dental
bone & tissue
regeneration

botiss
biomaterials

cerabone®

Natural bovine bone grafting material

Scientific & Clinical Evidence

by Dr. Marius Steigmann et al.

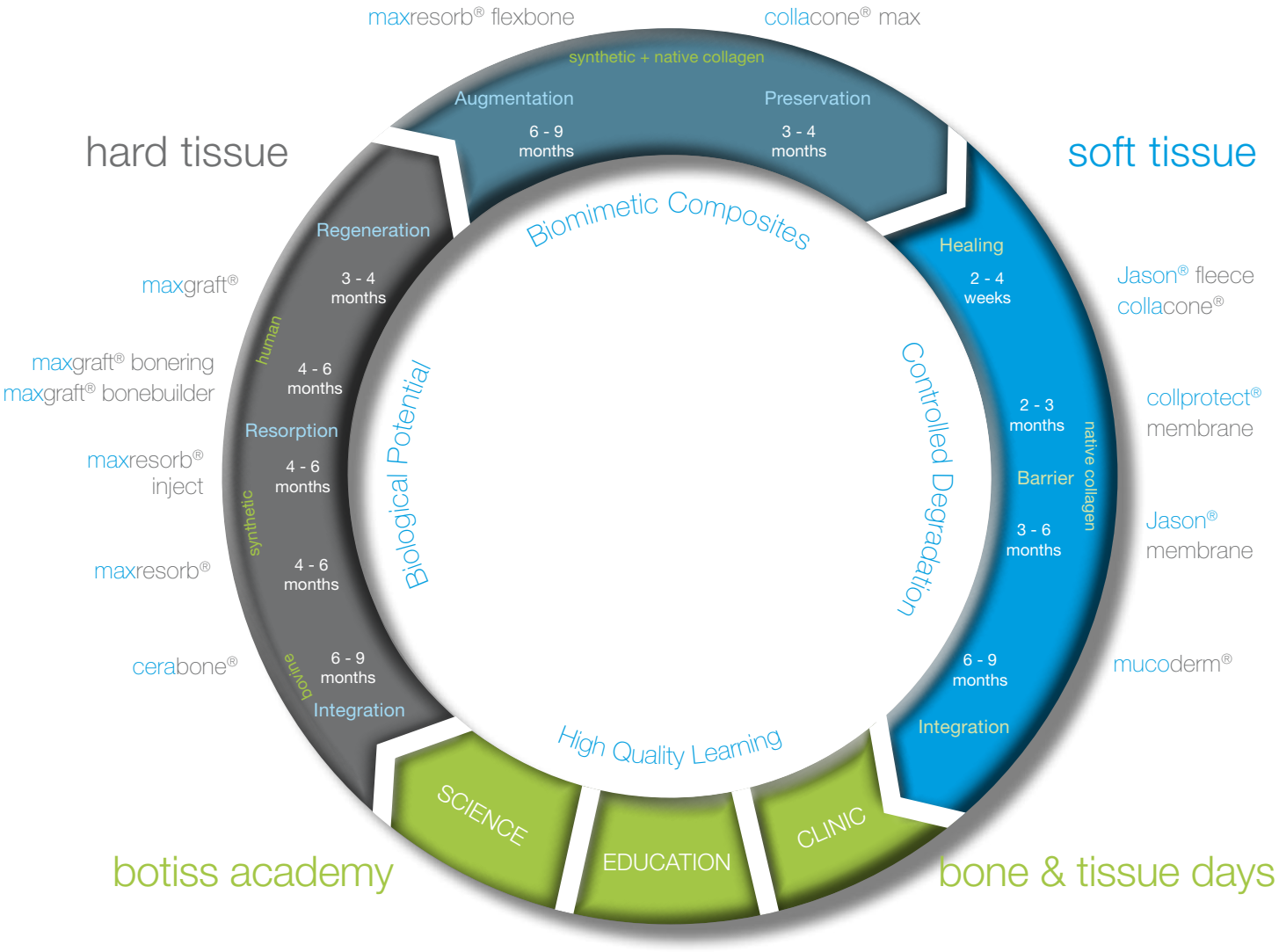
hard tissue

natural

safe

pure

botiss regeneration system



cerabone®

natural bovine bone graft

maxresorb®

bi-phasic calcium phosphate

maxresorb® inject

synthetic injectable bone paste

maxgraft®

processed allogenic bone graft

maxgraft® bonering

processed allogenic bone rings

maxgraft® bonebuilder

patient matched allogenic bone implants

maxresorb® flexbone

flexible blocks (CaP/collagen composite)

collacone® max

cone (CaP/collagen composite)

mucoderm®

3D-stable soft tissue (collagen) graft

Jason® membrane

native pericardium GBR/ GTR membrane

collprotect® membrane

native collagen membrane

Jason fleece® collacone®

collagenic haemostypt (sponge/cone)

Dr. medic. stom.
IMF Neumarkt
Marius Steigmann, PhD

academy
Berlin

- Adjunct. Assistant Professor of Oral and Maxillofacial Surgery at Boston University
- Visiting Professor at the University of Michigan
- Honorary Professor of the “Carol Davila“ University Bucharest, Invited Senior Guest
- Visiting Professor at the University of Szeged, Faculty of Dentistry
- Visiting Professor at the Department of Implantology of Temeschburg
- Diplomate of the ICOI

Dr. medic. stom. IMF Neumarkt
Marius Steigmann, PhD

- Dr. Marius Steigmann received the „Semmelweiss“ medal from Budapest University Dental School, Dept. of Oral and Maxillofacial Surgery
- Dr. Steigmann received his PhD with Summa cum laude from the University of Neumarkt
- Founder and scientific chairman of “Update Implantologie Heidelberg”
- Founder and director of the “Steigmann Implant Institute” in Neckargemünd

The Steigmann Implant Institute

The Steigmann Implant Institute is a private teaching institution founded in 2006. The mission is to teach dentists all aspects of dental implants and biologics. However the main focus is on aesthetics with soft tissue management and bone regeneration.
Dr. Steigmann is considered a specialist and pioneer of modern dental implantology.

