Pre-clinical \textit{(in vitro \& in vivo)} studies

   

   \url{https://www.ncbi.nlm.nih.gov/pubmed/22297272}

   An autologous bone graft is still the ideal material for the repair of craniofacial defects, but its availability is limited and harvesting can be associated with complications. Bone replacement materials as an alternative have a long history of success. With increasing technological advances the spectrum of grafting materials has broadened to allografts, xenografts, and synthetic materials, providing material specific advantages. A large number of bone-graft substitutes are available including allograft bone preparations such as demineralized bone matrix and calcium-based materials. More and more replacement materials consist of one or more components: an osteoconductive matrix, which supports the ingrowth of new bone; and osteoinductive proteins, which sustain mitogenesis of undifferentiated cells; and osteogenic cells (osteoblasts or osteoblast precursors), which are capable of forming bone in the proper environment. All substitutes can either replace autologous bone or expand an existing amount of autologous bone graft. Because an understanding of the properties of each material enables individual treatment concepts this review presents an overview of the principles of bone replacement, the types of graft materials available, and considers future perspectives. Bone substitutes are undergoing a change from a simple replacement material to an individually created composite biomaterial with osteoinductive properties to enable enhanced defect bridging.

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


   \url{https://www.ncbi.nlm.nih.gov/pubmed/25183228}

   OBJECTIVES: Allograft material for alveolar ridge reconstruction is quite promising and appears to be as equally successful as bone autograft material. The aim of the present study was to compare four different allogeneic bone grafts in terms of their histologic structure and DNA content before grafting. STUDY DESIGN: Four allograft specimens from different suppliers were analyzed histologically, and the DNA content was analyzed before clinical use of the allografts. RESULTS: Organic tissue remnants were detected in all of the evaluated samples. In the present samples adipocytes, fibroblasts, osteocytes, and chondrocytes were identified and DNA isolation and purification was possible. CONCLUSION: Demineralized freeze-dried allogeneic bone transplants can stimulate new bone formation and are a viable alternative to bone autograft material.
However, the well-tolerated use of allograft material in regard to our findings should be further investigated.

3. Evaluation of implant-materials as cell carriers for dental stem cells under in vitro conditions.

   BACKGROUND: Dental stem cells in combination with implant materials may become an alternative to autologous bone transplants. For tissue engineering different types of soft and rigid implant materials are available, but little is known about the viability and the osteogenic differentiation of dental stem cells on these different types of materials. According to previous studies we proposed that rigid bone substitute materials are superior to soft materials for dental tissue engineering. METHODS: We evaluated the proliferation, the induction of apoptosis and the osteogenic differentiation of dental stem/progenitor cells on a synthetic bone-like material and on an allograft product. The soft materials silicone and polyacrylamide (PA) were used for comparison. Precursor cells from the dental follicle (DFCs) and progenitor cells from the dental apical papilla of retained third molar tooth (dNC-PCs) were applied as dental stem cells in our study. RESULTS: Both dental cell types attached and grew on rigid bone substitute materials, but they did not grow on soft materials. Moreover, rigid bone substitute materials only sustained the osteogenic differentiation of dental stem cells, although the allograft product induced apoptosis in both dental cell types. Remarkably, PA, silicone and the synthetic bone substitute material did not induce the apoptosis in dental cells. CONCLUSIONS: Our work supports the hypothesis that bone substitute materials are suitable for dental stem cell tissue engineering. Furthermore, we also suggest that the induction of apoptosis by bone substitute materials may not impair the proliferation and the differentiation of dental stem cells.

4. Three-dimensional scanning electron microscopy of maxillofacial biomaterials.

   Report on a method of 3-dimensional scanning electron microscopy (3D-SEM) to visualize maxillofacial biomaterials. 3D visualization of mucoderm®, Mucograft®, and maxgraft®.
5. **Hydrophilicity, Viscoelastic, and Physicochemical Properties Variations in Dental Bone Grafting Substitutes.**


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5848912/

The indication-oriented Dental Bone Graft Substitutes (DBGS) selection, the correct bone defects classification, and appropriate treatment planning are very crucial for obtaining successful clinical results. However, hydrophilic, viscoelastic, and physicochemical properties’ influence on the DBGS regenerative potential has poorly been studied. For that reason, we investigated 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.
6. Comparison of autogenous and allograft bone rings in surgically created vertical bone defects around implants in a sheep model.

