chronOS™
Synthetic cancellous bone graft substitute (β-tricalcium phosphate)

Remodels
– Replaced by bone in 6–18 months

Easy to use
– Granules, blocks, wedges, cylinders

Safe
– Synthetic origin provides unsurpassed safety
### Handling

Chronos is preferably soaked with autogenous blood. Soaking the blocks, wedges and cylinders fills the pores and drives out remaining air. This procedure enhances the rapid exchange of fluids inside Chronos and initiates the start of the remodelling process. For an easier perfusion a syringe can be used. Soaking granules with autogenous blood results in a consistency that allows an easier placement into the surgical site.

In order to achieve its osteogenic potential, Chronos can be mixed with cancellous bone or bone marrow.

The blocks, wedges and cylinders can be easily formed to the desired shape with a suitable instrument, e.g. a scalpel.

### Indications

Chronos can be used wherever cancellous bone graft would normally be used. Depending on the size, voids of undefined geometric shape can be filled with granules or combinations of granules and blocks. Voids with defined geometric shape can be filled with blocks, wedges or cylinders.

**Trauma and orthopaedics**

Filling of voids caused by benign tumours, cysts and osteotomies, filling of defects arising from impacted fractures, refilling of cancellous bone harvesting sites, arthrodesis, non-unions and pseudoarthrosis.

**Spine surgery**

Postero-lateral fusion, interbody fusion (as cage filling material), vertebrectomies (as filling material of the vertebral implants).

**Cranio-maxillofacial surgery**

Reconstruction of mandibular cyst defects and voids after tooth socket extractions, augmentation of the alveolar ridge and the maxillary sinus.

The use of Chronos is restricted to applications with minor loading, unless supported with internal fixation devices.
Remodels

Chronos is replaced by host bone in 6–18 months. The remodelling process (simultaneous resorption and new bone formation) is possible due to the specific chemical composition and the optimised scaffold of Chronos.

Easy to use

The off-the-shelf product is available in different shapes and sizes: granules, blocks, wedges and cylinders. Chronos does not require preparation and is sterile packed.

Avoids bone harvesting

Autologous bone grafting is associated with several shortcomings and potential complications. Studies have shown an incidence of up to 20.6% of minor complications and 8.6% of major complications associated with the use of autograft material (Younger et al. 1989).

Chronos is an advantageous alternative to bone harvesting. It shortens operative time, solves the limitations in quantity and quality of available bone graft and avoids donor site morbidity.

Safe

The synthetic origin of Chronos provides high biocompatibility and unsurpassed safety, preventing any risk of transmission of infectious disease.
### Synthetic material characteristics

#### Strength of cancellous bone

The compressive strength of Chronos is consistently 7.5 ± 1 MPa. The standardized manufacturing process guarantees constant quality and provides reliable mechanical stability. The compressive strength of Chronos is similar to that of cancellous bone which is typically between 2 and 10 MPa (Van Auderkercke, Martens 1984).

#### Right choice of chemical composition

Differences in chemical composition of biomaterials have profound effects on their *in vivo* behaviour. Chronos consists of pure β-tricalcium phosphate which remodels completely. Hydroxyapatite, in contrast, resorbs very slowly, therefore remaining in the body for many years (Gazdag et al. 1995).

#### No adverse reactions

All investigations, according to ISO 10993-1, demonstrate the excellent biocompatibility of Chronos. No adverse reactions have been observed in the 20 years of clinical applications (Steffen et al. 2001, Roesgen 1991,Gattì et al. 1990).

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<table>
<thead>
<tr>
<th>Other bone graft substitutes</th>
<th>Chronos</th>
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<tbody>
<tr>
<td>Hydroxyapatite</td>
<td>β-tricalcium phosphate</td>
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<tr>
<td>Ca₁₀(PO₄)₆(OH)₂</td>
<td>β-Ca₃(PO₄)₂</td>
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**No remodelling**

**Remodelling**
Optimised scaffold

To induce the bone remodelling process osteoconductivity must occur. It is mainly influenced by three factors: the overall porosity, the interconnected macropores and the micropores. Chronos has been designed to optimise these features in order to mimic cancellous bone and provide an ideal scaffold for bone tissue infiltration.

Overall porosity

Chronos has a total porosity of 60% for the granules and 70% for the blocks, wedges and cylinders. A high porosity enhances the osteoconductivity, although a porosity which is too high weakens the material’s mechanical strength. Chronos benefits from the highest possible degree of porosity, without compromising the mechanical strength.

Interconnected macropores

The macropores of Chronos are mainly distributed within a range from 100–500 µm. This offers the optimal environment for vascularisation and migration of osteoclasts and osteoblasts (Gazdag et al. 1995). In addition, the macropores are interconnected to allow bone formation throughout the entire implant.

Micropores

Chronos contains micropores, which are defined as the space within the material smaller than 10 µm. The microporosity accelerates the remodelling process by increasing the surface area and allowing for circulation of body fluids.
Remodelling is the key to success

Desired remodelling process

The key to success of Chronos is the remodelling process. Resorption and new bone formation happen simultaneously and are completed in 6–18 months. This is the result of both the choice of the specific chemical composition and the optimised scaffold as described previously.

Replaced in 6–18 months

Timing is the critical factor for a bone graft to remodel into natural bone. If the resorption is too rapid, the osteoblasts lose the scaffold needed for the formation of new bone. If the resorption is too slow or incomplete, the graft will not be replaced by bone in an adequate time span. Chronos has been designed to remodel in an ideal time span, being replaced by host bone in 6–18 months.

Simultaneous resorption and new bone formation

As Chronos is structurally and chemically similar to bone, osteoclasts resorb Chronos like endogenous bone. During resorption, osteoclasts attach to the matrix and create lacunae on the implant surface. As this resorption takes place, new bone is formed: osteoblasts fill the lacunae, thus synthesising extracellular matrix, which is subsequently calcified.
**Successful spinal interbody fusion**

Cages filled with Chronos granules were used to achieve intervertebral fusion in sheep. The following figures show non-decalcified sections stained with toluidine blue: grey represents Chronos, blue represents bone, white represents medullary space (Steffen et al. 2001; histologies by R. K. Schenk, Berne).

<table>
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<tr>
<th>TimePost operative</th>
<th>Description</th>
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<tr>
<td>8 weeks</td>
<td>Bone surrounds Chronos granules and integrates in its pores.</td>
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<tr>
<td>16 weeks</td>
<td>Some of the granules are still surrounded by initially formed bone with low mineral content, woven bone. Other parts of Chronos are already covered by dense oriented bone, lamellar bone.</td>
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<tr>
<td>32 weeks</td>
<td>Extensive substitution of Chronos granules. Remodelling has replaced mostly all tricalcium phosphate particles and simultaneously, the mean volume of bone matrix has increased constantly.</td>
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Twenty years of clinical experience

Chronos has been used successfully in dental applications for twenty years. As early as 1988, P. S. Eggli et al. had suggested that Chronos underwent osteoclastic resorption and in 1990 J.-P. Pochon wrote about Chronos as an advantageous bone graft for bone defects in children (under the name Ceros-82). Since these publications, several studies have shown the excellent behaviour of Chronos as a bone graft in trauma, spinal and dental applications.

Clinical and animal studies


Other studies


Presented by: