Relevant Publications - cerabone®

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

1. **Bone ingrowth in bFGF-coated hydroxyapatite ceramic implants.**
   Schnettler R, Alt V, Dingeldein E, Pfefferle H.-J, Kilian O, Meyer C, Heiss C and Wenisch S. Biomaterials 2003; 24(25):4603–4608.

   http://www.ncbi.nlm.nih.gov/pubmed/12951003

   This experimental study was performed to evaluate angiogenesis, bone formation, and bone ingrowth in response to osteoinductive implants of bovine-derived hydroxyapatite (HA) ceramics either uncoated or coated with basic fibroblast growth factor (bFGF) in miniature pigs. A cylindrical bone defect was created in both femur condyles of 24 miniature pigs using a saline coated trephine. Sixteen of the 48 defects were filled with HA cylinders coated with 50 microg rhbFG, uncoated HA cylinders, and with autogenous transplants, respectively. Fluorochrome labelled histological analysis, histomorphometry, and scanning electron microscopy were performed to study angiogenesis, bone formation and bone ingrowth. Complete bone ingrowth into bFGF-coated HA implants and autografts was seen after 34 days compared to 80 days in the uncoated HA group. Active ring-shaped areas of fluorochrome labelled bone deposition with dynamic bone remodelling were found in all cylinders. New vessels could be found in all cylinders. Histomorphometric analysis showed no difference in bone ingrowth over time between autogenous transplants and bFGF-coated HA implants. The current experimental study revealed comparable results of bFGF-coated HA implants and autogenous grafts regarding angiogenesis, bone synthesis and bone ingrowth.

2. **Comparison of different methods for the preparation of porous bone substitution materials and structural investigations by synchrotron µ-computer tomography**
   Tadic D, Beckmann F, Donath T and Epple M. Materialwissenschaft und Werkstofftechnik 2004, 35(4): 240–244.

   http://onlinelibrary.wiley.com/doi/10.1002/mawe.200400730/abstract

   The preparation of porous biomaterials for bone substitution is an important clinical issue in current biomedical technology because the ingrowth of bone can only occur if a suitable number of sufficiently large pores is available. Different procedures are compared here: The combined chemical-thermal treatment of bovine and human cancellous bone, the calcination of bovine cancellous bone, mechanical hole-drilling, and the extraction of porogens (in this case: salt crystals). The inner structure and the porosity of all samples were studied using high-resolution synchrotron µ-computer tomography.

3. **A thorough physicochemical characterisation of 14 calcium phosphate-based bone substitution materials in comparison to natural bone.**
   Tadic D and Epple M. Biomaterials. 2004; 25(6):987-94.

   https://www.ncbi.nlm.nih.gov/pubmed/14615163

Fourteen different synthetic or biological bone substitution materials were characterised by high-resolution X-ray diffractometry, infrared spectroscopy, thermogravimetry, and scanning electron microscopy. Thus, the main parameters chemical composition, crystallinity, and morphology were determined. The results are compared with natural bone samples. The materials fall into different classes: Chemically treated bone, calcined bovine bone, algae-derived hydroxyapatite, synthetic hydroxyapatite, peptide-loaded hydroxyapatite, and synthetic beta-TCP ceramics.

4. **Evaluation of a novel nanocrystalline hydroxyapatite paste and a solid hydroxyapatite ceramic for the treatment of critical size bone defects (CSD) in rabbits.**
   Huber FX, Berger I, McArthur N, Huber C, Kock HP, Hillmeier J, Meeder PJ. J Mater Sci: Mater Med. 2008; 19(1):33-8. Epub 2007.

   https://www.ncbi.nlm.nih.gov/pubmed/17569013

   The purpose of our study was to test the effectiveness of Ostim nanocrystalline hydroxyapatite paste and cerabone ceramic by treating a critical size bone defect (CSD) on the right foreleg of a white New Zealand rabbit. Evaluation was carried out by comparing four groups each with a different CSD filling: an only OSTIM bone filling, an only cerabone filling, an OSTIM-cerabone combination, and a control group with no filling of the CSD. The results of this study display a rapid and uniform bone ingrowth following the CSD filling with Ostim. The histological and histomorphometrical data have shown similarly excellent results for both the Ostim and cerabone-Ostim groups. The control group fared poorly in comparison, as three cases of non-union were observed and none of the defects were totally refilled with fresh bone within 60 days. The successful bone healing with osseous consolidation verifies the importance of the nanocrystalline hydroxyapatite in the treatment of metaphyseal osseous volume defects in the metaphyseal spongiosa.

5. **Impact of Citric Acid Etching on Biocompatibility and Osseous Organisation of a Natural Bovine Bone Mineral: Preliminary Results of an In-Vitro/In-Vivo Study**
   Rothamel D, Schwarz F, Herten M, Berndsen K, Fienitz T, Ritter L, Dreiseidler T and Zöller J in Magjarevic R, Dössel O and Schlegel WC (Eds.), IFMBE Proceedings 2009; 25(11): 259–262.

   http://link.springer.com/chapter/10.1007/978-3-642-03891-4_69

   The aim of the present study was to evaluate the influence of superficial etching of a xenogenous bone mineral on cell proliferation and bone regeneration. A granular bone substitute material [BSM] (cerabone® [CB], botiss medical, Berlin, Germany) was superficially etched using citric acid (Acid [CBA]). CB and CBA were allocated into 96 non-binding well plates and incubated with 1×104 human osteoblast-like cells (SaOs-2) per well under standardized conditions. After 2 hours, 3 and 7 days a LDH-Assay was used for photometric evaluation of cell proliferation (n=8). LDH values were transferred into cell amounts using a standard curve and analyzed for statistical difference. Additionally, cell morphology was investigated using scanning electron microscopy (SEM) (n=3). In the in-vivo part, CB and CBA granules were used for lateral augmentation of the maxillae of four beagle dogs and covered with a collagen membrane (Jason® Membrane, botiss medical). Healing periods were set at 3 and 8

weeks (n=2, respectively). In-vitro evaluation revealed statistically significant higher cell proliferation after 3 and 7 days on CBA compared to CB ($p<0.05$, Wilcoxon test). SEM observation presented flat and star-shaped SaOs-2- osteoblasts displaying high numbers of lamellopodia on both CB and CBA surfaces. In vivo, both BSM showed osteoconductive properties and osseous organisation after 8 weeks. However, the number of the in-vivo applications did not allow further statistical analysis. Within the limits of the present study it was concluded that superficial etching of natural bone minerals using citric acid may support osteoblast-like cell proliferation. Further studies are necessary to specify the impact on bone regeneration.

