NanoBone®

POWER TO REMODEL RAPIDLY



Technical Monograph

Biocomposites®

Contents

Page

1. Overview 4

2. Introducing NanoBone 4

3. Indications for NanoBone 5

4. Applications for NanoBone 5

5. The composition of NanoBone 6

6. The mode of action of NanoBone 7

7. The advantages of NanoBone 8

7.1 Bioactivity and biocompatibility of nanostructured hydroxyapatite platelets 8

7.1.1 Study 1: Nanostructured bone grafting substitutes – A pathway to osteoinductivity 8

7.2 The role of the silica gel matrix 10

7.2.1 Study 1: Coupling of osteogenesis and angiogenesis in bone substitute healing – A brief overview 10

7.3 Angiogenic properties of NanoBone 12

7.3.1 Study 1: A preliminary study in osteoinduction by a nanocrystalline hydroxyapatite in the mini pig 12

8. Clinical studies 15

8.1 Study 1: Nanocrystalline hydroxyapatite bone substitute leads to sufficient bone tissue formation already after 3 months: Histological and histomorphometrical analysis 3 and 6 months following human sinus cavity augmentation 15

8.2 Study 2: Using nanotechnology as stand-alone bone grafting in open fracture bone defects and nonunions 17

8.3 Study 3: Evaluating a nanocrystalline hydroxyapatite bone graft substitute for the treatment of benign bone tumors 18

9. Case studies 19

9.1 Study 1: Calcaneal fracture 19

9.2 Study 2: Distal tibia bone infarction 20

9.3 Study 3: Femoral fracture 21

9.4 Study 4: Proximal tibia fracture 22

10. References 23

1. Overview

NanoBone® is a synthetic bone graft substitute that supports bone regeneration at every stage of the healing process. This technical monograph introduces NanoBone, discusses its indications and applications, and details its composition and mode of action. We will present the science behind the mechanism for the angiogenic properties of NanoBone, including the exchange of silica for an organic matrix of autologous proteins, and new bone formation and remodeling resulting from NanoBone's unique composition. Finally, we will discuss some of the clinical evidence for NanoBone.

2. Introducing NanoBone

NanoBone is a reliable and convenient, next generation, fully synthetic bone graft substitute. It can be placed in wet or dry sites and can be used in a variety of orthopaedic surgeries and in posterolateral spine. It provides the fullest support for bone regeneration at every stage of the healing process. NanoBone has the ideal properties for a bone graft as it is easy to prepare and apply, offers rapid and reliable bone formation, and completely absorbs.

NanoBone bone graft substitute consists of unique nanostructured hydroxyapatite (HA) platelets embedded in a silica gel matrix suspended in a hydrogel/polymer silica carrier. NanoBone integrates in the natural bone turnover and completely absorbs at a physiological rate with a comparable healing rate to autograft, without the costs and complications associated with harvesting the autograft.[1] The silica modified carrier facilitates ease of use of the putty. Bioavailable silica from the matrix and carrier is released within approximately 10 days to accelerate neovascularization and is exchanged by an organic matrix of autologous proteins, including BMPs, osteocalcin, osteopontin and glycoproteins.[2,3,4]

The NanoBone HA platelets are similar in size and shape to those that are complexed with collagen in human bone and are therefore available for biodegradation by osteoclasts. The nanostructure of NanoBone features interconnecting pores and high porosity, encouraging integration of newly formed blood vessels into the material and promoting rapid deposition of new bone in and around the bone graft substitute. High inner surface area is key to biological efficiency. Increasing the interaction between NanoBone and serum increases autologous protein enrichment and formation of an extracellular matrix to start bone healing. The organic matrix-coated HA platelets create optimal conditions for angiogenesis, bone formation, and remodeling.[2,5,6]

The combination of nanostructured HA and silica give NanoBone its osteoconductive properties.[7]

3. Indications for NanoBone

NanoBone is an implant intended to fill bony voids or gaps of the skeletal system (i.e., extremities, posterolateral spine and pelvis).[8] These osseous defects are surgically created or the result of traumatic injury to the bone and are not intrinsic to the stability of the bony structure. NanoBone resorbs and is replaced with bone during the healing process.

4. Applications for NanoBone

NanoBone can be used for all fields of application for which autologous cancellous bone could be used, including: posterolateral spine, depressed tibia plateau fracture, radial fracture, pathologic fracture, pseudarthrosis, acetabulum reconstruction, displacement osteotomy, bone necrosis, and defect fill after tumor or cyst removal.[8]

5. The composition of NanoBone

NanoBone is a fully synthetic bone graft substitute that consists of nanostructured HA platelets embedded in a silica gel matrix. This material is then suspended in a hydrogel/polymer silica carrier, achieved through a specific sol-gel process. NanoBone is specifically formulated with nanostructured HA that mimics HA in natural human bone.

NanoBone is created through a proprietary process. The highly biodegradable nanostructured HA in NanoBone, with dimensions of approximately 50 nm x 30 nm x 3 nm, closely mimics HA in natural human bone.[2,9] This is in contrast to other HA bone graft substitutes containing very large crystals of non-porous HA, which can take years to absorb. Materials often used in bone substitutes such as HA are sintered at a high temperature to remove all organic material, achieve higher density, and increase the mechanical strength of the material. This results in decreased material porosity and formation of large HA crystals. These two factors may negatively influence the ability of the product to be integrated in the natural bone turnover, thus increasing the risk of inflammation and foreign body reaction.[7] Natural HA constitutes 65 to 70% by mass of human bone, however synthetic sintered HA has low solubility in physiological environments and therefore exhibits a slow absorption rate (1-2% per year), preventing full remodeling of the implant site to the original bone architecture, and leaving a bone/HA composite instead of true trabecular bone.[10] Due to its size, sintered HA cannot be used as effectively during remodeling like HA in natural bone.

Silicon is an essential trace element in human bone mineralization and calcification.[10] Silica in the carrier and gel matrix in NanoBone offers a weakly crosslinked structure, making it available in biochemical processes in the host. Silica normally occurs in a crystalline and/or crosslinked structure like in minerals, which do not actively contribute biochemically in higher life forms. It is believed that the silica in NanoBone aids in non-fibrous connective tissue formation which then supports neogenesis, the proliferation of osteoblasts and osteoclasts, and bone matrix mineralization.[2] The silica gel matrix specifically has a high amount of open bonds, giving NanoBone a larger internal surface area and increased porosity to attract autologous proteins and promote degradation of the matrix and replacement by autologous proteins. This coupled with the high affinity of proteins to the surface of the HA platelets results in the silica gel matrix being rapidly replaced by an organic matrix containing host proteins important in bone regeneration and angiogenesis, which in turn supports new bone growth.[2]

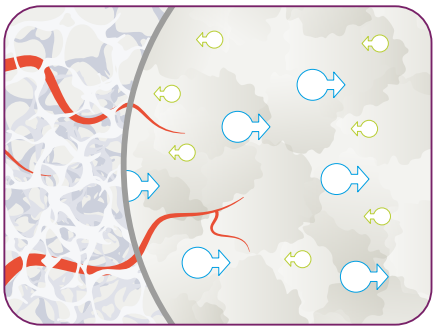
6. The mode of action of NanoBone

Bone healing is a multi-dimensional process. The silica gel matrix in NanoBone is quickly transformed by the body into a biomimetic organic matrix that enables physiological bone turnover at a very early stage.[2,3]

Phase 1 approx. 10 days

Neovascularization of the defect and attraction of autologous proteins

Silica from the carrier and the granules is released to accelerate neovascularization and is then exchanged for an organic matrix of autologous proteins: inc. BMPs, osteocalcin, osteopontin, glycoproteins.[2,3,4]



Phase 2 approx. 100 days

Remodeling – absorption of nanostructured hydroxyapatite and proteins

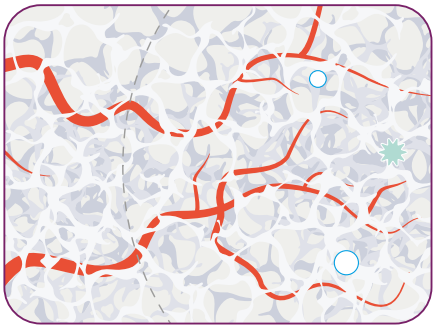
Combination of nanostructured hydroxyapatite and organic matrix of autologous proteins promotes rapid bone remodeling and formation of woven bone.[2,3,4]



Phase 3 beyond 100 days

Completion – absorption of woven bone and formation of lamellar bone

Remaining nanostructured hydroxyapatite and organic matrix of autologous proteins are biodegraded by osteoclasts, and osteoblasts form new lamellar bone.[3,4]



7. The advantages of NanoBone

7.1 Bioactivity and biocompatibility of nanostructured hydroxyapatite platelets

Through a proprietary manufacturing process NanoBone contains HA that forms small platelets approximately 50 nm x 30 nm x 3 nm, similar in morphology to innate HA in natural human bone.

7.1.1 Study 1:

Nanostructured bone grafting substitutes – A pathway to osteoinductivity

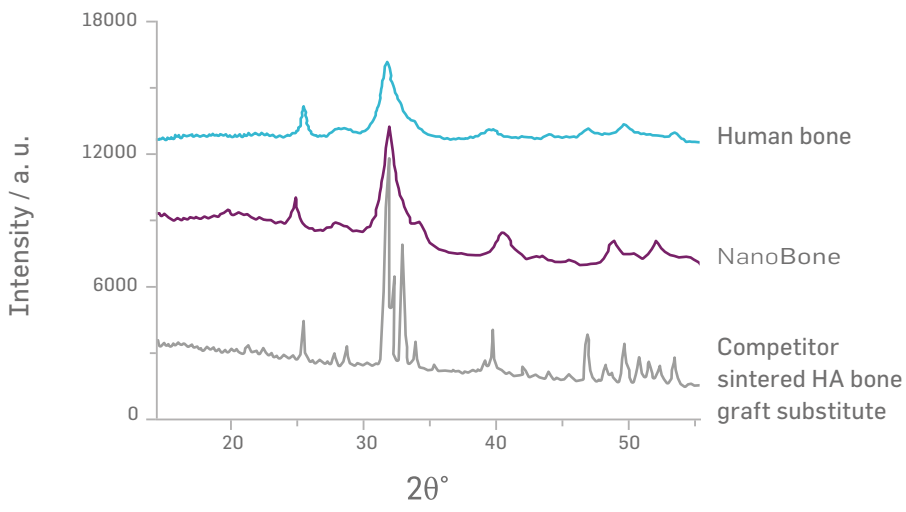
The comparative investigation of a highly nanoporous bone grafting material (NanoBone) and a sintered hydroxyapatite ceramic (Cerabone) aimed to show the influence of the structure of the grafting material on osteoinductivity.

