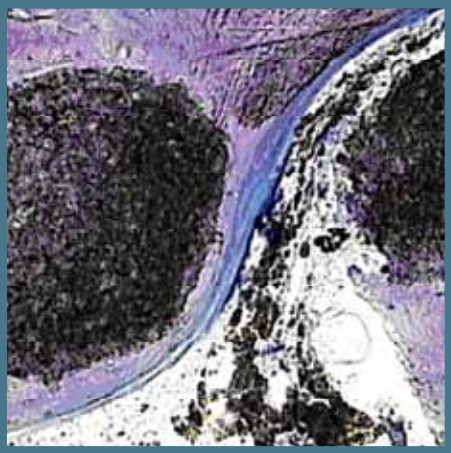
LINK®



BoneLink®

Setting new standards in bone regeneration

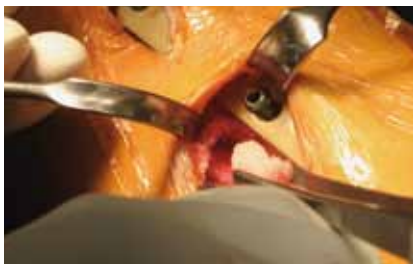
The goal of all treatment methods of bone regeneration is restitutio ad integrum.

To achieve this, the bone regenerative materials must have a capacity for complete integration into the natural processes. Ideally, therefore, the material should have osteogenic, osteoconductive and osteoinductive properties.

Up to now, only the patient's autologous bone has fulfilled this function, which is currently the gold standard in medicine. The disadvantage with this method is that a second intervention is necessary, in which the autologous tissue is harvested. The surgery can cause significant stress and dysfunctions and holds an array of additional risks for the patient. If allogenic or xenogenic materials are substituted for autologous bone, immunological rejection may occur. Furthermore, these materials have the potential to transmit infections and diseases of animal or human origin.

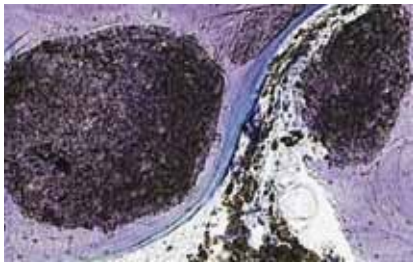
■ Mixture of BoneLink® and autologous blood

The limited availability of endogenous bone and the problems associated with the use of allogenic or xenogenic materials have prompted the increasing use of synthetic products in orthopedics. The suitability of synthetic bone substitutes comes down to whether they are bioconductive materials that have a capacity for complete integration into the natural regenerative processes of the bone.



■ Filling the bone defect

Predominantly inorganic components are used for most synthetic bone substitutes. Their structure lends them to use as an osteoconductive scaffold. The most commonly used materials are calcium phosphate compounds (e.g. hydroxyapatite), as they are most similar to the natural inorganic bone matrix. But this criterion alone is no guarantee of success. Deficiencies in the composition of the material can greatly diminish the success of treatment, because physiological processes are thrown off balance or become impaired.



■ Precipitated bone formation

In addition, certain manufacturing processes can significantly affect the suitability of the material. A good bone regenerative material should ultimately permit physiological processes at cell level, offer controlled resorption with good biocompatibility and stimulate the formation of bone.

BoneLink® - Innovative product for successful bone regeneration

Orthopaedic indications

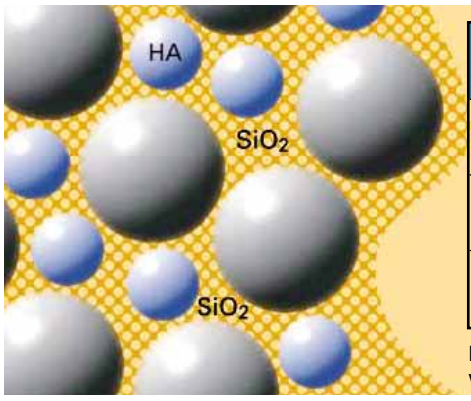
- After harvesting corticocancellous bone chips
- After tumor resections
- In the case of acetabular defects in hip revisions
- In the case of surgical spondylodeses
- In the case of pseudo-arthroses
- In the case of fractures treated using certain methods of osteo-synthesis

BoneLink® is a synthetic bone regenerative material designed to support reconstruction in bone defects.

