

NanoBone[®]

■ Bone Formation in a New Dimension

Information on the synthetic bone
grafting material NanoBone[®]



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NanoBone®

Introduction



1 | Prof. Dr. Gerber and Dr. Gerike,
managing partners of ARTOSS

The idea of developing new biomaterials for bone regeneration and many years of scientific cooperation with the university have resulted in the creation of our synthetic bone grafting material **NanoBone®**. The cooperation between universities and the researching company is playing an important role in our company philosophy still today, after more than ten years of development. In the meantime, we look back on more than 100,000 treatments with **NanoBone®** and cooperate with more than 20 universities. We produce and develop the **NanoBone®** technology at our company headquarters in Rostock-Warnemünde. Our R&D team is permanently working on further developments here.

With the particular structure of our bone grafting material **NanoBone®**, we offer you an innovative product. For our products, we use nanostructures for which nature is taken as a role model. A large number of clinical long-term studies show clearly that the **NanoBone®** technology meets the expectations. But as if that were not enough: Our technology offers many possibilities to treat various indications with special products and to always set new standards thanks to further research.

So stay curious about the products we are going to develop in future. We are looking forward to interesting conversations and the exciting cooperation with you.

Handwritten signature of Prof. Dr. Thomas Gerber in black ink.

Prof. Dr. Thomas Gerber
Managing partner

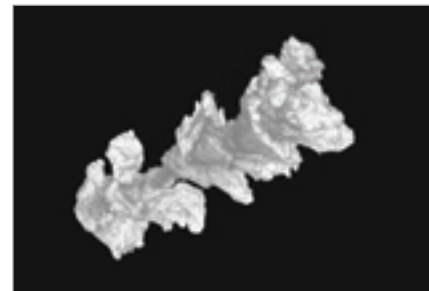
Handwritten signature of Dr. Walter Gerike in black ink.

Dr. Walter Gerike
Managing partner

What is nano?

Nano is the dimension in which intracellular processes take place. Nano can achieve the largest possible surface and stimulate processes that take place in our body.

During the natural bone formation and resorption, the remodelling, our bone is constantly regenerating. **NanoBone®** participates actively in this remodelling and thus promotes a natural process. The secret to success is the efficient nanostructure: Nanocrystalline hydroxylapatite (HA) as main element of autologous bone is embedded in a highly porous silica gel matrix. The silica gel stimulates the formation of collagen and bone.



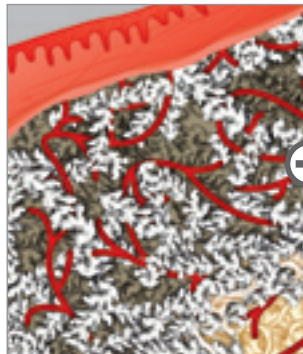
2 | NanoBone® granules

What does the NanoBone® technology do?

Macro world



3 | NanoBone® in the bone defect



4 | Fast angiogenesis through NanoBone®



5 | Fast defect healing

3 | Autologous proteins from the blood come into the nanopores and cover the entire internal surface ($> 80 \text{ m}^2/\text{g}$) of the granules. Thus, the body recognises NanoBone® as a material peculiar to the body.

4 | The fluffy structure allows for the quick growth of capillaries. This process is facilitated by the change of matrix.

5 | NanoBone® is completely substituted by bone during the process. With stabilised volume, NanoBone® is resorbed to the extent to which new, autologous bone is formed. * Meier et al.

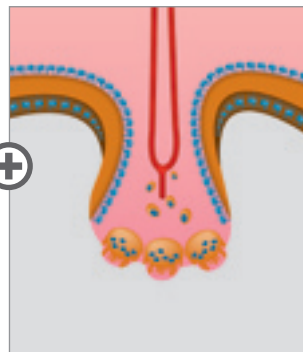
Nano world



6 | Hydroxylapatite in silica gel matrix, autologous proteins in the nanopores



7 | Change of matrix – substitution of the silica gel by organic autologous matrix



8 | Remodelling with osteoclasts and osteoblasts

6/7 | Within a few days, the silica gel matrix is replaced by an organic matrix that contains important proteins for osteogenesis (BMP, osteocalcin, osteopontin etc.). * Götz et al.

8 | Osteoclasts resorb the NanoBone® granules like bone. At the same time, osteoblasts form new natural bone. This resorption of the bone augmentation material and the formation of new, autologous bone take place in the same way as natural remodeling.

