OSTEOXENON® by BIOACTIVA®

OX® Bone Substitutes

Surgical procedures

Index

1. Notes on this guide

This guide has been created to describe the main features and indications of the **OX** bone grafts. It describes also the guidelines for the use of the several **OX** codes.

When application modalities are described, literature-based application techniques are given first. When a reference is not available, the technique described has been accepted through a “consensus” of selected users.

Application modalities described in this guide are the ones, therefore, that – according to the experience of the current users of the **OX** medical devices – give the best predictability. These are the techniques a selected panel of oral surgeons gave their consensus about.

Even if *other* application techniques are possible, beyond the ones described in this present guide, the manufacturer willingly excluded them from this document, believing that they are still not sufficiently predictable given the current level of evidence.

For this reason this guide will undergo periodical revision, in order to describe possible new techniques (or variations of the current ones) when evidence will be collected about their predictability.

2. General notes on bone regeneration

Even if this guide is not aimed to give medical indications the surgeon should already be aware of, we deem useful **reminding the main contraindications to bone regeneration surgery**.

Bone regeneration surgery for patients showing one or more of the following conditions is to be considered at risk, or totally contraindicated.

- **Patients irradiated in the head and neck area**
- **Immunosuppressed or immunocompromised patients**
- **Patients who took or are taking amino-bisphosphonates intravenously**
- **Patients with active periodontitis poor oral hygiene and motivation**
- **Uncontrolled diabetes**
- **Pregnancy or lactation**
- **Addiction to alcohol or drugs**
- **Psychiatric problems**
- **Acute or chronic infection in the area intended for augmentation/implant placement**
- **Smokers (> 10 cigs/day)**

3. Practical hints

Preparing the grafts:

A - Hydrating solution

There are cases in which the graft should be not hydrated (see next chapters). When hydration is needed, perform it with sterile physiologic solution, at room temperature, for 1-2 minutes.

B - Adding autologous bone to granular grafts

There's no direct evidence, in literature, about the real benefit of adding autologous bone to granular grafts. Nonetheless, clinical and histological data coming from the current users of the **OX** (granular) substitutes suggest a positive effect on the final result of the bone regeneration. Therefore, we suggest adding autologous bone – when possible – from 30 to 50% (in volume) to the mixture.

C - Adding anti-inflammatory drugs to the hydrating solution

Anti-inflammatory drugs must never be added to the hydrating solution. They would stop the first regeneration steps, leading surgery to a failure (there's no contraindication, instead, in administering such kind of drugs systemically).

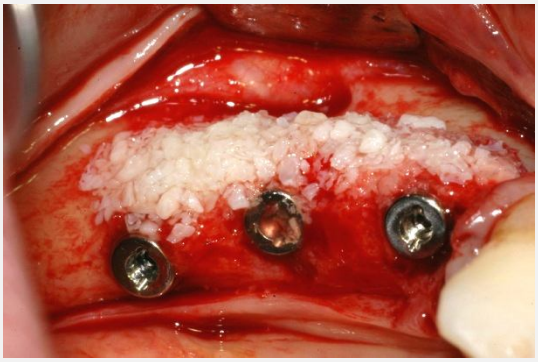
D - Preparing the receiving site

The grafting site must be carefully prepared. All fibrous tissue must be eliminated. The cortical wall must be perforated with a blur, or abraded with a bone scraper, in order to prompt blood supply and initial angiogenesis.

E - Adapting the graft to the receiving site

The adhesion of the onlay graft to the bone surface must be the best possible one. If gaps are present they won't be trespassed by blood vessels: angiogenesis won't occur and cells won't be able to reach the grafted site. If angiogenesis doesn't occur the graft will be enveloped by fibrous tissue, and no regeneration will be observed.

Example: good and failed blood imbibition

	After positioning the granules, blood permeates them completely.
	Blood doesn't fill the spaces between the granules: probably regeneration will fail. Courtesy Dr. Danilo Di Stefano

F - Graft stability

All grafts, either granules or blocks, must be stable and still. Every micro-movement can hinder the formation of the new vessels network, leading regeneration to a failure.

4. Probable causes of failure

Which causes?

Even when using the best bone substitutes, and even if contraindications are not present, failure can occur. What are the possible causes?

1 - Possible presence of residual antigens in the graft

This possibility must be **completely excluded**. The great number of tests that are periodically performed on the product show it is perfectly clean.

OX bone substitutes, during years of usage (the Orthopedic format has been used since 1995) never showed **any foreign body or inflammatory reaction**.

The most common failure causes are different:

2 - Failure when using granules

The most common causes of failure when using granules are:

a) Granules are not stable. If granules are not stable, they are enveloped by fibrous tissue.

b) Granules are too pressed. If granules are too pressed, angiogenesis is hindered. The graft doesn't osseo integrate. On re-opening different situations can be observed: a) the graft is there, unchanged or b) the graft is enveloped by fibrous tissue or c) the graft has been absorbed and a curdy, whitish substance is present. **The patient doesn't show any symptom.**

c) In sinus lifts: the nasal wall is not exposed because the Schneider membrane has not been detached correctly. In this case, a bone wall is missing. That means the granules won't be stable and, mainly, that angiogenesis won't be optimal. Blood vessels can develop only from the remaining walls that are atrophic.

3 - Failures when grafting blocks

The most common causes of failure with blocks are:

a) Unstable fixation. If blocks are not fixed properly, they will be enveloped by fibrous tissue. Using a single fixation device (one screw, for example) is at risk.

b) Bad contact with the receiving bone surface. If the contact between the receiving bone surface and the block is not precise, the zones where there's no contact won't be vascularized. Possibly part of the block or all the block, won't integrate. At re-opening the block will be found unchanged.

c) Unproper receiving sites, or sites that are not correctly prepared. Unfortunately, biology can not be changed by surgery. If the receiving atrophic bone shows **a) a too great atrophy degree** or **b) a very poor vascular condition, then all the grafts positioned over it won't regenerate into bone due to a lack in**

vascularization. On second surgery, the block will be found unchanged. The same negative result will be observed if the receiving site has been prepared unproperly. **If the site is not bleeding, or if the graft is not filled with the blood coming from the receving surface, the regeneration will probably fail.**

d) Positioning blocks with fantasy. Block positioning must follow the protocol given by the manufacturer (see proper chapter). **Any action, different than the ones described, even if it is done in order to improve the outcome of regeneration adds an uncontrolled variable to the procedure, increasing the risk of failure.** For example, the following actions must not be done, since their benefit has not been demonstrated: adding antibiotics, adding blood derivatives such as PRP, PRGF etc.

4 - Failure with other graft formats

The main failure causes are the same previously described.

5 - Bad flap management

If flaps are not managed properly, every bone regeneration surgery will be a failure. **Perform a bone regeneration surgery only when you are certain you will be able to manage the flaps properly.**

5. OX bone substitutes, features and indications

OX® Bone granules

OX30: Cancellous granules, 0.5 – 1 mm, 0.5 g ≅ 1 cc.
OX31: Cortical-cancellous granules (MIX), 0.5 – 1 mm, 0.5 g ≅ 1 cc.
OX32: Cortical-cancellous granules (MIX), 0.5 – 1 mm, 1 g ≅ 2 cc.
OX33: Cancellous granules, 2-3 mm, 1 g ≅ 2 cc.
OX34: Cancellous granules, 2-4 mm, 1 g ≅ 2 cc.

Type:	**OX bone granules**
Features:	Cortical-cancellous or cancellous-only natural granular bone grafts, enzyme-deantigenated, showing bone collagen preserved and different granule sizes.
Use:	1. Collect some autologous bone, if possible (blur, scraper) and put it in a sterile container 2. Open the bottle 3. Drop the bottle content into the sterile container 4. Hydrate with sterile physiological solution for 1-2 minutes 5. Graft the mixture 6. Protect the grafted site with a proper membrane
General hints and precautions:	**Grafting the granules:** Place the granules in the grafting site in order to make them stable and still. Avoid excessive compression. Too much compression can make the space between adjacent granules decrease to such a point that angiogenesis is hindered.
OX30: Cancellous granules, 0.5 – 1 mm, 0.5 g ≅ 1 cc.	They are indicated for small reconstructions, in 4-walls cavities, or where they can be stabilized with membranes or other, in order to avoid their dispersion and movement. Their remodeling time (complete substitution with new formed bone) is around 4-6 months. **Indications:** **1. Peri-implant defects (up to three threads exposed):** Hydrate the granules as described above ("Use") and place them around the exposed threads. Protect the graft with:

	a) A **XC30** membrane, if 3 or less threads are exposed b) A Heart **HRT-001** pericardium membrane if more than 3 threads are exposed **They can be used also for:** - Periodontal defect (every type of) - Post-extractive sockets - Sinus lift (traditional Misch approach) - Sinus lift (Misch approach, Tulasne variation) - Sinus lift (crestal approach, Summers)
OX31: Cortical-cancellous granules (MIX), 0.5 – 1 mm, 0.5 g ≅ 1 cc. **OX32**: Cortical-cancellous granules (MIX), 0.5 – 1 mm, 1 g ≅ 2 cc.	They are indicated for medium-size reconstruction, in 4-3 walls cavities. The cancellous components remodels in 4-6 months, the cortical one in 8-12 months (the remodeling time is approximate since, as a cell-mediated remodeling process occurs, the total substitution time depends on the beginning anatomical condition: the ratio between the receiving vital bone surface and the grafted volume). The cortical component needs more time to be remodeled given its greater density. Remodeling, anyway, is total (the bone substitute will be replaced with new formed bone). **Indications:** 1. **Intact post-extractive sockets, in order to preserve the vestibular wall, anticipating an implant placement** Hydrate the granules as described in the "Use" paragraph. Place them in the post-extractive socket after cleaning and preparing it. Detach slightly the flap around the socket and place a pericardium Heart, **HRT-001** membrane, after shaping it. The edges of the membrane must be inserted below the edges of the flap. Suture with a cross stitch. **2. Sinus lift (traditional Misch approach, or Misch approach and Tulasne variation)** Prepare the cavity according to the technique described by Misch. Prepare the granular mixture as described in the "Use" paragraph, and proceed to graft the mixture as already described. Even if there's no total agreement in literature about the use of a collagen membrane, we advise for the covering of the access window with a **XC30**, collagen membrane. For the variation according Tulasne, see the paragraph regarding the **OX02** cortical sheet. 3. **Filling the ridge after a "split crest"** Perform the crest splitting according to the preferred surgical approach; place the implants or use bone distracters to increase the gap width. Prepare the granular mixture as described in the "Use" paragraph, and proceed to graft the mixture as already described. Protect the graft with a Heart, **HRT-001**

pericardium membrane is preferred.

