Original Article

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# Healing of dehiscence defect around implants using β-tricalcium phosphate/calcium sulfate versus conventional guided bone regeneration: a pilot study

Aksornsan Pongsettakul[1], Narit Leepong[2], Srisurang Suttapriyasri[2]

[1] *Master of Science Program in Oral and Maxillofacial Surgery and Implantology, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Prince of Songkla University, Hatyai, Songkhla, Thailand*

[2] *Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Prince of Songkla University, Hatyai, Songkhla, Thailand*

Objectives: To evaluate and compare the healing outcomes of buccal dehiscence defects around dental implants using beta-tricalcium phosphate calcium sulfate (β-TCP/CS) and deproteinized bovine bone mineral mixed with a collagen membrane (DBBM/CM).

Materials and Methods: Two distinct groups were established for the study: the β-TCP/CS group (n=5) and the DBBM/CS group (n=5). The clinical evaluation was assessed by comparing the percentage of total volume alteration between pre-operative and 6 months post-operative 3D analyses. Radiological evaluations were conducted to assess bone graft thickness at the implant placement date and after a 6-month healing period.

Results: Both groups exhibit uneventful defect healing and 100% implant survival after 6-month healing period. Regarding the total volume alteration at the grafted site, β-TCP/CS exhibited 5.10%±2.32 alteration, while DBBM/CM exhibited 6.04%±3.07 alteration and no statistically significant difference ($p$>0.05) was observed. In Cone Beam Computed Tomography radiographic measurement, buccal bone thickness at 6 months at the platform level (BT0), 2mm (BT2), and 4mm (BT4) from the platform level after 6 months were 0.65±0.39 mm, 1.25±0.75 mm, and 2.79±0.37 mm in the β-TCP/CS group. For the DBBM/CM group, the corresponding values were 0.93±0.38 mm, 2.73±0.39 mm, and 3.22±0.99 mm, respectively. A statistically significant difference was observed between the two groups at BT2 ($p$=0.004). The percentage of bone graft thickness alteration at various points (%ΔBT0, %ΔBT2, and %ΔBT4) in the β-TCP/CS group showed 65.38%±20.44,58.49%±26.86 and 33.10%±18.28 respectively, when compared to the DBBM/CM group, where the corresponding values were 48.71%±26.03, 19.78%±9.29 and 8.72%±7.34 with a significant difference at %ΔBT2($p$=0.016) and %ΔBT4($p$=0.024).

Conclusions: β-TCP/CS demonstrated comparable overall clinical healing of small dehiscence defects around implants. However, β-TCP/CS resulted in greater graft reduction and less bone graft stabilization at 6-month follow-up.

Keywords: beta-tricalcium phosphate calcium sulfate, buccal dehiscence defect, deproteinized bovine bone, guided bone regeneration

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## Introduction

In contemporary dentistry, dental implants have emerged as a successful and viable alternative for the restoration of missing teeth. The quantity and quality of bone encompassing the implant play pivotal roles in determining the efficacy of dental implant therapy. Nonetheless, the natural process of alveolar bone resorption, particularly six months post-tooth extraction [1], inevitably impacts the outcome of dental implant placement.

Corresponding author: Aksornsan Pongsettakul
Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Prince of Songkla University
Hat Yai, Songkhla 90110, Thailand
Tel: +667 428 7596, +668 3186 1479
E-mail: pmiogo.moo@gmail.com
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A previous study indicated that over 40% of implant locations required bone graft augmentation [2]. Guided Bone Regeneration (GBR) has become a frequently employed treatment approach to attain the requisite bone volume for dental implant coverage [3-5]. Within GBR, barrier membranes in conjunction with particulate bone grafts are employed to direct the formation of new bone. According to a meta-analysis by Thoma DS *et al.* 2019 [6], xenogeneic bovine bone graft particles and resorbable membranes are currently the most popular materials for treating peri-implant bone deficiencies. In addition, many studies used demineralized bovine bone mineral with a resorbable membrane as a control standard for comparing various types of materials or techniques. Despite their widespread use as a result of their simplicity of application and lack of quantity restrictions, the same study [6] indicated that these materials did not significantly enhance peri-implant defect resolution. Noteworthy limitations of xenografts with resorbable membranes encompass the potential for buccal bone graft collapse at the platform level and associated risks of disease transmission. Furthermore, the combined use of multiple materials may potentially escalate patient costs and prolong recovery times.