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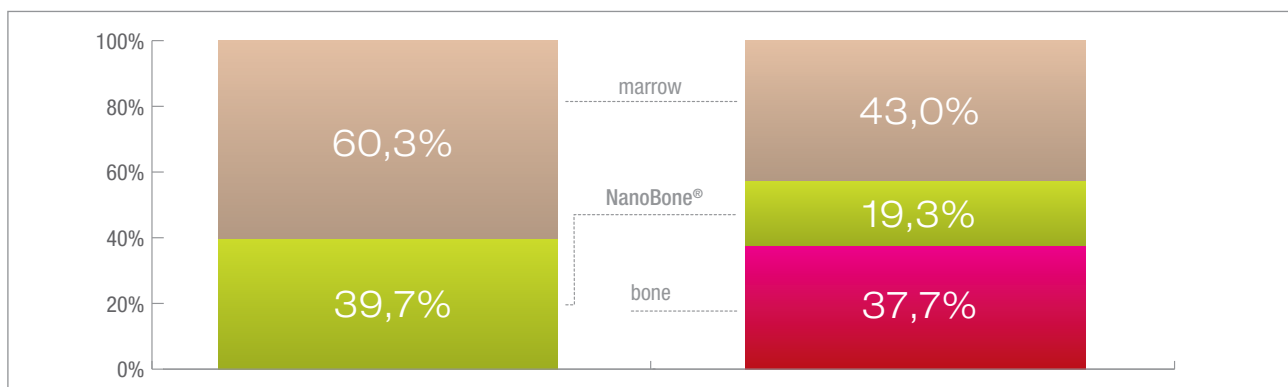
NanoBone®

Good reasons for NanoBone®

1 Faster bone formation

The special structure of NanoBone® results in an extremely fast bone formation. Clinical studies show that a stable implant bed is available in case of sinus floor elevation already after three months. Other bone replacement materials state an incorporation period of 9 – 12 months for this case. This is how the use of NanoBone® can considerably reduce the treatment period as well.

Meier et al. show: after three months, 37.7% bone, 43.0% marrow space and not more than 19.3% NanoBone® are detected. In this context, the angiogenic osteogenesis in NanoBone® constitutes a real difference in quality. For other bone replacement materials, however, only bone formation starting at the border was detected.

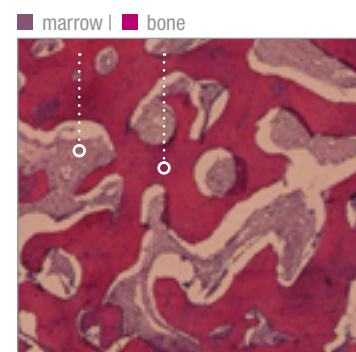


1 | Augmentation

2 | 3 months later

2 Complete remodelling

On account of the nature-identical component HA and the organic matrix formed after a short time (matrix change of silica gel), the body recognises NanoBone® as material peculiar to the body and the natural bone formation and resorption - the remodelling - starts. Osteoclasts resorb the granules. At the same time, osteoblasts form autologous bone. During the process, NanoBone® is completely substituted by bone so that, in contrast to xenogenic bone replacement material, no residual foreign substances can influence natural biomechanics. Considering the fact that a portion of approx. 16% of these bone replacement materials can still be detected after nearly 10 years, the complete remodelling of NanoBone® constitutes a decisive advantage.

