

## Selezione bibliografica degli studi pubblicati su materiali a base di idrossiapatite in soluzione acquosa.

Clin Oral Implants Res. 2009 Oct;20(10):1078-83. Epub 2009 Jun 10.

### **Sinus augmentation analysis revised: the gradient of graft consolidation.**

Busenlechner D, Huber CD, Vasak C, Dobsak A, Gruber R, Watzek G. Department of Oral Surgery, Medical University of Vienna, Vienna, Austria.

#### **Objective**

Graft consolidation follows a gradient that reflects the properties of bone substitutes at sites of sinus augmentation. This study presents an analytical method to examine the process of graft consolidation in consideration of the instance from the maxillary host bone.

#### **Materials & Methods**

Histological specimens of minipigs harvested 6 and 12 weeks after the sinus augmentation were analysed. The bone substitutes Bio-OssR, a deproteinized bovine bone mineral, and OstimR, an aqueous paste of synthetic nanoparticulate hydroxyapatite, were applied. The changes in histomorphometric parameters within a given distance from the maxillary host bone were presented.

#### **Results**

Three regions of interest were defined: R1 (0 – 1 mm) the bridging distance where new bone is laid onto the host bone, R2 (2 – 3 mm) a region of osteoconduction where new bone exclusively grows on the biomaterial, R3 (4 – 5 mm) and a region of osteoconduction where bone formation has reached its maximal extension. Qualitative and quantitative analysis of the three regions can show differences in graft consolidation, depending on the bone substitutes and the observation period. Bone volume (BV) per tissue volume after 6 weeks: R1: 19.3% for Bio-OssR and 42.9% for OstimR (P = .03), R2: 3.2% for Bio-OssR and 14.7% for OstimR (P = 0.03), R3: 5.4% for Bio-OssR and 5.3% for OstimR (P = 0.86). BV per tissue volume after 12 weeks: R1: 38.0% for Bio-OssR and 53.3% for OstimR (P = 0.04), R2: 14.2% for Bio-OssR and 26.4% for OstimR (P = 0.18), R3: 6.6% for Bio-OssR and 10.7% for OstimR.

#### **Conclusion**

Based on the graft consolidation gradient, the differences of bone substitutes in the process of bone formation and the kinetic of degradation within a distinct region of the augmented sinus can be investigated.

Clin Oral Investig. 2009 Aug 13. [Epub ahead of print]

### **Clinical effects of nanocrystalline hydroxyapatite paste in the treatment of intrabony periodontal defects: A randomized controlled clinical study.**

Heinz B, Kasaj A, Teich M, Jepsen S; Hamburg, Germany **Objective** In this present randomized controlled clinical study the clinical outcomes of papilla preservation flap surgery alone was compared to open flap surgery with additional application of nanocrystalline hydroxyapatite bone substitution material.

#### **Materials & Methods**

Fourteen patients with paired intrabony periodontal defects of  $\geq 4$  mm were included in this split-mouth design study. The defects in each subject were randomly assigned to be treated with a nanocrystalline hydroxyapatite paste in conjunction with papilla preservation flaps or papilla preservation flaps alone. At baseline, during surgery and after 6 months following surgery probing bone levels (PBL) from a customized acrylic stent and probing pocket depths (PPD) were measured. No differences in any of the investigated parameters were observed at baseline between the two groups.

#### **Results**

Both treatments resulted in significant improvements between baseline and 6 months ( $p < 0.05$ ). At 6 months after therapy, the sites treated with nano-HA paste showed a reduction in mean PPD from 8.3  $\pm$  1.2 to 4.0  $\pm$  1.1 mm and a gain in PBL of 4.3  $\pm$  1.4 mm, whereas in the control group, the mean PPD changed from 7.9  $\pm$  1.2 mm to 5.0  $\pm$  1.2 mm and PBL gain was 2.6  $\pm$  1.4 mm. Results demonstrated statistically greater PPD reduction and PBL gain ( $p < 0.05$ ) in the test group as compared with the control group.