BoneLink® comprises a mixture of calcium phosphate hydroxyapatite (HA) and ß-tricalcium phosphate (ß-TCP), both nanocrystalline, in the proven ratio of 60:40. In contrast to conventional HA and ß-TCP ceramics or bioglasses, BoneLink® is manufactured by a sol-gel method (without sintering), in which the nanocrystalline calcium phosphates are embedded in a bioactive silicon dioxide matrix.
This special low-temperature manufacturing process results in high porosity within the individual granules. An interconnecting pore system on the nanometer and micrometer scale gives the product a very large internal surface area of approx. 90 m^2/g.
After mixing with the patient's autologous blood, the granules become exceptionally dimensionally stable. The simple and safe application combined with the good site stability of the granules means that BoneLink® can be used for even hard-to-reach and large defects. One gram of BoneLink® fills bone defects up to a size of approx. 2 cm^3.

Good compatibility

BoneLink® offers good biocompatibility and also facilitates complication-free wound-healing. Its good compatibility and safety in use have been proven in biocompatibility tests, toxicological and clinical studies.



HA	ß-TCP	SiO_2
60 : 40		
87%		13%
90 nm	400 nm	Nano-porous scaffold

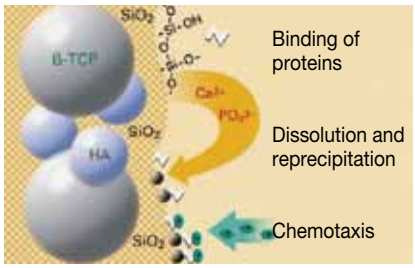
Manufacture: patented sol-gel method without sintering (DE10003824)

■ Granules

■ Bone regenerative material with optimized composition

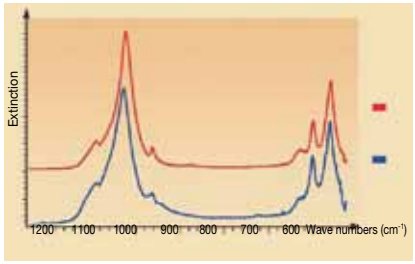
BoneLink® is perfectly adapted to physiological processes

A key feature behind BoneLink® is the presence of silicon in a bioactive compound. It has been known for a long time that silicon has both a stimulating and regulating influence on endogenous mineralization and also forms an important basis for the synthesis of collagens [1, 2].



■ Apatite elimination on BoneLink® surface (nucleation)

As a result of a gentle low-temperature manufacturing process, the silicon component is available in the form of a hydrated silicon dioxide scaffold. This gives a highly important property for osteogenesis: the ability to form a nanocrystalline layer on the surface of the material after introduction to a physiological site.



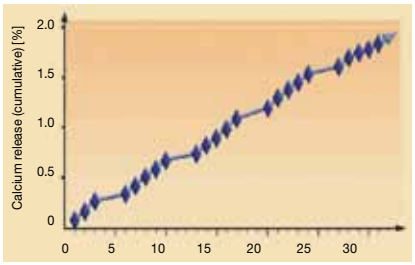
■ FT IR spectrum of the BoneLink® surface after incubation for 90 minutes in physiological solution (blue) compared with synthetic, fine-crystalline hydroxyapatite (red).

The FT IR spectrum clearly shows the correlation between an in vitro-induced apatite phase at the surface and synthetic, fine-crystalline hydroxyapatite.

BoneLink® is thus the nucleation agent for the formation of a layer, which is very similar in composition and habitus to new bone. Such reprecipitation on unsintered silicon dioxide surfaces is frequently described in the scientific literature and is regarded as a cause of rapid osteogenesis [3, 4]. This newly formed bioactive layer also prevents the premature dissolution of the silicon dioxide matrix underneath.

Controlled calcium release

The embedding of the two calcium phosphates HA and ß-TCP in the silicon dioxide scaffold produces an ion concentration at the bone defect site, which increases locally over a long period of time, and thus stimulates rapid osteogenesis and elevates bone remodeling [5]. The degradation of the bone regenerative material through cellular processes involves the material in bone metabolism (bone remodeling) and replaces it with new bone.



■ Ca release (cumulative) with 24-hour cycle/day in Tris/HCl buffer, pH 7.3

Interconnecting pore system

The bone regenerative material features an porosity of approx. 70 +/- 5 %. The interconnecting pore system on the nanometer and micrometer scale with its high capillarity and adsorbability facilitates complete diffusion of biological fluids, binds important growth factors in the blood and promotes bone formation as a result. Furthermore, the material acts as a scaffold and conductor for bone cells during osteogenesis.

