NanoBone®

Bibliography

Bone Formation in a New Dimension

Bibliografie

Knochenaufbau in neuer Dimension

artoss

Important notice:
The package insert provided by us sets out procedures for the application of **NanoBone®**. The following applications may deviate from the package insert. The physician is responsible for the choice of procedure. The manufacturer is not liable should an unsuitable procedure be chosen.

Hinweis:
Für die Anwendung von **NanoBone®** ist die von uns herausgegebene Gebrauchsanleitung maßgeblich. Die im Folgenden dargestellten Anwendungen können von der Gebrauchsanleitung abweichen. Die Auswahl der Behandlungsmethode obliegt eigenverantwortlich dem Behandler. Eine Haftung durch den Hersteller ist bei Auswahl einer nicht geeigneten Behandlungsmethode ausgeschlossen.

Canullo L, Patacchia O, Sisti A, Heinemann F

Implant Restoration 3 months after One Stage Sinus Lift Surgery in Severely Resorbed Maxillae: 2-Year Results of a Multicenter Prospective Clinical Study

Clin Implant Dent Relat Res 2010, in press

Objectives: This multicenter prospective study was aimed to clinically evaluate implant behavior inserted in severely resorbed maxillae and restored 3 months after sinus grafting.
Materials and Methods: In three clinical centers, 67 totally rough wide diameter implants were inserted during 30 consecutive sinus lifts. Computed tomography and panoramic analysis were preoperatively requested for each patient. Sinus grafting was performed using a nano-crystalline hydroxyapatite sole bone filler; no membrane was used to cover the buccal window. Preoperative residual bone height ranged between 1–4 mm (mean value: 2.70 mm, standard deviation [SD]: 0.9 mm). Uncovering procedure was carried out following 3 months of healing; 2 weeks later, a definitive restoration was seated using platform switching concept. To monitor stability changes, resonance frequency analysis was performed and implant stability quotient (ISQ) values were collected at the first surgery (baseline, T0), at the abutment connection (T1), and at 2-year follow-up (T2). To measure bone changes, patients underwent panoramic analysis after 2-year follow-up. The image analysis software calculated the grafted bone height changes at level of implant site comparing pre-operative and follow-up panoramic films; the software compensated for eventual radiographic distortion.
Results: Mean ISQ value was 35.7 (SD: 8.8) at baseline, 66.61 (SD: 4.76) at T1, and 77.9 (SD: 4.7) at T2. Statistically significant differences (p 2 0.005) regarding ISQ mean values were found between T1 and T0, as well as between T1 and T2. After 24 months of functional loading, only two implants were lost (cumulative survival rate: 97%). During the same observation period, the mean value of radiographic vertical height of grafted sinus was 13.75 mm (SD = 1.3 mm), with a mean gain of 11 mm.
Conclusions: Within the limits of this study, despite of preoperative residual bone height ranging 1 to 4 mm and absence of the membrane covering the buccal bone wall, maxillary sinus lift restoration 14 weeks after first surgery seems to be a reliable procedure using totally-rough surfaced implants restored using platform switching concept and nano-structured hydroxyapatite as sole bone filler.

Heinemann F, Mundt T, Biffar R, Gedrange T, Götz W

A 3-year clinical and radiographic study of implants placed simultaneously with maxillary sinus floor augmentations using a new nanocrystaline hydroxyapatite

J Physiol Pharmacol 2010, in press

The aims of this case series was to evaluate the success rate of implants and their restorations, the sinus bone graft resorption, and the marginal bone loss around the implants when nanocristalline HA embedded in a silica matrix was exclusively used as grafting material. In 13 partially edentulous patients of a private practice having missing teeth in the posterior maxilla and a subantral bone height between 3 and 7 mm, 19 sinus augmentations (100% **NanoBone®**, Artoss, Rostock, Germany) by the lateral lift technique were performed. The implants (Tiolox/ Tiologic Implants, Dentaurum, Ispringen, Germany) were simultaneously placed. After 6 to 9 months 37 implants were restored with fixed dental prostheses. The radiographic bone heights over time were estimated with linear mixed models. The implant success rate was 100% after three years. The mean rates of the marginal bone loss over the first year were higher (mesial: -0.55, distal: -0.51 mm) than the annual rates thereafter (mesial:-0.09 mm, distal: -0.08 mm). The mean rates of changes in the total bone height were neglectable (< 0.2 mm) and not significant. The prosthodontic and esthetic evaluation revealed a successful outcome. Within the limits of this clinical report it may be concluded that maxillary sinus augmentation using 100% nanocristalline HA embedded in a silica matrix to support implants is a reliable procedure.

Klein MO, Gotz H, Duschner H, Wagner W

Knöcherne Integration eines alloplastischen Knochenersatzmaterials (NanoBone®) im Sinuslift

Bony integration of an alloplastic bone substitute material (**NanoBone®**) after maxillary sinus augmentation

Z Zahnärztl Impl 2009; 25 (4):20-28

Moderne Knochenersatzmaterialien (KEM) müssen zahlreichen strukturellen und biologischen Anforderungen gerecht werden. Entsprechend groß ist der Stellenwert morphologischer in vitro Analysen und histomorphometrischer ex vivo Untersuchungen zur Abschätzung der Biokompatibilität. Ziel der Untersuchung war die entsprechende Beurteilung eines modernen alloplastischen KEM (**NanoBone®**). Die strukturelle in vitro Analyse des nativen Knochenersatzmaterials erfolgte mittels Rasterelektronenmikroskopie und Mikrocomputertomographie (µ-CT) unter besonderer Berücksichtigung der Porosität. 14 Monate nach erfolgter Sinuslift- Operation mit **NanoBone®** und aufgefangenen autologen Bohrspänen bei einem einzelnen Patientenfall wurde eine repräsentative Trepanbiopsie des Augmentates gewonnen und histomorphometrisch durch konventionelle Dünnschliffhistologie sowie durch µ-CT untersucht. Über eine Analyse der 2D-Phasenverteilung der Dichte konnten die Volumenanteile neugebildeten Knochens und residualer KEM-Partikel bestimmt werden. Das in vitro untersuchte Knochenersatzmaterial zeigte eine kantige Makrostruktur mit einer Gesamtporosität von > 65 % sowie einem hohen Anteil großvolumiger Poren > 250 µm, welche sich fast ausschließlich interpartikulär befanden. Die histomorphometrische Analyse des gewonnenen Knochenzylinders bot eine gute knöcherne Integration des Knochenersatzmaterials mit Zeichen der Resorption mit Ersatz durch vitales Knochengewebe nach 14 Monaten. Der Volumenanteil neugebildeten Knochens betrug 37 %. Die hier vorgestellten Methodiken zur präklinischen und klinischen Beurteilung moderner Knochenersatzmaterialien ergänzen sich sinnvoll.

Modern bone substitute materials (BSM) have to meet numerous structural and biological requirements. Accordingly, morphological in vitro analysis and histomorphometric ex vivo investigations are of great significance to estimate BSM biocompatibility. Aim of the study was a respective evaluation of a modern alloplastic BSM (NanoNone). Structural in vitro analysis of the native BSM was carried out by electron microscopy and microcomputed tomography (µ-CT) with special regard to porosity. 14 months after maxillary sinus augmentation with **NanoBone®** and collected autologous bone particles in one individual patient case, a representative trephine biopsy out of the augmentation volume was histomorphometrically analysed employing conventional histology and µ-CT. Volume ratios of newly formed bone and remaining BSM particles were calculated via assessment of 2-D phase distribution of tissue density. In vitro investigation of the BSM showed a chiselled macrostructure with a total porosity of > 65 % as well as a high ratio of pores > 250 µm, which were almost exclusively localized interparticulary. Histomorphometric analysis of the trephine biopsy revealed a good bony integration of the BSM with evidence of BSM resorption and replacement by vital bone tissue after 14 months. The volume ratio of newly formed bone was 37 %. The presented methods for pre-clinical and clinical evaluation of modern BSM complement one another in a reasonable manner.

Mertens C, Steveling H

Use of Synthetic Bone Blocks as an Alternative to Autologous Bone Block Grafts

Implants, International Magazine of Oral Implantology 2009; 4:30-32

In modern implantology, correct three-dimensional positioning of implants, as well as sufficient bone material are of great importance in order to reach satisfactory and predictable results. Resorption processes, traumatic tooth losses or chronic inflammatory processes such as chronic periodontal diseases, however, often result in severe reduction of bone material. If affected areas are intended to serve as implant beds, augmentation will often be required during the same or in a previous intervention. While autologous bone is still considered to be the gold standard, bone substitute materials have proven successful particularly in cases of rather small defects. Their use may decrease patient's morbidity, shorten treatment duration and reduce treatment costs. However, if the defect exceeds a certain size, autologous bone grafts will have to be used, usually in the form of blocks. Intraoral bone

removal poses the problem of limited availability. Extraoral donor sites, however, require treatment under general anesthesia or under in-patient conditions, which is why patients frequently reject this type of surgery. In particular in cases of edentulism in the molar and premolar region, patients tend to prefer fixed dental prostheses, however, the problem of a significantly narrowed alveolar ridge often occurs in the molar area of the mandible.
The use of the **NanoBone® | block** (Artoss, Germany) constitutes a possible alternative to autologous bone blocks. The nanocrystalline material, that has already proven reliable in many trials in a particulate form, has been available on the market in the form of blocks for a short time. Preclinical trials using animal models have shown high rates of bone formation within a relatively short period of time. The following follow-up observation was initiated to find out whether the bone substitute material used in the form of blocks proves successful as a possible alternative to autologous bone.
The nanocrystalline blocks used constitute a possible alternative to autologous bone blocks. The block provides a sufficient primary stability to be used safely for augmentation. The clinical procedure, however, differs from the use of e.g. autologous blocks removed from the retromolar space. The special structure of the block provides for the complete osseointegration of the augmentation materialand thus for a sufficient gain in volume for safe implantation

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Meier J
Experiences with the nanostructured bone substitute NanoBone™ in particular and block form: Prospective histological and clinical trial with 3 years follow-up
EAO 18th International Meeting Monaco 2009, Poster 245

This study presents the results of different augmentation procedures using the new and nanostructured bone substitute (BS) **NanoBone™** with special regard to the histologic features and demonstrates that former therapy protocols can be changed to remarkable shorter healing periods which can be carried out with reliable results. The structural changes were analysed histologically and the cellular ingrowth of bone forming cell lines and blood vessels could be verified. Based on 86 sinus floor elevations (SFE) and 75 lateral augmentations (LAT) performed on average 3 or more years ago there is no measurable difference in bone height and dimension. Histomorphometry of SFE samples showed about 40 vol.% of de novo bone formation after only 2-3 months which must be compared to other BS.
The preliminary results following augmentations with **NanoBone Blocks™** are encouraging and suggest that this might be a way to abandon the transplantation of bone blocks of other origin.