6. **Biocompatibility and biodegradation of a native porcine pericardium membrane: results of in vitro and in vivo examinations. (Thommen study)**
   Rothamel D, Schwarz F, Fienitz T, Smeets R, Dreiseidler T, Ritter L, Happe A and Zoller J. Int J Oral Maxillofac Implants. 2012; 27(1):146-54.

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

   The objective of this pilot study was to examine, in vitro and in vivo, a novel native collagen membrane extracted from porcine pericardium. Materials and Methods: The morphologic structure of two different native collagen membranes (Remotis, Thommen Medical; Bio-Gide, Geistlich Biomaterials) was examined using a scanning electron microscope. For biocompatibility testing, membranes were incubated with SaOs-2 osteoblastlike cells. After 2 hours, 3 days, and 7 days, proliferation of the cells on the membranes was determined. Evaluation of the biodegradation pattern was performed in a dog model with simultaneous bone augmentation with Bio-Oss (Geistlich Biomaterials) or cerabone® (Botiss Biomaterials) in the lateral anterior maxilla in eight animals with histologic examination after 4, 8, 12, and 24 weeks. Results: An interconnective pore system was identifiable for Remotis, while Bio-Gide displayed a more fibrous structure. In vitro, Remotis showed considerable cell proliferation, which was significantly superior to that observed with Bio-Gide, especially after 7 days (2,910 ± 1,273 and 707 ± 706, respectively). In vivo, both membranes integrated into the surrounding tissue without any inflammatory reaction. Both membranes allowed early vascularization. However, considerable biodegradation was noted within 4 to 8 weeks with Bio-Gide, while Remotis resorbed generally within the first 8 to 12 week. Both membranes supported underlying bone formation. Conclusion: Both examined membranes indicate a high level of biocompatibility. Both are resorbed without inflammation within 8 weeks (Bio-Gide) or 12 weeks (Remotis). The compact interconnective pericardium collagen of Remotis may have stabilized the resorption process.

7. **Effect of Guided Tissue Regeneration on Newly Formed Bone and Cementum in Periapical Tissue Healing after Endodontic Surgery: An In Vivo Study in the Cat.**
   Artzi Z, Wasersprung N, Weinreb M, Steigmann M, Prasad H.S. and Tsesis I. J Endod. 2012;38(2):163-9. Epub2011.

   https://www.ncbi.nlm.nih.gov/pubmed/22244630

The purpose of this study was to evaluate the influence of anorganic bovine bone as a grafted biomaterial on newly formed bone and cementum in periapical regions after surgical endodontic treatment in cats.

Methods: After inducing apical periodontitis in 9 cats, root canal and surgical endodontic treatment were performed on 72 roots of first and second maxillary premolars. Bone defects were treated with biomaterial particles + a membrane, biomaterial only, a membrane only, or left unfilled (control). Histomorphometry on nondecalcified sections were performed at 3 and 6 months after surgery. Analysis of variance with repeated measures was used within 2 and 3 subject factors to analyze newly formed bone, cementum, biomaterial conduction, and resorption.

Results: At each time period, bone formation was greater at the grafted membrane-protected sites than in the grafted unprotected sites. At 6 months, the bone area fraction at membrane nongrafted sites was greater than in the grafted-protected sites. The new cementum was significantly greater at 6 months than at 3 months and greater at the grafted membrane-protected sites over the unprotected ones at 6 months. Statistically, the grafted biomaterial, the membrane, and the time contributed significantly to the amount of new bone ($P < .05$) with no significant interaction. Biomaterial osteoconduction was significantly affected by the time. All 3 variables showed a significant interaction on new cementum.

Conclusions: There was significantly more bone formation after surgical endodontic treatment when membrane and bone grafts were used as compared with bone grafts only or unfilled control sites. However, it appears that the key factor to the enhanced tissue regeneration is the membrane and not the grafted biomaterial.

8. **Comparison of six bone-graft substitutes regarding to cell seeding efficiency, metabolism and growth behaviour of human mesenchymal stem cells (MSC) in vitro.**

Seebach C, Schultheiss J, Wilhelm K, Frank J, Henrich D. Int J Oral Maxillofac Surg. 2014;43(4):514- Epub 2013.

https://www.ncbi.nlm.nih.gov/pubmed/20233614

This in vitro study investigates cell seeding efficiency, metabolism, gene expression and growth behaviour of MSC sown on six commercially clinical available bone-graft substitutes in order to define their biological properties: synthetic silicate-substituted porous hydroxyapatite (Actifuse ABX), synthetic alpha-TCP (Biobase), synthetic beta-TCP (Vitoss), synthetic beta-TCP (Chronos), processed human cancellous allograft (Tutoplast) and processed bovines hydroxyapatite ceramic (cerabone®). 250,000 MSC derived from human bone marrow (n=4) were seeded onto the scaffolds, respectively. On days 2, 6 and 10 the adherence of MSC (fluorescence microscopy) and cellular activity (MTT assay) were analysed. Osteogenic gene expression (cbfa-1) was analysed by RT-PCR and scanning electron microscopy was performed.