NanoBone is a highly porous bone graft substitute with a porosity of approximately 80% and a large specific surface area of around 207 m^2/g. By contrast the competitor sintered HA bone graft substitute has a specific surface area of 0.4 m^2/g.[2,6]

Direct comparison using XRD analysis showed that the nanostructured HA platelets are comparable in size to biological HA in human bone and have similar platelet morphology. The sharp peaks of the competitor sintered HA ceramic (**Figure 1a**) are indicative of the larger dimensions of the HA crystals, which are larger than 1 µm (**Figure 1b**).[6] By contrast, the non-sintered HA platelets shown in **Figure 1c** are 3 nm thick, 30 nm wide and 50 nm long, which are similar dimensions to HA platelets in human bone.[6]

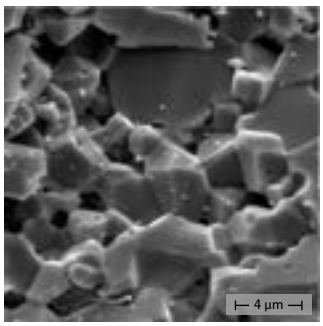
Figure 1

1a

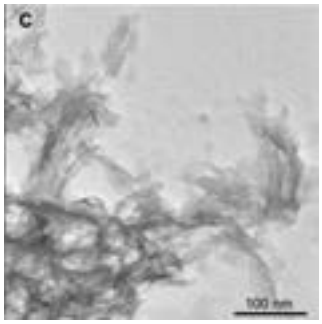


Narrow peaks represent larger HA crystals

1b



1c



Each graft material was implanted superficially into the trapezius muscle and subcutaneously in adipose tissue in the neck region of 18 sheep for 6, 12, and 26 weeks.

At 6 weeks neovascularization was present, and small vessels were present within the NanoBone granules.[6] Histology and immunohistochemistry demonstrated osteoclast-like cells and bone remodeling cells on the surface of NanoBone granules after 6 weeks. Figure 2A shows osteoclast like cells and TRAP-positive cells as red stained areas. Signs of early bone remodeling on the surface of the NanoBone granules were present.

Figure 2

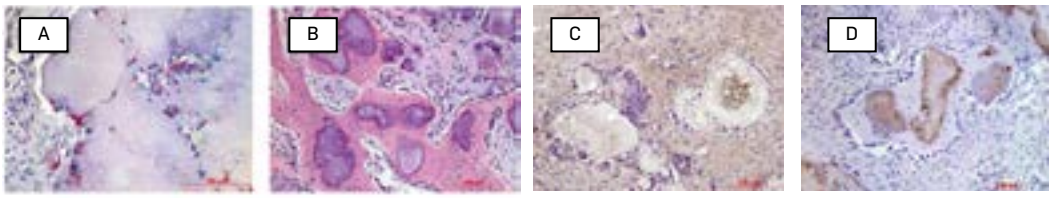
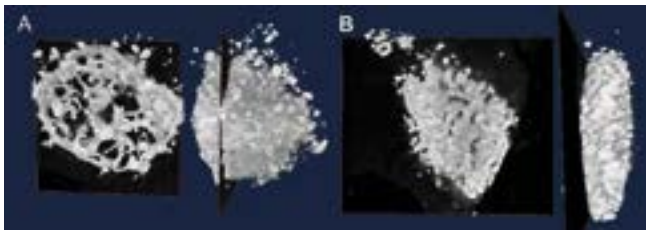


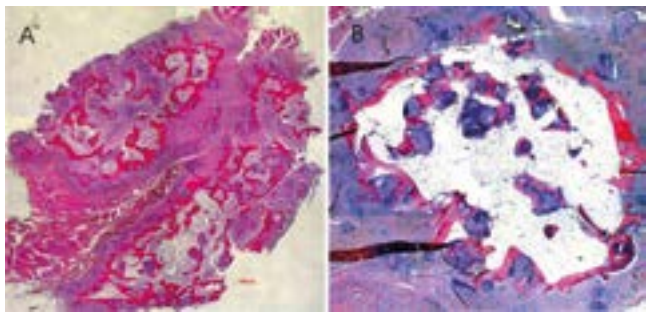
Figure 2B demonstrated early ectopic bone formation, with light pink staining signifying bone. The matrix of NanoBone granules showed strong immunoreactivity (brown staining) for Osteocalcin in Figure 2C. The strongest staining was detectable in the center of the granules. The immunoreactivity pattern (brown staining) of Osteopontin in and around the granules was similar to that of Osteocalcin, except for a stronger staining at the interfaces between granules and newly formed bone tissue (Figure 2D).

Figure 3



Micro-CT scanning in Figure 3 showed the implantation site 26 weeks after implantation in sheep and the presence of ectopic bone after implantation in both muscle (A) and subcutaneous adipose tissue (B).

Figure 4



The quality of new bone showed no difference to lamellar bone. Bone marrow was also present, that is typically found in the interior of the long bone, following the implantation into muscle tissue (Figure 4). At 12 weeks (A) the presence of bone marrow was observed in some implantation sites, by 26 weeks (B) a central marrow was observed. Therefore, NanoBone's mode of action follows a similar remodeling pattern to natural bone.[6]

The results suggest that the nanostructure and composition of NanoBone initiated the replacement of the silica gel matrix from NanoBone with an organic non collagenous matrix similar to the extracellular matrix available in bone.

While the *in vivo* study demonstrates osteoinductive potential under preclinical conditions, these findings do not necessarily translate to equivalent clinical outcomes. NanoBone's osteoinductivity has not been validated or approved.