4. **Vertical ridge augmentation, Ludovichetti technique with a Cortical Flex Sheet**
See the paragraph regarding the **OX02** cortical sheet.

5. **As a filler for the remaining gaps between adjacent blocks after an onlay graft**
Prepare the granular mixture as described in the "Use" paragraph, and proceed to graft the mixture as already described (protect the graft with a Heart Pericardium membrane, **HRT-001** or **HRT-002**).

They can be used also for:

- Periodontal defects (every type of)
- Peri-implant defects
- Sinus lift, crestal approach according to Summers

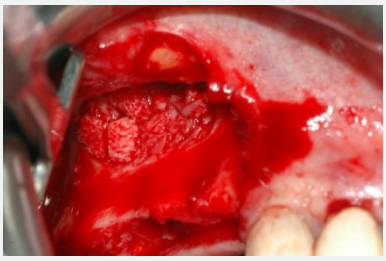
OX33:
Cancellous granules, 2-3 mm, 1 g ≅ 2 cc.
OX34:
Cancellous granules, 2-4 mm, 1 g ≅ 2 cc.

They are indicated specifically for the **sinus lift performed through the lateral approach (Misch)**: the greater granule size allows for a faster filling, prevents excessive compression (if compression is excessive vessels could not invade the graft), and allows for a better stabilization of the granules (which will be less subjected to the mechanical stimulation due to the sinus membrane movements).

Indications:
1. **Sinus lift, lateral approach (Misch technique, possible Tulasne variation)**
Prepare the sinus cavity as described by Misch. Prepare the granular mixture as described in the "Use" paragraph, and proceed to graft the mixture as already described. Even if there's no total agreement in literature about the use of a collagen membrane, we advise for the covering of the access window with a **XC30**, collagen membrane. For the variation according Tulasne, see the paragraph regarding the **OX02** cortical sheet.

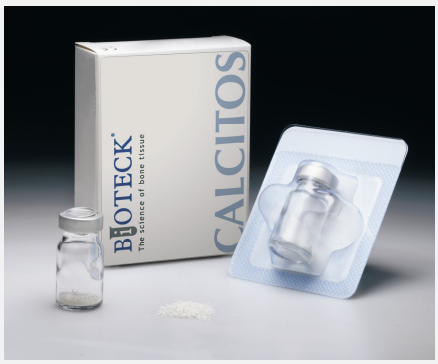
Example: using OX34 granules to perform a sinus lift.


OX34 cancellous granules are mixed with autologous bone


The mixture is grafted in the sinus cavity


The access window is protected with a **XC30** collagen membrane

Courtesy
Dr. Danilo Di Stefano



Calcitos **Bone granules**

OMC-030: Cortical granules, 0.5 – 1 mm, 0.5 g ≅ 1 cc.

Type:	**"Calcitos" bone granules**
Features:	Natural bone granules, without bone collagen and slowly resorbable, since thermally-treated, indicated for preserving volume in esthetic reconstructions and to stabilize cancellous, autologous grafts.
Use:	1. Open the bottle 2. Drop the content of the bottle in a sterile container 3. Hydrate with physiologic solution for 1-2 minutes 4. Graft the mixture 5. Protect the grafted site with a proper membrane
General hints and precautions:	The same as previously said. The aim in using these granules is to create a bone volume containing both regenerated bone and osseointegrated biomaterial granules that are going to preserve the grafted volume.
OMC-030 Cortical granules, 0.5 – 1 mm, 0.5 g ≅ 1 cc.	**Indications:** 1. **Reconstructing bone volumes for esthetic purposes** Prepare the bone granules as described in the "Use" section. Protect the graft with a proper membrane.

OX® Mix gel

OX21 - Gel, cancellous-cortical bone granules - 2 syr. / 0.25 ml.
OX22 - Gel, cancellous-cortical bone granules - 2 syr. / 0.5 ml.
OX23 - Gel, cancellous-cortical bone granules - 1 syr. / 1.0 ml.

Note: size granules is 0.5-1 mm for all codes

Type:	**Gel bone granules**
Features:	Natural cancellous and cortical bone granules, enzyme-deantigenated, with preserved bone collagen, (as **OX31** e **OX32**) **already mixed with a water-based gel.**
Use:	1. Open the blister and the syringe cap 2. Extrude the needed quantity in the grafting site 3. Model the graft, if necessary, without applying excessive pressure 4. Protect the grafted site with a proper membrane
General hints and precautions:	The graft is ready to use. The syringe, once open, cannot be used again.
OX21 Gel, cancellous-cortical bone granules 2 syr. / 0.25 ml. **OX22** Gel, cancellous-cortical bone granules 2 syr. / 0.5 ml. **OX23** Gel, cancellous-cortical bone granules 1 syr. / 1.0 ml.	This syringe formulation (whose bone component corresponds to **OX31** or **OX32**) features some operative advantages: being a ready- to-use mixture, all the steps that are needed to prepare standard granules can be avoided (hydration, mixing, bringing the material from the container to the grafting site). The bone substitute, in fact, can be extruded directly from the syringe into the grafting site. Indications are the same as for the granules. Moreover, grafting periodontal defects becomes easier, since granules can be extruded directly into the defect. **Indications:** 1. **Regenerating periodontal defects** After preparing the grafting site, extrude directly the granules from the syringe into the defect, filling it. Model with a sterile instrument if necessary. For intrabony defects (1 to 3 walls) or furcation defects, protect the site with a pericardium Heart membrane**HRT-001** shaping it properly. For smaller defects, where placing a shaped membrane is difficult protect the graft with **OX** Collagen Gel (**OX06** or **OX07**).

2. **Sinus lift (Summers technique)**
After preparing the access to the sinus through the crestal approach, according to Summers, extrude directly the bone substitutes into to access tunnel from the syringe and proceed to introduce it in the prepared volume according to the Summers procedure.

- **They can be used also for:**
  - Regenerating intact post-extractive sockets in order to preserve the vestibular wall, anticipating implant placement
  - Sinus lift (Misch technique, also Tulasne variation)
  - Filling the space created during a split crest surgery
  - Vertical ridge augmentation, Ludovichetti technique with **OX** Cortical Flex
  - Filling gaps remaining after onlay grafts

Example: using OX21 (OX Mix Gel) together with OX06 (OX Collagen Gel) to fill periodontal defects.

	Opening the flap. Intrasulcular incision, preserving the papillae.
	Receiving bone is prepared, defects are filled with **OX** Mix Gel.
	The graft is stabilized and covered with **OX** Collagen Gel.
	Suture. Courtesy Dr. Maurizio Ludovichetti

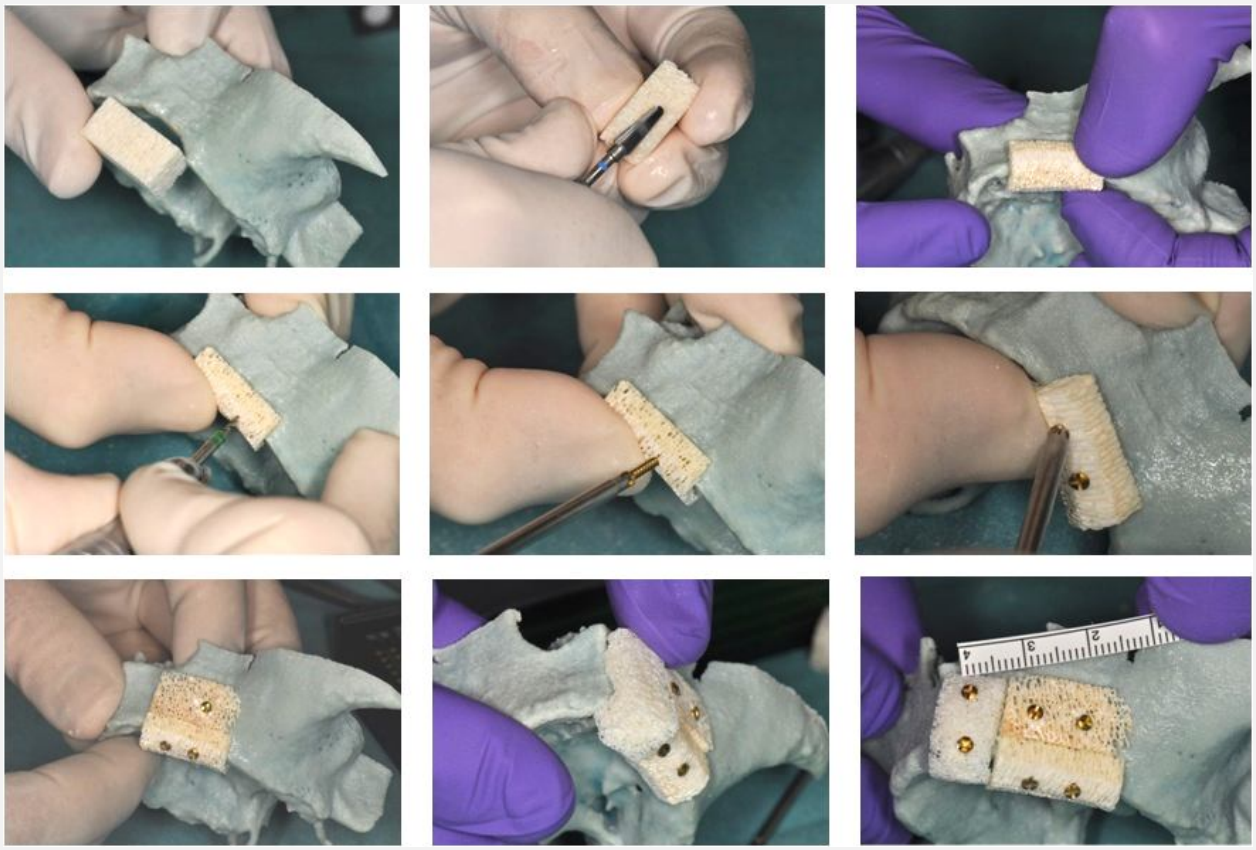
OX® Cancellous Blocks

OX51 - Cancellous block - 1 pc. 10 x 10 x 10 mm.
OX52 - Cancellous block - 1 pc. 10 x 10 x 20 mm.
OX54 - Cancellous block - 2 pc. 10 x 20 x 3 mm.
OX55 - Cancellous block - 2 pc. 10 x 20 x 5 mm.