Xu W, Holzhüter G, Sorg H, Wolter D, Lenz S, Gerber T, Vollmar B
Early matrix change of a nanostructured bone grafting substitute in the rat.
J Biomed Mater Res B Appl Biomater. 2009 Nov; 91(2):692-9

A nanocrystalline bone substitute embedded in a highly porous silica gel matrix (**NanoBone®**) has previously been shown to bridge bone defects by an organic matrix. As the initial host response on the bone graft substitute might be a determinant for subsequent bone formation, our present purpose was to characterize the early tissue reaction on this biomaterial. After implantation of 80 mg of **NanoBone®** into the adipose neck tissue of a total of 35 rats, grafts were harvested for subsequent analysis at days 3, 6, 9, 12, and 21. The biomaterial was found encapsulated by granulation tissue which partly penetrated the implant at day 3 and completely pervaded the graft at day 12 on implantation. Histology revealed tartrate-resistant acid phosphatase (TRAP)-positive giant cells covering the biomaterial. ED1 (CD68) immunopositivity of these cells further indicated their osteoclast-like phenotype. Scanning electron microscopy revealed organic tissue components within the periphery of the graft already at day 9, whereas the central hematoma region still presented the silica-surface of the biomaterial. Energy dispersive X-ray spectroscopy further demonstrated that the silica gel was degraded faster in the peripheral granulation tissue

than in the central hematoma and was replaced by organic host components by day 12. In conclusion, the silica gel matrix is rapidly replaced by carbohydrate macromolecules. This might represent a key step in the process of graft degradation on its way toward induction of bone formation. The unique composition and structure of this nanoscaled biomaterial seem to support its degradation by host osteoclast-like giant cells.

Reichert C, Al-Nawas B, Smeets R, Kasaj A, Götz W , Klein MO
In vitro proliferation of human osteogenic cells in presence of different commercial bone substitute materials combined with enamel matrix derivatives
Head & Face Medicine 2009, 5:23

Background: Cellular reactions to alloplastic bone substitute materials (BSM) are a subject of interest in basic research. In regenerative dentistry, these bone grafting materials are routinely combined with enamel matrix derivatives (EMD) in order to additionally enhance tissue regeneration.
Materials and methods: The aim of this study was to evaluate the proliferative activity of human osteogenic cells after incubation over a period of seven days with commercial BSM of various origin and chemical composition. Special focus was placed on the potential additional benefit of EMD on cellular proliferation.
Results: Except for PerioGlas®, osteogenic cell proliferation was significantly promoted by the investigated BSM. The application of EMD alone also resulted in significantly increased cellular proliferation. However, a combination of BSM and EMD resulted in only a moderate additional enhancement of osteogenic cell proliferation.
Conclusion: The application of most BSM, as well as the exclusive application of EMD demonstrated a positive impact on the proliferation of human osteogenic cells in vitro. In order to increase the benefit from substrate combination (BSM + EMD), further studies on the interactions between BSM and EMD are needed.

Punke C, Zehlicke T, Boltze C, Pau HW
Investigation of a new highly porous hydroxyapatite matrix for obliterating open mastoid cavities - application in guinea pigs bulla
Laryngorhinootologie 2009 Apr; 88(4):241-6

Background: Many different techniques for obliterating open mastoid cavity have been described. The results after the application of alloplastic materials like Hydroxyapatite and Tricalciumphosphate were poor due to long-lasting resorption. Extrusion of those materials has been described. We investigated the applicability of a new high-porosity ceramic for obliterating large open mastoid cavities and tested it in an animal model (bulla of guinea pig).
Methods: A highly porous matrix (**NanoBone®**) bone-inductor fabricated in a sol-gel-technique was administered unilaterally into the opened bullae of 30 guinea pigs. In each animal the opposite bulla was filled with Bio-Oss, a bone substitute consisting of a portion of mineral bovine bone. Histological evaluations were performed 1, 2, 3, 4, 5 and 12 weeks after the implantation.
Results: After the initial phase with an inflammatory reaction creating a loose granulation tissue, we observed the formation of trabeculare bone within the fourth week in both groups. From the fifth week on we found osteoclasts on the surface of **NanoBone®** and Bio-Oss with consecutive degradation of both materials.
Conclusion: In our animal model study we found beneficial properties of the used bone-inductors **NanoBone®** and Bio-Oss for obliterating open mastoid cavities.

Canullo L, Vozza I, Caricato F, Dellavia C
Maxillary sinus floor augmentation using a nano-crystalline hydroxyapatite silica gel
A prospective study—Histological results after 3 months of healing
Implants, International Magazine of Oral Implantology 2009; 2:24-27

Background: The aim of this prospective study was to evaluate tissue composition of augmented maxillary sinus floor 3 months after using of a nano-crystalline hydroxyapatite bone substitute. Histological analysis and bone-to-implant contact (BIC) assessment between the grafting material and inserted miniimplant were achieved.
Methods: Five patients (2 men and 3 women) in need for fixed implant-supported prosthesis in the posterior maxillae were consecutively recruited for the present study. Preoperatively, computerized tomography and digital panoramic examinations were acquired for antral anatomy evaluation. A rectangular or oval-shaped osteotomy was then prepared on the lateral aspect of the alveolar ridge under copious normal saline irrigation. The resulted detached "window" was elevated medially and apically while simultaneously reflecting the sinus membrane. **NanoBone®** mixed with antibiotic solution was placed incrementally at the superior aspect of the sinus and against the medial aspect of the grafted compartment created in the sinus cavity. A mini screw for osteosynthesis of 1.2 mm diameter and 13 mm in length was then positioned to maintain the space opened. After a 3 month healing period , a bioptical core containing the mini-implant was retrieved using a 3 mm trephine bur. In the same surgical step, implants were inserted. After 3 months of submerged healing, implants were restored.
Results: After 3 months of healing, varying amounts of newly formed bone were found through the specimens. From the histomorphometric analysis, **NanoBone®** residuals accounted for 47.35 % ± 5.20 % of the extracted bone volume, marrow spaces presented 19.30 % ± 3.20 % and bone occupied 33.35 % ±4.1 % (new bone: 22.23 % ± 4.10 %, and native bone: 11.12 % ± 4.20 %). Well-mineralized regenerated bone with lamellar parallel-fibred structure and Haversian systems surrounded the residual **NanoBone®** particles. Mean BIC was 17.75 % ± 2.9 %. No connective tissue was observed at the implant boundary surface.
Conclusion: Within the limits of this clinical prospective study, it can be concluded that nano-crystalline hydroxyapatite bone substitute showed good histological outcomes for augmenting maxillary sinus floor in critical bone volume conditions. Furthermore, the absence of covering membrane and 3-month healing period could clinically demonstrate the potential of this grafting biomaterial. In such a critical condition the use of a rough-surfaced mini-implant showed BIC values supposed to be effective also in case of functional loading.

Stübinger S, Ghanaati S, Orth C, Hilbig U, Saldamli B, Biesterfeld S, Kirkpatrick CJ, Sader RA
Maxillary sinus grafting with a nano-structured biomaterial: preliminary clinical and histological results.
Eur Surg Res. 2009;42(3):143-9. Epub 2009 Jan 29.

Background: In this study the potential of a new and entirely synthetic, nano-structured hydroxyapatite-based biomaterial for sinus floor augmentation is evaluated.
Methods: 20 sinus floor elevations were carried out in a total of 20 patients. After a healing period of 6 months, in 10 cases cylinder-shaped bone biopsies were taken from the augmented maxillary region using trephine burs.
Results: The healing period progressed without any complications. General and specific histological analysis of the bone biopsies showed a high osteoclast activity at the margin of the biomaterial which was well integrated into the newly formed bone.
Conclusion: This study demonstrates that new trabecular bone is formed after grafting with the nanocrystalline bone substitute after 6 months. Ongoing histomorphological studies are necessary to quantify the biomaterial-bone ratio and the exact amount of newly built bone in the augmented cavity after 6 months.

Canullo L, Dellavia C
Sinus lift using a nano-crystalline hydroxyapatite silica gel in severely resorbed maxillae: histological preliminary study
Clin Implant Dent Relat Res 2009 Oct; 11 Suppl 1:e7-13. Epub 2009 Feb 13

Objectives: The aim of this prospective study was to evaluate histologically, radiographically and clinically a new nano-structured hydroxyapatite in maxillary sinus floor grafting in severely resorbed maxillae. Materials and methods: A total of 33 totally length micro-textured implants were placed during 16 consecutive sinus lift. No membrane was used to close the buccal window. Preoperative residual bone level ranged between 1-3 mm (mean value of 2.03 mm). After 3-4 months of healing, definitive restorations were seated using platform switching concept. Results: After 18 months of functional loading, no implant was lost. During the same observation period, the mean value of radiographic vertical height of grafted sinus floor was 14.2 mm (SD=0.505 mm) and the mean value of grafted bone filler absorption rate was 4.4 % (SD=0.456 mm). Histological analysis showed significant new bone formation, and remodeling of the grafted material. In the cores obtained at 5 months, regenerated bone, residual **NanoBone**® and bone marrow occupied respectively 48±4.63 %, 28±5.33 % and 24±7.23 % of the grafted volume. In the specimens taken 3 months after grafting, mean new bone was 8±3.34 %, mean **NanoBone**® was 45±5.10 % and mean bone marrow was 47±6.81 % of the bioptical volume. Conclusions: Within the limits of this study, it was concluded that grafting of maxillary sinus using nano-structured hydroxyapatite as only bone filler is a reliable procedure also in critical conditions.

