maxgraft®
maxgraft® bonering
maxgraft® bonebuilder
Processed Human Allograft

Dr. B. Giesenhagen & Dr. M. Schlee et al.
Various bone graft materials are available to replace and regenerate bone matrix lost by tooth extraction, cystectomy or bone atrophy following loss of teeth or inflammatory processes.

Of all grafting options autologous bone is considered the „gold standard“, because of its biological activity due to vital cells and growth factors.

Yet, the availability of sufficient quantities of autologous bone from intra-oral donor sites is restricted and the bone tissue obtained from the iliac crest is described to be subject to fast resorption. Moreover, the harvesting of autologous bone requires a second surgical site associated with an additional bone defect and potential donor site morbidity. Thus, application of processed allogenic bone tissue appears a sufficient alternative.

New bone formation after grafting with allogenic bone tissue begins with an acute inflammatory response, within which granulation tissue gradually accumulates, and by activation of osteoclasts. The incorporation process begins with the vascularization of the allograft. By activation of osteoclasts the immune system will facilitate the remodelling of the graft. These large cells completely degrade medullary bone thereby allowing its substitution by osteoblasts. The immunological compatibility of processed allogenic bone is not different from autologous tissue. In patients who had allograft surgery no circulating antibodies could be detected in blood samples1.

Moreover, several histological studies have well documented that there was no difference in the final stage of incorporation between allograft and autologous graft2,3.

Classification

**Autologous:**
- patient’s own bone, mostly harvested intra-oral or from the iliac crest
- intrinsic biologic 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

C+TBA is a non-profit organization aiming to maintain the continuity of the medical supply of allografts under pharmaceutical conditions. Serving as a platform for the definition of safety standards and assurance of compliance with defined product qualities, C+TBA focuses on the specifications of human bone tissue as required in a large number of diseases that are associated with the loss of bone tissue.

C+TBA is certified and audited by the Austrian Ministry of Health in accordance to the European Directives and regulated by the Austrian Tissue Safety Act (GSG 2009).

In Directive 2004/23/EU of 31 March 2004, the European Parliament and the Council of the European Union defined the future general conditions and quality standards for the handling of tissue of human origin, which were further specified in Directives 2006/17EC and 2006/86EC. Regulating in detail the removal, quality control, processing, stockpiling, storage, and distribution of human tissue and cells, provisions have been obligatory for all member states since April 2006. The individual measures are to be undertaken at pharmaceutical level within the framework of a GMP-compliant quality management system.
Tissue Donation and Procurement

Donor tissue is only approved for processing when passed through the incoming inspection, consisting of a strict serological screening protocol.

maxgraft® is exclusively produced from bone tissue of German, Swiss and Austrian donors. All pure cancellous bone regeneration material originates from living donors by explantation of femoral heads during total hip replacement surgery, while products with a high proportion of cortical bone originate from recently deceased donors.

The procurement, standardized by a predefined removal protocol, is carried out by certified procurement centers. All donations are based on the written consent from the patient and highly selective exclusion criteria with regard to the patient’s state of health. maxgraft® uni-cortical blocks exclusively originate from Austrian organ donors. For all donors the highest ethical and safety-related requirements are met and a donation is only accepted with the written consent of the donor.

Family members of the deceased are obligated to answer a questionnaire to ensure compliance with the stated exclusion criteria.

After donor acceptance a series of serological testing is performed. Aside from antibody screening (Ab) nucleic acid tests (NAT) are executed to span the diagnostic window.

Serological testing

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<td>Human Immunodeficiency Virus (HIV 1/2)</td>
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<td>Human T-lymphotropic Virus (HTLV 1/2)</td>
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<td>Bacteria</td>
<td>Test</td>
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<tr>
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<td>Liver parameters</td>
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<tr>
<td>ALT/ALAT</td>
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Blood samples are taken simultaneously to tissue explantation during total hip replacement surgery or within 24h of death in case of organ donation.
The C+TBA Cleaning Process

After shaping and crude cleaning, the donor tissue undergoes ultrasonication to remove blood, cells and tissue components, but mainly to promote the removal of fat from the cancellous structure of the bone, improving the penetration of subsequent substances.

In a chemical treatment all non-collagenic proteins are denatured, potential viruses are inactivated and bacteria are destroyed.

In the subsequent oxidative treatment, persisting soluble proteins are denatured and potential antigenicity is eliminated.

