Biodegradable inductive load-bearing bone regeneration scaffold
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Reconstruction of critical-size large bone defects remains a significant clinical problem. The high clinical failure rates observed with natural and synthetic bone grafts are attributed to the lack of vascularity in the interior parts of the implant. In this regard, tissue engineered (TE) scaffolds that can initiate the cascade of vascularized osteogenesis hold great promise for the treatment of large skeletal defects. We hypothesized that the osteopontin-derived SVVYGLR peptide (OPD) and the rhBMP-2 derived LYLTSIASLETPVSSAKPIK peptide (BMP2), grafted to a crosslinked scaffold with well-defined pore geometry and degradation profile, work together to synergistically enhance the cascade of cell migration, differentiation, and maturation of bone marrow stromal (BMS) cells to produce a mineralized vascular matrix. A novel star in-situ crosslinkable acrylate-terminated lactide-co-glycolide (sLGAA) macromer will be used to fabricate the biodegradable scaffold by rapid prototyping/injection molding technology. The salient feature of this macromer is that very short lactide-co-glycolide (LG) segments are used to control degradation while the multi-arm core controls the rate of hardening and mechanical strength. In this project, we will develop and test a scaffold that provides: a) an osteoconductive matrix for temporary structural support to the regenerating region and b) BMP2 and OPD peptide grafted sites to initiate the cascade of vascularized osteogenesis of migrated BMS cells. In Aim 1, we will determine the effect of the composition of sLGAA polymerizing mixture, reinforced with hydroxyapatite (HA) nanocrystals, on degradation and mechanical strength of the scaffolds. In Aim 2, we will determine the effect of BMP2 and OPD peptides, grafted to sLGAA scaffold, on differentiation of BMS cells in-vitro in a dynamic cell culture system. In Aim 3, we will evaluate the peptide-grafted sLGAA scaffold for the extent of bone formation in-vivo by implantation in rat calvarial defect model. The effect of OPD and BMP2 peptides will be evaluated radiographically, mechanically, histologically, and by histomorphometry. Success will be judged by the continuous bridging of new bone across the scaffold, and the highest mineral and vascular density.