7.2 The role of the silica gel matrix

Silicon is an essential element in human bone mineralization. The silica component with the nanostructured HA of NanoBone is believed to be responsible for inducing connective tissue formation, which then supports the proliferation of osteoblasts and bone matrix mineralization. The silica gel matrix is characterized by a high density of open bonds, resulting in a large specific surface area, thus causing neovascularization of the defect and attraction of autologous proteins.[2] NanoBone's unique silica structure induces osteogenesis by being rapidly exchanged by a readily available organic matrix of autologous proteins (e.g. BMP-2).

7.2.1 Study 1:

Coupling of osteogenesis and angiogenesis in bone substitute healing – A brief overview

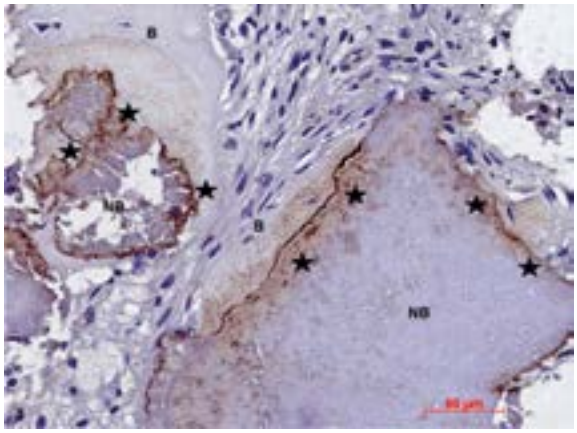
In this paper, Götz et al. discuss neoangiogenesis, which is critical for new bone formation in healing and repair and is important for a healthy blood supply in bone healing. There is a close relationship between osteogenesis and angiogenesis. NanoBone contains nanostructured non-sintered HA particles embedded in a silica gel matrix. The granules are innervated with new blood vessels that branch from existing blood vessels after implantation.[11]

NanoBone's highly porous structure facilitates the growth of new blood vessels. This is critical because a reduced rate of angiogenesis could be a reason for clinically unsuccessful healing or osteogenesis due to local problems in vascularization.

It is suggested that the silica gel matrix is replaced by an organic proteinaceous matrix that attracts cells such as fibroblasts, osteoblasts and osteoclasts. Osteopontin was present in the organic matrix, which is one of the proteins responsible for attracting bone cells that also has an angiogenic effect.[11]

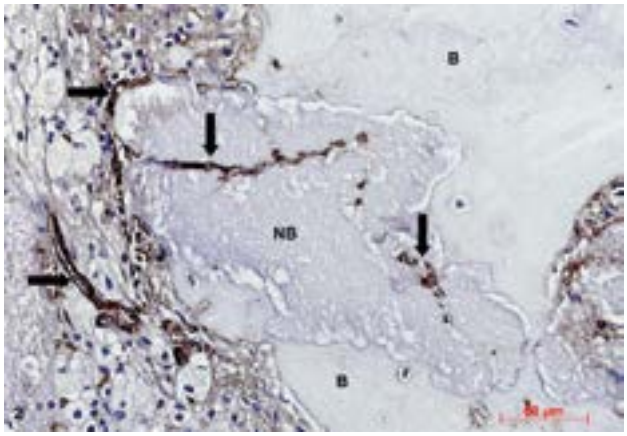
Osteopontin is indicated by stars in Figure 5 below and is shown to be present at the periphery between NanoBone granules (**NB**), and new bone formation (**B**) in a mandible biopsy.

Figure 5



It was also observed that NanoBone supports later stages of osteogenesis with the formation of capillaries. Figure 6 shows capillaries marked by arrows innervated into the NanoBone granule (NB). The ability of the material to accommodate capillaries results from the high porosity and matrix change of silica in NanoBone.[11]

Figure 6



7.3 Angiogenic properties of NanoBone

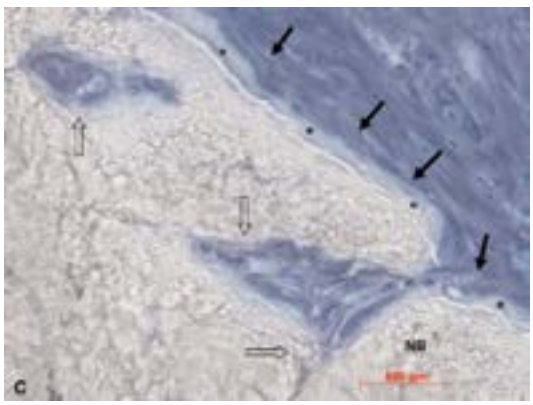
Angiogenesis is the process of forming new blood capillaries from existing blood vessels.[11] This is key for biomaterial implantations as a sufficient blood supply is vital for successful bone healing and osteogenesis. Sufficient blood circulation alongside adequate surface structure, porosity, and chemical properties that are biocompatible, are favorable in bone graft substitutes as they provide an osteoconductive potential.[4] NanoBone has osteoconductive properties, as the graft material acts as a scaffold that encourages bone growth onto its surface and within its pores.[12] NanoBone's osteogenic and osteoconductive properties support the promotion of new bone formation using cells from the surrounding tissue and complete replacement of the grafting material.

