Scientific and clinical evidence

cerabone®

100% PURE BOVINE BONE MINERAL

hard tissue
Bone and tissue regeneration techniques

THE USE OF BONE GRAFT MATERIALS

Bone graft materials are applied to replace and regenerate bone matrix lost by various reasons such as tooth extraction, cystectomy or bone atrophy following loss of teeth or inflammatory processes.

For the filling of bone defects, the patient’s own (autologous) bone is considered the „gold standard“, because of its biological activity due to vital cells and growth factors. Nevertheless, the harvesting of autologous bone requires a second surgical site associated with an additional bony defect and potential donor site morbidity.

In addition, the quantity of autologous bone is limited. Today, due to a constant development, bone graft materials provide a reliable and safe alternative to autologous bone grafts.

Clinicians can choose between a variety of different bone graft materials and augmentation techniques. Bone graft materials are classified by their origin into four groups (see classification on right side).

The GBR/GTR technique

The principle of Guided Bone Regeneration (GBR) or Guided Tissue Regeneration (GTR) is based on the separation of the grafted site from the surrounding soft tissue by application of a barrier membrane. Membranes act as a barrier to avoid the ingrowth of the faster proliferating fibroblasts and/or epithelium into the defect, and to maintain the space for controlled regeneration of bone.

The application of a bone graft material into the defect prevents a collapse of the membrane, acting as a place holder for the regenerating bone and as an osteoconductive scaffold for the ingrowth of blood vessels and bone forming cells.

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Classification

Autologous:
- Patient’s own bone, mostly harvested intraorally or from the iliac crest
- Intrinsic biological activity

Allogenic:
- Bone from human donors (tissue donors or femoral heads of living donors)
- Natural bone composition and structure

Xenogenic:
- From other organisms, mainly bovine origin
- Long-term volume stability

Alloplastic:
- Synthetically produced, preferably calcium phosphate ceramics
- No risk of disease transmission

For large defects a mixture of autologous or allogenic bone, which has excellent biological potential, and a bone graft material for volume stability of the grafting site, is recommended.
Xenogenic bone graft materials

Xenogenic bone grafts are derived from animals, preferably of bovine origin. Bovine bone materials can be deproteinized by heating (sintering) to minimize the risk of allergic reactions and disease transmission.

Bovine bone materials have a long tradition, are very well documented, and their clinical application has found wide-ranging acceptance. The removal of all proteins transforms them into biologically derived hydroxyapatite ceramics. It’s important to choose a manufacturing process that preserves the natural three-dimensional bone structure with interconnecting pores, so that the material strongly resembles the human bone. In addition, a highly structured surface supports the formation of new bone matrix and thus the osseous integration that is the basis for an excellent volume stability of the augmented site.

cerabone® – NATURAL BOVINE BONE GRAFTING MATERIAL

cerabone® is a 100% pure bone mineral of bovine origin manufactured by a unique 1200°C production process providing maximum safety. Beside safety and reliability of the product and the production process, the material fulfills all other important requirements for the clinical success of a bovine bone graft material:

- Phase pure hydroxyapatite without organic components
- Rough and open porous structure comparable to native human bone
- Excellent hydrophilicity enabling a rapid uptake of blood
- Optimal biocompatibility proven in various in vitro and in vivo tests
- Rapid and controlled osseous integration
- Ultimate volume stability

These characteristics are the basis for the excellent clinical results of cerabone® demonstrated by high volume stability of the grafted site, complete integration into newly formed bone matrix and the resulting high bone density.

Indications for cerabone®

**Implantology, Periodontology, Oral- and CMF Surgery**
- Sinus lift
- Horizontal and vertical augmentation
- Periodontal bone defects
- Peri-implant defects
- Socket and ridge preservation
- Furcation defects (class I and II)

### Product Specifications

cerabone® granules

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<th>Art.-No.</th>
<th>Particle Size</th>
<th>Content</th>
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<td>1525</td>
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cerabone®: Safety and reliability made in Germany

cerabone® is made of cancellous bone from the femoral heads of domestic cattle. The processes of procurement and processing/production of this bovine material meets strict safety requirements. Thus the risk of BSE transmission can be considered negligible.