Abshagen K, Schrodi I, Gerber T, Vollmar B
In vivo analysis of biocompatibility and vascularization of the synthetic bone grafting substitute NanoBone®
J Biomed Mater Res A 2009 Nov; 91(2):557-66

One of the major challenges in application of bone substitutes are adequate vascularization and biocompatibility of the implant. Thus, the temporal course of neovascularization and the microvascular inflammatory response of implants of **NanoBone**® (fully synthetic nanocrystalline bone grafting material) were studied in vivo by using the mouse dorsal skinfold chamber model. Angiogenesis, microhemodynamics and leukocyte-endothelial cell interaction were analyzed repetitively after implantation in the center and in the border zone of the implant up to 15 days. Both **NanoBone**® granules and plates exhibited high biocompatibility comparable to that of cancellous bone, as indicated by a lack of venular leukocyte activation after implantation. In both synthetic **NanoBone**® groups, signs of angiogenesis could be observed even at day 5 after implantation whereas granules showed higher functional vessel density compared with **NanoBone**® plates. The angiogenic response of the cancellous bone was markedly accelerated in the center of the implant tissue. Histologically, implant tissue showed an ingrowth of vascularized fibrous tissue into the material combined with an increased number of foreign-body giant cells. In conclusion, **NanoBone**®, particularly in granular form, showed high biocompatibility and high angiogenic response, thus improving the healing of bone defects. Our results underline, that beside the composition and nanostructure, also the macro-structure is of importance for the incorporation of the biomaterial by the host tissue.

Kruse A, Jung RE, Nicholls F, Zwahlen RA, Hämmerle CHF, Grätz KW, Weber FE
Comparison of synthetic HA/SiO_2 matrix and bovine derived HA
EAO 17th International Meeting Warszaw 2008, Poster 243

Background: The substitution of autologous bone with synthetic materials for the treatment of bone defects is still a challenge. Calcium phosphate salts, like hydroxyapatite, are often used to develop synthetic bone substitutes since they are main constituent of natural bone material. During synthesis, most synthetic bone substitutes are sintered

yielding in a more compact and less porous material, where osteoconductivity can be reduced. **NanoBone®**, is a non-sintered nanocristaline hydroxyapatite embedded in a high porous silica gel matrix. In order to guarantee a high osteoinductive property and a biodegradability, the granula are loosely packed and present a porosity >50 %.
Purpose: The aim of the present study was to test whether or not a synthetic hydroxyapatite/silica oxide based bone substitute material (**NanoBone®**) enhances bone regeneration compared to a xenogenic hydroxyapatite based bone substitute material (BioOss®) or empty control sites.
Material and methods: A rabbit calvarial defect model was used to compare the different bone substitute materials. The handling characteristics of both materials was similar. The samples were embedded Goldner Trichrome stained and middle sections were used fo evaluation. In none of the sections any signs of inflammation was detectable.
Results: Bone tissue in the defect: The results of the histomorphometric analysis revealed a significant difference between the percentages between bone formed in the empty and the synthetic hydroxyapatite/silica oxide based granules group. Bone bridging: Bony bridging is the percentage of the defect where new bone has occurred. The box-plot shows median, the standard deviation and the 95 %-confidence interval (red box). The P values determined by an ANOVA according the Fisher least significant difference Post hoc procedure showed a highly significant increase in bone bridging when the untreated defect group was compared to the group treated with synthetic hydroxyapatite/silica oxide based granules (P=0.032). When these two groups were compared by a paired t-test the difference was still significant (P=0.067). Both materials show a excellent bone integration.
Conclusion: Compared to empty defects: significantly more bone forms if the defects are treated with synthetic hydroxyapatite/silica oxide granules (**NanoBone®**) significantly more of the defect is bridged by bone when synthetic hydroxyapatite/silica oxide granules are applied (**NanoBone®**). In this in vivo model system no significant difference is seen between hydroxyapatite/silica oxide granules (**NanoBone®**) and xenogenic hydroxyapatite based material (BioOss®).

Lenz S, Kirchhoff M, Gerber T
Enhanced osseointegration of implants with a nanostructured bioactive coating
EAO 17th International Meeting Warszaw 2008, Poster 391

Objectives: In this study we tried to investigate weather it is possible to use the properties of the bone grafting material **NanoBone®** for coating of dental implants to improve their osseointegration.
Material and methods: The implants (group A: Semados®, sand blasted surface, group B ixx2®, sand blasted and acid etched surface) were coated with a silica matrix covering nanocrystalline hydroxyapatite by sol-gel technique. The implants showed differences in screw thread and roughness. Coated (n=18) and uncoated (n=18) implants were inserted in the frontal bone of 8 minipigs. Specimens were excised after 2, 4 and 6 weeks and processed according to the sawing and grinding technique. The bone to implant contact (BIC) was measured by semiautomatic software.
Results: All coated implants showed a higher rate of BIC compared to the uncoated implants. The mean percentage of BIC for coated implants group A was 60.2 %-2 weeks, 66.6 %-4 weeks, and 74.5 %-6 weeks. The uncoated implants of this group reached 57.0 %-2 weeks, 61.3 %-4 weeks and 64.4 %-6 weeks. In group B the BIC was 73.4 %-2 weeks, 70.6 %-4 weeks and 78.0 % for the coated ones. The uncoated implants in this group reached a BIC of 68.5 %-2 weeks, 60.9 %-4 weeks and 45.8 %-6 weeks.
Conclusion: The applied coating of implants enhances the BIC. Earlier loading of such modified implants can be considered.

Meier J, Wolf E, Bienengräber V

Einsatz des synthetischen nanostrukturierten Knochenaufbaumaterials NanoBone® bei Sinusbodenelevation

Implantologie 2008;16(3):301-314

Ziel der vorliegenden Untersuchung war die Evaluierung des Knochenanbaus (Modeling), Knochenumbaus (Remodeling) und des Verlaufs der Biodegradation des neuen Knochenaufbaumaterials **NanoBone®** im Rahmen einer prospektiven klinisch-histomorphologischen Studie. Eingeschlossen sind die Daten von 17 Patienten, bei denen **NanoBone®** zur Sinusbodenelevation als Knochenaufbaumaterial bei zweizeitiger Vorgehensweise zum Einsatz kam. Auswahlkriterium war eine subantrale Knochenhöhe unter 5 mm. Der Zweiteingriff zur Implantatinsertion erfolgte nach acht bis elf bzw. 12 bis 15 Wochen, hierbei wurden zur histologischen Aufarbeitung 43 Knochenzylinder gewonnen, die mittels Hartschnitt- bzw. Trenn-Dünnschliff-Technik bearbeitet wurden. Klinisch fand sich eine solide Ossifikation mit Knochenqualitäten von D1 bis D2. Dem entsprach das histologische Bild mit einer ausgeprägten Hyperostose. Die Resorption von **NanoBone®** und die Knochenneubildung laufen parallel ab. Somit erfüllt **NanoBone®** die Kriterien für ein Knochenaufbaumaterial und verhält sich nach der Augmentation im Sinus wie transplantierter autologer Knochen. Der im Vergleich zu anderen Knochenersatzmaterialien deutlich raschere knöcherne Umbau liefert bereits nach drei Monaten ein solides Lager für eine primär stabile Implantatinsertion im augmentierten Sinus. Durch die zeitnahe Implantation und eine frühzeitige funktionelle Belastung der Implantate tritt kein Volumenverlust ein.

This prospective study evaluated the structural changes (modeling and remodeling) as well as the biodegradation of the new bone grafting material **NanoBone®** based on clinical and histologic investigation. Sinus floor elevations were performed on 17 patients using a two-stage protocol when the subantral bone height was less than 5 mm. The 43 bone samples were collected during implant placement, which was carried out after healing periods of 8–11weeks (group I) or 12–15 weeks (group II), and subjected to undecalcified tissue processing by applying a hard specimen cutting-grinding technique. The clinical findings showed a solid ossification with bone qualities of D1 or D2, that could be verified in the histologic sections showing impressive hyperostosis. The resorption of **NanoBone®** and the de novo bone formation took place simultaneously, similar to the processes following transplantation of autogenous cancellous bone. Compared with other bone substitutes, we observed an accelerated organization and new bone formation that, after only 3 months, yielded a solid bony layer for primary stable implant placement in the augmented maxillary sinus. Early implantation and functional loading stimulated the new bone and prevent a los.