In addition, BoneLink® is an ideal carrier for drugs. During in-vitro trials, the bone regenerative material demonstrated a high retention capacity for antibiotics, where release of the antibiotic over a period of several weeks was observed [6].

In vitro and in vivo results

Cell culture experiments show that BoneLink® supports both the growth and function of the cells responsible for bone formation (osteoblasts) in a highly effective way [7].

In a randomized clinical study, the main advantages of BoneLink® over a conventionally manufactured, sintered bone substitute made of ß-TCP were more rapid bone formation along with little pronounced redness and swelling in the wound site, and simple and safe application [8].

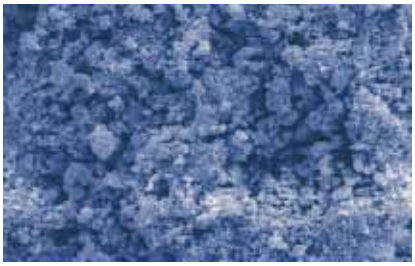

ZERTIFIKAT ◆ CERTIFICATE ◆ 证书 ◆ CERTIFICADO ◆ CERTIFICAT

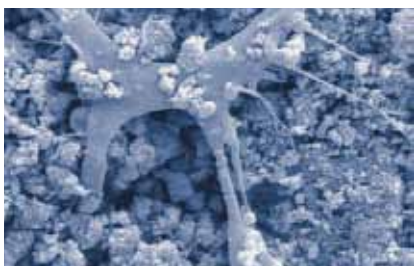
EC Design Examination Certificate

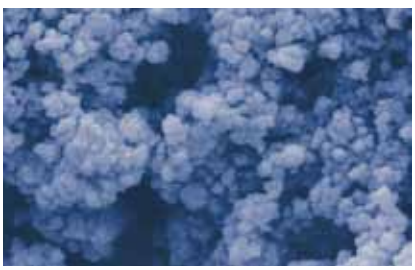
Manufacturer: Waldemar Link GmbH & Co. KG

Product: Non-Active Implants


■ SEM 80x


■ SEM 1000x


■ SEM 2000x,
mesenchymal stem cell


■ SEM 10000x

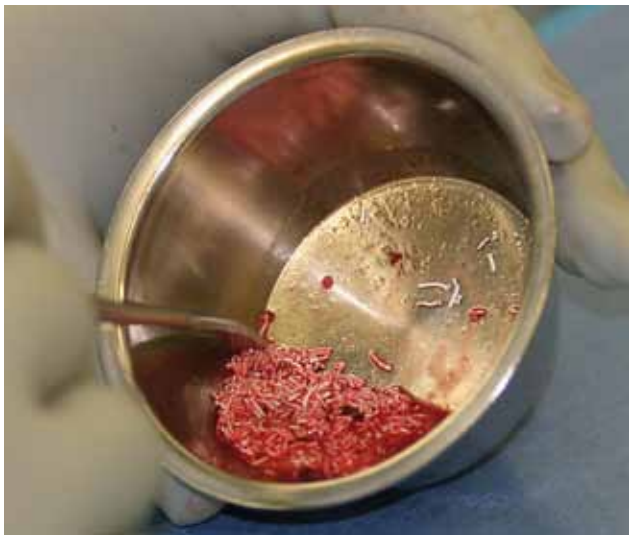
BoneLink® – Advantages at a glance

- Fully synthetic
- Completely resorbable
- Highly porous
- High capillarity
- Spacer function
- Physiologically adapted
- Excellent compatibility

