Pre-clinical (*in vitro* & *in vivo*) studies

1. Stability of Implants Supported By Three Types of Bone Grafting Materials in Dogs

Gholami M, Ahrari F, Sedigh HS, Bourauel C, Ahmadi L. Research Square; 2021 Nov. doi: 10.21203/rs.3.rs-1063509/v1.

https://europepmc.org/article/ppr/ppr420609

Background: This study was conducted to assess the stability of implants placed in a simultaneous procedure with different grafting materials (autogenous, xenogenous, and synthetic) in experimentally induced bone defects in dogs. **Methods:** Thirteen dogs were included and divided into three groups according to the time of sacrificing. Oversized osteotomies were prepared in the sternum, and the implants were placed in bone defects. A total of 3 to 5 implants were placed per animal. Each group of animals contained 3 subgroups according to the grafting material utilized. In subgroup 1, autograft was applied, whereas in subgroups 2 and 3, bovine bone mineral (Cerabone) and a synthetic calcium phosphate substitute (Osteon II) were employed. At the end of the specified healing periods (2 months, 4 months, or 6 months), the animals were sacrificed and the implant stability was determined through measuring the resonance frequency. **Results:** Forty-five integrated implants were obtained from this study and nine were lost (failure rate 17%). The two-way analysis of variance revealed no significant difference in ISQ measurements either between the bone graft materials (autogenous, xenogenous, and synthetic; P=0.950) or between the healing intervals (2 months, 4 months, and 6 months; P=0.769). **Conclusions:** The stability of implants augmented with autogenous, xenogenous (Cerabone) or synthetic (Osteon II) graft materials was comparable at 2, 4 and 6 months after placement. This indicates that both Cerabone and Osteon II could be considered as suitable substitutes for regeneration of bone defects to overcome the limitations of autografts.

2. Effects of Systemic Propranolol Application on the New Bone Formation in Periimplant Guided Bone Regeneration

Gunes N, Gül M, Dundar S, Artas G, Kobat MA, Tekin S, Bozoglan A, Isayev A. J Oral Maxillofac Res. 2021 Sep;12(3):e2. doi: 10.5037/jomr.2021.12302.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8577584/

Objectives: The aim of this experimental animal study was to evaluate the effects of systemic propranolol on new bone formation in peri-implant bone defects. **Material and Methods:** Implant slots were created 4mm long and 2.5 mm wide. After the titanium implants were placed in the sockets,

2 mm defects were created in the neck of the implants. Bone grafts were placed in these defects. Then the rats were randomly divided into three equal groups: control (n = 8), propranolol dose-1 (PRP-1) (n = 8), and propranolol dose-2 (PRP-2) (n = 8) groups. In the control group, the rats received no further treatment during the eight-week experimental period after the surgery. The rats in the PRP-1 and PRP-2 groups were given 5 mg/kg and 10 mg/kg propranolol, respectively, every three days for the eight-week experimental period after the surgery. At the end of the experimental period, the rats were euthanized. Blood serum was collected for biochemical analysis, and the implants and surrounding bone tissues were used for the histological analysis. **Results:** There were no significant differences in the histological analysis results and the biochemical parameters (alkaline phosphatase, calcium, creatinine and phosphorus) of the groups (P > 0.05). Also, in the test groups, there was numerically but not statistically more new bone formation detected compared with the controls.

3. Critical-size Defect Augmentation Using Sintered and Non-Sintered Bovine Bone Matrix - An Experimental Controlled Study in Minipigs

Schorn L, Fienitz T, De Donno F, Sterner-Kock A, Maul AC, Holtmann H, Lommen J, Rothamel D. J Oral Maxillofac Surg. 2021 Sep;79(9):1866-1873. doi: 10.1016/j.joms.2021.03.025.

https://pubmed.ncbi.nlm.nih.gov/34051155/

Purpose: Xenogeneic bone substitute materials are often used for augmentation of larger bone defects. Purification methods for these materials vary, mainly in terms of temperature. The aim of this study was to determine *in vivo* how sintering affects quantitative and qualitative bone regeneration of 2 bovine augmentation materials. **Methods:** A total of 56 critical size defects were set at the frontal bone of 14 domestic pigs (4 each) and filled randomly with either bovine, sintered hydroxyapatite (BO), bovine, non-sintered hydroxyapatite (BOS), local autologous bone (AB) or left empty. All defects were additionally covered with a collagen membrane. Specimens were harvested after 4 and 8 weeks and were evaluated histologically and histomorphometrically. **Results:** Histologically new bone could be seen in every group. Significantly highest new bone formation was found in AB. No significant difference could be detected between BO and BOS. **Conclusions:** According to the results of this study, sintered bone substitute material remains histologically distinguishable but does not affect quantitative and qualitative bone regeneration.

4. Comparative barrier membrane degradation over time: Pericardium versus dermal membranes

Bornert F, Herber V, Sandgren R, Witek L, Coelho PG, Pippenger BE, Shahdad S. Clin Exp Dent Res. 2021 Oct;7(5):711-718. doi: 10.1002/cre2.414.

https://pubmed.ncbi.nlm.nih.gov/33949796/

Objective: The effectiveness of GBR procedures for the reconstruction of periodontal defects has been well documented. The objective of this investigation was to evaluate the degradation kinetics and biocompatibility of two resorbable collagen membranes in conjunction with a bovine xenograft material. **Materials and methods:** Lower premolars and first molars were extracted from 18 male Yucatan minipigs. After 4 months of healing, standardized semi-saddle defects were created (12 mm × 8 mm × 8 mm [l˙ × W˙ × d]), with 10 mm between adjacent defects. The defects were filled with a bovine xenograft and covered with a either the bilayer collagen membrane (control) or the porcine pericardium-derived collagen membrane (test). Histological analysis was performed after 4, 8, and 12 weeks of healing and the amount of residual membrane evaluated. Non-inferiority was calculated using the Brunner-Langer mixed regression model. **Results:** Histological analysis indicated the presence of residual membrane in both groups at all time points, with significant degradation noted in both groups at 12 weeks compared to 4 weeks (p = .017). No significant difference in ranked residual membrane scores between the control and test membranes was detected at any time point. **Conclusions:** The pericardium-derived membrane was shown to be statistically non-inferior to the control membrane with respect to resorption kinetics and barrier function when utilized for guided bone regeneration in semi-saddle defects in minipigs. Further evaluation is necessary in the clinical setting.

5. Novel Histomorphometrical Approach to Evaluate the Integration Pattern and Functionality of Barrier Membranes

Ottenbacher N, Alkildani S, Korzinskas T, Pissarek J, Ulm C, Jung O, Sundag B, Bellmann O, Stojanovic S, Najman S, Zechner W, Barbeck M. Dent J (Basel). 2021 Oct;9(11):127. doi: 10.3390/dj9110127.

https://pubmed.ncbi.nlm.nih.gov/34821591/

GBR (guided bone regeneration) is a standard procedure for building up bony defects in the jaw. In this procedure, resorbable membranes made of bovine and porcine collagen are increasingly being used, which, in addition to many possible advantages, could have the potential disadvantage of a shorter barrier functionality, especially when augmenting large-volume defects. Thus, it is of importance to evaluate the integration behavior and especially the standing time of barrier membranes using specialized methods to predict its respective biocompatibility. This study is intended to establish a new histomorphometrical analysis method to quantify the integration rate of collagen-based barrier membranes. Three commercially available barrier membranes, i.e., non-crosslinked membranes (BioGide® and Jason® membrane), a ribose-crosslinked membrane (Ossix® Plus), and a newly developed collagen-hyaluronic acid-based (Coll-HA) barrier membrane were implanted in the subcutaneous tissue of 48 6-8-week-old Wistar rats. The explants, after three timepoints (10, 30, and 60 days), were processed and prepared into histological sections for histopathological (host tissue response) and histomorphometrical (cellular invasion) analyses. 10 days after implantation, fragmentation was not evident in any of the study groups. The sections of the Coll-HA, Jason® and

BioGide® membranes showed a similar mild inflammatory reaction within the surrounding tissue and an initial superficial cell immigration. Only in the Ossix® Plus group very little inflammation and no cell invasion was detected. While the results of the three commercially available membranes remained intact in the further course of the study, only fragments of the Coll-HA membrane were found 30 and 60 days after implantation. Histomorphometrically, it can be described that although initially (at 10 days post-implantation) similar results were found in all study groups, after 30 days post-implantation the cellular penetration depth of the hyaluronic acid-collagen membrane was significantly increased with time (**** $p < 0.0001$). Similarly, the percentage of cellular invasion per membrane thickness was also significantly higher in the Coll-HA group at all timepoints, compared to the other membranes (**** $p < 0.0001$). Altogether, these results show that the histomorphometrical analysis of the cellular migration can act as an indicator of integration and duration of barrier functionality. Via this approach, it was possible to semi-quantify the different levels of cellular penetration of GBR membranes that were only qualitatively analyzed through histopathological approaches before. Additionally, the results of the histopathological and histomorphometrical analyses revealed that hyaluronic acid addition to collagen does not lead to a prolonged standing time, but an increased integration of a collagen-based biomaterial. Therefore, it can only partially be used in the dental field for indications that require fast resorbed membranes and a fast cell or tissue influx such as periodontal regeneration processes.

6. Comparative *In Vivo* Analysis of the Integration Behavior and Immune Response of Collagen-Based Dental Barrier Membranes for Guided Bone Regeneration (GBR)

Radenković M, Alkildani S, Stoewe I, Bielenstein J, Sundag B, Bellmann O, Jung O, Najman S, Stojanović S, Barbeck M. Membranes (Basel). 2021 Sep;11(9):712. doi: 10.3390/membranes11090712.

https://pubmed.ncbi.nlm.nih.gov/34564529/

Collagen-based resorbable barrier membranes have been increasingly utilized for Guided Bone Regeneration (GBR), as an alternative to non-resorbable synthetic membranes that require a second surgical intervention for removal. One of the most important characteristics of a resorbable barrier membrane is its mechanical integrity that is required for space maintenance and its tissue integration that plays a crucial role in wound healing and bone augmentation. This study compares a commercially available porcine-derived sugar-crosslinked collagen membrane with two non-crosslinked collagen barrier membranes. The material analysis provides an insight into the influence of manufacturing on the microstructure. *In vivo* subcutaneous implantation model provides further information on the host tissue reaction of the barrier membranes, as well as their tissue integration patterns that involve cellular infiltration, vascularization, and degradation. The obtained histochemical and immunohistochemical results over three time points (10, 30, and 60 days) showed that the tissue

response to the sugar crosslinked collagen membrane involves inflammatory macrophages in a comparable manner to the macrophages observed in the surrounding tissue of the control collagen-based membranes, which were proven as biocompatible. The tissue reactions to the barrier membranes were additionally compared to wounds from a sham operation. Results suggest wound healing properties of all the investigated barrier membranes. However, the sugar-crosslinked membrane lacked in cellular infiltration and transmembraneous vascularization, providing an exclusive barrier function in GBR. Moreover, this membrane maintained a similar swelling ratio over examined timepoints, which suggests a very slow degradation pattern and supports its barrier function. Based on the study results, which showed biocompatibility of the sugar crosslinked membrane and its stability up to 60 days post-implantation, it can be concluded that this membrane may be suitable for application in GBR as a biomaterial with exclusive barrier functionality, similar to non-resorbable options.

7. Cytocompatibility of Bone Substitute Materials and Membranes

Schafer S, Al-Qaddo H, Gosau M, Smeets R, Hartjen P, Friedrich RE, Nada OA, Vollkommer T, Rashad A. 2021 Jul-Aug;35(4):2035-2040. doi: 10.21873/invivo.12472.

https://pubmed.ncbi.nlm.nih.gov/34182478/

Background/aim: With the demographic change and associated chronic bone loss, the need for cytocompatible bone replacement materials arise in modern medicine. The aim of this *in vitro* study was to investigate the cytocompatibility of eleven different bone substitute materials and membranes. **Materials and methods:** Seven bone substitute materials and four membranes were assessed *in vitro*. The specimens were tested based on their interaction with MC3T3 pre-osteoblasts, through the utilization of viability, proliferation, and cytotoxicity assays. Cell vitality was evaluated using live-dead staining. **Results:** Although we found minor differences in cytocompatibility among the assessed materials, all tested materials can be considered as cytocompatible with a viability of more than 70% of the negative control, which indicates the non-toxic range as defined in current, international standards (DIN EN ISO 10993-5:2009, German Institute for Standardization, Berlin, Germany). Direct live-dead staining assays confirmed satisfactory cytocompatibility of all tested membranes. **Conclusion:** All examined bone substitute materials and membranes were found to be cytocompatible. In order to assess whether the observed minor differences can impact regenerative processes, further *in vivo* studies need to be conducted.

8. Osseointegration of different implant surfaces in areas grafted with deproteinized bovine bone associated or not with fresh bone marrow-Preclinical study in rabbits

Leocádio ACS, Silva M Jr, de Oliveira GJPL, Marcantonio É Jr. Clin Oral Implants Res. 2021 Jun;32(6):767-775. doi: 10.1111/clr.13746.

https://pubmed.ncbi.nlm.nih.gov/33749041/

Objectives: To assess the influence of two different implant surfaces on osseointegration in maxillary sinuses of rabbits previously grafted with deproteinized bovine bone (DBB) associated or not with fresh bone marrow (BM). **Material and methods**: Sixteen New Zealand albino rabbits (males, 3.5/4.5 kg and 9-12 months old) were randomly divided into two groups with 8 rabbits each, according to the type of association of biomaterials used to fill the animals' maxillary sinuses: DBB (Deproteinized Bovine Bone) and DBB/BM (Deproteinized bovine bone associated with fresh autologous bone marrow). Ninety (90) days following the grafting procedure, the animals received implants in the area with two different microstructures (SA-Sandblasting + acid attack and SA-H-Sandblasting + acid attack + immersion in 0.9% sodium chloride isotonic solution). All rabbits were euthanized 90 days after implant placement. The microtomographic analysis was performed to verify the number of mineralized tissues around the implants throughout their length (%BV/TV), while the histomorphometric analysis was performed to verify the percentage of bone-implant contact around the implants throughout their length (%BIC). **Results:** We observed no differences in the quantity for %BV/TV (DBB-SA:33.25 ± 19.67; DBB-SA-H:35.15 ± 22.17; DBB/BM-SA:39.71 ± 24.21; DBB/BM-SA-H:36.40 ± 23.07) and %BIC (DBB-SA:58.94 ± 24.37; DBB-SA-H:52.52 ± 24.36; DBB/BM-SA: 61.66 ± 14.60; DBB/BM-SA-H: 64.06 ± 23.30) between the groups assessed. **Conclusions:** The addition of BM and the type of surface did not influence the osseointegration of implants installed in areas grafted with sintered deproteinized bovine bone at high temperatures in the late period assessed.

9. *In Vivo* Analysis of the Biocompatibility and Bone Healing Capacity of a Novel Bone Grafting Material Combined with Hyaluronic Acid

Pröhl A, Batinic M, Alkildani S, Hahn M, Radenkovic M, Najman S, Jung O, Barbeck M. Int J Mol Sci. 2021 May;22(9):4818. doi: 10.3390/ijms22094818.

https://pubmed.ncbi.nlm.nih.gov/34062885/

The present *in vivo* study analyses both the inflammatory tissue reactions and the bone healing capacity of a newly developed bone substitute material (BSM) based on xenogeneic bone substitute granules combined with hyaluronate (HY) as a water-binding molecule. The results of the hyaluronate containing bone substitute material (BSM) were compared to a control xenogeneic BSM of the same chemical composition and a sham operation group up to 16 weeks post implantationem. A major focus of the study was to analyze the residual hyaluronate and its effects on the material-dependent healing behavior and the inflammatory tissue responses. The study included 63 male Wistar rats using the calvaria implantation model for 2, 8, and 16 weeks post implantationem. Established and Good

Laboratory Practice (GLP)-conforming histological, histopathological, and histomorphometrical analysis methods were conducted. The results showed that the new hyaluronate containing BSM was gradually integrated within newly formed bone up to the end of the study that ended in a condition of complete bone defect healing. Thereby, no differences to the healing capacity of the control BSM were found. However, the bone formation in both groups was continuously significantly higher compared to the sham operation group. Additionally, no differences in the (inflammatory) tissue response that was analyzed via qualitative and (semi-) quantitative methods were found. Interestingly, no differences were found between the numbers of pro- and anti-inflammatory macrophages between the three study groups over the entire course of the study. No signs of the HY as a water-binding part of the BSM were histologically detectable at any of the study time points, altogether the results of the present study show that HY allows for an optimal material-associated bone tissue healing comparable to the control xenogeneic BSM. The added HY seems to be degraded within a very short time period of less than 2 weeks so that the remaining BSM granules allow for a gradual osteoconductive bone regeneration. Additionally, no differences between the inflammatory tissue reactions in both material groups and the sham operation group were found. Thus, the new hyaluronate containing xenogeneic BSM and also the control BSM have been shown to be fully biocompatible without any differences regarding bone regeneration.

