IngeniOs™ß-TCP Bioactive Synthetic Bone Particles Technical Data Sheet[1]

1. CHARACTERISTICS

IngeniOs β-TCP Bioactive Synthetic Bone Particles are an open-cell, non-biologic resorbable bioceramic for bone regeneration. By using a phase-pure beta tricalcium phosphate with a biocompatible open-cell structure, a bioactive and osteoconductive material is achieved. The synthetic material and the ceramic sintering process result in a material free of germs and pyrogens. A potential for allergenic response can be precluded.

IngeniOs β-TCP Bioactive Particles are an open-cell material with a porosity of up to 75%. *IngeniOs* β-TCP Bioactive Particles are available in two volumes 250-1000 µm and 1000-2000 µm and serve to fill oral and maxillofacial defects. Blood components can permeate the material quickly due to the high porosity of the particles, which results in the potential for osseous integration and vascularization.

The doping of 4% sodium-magnesium-silicate on interstitial spaces of TCP-crystal-lattice is designed to ensure maximum mechanical stability of the substance while increasing its bioactive potential.

1.1 Substance

Phase-pure β-TCP $Ca_3(PO_4)_2$

A biocompatible and osteoconductive bioactive material is made available through the use of phase-pure ß-tricalcium phosphate (ß-TCP) with open sintering structure. Phase impurities in beta-tricalcium phosphate increase the risk of foreign body reactions. Especially worthy of critical evaluation are phase impurities in beta-tricalcium that are very difficult to dissolve such as hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). Therefore, the American Society for Testing and Materials (ASTM F 1088-04) requires a phase purity ≥ 95%. This is achieved and confirmed by *IngeniOs* β-TCP Bioactive Particles with validated procedures.

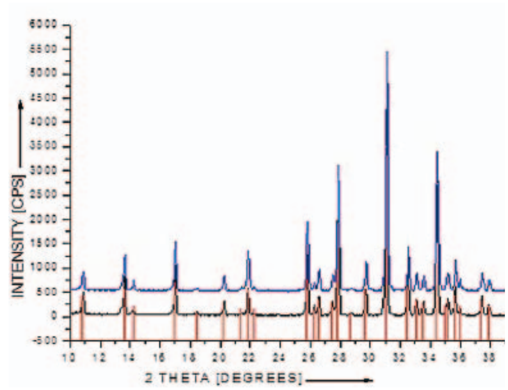

Fig. 1 *X-ray powder diffractogram of phase-pure ß-tricalcium phosphate Riemser Cerasorb* material in comparison with* IngeniOs *ß-TCP Bioactive Particles (10-40° 2 Θ, 0.04° resolution, measurement time 7 sec, ßΘ/Θ-diffractometer, reflection Cu-Kα, U=40 kV, I=30 mA, planar graphite monochromatic filter, scintillation counter, continuous sample rotation). The red bars mark the reflection positions of the reference file (PDF #55-898 (2005), which replaced #9-169 (1959)). It can clearly be seen that the reflections agree with the reference substance and that no other foreign reflections that indicate phase impurities occur.*

**Cerasorb is a registered trademark of Riemser Arzneimittel AG.*

1.2 Analytic Values

Heavy Content	ASTM Requirement	Achieved in IngeniOs ß-TCP Bioactive Particles
Lead	‹ 30 ppm	‹ 5 ppm
Mercury	‹ 5 ppm	‹ 0.1 ppm
Arsenic	‹ 3 ppm	‹ 0.5 ppm
Cadmium	‹ 5 ppm	‹ 1 ppm
Total heavy metals calculated as lead	‹ 50 ppm	‹ 50 ppm

Table 1 *Heavy metal content in* IngeniOs *ß-TCP Bioactive Particles determined with standardized and validated procedures using ICP-AAS and x-ray fluorescence spectroscopy.*

Ca/P Ratio Stoichiometric: 1.5

The stoichiometric Ca/P ratio relates to the chemical composition of the beta-tricalcium phosphate.