#### **Conclusion**

The additional treatment with nanocrystalline hydroxyapatite compared to open flap surgery alone led to significant more favourable clinical improvements in intrabony periodontal defects.

J Oral Sci. 2008 Sep;50(3):279-85.

### **Ability of nanocrystalline hydroxyapatite paste to promote human periodontal ligament cell proliferation.**

Kasaj A, Willershausen B, Reichert C, Rohrig B, Smeets R, Schmidt M. Department of Operative Dentistry and Periodontology, Johannes Gutenberg University, Mainz, Germany.

#### **Objective**

This study was conducted with the aim of investigating the effects of nanocrystalline hydroxyapatite (nano-HA) paste on the proliferation of human periodontal ligament (PDL) cells. In relation to that, alterations in intracellular signaling mechanisms were to be explained.

#### **Materials & Methods**

PDL cells were cultured stimulated either with nano-HA paste or with enamel matrix derivative (EMD) in a soluble form. Proliferation of PDL cells was determined by incorporation of bromodeoxyuridine in the DNA of proliferating cells. In order to understand the signaling mechanisms underlying the increased cell proliferation of PDL cells exposed to nano-HA, the phosphorylation status of the serine/threonine protein kinase Akt, of the signal regulated kinases ERK ½ and of the epidermal growth factor receptor (EGFR) was analyzed by Western blotting using phospho-specific antibodies.

#### **Results**

As compared to the negative control group nano-HA paste as well as EMD promoted the proliferation of PDL fibroblasts. Even though nano-HA paste caused two-fold less cell proliferation than EMD, both substrates enhanced the proliferation rate significantly ( $P < 0.05$ ). The increased proliferation rate of PDL cells in the presence of nano-HA paste was mechanistically linked to activation of the epidermal growth factor receptor (EGFR) and its downstream targets ERK ½ and Akt.

#### **Conclusion**

The study results suggest that nano-HA paste is a stimulator of cell proliferation, thereby possibly supporting the main processes of periodontal tissue regeneration. *Biomaterials*. 2008 Aug;29(22):3195-200. Epub 2008 May 2.

### **Simultaneous in vivo comparison of bone substitutes in a guided bone regeneration model.**

Busenlechner D, Tangl S, Mair B, Fugger G, Gruber R, Redl H, Watzek G. Department of Oral Surgery, Medical University of Vienna, Vienna, Austria.

#### **Objective**

Aim of this study was to establish a preclinical model for guided bone regeneration wherein various bone substitutes can be tested simultaneously in a one-wall defect situation.

#### **Materials & Methods**

To establish the critical size model for regeneration, 8 titanium hemispheres were filled with and without Bio-Oss, a deproteinized bovine bone mineral, Ostim, an aqueous paste of synthetic nanoparticulate hydroxyapatite, and Osteoinductal, an oily calcium hydroxide suspension, before being positioned on the calvaria of minipigs. After 6 and 12 weeks, titanium hemispheres were examined histologically and histomorphometrically.

#### **Results**

In accordance with the documented osteoconductive properties of Bio-Oss and Ostim, titanium hemispheres were almost completely filled with bone. Moreover, the expected degradation profile of Bio-Oss and Ostim could be confirmed by histologic and histomorphometric analysis. Under the same conditions, Osteoinductal failed to exert osteoconductive properties, rather a progressive resorption of the host bone was observed.

#### **Conclusion**

The results show that the preclinical model presented here is suitable to compare simultaneously different bone substitutes. This model based on the titanium hemispheres allows evaluating graft consolidation under standardized conditions thereby avoiding intra-individual variations. *Arch Oral Biol*. 2008 Jul;53(7):683-9. Epub 2008 Mar 5.

### **Human periodontal fibroblast response to a nanostructured hydroxyapatite bone replacement graft in vitro.**

Kasaj A, Willershausen B, Reichert C, Gortan-Kasaj A, Zafiroopoulos GG, Schmidt M. Department of Operative Dentistry and Periodontology, Johannes Gutenberg University, Mainz, Germany.