7.3.1 Study 1:

A preliminary study in osteoinduction by a nanocrystalline hydroxyapatite in the mini pig

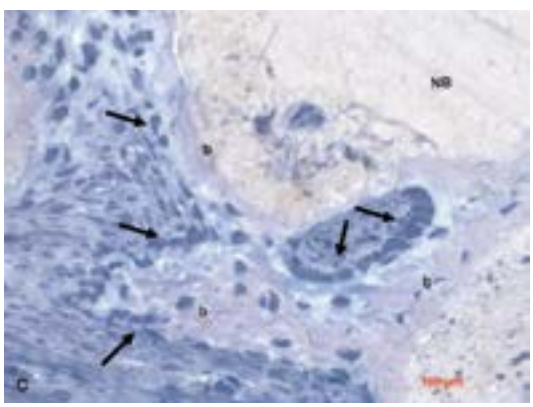
The aim of this study was to test the hypothetic osteoinductive properties of NanoBone. NanoBone was implanted subcutaneously and intramuscularly into the back region of mini pigs and bone formation was characterized post-operatively.[7]

Figure 7



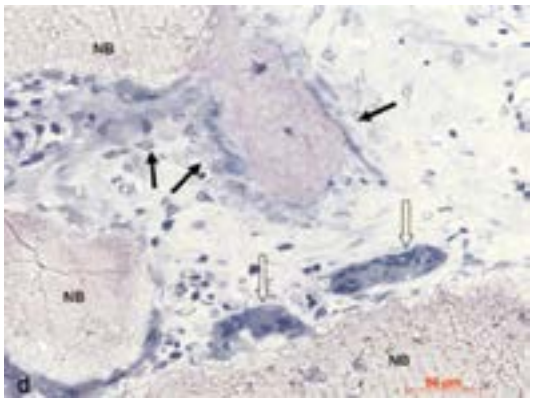
Five weeks after implantation NanoBone material was observed in histology samples, showing a connective tissue matrix at both the subcutaneous implantation sites and muscle. Figure 7 shows osteoblasts (black arrows) and an osteoid seam (asterisks) along the borders of the NanoBone (**NB**) material, indicating the leading edge of bone remodeling in the subcutaneous implantation site. Osteoclasts are also present. In the majority of animals, osteoblast-like cells with osteoid underneath were also identified, signifying early-stage osteogenesis.[7]

Figure 8



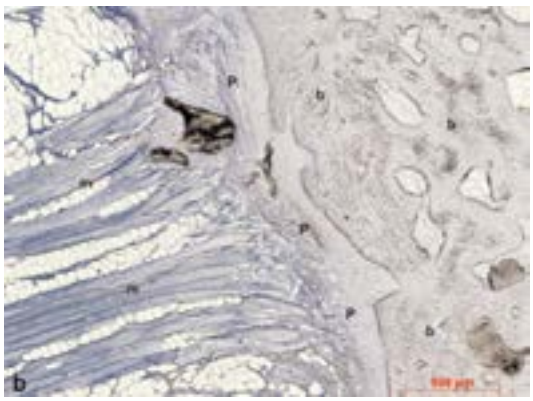
At 10 weeks no NanoBone or new bone tissue was observed from the histological samples at the muscle implantation sites. However after 10 weeks, the subcutaneous sites showed increased osteogenesis and degradation of NanoBone granules compared to 5 weeks (Figure 8).
Newly formed mineralizing bone substance (**b**) can be seen surrounding undegraded NanoBone granules (**NB**) covered with osteoblasts (black arrows).[7]

Figure 9



Four months after implantation of NanoBone, minor or no osteogenesis was observed in the intramuscular implantation sites. At the subcutaneous implantation sites, advanced osteogenesis was observed with the bony tissue showing woven bone with lamellar structures (Figure 9). Any residual nanostructured HA granules were incorporated into the bone. Large osteoclasts (open arrows) could be seen on the surface of the NanoBone granule with osteoblasts (black arrows) secreting bone matrix around the NanoBone granules.[7]

Figure 10



After 8 months post-implantation, advanced osteogenesis was visible in the subcutaneous implantation sites by microscopy in 4 out of 9 animals. In 4 cases, cancellous bone was observed with loose vascularized connective tissue or adipose tissue resembling bone marrow.[7]

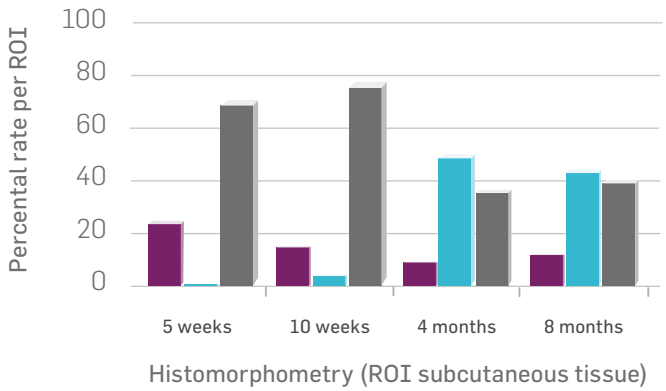
Figure 10 shows newly formed cancellous bone (**b**) that could be observed by histology surrounded with a periost-like structure (**P**) connected to muscle fibers (**m**) in the subcutaneous implantation sites.