Finally, the tissue undergoes lyophilization, a dehydration technique which facilitates the sublimation of frozen tissue water from solid phase to gas phase, thereby preserving the structural integrity of the material.

The tissue can be reconstituted rapidly due to microscopic pores within the material, which were created by the sublimating ice crystals. It has been well established that the lyophilization process preserves structural properties that improve graft incorporation.

The final sterilization by gamma irradiation guarantees a sterility assurance level (SAL) of $10^{-6}$ while ensuring structural and functional integrity of the product and its packaging.

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Step 1: After crude removal of surrounding soft tissue, fat and cartilage, the donor tissue is brought into its final shape.

Step 2: The defatting of the donor tissue by ultrasonication allows moderate penetration of subsequent substances.

Step 3: A treatment with alternating durations of diethyl ether and ethanol leaches out cellular components and denatures non-collagenic proteins, thereby potential viruses.

Step 4: An oxidative treatment further denatures persisting soluble proteins, thereby eliminating potential antigenicity.

Step 5: Freeze-drying by lyophilization preserves the natural structure of the tissue and maintains a residual moisture of < 5%, allowing quick rehydration and easy handling.

Step 6: Double packing and final sterilization by gamma-irradiation guarantees a 5 year shelf-life at room temperature.

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Safety and Quality

Test samples are taken from every donor tissue to perform a LAL test (Limulus Amebocyte Lysate) for bacterial endotoxin. Reference samples are filed for a minimum of 15 years.

Limulus Amebocyte Lysate test:

Endotoxin activates a serine protease catalytic coagulation cascade in the Limulus’ hemolymph. The first component of the cascade, Factor C (FC), is activated by endotoxin binding. After downstream activation of clotting enzyme, application of a chromogenic substrate results in color change.

Virus inactivation

The critical viral inactivation steps of the process – dynamic immersion in ethanol, hydrogen peroxide and gamma irradiation – have been validated for reliability and reproducibility by an independent test facility. Suspensions of model viruses for non-enveloped and enveloped DNA viruses (HBV), and non-enveloped (HAV) and enveloped RNA viruses (HIV, HCV, HTLV) have been applied. The process shows an overall efficacy in inactivating all test viruses globally > 6 logs (reference value for efficient viral inactivation > 4 logs) and therefore can be considered effective in removing potential viral contaminants.

Biomechanical properties have been recently analyzed by the Institute of Material Science of the Technical University of Vienna, Austria. After the determination of E-modulus and pressure resistance no significant alterations were detected in irradiated products (post rad.) compared to non-irradiated ones (post proc.).

CTBA’s allograft products provide a stable scaffold for revascularization and osteoblast migration. Simultaneously, due to the preserved collagen content, the graft presents high flexibility supporting physiological bone formation and remodeling.
maxgraft® is a sterile, high-safety allograft product, derived from human donor bone, processed by the Cells + Tissue Bank Austria. C+TBA, a high-quality bone bank, is regulated, audited and certified by the Austrian Ministry of Health and fulfills the highest EU safety standards.

For experienced oral and maxillofacial surgeons, allograft bone blocks for block augmentation are the only real alternative to harvesting patients’ autologous bone, preventing well known risks as donor-site morbidity, infection, postoperative pain and loss in bone stability. The high biologic regeneration capability of maxgraft® results in a predictable clinical outcome.

Properties
- Preserved biomechanical properties
- Sterile without antigenic effects
- Storable at room temperature for 5 years
- Osteoconductive properties supporting natural and controlled tissue remodelling

Indications:
Implantology, Periodontology, Oral Surgery & CMF

Granules
- Localized augmentation of the ridge for future implant placement
- Reconstruction of the ridge for prosthetic therapy
- Filling of osseous defects, such as extraction sockets
- Elevation of maxillary sinus floor
- Repair of intrabony periodontal defects

Blocks
- A predictable and highly effective alternative to traditional block grafting
- Ridge augmentation
The thermogravimetric analysis shows the mass reduction following heating and helps to determine the content of water and organic components like collagen. Heating from room temperature up to 1000°C resulted in a staged mass reduction. The first reduction of 34.64% can be attributed to the vaporization of water and the combustion of collagen, the second (3.88%) to the vaporization of carbon dioxide.

