Performance of Degradable Long-Fibre Composites for Craniofacial Bone Repair in a Calvarial Defect Model

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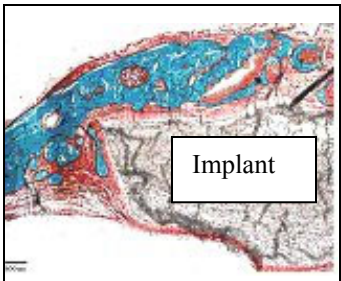
Introduction: Current procedure for bone tissue replacement or fracture fixation of the face or skull often involves the use of titanium or degradable polymers such as poly(lactic acid), both of which have significant disadvantages. Therefore a long-fibre composite is under development for craniofacial and maxilliofacial bone repair. The polymer composite is based on a polycaprolactone (PCL) matrix reinforced with degradable phosphate glass fibres. The composite is manufacture using a novel polymerization method to produce a material with controllable degradation rate and which supports osteoblast attachment and growth. The aim of this study was to make a first assessment of the composite in an in vivo model. To achieve this in a clinically analogous environment, a critical size rat calvarial defect model was chosen.

Methods: The study was performed on young adult male Wistar rats. Eight animals were included in each experimental group per time point. An 8mm diameter calvarial defect was created in the midline or paramedian area of the skull of each animal. Implants were then press fit into the defects, the periosteal flap placed back over the defect and the wound closed. Implants were 8mm diameter x 1mm thick. These were post formed to a dome (8.5mm radius of curvature) to more accurately fit the defect. Implants were either PCL alone, PCL/phosphate glass (20mol% Ca, 30 mol% magnesium, 50 mol % sodium phosphate) or PCL/45S5 Bioglass fibres. Both experiemental composites had a fibre volume fraction of 30%. Glass fibres were sized using amino propyltrioxyethyl silane. Controls used were either the empty defect or defect grafted with autologous bone. Sacrifice was carried out at 2, 4, 8, 12, and 26 weeks post implantation. Explanted samples were either decalcified and processed for wax histology or resin embedded, undecalcified for assessment by light microscopy (methyl methacrylate) or SEM (glycomethacrylate).

Results & Discussion: All wounds healed cleanly without any evidence of infection. At sacrifice the material was seen to be covered with a healthy periosteum. The critical sized defects did not exhibit any evidence of closure, either macroscopically or histologically, thus validating the model. In all experimental groups a thin fibrous capsule was present around the implant. This varied with experimental period and implant type. In the decalcified tissue series this was more marked on PCL alone, composites appeared to have a close bone/implant configuration. No obvious superiority was apparent for either of the composites studied. A reduction in capsule thickness with time was noted. No indication of necrosis or significant inflammatory response was observed. A few inflammatory cells were seen at 2 weeks in all groups. Macrophage/giant cell activity was associated with bone debris and possibly surgical suture at these early timepoints, however this became insignificant with increasing implantation time, most likely associated with the healing process. In later specimens, no evidence of any inflammatory response was detected, with the exception of an occasional giant cell associated with debris at the periphery of the implant. New bone growth was most commonly observed below the implant, or in the gap between implant edge and the edge of the defect. Bone formation above the implant was limited and rare, occurring mainly in PCL/phosphate glass samples. Bone ingrowth below the implant was shown to be more extensive with the composite samples than the PCL only samples. In some cases there was a seven fold difference in the extent of defect filling between these groups.



Bone growth around a PCL/phosphate glass implant 26 weeks post implantation. Bone is indicated by blue/green staining, osteoid in orange, with red indicating fibrous soft tissue. The section is a transverse section the implant/tissue sample, with the ventral aspect of the sample at the bottom of the micrograph.

Implant degradation was limited over the course of the experiment, with no substantial reduction in the dimensions of the implant. As such, qualitative assessment of implant degradation was made using morphological observations of cross sections through the centre of implant/tissue samples by BSE SEM imaging. Typically, evidence of degradation was observed at the perimeter face of the implants. Degradation was most advanced in the two composite implants by the end of the study. The phosphate glass reinforced composites more severe evidence of degradation with small crevice formation, irregular implant edges.

Conclusions: This study has allowed us to confirm that the material shows considerable promise for progression to trials in patients. In particular, it is well tolerated in a clinically analogous environment and its degradation is sufficiently slow to overcome the deficiencies of competitor materials. The study was designed to test a number of options of candidate materials in the simplest craniofacial bony model. As such the thinness of the rat calvarium allowed only a 'butt' end joint between bone and material, micromovement was inevitable, interface contact very limited and a full assessment of the ability of the material to integrate with bone was not possible. The close proximity of bone to material and surface erosion of implants at 26 weeks indicates a promising bone material interface, this will investigated further in a more clinically analogous model.