10. Microtomographic reconstruction of mandibular defects treated with xenografts and collagen-based membranes: A pre-clinical minipig model

Gomez J, Bergamo ET, Tovar N, Talib HS, Pippenger BE, Herdia V, Cox M, Coelho PG, Witek L. Med Oral Patol Oral Cir Bucal. 2021 Nov;26(6):e825-e833. doi: 10.4317/medoral.24811.

https://pubmed.ncbi.nlm.nih.gov/34564687/

Background: The goal of this study was to evaluate hard tissue response following guided bone regeneration using commercially available bovine bone grafts and collagen membranes; bilayer collagen membrane and porcine pericardium-based membrane, by means of a non-destructive three-dimensional (3D) computerized volumetric analysis following microtomography reconstruction. **Material and methods:** Bone regenerative properties of various bovine bone graft materials were evaluated in the Göttingen minipig model. Two standardized intraosseous defects (15mm x 8mm x 8mm) were created bilaterally of the mandible of eighteen animals (n=72 defects). Groups were nested within the same subject and randomly distributed among the sites: (i) negative control (no graft and membrane), (ii) bovine bone graft/bilayer collagen membrane (BOB) (iii) Bio-Oss® bone graft/porcine pericardium-based membrane (BOJ) and (iv) cerabone® bone graft/porcine pericardium-based membrane (CJ). Samples were harvested at 4, 8, and 12-week time points (n=6 animal/time point). Segments were scanned using computerized microtomography (µCT) and three dimensionally reconstructed utilizing volumetric reconstruction software. Statistical analyses were performed using IBM SPSS with a significance level of 5%. **Results:** From a temporal perspective, tridimensional

evaluation revealed gradual bone ingrowth with the presence of particulate bone grafts bridging the defect walls, and mandibular architecture preservation over time. Volumetric analysis demonstrated no significant difference between all groups at 4 weeks ($p>0.127$). At 8 and 12 weeks there was a higher percentage of new bone formation for control and CJ groups when compared to BOB and BOJ groups ($p<0.039$). The natural bovine bone graft group showed more potential for graft resorption over time relative to bovine bone graft, significantly different between 4 and 8 weeks ($p<0.003$). **Conclusions:** Volumetric analysis yielded a favorable mandible shape with respect to time through the beneficial balance between graft resorption/bone regenerative capacity for the natural bovine bone graft.

11. Expression of TNF- and MMP-13 Following Subcutaneous Implantation of Demineralized Freeze Dried Bovine Cortical Bone Membrane in Rat's Dorsum

Mulyawan I, Rizqiawan A, Soesilowati P, Kamadjaja DB. J Intern Dent Med Res. 2021 Jan;14(1), 74-78.

https://scholar.unair.ac.id/en/publications/expression-of-tnf-and-mmp-13-following-subcutaneous-implantation-

Guided Bone Regeneration (GBR) for alveolar bone augmentation requires combination of bone graft and tissue barrier in the form of biodegradable membrane. Bovine pericardium collagen membrane (BPCM) is the most commonly used resorbable membrane. Demineralized freeze dried bovine cortical bone membrane (DFDBCBM) was known to undergo faster biodegradation compared to BPCM. The study attempts to reveal the mechanism of DFDBCBM degradation by analyzing Tumor Necrosis Factor-Alpha (TNF-) and Matrix Metalloproteinase - 13 (MMP-13) expression after implantation of DFDBCBM and BPCM in rat's dorsum. This experimental study used 60 male rat's which are divided into 2 groups. Subcutaneous implantation of DFDBCBM were done in the first group, while BPCM implanted in the control group. On day 2, 5, 7, 14, 21 and 28 post implantation five rats were sacrificed from each group for immunohistochemistry staining to analyze TNF-α and MMP-13 expression. Comparative and correlation study were done to analyze the two parameters. There was no significant differences in TNF-α and MMP-13 expression between the two groups over all observation periods. However, no correlation was found between TNF-α and MMP-13 expression in both groups. The implantation of DFDBCBM does not induce excessive inflammatory response and it undergoes comparable biodegradation process with BPCM until 28 days post implantation. The level of inflammatory response does not correlate with the magnitude of membrane degradation.

12. Collagen membranes of dermal and pericardial origin-In vivo evolvement of vascularization over time

Dau M, Volprich L, Grambow E, Vollmar B, Frerich B, Al-Nawas B, Kämmerer PW. J Biomed Mater Res A. 2020 Dec;108(12):2368-2378. doi: 10.1002/jbm.a.36989.

https://pubmed.ncbi.nlm.nih.gov/32363796/

Aim of the study was to compare the evolvement of vascularization over time of collagen membranes (CMs) of dermal and pericardial origin in an in vivo animal study. Twenty-eight mice underwent implantation of three commercially available CM derived from porcine dermis (homogenous structure: CM1 (Control 1) and bilayer structure: CM2 [Control 2]), from porcine pericardium (CM3; Test 1) as well as CM3 sprayed with silica-enhanced nanostructured hydroxyapatite (CM4, Test 2). After 3, 6, 9, and 12 days, intravital fluorescence microscopy was conducted for determination of capillary diameter, density, flow, and length. At Day 12, samples were examined immunohistologically for expression of fibroblast growth factor receptor 4 (FGFR4), CD11b, CD68, αSMA, and CD34. In all CM, intravital fluorescence microscopy over time showed increasing values for all parameters with the highest levels in CM4 and the lowest values in CM1. Significant lower amounts of FGFR4, CD11b, and CD68 were detected in CM4 when compared to CM2 ($p < .05$). In contrast to CM3, lower values of αSMA and higher numbers of CD34 positive-marked vessels were observed in CM4 ($p < .05$). In conclusion, dermal bilayer as well as pericardial CM seem to have a higher vascularization rate than dermal homogenous CM. Additional coating of pericardial CM with a silica-enhanced hydroxyapatite increases the speed of vascularization as well as biological remodeling processes.

13. A Novel Xenograft Bone Substitute Supports Stable Bone Formation in Circumferential Defects Around Dental Implants in Minipigs

Catros S, Sandgren R, Pippenger BE, Fricain JC, Herber V, El Chaar E. Int J Oral Maxillofac Implants. 2020 Nov/Dec;35(6):1122-1131. doi: 10.11607/jomi.8265.

https://pubmed.ncbi.nlm.nih.gov/33270052/

Purpose: The aim of this study was to evaluate and compare bone growth and implant integration in circumferential defects with two commercially available bone substitutes (demineralized bovine bone mineral [DBBM]). **Materials and methods:** Circumferential defects were created in the mandibles of minipigs (n = 10), and Bone Level Tapered implants (Straumann Roxolid with SLActive surface) were placed. The defects (4-mm-deep circumferential defect, 2 mm around each implant) were augmented with either sintered bovine bone mineral (test, cerabone) or natural bovine bone mineral (control, Bio-Oss). Bone formation and tissue composition in augmented sites were histomorphometrically assessed after 8 and 12 weeks of healing time (n = 5 each), respectively, in terms of the percentage of area of newly formed bone to total area, bone-to-implant contact (BIC), and crestal bone height relative to the implant shoulder (first bone-to-implant contact [fBIC]). **Results:** Bone formation in all defect sites was adequate and equivalent for both groups at individual healing time points. The amount of residual graft material was comparable in both groups after 8 and 12 weeks, with no significant resorption in either group. The mean newly formed bone area in the test group amounted to 46.7% ± 5.1% and 48.7% ± 4.0% after 8 and 12 weeks vs 47.0% ± 4.8% and 47.8% ± 7.3% in the control group, respectively. BIC and

fBIC as individually assessed for the lingual and buccal aspects were comparable at both healing time points without any statistically significant differences between the groups. A slightly greater variability of fBIC was observed within the test group. **Conclusion:** The results of this study indicate that test and control materials both represent viable bovine bone graft material that equivalently support the formation of new and stable bone volume specifically when used for simultaneous augmentation around implants.

14. *In Vitro* and *In Vivo* Biocompatibility Analysis of a New Transparent Collagen-based Wound Membrane for Tissue Regeneration in Different Clinical Indications

Jung O, Radenkovic M, Stojanović S, Lindner C, Batinic M, Görke O, Pissarek J, Pröhl A, Najman S, Barbeck M. *In Vivo*. 2020 Sep-Oct;34(5):2287-2295. doi: 10.21873/invivo.12040.

https://pubmed.ncbi.nlm.nih.gov/32871752/

Background/aim: For the treatment of different tissue defects such as jawbone defects, open wound defect, chronic ulcers, dura mater defects and corneal defects, different biomaterials are available. The use of collagen-based materials for these applications has been significantly increased over the past decades due to its excellent biocompatibility and degradability. However, no transparent collagen-based biomaterial is available until now. Thus, a newly developed transparent collagen membrane (TCM) based on natural derived porcine pericardium, which offers numerous application possibilities, was developed. The present study aimed to analyze the *in vitro* and *in vivo* biocompatibility using established methods. **Materials and methods:** The new TCM membrane and a commercially available collagen membrane (CM, Jason membrane, botiss biomaterials GmbH, Zossen, Germany) were tested for its *in vitro* cytocompatibility. Furthermore, the *in vivo* biocompatibility was analyzed using sham operations as control group. I*n vitro*, cytocompatibility was tested in accordance with EN ISO 10993-5/-12 regulations and Live-Dead-stainings. *In vivo*, a subcutaneous implantation model in BALB/c mice was used and explants were prepared for analyses by established histological, immunohistochemical and histomorphometrical methods. **Results**: *In vitro*, both membranes showed promising cytocompatibility with a slightly better direct cell response in the Live-Dead staining assay for the TCM. *In vivo*, TCM induced a comparable inflammatory immune response after 10 and 30 days with comparable numbers of M1- and M2-macrophages as also found in the control group without biomaterial insertion. **Conclusion:** The newly transparent collagen membrane is fully biocompatible and is supporting safe clinical application in tissue repair and surgery.

15. The Impact of Compaction Force on Graft Consolidation in a Guided Bone Regeneration Model

Viteri-Agustín I, Brizuela-Velasco A, Lou-Bonafonte JM, Jiménez-Garrudo A, Chávarri-Prado D, Pérez-Pevida E, Benito-Garzón L, Gruber R. Int J Oral Maxillofac Implants. 2020 Sep/Oct;35(5):917-923. doi: 10.11607/jomi.8082.

https://pubmed.ncbi.nlm.nih.gov/32991641/

Purpose: Compaction of particulated grafts is done manually; thus, the effect of compression force on bone regeneration remains unclear. The aim of this study was to evaluate the impact of two different compression forces on the consolidation of particulated bovine hydroxyapatite. **Materials and methods:** Two titanium cylinders were fixed on the calvarium of eight New Zealand rabbits. Both defects were filled with particulated bovine hydroxyapatite subjected to a compression force of 0.7 kg/cm2 or 1.6 kg/cm2 before being covered with a resorbable collagen membrane. A handheld device that uses a spring to control the compression force applied by the plugger was used. At 6 weeks, histomorphometry of the area immediately adjacent to the calvaria bone and to the collagen membrane was performed. **Results:** It was shown that next to the calvaria, the bone volume per tissue volume (BV/TV) was 29.0% ± 8.8% and 27.6% ± 8.2% at low and high compression force, respectively; the bone-to-biomaterial contact (BBC) was 58.2% ± 25.0% and 69.3% ± 22.9%, respectively (P > .05). In the corresponding area next to the collagen membrane, BV/TV was 4.9% ± 5.1% and 5.7% ± 4.7%, and the BBC was 18.3% ± 20.8% and 20.1% ± 15.9%, respectively (P > .05). In addition, the number and area of blood vessels were not significantly affected by compression force. **Conclusion:** Both compression forces applied resulted in similar consolidation of bovine hydroxyapatite expressed by new bone formation and vascularization based on a rabbit calvaria augmentation model.

16. Biofunctionalization of porcine-derived collagen matrices with platelet rich fibrin: influence on angiogenesis *in vitro* and *in vivo*

Blatt S, Burkhardt V, Kämmerer PW, Pabst AM, Sagheb K, Heller M, Al-Nawas B, Schiegnitz E. Clin Oral Investig. 2020 Oct;24(10):3425-3436. doi: 10.1007/s00784-020-03213-8.

https://pubmed.ncbi.nlm.nih.gov/32030513/

Objectives: Porcine-derived collagen matrices (CM) can be used for oral tissue regeneration, but sufficient revascularization is crucial. The aim of this study was to analyze the influence of platelet-rich fibrin (PRF) on angiogenesis of different CM *in vitro* and *in vivo*. **Materials and methods:** Three different CM (mucoderm®, jason®, collprotect®) were combined with PRF in a plotting process. Growth factor release (VEGF, TGF-β) was measured *in vitro* via ELISA quantification after 1,4 and 7 days in comparison to PRF alone. In ovo yolk sac (YSM) and chorion allantois membrane (CAM) model, angiogenic potential were analyzed *in vivo* with light- and intravital fluorescence microscopy after 24 h, then verified with immunohistochemical staining for CD105 and αSMA. **Results:** Highest growth factor release was seen

after 24 h for all three activated membranes in comparison to the native CM (VEGF 24 h: each $p < 0.05$; TGF-β: each $p < 0.001$) and the PRF (no significant difference). All activated membranes revealed a significantly increased angiogenic potential *in vivo* after 24 h (vessels per mm2: each $p < 0.05$; branching points per mm2: each $p < 0.01$; vessel density: each $p < 0.05$) and with immunohistochemical staining for CD105 (each $p < 0.01$) and αSMA (each $p < 0.05$). **Conclusions:** PRF improved the angiogenesis of CM *in vitro* and i*n vivo*.

17. Evaluation of air polishing with a sterile powder and mechanical debridement during regenerative surgical periimplantitis treatment: a study in dogs

Solderer A, Pippenger BE, Donnet M, Wiedemeier D, Ramenzoni LL, Schmidlin PR. Clin Oral Investig. 2021 May;25(5):2609-2618. doi: 10.1007/s00784-020-03572-2.

https://pubmed.ncbi.nlm.nih.gov/32914269/

Objectives: To evaluate the effectiveness of mechanical debridement and/or air polishing on the healing of ligature-induced buccal periimplantitis dehiscence defects in dogs. **Material and methods:** Forty-eight implants were placed in the mandibles of twelve beagle dogs, and periimplantitis was induced for 2 months using ligatures. The resulting buccal dehiscence-type defects were surgically cleaned and augmented (xenogenic filler and resorbable membrane) according to one of the following treatments: (1) Cleaning with carbon curette (debridement - D) and guided bone regeneration (GBR/G): DG, (2) air polishing cleaning (A) and GBR: AG, (3) a combination of D/A/G: DAG, and (4) D/A without GBR: DA. After 2 months, histomorphometric and inflammatory evaluations were conducted. **Results:** The median bone gain after therapy ranged between 1.2 mm (DG) and 2.7 mm (AG). Relative bone gain was between 39% (DG) and 59% (AG). The lowest inflammation scores were obtained in DA without GBR (5.84), whereas significantly higher values between 8.2 and 9.4 were found in the groups with augmentation. At lingual sites without defects, scores ranged from 4.1 to 5.9. According to ISO, differences above 2.9 were considered representative for irritative properties. **Conclusions:** All treatments resulted in partial regeneration of the defects. No treatment group showed a significantly ($p < 0.05$) better outcome. However, pretreatment with air polishing showed a tendency for less inflammation. Noteworthy, inflammation assessment showed an overall irritative potential after GBR in the evaluated early healing phase. **Clinical relevance:** Periimplantitis treatment still represents a big issue in daily practice and requires additional preclinical research in order to improve treatment concepts.

