCM inconsistency that was undetectable in one of four

sites at 8, 16, and 24 weeks. Membrane ossification was observed in all GLYM sites and in only one BCM site, which progressed with time to 24 weeks. Bone increased by approximately 1 mm on the lingual side, where the GLYM membrane was in direct contact with bone. Conclusions: Both membranes were safe and effective in supporting bone regeneration in critical size alveolar ridge defects in dogs and completely degraded within 24 weeks with marked BCM inconsistency. In areas of direct contact with bone, all GLYM sites were progressively ossified with time and augmented the original alveolar ridge. To the best of our knowledge, this is the first report of complete ossification of a collagen barrier membrane in GBR procedures.

13. Growth factors and carriers

Vertical Ridge Augmentation Using an Equine Bone and Collagen Block Infused With Recombinant Human Platelet-Derived Growth Factor-BB: A Randomized Single-Masked Histologic Study in Non-Human Primates

Nevins M, Hezaimi KA, Schupbach P, Karimbux N, Kim DM.
J Periodontol 2012.

Background: This study tests the effectiveness of hydroxyapatite and collagen bone blocks of equine origin (eHAC), infused with recombinant human platelet-derived growth factor-BB (rhPDGF-BB), to augment localized posterior mandibular defects in non-human primates (Papio hamadryas). Methods: Bilateral critical-sized defects simulating severe atrophy were created at the time of the posterior teeth extraction. Test and control blocks (without growth factor) were randomly grafted into the respective sites in each non-human primate. Results: All sites exhibited vertical ridge augmentation, with physiologic hard- and soft-tissue integration of the blocks when clinical and histologic examinations were done at 4 months after the vertical ridge augmentation procedure. There was a clear, although non-significant, tendency to increased regeneration in the test sites. As in the first two preclinical studies in this series using canines, experimental eHAC blocks infused with rhPDGF-BB proved to be a predictable and technically viable method to predictably regenerate bone and soft tissue in critical-sized defects. Conclusion: This investigation supplies additional evidence that eHAC blocks infused with rhPDGF-BB growth factor is a predictable and technically feasible option for vertical augmentation of severely resorbed ridges.

Prefabrication of vascularized bone grafts using recombinant human osteogenic protein-1--part 3: dosage of rhOP-1, the use of external and internal scaffolds.

Terheyden H, Menzel C, Wang H, Springer IN, Rueger DR, Acil Y.
Int J Oral Maxillofac Surg 2004; 33(2): 164-72.

In a previous study vascularized bone grafts were prefabricated with recombinant human osteogenic protein-1 (rhOP-1) using blocks of xenogenic bone mineral (Bio-Oss) as scaffolds. The present study addressed the dosage of rhOP-1 and the combination of an external (mould) and internal scaffold (granular Bio-Oss). In five Gottingen minipigs six prefabrication sites in the latissimus dorsi muscles were randomly assigned to groups a-f. Moulds were prepared by shaping collagen/polylactide membranes in a cylindrical form which was filled with 1g Bio-Oss granules and rhOP-1 (a: 0; b: 50; c, f, e: 250; d: 1000 microg of rhOP-1, a-e: cylinder open to muscle, e cylinder perforated, f: cylinder open to subcutaneous fat). After 6 weeks a dose dependency of bone density (a-d: 0%; 9.4%; 15.8%; 31.1%) and vessel density (a-d: 0.3; 2.4; 7.9; 25.4 counts/view) was observed histomorphometrically. Muscular surrounding was advantageous to subcutaneous tissue. Perforations of the membranes increased vessel density and did not impair bone formation. Bone density decreased in the proximity of the polylactide membranes. The membrane material was too soft and partly collapsed and therefore needs not to be reconsidered. The use of Bio-Oss granules with 1000 microg rhOP-1 per gram proved to be a suitable concept for prefabrication of bone transplants.

Platelet-Derived Growth Factor Enhancement of a Mineral-Collagen Bone Substitute

E.B. Stephan, R. Renjen, S.E. Lynch, R. Dziak
J Periodontol 2000; 71.