#### **Objective**

Aim of this study was to determine the effects of a nanostructured hydroxyapatite (NHA) on cellular adhesion, mitogenic responses in human periodontal ligament (PDL) cells and characterized associated changes in cellular signaling pathways.

#### **Materials & Methods**

First step of the test was to stimulate cultured PDL cells with a NHA. Evidence of cell division was made visible by incorporating bromodeoxyuridine in the DNA of the proliferating cells. Furthermore, colorimetric tests were applied to measure changes in adhesion properties of the PDL fibroblasts, among them an analysis of integrin, a protein with cell-connecting properties.

In addition, mechanisms responsible for altered signaling pathways that enhance heightened cell proliferation in PDL cells were revealed by testing the phosphorylation status of the serine/threonine protein kinase Akt and of the signal regulated kinases ERK 1/2.

#### **Results**

Alpha5beta1 was the trigger for a mechanism that led to integrin-mediated cellular adhesion of PDL fibroblasts. The augmentation of PDL cell proliferation mediated by nanostructured hydroxyapatite was generated by activation of the epidermal growth factor receptor (EGFR) pathway and its downstream targets ERK 1/2 and Akt.

#### **Conclusion**

The results indicated that nanostructured hydroxyapatite is an effective stimulator of PDL cell attachment and PDL cell proliferation.

J Periodontol. 2008 Mar;79(3):394-400.

#### **Clinical evaluation of nanocrystalline hydroxyapatite paste in the treatment of human periodontal bony defects – a randomized controlled clinical trial: 6-month results.**

Kasaj A, Rohrig B, Zafiroopoulos GG, Willershausen B. Department of Operative Dentistry and Periodontology, Johannes Gutenberg University, Mainz, Germany.

#### **Objective**

In this study the efficacy of the nanoparticulate hydroxyapatite Ostim (NHA) in intrabony defects was compared to conventional flap surgery alone.

#### **Materials & Methods**

Twenty-eight patients with intrabony defects were included in this study. The defects showed a probing depth of at least 6 mm and radiographic evidence of an intraosseous component  $\geq 3$  mm. Subjects were allocated randomly to one of the two groups: treatment with open flap debridement plus Ostim application (test group, n = 14) or open flap debridement alone (control group, n = 14). At baseline and at 6 months after surgery, the following clinical parameters were recorded by a masked examiner: Plaque index, gingival index, PD, clinical attachment level (CAL) and gingival recession.

#### **Results**

The clinical parameters PD and CAL showed a significant improvement in both treatment groups ( $P < 0.001$ ) 6 months after surgery compared to baseline. At 6 months following therapy, the test group showed a reduction in mean PD from  $7.4 \pm 1.3$  mm to  $3.4 \pm 1.2$  mm and a change in mean CAL from  $8.0 \pm 1.3$  mm to  $4.4 \pm 1.7$  mm, whereas in the control group the mean PD decreased from  $7.4 \pm 0.8$  mm to  $4.9 \pm 0.9$  mm, and mean CAL decreased from  $8.1 \pm 1.2$  mm to  $6.4 \pm 1.3$  mm. The intergroup comparison demonstrated significantly more PD reductions ( $P = 0.012$ ) and CAL gains ( $P = 0.005$ ) in the test group compared to the control group. No complications were observed during the observation period, the postoperative healing was uneventful in all cases.

#### **Conclusion**

Treatment of intrabony periodontal defects with the nanoparticulate hydroxyapatite Ostim resulted in significant clinical improvements compared to open flap debridement alone.

Clin Oral Implants Res. 2007 Dec;18(6):743-51. Epub 2007 Sep 20.

