

# **The Bone Graft Substitute $\beta$ -TCP in Oral Surgery and Dental Applications: A Literature Review**

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# TABLE OF CONTENTS

<b>1. INTRODUCTION .....</b>	<b>3</b>
<b>2. CLINICAL STUDIES: β-TCP IN MAXILLO-FACIAL AND DENTAL APPLICATIONS ....</b>	<b>3</b>
2.1. SINUS FLOOR AUGMENTATION .....	3
2.2. GUIDED BONE REGENERATION (GBR) USING MEMBRANES .....	5
2.3. PERIODONTAL BONE DEFECTS.....	5
2.4. CYSTECTOMY .....	6
2.5. OTHER APPLICATIONS OF β-TCP IN ORAL SURGERY.....	7
2.6. APPLICATION OF β-TCP TOGETHER WITH AUTOLOGOUS BONE, PLATELET RICH PLASMA (PRP) AND RECOMBINANT GROWTH FACTORS .....	8
2.6.1. <i>Application of β-TCP in combination with autologous bone</i> .....	8
2.6.2. <i>β-TCP in combination with platelet-rich plasma (PRP)</i> .....	8
2.6.3. <i>Application of β-TCP together with recombinant human platelet-derived growth factor (hrPDGF)</i> .....	9
<b>3. CONCLUSIONS .....</b>	<b>10</b>
<b>4. BIBLIOGRAPHY .....</b>	<b>11</b>
4.1. REFERENCES: CLINICAL STUDIES: β-TCP IN MAXILLO-FACIAL AND DENTAL APPLICATIONS	11
4.1.1. <i>References: sinus floor augmentation</i> .....	11
4.1.2. <i>References: guided bone regeneration (GBR) using membranes</i> .....	14
4.1.3. <i>References: periodontal bone defects</i> .....	15
4.1.4. <i>References: cystectomy</i> .....	17
4.1.5. <i>References: other applications of β-TCP in dentistry</i> .....	17
4.1.6. <i>References: application of β-TCP together with autologous bone, platelet rich plasma (PRP) and recombinant growth factors</i> .....	19
4.2. REFERENCES: CONCLUSIONS .....	21
<b>5. DISCLAIMER.....</b>	<b>21</b>

## 1. Introduction

$\beta$ -TCP is known to be highly biocompatible, resorbable and osteoconductive. Due to these properties,  $\beta$ -TCP is currently used in many dental applications in order to heal or augment bone defects.

Here, clinical studies are presented where  $\beta$ -TCP was applied as a bone substitute in various applications, and that confirm the properties of this biomaterial. Care was taken to represent the main findings of the presented literature with an emphasis on quantitative data. The aim of this literature review is to support the clinician with unbiased information.

Methodology: A literature search was performed in the databases Silverplatter Medline (Advanced, Direct, Serfile), Compendex and PubMed. The literature was classified according to indications. The studies using  $\beta$ -TCP were evaluated without discerning possible influences of porosity, phase purity or granule size on the clinical outcome or on the degradation rate of  $\beta$ -TCP.

## 2. Clinical studies: $\beta$ -TCP in maxillo-facial and dental applications

### 2.1. Sinus floor augmentation

Augmentation of the maxillary sinus floor has become a well-established method to increase the amount of bone above deficient alveolar ridges in the posterior maxilla.

Reinhardt and Kreusser (Reinhardt and Kreusser 2000) reported successful sinus floor augmentations using  $\beta$ -TCP granules in 50 patients. In six cases, complications (sinusitis, thread dehiscence) that could be easily treated with antibiotics were reported. Radiographic images suggested that the  $\beta$ -TCP granules were resorbed within 6 to 9 months postoperatively. Lamellar bone was found in a histological analysis from the augmented areas 6 months after the intervention. 99% of the 101 implants were osseointegrated after 3,5 years.

Similarly, Kreusser (Kreusser 1998) reported sinus floor elevation with  $\beta$ -TCP and placement of 103 implants in 45 patients. None of the implants were lost and healing was uneventful.

Plöger (Plöger 2000) describes the use of  $\beta$ -TCP granules for sinus floor elevation in one patient emphasizing that round granules are well suited for this application since rupture of the Schneiderian membrane that lines the maxillary sinus may be less likely.

Zerbo (Zerbo et al. 2001) augmented the sinus floor of an edentulous patient with an atrophic maxilla. 8 months postoperatively, the volume of newly formed bone was 20%, 44% of the volume was occupied by  $\beta$ -TCP granules that were not yet resorbed. Bone and osteoid were found in close contact with the remaining granules, histological signs of inflammation were absent. The authors point out that  $\beta$ -TCP granules are a suitable biodegradable bone substitute.

Füssinger and Füssinger (Füssinger and Füssinger 2005) report sinus floor elevation in 17 patients from who histological samples were taken from the area augmented with  $\beta$ -TCP. Already after 4 months, bone neogenesis was observed around the  $\beta$ -TCP granules. Mature lamellar bone was seen after 6 months whereas degradation of  $\beta$ -TCP granules proceeded along with bone formation. In the same study, the long-term stability of 70 implants that were placed after sinus elevation was 94.4% in a study with 28 patients that were followed for 1.5 to 7 years. Based on their findings,

the authors suggest that implants may be placed 4.5 months after sinus floor elevation.

In order to understand osteogenesis and the degradation of  $\beta$ -TCP in the augmented maxillary sinus floor, Zerbo and coworkers (Zerbo et al. 2005) analyzed the localization of cells with osteogenic or osteoclastic potential in relation to the TCP particles in histological samples of 12 patients after 6 months. The findings suggest that  $\beta$ -TCP particles attract osteoprogenitor cells that migrate into the interconnecting micropores of the bone substitute material. The lack of large multinucleated TRAP (Tartrate Resistant Acid Phosphatase) positive cells suggests that resorption of the  $\beta$ -TCP material by osteoclasts plays only a minor role in its replacement by bone.

These findings were confirmed by Knabe and coworkers (Knabe et al. 2008) in 20 patients whose maxillary sinus floor has been augmented with a mixture of  $\beta$ -TCP and autologous bone (ratio bone: $\beta$ -TCP 4:1). After six months, cells that expressed proteins characteristic for osteoblastic differentiation like collagen type 1, alkaline phosphatase, osteocalcin and bone sialoprotein were observed in close contact with the degrading  $\beta$ -TCP particles in the augmented sinus. In accordance with Zerbo and coworkers (Zerbo et al. 2005), multinucleated, TRAP-positive cells were not observed suggesting that osteoclasts do not play a major role in degradation of the  $\beta$ -TCP particles. The predominant mechanism of  $\beta$ -TCP degradation is thus most likely chemical dissolution.

Besides  $\beta$ -TCP, autologous bone grafts are in use for sinus floor augmentation. However, the availability of autologous bone is limited, and in many cases its collection requires a secondary surgical procedure with all the associated risks. More than 50% of 97 patients still had problems at the autologous graft donor site one year after the operation (Wippermann et al. 1997), 37% reported pain at the donor site 6 months post-operatively (Goulet et al. 1997), and, depending on the intervention site, 3-50% of the patients had decreased or altered sensitivity at the donor site after 18 months (Clavero and Lundgren 2003). The following studies compared autologous bone and  $\beta$ -TCP in sinus floor elevation. They agree that  $\beta$ -TCP is a valuable alternative to replace autologous bone grafts in this application.

Szabó and coworkers (Szabo et al. 2001) compared the performances of  $\beta$ -TCP and autologous bone grafts. Sinus floor elevation was carried out in 4 patients with severe ridge atrophies of the anterior and the posterior maxillary. From 16 histological samples that were taken after 6 months, the authors conclude that the formation of new bone was independent of the graft material but rather depended on patient's ability to regenerate bone. Remnant  $\beta$ -TCP granules were found after 6 months. No postoperative complications occurred in any of the patients.

