Repair of calvarial defects with customised tissue-engineered bone grafts. II. Evaluation of cellular efficiency and efficacy in vivo.

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Publication Date: 2003

Abstract:

We have demonstrated in Part I of this study [see Schantz, J.-T., et al, Tissue Eng. 2003;9(Suppl. 1): S-113-S-126; this issue] that bone marrow-derived progenitor-cells and calvarial osteoblasts could be successfully directed into the osteogenic lineage and cultured in three-dimensional (3-D) polycaprolactone (PCL) scaffolds. The objective of the second part of the study was to evaluate and to compare tissue engineered cell-polymer constructs using calvarial osteoblasts (group I) and mesenchymal progenitor cells (MPCs; group II) for the reconstruction of critical-size and three-dimensionally complex cranial defects. In 30 New Zealand White rabbits, bilateral parietal criticalsize defects were created. On the basis of computed tomography scans, customized PCL scaffolds with precisely controlled microarchitecture were fabricated, using a rapid prototyping technology. Bone marrow-derived progenitor cells and osteoblasts were isolated and expanded in culture. Osteoblasts (group I) and mesenchymal progenitor cells (group II) were seeded in combination with a fibrin glue suspension into 40 PCL scaffolds. After incubating for 3 days in static culture, the PCL scaffold-cell constructs as well as nonseeded PCL scaffolds (control group) were implanted into 15-mm-diameter calvarial defects. Reconstruction of the cranium and bone formation were evaluated after 3 months. In vivo results indicated osseous tissue integration within the implant and functionally stable restoration of the calvarium. Islands of early bone formation could be observed in X-ray radiographs and in histological sections. Implants showed a high cell:ECM ratio and a dense vascular network. Mechanical testing of the reconstructed area revealed partial

integration with the surrounding corticocancellous calvarial bone. The amount (area) of calcification, measured by clinical computed tomography, indicated that cell-seeded constructs measured about 60% more than unrepaired or unseeded scaffolds. Mechanical investigations revealed that stiffness reached 52 +/- 29 and 44 +/- 16 MPa for MPC- and osteoblast-seeded scaffolds, respectively. The yield strength for the push-out tests was 180 +/- 36 N for normal calvarial bone, 90 +/- 1 N for unrepaired site, and 106 +/- 10 N for unseeded constructs, which is about 60% of normal bone strength. MPC- and osteoblast-seeded scaffolds indicated a yield strength of 149 +/- 15 and 164 +/- 42 N, respectively, which is about 85-90% of normal bone. This study demonstrated that customized biodegradable polymeric implants may be used to delivery osteogenic cells and enhance bone formation within critically-sized defects in vivo. The use of rapid prototyping technology to produce scaffolds with controlled external geometry and microarchitecture offers new possibilities in the functional and aesthetic reconstruction of complex craniofacial defects.