#### **Lateral alveolar ridge augmentation using a synthetic nano-crystalline hydroxyapatite bone substitution material (Ostim): Preliminary Results.**

Strietzel FP, Reichart PA, Graf HL. Department for Oral Surgery and Dental Radiology, Campus Virchow Clinic Charite Centre 3 for Dental Medicine, Charite-Medical University Berlin, Germany

#### **Objective**

The aim of this clinical prospective study was to assess the tissue composition of augmented sites following application of a nano-crystalline hydroxyapatite bone substitution material by clinical and histological examinations.

#### **Materials & Methods**

14 patients requiring lateral ridge augmentation were included in this two-center study. 10 patients were treated 6 to 7 months prior to implant placement, whereas 4 patients received implants and augmentation simultaneously. The

bone substitution material was used without any additives and covered by a titanium mesh for space maintenance. Clinical and radiographic parameters were evaluated. Bone biopsy cores were obtained 6 – 7 months following augmentation and analyzed histologically and histomorphometrically.

#### **Results**

The width of the fixed gingival and the alveolar ridge height did not change significantly at least 6 months following augmentation ( $P > 0.5$ ), whereas a significant gain in alveolar ridge width ( $P = 0.01$ ) was noted. No implant loss was observed during the observation period of approximately 24 months of prosthetic loading. Histology revealed hydroxyapatite remnants in biopsy cores obtained from seven patients after at least 6 months showed no histological symptoms of inflammation. Histomorphometric results of bone cores revealed no significant differences of the mean percentage area of nCHA in peripheral (23.4%) and central (15.1%) parts of biopsy cores ( $P = 0.262$ ).

#### **Conclusion**

The former defect space was filled with bone. The alveolar ridge width gain was found to be significant after lateral augmentation utilizing nCHA, providing a quantitatively and qualitatively sufficient site for primary stable implant placement.

J Biomed Mater Res B Appl Biomater. 2007 Aug;82(2):494-505.

#### **Injectable nanocrystalline hydroxyapatite paste for bone substitution: In vivo analysis of biocompatibility and vascularization.**

Institute for Clinical and Experimental Surgery, University of Saarland, Homburg, Germany.

#### **Objective**

The objective of this study was to investigate in vivo the inflammatory and angiogenic host tissue response to the nanocrystalline hydroxyapatite paste Ostim after implantation into the dorsal skinfold chambers of Syrian golden hamsters. The hydroxyapatite ceramic Cerabone and isogenic transplanted cancellous bone served as controls.

#### **Materials & Methods**

Angiogenesis, microhemodynamics, microvascular permeability, and leukocyte-endothelial cell interaction of the host tissue were analyzed over 2 weeks using intravital fluorescence microscopy. In comparison to Cerabone and the transplanted cancellous bone, Ostim showed comparable biocompatibility. With respect to the angiogenic response cancellous bone induced more neovascularisation than the synthetic materials. However, among the synthetic materials, the implantation of Ostim led to a higher degree of proliferation of vascularized tissue.

#### **Conclusion**

Ostim may optimize the conditions for the formation of new bone at sites of bone defects by supporting a guided vascularization during biodegradation.

Mund Kiefer Gesichtschir. 2007 Aug;11(3):131-7. Epub 2007 Jul 5.

#### **Treatment of jaw cysts with a new kind of nanoparticulate hydroxyapatite**

Gerlach KL, Niehues D. Otto-von-Guericke-Universität Magdeburg, Klinik für Mund-, Kiefer- und Gesichtschirurgie, Magdeburg, Germany.

#### **Objective**

This article reports on the treatment of maxillofacial bone defects with the bone substitute material Ostim. **Materials & Methods**

40 patients with ages ranging between 15 and 80 years were treated with the nanoparticulate, phase-pure hydroxyapatite Ostim in the following indications: odontogenic cysts, odontogenic keratocysts, impacted and ectopic teeth and apicoectomies. On average 3.2 ml of Ostim were used. Wounds were closed saliva-proof. X-ray controls were performed after 3 – 5, 6 resp. 12 months.