Global clinical and scientific network include: Prof. Dr. Hom-Lay Wang, Prof. Dr. Anton Sculean, Dr. Maurice Salama, Dr. Philippe Russe, Dr. Tiziano Testori, Dr. Scott Ganz, Dr. Olaf Daum, PD Dr. Dr. Daniel Rothamel, Dr. Damir Jelušić, Dr. Ophir Fromovich.

Clinical contribution: Dr. Marius Steigmann, Dr. Damir Jelušić
Scientific contribution: PD Dr. Dr. Daniel Rothamel, Dr. Dr. Shahram Ghanaati, Prof. Dr. Zvi Artzi, Prof. Dr. Carla Vogt, Prof. Dr. Barbara Zavan, Prof. Dr. Herbert Jennissen, Dr. Markus Laub, Dr. Christoph Reichert

Bone and Regeneration Techniques

cerabone® 1.0-2.0mm

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 patients 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.

cerabone® 0.5-1.0mm

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.

Classification

Autologous:
- patients own bone, mostly harvested intraorally or from the iliac crest
- intrinsic biological activity

Allogenic:
- bone from human donors (cadaver bone or femoral heads of living donors)
- natural bone composition and structure

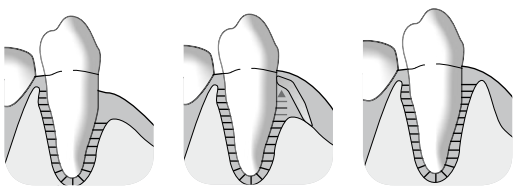
Xenogenic:
- from other organisms, mainly bovine origin
- Long term volume stability

Alloplastic:
- synthetically produced, preferably calcium phosphate ceramics
- no risk of disease transmission

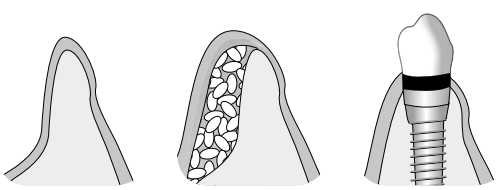
The GBR/GTR technique

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. Collagen membranes act as a resorbable matrix 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 collagen 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.

Guided Tissue Regeneration (GTR)



Guided Bone Regeneration (GBR)



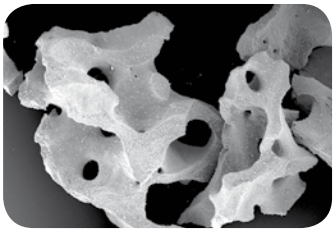
For large defects a mixture of autologous or allogenic bone, which has excellent biological potential, and a bone graft material for volume stability of the grafting site, is recommended.

Histology of cerabone® 6 months after sinus lift; optimal integration and bone healing

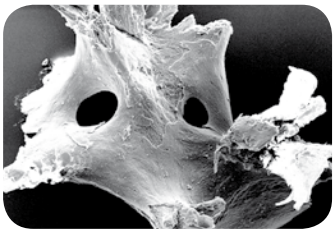
Xenogenic bone graft materials

Xenogenic bone grafts are derived from animals, preferably of bovine origin. Bovine bone materials are deproteinized by heating (sintering) to exclude the risk of allergic reactions and infection transmission[1].

The 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. They are characterized by their preserved three dimensional natural bone structure with interconnecting pores, strongly resembling the human bone structure. Their guided osseous integration rather than rapid resorption leads to excellent volume stability of the graft, with the formation of new bone on the highly structured bovine bone surface.



SEM: cerabone® macro- and micropores resembling human bone



SEM picture of human bone

cerabone® – natural bovine bone grafting material

cerabone® is derived from bovine bone in an established high temperature heating process (sintering) guaranteeing its safety[2].

Beside safety and reliablity of the product and the production process, the material fulfills all other important requirements for the clinical success of a bovine bone graft material:

cerabone® excellent biofunctionality; superior hydrophilicity and blood uptake

- 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 proved in various in vitro and in vivo tests
- rapid and controlled osseous integration

These characteristics are the base for the excellent clinical results of cerabone® demonstrated by high volume stability at the graft site, complete integration into newly formed bone matrix with satisfactory bone density[3].

[1] Murugan et al., Heat-deproteinated xenogenic bone from slaughterhouse waste: Physico-chemical properties, Bull. Mater. Sci, Vol 26, No. 5, 2003

[2] BSE risk cerabone, aap biomaterials, GmbH

[3] D. Rothamel et al., Sinus floor Elevation using a sintered, natural bone mineral, zzi, 2011; 27(1)

cerabone®: Safety & Reliability Facts Made in Germany

threefold sterility

Sintering

Heating up to 1250 °C

BSE free

cerabone® is gained from the cancellous bone of femur condyles of cattle older than 48 months. All cattle have been tested for BSE with negative results. Because of the choice of the raw material (food industry) and the special processing, cerabone® is BSE free.