Anorganic bovine bone-collagen matrix (Bio-Oss® Collagen) is commercially available for bone regeneration procedures. Platelet-derived growth factor BB (PDGF-BB) has been demonstrated to stimulate bone formation in vivo and in vitro. It was the aim of these studies to examine 1) the interaction of Bio-Oss® Collagen with PDGF-BB and 2) determine if the adsorption of PDGF-BB to Bio-Oss® Collagen stimulates osteoblastic cell proliferation above that of the untreated matrix.
Methods: Measurement of PDGF-BB adsorption and release was accomplished using ^{125}I radiolabled growth factor. The PDGF-BB was incubated with Bio-Oss® Collagen and radiolabled PDGF-BB was adsorbed to the matrix material, then the samples were incubated in buffer for various time periods. The amount of PDGF-BB retained on the matrix was measured and the percent of growth factor released calculated. The biological activity was tested in an in vitro assay with primary culture neonatal rat osteoblastic cells. Osteoblastic cells were cultured on Bio-Oss® Collagen with known amounts of adsorbed PDGF-BB. Proliferation of the cells was assessed by ^{3}H-thymidine incorporation and cell attachment measured by prelabeling cells with ^{3}H-leucine.
Results: PDGF-BB adsorbed to Bio-Oss® Collagen in a rapid, concentration-dependent fashion. The growth factor was slowly released from the matrix such that approximately 30% of the adsorbed protein was liberated over 10 days. PDGF-BB treated Bio-Oss® Collagen displayed significantly ($P<0.05$, ANOVA) enhanced proliferation of cultured osteoblastic cells compared to Bio-Oss® Collagen alone.
Conclusions: These results suggest that PDGF-BB is rapidly adsorbed then slowly released Bio-Oss® Collagen. PDGF-BB adsorbed to this material is able to stimulate proliferation of the attached osteoblastic cells. These data suggest that it may be clinically feasible to adsorb PDGF to Bio-Oss® Collagen and that this combination of bone growth factor and Bio-Oss® Collagen has the potential for clinical applications.

Recombinant human osteogenic protein 1 in the rat mandibular augmentation model: differences in morphology of the newly formed bone are dependent on the type of carrier

H. Terheyden, S. Jepsen, St. Vogeler, M. Tucker, D.C. Rueger
Mund Kiefer Gesichtschir 1997; 1: 272-275.

Recombinant human osteogenic protein 1 (rhOP1), also known as bone morphogenetic protein 7, was investigated in a newly developed experimental model, the rat lateral mandibular augmentation model. Algipore® and Bio-Oss® Block were applied as carrier materials. Extensive induction of newly formed bone was demonstrated on the test side containing rhOP1 and did not occur on the control side without rhOP1. The interstitial bone formation was limited to the augmented area and was not observed in the surrounding masseter muscle. The morphology of the newly formed bone differed in both carrier systems, which may be an important characteristic for the clinical indication of carrier systems in combination with bone morphogenetic proteins.

14. PRP and stem cells

In vivo Comparison of Hard Tissue Regeneration with Human Mesenchymal Stem Cells processed with either the FICOLL- or the BMAC-Method.

Sauerbier S, Stricker A, Kuschnierz J, Buehler F, Oshima T, Xavier SP, Schmelzeisen R, Gutwald R.
Tissue Eng Part C Methods 2009

Objective: Comparison of new bone formation in maxillary sinus augmentation procedures by using biomaterial associated with mesenchymal stem cells (MSCs) separated by two different isolation methods. Background: In regenerative medicine open cell concentration systems are only allowed for clinical application under GMP-conditions. Methods: Mononuclear cells including MSCs were concentrated with either the FICOLL method (classic open system - control group, n=6 sinus) or BMAC method (closed system - test group, n=12 sinus) and transplanted in combination with biomaterial. A sample of the cells was characterized by their ability to differentiate. After 4.1 (SD+/-1.0) months bone biopsies were obtained and analyzed. Results: The new bone formation in the BMAC-group was 19.9% (90%CI, 10.9 to 29), and 15.5% (90%CI, 8.6 to 22.4) in the FICOLL-group. The 4.4%-difference was not significant (90%CI, - 4.6 to 13.5; p=0.39). MSCs could be differentiated into osteogenic, chondrogenic and adipogenic lineages. Conclusion: MSCs harvested from bone marrow aspirate in combination with bovine bone matrix particles can form lamellar bone and provide a reliable base for dental implants. The closed BMAC-system is suited to substitute the open FICOLL-system in bone regeneration procedures.

Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane.

Döri F, Huzar T, Nikolidakis D, Arweiler N.B., Gera I, Sculean A.
J Clin Periodontol 2007: 34: 254-261.

BACKGROUND: Regenerative periodontal therapy with a combination of platelet-rich plasma (PRP)+a natural bone mineral (NBM)+guided tissue regeneration (GTR) has been shown to result in significantly higher probing depth reductions and clinical attachment-level gains compared with treatment with open flap debridement alone. However, at present, it is unknown to what extent the use of PRP may additionally enhance the clinical outcome of the therapy compared with treatment with NBM+GTR. AIM: To clinically compare treatment of deep intra-bony defects with NBM+PRP+GTR with NBM+GTR. MATERIAL AND METHODS: Thirty patients suffering from advanced periodontal disease, and each of whom displayed one advanced intra-bony defect were randomly treated with a combination of either NBM+PRP+collagen membrane (GTR) or NBM+GTR. The following clinical parameters were evaluated at baseline and at 1 year after treatment: plaque index, gingival index, bleeding on probing, probing depth (PD), gingival recession and clinical attachment level (CAL). CAL changes were used as the primary outcome variable. RESULTS: No differences in any of the investigated parameters were observed at baseline between the two groups. Healing was uneventful in all patients. At 1 year after therapy, the sites treated with NBM+PRP+GTR showed a reduction in mean PD from 8.9+/-2.3 mm to 3.4+/-2.0 mm ($p<0.001$) and a change in mean CAL from 10.9+/-2.2 mm to 6.4+/-1.8 mm ($p<0.001$). In the group treated with NBM+GTR, the mean PD was reduced from 8.9+/-2.5 mm to 3.4+/-2.3 mm ($p<0.001$), and the mean CAL changed from 11.1+/-2.5 mm to 6.5+/-2.3 mm ($p<0.001$). In both groups, all sites gained at least 3 mm of CAL. CAL gains of $\geq$ 4 mm were measured in 80% (i.e. in 12 out of 15 defects) of the cases treated with NBM+PRP+GTR and in 87% (i.e. in 13 out of 15 defects) treated with NBM+GTR. No statistically significant differences in any of the investigated parameters were observed between the two groups. CONCLUSIONS: Within its limits, the present study has shown that (i) at 1 year after regenerative surgery with both NBM+PRP+GTR and NBM+GTR, significant PD reductions and CAL gains were found, and (ii) the use of PRP has failed to improve the results obtained with NBM+GTR.

The effect of platelet-rich plasma on bone healing around implants placed in bone defects treated with Bio-Oss: a pilot study in the dog tibia.

You TM, Choi BH, Li J, et al.
Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007, 103, e8 – e12.

OBJECTIVE: The aim of this study was to examine the influence of platelet-rich plasma (PRP) used as an adjunct to Bio-Oss for the repair of bone defects adjacent to titanium dental implants. STUDY DESIGN: In 6 mongrel dogs, 12 screw-shaped titanium dental implants were inserted into the osteotomy sites in the dogs' tibias. Before implantation, a standardized gap (2.0 mm) was created between the implant surface and the surrounding bony walls. The gaps were filled with either Bio-Oss cancellous granules alone or Bio-Oss cancellous granules mixed with PRP. RESULTS: After 4 months, the Bio-Oss-treated defects revealed a significantly higher percentage of bone-implant contact than the defects treated with Bio-Oss and PRP (60.1% vs. 30.8%; P < .05). CONCLUSION: The results indicate that when PRP is used as an adjunct to Bio-Oss in the repair of bone defects adjacent to titanium dental implants, PRP may decrease periimplant bone healing.