The amount of NanoBone biomaterial, new bone and soft tissue was quantified by histomorphometry. Over the time periods tested in subcutaneous tissue, the amount of NanoBone decreased from 26% to 11%. New bone formation was reported at 53% at 4 months, and was noticeable at 48% at 8 months post-implantation, as shown in Figure 11a. The amount of soft tissue decreased at 4 months from 80% to 41%, then at 8 months post-implantation the amount of soft tissue remained steady at around 42%.[7]

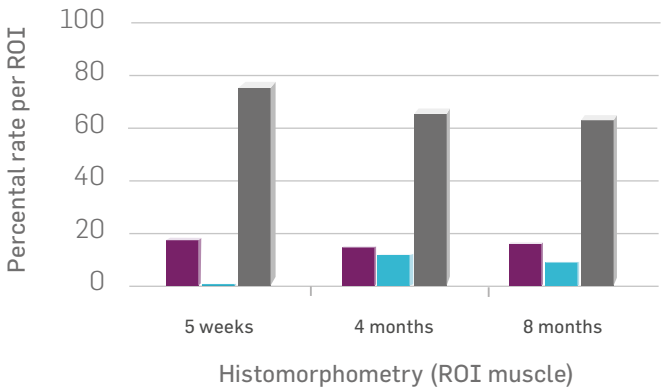
In the intramuscular sites the NanoBone material was consistently around 20% at each time point. New bone formation was detected after 4 months and accounted for 11% at 8 months. The amount of soft tissue decreased from 80% at 5 weeks to 71% at 4 months and 70% at 8 months, as shown in Figure 11b.[7]

Figure 11

11a



11b





In summary, implantation of NanoBone intramuscularly or subcutaneously induced new bone formation. The new bone was minimal at 11% in the intramuscular sites but substantial at roughly 50% of the subcutaneous sites. This demonstrates that NanoBone has potential to stimulate new bone formation outside of bony sites.

While the *in vivo* study demonstrates osteoinductive potential under preclinical conditions, these findings do not necessarily translate to equivalent clinical outcomes. NanoBone's osteoinductivity has not been validated or approved.

8. Clinical studies

NanoBone has been used successfully in over 100,000 clinical cases.

8.1 Study 1:

Nanocrystalline hydroxyapatite bone substitute leads to sufficient bone tissue formation already after 3 months: Histological and histomorphometrical analysis 3 and 6 months following human sinus cavity augmentation

In this study, the potential for new bone formation following use of NanoBone was assessed in 14 patients with severe atrophic maxillary bone after sinus cavity augmentation. Samples were analyzed 3 and 6 months after implantation using histology and histomorphometry.[13]

The surgical cavity was augmented with NanoBone, after being mixed with blood gained from the surgical site. Fourteen biopsies were taken in total during second stage surgery 3 or 6 months post-implantation of NanoBone.[13] Seven biopsies from each time point were prepared and then anaylzed using histology and histomorphometries.

After 3 months, the augmentative area showed connective tissue from around NanoBone (NB) and bone trabeculae formation on the surface of the NanoBone. Multinucleated cells (arrow heads), produced in the connective tissue (CT), assisted the cellular degradation of the bone substitute as seen in Figure 12a. Newly formed bone (B) was observed in the majority of samples as seen in Figure 12b.

Figure 12a

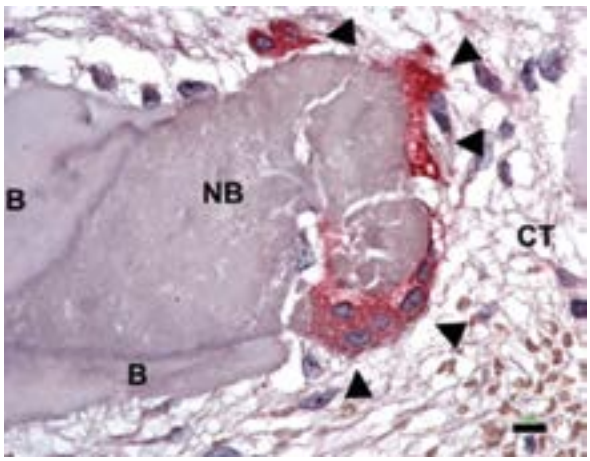
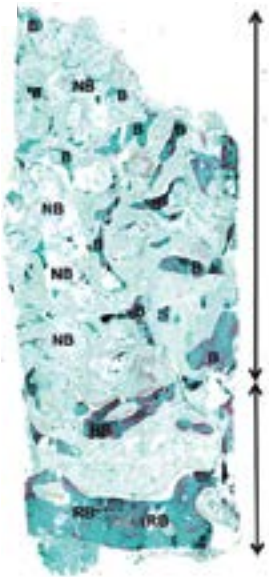


Figure 12b



By 3 months, the percentage distribution of bone substitute, new bone and connective tissue were 29%, 25% and 46% respectively.[13] The histomorphometric results of the augmented region demonstrated a higher proportion of tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells, similar to osteoclast-like cells, compared to residual bone fractions.[13]

Figure 13

Tissue distribution within the fraction of the augmented area

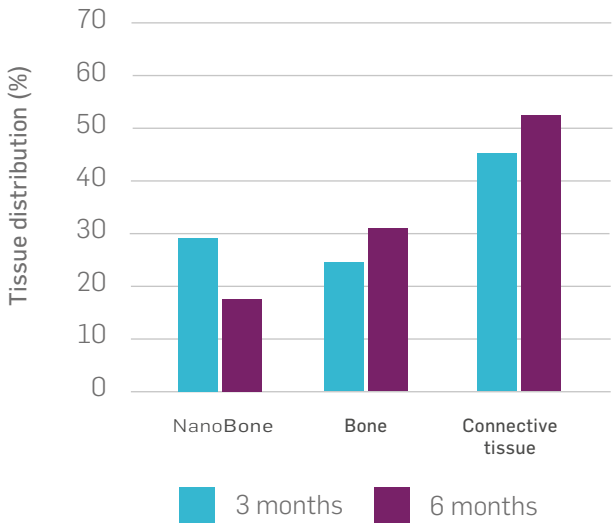
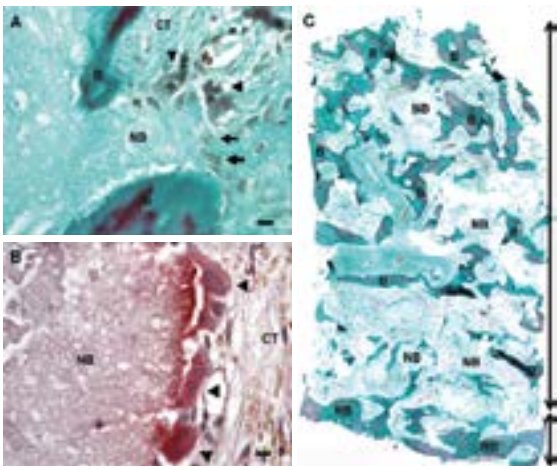