Patented Manufacturing Process

Both product and production process are fulfilling the German and EU-regulatory and security requirements for bovine bone grafts including EN ISO 22442-1 and EN ISO 22442-2.
The proprietary manufacturing process of cerabone® is based on high temperature heating (sintering) and special surface treatment that result in:

- cell-friendly, biomimetically structured, rough surface
- complete removal of organic components and albuminous impurities
- no risk of allergic reactions or rejection

CE Certification

- CE certification of cerabone® was issued in 2002
- the product is on the market since January 2002
- no single adverse event reported in association with the product

Sterile & Storable

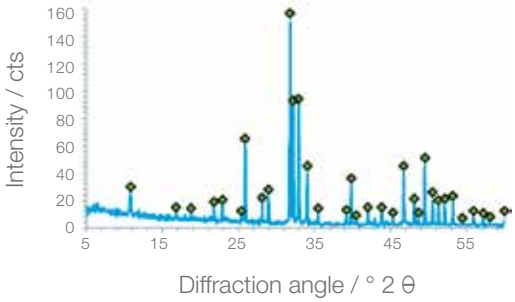
cerabone® is available as granules and in block form. The product is packed in sterile vials, sealed in primary and secondary blister packaging and sterilized with gamma irradiation. cerabone® can be stored at room temperature for up to three years.

cerabone®: 100% Pure Mineral Bone Phase

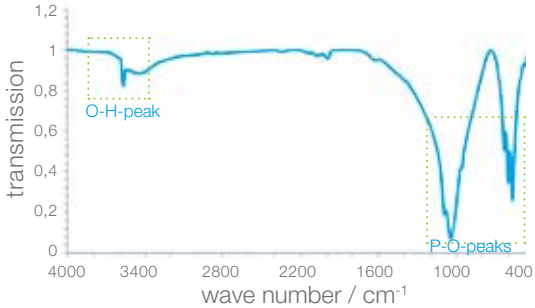
cerabone® consists of the pure mineral phase of bovine bone.

No other phases besides hydroxyapatite are detectable. The high phase purity leads to maximal volume stability. In addition, the absence of organic components warrants for the high safety of cerabone®.

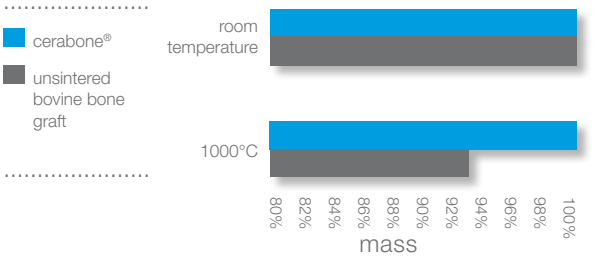
Results from Prof. Dr. C. Vogt, University of Hannover



X-ray diffractometry: mineral phases and crystallinity.
Narrow peaks and low baseline[4].
cerabone® shows high crystallinity and 100% purity.



Infrared spectroscopy:
molecular fingerprint.
Characteristic peaks of phosphate and hydroxy groups of the hydroxyapatite[4].
No other organic phases detectable.

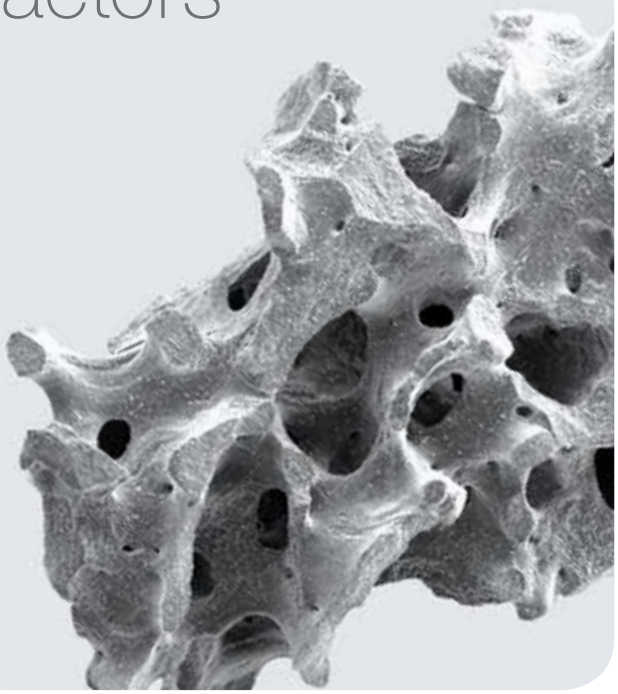


Thermogravimetric analysis showing combustion of organic components.
No mass loss by heating cerabone® up to 1000°C[5].
Complete removal of organic components (cells, collagen) by sintering process.

Particle size 1.0-2.0mm 0.5-1.0mm

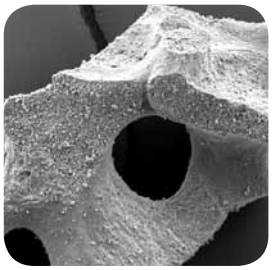
[4] Prof. C. Vogt, Leibniz University Hannover, Protocol on the analysis of bone graft material, 2012.
[5] Tadic et al., A thourough physicochemical characterization of 14 calcium phosphatebased bone substitute materials in comparison to natural bone, Biomaterials 25 (2004) 987-994

Topography and Hydrophilicity as key success factors

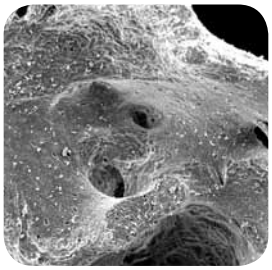


Optimal adhesion and ingrowth of cells, proteins and blood vessels

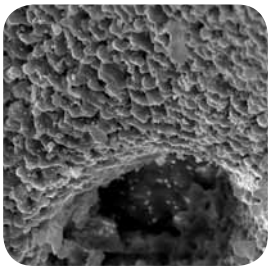
Scanning electron microscope (SEM) pictures show the highly structured surface of cerabone® as well as the macro and micro pores.