The highest number of adhering cells was found on Tutoplast (e.g. day 6: 110.0+/-24.0 cells/microscopic field; $p<0.05$) followed by Chronos (47.5+/-19.5, $p<0.05$), Actifuse ABX (19.1+/-4.4), Biobase (15.7+/-9.9), Vitoss (8.8+/-8.7) and cerabone® (8.1+/-2.2). MSC seeded onto Tutoplast showed highest metabolic activity and gene expression of cbfa-1. These data are confirmed by scanning electron microscopy. The cell shapes varied from round-shaped cells to wide spread cells and cell clusters,

depending on the bone-graft substitutes. Processed human cancellous allograft is a well-structured and biocompatible scaffold for ingrowing MSC in vitro. Of all other synthetical scaffolds, beta-tricalcium phosphate (Chronos) have shown the best growth behaviour for MSC.
DISCUSSION: Our results indicate that various bone-graft substitutes influence cell seeding efficiency, metabolic activity and growth behaviour of MSC in different manners. We detected a high variety of cellular integration of MSC in vitro, which may be important for bony integration in the clinical setting.

9. **High-temperature sintering of xenogeneic bone substitutes leads to increased multinucleated giant cell formation: In vivo and preliminary clinical results. (BEGO study)**
Barbeck M, Udeabor S, Lorenz J, Schlee M, Grosse Holthaus M, Raetscho N, Choukroun J, Sader R, Kirkpatrick C.J. and Ghanaati S. J Oral Implantol.2014; 41(5):e212-22.

http://www.ncbi.nlm.nih.gov/pubmed/25105868

The present preclinical and clinical study assessed the inflammatory response to a high temperature-treated xenogeneic material (Bego-Oss®) and the effects of this material on the occurrence of multinucleated giant cells, implantation bed vascularization and regenerative potential. After evaluation of the material characteristics via scanning electron microscopy, subcutaneous implantation in CD-1 mice was used to assess the inflammatory response to the material for up to 60 days. The clinical aspects of this study involved the use of human bone specimens six months after sinus augmentation. Established histological and histomorphometric analysis methods were applied. After implantation, the material was well integrated into both species without any adverse reactions. Multinucleated giant cells were observed in both species and were associated with enhanced vascularization. These results revealed that the high heat treatment led to an increase in the inflammatory tissue response to the biomaterial and a combined increase in multinucleated giant cell formation. Further clarification of the differentiation of the multinucleated giant cells toward so-called osteoclast-like cells or foreign body giant cells is needed to relate these cells to the physicochemical composition of the material.

10. **Bone substitute material composition and morphology differentially modulate calcium and phosphate release through osteoclast-like cells.**
Konermann A, Staubwasser M, Dirk C, Keilig L, Bourauel C, Götz W, Jäger A, Reichert C. Int J Oral Maxillofac Surg. 2014; 43(4):514-21. Epub 2013.

https://www.ncbi.nlm.nih.gov/pubmed/24268900

The aim of this study was to determine the material composition and cell-mediated remodelling of different calcium phosphate-based bone substitutes. Osteoclasts were cultivated on bone substitutes (cerabone®, maxresorb®, and NanoBone) for up to 5 days. Bafilomycin A1 addition served as the control. To determine cellular activity, the supernatant content of calcium and phosphate was measured by inductively coupled plasma optical emission spectrometry. Cells were visualized on the materials by scanning electron microscopy. Material composition and surface characteristics were assessed by energy-dispersive X-ray spectroscopy. Osteoclast-induced calcium and phosphate release was material-specific. maxresorb® exhibited the highest ion release to the medium ($P = 0.034$; calcium

40.25mg/l day 5, phosphate 102.08 mg/l day 5) and NanoBone the lowest (P = 0.021; calcium 8.43 mg/l day 5, phosphate 15.15 mg/l day 5); cerabone® was intermediate (P = 0.034; calcium 16.34 mg/l day 5, phosphate 30.6 mg/l day 5). All investigated materials showed unique resorption behaviours. The presented methodology provides a new perspective on the investigation of bone substitute biodegradation, maintaining the material-specific micro- and macrostructure.

11. Polymeric vs hydroxyapatite-based scaffolds on dental pulp stem cell proliferation and differentiation.

Khojasteh A, Motamedian SR, Rezai Rad M, Hasan Shahriari M, Nadjmi N. World J Stem Cells. 2015; 7(10): 1215–1221.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4663374/

The aim was to evaluate adhesion, proliferation and differentiation of human dental pulp stem cells (hDPSCs) on four commercially available scaffold biomaterials.

METHODS: hDPSCs were isolated from human dental pulp tissues of extracted wisdom teeth and established in stem cell growth medium. hDPSCs at passage 3-5 were seeded on four commercially available scaffold biomaterials, SureOss (Allograft), cerabone (Xenograft), PLLA (Synthetic), and OSTEON II Collagen (Composite), for 7 and 14 d in osteogenic medium. Cell adhesion and morphology to the scaffolds were evaluated by scanning electron microscopy (SEM). Cell proliferation and differentiation into osteogenic lineage were evaluated using DNA counting and alkaline phosphatase (ALP) activity assay, respectively.

RESULTS: All scaffold biomaterials except SureOss (Allograft) supported hDPSC adhesion, proliferation and differentiation. hDPSCs seeded on PLLA (Synthetic) scaffold showed the highest cell proliferation and attachment as indicated with both SEM and DNA counting assay. Evaluating the osteogenic differentiation capability of hDPSCs on different scaffold biomaterials with ALP activity assay showed high level of ALP activity on cells cultured on PLLA (Synthetic) and OSTEON II Collagen (Composite) scaffolds. SEM micrographs also showed that in the presence of Cerabone (Xenograft) and OSTEON II Collagen (Composite) scaffolds, the hDPSCs demonstrated the fibroblastic phenotype with several cytoplasmic extension, while the cells on PLLA scaffold showed the osteoblastic-like morphology, round-like shape.

CONCLUSION: PLLA scaffold supports adhesion, proliferation and osteogenic differentiation of hDPSCs. Hence, it may be useful in combination with hDPSCs for cell-based reconstructive therapy.

12. Characterization of Bone Marrow Mononuclear Cells on Biomaterials for Bone Tissue Engineering In Vitro

Henrich D, Verboket R, Schaible A, Kontradowitz K, Oppermann E, Brune J.C, Nau C, Meier S, Bonig H, Marzi I and Seebach C. Biomed Res Int. 2015; 3: 1–12.

