Bio-Oss®
Bio-Gide®

Advanced techniques for bone regeneration

Geistlich
Biomaterials
Regenerative procedures

Autogenous bone is irreplaceable in the treatment of large bony defects and is regarded as the gold standard. However, bone regeneration using autologous bone alone has certain limitations:

1. Restricted oral availability: Accessing the hip is an additional burden for the patient and cost-intensive.

2. Accelerated resorption of autogenous cancellous bone compared to autogenous cortical bone:
   - Less stability of implant anchorage in two-step procedures when an augmentation is performed with autogenous cancellous bone alone.
   - Short therapeutic time schedule: The optimum implantation time with autogenous cancellous bone is after 2-3 months. The treatment time plan has to be followed meticulously, to prevent resorption and to maintain the dimensional stability.

Such limitations of autogenous grafts can be countered by the addition of a slow-resorbing bone substitute such as Bio-Oss®.

Numerous scientific studies have shown that Bio-Oss® is highly osteoconductive and integrates into the bone remodelling process (cf. p. 7-9). Bio-Oss® has been clinically tested in over 90 universities and has been scientifically documented in detail in over 350 publications over the last 15 years. Bio-Oss® has already been used in over one million patients worldwide.

Structure of Bio-Oss® Spongiosa (SEM 40 x). Bio-Oss® consists of the mineralised part of bone and bears a great similarity to natural bone. Therefore Bio-Oss® is an ideal guide rail for bone regeneration.

Advantages of using Bio-Oss®

- The slow resorption of Bio-Oss® helps to preserve the volume of the bone/bone substitute augmentation graft. This extends the therapeutic time scale and improves the aesthetic outcome.

- Defects regenerated with Bio-Oss® show higher mineral density than local bone, which aids stable anchorage of the implant.

- The combination of oral bone and a bone substitute can in some cases render it unnecessary to access the hip, even in relatively extensive defects. Not infrequently, this allows to avoid a more major and more cost-intensive procedure under general anaesthesia to be avoided.

Abb. 1a
Bone augmentation with an autogenous block graft alone (Case: C. Maiorana)

Abb. 1b
5 months post-operatively, marked resorption of the autogenous bone has taken place in the absence of Bio-Oss® contouring.
Methods of treatment

The method of treatment for successful regeneration always depends on the local conditions (defect size, bone quality, etc.) and on the assessment of the treating surgeon. However, the following treatment options can be proposed on the basis of the many years of clinical experience acquired with the use of Bio-Oss® and Bio-Gide®.

Treatment options with natural biomaterials for advanced regenerative techniques

- **defect class 1**
  - 3+ and 4-wall horizontal defects
    - Bio-Oss® + Bio-Gide®
  - 2-wall horizontal defects
    - Bio-Oss® (+ autogenous bone chips) + Bio-Gide®
  - 1-wall horizontal defects
    - Autogenous block graft, contoured with Bio-Oss® + Bio-Gide®

- **defect class 2 + 3**
  - vertical or combined vertical/horizontal defects
    - Autogenous block graft, contoured with Bio-Oss® + Bio-Gide®
  - Sinus floor augmentation
    - Bio-Oss® with residual bone height of more than 5mm**
    - Autogenous block graft, contoured with Bio-Oss® + Bio-Gide®

- **defect class 2 + 3**
  - Bio-Oss® + autogenous bone chips + titanium-reinforced membrane
  - Bio-Oss® + autogenous bone chips + titanium-reinforced membrane or TiMesh
  - Bio-Oss® + autogenous bone chips with residual bone height of less than 5mm**

** Note: (Abensur, Information Dentaire, 1998)

Comments:

**Bio-Gide® application**
- It is always advisable to cover the augmentation graft with a membrane barrier in order to achieve undisturbed bone regeneration.
- In general terms, it is advisable to fix the membrane with minipins or to stabilise the membrane using the double-layer technique (cf. p.11).
- To ensure new bone formation, Bio-Oss® should be used only in direct bony contact with well vascularised bone beds (if necessary, roughen).
- Implantation into implant beds prepared with Bio-Oss® should take place 4-6 months after defect filling.
- In the case of sinus floor elevations, bony integration of the augmentation graft takes 6-12 months.
Indications