The macroporous structure enables migration of cells, penetration of blood vessels and integration of the particles

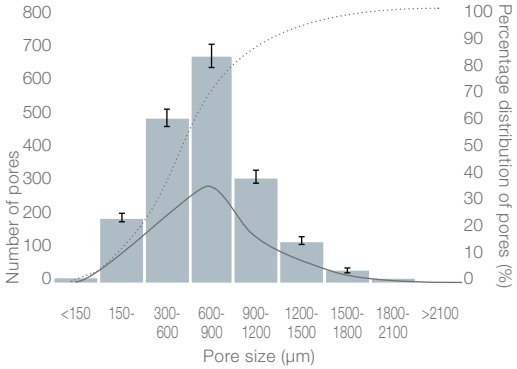


The capillary effect of the micro pores leads to a quick blood uptake of the material



The rough surface ensures an excellent and homogenous surface adhesion, cells and proteins

Pore distribution of cerabone®[6]



Excellent hydrophilicity of cerabone®

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

Good hydrophilicity and fast blood uptake of cerabone®[6]

Its strong capillary action enables the fast and efficient penetration of the material particles with fluids, nutrients and blood through the 3-dimensional, porous trabecular bone network, resulting in excellent handling, reliability and predictability in the daily clinical use.

Hydrophobicity of a non sintered bovine bone graft material[6]

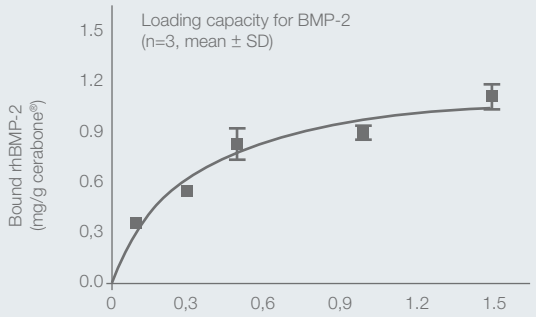
[6] Seidel P. and Dingeldein E. Cerabone® - Bovine Based Spongiosa Ceramic. Mat.-wiss. u. Werkstofftech. 2004, 35, No. 4.

cerabone® serves as an excellent matrix for bone regeneration

cerabone® and growth factors

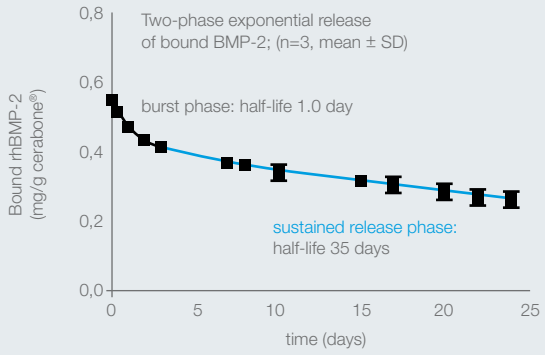
In vitro experiments from Prof. Dr. H. Jennissen und Dr. M. Laub University of Duisburg-Essen/Morphoplant GmbH

A



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

B

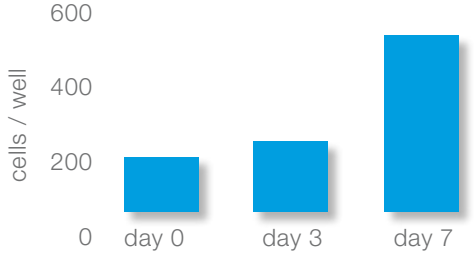


Two-phase controlled exponential release of BMP-2 may provide cerabone® with enhanced osseointegration (Morphoplant GmbH; patent application WO 2009/056567).

Growth of osteoblasts and osteoclasts on cerabone®
In vitro results from PD Dr. Dr. D. Rothamel, University of Collogne and Dr. C. Reichert, University of Bonn

The rough surface also promotes the adherence 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. In another study, good adherence of osteoclasts promoted the superficial remodeling of the particles.

Proliferation of osteoblasts on cerabone®



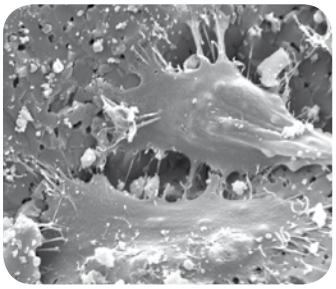
[7] Konermann A., Staubwasser M., Dirk C., Keilig L., Bourauel C., Götz W., Jäger A., Reichert C.: Bone substitute material composition and morphology differentially modulate calcium and phosphate release through osteoclast-like cells. Int. J. Oral Maxillofac. Surg. 2013

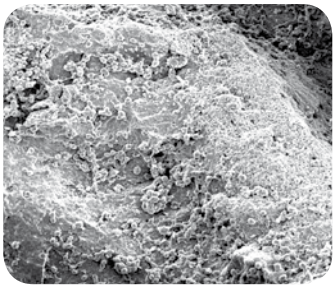
Bone biology:

Scientific results from in vitro experiments

BMP-2 structure

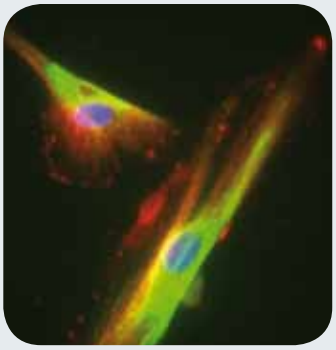
Colonialization of cerabone® by osteoblasts
Priv.-Doz. Dr. Dr. Daniel Rothamel