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

Bone marrow mononuclear cells (BMCs) are suitable for bone tissue engineering. Comparative data regarding the needs of BMC for the adhesion on biomaterials and biocompatibility to various biomaterials are lacking to a large extent. Therefore, we evaluated whether a surface coating would

enhance BMC adhesion and analyze the biocompatibility of three different kinds of biomaterials. BMCs were purified from human bone marrow aspirate samples. Beta tricalcium phosphate (β-TCP, without coating or coated with fibronectin or human plasma), demineralized bone matrix (DBM), and bovine cancellous bone (BS) were assessed. Seeding efficacy on β-TCP was 95% regardless of the surface coating. BMC demonstrated a significantly increased initial adhesion on DBM and β-TCP compared to BS. On day 14, metabolic activity was significantly increased in BMC seeded on DBM in comparison to BMC seeded on BS. Likewise increased VEGF-synthesis was observed on day 2 in BMC seeded on DBM when compared to BMC seeded on BS. The seeding efficacy of BMC on uncoated biomaterials is generally high although there are differences between these biomaterials. Beta-TCP and DBM were similar and both superior to BS, suggesting either as suitable materials for spatial restriction of BMC used for regenerative medicine purposes in vivo.

13. Comparison of three different types of scaffolds preseeded with human bone marrow mononuclear cells on the bone healing in a femoral critical size defect model of the athymic rat.

Janko M, Sahm J, Schaible A, Brune JC, Bellen M, Schroder K, Seebach C, Marzi I, Henrich D. J Tissue Eng Regen Med. 2017. Epub ahead of print.

https://www.ncbi.nlm.nih.gov/pubmed/28548246

Comparison of three different scaffolds serving as carrier for BMC in a rat femoral critical size defect with regard to the osteogenic activity in the defect zone. Human demineralized bone matrix (DBM), bovine cancellous bone hydroxyapatite ceramic (BS), or β-TCP were seeded with human BMC and hereafter implanted into critically sized bone defects of male athymic nude rats. Autologous bone served as control. Gene activity was measured after one week, bone formation was analysed histologically and radiologically after 8 weeks. Generally, regenerative gene expression (BMP2, RUNX2, VEGF, SDF-1, RANKL) as well as bony bridging and callus formation was observed to be most pronounced in defects filled with autologous bone, followed in descending order by DBM, β-TCP and BS. Although DBM was superior in most aspects of bone regeneration analysed in comparison to β-TCP and BS, the level of autologous bone could not be attained.

14. Resol based chitosan/nano-hydroxyapatite nanoensemble for effective bone tissue engineering.

Shakir M, Jolly R, Khan AA, Ahmed SS, Alam S, Rauf MA, Owais M, Farooqi MA. Carbohydr Polym. 2018; 179:317-327. Epub 2017.

https://www.ncbi.nlm.nih.gov/pubmed/29111057

It is the first report where different amounts of resol resin (RS) were incorporated with chitosan-hydroxyapatite (CHA) to develop a triconstituent nanoensemble CHA-RS (0.5,1,2), via simple co-precipitation method. The results of SEM, TEM, TGA and mechanical analysis revealed irregular interconnected rough morphology with homogenous distribution of needle shaped particles having average size ranging between 12 and 19nm, possessing higher thermal stability and mechanical strength, respectively relative to CHA (binary) nanocomposite. The CHA-1RS nanocomposite showed enhanced protein adsorption and ALP activity with excellent apatite formation ability compared to

CHA-RS (0.5,2) and CHA nanocomposites. Thus, CHA-1RS nanocomposite was selectively tested as bare implant in the repair of critical-size calvarium defect (8mm) in albino rat. The histopathological and radiological investigations indicated that CHA-1RS prompted the bone regeneration ability as early as 2 weeks postimplantation demonstrating remarkably faster healing of calvarial defect relative to cerabone. These findings have placed CHA-1RS on the pedestal to be employed as a potential alternative biomaterial for bone tissue engineering.

15. **Hydrophilicity, Viscoelastic, and Physicochemical Properties Variations in Dental Bone Grafting Substitutes.**

Trajkovski B, Jaunich M, Müller WD, Beuer F, Zafiropoulos GG, Houshmand A. Materials (Basel). 2018; 11(2).

https://www.ncbi.nlm.nih.gov/pubmed/29385747

Investigation of the dimensional changes and molecular mobility by Dynamic Mechanical Analysis (DMA) of xenograft (cerabone®), synthetic (maxresorb®), and allograft (maxgraft®, Puros®) blocks in a wet and dry state. While no significant differences could be seen in dry state, cerabone® and maxresorb® blocks showed a slight height decrease in wet state, whereas both maxgraft® and Puros® had an almost identical height increase. In addition, cerabone® and maxresorb® blocks remained highly rigid and their damping behaviour was not influenced by the water. On the other hand, both maxgraft® and Puros® had a strong increase in their molecular mobility with different damping behaviour profiles during the wet state. A high-speed microscopical imaging system was used to analyze the hydrophilicity in several naturally derived (cerabone®, Bio-Oss®, NuOss®, SIC® nature graft) and synthetic DBGS granules (maxresorb®, BoneCeramic®, NanoBone®, Ceros®). The highest level of hydrophilicity was detected in cerabone® and maxresorb®, while Bio-Oss® and BoneCeramic® had the lowest level of hydrophilicity among both naturally derived and synthetic DBGS groups. Deviations among the DBGS were also addressed via physicochemical differences recorded by Micro Computed Tomography, Scanning Electron Microscopy, Fourier Transform Infrared Spectroscopy, X-ray powder Diffractometry, and Thermogravimetric Analysis. Such DBGS variations could influence the volume stability at the grafting site, handling as well as the speed of vascularization and bone regeneration. Therefore, this study initiates a new insight into the DBGS differences and their importance for successful clinical results.