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


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

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4896248/

The sinus lift was first described in 1974 and it has proven to be a predictable procedure ever since. The complications of this surgical procedure are reported in the literature to be low, and can include acute maxillary sinusitis, scattering of the grafting material into the sinus cavity, wound dehiscence and Schneiderian membrane perforations. 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.


OBJECTIVES: The aim of this study was to evaluate implant survival rate and to measure peri-implant bone changes in full-arch rehabilitations with immediate placement and immediate loading implants with platform switching and Morse taper connection, in addition to platelet-rich fibrin (PRF) and buccal bone augmentation, after 4 years of follow-up. METHOD AND MATERIALS: In this retrospective controlled study, patients who had been fully rehabilitated with immediate placement and immediate loading implants were evaluated 4 years post-loading. Implants with platform switching and Morse taper connections were used (In-Kone Universal System, Global D) and PRF and buccal bone augmentation were applied. The radiographic bone loss was calculated by subtracting the bone level at baseline (BLT0) from that at the 4-year follow-up (BLT4) in immediate and delayed implants. Measurements were made at the distal, mesial, vestibular, and oral sites of the implants and the deepest value was recorded. Implants placed in extraction sites and implants placed in healed sites were considered. A comparison between the groups was performed using the Mann-Whitney test. The implant survival rate was calculated using the Kaplan-Meier analysis. RESULTS: In total, 42 patients (28 females and 14 males; average age 55.8 years old, age range 45 to 77) were recruited to this study. A total of 334 implants were put in place (226 in the maxilla, 108 in the mandible). The implant survival rate was 97.8% for the maxilla and 98.1% for the mandible, 98.3% for immediate implants and 96.9% for delayed implants. No statistically significant differences (P > .05) in the mean radiographic bone loss (mBL) were observed when comparing the immediate and delayed implants and the anterior and posterior implants. Statistically significant differences were found in the mBL between the mandibular and maxilla implants in the vestibular (P = .01) and mesial (P = .001) sites. CONCLUSION: Within their limits, the present results suggest that rehabilitation with platform switching and taper connection implants, in addition to buccal bone augmentation and the use of PRF, can lead to predictable results.

10. Lateral bone augmentation in narrow posterior mandibles, description of a novel approach, and analysis of results.


BACKGROUND: Combination of particulate grafts and collagen membranes is widely used for augmentation of bony defects for implant placement. Fixation of the barrier membrane may avoid complications due to unfavorable mechanical properties and poor stability leading to collapse of
The use of mineralized bone allograft as a single grafting material in maxillary sinus lifting with severely atrophied alveolar ridge (1-3 mm) and immediately inserted dental implants. A 3- up to 8-year retrospective study.


The primary aim of our study was to evaluate the efficacy of mineralized bone allograft alone in sinus floor augmentation with simultaneous implant placement in cases with severe atrophy of the residual maxillary bone (bone height < 4 mm). METHODS: Thirty-five dental implants were placed in 29 patients who underwent sinus augmentation via traditional lateral window technique from 2008 to 2013. Patients with residual alveolar height between 1 and 3 mm at the site of implantation were included in the study. The height of residual bone was initially estimated by plain panoramic X-ray and reevaluated intraoperatively by precise micrometric measurement at the site of implantation. Implants of 13 mm height and 3.5 or 4.3 mm in diameter were inserted simultaneously. Mineralized bone allograft was used alone to augment the sinus floor. RESULTS: No wound dehiscence was recorded. In one case there was a postoperative site infection which subsided with antibiotics without implant failure. One implant migrated during the postoperative period to the maxillary sinus and was removed. One implant failed. The remaining 33 implants were successfully loaded. Follow-up ranged from 3 to 8 years. CONCLUSIONS: Maxillary sinus lift in severely absorbed alveolar ridges with simultaneous implant placement could be safely performed using mineralized allograft alone, rendering the procedure less invasive and less time-consuming.
12. Comparison of allogeneic and autogenous bone grafts for augmentation of alveolar ridge defects – a 12-month retrospective radiographic evaluation


The aim of this study was to compare three-dimensional alterations following the use of autogenous versus allogeneic onlay grafts for augmentation at single tooth defects. Materials and methods: Alveolar bone width at specific implant sites were assessed using sagittal and cross-sectional CBCT images prior grafting and at three subsequent time points. 21 patients received autogenous bone blocks harvested from the retromolar region and another 21 patients received freeze-dried cancellous allogeneic bone blocks. Results: The vertical and horizontal dimensions did not significantly differ between autogenous and allogeneic bone grafts at any time point. In addition, there were no statistically significant differences in graft remodeling rates between autogenous (mean shrinkage rate after 12 months: 12.5 ± 7.8 %) and allogeneic onlay grafts (mean shrinkage rate after 12 months: 14.4 ± 9.8 %). Conclusions: Freeze-dried cancellous allogeneic bone blocks showed equivalent volumetric shrinkage rates as autogenous bone blocks when used for treating circumscribed bone defects classified as Type-II to Type-IV according to the ITI-treatment guide categories. Therefore, it is not necessary to over-contour the alveolar ridge when using allogeneic blocks for treating single tooth defects, but to apply the same procedure as when using autogenous blocks.