Recently, a novel alloplastic bone substitute composed of calcium sulfate and beta-tricalcium phosphate has been developed, offering advantages in terms of biodegradability and facilitating minimally invasive bone reconstruction [7]. Additionally, this newly devised material has been suggested to possess the capability for bone grafting in the context of Guided Bone Regeneration (GBR) procedures, eliminating the need for a membrane [8-10]. This notion is substantiated by the ability of calcium sulfate to shield fibroblast cells from infiltration by the self-hardening interlocking rod structure that forms upon material setting [11]. Nevertheless, this material still lacks comprehensive clinical research, despite earlier studies [8,12-14] demonstrating its potential in fostering positive bone regenerating outcomes.

The objectives of this study were to assess and compare the healing outcomes of buccal dehiscence defects surrounding dental implants using beta-tricalcium phosphate calcium sulfate (βTCP/CS) and deproteinized bovine bone mineral combined with a collagen membrane (DBBM/CM) by using total volume 3D analysis and CBCT bone thickness analysis for assessment.

## Materials and Methods

The pilot study was designed as a prospective, randomized, controlled clinical trial. The study protocol received approval from the Research Ethics Committee at the Faculty of Dentistry, Prince of Songkla University, Songkhla, Thailand (EC6402-009).

### Patient selection

Patients ranging in age from 20 to 65 years, who are in good general health and require single posterior dental restoration, wherein an infrabony small buccal dehiscence defect measuring 2–5 mm is suspected during implantation, and with an adequate amount of keratinized tissue, were included. Patients with severe systemic diseases, chronic periodontitis affecting adjacent teeth, medication interfering with bone or soft tissue healing, pregnancy, and heavy smokers (consuming 10 or more cigarettes per day) were excluded.

### Patients' allocation method

Based on the aforementioned inclusion criteria, all patients were selected from the oral and maxillofacial clinic at Prince of Songkla University. Block randomization was used to divide 10 patients into 2 groups at random. The block randomization used in this investigation was created using generated by website at http://www.randomization.com.

## Pre-surgical procedures

Intraoral scans using an intraoral 3D scanner (TRIOS®,3Shape Dental Systems, Copenhagen, Denmark) and cone-beam computed tomography (CBCT) (Morita Co., Tokyo, Japan) were performed. The CBCT images were transferred to implant planning software One Volume Viewer (J Morita Manufacturing) to simulate the implant position and forecast the bone defect.

## Surgical procedure

Prior to surgery, patients were administered oral antibiotics (1000 mg Amoxicillin) and a mouth rinse containing 0.12% chlorhexidine for one minute. Under local anesthesia (4% Articaine hydrochloride, Ubistesin 1:200,000; 3M ESPE, Platz, Seefeld, Germany), the implant osteotomy site was prepared according to a manufacturer' s protocol. Briefly, a full thickness flap was raised, for the β-TCP/CS group minimal flap releasing was considered to reduce the bleeding from the surgical site, which may affect the setting time of the material. The osteotomy site was implanted with the ITI Dental Implant System (Institute Straumann®, Waldenburg, Switzerland) according to the manufacturer's protocol. After implant placement, defects were identified and treated with the allocated materials for each group.

In the β-TCP/CS group, the defect was filled with ethOss® (ethOss®, Regeneration Ltd. 8 Ryefield Court, Silsden, UK; 65% β-TCP and 35% CS) mixed with standard sterile saline (0.9% Sodium Chloride) to create a paste within the syringe package. This paste was then applied to the peri-implant defect site.

In the DBBM/CM (control) group, the defect was filled with demineralized bovine bone mineral (Bio-Oss®, Geistlich AG, Wolhusen, Switzerland; granule size 0.25-1.0 mm; 0.5 g ~ 1 cc) until reaching the desired quantity. A resorbable collagen membrane (Bio-Gide®, Geistlich Pharma, Wolhusen, Switzerland) was then used to cover the defects and secured with two titanium tacks for stabilization.