16. **Inflammatory-driven angiogenesis in bone augmentation with bovine hydroxyapatite, B-tricalcium phosphate and Bioglasses. Comparative study.**

Anghelescu VM, Neculae I, Dincă O, Vlădan C, Socoliuc C, Cioplea M, Nichita L, Popp C, Zurac S, Bucur A. JImmunolRes 2018. Accepted 25 July 2018

https://www.hindawi.com/journals/jir/aip/9349207/

Introduction:

The clinical use of bioactive materials for bone augmentation has remained a challenge because of predictability and effectiveness concerns, as well as increased costs. The purpose of this study was to

analyze the ability to integrate bone substitutes by evaluating the immunohistochemical expression of the platelet endothelial cells adhesion molecules (PECAM-1), vascular endothelial growth factor (VEGF), collagen IV, laminin and osteonectin, in the vicinity of bone grafts, enabling tissue revascularization and subsequent appearance of bone lamellae. There is still a lack of in vivo studies of inflammatory-driven angiogenesis in bone engineering using various grafts, although angiogenesis is a key factor of bone regeneration with crucial role in the success rate of bone augmentation.
Methods: The study was performed in animal experimental model on the standardized monocortical defects in the tibia of 20 New Zeeland rabbits. The defects were augmented with the three types of bone substituents. The used bone substituents were Beta Tricalcium Phosphate, bovine hydroxyapatite and bioactive glasses. After a period of 6 months, bone fragments were harvested for histopathologic examination. Endothelial cell analysis was done by analysing vascularization with PECAM / CD31 and VEGF and fibrosis with collagen IV, laminin and osteonectin stains. Statistical analysis was realized by descriptive analysis which was completed with the Kurtosis and Skewness as well as the Kruskal-Wallis and Mann Whitney statistical tests. Results: The discoveries show that the amount of bone that is formed around Beta Tricalcium Phosphate and bovine hydroxyapatite is clearly superior to the bioactive glasses. Both the lumen diameter and the number of vessels were slightly increased on the studied slides in favor of Beta Tricalcium Phosphate. Conclusion: Based on the results of this study, we can conclude that bone substitutes as Bovine bone and beta tricalcium phosphate have significant increased angiogenesis (and subsequent improved osteogenesis) compared to the bioactive glass. In our study, significant angiogenesis is linked with a greater tissue formation, indicating that in bone engineering with the allografts we used, inflammation has more benefic effects, the catabolic action being exceeded by the tissue formation

Clinical studies and case series

17. Sinus floor elevation using a sintered, natural bone mineral - A histological case report study. (BEGO study)

Rothamel, D, Smeets, R, Happe, A, Fienitz, T, Mazor, Z, Schwarz, F, Zöller, J (2011), Zeitschrift für zahnärztliche Implantologie, 27(1): 60-70.

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 approach, 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.

18. Influence of Material Properties on Rate of Resorption of Two Bone Graft Materials after Sinus Lift Using Radiographic Assessment.

Riachi F, Naaman N, Tabarani C, Aboelsaad N, Aboushelib MN, Berberi A and Salameh Z. Int J Dent. 2012:737262.

https://www.ncbi.nlm.nih.gov/pubmed/22899930

The aim of this study was to investigate the influence of chemical and physical properties of two graft materials on the rate of resorption.

Materials and Methods. Direct sinus graft procedure was performed on 22 patients intended for implant placement. Two types of graft materials were used (Bio-Oss and cerabone®) and after 8 months healing time the implants were inserted. Radiographic assessment was performed over the period of four years. Particle size, rate of calcium release, and size and type of crystal structure of each graft were evaluated. Results. The average particle size of Bio-Oss (1mm) was much smaller compared to cerabone® (2.7 mm). The amount of calcium release due to dissolution of material in water was much higher for Bio-Oss compared to cerabone®. X-ray image analysis revealed that Bio-Oss demonstrated significantly higher volumetric loss (33.4 ± 3.1%) of initial graft size compared to cerabone® (23.4 ±

3.6%). The greatest amount of vertical loss of graft material volume was observed after one year of surgery.

19. **Nasal floor elevation combined with dental implant placement: a long-term report of up to 86 months.**
Lorean A, Mazor Z, Barbu H, Mijiritsky E, Levin L. Int J Oral Maxillofac Implants. 2014;29(3):705-8.

https://www.ncbi.nlm.nih.gov/pubmed/24818211

The aim of this paper is to present a large-scale long-term follow-up of dental implants placed simultaneously with nasal floor augmentation using osteoconductive bovine bone substitutes.
MATERIALS AND METHODS: Patients who received dental implants combined with nasal floor elevation in three dental centers between 2006 and 2012 were included in this report. Preoperative available bone height was measured on computed tomographic scans. Implant parameters as well as implant survival rates were recorded. The cohort consisted of long-term follow-up of this previously reported cohort, combined with a cohort of newly treated patients.
RESULTS: Overall, 67 patients were included in this study. Cigarette smoking was reported by 16 patients. Two hundred three implants were inserted in combination with nasal floor elevation. No nasal mucosa perforations were observed. The mean follow-up periods were 65.93 ± 13.2 months (range, 33 to 86 months) for the original cohort and 23.14 ± 9.4 months (range, 7 to 44 months) for the newly treated patients. The available bone height prior to bone augmentation was 8.89 ± 1.1 mm (range, 5 to 11.2 mm) and a mean of 3.65 ± 0.9 mm (range, 1.1 to 7 mm) of additional height was achieved with nasal floor elevation. During the follow-up period, no implants were lost, resulting in a 100% survival rate.
CONCLUSION: Nasal floor augmentation, as shown in this report, might serve as a reliable method for reconstruction of the anterior atrophic maxilla when residual height is insufficient.