In a larger study (Suba et al. 2006) with 17 patients with atrophied alveolar ridges, the sinus floor was augmented bilaterally, on one side with autogenous bone and the other side with  $\beta$ -TCP. Histological analysis of 68 bone samples taken during implant placement 6.5 months after the intervention showed that the new bone densities did not differ significantly between the two graft materials after 6 months ( $32.4 \pm 10.9\%$  for  $\beta$ -TCP and  $34.7 \pm 11.9\%$  for autologous bone, respectively). Six months after the intervention, the bone of the augmented sinus floor was strong and suitable for anchorage of dental implants.

Likewise, Szabo et al. (Szabo et al. 2005) conducted bilateral sinus floor augmentation on 20 selected patients with  $\beta$ -TCP on one side and autogenous bone on the other side. Implants were placed 6 months after the procedure. Two- and three-dimensional computerized tomographic examinations revealed no significant

difference between the experimental and control grafts in terms of the quantity and rate of ossification. The mean percentage bone areas in histological sections were  $36.5\% \pm 6.9\%$  and  $38.3\% \pm 7.4\%$ , respectively without a significant difference between  $\beta$ -TCP and autologous bone.

6 months after sinus floor elevation in a split mouth model in 5 patients, Zerbo and coworkers (Zerbo et al. 2004), found an average bone volume of  $41 \pm 10\%$  on the site augmented with an autologous bone whereas the average bone volume was  $19 \pm 5\%$  on the site augmented with  $\beta$ -TCP. Despite the difference between the two grafting materials, Zerbo and coworkers concluded that  $\beta$ -TCP is an acceptable bone substitute material for augmentation of the maxillary sinus. They speculate that due to the osteoconductive, but not osteoinductive properties of  $\beta$ -TCP, bone formation may be delayed in comparison to autologous bone.

In a study with 48 sinus lift procedures, Simunek and coworkers (Simunek et al. 2008) compared bone formation in the augmented region. Various materials were compared, among them  $\beta$ -TCP and autologous bone. A histomorphometrical analysis after 9 months found  $49 \pm 3\%$  bone if autologous bone was grafted and  $21 \pm 8\%$  newly formed bone with  $\beta$ -TCP.

## 2.2. Guided bone regeneration (GBR) using membranes

Many investigations have been performed in order to augment bone using GBR (Guided Bone Regeneration) techniques with  $\beta$ -TCP covered with a polytetrafluorethylene (PTFE) membrane (Hempton and Fugazzotto 1994; Scher and Speight 1996; Fugazzotto et al. 1997). Besides the studies presented in this paragraph, GBR was frequently used in the treatment of periodontal pockets (See paragraph 2.3).

Scher (Scher and Speight 1996) reported a case of anterior maxillary damage treated with a mixture of  $\beta$ -TCP granulate and demineralized freeze-dried cortical bone (DFDB) covered with a membrane. No evidences of inflammation or of osteoclastic activity were found at 8 months and 17 months postoperatively. Formation of normal bone was observed 17 months after the complex ridge augmentation procedure.

Similarly, Hempton (Hempton and Fugazzotto 1994) augmented the mandibular alveolar ridge with a mixture of  $\beta$ -TCP granulate and DFDB covered with a PTFE membrane permitting the placement of a root form implant in previously untenable site.

In a large-scale study, Fugazzotto (Fugazzotto, Shanaman et al. 1997) carried out GBR around 1503 implants using  $\beta$ -TCP mixed with DFDB. Dehiscent or fenestrated implants and implants that were inserted into immediate extraction sockets were treated. In 97.0% of all cases, a recovery of the hard tissue was observed demonstrating the potential of GBR.

## 2.3. Periodontal bone defects

Treatments of periodontal bone defects are reported in the literature. However, the efficiency of  $\beta$ -TCP granules insertion into periodontal pockets for bone augmentation still is ambiguous. Early studies reported a lack of osseointegration of the  $\beta$ -TCP in periodontal defects whereas more recent findings with larger patient groups indicate a positive effect of  $\beta$ -TCP on different clinical parameters.

Stahl and Froum (Stahl and Froum 1986) treated eight periodontal sites with  $\beta$ -TCP granules. Lesions healed uneventfully without any inflammatory response to the granules. However, the granules were walled off by collagen eight months

postoperatively. Although the implantation of  $\beta$ -TCP permits a clinical gain in closure of the defect, no evidence of osteogenesis or cementogenesis was found.

Similar results are reported by the same authors (Froum and Stahl 1987) for the treatment of five bony periodontal lesions in one patient. However, the patient demonstrated some signs of inflammation, which, according to the authors, explains the variations in resorption and regeneration seen within the same surgical site at 18 months.

Baldock (Baldock et al. 1985) treated 13 periodontal osseous defects in two patients. He found promising clinical and radiographic results but histological investigations revealed no bone formation and little connective tissue attachment.

Palti and Hoch (Palti and Hoch 2002) reported a case where the use of  $\beta$ -TCP permitted to reduce the periodontal pocket depth by 4 mm at 18 months postoperatively. At this time,  $\beta$ -TCP granules were completely resorbed as judged from radiographs.

Positive results in the treatment of periodontitis with  $\beta$ -TCP were confirmed in a report (Foitzik and Stamm 1997) with 86 patients. Radiographic imaging showed that the clinical situation improved for most patients over a period of 20 months.

In a larger, retrospective study (Foitzik and Staus 1999) with more than 600 patients, the same authors assess the rate of infections and inflammatory complications for the treatment of periodontal defects with  $\beta$ -TCP. They find that this rate is lower for three-walled defects (3.4-5.6%) than for one-walled defects (9.5-11.8%). Furthermore, they report that the complication rate depends on the defect location. Generally, the complication rates are higher for defects in posterior regions compared to anterior regions and for defects in the mandible compared to maxillary defects.

In another report (Foitzik and Staus 1999), Foitzki and Staus point out that deep, solitary periodontal defects are very well suited for treatment with  $\beta$ -TCP granulate and that application of a membrane may be beneficial based on a clinical experience of 4 years.

Bokan et al. (Bokan et al. 2006) used a combination of  $\beta$ -TCP and an enamel matrix derivative (EMD) to treat deep intrabony periodontal defects in 19 patients. Measurements after 12 months showed that the combination of  $\beta$ -TCP and EMD leads to a significant clinical improvement reducing the probing pocket depth, and an increase in the probing attachment level.

A study (Dori et al. 2008) performed on 28 patients with deep intrabony periodontal defects showed that the clinical situation was significantly improved one year after closing the defect with  $\beta$ -TCP and an expanded polytetrafluorethylene membrane. The probing depth of the defects was reduced by  $5.4 \pm 0.7$  mm and a gain of  $3.9 \pm 0.9$  mm in the clinical attachment level was detected.

Similarly, Yassibag-Berkman and coworkers (Yassibag-Berkman et al. 2007) reported a gain of the attachment level after 12 months in a study where they treated intrabony periodontal defects in 25 patients. They also recorded the radiographic bone fill, which increased quickly during the first 6 months after the treatment and continued to increase in the six months thereafter.

## 2.4. Cystectomy

Zerbo and coworkers (Zerbo et al. 2001) reported the use of  $\beta$ -TCP granules for the treatment of bone defects, which resulted from cyst enucleation. At 9.5 months, remnants of granules were found in close contact with newly formed bone in a

histological analysis. No signs of inflammation were observed. From this report, it was concluded that  $\beta$ -TCP granules were effective in the treatment of large bone defects that result from cystectomy.

Palm and coworkers (Palm et al. 2006) assessed the capacity of  $\beta$ -TCP to stimulate the reossification of 64 defects that resulted from cystectomy in 63 patients. They found that new bone formation depended on the defect size. After 9 months, even in the largest lesions with diameters of more than 2.5 cm,  $\beta$ -TCP has been replaced by newly formed bone as judged from radiographs.