Vicryl® 4-0 (Ethicon, Somerville, NJ, USA) was utilized for flap closure in both groups as the primary closure method once the grafting procedure was completed. Post-surgery, patients were prescribed nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics (Amoxicillin 500 mg), and a mouthwash containing 0.12% chlorhexidine. Each medication was prescribed for a seven-day duration.

## Follow-up visits

At baseline (T0), surgical procedure (T1), 2 weeks, 1 month, 3 months and 6 months (T2) follow-up intraoral clinical examinations were planned for all patients.

## Quantitative sssessment of total volume

The alveolar ridge was subjected to sequential scanning at the pre-operative stage (T0) and six months postoperatively (T2). Intraoral scanning was performed using the Intraoral 3D scanner (TRIOS®, 3Shape Dental Systems, Copenhagen, Denmark) in accordance with the manufacturer's protocols, thereby generating STL files. Utilizing surface-matching software (Geomagic® Control X 3D measuring software). The Region of Interest (ROI) was extracted from the merged files using adjacent teeth near the grafted site as a reference. Subsequently, after merging the two files, the 3D file with superimposed data was segmented to isolate only the grafted area for calculating dimensional changes. The change in total volume was expressed as a percentage and in a variety of color tones from the 3D superimposed picture.

### Radiographic Measurements

**Buccal bone thickness**

CBCT scans were promptly conducted post-operatively (T1) and at the six-month mark (T2) utilizing the 3D Accuitomo 170 by J. Morita, Kyoto, Japan, under meticulously specified parameters. Access to the CBCT images was facilitated through the One Volume Viewer interface. Reference markers were established from the coronal slice orientation of the CBCT, utilizing the implant center as a cardinal reference point. Assessment of mid-buccal bone thickness transpired at three discrete levels: the implant platform (BT0), 2mm (BT2), and 4mm (BT4) distance from the implant platform reference (yellow line) Figure 1, aligned in the buccal orientation perpendicular to the implant surface.

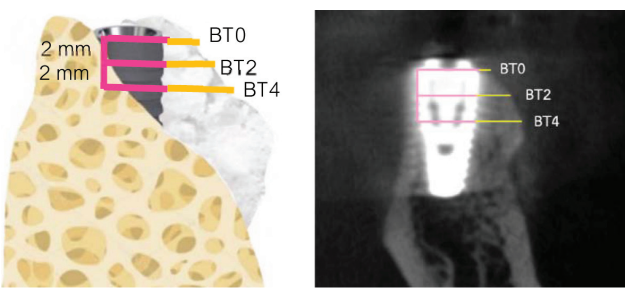


Figure 1 Radiographic measurements of buccal bone thickness. The vertical reference lines aligned with the implant center, in conjunction with horizontal lines at three specific levels ; at implant platform(BT0), 2- mm (BT2), and 4-mm (BT4) below the platform level.

### Statistical analysis

Data presentation encompassed mean values alongside their corresponding standard deviations. The statistical analysis was executed employing IBM SPSS (version 25, SPSS, Chicago, IL, USA). Distribution normality underwent verification via the Shapiro-Wilk test. Distinctions between groups were ascertained through either independent t-tests or the Mann-Whitney test. A significance level of $p< 0.05$ was established to denote statistical significance.

## Results

All implants showed a 100% survival rate. The study comprised ten patients (6 males, 4 females), encompassing 10 implant sites, with an average age of 53.3±12.25 years. Clinically, the majority of implants in this study were completed defect fill. The demographic data and baseline clinical defects of the participants involved in the study are presented in Table 1. There were no statistically significant differences observed between the two groups ($p>0.05$)

### The total volume alteration

In general, the differentiation of the volume presented in the color mapping from the generated picture from the software as shown in Figure 2. The overall mean total volume change between the 2 groups shows no statistical difference.