20. **Reconstruction of advanced bone defect associated with severely compromised maxillary anterior teeth in aggressive periodontitis: a case report.**
Kamil W, Al Bayati L, Hussin AS, Hassan H. J Med Case Rep. 2015; 9:211.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4582840/

Report of a successful intervention outcome of a challenging case in the aesthetic zone of a patient with aggressive periodontitis.
A 34-year-old systemically healthy Malay woman was referred to the Periodontics Specialist Clinic of the Kulliyyah of Dentistry, International Islamic University Malaysia, with a chief complaint of bleeding gums and mobility of the upper anterior teeth. A diagnosis of localized aggressive periodontitis was made. A thorough non-surgical periodontal treatment was provided, followed by a series of regenerative periodontal surgeries to manage advanced bone defects. A successful treatment outcome with a good prognosis was achieved. Maintenance through the supportive treatment phase showed marked bone gain. CONCLUSIONS: Teeth with severely compromised periodontium of unpredictable prognosis can still be maintained with satisfactory restoration of the function, support, and aesthetics,

despite the baseline unpredicted treatment outcome. Proper selection of an advanced periodontal treatment plan can exclude the option of tooth extraction or prosthetic replacement.

21. **Flapless implant surgery: A review of the literature and 3 case reports.**
Romero-Ruiz, M., Mosquera-Perez, R., Gutierrez-Perez, J. and Torres-Lagares, D. J Clin Exp Dent. 2015 Feb; 7(1): e146–e152.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4368003

The present work aims to produce a thorough review of the literature published on the field of Implantology with flapless surgery, to determine the current scientific evidence of the technique, along with illustrating the results with different clinical cases. After presenting the clinical cases, and the review of literature, we can say that flapless surgeries should be restricted to well-selected cases in which a proper clinical and radiological planning has been made. Patients treated with anticoagulant drugs or medically compromised equally can get benefitted by this minimal invasion technique.

22. **Comparison of two different xenografts in bilateral sinus augmentation: Radiographic and histologic findings.**
Panagiotou D, Özkan Karaca E, Dirikan İpçi Ş, Çakar G, Olgaç V and Yılmaz S. Quintessence Int. 2015; 46(7):611-9.

http://www.ncbi.nlm.nih.gov/pubmed/25699296

The aim of this study was to evaluate the radiographic and histomorphometric results of two different xenografts in bilateral sinus augmentation in patients with posterior maxillary atrophy. Method and Materials: Eight patients with less than 5 mm residual alveolar bone height were included in this study. One side was augmented with bovine bone graft-1 and the other side with bovine bone graft-2. Radiographic analyses were performed before and after augmentation, and before the implant placement. After 8 months of healing period, bone biopsies were obtained during implant placement. Results: No statistically significant difference was found between the groups, based on post-augmentation and pre-implantation graft heights (P>.05). Histomorphometric evaluation demonstrated 24.63% and 29.13% newly formed bone in the graft-1 and graft-2 groups, respectively. Intergroup differences were not significant for the mean percentage of new bone formation (P > .05). Conclusion: Within the limitations of this study, it can be concluded that xenograft materials resulted in satisfactory bone height and trabecular new bone formation, and they could be used for the rehabilitation of atrophic maxillae.

23. **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. (Alpha Bio).**
Fienitz T, Moses O, Klemm C, Happe A, Ferrari D, Kreppel M, Ormianer Z, Gal M, Rothamel D (2016), Clinical Oral Investigations 2017; 21(3):787-794. Epub 2016

https://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, BioOss®) 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.

24. 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. and 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. This will be reported in a subsequent article.

25. Tuberosity-alveolar block as a donor site for localised augmentation of the maxilla: a retrospective clinical study.

Khojasteh A, Nazeman P, Tolstunov L. Br J Oral Maxillofac Surg. 2016; 54(8):950-955.

https://www.ncbi.nlm.nih.gov/pubmed/27453038

Retrospective assessment of the efficacy of tuberosity-alveolar block bone (posterior maxillary alveolar ridge) in the augmentation of adjacent defects in the maxilla using data from 14 patients (10 men and four women, mean (range) age 55 (38-69) years) who had had 20 bony augmentations with block bone from the alveolar tuberosity during 2014. Patients were divided into three groups according to the technique by which the bone was collected. The first group had a graft from the alveolar tuberosity covered with titanium mesh (titanium mesh group); the second group had the block bone covered by platelet rich fibrin and collagen membrane (platelet rich fibrin group), and in the third group the graft was covered only with periosteum (periosteum group). The primary width of the bone was recorded at the time of placement of the graft and changes were evaluated 4-6 months later when the implant was inserted. The changes in the width of the bone were 4.1, 3.3, and 2.5 in the platelet rich fibrin, titanium mesh, and periosteum groups, respectively. The difference in bony change among groups was not significant except between the platelet rich fibrin and and periosteum groups (p = 0.005). Tuberosity-alveolar block bone graft may be a good source of bone for augmentation of deficient ridges, and more favourable results can be expected by the addition of resorbable membranes and growth factors.

26. Management of acute maxillary sinusitis after sinus bone grafting procedures with simultaneous dental implants placement - a retrospective study.

Chirilă L, Rotaru C, Filipov I, Săndulescu M. BMC Infect Dis. 2016; 16(1):94.

https://www.ncbi.nlm.nih.gov/pubmed/27169511

The sinus lift was first described in 1974 and it has proven to be a predictable procedure ever since. We aimed to evaluate the rate of acute maxillary sinusitis after sinus lift procedures and the appropriate management strategies.

Methods: Between 2013 and 2015, 245 dental implants were placed in 116 patients (76 males and 40 females) with concomitant bone augmentation of the maxillary sinus floor. The sinus lifting procedure was bilateral in 35 patients and unilateral in 81 patients (a total of 151 sinuses).