## 2.5. Other applications of $\beta$ -TCP in oral surgery

Trisi and coworkers (Trisi et al. 2003) studied the replacement of  $\beta$ -TCP in artificial jaw bone defects in 5 volunteers. After 6 months, the density of the newly formed bone measured  $27.8 \pm 24.7\%$  in the defects that have been treated with  $\beta$ -TCP and  $17.9 \pm 4.3\%$  in the empty control defects. The difference was statistically not relevant. The pure  $\beta$ -TCP was resorbed simultaneously with new bone formation.

$\beta$ -TCP granules were used in the treatment of chronic periapical abscesses (Barkhordar and Meyer 1986). However, in the presented case, infection could not be eliminated and additional bone destruction was observed. It was therefore concluded that ceramic implant material should not be inserted in areas where a chronic bacterial infection is present.

Palti (Palti and Hoch 2002) reported the treatment of lesions after apicoectomy, cystectomy and the treatment of alveolar defects with  $\beta$ -TCP granules. No complications were observed in 97.8% of 958 treatments of dental bone defects with  $\beta$ -TCP.

The application of  $\beta$ -TCP as a bone substitute in 152 patients was reported by Horch and colleagues (Horch et al. 2006).  $\beta$ -TCP was used to fill large mandibular cysts, for secondary and tertiary alveolar cleft grafting, to fill periodontal defects and for maxillary sinus floor augmentation. Complete replacement of  $\beta$ -TCP by autologous bone was detected after approximately 12 months, histological analysis in 16 biopsied cases showed a complete bony regeneration. Partial loss of the bone substitute material occurred in 5.9% of the patients whereas a total loss of the  $\beta$ -TCP graft was found in only 2% of the cases. The authors conclude that synthetic, phase-pure  $\beta$ -TCP is a suitable material for the treatment of bone defects in the alveolar region.

A study with 26 patients (Füssinger and Füssinger 2005) assessed the long-term stability of 40 implants in the alveolar crest augmented with  $\beta$ -TCP. In 22 patients, augmentation and implant placement took place in one step. In a period of 1 to 7 years, none of these implants have been lost.

In a larger study, Ormianer and coworkers (Ormianer et al. 2006) assessed the survival of 1065 immediately loaded dental implants in augmented alveolar bone sites in 338 patients.  $\beta$ -TCP mixed with blood from the surgical site was used to augment the alveolar ridge level, fill spaces between the implant and the socket wall or, if necessary, to augment the sinus floor. The implants placed in augmented areas were splinted to implants in nonaugmented sites for stability. 97.6% of the implants survived during the observation period of 12 to 48 months. Thus, immediate loading of splinted implants in augmented sites is a predictable procedure.

In a prospective case-cohort study, Thoma and coworkers (Thoma et al. 2006) inserted custom-fit root analogs made of thermally molded PLGA-coated  $\beta$ -TCP granules into extraction sockets above which communications between the oral

cavity and the maxillary sinus have been opened. In all 14 patients, the oroantral communications were closed successfully. Furthermore, the authors noted that pain and swelling were less intense with this method compared to oroantral communication closure with mucoperiosteal flaps. They conclude that this method constitutes a valuable alternative to close oroantral communications.

Brkovic (Brkovic et al. 2008) demonstrated the use of a  $\beta$ -TCP-collagen material to prevent alveolar atrophy following tooth extraction in a case report. Healing was uneventful, mineralized bone and bone marrow was observed 9 months after the intervention in a histological sample. Only small amounts of  $\beta$ -TCP that were in close contact with bone have remained.

## **2.6. Application of $\beta$ -TCP together with autologous bone, platelet rich plasma (PRP) and recombinant growth factors**

$\beta$ -TCP is versatile and can be applied in combination with autologous bone or other bone regeneration materials. Furthermore, most formulations of  $\beta$ -TCP are porous and can thus serve as carriers for cells or liquid substances. Here, studies that describe and compare the most widespread applications are presented.

### **2.6.1. Application of $\beta$ -TCP in combination with autologous bone**

Aguirre-Zorzano et al. (Aguirre Zorzano et al. 2007) found that  $\beta$ -TCP mixed with autologous bone from the site of the intervention can be used for sinus floor elevation. Implant placement took place at the same time as sinus floor elevation in 22 patients. Histological analysis after the osseointegration period proved the formation of lamellar bone. Remnants of  $\beta$ -TCP were observed in close bone contact.

A second study (Princ et al. 2006) showed that, after three years, 97% of the 34 implants that have been placed in 10 patients after sinus floor augmentation with a mixture of  $\beta$ -TCP and autologous bone were stably integrated.

By comparing combinations of different graft materials in 48 sinus floor elevations, Simunek and coworkers (Simunek et al. 2008) found that adding 10% or 20% autologous bone to  $\beta$ -TCP did not result in a significantly increased bone formation compared to  $\beta$ -TCP alone in the augmented sinus floor after 9 months.

### **2.6.2. $\beta$ -TCP in combination with platelet-rich plasma (PRP)**

A case report (Nikolidakis et al. 2008) suggests that allogeneic PRP (aPRP) can be used in combination with  $\beta$ -TCP granules for sinus floor augmentation.

Another case was reported by Taner and coworkers (Taner et al. 2006) where a mixture of  $\beta$ -TCP, PRP and autologous bone was used for onlay grafting to augment the alveolar crest.

Antoun and coworkers (Antoun et al. 2008) report the use of bovine hydroxyapatite combined with PRP on one side and  $\beta$ -TCP combined with PRP on the other side of a bilateral sinus floor elevation. The results suggested that both materials are suited for this procedure. Interestingly, lamellar bone was found 6 months after grafting in the  $\beta$ -TCP but not in the bovine hydroxyapatite graft.

Yassibag-Berkman and coworkers (Yassibag-Berkman et al. 2007) treated 30 anterior, intrabony, interproximal lesions in 25 patients either with  $\beta$ -TCP alone,  $\beta$ -TCP combined with PRP, and  $\beta$ -TCP with PRP covered with a collagen membrane in order to assess the clinical gain of PRP in the treatment of periodontal defects. They found that all three options were effective in the treatment of the periodontal defects. The use of PRP together with a membrane lead to a higher clinical bone fill after six

months compared to  $\beta$ -TCP or  $\beta$ -TCP/PRP. After 12 months, this difference had disappeared.

Christgau and coworkers (Christgau et al. 2006) treated 25 patients with two intrabony lesions each. One defect was filled with  $\beta$ -TCP whereas the other was filled with  $\beta$ -TCP mixed with autologous platelet concentrate (APC) in every patient. Both defects were covered with a resorbable membrane. APC contained 7.9 times more platelets than venous blood and high concentrations of platelet-derived growth factor-AB (PDGF-AB) and PDGF-BB, transforming growth factor-beta1, and insulin-like growth factor-1. However, the potential influence of APC on periodontal regeneration remained unclear.

A study with 28 patients (Dori et al. 2008) did not find a significant additional clinical benefit if PRP was added to  $\beta$ -TCP to treat periodontal lesions. The application of  $\beta$ -TCP with and without PRP resulted in similar probing depth reduction of the defect and clinical attachment level gains.

### **2.6.3. Application of $\beta$ -TCP together with recombinant human platelet-derived growth factor (hrPDGF)**

Byun (Byun and Wang 2008) reports a case where a fenestration defect and fracture of the labial plate was repaired using autologous bone as an inner grafting material, which was overlaid with  $\beta$ -TCP combined with recombinant human platelet-derived growth factor BB (rhPDGF-BB) and tented with a collagen membrane. After 5 months, complete healing of the defect was observed suggesting that combination of rhPDGF-BB and  $\beta$ -TCP may be suitable materials for bone augmentation.