Table 1 Demographic data and baseline clinical defect between the two groups, with the mean and SD of the difference.

| Characteristic | β-TCP/CS (N =5) | DBBM/CM (N =5) | *p*-value |
|---|---|---|---|
| Age, (years) Mean ± *SD.* | 56.6±10.53 | 50.0±14.12 | $p = 0.991$ |
| Sex (%) | | | $p = 0.527$ |
| Male | 4 (80%) | 2 (40%) | |
| Female | 1 (20%) | 3 (60%) | |

(a)

(b)

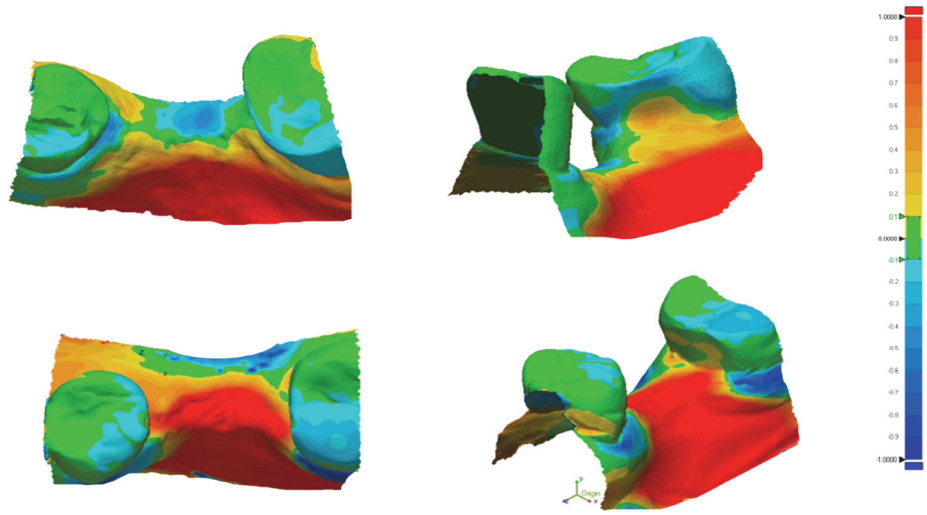

Figure 2 The pictures illustrate the dimensional changes of superimposed STL files from pre-operation and 6 months post operation. Each color mapping area represented a different level of volume thickness, which was interpreted using the bar color chart on the right site. (a) Sample case from β-TCP/CS; (b) Sample case from DBBM/CM group.

The percentage of total volume alteration in the β-TCP/CS group was 5.10%±2.32, while in the DBBM/CM group was 6.04%±3.07. No statistically significant difference in the percentage of total volume change was observed between the two groups ($p$=0.598) (Table2).

## Radiographic measurements: Buccal bone thickness

At baseline the bone graft thickness augmentation showed no statistical difference in any level from the platform. The average bone thickness at six months (T2) in the β-TCP/CS group was documented as 0.65 ± 0.39 mm at BT0, 1.25 ± 0.75 mm at BT2, and 2.79 ± 0.37 mm at BT4. In the DBBM/CM group, the corresponding values were 0.93±0.38 mm, 2.73±0.39 mm, and 3.22±0.99 mm, respectively. Notably, a significant difference was found between the two groups at the 2 mm level (BT2) from the implant platform ($p$=0.004). In β-TCP/CS, the percentage of bone graft thickness alteration at platform level (%ΔBT0) was 65.38%±20.44, platform to 2 mm (%ΔBT2) was 58.49%±26.86 and 33.10%±18.28 in platform level to 4 mm (%ΔBT4). In DBBM/CM group the corresponding value were 48.71%±26.03, 19.78%±9.29 and 8.72%±7.34, respectively. There are statistical differences between the two groups in %ΔBT2 ($p$=0.016) and %ΔBT4 ($p$=0.024) (Table 3, Figure 3).