HEATING UP TO >1200°C

cerabone® is produced by a unique production process utilizing heat and water only (free of chemical additives).

UNIQUE MANUFACTURING PROCESS

Both, product and process of procurement of the raw material as well as the production process are fulfilling the German and EU-regulatory and security requirements for bovine bone grafts including EN ISO 22442-1, -2 and -3, as well as Commission Regulation (EU) No 722/2012.

The proprietary manufacturing process of cerabone® is based on a 1200°C high-temperature treatment resulting in excellent product characteristics:
- Cell-friendly, biomimetically structured, rough surface
- Complete removal of organic components and albuminous impurities
- Negligible risk of allergic reactions or rejection

CE MARKING SINCE 2002

cerabone® has been available in the orthopaedic field amongst others since 2002. The product optimized for the dental field was launched in 2007.

STERILE AND STORABLE

cerabone® is available as granules of two different sizes, which are sealed in primary and secondary blister packaging and sterilized with gamma irradiation.

cerabone® can be stored at room temperature for up to three years.
cerabone®: 100% pure bone mineral

cerabone® consists of the pure mineral phase of bovine bone. The high phase purity leads to maximal volume stability. In addition, the absence of organic components ensures the high safety of cerabone®.

Results from Prof. Dr. C. Vogt, University of Hannover


X-ray diffractometry: mineral phases and crystallinity. Narrow peaks and low baseline. cerabone® shows high crystallinity and 100% purity.

Thermogravimetric analysis showing combustion of organic components. No mass loss by heating cerabone® up to 1000°C. Complete removal of organic components (cells, collagen) by sintering process.

1 Prof. C. Vogt, Leibniz University Hanover, Protocol on the analysis of bone graft material, 2012.
Topography and hydrophilicity as key success factors

Optimal adhesion and ingrowth of cells, proteins and blood vessels

Scanning electron microscope (SEM) pictures show the highly structured surface of cerabone® as well as the macro- and micropores.

The macroporous structure enables migration of cells, penetration of blood vessels and integration of the particles.
The capillary effect of the micropores leads to a quick blood uptake of the material.
The rough surface ensures an excellent and homogenous adhesion of cells and proteins.

Excellent hydrophilicity of cerabone®

cerabone®’s rapid and complete hydration with blood or saline solution is crucial for excellent handling characteristics, new bone formation and for the final clinical success.

Its strong capillary action facilitates fast and efficient penetration of the material particles with fluids, nutrients and blood through the three-dimensional, porous trabecular bone network, resulting in excellent handling and reliability in the daily clinical use.

Good hydrophilicity and fast blood uptake of cerabone®

Hydropobicity of a non sintered bovine bone graft material

cerabone® serves as an excellent matrix for bone regeneration

**cerabone® and growth factors**
*In vitro* experiments from Prof. Dr. H. Jennissen and Dr. M. Laub
University of Duisburg-Essen/Morphoplant GmbH

-In vitro- experiments show that cerabone® can be loaded with up to 1 mg BMP-2/g.

**Bone biology:**

**Scientific results from in vitro experiments**

**Growth of osteoblasts and osteoclasts on cerabone®**
*In vitro* results from Prof. Dr. D. Rothamel, Clinic Mönchengladbach,
University of Düsseldorf and PD Dr. C. Reichert, University of Bonn

The rough surface also promotes the adhesion of serum proteins and cells onto the surface. Osteoblast-like cells quickly adhere to the cerabone® particles. Only attached osteoblasts can start to produce new bone matrix leading to the osseous integration of the cerabone® particles. Another study indicated that the good adherence of osteoclasts promotes the superficial remodeling of the particles.