Augmentation of 3 to 4 wall defects around implants
Dr. Dr. St. Hauk
Practice for maxillofacial surgery, Bad Soden, Germany

Abb. 2a
Initial clinical situation showing the strongly atrophied maxilla

Abb. 2b
Application of Bio-Oss® after insertion of the immediate implant in the split crest

Augmentation of alveolar 2 wall defects
Dr. K.-L. Ackermann,
Practice for oral surgery, Filderstadt, Germany

Abb. 3a
After extraction and insertion of 7 implants the large and optimally prepared augmentation areas are easily seen.

Abb. 3b
The Bio-Gide® membranes are partially fixed with resorbable pins (Resor-Pin®). The defects are then filled with 1-2 mm granules of Bio-Oss®.

Combined vertical/horizontal ridge augmentation
Dr. A. Baruffaldi,
Dep. of oral surgery, University of Parma, Italy

Abb. 4a
View of the defect region

Abb. 4b
Fixing of the autogenous block graft

Ridge reconstruction
Prof. Dr. C. Maiorana,
Dep. of oral surgery, University of Milan, Italy

Abb. 5a
Clinical starting situation

Abb. 5b
Exposition of the severely atrophied maxilla
Abb. 2c  Covering the augmented area with Bio-Gide®

Abb. 2 d  Tension-free wound closure

Abb. 2 e  Because of instability, one implant had to be removed after 2 weeks. During reopening at 4.5 months post-operatively, one can see the clearly improved bone availability in the augmented area.

Abb. 3a  In the interforaminal area, Bio-Gide® membrane is fixed on the right and on the left of the median plane.

Abb. 3b  Three further implants are inserted. The original implants have become completely osteointegrated by this time.

Abb. 3c  Radiological findings pre-operatively and 15 months post-operatively after augmentation.

Abb. 3d  Radiological findings pre-operatively and 6 months post-operatively after implant insertion.

Abb. 3e  Radiological findings pre-operatively and 5 months post-operatively after implant insertion.

Abb. 4c  Contouring of block graft with Bio-Oss® Spongiosa.

Abb. 4d  Re-entry after 2 months for implant insertion.

Abb. 4e  Radiological findings pre-operatively and 6 months post-operatively after implant insertion.

Abb. 5c  Ridge reconstruction with Bio-Oss® and autogenous bone (mixing ratio 1:1), using titanium mesh.

Abb. 5d  Re-entry and removal of titanium mesh after 5 months.

Abb. 5e  Radiological findings pre-operatively and 5 months post-operatively after implant insertion.
Sinus floor augmentation

Case from Dr. K.-L. Ackermann, Practice for oral surgery, Filderstadt, Germany

Sinus floor elevation with Bio-Oss® alone or in combination with autogenous bone is a widely used and well-documented surgical technique that has been performed for more than a decade in numerous hospitals and practices worldwide.

Long-term results in sinus floor elevation with Bio-Oss®
by Dr. A. Kirsch and Dr. K.-L. Ackermann:

| number of sinus floor elevations: | 1112 |
| inserted implants: | 2,200 |
| (81% single step, 15% two step, 4% combined) |
| time of implantation: | Sept. 1988 – August 2001 |
| loss: | 29 implants |
| success rate: | 98.7% |
| over 70% of the cases were treated with Bio-Oss® or with a combination of Bio-Oss® and autogenous bone |

Abb. 6a
Before starting the treatment, substantial bone loss is evident in the abutment teeth in the posterior maxilla, and large alveolar bony defects in the right side of the maxilla.

Abb. 6b
Right posterior maxilla: Immediate implantation is first performed in extraction socket 14. At the same time, preparations for sinus floor elevation are made by creating a lateral window.

Abb. 6c
To regenerate the defect in regio 15, a monocortical block is removed from the tuber. This is secured with a CorticoFix screw in the region of the alveolar defect. Sinus floor augmentation is performed with Bio-Oss®.