Table 2 The mean total volume reduction from baseline to 6 months compared between β-TCP/CS and DBBM/CM groups.

| Group | β-TCP/CS (n=5) | DBBM/CM (n=5) | *p*-value |
|---|---|---|---|
| Percentage of Total volume alteration | 5.10%±2.32 | 6.04% ±3.07 | 0.598 |

Table 3 The buccal bone thickness parameter from immediate after surgery to 6 months re-entry and alteration of bone graft, with mean and SD. *Significant difference between the two groups.

| Radiographic: Bone thickness parameter | | β-TCP/CS (n=5) | DBBM/CM (n=5) | *p*-value |
|---|---|---|---|---|
| Buccal bone thickness baseline (mm.) | BT0 (T1) | 1.87± 0.65 | 2.09 ± 0.81 | 0.652 |
| | BT2 (T1) | 3.42±1.24 | 2.94±0.97 | 0.521 |
| | BT4 (T1) | 4.39±1.09 | 3.56±1.23 | 0.293 |
| Buccal bone thickness (mm.) | BT0 (T2) | 0.65±0.39 | 0.93±0.38 | 0.285 |
| | BT2 (T2) | 1.25±0.75 | 2.73±0.39 | 0.004* |
| | BT4 (T2) | 2.79±0.37 | 3.22 ±0.99 | 0.384 |
| Percentage of buccal bone thickness alteration (%) | %ΔBT0 | 65.38±20.44 | 48.71±26.03 | 0.293 |
| | %ΔBT2 | 58.49±26.86 | 19.78±9.29 | 0.016* |
| | %ΔBT4 | 33.10±18.28 | 8.72±7.34 | 0.024* |

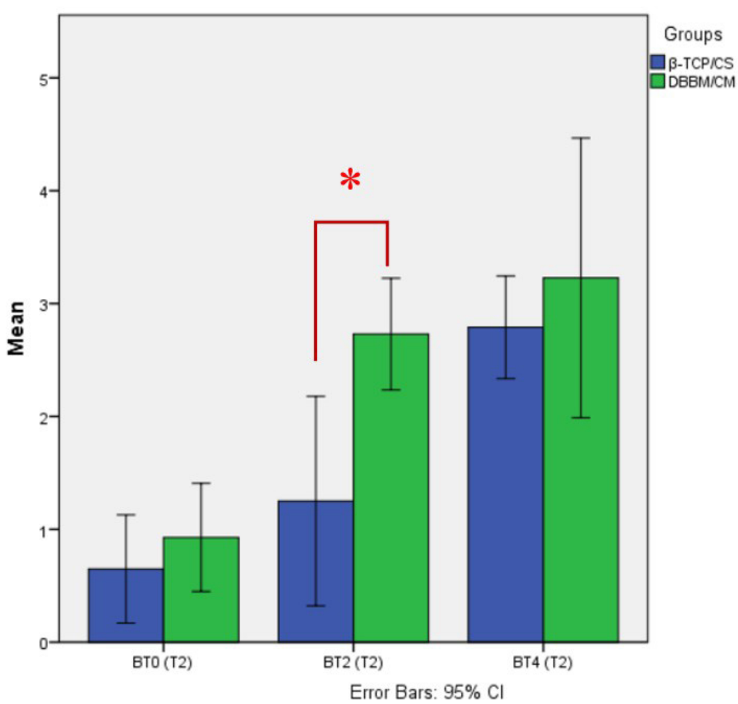


Figure 3 The bar graphs demonstrated a comparison of the mean buccal bone thickness at 6 months.
* $p< 0.05$: statistically significant difference

## Discussion

Guided Bone Regeneration (GBR) serves as a reliable approach for facilitating bone regeneration around dental implants. The standard technique commonly employs xenografts accompanied by resorbable collagen membranes; however, these materials bear the drawback of necessitating multiple surgical procedures, thereby increasing both cost and duration. This study's objective entailed a comparison of the clinical and radiographic outcomes of post peri-implant dehiscence defect augmentation between β-TCP/CS and conventional GBR utilizing DBBM with a collagen membrane.

From the clinical point, majority of the cases in both groups present complete heal at the buccal defect. Based on this preliminary data, the percentages of clinical total volume change from 3D analysis exhibited comparability. There was no significant difference between the two groups in terms of total volume change. However, these changes must be interpreted with caution due to the fact that these results depended on the volumes of the underlying hard and soft tissues, which may demonstrate a smaller change than the sole result of bone volume. In addition, the present study did not specify the tissue biotype of the patients enrolled in the study which could be effect on total volume differentiation. A study by Basler T *et al.* in 2018 [15] observed 3 years of dimensional change of total volume after implant and GBR with either resorbable or non-resorbable membrane. The authors revealed that only minor changes in the total dimensional change in both groups and peri-implant tissues are still ongoing changes after crown insertion. In this investigation, the total volume reduction was only determined six months after surgery. Consequently, these results may require an extended duration to obtain the variation of the difference.

