maxresorb® &
maxresorb® inject

INNOVATIVE BIPHASIC CALCIUM PHOSPHATE

Scientific and clinical evidence
Bone is a highly specialized tissue with properties strongly adapted to its supporting and skeletal function. Bones are composed of ~65% inorganic matrix, the mineral phase, ~25% organic phase and ~10% water.

The main component of the mineral bone phase (~90%) is hydroxyapatite (biological apatite). This inorganic part is responsible for the high stability and compressive strength of the bone.

The organic phase mainly consists of collagen type I (~90%) being accountable for elasticity (tensile strength, ductility). Basis for bones’ resistance to different mechanical forces is the interplay of collagen fibrils, non-collagenous proteins and deposited mineral crystals.
Bone biology and remodeling

**COMMUNICATION OF CELLS**

Despite its high stability bone is in no way a rigid tissue, but is characterized by a high metabolism and is subject to constant remodeling. This dynamic is necessary to save the skeleton from degradation by the repair of structural damages (micro fractures).

Furthermore, the continuous rebuilding serves to adapt the microstructure of the bone (direction and density of trabeculae) to changing loads. These adaptations are the reason for bone atrophy following missing load (e.g. atrophy of the jaw bone after tooth loss).

Three different types of bone cells contribute to bone remodeling. The degradation of old bone matrix is carried out by osteoclasts. In the course of this process so called resorption lacunae are built that afterwards are filled with new bone matrix by cells called osteoblasts. The osteoblasts are sealed by the mineralization of the extracellular matrix. These mature bone cells that are no longer able to produce osteoid are called osteocytes. Osteocytes are involved in the formation and restructuring of the bone and are therefore important for maintaining the bone matrix.

**Bone remodeling**

Balance between bone degradation by osteoclasts and bone formation by osteoblasts.

**Bone and 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 progressive 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 placing 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 bone graft material into the defect prevents the 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.

**Classification**

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

**Allogenic:**
- Bone from human donors (multi-organ 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

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**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.**

**Guided Tissue Regeneration (GTR)**

**Guided Bone Regeneration (GBR)**

[References]


Bone remodeling

**Bone and regeneration techniques**
Development of bone regeneration materials – usage of calcium phosphates

The benefit of calcium phosphate ceramics as bone regeneration materials was realized long ago, as they are the main component of bones and therefore provide an excellent biocompatibility without any foreign body reactions.

In contrast with the first solely bioinert biomaterials, the advantages of calcium phosphates are their bioactive properties as well as their resorbability. Calcium phosphates support the attachment and proliferation of bone cells and undergo a natural remodeling process that includes osteoblasts and osteoclasts and that is characterized by an initial integration of the material into the surrounding bone matrix and a gradual degradation. Among the calcium phosphates, hydroxyapatite (HA), alpha-tricalcium phosphate (α-TCP) and beta-tricalcium phosphate (β-TCP) or biphasic CaPs are most commonly used as bioerodizing materials. Compared to all other calcium phosphates, hydroxyapatite shows the slowest solubility, therefore providing the highest stability. By contrast, the alkaline β-TCP demonstrates a higher solubility and thereby fast resorption kinetics.

Hydroxyapatite (HA)

\[
\text{Ca}_10(\text{PO}_4)_6(\text{OH})_2
\]

Beta-tricalcium phosphate (β-TCP)

\[
\text{Ca}_3(\text{PO}_4)_2
\]

An ideal bone regeneration material should be resorbed in pace with new bone matrix formation. The basic principle of the biphasic calcium phosphates is a balance between the stable hydroxyapatite, which can be found years after the implantation, and the fast resorbing β-TCP. Bone regeneration materials based on mixtures of HA and β-TCP have successfully been applied in dental regenerative surgery for more than 20 years.

Injectable calcium phosphates – cements and putties

Bone regeneration materials based on calcium phosphates are available as powders, granules and as porous blocks. The development of injectable bone regeneration materials started with the discovery of calcium cements in the 90’s. Cements result from the mixing of calcium phosphate powder with an aqueous solution. Following application, the hardening occurs in vivo. Cements create the possibility for several minimal invasive therapies of bony defects and offer an easier handling in many indications. The main disadvantage of the calcium phosphate cements is the reduced vascularization and natural remodeling experienced due to the stiffness and lack of interconnecting pores within the polymerised matrix. By mixing calcium phosphate granules with a water-based gel made of nano/micro hydroxyapatite granules (nano/micro HA), a moldable and non-hardening bone paste (putty) can be created. An example of such a non-hardening putty is maxresorb® inject.