Abb. 6d
At the same time, a sinus floor elevation is also performed in the left side of the maxilla with Bio-Oss® and three endosteal implants are inserted. Despite considerable alveolar destruction, primary implant stability is achieved.

Abb. 6e
After implant insertion, the sinus floor and the lateral alveolar bony defect are further augmented with Bio-Oss®.

Abb. 6f
After complete augmentation, the entire augmentation graft and the implants themselves are covered with a Bio-Gide® membrane. The membrane is fixed three-dimensionally with resorbable pins (Resorb-Pins®).

Abb. 6g
14 months after augmentation, the implants inserted using a one-stage procedure (left maxilla) and those inserted using a two-stage procedure (right maxilla) are well integrated.

Abb. 6h
Final radiological check, 20 months after augmentation and 6 months after prosthetic restoration.

Scientific references for sinus floor elevation with Bio-Oss®:

- Malorana et al. (Int J of Oral & Maxillofac Impl 2000)
- Yıldırım et al. (Clin Oral Impl Res 2000)
- Valentinii (Int J Periodont Rest Dent 2000)
- Platiel et al. (Int J Oral & Maxillofac Impl, 1999)
- McAllister et al. (Int J Oral & Maxillofac Impl 1999)
- Terheyden et al. (Clin Oral Impl Res 1998)
- Margolin et al. (J Periodontol 1998)
- Haas et al. (Clin Oral Impl Res 1998)
- Haas et al. (Clin Oral Impl Res 1998)
- McAllister et al. (Int J Periodont Rest Dent 1998)
- Valentinii et al. (Clin Oral Impl Res 1998)
- Hürzeler et al. (Clin Oral Impl Res 1997)
- Valentinii Abensur (Int J Periodont Rest Dent 1997)
- Wetzel et al. (Clin Oral Impl Res 1995)
Natural properties of Bio-Oss®

The extremely close similarity of
Bio-Oss® to endogenous human bone
is assumed to be the reason for its
good bone regeneration.

High porosity –
just like natural bone
encourages blood vessels to infiltrate and
bone cells to migrate through the wide-
mesh, interconnecting pore system.

Large internal surface area –
just like natural bone
allows close contact with new bone tissue.

Fine crystalline structure –
just like natural bone
facilitates integration into bone's natural
remodelling process.

Chemical composition –
just like natural bone
leads to high tissue compatibility of the
natural bone apatite.
(CaP-Index: Bio-Oss® 2,03,
human bone 2,03)

"The pore size and, associated with this, the size of
the specific surface area of bone substitute materials
influences their in vivo behaviour."
(Weibrich et al., Mund Kiefer GesichtsChir, 2000)

Specific surface area of bone substitute materials (m²/g)

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<thead>
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<th>Material</th>
<th>Specific Surface Area (m²/g)</th>
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<tr>
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<tr>
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<tr>
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</table>

Scientific references for the high osteoconductivity
of Bio-Oss®:
Zitzmann et al. (Int. J. Maxillofac. Implants 2001)
Zitzmann et al. (J. Periodontics Restorative Dent 2001)
Araujo et al. (J. Clin. Periodontal 2001)
Maiorana et al. (Int. J. Oral Maxillofac. Implants 2000)
Valentini et al. (J. Periodontics Restorative Dent 2000)
Camelo, Neves et al. (Int. J. Periodontal Rest Dent 1998)
Hürzeler et al. (Clin. Oral Impl Res 1997)
Valentini, Abensur (Int. J. Periodontal Rest Dent 1997)
Schmitt et al. (J. Periodontal 1997)
Jensen et al. (Int. J. Oral Maxillofac. Implants 1996)

Abb. 7a
Human bone
Structure and porosity of cancellous bone
(SEM 50x)

Abb. 7b
Bio-Oss®
Close similarity with human bone in terms of
structure and porosity (SEM 50x)
Bio-Oss® – prevents premature graft resorption

Bio-Oss® is integrated into bone’s natural remodelling process. The slow-resorbing matrix structure of Bio-Oss® gives the augmentation graft a high degree of stability and prevents premature resorption of the newly formed bone.

The preservation of dimensional stability is achieved over a prolonged period and so extends the therapeutic time-scale. This is particularly important in pre-prosthetic surgery in aesthetically demanding indications.

Long-term preservation of the ridge height with Bio-Oss®

Bone resorption after 4 years:
- Combined treatment with Bio-Oss® and autogenous bone 20%
- Treatment with autogenous bone alone 60%

Bone resorption after 9 years:
- Combined treatment with Bio-Oss® and autogenous bone < 30%

(Boyne, 1991, 1997)

Scientific references for bone-volume preservation with Bio-Oss®:
- Artzi et al. (J Periodontal 2000)
- Kloss et al. (Z Zahnärztl Implantol 2001)
- Maisharan C (In: Osteointegra Avancata, RC Libri 2001)
- McAllister et al. (Int J Oral Maxillofac Implants 1999)
- Boyne P. (In: Osseous Reconstruction of the Maxilla and the Mandible, Quintessenz 1997)
- Boyne P. (Unfallheilkunde 1991)

Long-term preservation of the ridge with Bio-Oss®

Fig. 8a
Baseline situation: Severely atrophied mandible (white arrows), which will be treated with Bio-Oss® and autogenous bone (mixing ratio 50:50) and restored with a removable full prosthesis 6 months post-operatively.

Fig. 8b
5 years after treatment with Bio-Oss® and an autograft, the mandible shows an unchanged ridge height (black arrows). “Bone preservation after 5 years is excellent.” (Prof. Dr. P. J. Boyne, 1997, University of Loma Linda, California)
Bio-Oss® - increases bone mineral content

Histological studies have shown that Bio-Oss® increases the mineral content of the regenerated area. This hard and compact regenerated tissue favors stable anchorage of the implant to be inserted.

Better implant anchorage with Bio-Oss®

Bone anchorage of 54 titanium implants after sinus floor elevation. The implants in the Bio-Oss® augmented region initially exhibit high tensile strength, which continues to increase up to week 26. The 45% greater tensile strength of Bio-Oss® test site compared to autogenous bone after 12 weeks indicates a better anchorage of the implant in the bone at the time. (Experimental study in the sheep, Haas et al. Clin Oral Implant Res 1998).

Increased mineralized structures in bone with Bio-Oss®

Fig. 9 a
Biopsy after sinus floor elevation with Bio-Oss®. The augmented region (top of picture) consists of a dense matrix of Bio-Oss® (purple), osseo-integrated by newly formed bone (pink).

The host bone (bottom of picture) contains cancellous bone of much less density.
(Case: P. Valenti, Paris, histology: R. Schenk, Bern)

Scientific references for the increase in bone mineral content with Bio-Oss®:

Maiorana C. (in: Osteointegrazione Avanzata, RC Libri 2001)
Valenti et al. (Int J Periodontics Restorative Dent 2000)
Maiorana et al. (Int J Oral Maxillofac Implants 2000)
McAllister et al. (Int J Oral Maxillofac Implants 1999)
Hämmerle et al. (Clin Oral Implant Res 1998)
McAllister et al. (J Periodont Rest Dent 1998)

Fig. 9 b
Detail enlargement from the regenerated region. Bio-Oss® (purpur) has been osseo-integrated by new bone, which has grown along the Bio-Oss® particle. Both osteoclasts (black arrow) and resorption lacunae (white arrow) can be seen on the surface of the Bio-Oss® particle.
Combination with the GBR technique: Bio-Gide®

Large augmentations in the hard tissue are frequently associated with complications in the soft tissue management. Collagen membranes have a positive influence on soft tissue healing and a tissue-friendly degradation.

Natural collagen encourages wound healing
Bio-Gide® consists of highly purified type I and III porcine collagen (source animal: pig) and has high biocompatibility. Good cell adhesion to the collagen membrane encourages wound healing. Even if a wound dehiscence does occur, it generally heals without complications.

Sufficiently long barrier function for undisturbed bone regeneration
Bio-Gide® provides a barrier function for 4–6 months and therefore allows undisturbed bone regeneration. There is no need for a second procedure to remove the membrane because it is resorbed. The breakdown occurs enzymatically and thus causes no irritation to the tissue from acidification.