Osteoclastic resorption of cerabone®
Dr. C. Reichert, University of Bonn[7]

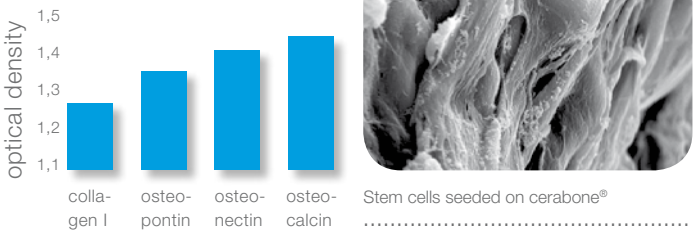
Stem Cell Research



Immuno fluorescence staining of stem cells

Interaction of cerabone® with stem cells
In vitro results from Prof. Dr. B. Zavan, University of Padova

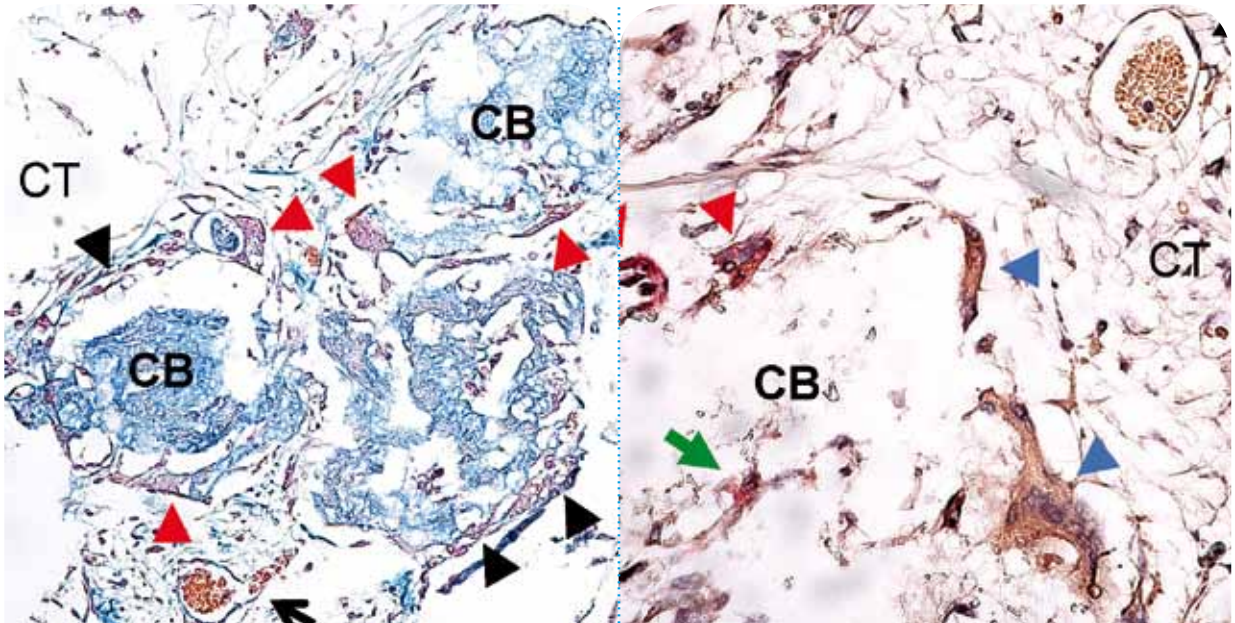
cerabone® supports the differentiation of attached stem cells into osteoblasts that produce new bone matrix.
Collagen, osteopontin, osteonectin and osteocalcin are proteins of the extracellular bone matrix that can be used as markers for bone formation. Their detection 14 days after seeding stem cells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



Stem cells seeded on cerabone®

Tissue integration and cellular degradation
In vivo data from a mouse model by Dr. Dr. S. Ghanaati, University of Mainz and University of Frankfurt a. M.

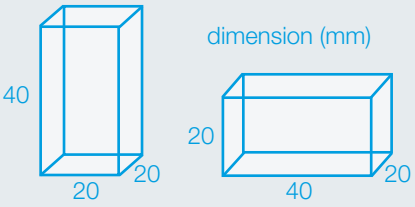
15 days after implantation into the subcutaneous tissue (CT) of mice, cerabone® (CB) is embedded within a well vascularized granulation tissue (blood vessels marked by arrows). No fibrous encapsulation or inflammatory reactions are observed. Mononuclear and multinuclear cells (arrow heads) indicate the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



Maximal Stability and good osseous integration of cerabone®

Histological studies 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



Endodontics

cerabone® – osteoconduction and bony regeneration

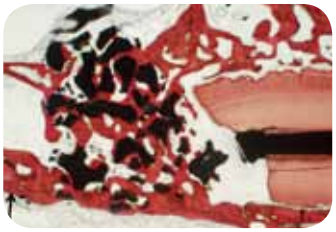
Optimal bone regeneration after bone defect treatment with cerabone® was demonstrated in an animal study.

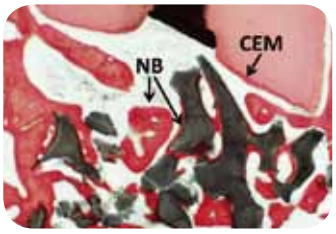
Bony defects following apicectomy, were filled with cerabone®.

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.