In this study, the alteration in bone thickness in both groups exhibited the most reduction in bone graft thickness at the platform level, with no statistically significant difference between β-TCP/CS and DBBM/CM groups. A previous in-vitro study by Mir-Mari *et al*. in 2016 [16] indicated that the volume stability of the augmented site relies on the method of stabilization and wound closure. They revealed that bone thickness in the coronal region predominantly experienced collapse following augmentation with a resorbable membrane. Corresponding to the findings of the present study, it may be inferred that primary flap closure exerted an influence on the bone thickness at the platform level in both β-TCP/CS and DBBM/CM groups.

In the current study, the use of β-TCP/CS resulted in a greater reduction in graft thickness than the application of xenograft particles covered with a resorbable membrane. The β-TCP/CS is a bioresorbable material; the material in our study is a combination of 65% β-TCP and 35% CS; both of these materials have rapid resorption properties [17-18], particularly the calcium sulfate component, which functions as a membrane but can withstand only an approximate 8 weeks [19]. Despite the company's assertion that CS could offer graft stabilization, it is noteworthy that calcium sulfate undergoes rapid resorption within 1–3 months [19-20] which is faster than the rate of new bone formation [20-21]. Moreover, the influence of flap manipulation within the β-TCP/CS group, where minimal flap reflection was recommended due to the necessity of controlling bleeding from nearby areas, might impact graft hardening capabilities [22-23]. This minimal flap operation could potentially result the negative impact on bone graft compression, especially when combined by the β-TCP and CS resorption properties, thus leading to a more pronounced loss of thickness over time.

According to previous studies [3] [11], the buccal bone thickness surrounding an implant should be at least 1–2 mm for long-term aesthetic and functional outcomes. Corresponding to our study which found that all levels of bone thickness gain in the DBBM/CM group were adequate for implant coverage, whereas in β-TCP/CS group, the average bone thickness at platform, 2mm, and 4mm from the platform were in the β-TCP/CS group was documented as 0.65 ± 0.39 mm at BT0, 1.25 ± 0.75 mm at BT2, and 2.79 ± 0.37 mm at BT4, respectively. This result, particularly at the platform level, may affect the clinically exposed implant surface in a long-term situation. Similar to the study of Fu JH *et al.*, 2014 [24] that also reported the mean bone thickness gain at the platform level of the implant was 0.04 ± 0.28 mm, which is augmented by Sandwich bone graft augmentation (SBA) technique by using allograft with pericardium membrane. However, a prior study from Jung RE, 2017 [25] found that even when small defects (5mm) around the implant site were present, there was still a high survival rate with strong and stable soft tissues after an 18-month follow-up. In our study, at the 6-month follow-up time point, all implants in the test group had a 100% survival rate with stable soft tissue coverage. However, this still does not prove the material efficacy; more long-term follow-up and more clinical case observed is still required.

Due to the limitations of this study, an analysis of the quality of new bone formation through the harvest of additional bone for histological assessment was not feasible. Regarding the clinical and radiographic findings, it could be considered that this material has the potential to offer cost and time savings for both patients and dental professionals. Further investigations may be required to thoroughly determine the effectiveness and appropriateness of this material for facilitating bone regeneration.

## Conclusion

From the results, it can be inferred that β-TCP/CS exhibited clinical effectiveness in facilitating healing within small dehiscence defects around the implant, comparable to the utilization of xenograft particles combined with a resorbable membrane. This material offers advantages in terms of cost and time savings, along with simplified handling. However, it's important to note that β-TCP/CS exhibited a higher degree of graft reduction and lower graft stabilization, this may depend on graft manipulation and flap closure factors. Further clinical investigations and long-term follow-up are essential to identify and enhance the factors that could potentially influence the observed outcomes.

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