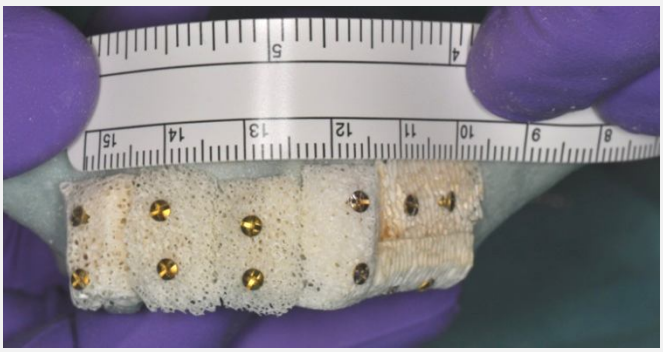
Type:	**Cancellous blocks**
Features:	Natural, enzyme-deantigenated, bone collagen preserved, rigid blocks
Use:	**A) Intraoperative shaping and graft** After exposing and preparing the grafting site: 1. Open the blister 2. With a rotating instrument (tungsten carbide), shape the block (without hydrating it), with short and fast movements (to avoid over-heating) 3. Prepare the seats for placing the fixation screws, by drilling proper holes through the block. The drill must be larger than the diameter of the screw body. After that, place the block over the grafting site, and prepare the screw(s) seat(s) into the receiving bone by drilling through the holes already prepared into the block 4. Hydrate the block for 1-2 minutes with sterile physiologic solution 5. Place the block and fix it with the screws 6. Fill the gaps, if any, with **OX31** granules or similar 7. Protect the grafted site with a Heart, **HRT-001** pericardium membrane 8. Release the flap properly and suture **B) Extraoperative shaping and graft** 1. Purchase a stereolitographic model of the arch where the defect is located 2. Adapt the bone block to the defect, **working on the model,** with rotating instruments, without hydrating it, with short and fast movements 3. Always **working on the model** prepare the seats for placing the fixation fixation screws, by drilling proper holes through the block 4. Send back the shaped, drilled block, to the manufacturing company. The company will clean and sterilize the block, that will be sent back to you, in a double sterile blister, ready to be grafted on the day of surgery 5. On the day of surgery, after preparing the grafting site and opening the

	blisters, proceed as in point 3-8 of procedure A)
General hints and precautions:	The use of bone blocks should be reserved to surgeons that are already used to place autologous bone blocks, or surgeons that have the possibility of learning the technique from a more experienced surgeon. Please remind that one of the most difficult steps in this kind of surgery is the correct flap management. **OX** bone blocks are indicated for vertical or vertical/horizontal augmentation in the upper jaw only. At the current time there's no sufficient evidence for its effectiveness in the posterior lower jaw, expecially for vertical augmentations. Please remind that vertical or horizontal augmentation greater than 5 mm show a greater risk of failure: in this case the non-regenerated portion of the block can expose.
OX51 Cancellous block 1 pc. 10 x 10 x 10 mm. **OX52** Cancellous block 1 pc. 10 x 10 x 20 mm. **OX54** Cancellous block 2 pc. 10 x 20 x 3 mm. **OX55** Cancellous block 2 pc. 10 x 20 x 5 mm.	The main feature of this block is that, since they show bone collagen preserved, they feature the same mechanical resistance to compression and elastic deformation of natural bone (superficial compression resistance is at least 300 kg/cm^2). This means that these blocks can be shaped and drilled with rotating instruments, or fixed with screws or implants, without breaking (if thickness is not less than 3 mm). **Indications:** 1. Horizontal or horizontal and vertical onlay grafts on the upper jaw 2. Inlay grafts

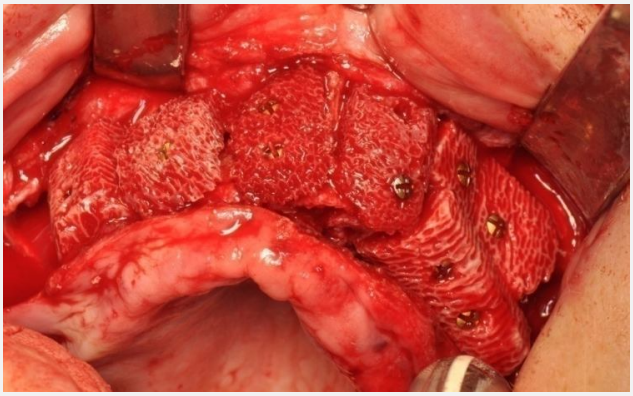
Example: OX52 blocks (OX Cancellous Block) are applied to perform an onlay augmentation for a wide atrophy of the maxilla. Blocks are shaped over a stereolitographic model.



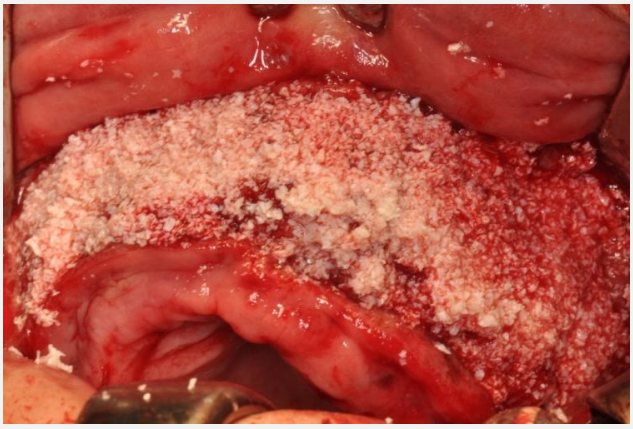
OX52 are shaped over a stereolitographic model: the regeneration is totally planned on the model some days before surgery



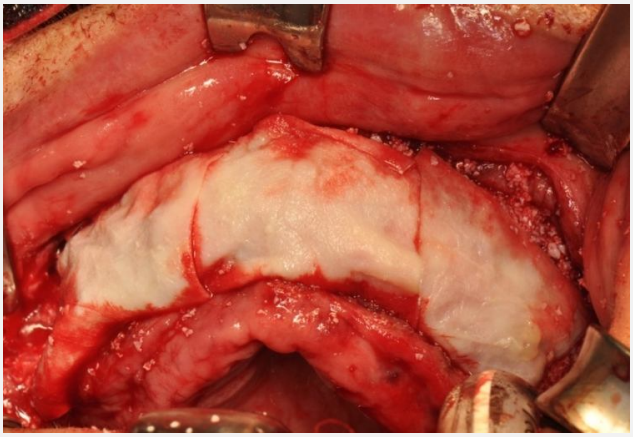
The reconstruction is complete. The blocks are removed from the model and sent back to the manufacturing company for cleaning and sterilization. They will be ready, packed into a sterile double blister, on the day of surgery .



During surgery blocks are placed according to what had been planned on the stereolitographic model. Note that block edges have been beveled in order to avoid interferences with the soft tissues .



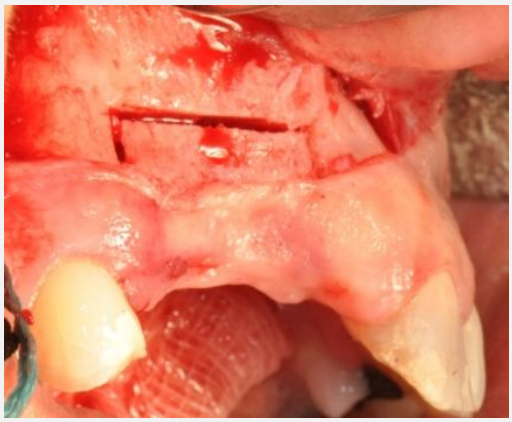
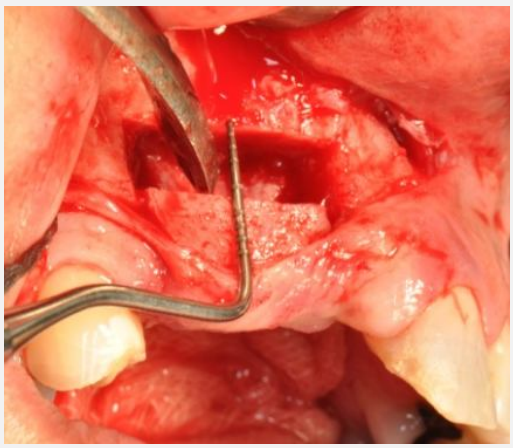
All the block reconstruction is covered with granules.

