One Year Evaluation of a PCL-TCP Putty In an Ovine Critical Sized Metaphyseal Defect Model.

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Statement of Purpose: Using a well-established metaphyseal defect model in sheep, the primary objective of this study was to evaluate the long-term in-vivo characteristics and local biocompatibility of two different formulations of poly ε-caprolactone / β-tricalcium phosphate composites and their controls, poly ε-caprolactone and a β-tricalcium phosphate.

Methods: A total of fifteen (15) skeletally mature (>2 years) female Swiss Alpine White Sheep were enrolled in this study and subjected to bilateral drill holes (10.5 mm diameter by 15 mm deep) in the proximal humerus and distal femur. Three animals were lost due to post-operative complications. Therefore, a total of twelve animals were available for inclusion into the study. The four treatment groups evaluated in this study had a sample size of six (n=6), and all animals had an in life duration of 6 or12 months

Four experimental groups were evaluated as follows:

- **Group A:** 30% PCL / 70% Coarse (0.7 – 1.4mm) β-TCP Granules
- **Group B:** 30% PCL / 70% Fine (0.5 – 0.7mm) β-TCP Granules
- **Group C:** PCL Cylinder (100% PCL)
- **Group D:** β-TCP Cylinder (100% β-TCP)

All samples were fixed in 70% ethanol and embedded in Technovit 7200 for undecalcified histology. Three 75-100 μm transverse cross sections were made using an Exakt saw and grinder. The center section was stained with H&E while the medial and lateral sections were stained with Sanderson's rapid bone stan/Van Gieson's stain for histology and histomorphometry.

For all data, significance was determined at the 95% confidence level, $p < 0.05$.

Results: At necropsy, macroscopic examination of the tissues revealed complete and normal healing of the surgical wounds in all animals. One animal (9073) had caseous material in one mesenteric lymph node consistent with pseudoteberculosis, but all other lymph nodes appeared normal. There was no evidence of abnormal tissue reaction or inflammation in the tissues overlying the fusion site in any of the animals.

Semi-quantitative microscopic evaluation of the implant sites revealed no evidence of adverse tissue reaction such as necrosis, degeneration or osteolysis in any of the test groups. A thin ring of fibrous tissue, completely or partially surrounding the defect area, was observed in two Group A samples (2/6) at 6 months and in one Group B sample (1/6) at 12 months. For Group C, minimal fibrous encapsulation was observed in all 6 month samples (6/6) and in four 12 month samples (4/6). Fibrous encapsulation was not observed at sites implanted with Group D (β-TCP Cylinder).

Group A and B had significantly greater mean inflammatory scores at both 6 and 12 months as compared to Groups C and D, $p < 0.05$. There were no differences in mean inflammatory scores between Group A and B or Group C and D at either 6 or 12 months (Table 1). Inflammation consisted primarily of macrophages and giant cells actively engaged in resorption of the implant material. Some sites had low numbers of lymphocytes and/or neutrophils, but these cells were always a minor component of the inflammatory cell population.

Histomorphometric evaluation of percent bone area and residual implant area were quantified for each group. Group D had statistically greater amounts of bone present within the defect at both 6 and 12 months when compared to all other groups, $p < 0.05$. Likewise, Groups A & B had significantly greater amounts of bone present at both 6 and 12 months when compared to Group C, $p < 0.05$. No differences were found between the two PCL-TCP treatment groups at either 6 or 12 months. Evaluation of the % Bone as a function of available space (ROI – residual implant area) resulted in similar % Bone (available) values for both PCL-TCP groups as compared to the pure β-TCP sample (Table 2).

Residual implant area for Group A & B decreased significantly from 6 to 12 months whereas Groups C & D showed little change. Group D demonstrated almost complete resorption by 6 months (Table 1).

Treatment Group	Mean Irritation Score		% Residual Implant	
	6 Months	1 Year	6 Months	1 Year
Group A	2.0 ± 0.9	2.0 ± 0.6	83.8 ± 5.6	65.3 ± 6.9
Group B	2.0 ± 0.8	2.0 ± 0.0	82.0 ± 6.6	68.4 ± 4.5
Group C	0.9 ± 0.6	0.3 ± 0.4	97.3 ± 3.8	94.2 ± 7.2
Group D	0.8 ± 0.6	0.8 ± 0.7	7.6 ± 5.3	5.1 ± 3.1

Table 1. Mean inflammatory score as determined by histopathology and % residual implant as determined by histomorphometry

Treatment Group	% Bone		% Bone (available)	
	6 Months	1 Year	6 Months	1 year
Group A	8.4 ± 4.4	17.3 ± 7.2	49.3 ± 22.0	49.6 ± 15.9
Group B	12.3 ± 2.9	15.7 ± 4.5	70.1 ± 13.2	50.7 ± 16.6
Group C	0.6 ± 1.0	0.1 ± 0.2	10.2 ± 8.2	1.7 ± 2.2
Group D	46.6 ± 6.8	41.7 ± 7.4	51.5 ± 10.1	44.0 ± 8.1

Table 2. Percent Bone and Percent Bone (available) as determined by histomorphometry.

Conclusions: The results of this study indicate that the affect of coarse (0.7 – 1.4mm) or fine (0.5 – 0.7mm) TCP granules does not influence the biological performance of the PCL- TCP material at 6 or 12 months in this model. These data further indicate that, while these PCL-TCP materials support less overall bone when compared to the pure β-TCP construct, the percentage of bone found within the PCL-TCP materials, with respect to available space, was similar to the pure β-TCP group. While PCL-TCP appears to illicit an elevated inflammatory response relative to the controls, it does not appear to adversely affect bone growth into the PCL-TCP construct.