Ridgway and coworkers (Ridgway et al. 2008) combined  $\beta$ -TCP with either 0.3 or 1.0 mg/ml human recombinant platelet-derived growth factor-BB (rhPDGF-BB) to treat periodontal defects around 16 teeth planned for extraction in 8 patients. Extraction took place 6 months after the treatment. Histological evaluation demonstrated that in 81.25 % of all cases, new bone, cementum and periodontal ligament were present suggesting that the combination of rhPDGF-BB and  $\beta$ -TCP can promote periodontal regeneration in human intraosseous defects.

Nevins and coworkers (Nevins et al. 2005) assessed the safety and effectiveness of rhPDGF-BB in a large, prospective, triple-blinded clinical trial with 180 patients requiring surgical treatment of 4 mm or greater intrabony periodontal defects. The patients were treated either with  $\beta$ -TCP + 0.3 mg/ml rhPDGF-BB,  $\beta$ -TCP + 1.0 mg/ml rhPDGF-BB or  $\beta$ -TCP with buffer as a control. The study demonstrated that the use of rhPDGF-BB is safe and effective.  $\beta$ -TCP in combination with rhPDGF-BB stimulated a significant increase in the rate of clinical attachment level gain and reduced gingival recession at 3 months post-surgery. The patients showed improved bone fill, which was assessed radiologically, after six months compared to the group treated with  $\beta$ -TCP and buffer.

### 3. Conclusions

The presented works describing the application of  $\beta$ -TCP in dentistry show that this biomaterial represents a valuable bone substitute for various indications.

- Treatment with  $\beta$ -TCP granules gives very good results in the cases of small or medium-sized bone defects. In large bone defects, replacement of the biomaterial by newly formed bone tissue generally took more time, most probably since  $\beta$ -TCP is osteoconductive but not osteoinductive. Consequently, for larger bone defects, addition of autologous bone to  $\beta$ -TCP is recommended.
- $\beta$ -TCP is biocompatible, no general complications related to the material were mentioned in the presented literature.
- $\beta$ -TCP was found to be resorbable within 24 months postoperatively and to be progressively replaced by newly formed bone tissue.
- No general conclusion on the influence of granules size or porosity on the regeneration of bone or on the degradation characteristics of the material could be extracted from the evaluated studies. However, the study by Knabe and coworkers (Knabe et al. 2008) and animal studies (Gauthier et al. 1998; Mastrogiacomo et al. 2006) clearly show that pore design and the granule geometry do impact the in vivo behavior of synthetic calcium phosphate ceramics.

## 4. Bibliography

### 4.1. References: clinical studies: $\beta$ -TCP in maxillo-facial and dental applications

#### 4.1.1. References: sinus floor augmentation

Reinhardt, C. and B. Kreusser (2000) **Retrospektive Studie nach Implantation mit Sinuslift und Cerasorb-Augmentation** Dent Implantol(4): 18-26.

<b>Aim of the study:</b>	Assess the clinical outcome of treatments with $\beta$ -TCP granules.
<b>Materials:</b>	$\beta$ -TCP granulate (particle size 1000-2000 $\mu\text{m}$ , > 99% $\beta$ -phase, 35 % microporosity)
<b>Number of Patients:</b>	50 patients, 101 implants
<b>Investigation methods:</b>	Clinical examination and histological analysis after 6 and 9 months.
<b>Complications:</b>	Sinusitis and thread dehiscence in 6 patients

Kreusser, B. (1998) **[Good results even without adding autologous cancellous bone]** DZW(12).

<b>Aim of the study:</b>	Report the results of sinus floor elevations with $\beta$ -TCP.
<b>Materials:</b>	$\beta$ -TCP granulate (> 99% $\beta$ -phase, 35 % microporosity)
<b>Number of Patients:</b>	45 patients, 103 implants
<b>Investigation methods:</b>	Clinical reports
<b>Complications:</b>	None reported.

Plöger, M. (2000) **beta-Tricalciumphosphat versus bovines Knochenersatzmaterial in äquivalenten OP-Arealen: Ein klinischer Vergleich** Dent Implantol(9): 200-207.

<b>Aim of the study:</b>	Offer guidance for the choice of the best suited augmentation material.
<b>Materials:</b>	$\beta$ -TCP granulate (particle sizes 500-1000 $\mu\text{m}$ and 1000-2000 $\mu\text{m}$ , > 99% $\beta$ -phase, 35 % microporosity), bovine hydroxy-apatite.
<b>Number of Patients:</b>	6 patients (case reports)
<b>Investigation methods:</b>	Clinical examination
<b>Complications:</b>	Loss of $\beta$ -TCP granules from the augmented ridge during the implant placing, formation of connective tissue capsules around $\beta$ -TCP granules.

Zerbo, I. R., A. L. Bronckers, G. L. de Lange, G. J. van Beek and E. H. Burger (2001) **Histology of human alveolar bone regeneration with a porous tricalcium phosphate. A report of two cases** Clin Oral Implants Res 12(4): 379-84.

<b>Aim of the study:</b>	Analyse bone formation in two cases where $\beta$ -TCP was used for sinus floor elevation and to fill a large mandibular bone defect.
<b>Materials:</b>	$\beta$ -TCP granulate (particle sizes 500-1000 $\mu\text{m}$ and 1000-2000 $\mu\text{m}$ , > 99% $\beta$ -phase, 35 % microporosity). The mandibular defect was filled with coarse-grained material, a mixture of was used for fine-grained and coarse grained $\beta$ -TCP was used for the sinus floor augmentation.
<b>Number of Patients:</b>	2 patients (case reports)
<b>Investigation methods:</b>	Histological analysis 8 and 9.5 months after the interventions
<b>Complications:</b>	None reported

Füssinger, R. and K. Füssinger (2005) **Résultats cliniques et histologiques à long terme, après régénération osseuse avec du phosphate tricalcique  $\beta$  et mise en place d'implants** Le Chirurgien-Dentiste De France 1223: 1-5.

<b>Aim of the study:</b>	Assess the long-term stability of implants that have been inserted in bone augmented with $\beta$ -TCP.
<b>Materials:</b>	$\beta$ -TCP granules (particle size 500-100 $\mu$ m, > 99% $\beta$ -phase, micro and macroporous)
<b>Number of Patients:</b>	54 patients, 28 with sinus floor elevations and 26 with augmented alveolar ridges.
<b>Investigation methods:</b>	Assessment of implant survival 1-7 years after implantation, histological analysis
<b>Complications:</b>	$\beta$ -TCP granules were surrounded by connective tissue in two cases where an implant was lost. One of the patients was a strong smoker.

Zerbo, I. R., A. L. Bronckers, G. de Lange and E. H. Burger (2005) **Localisation of osteogenic and osteoclastic cells in porous beta-tricalcium phosphate particles used for human maxillary sinus floor elevation** *Biomaterials* 26(12): 1445-51.

<b>Aim of the study:</b>	Advancing the understanding of $\beta$ -TCP degradation and osteogenesis in the augmented sinus floor by analysis of cells with osteogenic and osteoclastic potential.
<b>Materials:</b>	$\beta$ -TCP granulate (particle size 1000-2000 $\mu$ m, > 99% $\beta$ -phase, 35 % microporosity)
<b>Number of Patients:</b>	12 patients
<b>Investigation methods:</b>	Histomorphometrical and immunohistochemical analysis 6 months after sinus floor elevation.
<b>Complications:</b>	None reported.

Knabe, C., C. Koch, A. Rack and M. Stiller (2008) **Effect of beta-tricalcium phosphate particles with varying porosity on osteogenesis after sinus floor augmentation in humans** *Biomaterials* 29(14): 2249-58.