Putties offer two significant advantages over cements: First, their increased porosity allows for the ingrowth of blood vessels and bone tissue, resulting in a fast and complete integration into new bone matrix and a rapid natural remodeling. Second, due to the large surface area, the nano/micro HA particles exhibit a high biologic activity resulting in an osteostimulating effect of these putties. Nano/micro HA particles support the adhesion of bone cells and thereby a fast formation of new bone as well as a fast particle degradation, offering additional space for the ingrowth of bone tissue.

The ideal composition: biphasic calcium phosphates

The resorption properties of biphasic calcium phosphates can be changed by varying the mixing ratio of HA and β-TCP. A HA/β-TCP ratio between 65:35 and 55:45 has been proven particularly suitable in many studies and offers a controlled resorption with parallel bone formation.

Injectable bone paste – maxresorb® inject

SOLUBILITY

- High
- Medium
- Low

- Crystalline structure of maxresorb®

- Schematic drawing of a calcium atom

CALCIUM

- Alkaline earth metal
- One of the most common elements
- Essential mineral for humans
- Important for regulation of metabolism
- Besides phosphate, the main component of bone
maxresorb®

INNOVATIVE BIPHASIC CALCIUM PHOSPHATE

maxresorb® is an innovative, safe, reliable, and fully synthetic bone substitute material that is characterized by controlled resorption properties and outstanding handling characteristics.

maxresorb® is composed of 60% slowly resorbing hydroxyapatite (HA) and 40% fast resorbing beta-tricalcium phosphate (β-TCP). The unique synthesis-based production process ensures a completely homogenous distribution of both mineral phases. The peculiar composition of maxresorb® promotes fast formation of new vital bone, while ensuring a long-term mechanical and volume stability. The osteoconductivity of maxresorb® is achieved by a matrix of interconnecting pores with an overall porosity of ~80% and a very rough surface. The nano-structured surface facilitates the uptake and adsorption of blood, proteins, and stem cells and promotes cell differentiation and osseous integration. maxresorb® offers a reliable alternative to bovine bone in a variety of indications.

Properties of maxresorb®
- 100% synthetic and resorbable
- Very high interconnected porosity
- Very rough and hydrophilic surface
- Safe, reliable and sterile
- 60% HA/40% beta-TCP
- Osteoconductive

INDICATIONS:
- Implantology,
- Periodontology and Oral and CMF Surgery
- Sinus lift
- Ridge augmentation
- Intraosseous defects
- Osseous defects
- Furcation defects
- Extraction sockets

maxresorb® inject

INNOVATIVE SYNTHETIC INJECTABLE BONE PASTE

maxresorb® inject is a highly innovative, injectable and non-hardening bone graft paste. The unique pasty material is composed of a water-based gel with nano-hydroxyapatite particles and biphasic maxresorb® granules (composed of 60% HA and 40% β-TCP), therefore showing an improved resorption profile.

The active nano-HA particles provide a large surface promoting cell-biomaterial-interaction. This leads to a fast cellular resorption and fast new bone formation, while the included maxresorb® granules support the volume maintenance. maxresorb® inject is gradually replaced by mature new bone.

The highly viscous paste allows perfect shaping and molding. It shows optimal fitting to the defect contours and bonding to the surrounding bone surface.

Properties of maxresorb® inject
- Non-hardening bone paste
- Injectable and easy handling
- Viscous and moldable
- Optimal adaptation to surface contours
- 100% synthetic, safe and resorbable
- Active nano/micro HA particles

INDICATIONS:
- Implantology,
- Periodontology and Oral and CMF Surgery
- Sinus lift
- Intraosseous defects
- Extraction sockets
- Osseous defects
- Small, contained defects
- Furcation defects

maxresorb® inject resorption profile

Four-phasic activity

maxresorb® inject syringe
Biology as a model

Interconnected porosity

The unique production process leads to porous ceramics, resembling the structure of human cancellous bone with fully interconnected pores.

These interconnected pores are like tunnels within the material, providing access for fluids (blood) and also giving space and a surface for the ingrowth and migration of cells and blood vessels, thereby enabling the formation of new bone not only superficially but also inside the particles.

Rough surface - optimal condition for adhesion of cells and proteins

Beside safety, the advantage of synthetic materials lies in the reproducibility and ability to influence the structure. Due to a unique production process, maxresorb® has a very rough surface. This roughness is the basis for the osteostimulative effect of maxresorb®. Proteins, such as growth factors, adhere to the surface and support the bony regeneration. Moreover, the nanostructured surface promotes the adhesion of cells and also their final differentiation. Likewise, the excellent hydrophilicity of maxresorb® is based on its surface roughness. Blood is very quickly absorbed, and proteins (e.g. growth factors) from the blood adhere to the inner and outer particle surface, promoting regeneration and integration.

Relevance of the structure of bone regeneration materials

Macro - guidance
Rapid vascularization
Osteoconduction
Bone formation in pores

Micro - communication
Ingrowth of cells
Blood uptake by capillary effects

Nano - nutrition
Adhesion of cells, proteins (growth factors) and nutrients

maxresorb® granules

Art.-No. | Particle Size | Content
--- | --- | ---
22025 | 0.5 - 1.0 mm (S) | 1 x 0.5 ml
22010 | 0.5 - 1.0 mm (S) | 1 x 1.0 ml
22105 | 0.8 - 1.5 mm (L) | 1 x 0.5 ml
22120 | 0.8 - 1.5 mm (L) | 1 x 2.0 ml

maxresorb® inject

Art.-No. | Unit | Volume
--- | --- | ---
22025 | 1 x syringe | 1 x 0.5 ml
22010 | 1 x syringe | 1 x 1.0 ml
22500 | 1 x syringe | 1 x 2.0 ml

maxresorb® inject

Art.-No. | Unit | Volume
--- | --- | ---
22025 | 1 x syringe | 1 x 0.5 ml
22010 | 1 x syringe | 1 x 1.0 ml
22105 | 0.8 - 1.5 mm (L) | 1 x 0.5 ml
22120 | 0.8 - 1.5 mm (L) | 1 x 2.0 ml
In vitro research

Proliferation of osteoblasts on maxresorb®
Prof. Dr. Dr. D. Rothamel,
Clinic Mönchengladbach, University Düsseldorf
Germany

The nanostructured surface of maxresorb® provides ideal conditions for the adhesion of osteoblasts. In vitro experiments demonstrated a fast proliferation of osteoblasts on maxresorb® granules.

After only seven days a dense colonization of cells was observed. The improved attachment and proliferation of osteoblasts promote the osseous regeneration, resulting in a fast integration of the particles into the newly formed bone matrix.

Osteoblasts on maxresorb® three and seven days after seeding.

Osteoblasts:
- Small, mononuclear cells, of embryonic mesenchymal cell origin
- Responsible for bone formation
- Settle on bone and release a collagenous basic substance (osteoid) into the intercellular space

Osteoclasts:
- Multi-nuclear giant cells formed by fusion of mononuclear progenitor cells of the bone marrow
- Main task is the resorption of bone substance by releasing protons (pH reduction) and proteolytic enzymes.

Research with growth factors–
Adsorption and release of BMP-2 from maxresorb®

In-vitro experiments show that maxresorb® can be loaded with up to 6 mg BMP-2/g (A). A two-stage, controlled exponential release of bound growth factors (B) indicates that maxresorb® is especially suitable to support the osseous integration.

Collagen, osteopontin, osteonectin and osteocalcin are proteins that are expressed from progenitor cells after they start to differentiate into osteoblasts. All of these marker proteins could be detected 14 days after seeding of stem cells on maxresorb® granules, indicating the correct differentiation of the stem cells.

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

maxresorb® supports the differentiation of stem cells
In-vitro experiments from Prof. Dr. B. Zivan and Prof. Dr. E. Bressan, University of Padova, Italy

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Immunofluorescence staining of stem cells grown on maxresorb®
red = osteopontin, green = osteocalcin

References:

References:
Predictable results for sinus floor elevation with maxresorb®

Results of a sinus lift study from
Prof. Dr. D. Rothamel, Clinic Mönchengladbach,
University Düsseldorf, Germany and
Dr. D. Jelušić, Privat Clinic Opatija, Croatia

In a prospective randomized clinical study on 30 + 30 patients maxresorb® was compared to a pure beta-TCP for the indication of two-stage sinus floor elevation. Application of maxresorb® led to highly predictable bone regeneration with better volume maintenance and radiological graft homogeneity compared to beta-TCP.