**Surface**

SEM pictures of maxgraft® illustrate the structure of the processed bone. Processing does not affect structural features and with its interconnecting macroporosity, maxgraft® strongly resembles natural human bone matrix. Because of the special production process without sintering, maxgraft® still contains the collagen matrix. At a higher magnification the structure of the mineralized collagen fibers can be recognized.
The maxgraft® bonering technique

maxgraft® bonering is a pre-fabricated ring of processed allogenic donor bone, which is placed press-fit into a trephine drill-prepared ring bed. At the same time an implant is inserted into the ring. The bone integration of both maxgraft® bonering, and the implant, occurs via the surrounding vital bone.

Compared to the classic, two-stage augmentation with i.e. bone blocks, this technique reduces the entire treatment period by several months and saves the re-entry.

The maxgraft® bonering allows vertical and horizontal augmentation and new bone formation, therefore simplifying the surgical treatment of 3-dimensional bone defects.

Indications
- Vertical augmentation (in combination with horizontal augmentation)
- Single tooth gap
- Edentulous space
- Sinus lift

Advantages
- bone augmentation and simultaneous implant placement
- no second surgical procedure
- significant reduction of treatment time
bone augmentation & immediate implant placement

Soft tissue management

maxgraft® bonering surgical kit

With this surgical kit, botiss provides all necessary instruments to apply the maxgraft® bonering technique. The kit includes two convenient sizes of trephines, which precisely fit together with the two maxgraft® bonering diameters. The planator allows paving of the local bone to create a congruent and fresh contact surface of the implant area. Trephines and planator are perfectly adjusted to the pilot drill. The diamond disc and the diamond ball mill serve to manipulate the maxgraft® bonering for excellent adjustment to the local bone and for improved soft tissue healing. Altogether, these instruments allow optimal preconditions for the bony ingrowth of maxgraft® bonering. All instruments are made of high quality surgical steel and produced in Germany.
maxgraft® bonebuilder provides clinical users a pre-fabricated allogenic bone implant, which is individually adjusted to the patient’s bone defect. With maxgraft® bonebuilder, harvesting of autologous bone and manual adjustment of the obtained transplant is no longer required. Therefore, pain, risk of infection, morbidity, operation time and costs can be significantly reduced. maxgraft® bonebuilder blocks are sterile and delivered directly to the clinical user.

The maxgraft® bonebuilder technology

In-house planning

botiss virtually designs the patient matched allogenic bone implant based on the CT/DVT-scan of the bone defect. The design of the bone implant undergoes the final inspection by the clinical user and is, by individual order, released for production. Alternatively, the clinical user can use a suitable software to design a block by himself (e.g. SUITE ONESCAN by 3D Med, Italy®). The botiss partner Cells +Tissuebank Austria receives a *stl milling file and the patient matched allogenic bone implant is produced under cleanroom conditions. The resulting allogenic bone implant is ready to be inserted into the defect with only minor adjustments.

After implantation, the maxgraft® bonebuilder block is to be fixed with osteosynthesis screws. The augmentation site should be covered with bone regeneration material and a collagen membrane – as a protection against potential resorption.

Its strong capillary action enables the fast and efficient penetration of the material 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.

The patient matched maxgraft® bonebuilder block allows optimal horizontal and vertical reconstruction of the atrophic ridge.

Indications
- Extensive bone defects
- Atrophic maxilla/mandibula
- Horizontal/vertical augmentation

Advantages
- Individualized allogenic bone implant
- Significant reduction of operation time
- Improved wound healing
The process flow

1. Upload of CT/DVT-data on www.botiss-bonebuilder.com

After registration, CT/DVT-data of the patient’s defect can be uploaded on the botiss server. All radiological data have to be single sliced, unlinked images (single-frame data images). The only data type suitable for 3D planning is DICOM (*dcm). Please find further information on the correct data format on our website.

2. Design of the customized allogenic bone block

botiss creates a 3-dimensional model of the radiological images and designs a virtual patient matched bone implant in consultation with the clinical user. Alternatively, the clinical user can design the bone block by himself and upload the final *.stl file of the designed implant on www.botiss-bonebuilder.com.

3. Design quality check

The clinical user receives a 3D PDF file containing the virtually constructed maxgraft® bonebuilder block and has to confirm its design. Alternatively, the virtual bone block will be individually adjusted due to requirements.

4. Individual order

The production of the block starts after the clinical user fills in the patient based order form for the bone block to the attention of C+TBA, the responsible tissue bank.

5. Production of the individual bone block

At C+TBA the *.stl data of the design is imported into a milling machine and a block of maximal 23x13x13mm is produced.