2. POROSITY

2.1 Description Interconnected-open cell

2.2 Total Porosity 75%

2.3 Pore Size 250-450 µm

2.4 Trabecula Width 15-20 µm

3. LIGHT MICROSCOPY IMAGES

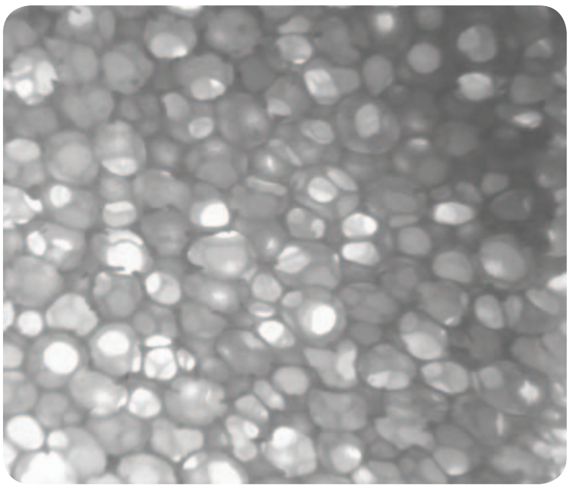

Fig. 2 *Transmission light microscope image of* IngeniOs *ß-TCP Bioactive Particles.*

A pile of particles shows both low density and intergranular intermediate areas due to the irregular width of the particles.

The Scanning electron microscope (SEM) image [Fig. 3] shows a highly porous material that consists of bars with a width of 15-20 µm. The pore system is interconnecting. The macrostructure (i.e. adoption of the foam structure) represents a completely spongious product. The microstructure shows small primary particles that are melted together. The subparticles (fragments of bridge widths) have an average size of more than 10 µm.

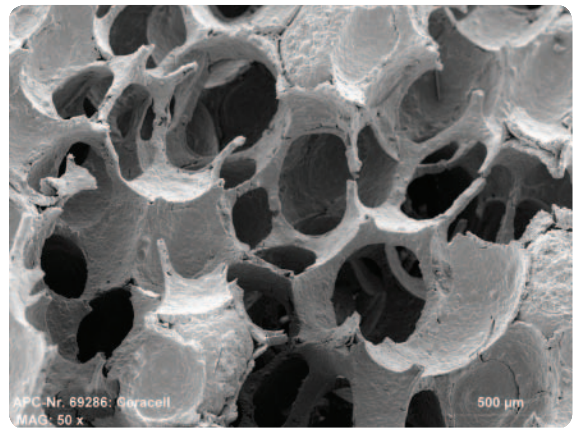

Fig. 3 *Scanning electron microscopy (SEM) image of* IngeniOs *ß-TCP Bioactive Particles. The open cellular scaffold structure is clearly visible.*

4. µ-CT IMAGES

The µ-CT images in Fig. 4 show a highly porous bulk material. The cylindrical shape comes from the geometry of the measuring instrument. Pores and intergranular spaces can also be seen.

Fig. 4 *µ-CT images of* IngeniOs *ß-TCP Bioactive Particles*

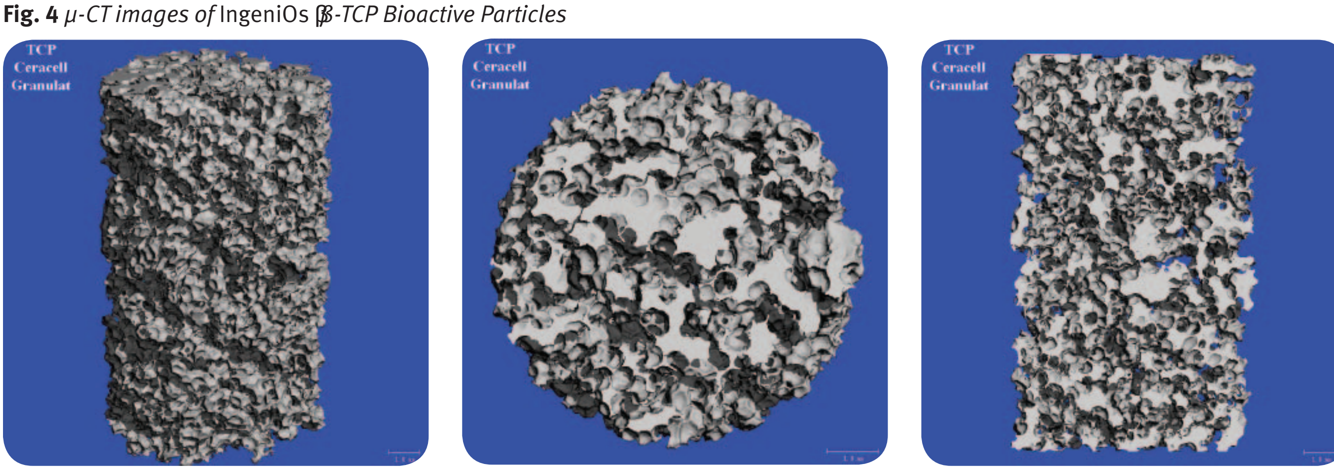

Fig. 4A *Three dimensional view.*

Fig. 4B *Horizontal section through the middle of the sample.*

Fig. 4C *Vertical section through the middle of the sample.*

Fig. 5 *False color representation of μ-CT images of* IngeniOs *ß-TCP Bioactive Particles.*