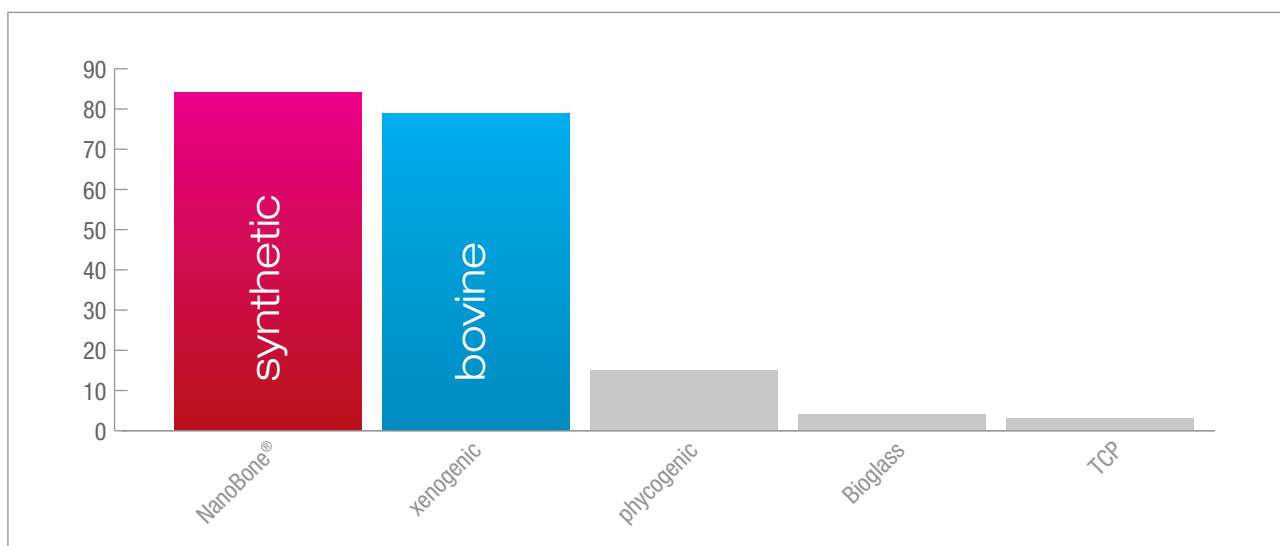


3 | Histology of a sinus biopsy

3 High-performance through nanostructure

The interconnecting nanopores and the nanocrystalline HA are the keys to success. Thanks to its porosity in the

nanometer range, **NanoBone®** has a very large surface thus reaching new dimensions.



4 | Specific surface of bone replacement materials (m²/g)

4 Synthetic and safe

An important advantage is offered in the context of the duty to inform the patient. **NanoBone®** is a safe product with respect to the possible triggering of allergies, the transmission of infections and ethical views. Moreover, the synthetic character also allows for the development of indication-related products. In this context, for example **NanoBone®** blocks for major defects are being developed based on the **NanoBone®** technology.



5 | The entire synthetic production at the company headquarters in Rostock-Warnemünde is subject to very strict safety regulations within the scope of quality management.

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Indications

1 Implantology

- sinus lift and/or sinus floor elevation (open/closed)
- augmentation of alveolar ridge defects (lateral/vertical bone deficits, unilateral or bilateral)
- filling of alveolar cavities for stabilising the bony alveolar ridge (socket preservation)

2 Maxillary and facial surgery

- reconstruction of the alveolar ridge
- defect filling after traumata

3 Periodontics

- filling of two-wall or multi-wall bone pockets
- sanitation of bi- or trifurcation defects

4 Oral surgery

- filling of defects after cystectomy, root end resection and removal of impacted teeth
- stabilisation of the alveolar ridge after series extraction

Application of NanoBone® granules

The NanoBone® granules have to be inserted in direct contact with the vital bone. On account of the mixing with blood, the proteins decisive for the successful bone formation have already been provided. The bone defect should be filled completely with the granules.



1 | NanoBone® granules



2 | Mixing the granules with blood



3 | Easy handling with spoon or spatula

Extract from references

Götz W, Gerber T, Michel B, Lossdörfer S, Henkel KO, Heinemann F: Immuno-histochemical characterization of nanocrystalline hydroxyapatite silica gel (NanoBone®) osteogenesis: A study on biopsies from human jaws, Clin Oral Impl Res 2008; 19:1016-1026

Meier J, Wolf E, Bienengraber V: Einsatz des synthetischen nanostrukturierten Knochenaufbaumaterials NanoBone® bei Sinusbodenelevation, Implantologie 2008; 16(3)

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

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 nanocrystalline bone grafting substitute NanoBone®, Chirurgisches Forum 2008, Band 37; 253:255

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

Stübinger S, Ghanaati S, Orth C, Hilbig U, Saldamli B, Biesterfeld S, Kirkpatrick J, Sader R: Maxillary sinus grafting with a nano-structured biomaterial: Preliminary clinical and histological results, J Periodontol, submitted

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

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, Poster: IADT 2008

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

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

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 in Barcelona

Ghanaati S, Stübinger S, Orth C, Biesterfeld S, Barbeck M, Booms P, Sader R, Kirkpatrick CJ: Poster: Presence of osteoclast-like cells in the subcutaneous tissue of Wistar rats: in vivo Biocompatibility analysis of a synthetic HA and SiO₂ matrix, 21st European Conference of Biomaterials, (Brighton, UK, 9-13th September 2007)

Hebecker R, Sola S, Mann S, Buchholz K, Piek J: Poster: 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, (Leipzig, Germany, September 20th-22nd, 2007)

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

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

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

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

Bienengraber 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

Henkel KO, Gerber T, Lenz S, Gundlach KH, Bienengraber 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

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

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

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.

Gerike W, Bienengraber 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.

Rumpel E, Wolf E, Kauschke E, Bienengraber 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.

- If you have any questions regarding the application, the product and/or on how to order **NanoBone®**, please do not hesitate to contact us.

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