**Proliferation of osteoblasts on cerabone®**

Stem cell research

Interaction of cerabone® with stem cells

*In vitro results from Prof. Dr. B. Zavan, University of Padova*

cerabone® supports the differentiation of attached stem cells into osteoblasts that produce new bone matrix. Collagen, osteopontin, osteonectin and osteocalcin are proteins of the extracellular bone matrix that can be used as markers for bone formation. Their detection 14 days after seeding stem cells on cerabone® indicates the correct differentiation of the cells.

![Graph showing optical density of collagen I, osteopontin, osteonectin, and osteocalcin](image)

Tissue integration and cellular degradation

*In vivo data from a mouse model by Prof. Dr. Dr. S. Ghanaati, University of Frankfurt a. M.*

15 days after implantation into the subcutaneous tissue (CT) of mice, cerabone® (CB) is embedded within a well vascularized granulation tissue (blood vessels marked by arrows). No fibrous encapsulation or inflammatory reactions are observed. Mononuclear and multinuclear cells (arrow heads) indicate the onset of cellular degradation of the cerabone® particles.

![Images showing tissue integration and cellular degradation](image)
Maximal stability and good osseous integration of cerabone®

Material study on cerabone®

Compressive force (N) 1670±120 4510±770
Compressive resistance (N/cm²) 420±32 564±96
Shear force (N/cm²) 124±35 338±200

Histological studies on cerabone®

Animal study
cerabone® - osteoconduction and bony regeneration
Optimal bone regeneration after bone defect treatment with cerabone® was demonstrated in an animal study.
Bony defects following apicoectomy were filled with cerabone®.
The histological examination showed a complete bridging of the osteotomy orifice after three months and a well established new bone (NB) and cementum formation (CEM) around the cerabone® particles.

Clinical study
cerabone® - osseous integration and optimal stability
Sinus lift study from Prof. Dr. Dr. D. Rothamel, Clinic Mönchengladbach, University of Düsseldorf
A study on 12 patients showed that cerabone® acts as an osteoconductive material that supports the regeneration of bone after sinus floor elevation surgery. After six months the particles of all biopsies were completely integrated into the newly formed bone matrix, while the grafted area showed excellent volume stability.

Results from Prof. Dr. Z. Artzi, University of Tel Aviv

In vivo

Section of maxillary block stained with Stevenels blue and Van Gieson's picro fuchsin

Biopsy taken six months after sinus floor elevation. cerabone® particles are covered by a layer of newly formed bone matrix

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CLINICAL CASE BY
Dr. Marius Steigmann, Neckargemünd, Germany

CERABONE® FOR COVERAGE OF IMPLANT DEHISCENCE AND RIDGE AUGMENTATION

Contour maintenance
For augmentations in the aesthetic region cerabone® provides long-term dimensional stability and therefore a good bone bed to support an optimal contour of the soft tissue and sustained aesthetic result.
Clinical situation with narrow alveolar ridge in the lower jaw

3.5 mm dental implants inserted with inefficient immersion of dental implant platforms

Implants inserted and cortical bone perforated, vestibular view

Alveolar ridge form and size renewal around implants with cerabone®

cerabone® particles size 0.5 - 1.0 mm in place

Covering augmentation site with collprotect® membrane

Situation at re-entry six months post-operative, implants partly covered by new bone matrix

Implants uncovered, good integration of cerabone® particles

Rehydration

Due to its excellent hydrophilicity, cerabone® particles adhere to each other after mixing with blood or sterile saline solution, allowing optimal handling and good adaptation to surface contours.