<b>Aim of the study:</b>	Compare the performance of two $\beta$ -TCP ceramics with different porosities in the augmented sinus floor.
<b>Materials:</b>	Two different $\beta$ -TCP granulates (both > 99% $\beta$ -phase, particle size 1000-2000 $\mu$ m, round particles with 35% microporosity and polygonal with a bulk porosity of 65%) mixed with autologous bone chips from the maxillary tuberosity (ratio 4:1).
<b>Number of Patients:</b>	20 patients
<b>Investigation methods:</b>	Histomorphometrical and immunohistochemical methods 6 months after sinus floor elevation
<b>Complications:</b>	None reported

Wippermann, B. W., H. E. Schrott, S. Steeg and H. Tscherne (1997) **Komplikationen der Spongiosaentnahme am Beckenkamm Eine retrospektive Analyse von 1191 Fällen** *Der Chirurg* 68(12): 1286-1291.

<b>Aim of the study:</b>	Analyse the frequency of complications after autologous bone graft harvesting at the iliac crest.
<b>Number of Patients:</b>	A total of 1191 patients, 97 patients were reassessed
<b>Investigation methods:</b>	Clinical examination after 1 year
<b>Complications:</b>	Local irritation, discomfort 1 year after the intervention

Goulet, J. A., L. E. Senunas, G. L. DeSilva and M. L. Greenfield (1997) **Autogenous iliac crest bone graft. Complications and functional assessment** *Clin Orthop Relat Res*(339): 76-81.

<b>Aim of the study:</b>	Assessment of the functional outcome and complications after iliac crest bone grafting.
<b>Number of Patients:</b>	192 patients
<b>Investigation methods:</b>	Questionnaire (6 months and 2 years after the grafting)
<b>Complications:</b>	Infection (2.4 % of the patients), pain

Clavero, J. and S. Lundgren (2003) **Ramus or chin grafts for maxillary sinus inlay and local onlay augmentation: comparison of donor site morbidity and complications** Clin Implant Dent Relat Res 5(3): 154-60.

- Aim of the study:** Document and compare the morbidity and the frequency of complications occurring at two intraoral bone graft donor sites: the mandibular symphysis and the mandibular ramus.
- Number of Patients:** 53 patients
- Investigation methods:** Questionnaire 18 months after surgery
- Complications:** Decreased sensitivity and permanently altered sensation around the graft donor site after 18 months

Szabo, G., Z. Suba, K. Hrabak, J. Barabas and Z. Nemeth (2001) **Autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevations (2- and 3-dimensional computed tomographic, histologic, and histomorphometric evaluations): preliminary results** Int J Oral Maxillofac Implants 16(5): 681-92.

- Aim of the study:** Evaluation of  $\beta$ -TCP granules and autogenous bone in sinus floor elevation.
- Materials:**  $\beta$ -TCP granulate (> 99%  $\beta$ -phase, 35 % microporosity) and autologous bone
- Number of Patients:** 4 patients
- Investigation methods:** Radiological, histomorphometrical and immunohistochemical assessment
- Complications:** None reported in abstract

Suba, Z., D. Takacs, D. Matusovits, J. Barabas, A. Fazekas and G. Szabo (2006) **Maxillary sinus floor grafting with beta-tricalcium phosphate in humans: density and microarchitecture of the newly formed bone** Clin Oral Implants Res 17(1): 102-8.

- Aim of the study:** Evaluation of  $\beta$ -TCP granules and autogenous bone in sinus floor elevation.
- Materials:**  $\beta$ -TCP granulate (particle size 500-1000  $\mu$ m, > 99%  $\beta$ -phase, 35 % microporosity) and autologous bone graft from the iliac crest.
- Number of Patients:** 17 patients
- Investigation methods:** Histomorphometric analysis 6 months after sinus floor elevation
- Complications:** Epistaxis in 2 patients

Szabo, G., L. Huys, P. Coulthard, C. Maiorana, U. Garagiola, J. Barabas, Z. Nemeth, K. Hrabak and Z. Suba (2005) **A prospective multicenter randomized clinical trial of autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevation: histologic and histomorphometric evaluation** Int J Oral Maxillofac Implants 20(3): 371-81.

- Aim of the study:** Evaluation of  $\beta$ -TCP granules and autogenous bone in bilateral sinus floor elevation.
- Materials:**  $\beta$ -TCP granulate (> 99%  $\beta$ -phase, 35 % microporosity) and autologous bone graft from the iliac crest.
- Number of Patients:** 20 patients
- Investigation methods:** Clinical evaluation, 2- and 3-dimensional computerized tomographic examinations, histomorphometric analysis 6 months after sinus floor elevation
- Complications:** None reported in abstract

Zerbo, I. R., S. A. Zijdeveld, A. de Boer, A. L. Bronckers, G. de Lange, C. M. ten Bruggenkate and E. H. Burger (2004) **Histomorphometry of human sinus floor augmentation using a porous beta-tricalcium phosphate: a prospective study** Clin Oral Implants Res 15(6): 724-32.

<b>Aim of the study:</b>	Evaluation of $\beta$ -TCP granules and autogenous bone in sinus floor elevation.
<b>Materials:</b>	$\beta$ -TCP granulate (particle size 1000-2000 $\mu$ m, > 99% $\beta$ -phase, 35 % microporosity) and autologous bone from the symphysis area.
<b>Number of Patients:</b>	5 patients
<b>Investigation methods:</b>	Histomorphometrical analysis after 6 months
<b>Complications:</b>	None reported

Simunek, A., D. Kopecka, R. V. Somanathan, S. Pilathadka and T. Brazda (2008)

**Deproteinized bovine bone versus beta-tricalcium phosphate in sinus augmentation surgery: a comparative histologic and histomorphometric study** Int J Oral Maxillofac Implants 23(5): 935-42.

<b>Aim of the study:</b>	Evaluation of bone graft substitutes with and without addition of autologous bone.
<b>Materials:</b>	$\beta$ -TCP, Deproteinized bovine bone, autologous bone, both $\beta$ -TCP and deproteinized bovine bone combined with 10% and 20% autologous bone.
<b>Number of Patients:</b>	48 sinus lift procedures
<b>Investigation methods:</b>	Histomorphometrical analysis after 9 months
<b>Complications:</b>	None reported in abstract

#### 4.1.2. References: guided bone regeneration (GBR) using membranes

Hempton, T. J. and P. A. Fugazzotto (1994) **Ridge augmentation utilizing guided tissue regeneration, titanium screws, freeze-dried bone, and tricalcium phosphate: clinical report** Implant Dent 3(1): 35-7.

<b>Aim of the study:</b>	Report a case that shows alveolar ridge augmentation with a mixture of TCP and freeze-dried bone covered with PTFE-membrane.
<b>Materials:</b>	$\beta$ -TCP, demineralized freeze-dried human cortical bone, expanded PTFE-membrane
<b>Number of Patients:</b>	1 patient
<b>Investigation methods:</b>	Clinical examination 4 and 8 months after the augmentation
<b>Complications:</b>	None reported in abstract

Scher, E. L. and P. M. Speight (1996) **Bone augmentation and biopsy: clinical report** Implant Dent 5(4): 251-4.

<b>Aim of the study:</b>	Report an accident case where an anterior maxillar damage was augmented with a mixture of TCP and freeze-dried bone covered with PTFE-membrane.
<b>Materials:</b>	$\beta$ -TCP mixed with demineralized freeze-dried cortical bone, expanded titanium-reinforced PTFE-membrane
<b>Number of Patients:</b>	1 patient
<b>Investigation methods:</b>	Clinical examination, histological assessment 17 months after the intervention
<b>Complications:</b>	None reported in abstract

Fugazzotto, P. A., R. Shanaman, T. Manos and R. Shectman (1997) **Guided bone regeneration around titanium implants: report of the treatment of 1,503 sites with clinical reentries** Int J Periodontics Restorative Dent 17(3): 292, 293-9.

<b>Aim of the study:</b>	Evaluation of the GBR technique for the treatment of dehiscence and fenestration defects, and for the treatment of implants inserted into immediate extraction sockets.
<b>Materials:</b>	$\beta$ -TCP in combination with deminarlized freeze-dried bone allograft (DFDBA), a decalcified DFDBA, a freeze-dried bone allograft granules covered with a GoreTex membrane.

**Number of Patients:** 1503 sites treated  
**Investigation methods:** Clinical examination  
**Complications:** No complications resulting from the application of TCP are reported in the abstract.

#### 4.1.3. References: periodontal bone defects

Stahl, S. S. and S. Froum (1986) **Histological evaluation of human intrasosseous healing responses to the placement of tricalcium phosphate ceramic implants. I. Three to eight months** J Periodontol 57(4): 211-7.

**Aim of the study:** Histological examination of eight periodontal lesions treated with  $\beta$ -TCP.  
**Materials:**  $\beta$ -TCP (> 99%  $\beta$ -phase, micro and macroporous)  
**Number of Patients:** 4 patients, 8 periodontal lesions  
**Investigation methods:** Clinical examination, histological analysis  
**Complications:** Although a clinical attachment gain was reported, neither osteogenesis nor cementogenesis has been observed.

Froum, S. and S. S. Stahl (1987) **Human intrasosseous healing responses to the placement of tricalcium phosphate ceramic implants. II. 13 to 18 months** J Periodontol 58(2): 103-9.

**Aim of the study:** Histological examination of eight periodontal lesions treated with  $\beta$ -TCP.  
**Materials:**  $\beta$ -TCP (> 99%  $\beta$ -phase, micro and macroporous)  
**Number of Patients:** 4 patients, 8 periodontal lesions  
**Investigation methods:** Clinical examination, histological analysis  
**Complications:** Although a clinical attachment gain was reported, neither osteogenesis nor cementogenesis has been observed.

Baldock, W. T., L. H. Hutchens, Jr., W. T. McFall, Jr. and D. M. Simpson (1985) **An evaluation of tricalcium phosphate implants in human periodontal osseous defects of two patients** J Periodontol 56(1): 1-7.

**Aim of the study:** Report the treatment of human periodontal defects with  $\beta$ -TCP in 2 patients.  
**Materials:**  $\beta$ -TCP  
**Number of Patients:** 2 patients  
**Investigation methods:** Clinical and histological analysis after 3,6 and 9 months  
**Complications:** Although the clinical probing and radiographic results were promising, the histological analysis indicated that TCP did not stimulate new bone growth.

Palti, A. and T. Hoch (2002) **A concept for the treatment of various dental bone defects** Implant Dent 11(1): 73-8.

**Aim of the study:** Assess the clinical outcome of treatments with  $\beta$ -TCP granules.  
**Materials:**  $\beta$ -TCP granulate (> 99%  $\beta$ -phase, 35 % microporosity)  
**Number of Patients:** 267 patients, 958 dental bone defects  
**Investigation methods:** Clinical reports  
**Complications:** Fistula formation or complications that made an explantation necessary were reported in 21 cases.

Foitzik, C. and M. Stamm (1997) **Einsatz von phasenreinem beta-Tricalciumphosphat zur Auffüllung von ossären Defekten - Biologische Materialvorteile und klinische Erfahrungen** Quintessenz 48: 1365-1377.

**Aim of the study:** Report on the clinical experience with  $\beta$ -TCP granules for the treatment of periodontal bone defects.  
**Materials:**  $\beta$ -TCP granulate (> 99%  $\beta$ -phase, 35 % microporosity)

**Number of Patients:** 86 cases  
**Investigation methods:** Clinical evaluation, 20 months after the treatment  
**Complications:** "In most cases, good results were attained"

Foitzik, C. and H. Staus (1999) **Pure beta-tricalcium phosphate bone substitution in periodontal disease** Quintessenz 50(10): 1049-1058.

**Aim of the study:** Report on the clinical experience with β-TCP granules for the treatment of periodontal bone defects with and without membranes  
**Materials:** β-TCP granulate (> 99% β-phase, 35 % microporosity), resorbable membrane (Atrisorb®, Curasan)  
**Number of Patients:** about 1000  
**Investigation methods:** Clinical evaluation after 12 months  
**Complications:** A total failure rate of 8.24 % is reported

Foitzik, C. and H. Staus (1999) **Parodontale Defektauffüllung mit phasenreinem beta-Trikalziumphosphat** ZWR(6): 378-383.

**Aim of the study:** Report on the clinical experience with β-TCP granules for the treatment of periodontal and other bone defects.  
**Materials:** β-TCP granulate (> 99% β-phase, 35 % microporosity)  
**Investigation methods:** Clinical evaluation  
**Complications:** Occasionally, particles are not resorbed but encapsulated into connective tissue.

Bokan, I., J. S. Bill and U. Schlagenhauf (2006) **Primary flap closure combined with Emdogain alone or Emdogain and Cerasorb in the treatment of intra-bony defects** J Clin Periodontol 33(12): 885-93.

**Aim of the study:** Evaluation of enamel matrix derivative alone and in combination with β-TCP in the treatment of periodontal defects.  
**Materials:** β-TCP granulate (> 99% β-phase, 35 % microporosity), enamel matrix derivative (Emdogain®, Biora, Malmö, Sweden)  
**Investigation methods:** Assessment of clinical parameters (probing depth, attachment level, gingival recession, plaque index, gingival index) 1 year after the treatment.  
**Complications:** None reported

Dori, F., T. Huszar, D. Nikolidakis, D. Tihanyi, A. Horvath, N. B. Arweiler, I. Gera and A. Sculean (2008) **Effect of platelet-rich plasma on the healing of intrabony defects treated with Beta tricalcium phosphate and expanded polytetrafluoroethylene membranes** J Periodontol 79(4): 660-9.

**Aim of the study:** Evaluation of PRP on the healing of deep intrabony defects treated with β-TCP and covered with resorbable membranes.  
**Materials:** β-TCP granulate (250-1000 μm, > 99% β-phase, 35 % microporosity), expanded PTFE membrane (W.L. Gore), PRP  
**Number of Patients:** 28 patients  
**Investigation methods:** Assessment of clinical parameters like probing depth and gingival recession and the clinical attachment level after 1 year.  
**Complications:** None reported

Yassibag-Berkman, Z., O. Tuncer, T. Subasioglu and A. Kantarci (2007) **Combined use of platelet-rich plasma and bone grafting with or without guided tissue regeneration in the treatment of anterior interproximal defects** J Periodontol 78(5): 801-9.

**Aim of the study:** Comparison of β-TCP, β-TCP with PRP, and β-TCP with PRP combined with a membrane for the treatment of periodontal, interproximal, intrabony defects

<b>Materials:</b>	$\beta$ -TCP granulate (particle size 500-100 $\mu$ m, > 99% $\beta$ -phase, 35 % microporosity), collagen membrane (Bio-Gide®, Geistlich), PRP
<b>Number of Patients:</b>	25 patients with 30 lesions
<b>Investigation methods:</b>	Clinical parameters (plaque index, gingival index, periodontal probing depth, relative attachment level, transgingival probing measurement and radiographic analysis) after 6, 9 and 12 months.
<b>Complications:</b>	None reported.

#### 4.1.4. References: cystectomy

Zerbo, I. R., A. L. Bronckers, G. L. de Lange, G. J. van Beek and E. H. Burger (2001) **Histology of human alveolar bone regeneration with a porous tricalcium phosphate. A report of two cases** Clin Oral Implants Res 12(4): 379-84. See 4.1.1 References: sinus floor augmentation

Palm, F., C. Hilscher and M. Kind (2006) **Einsatz einer neuen synthetischen, phasenreinen  $\beta$ -TCP Keramik in der Mund-, Kiefer- und Gesichtschirurgie** Implantologie Journal 10(4).

