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Biodegradable, Phosphate-containing, Dual-Gelling Macromers for Cellular Delivery in Bone Tissue Engineering

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Abstract: Injectable, biodegradable, dual-gelling macromer solutions were used to encapsulate mesenchymal stem cells (MSCs) within stable hydrogels when elevated to physiologic temperature. Pendant phosphate groups were incorporated in the N-isopropyl acrylamide-based macromers to improve biointegration and facilitate hydrogel degradation. The MSCs were shown to survive the encapsulation process, and live cells were detected within the hydrogels for up to 28 days *in vitro*. Cell-laden hydrogels were shown to undergo significant mineralization in osteogenic medium. Cell-laden and acellular hydrogels were implanted into a critical-size rat cranial defect for 4 and 12 weeks. Both cellular and acellular gels were shown to degrade *in vivo* and help to facilitate bone growth into the defect. Improved bone bridging of the defect was seen with the incorporation of cells, as well as with higher phosphate content of the macromer. Furthermore, direct bone-to-hydrogel contact was observed in the majority of implants, which is not commonly seen in this model. The ability of these macromers to deliver stem cells while forming *in situ* and subsequently degrade while facilitating bone ingrowth into the defect makes this class of macromers a promising material for craniofacial bone tissue engineering.

Key words: hydrogel, poly(N-isopropyl acrylamide), monoacryloxyethyl phosphate, rat cranial defect, mesenchymal stem cell encapsulation

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