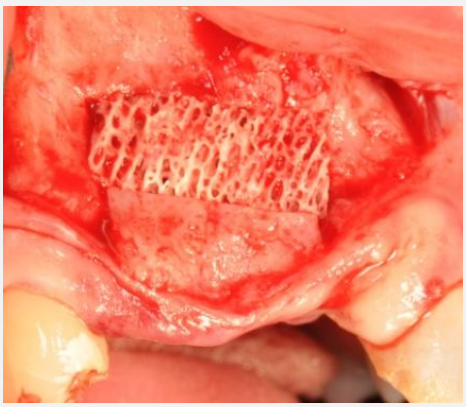
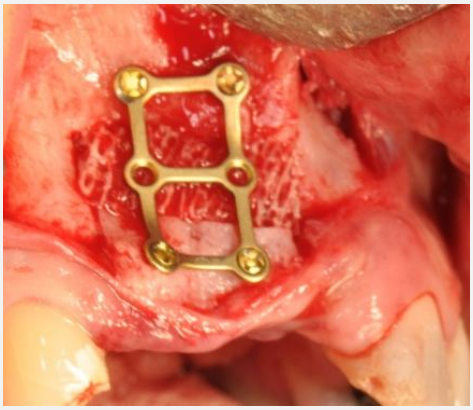
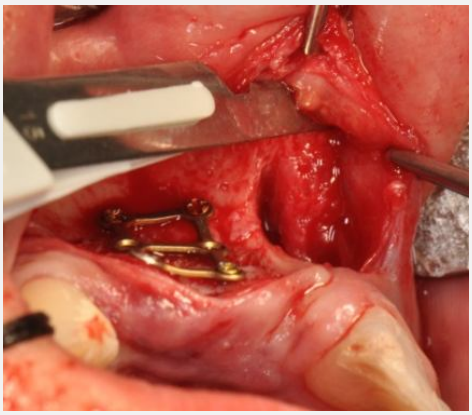
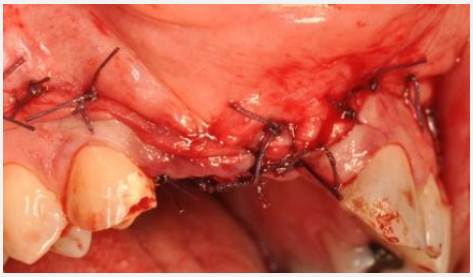


And protected with some resorbable membranes.

Courtesy Dr. Roberto Pistilli

Example: Using OX52 (OX Blocco Spongiosa) (OX Cancellous Block) is applied to perform an inlay graft in the upper jaw.

	The ridge is cut on the vestibular side with a piezo osteotomy insert.
	Incision is complete.
	Bone is distracted, preparing it to receive the inlay graft.

	**OX52** bone block is grafted as an inlay.
	The block and the distracted bone portion are stabilized with a proper plaque.
	The flap is released properly.
	Suture. Courtesy Dr. Roberto Pistilli

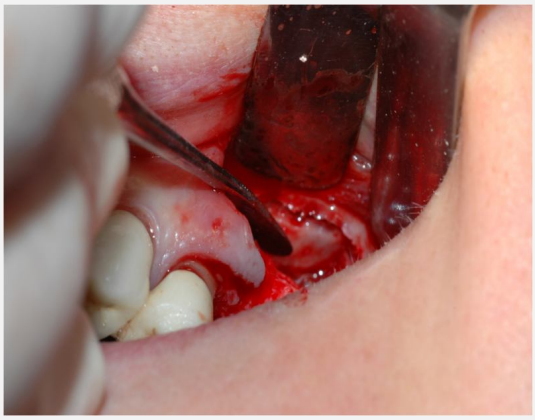
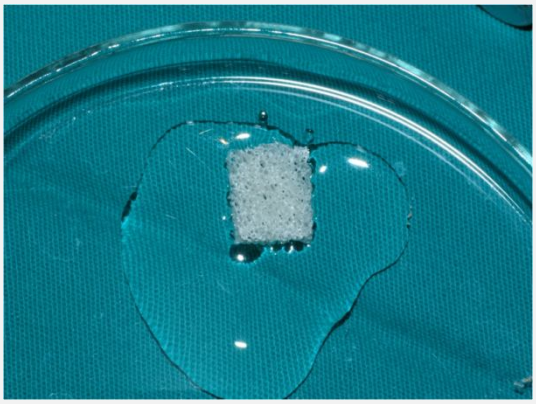
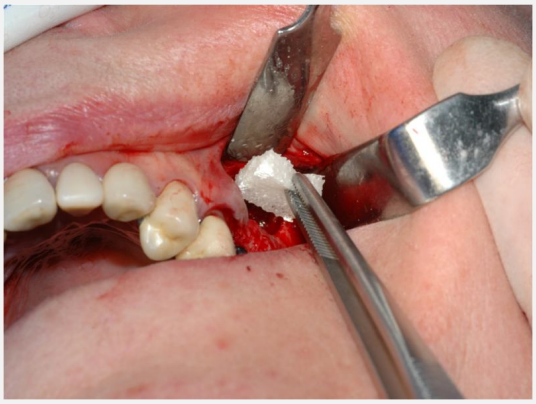
OX® Flex cancellous bone sheet

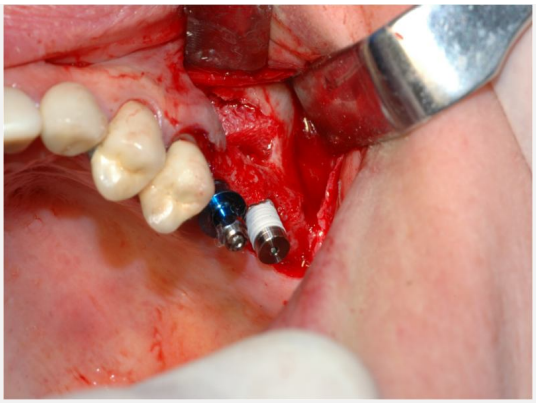
OX01 - Cancellous sheet - 1 pc. 25 x 25 x 3 mm.

Type:	**Flexible spony sheet.**
Features:	Natural bone collagen-preserved, enzyme-deantigenated, cancellous bone. It is partially demineralized to make it flexible.
Use:	**a) For horizontal onlay grafts** After exposing and preparing the grafting site: 1. Open the blister 2. Shape the graft without hydrating it (sterile scissors are sufficient) 3. Prepare the seats for placing the fixation screw(s) (drill the proper hole(s) through the graft, then drill the corresponding hole(s) in the receiving bone either through the graft or using a sterile template) 4. Hydrate the sheet for 1-2 minutes with sterile physiologic solution 5. (Optional). Spread an osteopromoter, like **OX11** (Angiostad) as a thin layer *either* on the receiving bone *or* on the side of the sheet that will be in contact with the receiving bone 6. Place the graft and fix it with the screw(s) 7. Protect the grafted site with a Heart pericardium membrane **HRT-001** 8. Release the flap properly and suture **b) To protect the Schneider membrane when performing a sinus lift, also as membrane tearing management** 1. Perform the sinus lift procedure, according to Misch, up to detaching completely the sinus membrane 2. Open the blister 3. Shape the graft without hydrating it (sterile scissors are sufficient) 4. Hydrate the sheet for 1-2 minutes with sterile physiologic solution 5. Place the graft under the Schneider membrane, inserting it through the window, keeping it bent with sterile pliers. When released in the cavity, the sheet will recover its original shape and will lift the membrane, protecting it 6. Graft the remaining volume with the desired bone substitute (for example,

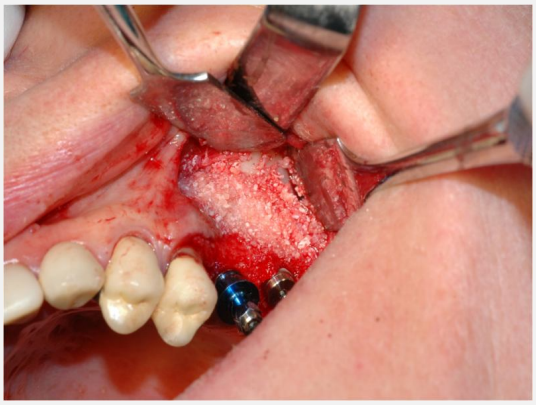
	granular grafts as **OX34/33** or **OX31/32**) 7. Cover the window with a **XC30** collagen membrane
General hints and precautions:	All the **OX** bone substitutes feature bone collagen preserved. This allows making them flexible by demineralizing them partially: since collagen is preserved, the mechanical resistance of the sheet decreases but it doesn't break. The advantage in using flexible grafts is that they adapt perfectly to curve profiles, and there's no need of shaping them (the only needed operation is cutting them to give them the proper size for being grafted). Precautions and suggestions for onlay grafts: **1. Application field** The flexible cancellous sheets have to be used for lateral onlay augmentations, when **implant placement will be performed in two steps**. Given the peculiar morphology of cancellous bone, in fact, these sheets will be colonized immediately by cells and vessels also in their inner parts. The substitution of the graft with new formed bone, therefore, will proceed both from the outer to the inner part, and from the inner to the outer part. The speed of the process is such that the time for a sufficient formation of new formed bone is quite predictable (from 6 to 8 months). It is therefore possible to plan properly the implant placement surgery. For these applications, preparing properly the receiving site is mandatory (see chapter 3 and the notes for the grafts with blocks). **2. Protection and stability of the graft** The perfect fixation of the flexible graft is mandatory in onlay augmentations. Be sure of having stabilized perfectly the sheet. A long lasting membrane is necessary too (such as the pericardium membrane Heart **HRT-001**). Shorter lasting membranes won't protect the graft for a sufficient time duration, leading to a partial, or even total, failure. Correct flap management is, as in all augmentation cases, a must.
OX01 Cancellous sheet 1 pc. 25 x 25 x 3 mm.	**Indications:** 1. Horizontal onlay grafts on the upper or lower jaw 2. Sinus lift, grafted to protect the Schneider membrane

Example: using OX01 (OX Flexible Cancellous Sheet) during a sinus lift, to protect the Schneider membrane.

	Lifting the bone window and the Schneider membrane.
	A piece of **OX01** has been cut, and is being hydrated with physiologic solution.
	The cancellous flexible sheet is placed below the sinus membrane.



The sheet protects the sinus membrane from the following operations (graft of granules or implant placement.