In vivo

Results from Prof. Dr. Z. Artzi, University of Tel Aviv [8]





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

Implantology

cerabone® – osseous integration and optimal stability

Sinus lift study from PD Dr. Dr. D. Rothamel, University of Cologne [9]

Biopsy taken 6 months after sinus floor elevation. cerabone® particles are covered by a layer of newly formed bone.

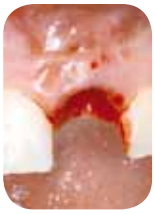
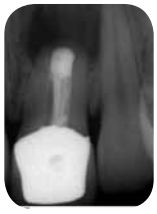
A study on 12 patients showed that cerabone® acts as an osteoconductive material that supports the regeneration of bone after sinus floor elevation surgery. After 6 months the particles of all biopsies were completely integrated into the newly formed bone matrix, while clinically the grafted area showed excellent volume stability.

[8] Effect of Guided Tissue Regeneration on Newly Formed Bone and Cementum in Periapical Tissue Healing after Endodontic Surgery: An In Vivo Study in the Cat
Artzi Z., Wasersprung N., Weinreb M., Steigmann M., Prasad H.S., Tsesis I.; JOE — Volume 38, Number 2, February 2012

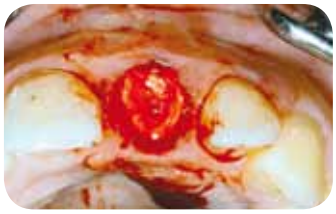
[9] Sinus floor elevation using a sintered, natural bone mineral – A histological case report study
Rothamel, D., Smeets, R., Happe, A., Fienitz, T., Mazor, Z., Schwarz, F., Zöller, J., Zeitschrift für zahnärztliche Implantologie, 2011;27(1):60

Clinical Case by Dr. Marius Steigmann

cerabone® for coverage of implant dehiscence and ridge augmentation

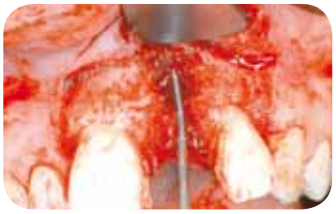



Extraction of tooth 21 after endodontic treatment



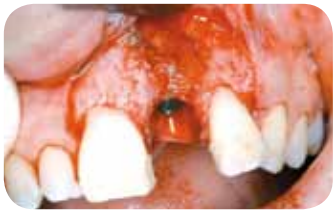
Application of collacone® for stabilization of the blood clot

Buccal bone defect after eight weeks healing time

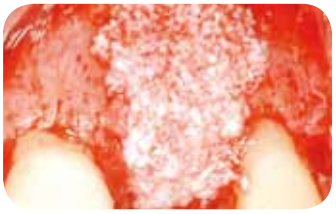


A periodontal probe demonstrates the vertical extension of the defect

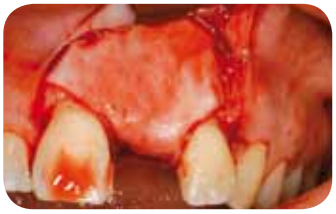
Implant placed into the former extraction socket



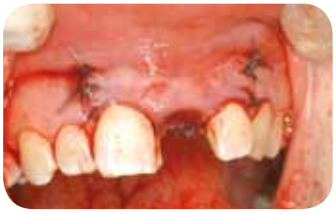
Surface of the implant is covered with autologous bone



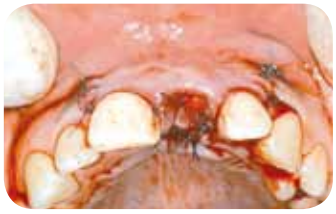
Coverage of the autogenous bone with cerabone® (0,5-1 mm)



Covering of the bone substitute with Jason® membrane



Closure of the site using single sutures after periosteum slitting



Tension-free suturing maintains undisturbed healing

Abutment installation after implant uncovering, six months after implantation

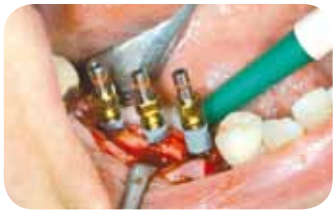
Final prosthetic restoration with a full-ceramic crown

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.

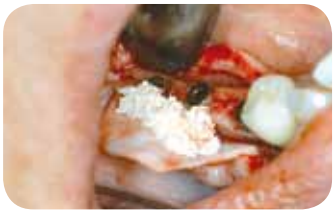
Clinical Case by Dr. Marius Steigmann

cerabone® for horizontal augmentation



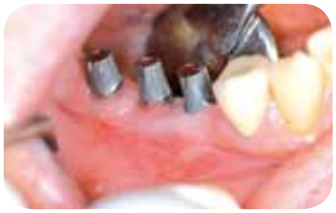
Three implants placed in a narrow posterior mandible

Due to resorption an augmentation of the buccal wall is necessary



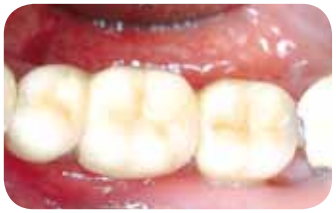
Augmentation of the buccal bone using cerabone® and Jason® membrane.

Tension-free suturing of the flap



Installation of individualized abutments three months post-OP

Good regeneration of the alveolar ridge with stable soft tissue conditions



Final prosthetic rehabilitation with ceramic crowns

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 mm) allow a good adaptation to surface contours; they are especially useful for lateral augmentations or to fill voids when working with autologous bone blocks.

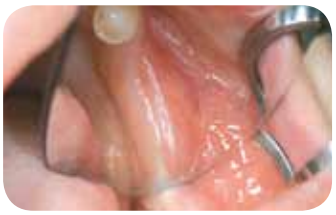
For sinus lift and extensive augmentations the use of cerabone® particle size 1-2 mm is recommended. The increased space between the large particles enable a better vascularization and improve the regeneration of larger defects.