Bio-Gide® demonstrates a high degree of similarity to human collagen membranes

Advantages of combining bone grafts with Bio-Gide®
- Promotes soft tissue healing with its guide rail function and leads to a high degree of tissue compatibility.
- Mechanical protection and stabilization of the graft, reduction of micromovements.
- Additional protection for autogenous bone chips against resorption and therefore optimization of the bone regeneration up to the coronal defect area.
- Prevents fibrous connective tissue from growing into the defect area and thereby optimizes esthetic results.

Scientific references for the combined use of Bio-Gide® and Bio-Oss®:
Zitzmann, Schäfer et al. (Int J Oral Maxillofac Implants 2001)
Camelo, Nevis et al. (Int J Periodontics Rest Dent 2001)
Zitzmann, Schäfer et al. (Int J Periodontics Rest Dent 2001)
Hämmerle, Lang (Clin Oral Implant Res 2001)
Melloni, J (Int J Periodontics Rest Dent 2000)
Camargo, Lekovic et al. (Int J Periodontics Rest Dent 2000)
Alpar, Leyhausen et al. (Clin Oral Invest 2000)
Höckers, Abensur et al. (Clin Oral Implant Res 1999)
Ohazama, Kitamura et al. (Jpn Soc Periodontol 1999)
Camelo, Nevis et al. (Int J Periodontics Rest Dent 1998)
Hürzeler, Köhler et al. (J Oral Maxillofac Surg 1998)
Zitzmann, Naef et al. (Int J Oral Maxillofac Implants 1997)
Kay, Wiener et al. (Proc Periodontics Aesthetic Dent 1997)
Hürzeler, Weng et al. (Deutsche Zahnärztl Zeitschrift 1996)
Double-layer technique

The development of natural collagen membranes such as Bio-Gide® constitute a considerable improvement in wound healing compared with ePTFE membranes and also simplify the surgical technique.

Furthermore, the membrane can be stabilised using the "double-layer technique". This technique affords greater graft stabilisation than does a single membrane layer, and so offers increased protection from micro-movements.

This application technique is used principally in the presence of defect sizes of 1–2 sockets in aesthetically demanding augmentations (e.g. in the front teeth).

Clinical study by N. Zitzmann et al. (Zurich): Improved prognosis with Bio-Gide®. In contrast to cases treated with ePTFE membranes, cases of dehiscence treated with Bio-Gide® healed without complications.

Diagram of double-layer technique

A surgical video from Prof. D. Buser on the use of Bio-Gide® with double-layer technique is available at Geistlich Biomaterials.
Today, tissue-engineering methods are being increasingly used to optimise surgical treatments and to develop new ones. The objectives are the accelerated healing of bone or soft-tissue defects, the enlargement of the regenerated graft volume or the treatment of borderline indications that could previously not been adequately treated.

Optimization of regenerative steps:
- platelet-rich plasma (PRP) harvested from the patient’s blood
- genetically engineered growth factors (BMP’s)
- autogenous cells enriched millions of times in the laboratory
- autogenous bone marrow (transplants), already containing cells and growth factors.

The properties of the carrier play an important role in the effect of these biological modulators. On one hand they act as a delivery system for the morphogenic factors and on the other hand they have to provide a stable matrix for cell adhesion and growth.

The osteoconductivity of these carriers plays an important part in the success of the treatment. For instance, a suitable carrier surface can encourage cell adhesion and help maintain the differentiation status of the bone-forming cells. The morphology of the newly formed bone is also decisively influenced by the carrier.

The rate of resorption is another important factor in the effectiveness of the carrier. Slow-resorbing materials such as Bio-Oss® offer the young bone long-term stability and in this way support permanent tissue regeneration.

Matrix based tissue-engineering

Abb. 12a

Abb. 12b
Osteoblast cell culture on Bio-Oss®. Several cell layers have formed on the osteoconductive surface of Bio-Oss® (P. Behrens, Lübeck).
Effect of the carrier on the regeneration outcome:

- Encourages cell adhesion
- Maintains the differentiation status of bone-forming cells
- Influences the morphology of the new bone
- Maintains space in the defect

Bio-Oss® + growth factors (BMPs)
In animal studies, Bio-Oss® was compared with a variety of other materials used as carriers for genetically engineered growth factors. The natural surface structure of Bio-Oss® produced advantageous results in terms of bone regeneration and apposition. Bio-Oss® was assessed as a suitable carrier for growth factors on the basis of various studies.