Figure 14



After 6 months, NanoBone was well integrated in the new surrounding tissue, and new bone was observed in all samples, as shown in Figure 13. Due to the presence of TRAP-positive and TRAP-negative multinucleated giant cells, degradation was still ongoing for the remaining biomaterial, as shown in Figure 14. It was noted that a significantly higher amount of total multinucleated cells were present at the augmentation region than in residual bone, which could support the suggestion that residual bone tissue remodeling is slower than the NanoBone remodeling process.[13] Between 3 and 6 months the NanoBone at the augmentation region underwent significant degradation, the amount of bone substitute decreased to 17% from 29%, and the new bone formation increased to 31% from 25%. This increase in new bone positively correlated with an increase of connective tissue. However, the biomaterial degradation is not associated with new bone formation alone, but rather with mixed tissue of bone and connective tissue.[13]

The data supports the osteoconductive properties of NanoBone, and increased production of vessels to ensure a sufficient blood supply for successful bone regeneration compared to residual bone. A high blood vessel density assists the increased metabolism for chemotaxis of inflammatory cells which support the degradation of NanoBone. The neovascularization properties of NanoBone also attract TRAP-positive multinucleated giant cells, also known as osteoclast-like cells, which support the degradation of biomaterial and dissolution.[13]

8.2 Study 2:

Using nanotechnology as stand-alone bone grafting in open fracture bone defects and nonunions

The objective of this study was to review outcomes and complications of open fracture defects and nonunions treated with nanotechnology-derived, stand-alone synthetic bone graft.[14]

This was a retrospective review of open fracture defects and nonunions treated with the addition of a novel, advanced bone graft material utilizing nanocrystalline hydroxyapatite (HA) that resemble the size, chemistry, and morphology of human HA particles. The HA particles are contained within an amorphous silica gel matrix. The matrix is highly nanoporous, hydrophilic, and releases silicon dioxide, which triggers angiogenesis and initial bone formation. The synthetic bone grafting material, NanoBone was used in cases between 2017 and 2019 by a single surgeon at a Level-I trauma center. Patients were treated using standard bone grafting techniques utilizing the synthetic product in open fractures with bone defects and radiographically defined nonunions.[14]

17 patients underwent the application of NanoBone - 9 patients with open fracture defects and 8 patients with nonunions. 7 of 9 open fracture defects (78%) were in the tibia, 1 of 9 (11%) was the radius, and 1 of 9 (11%) was in the distal humerus. The nonunions included 3 of 8 distal femur (38%), 4 of 8 tibia (50%), and 1 of 8 calcaneus (12%). The average age was 37 years (range 22-83). Patients were observed for an average of 13 weeks postoperatively (range 8 weeks to 26 months). There were no patients lost to follow-up. Union was observed in 9 of 9 (100%) of the open fracture defects and 8 of 8 of the nonunions. The average time to union was 7.5 weeks (range 6-12 weeks) when including open fracture defects and nonunions. There were no intraoperative or late complications. Early postoperative complications included a superficial infection of the radius open fracture that required oral antibiotics.[14]

Using nanotechnology with nanocrystalline HA particles that are contained in a silica gel matrix is a successful treatment as stand-alone bone graft in both open fracture defects and nonunions. This preliminary data shows evidence of low complication rates, high union rates, and early healing. This data suggest that using nanocrystalline HA particles may be an alternative to other methods of autologous bone grafts, allografts, and/or synthetic bone grafts. Although, this study did not quantify the bone density healing, it shows more subjective bony consolidation at much earlier stages of healing when compared to the authors previous gold standard, autologous bone. The authors further stated that they have switched from using autologous bone grafts to mainly using the nanocrystalline HA particles, as they believe the preliminary findings show high and early healing rates with the reduction of risks and comorbidities associated with autologous bone graft.[14]

8.3 Study 3:

Evaluating a nanocrystalline hydroxyapatite bone graft substitute for the treatment of benign bone tumors

Ninety-eight patients were studied following the implantation of NanoBone between August 2018 and February 2021 for the treatment of benign tumors.[15] Patients were followed for a minimum of 6 months out to 2.5 years (range 6-36 months). Radiographic follow-up was performed post-operatively at 6 weeks, 12 weeks, 6 months and 12 months, and then biannually. Physical examinations, range of motion and strength assessments, and radiographic study were performed.[15]

Within this study, the most common tumor types were unicameral bone cysts (22), non-ossifying fibroma/fibrous cortical defects (19) and aneurysmal bone cysts (15). With the most common location being proximal humerus (38), distal femur (21) or hands/feet (12).[15]

After the removal of the tumor, between 1-25 cc of NanoBone was implanted. It was reported that the surgical time for preparation and insertion of NanoBone was under five minutes due to the product being pre-packaged and requiring no additional preparation.