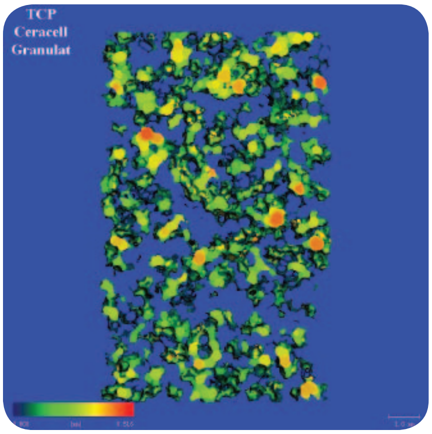

Fig. 5A *Vertical section through the middle of the sample (50 Layers per 16 μm)*

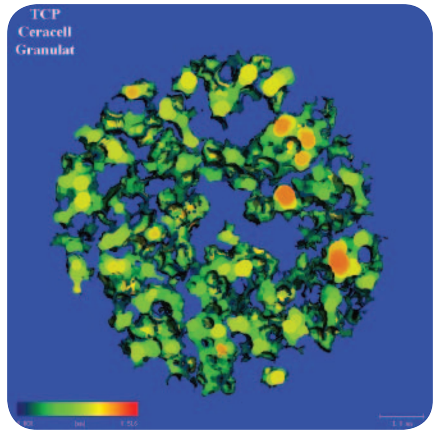

Fig. 5B *Horizontal section through the upper part of the sample (50 layers per 16 μm)*

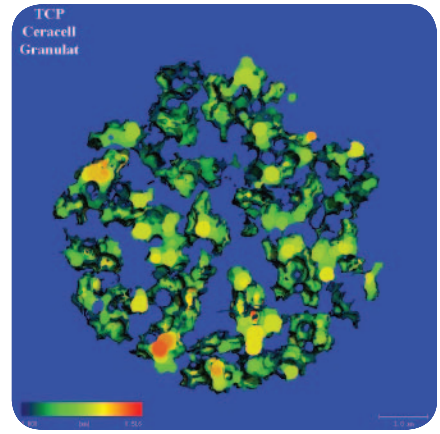

Fig. 5C *Horizontal section through the lower part of the sample (50 layers per 16 μm)*

Fig. 5 shows that the bridge width of *IngeniOs* β-TCP Bioactive Particles are strongly emphasized. Blue areas show a cavity, green areas a simple bridge width, and yellow to red areas show stronger compound materials. The materials which are shown yellow to red are radiopaque. The figures of B and C show an equally dense structure, in all areas of the bulk material. This indicates a high regularity of pore distribution and the bridge width.

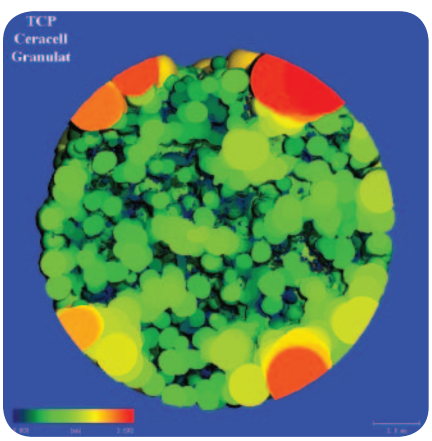

Fig. 6 *Pore imaging of IngeniOs ß-TCP Bioactive Particles. Horizontal section through the middle of the sample shown.*

The pore illustration in Fig. 6 (above) shows a horizontal section through the middle of the sample. The open-cell structure of the material is clearly visible and consistent with scanning electron microscope (SEM) images.

5. PRODUCTION

Reticulated sponges (a sponge with a net-like pattern) with consistent, open-cellular porosity serve as a sintering matrix. The pore size of open-cell sponges is calculated in "pores per inch" (ppi).

The production of beta-tricalcium phosphate occurs by means of a high temperature sintering process according to the reaction shown below:

$$2\ CaHP0_4 + CaC0_3 \rightarrow Ca_3(P0_4)_2 + C0_2 \uparrow + H_20 \uparrow$$

Heating to more than 1000° C eliminates germs and pyrogens.

The β-TCP slurry is kneaded into the regular open-cell sponges. By a thermal sintering process the sponge burns away without leaving residue, the liquid of the slurry is evaporated and the ceramic particles are sintered with each other. What remains is a shape of TCP ceramic and open-cell porosity of the sponge. By using a cutting mill the open-cellular foams are grinded to the desired size of granules and are mixed in different pore sizes with each other.

1. Data on file with curasan AG.