Topographical cues accelerate endogenous regeneration of long peripheral nerve gaps

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Introduction

The clinical "gold standard" for bridging peripheral nerve gaps is autografts. However, their usefulness is limited by several issues including the requirement for multiple nerve segments, mismatch between injured nerve and nerve grafts, and the loss at the donor site [1]. Empty hollow conduits created from natural and synthetic materials have been used to bridge nerve gaps. These scaffolds have shown promising outcomes in small gaps but fail when the nerve gap is longer than 10 mm in rats or more than 30 mm in humans. Tissue engineering strategies that involve the use of luminal fillers have been used to augment the rate as well as efficacy of nerve regeneration across long gaps.[2,3] But the *mechanisms* by which they affect nerve regeneration are not completely understood.

In this study, we design fiber based films with aligned, random and smooth topographies to understand how these topographical features affect nerve regeneration.

Materials and Methods

Ten micron thick oriented nanofiber films were fabricated by electrospinning poly(acrylonitrile-co-methylacrylate) (PAN-MA) on a high-speed rotating metal drum while random fibers were spun using a flat target. Polymer film was casted by solvent evaporation. The morphology of these fibers and the film were evaluated using scanning electron microscope.

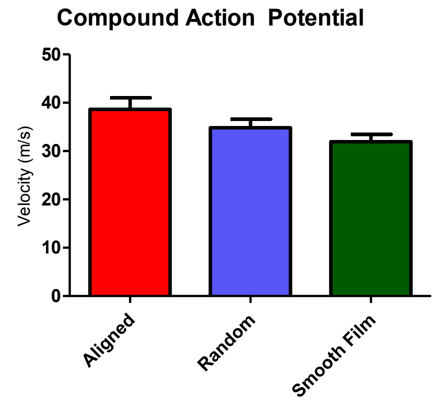
These films were loaded in a polysulfone conduit and implanted in vivo in a 15 mm long peripheral gap. The schematic of the scaffolds are shown in Figure 1.

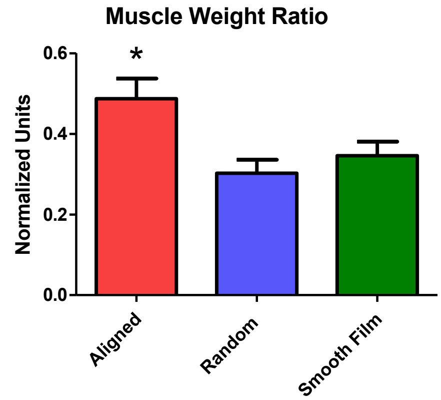
Results

These scaffolds were implanted in vivo for 22 weeks and functional nerve regeneration was quantified based on compound action potentials as well as muscle weight ratios. Figure 2 shows how compound action potential (CAP) velocity is affected by the presence of topography. We observed no difference between the different topographies for the CAP velocity. There were significant differences seen in terms of muscle weights for the different topographies. Relative gastrocnemius muscle weights were significantly higher in animals implanted with Aligned fibers compared to random fibers and smooth films.

Discussion and Conclusions

Several strategies to enhance peripheral nerve regeneration have been proposed. In order to develop scaffolds that augment PNS repair, it is vital to understand how topographical cues influence the different steps of regeneration in peripheral nerve.





In this study we suggest that aligned fibers enable enhanced regeneration by stimulating faster reinnervation of gastrocnemius muscle. While other topographies also support nerve regeneration, as shown by the similar CAP velocity, aligned fibers are able to increase the rate of regeneration. Hence we suggest that 3D scaffolds created from oriented nanofiber films will enhance nerve regeneration *in vivo* by providing topographical cues necessary to induce the regenerative phenotype of Schwann cells and aid in neurite bridging peripheral nerve gaps.

References

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Acknowledgments

The authors gratefully acknowledge funding from NIH NS44409 and GTEC NSF EEC-9731643