The remaining volume is filled with **OX31** granules.

A **XC30** collagen membrane is placed to cover the access window after hydrating it .

Courtesy Dr. Maurizio Ludovichetti.

OX® Flex Cortical Sheet

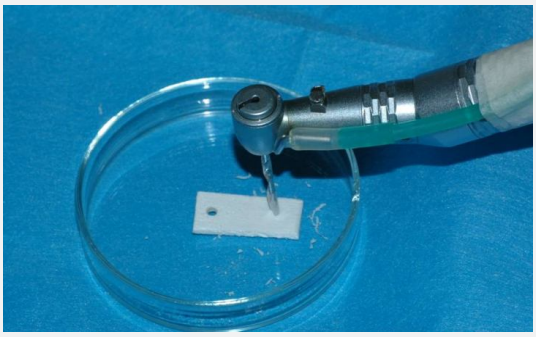
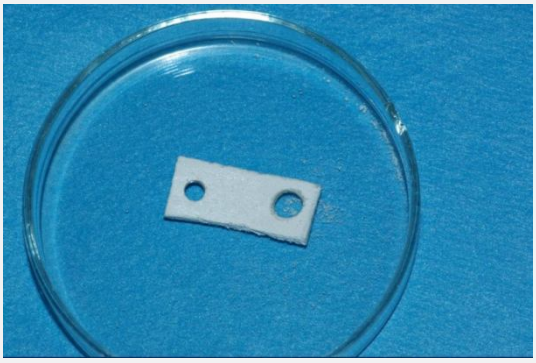
OX02 - Cortical sheet - 1 pc. 25 x 25 x 2-2.5 mm.

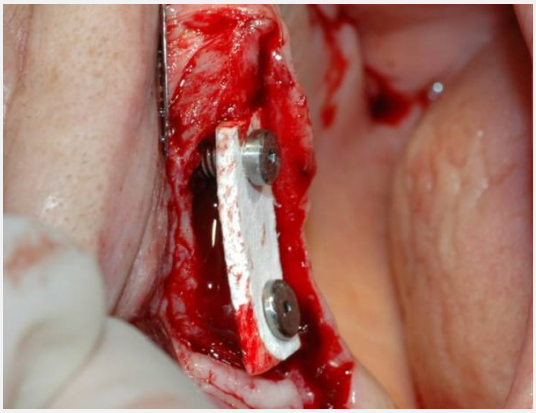
Type:	**Flexible cortical sheet**
Features:	Natural bone collagen-preserved, enzyme-deantigenated, cortical bone. It is partially demineralized to make it flexible.
Use:	**a) For vertical augmentation and contemporary implant placement** After exposing and preparing the grafting site: 1. Prepare the implant seats 2. Open the blister 3. Shape the graft without hydrating it (sterile scissors are sufficient) 4. With a sterile template, replicate the position of the implants over cortical sheet 5. Drill the graft, preparing the seats for the implants 6. Position the graft, by placing the implant(s) through the sheet into the receiving bone 7. Block the graft with the implant cover screws (the diameter of the cover screw should be greater than the one for that implant, e.g. use a 4 mm cover screw if you placed a 3 mm implant) 8. Graft the volume below the sheet with, for example, granules (like **OX31/32**) mixed, if desired, with **OX11** (Angiostad) and **OX14** (Activagen) osteopromoters 9. Eliminate the sharp edges of the graft with a rotating blur 10. Protect the site with a long lasting membrane (for example: Heart pericardium membrane, **HRT-001**) **b) To protect the Schneider membrane during a sinus lift (modified Tulasne technique)** 1. Perform the sinus lift procedure, according to Misch, up to detaching completely the sinus membranes

	2. Prepare, on the two upper sides of the access window, two slots for the following sheet placement 3. Open the blister 4. Shape the graft without hydrating it (sterile scissors are sufficient); if necessary, adjust the shape by using a sterile template, inserting it between the slots in a trial and errors procedure 5. Place the sheet below the sinus membrane, making it slide into the two slots. The sheet must slide up to touch the nasal wall of the sinus. The sheet, being inserted in the two slots, and being in touch with the nasal wall, must be perfectly stable 6. Graft the remaining volume with the desired bone substitute (for example, granular grafts as **OX34/33** or **OX31/32**) 7. If needed, eliminate the protruding part of the sheet with a rotating instrument 8. Cover the window with a **XC30** collagen membrane
General hints and precautions:	Flexible cortical sheets, 2 mm. thick, are used mainly for vertical augmentations, when **implant placement is performed in one step**. Typically, these sheets are shaped and drilled when dry, and fixed with the implants themselves, in order to create a cortical wall, at the level of the ridge surrounding the vertical defect. The volume under the sheet is then grafted with granular substitutes, and all the reconstruction is covered with a long lasting membrane (like the pericardium ones). The remodeling process of these sheets goes from their outer to their inner parts only, since they are cortical – and therefore do not show internal spaces that can be filled by cells and vessels. The remodeling process occurs through a mechanism called *creeping substitution*: osteoclasts degrade a part of the cortical bone, and osteoblasts replace it with new formed bone, and so on. The process can be quite long, so the total remodeling time for these grafts is surely greater than one year. That's why they can be used only for one-step implant placement surgeries. As cancellous ones, also cortical sheets can be used during sinus lift procedures. They can be extremely useful if the membrane tears: after preparing the access window to the sinus, and detaching the membrane, two slots are prepared on the upper side of the window. The sheet will slide into the slots and will touch finally the sinus nasal wall. The final result is that the sinus membrane and the lower space are physically and mechanically isolated, and if membrane tears are present, surgery can be nonetheless carried on. This technique mimics the Tulasne technique, which was performed, though, with calvaria grafts, and is rarely applied nowadays, given its invasiveness.

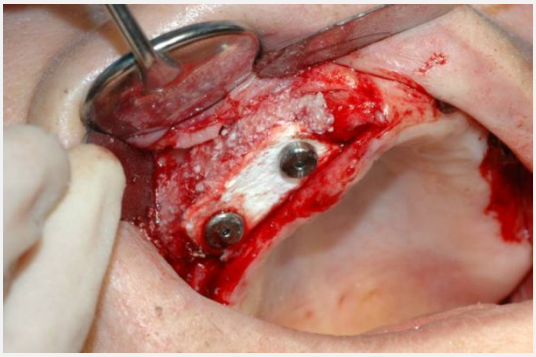
OX02 Cortical sheet 1 pc. 25 x 25 x 2 -2.5 mm.	**Indications:** 1. Vertical augmentation, on the upper or lower jaw, with contemporary implant placement 2. Sinus lift; protection of the Schneider membrane, mimicking the Tulasne technique

Example: using OX02 (OX Flexible Cortical Sheet) for a lower jaw vertical augmentation and contemporary implant placement.

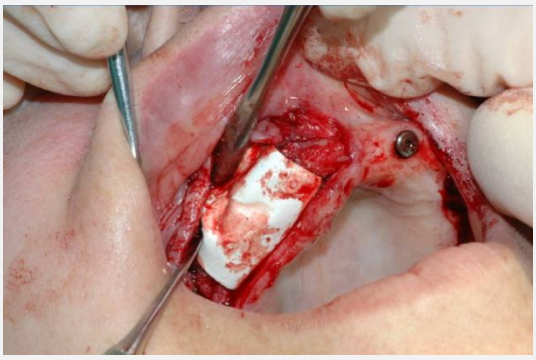
	The cortical sheet is drilled, still dry (the position of the holes was replicated with a sterile template, from the position of the implant seats on the receiving bone, already prepared).
	Two holes are prepared, corresponding to the size of the implants that are going to be placed.



The sheet is fixed with the implants (the first implant is positioned through the sheet and then on the receiving bone; then the second implant is placed).
The sheet is stable thanks to the use of two cover screws featuring a larger size than the implants diameter.



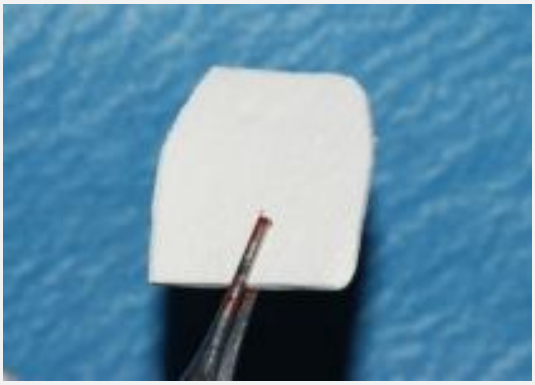
The space under the sheet is filled with a granular mixture (**OX31** and autologous bone collected with a scraper). Sharp edges are eliminated to avoid troubles with the soft tissues [not showed].



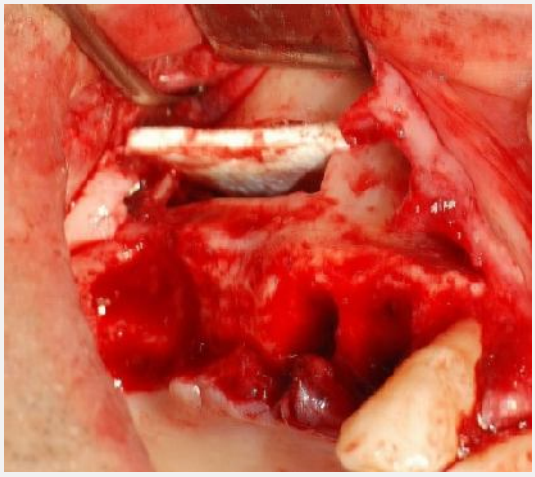
All the graft is covered with a Heart **HRT-002** pericardium membrane.

Courtesy Dr. Maurizio Ludovichetti.

Example: using OX02 (OX Flexible Cortical Sheet) to protect the Schneider membrane, during a sinus lift, mimicking the Tulasne technique.



The flexible cortical sheet is shaped, without hydrating it.



