PERFORMANCE OF β-TRICALCIUM PHOSPHATE BONE SUBSTITUTE WHEN TREATED WITH BONE MARROW ASPIRATE

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Introduction

Synthetic ceramic bone substitutes have evolved as alternatives to the use of autograft or allograft tissues. Ceramics are osteconductive, but are not osteogenic or osteoinductive when used alone. The technique of combining ceramics with autologous bone marrow aspirate may provide an effective method of improving bone healing by imparting osteogenic and/or osteoinductive qualities to ceramic bone substitutes.[1-3]

Objective

Determine if autologous bone marrow increases the rate of osseous healing when combined with a highly porous ceramic bone substitute.

Materials and Methods

A resorbable β-TCP bone substitute was produced using the TheriForm™ 3D fabrication process (Fig 1). The implant was composed of multiple 5x5x3mm crosses, which had a mean pore diameter of 60μm and range of 7-640μm, and a packed porosity of 70% (Fig 2).

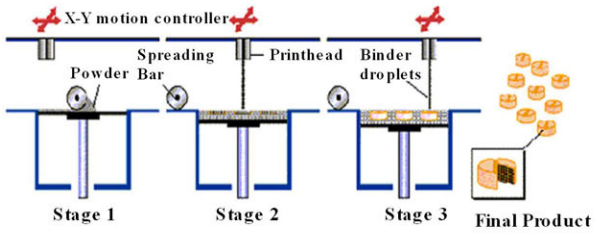

Figure 1. Diagram of the TheriForm™ process

Figure 2. The implant device was composed of multiple ceramic crosses (5x5x3mm).

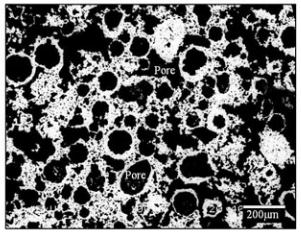

Figure 3. SEM image of device cross-section. The internal structure of the device is a highly porous, open network.

Table 1. In Vivo Study Design

Timepoint	Comparison	N	Analysis
Week 6	β-TCP vs. β-TCP & Marrow	5	Histology
Week 12	β-TCP vs. β-TCP & Marrow	6	Histology

A bilateral proximal humeral defect (5cm deep x 1.3cm diameter) was created in eleven canines[4]. Left humeral defects were filled with 5cc β-TCP implant and right humeral defects were filled with 5cc β-TCP implant that had been combined with 3cc of autologous marrow aspirated from the iliac crest.

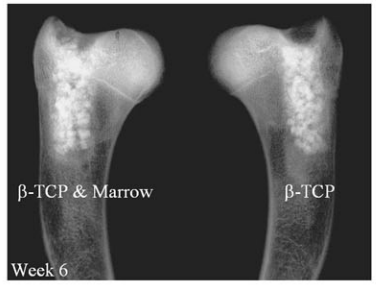

Figure 4. Radiograph of Week 6 explants. Implant material can be seen filling the defect. Each animal received both treatments to minimize variability.

At Week 6 or 12, animals were sacrificed and three transverse histological sections were produced from each defect site and stained with toluidine blue (Skeletech, Bothell, WA). Sections were graded histopathologically for tissue reaction and osteogenesis, and the percent of the defect occupied by new bone and residual implant material were measured using histomorphometric techniques. Treatments were compared using a two-tailed paired t-test for means at a significance level of $p < 0.05$.

Results

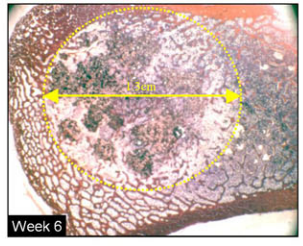

Figure 5. Typical Week 6 section. Bone ingrowth observed throughout the defect and into the implant (gray).

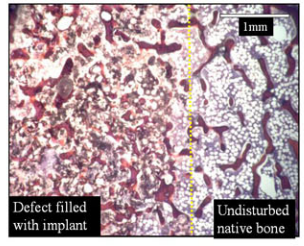

Figure 6. Week 12 section showing bone ingrowth and marrow development within the treated defect.

Table 2. Histopathological Analysis

	Tissue Reaction Score		Osteogenesis Score	
Timepoint	β-TCP	β-TCP & Marrow	β-TCP	β-TCP & Marrow
Week 6	7.5 ± 1.9	7.5 ± 1.9	2.5 ± 0.4	2.8 ± 0.3
Week 12	4.5 ± 1.5	4.5 ± 1.5	2.5 ± 0.6	2.5 ± 0.4

Sections were scored for tissue reaction using a 0-15 scale; higher scores indicate an increased level of reaction. Ostegenesis was scored on a 0-3 scale; higher scores indicate an increased level of osteogenic activity. Tissue reaction decreased significantly for both treatments from Week 6 to 12. There were no significant differences between the treatments for tissue reaction or osteogenic activity.

Table 3. Histomorphometric Analysis

	New Bone		Residual Material	
Timepoint	β-TCP	β-TCP & Marrow	β-TCP	β-TCP & Marrow
Week 6	16.7 ± 4.7	18.5 ± 5.4	28.4 ± 6.4	30.2 ± 4.1
Week 12	17.1 ± 4.3	17.6 ± 3.4	20.1 ± 5.3	21.6 ± 5.5

The percent of the defect area filled with new bone (mineralized tissue) and residual implant material was measured using histomorphometric techniques. There were no significant differences in new bone between Week 6 and 12, nor between treatments. Both treatments had levels of mineralized tissue similar to surrounding native bone (12-21%) by Week 6. The amount of residual material did decrease significantly for both treatments from Week 6 to 12; however, there were no significant differences between β-TCP alone or combined with marrow.

Discussion

There were no significant differences between the treatments: β-TCP or β-TCP combined with marrow as measured by tissue reaction, osteogenic activity, percent new bone, or percent residual material within the defect at Week 6 or 12.

Possible factors:

- Healing benefits of marrow addition may have diminished by Week 6
- Defect site has rich supply of local marrow; β-TCP only treatment may have wicked local marrow
- Porous β-TCP device already enhances healing
- Marrow addition does not impart osteogenic qualities

Both treatments had moderate tissue reaction scores at Week 6, which is anticipated for such treatments; however, tissue reactions declined by Week 12. This decline is likely related to the decrease in the amount of residual implant material.

References

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4. Turner TM, Urban RM, Gitelis S, Kuo KN, Andersson GBJ. Radiographic and histologic assessment of calcium sulfate in experimental animal models and clinical use as a resorbable bone-graft substitute, a bone-graft expander, and a method for local antibiotic delivery. J Bone and Joint Surg 2001:83A;8-18.