The maxgraft® bonebuilder technology allows complex reconstruction in cases of extensive jaw atrophy.
Clinical Application

Clinical Case by Dr. Fernando Rojas-Vizcaya, Castellón, Spain

Socket preservation with maxgraft® granules

Clinical Situation in the maxilla before extraction

Situation after tooth extraction and mobilization of mucosal flap

Augmentation of the maxillary ridge and filling of extraction sockets with maxgraft® granules. Placement of mucoderm® to improve soft tissue situation and Jason® membrane to cover surgical site

Mobilization and pre-fixation of the surrounding soft tissue

Tension-free wound closure

4 months post OP: bone is at the level of the planned crowns

Clinical situation 4 months post-OP

Maxillary ridge in situ after preparation of mucosal flap

Insertion of four implants

Placement of abutments

Positioning of prosthesis

Closure of mucosal flap

After immediate loading protocol: Prosthesis will guide soft tissue during healing process

Antibiotics

When performing hard tissue augmentation, you should treat the patient with a sufficient dose of antibiotics to minimize the risk of infection and related possible graft loss. A potential treatment plan could include starting the antibiosis one day prior or at least one hour before surgery by ingestion of a full daily dose. In case of extensive jaw reconstruction a bacteriological screening (saliva sample) should be considered.
Clinical Application

Clinical Case by Dr. Damir Jelušić, Opatija, Croatia

Ridge augmentation with maxgraft® cancellous block

X-ray and CAD/CAM-based 3D image of maxillary ridge before surgery

Manual adjustment of maxgraft® blocks on a CAD/CAM-based model

Clinical situation

Atrophic maxillary ridge after preparation of mucosal flap

Fixation of the prepared maxgraft® blocks

Filling of residual gaps with cerabone® and covering with Jason® membrane

Tension-free closure of mucosal flap

CAD/CAM-based 3D image

Clinical situation 5 months post-OP

X-ray 5 months post-OP

Insertion of 3 implants and gingiva formers

6 months after re-entry: Patient is ready for final prosthesis

GBR/GTR

Collagen membranes act as a resorbable matrix to avoid the ingrowth of the faster proliferating fibroblasts and epithelium into the defect and maintain the space for controlled regeneration of bone. Jason® membrane is a pericardium membrane providing a long-lasting barrier function for ~3-6 months. mucoderm®, a 3-dimensional stable matrix, supports revascularization and fast soft tissue integration and thus, is a valid alternative for patients’ own connective tissue. When applying mucoderm® simultaneously to a bone graft material please assure adequate mobilization of the surrounding soft tissue.
Clinical Application

Clinical Case by
Dres. Bernhard Giesenhagen and Orcan Yüksel, Frankfurt, Germany

Part I: Vertical augmentation with maxgraft bonering®

**Preparation of the ring bed in an atrophic mandibula (third quadrant)**

**Vertical augmentation by placing a maxgraft® bonering**

**Simultaneous horizontal augmentation**

**Stabil implant insertion**

**Insertion of second maxgraft® bonering and implant**

**Filling of the residual defect volume with cerabone® and covering the operation site with a Jason® membrane**

**Augmentation with maxgraft® bonering**

For the reconstruction in an atrophic jaw a vertical augmentation of up to 3mm above local bone level can easily be achieved. If more vertical height is desired, one should apply enhancing additives like bone morphogenic proteins (BMP) or growth factors. In a severely atrophic mandibular the ridge has to present with a broadness of at least 4mm (in case of a parallel-walled ridge) to successfully apply maxgraft® bonering for vertical and horizontal augmentation.

By providing primary stability maxgraft® bonering allows direct implant insertion during sinus lifting. Since allogenic bone is not a common grafting material for this procedure the sinus cavity has to be filled with an additional grafting material (e.g. cerabone®, maxresorb® or maxresorb® inject).
Part II: Sinus lift with maxgraft bonering®

Preparation of a lateral window for sinus floor elevation in the first quadrant

Placement of maxgraft® bonering

Implant implant insertion passing through maxgraft® bonering from the crestal side

Filling of the residual sinus cavity with cerabone®

Preparation of the defect with a trephine

Press-fit placement of maxgraft® bonering into the defect

X-ray 9 months post-OP: full integration of maxgraft® bonering and implants and proceeding remodelling of the grafts

Tension-free suturing after placement of Jason® membrane

Rehydration of maxgraft® bonering by careful aspiration of physiological saline in a syringe (2-3 times)