18. The Condensation of Collagen Leads to an Extended Standing Time and a Decreased Pro-inflammatory Tissue Response to a Newly Developed Pericardium-based Barrier Membrane for Guided Bone Regeneration

Gueldenpfennig T, Houshmand A, Najman S, Stojanovic S, Korzinskas T, Smeets R, Gosau M, Pissarek J, Emmert S, Jung O, Barbeck M. *In Vivo*. 2020 May-Jun;34(3):985-1000. doi: 10.21873/invivo.11867.

https://pubmed.ncbi.nlm.nih.gov/32354884/

Background/aim: A new manufacturing process has been established for the condensation of collagen derived from porcine pericardium to develop a new dental barrier membrane (CPM) that can provide a long barrier functionality. A native collagen membrane (PM) was used as control. **Materials and methods:** Established *in vitro* procedures using L929 and MC3T3 cells were used for cytocompatibility analyses. For the *in vivo* study, subcutaneous implantation of both membrane types in 40 BALB/c mice and established histological, immunohistochemical and histomorphometrical methods were conducted. **Results:** Both the *in vitro* and *in vivo* results revealed that the CPM has a biocompatibility profile comparable to that of the control membrane. The new CPM induced a tissue reaction including more M2-macrophages. **Conclusion:** The CPM is fully biocompatible and seems to support the early healing process. Moreover, the new biomaterial seems to prevent cell ingrowth for a longer period of time, making it ideally suited for GBR procedures.

19. A Comprehensive Comparison of Bovine and Porcine Decellularized Pericardia: New Insights for Surgical Applications

Zouhair S, Sasso ED, Tuladhar SR, Fidalgo C, Vedovelli L, Filippi A, Borile G, Bagno A, Marchesan M, Giorgio R, Gregori D, Wolkers WF, Romanato F, Korossis S, Gerosa G, Iop L. Biomolecules. 2020 Feb;10(3):371. doi: 10.3390/biom10030371.

https://pubmed.ncbi.nlm.nih.gov/32121155/

Xenogeneic pericardium-based substitutes are employed for several surgical indications after chemical shielding, limiting their biocompatibility and therapeutic durability. Adverse responses to these replacements might be prevented by tissue decellularization, ideally removing cells and preserving the original extracellular matrix (ECM). The aim of this study was to compare the mostly applied pericardia in clinics, i.e. bovine and porcine tissues, after their decellularization, and obtain new insights for their possible surgical use. Bovine and porcine pericardia were submitted to TRICOL decellularization, based on osmotic shock, detergents and nuclease treatment. TRICOL procedure resulted in being effective in cell removal and preservation of ECM architecture of both species' scaffolds. Collagen and elastin were retained but glycosaminoglycans were reduced, significantly for bovine scaffolds. Tissue hydration was varied by decellularization, with a rise for bovine pericardia and a decrease for porcine ones. TRICOL significantly increased porcine pericardial thickness, while a non-significant reduction was observed for the bovine counterpart. The protein secondary structure and thermal denaturation profile of both species' scaffolds were unaltered. Both pericardial tissues showed augmented biomechanical compliance after decellularization. The ECM bioactivity of bovine and porcine pericardia was

unaffected by decellularization, sustaining viability and proliferation of human mesenchymal stem cells and endothelial cells. In conclusion, decellularized bovine and porcine pericardia demonstrate possessing the characteristics that are suitable for the creation of novel scaffolds for reconstruction or replacement: differences in water content, thickness and glycosaminoglycans might influence some of their biomechanical properties and, hence, their indication for surgical use.

20. Osseous ingrowth in allogeneic bone blocks applied for vertical bone augmentation: a preclinical randomised controlled study

Moest T, Frabschka J, Kesting MR, Schmitt CM, Frohwitter G, Lutz R, Schlegel KA. Clin Oral Investig. 2020 Aug;24(8):2867-2879. doi: 10.1007/s00784-019-03151-0.

https://pubmed.ncbi.nlm.nih.gov/31828520/

Objectives: The aim of the present study was the qualitative and quantitative evaluation of osseous graft consolidation using allogeneic bone blocks for vertical bone augmentation in an animal model. **Material and methods:** Standardised allogeneic and autologous bone blocks were fixed on the frontal skull of 20 adult female pigs and covered with a resorbable collagen membrane. Animals were sacrificed after 2 and 6 months. Specimens were histologically and histomorphometrically analysed focusing on the amount of vital bone, residual bone substitute material and connective tissue. Furthermore, the amount of expression of bone matrix proteins (collagen type I and osteocalcin) and de novo vessel formation (von Willebrand factor) were quantified by immunohistochemistry. **Results:** Significantly more allogeneic bone blocks failed for both evaluation time points ($p < 0.05$). Allogeneic blocks showed significantly less vital bone with more connective tissue formation compared to autologous bone blocks. Increased vessel formation could be detected for both evaluation time points in the contact area of autologous bone with local bone. The expression of collagen type I and osteocalcin was significantly lower in the allogeneic bone graft. **Conclusions:** Allogeneic cancellous bone blocks showed a significantly higher failure rate compared to autologous bone blocks. Allogeneic bone blocks seemed to negatively affect bone formation or negatively influence the host in the long term, and increased connective tissue formation and block loss should be anticipated.

21. Histologic analyses of flapless ridge preservation in sockets with buccal dehiscence defects using two alloplastic bone graft substitutes.

Naenni N, Bienz SP, Jung RE, Hämmerle CHF, Thoma DS. Clin Oral Investig. 2019; 23(9):3589-3599.

https://www.ncbi.nlm.nih.gov/pubmed/30617661

Investigation whether one of two synthetic bone substitute materials used for ridge preservation in the extraction sockets with buccal dehiscence defects was superior regarding new bone formation and ridge preservation compared to sites left for spontaneous healing. **MATERIALS AND METHODS:**

In sixteen dogs, P3 and P4 were hemi-sectioned and the respective distal roots were extracted. Following preparation of a mucoperiosteal flap without vertical releasing incisions, 50% of the buccal bone was carefully removed. The extraction sites were randomly assigned either to a ridge preservation procedure (alloplastic bone substitute material (two test groups)) or to spontaneous healing (control group). Descriptive histology and histomorphometric analyses were performed at healing times of 4, 8, and 16 weeks. In case of homogeneous variances, the results were analyzed by one-way ANOVA, followed by Tukey's post-hoc test. If inhomogeneous, the data was analyzed using Welch-type ANOVA, followed by the Games-Howell post-hoc test. **RESULTS:** The use of bone substitute material led to significantly greater horizontal dimensions amounting to 3.3 mm and 3.5 mm compared to spontaneous healing at 16 weeks of healing. A significant difference was observed between spontaneous healing and the test groups in terms of newly formed bone tissue at 4, 8, and 16 weeks, but there were no significant differences between the test groups. The final ridge profile was more favorable after ridge preservation as demonstrated by a loss of 28.8% (spontaneous healing) and an increase in both test groups at 16 weeks. **CONCLUSIONS:** The use of alloplastic materials rendered greater horizontal dimensions and a more favorable maintenance of the ridge profile.

22. PRGF-Modified Collagen Membranes for Guided Bone Regeneration: Spectroscopic, Microscopic and Nano-Mechanical Investigations

Ratiu C, Brocks M, Costea T, Moldovan L and Cavalu S. Appl. Sci. 2019, 9(5): 1035

https://www.mdpi.com/2076-3417/9/5/1035

Evaluation of the properties of different commercially available resorbable collagen membranes for guided bone regeneration, upon addition of plasma rich in growth factors (PRGF). The structural and morphological details, mechanical properties, and enzymatic degradation were investigated in a new approach, providing clinicians with new data in order to help them in a successful comparison and better selection of membranes with respect to their placement and working condition. Particular characteristics such as porosity, fiber density, and surface topography may influence the mechanical behavior and performances of the membranes, as revealed by SEM/AFM and nanoindentation measurements. The mechanical properties and enzymatic degradation of the membranes were analyzed in a comparative manner, before and after PRGF-modification. The changes in Young modulus values are correlated with the ultrastructural properties of each membrane type. The enzymatic (trypsin) degradation test also emphasized that PRGF-modified membranes exhibit a slower degradation compared to the native ones.

23. Can the Macrogeometry of Dental Implants Influence Guided Bone Regeneration in Buccal Bone Defects? Histomorphometric and Biomechanical Analysis in Beagle Dogs.

Fernández-Domínguez M, Ortega-Asensio V, Fuentes-Numancia E, Aragoneses JM, Barbu HM5, Ramírez-Fernández MP, Delgado-Ruiz RA, Calvo-Guirado JL, Samet N, Gehrke SA. 2019. J Clin Med.;8(5). pii: E618.

https://www.ncbi.nlm.nih.gov/pubmed/31067735

The aim of this experimental animal study was to assess guided bone regeneration (GBR) and implant stability (ISQ) around two dental implants with different macrogeometries. **Material AND METHODS:** Forty-eight dental implants were placed within six Beagle dogs. GBR was performed to fill buccal defects using maxresorb® bone grafting material and Jason® membrane to cover the graft. The implants were divided into two groups (n = 24 per group): G1 group implants presented semi-conical macrogeometry, a low apical self-tapping portion, and an external hexagonal connection (whereby the cervical portion was bigger than the implant body). G2 group implants presented parallel walls macrogeometry, a strong apical self-tapping portion, and an external hexagonal connection (with the cervical portion parallel to the implant body). Buccal (mouth-related) defects of 2 mm (c2 condition) and 5 mm (c3 condition) were created. For the control condition with no defect (c1), implants were installed at crestal bone level. Eight implants in each group were installed under each condition. The implant stability quotient (ISQ) was measured immediately after implant placement, and on the day of sacrifice (3 months after the implant placement). Histological and histomorphometric procedures and analysis were performed to assess all samples, measuring crestal bone loss (CBL) and bone-to-implant contact (BIC). **RESULTS:** The data obtained were compared with statistical significance set at $p < 0.05$. The ISQ results showed a similar evolution between the groups at the two evaluation times, although higher values were found in the G1 group under all conditions. Within the limitations of this animal study, it may be concluded that implant macrogeometry is an important factor influencing guided bone regeneration in buccal defects. Group G1 showed better buccal bone regeneration (CBL) and BIC [%] at 3 months follow up, also parallel collar design can stimulate bone regeneration more than divergent collar design implants. **CONCLUSION:** The apical portion of the implant, with a stronger self-tapping feature, may provide better initial stability, even in the presence of a bone defect in the buccal area.

24. Evaluating the adhesion of human gingival fibroblasts and MG-63 osteoblast-like cells to activated PRP-coated membranes.

Vahabi S, Yadegary Z, Karamshahi M. 2019. Cell Tissue Bank. [Epub ahead of print].

https://www.ncbi.nlm.nih.gov/pubmed/31098701

Regeneration of periodontal tissues is affected by the biological and morphological characteristics of the membrane surface. The current study evaluated the adhesion of human gingival fibroblasts (HGF) and MG-63 osteoblast-like cells to membranes, with and without activated PRP. **MATERIAL AND**

METHODS: The line of human gingival fibroblast cells and MG-63 osteoblast-like cells were first prepared and cultured on three types of membranes, including Jason® membrane, CenoMembrane and TXT-200 in three groups (FBS 10%, FBS 0.5% and activated PRP). Cell viability was investigated by MTT assay and electron microscopy (SEM) was used to evaluate the cell morphology and adhesion on these membranes after 24 and 72 h. Two-way ANOVA was carried out at the significant level of 0.05. **RESULTS:** The highest adhesion in the 10% FBS group for HGF and the MG-63 osteoblast-like cells was observed to the Jason® membrane during 24 h and 72 h ($p < 0.05$). However, there were no significant differences among the three membranes in PRP and FBS groups for HGF during 24 h and for MG-63 cells during 72 h ($p > 0.05$). Activated PRP had a positive effect on the viability and adhesion of both human gingival fibroblasts and osteoblast-like cells as compared to the FBS 0.5% group, but these effects were not as 10% FBS group. **CONCLUSION:** The results also showed that Jason® membrane had the highest amount of cell viability and adhesion.

25. Osseointegration of Superhydrophilic Implants Placed in Defect Grafted Bones.

El Chaar E, Zhang L, Zhou Y, Sandgren R, Fricain JC, Dard M, Pippenger B, Catros S. 2019. Int J Oral Maxillofac Implants; 34(2):443–450.

https://www.ncbi.nlm.nih.gov/pubmed/30703182

Only limited information on the effect of implant surface hydrophilicity in conjunction with simultaneous bone augmentation is available**.** In this study, new bone growth around implants with a superhydrophilic modSLA (SLActive) and hydrophobic SLA (SLA) surface were compared in circumferential defects when grafted in conjunction with mineralized cancellous bone allograft (MCBA, maxgraft®) or sintered bovine bone mineral (SBBM, cerabone®) both covered with Jason® membrane. **MATERIALS AND METHODS:** The osseointegration and bone formation in circumferential defects in minipig mandibles around Straumann Roxolid, Ø 3.3 mm, length 8 mm; either SLA or SLActive, were evaluated. Following implant placement, the 2-mm circumferential defects around the implants were filled with MCBA or SBBM. Distance from implant shoulder to first bone-to-implant contact (f-BIC), percentage of bone-to-implant contact (BIC), and bone aggregate percentage (amount of new bone and remaining graft) within the defect area were evaluated after 8 weeks of healing. **RESULTS:** In the SBBM group, lingual fBIC and buccal BIC were significantly lower for SLA (mean -0.404 ± 0.579 mm for modSLA versus -1.191 ± 0.814 mm for SLA, P = .021 and mean 62.61% ± 9.49% for modSLA versus 34.67% ± 24.41% for SLA, P = .047, respectively). Bone aggregate percentage was significantly higher for modSLA versus SLA implants in SBBM (77.84% ± 6.93% versus 64.49% ± 13.12%; P = .045). The differences between implant surfaces in MCBA showed a similar trend but were less pronounced than in the SBBM group and did not reach a statistically significant level. **CONCLUSION:** The results suggest that implants with a superhydrophilic modSLA surface are more conducive to faster osseointegration even in conjunction with simultaneous bone grafting procedures.

26. Comparison of autogenous and allograft bone rings in surgically created vertical bone defects around implants in a sheep model.

Benlidayi ME, Salimov F, Tukel HC, Yüksel O. 2018. Clin Oral Implants Res. [Epub ahead of print].

https://www.ncbi.nlm.nih.gov/pubmed/30281857

OBJECTIVES: The aim of this study was to compare autogenous and allograft bone rings in surgically created vertical bone defects. **MATERIAL AND METHODS:** Four male, 1-year-old sheep were used in this study. In each sheep, 8 vertical bone defects 7mm in diameter were created using trephine drill in the iliac wing. Autogenous and allograft bone rings 5mm in height and 7mm in diameter were used for vertical augmentation around implants and covered with Jason® membrane. The study consisted of four groups according to the bone ring type and amount of vertical augmentation; autogenous 2mm, allograft 2mm, autogenous 4mm and allograft 4mm. Two of the animals were sacrificed after 4 months and the remaining two animals were sacrificed after 8 months. Undecalcified sections were prepared from harvested samples. Histological assessment and histomorphometric analysis were performed. **RESULTS**: Autogenous 2mm group showed higher values than allograft 2mm group and autogenous 4mm group showed higher values than allograft 4mm group in terms of bone area and bone to implant contact (BIC) after 4 months. However, allograft 2mm group showed higher bone area and BIC values than autogenous 2mm group after 8 months. Also, autogenous 4mm and allograft 4mm groups showed comparable results after 8 months. Allograft 2mm and allograft 4mm groups showed higher bone area and BIC values at 8 months compared to 4 months. Jason® membrane led to satisfactory bone regeneration and BIC. **CONCLUSIONS:** Allograft bone ring looks promising in augmentation of surgically created vertical bone defects around implants after 8 months of healing.

27. Effect of flapless ridge preservation with two different alloplastic materials in sockets with buccal dehiscence defects—volumetric and linear changes.