Results: Maxillary sinusitis occurred in 5 patients (4.3 %). The clinical signs of infection were: headache, locoregional pain, cacosmia, inflammation of the oral buccal mucosa and rhinorrhea or unilateral nasal discharge. A mucosal fistula was observed during inspection in one patient. The management included only the removal of the grafting material in 3 patients, in 1 patient the grafting material was removed together with all the implants, and in 1 patient only 2 implants and the grafting material were removed, 1 implant being left in place. The sinus cavity was irrigated with metronidazole solution and antibiotic therapy with clindamycin and metronidazole was prescribed for 10 days. Subsequently, all signs of infection disappeared within 5 to 7 days and normal sinus function and drainage were restored.
Conclusions: Although sinus lift is regarded as a safe and reliable procedure, acute sinusitis is a possible complication which has to be managed immediately in order to reduce the risk of further complications like pansinusitis, osteomyelitis of the maxillary bone, and spreading of the infection in the infratemporal space or orbital cavity. To minimize risk, caution must be taken with all the steps of the procedure, in order not to obliterate the ostium, impairing maxillary sinus clearance.

27. Histological and histomorphometric study using an ultrasonic crestal sinus grafting procedure. A multicenter case study. (BEGO 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.

28. Conservative Socket Regeneration with Buccal Wall Defect Using Guided Tissue.

Al-Juboori MJ. Open Dent J. 2016; 10:561-567.

https://www.ncbi.nlm.nih.gov/pubmed/27857817

This case report discusses an irreparable lower left second premolar tooth with a periodontal lesion on the buccal side. A preservative tooth extraction was performed. Then, the socket was grafted with bovine bone, a collagen membrane was placed between the buccal bone and the attached gingiva,

covering the bone dehiscence buccally, and the socket without a flap was raised. After a 6-month healing period, there was minimal socket width resorption and a shallow buccal vestibule. The implant was placed with high primary stability and sufficient buccal plate thickness. In conclusion, this guided tissue regeneration technique can minimize alveolar bone resorption in a socket with buccal dehiscence, but technical difficulties and shallowing of the buccal vestibule still exist.

29. The influence of initial alveolar ridge defect morphology on the outcome of implants in augmented atrophic posterior mandible: an exploratory retrospective study.

Khojasteh A, Motamedian SR, Sharifzadeh N, Zadeh HH, Clin Oral Implants Res. 2017; 28(10):e208-e217.

https://www.ncbi.nlm.nih.gov/pubmed/27804178

The purpose of this retrospective study was to examine the influence of initial atrophic posterior mandible morphology on the outcome of implants placed following augmentation.

MATERIALS AND METHODS: A total of 52 patients contributed 71 edentulous sites, and 185 implants were placed with mean follow-up of 37.97 months. The initial defect morphology was classified according to ABC classification (Journal of Oral Implantology, 37, 2013a and 361). Ridge augmentation was performed by "cortical autogenous tenting" (CAT) followed by either simultaneous or delayed implant placement after 4-6 months of healing. The European Academy of Osseointegration success criteria were used to evaluate implant outcomes.

RESULTS: The overall survival and success rates of dental implants were 98.91% and 80%, respectively. Cumulative success and survival rates in CAT group were 95% and 100% after 2 years of follow-up. The highest marginal bone loss (MBL) was observed (1.26 mm ± 0.99) around implants placed in augmented edentulous sites with initially narrow and flat alveolar crest (defect class CII). Conversely, least MBL (0.48 mm ± 0.78) was detected around implants placed into edentulous sites with two sloped boney walls (defect class AII). Differences between MBL observed around implants placed into initial defect class C, initial defect type and class A (I, II), as well as class BII, were statistically significant ($P < 0.05$). Among all implants, 148 were considered as successful, 26 exhibited satisfactory survival, nine with compromised survival, and two implants failed.

CONCLUSION: The present data confirmed the effect of initial ridge morphology on the outcome of implants placed into augmented bone. Specifically, class A and class B atrophic ridge defects, with one and two vertical boney walls, respectively, may be considered as more favorable recipient sites than class C defects with flat morphology. This conclusion is based on least MBL around implants placed into initial defect class A and class B augmented sites, and higher MBL in implants placed into class C recipient sites. A randomized controlled trial is warranted to examine these exploratory observations.

30. Cortical lamina technique: A therapeutic approach for lateral ridge augmentation using guided bone regeneration.

Deepika-Penmetsa SL, Thomas R, Baron TK, Shah R, Mehta DS5. J Clin Exp Dent. 2017; 9(1):e21-e26.

https://www.ncbi.nlm.nih.gov/pubmed/28149458

The present study aimed at evaluating the efficacy of a novel technique, the bone lamina technique, in horizontal ridge augmentation clinically & radiographically using a combination of allogenic cortical shell, particulate xenograft and resorbable collagen membrane.

MATERIAL AND METHODS: Localized horizontal ridge defects, in ten patients (6 male, 4 female), with bucco-palatal ridge width less than 5 mm were included in this study. Localised ridge augmentation was performed using bone lamina technique with mineralised allogenic shell of 1 mm thickness trimmed to the appropriate size using stereo-lithographic models and fixed to the recipient site with stainless steel micro-screws of 1 mm diameter. The space between the shell & host bone was filled with particulate xenograft followed by placement of collagen membrane and primary closure of the site. Clinical parameters including ridge width before & after flap reflection & radiographic (CBCT) ridge width measurements were recorded pre-operatively, and six months after the augmentation procedure. Results obtained were analyzed statistically.

RESULTS: The mean clinical ridge width before flap reflection (BFR), after flap reflection (AFR) & radiographically was 3.7 ± 0.74 mm, 2 ± 0.70 mm & 1.77 ± 0.71 mm respectively at baseline which increased to 6.8 ± 0.95 mm, 5.15 ± 0.98 mm & 4.90 ± 0.90 mm with a mean gain in ridge width of 3.1 ± 0.63 mm ($p< 0.005$), 3.15 ± 0.63 mm ($p<0.005$) & 3.13 ± 0.70 mm ($p< 0.005$) respectively.

CONCLUSIONS: The present study demonstrates that bone lamina technique can be effective means of horizontal ridge augmentation and the use of mineralized allograft in combination with xenograft and collagen membrane leads to good amount of bone regeneration for subsequent implant placement.

Key words: Dental implant, guided bone regeneration, horizontal ridge defect, ridge augmentation.

