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## ACCEPTED MANUSCRIPT

Multi-tubule conduit-filler constructs loaded with gradient-distributed growth factors for neural tissue engineering applications

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Abstract: Chitosan/silk fibroin/glycerophosphate gels were loaded with nerve growth factor (NGF) and further processed into multi-tubule fillers. NGF was loaded into the fillers in such a way so that a NGF gradient was established longitudinally along the filler length. A type of poly(lactide-co-glycolide)(PLGA)/chitosan(CH) porous conduit was fabricated using a pre-crosslinking method. The filler was fully filled into the lumen of conduits to build multi-tubule conduit-filler constructs that are intended for long-gap peripheral nerve repair. In vitro degradation in a lysozyme-contained medium revealed that constructs had degradation-tolerant features and the optimized multi-tubule filler was capable of maintaining its multi-tubules unblocked for around 10-week. After being degraded for various periods up to 8 weeks, the optimal conduit-filler constructs showed confirmative

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