Following a healing phase of six months, biopsies from trephines taken at implant bed preparation demonstrated the osteoconductive properties of maxresorb®, supporting the formation of new bone matrix. Three-dimensional radiological control images showed an excellent volume stability of the grafts, facilitating the insertion of the planned implants. No implant failures were observed in a first follow-up one year post-operative, emphasizing the safety and reliability of the biphasic material.

In-vivo pre-clinical testing
Enhanced bone formation and controlled resorption of maxresorb®
Histomorphometric and degradation study of maxresorb® in critical size defects in rabbits
Prof. Dr. J. L. Calvo-Guirado, University of Murcia, Spain

Critical size defects were created in the tibia of rabbits and filled with maxresorb®. Nearly complete closure of the cortical defect after only 15 days. After 60 days, increase of medullary radiopacity, resembling cancellous bone. The percentage of maxresorb® after 60 days is 27%.

Fast integration and natural remodeling of maxresorb® inject
In vivo results of maxresorb® inject for filling of femoral defects in rats,
Prof. Dr. R. Schnettler, University of Gießen, Germany

Only three weeks after implantation, particles are covered by a layer of new bone matrix. A close contact between the newly formed bone and both components of the material (β-TCP and HA) can be seen.

Active osteoblasts (right picture) and osteoclasts (left picture) on the surface of the HA as well as the β-TCP component.

The presence of these cells is a sign for the natural remodeling of maxresorb® inject, with a degradation by osteoclasts and formation of new bone matrix by osteoblasts.

**CLINICAL CASE BY**

Dr. Steffen Kistler, Landsberg am Lech, Germany

**SINUS LIFT WITH TWO-STAGE IMPLANTATION**

- **DVT control after sinusitis surgery, residual bone height one millimeter**
- **Access to the sinus cavity by a lateral approach, minor perforation of the Schneiderian membrane**
- **Covering of the perforation with Jason® fleece**
- **Transversal section to determine the depth of the sinus floor**
- **Covering of the sinus window with colprotect® membrane fixed with two pins**
- **maxresorb® mixed with venous blood and collected bone chips**
- **Augmentation of the sinus wall with a mixture of autologous bone and maxresorb®**
- **Consolidation of graft material with minimal hyperplasia of sinus mucosa before implantation**

**Tip:**
For easy application and optimal revascularization, the graft material should be mixed with blood collected from the defect, or with venous blood when larger volumes are needed.

- **Primary stable insertion of two implants after only eight weeks**
- **OPG control of implant insertion**
- **Uncovering of implants ten weeks post-operative**
- **X-ray control after uncovering, showing dense regeneration of the graft material**

- **Post-operative DVT control showing cavity between mucosa of the maxillary sinus and the membrane**
- **OPG control of inserted implants along the anterior sinus floor**

**Tip:**
To achieve an even contour when stabilizing bone splitting in lateral augmentations, the smaller granules (0.5 - 1.0 mm) should be used.

**CLINICAL CASE BY**

PD Dr. Jörg Neugebauer, Landsberg am Lech, Germany

**CIRCULAR BONE SPLITTING IN THE UPPER JAW**

- **Three-dimensional implant planning with a radio-opaque scan template**
- **Surgical presentation of the alveolar ridge with reduced amount of horizontal bone available**
- **Lateral deposition of maxresorb® to prevent resorption of the vestibular wall**
- **Covering of the augmentation site with the initially inserted membrane**

**Tip:**
To achieve an even contour when stabilizing bone splitting in lateral augmentations, the smaller granules (0.5 - 1.0 mm) should be used.

- **Deep bone splitting with oscillating saw in regio 15 to 25**
- **Positioning of colprotect® membrane for application of bone graft material**
- **Tight wound closure with a continuous seam following the periost splitting**
- **Complication-free healing of the augmented ridge**

- **Re-entry surgery in combination with vestibuloplasty to form the vestibulum**
- **Soft tissue situation after healing with inserted abutments**
- **Inserted bridge with terminally screwed and anteriorly cemented implants**
### CLINICAL CASE BY
Dr. Frank Kistler, Landsberg am Lech, Germany

