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A chemical and engineering approach towards "smart" synthetic bone grafts

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The design of synthetic bone grafts that possess structural and biochemical microenvironment emulating the extracellular matrix of bone and exhibit good surgical handling characteristics is of significant importance to orthopedic applications. Using a combination of chemical and engineering tools, our lab has developed a number of osteogenic composite bone grafts that possess elastomeric or self-deployable shape memory properties facilitating the repair and regeneration of segmental bony defects.

The first type of grafts are composites of poly(2-hydroxyethyl methacrylate) (pHEMA) and hydroxyapatite/tricalcium phosphate (HA/TCP) possessing osteoconductive mineral content approximating that of human bone. The grafts are fabricated by cross-linking pHEMA hydrogel in the presence of different types of HA/TCP powder using viscous ethylene glycol as a solvent. Despite the high HA/TCP contents, these composites exhibit elastomeric property and unusually high fracture resistance under physiological compressive loading. We demonstrate that tailored microstructural properties and compressive behavior of the composites can be achieved by the selective use of HA/TCP powder of varied sizes and aggregation. When subcutaneously implanted in rats, the mineral component dissolved slowly and osteoblastic differentiation of the bone marrow stromal cells pre-seeded on the substrates was observed. *In vitro* cell culture studies show that these composites are able to retain and locally release exogenous growth factors and cytokines regulating graft healing in a sustained manner. These grafts in facilitating the repair of critical-sized bony defects are being investigated using a rat femoral segmental defect model.

The second type of composite grafts consist cross-linked poly(ester-urethane) that is strengthened by Si-based nanoparticles. Using ring-opening polymerization, biodegradable polylactide of varying lengths is first grafted to Si nanoparticles to generate star-shaped macromers. Using a solvent casting technique, these macromers are then crosslinked to generate composite grafts with tailored bone-like flexural moduli, tunable biodegradation rates consistent with the time frame of normal bone fracture healing, and physiologically relevant glass transition temperatures. These grafts possess unique shape memory properties that enable the grafts to efficiently recover (within seconds) from a temporary shape facilitating surgical insertion to a pre-programmed "permanent" shape matching the defect size upon mild thermal activation. The potential of these composites as deployable bone grafts for assisting the repair and regeneration of musculoskeletal defects are being explored.

The author has no conflict of interest.

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