

Summary of the Publication:



Histology of Bone Regeneration in the Human Maxilla: Augmentation by Monocortical Bone Blocks or β -Tricalcium Phosphate Particles

Zerbo, Ilara R
 PhD-Thesis, Amsterdam 2004

Purpose:

The thesis has concentrated on two methods of bone augmentation in the maxilla: the monocortical bone block and the use and success rate of Cerasorb®¹, a $\geq 99\%$ pure-phase β -Tricalcium Phosphate. Augmentations in the human maxilla were examined in several clinical studies. During insertion of the implants, biopsies were taken and histomorphometrically investigated. In a prospective split-mouth study, Cerasorb®¹ was compared with autologous bone. To evaluate resorption and new bone formation for an extended period, biopsies were taken after 9 and 14 months of healing.

Clinical Studies and Results:

1. A two case histological study was performed as a pilot study to gain information concerning the relatively new bone substitute, Cerasorb®¹ prior to implantation. In one patient a large defect resulting from a cystectomy in the mandibula was filled with Cerasorb®¹ (granule size 1000-2000 μ m) and

covered with a TefGen²) foil. In a second case a sinus floor augmentation was performed with Cerasorb®¹ (granule size 500-1000 and 1000-2000 μ m).

Both cases exhibited complication-free ingrowth of the material without foreign body reactions. Active bone formation as well as the presence of woven and lamellar bone proved active remodelling at the implant site. The study reports the ability of the material to be substituted by bone and laid the basis for a larger prospective study where the capability of this material would be compared with autologous trabecular bone, the "gold standard".

2. In the prospective controlled human study, the bilateral sinus floor augmentation procedure was used as a model in which to have an intra-patient control (split-mouth technique). In 9 patients augmentation by means of Cerasorb®¹ was compared with the autologous graft (bone chips from the symphysis) as control. Biopsies were retrieved after 6 months healing from 5 controlled (bilateral sinuses) and 4 uncontrolled (unilateral) patients. The histological findings confirm the osteoconductive

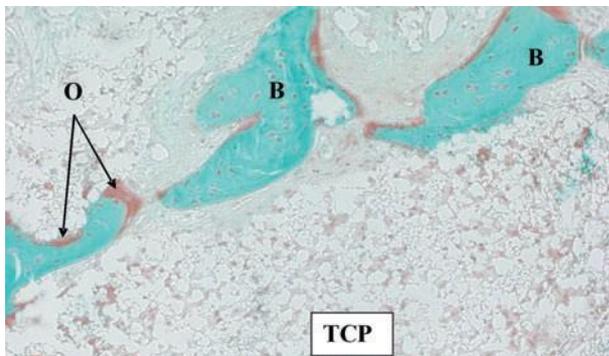


Figure 1: Undecalcified Goldner-stained section showing bone formation in and around TCP particles. B: immature woven bone stains blue-green; O: osteoid, red; TCP material infiltrated with connective tissue cells, the nuclei of which stain red (original magnification x 100).

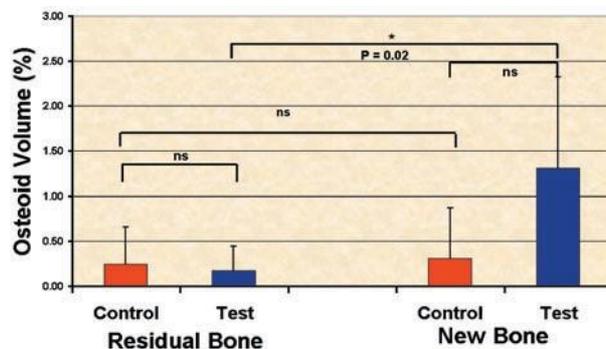


Figure 2: Osteoid volume of residual bone and new (augmented) bone at 6 months healing after grafting with either test or control material (data shown for all 9 patients, means and standard deviations).



properties of the TCP material. The average bone volume formed at the test side (Cerasorb®¹) was significantly lower to that of the control side, osteoid formation however tended to be higher in the test side, indicating ongoing bone formation in the TCP material. The $\geq 99\%$ pure-phase β -Tricalcium Phosphate Cerasorb®¹ is able to produce a similar bone height as the autologous bone material (3.2 - 3.5 mm in 6 months). After 6 months the edges of the round TCP-particles were partially penetrated by bone and connective tissue. It was found that Cerasorb®¹ is an acceptable bone substitute at 6 months.

3. In order to better understand the transformation of the Cerasorb®¹ into bone, the appearance of the potentially osteogenic and osteoclastic cells were investigated in biopsies samples. Runx2/ Cbfa-1 (an essential, early transcription factor for osteoblast differentiation) as well as bone sialoprotein and osteopontin positively identified the osteogenic potential of cells found within TCP particles. This suggested that the TCP particles attracted osteoprogenitor cells to migrate into the micropores of Cerasorb®¹.

It was also studied whether the degradation of the TCP material was due to chemical dissolution or due to resorption via osteoclasts, using the osteoclast marker tartrate-resistant acid phosphatase (TRAP). The histochemical results showed much degradation of the particles occurred in areas of high cell density but without large numbers of TRAP positive cells (presumably osteoclasts). Thus it is unlikely that osteoclasts play a major role in the degradation of TCP. Chemical dissolution, possibly stimulated by local acidity due to high cellular activity, remains the likely mechanism for TCP degradation.

4. In a long-term case study with 3 patients, long-term results were assessed as to how bone quantity (percentage of bone volume) and bone quality (percentage of lamellar bone) after a sinus floor elevation with Cerasorb®¹ (1000-2000 μ m) are influenced by a healing of 9 and 14 months, respectively. Indeed higher bone volumes were found after 9 and 14 months than after 6 months and also a much higher amount of lamellar

bone. The height of bone augmentation had also doubled compared to six months. This indicates that bone continues to be deposited in this material and that remodelling of woven bone into lamellar bone is taking place. It is concluded that 9 months is an acceptable healing time for placement of implants, in sinuses augmented with 100% Cerasorb®¹.

Discussion:

The data show that Cerasorb®¹ acts as an osteoconductive material. Bone progenitor cells migrate from the existing bone in and around the particles of the $\geq 99\%$ pure-phase β -Tricalcium Phosphate, followed by their differentiation into osteoblasts which secrete osteoid. This cell migration can be stimulated by the blood coagulum which contains a large amount of fibrin and, thus, fibronectin, an adhesive glyco-protein which contains integrin receptors of the cellular membranes with extra-cellular matrix molecules of the Asp-Gly-Arg sequence (RGD). This facilitates the cell migration.

It was observed that the biodegradation of the β -TCP corresponds with the measured physio-chemical data of 0.57% dissolution per day in Tris-HCl-solution. The degradation of the material is more due to a chemical dissolution than to osteoclastic resorption.

After a 9-month healing period, the achieved bone height had doubled in comparison with the 6-month results.

Conclusion:

Cerasorb®¹ is an augmentation material well-suited for the sinus floor augmentation. It is not encapsulated by soft connective tissue, but replaced by bone. Bone formation occurred by osteoconduction. The newly formed bone in autogenously augmented defects shows an earlier onset of maturation. When Cerasorb®¹ is used in sinus floor augmentation, a considerable increase in bone height is evident with the progressing healing process. Increasing the healing times from 6 to 9 months strongly increases the bone quantity and quality.

¹Trade name CERASORB® Classic since 2011

²TefGen-Membranes are not available since 2008.
The non-resorbable Cytoplast TXT-200 Membranes [produced by Osteogenics, USA, distributed (in some countries) by RIEMSER Arzneimittel AG] are a very good alternative.

Reprint of figures with permission of Blackwell Publishing Ltd.

Original publication in "Clinical Oral Implants Research", 12, 2001:379-384, Histology of human alveolar bone regeneration with a porous tricalcium phosphate, Ilara R. Zerbo et al