<b>Aim of the study:</b>	Comparison of $\beta$ -TCP, $\beta$ -TCP with PRP, and $\beta$ -TCP with PRP combined with a membrane for the treatment of periodontal, interproximal, intrabony defects
<b>Materials:</b>	$\beta$ -TCP granulate (particle size 1000-2000 $\mu$ m, > 99% $\beta$ -phase, 35 % microporosity)
<b>Number of Patients:</b>	121 patients, 63 patients with 64 bone defects from cystectomy, 58 patients with 79 sinus lifts.
<b>Investigation methods:</b>	Clinical evaluation and histological analysis
<b>Complications:</b>	None reported

#### 4.1.5. References: other applications of $\beta$ -TCP in dentistry

Trisi, P., W. Rao, A. Rebaudi and P. Fiore (2003) **Histologic effect of pure-phase beta-tricalcium phosphate on bone regeneration in human artificial jawbone defects** Int J Periodontics Restorative Dent 23(1): 69-77.

<b>Aim of the study:</b>	Study the in vivo properties of $\beta$ -TCP granules in human artificial jawbone defects.
<b>Materials:</b>	$\beta$ -TCP granulate (> 99% $\beta$ -phase, 35 % microporosity)
<b>Number of Patients:</b>	5 volunteers
<b>Investigation methods:</b>	Histological analysis after 6 months
<b>Complications:</b>	None reported in abstract

Barkhordar, R. A. and J. R. Meyer (1986) **Histologic evaluation of a human periapical defect after implantation with tricalcium phosphate** Oral Surg Oral Med Oral Pathol 61(2): 201-6.

<b>Aim of the study:</b>	Report a case where $\beta$ -TCP was used to treat a periapical abscess.
<b>Materials:</b>	$\beta$ -TCP (> 99% $\beta$ -phase, micro and macroporous)
<b>Number of Patients:</b>	1 patient
<b>Investigation methods:</b>	Clinical evaluation and histological analysis
<b>Complications:</b>	Persistent infection and additional bone destruction

Palti, A. and T. Hoch (2002) **A concept for the treatment of various dental bone defects** Implant Dent 11(1): 73-8. See 4.1.3 References: periodontal defects

Horch, H. H., R. Sader, C. Pautke, A. Neff, H. Deppe and A. Kolk (2006) **Synthetic, pure-phase beta-tricalcium phosphate ceramic granules (Cerasorb) for bone regeneration in the reconstructive surgery of the jaws** Int J Oral Maxillofac Surg 35(8): 708-13.

<b>Aim of the study:</b>	Investigation of the long-term effect of $\beta$ -TCP at different sites.
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<b>Materials:</b>	$\beta$ -TCP granulate (500-2000 $\mu\text{m}$ , > 99% $\beta$ -phase, 35 % microporosity), mixed 1:1 with autologous bone from the retromolar area, the maxillary tuberosity, or the chin region if defect sizes exceeded 2 cm.
<b>Number of Patients:</b>	152 patients with 156 defects
<b>Investigation methods:</b>	Clinical evaluation and histological analysis up to 5 years after the intervention.
<b>Complications:</b>	9.2 % of the patients experienced some form of wound healing disturbance. Partial loss of the implanted material was seen in 5.9% of all cases, a total loss in 2%.

Füssinger, R. and K. Füssinger (2005) **Résultats cliniques et histologiques à long terme, après régénération osseuse avec du phosphate tricalcique  $\beta$  et mise en place d'implants** Le Chirurgien-Dentiste De France 1223: 1-5. See 4.1.1 References: *sinus floor augmentation*

Ormianer, Z., A. Palti and A. Shifman (2006) **Survival of immediately loaded dental implants in deficient alveolar bone sites augmented with beta-tricalcium phosphate** Implant Dent 15(4): 395-403.

<b>Aim of the study:</b>	Assessment of the survival of immediately loaded dental implants placed in deficient alveolar bone sites at grafting with $\beta$ -TCP.
<b>Materials:</b>	$\beta$ -TCP
<b>Number of Patients:</b>	338 patients with 1065 implants
<b>Investigation methods:</b>	Assessment of implant stability over a time period of 12-48 months.
<b>Complications:</b>	None reported in abstract

Thoma, K., G. F. Pajarola, K. W. Gratz and P. R. Schmidlin (2006) **Bioabsorbable root analogue for closure of oroantral communications after tooth extraction: a prospective case-cohort study** Oral Surg Oral Med Oral Pathol Oral Radiol Endod 101(5): 558-64.

<b>Aim of the study:</b>	Assessment of the clinical capacity of a bioresorbable root analog to close oroantral communications.
<b>Materials:</b>	Thermally moulded polylactide-coated $\beta$ -TCP-granules (particle size 500-1000 $\mu\text{m}$ , > 99% $\beta$ -phase, 55 % microporosity)
<b>Number of Patients:</b>	20 patients (14 patients were treated with polylactide-coated $\beta$ -TCP, 6 patients with mucoperiosteal flaps)
<b>Investigation methods:</b>	Clinical evaluation
<b>Complications:</b>	The root analog was lost in one patient after 5 days, which did not affect healing of the oroantral communication.

Brkovic, B. M., H. S. Prasad, G. Konandreas, R. Milan, D. Antunovic, G. K. Sandor and M. D. Rohrer (2008) **Simple preservation of a maxillary extraction socket using beta-tricalcium phosphate with type I collagen: preliminary clinical and histomorphometric observations** J Can Dent Assoc 74(6): 523-8.

<b>Aim of the study:</b>	Reporting a case where a cone made of a $\beta$ -TCP/collagen composite was used for alveolar socket preservation
<b>Materials:</b>	porous $\beta$ -TCP/collagen cone
<b>Number of Patients:</b>	1 patient
<b>Investigation methods:</b>	Clinical evaluation and histological analysis after 9 months.
<b>Complications:</b>	None reported

#### 4.1.6. References: application of $\beta$ -TCP together with autologous bone, platelet rich plasma (PRP) and recombinant growth factors

Aguirre Zorzano, L. A., M. J. Rodriguez Tojo and J. M. Aguirre Urizar (2007) **Maxillary sinus lift with intraoral autologous bone and B--tricalcium phosphate: histological and histomorphometric clinical study** Med Oral Patol Oral Cir Bucal 12(7): E532-6.

<b>Aim of the study:</b>	Assessment of the potential of a $\beta$ -TCP/autologous bone mixture for sinus floor elevation.
<b>Materials:</b>	$\beta$ -TCP granulate (> 99% $\beta$ -phase, 35 % microporosity), mixed in a ration of 2:1 or 5:1 with autologous bone collagen from the surgical site, collagen membrane (Bio-Gide®, Geistlich Biomaterials)
<b>Number of Patients:</b>	22 patients
<b>Investigation methods:</b>	Clinical evaluation, histological analysis, assessment of implant stability after 36 months.
<b>Complications:</b>	Rupture of the Schneiderian membrane in one patient.

Princ, G., M. Bert and J. C. Ifi (2006) **Utilisation du substitut osseux beta-phosphate tricalcique (beta-TCP) Résultats à 3 ans.** Le Chirurgien-Dentiste De France(1250/1251): 29-32.

<b>Aim of the study:</b>	Testing implant stability after sinus floor elevation
<b>Materials:</b>	$\beta$ -TCP granulate (> 99% $\beta$ -phase, 35 % microporosity) and autologous bone from the illiac crest, retromolar areas or the symphysis
<b>Number of Patients:</b>	10
<b>Investigation methods:</b>	Clinical evaluation, histological analysis after 6 months, assessment of implant stability
<b>Complications:</b>	Implant loss in one patients.

Simunek, A., D. Kopecka, R. V. Somanathan, S. Pilathadka and T. Brazda (2008) **Deproteinized bovine bone versus beta-tricalcium phosphate in sinus augmentation surgery: a comparative histologic and histomorphometric study** Int J Oral Maxillofac Implants 23(5): 935-42. See 4.1.1 References: sinus floor elevation

Nikolidakis, D., G. J. Meijer and J. A. Jansen (2008) **Sinus floor elevation using platelet-rich plasma and beta-tricalcium phosphate: case report and histological evaluation** Dent Today 27(5): 66, 68, 70; quiz 71.