#### **Results**

The x-ray control showed a complete osseous integration in defects up to 3 cm after 3 months, in more voluminous defects after 6 months and in particular cases within 12 months. No serious complications were observed.

#### **Conclusion**

Due to the good clinical results with mainly uncomplicated healing, effective resorption and obvious bone regeneration, the use of Ostim can be recommended for the treatment of bone defects originating from jaw cysts and surgical tooth removal.

J Clin Periodontol. 2006 Jul;33(7):491-9.

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

Schwarz F, Bieling K, Latz T, Nuesry E, Becker J. Department of Oral Surgery, Heinrich Heine University, Dusseldorf, Germany.

### **Objective**

The objective of this case series was to assess the healing of intrabony peri-implantitis defects following application of a nanocrystalline hydroxyapatite or a bovine-derived xenograft in combination with a collagen membrane.

### **Materials & Methods**

Twenty-two patients having moderate peri-implantitis (n = 22 intrabony defects) were examined. One half of patients were treated with access flap surgery and the application of Nanocrystalline hydroxyapatite, the other half with access flap surgery and the application of a bovine-derived xenograft in combination with a collagen membrane. Clinical parameters were recorded at baseline and after 6 months of nonsubmerged healing. Postoperative wound healing revealed that NHA compromised initial adhesion of the mucoperiosteal flaps in all patients. At 6 months after therapy, the group treated with nanocrystalline hydroxyapatite showed a reduction in the mean PD from 7.0 ± 0.6 to 4.9 ± 0.6 mm and a change in the mean clinical attachment loss (CAL) from 7.5 ± 0.8 to 5.7 ± 1.0 mm. In the group with the bovine-derived xenograft, the mean PD was reduced from 7.1 ± 0.8 to 4.5 ± 0.7 mm and the mean CAL changed from 7.5 ± 1.0 to 5.2 ± 0.8 mm.

### **Conclusion**

Within the limits of the present case series, the results indicated that both treatment procedures led to clinically important reductions in pocket depths and CAL gains at 6 months after surgery. Both methods improved the healing of intrabony peri-implantitis defects in this case study.

J Oral Maxillofac Surg. 2005 Nov;63(11):1626-33.

### **Bone regeneration in osseous defects using a resorbable nanoparticulate hydroxyapatite.**

Thorwarth M, Schultze-Mosgau S, Kessler P, Wiltfang J, Schlegel KA. Department of Oral and Maxillofacial Surgery/Plastic Surgery, University of Jena, Jena, Germany.

### **Objective**

Aim of this animal study was to compare the regenerative potential in bone defects of a hydroxyapatite bone substitution material alone with a combination of hydroxyapatite and 25% autogenous bone and autogenous bone alone. The regenerative potentials of the tested materials were compared with each other.

### **Materials & Methods**

24 pigs were included in the test. Each obtained nine 1 cm diameter defects in the frontal bone. Three defects were filled with autogenous bone, three with Ostim and three with Ostim combined with 25% autogenous bone. A total observation period of 6 months was selected. Microradiographic and histologic evaluation of the bone specimens was completed at 8 defined times.

### **Results**

Microradiographic images of the 2 bone substitute groups indicated high mineralization rates that were not significantly lower than those found in the autogenous bone reference group. Histologically, there was sufficient Osseointegration and osteoconduction of the used material used in both groups. Complete resorption of the nanoparticle hydroxyapatite had taken place after 12 weeks.

### **Conclusion**

Based on the evaluation of all data it can be concluded that the nanoparticulate hydroxyapatite met the clinical requirements for a bone substitute material within the limits of this experimental setting. Due to its nanocrystalline microstructure, complete resorption took place during the course of this study.

Stomatologija (Mosk). 1998;77(1):31-5.

### **The surgical treatment of jaw cysts using hydroxyapatite with an ultrahigh degree of dispersity.**

Bezrukov VM, Grigor'iants LA, Zuev VP, Pankratov AS. Maxillofacial Surgery and Stomatology Chair of the Russian State Medical University, Moscow, Russia

### **Objective**

Purpose of this study was to assess the clinical efficacy of a nanocrystalline hydroxyapatite in surgical treatment of jaw cysts.