Götz W, Gerber T, Michel B, Lossdörfer S, Henkel KO, Heinemann F

Immunohistochemical characterization of nanocrystalline hydroxyapatite silica gel (NanoBone®) osteogenesis: A study on biopsies from human jaws

Clin Oral Impl Res 2008; 19;1016-26

Bone substitute biomaterials may be osteogenic, osteoconductive or osteoinductive. To test for these probable characteristics in a new nanoporous grafting material consisting of nanocrystalline hydroxyapatite embedded in a porous silica gel matrix (**NanoBone®**), applied in humans, we studied biopsies from 12 patients prior to dental implantation following various orofacial augmentation techniques with healing times of between 3.5 and 12 months. Sections from decalcified specimens were investigated using histology, histochemistry (PAS, alcian blue staining, TRAP) and immunohistochemistry with markers for osteogenesis, bone remodelling, resorption and vessel walls (alkaline phosphatase, bone morphogenetic protein-2, collagen type I, ED1, osteocalcin, osteopontin, runx2, vWF). Histologically, four specific stages of graft transformation into lamellar bone could be characterized. During early stages of healing, bone matrix proteins were absorbed by **Nanobone®** granules, forming a proteinaceous matrix, which was invaded by small vessels and cells. We assume that the deposition of these molecules promotes early osteogenesis in and around **NanoBone®** and supports the concomitant degradation probably by

osteoclast-like cells. TRAP-positive osteoclast-like cells were localized directly on the granular surfaces. Runx2-immunoreactive pre-osteoblasts, which are probably involved in direct osteogenesis forming woven bone which is later transformed into lamellar bone, were attracted. Graft resorption and bone apposition around the graft granules appear concomitantly. We postulate that **NanoBone®** has osteoconductive and biomimetic properties and is integrated into the host's physiological bone turnover at a very early stage.

Punke C, Zehlicke T, Boltze C, Pau H-W
Experimental Studies on a New Highly Porous Hydroxylapatite Matrix for Obliterating Open Mastoid Cavities
Otol Neurotol 2008 Sep; 29(6):807-11

Objective: In an initial preliminary study, the applicability of a new high-porosity hydroxyapatite (HA) ceramic for obliterating large open mastoid cavities was proven and tested in an animal model (bulla of guinea pig).
Study Design: Experimental study.
Methods: **NanoBone®**, a highly porous matrix consisting of 76 % hydroxylapatite and 24 % silicone dioxide fabricated in a sol-gel technique, was administered unilaterally into the opened bullae of 30 guinea pigs. In each animal, the opposite bulla was filled with Bio-Oss, a bone substitute consisting of a portion of mineral bovine bone. Histologic evaluations were performed 1, 2, 3, 4, 5 and 12 weeks after the implantation.
Results: After an initial phase in which the ceramic granules surrounded by inflammatory cells (1Y2 wk), there were increasing signs of vascularization. Osteoneogenesis and – at the same time - resorption of the HA ceramic were observed after the third week. No major difference in comparison to the bovine bone material could be found.
Discussion: Our results confirm the favorable qualities of the new ceramic reported in association with current maxillofacial literature. Conventional HA granules used for mastoid obliteration to date often showed problems with prolonged inflammatory reactions and, finally, extrusions. In contrast to those ceramics, the new material seems to induce more osteoneogenesis and undergoes early resorption probably due to its high porosity. Overall, it is similar to the bovine bone substance tested on the opposite ear in each animal. Further clinical studies may reveal whether **NanoBone®** can be an adequate material for obliterating open mastoid cavities in patients.

Harms C, Helms K, Taschner T, Stratos I, Gerber T, Lenz S, Vollmar B, Mittlmeier T
Histomorphometric and micro-CT analysis of the osteoneogenic capacity in the metaphysis of the sheep after implantation of nanocristalline bone grafting substitute NanoBone™
Chirurgisches Forum 2008, Band 37; 253:255

Abstract: Autologous cancelous bone transplantation is today the gold standard to substitute large bone defects. However a high rate of transplantmorbidity and a limited transplant availability reduce the use of this therapy. The synthetic material **NanoBone™** (hydroxylapatit nanocristallines embedded in a porous silica gel matrix) has been shown to have in vivo osteoconductive properties on desmal bone. Up to now positive clinical experience with **NanoBone™** has been reported after ventral body fusions and in mandibular surgery. Goal of our study was to examine in vivo the applicability of **NanoBone™** on long bones, using a standardized bone defect model for the sheep tibial metaphysis. Therefore we used 18 full-grown sheep and milled a 1.05 cm^3 standardized defect under the articular surface of the medial tibia condyles on both hind legs. The defect on the right was filled up with **NanoBone™** and the defect on the contralateral leg was left empty. Because of the compact cancelous structure of the tibia head and the integrity of the lateral condyles, a further stabilization was not needed. The defect was partially loaded under full load of the hind leg. Animals were sacrificed after 6 weeks (n = 6), 12 weeks (n = 6) and 26 weeks (n = 6). Operated bones were explanted, taken into account their periostal integrity. Specimens were macroscopically and microscopically analyzed. Radiographic analysis was performed bymeans of X-ray, macro- and micro-CT. By compiling the volume distribution and radiographic density from the micro-CT data, a minimal value for osteoneogenesis was calculated. Upon decalcification samples were histomorphometrically analyzed.

The histological and radiological analysis of the defect on the left control-side showed no bone formation after 6, 12 and 26 weeks. In contrast, the micro-CT analysis of the right with **NanoBone™** filled defect showed a 55 % volume fraction of structures with bone density. Furthermore the quantitative histochemichal analysis of 6 weeks revealed an osteoneogenesis of 22 % and of 12 weeks 34 %. After 12 weeks the micro-CT analysis showed an increase of the structures with bone density to 72 % and after 26 weeks to 74 %. HE-sections demonstrated multinucleated giant cells on the surface of the biomaterial and resorption lacunae, indicating resorption by osteoclasts. In conlusion **NanoBone™** is a highly potent bone replacement material with osteoconductive properties in sheep, supporting the potential use of **NanoBone™** also in humans.

Einleitung: Die Transplantation von autologer Spongiosa stellt auch heute noch den Goldstandard zur Füllung von Knochendefekten dar. Allerdings bestehen eine Hebemorbidität sowie eine begrenzte Verfügbarkeit. Das hier untersuchte vollsynthetische Knochenaufbaumaterial **NanoBone®** (ein in hochporöse Kieselgelmatrix eingebettetes nanokristallines Hydroxylapatit) weist im Großtiermodell am desmalen Knochen eine sehr gute osteokonduktive Potenz auf [1, 2]. Bislang liegen positive klinische Erfahrungen zu **NanoBone®** als Fusionsmaterial bei Wirbelkörperfusion sowie im Bereich der Oralchirurgie vor. Eine Untersuchung am Röhrenknochen im standardisierten Großtiermodell am Schaf sollte die Anwendbarkeit von **NanoBone®** bei metaphysären Knochendefekten bestätigen.
Methodik: Bei 18 ausgewachsenen Schafen wurde unter der Gelenkfläche der medialen Tibiakondyle beider Hinterläufe unter standardisierten Bedingungen ein definierter Knochendefekt von 1.05 cm^3 gefräst. Der rechtsseitige Defekt wurde mit Biomaterial gefüllt, während der linksseitige Defekt leer belassen wurde. Beide Defekte wurden mit einem Fascienstreifen gedeckt. Unter Berücksichtigung der festen spongiösen Struktur des Tibiakopfes und der Intaktheit der lateralen Tibiakondyle konnte auf eine zusätzliche Stabilisierung verzichtet werden. Der Defekt war – bei voller Belastbarkeit des Hinterlaufes – teilbelastet. Die Tiere wurden nach 6 Wochen (n = 6), 12 Wochen (n = 6) bzw. nach 26 Wochen (n = 6) getötet. Die operierten Knochen wurden unter Berücksichtigung der periostalen Integrität entnommen. Die Proben wurden makroskopisch und mikroskopisch beurteilt. Die radiologische Untersuchung schloss neben einer nativröntgenologischen Bildgebung eine Makro- und Mikrocomputertomographie ein. Durch Auswertung der Mikro-CT Daten konnte anhand der Volumenverteilung der radiologischen Dichte ein Mindestwert für die Knochenneubildung ermittelt werden. Nach Entkalken der Proben und Hämatoxylin-Eosin-Färbung wurden zusätzlich histologische und histomorphometrische Untersuchungen durchgeführt.
Ergebnisse: Die histologischen und radiologischen Untersuchungen zeigten, dass die zur Kontrolle angelegten Leerdefekte sowohl nach 6, 12 als auch nach 26 Wochen nicht mit Knochen gefüllt waren. Im Gegensatz dazu zeigte sich nach 6 Wochen in den mit dem Biomaterial gefüllten Defekten nach der Auswertung der Mikro-CT-Daten ein Volumenanteil der knochendichten Strukturen von 55 %. Parallel dazu wies die quantitative Analyse der histologischen Schnittbilder nach diesem Zeitraum eine Knochenneubildung von 22 % auf. Nach 12 Wochen ergab sich histomorphometrisch eine Knochenneubildung von 34 %. Die Mikro-CT Auswertung zeigte nach 12 Wochen eine weitere Zunahme der knochendichten Strukturen auf 72 %, nach 26 Wochen auf 74 %. Histologisch waren auf der Oberfläche des Biomaterials mehrkernige Riesenzellen und Resorptionslakunen nachweisbar, was auf einen Abbau durch Osteoklasten hinweist.
Diskussion/Schlussfolgerung: Das eingesetzte nanostrukturierte Knochenaufbaumaterial **NanoBone®** hat sich auch beim Einsatz im Schafsmodell als ein hochpotenter Knochenersatzstoff mit ausgeprägten osteokonduktiven Eigenschaften bewährt. Diese Eigenschaften lassen das getestete Material auch beim Menschen im klinischen Einsatz zum bevorzugten Knochenaufbaumaterial werden.