The sheet is positioned to protect the sinus membrane. The sheet is still dry. Note that **a) the width between the two slots' extremities is a little smaller than the sheet's width (to allow a better stabilization of the sheet itself and b) [not visible] that the sheet must be pushed in up to touching the nasal wall of the sinus**. The part that still protrudes out of the window will be eliminated with a rotating instrument. Filling of the remaining volume is performed as usual.

Courtesy Dr. Maurizio Ludovichetti.

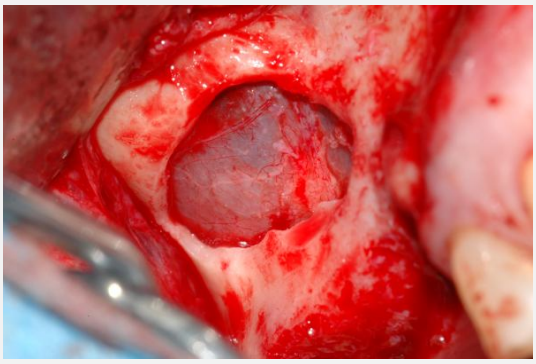
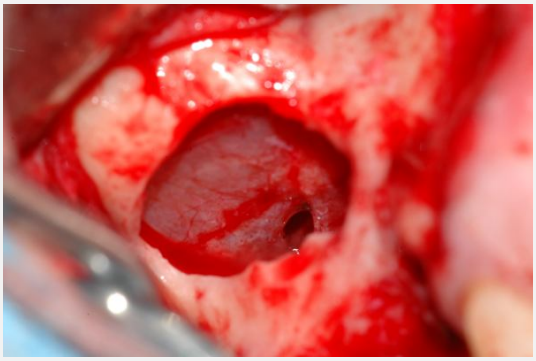
OX® Collagen membrane

XC30 – Collagen membrane - 1 pc. 30 x 25 x 0.2 mm.

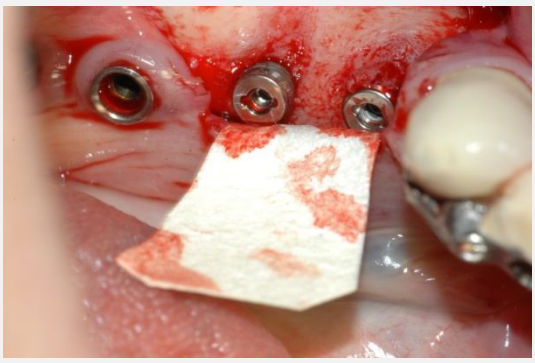
Type:	**Collagen membrane**
Features:	Resorbable membrane made of collagen from natural Achilles' tendon.
Use:	After performing the graft: 1. Open the bottle 2. Shape the membrane, if necessary, without hydrating it 3. Hydrate the membrane for 1-2 minutes with sterile physiologic solution 4. Cover the graft with the membrane
General hints and precautions:	The **protection time** of this kind of membrane is **4-6 weeks**. After this period its integrity is no more guaranteed, and connective tissue can invade the graft. For this reason, these membranes are indicated for very small grafted sites only. The collagen membrane needs no fixation. Since it is made of collagen, it adheres rapidly to sites where blood is present. The **XC30** collagen membrane can be used dry, to cover sites showing unusual bleeding, or where a stronger adhesion is desired. It can partially work as a haemostatic. When dry, the membrane can be placed under the flaps more easily. It can also work as a wall to keep granules in the proper position when they are placed into the grafting site.
XC30 Collagen membrane 1 pc. 30 x 25 x 0.2 mm.	**Indications:** 1. To protect small peri-implant grafted sites (less than 3 threads exposed) 2. To protect small periodontal grafted sites

	3. To protect the access window after performing a sinus lift according to Misch 4. To repair small sinus membrane tears (up to 2-3 mm), during sinus lift procedures

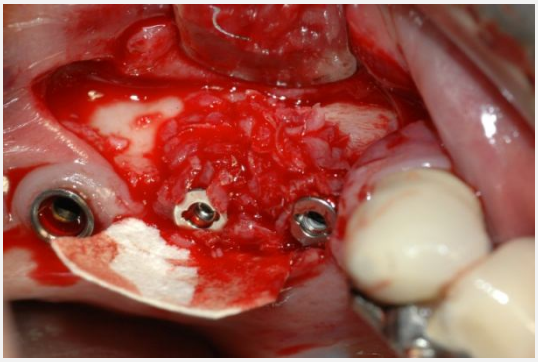
Example: using XC30 (OX collagen membrane) to repair a little tear of the Schneider membrane.

	The sinus membrane is detached during a sinus lift.
	The membrane shows a little tear.
	A collagen XC30 membrane is placed to repair the tear. Note that, in order to facilitate its adhesion, it is placed still dry. Courtesy Dr. Danilo Di Stefano.

Example: using a XC30 membrane (OX collagen membrane), still dry, as a wall to keep the granules in the right position.



The membrane, still dry and shaped, is placed under the flap.



The granules are placed exploiting the membrane as a wall.

Courtesy Dr. Danilo Di Stefano.

OX® Collagen gel

OX06 - Collagen gel - 2 syr. / 0.25 ml.
OX07 - Collagen gel - 2 syr. / 0.50 ml.

Type:	**Collagen gel**
Features:	Resorbable collagen gel, made of collagen from natural Achilles' tendon and water-based gel.
Use:	After performing the graft: 1. Open the syringe 2. Extrude the gel directly where desired 3. Model the gel with a sterile instrument
General hints and precautions:	For very small grafted sites, the classic collagen membrane can be replaced with a *collagen gel*, achieved by mixing the same collagen the membrane is made of (extracted from natural Achilles' tendon), as a powder, with a water based gel. This paste, when placed over granular grafts, in some cases, can act as a mechanical stabilizer of the granules and as a protecting film that works also as a membrane. Using this paste as an alternative to the membrane allows for a cleaner and faster surgery, since there's no need for preparation and time is not wasted in shaping a standard membrane (the paste is easily modeled). Even if the protection time of the gel can be compared to the one of the membrane (4-6 weeks), **this gel cannot be used as a collagen membrane in all cases, but only for very small grafted sites**. The product is ready to use. The syringe, once open, cannot be used again.

OX06 Collagen gel 2 syr. / 0.25 ml. **OX07** Collagen gel 2 syr. / 0.50 ml.	**Indications:** 1. To protect small peri-implant grafted sites (less than 3 threads exposed) 2. To protect small periodontal grafted sites

Example: using OX06 (OX Gel di Collagene) (OX Collagen Gel) to protect a periodontal defect grafted with OX21 (OX Mix Gel).

	The two products: OX Mix Gel (**OX21**, top) and OX Collagen Gel (**OX06**) bottom. Usually the two products are extruded directly from the syringe into the grafting site (this picture is showed for sake of explanation).
	Periodontal defects.
	Filling one of the defects with OX Mix Gel (**OX21**).

The graft is covered with **OX** Collagen Gel (**OX06**). Suture will be then performed following standard procedures.

Courtesy Dr. Maurizio Ludovichetti.

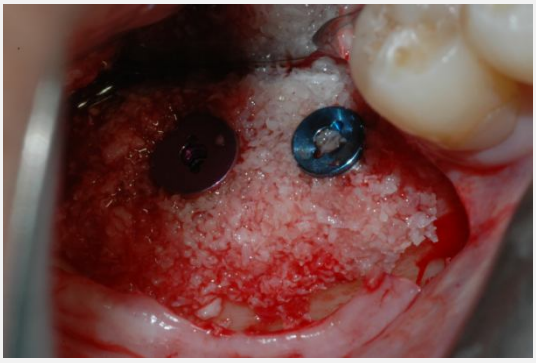
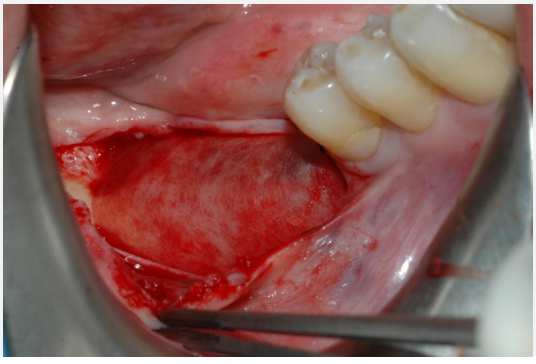
Heart® Pericardium Membrane

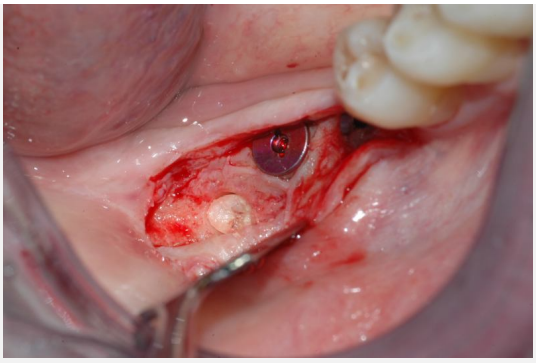
HRT-001 - Pericardium membrane - 1 pc. 30 x 25 x 0.2 mm.
HRT-002 - Pericardium membrane - 1 pc. 50 x 30 x 0.2 mm.

Type:	**Pericardium membrane**
Features:	Resorbable membrane, natural pericardium.
Use:	After performing the graft: 1. Open the blister 2. Shape the membrane, if necessary, without hydrating it 3. Hydrate the membrane for 1-2 minutes with sterile physiologic solution 4. Cover the graft with the membrane
General hints and precautions:	The **protection time** for this kind of membrane is **3-4 months**. Such a long protection time is due to the fact that the treatment the pericardium undergoes to achieve these membranes does not alter the tridimensional structure, and the bonds among the collagen and elastin fibers the pericardium is made of. Thus, the time needed for degradation is longer. This membrane is, therefore, structured and features a peculiar mechanical resistance to tearing. **It can be sutured** without tearing. **This membrane needs not fixation**; its adhesiviness is only slightly smaller than the one of the classic collagen membranes. It's the best choice for most bone regeneration surgeries.
HRT-001 Pericardium membrane 1 pc. 30 x 25 x 0.2 mm. **HRT-002** Pericardium membrane 1 pc. 50 x 30 x 0.2 mm.	**Indications:** **To protect most medium to large-sized bone grafts, and in particular:** a) To protect grafted peri-implant defects showing more than 3 exposed threads b) To protect every kind of grafted periodontal site c) To protect grafted post-extractive sites even when one or more walls are

	missing d) To cover GBR granular grafts e) To cover horizontal and/or vertical onlay grafts performed with sheets or blocks f) To protect inlay grafts

Example: using HRT-001 pericardium membrane) to protect a peri-implant defect grafted with OX31 granules (cortical-cancellous bone granules, sized 0.5-1 mm).

