Multiple Layer Nerve Guide Using Carbon Nanotubes for Peripheral Nerve Regeneration

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Statement of Purpose: The key to successful treatment of a peripheral nerve lesion is to direct the axonal regeneration towards the distal endoneural stump. After reconnection, electrical signals can reestablish the neural function. The role of a tubular nerve guide is not only to serve as a conduit to enable the proximal neurons to grow in the direction of and eventually reconnect to their distal partner, but also to protect the axons and Schwann cells from being diverted from their desired pathway by the inflammatory response of infiltrating macrophages and fibroblasts. In addition, a nerve guide can also avoid the morbidity associated with an autograft donor site and any immunogenic side-effect due to allografting. Nerve guide conduits have the potential to be the preferred option in clinical nerve repair for gaps of up to 30 mm [1]. The nerve guide must have sufficient compression resistance to serve as a protective envelope around the nerve during the period of nerve regeneration.

The 3 objectives of this study were:
i) To fabricate 3 hollow tubular concentric double layer braided nerve guides from resorbable PLA yarns, a) the first with 200 layers of oriented CNT's and an electrospun web of polyethylene oxide (PEO) nanofibers between the two layers, b) 100 layers of oriented CNT's and electro-spun web of polyethylene oxide (PEO) nanofibers between the two layers, and c) no additional core material inserted between the layers.
ii) To determine the mechanical properties of the 3 braided nerve guides described above.
iii) To determine the relative biocompatibility of the 3 braided nerve guides described above.

Methods: Polylactic acid (PLA) braided tubes are flexible, biocompatible and biodegradable. Carbon nanotubes (CNTs) are nano-scale materials with electrical conductivity. A double layer PLA braided structure has been shown to have excellent kink recovery and compression resistance [2]. In this study, by adding aligned carbon nanotubes within the double layer PLA braided structure, we hypothesize that the presence of carbon nanotubes can improve the mechanical properties, such as tensile strength, compression resistance and kink recovery. In order to evaluate the biocompatibility, the nerve guide samples were cultured in vitro for 7 days with 3T3 fibroblast cells.

Results: Physical property tests have shown that the presence of carbon nanotubes improves the tensile strength, compression resistance and kink recovery of the prototype nerve guides. A live and dead assay shows that the nerve guide prototypes were found to be biocompatible and provided equivalent attachment and proliferation of fibroblasts regardless of whether they contained carbon nanotubes or not.

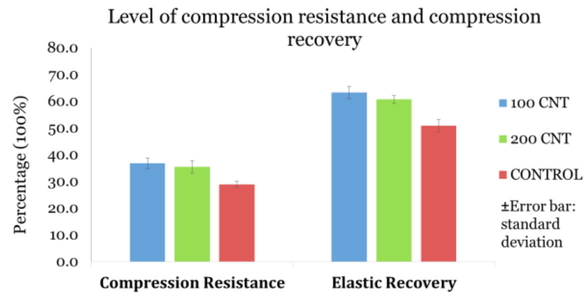

Figure 1. Samples with CNTs show improved compression resistance and recovery.

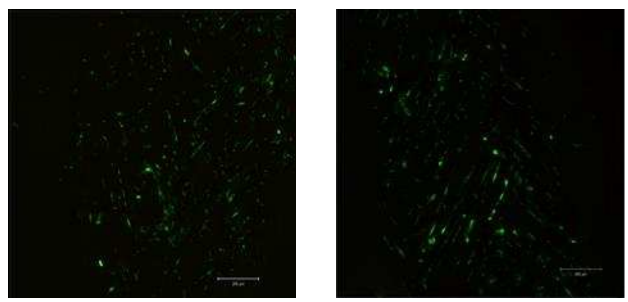

Figure 2. Laser scanning confocal images with "live and dead" staining showing cell proliferation along the length of the braided tubes, with CNTs (left), and without CNTs (right).

Conclusions: In the design of double layer PLA braided structure the addition of directional carbon nanotubes has been found to improve the tensile strength, compression resistance and kink recovery as well as confirm the biocompatibility. In a future study, we plan to apply an external electrical potential so as to determine whether or not the cells will migrate in the direction of the aligned CNTs. In conclusion, this multiple layer nerve guide using aligned carbon nanotubes has the potential to be used for peripheral nerve regeneration.

References: 1. Ray, W. Z., & Mackinnon, S. E. (2010). Management of nerve gaps: autografts, allografts, nerve transfers, and end-to-side neurorrhaphy. Experimental Neurology; Regeneration in the Peripheral Nervous System, 223(1), 77-85.
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