Schrodi I, Abshagen K, Gerber T, Vollmar B
In vivo analysis of biocompatibility and vascularization of the synthetic bone grafting substitute NanoBone™
Chirurgisches Forum 2008, Band 37; 251:252

Abstract: One of the major challenges in tissue engineering of bone substitutes are adequate vascularization and biocompatibility of the implant. Thus, the temporal course of neovascularization and the microvascular inflamma-

tory response of implants of **NanoBone**™ (fully synthetic nanocrystalline bone grafting material) were studied in vivo by using the dorsal skinfold chamber model. Angiogenesis, microhemodynamics and leukocyte-endothelial cell interaction were analyzed repetitively after implantation in the center and in the border zone of the implant up to 15 days. Both **NanoBone**™ granules and plates exhibited high biocompatibility comparable to that of cancellous bone, as indicated by a lack of venular leukocyte activation after implantation. In both synthetic **NanoBone**™ groups, signs of angiogenesis could be observed even at day 5 after implantation whereas granules showed higher functional vessel density compared with **NanoBone**™ plates. The angiogenic response of the cancellous bone was markedly accelerated in the center of the implant tissue. Histologically, implant tissue showed an ingrowth of vascularized fibrous tissue into the material combined with an increased number of foreign-body giant cells. In conclusion, **NanoBone**™, particularly in granular form, shows high biocompatibility and high angiogenic response, thus improving the healing of bone defects. Our results underline, that beside the composition and nanostructure, also the macro-structure is of importance for the incorporation of the biomaterial by the host tissue.

Einleitung: Ein großes Problem bei der Anwendung von Knochenersatzstoffen stellt die fehlende Vaskularisierung und schlechte Biokompatibilität des Implantats dar. Eine gute Gewebeintegration ist aber von besonderer Bedeutung, um eine dauerhafte Vitalität und Funktionalität des implantierten Biomaterials zu erreichen. **NanoBone**® repräsentiert ein vollsynthetisches hochporöses nanokristallines Knochenaufbaumaterial mit hohem osteokonduktivem und osteoinduktivem Potential, welches im Rahmen des physiologischen »Bone Remodellings« vollständig biodegradiert wird [1, 2]. Da bisher die mikrovaskuläre Antwort auf **NanoBone**® nicht bekannt ist, untersuchten wir im Modell der Rückenhautkammer der Maus [3] die inflammatorische und angiogene Wirkung dieses Biomaterials nach Implantation.
Methodik: Mittels intravitaler Fluoreszenzmikroskopie wurde über einen Zeitraum von 15 Tagen Angiogenese, Mikrohämodynamik und Leukozyten-Endothelzell-Interaktion des Empfängergewebes quantitativ analysiert. Hierzu wurde männlichen C57BL/6J Tyr Mäusen unter Ketamin/Xylazin-Anästhesie (90/25mg/kg ip) eine Rückenhautkammer präpariert, in die 3 Tage später die Materialien implantiert wurden. **NanoBone**® wurde sowohl als Plättchen (P, n = 7) als auch in Granulatform(G, n = 7) implantiert. Isogen transplantiertes Spongiosagewebe (S, n = 6) diente als Standard. Die nachfolgende in vivo Mikroskopie erfolgte repetitiv 20 min, 3, 5, 7, 10 und 15 Tage nach Implantation im Randbereich und Zentrum des Implantats als auch im peripheren Kammergewebe. Des Weiteren wurde die Anzahl Angiogenese-positiver Felder bestimmt und zusätzlich die Gefäßdichte in diesen Feldern analysiert. Zur weiteren Charakterisierung der Biointegrität des Implantats diente die histologische Bewertung des Gewebes am Tag 15 nach Implantation. Mittelwerte ± Standardfehler des Mittelwertes. ANOVA mit nachfolgendem Paarvergleich (*$p < 0,05$ vs. S; #$p < 0,05$ vs. P).
Ergebnisse: Sowohl **NanoBone**®-Granulat als auch **NanoBone**®-Plättchen sind durch gute Biokompatibilität, vergleichbar der von spongiösem Knochen, gekennzeichnet, was sich in einer fehlenden venulären Leukozyten-Akkumulation zu allen Untersuchungszeitpunkten widerspiegelt. Erste Zeichen von Angiogenese konnten bereits am 5. Tag nach Implantation der Biomaterialien nachgewiesen werden. Diese waren im Randbereich der Implantate durch kapillare Gefäßaussprossungen charakterisiert, welche bis zum 15. Tag ein dichtes, mikrovaskuläres Netzwerk ausbildeten. Während beim Granulat -im Gegensatz zum Plättchen- eine schwache angiogene Reaktion im Zentrum beobachtet werden konnte (Tag 7, [cm/cm^2], G 36±14; P 5±3), ergaben sich bei der Analyse der randständigen Angiogenese deutlichere Unterschiede. Bereits 7 Tage nach Implantation beider Materialien zeigten ca. 62–80 % der randständig gelegenen Felder klare Zeichen der Angiogenese, jedoch war die Gefäßdichte beim **NanoBone**®-Granulat gegenüber dem Plättchen und der Spongiosa (Tag 7, [cm/cm^2], G 713±59*#, P 462±28, S 357±10) signifikant erhöht. Im Gegensatz zu den synthetischen Materialien ist die angiogene Antwort im Zentrum der Spongiosa wesentlich stärker ausgeprägt, was sich durch eine Vielzahl Angiogenese-positiver Felder (Tag 7, [%], S 61±7, G 23±8, P 2±1*) sowie einer erhöhten Gefäßdichte (Tag 7, [cm/cm^2], S 126±13, G 36±14*, P 5±3*) im Zentrum zeigte. Histologisch konnte im Randbereich der Implantate die Ausbildung eines gut vaskularisierten Granulationsgewebes nachgewiesen werden.
Zusammenfassung: In der vorliegenden Studie konnten wir zeigen, dass **NanoBone**® in Granulatform ein Knochenaufbaumaterial mit geringem inflammatorischem Potential und stark angiogener Wirkung ist und somit optimale Bedingungen für die Neubildung von Knochen in Defekten schafft. Diese Ergebnisse zeigen weiterhin, dass, neben der Zusammensetzung und Nanostruktur von Implantaten, auch die Makrostruktur Einfluss auf die Inkorporation des implantierten Biomaterials im Empfängergewebe hat.

Kasaj A, Willershausen B, Reichert C, Gortan-Kasaj A, Zafiropoulos GG, Schmidt M
Human periodontal fibroblast response to a nanostructured hydroxyapatite bone replacement graft in vitro
Archives of Oral Biology 2008; 53:683-689

Objective: The efficacy of nanostructured hydroxyapatite (NHA) for the treatment of osseous defects has been demonstrated in recent studies, even though the underlining biological mechanism is still poorly known. This study examined the alterations in cellular adhesion and mitogenic responses in human periodontal ligament (PDL) cells treated with a novel nanostructured hydroxyapatite bone graft substitute and characterized associated changes in cellular signalling pathways.
Methods: Cultured PDL cells were stimulated with NHA in a surface coated form. Proliferation was determined by bromodeoxyuridine (BrdU) incorporation and cell adhesion was analysed by a colorimetric assay. In order to understand altered adhesion properties of PDL fibroblasts their integrin profile was analysed and the phosphorylation status of focal adhesion kinase (FAK) and b1 integrin was determined by immunoblotting. In order to understand the signalling mechanisms of increased cell proliferation of PDL cells caused by NHA, the phosphorylation status of the serine/threonine protein kinase Akt, of the signal regulated kinases ERK1/2 and of the epidermal growth factor receptor (EGFR) was analysed by western blot using phospho-specific antibodies.
Results: The results indicated that NHA is a strong stimulator of PDL cell attachment and proliferation. Mechanistically, a5b1 integrin-mediated cellular adhesion of PDL fibroblasts, which resulted in altered phosphorylation and activation levels of FAK. Proliferation mediated by NHA was mechanistically caused by activation of the epidermal growth factor receptor (EGFR) pathway and its downstream targets ERK1/2 and Akt.
Conclusions: In sum, our findings present evidence that a5b1 integrin-mediated cellular adhesion of NHA to PDL fibroblasts, whereas proliferation was caused by activation of the epidermal growth factor receptor (EGFR) and the MAP kinase (ERK1/2) and Akt pathways.

Stübinger S, Ghanaati SM, Orth C, Booms P, Kirkpatrick C, Sader R
A new nano-structured and synthetic biomaterial promotes reconstruction of alveolar ridge defects after dental trauma: A preliminary report of clinical and animal studies
IADT 2008, Poster

Objectives: The following study was undertaken to clinically evaluate the properties of **NanoBone**™ (a new entirely synthetic and nano-structured hydroxylapatite based biomaterial) as a grafting material for guided bone regeneration after dental trauma. This study was triggered by initial in vivo analysis of the host-biomaterial-interaction in the subcutaneous implantation model in Wistar-rats.

Meier J, Wolf E
Zeitgewinn bei der Hartgewebsregeneration durch Einsatz nanostrukturierter Knochenersatzmaterialien?
4. Gemeinschaftstagung DGI, ÖGI und SGI, Wien, November 2007, Poster

Zusammenfassung: Hier wird auf der Basis der Erfahrungen der letzten zweieinhalb Jahre dargestellt, wie sich im klinischen Verlauf, in den radiologischen Befunden und besonders in der Histologie der (Re-)Generationsprozess nach Augmentationen mit einem nanostrukturierten Knochenersatzmaterial (**NanoBone**®) im Vergleich mit anderen Knochenersatzmaterialien (KEM) verhält.
Im Vergleich mit Literaturangaben zu quantitativen Befunden 6 bis 12 Monate nach Sinusbodenelevation mit KEM boviner Herkunft (BBM) oder ß-Tri-Calcium-Phosphaten (ß-TCP) zeigen die Präparate mit **NanoBone**® eine ähnliche oder höhere Rate an Knochenneubildung nach 2 bis 3 Monaten, wie sie von den anderen Präparaten erst nach 9

bis 12 Monaten berichtet wird. Die zeitliche Korrelation und der auffällige Kontrast in den histologischen Befunden, welche eine wesentlich raschere und umfassendere Knochenneubildung bei Verwendung von **NanoBone®** zeigen, stützt unsere Aussage, dass eine wesentliche Verkürzung der Behandlungszeiten möglich wird.