### **Materials & Methods**

In 49 patients ultrahigh dispersed hydroxyapatite in combination with lincomycin was used for filling the bone cavity formed after cystectomy. In controls (n = 43) the postoperative cavity was filled with blood clot. Antimicrobials and oral lincomycin were administered postoperatively.

### **Results**

The results of clinical, x-ray, and radiovisiographic examinations indicate that the use of nanocrystalline hydroxyapatite decreased the incidence of postoperative complications and created the optimal conditions for bone repair at the site of defects of different size. The therapeutic efficacy was most beneficial in patients with former inflamed cysts.

#### **Conclusion**

Ultrahigh dispersion hydroxyapatite formulations are optimal for the treatment of bone cavities after cystectomy with normal height of alveolar process.

Stomatologija (Mosk). 1996;75(5):31-4.

#### **The comparative characteristics of stimulators of reparative osteogenesis in the treatment of periodontal diseases.**

Zuev VP, Dmitrieva LA, Pankratov AS, Filatova NA. Maxillofacial Surgery and Stomatology Chair of the Russian State Medical University, Moscow, Russia

#### **Objective**

Aim of this study was to compare the efficacy of ultra highly dispersed hydroxyapatite and demineralized bone matrix implanted to 395 patients for repair of bone defects.

#### **Materials & Methods**

395 patients were examined of whom 200 patients formed the main group and 195 patients the reference group. During flap surgery the vertical bone defects of the main group were filled with nanocrystalline hydroxyapatite whereas the patients of the reference group received demineralised bone matrix. All patients were examined on days 3, 7 and 21 and also 1, 3 and 6 months after surgery. X-ray examinations, periodontal and gingival indices were determined.

#### **Results**

Nanocrystalline hydroxyapatite seemed to be not inferior to demineralised bone matrix, but does not show its shortcomings. Complications occurred in 1.5% cases but never involved to the site of osteoplasty, whereas in the group with transplanted bone matrix 3.6% of the patients showed complications, which were frequently associated with graft rejection. Nanocrystalline hydroxyapatite was especially effective in the treatment of periodontitis at the stage of abscesses.

#### **Conclusion**

Nanocrystalline hydroxyapatite is convenient and recommended in combination with guided tissue regeneration membranes for surgical treatment of patients with periodontal diseases.

#### **The use of hydroxyapatite with ultrahigh dispersity in the combined treatment of patients with mandibular fractures.**

Pankratov AS, Zuev VP, Alekseeva AN. Maxillofacial Surgery and Stomatology Chair of the Russian State Medical University, Moscow, Russia

#### **Results**

Such implantations were found easy to perform, well tolerated by the patients, and causing no side effects. The incidence of complications in this group was by 6.78% lower than in controls treated by the traditional methods alone and by 7.16% lower than in all patients with mandibular fractures treated over a year. The mean disability period was reduced by 4.8 days when this preparation was used.

#### **Conclusion**

This clinical study confirms the efficacy of Ostim in the treatment of patients with mandibular fractures showing that the implantation was easy to perform; the material was well tolerated by patients and did not cause any adverse reactions. Compared to the control group, the utilization of Ostim reduced the period of disability and accelerated bone healing.

#### **Objective**

Aim of this study was to analyse the clinical effect of ultrahighly dispersed hydroxyapatite (Ostim) in the complex treatment of patients with mandibular fractures.

#### **Materials & Methods**

125 patients with various mandibular fractures were analysed. 65 patients were treated additionally with Ostim. The other 60 patients received conventional treatment without Ostim. Both groups were constantly followed up during the treatment period. This included laboratory tests as well as X-ray examinations, which were performed on admission, 2 – 4 days after treatment and on the 21st, 28th and 35<sup>th</sup> day after trauma. Stomatologija (Mosk). 1995;74(4):22-5.