Naenni N, Sapata V, Bienz SP, Leventis M, Jung RE, Hämmerle C.H.F, Thoma DS. 2018. Clin Oral Investig. ; 22(6):2187-2197. [Epub 2017].

https://www.ncbi.nlm.nih.gov/pubmed/29280075

The objective was to test whether or not one out of two alloplastic materials used for ridge preservation (RP) is superior to the other in terms of volumetric and linear ridge changes over time. **MATERIALS AND METHODS:** In 16 adult beagle dogs, the distal roots of P3 and P4 were extracted and 50% of the buccal bone plate removed. Ridge preservation was performed randomly using two different alloplastic bone grafting substitutes (poly lactic-co-glycolic acid (PLGA) coated biphasic calcium phosphate particles consisting of 60% hydroxyapatite (HA) and 40% beta-tricalcium phosphate (ß-TCP=test 1), (a biphasic calcium phosphate consisting 60% HA and 40% ß-TCP=test 2) and a resorbable collagen membrane or a control group (sham). Sacrifice was performed at three

time-points (4, 8, 16 weeks later). Impressions were taken before extraction, after RP, and at sacrifice, allowing for assessment of volumetric changes. A multi-way ANOVA was computed, and partial Type-II F tests were performed. **RESULTS:** Both ridge preservation procedures minimized the volume loss compared to spontaneous healing. The median buccal volume changes between pre-extraction and sacrifice were - 1.76 mm (Q1 = - 2.56; Q3 = - 1.42) for test 1, - 1.62 mm (Q1 = - 2.06; Q3 = - 1.38) for test 2, and - 2.42 mm (Q1 = - 2.63; Q3 = - 2.03) for control. The mean ridge width measurements did not show statistically significant differences between test 1 (- 2.51 mm; Q1 = - 3.25; Q3 = - 1.70) and test 2 (- 2.04 mm; Q1 = - 3.82; Q3 = - 1.81) (p = 0.813), but between test and control (- 3.85 mm; Q1 = - 5.02; Q3 = - 3.27) (p = 0.003). **CONCLUSIONS:** Both RP techniques were successful in maintaining the buccal contour from pre-extraction to sacrifice to a similar extent and more favorable compared to spontaneous healing.

28. New nano-hydroxyapatite in bone defect regeneration: A histological study in rats.

Kubasiewicz-Ross P, Hadzik J, Seeliger J, Kozak K, Jurczyszyn K, Gerber H, Dominiak M, Kunert-Keil C. 2017. Ann Anat.; 213:83-90.

https://www.ncbi.nlm.nih.gov/pubmed/28655570

The purpose of the study was to evaluate the osseoconductive potential and bone defect regeneration in rat calvarial bone defects treated with new synthetic nano-hydroxyapatite. The study was performed on 30 rats divided into 5 equal groups. New preproduction of experimental nano-hydroxyapatite material by NanoSynHap (Poznań, Poland) was tested and compared with commercially available materials. Five mm critical size defects were created and filled with the following bone grafting materials: 1) Geistlich Bio-Oss® 2) Nano-hydroxyapatite+β-TCP 3) Nano-hydroxyapatite; 4) Nano-hydroxyapatite + collagen membrane (Jason® membrane). A last group served as control without any augmentation. Bone samples from calvaria were harvested for histological and micro-CT evaluation after 8 weeks. New bone formation was observed in all groups. Histomorphometric analysis revealed an amount of regenerated bone between 34.2 and 44.4% in treated bone defects, whereas only 13.0% regenerated bone was found in controls. Interestingly, in group 3, no significant particles of the nano-HA material were found. In contrast, residual bone substitute material could be detected in all other test groups. Micro-CT study confirmed the results of the histological examinations. The new nano-hydroxyapatite provides comparable results to other grafts in the field of bone regeneration.

29. Comparison of Two Porcine Collagen Membranes Combined with rhBMP-2 and rhBMP-9 on Osteoblast Behavior *in Vitro*.

Fujioka-Kobayashi M, Schaler B, Shirakata Y, Nakamura T, Noguchi K, Zhang Y, Miron RJ. 2017. Int J Oral Maxillofac Implants.; 32(4):e221-e230.

http://onlinelibrary.wiley.com/doi/10.1002/cre2.55/pdf

The aim was to investigate the bone-inducing properties of two types of collagen membranes in combination with recombinant human bone morphogenetic protein (rhBMP)-2 and rhBMP-9 on osteoblast behavior. **MATERIALS AND METHODS:** Porcine pericardium collagen membranes (PPCM) and porcine dermis-derived collagen membranes (PDCM) were coated with either rhBMP-2 or rhBMP-9. The adsorption and release abilities were first investigated via enzyme-linked immunosorbent assay up to 10 days. Moreover, murine bone stromal ST2 cell adhesion, proliferation, and osteoblast differentiation were assessed by MTS assay; real-time polymerase chain reaction for genes encoding runt-related transcription factor 2 (Runx2); alkaline phosphatase (ALP); and osteocalcin, ALP assay, and alizarin red staining. **RESULTS:** Both rhBMP-2 and rhBMP-9 adsorbed to collagen membranes and were gradually released over time up to 10 days. PPCM showed significantly less cell attachment, whereas PDCM demonstrated comparable cell attachment with the control tissue culture plastic at 8 hours. While both rhBMPs were shown not to affect cell proliferation, collagen membranes combined with rhBMP-9 significantly increased ALP activity at 7 days and ALP mRNA levels at either 3 or 14 days compared with the control tissue culture plastic. Furthermore, rhBMP-9 increased osteocalcin mRNA levels and alizarin red staining at 14 days compared with the control tissue culture plastic. **CONCLUSION:** The results from this study suggest that both porcine-derived collagen membranes combined with rhBMP-9 accelerated the osteopromotive potential of ST2 cells. Interestingly, rhBMP-9 demonstrated additional osteogenic differentiation compared with rhBMP-2 and may serve as a suitable growth factor for future clinical use.

30. Collagen Membranes Adsorb the Transforming Growth Factor-β Receptor I Kinase-dependent Activity of Enamel Matrix Derivative.

Stähli A, Miron RJ, Bosshardt DD, Sculean A, Gruber R. 2016. J Periodontol.; 87(5):583-90.

http://www.ncbi.nlm.nih.gov/pubmed/26777762

Enamel matrix derivative and collagen membranes are simultaneously applied in regenerative periodontal surgery. Here, we studied the ability of two collagen membranes and a collagen matrix to adsorb the activity intrinsic to enamel matrix derivative that provokes transforming growth factor-beta (TGF-β) signaling in oral fibroblasts. **MATERIAL AND METHODS**: Three commercially available collagen products were exposed to enamel matrix derivative or recombinant TGF-β1, followed by vigorous washing. Oral fibroblasts either were seeded directly onto the collagen products or were incubated with the respective supernatant. The expression of the TGF-β target genes interleukin 11 and proteoglycan 4 was evaluated by real time PCR. To study the fraction of enamel matrix derivative proteins binding to collagen, we used proteomic analysis. **RESULTS:** Enamel matrix derivative or TGF-β1 provoked a significant increase of interleukin 11 and proteoglycan 4 expression of oral fibroblasts when seeded onto the collagen products and when incubated with the respective supernatant. Gene

expression was blocked by the TGF-β receptor I kinase inhibitor SB431542. Amelogenins bound most abundantly to gelatin coated culture dishes. Incubation of palatal fibroblasts with recombinant Amelogenins, however, did not alter expression of interleukin 11 and proteoglycan 4. **CONCLUSIONS:** These *in vitro* findings suggest that collagen products adsorb a TGF-β receptor I kinase-dependent activity of enamel matrix derivative and make it available for potential target cells.

31. Porcine dermis and pericardium-based, non-cross-linked materials induce multinucleated giant cells after their *in vivo* implantation: A physiological reaction?

Barbeck M, Lorenz J, Grosse Holthaus M, Raetscho N, Kubesch A, Booms P, Sader R, Kirkpatrick CJ, Ghanaati S. J Oral Implantol. 2015; 41(6):e267-81. [Epub 2014].

http://www.ncbi.nlm.nih.gov/pubmed/25386662

The present study analyzed the tissue reaction to two novel porcine-derived collagen materials, i.e. pericardium versus dermis. By means of the subcutaneous implantation model in mice, the tissue reactions were investigated at five different time points: 3, 10, 15, 30 and 60 days after implantation. Histological, histochemical, immunohistological and histomorphometrical analysis methodologies were applied. The dermis-derived material underwent an early degradation while inducing mononuclear and together with some multinucleated giant cells along with a mild vascularization. The pericardium-derived membrane induced two different cellular tissue reactions. The compact surface induced mononuclear and multinucleated giant cells and underwent a complete degradation until day 30. The spongy surface of the membrane induced mainly mononuclear cells and served as a stable barrier membrane for up to 60 days. No transmembraneous vascularization was observed within the spongy material surface layer. The present data demonstrates the diversity of the cellular tissue reaction towards collagen-based materials from different tissues. Furthermore, it becomes obvious that the presence of multinucleated giant cells is associated with the material breakdown/degradation and vascularization.

*Study refers to BEGO collagen membrane, which is a private label of Jason® membrane

32. Biocompatibility and Biodegradation of a Native, Porcine Pericardium Membrane. Results from *in vitro*/*in vivo* Examination.

Rothamel D, Smeets R, Ritter L, Dreiseidler T, Fienitz T, Zöller J. Int J Oral Maxillofac Implants 2012, 27(1):146-54.

http://www.ncbi.nlm.nih.gov/pubmed/22299091

The aim of this pilot study was the *in vitro* and *in vivo* examination of a novel native collagen membrane extracted from porcine pericardium. **MATERIAL AND METHODS:** Two different native collagen membranes (Remotis pericardium collagen membrane [RPCM]), porcine pericardium, Thommen Medical, Waldenburg, Switzerland and Bio Gide [BG], porcine, Geistlich Pharma AG, Wolhusen, Switzerland were incubated with $1*10^4$ SaOs-2 osteoblast-like cells for biocompatibility testing. After 2 hours, 3 and 7 days proliferation of the cells on the surface was determined. Morphological structure of the membranes was conducted using a scanning electron microscope. Evaluation of the biodegradation pattern was performed in a dog model with simultaneous bone augmentation with Bio-Oss (Geistlich Pharma AG) or cerabone® (botiss dental GmbH) in the lateral anterior maxilla in 4 animals and histological examination after 4, 8, 12 and 24 weeks. **RESULTS:** *In vitro*, RPCM showed considerable cell proliferation, which was significantly superior to that observed with BG (p 0.05, Wilcoxon test). With respect to the morphological analysis, an interconnected multilayer system was identifiable for RPCM, while BG displayed more of a fibrous structure. *In vivo*, both membranes integrated into the surrounding tissue without any inflammatory reaction. Both membranes revealed an early vascularization of the membrane body. However, a considerable biodegradation was noted within 4–8 weeks with BG, while the resorption of RPCM primarily occurred within the first 8–12 weeks. It was concluded that both examined membranes indicate a high level of biocompatibility. **CONCLUSION**: Both native RPCM and BG are resorbed without inflammation within 8 (BG) or 12 weeks (RPCM). The compact multilayer collagen of RCPM may have positively influenced the resorption stability.

*Study refers to Remotis membrane, which was a former private label of Jason® membrane.

33. Clinical aspects of novel types of collagen membranes and matrices: Current issues in soft- and hard-tissue augmentation.

Rothamel D, Toeroek R, Neugebauer J, Fienitz T, Scheer M, Kreppel M, Mischkowski R, Zöller J. EDI Journal 1/2012; 64.

http://www.teamwork-media.de/wp-content/uploads/2015/11/edi1_12_rothamel_lit.pdf

In recent years, the use of bone substitutes has increasingly become established for augmenting localized defects of the alveolar ridge as an alternative to autologous bone grafts. Bone substitutes are available in unlimited quantities, are not associated with any harvest-related morbidity and are well accepted by patients. To prevent connective-tissue encapsulation of the material introduced, it should be separated from the adjacent soft tissue by membranes, following the principles of guided tissue regeneration (GTR). However, it should be noted that especially resorbable collagen membranes differ with regard to their handling properties and mechanism of biodegradation and, hence, the resulting incidence of complications. But technical progress in the area of collagenous membranes has led to thicker collagen matrices with more stable volumes, opening up new possibilities. New indications for these matrices might reduce the morbidity related to the harvesting of palatal soft-tissue grafts.

34. 3D-Printed Soft Membrane for Periodontal Guided Tissue Regeneration

Farshid Vahdatinia, Amirarsalan Hooshyarfard, Shokoofeh Jamshidi, Setareh Shojaei, Kishan Patel, Erfan Moeinifard, Rasool Haddadi, Maryam Farhadian, Leila Gholami, Lobat Tayebi. 2023 Feb 6;16(4):1364. doi: 10.3390/ma16041364. PMID: 36836994; PMCID: PMC9967512.

https://pubmed.ncbi.nlm.nih.gov/36836994/

Objectives: The current study aimed to perform an in vivo examination using a critical-size periodontal canine model to investigate the capability of a 3D-printed soft membrane for guided tissue regeneration (GTR). This membrane is made of a specific composition of gelatin, elastin, and sodium hyaluronate that was fine-tuned and fully characterized in vitro in our previous study. The value of this composition is its potential to be employed as a suitable replacement for collagen, which is the main component of conventional GTR membranes, to overcome the cost issue with collagen. **Methods:** Critical-size dehiscence defects were surgically created on the buccal surface of the roots of canine bilateral mandibular teeth. GTR treatment was performed with the 3D-printed membrane and two commercially available collagen membranes (Botiss Jason® and Smartbrane-Regedent membranes) and a group without any membrane placement was considered as the control group. The defects were submerged with tension-free closure of the gingival flaps. Histologic and histometric analyses were employed to assess the periodontal healing over an 8-week experimental period. **Results:** Histometric evaluations confirmed higher levels of new bone formation in the 3D-printed membrane group. Moreover, in all defects treated with the membranes, the formation of periodontal tissues, bone, periodontal ligaments, and cementum was observed after 8 weeks, while in the control group, only connective tissue was found in the defect sites. There was no clinical sign of inflammation or recession of gingiva in any of the groups. **Significance:** The 3D-printed gelatin/elastin/sodium hyaluronate membrane can be safe and effective for use in GTR for periodontal tissue regeneration therapies, with better or comparable results to the commercial collagen membranes.

35. Analyses of the Cellular Interactions between the Ossification of Collagen-Based Barrier Membranes and the Underlying Bone Defects

Alkildani S, Ren Y, Liu L, Rimashevskiy D, Schnettler R, Radenković M, Najman S, Stojanović S, Jung O, Barbeck M. Int J Mol Sci. 2023 Apr 6;24(7):6833. doi: 10.3390/ijms24076833. PMID: 37047808; PMCID: PMC10095555.

https://pubmed.ncbi.nlm.nih.gov/37047808/

Barrier membranes are an essential tool in guided bone Regeneration (GBR), which have been widely presumed to have a bioactive effect that is beyond their occluding and space maintenance functionalities. A standardized calvaria implantation model was applied for 2, 8, and 16 weeks on Wistar rats to test the

interactions between the barrier membrane and the underlying bone defects which were filled with bovine bone substitute materials (BSM). In an effort to understand the barrier membrane's bioactivity, deeper histochemical analyses, as well as the immunohistochemical detection of macrophage subtypes (M1/M2) and vascular endothelial cells, were conducted and combined with histomorphometric and statistical approaches. The native collagen-based membrane was found to have ossified due to its potentially osteoconductive and osteogenic properties, forming a "bony shield" overlying the bone defects. Histomorphometrical evaluation revealed the resorption of the membranes and their substitution with bone matrix. The numbers of both M1- and M2-macrophages were significantly higher within the membrane compartments compared to the underlying bone defects. Thereby, M2-macrophages significantly dominated the tissue reaction within the membrane compartments. Statistically, a correlation between M2-macropahges and bone regeneration was only found at 2 weeks post implantationem, while the pro-inflammatory limb of the immune response correlated with the two processes at 8 weeks. Altogether, this study elaborates on the increasingly described correlations between barrier membranes and the underlying bone regeneration, which sheds a light on the understanding of the immunomodulatory features of biomaterials.

Clinical studies and case series

1. The effect of acemannan in implant placement with simultaneous guided bone regeneration in the aesthetic zone: a randomized controlled trial

   Deesricharoenkiat N, Jansisyanont P, Chuenchompoonut V, Mattheos N, Thunyakitpisal P. Int J Oral Maxillofac Surg. 2022 Apr;51(4):535-544. doi: 10.1016/j.ijom.2021.07.017.

   https://pubmed.ncbi.nlm.nih.gov/34429224/

   Acemannan, a linear polysaccharide produced by Aloe vera, has been shown to have important biological effects promoting wound healing and tissue regeneration. The aim of this randomized clinical trial was to investigate the impact of acemannan in guided bone regeneration (GBR) with simultaneous implant placement. Twenty patients were randomly allocated to a test group (deproteinized bovine bone with particulate acemannan (mean size 32.45 µm)) and a control group (deproteinized bovine bone only). Twenty implants were placed with simultaneous GBR. Radiographic measurements were conducted on cone beam computed tomography (CBCT) scans immediately post-surgery and at 3 and 6 months. Vertical and horizontal dimensions of the buccal bone were measured at the implant platform (0) and at points 2, 4, 6, and 8 mm apically. The dimensional reduction of vertical and horizontal buccal bone was significantly smaller in the test group at 3 months postoperative ($P < 0.05$) at every position measured (0, 2, 4, 6, 8 mm), but the difference was not statistically significant at 6 months. Acemannan was found to be a safe and predictable biomaterial for GBR, which resulted in enhanced dimensional stability of the regenerated tissue at 3 months. However, these results were not replicated at 6 months. Further studies are required to document the long-term efficacy and potential of acemannan use as a supplement in bone regeneration.