15. Major Bone Augmentation

Resorbable collagen membrane in surgical repair of fistula following palatoplasty in nonsyndromic cleft palate.

Sader R, Seitz O, Kuttenberger J..
Int J Oral Maxillofac Surg 2010..

Treatment of palato-nasal fistula following primary palatoplasty in patients with nonsyndromic cleft palate is often complicated by recurrence. The authors have tested the feasibility of a surgical technique adding a resorbable collagen membrane at the bony edge of the fistula and report the outcome in the first 14 patients in an open, non-comparative, preliminary investigation. The procedure was well tolerated by all patients, with no relapses during follow up ranging from 4 to 12 months.

Horizontal ridge augmentation with a collagen membrane and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: a prospective case series in 25 patients.

Urban IA1, Nagursky H, Lozada JL, Nagy K.
Int J Periodontics Restorative Dent. 2013 May-Jun;33(3):299-307. doi: 10.11607/prd.1407.

This prospective case series evaluated the use of a resorbable natural collagen membrane with a mixture of autogenous bone and anorganic bovine bone-derived mineral (ABBM) for lateral ridge augmentation and subsequent implant placement. A mixture (1:1) of particulated autogenous bone and ABBM was used for lateral ridge augmentation and covered with a resorbable, natural collagen bilayer membrane to treat knife-edge ridges and prepare them for implant placement. Ridge measurements were obtained pre- and postsurgery, complications recorded, and biopsy specimens examined histologically. Seventy-six implants were placed in 25 patients with 31 knife-edge ridge surgical sites. One defect had a bone graft complication (3.2%; exact 95% confidence interval: 0.1%, 16.7%). Clinical measurements revealed an average of 5.68 mm (standard deviation [SD] = 1.42 mm) of lateral ridge augmentation after a mean 8.9-month (SD = 2.1 months) graft healing period. Clinically, all treated ridges were sufficient in width for subsequent implant placement. All implants survived with an average follow-up of 20.88 months (SD = 9.49 months). Histologic analysis of nine surgical sites showed that ABBM was connected with a dense network of newly formed bone with varying degrees of maturation. Histomorphometric analysis demonstrated that autogenous bone represented a mean of 31.0% of the specimens, ABBM 25.8%, and marrow space 43.2%. The treatment of horizontally deficient alveolar ridges with the guided bone regeneration technique using autogenous bone mixed with ABBM and a natural collagen resorbable barrier membrane can be regarded as successful. Implant success and survival need to be confirmed with long-term follow-up examinations.

Comparison of four different allogeneic bone grafts for alveolar ridge reconstruction: a preliminary histologic and biochemical analysis.

Fretwurst T1, Spanou A2, Nelson K3, Wein M4, Steinberg T4, Stricker A3.
Oral Surg Oral Med Oral Pathol Oral Radiol. 2014 Oct;118(4):424-31. doi: 10.1016/j.0000.2014.05.020. Epub 2014 Jun 13.

OBJECTIVES: Allograft material for alveolar ridge reconstruction is quite promising and appears to be as equally successful as bone autograft material. The aim of the present study was to compare four different allogeneic bone grafts in terms of their histologic structure and DNA content before grafting.

STUDY DESIGN: Four allograft specimens from different suppliers were analyzed histologically, and the DNA content was analyzed before clinical use of the allografts.

RESULTS: Organic tissue remnants were detected in all of the evaluated samples. In the present samples adipocytes, fibroblasts, osteocytes, and chondrocytes were identified and DNA isolation and purification was possible.

CONCLUSION: Demineralized freeze-dried allogeneic bone transplants can stimulate new bone formation and are a viable alternative to bone autograft material. However, the well-tolerated use of allograft material in regard to our findings should be further investigated.

Piezoelectric decortication applied in periodontally accelerated osteogenic orthodontics.

Yu H1, Jiao F, Wang B, Shen SG.
J Craniofac Surg. 2013;24(5):1750-2. doi: 10.1097/SCS.0b013e3182902c5a.