Summary: Based on experiences made during the last two and a half years we present data on clinical and radiological findings as well as histologic specimens after augmentative treatment using a nanostructured bone substitute (**NanoBone™**) in comparison to other bone substitutes.
Comparing reports on quantitative evaluations 9 to 12 months after sinus floor elevation with bovine bone matrix (BBM) or ß-TCPs in literature to those specimens where we have used **NanoBone™** it becomes evident that **NanoBone™**-cases show a similar or even higher amount of de novo bone formation after only 2 to 3 months. Correlating those results with time and the impressive contrast in the histological sections which show faster and more complete de novo bone formation when **NanoBone™** was used our proposal to a substantial shortcut of therapy protocols gets support.

Meier J
Fördert der Zusatz autologen Knochens die Knochenneubildung bei Augmentation mit nanokristallinem Knochenersatzmaterial – Split-mouth Untersuchung bei Sinusbodenelevation
4. Gemeinschaftstagung DGI, ÖGI und SGI, Wien, November 2007, Poster

Zusammenfassung: Hier werden die Daten präsentiert, die anhand von Sinusbodenelevationen bei 14 Patienten gewonnen wurden, die sich im Rahmen der Implantatversorgung zur Verbesserung des Knochenlagers bilateraler Sinusbodenelevationen unterziehen mussten. Zur Bewertung des eventuellen Einflusses autologer Knochenspäne (AK) auf die Knochenneubildung wurden nach dem Zufallsprinzip auf einer Seite nur das Knochenersatzmaterial (KEM) **NanoBone®**, auf der anderen Seite **NanoBone®** mit autologen Knochenspänen gemischt eingesetzt.
Beim Zweiteingriff nach 8 bis 14 Wochen wurden Bohrzylinder gewonnen, die histologisch und histomorphometrisch untersucht wurden. Dabei ergab sich für die alleinige Anwendung des **NanoBone®** eine Knochenneubildungsrate von 39,5 % während bei Zusatz autologen Knochens 40,7 % neu gebildete Knochensubstanz gefunden wurde. Diese Differenz ist statistisch nicht signifikant.
Summary: This study presents data found in14 individuals where bilateral sinus floor elevation had to be preform-ed prior to implant therapy. To evaluate the influence of added autogenous bone on the de novo bone formation in sinuses at randomly chosen sides **NanoBone™** was used as bone substitute either without or in a mixture with autogenous bone chips. At the second stage procedure 8 to 14 weeks later bone cylinders were collected for histological and histomorphometric analysis. **NanoBone™** without additional bone revealed an average of 39.5 % de novo bone while in the group with both bone and **NanoBone™** 40.7 % of new bone could be measured. The difference is of no statistical significance

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Meier J, Heine M, Wolf E
Shortening Therapy Protocols by using the Nanocrystalline Bone Substitute NanoBone™ for Sinus Floor Elevations and Augmentation of other Bone Defects
EAO 2007, Barcelona, Poster

Introduction: The preparation of a sufficient bony layer prior or simultaneously to implantations is mandatory for good long term results. Depending on the amount of bone missing this can be achieved by one- or two-staged approaches. Those bone substitutes that were introduced previously are characterized by long healing periods of (6-) 9 to 12 months that are required to gain sufficient bone regeneration (bovine bone matrix as well as ß-TCP). The use of nanocrystals leads to a faster turnover due to the enlarged surface. The most important question now

is whether those bone substitutes can guarantee the growth of de novo bone and the remodelling that is necessary for the primary stability of endosseous implants. We performed several studies to prove the bony integration of **NanoBone**™ and estimate the time required for the generation of bone that provides us with the reliable conditions to insert implants at shorter therapy intervals compared to other bone substitutes.

Ghanaati S, Stübinger S, Orth C, Biesterfeld S, Barbeck M, Booms P, Sader R, Kirkpatrick CJ
Presence of osteoclast-like cells in the subcutaneous tissue of Wistar rats: in vivo Biocompatibility analysis of a synthetic HA and SiO_2 matrix
21st European Conference of Biomaterials, Poster (Brighton, UK, 9-13th September 2007)

Sol-gel technology results in a variety of biomaterial surfaces and leads to an enlargement of the interface between the biomaterial and the peri-implant tissue. The bone substitute **NanoBone**® consists of nanocrystalline hydroxyapatite embedded in a highly porous matrix of silica gel and is produced in a sol-gel process at a temperature of < 700°C.
Evaporation leads to the formation of small pores (Ø 5-100 µm). The crystallites are loosely packed and held together by SiO_2 which connect the HA crystals and leads to nano-pores (Ø10-20 nm).
This interconnective porosity is the characteristic of this new biomaterial and assumed to be responsible for induction of the new bone. Up to now there is no in vivo investigation analysing the biodegradation of this biomaterial and its influences on peri-implant cells in the subcutaneous implantation model. Using histological and histochemical methods our aim was to analyse the biocompatibility of **NanoBone**™ and t identify the cells involved in this degradation.

Hebecker R, Sola S, Mann S, Buchholz K, Piek J
Lumbar Interbody Fusion with a New Nanostructured HA Bone Substitute (NanoBone™) – A Prospective Clinical and CT Study with 15 Patients
Biospine 2, 2nd International Congress Biotechnologies for Spinal Surgery, Poster (Leipzig, Germany, September 20th-22nd, 2007)

In spinal surgery limited availability of autologeous bone graft and donor site morbidity are challenge for bone substitutes becoming more and more important. A variety of materials have been introduced for intervertebral cage filling. Therefore bioceramics as well as osteogenetic growthfactors have mainly been used in recent studies. As a new hydroxyapatite (HA)-based bone substitute (**NanoBone**™) has already been established for use in craniomaxillofacial surgery with promising results we initiated a prospective study to prove its sufficient bone graft potential for interbody fusion.

Meier J, Wolf E
Umbau des nanokristallinen Knochenersatzmaterials NanoBone® im histologischen und immunhistochemischen Bild
Jahrestagung der Deutschen Gesellschaft für Implantolgie, Poster (München, Mai 2007)

Bei alloplastischen und xerogenen Knochenersatzmaterialien (KEM) waren bislang je nach Präparat Einheilzellen von 6 – 9 – 12 Monaten üblich. Die nanokristalline Struktur des hier beschriebenen **NanoBone**® bestehend aus Hydroxylapatit, der initial in einer Kieselgelmatrix vorliegt, führt zu einer hohen Adsorption von Plasmaproteinen und Proteoglykanen, was eine wesentlich raschere Besiedlung mit Osteoprogenitorzellen und damit auch eine

erhebliche beschleunigung des knöchernen Um- und Einbaus bewirkt.
Dem klinischen Eindruck der teilweise massiven, erheblich dichteren Knochengeneration nach Sinusbodenelevation innerhalb von 3 Monaten entspricht die Morphologie bei der feingeweblichen Aufarbeitung. Histomorphometrisch findet sich durchschnittlich 39,5 % neu gebildeter Knochen neben einem Restvolumenanteil von 17,7 % KEM, so dass nur noch 42,8 % Markraum verbleiben. Im ortständigen Oberkieferalveolarfortsatz beträgt der Anteil des Markraums durchschnittlich 60,3 %.
Der Abbau des KEM **NanoBone®** erfolgt durch osteoklasten und Phagozytose. In den ersten drei Monaten wird etwa die Hälfte des KEM resorbiert, die Restpartikel finden sich zu diesem Zeitpunkt in einem innigen Verbund mit dem neu gebildeten Knochen, der diese umschließt und teilweise durchdringt und so die Festigkeit und ein für frühzeitige Implantationen gut geeignetes Lager bietet.

Meier J, Wolf E
Histomorphological and immunohistological findings after sinuslift procedures
Osteology Symposium (Monaco – May 10th–12th, 2007), Poster

The production of bone substitute with nanostructure has significantly enhanced the bone (re)modelling by better absorption of osteogenetic substances at the enormously surface and the high porosity. The nanostructured new bone substitute **NanoBone**™ provides a a material that can be used for sinus floor elevations succeeded by the insertion of dental implants after a healing period of about 3 months in two stage procedures or the beginning of functional loading in one stage procedures after only 3 to 4 months.
Here the cellular ingrowth and formation of new bone surrounding the particle of this bone substitute is presented in histologic sections and compared to others with special regard to the rate of bone formation which was evaluated not only by morphologic apperance but by histomorphometry.

Henkel KO, Kirchhoff M, Gerber T, Bienengräber V
Klinische Anwendung eines innovativen nanokristallinen Knochenersatzmaterials - eine Bizenterstudie
57. Jahrestagung der AGKI in Wiesbaden, Mai 2007, Poster

Hochporöse, nanostrukturierte Knochenaufbaumaterialien (KAM) können im Gewebeverbund aufgrund ihrer extrem großen inneren Oberfläche körpereigene Wachstumsfaktoren binden. So wirken sie nicht nur osteokonduktiv, sondern regen zugleich die Knochenregeneration an. Erste klinische Resultate werden vorgestellt.

Bienengräber V, Lenz S, Gerber T, Henkel KO
Kann ein synthetisches Knochenersatzmaterial osteoinduktiv wirken?
(Osteoinductivity of a synthetic bone replacement material)
57. Jahrestagung der AGKI in Wiesbaden, Mai 2007, Poster

Das zu testende neuartige Knochenaufbaumaterial (KAM) – eine nanostrukturierte Hydroxylapatit (HA)-Kieselgel (SiO_2)-Matrix – wirkt stark osteokonduktiv und ist vollständig biodegradierbar. Eine extraskelettale Knochenbildung soll induziert werden, um einen möglichen osteoinduktiven Effekt dieses KAM zu erfassen.