2. A 3-year prospective randomized clinical trial of alveolar bone crest response and clinical parameters through 1, 2, and 3 years of clinical function of implants placed 4 months after alveolar ridge preservation using two different allogeneic bone-grafting materials

   Solakoğlu Ö, Ofluoğlu D, Schwarzenbach H, Heydecke G, Reißmann D, Ergun S, Götz W. Int J Implant Dent. 2022 Feb;8(1):5. doi: 10.1186/s40729-022-00402-w.

   https://pubmed.ncbi.nlm.nih.gov/35102440/

   Purpose: The aim of this study was to longitudinally evaluate changes in alveolar bone crest (ABC) levels and differences in resorption rates (RR) between the tested grafting materials following alveolar ridge

preservation (ARP) after tooth extraction after 1, 2, and 3 years (T1-T8) of clinical function. **Methods:** Patients were randomly assigned to two different bone allografts (group 1 maxgraft®, group 2 Puros®) for ARP. Non-restorable teeth were minimal traumatically extracted. Sockets were augmented with the tested materials and covered with a pericardium membrane. After 4 months of healing, 36 implants were placed and sites were clinically and radiographically monitored in the mesial (ABC-M), the distal (ABC-D, T1-T8), the bucco-lingual (ABC-BL), buccal (ABC-B) and oral (ABC-O) aspect (T1-T4). **Results:** Changes in (ABC-M), (ABC-D), (ABC-BL), (ABC-B), and (ABC-O) levels showed statistically highly significant differences between T1 and T2 for both bone allografts ($p < 0.001$). Changes at the ABC-M and ABC-BL levels between T2 and T3 of group 1 showed a statistically significant difference ($p < 0.001$). Both groups achieved and maintained increased ABC levels without statistically significant differences throughout the monitoring periods of 1-3 years (T6-T8) of clinical function. No failures or adverse events were observed. **Conclusions:** To the best of our knowledge, this study is within its limitations the first study to directly compare ABC-changes and differences in RR of two different allogeneic grafting materials for a period of 3 years after ARP. It was demonstrated to be, despite significant differences in RR, a successful method of preserving increased ABC levels through 1, 2, and 3 years of clinical function. Trial registration DRKS00013010, registered 07/30/2018, http://apps.who.int/trialsearch.

3. Characterization of circulating molecules and activities in plasma of patients after allogeneic and autologous intraoral bone grafting procedures: a prospective randomized controlled clinical trial in humans

Solakoglu Ö, Steinbach B, Götz W, Heydecke G, Schwarzenbach H. BMC Oral Health. 2022 Jan;22(1):24. doi: 10.1186/s12903-021-02036-7.

https://pubmed.ncbi.nlm.nih.gov/35094679/

Background: The objective was to assess whether intraoral bone augmentation procedures have an impact on the patient's plasma levels of circulating nucleic acids, exosomes, miRNA levels and caspase activities. The null hypothesis was tested, that no significant differences between the two groups will be found. **Methods**: In this prospective randomized controlled clinical trial 35 systemically healthy non-smoking participants were randomly allocated using sealed envelopes by a blinded clinician not involved in the clinical setting. Plasma samples were collected preoperatively and 3 times postoperatively (immediately, 5 weeks and 4 months postoperatively). The test group consisted of twenty-five patients who received allogeneic bone grafting material and the control group of ten patients who received autologous bone grafts. Levels of cell-free DNA (cfDNA) and microRNAs (miR-21, miR-27a, miR-218) were quantified by real-time PCR, caspase activities and exosome concentrations were determined by ELISA. **Results:** Statistical evaluation reveled a significantly higher exosome level before surgery ($p = 0.013$) and the first postsurgical sample ($p = 0.017$) in the control group compared

to the test group. The levels of miR-27a and miR-218 significantly differed between the plasma samples before surgery and after surgery in both groups. The levels of miR-21 only significantly differed between the pre- and postsurgical plasma samples in the test group, but not in the control group. All patients completed the study, no adverse events were recorded. **Conclusions:** Our data show the diagnostic potential of the plasma levels of miR-27a, miR-218 and miR-21 in detecting changes in bone metabolism after alveolar bone augmentation. Our very promising results indicate that there might be a high diagnostic potential in evaluating the plasma levels of the before mentioned miRNAs in order to detect bone resorption activities before they become clinically relevant.

4. Comparing membranes and bone substitutes in a one-stage procedure for horizontal bone augmentation. Three-year post-loading results of a double-blind randomized controlled trial.

Merli M, Moscatelli M, Mariotti G, Pagliaro U, Raffaelli E, Nieri M. Eur J Oral Implantol. 2018;11(4):441-452.

https://pubmed.ncbi.nlm.nih.gov/30515484/

Purpose: The objective of this 3-year post-loading parallel randomised controlled trial is to compare two bone substitutes and resorbable membranes in a one-stage procedure for horizontal bone augmentation: anorganic bovine bone and porcine collagen membranes (BB group) versus synthetic resorbable bone graft substitute made of pure β-tricalcium phosphate and porcine pericardium collagen membranes (CJ group).
Materials and methods: Patients in need of implant treatment having at least one site with horizontal osseous defect at a private clinic in Rimini, Italy, were included in this study. Patients were randomised to receive either BB or CJ in a one-stage procedure for horizontal bone augmentation in a submerged approach. Randomisation was computer-generated with allocation concealment by opaque sequentially numbered sealed envelopes. Patients and the outcome assessor were blinded to group assignment. The abutment connection was made after 6 months of healing. The application of the provisional prosthesis was performed after abutment connection and a definitive metal-ceramic prosthesis was placed 6 months post-loading. The patients were followed-up to 3 years post-loading. Primary outcome measures were: implant failure, complications and peri-implant margin bone level changes. Secondary outcome measures were: visual analogue scale (VAS) for functional and aesthetic satisfaction and pink aesthetic score (PES).
Results: Twenty-five patients with 32 implants were randomly allocated to the BB group and 25 patients with 29 implants to the CJ group. All 50 randomised patients received the treatment as allocated and there were 7 drop-outs in the BB group and 11 drop-outs in the CJ group up to 3 years' post-loading. There were no implant failures. There were six complications in five patients of the BB group and three complications in three patients of the CJ group (relative risk: 1.32, 95% CI from 0.37 to 4.64, P = 1.0000). Radiographic bone loss was 1.61 mm for the BB group and 1.02 mm for the CJ group (difference 0.54 mm, 95% CI from -0.53 to 1.60, P = 0.3100). The functional VAS was 9.0 for the BB group and 9.6 for the CJ group (difference 0.6, 95% CI from -0.4 to 1.5, P = 0.2393). The aesthetic

VAS was 9.4 for the BB group and 9.6 for the CJ group (difference 0.2, 95% CI from -0.5 to 0.8, P = 0.6141). PES was 8.7 for the BB group and 8.5 for the CJ group (difference -0.1, 95% CI from -2.9 to 2.7, P = 0.9360).
Conclusions: No significant differences were observed in this randomised controlled trial comparing anorganic bovine bone with porcine collagen membranes versus synthetic resorbable bone made of pure β-tricalcium phosphate with pericardium collagen membranes for horizontal augmentation.

5. Hard Tissue Volume Stability Effect beyond the Bony Envelope of a Three-Dimensional Preformed Titanium Mesh with Two Different Collagen Barrier Membranes on Peri-Implant Dehiscence Defects in the Anterior Maxilla: A Randomized Clinical Trial

   Lee SR, Jang TS, Seo CS, Choi IO, Lee WP. Materials (Basel). 2021 Sep;14(19):5618. doi: 10.3390/ma14195618.

   https://pubmed.ncbi.nlm.nih.gov/34640019/

   This single-blinded, randomized, controlled study aimed to clinically and radiographically evaluate hard tissue volume stability beyond the bony envelope using three-dimensional preformed titanium mesh (3D-PFTM) for peri-implant dehiscence defects in the anterior maxilla. A total of 28 patients who wished to undergo implant surgery combined with guided bone regeneration (GBR) after extraction of a single maxillary anterior tooth were randomly assigned to two groups depending on the type of collagen membrane used, additionally with the 3D-PFTM-test (n = 14, cross-linked collagen membrane; CCM) and control (n = 14, non-cross-linked collagen membrane; NCCM) groups. Each implant was evaluated radiographically using CBCT at baseline, immediately after surgery, and at 6 months postoperatively. The relative position and distances from the bony envelope to the outlines of the augmented ridge were further determined immediately after GBR and 6 months after healing. At the platform level, the mean horizontal hard tissue gain (HG) at all the sites was 2.35 ± 0.68 mm at 6 months postoperatively. The mean HG rate was 84.25% ± 14.19% in the CCM group and 82.56% ± 13.04% in the NCCM group, but the difference was not significant between the groups. In all cases, HG was maintained beyond the bony envelope even after 6 months of GBR. This study suggests that 3D-PFTM should be considered a valuable option for GBR for peri-implant dehiscence defects in the anterior maxilla. In addition, 3D-PFTM may confer predictable hard tissue volume stability even after the healing period of hard tissue augmented outside the bony envelope by GBR.

6. The use of Bone Allograft material and Enamel matrix derivates in the regenerative treatment of mandibular furcation class II defects in localised periodontitis with trauma from occlusion: a report of two cases and a narrative review of the literature

Solakoglu Ö, Amiri N, Ahlers MO. Dtsch Zahnärztl Z Int 2021 Mar;3:8–110. doi: 10.3238/dzz-int.2021.0012.

https://www.online-dzz.com/archive/issue/article/dzzint-3-2021/5685-103238-dzz-int20210012-the-use-of-bone-allograft-material-and-enamel-matrix-derivates-in-the/

Introduction: Periodontitis can result in irreversible loss of connective tissue and supporting alveolar bone. Despite advances in regeneration therapy, treatment of periodontal furcation defects is still a challenge. This case report describes a combined regenerative approach in the treatment of grade II furcation defects in mandibular molars. **Material and Methods:** In the present case study, 2 clinical cases with advanced localised periodontitis and an occlusal trauma as a cofactor were studied over 8 and 5 years, respectively. Following initial occlusal adjustment, the periodontal defects were treated successfully with guided tissue regeneration along with allogenic cancellous bone, enamel matrix proteins and endogenous growth factors. **Results:** The treatment was effective in the regenerative therapy of destructive periodontal disease in both patients. Significant amount of bone fill was seen in clinical and radiographic re-evaluation and clinical results were maintained in the follow-up after 8 and 5 years. **Conclusion:** Successful regeneration of periodontal tissues can be achieved using the combination of guided tissue regeneration (GTR), Allograft bone substitute, Emdogain and plasma rich in growth factor (PRGF). The combination therapy resulted in regeneration of tooth supporting tissue with improved clinical attachment levels and healthy gingiva.

7. Retrospective Analysis of the Effect of Three-Dimensional Preformed Titanium Mesh on Peri-Implant Non-Contained Horizontal Defects in 100 Consecutive Cases

Choi I-O, Oh J-S, Yu S-J, Kim B-O, Lee W-P. Appl Scien. 2021 Jan;11(2):872. doi : 10.3390/app11020872.

https://www.mdpi.com/2076-3417/11/2/872

This study aimed to clinically and radiographically evaluate the results of guided bone regeneration (GBR) using three-dimensional preformed titanium mesh (3-D-PFTM) for non-contained horizontal defects in 100 consecutive cases. This study involved 100 patients (129 implants) with peri-implant non-contained horizontal defects. The patients were divided into three groups: 3-D-PFTM alone (Group 1), 3-D-PFTM plus cross-linked collagen membrane (Group 2), and 3-D-PFTM plus non-cross-linked collagen membrane (Group 3). Each implant was evaluated radiographically using CBCT at baseline and 6 months postoperatively. At the platform level, the mean horizontal hard tissue gain of all the sites was 3.1 ± 1.3 mm at 6 months postoperatively. The mean rate of mesh exposure was 11.8% in Group 1, 4.2% in Group 2, and 5.0% in Group 3. The mean hard tissue gain rate was 71.0 ± 23.0% in group 1, 84.2 ± 21.5% in group 2, and 84.0 ± 22.9% in group 3. Groups 2 and 3 showed significantly higher hard

tissue gain rates than group 1. However, there was no significant difference between the rates in groups 2 and 3. Within the limitations of this study, 3-D-PFTM should be considered as a valuable option for GBR for peri-implant non-contained horizontal defects. The use of an additional resorbable collagen membrane provides additional advantages.

8. Alveolar ridge augmentation using the shell technique with allogeneic and autogenous bone plates in a split-mouth design—A retrospective case report from five patients

   Tunkel J, de Stavola L, Kloss-Brandstätter A. Clin Case Rep. 2020 Dec;9(2):947-959. doi: 10.1002/ccr3.3626.

   https://pubmed.ncbi.nlm.nih.gov/33598278/

   Atrophic alveolar ridges of five patients were augmented with allografts and autografts on opposite sites, followed by dental implantation. Both augmentation materials led to equivalent bone gains. Allografts did not compromise the clinical outcome.

9. Immediate Implant Placement and Provisionalization in the Esthetic Zone Revisited: The Marginal Migration Concept (MMC)

   Valavanis K, Vergoullis I, Papastamos M, Salama H. Applied Sciences. 2020; 10(24):8944. doi: 10.3390/app10248944.

   https://www.mdpi.com/2076-3417/10/24/8944

   Immediate implant placement and provisionalization in the esthetic zone is a desirable approach that presents several advantages but at the same time embosses several risk factors that can lead to sever esthetic complications. The purpose of this article was to propose a new protocol that could allow for the maintenance and even the improvement of the hard and soft tissue topography, leading to superior esthetic results. The proposed protocol, when certain criteria are met, could be applied even for cases where the extraction socket morphology is currently proposed as a contra-indication for immediate implant placement and provisionalization.

10. Ridge Augmentation Using Customized Allogeneic Bone Block: A 3-Year Follow-up of Two Case Reports

    Landsberg C, Moses O. Int J Periodontics Restorative Dent. 2020 Nov/Dec;40(6):881-889. doi: 10.11607/prd.3354.

    https://pubmed.ncbi.nlm.nih.gov/33151194/

A variety of surgical techniques and grafting materials for the purpose of ridge augmentation have been developed during the last three decades. Recently, the use of customized allogeneic bone blocks, prepared by CAD/CAM techniques, has been introduced. This new augmentation technology may significantly reduce surgical time and improve donor-recipient fit and adaptation. However, promising clinical and histologic results have been published in only a few short-term case reports. The 3-year follow-ups of these two case reports may provide more clinical data on the use of the customized bone blocks for horizontal and vertical ridge augmentation in the posterior mandible.

11. Randomized and Controlled Clinical Trial of Bone Healing After Alveolar Ridge Preservation Using Xenografts and Allografts Versus Plasma Rich in Growth Factors

Stumbras A, Januzis G, Gervickas A, Kubilius R, Juodzbalys G. J Oral Implantol. 2020 Oct;46(5):515-525. doi: 10.1563/aaid-joi-D-19-00179.

https://pubmed.ncbi.nlm.nih.gov/32315435/

Abstract: The aim of this study was to compare bone regeneration in the anterior maxilla between bone substitutes and autologous platelet concentrate in alveolar ridge preservation. Forty patients requiring tooth extraction in the anterior maxilla were randomly allocated to the following 4 treatment modalities: spontaneous healing (control), natural bovine bone mineral covered with resorbable native collagen membrane (BBM/CM), freeze-dried bone allograft covered with resorbable native collagen membrane (FDBA/CM), and plasma rich in growth factors (PRGF) alone. Bone biopsies and histomorphometrical analysis were performed after 3 months of healing. The following parameters were assessed: newly formed mineralized tissue, newly formed nonmineralized tissue, and residual bone-grafting material (if applicable). Statistical analysis was performed to provide descriptive analysis and to compare the parameters of the bone regeneration between the study groups. Histomorphometrical analysis revealed the highest new mineralized tissue formation in the PRGF group. Statistically significant differences in new mineralized tissue formation were found between control/PRGF (46.4% ± 15.2% vs 75.5% ± 16.3%), control/(BBM/CM) (46.4% ± 15.2% vs 20.3% ± 21.9%), control/(FDBA/CM) (46.4% ± 15.2% vs 7.2% ± 8.6%), PRGF/(BBM/CM) (75.5% ± 16.3% vs 20.3% ± 21.9%), and PRGF/(FDBA/CM) (75.5% ± 16.3% vs 7.2% ± 8.6%) groups. The new mineralized tissue formation was in the following order: PRGF > control > BBM > FDBA. Alveolar ridge preservation in the esthetic zone with PRGF was the most effective for bone regeneration of the alveolar ridge.