Our aim was to evaluate the application of piezoelectric decortication in periodontally accelerated osteogenic orthodontics (PAOO). One hundred fifty-six patients with severe skeletal malocclusions were enrolled in this study. Ultrasonic decortications were performed in 187 labial or lingual PAOO of the maxillary and mandibular anterior teeth. Orthodontic decompensation started from the fifth day after operation. All patients healed uneventfully and no severe periodontic complications were recorded. Rapid teeth movement and relatively short treatment duration were realized. Alveolar fenestration and bony dehiscence was successfully addressed. With physical and mechanical properties of absence of macrovibration, ease of use and control, piezosurgery showed its great values in PAOO.

Bone level variation after vertical ridge augmentation: resorbable barriers versus titanium-reinforced barriers. A 6-year double-blind randomized clinical trial.

Merli M, Moscatelli M, Mariotti G, Rotundo R, Bernardelli F, Nieri M.
Int J Oral Maxillofac Implants. 2014 Jul-Aug;29(4):905-13. doi: 10.11607/jomi.3203.

PURPOSE: To compare the efficacy of two different techniques for vertical bone regeneration at implant placement with particulate autogenous bone at 6 years after loading by means of a double-blind, superiority, parallel-group randomized clinical trial.
MATERIALS AND METHODS: The study was conducted in a private center in Italy between April 2004 and December 2011. Patients in whom vertical bone augmentation was indicated in combination with the placement of single or multiple implants were eligible for inclusion in this trial. Patients were randomized to receive either resorbable collagen barriers supported by an osteosynthesis plate (test group) or nonresorbable titanium-reinforced expanded polytetrafluoroethylene barriers (control group). The outcome variables-radiographic bone variation at implant sites, implant failures, and complications- were evaluated 6 years after loading. Randomization was done by computer, with allocation concealed by opaque sequentially numbered sealed envelopes. The patients and the radiographic examiner were blinded to group assignment.
RESULTS: Twenty-two patients were randomized: 11 to the resorbable barrier group and 11 to the nonresorbable (control) group. One control group patient dropped out. The mean bone level 6 years after surgery was 1.33 mm for the resorbable group and 1.00 mm for the nonresorbable group. The adjusted difference in bone changes between groups was 0.15 mm (95% confidence interval, -0.39 to 0.69, P = .5713). No implant failures or complications occurred after loading.
CONCLUSION: No differences were observed in this comparison of resorbable and nonresorbable barriers with simultaneous implant placement for vertical ridge augmentation.

Induction of multinucleated giant cells in response to small sized bovine bone substitute (Bio-Oss™) results in an enhanced early implantation bed vascularization.

Barbeck M1, Udeabor SE2, Lorenz J2, Kubesch A1, Choukroun J3, Sader RA2, Kirkpatrick CJ4, Ghanaati S1.
Ann Maxillofac Surg. 2014 Jul-Dec;4(2):150-7. doi: 10.4103/2231-0746.147106.

PURPOSE: The host tissue reaction to the xenogeneic bone substitute Bio-Oss™ (Geistlich Biomaterials, Wolhousen, Switzerland) was investigated focusing on the participating inflammatory cells and implantation bed vascularization.
MATERIALS AND METHODS: Bio-Oss™ was implanted subcutaneously into CD1 mice for up to 60 days and analyzed by means of specialized histological and histomorphometrical techniques after explantation.
RESULTS: Bio-Oss™ induced within the first 15 days an early high vascularization combined with a marked presence of multinucleated giant cells. The latter cells were associated mainly with the smaller sized granules within the implantation bed. Toward the end of the study the number of multinucleated giant cells decreased while the tissue reaction to the larger granules was mainly mononuclear.
CONCLUSION: The results of the present study showed that smaller xenogeneic bone substitute granules induce multinucleated giant cells, whereas the larger-sized ones became integrated within the implantation bed by means of a mononuclear cell-triggered granulation tissue. Obviously, the presence of multinucleated giant cells within biomaterial implantation beds is not only related to the type of synthetic bone substitute material, but also to the granule size of the natural-based xenogeneic bone substitute material.