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CONSTRUCTING NEUROTROPHIC GRADIENT-GENERATING PERIPHERAL NERVE CONDUITS AND ASSAYS TO MEASURE FUNCTIONAL OUTCOMES

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Severe injury and trauma often results in peripheral nerve injuries. With current surgical practices such as the use of autografts, regeneration from nerve injuries is slow and incomplete resulting in loss of motor and sensory function. Previous studies indicate that the combination of a synthetic nerve conduit and neurotrophic factors aide in the regeneration process. It is also known that nerves will grow toward a chemotactic gradient. This study aims to demonstrate that a nerve conduit that implements a neurotrophic gradient can improve functional recovery following peripheral nerve damage. To do this, biodegradable gradient-producing nerve conduits are manufactured. The gradient device is composed of multiple pieces, all constructed from poly-L lactic acid (PLLA). There are two concentric tubes (an inner and outer conduit) enclosing a reservoir from which neurotrophic drugs will diffuse through holes that are cut with a laser into the inner conduit. Location and size of the diffusion holes is altered resulting in varying gradient patterns. Two, o-shaped endcaps are placed between the inner and outer conduits and are then sealed to prevent drug leakage. Drug diffusion from the device is initially tested using a fluorescent dye. After implantation of the devices across a nerve gap, a functional assay is employed to assess recovery following a peripheral nerve injury. After designing and manufacturing a horizontal ladder rung test, healthy mice are trained to walk over at a constant pace. After being injured, the mice are then run across the ladder again and differences in functional ability are identified from counting how often and to what extent their leg slips off a rung. Full functional recovery is ideal after a peripheral nerve injury and the gradient design conduit has the potential to expedite this optimal recovery.