12. Radiological and histological evaluation of horizontal ridge augmentation using corticocancellous freeze-dried bone allograft with and without autogenous bone: A randomized controlled clinical trial

Hashemipoor M, Asghari N, Mohammadi M, Kalantari M, Arabsolghar M, Ranjbar H. Clin Implant Dent Relat Res. 2020 Oct;22(5):582-592. doi: 10.1111/cid.12935.

https://pubmed.ncbi.nlm.nih.gov/32902105/

Purpose: The purpose of this study was radiological and histological evaluation of horizontal ridge augmentation using corticocancellous freeze-dried bone allograft (FDBA) with and without autogenous bone (AB). **Materials and methods:** The present research was conducted on 42 patients (27 females and 15 males) with insufficient width of edentulous ridge. The patients were randomly assigned into two groups, FDBA alone + collagen membrane (n = 21) and the combined FDBA and AB + collagen membrane (n = 21). The horizontal alveolar ridge dimensions were measured using cone-beam computerized tomography before and 6 months after alveolar ridge augmentation. At the time of insertion of implants, biopsy of new bone was taken from 11 patients in each group and was analyzed histologically. The obtained data were statistically analyzed with paired t test and two-sample t test. The registration number was IRCT201109165305N3. Results: The mean ± SD ridge width gain after 6 months at the distance of 0, 2, 4, and 6 mm from crest of alveolar ridge was 2.78 ± 1.44, 3.05 ± 1.21, 2.82 ± 1.62, and 2.23 ± 1.95 mm in the FDBA group and 2.40 ± 1.60, 3.10 ± 1.80, 3.60 ± 1.87, and 2.65 ± 2.39 mm in the combined group, respectively, which was statistically significant in both groups using paired t test ($P < .001$). However, the difference between two groups analyzed by two-sample t test was not statistically significant ($P > .05$). Amount of new bone generation, remained particles, and connective tissue was not statistically different between two groups ($P = .367$, $P = .428$, and $P = .598$, respectively). **Conclusion:** Based on the results of this study, corticocancellous FDBA granules along with collagen membrane can successfully be used for horizontal augmentation of edentulous ridge, and adding AB to the granules of FDBA does not significantly increase the quality and quantity of regenerated bone.

13. Horizontal ridge augmentation using native collagen membrane vs titanium mesh in atrophic maxillary ridges: Randomized clinical trial

Atef M, Tarek A, Shaheen M, Alarawi RM, Askar N. Clin Implant Dent Relat Res. 2020 Apr;22(2):156-166. doi: 10.1111/cid.12892.

https://pubmed.ncbi.nlm.nih.gov/32185856/

Background: Several techniques have been proposed to reconstruct deficient alveolar ridges including bone blocks, ridge splitting and guided bone regeneration (GBR). GBR has been successfully established in restoring horizontal bone deficiency. However, yet still there is a debate regarding the ideal barrier for GBR. Purpose: To evaluate the quantity and the quality of the bone gained using collagen membrane with 1:1 mixture of autogenous and anoraganic bovine bone mineral compared to titanium mesh with the same mixture of bone for GBR of horizontally deficient maxillary ridges. **Materials and methods:** Two different grafting techniques were evaluated, 10 patients receiving GBR using native collagen membrane using 1:1 autogenous and anorganic bovine bone mineral (ABBM) bone mixture, and 10 patients receiving GBR using titanium mesh with same mixture of bone. **Results:** Statistical analysis showed a significant increase in alveolar bone width in both techniques with a mean bone gain of 4.0 mm for Collagen group and 3.7 mm for titanium mesh group. Bone area percent was almost 28% for both groups. For Ti-mesh group, six sites soft tissue healing was uneventfully with no signs of wound dehiscence. However, four cases showed mesh exposure first 3 patients showed this exposure 3 weeks postoperatively while the fourth patient showed exposure 4 months postoperatively. The mean graft resorption in the Collagen and mesh group 6 months postoperative was considered nonsignificant. **Conclusions:** GBR with both collagen membrane and titanium mesh using a 1:1 mixture of autogenous and ABBM is a viable technique for horizontal augmentation of deficient maxillary alveolar ridges. Titanium mesh is a more technique sensitive compared to collagen membrane. Soft tissue dehiscence and difficulty during second stage removal should limit its use in augmentation of horizontally deficient maxillary ridges.

14. Alveolar ridge preservation in the esthesic zone: predictable decisions in a severly affected site.

Oddo P, Klein C, Contreras A. Int. j interdiscip. dent. 2020 Apr;13(1):30-34. doi: 10.4067/S2452-55882020000100030.

https://scielo.conicyt.cl/scielo.php?script=sci_abstract&pid=S2452-55882020000100030&lng=es&nrm=iso&tlng=en

Introduction: The specific assessment of a severely compromised sites involves: the consideration of healing time according to the different kinds of tissues involved and the knowledge of the evidence available concerning biomaterials and surgical techniques. **Material and methods:** Female patient attends the postgraduate school of periodontics, UDD University in Santiago de Chile, because of pain and chronic infection compromising tooth 2.1. At clinical evaluation, the site has an extensive defect, with active fistula that compromises the buccal and palatal bone plates. The treatment consisted of

exodontia and guided bone regeneration, implantation six months after initial exodontia and abutment connection surgery seven months after implant insertion. **Results:** the treatment of combined defects associated with a long-standing infectious process can be very predictable and successful, only if the measures of time and tissue handling are considered and applied.

15. The effect of different types of attachment system in implant assisted over denture on rate of resorption of grafted anterior mandible (prospective clinical study)

Nawar N, Sleem H. Egypt. J. Oral Maxillofac. Surg. 2020 Apr;11(2), 36-43. doi : 10.21608/OMX.2020.29369.1063.

https://omx.journals.ekb.eg/article_159905_20843.html

Purpose: Mandibular implant assisted overdentures have been considered as satisfactory treatment plan of mandibular edentulism and might be hindered by limited bone height and or width in interforaminal region which necessitate implementation of bone grafts. However, bone graft resorption is expected after loading where the design of retention system could influence resorption rate. So the objective of this study is to assess the effect of using retention sil versus PEEK matrix as a retention system of overdenture on supporting bone of augmented anterior mandible. **Material and Methods:** Fourteen patients were randomly assigned into two groups after being subjected to anterior mandibular bone grafting and implant insertion., for group I patients. Implants were loaded by mandibular overdentures using the OLS attachments system (PEEK female) and for group II implants were loaded using silicone matrix (Retention Sil 400) over the locator abutments with its dual retention mechanism. Implant stability was assessed using (osstell). Peri-implant bone loss was radiographically assessed after loading (at 6 months and 1 year intervals). **Results:** There was no significant increase in implant stability between the two groups. However, group II presents significantly lower bone loss one year after loading ($p \leq 0.01$) than group I. **Conclusion:** It could be concluded that resilient matrix (retention sil) for locator attachment induce less bone resorption than peek matrix in anterior grafted mandibular bone.

16. Tomographic Assessment on the Influence of the Use of a Collagen Membrane on Dimensional Variations to Protect the Antrostomy After Maxillary Sinus Floor Augmentation: A Randomized Clinical Trial

Imai H, Lang NP, Ferri M, Hirota A, Apaza Alccayhuaman KA, Botticelli D. Int J Oral Maxillofac Implants. 2020 Mar/Apr;35(2):350-356. doi: 10.11607/jomi.7843.

https://pubmed.ncbi.nlm.nih.gov/32142572/

Purpose: To evaluate the dimensional variations after elevation of the maxillary sinus floor and the healing of the antrostomy left unprotected or protected by a collagen membrane. **Materials and methods:** Twenty patients were included in the study. After the elevation of the sinus mucosa, natural bovine bone was grafted into the elevated space. In 10 randomly selected patients, a native collagen membrane made of porcine corium was placed on the antrostomy (membrane group). In the other 10 patients, the antrostomy was left uncovered (no-membrane group). Cone beam computed tomography (CBCT) images were taken for all patients before surgery (T0), 1 week after sinus floor augmentation (T1), and after 9 months of healing (T2), and evaluations of dimensional variations over time of soft and hard tissues were performed. **Results:** At T1, the elevation of the sinus floor in the middle aspect was 12.5 ± 3.8 mm and 11.9 ± 3.6 mm in the membrane and no-membrane groups, respectively. At T2, the reduction in height of the elevated space was 0.6 ± 0.9 mm and 0.8 ± 0.8 mm in the membrane and no-membrane groups, respectively. The elevated area decreased between ~10% and 11% in the membrane group and between ~15% to 20% in the no-membrane group. However, no statistically significant differences were found. **Conclusion:** The use of a collagen membrane to cover the antrostomy after sinus floor elevation did not produce significant clinical effects on dimensional variations over time.

17. Customized allogeneic bone grafts for maxillary horizontal augmentation: A 5-year follow-up radiographic and histologic evaluation

Kloss FR, Offermanns V, Donkiewicz P, Kloss-Brandstätter A. Clin Case Rep. 2020 Mar;8(5):886-893. doi: 10.1002/ccr3.2777.

https://pubmed.ncbi.nlm.nih.gov/31969253/

The use of cold atmospheric pressure plasma (CAPP) as a bacterial decontaminant for chronic wounds has shown good results. The purpose of this *in vitro* study was to evaluate the bactericidal effects of CAPP on the cancellous area of the bone. Sterile glass slides and processed sterile human bone allografts 1, 2, 3, and 4mm thick were used for initial contamination and further CAPP treatment. Each block was contaminated with Staphylococcus aureus suspension on one side. Each slide was turned 180° and treated on the reverse side. The bacterial count in colony-forming units (CFU) was then measured and compared with that of a control group, and the bactericidal effects of CAPP in relation to bone density evaluated. A significant reduction in count was measured between treated and untreated groups (groups A-D: $p<0.01$ and group E: $p=0.04$). A strong positive linear relation was found between bone density and the S aureus count ($r=0.844$, $p=0.156$). Treatment with CAPP had a bactericidal effect on bone structures with a penetration depth of up to 4mm. It might be used for all diseases involving infected bone, and so extends the existing range of treatments.

18. Interantral alveolar ridge splitting for maxillary horizontal expansion and simultaneous dental implant insertion: A case report.

Berger S, Hakl P, Sutter W, Meier M, Roland H, Bandura P, Turhani D. Ann Med Surg (Lond). 2019; 48:83-87.

https://www.ncbi.nlm.nih.gov/pubmed/31737265

Tooth loss caused by caries, periodontal disease or systemic factors often results in a decline of the bucco-lingual alveolar ridge dimension. Within one year the initial bone width can be resorbed up to 50%. As a consequence dental implants may be limited for rehabilitation and cannot be performed in a conventional manner because of the risk of dehiscence and fenestrations. **Case presentation:** Presentation of a 51-year old female patient, who has had a full denture for about 30 years. The reason for consultation was the demand for a fixed prosthesis. Dental implants in combination of the ARST with GBR allowed us to correct horizontal deformities of the alveolar ridge. **Discussion:** We discuss the possibility of using the ARST in the interantral region for a full arch rehabilitation of the maxilla with simultaneous dental implant placement in a narrow alveolar ridge. **Conclusion:** The ARST in addition to simultaneous implant placement with a GBR can be successfully used for a full arch rehabilitation of the maxilla in a narrow alveolar ridge.

19. Multidisciplinary oral rehabilitation of an adolescent suffering from juvenile Gorlin-Goltz syndrome - a case report.

Nilius M, Kohlhase J, Lorenzen J, Lauer G, Schulz MC. 2019. Head Face Med;15(1):5.

https://www.ncbi.nlm.nih.gov/pubmed/30736811

The Gorlin-Goltz syndrome is an autosomal dominant disorder characterized by keratocystic odontogenic tumors in the jaws, multiple basal cell carcinomas and skeletal abnormities. Frequently, the manifestation of the syndrome occurs in the adolescent years. **CASE PRESENTATION:** An 11-year-old boy was referred to our clinic due to the persistence of the lower deciduous molars. The further diagnosis revealed bilateral keratocystic odontogenic tumors in the region of teeth 33 and 45 representing a symptom of a Gorlin-Goltz syndrome. This case of the oral rehabilitation of an adolescent with bilateral keratocystic odontogenic tumors shows the approach of a multidisciplinary treatment concept including the following elements: Enucleation and bone defect augmentation using a prefabricated bone graft; distraction osteogenesis to extend the graft-block vertically after cessation of growth; accompanying orthodontic treatment, guided implant placement and prosthetic rehabilitation. Six months after implant insertion, a new keratocystic odontogenic tumor in the basal part of the left sinus maxillaris had to be removed combined with the closure of the oroantral fistula. During the follow-up period of 18 months in semi-annual intervals, the patient showed no sign of

pathology. **CONCLUSION:** In the presented case could be shown that distraction osteogenesis of prefabricated bone blocks is possible. With a multidisciplinary approach in a long-term treatment, a sufficient oral rehabilitation of the patient suffering from extended keratocystic odontogenic tumors was possible.

20. Bilateral maxillary augmentation using CAD/CAM manufactured allogenic bone blocks for restoration of congenitally missing teeth: A case report.

Blume O, Donkiewicz P, Back M1, Born T. 2019. J Esthet Restor Dent.;31(3):171-178.

https://www.ncbi.nlm.nih.gov/pubmed/30756449

OBJECTIVE: Various biomaterials have been successfully applied in alveolar bone regeneration, however, the reconstruction of extensive osseous defects remains challenging and is often unfeasible with granular grafting materials. Several studies have outlined allogenic bone blocks as valid alternative to autologous block grafting. **CLINICAL CONSIDERATIONS:** In this report, we demonstrate the regeneration of two large osseous defects in the maxilla with allogenic bone blocks made from human donor bone. The bone blocks were customized using the CAD/CAM technology in order to enable the insertion of four dental implants. Both grafted areas were covered with a resorbable collagen membrane (Jason® membrane). **CONCLUSIONS:** Both blocks perfectly matched the defect geometry, showed limited resorption, led to the formation of sufficient amounts of mineralized bone in both horizontal and vertical dimensions and enabled the installation of implants according to the treatment plan. The implementation of innovative technologies for individualization of allogenic bone blocks simplifies the restoration of complex and extensive osseous defects and poses great benefits for both practitioners and patients. **CLINICAL SIGNIFICANCE:** The here presented procedure demonstrates the successful regeneration of two extensive osseous defects in a patient suffering from hypodontia using two CAD/CAM manufactured allogenic bone blocks, rendering the procedure far less invasive as compared to guided bone regeneration carried out with autologous transplants. Furthermore, to the best of our knowledge, this is the first case report that radiographically demonstrates the new formation of a cortical bone layer following block grafting with solely cancellous bone blocks.

21. Comparison of allogeneic and autogenous bone grafts for augmentation of alveolar ridge defects - a 12-month retrospective radiographic evaluation.

Kloss FR, Offermanns V, Kloss-Brandstätter A. Clin Oral Impl Res. 2018; 29:1163–1175.

https://www.ncbi.nlm.nih.gov/pubmed/30303581

OBJECTIVES: The aim of this study was to compare three-dimensional alterations following the use of autogenous versus allogeneic onlay grafts for augmentation at single tooth defects. **MATERIALS AND METHODS:** Alveolar bone width at specific implant sites was assessed using sagittal and cross-

sectional CBCT images prior grafting and at three subsequent time points. 21 patients received autogenous bone blocks harvested from the retromolar region and another 21 patients received freeze-dried cancellous allogeneic bone blocks covered with Jason® membrane. **RESULTS:** The vertical and horizontal dimensions did not significantly differ between autogenous and allogeneic bone grafts at any time point. In addition, there were no statistically significant differences in graft remodeling rates between autogenous (mean shrinkage rate after 12 months: 12.5 ± 7.8 %) and allogeneic onlay grafts (mean shrinkage rate after 12 months: 14.4 ± 9.8 %). **CONCLUSIONS:** Freeze-dried cancellous allogeneic bone blocks showed equivalent volumetric shrinkage rates as autogenous bone blocks when used for treating circumscribed bone defects classified as Type-II to Type-IV according to the ITI-treatment guide categories. Therefore, it is not necessary to over-contour the alveolar ridge when using allogeneic blocks for treating single tooth defects, but to apply the same procedure as when using autogenous blocks.