Clinical Case by Dr. Marius Steigmann

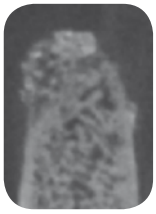
cerabone® for horizontal augmentation

Atrophic alveolar ridge in the left mandible

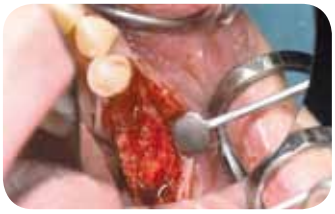
After mucoperiosteal flap elevation, the extensive bone resorption is visible



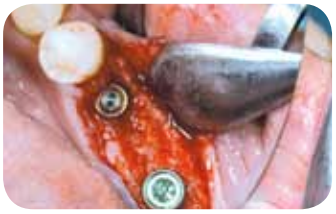
Clinical view six months after augmentation reveals healthy soft tissue situation



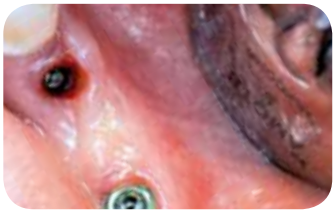
Pre-operative cone beam scan revealing good osseous formation of the augmented site



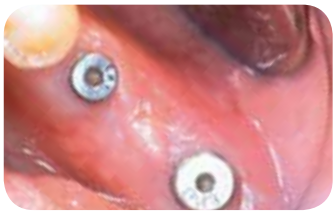
Excellent bone regeneration six months after application of cerabone® particles and Jason® membrane



The wide ridge allows for stable insertion of the two implants



Situation after healing of the soft tissue



Insertion of gingiva formers allow for soft tissue maturation

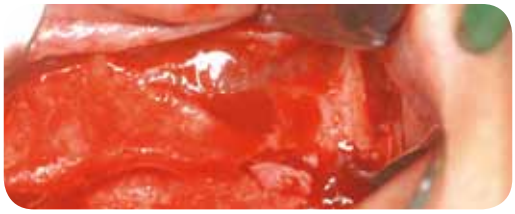
Final prosthetic restoration with ceramic bridge

Antibiotic prophylaxis

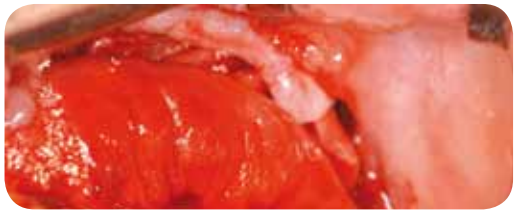
Make sure that the patient's blood contains a sufficient concentration of antibiotics before starting the augmentation (especially for larger augmentation volumes), e.g. by starting the antibiosis one day prior surgery or at least one hour before by ingestion of a full daily dose.

Clinical Case by Dr. Marius Steigmann

cerabone® for sinus floor elevation

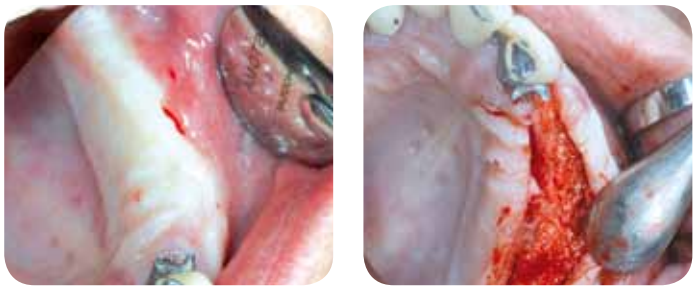


Combined lateral and vertical defect of the anterior and lateral maxilla requiring augmentation. Situation after preparation of the Schneiderian membrane

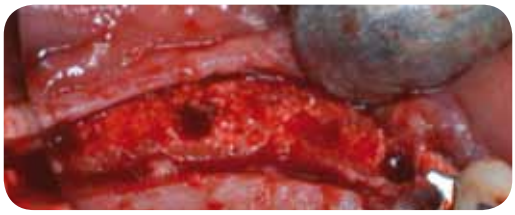


Sinus lift and additional horizontal augmentation with cerabone® and Jason® membrane

Pre-operative CT scan for implant positioning reveals excellent bone regeneration in both lateral and sinus applications



Good soft tissue situation and excellent bone formation six months after augmentation. cerabone® particles are integrated into newly formed bone matrix



Successful bone regeneration allows for prosthetically driven implant positioning

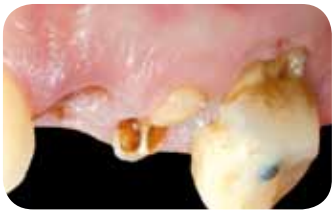
Situation after insertion of three implants in positions 22, 25 and 26

Schneiderian membrane perforation

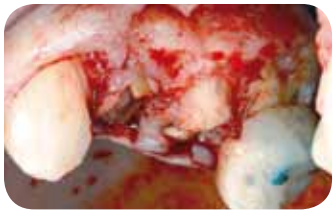
In case of a small perforation (< 5 mm) of the Schneiderian membrane during sinus floor elevation, the application of a collagen membrane (e.g. Jason® membrane or collprotect® membrane) is a useful tool for perforation coverage. Make sure that the patient doesn´t sneeze for two weeks and prescribe antibiotics 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