<b>Aim of the study:</b>	Presentation of a case where $\beta$ -TCP was used in combination with allogeneic PRP for sinus floor augmentation.
<b>Materials:</b>	$\beta$ -TCP granulate (1000-2000 $\mu$ m, > 99% $\beta$ -phase, 35 % microporosity), PRP from 250 ml allogeneic blood
<b>Number of Patients:</b>	1
<b>Investigation methods:</b>	Clinical evaluation after 6 months and 1 year, histological analysis after 6 months
<b>Complications:</b>	None reported

Taner, T. U., D. Germec, N. Er and I. Tulunoglu (2006) **Interdisciplinary treatment of an adult patient with old extraction sites** Angle Orthod 76(6): 1066-73.

<b>Aim of the study:</b>	Present an interdisciplinary treatment of a patient with old, atrophied extraction sites.
<b>Materials:</b>	$\beta$ -TCP granulate (> 99% $\beta$ -phase, 35 % microporosity) combined with autologous from the maxillary tuberosity and PRP.
<b>Number of Patients:</b>	1
<b>Investigation methods:</b>	Clinical evaluation after 1 year
<b>Complications:</b>	None reported

Antoun, H., H. Bouk and G. Ameer (2008) **Bilateral sinus graft with either bovine hydroxyapatite or beta tricalcium phosphate, in combination with platelet-rich plasma: a case report** *Implant Dent* 17(3): 350-9.

**Aim of the study:** Comparison of the performance of β-TCP granulate and bovine hydroxyapatite in sinus floor augmentation.  
**Materials:** β-TCP granulate, bovine hydroxyapatite, PRP.  
**Number of Patients:** 1  
**Investigation methods:** Clinical evaluation, histomorphometric analysis after 6 months  
**Complications:** None reported in abstract

Yassibag-Berkman, Z., O. Tuncer, T. Subasioglu and A. Kantarci (2007) **Combined use of platelet-rich plasma and bone grafting with or without guided tissue regeneration in the treatment of anterior interproximal defects** *J Periodontol* 78(5): 801-9. See 4.1.1  
*References: sinus floor augmentation*

Christgau, M., D. Moder, K. A. Hiller, A. Dada, G. Schmitz and G. Schmalz (2006) **Growth factors and cytokines in autologous platelet concentrate and their correlation to periodontal regeneration outcomes** *J Clin Periodontol* 33(11): 837-45.

**Aim of the study:** Determination of the concentration of naturally available biological mediators in autologous platelet concentrates and their correlation with periodontal regeneration outcome  
**Materials:** β-TCP granulate (β-TCP, bulk porosity 60%) autologous platelet concentrate, bioresorbable membrane (ResolutXT, W.L. Gore).  
**Number of Patients:** 25 patients with 2 periodontal defects per patient  
**Investigation methods:** Evaluation of clinical parameters and estimation of the bone density by radiological methods (vertical relative attachment gain) after 3, 6 and 12 months  
**Complications:** None reported

Dori, F., T. Huszar, D. Nikolidakis, D. Tihanyi, A. Horvath, N. B. Arweiler, I. Gera and A. Sculean (2008) **Effect of platelet-rich plasma on the healing of intrabony defects treated with Beta tricalcium phosphate and expanded polytetrafluoroethylene membranes** *J Periodontol* 79(4): 660-9. See 4.1.3 *References: periodontal bone defects*

Byun, H. Y. and H. L. Wang (2008) **Sandwich bone augmentation using recombinant human platelet-derived growth factor and beta-tricalcium phosphate alloplast: case report** *Int J Periodontics Restorative Dent* 28(1): 83-7.

**Aim of the study:** Presentation of a case where β-TCP was used in combination with rhPDGF-BB to augment a buccal fenestration defect.  
**Materials:** β-TCP, rhPDGF-BB, collagen membrane.  
**Number of Patients:** 1 patient  
**Investigation methods:** Clinical evaluation during a second stage surgery 5 months after the intervention.  
**Complications:** None reported in abstract

Ridgway, H. K., J. T. Mellonig and D. L. Cochran (2008) **Human histologic and clinical evaluation of recombinant human platelet-derived growth factor and beta-tricalcium phosphate for the treatment of periodontal intraosseous defects** *Int J Periodontics Restorative Dent* 28(2): 171-9.

**Aim of the study:** Evaluation of β-TCP in combination with rhPDGF-BB in the treatment of periodontal intraosseous defects.  
**Materials:** β-TCP combined with rhPDGF-BB (0.3 and 1.0 mg/ml)  
**Number of Patients:** 16  
**Investigation methods:** En bloc removal and histological analysis of the treated teeth after a minimum healing period of 6 months.  
**Complications:** None reported in abstract.

Nevins, M., W. V. Giannobile, M. K. McGuire, R. T. Kao, J. T. Mellonig, J. E. Hinrichs, B. S. McAllister, K. S. Murphy, P. K. McClain, M. L. Nevins, D. W. Paquette, T. J. Han, M. S. Reddy, P. T. Lavin, R. J. Genco and S. E. Lynch (2005) **Platelet-derived growth factor stimulates bone fill and rate of attachment level gain: results of a large multicenter randomized controlled trial** J Periodontol 76(12): 2205-15.

**Aim of the study:** Evaluation of the safety and effectiveness  $\beta$ -TCP combined with rhPDGF-BB in the treatment of periodontal defects in a large multicenter study.

**Materials:**  $\beta$ -TCP combined with rhPDGF-BB (0.3 and 1.0 mg/ml)

**Number of Patients:** 180

**Investigation methods:** Assessment of clinical parameters (clinical attachment levels, gingival recession, linear bone growth) and radiographical estimation of the bone fill after 3 and 6 months.

**Complications:** No serious adverse events were reported

#### 4.2. References: conclusions

Knabe, C., C. Koch, A. Rack and M. Stiller (2008) **Effect of beta-tricalcium phosphate particles with varying porosity on osteogenesis after sinus floor augmentation in humans** Biomaterials 29(14): 2249-58. See 4.1.1 References: sinus floor augmentation

Gauthier, O., J. M. Bouler, E. Aguado, P. Pilet and G. Daculsi (1998) **Macroporous biphasic calcium phosphate ceramics: influence of macropore diameter and macroporosity percentage on bone ingrowth** Biomaterials 19(1-3): 133-9.

**Aim of the study:** Determine the influence of macropores on bone ingrowth into calcium phosphate ceramics.

**Materials:** macroporous biphasic calcium phosphate ceramics

**Investigation methods:** The ceramics were implanted into a distal femoral site of 30 rabbits. Bone ingrowth was analyzed by backscattered electron microscopy.

Mastrogiacomo, M., S. Scaglione, R. Martinetti, L. Dolcini, F. Beltrame, R. Cancedda and R. Quarto (2006) **Role of scaffold internal structure on in vivo bone formation in macroporous calcium phosphate bioceramics** Biomaterials 27(17): 3230-7.

**Aim of the study:** Analysis of the role of density and pore interconnection pathway in scaffolds to be used as bone substitutes.

**Materials:** Two hydroxyapatite ceramics with identical microstructure and different macropore structures.

**Investigation methods:** Implantation of hydroxyapatite loaded with osteoprogenitor cells into immunodeficient mice. Histological analysis after 2, 4 and 8 weeks.

## 5. Disclaimer

Although Degradable Solutions AG takes all possible care to ensure the correctness of this literature review about the application of  $\beta$ -TCP in oral surgery and dental fields, no warranty can be accepted regarding the correctness, accuracy, up-to-dateness, reliability and completeness of the content of this information.

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