Particle Size

Small cerabone® particles (0.5 - 1.0 mm) allow good adaptation to surface contours; they are especially useful for lateral augmentations or to fill voids when working with autologous bone blocks. For sinus lift and extensive augmentations the use of large cerabone® particles (1.0 - 2.0 mm) is recommended. The increased space between the large particles enables a better vascularization and improves the regeneration of larger defects.
Preoperative cone beam scan revealing good osseous formation of the augmented site

Excellent bone regeneration six months after augmentation with cerabone® particles and Jason® membrane

Insertion of gingiva formers allow for soft tissue maturation

Final prosthetic restoration with ceramic bridge

Antibiotic prophylaxis
Especially before large volume augmentations the patient can be prophylactically administered antibiotics, e.g. by starting the antibiosis one day prior to surgery or at least one hour before the surgery by ingestion of a full daily dose.
CLINICAL CASE BY
Dr. Paolo Di Capua, Tel Aviv, Israel

SOCKET PRESERVATION WITH CERABONE®, JASON® MEMBRANE AND PERMAMEM®

- Situation after tooth extraction
- Socket grafted with cerabone®
- Placement of Jason® membrane over the augmented socket
- Augmented socket completely covered with Jason® membrane
- Placement of permamem®
- Augmented socket completely covered with permamem®
- Membrane stabilized with cross suture. Open healing of the membrane
- Situation four weeks post-operative
- Situation four weeks post-operative after removal of permamem®
- Situation five weeks post-operative
- Re-entry
- Implant placement
- Primary wound closure
- Radiographic control
In case of a small perforation (< 5 mm) of the Schneiderian membrane during sinus floor elevation, the application of a collagen membrane (e.g. Jason® membrane or collprotect® membrane) is a useful tool for perforation coverage. Instruct the patient to avoid sneezing for two weeks and prescribe antibiotics and swelling prophylaxis (e.g. xylomethazoline). Never continue if you find an acute sinusitis with presence of pus.
CLINICAL CASE BY
Dr. Damir Jelušić, Opatija, Croatia

SINUS FLOOR ELEVATION WITH CERABONE® AND JASON® MEMBRANE

Preoperative OPG
Preparation of a lateral window for sinus floor elevation
Perforation of the Schneiderian membrane visible after preparation of the lateral window
Jason® fleece inserted into the sinus cavity to cover the Schneiderian membrane

Filling of the sinus cavity with cerabone® (particle size 1.0 - 2.0 mm)
Simultaneous placement of three implants
Jason® fleece covering the lateral sinus window
Additional horizontal augmentation with cerabone® (particle size 1.0 - 2.0 mm)

Covering of the augmentation site with Jason® membrane
Re-opening six months after implantation, stable integration of the cerabone® particles
Placement of gingiva formers
Good situation after removal of gingiva formers, six weeks after re-opening

Membrane coverage
For better and more predictable results we always recommend to cover the augmentation area (and the lateral sinus window after sinus floor elevation) with a collagen membrane (e.g. collprotect® membrane or Jason® membrane).
Filling of the sockets with cerabone®

Application of the granules
Avoid to compress the cerabone® particles excessively at the defect site. Open space between the particles permits blood vessel ingrowth and the formation of new bone matrix.

SOCKET PRESERVATION WITH CERABONE®

CLINICAL CASE BY
Dr. Damir Jelušić, Opatija, Croatia

Preoperative CT of teeth 11 and 21 after endodontic treatment

Teeth 11 and 21 not worth saving and planned for extraction

Situation after extraction of the front teeth

Jason® membranes placed within the extraction sockets

Filling of the sockets with cerabone®

Jason® membrane turned down over the socket and sutured

Post-operative CT four months after extraction, good preservation of the ridge

Flapless implant placement (punch technique) four months after socket preparation; good integration of cerabone® particles

Placement of gingiva formers

Final prosthetic situation with individual emergence profile created with provisional crowns (Four months post implantation)

Individualized zirconium abutments

Final prosthetic restoration with ceramic crowns
CLINICAL CASE BY
PD Dr. Raluca Cosgarea and Prof. Dr. Dr. Anton Sculean,
University of Marburg, Germany and University of Bern, Switzerland

REGENERATION OF INTRABONY DEFECTS WITH CERABONE® AND
COLLPROTECT® MEMBRANE

Sterile application
Pay attention to sterile application of the substitute, e.g. by using new instruments for granule insertion (and trimming of membranes). Prior contact to saliva may contaminate your graft.
Innovation.
Regeneration.
Aesthetics.

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