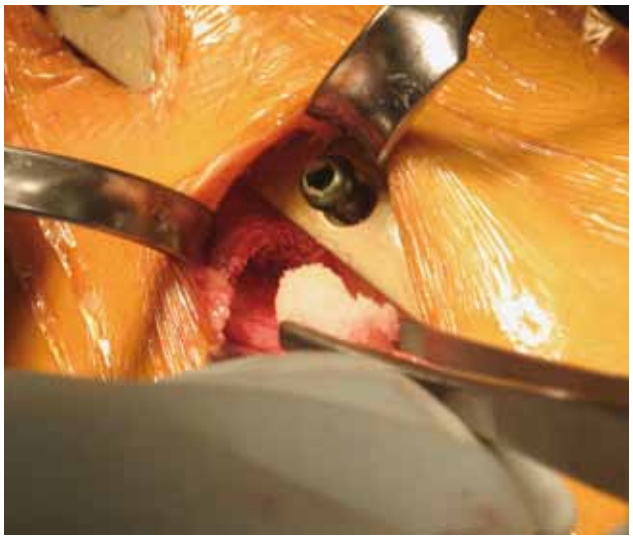
Step-by-step application

BoneLink® is a synthetic, bioactive, completely resorbable material for filling and reconstructing bone defects.
Direct contact with the vital bone tissue is absolutely essential for BoneLink® to function. For that reason, the bone regenerative material may only be applied in revivified defects. For application purposes, it is vital to mix BoneLink® with the patient's autologous blood and, if necessary, with autologous bone marrow to form a workable paste. Autologous cancellous bone or bone chips can be added with the autologous blood after incubation of BoneLink®, since they additionally support bone formation.

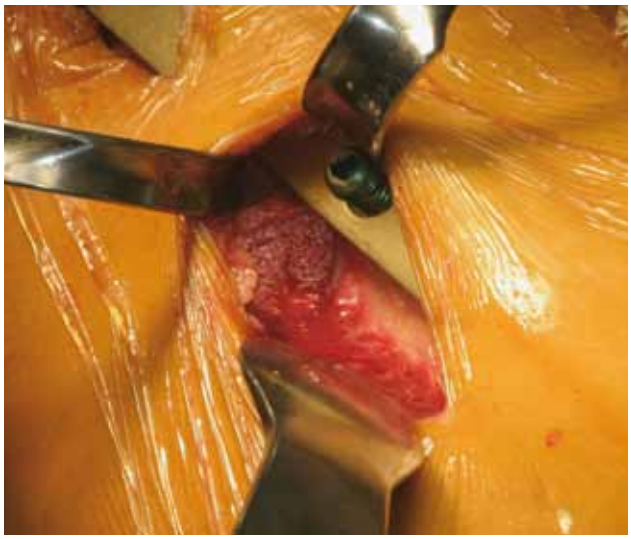
When mixed, the material is easy to model and displays good stability in the defect. The material dose is governed by the type and size of the bone defect. Note that the bone defect should be completely filled. One gram of BoneLink® is sufficient to fill a defect of approx. 2 cm^3. The material must be loosely filled in. Avoid packing the material, or macroporosity will be reduced.



■ Mixing the material with autologous blood/bone marrow/ bone chips



■ Filling the defect



■ Filling defect

Granule and pack sizes

Item-No.	932-001/01
Packaging size	1 g
Granule size	0.6 x 4 mm

Item-No.	932-001/05
Packaging size	5 g
Granule size	0.6 x 4 mm

Item-No.	932-001/10
Packaging size	10 g
Granule size	0.6 x 4 mm

Literature

[1] E.M. Carlisle „Silicon as a trace nutrient." Sci Total Environ (1988), 73 (1-2): 95-106
[2] S. Hidaka, Y. Okamoto, K. Abe „Possible regulatory roles of silicic acid, silica and clay minerals in the formation of calcium phosphate precipitates." Arch Oral Biol (1993), 38 (5): 405-413
[3] P. Li, C. Ohtsuki, T. Kokubo, K. Nakanishi, N. Soga „Apatite formation induced by silica gel in simulated body fluid.", J Am Ceram Soc (1992), 75: 2094-2097
[4] S. Radin, S. Falaize, MH Lee, P. Ducheyne „In vitro bioactivity and degradation behaviour of silica xerogels intended as controlled release materials." Biomaterials (2002), 23: 3113-3122
[5] S. Overgaard "Calcium phosphate coatings for fixation of bone implants." Acta Orthop Scand (2000), Suppl. 297 (71): 1-74
[6] Teller M, Becker P and Neumann HG. „Antibiotic Loaded Sol-Gel-Derived Calcium Phosphate/Silica Composite for Bone Regeneration." Key Engineering Mat. 2005; 284-286:415-418
[7] F. Lüthen et al. „Adhesion and gene expression in osteoblasts on sol-gel-derived calcium phophate coatings.", Proceedings ESB 2003 Stuttgart P 081
[8] Mitteilungsblatt der Zahnärztekammer und der KZV Mecklenburg-Vorpommern 1/2005: 20-22

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