22. Sinus Floor Elevation Using the Lateral Approach and Window Repositioning and a Xenogeneic Bone Substitute as a Grafting Material: A Histologic, Histomorphometric, and Radiographic Analysis.

Tawil G, Barbeck M, Unger R, Tawil P, Witte F. 2018. Int J Oral Maxillofac Implants.; 33(5):1089–1096.

https://www.ncbi.nlm.nih.gov/pubmed/29894551

PURPOSE: Sinus floor elevation using the lateral approach and bone window repositioning and a xenogeneic bone substitute (cerabone®) has been well documented clinically. The purpose of this histologic and histomorphometric study was to determine the fate of the window, its contributing role in the healing process, and the osseoconductivity and resorption potential of the high-temperature sintered bovine bone used, as well as to correlate the histomorphometric results with sinus depth and lateral wall thickness as determined on cone beam computed tomography (CBCT).
MATERIALS AND METHODS: Thirty biopsy specimens were harvested from the lateral side of the maxilla of patients operated on for sinus floor elevation and implant placement at two postoperative periods: early, group 1 (mean: 5.73 ± 0.44 months); and late, group 2 (mean: 8.68 ± 1.76 months). Sinus depth and lateral wall thickness were determined on CBCT and correlated to graft maturation.
RESULTS: The repositioned bone window was microscopically detectable in both study groups and looked well integrated. Bone was found growing out of the repositioned window toward the center of the graft, most often forming a trabecular network independently from the bone matrix, which is in favor of osteogenic potential of the window. Also, newly built bone was found directly attached to the surfaces of the window, indicating bone growth via osseoconduction. Repositioned window sides showed signs of low-grade inflammation. Active osteoclasts were only found to be associated with the newly built bone matrix, hinting at an active bone remodeling process. No signs of biodegradation or remodeling of the window were detected using the tartrate-resistant acid phosphatase (TRAP) technique. The histomorphometric analysis of the tissue distribution showed similar values of newly formed bone in group 1 (22.77% ± 5.89%) and in group 2 (26.15% ± 11.18%) and connective tissue

values in both study groups (42.29% ± 8.98% for group 1 vs 46.03% ± 5.84% for group 2). No significant differences were found between group 1 (34.94% ± 7.10%) and group 2 (27.82% ± 11.97%) for xenogeneic bone substitute values. Statistically significant differences were only found between connective tissue values and newly built bone values (P < .01 and P < .001, respectively). Furthermore, a significant difference was found between connective tissue values and that of bone substitute up to 12 months (P < .01). No significant correlation was found between sinus depth and lateral window thickness and histomorphometric results. **CONCLUSION:** The repositioned window technique appears to be a good osteoconductive barrier for bone formation. Its osteogenic potential needs to be confirmed immunochemically. High-temperature sintered bovine bone proved to be an effective slowly resorbing osseoconductive material.

23. A preliminary randomized clinical trial comparing diode laser and scalpel periosteal incision during implant surgery: impact on postoperative morbidity and implant survival.

Shahnaz A, Jamali R, Mohammadi F, Khorsand A, Moslemi N, Fekrazad R. Lasers Med Sci. 2018; 33(1):19-25.[Epub 2017].

https://www.ncbi.nlm.nih.gov/pubmed/28861729

The aim of this preliminary randomized clinical trial was to compare: (1) post-operative morbidity after application of laser or scalpel incision for flap advancement during implant surgery and bone grafting and (2) implant survival rate following flap advancement with laser or scalpel incision after 6 months of loading. **MATERIAL AND METHODS:** Eighteen patients who were scheduled for dental implant placement and simultaneous bone grafting were randomly assigned to test or control groups. Diode laser (810 nm, 2W, pulse interval 200 µs; pulse length 100µs, 400-µm initiated fiber tip), or scalpel (control) was used to sever the periosteum to create a tension-free flap. Visual analogue scale (VAS) pain score, rate of nonsteroidal anti-inflammatory drug (NSAID) consumption, intensity of swelling, and ecchymosis were measured for the six postsurgical days. **RESULTS:** Six months after loading, implant survival was assessed. VAS pain score (during the first four postoperative days), rate of NSAID consumption (during the first three postoperative days), and intensity of swelling (during the first five postoperative days) were significantly lower in the test group compared to the control group (All P values < 0.05). One patient in the control group experienced ecchymosis. All implants were successful in function. Application of laser for performing periosteal releasing incision reduced the incidence and severity of postoperative morbidity of the patients undergone implant surgery in conjunction with bone augmentation procedure. **CONCLUSION:** We did not find any detrimental effect of laser incision on the implant survival within 6 months of loading.

*Study refers to Bone protect membrane, which is a private label of Jason® membrane.

24. Mandibular Torus Harvesting for Sinus Augmentation: Two-Year Follow-Up.

Karaca, I.R., Ozturk, D.N. & Akinci, H.O. J. 2019. Maxillofac. Oral Surg. 18(1):61-64. [Epub 2018].

https://link.springer.com/article/10.1007/s12663-018-1135-y

Maxillary sinus grafting is a commonly used treatment alternative in cases with insufficient bone height to enable insertion of implants in the posterior maxilla. It is commonly carried out with autogenous grafts, biomaterials or both. Autogenous bone grafts are considered gold standard for this procedure; however, due to donor site morbidity, it is not as commonly used as other biomaterials. Mandibular tori are hyperostoses on the lingual side of the mandible in the premolar region. This a case in which mandibular tori were used for a sinus augmentation procedure. The patient was then followed up for 2 years with no complaints, or objective symptoms.

25. A modification to Schneiderian membrane perforation repair technique: The Hammock Approach.

Cuadrado-González L, Jiménez-Garrudo A, Brizuela-Velasco A, Pérez-Pevida E, Chávarri-Prado D, Diéguez-Pereira M, Pacho-Martínez JM. 2018. J Oral Implantol. [Epub ahead of print].

https://www.ncbi.nlm.nih.gov/pubmed/29608401

Schneiderian membrane perforation is one of the most common intra-surgical complications occurring during maxillary sinus elevation procedures. The management of these perforations is essential to accurate treatment prognosis. Several techniques have been shown to repair sinus membrane perforation using different materials such as connective tissue, fat pads, and resorbable collagen membranes. This short communication presents a modification to the classical sinus perforation repair technique using a resorbable collagen membrane (Jason® membrane). The hammock approach is based on enhancing the stabilization of the collagen membrane by suturing the membrane to both the buccal and palate plates with double perforations.

26. Lateral Ramus Cortical Bone Plate in Alveolar Cleft Osteoplasty with Concomitant Use of Buccal Fat Pad Derived Cells and Autogenous Bone: Phase I Clinical Trial.

Khojasteh A, Kheiri L, Behnia H, Tehranchi A, Nazeman P, Nadjmi N, and Soleimani M. 2017. Biomed Res Int.; 2017:6560234.

https://www.ncbi.nlm.nih.gov/pubmed/29379800

Tissue regeneration has become a promising treatment for craniomaxillofacial bone defects such as alveolar clefts. This study sought to assess the efficacy of lateral ramus cortical plate with buccal fat pad derived mesenchymal stem cells (BFSCs) in treatment of human alveolar cleft defects. **MATERIAL AND METHODS:** Ten patients with unilateral anterior maxillary cleft met the inclusion criteria and were assigned to three treatment groups. First group was treated with anterior iliac crest (AIC) bone and a collagen membrane (AIC group), the second group was treated with lateral ramus cortical bone

plate (LRCP) with BFSCs mounted on a natural bovine bone mineral (LRCP+BFSC), and the third group was treated with AIC bone, BFSCs cultured on natural bovine bone mineral, and a collagen membrane (AIC+BFSC). The amount of regenerated bone was measured using cone beam computed tomography 6 months postoperatively. **RESULTS:** AIC group showed the least amount of new bone formation (%). LRCP+BFSC group demonstrated defect closure and higher amounts of new bone formation (%) but less than AIC+BFSC (%), suggesting that use of BFSCs within LRCP cage and AIC may enhance bone regeneration in alveolar cleft bone defects; however, the differences were not statistically significant.

27. Monophasic ß-TCP vs. biphasic HA/ß-TCP in two-stage sinus floor augmentation procedures - a prospective randomized clinical trial.

Jelusic D, Zirk ML, Fienitz T, Plancak D, Puhar I, Rothamel D. 2016. Clin Oral Implants Res.; 28(10):e175-e183.

https://www.ncbi.nlm.nih.gov/pubmed/27683073

Comparison of a monophasic (100% ß-TCP) and a biphasic (60% HA and 40% ß-TCP) bone substitute material (BSM) regarding biocompatibility, osteoconductivity and implant stability using histological, radiological and resonance frequency analysis. **MATERIAL AND METHODS:** Sixty-seven sinus floor elevations were performed in 60 patients. One patient group (monophasic bone substitute [MBS], 30 patients, 32 sinuses) was augmented by the use of the monophasic material (Bioresorb®, Sybron Implant Solutions, Bremen, Germany), while the second group (biphasic bone substitute (BBS), 30 patients, 35 sinuses) received a biphasic material (maxresorb®, Botiss Biomaterials, Berlin, Germany). Cone beam CT images were taken immediately after augmentation and prior to implant placement after 6 months. Trephines were harvested, while the implant bed was prepared. Resonance frequency analysis was performed immediately after implant placement and 6 months later. Descriptive analysis was performed on all augmented sinus (n = 67). For statistical comparison of the groups, one sinus of each bilaterally treated patient was randomly excluded, resulting in 30 sinuses grafted with MBS and 30 sinuses grafted with BBS (n = 60). **RESULTS:** Histomorphometrical analysis of all sinuses displayed comparable results for both groups regarding new bone matrix (MBS 36.16 ± 19.37%, BBS 38.42 ± 12.61%), residual BSM (MBS 30.26 ± 11.7%, BBS 32.66 ± 12.57%) and non-mineralized tissue (MBS 34.29 ± 18.32%, BBS 28.92 ± 15.04) %) ($P > 0.05$, respectively). Radiological volume of BBS was significantly more stable (volume loss of 22.2% for MBS, 6.66% for BBS; $P < 0.001$), and homogeneity of the graft after 6 months was higher for BBS than that for MBS ($P < 0.05$). Resonance frequency analysis endorsed a higher implant stability quotient for BBS after 6 months than that for MBS (MBS 78.31 ± 5.81, BBS 80.42 ± 6.31; $P < 0.05$, Mann-Whitney U-test, respectively). **CONCLUSION:** Both monophasic and biphasic materials show good biocompatibility and osteoconductivity with satisfactory support on implant stability. BBS remains more stable in terms of volume maintenance and radiological graft homogeneity after a healing period of 6 months.

28. Sinus Floor Elevation Using the Lateral Approach and Bone Window Repositioning I: Clinical and Radiographic Results in 102 Consecutively Treated Patients Followed from 1 to 5 Years.

Tawil G, Tawil P, Khairallah A. 2016. Int J Oral Maxillofac Implants.; 31(4):827-34.

https://www.ncbi.nlm.nih.gov/pubmed/27447149

The study determines potential complications and clinical outcomes using the lateral sinus elevation technique with window repositioning. **MATERIALS AND METHODS**: One hundred nine sinus elevations were performed on 102 consecutively treated patients. Following lateral window outward fracturing, sinus mucosa was elevated, and the sinus was grafted with anorganic bovine bone. Two hundred five implants were placed: 160 concomitantly with grafting, and 45 six months after grafting. Seventeen implants replaced single missing molars. One hundred eighty-eight implants replaced multiple missing posterior teeth. The bone window was repositioned over the osteotomy site and the flap sutured. Implants were connected at 6 months and followed up from 12 to 60 months (mean: 29.8 months). In 30 cases, biopsy specimens were harvested from the lateral wall of the sinus for histomorphometric analysis. The Fisher exact test and Kruskal-Wallis test followed by the Mann-Whitney test were used for statistical analysis. **RESULTS:** No clinically significant complications were encountered in using this technique (mucosa tear, intraoperative bleeding, window sequestration). In three cases, the window was separated in two before outfracturing. In 20 cases, it was stabilized with a collagen fleece. Limited sinus mucosa tears occurred in 14 cases during elevation. They were patched with a collagen membrane, and 18 implants were placed in these cases. All of the latter cases osseointegrated at abutment connection with no statistically significant difference in the outcome compared with implants placed with no tear of the membrane ($P < .05$). The reconstruction of the lateral wall was confirmed in all cases. No significant differences in outcomes were found between the immediately and delayed placed implants ($P < .05$). One implant failed in the immediately placed group due to a sinus infection. All other implants were loaded and remained in function during the observation period. **CONCLUSION:** Lateral sinus elevation with window repositioning is safe and effective with minimal risks, such as mucosal tear, intraoperative bleeding, or window sequestration. The repositioned window can serve as an alternative for collagen membrane in containing the graft. Graft maturation, percent of vital bone formation, and the potential of the window to serve as a source of osteogenic cells need to be confirmed histomorphometrically.

29. Histological and radiological evaluation of sintered and non-sintered deproteinized bovine bone substitute materials in sinus augmentation procedures. A prospective, randomized-controlled, clinical multicenter study.

Fienitz T, Moses O, Klemm C, Happe A, Ferrari D, Kreppel M, Ormianer Z, Gal M, Rothamel D. 2017. Clin Oral Investig.; 21(3):787-794. Epub 2016.

http://www.ncbi.nlm.nih.gov/pubmed/27129584

The objective of this study is to compare histologically and radiologically a sintered and a non-sintered bovine bone substitute material in sinus augmentation procedures. **MATERIALS AND METHODS:** Thirty-three patients were included in the clinically controlled randomized multicentre study resulting in a total of 44 treated sinuses. After lateral approach, sinuses were filled with either a sintered (SBM, Alpha Bio's Graft®) or a non-sintered (NSBM, Bio Oss®) deproteinized bovine bone substitute material. The augmentation sites were radiologically assessed before and immediately after the augmentation procedure as well as prior to implant placement. Bone trephine biopsies for histological analysis were harvested 6 months after augmentation whilst preparing the osteotomies for implant placement. **RESULTS:** Healing was uneventful in all patients. After 6 months, radiological evaluation of 43 sinuses revealed a residual augmentation height of 94.65 % (±2.74) for SBM and 95.76 % (±2.15) for NSBM. One patient left the study for personal reasons. Histological analysis revealed a percentage of new bone of 29.71 % (±13.67) for SBM and 30.57 % (±16.07) for NSBM. Residual bone substitute material averaged at 40.68 % (±16.32) for SBM compared to 43.43 % (±19.07) for NSBM. All differences between the groups were not statistically significant ($p > 0.05$, Student's t test). **CONCLUSION:** Both xenogeneic bone substitute materials showed comparable results regarding new bone formation and radiological height changes in external sinus grafting procedures. **CLINICAL RELEVANCE:** Both bone substitute materials allow for a predictable new bone formation following sinus augmentation procedures.

*Study refers to Alpha Bio's collagen membrane, which was a former private label of Jason® membrane.

30. Successful treatment of a large implant periapical lesion that caused paraesthesia and perimandibular abscess.

Jafarian M, Rayati F, Najafi E. Dent Res J 2016; 13: 188-92.

https://www.ncbi.nlm.nih.gov/pubmed/27076835

Presentation of a successful treatment of a large implant periapical lesion (IPL) that caused paraesthesia and perimandibular abscess. IPL is a pathologic phenomenon that rarely involves implants. This event first described in 1992 with an incidence rate of 0.26-9.9% and the origin is not well known. The most likely suggested causes are presence of preexisting bone pathology, contamination of implant surface, bone overheating during implant surgery, vascular ischemia, excessive tightening of the implant, fenestration of the buccal plate and different implant surface designs. In the present case report, we describe relatively large periapical lesions involving several implants caused severe abscess accompanied by transient inferior alveolar nerve paraesthesia and its successful management. A brief review of the literature and a discussion of possible causes and different treatment plans are also included.

31. Histological and histomorphometric study using an ultrasonic crestal sinus grafting procedure. A multicenter case study.