13. Characterization of circulating DNA in plasma of patients after allogeneic bone grafting.
Solakoglu Ö, Steinbach B, Götz W, Heydecke G, Pantel K, Schwarzenbach


Cell-free DNA (cfDNA) harboring mutations has been found in patients with diseases. Experimental studies have shown that cfDNA can be transmitted, leading to transformations in the host. In the present study, we evaluated whether bone allograft material contains cfDNA and whether this foreign cfDNA can be released into the patient’s blood circulation.
MATERIALS AND METHODS: Plasma samples were collected preoperatively and postoperatively on the same day, at 5 weeks, and 4 months from 25 women who received bone allograft material (test group) from male donors and from 10 women who were treated with autologous graft (control group, only pre- and postoperative samples were collected). DNA was quantified and characterized in bone material and plasma samples by quantitative PCR with primers specific for glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and Y chromosome and gel electrophoresis. DNA in bone material was digested by different concentrations of DNase I.
RESULTS: We detected between 1 and 1.8 μg cfDNA fragments at a length around 601 base pairs (bp) and smaller in each 100 mg allograft. Treatment of the allograft with DNase I completely degraded the longer but not the shorter DNA 90-bp fragments. Y-DNA was not detected in the patients' bloodstream at any time during the treatment and follow-up, but elevated levels of circulating cfDNA could be measured immediately postoperatively.

CONCLUSIONS: Our results suggest that a transmission of DNA from allografts used for alveolar ridge reconstruction in humans is unlikely. The observed increase in circulating cfDNA in allograft and autograft patients immediately postoperatively may be elicited by the surgical procedure.

CLINICAL RELEVANCE: The results support the safety of allograft materials. The results suggest that human allograft materials seem not to release DNA into the blood since we did not measure Y-DNA with our technique.

Clinical case reports


Implant rehabilitation of the atrophic right posterior mandible in a 48-year-old woman using dehydrated homologous bone block, shaped with a computer aided design-computer aided manufacturing (CAD-CAM) system, to avoid harvesting of autologous bone block and to assure a perfect fitting of the block above the alveolar crest. RESULTS: After 7 months, 6.09, 7.36, and 8.08 mm (mean, 7.18 mm) of total horizontal bone gain was observed at sites 6, 12, and 18 mm posterior to the right mental foramen, respectively. CONCLUSIONS: The use of a bone block with CAD-CAM system for alveolar ridge augmentation is a valuable alternative to autograft because it reduces time, cost, and complications for the patients. Data from a computerized tomographic scan can be used to shape a precise 3-dimensional homologous bone block using a CAD-CAM system.
The management of facial defects has rapidly changed in the last decade. Functional and esthetic requirements have steadily increased along with the refinements of surgery. In the case of advanced atrophy or jaw defects, extensive horizontal and vertical bone augmentation is often unavoidable to enable patients to be fitted with implants. Loss of vertical alveolar bone height is the most common cause for a non primary stability of dental implants in adults. At present, there is no ideal therapeutic approach to cure loss of vertical alveolar bone height and achieve optimal pre-implantological bone regeneration before dental implant placement. Recently, it has been found that specific populations of stem cells and/or progenitor cells could be isolated from different dental resources, namely the dental follicle, the dental pulp and the periodontal ligament. Our research group has cultured palatal-derived stem cells (paldSCs) as dentospheres and further differentiated into various cells of the neuronal and osteogenic lineage, thereby demonstrating their stem cell state. In this publication will be shown whether paldSCs could be differentiated into the osteogenic lineage and, if so, whether these cells are able to regenerate alveolar bone tissue in vivo in an athymic rat model. Furthermore, using these data we have started a proof of principle clinical- and histological controlled study using stem cell-rich palatal tissues for improving the vertical alveolar bone augmentation in critical size defects. The initial results of the study demonstrate the feasibility of using stem cell-mediated tissue engineering to treat alveolar bone defects in humans.

