Long-Term Effects of Poly (ε–caprolactone) Implantation in a Bone Defect Model

Petticoffer AC[1], Recber A[1], Boure L[2], Arens D[2], Liu X[1], Fulmer M[1] and Harten R[1]
[1]DePuy Synthes, West Chester, PA. [2]AO Research Institute, Davos, Switzerland

Statement of Purpose: Poly (ε-caprolactone) (PCL) is widely investigated as a potential bioresorbable material for orthopaedic indications. The primary objective of this study was to determine the long-term in vivo degradation characteristics of PCL out to five (5) years.

Methods: Sixteen Swiss alpine sheep received drill-hole defects (8 mm in diameter by 12 mm in depth) bilaterally, in the proximal humerus, proximal and distal femur and proximal tibia. Each hole was filled with a pre-formed cylinder of PCL. The PCL implants had four different initial levels of pre-degradation; 25%, 50%, 75%, or Non-degraded. Samples were pre-degraded by being placed in phosphate buffered saline solution at elevated temperatures for fixed times and degradation state was confirmed via GPC analysis. Each animal received two samples of each material. Four animals at each time-point were evaluated; 6, 12, 24, and 60 months post-operatively After the animals were sacrificed, each sample was scanned using a Scanco MicroCT80 for 2D imaging and analyzed for residual PCL Volume/Total Volume (PCL V/TV) and density. Post scanning, a portion of each site was extracted and GPC testing was performed to obtain molecular weight (Mw).

Samples were then processed for undecalcified histology. Thick ground slides were prepared and histomorphometry was performed using OsteomeasureXP.

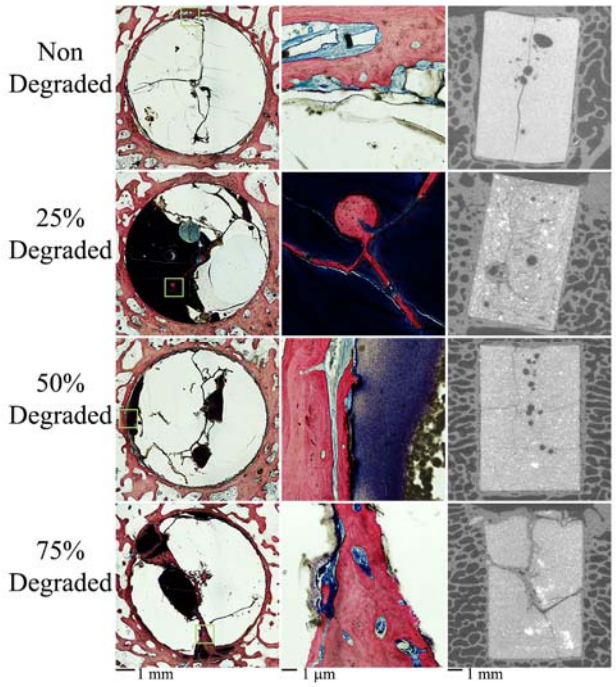

Figure 1. 60 month images of ground sections stained for Sanderson's Rapid Bone stain/Van Gieson's (2X & 10X magnification), and 2D µCT images.

Results: Microcomputed Tomography (µCT) analysis showed that the 75% degraded PCL implants experienced greater mass loss than the Non-degraded samples over the course of the study, as seen in Fig. 2A. Qualitatively, µCT imaging demonstrated that the more highly degraded versions of PCL experienced a greater amount of cracking and fragmentation despite having relatively limited mass loss. Micro-CT imaging also revealed robust new formation within the voids and fissures of the PCL implants as seen in Figs. 1 and 3.

Histomorphometric analysis showed similar trends in residual PCL, however, the only significant differences were observed at 60 months between the 25% and 50% groups. Bone Area/Total Area (Bar/Tar) showed no significant differences.

GPC analysis showed a significant and consistent drop in Mw over time for all four treatments at all four time points, as shown in Fig. 2B.

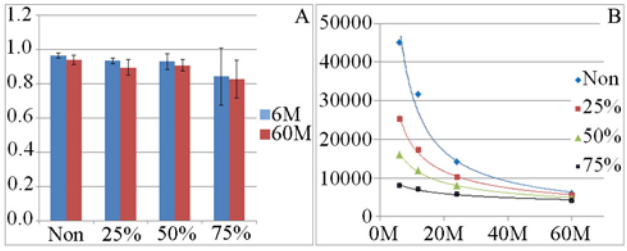

Figure 2. Mean values for A) PCL V/TV (mm^3) and B) Mw (Dalton)

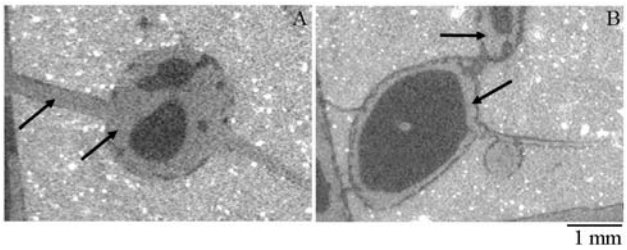

Figure 3. 2D µCT images at A. 6 months and B. 60 months. Arrows denote newly formed bone within the PCL.

Conclusions: These data demonstrate that the PCL material was well tolerated and integrated into the osseous defects after 5 years of implantation. Despite the lack of significant mass loss in this implant configuration, the results demonstrate that the polymer was steadily degrading over time. Specifically, the non-degraded PCL implants lost 86.6% of their molecular weight between the 6 and 60 month time periods. Using this model, longer time periods would be required to ultimately determine the rate of mass loss over time. Taken together, these data demonstrate that PCL may be a suitable polymer for orthopaedic indications where rapid resorption is not a critical attribute.