Placement of Jason® membrane

Clinical Application

Rehydration

The processing of maxgraft® products preserves the natural collagen content of the bone tissue and a residual moisture of ~5%. Thus, the products don’t have to be re-hydrated but are ready for instant use. Nevertheless, reconstitution in physiological saline, as described in the case beneath, can be beneficial for the blood diffusion of the graft. This technique can be used for all maxgraft® products. Be aware that hyper-hydration can result in the loss of structural integrity!
Clinical Application

Clinical Case by
Dr. Darius Pocebutas, Kaunas, Lithuania

Horizontal augmentation in a single tooth gap with maxgraft® bonering

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**Clinical situation pre-OP**

**Pilot drill in the recipient site**

**Preparation of the ring bed with the trephine**

**Paving of the local bone using the planator from maxgraft® bonering surgical kit**

**Measurement of the defect**

**Adjustment of maxgraft® bonering to desired height**

**Placement of the ring into the ring bed**

**Due to its structure the ring is instantly soaked with blood**

**Implant insertion passing through maxgraft® bonering; the shape of the ring mimics the anatomic structure of the ridge**

**Gaps are filled with cerebone® and the augmentation site is covered with a Jason® membrane**

**Tension-free wound closure**

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**Graft exposure**

Wound dehiscence and graft exposure is a common complication of block augmentation. After removal of necrotic tissue (cut out the soft tissue with a scalpel and remove infected hard tissue with rotating instruments if necessary) the augmented area should be rinsed with chlorhexidine. Subsequently, the graft has to be covered again, if necessary, by harvesting a palatal soft tissue transplant.
Clinical Application

Clinical Case by Dr. Markus Schlee, Forchheim, Germany

Ridge augmentation with maxgraft® bonebuilder

3D design of maxgraft® bonebuilder
Patient matched maxgraft® bonebuilder block
Clinical situation in situ

Fixation of maxgraft® bonebuilder with screws for osteosynthesis
Covering of the block with Jason® membrane
Tension-free suturing of the wound

Re-entry 5 months post-OP: full ingrowth of the block
Implant insertion
Wound closure around gingiva formers

Design quality check
The design of maxgraft® bonebuilder has to be checked very carefully before it is released for production. Only the surgeon himself can assess the patients’ soft tissue situation and therefore, the required dimension of the block. The botiss construction team will adjust the design of the block until it perfectly meets the expectations of the clinician.
Clinical Application

Clinical Case by Dr. Michele Jacotti, Brescia, Italy

Ridge augmentation with maxgraft® bonebuilder

Virtual planning of the block using OneGraft3D (by 3D Med)
Patient matched maxgraft® bonebuilder
Situation after preparation of mucosal flap and perforation of the cortical layer
Exact positioning of the maxgraft® bonebuilder block

Fixation of the block with screws for osteosynthesis
Careful wound closure
Clinical situation at re-entry 5 months post-OP
Full bony ingrowth of the block

3D implant positioning using OnePlan3D (by 3D Med)
Stable implant insertion
Abutment placement after ingrowth of the implants
Final prosthesis

3D construction
The surgeon is free to design his own maxgraft bonebuilder® block by using a suitable software package (e.g. SUITE ONE-SCAN by 3D Med, Italy®). The output format of the design file has to be *.stl to import it into the C+TBA milling machine.
Ridge augmentation with maxgraft® bonebuilder

Clinical situation before augmentation

CT scan of region 36, 37 before surgery

Situation after tooth extraction and mobilization of mucosal flap

maxgraft® bonebuilder

Immediate implant insertion in regio 34, 35; positioning and fixation of maxgraft® bonebuilder

Filling of residual volume with cerabone®

Covering of the augmentation site with collprotect® membrane

Wound closure and suturing

CT scan of region 36, 37 after surgery

**Fixation**

maxgraft® blocks are to be fixed with screws for osteosynthesis, preferably with flat-headed screws to avoid perforation of the surrounding soft tissue.
Product Specifications

maxgraft® cancellous granules

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<tr>
<th>Art.-No.</th>
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maxgraft® cortical granules

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maxgraft® blocks

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PMfa Individual planning and production of a bone implant from a 20x10x10mm cancellous block.
maxgraft® bonering surgical kit

The maxgraft® bonering surgical kit is delivered in an autoclavable instrument rack.
Innovation.
Regeneration.
Aesthetics.

soft tissue
education
hard tissue

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