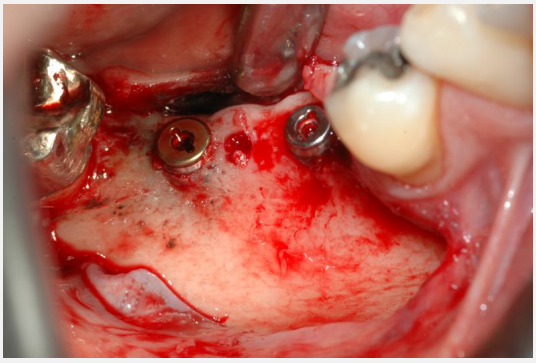
	The implants show a small exposition, that could compromise the esthetic of the final restoration.
	The two defects are filled with **OX31** granules (cortical-cancellous bone granules, sized 0.5-1 mm).
	The reconstruction is protected with a **HRT-001** pericardium membrane.



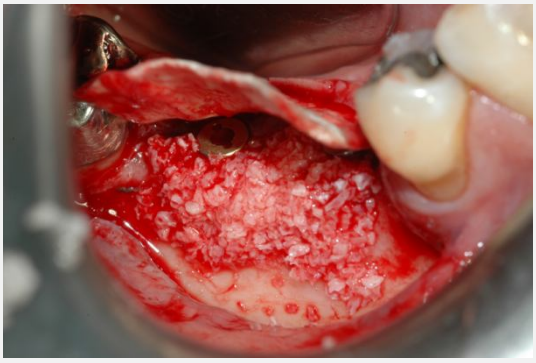
Second look (4 months). The picture shows also the collection of a bone core for the histological tests.

Courtesy Dr. Danilo Di Stefano

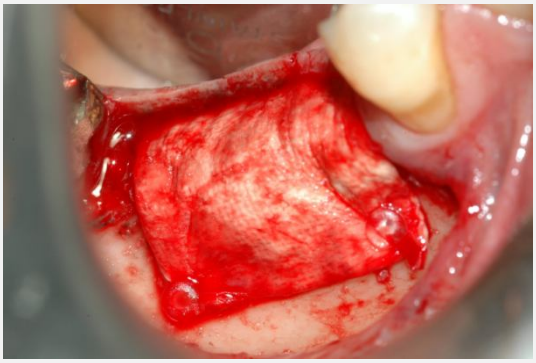
Example: using HRT-001 (Heart pericardium membrane) to protect a graft with granules to perform a lateral GBR.



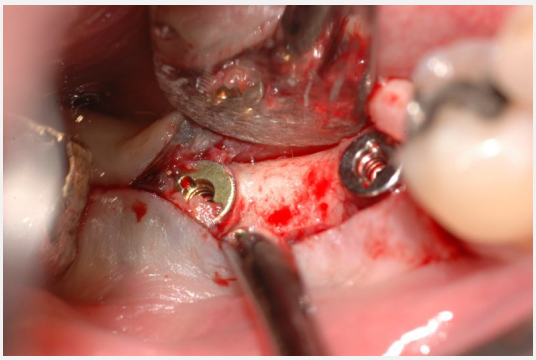
Two implants are placed, but a large lateral defect is present.



The defect is filled with a mixture of cortical-cancellous bone granules **OX31** and autologous bone, collected with a scraper.



The defect is protected with a **HRT-001** Heart pericardium membrane.



Second look (6 months).

Courtesy Dr. Danilo Di Stefano.

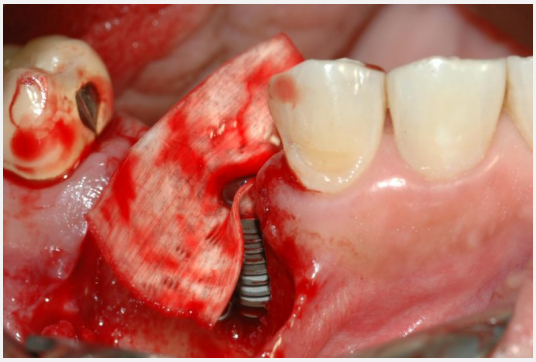
OX® Cortical Membrane

OX03 - Cortical membrane - 1 pc. 25 x 25 x 0.2 mm.
OX04 - Cortical membrane - 1 pc. 50 x 25 x 0.2 mm.

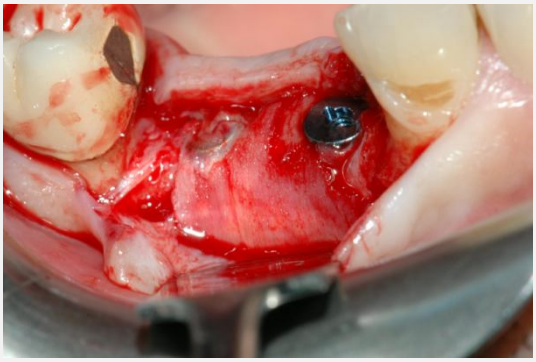
Type:	**Cortical membrane**
Features:	Long lasting natural cortical bone membrane.
Use:	After performing the graft: 1. Open the blister 2. Shape the membrane, if necessary, without hydrating it 3. Prepare the proper holes into the membrane, where the fixation devices (screws, pins) will be placed 4. Hydrate the membrane for 1-2 minutes with sterile physiologic solution 5. Cover the graft with the membrane 6. Fix the membrane with the chosen fixation devices
General hints and precautions:	The **protection time** of this kind of membrane is greater than **6 months**. The same demineralization process that is applied to achieve the flexible bone sheets (**OX** Cancellous Flexible Sheet, **OX01**, and **OX** Cortical Bone Sheet, **OX02**, is applied to achieve very thin (0.2 mm) cortical layers. Such layers act as flexible bone membranes with a very long resorption time: histological evidence shows that 6 months after being grafted these membranes are still completely occlusive. Being bone grafts, they will be anyway remodeled by osteoclasts and will be totally replaced, over time, by new formed bone. The total remodeling time is about 10-12 months (estimated). Given their long protection time, they are indicated to protect large onlay reconstruction, and for all the cases when the ratio between the volume to be regenerated and the area of vital bone surrounding the graft is so small, that a very slow regeneration process is expected. Since they are bone grafts, they must be fixed with proper devices. .
OX03	**Indications:**

Cortical membrane 1 pc. 25 x 25 x 0.2 mm. **OX04** Cortical membrane 1 pc. 50 x 25 x 0.2 mm.	**To protect most medium to large-sized bone grafts, and in particular:** a) To protect grafted peri-implant defects showing more than 3 exposed threads b) To cover horizontal and/or vertical onlay grafts performed with flexible sheets or blocks c) To maintain bone profiles (vestibular ridge reconstruction)

Example: using OX03 (OX Cortical membrane) to protect a granular graft, performed with OSP-OX31 to reconstruct a severe peri-implant defect.

	A severe peri-implant defect. The implant has primary stability, but it is highly exposed (both on the vestibular and the palatal side).
	A cortical **OX03** membrane is placed, before the granules, stabilizing it with the implant cover screw. The edges of the membrane will be placed under the flap borders.

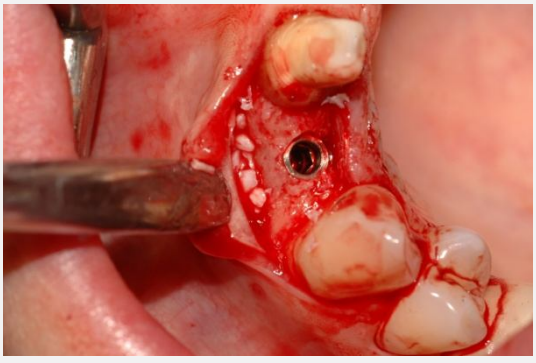
The defect is filled with **OX31** (cortical-cancellous bone granules sized 0.5-1 mm.).



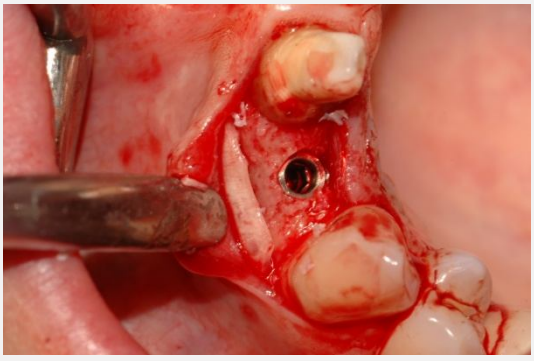
Second look (6 months). The membrane is still present and undergoing remodeling. The surgical opening is so wide since a portion of the membrane will be removed to perform histological tests.

Courtesy Dr. Danilo Di Stefano.

Example: using OX03 (Cortical Membrane) to regenerate a vestibular defect.



The cortical membrane is placed under the flap, creating a wall containing the granular graft.
If the membrane is stable, and held still by the flap, fixation can not be necessary.



When the filling is complete, the membrane acts as a new vestibular wall.

Courtesy Dr. Danilo Di Stefano.