Bio-Oss® + PRP
Today, patient-endogenous platelet-rich plasma (PRP) is being discussed as a new way of optimising bone regeneration with substitute materials. Because PRP can only exert an effect on bone cells that have already undergone differentiation, bone cells, in the form of autogenous bone chips, must always be added.

The early results of extensive studies show that Bio-Oss®, in combination with bone chips, is a suitable carrier for PRP.

BMP-guided bone healing
Healing of a bony defect after application of BMP to a carrier in granule form (light yellow particles). BMPs are delivered by the carrier and stimulate mesenchymal stem cells in the soft tissue and medullary cavity. The stem cells divide and become differentiated. As the carrier is osteoconductive, the osteoprogenitor cells settle on it, become differentiated into osteoblasts and form bone there.

Even though PRP has already been used in combination with bone substitute materials in patients on a number of occasions, many questions about the harvesting methods and the clinical benefits of PRP remain unanswered.

Scientific references for Bio-Oss® as a carrier for growth factors:

- Boyne et al. (Int J Periodontics Restorative Dent 2001)
- Stephan et al. (J Periodontol 2000)
- Acl et al. (J Biomed Mater Res 2000)
- Terheyden et al. (Int J Maxillofac Surg 1999)
- Jiang et al. (J Clin Periodontol 1999)
- Terheyden et al. (Clin Oral Impl Res 1999)
- Terheyden, et al. (Mund Kiefer Gesichts Chir 1997)
- Sigurdsson et al. (Int J Periodont Rest Dent 1996)
Bio-Oss® owes its unique properties to its natural source. The mineral structure of Bio-Oss® comes from carefully selected bone of bovine origin. Strict controls ensure a high standard of quality and safety.

The high safety standard is achieved by:

**The controlled production process**

The mineral structure of Bio-Oss® is produced through a combination of chemical processes and heat treatment. Amongst other processes, the bone material is subjected to treatment at a high temperature for over 15 hours and to several hours of strong alkali treatment. This gives rise to a highly cleaned mineral bone structure.

**The choice of raw material**

The raw material used for Bio-Oss® is derived from bone harvested from bovine extremities. Unlike the brain, gut or spinal cord, these bones are classified as a safe tissue by experts, because no prions have been found in them. The raw material comes from three officially controlled abattoirs in the USA. The animals have to be pronounced healthy by veterinary inspectors.

**Official controls**

Bio-Oss® meets in full the strict official safety requirements that apply to medical devices* and is subject to a quality assurance system that complies with international standards (ISO 9001/EN 46001). This is regularly checked by recognised auditing institutes and international authorities. Bio-Oss® is CE-certified and is approved as a medical device by the US health authority, the FDA.

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* Wenz B, Oesch G, Horst M
Analysis of the Risk of Transmitting Bovine Spongiform Encephalopathy through Bone Grafts derived from Bovine Bone, Biomaterials 2001; 22; 1599-1606.
**Product line**

**GBR-System**
System for natural bone regeneration

Bio-Oss® Spongiosa 0.25–1 mm
- 0.25g, 0.5g and 2.0g vials
- Treatment of small defects
- For contouring, to aid autogenous block grafts

Bio-Oss® Spongiosa 1–2 mm
- 0.5g and 2.0g vials
- Augmentation of defects involving 2 or more sockets
- Sinus floor augmentations
- For mixing with autogenous bone chips

Bio-Gide®
- GBR in the presence of minor defects

Bio-Gide® 30 x 40 mm
- GBR in the presence of major defects
- Use of the double-layer technique

Resor-Pin®
- Resorbable pin
  - 5x2 pins
  - Fixing of resorbable membranes

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**CE**
Bio-Oss®, Bio-Gide® and Resor-Pin® have been approved for use in Europe (CE certified) and in the USA (FDA).