The surgery was successful in all 98 patients, with no infections or other complications related to the bone graft reported. No evidence of heterotopic ossification or complications were reported with the surrounding soft tissue, and any excess NanoBone in the soft tissue was absorbed within 12 weeks.[15]

Radiographic evidence demonstrated the gradual diminishing and remodeling of the bone graft/host bone interface with healing times ranging from 4 to 12 weeks. By 12 weeks, new bone growth and development of trabeculae was observed. All patients achieved successful clinical outcomes and were fully active and weight-bearing.[15]

In cases where adjuvant margin enhancers such as liquid nitrogen or cryosurgery were used, NanoBone still incorporated at the same rate and the quality of bone formed was deemed equivalent to the non “frozen” bone. No late fractures, infections or differences in remodeling were noted in the radiographs in comparison with the non-frozen bone.[15]

It was concluded that NanoBone is a safe, synthetic bone graft and was shown to be an effective treatment for benign bone tumors in the appendicular skeleton, even in hostile environments such as following the use of chemical or cryosurgery.[15]

9. Case studies

9.1 Study 1:

Courtesy of Dr. Arndt P. Schulz[16]

Consultant Medical Researcher in Orthopaedics, Lübeck, Germany

Clinical particulars

62-year-old male sustained a calcaneal fracture of the left foot with severe depression of the joint line after a fall.

Treatment

Following 1 week of conservative treatment to reduce swelling, an osteosynthesis was performed to reconstruct the joint surface with a calcaneal plate and locking screws, and 2.5 ml of NanoBone was applied to fill the remaining defect.

Outcome

At 6 months, hardware was removed and x-rays confirmed full bony consolidation. At 1 year follow-up, the patient was independently ambulatory with normal range of motion and no pain.



Presentation



Post-operative



6 months



1 year

9.2 Study 2:

Courtesy of Dr. Arndt P. Schulz[16]

Consultant Medical Researcher in Orthopaedics, Lübeck, Germany

Clinical particulars

Patient presented 6 months after treatment at a different clinic for reduction of a Maisonneuve's injury with persistent pain and recurrent swelling of the right upper ankle. Two screws used for the reduction had been previously removed after complaints of pain and swelling in the upper ankle area. Diagnostics confirmed a post-traumatic bone infarction in the area of the distal right tibia. The patient was admitted for diagnostic arthroscopy of the right ankle joint and potential removal of the infarction zone with sample collection. The reason for bone necrosis was not clear.

Treatment - Stage 1

Stage 1 of treatment involved fenestration of the tibia and removal of all necrotic material. Samples were collected for histopathological and microbiological examination. Additionally, an ankle arthroscopy was performed to eliminate the possibility of cartilage damage.

Treatment - Stage 2

Two weeks later, the patient was readmitted after any malignancy or deep infection was excluded. Stage 2 of treatment involved surgical revision, debridement, and filling of the defect zone with 5 ml of NanoBone.

Outcome

At discharge following stage 2 surgery, the patient was independently ambulatory and fully weight-bearing. At 1 year follow-up, the patient remains pain and symptom free.



Presentation



Stage 1 - Post-operative



Stage 2 - Post-operative



Stage 2 - Post-operative



Stage 2 - 1 year



Stage 2 - 1 year

9.3 Study 3:

Courtesy of Dr. Arndt P. Schulz[16]

Consultant Medical Researcher in Orthopaedics, Lübeck, Germany

Clinical particulars

30-year-old male involved in a motor vehicle accident sustained multiple injuries, including an AO C3 distal femoral shaft fracture with open wound site less than 1 cm (Gustilo - Anderson classification - grade I).

Treatment

An open reduction internal fixation was performed with a locked femoral plate. The remaining bone void was filled with 2.5 ml of NanoBone.

Outcome

1 year post-operative x-rays show full bony consolidation. The patient was fully independently ambulatory with normal range of motion and no pain.



Presentation



Post-operative



Post-operative



1 year



1 year

9.4 Study 4:

Courtesy of Dr. Arndt P. Schulz[16]

Consultant Medical Researcher in Orthopaedics, Lübeck, Germany

Clinical particulars

42-year-old male involved in a motor vehicle accident sustained multiple injuries, including a proximal tibia fracture with a large bone-cartilage defect of the lateral condyle.

Treatment - Stage 1

Following the reduction of swelling, osteosynthesis was performed to address the proximal tibia defect, utilizing 7.5 ml of NanoBone. Stabilization was achieved using a locked proximal tibia plate. Subsequently, a cartilage defect remained.

Treatment - Stage 2

After 5 months the patient was readmitted for arthroscopy and re-evaluation of cartilage defect, revealing a traumatic chondral lesion. This was subsequently treated with autologous matrix-induced chondrogenesis (AMIC), involving microfracturing with application of a porcine collagen matrix. The bony status of the former proximal tibia defect allowed for the procedure without complications. To support the bony structures, the proximal tibia plate was removed and replaced with a thin locked support plate.

Outcome

At 7 months following stage 2 surgery, x-rays show full bony consolidation. Follow-up at 19 months revealed a range of motion of 125 degrees, indicating recovery, restored function and mobility.



Presentation



Stage 1 - Post-operative



Stage 2 - 7 months



Stage 2 - 7 months



Stage 2 - 19 months



Stage 2 - 19 months

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For indications, contraindications, warnings and precautions see Instructions for Use.

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