The objective of this case report is to introduce a customized CAD/CAM freeze-dried bone allograft (FDBA) block for its use in Guided Bone Regeneration (GBR) procedures for severely deficient maxillary bones. Additionally, a special newly developed remote incision technique is presented to avoid wound dehiscence. The results show optimal integration behavior of the FDBA block after six months and the formation of new vital bone. Thus, the results of the present case report confirm the use of the customized CAD/CAM bone block for augmentation of complex defects in the maxillary aesthetic zone as a successful treatment concept.

This case report describes a technique for aesthetic single implant placement with simultaneous bone grafting and soft tissue thickening. At the time of implant surgery, allogenic (maxgraft®, Botiss Biomaterials, Germany) and xenogenic bone substitute (cerabone®, Botiss Biomaterials, Germany) was used for bone grafting, soft tissues were augmented simultaneously with collagen tissue matrix derivate membrane (mucoderm®, Botiss Biomaterials, Germany). After 4 months during second stage surgery the implant was exposed. Subsequently healing abutment was replaced with provisional crown for gingival contouring. An individual zirconia abutment was made and a cemented full-ceramic crown was placed for final restoration. The 12-month follow-up check-up revealed a pleasing aesthetic treatment outcome, as well as clinically healthy peri-implant soft tissues. Radiological examination showed a stable bone crest with minor bone remodelling around the implant platform. The use of a collagen tissue matrix derivate, simultaneously with GBR, in the aesthetic area can provide excellent results, by establishing and maintaining facial bone wall and thick soft tissue in aesthetic area.

18. Custom-milled individual allogeneic bone grafts for alveolar cleft osteoplasty—A technical note


INTRODUCTION: Bone grafts from the iliac crest are most commonly used for osteoplasties of the cleft alveolus. To preclude undue donor site morbidity custom-milled allogeneic bone grafts might be an appropriate choice. MATERIAL AND METHODS: This technical note showcases the repair of an alveolar cleft using an individualized allogeneic bone graft in a 36-year old female patient. She was asking for an alternative to the iliac crest bone grafting. Her alveolus was successfully build up by a custom-milled cancellous bone block allograft (maxgraft® bonebuilder). RESULTS: Custom-milled cancellous bone block allografts can greatly facilitate alveolar cleft repair and may present an effective treatment option under the premise that resorption resistance corresponds to autografts. CONCLUSION: Further clinical studies are needed to explore the potential of bone block allografts for alveolar cleft osteoplasty.


OBJECTIVE:

Various biomaterials have been successfully applied in alveolar bone regeneration, however, the reconstruction of extensive osseous defects remains challenging and is often unfeasible with granular grafting materials. Several studies have outlined allogenic bone blocks as valid alternative to autologous block grafting.

CLINICAL CONSIDERATIONS: In this report, we demonstrate the regeneration of two large osseous defects in the maxilla with allogenic bone blocks made from human donor bone. The bone blocks were customized using the CAD/CAM technology in order to enable the insertion of four dental implants.

CONCLUSIONS: Both blocks perfectly matched the defect geometry, showed limited resorption, led to the formation of sufficient amounts of mineralized bone in both horizontal and vertical dimensions and enabled the installation of implants according to the treatment plan. The implementation of innovative technologies for individualization of allogenic bone blocks simplifies the restoration of complex and extensive osseous defects and poses great benefits for both practitioners and patients.

CLINICAL SIGNIFICANCE: The here presented procedure demonstrates the successful regeneration of two extensive osseous defects in a patient suffering from hypodontia using two CAD/CAM manufactured allogenic bone blocks, rendering the procedure far less invasive as compared to guided bone regeneration carried out with autologous transplants. Furthermore, to the best of our knowledge, this is the first case report that radiographically demonstrates the new formation of a cortical bone layer following block grafting with solely cancellous bone blocks.
20. Vertical bone augmentation in a single-tooth gap with an allogenic bone ring: Clinical considerations


OBJECTIVE: The main objective of this case report is to introduce a one-stage bone block augmentation with a cylindrical freeze-dried bone allograft (FDBA) and simultaneous implantation for the reconstruction of a single-tooth bone defect. Clinical Considerations: The report describes this method on the basis of radiographical and clinical images derived from a single patient. CONCLUSIONS: The report demonstrates the time-saving and successful application of this treatment concept, which has the potential to increase patient satisfaction and comfort. CLINICAL SIGNIFICANCE: The application of the presented technique enabled a prosthetic rehabilitation of the extracted tooth about 3 months earlier as compared to the conventional procedure, while demonstrating no compromises regarding clinical outcome, functionality and esthetics.