Immediate implant placement in one stage surgery

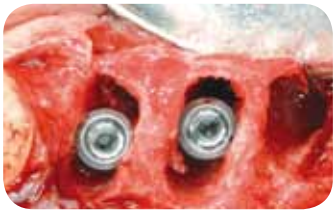


Clinical situation before extraction and implantation



View after preparation of the mucosal flap, teeth 24 to 26 planned for extraction

Situation after extraction of teeth 24 to 26

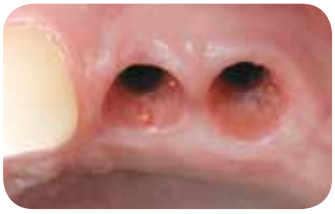


Immediate placement of two implants into the extraction sockets in position 24 and 25

Placement of healing abutments and filling of the gaps and of the extraction socket in position 26 with cerabone®

Covering of the augmentation area in position 26 with Jason® fleece

Wound closure



Situation four months after healing, good soft tissue situation, vestibular view

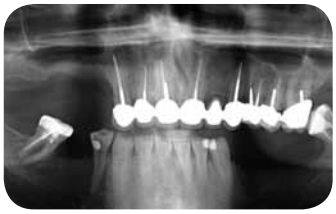
Situation four months after healing, good soft tissue situation, occlusal view

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.

Clinical Case by Dr. Damir Jelušić, Opatija, Croatia

Sinus floor elevation



Pre-operative OPG

Preparation of a lateral window for sinus floor elevation

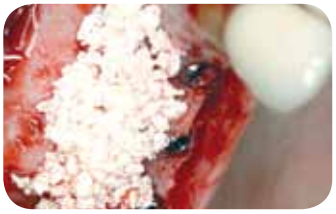
Perforation of the Schneiderian membrane visible after preparation of the lateral window

Jason® fleece introduced into the sinus cavity to cover the Schneiderian membrane

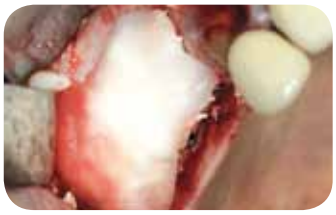
Filling of the sinus cavity with cerabone® (particle size 1-2 mm)

Simultaneous placement of three implants

Jason® fleece covering the lateral sinus window



Additional horizontal augmentation with cerabone® (particle size 1-2 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

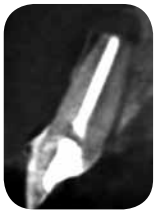
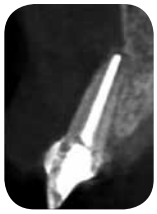
Good situation after removal of ginigva formers, six weeks after re-opening

Membrane coverage

For better and more predictable results we recommend always 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).

Clinical Case by Dr. Damir Jelušić, Opatija, Croatia

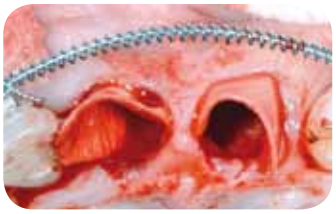
Socket preservation

Pre-operative CT of teeth 11 and 21 after endodontic treatment

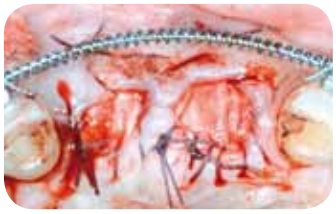
Teeth 11 and 21 not worth saving and planned for extraction

Situation after extraction of the front teeth

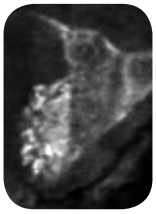
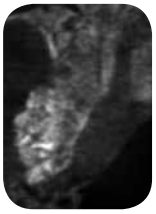


Jason® membranes placed within in the extraction sockets, covering the vestibular wall

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; complete integration of cerabone® particles

Placement of gingiva formers

Final prosthetic situation with individual emergence profile created with provisional crowns (4 months post implantation)

Individualized zirconium abutments

Final prostethic restoration with ceramic crowns

Density

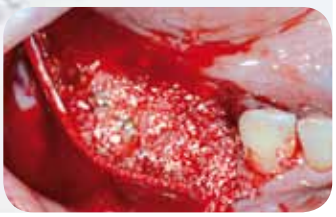
Avoid to compress the cerabone® particles excessively at the defect site. Open space between the particles permits blood vessel in-growth and the formation of new bone matrix.

Indications for cerabone®

cerabone® product family

Periodontology

Intraosseous defects (1-3 walls)
Furcation defects (class I-II)



Implantology, Oral & CMF surgery

Sinus floor elevation

Horizontal augmentation

Vertical augmentation

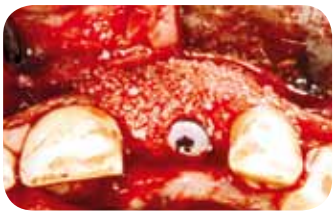
Ridge preservation

Peri-implant defects

Extraction sockets

Socket preservation

Bone defect augmentation



Product Specifications

cerabone® packaging

cerabone® granules

Article No.	Particle Size	Content
1510	0.5-1.0mm	1x0.5cc (ml)
1511	0.5-1.0mm	1x1.0cc (ml)
1512	0.5-1.0mm	1x2.0cc (ml)
1515	0.5-1.0mm	1x5.0cc (ml)
1520	1.0-2.0mm	1x0.5cc (ml)
1521	1.0-2.0mm	1x1.0cc (ml)
1522	1.0-2.0mm	1x2.0cc (ml)
1525	1.0-2.0mm	1x5.0cc (ml)

cerabone® block

Article No.	Dimension	Content
1720	20x20x10mm	1xblock

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bone & tissue
regeneration

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