

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

### 1. 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. 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  $1 \cdot 10^4$  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. *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 interconnective 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 vascularisation 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. Both native RPCM and BG are resorbed without inflammation within 8 (BG) or 12 weeks (RPCM). The compact multilayer collagen of RPCM may have positively influenced the resorption stability.

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

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2. 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.

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

Rothamel D, Torök 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](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.

#### 4. Collagen Membranes Adsorb the Transforming Growth Factor- $\beta$ Receptor I Kinase-dependent Activity of Enamel Matrix Derivative.

Stähli A, Miron RJ, Bosshardt DD, Sculean A, Gruber R. *J Periodontol.* 2016; 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- $\beta$ ) signaling in oral fibroblasts.

**MATERIAL AND METHODS:** Three commercially available collagen products were exposed to enamel matrix derivative or recombinant TGF- $\beta$ 1, followed by vigorous washing. Oral fibroblasts were then either seeded directly onto the collagen products or were incubated with the respective supernatant. The expression of the TGF- $\beta$  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- $\beta$ 1 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- $\beta$  receptor I kinase inhibitor SB431542. Amelogenin bound most abundantly to gelatin coated culture dishes. Incubation of palatal fibroblasts with recombinant amelogenin, however, did not alter expression of interleukin 11 and proteoglycan 4.

**CONCLUSIONS:** These in vitro findings suggest that collagen products adsorb a TGF- $\beta$  receptor I kinase-dependent activity of enamel matrix derivative and make it available for potential target cells.

#### 5. 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. *Int J Oral Maxillofac Implants.* 2017; 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.

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

Kubasiewicz-Ross P, Hadzik J, Seeliger J, Kozak K, Jurczynszyn K, Gerber H, Dominiak M, Kunert-Keil C. *Ann Anat.* 2017; 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). The last group served as controls 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.

## 7. 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. *Clinical Oral Investigations*. 2017. [Epub ahead of print]

<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 ( $\beta$ -TCP=test 1), (a biphasic calcium phosphate consisting 60% HA and 40%  $\beta$ -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.

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## Clinical studies and case series

### 8. 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](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 clinical 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 collagen membrane, which is a private label of Jason® membrane.

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9. The concept of Screw-Guided Bone Regeneration (S-GBR). Part 1: From sinus-lift to general applications in the resorbed maxilla and mandible.

Toeroek R, Mazor Z, del Corso M and Dohan Ehrenfest D. M; POSEIDO. 2013; 1(2): 69-84.

<http://www.poseido.info/publication/volume-1-2013/poseido-20131269-84-toeroek.pdf>

The concept of Guided Bone Regeneration (GBR) is quite old and is now covering a large quantity of techniques and combinations of grafting materials and resorbable or nonresorbable membranes. For the treatment of the resorbed posterior mandible, the efficiency of the GBR concept is relatively difficult to fully validate, as it remains difficult operator-dependent techniques where no consensus on the material combination exists. The terminology used in the literature is quite confusing about these techniques, as it covers in fact many different approaches. In this article, we isolate and describe for the first time one very specific approach named Screw-Guided Bone Regeneration (S-GBR), where the osteosynthesis screws and/or screw implants are used as pillars of the bone regenerative compartments during GBR strategies.

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

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

Toeroek R. and Dohan Ehrenfest D. M.; POSEIDO. 2013; 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.

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

Jelusic 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.

## 12. 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  $\beta$ -tricalcium phosphate (Ceros TCP) and porcine pericardium collagen membranes (Jason) (CJ group).

**MATERIALS 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  $\beta$ -tricalcium phosphate with pericardium collagen membranes for horizontal augmentation.

### 13. 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., *Int J Periodontics Restorative Dent.* 2015; 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 ( $P = .0759$ ).

14. 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. *Scripta Scientifica Medicinae Dentalis* 2015; 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.

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

Khajasteh A, Hosseinpour S, Nazeman P, Dehghan MM. *Int J Oral Maxillofac Surg*. 2016;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. 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. 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. Although the two groups had comparable results at the 12-month follow-up, it was observed

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that the modified technique accelerated neural healing within 6 months and reduced the length of the discomfort period.

**16. 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.**

Khajasteh 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 (BFPCs) with iliac bone block grafting for the treatment of extensive human alveolar ridge defects. 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 BFPCs. 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. 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. The application of BFPCs in conjunction with iliac bone block grafts may increase the amount of new bone formation and decrease secondary bone resorption in extensively atrophic jaws.

**17. 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 transcresal 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  $33.4\% \pm 17.05\%$ , and  $43.6\% \pm 16.70$  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 subantrally.

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

## 18. 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>

**Clinical case 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.

## 19. 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. *Clin Oral Investig.* 2016; 21(3):787-794. [Epub ahead of print]

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

**The objective of this study is to histologically and radiologically compare 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 % ( $\pm 2.74$ ) for SBM and 95.76 % ( $\pm 2.15$ ) for NSBM. One patient left the study for personal reasons. Histological analysis revealed a percentage of new bone of 29.71 % ( $\pm 13.67$ ) for SBM and 30.57 % ( $\pm 16.07$ ) for NSBM. Residual bone substitute material averaged at 40.68 % ( $\pm 16.32$ ) for SBM compared to 43.43 % ( $\pm 19.07$ ) 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.

## 20. 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. *Int J Oral Maxillofac Implants.* 2016; 31(4):827-34.

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

[Determination of 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.

## 21. Monophasic $\beta$ -TCP vs. biphasic HA/ $\beta$ -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. *Clin Oral Implants Res.* 2016; 28(10):e175-e183.

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

Comparison of a monophasic (100%  $\beta$ -TCP) and a biphasic (60% HA and 40%  $\beta$ -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  $36.16 \pm 19.37\%$ , BBS  $38.42 \pm 12.61\%$ ), residual BSM (MBS  $30.26 \pm 11.7\%$ , BBS  $32.66 \pm 12.57\%$ ) and non-mineralized tissue (MBS  $34.29 \pm 18.32\%$ , BBS  $28.92 \pm 15.04\%$ ) ( $P > 0.05$ , 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  $78.31 \pm 5.81$ , BBS  $80.42 \pm 6.31$ ;  $P < 0.05$ , 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.

## 22. 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. *Biomed Res Int.* 2017; 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. 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. 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.

## 23. Immediate One-Time Low-Profile Abutment to Enhance Peri-implant Soft and Hard Tissue Stability in the Esthetic Zone.

Pelekanos S and Pozidi G. *Int J Periodontics Restorative Dent.* 2017; 37(5):729-735.

<https://www.ncbi.nlm.nih.gov/pubmed/28817139>

Reductions in peri-implant bone height have been acknowledged as a normal consequence of implant therapy. Various restorative factors contribute to this phenomenon. One is repeated abutment retightening, which causes a mechanical disruption at the implant-abutment interface, leading to soft tissue recession. Several investigators proposed placement of the definitive abutment after implant placement as a solution to the problem. The definitive use of an intermediate abutment after implant placement seems to positively affect the soft tissue response. [This article aims to present a prosthetic sequence for achieving peri-implant tissue stability in the esthetic zone.](#)

## 24. 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.

<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. 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. 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. 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.

## 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. *J Oral Implantol.* 2018. [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.