OX® Osteopromoters

OX11 – 2 syr. 0.5 ml/syr. "OX Angiostad"
OX14 – 1 btl. 0.5 cc. "OX Activagen"

Type:	**Osteopromoters (demineralized bone matrixes - DBM)**
Features:	Natural demineralized bone matrixes showing osteopromoting effects .
Use:	**OX "Angiostad"** **a) When blocks are grafted (vertical and/or horizontal onlay)** 1. Prepare the receiving bone surface (with a blur, or with a scraper) 2. Spread a thin (< 1 mm) layer of **OX** Angiostad (**OX11**) over the receiving bone surface or, as an alternative, on the side of the graft that will be in touch with it 3. Place the graft, protect it with a proper membrane, release the flaps, and suture according usual surgical procedures **b) When granules are grafted** 1. When granules are hydrated (and, if possible, mixed with autologous bone), add **OX** Angiostad (**OX11**) to the mixture (1:3 in volume approximately) 2. Graft as already described

	OX "Activagen" When granules are grafted: 1. When granules are hydrated (and, if possible, mixed with autologous bone), add **OX** Activagen (**OX14**) to the mixture (1:1 in volume approximately) 2. Graft as already described
General hints and precautions:	These **osteopromoting medical devices** are achieved by complete demineralization of bone tissue: they are made, therefore, of type I bone collagen, still containing – since they have been preserved selectively through the Bioteck enzymatic deantigenation system – **growth factors (peptides of). These factors, physiologically present into the bone tissue, have a stimulating effect over the angiogenetic and the morphogenetic processes (these devices are, from a technical point of view, demineralized bone matrixes).** As a general indication, they should be used in all the cases where the anatomy of the defect, and the surgical technique that is going to be applied, let the surgeon suppose that the regeneration will be difficult and slow. Their use should be planned to achieve a higher success rate, rather than an increase of regeneration speed. According to the type of peptides that has been selected, the effect can be different, and two formulations are available: **Osteopromoter, angiogenic activator ("OX Angiostad", OX11)** It's a water-based gel containing demineralized bone matrix. Its main use is as an adjuvant when onlay grafts are performed. It is used by spreading a thin layer on the receiving bone surface, after preparing it by drilling or scraping. The stimulation of the pro-angiogenic peptides, in fact, will take place where new vessels grow, i.e. the bone-graft interface. **Osteopromoter, morphogenic activator ("OX Activagen", OX14)** It's made of demineralized bone matrix granules, used as an adjuvant for granular grafts. It is used by mixing it to granules, and its action will be the stimulation of morphogenesis (the differentiation of mesenchimal cells into active osteoblasts). Its main function is to permit achieving, after the same time span, a greater bone density.

OX11 "OX Angiostad" 2 syr. 0.5 ml/syr. **OX14"OX Activagen"** 1 btl. 0.5 cc.	**Indications:** To achieve osteopromotion, when used together with an osteoconductive graft, in all those sites whose anatomy (ratio between vital bone surface and bone volume to regenerate) make the surgeon expect a very slow and difficult regeneration. **These devices should be used to achieve a greater success rate, and not an increase in regeneration speed.** Their application in small sites, or in sites showing a great regenerative potential (reduced volume and four walls surrounding the defect) is probably not useful.

Example: using OX11 (OX Angiostad) over an OX01 sheet (OX Flex Cancellous Sheet) for an onlay lateral augmentation.

The osteopromoter **OX11** (OX Angiostad) is spread over an **OX01** sheet (**OX** Flex Cancellous Sheet), on the side that will be in contact with the receiving bone surface (there's blood over the sheet since the surgeon already tried to fit it over the defect).

Courtesy Dr. Danilo Di Stefano.

Example: mixing OX14 (OX Activagen) with OX31 (OX Cortical-cancellous granules).

The osteopromoter **OX14** (OX Activagen)) is placed into the sterile container to be mixed with the granules before hydration with saline.

Osteopromoter (bottom) and granules (top). Note that the quantity of osteopromoter is still not optimal: another vial should be used to get a volume approximately equal to the one of the granules. The mixture will be then hydrated and grafted as usual..

Courtesy Dr. Danilo Di Stefano.

6. Current level of evidence for the proposed clinical protocols

Protocol	***Evidence***
Using **OX30** (cancellous granules, 0.5-1 mm.) to graft peri-implant defects, and protect them with a resorbable membrane.	*GBR-based restoration of a peri-implant defect with an equine flexible cortical bone membrane and heterologous equine bone.* *D.A. Di Stefano, R. Vinci, G. Cremaschini, S. Pagnutti, and E.F. Gherlone.* *Italian Oral Surgery 2011 (in press).*
Using **OX31/32** (cortical cancellous granules, sized 0.5-1 mm.) to graft intact post-extractive sockets, and placing a **HRT-001** Heart pericardium membrane as a protection.	*Consensus of users.*
Performing a sinus lift, according to the traditional Misch approach or to the traditional Misch approach and Tulasne variation (graft with **OX31/32**, cancellous-cortical granules sized 0.5-1 mm – possibly mixed with autologous bone; **OX02** Flex Cortical Sheet for the Tulasne variation).	*Stievano D, Di Stefano A, Ludovichetti M, Pagnutti S, Gazzola F, Boato C, Stellini E. Maxillary sinus lift through heterologous bone grafts and simultaneous acid-etched implants placement. Five year follow-up. Minerva Chir. 2008 Apr;63(2):79-91.* *Piattelli A, Perrotti V, Piccirilli M, Artese L, Pagnutti S, Di Stefano DA. Sinus lift with autologous bone alone or in addition to equine bone: an immunohistochemical study in man. Submitted to Implant Dentistry.*
Filling a ridge after a split crest with **OX31/32** cortical-cancellous granules and a **XC30** collagen membrane or **HRT-001** Heart pericardium membrane.	*Consensus of users.*
Performing a vertical ridge augmentation following the Ludovichetti technique with a cortical flexible sheet (**OX02**), cortical-cancellous granules (**OX31/32**) and a pericardium membrane (Heart, **HRT-001**).	*Ludovichetti M, Di Stefano DA, Pagnutti S, Vaccari E, Ludovichetti FS, Celletti R.* *Vertical Ridge Augmentation Using a Flexible Heterologous Cortical Bone Sheet: Three-Year Follow-up. Int J Periodontics Restorative Dent. (2011, accepted).*

Using cortical-cancellous granules (**OX31/32**) as a filler after an onlay graft.	*Consensus of users.*
Using larger cancellous granules (**OX33/34**, sized 2-3 or 2-4 mm respectively) for sinus lift, traditional lateral approach (Misch), **XC30** collagen membrane to cover the access window.	*Di Stefano DA, Andreasi Bassi M, Savin G, Ludovichetti M, Pagnutti S. Maxillary sinus lift with collagenic equine bone substitutes. Histomorphometric analysis. IOS (2011, accepted).*
Using **OMC-030** Calcitos bone granules to preserve bone volume for esthetic purposes.	*Consensus of users.*
Using **OX** Mix Gel (**OX21/22/23**) to fill periodontal defects in association with a BCG-**XC30** collagen membrane, or a Heart **HRT-001** pericardium membrane or the **OX06** Collagen gel stabilizer.	*Consensus of users.*
Using **OX** Cancellous Blocks (**OX51 – 55**) to perform onlay vertical or horizontal augmentations together with a Heart HRT-001 pericardium membrane or a **OX03** Cortical membrane.	*Consensus of users.*
Using **OX** Cancellous Blocks (**OX51 – 55**) to perform inlay vertical or horizontal augmentations	*Consensus of users.*
Using **OX** Flex Cancellous bone sheet (**OX01**) as an onlay graft, in association with a long-lasting membrane.	*Di Stefano DA, Artese L, Iezzi G, Piattelli A, Pagnutti S, Piccirilli M, Perrotti V. Alveolar ridge regeneration with equine spongy bone: a clinical, histological, and immunohistochemical case series. Clin Implant Dent Relat Res. 2009 Jun;11(2):90-100.*

Using **OX** Flex Cancellous bone sheet (**OX01**) or **OX** Flex Cortical bone sheet (**OX02**) during a sinus lift (lateral approach) to protect the Schneider membrane (mimicking the Tulasne technique).	*Di Stefano DA, Cazzaniga A, Andreasi Bassi M, Savin G, Ludovichetti FS, Pagnutti S, Ludovichetti M, Celletti R. Using Flexible and Rigid Heterologous Sheets to Mimic Tulasne's Technique. 7-years Follow-up of a Series of Cases. Submitted to Int J Periodontics Restorative Dent (2011).* *Stievano D, Di Stefano A, Ludovichetti M, Pagnutti S, Gazzola F, Boato C, Stellini E. Maxillary sinus lift through heterologous bone grafts and simultaneous acid-etched implants placement. Five year follow-up. Minerva Chir. 2008 Apr;63(2):79-91.*
Using **OX** Osteopromoters (**OX11** "**OX** Angiostad" and **OX14** "**OX** Activagen") to increase the probability of success of bone regeneration.	*Ludovichetti M., Pagnutti S., Pennelli N. A new biological approach to sinus lift Quintessenza 2007; 23, 7-13.* *Effects of OX Angiostad on endothelial cells growth in: Bellone G, Scirelli T, Emanuelli G. Osteo-promoting activity of Osteoplant Angiostad in vitro. Minerva Stomatol. 2008 Apr;57(4):189-98.* *Stievano D, Gazzola F, Stellini E, Boato C. Morpho-functional pre-prosthetic rehabilitation with the osteogenic accelerator Osteplant Activagen. A case report). Atti 13° Congresso Nazionale del "Collegio dei Docenti di Odontoiatria", Roma 5-8 Aprile 2006.*

7. Current references on OX bone substitutes

*Note: as known, **OX** bone substitutes are the dental version (for size and formats) of a class of medical devices that are being used in Orthopedics since 1995. This class of Orthopedic medical devices is marketed under the commercial name of "Osteoplant®" (from a regulatory point of view, the CE mark of the **OX** medical device, in fact, is the same and the correct, complete, burocratic name of the OX bone substitutes is actually "Osteoplant Osteoxenon", called "**OX**" for sake of brevity).*

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