Bienengräber V, Lenz S, Rumpel E, Gerber T, Henkel KO
A New Osteoinductive Bone Replacement Material
International Proceedings, XVIII Congress of the European Association for Cranio-Maxillo facial Surgery, Barcelona (Spain), September 12-15, 2006, 19-22

Introduction Hydroxyapatite (HA) is the main component of bone and an important material used for bone substitutes. Conventional HA ceramics are osteoconductive, but poorly degradable. A new HA-silica-matrix is presented being highly osteoconductive and fully biodegradable. Ectopic bone formation was induced when implanted subcutaneously into fatty tissue proving osteoinductive properties of the new biomaterial.

Henkel KO, Gerber T, Lenz,S, Gundlach KH, Bienengräber V
Macroscopical, histological, and morphometric studies of porous bone-replacement materials in minipigs 8 months after implantation
Oral Surg Oral med Oral Pathol Oral Radiol Endod 2006; 102:606-13

Objective: The aim of this investigation was to test the induction of bone formation and biodegradation of different biomaterials based on calcium phosphate (CaP). Up to now, hydroxyapatite and ß-tricalcium phosphate ceramics have routinely been sintered at temperatures of 1300°C. The new CaP biomaterials tested are fabricated by a sol-gel process at only 700°C.
Study design: Critical-size defects (>5 cm^3) in the mandible of 15 adult Goettingen minipigs were filled with 1 of the 2 new types of CaP biomaterials, or with 1 of 2 well-known old-type ceramics, or with a gelatin sponge (in the control group). Macroscopical, histological, and morphometric examination of the former defect areas were made 8 months postoperatively.
Results: Eight months after implantation of the new CaP biomaterials, complete bone formation was observed in the defect area, and at the same time, the foreign material was resorbed almost completely. After implantation of the classical types of ceramics, only incomplete bone formation and a lesser resorption rate of the foreign bodies were noted. The difference in the bone formation rate was significant: more than 93 % for the new CaP biomaterials versus less than 58 % for the classical types of ceramics ($P < 0.01$).
Conclusion: The biological behavior of the new CaP biomaterials was better than that of the old-type sintered ceramic bone-grafting materials. These new CaP matrices are suitable for filling bone defects and are of interest for dentists, including implantologists, craniomaxillofacial and orthopedic surgeons, as well as traumatologists.

Kirchhoff M, Bienengräber V, Lenz S, Gerber T, Henkel KO
A new synthetic bone replacement material with osteoinductive properties – in vivo investigations
BIOmaterialien 7 (S1),2006;80

Introduction: Hydroxyapatite (HA) being the main component of bone is an important material used for bone substitutes. Conventional HA ceramics are osteoinductive, but poorly degradable. A new HA matrix is presented being highly osteoconductive and at the same time fully biodegradable. Ectopic bone formation was induced when implanted subcutaneously into fatty tissue proving the osteoinductive properties of the new material.

Gerber T, Holzhüter G, Götz W, Bienengräber V, Henkel KO, Rumpel E
Nanostructuring of Biomaterials – A Pathway to Bone Grafting Substitute
Eur J Trauma 2006;32:132-40

Background The bone substitute **NanoBone**™ consists of nanocrystalline hydroxyapatite embedded in a highly porous matrix of silica gel. It promotes the healing of bone defects and is degraded by osteoclasts during bone remodeling. The present study investigates the interactions of **NanoBone**™ with bone tissue.
Methods: Granules of **NanoBone**™ were implanted in defects of critical size in the mandible of minipigs. Samples were taken after 5 and 10 weeks and demineralized. The composition of the implanted granules was analyzed by means of transmission and scanning electron microscopy and EDX. Enzymeand immunohistochemistry was used to investigate organic components of **NanoBone**™ granules that arised after implantation in the host.
Results: EDX demonstrated that 5 weeks after implantation the silica gel was degraded and replaced by an organic matrix. Ultrastructurally, the matrix appeared amorphous with only single collagen fibrillae. PAS-staining indicated the presence of carbohydrates. Immunohistochemically, the bone proteins osteopontin, osteocalcin and BMP-2 were found as constituents of the new matrix. Alkalic phosphatase activity was located in osteoblasts and newly formed bone on **NanoBone**™ and focally in particles. Osteoclasts with ruffled borders, sealing zones, and acid phosphatase activity were situated in resorption lacunae at granule surfaces not covered by new bone.
Conclusions: In vivo, the silica gel of **NanoBone**™ is replaced by bone matrix glycoproteins with known functions in attraction, adhesion, and differentation of bone cells as osteoblasts and osteoclasts. We assume that the deposition of these molecules supports the early phase of **NanoBone**™ degradation by osteoclasts and promotes the production of new bone tissue.

Dietze S, Bayerlein T, Proff P, Hoffmann A, Gedrange T
The ultrastructure and processing properties of Straumann Bone Ceramic and NanoBone™.
Folia Morphol (Warsz). 2006 Feb;65(1):63-5.

The ultrastructure, fundamental chemistry, and processing modes of fully synthetic bone grafting materials are relevant to the reconstruction of osseous defects. Rapid progress in the profitable market of biomaterials has led to the development of various bone substitutes. Despite all these efforts, an ideal and full substitute of autologous bone is not yet in sight. With regard to anorganic calcium phosphate ceramics, Straumann Bone Ceramic and **NanoBone**™ are compared. These have a similar composition and are osteoconductive, which indispensably requires contact with well-vascularised bone.

Gerike W, Bienengräber V, Henkel KO, Bayerlein T, Proff P, Gedrange T, Gerber T
The manufacture of synthetic non-sintered and degradable bone grafting substitutes.
Folia Morphol (Warsz). 2006 Feb;65(1):54-5.

A new synthetic bone grafting substitute (**NanoBone**™, ARTOSS GmbH, Germany) is presented. This is produced by a new technique, the sol-gel-method. This bone grafting substitute consists of nanocrystalline hydroxyapatite (HA) and nanostructured silica (SiO_2). By achieving a highly porous structure good osteoconductivity can be seen. In addition, the material will be completely biodegraded and new own bone is formed. It has been demonstrated that **NanoBone**™ is biodegraded by osteoclasts in a manner comparable to the natural bone remodelling process.

Rumpel E, Wolf E, Kauschke E, Bienengräber V, Bayerlein T, Gedrange T, Proff P.
The biodegradation of hydroxyapatite bone graft substitutes in vivo.
Folia Morphol (Warsz). 2006 Feb;65(1):43-8.

Hydroxyapatite (HA) ceramics are widely used for bone reconstruction. They are osteoconductive and serve as structural scaffolds for the deposition of new bone. Generally, scaffold materials should be degradable as they affect the mechanical properties of the reconstructed bone negatively. Degradation by osteoclasts during the bone remodelling process is desirable but often does not take place. In the current study we analysed by light microscopy the degradation of two granular HA implants in critically sized defects in the mandibula of Goettingen mini-pigs five weeks after implantation. Bio-Oss consists of sintered bovine bone and **NanoBone**™ is a synthetic HA produced in a sol-gel process in the presence of SiO_2. We found that both biomaterials were degraded by osteoclasts with ruffled borders and acid phosphatase activity. The osteoclasts created resorption lacunae and resorptive trails and contained mineral particles. Frequently, resorption surfaces were in direct contact with bone formative surfaces on one granule. Granules, especially of **NanoBone**™, were also covered by osteoclasts if located in vascularised connective tissue distant from bone tissue. However, this usually occurred without the creation of resorption lacunae. The former defect margins consisted of newly formed bone often without remnants of bone substitutes. Our results show that the degradation of both biomaterials corresponds to the natural bone degradation processes and suggest the possibility of complete resorption during bone remodelling.

Kauschke E, Rumpel E, Fanghänel J, Bayerlein T, Gedrange T, Proff P.
The in vitro viability and growth of fibroblasts cultured in the presence of different bone grafting materials (NanoBone™ and Straumann Bone Ceramic).
Folia Morphol (Warsz). 2006 Feb;65(1):37-42.

Different clinical applications, including dentistry, are making increasing demands on bone grafting material. In the present study we have analysed the viability, proliferation and growth characteristics of fibroblasts cultured in vitro together with two different bone grafting materials, **NanoBone**™ and Straumann Bone Ceramic, over a period of 24 and 28 days respectively. Viability was measured at least every 72 hours by using the alamarBlue assay, a test that measures quantitatively cell proliferation and viability but does not require cell fixation or extraction. After one week of culture fibroblast viability was as high as in controls for both grafting materials and remained high (> 90 %) for the duration of the experiment. Cell growth was evaluated microscopically. Scanning electron microscopy revealed a dense fibroblast growth at the surface of both bone grafting materials after three weeks of in vitro culture. Generally, our in vitro analyses contribute to further insights into cell - scaffold interactions.

Streckbein R, Streckbein Ph
Kombinierter Einsatz von Knochenersatzmaterialien mit neuen, antibiotikahaltigen Kollagenmembranen
Implantologie Journal 7/2006:40-44

Mit den Techniken der gesteuerten Knochenregeneration (GBR) und Geweberegeneration (GTR) konnten seit Mitte der 80er-Jahre des letzten Jahrhunderts in der Parodontologie nachhaltige Erfolge beim Bemühen um den Wiederaufbau verloren gegangener Stützgewebe erzielt werden (Dahlin, Linde et al., 1988).

Maas W, Bienengräber V, Wolf E
Sicher Augmentieren
Splitmouth-Fallstudie zur Augmentation mittelgroßer Knochendefekte
Implantologie Journal 5/2006:40-44

In den vergangenen Monaten wurde die Fachpresse durch eine heftige Diskussion über die medizinische und juristische Problematik von bovinen Augmentationsmaterialien durchzogen. Auslöser war das Urteil des OLG Stuttgart vom Juli 2005, das einen Zahnarzt unter anderem wegen unzureichender Aufklärung über die Herkunft des Augmentationsmaterials Bio-Oss® zu einem Schmerzensgeld von 5.000,– Euro verurteilt.