**SINUS FLOOR ELEVATION WITH SIMULTANEOUS BONE SPLITTING AND IMPLANTATION**

- DVT image demonstrating horizontal and vertical amount of bone available
- Reduced amount of bone on both sides of the upper jaw
- Surgical presentation of the ridge with mobilization of the sinus mucosa through a lateral window
- Splitting of the ridge after crestal osteotomy with bone condenser
- Covering of augmentation site with collprotect® membrane
- Single sutures for tight wound closure after periost splitting
- Good consolidation of the bone graft material with wide alveolar ridge
- Reduction of mucosal situation at re-entry surgery
- DVT image to control the inserted graft material
- Control three months after augmentation of the alveolar ridge
- Crestally stable bone level at re-entry

**Tip:**
For stabilization of bone splitting, a combined application of graft material and membrane shows the best long-term results.

### CLINICAL CASE BY
Dr. Georg Bayer, Landsberg am Lech, Germany

**LATERAL AUGMENTATION**

- DVT image showing the reduced amount of bone available in the area of the mental foramen
- Lateral bone defect following root tip resection
- After preparation of the implant bed the thin vestibular wall is visible
- Insertion of implant in the reduced bone amount
- Lateral augmentation with maxresorb® and application of a dry collprotect® membrane
- Complete covering of augmentation site and implant with the membrane
- Wound closure by soft tissue expansion without vertical releasing incisions
- Stable keratinized gingiva after insertion of healing abutment at re-entry
- X-ray control at re-entry
- Tip:
For lateral augmentation with minimally invasive surgery, initial placement of a membrane and subsequent application of a graft material is advantageous.
**CLINICAL CASE BY**
Prof. Dr. Dr. Daniel Rothamel,
Clinic Mönchengladbach, University Düsseldorf, Germany

**SINUS LIFT WITH TWO-STAGE IMPLANTATION**

- Pre-operative radiograph
- Clinical situation before sinus lift
- Preparation of a lateral sinus window
- Filling of sinus cavity with maxresorb®
- Covering with Jason® membrane
- Tension-free wound closure with interrupted sutures
- Post-operative radiograph to control applied grafting material
- Good osseous integration of the maxresorb® particles without soft tissue ingrowth six months post-operatively at re-entry
- Stable insertion of two implants into sufficient bone matrix
- Histology showing good integration of the maxresorb® particles into the newly formed bone matrix
- X-ray control after implantation

**Tip:** For sinus floor elevation, the large maxresorb® granules (particle size 0.8 - 1.5 mm) are especially suitable to gain sufficient space for osteogenesis and revascularization, even when larger volumes of the bone graft material are applied.

**CLINICAL CASE BY**
Dr. Frank Kistler, Landsberg am Lech, Germany

**INTERNAL SINUS LIFT**

- Endodontically treated tooth 26 with apical cyst formation
- X-ray control before implantation with partially regenerated extraction socket
- Presentation of the soft tissue situation before implantation
- Preparation of the implant bed for internal sinus lift with bone condenser
- The maxresorb® inject paste is brought to instrument for application
- Insertion of maxresorb® inject for internal sinus lift
- Augmentation of the sinus floor by a crestal approach
- Insertion of maxresorb® inject with bone condenser
- Inserted implant before wound closure
- X-ray control clearly showing the inserted maxresorb® inject

**Tip:** For internal sinus lift, the moldable graft material maxresorb® inject is ideally applied by a lateral approach as no further mixing with blood is needed.
Extraction of tooth 14 and 15

Immediate implant insertion in extraction sockets of tooth 14 and 15

Buccal dehiscence of the bone wall of tooth 14

Placement of the healing abutments

Osteotome technique with insertion of maxresorb® inject (transalveolar) at tooth 15

Placement of Jason® membrane at the buccal bone wall

maxresorb® inject placed at buccal wall and protected by Jason® membrane

Wound closure and suturing

Tissue situation after five months of healing

3D CBCT four months post-operative

Situation after removal of healing abutments

Clinical view at control one year after surgery

Preoperative x-ray

Clinical situation before surgery

Implant insertion in regio 12, 11 and 23

Insertion of healing caps

Extraction of tooth 21 and 22, defects of the buccal wall visible

Filling of the extraction sockets with maxresorb® inject

Covering of socket and buccal wall with Jason® membrane

Wound closure and suturing

Situation after six months healing time

Situation after removal of healing caps

Final prosthetic restoration

X-ray control eight months after extraction and implantation
Innovation.  
Regeneration.  
Aesthetics.

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