31. Ridge augmentation with titanium mesh: A case report.

Jegham H, Masmoudi R, Ouertani H, Blouza I, Turki S, Khattech MB. J Stomatol Oral Maxillofac Surg. 2017; 118 (3):181-186.

https://www.ncbi.nlm.nih.gov/pubmed/28363847

The aim of this case was to demonstrate that the use of rigid titanium occlusive barrier is a reliable alternative to perform a lateral alveolar bone augmentation and treat localized ridge deformities before reaching an ideal implant placement.

A 25-year-old healthy male was referred for implant placement in the maxillary central incisor. The alveolar bone width at the implant site 21 was less than 5mm. Hard tissue augmentation was accomplished using guided bone regeneration. A rigid titanium occlusive barrier was customized to desired shape of future alveolar ridge then secured with tent and fixing screws. Autogenous bone graft harvested with an auto-chip-maker adjacent to the surgical site were mixed with a xenograft and putted under the barrier. The wound was closed using a vestibular mucoperiosteal flap. At 4 months, the rigid barrier was removed, and a 7mm crestal width transversal bone was observed. At the same time, a fixture (4×10mm) was placed. A definitive ceramometal crown was completed after full osseointegration with periodical clinical maintenance. The exposure of the titanium mesh occurred in this case and was visible with a circular flap dehiscence at 1-month follow-up visit. This exposure did not affect the successful regenerative outcomes. After removal of the titanium mesh from the grafted defects, the space beneath the membrane enclosure was seen to be almost completely filled with new hard tissue covered by a thin layer of soft tissue. The postoperative follow-ups revealed that the

implant was stable with excellent osseointegration and the buccal depression of the surgical area was reconstructed.
CONCLUSION: The use of rigid titanium occlusive screwed barrier with autogenous and bovine bone graft might be a reliable technique for alveolar ridge reconstruction. This approach achieve excellent final esthetic outcome of the implant-supported restoration.

32. Presurgical Cone Beam Computed Tomography Bone Quality Evaluation for Predictable Immediate Implant Placement and Restoration in Esthetic Zone.
Cristache CM. Case Rep Dent. 2017; 2017:1096365.

https://www.ncbi.nlm.nih.gov/pubmed/28321342

Despite numerous advantages over multislice computed tomography (MSCT), including a lower radiation dose to the patient, shorter acquisition times, affordable cost, and sometimes greater detail with isotropic voxels used in reconstruction, allowing precise measurements, cone beam computed tomography (CBCT) is still controversial regarding bone quality evaluation. This paper presents a brief review of the literature on accuracy and reliability of bone quality assessment with CBCT and a case report with step-by-step predictable treatment planning in esthetic zone, based on CBCT scans which enabled the clinician to evaluate, depending on bone volume and quality, whether immediate restoration with CAD-CAM manufactured temporary crown and flapless surgery may be a treatment option.

33.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.

34. 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, 2 W, pulse interval 200 μs; pulse length 100 μs, 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 nonsteroid 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.

35. Risk factors and clinical outcomes of sinus membrane perforation during lateral window sinus lifting: analysis of 120 patients.

Tükel HC, Tatli U. Int J Oral Maxillofac Surg. 2018; 47(9):1189-1194.

https://www.ncbi.nlm.nih.gov/pubmed/29655818

The aim of this study was to identify the risk factors associated with sinus membrane perforation and the effect of sinus membrane perforation and other risk factors on graft success and postoperative sinusitis. Sinus membrane perforation, graft failure, and postoperative sinusitis were tested for an association with age, sex, operator experience, side of the operation, residual bone height, presence of septa, presence of a mucous retention cyst, and smoking ($\chi 2$ test). Logistic regression analysis was used to model the odds ratio (OR) with corresponding risk factors. One hundred and twenty patients were included in this study. A total of 22 (18.3%) perforations occurred. A residual bone height of 3-6mm (OR 6.808, P=0.002) and presence of septa (OR 4.023, P=0.025) were identified as significant risk factors. Twenty-eight (23.3%) sinus grafts were classified as failed. Membrane perforation (OR 16.819, P<0.005) and residual bone height of 3-6mm (OR 5.363, P=0.01) were identified as significant risk factors for graft failure. None of the risk factors investigated in this study was significantly associated with postoperative sinusitis. These results suggest that the presence of septa and a residual bone height of 3-6mm are associated with an increased risk of sinus membrane perforation, and that sinus membrane perforation has a negative effect on graft success.

36. **Radiographic Comparison of Bovine Bone Substitute Alone Versus Bovine Bone Substitute and Simvastatin for Human Maxillary Sinus Augmentation. (Dentegris study)**
Yaghobee S, Ghahroudi AARR, Khorsand A, Mahmoudi S, Rafiei SC. J Dent (Tehran). 2018; 15(1):20-29.

https://www.ncbi.nlm.nih.gov/pubmed/29971118

The aim of this study was the comparison of the efficacy of bovine bone substitute (Compact Bone B. ®) alone versus bovine bone substitute and simvastatin for human maxillary sinus augmentation.
Materials and Methods: This study was conducted on 16 sinuses in eight patients. Radiographic assessments were done preoperatively (T0), immediately (T1) and at nine months after sinus grafting (T2). Alveolar bone height and density were assessed on cone beam computed tomography (CBCT) scans using Planmeca Romexis™ Imaging Software 2.2.
Results: The change in alveolar bone height and density between T0, T1 and T2 was significant in both groups. Alveolar bone height (h0, h1, h2) and vertical height of the grafted bone (g1, g2) in three lines (anterior, middle and posterior) were not significantly different between groups. The grafted bone height shrinkage (%) in the anterior, middle and posterior limits of the augmented area were not significantly different between groups. The existing alveolar and grafted bone density increased significantly in both groups between T1 and T2, except for the existing alveolar bone density in the control group. There were no statistically significant differences between the alveolar bone density values obtained in TI and T2 between groups, except for the existing alveolar bone density at T1.
Conclusions: This study did not show any significant positive effect for simvastatin in maxillary sinus augmentation based on radiographic examination.