Bienengräber V, Gerber Th, Wolf E, Henkel KO
Biologische Grundlagen eines synthetischen Knochenaufbaumaterials - NanoBone®
Implantologie Journal 4/2006:48-51

Hydroxylapatit (HA) ist als Hauptbestandteil der Knochenmatrix ein wichtiges Ausgangsmaterial für Knochenaufbaumaterialien. Im Sinterverfahren hergestellte HA-Keramiken sind zwar ausreichend osteokonduktiv, jedoch nur schwer biodegradierbar. Es wird ein nichtgesintertes Knochenaufbau-material vorgestellt, bei dem nanokristallines HA in einer hochporösen Kieselgelmatrix eingebettet ist.

Chuchracky N
NanoBone® Augmentation Material and Bego Semados® - S-Implants: A Powerful Combination for Today`s Dental Implantology Applications?
implants 1_2006:06-09

NanoBone® Bone Augmentation Material
The spezial properties of the all-new **NanoBone™** Augmentation material derive from the material`s nanostructure, which means that identical chemical compounds can have completely different properties. **NanoBone™** has a very large surface area relative to its volume. Numerous studies have shown that the surface properties of bone augmentation materials are of decisive importance for the development of optimal biological activity and the formation of new bone bone (osteogenesis). The deposition of hydroxyapatite in a SiO_2 structure forms the basis of the material. Silicon dioxide molecules ares used to achieve the additional effect of “fixing” proteins in the surface. Silicon dioxide is particulary important here because it stimulates the formation of collagen and bone.

Bienengräber V
Anforderungen an ein innovatives und praxistaugliches Knochenersatzmaterial
DENTAL MAGAZIN 1/2006:35-38

Knochenersatzmaterialien spielen eine zunehmend größere Rolle in der Praxis, nicht zuletzt im Zuge der wachsenden Zahl der Implantatinsertionen. Autogener Knochen gilt zwar als „Goldstandard“, die Entnahme belastet aber den Patienten. So sind viele unterschiedliche Knochenersatzmaterialien im Angebot, der chirurgisch tätige Zahnarzt hat die „Qual der Wahl“.

Henkel KO, Gerber Th, Dörfling P, Gundlach KH, Bienengräber V
Repair of bone defects by applying biomatrices with and without autologous osteoblasts
Journal of Cranio-maxillofacial Surgery (2005) 33, 45-49

Question: Is it possible to stimulate osteoconduction and osteogenesis to improve bone formation in critical-size defects in order to avoid bone grafting? Material and methods: Full thickness, critical-sized defects were created in the anterior mandible of 16ad ult mini-pigs. The defects were filled with a new bioactive matrix (60 % hydroxyapatite and 40 % ß-tricalciumphosphate), produced by an innovative low temperature sol–gelprocess (120 1C). The biomatrix was tested alone and in combination with cultured autologous osteoblasts. In a control group, periosteum was the only bone producing source. Five weeks postoperatively, the animals were sacrificed and the defects analysed macroscopically, histologically and radiographically.

Henkel KO, Bienengräber V, Lenz S, Gerber T
Comparison of a new kind of calcium phosphate formula versus conventional calciumphosphate matrices in treating bone defects – A long-term investigation in pigs
Key Engineering Materials Vols. 284-286 (2005) pp. 885-888
In clinical practice arises an increasing need for bone substitute materials. The main inorganic part of bone is the hydroxyapatite (HA). A new hydroxyapatite formula was created by a sol-gel-process at
low temperature level [4]. The aim of this investigation was to test the biodegradation and the induction of bone formation by this new material and to compare these versus conventional fabricated HA and ß-TCP. 30 one-year-old Goettingen minipigs were divided into five groups. Critical size defect (>5 cm^3) in the mandible was treated differently in all 5 groups: group I- filling with pure HA, which was fabricated by sol-gel-technique, group II- control, only gelatinous material was given, group III- conventional ß-TCP [Cerasorb®], in group IV- conventional HA [Endobone®] and in group V [Targobone®], a non denatureted bovine collagen matrix was used. Macroscopical and microscopical investigations of the former defects were made eight months postoperatively. The bone formation was superior in the sol-gel-HA-group (group I) in comparison with the control groups (group II) and the conventional fabricated ceramics groups (III and IV). In the sol-gel-HA group, the biodegradation of this new biomaterial was considered to very good with a resorption rate of more than 98 %; eight months postoperatively. In this group complete bone formation was seen in former defects. In the control group, only an incomplete bone formation with 48.4 % of the defect area was noted. This difference was significant ($p<0,001$).
A less bone formation was also observed in group III and IV with 57.6 % and 56.9 %. The
bovine non-denaturated collagen matrix (group V) leads to only 20 % of new formed bone. The new calcium phosphate formula made by a sol-gel method seems to be superior and suitable for filling bone defects.

Henkel KO, Lenz JH, Gerber T, Bienengräber V
Ein qualitativ neuartiges Knochenaufbaumaterial auf Hydroxylapatit-Xerogel-Basis
ZWR 114, Jahrg. 2005, Nr. 9:416-418

Es wird ein neuartiges Knochenaufbaumaterial auf Hydroxylapatit-Xerogel-Basis vorgestellt, das mittels innovativer Sol-Gel-Technologie im Niedertemperaturbereich unter Zusatz von Siliziumdioxid hergestellt wird und strukturell die natürliche Knochenmatrix weit gehend imitiert. Daraus resultieren eine hohe Osteokonduktivität und ein osseoprotektiver Effekt sowie eine vollständige, dem Knochenanbau angepasste Biodegradation im Rahmen des natürlichen Knochen-Remodelings. 2 Fallberichte werden vorgestellt.

Henkel KO, Gerber T, Dietrich W, Bienengräber V

Neuartiges Knochenaufbaumaterial auf Kalziumphosphatbasis – Erste In-vivo-Langzeitergebnisse

Mund Kiefer GesichtsChir 5 2004, 277-281

Hintergrund: Alle bisher angebotenen synthetischen Knochenersatzmaterialien auf Hydroxylapatit (HA)- und ß-Trikalziumphosphat (TCP)-Basis werden im Sinterverfahren bei Temperaturen von 1100–1500°C produziert. 2 innovativ im Sol-Gel-Verfahren bei 200°C hergestellte Knochenaufbaumaterialien auf Kalziumphosphatbasis mit Siliziumoxid (SiO_2) weisen aufgrund des Herstellungsunterschieds neuartige Materialeigenschaften auf und wurden als Adjuvans im Langzeittierversuch getestet. Es sollte geklärt werden, in welchem Umfang diese im Niedertemperaturbereich hergestellten Knochenaufbaumaterialien die Osteogenese in Critical-size-Defekten stimulieren und welches Resorptionsverhalten sie aufweisen.

Material und Methode: Bei 18 adulten Göttinger Minischweinen wurden im Bereich der anterioren Mandibula perforierende Critical-size-Defekte (>5 cm^3) gesetzt. In Gruppe I (n=6) wurden diese mit einer biphasischen (60 % HA und 40 % ßTCP), in Gruppe II (n=6) mit einer monophasischen Variante (100 % HA) des neuartigen Knochenaufbaumaterials aufgefüllt.Gruppe III (n=6) bildete die Leerkontrolle. Nach 8 Monaten wurde die Defektregion klinisch und histologisch/morphometrisch untersucht. Die statistische Evaluation erfolgte mittels Varianzanalyse für Mehrfachvergleiche.

Ergebnisse: In beiden Versuchsgruppen waren klinisch eine vollständige Reossifikation der Defekte sowie ein hoher Biodegradationsgrad der Testmaterialien zu beobachten. In Gruppe II (reines HA) waren nach 8 Monaten 98,7 % des Biomaterials resorbiert. Dieser Wert lag in Gruppe I (HA und ßTCP) mit 93,7 % etwas niedriger,wobei die Gruppendifferenz statistisch nicht signifikant war (p=0,483). Beide Knochenaufbaumaterialien stimulieren die Knochenneubildung deutlich. Die Defekte waren nach 8 Monaten zu mehr als 93 % mit Knochen aufgefüllt. In der Kontrollgruppe lag die knöcherne Durchbaurate der Defekte bei 48,4 %. Dieser Unterschied war statistisch hoch signifikant (p<0,001).

Schlussfolgerung: Im Sol-Gel-Verfahren bei 200°C hergestellte Knochenaufbaumaterialien auf Kalziumphosphatbasis weisen in vivo neben einer sehr guten Osteokonduktivität ein verbessertes Resorptionsverhalten gegenüber herkömmlichen Biokeramiken auf. Sie erscheinen daher für die Therapie knöcherner Defekte beim Menschen geeignet.

Background: Up to now hydroxyapatite (HA) and ß-tricalciumphosphate (ß-TCP) ceramics have been routinely sintered at temperatures between 1100° and 1500°C. Our new calcium ceramic is fabricated by a sol-gel process at 200°C. The aim of this investigation was to test the biodegradation of and the induction of bone formation by this material.

Material and methods: Eighteen 1-year-old Goettingen minipigs were divided into three groups. Critical size defects (>5 cm^3) in the mandible were treated differently in all three animals (group 1: filling with 40 % ß-TCP plus 60 % HA, group 2: pure HA was applied, group 3 served as controls: only gelatinous material was given). Macroscopic and microscopic investigations of the former defects were made 8 months postoperatively.

Results: In groups 1 and 2 biodegradation of more than 93 % of the new calcium phosphate formula was found 8 months postoperatively and considered to be very good. No difference was observed between pure HA (group 2) and the combination of HA and ß-TCP (group 1). In both groups complete bone formation was seen macroscopically in the former defects. In the control group only incomplete bone formation with 48.4 % of the defect area was noted. This difference was significant (p<0.001).

Discussion: The new calcium phosphate formula made by a sol-gel method at 120°C seems to be suitable for filling bone defects and is of interest for orthopedic surgery, traumatology, craniomaxillofacial surgery, and dentistry.

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