Wainwright, M., Torres-Lagares, D., Pérez-Dorao, B., Serrera-Figallo, M.A., Gutierrez-Perez, J.L., Troedhan, A., Kurrek, A. Med Oral Patol Oral Cir Bucal.2016; 21(3):e367-73.

https://www.ncbi.nlm.nih.gov/pubmed/26946203

The aim of this study was to evaluate the efficacy of a hydrodynamic ultrasonic driven transcrestal sinus grafting procedure (Intralift®, Acteon Company, Bordeaux, France) and the use of a bovine high temperature sintered grafting material in sinus sites with less than 5 mm remaining bone height with no additional autogenous bone in order to create a sufficient recipient site for implants. **MATERIAL and METHODS:** 12 patients (16 sinus) in this multicenter case study were included. Using a crestal approach, bone under the sinus was prepared with ultrasonic tips until the Schneiderian membrane was reached. With a trumpet shaped instrument, the Schneiderian membrane was elevated. In the new created subantral space a high temperature sintered bovine grafting material was introduced (Bego Oss, BEGO Implant Systems GmbH & Co. KG, Bremen, Germany). After 6 months biopsies were taken with a trephine bur and histologies were generated following histomorphometric analysis. **RESULTS:** The results showed new vital bone in average of 33.4% ± 17.05%, and 43.6% ± 16.70 of bone substitute material. No signs of abnormal inflammation were observed. **CONCLUSIONS:** This procedure (Intralift®) allows, using a bovine material with no additional autogenous bone, new bone formation in the sinus in order to allow place implant subantraly.
*Study refers to BEGO collagen membrane, which is a private label of Jason® membrane.

32. Application of buccal fat pad-derived stem cells in combination with autogenous iliac bone graft in the treatment of maxillomandibular atrophy: a preliminary human study.

Khojasteh A, Sadeghi N. Int J Oral Maxillofac Surg. 2016; 45(7):864-71.

https://www.ncbi.nlm.nih.gov/pubmed/26846793

Stem cell therapy for the treatment of bone defects is an alternative or adjunct to autologous bone grafting. This study assessed the efficacy of buccal fat pad-derived stem cells (BFPSCs) with iliac bone block grafting for the treatment of extensive human alveolar ridge defects. **MATERIAL AND METHODS:** Eight patients with extensive jaw atrophy were selected for this study. The jaws were reconstructed with non-vascularized anterior iliac crest bone blocks. Gaps between the blocks were filled with freeze-dried bone granules and covered with a collagen membrane. In the test group (n=4), these granules were seeded with BFPSCs. Cone beam computed tomography scans were used to assess the amount of new bone formed at six sites in each patient. Trephine biopsies of 2-mm were

also taken from the graft site during implant placement for histomorphometric analysis. **Results:** The mean bone width change at the graft site was greater in the test group than in the control group (3.94±1.62mm vs. 3.01±0.89mm). New bone formation was 65.32% in the test group versus 49.21% in the control group. **CONCLUSION:** The application of BFPSCs in conjunction with iliac bone block grafts may increase the amount of new bone formation and decrease secondary bone resorption in extensively atrophic jaws.

33. The effect of a platelet-rich fibrin conduit on neurosensory recovery following inferior alveolar nerve lateralization: a preliminary clinical study.

Khojasteh A, Hosseinpour S, Nazeman P, Dehghan MM. 2016. Int J Oral Maxillofac Surg.; 45(10):1303-8.

https://www.ncbi.nlm.nih.gov/pubmed/27371997

This retrospective study aimed to assess the recovery of neurosensory dysfunction following modified inferior alveolar nerve (IAN) lateralization surgery compared to the conventional approach. **MATERIAL AND METHODS:** Data from two groups of patients who underwent IAN lateralization in 2014 were included in this study. In one group, platelet-rich fibrin was placed over the IAN and this was protected with a collagen membrane conduit; the other group underwent the conventional IAN lateralization procedure. Implants were placed immediately. Neurosensory dysfunction was evaluated at 3, 6, and 12 months post-surgery. Demographic, neurosensory disturbance (NSD), subjective two-point discrimination test (TPD), and static light touch test (SLT) data were obtained. **RESULTS:** Twenty-three IAN lateralization procedures with the placement of 51 implants were performed in 14 patients. At the 6-month follow-up, the number of patients experiencing normal sensation was greater in the modified surgery group, but the 12-month follow-up results were the same in the two groups. More precise sensation was observed with the TPD in the modified group at 6 months, and the modified group demonstrated better SLT scores at 6 months. **CONCLUSION:** Although the two groups had comparable results at the 12-month follow-up, it was observed that the modified technique accelerated neural healing within 6 months and reduced the length of the discomfort period.

34. Comparison of the rates of bone regeneration of in sinus lift grafting with a calcium phosphate paste between the 6th and the 9th month - a clinical case.

Papanchev G , Georgiev T, Peev S, Arnautska H, Zgurova N, Borisova-Papancheva T, Dzhongova E. 2015. Scripta Scientifica Medicinae Dentalis; 1(1): 41-49.

http://press.mu-varna.bg/ojs/index.php/ssmd/article/view/635

Maxillary sinus floor augmentation has been used for occlusal rehabilitation with prosthetic appliances installed over dental implants in the posterior maxilla despite the fact that this region often

presents loss of alveolar bone and increased maxillary sinus pneumatization, particularly when all of the molars are absent. The shortage and quality of the remaining bone often implies a challenge when rehabilitating with dental implants. Different kinds of grafts have been used in an endeavor to solve these problems. The aim of this study is to find out if there is a significant difference in the bone formation between the 6th and the 9th month periods after sinus lift grafting with a calcium phosphate paste (maxresorb®inj., botiss dental, Berlin, Germany). For this purpose a bilateral sinus lift has been made by own methodology. Results showed no significant difference in the percentage of newly formed bone in the six and the ninth month, which warrants the dental implants to be placed on the six-month post-sinus lifting.

35. Membranes and Bone Substitutes in a One-Stage Procedure for Horizontal Bone Augmentation: A Histologic Double-Blind Parallel Randomized Controlled Trial.

Merli M, Moscatelli M, Mariotti G, Pagliaro U, Breschi L, Mazzoni A, Nieri M. 2015. Int J Periodontics Restorative Dent.; 35(4):463-71.

http://www.ncbi.nlm.nih.gov/pubmed/26133135

The aim of this histologic, double-blind, parallel, randomized controlled trial was to compare anorganic bone mineral-collagen membranes (BB) and betatricalcium phosphate-pericardium collagen membranes (CJ) in a one-stage procedure for horizontal bone augmentation. A biopsy was performed in the regenerated area at abutment connection 6 months after surgery. Five patients were assigned and treated with the BB combination and five patients were treated with the CJ combination. At abutment connection, 6 months after grafting, no significant differences were evident in the histomorphometric comparisons, even if the percentage of residual graft, using the marrow spaces and soft tissue as a reference, tended to be greater in the CJ group (P = .0759).

36. Comparing membranes and bone substitutes in a one-stage procedure for horizontal bone augmentation. A double-blind randomized controlled trial.

Merli M, Moscatelli M, Mariotti G, Pagliaro U, Raffaelli E, Nieri M., Eur J Oral Implantol. 2015; 8(3):271-81.

http://www.ncbi.nlm.nih.gov/pubmed/26355171

The objective of this parallel randomized controlled trial is to compare two bone substitutes and collagen membranes in a one-stage procedure for horizontal bone augmentation: anorganic bovine bone (Bio-Oss) and collagen porcine membranes (Bio-Gide) (BB group) versus a synthetic resorbable bone graft substitute made of pure β-tricalcium phosphate (Ceros TCP) and porcine pericardium collagen membranes (Jason® membrane) (CJ group). **MATERIAL AND METHODS:** Patients in need of implant treatment having at least one site with horizontal osseous defects at a private clinic in Rimini

(Italy) were included in this study. Patients were randomized to receive either the BB or CJ treatment. Randomization was computer-generated with allocation concealment by opaque sequentially numbered sealed envelopes. Patients and the outcome assessor were blinded to group assignment. The main outcome measures were implant failure, complications, clinical bone gain at augmented sites, and complete filling of the bone defect. Secondary outcome measures were chair-time, postoperative pain and peri-implant marginal bone level changes. **RESULTS:** Twenty-five patients with 32 implants were allocated to the BB group and 25 patients with 29 implants to the CJ group. All 50 randomized patients received the treatment as allocated and there were no dropouts up to 6-months post-loading (12 months post-surgery). There were no failures and there were three complications in the BB group and three complications in the CJ group (relative risk: 1.00, 95% CI from 0.22 to 4.49, P = 1.00). The estimated difference between treatments in the vertical defect bone gain was -0.15 mm (95% CI from -0.65 to 0.35, P = 0.5504) favoring the BB group, and the estimated difference between treatments in the horizontal defect bone gain was -0.27 mm (95%CI from -0.73 to 0.19, P = 0.3851) favoring the BB group. There was no difference in the complete filling of the defect (relative risk: 0.88, 95%CI from 0.58 to 1.34, P = 0.7688). No significant differences were detected for chair-time (P = 0.3524), for VAS pain immediately after surgery (P = 0.5644), VAS pain after 1 week (P = 0.5074) and VAS pain after 2 weeks (P = 0.6950). A slight difference (0.24 mm, 95%CI from 0.0004 to 0.47, P = 0.0464) was detected in radiographic peri-implant bone loss favoring the CJ group. **CONCLUSIONS:** No significant differences, except for radiographic bone loss, were observed in this randomized controlled trial comparing anorganic bovine bone with collagen porcine membranes versus synthetic resorbable bone made of pure β-tricalcium phosphate with pericardium collagen membranes for horizontal augmentation.

37. Assessment of Implant Stability Following Sinus Lift Procedures with Different Grafting Materials.

Jelušić D, Puhar I, Plancak D. Acta Stomatol Croat. 2014; 48(1): 25–32.

https://www.ncbi.nlm.nih.gov/pubmed/27688348

The objective of this research was to evaluate implant stability following sinus lift with two grafting materials, and to compare it with the results obtained for the implants placed in a pristine posterior maxilla. **MATERIALS AND METHODS:** The study included 44 healthy patients with an existing indication for sinus lift procedure (test group). 46 implants were placed following sinus lift with a pure-phase beta-tricalcium phosphate, while 39 implants were placed following augmentation with 60% hydroxyapatite with 40% beta-tricalcium phosphate material. The control group consisted of 48 healthy patients who were treated with 85 implants but without bone augmentation in posterior maxilla. Astra Tech OsseoSpeed implants were placed in all subjects. Resonance frequency analysis was used in both groups for determining implant stability 4 months after insertion. A mean implant stability quotient (ISQ) was calculated on the basis of 3 measurements. **RESULTS:** No statistical difference was observed in ISQ values of implants placed with and without augmentation procedure

(p=0,789). Statistically significant difference was not found when ISQ values of implants placed following particular grafting material were compared with ISQ values of corresponding implants in a pristine bone (p=0.697 and p=0.402). **CONCLUSIONS:** This study demonstrated that the implant stability is comparable among implants placed in the posterior maxilla regardless of sinus lift and grafting procedure. Implants placed in the grafted posterior maxilla can be predictably loaded as the implants placed in a non-grafted, pristine maxilla.

38. The concept of Screw-Guided Bone Regeneration (S-GBR). Part 3: Fast Screw-Guided Bone Regeneration (FS-GBR) in the severely resorbed pre-implant posterior mandible using allograft and Leukocyte- and Platelet-Rich Fibrin (L-PRF): a 4-year follow-up.

Toeroek R. and Dohan Ehrenfest D. M. 2013. POSEIDO.; 1(2): 93-100.

http://www.poseido.info/publication/volume-1-2013/poseido-20131293-100-toeroe.pdf

In this series of article, we developed and illustrated the concept of Screw-Guided Bone Regeneration (S-GBR), with excellent results in the posterior mandible. In this form of GBR, the barrier between the bone and gingival compartment is supported and protected through the presence of screws, serving both as tent pegs to maintain the regenerative chamber space and as bone growth pillars. Many combinations of bone materials and membranes are possible to get adequate results with various healing times, but the use of Leukocyte- and Platelet-Rich Fibrin (L-PRF) membranes as interposition, healing and maturation material became a common standard for us. L-PRF (Intra-Spin system and Xpression kit, Intra-Lock, Boca-Raton, FL, USA) is an optimized blood clot or membrane, which concentrates most of the platelets and half of the leukocytes of a blood sample.

*Study refers to Bone protect membrane, which is a private label of Jason® membrane.

39. Sinus floor elevation using a sintered, natural bone mineral - A histological case report study.

Rothamel D, Smeets R, Happe A, Fienitz T, Mazor Z, Schwarz F, Zöller J. Zeitschrift für zahnärztliche Implantologie, 2011; 27(1):60.
http://www.online-jdi.com/media/article/2011/1/00365097-4D06-438D-A1E8-AA217B7773F8/003650974D06438DA1E8AA217B7773F8_oa_rothamel_engl_1_original.pdf

The aim of the present study was the histological and c1inical evaluation of the xenogeneic bone substitute material (BEGO OSS, BEGO Implant Systems, Bremen) for the indications one-stage and two-stage sinus floor elevation. **MATERIALS AND METHOD:** Twelve patients were included in the study, undergoing 15 simultaneous or staged sinuslift operations. Data were evaluated clinically and, for two-stage approaches, histologically and histomorphometrically after trephine harvesting during implant bed preparation. **RESULTS:** Healing was uneventful in all cases. All patients showed good hard tissue regeneration of the lateral window of the sinus. Neither resorption nor dislocation of the granular bone

substitute material was observed. Radiologically, good volume stability of the graft was observed. Histologically, bone substitute particles displayed complete osseous integration in newly formed bone matrix. The proportion of newly formed bone within the graft was 25.8-49.6 %, whereas the proportion of remaining bone substitute material varied from 28.6-38.5 %. **CONCLUSION:** It was concluded that BEGO Oss acts as an osteoconductive material to support hard tissue regeneration after sinus floor elevation. Showing excellent volume stability, it is integrated into newly formed bone matrix within a six-month healing period.
*Study refers to BEGO Oss and BEGO collagen membrane, which are private labels of cerabone® and Jason® membrane.

40. Regeneration of Horizontal Bone Defect in Edentulous Maxilla Using the Allogenic Bone-Plate Shell Technique and a Composite Bone Graft-A Case Report.
Kovac Z, Cabov T, Blaskovic M, Morelato L. Medicina (Kaunas). 2023 Mar 2;59(3):494. doi: 10.3390/medicina59030494. PMID: 36984495; PMCID: PMC10053208.

An insufficient volume of the alveolar bone may prevent implants from being placed in the prosthetically optimal position. Complex restoration of bony structures is required to achieve long-term peri-implant bone stability and represents an adequate prosthetic solution. **Background and Objectives:** The shell technique has become a widespread and important method for guided bone regeneration in dentistry. Allogeneic bone materials appear to be the most similar substitution for autogenous bone transplants. However, there are few studies using cortical bone allografts in combination with a mix of autogenous and xenograft materials for the augmentation of horizontal ridge defects. This combination offers the advantage of reduced patient morbidity while adding adequate volume and contour to the alveolar ridge. **Case report:** The present case study aimed to clinically and radiographically **evaluate** the efficacy of allogenic cortical bone lamina combined with a composite bone graft in the augmentation of a horizontal bone defect in the edentulous maxilla during a 6-year follow-up period. Three CB CT scans taken before treatment, 6 months after the augmentation period/before implant placement, and after a 6-year follow-up period, were analyzed using stable referent points. After the 6 -year follow-up period, the average resorption rate was 21.65% on the augmented buccal side, with no implant exposure being observed. **Conclusions:** The bone shell technique used in conjunction with allogenic bone plates combined with autogenous bone, xenografts, and collagen membranes is an effective technique to manage horizontal ridge defects.

41. Implantological and mucogingival treatment approach in a patient with cerebral palsy
Dr. Mariajosé González Villarreal, Dr. Edson Josué Pacheco Herrera, Dr. Martha Margarita Aguado Arzola, Dr. Jesús Alfredo Aguado Arzola, Dr. Gilberto Zatarain Hernández, Dr. María de los Ángeles Pietschmann Santa María. Implantological and mucogingival treatment approach in a patient with cerebral palsy. Int J Appl Dent Sci 2022;8(1):322-327.

https://www.oraljournal.com/archives/2022/8/1/E/8-1-60

This article includes the report of a clinical case of a 41-year-old female patient with cerebral palsy and hypothyroidism. The treatment comprised the three stages of periodontal therapy comprising hygienic phase I accompanied by phase II that compromises guided implant placement and horizontal guided bone regeneration with soft tissue conditioning through the placement of a connective tissue graft through the VISTA technique and finally phase III of maintenance.

06/2023