Remodeling of an Injectable/Settable Bone Graft in a Sheep Femoral Defect Model

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Statement of Purpose: Injectable/settable bone grafts offer several advantages over preformed implants, including the ability to conform to the graft site and compatibility with minimally invasive surgical approaches. A novel injectable/settable composite graft, consisting of a granular osteoconductive matrix in a porous poly(ester urethane) (PEUR) carrier, has previously demonstrated the ability to support formation of new bone in small animal models. This study tests the material in a critical-sized sheep femoral defect repair model to assess bone formation, osseointegration, and polymer degradation. We present radiographic and histological results at 16 weeks and 12 months post implantation

Methods: Bilateral distal lateral femoral defects (11 mm diameter x 20 mm depth) were created in the cancellous bone of female skeletally-mature sheep. Test implant materials were prepared intraoperatively by mixing polyol, prepolymer, and catalyst components with either mineralized allograft bone or MASTERGRAFT® Mini Granules (Medtronic, Memphis, TN). The control group consisted of MASTERGRAFT® Mini Granules alone. Test groups were injected into the defect site through a trocar and allowed to react *in-situ* to form a set implant. Approximately 2 cc of graft material was implanted in each defect. Specimens were harvested at 16 weeks. Plain radiographs and micro-CT images of the implant and surrounding bone were taken at necropsy. Sagittal ground plastic sections were prepared from the approximate center of each defect and stained with Stevenel's blue-van Gieson stain. Sections were scored semi-quantitatively to evaluate residual implant material, new bone formation, and cellular response.

Results: Post-implantation radiographs showed evenly distributed radiodense material filling the defects in all groups. Newly formed bony trabecular structures were visible in all three groups at 16 weeks. Histologically, new calcified bone scores were higher for the control MASTERGRAFT® Mini Granules group than for the test groups. Median new calcified bone scores were not significantly different between the test groups (between 26% and 50% calcified bone within the implant area). Bone fill was not complete at the center of both test groups where residual PEUR material was present, though bone formation was ongoing. Necrosis and/or localized inflammation in native bone adjacent the implant was not seen in any groups. Residual allograft and MASTERGRAFT® were well integrated with newly formed bone (Fig. 1) except where surrounded by residual polymer. Cellular response was similar for all groups, with cell types being predominantly macrophages and giant cells (GCs). Cell response was generally low for all groups. (Note: Data are only available for the 16 week time point at the time of abstract submission.)

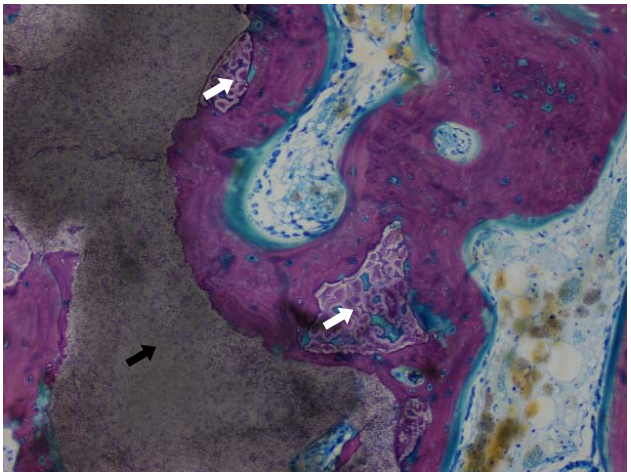

Figure 1. PEUR MASTERGRAFT® implant material at 16 weeks post-implantation, 100X magnification. Lamellar bone formation adjacent to residual MASTERGRAFT® material (black arrow). Residual polymer (white arrows) is incorporated within new bone.

Conclusions: At 16 weeks, new bone formation was evident in all three groups, though was more extensive for control MASTERGRAFT® groups than for PEUR MASTERGRAFT® and allograft groups. Substantial osseointegration of implant materials was evident for all groups tested. The polymer material did not appear to stimulate a significant cellular response, and residual polymer was shown incorporated within new bone. We anticipate controlled degradation of the PEUR material to lead to equivalent healing of the bony defects in all groups at the 12 month time point.

References: [1]Dumas et al. (2010) Tissue Eng Part A 16(8):2505-18. [2]Hafeman et al. (2011) Biomaterials 32(2):419-29.

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