Prevention of Neuromas with a Porcine SIS Nerve Cap: A Histopathologic Evaluation

Shahryar Tork, MD[1], Jennifer Faleris, BS[2], Anne Engemann, PhD[2], Curt Deister, PhD[2], Erick DeVinney, BS[2] and Ian L. Valerio, MD, MS, MBA[1]

1-Department of Plastic Surgery, The Ohio State University, Wexner Medical Center, Columbus, OH, 2-AxoGen Corporation, Alachua, FL

Introduction

Following traumatic or oncologic nerve amputations, the aberrant axonal regeneration may result in painful neuroma formation. Studies suggest that isolating the nerve-end within a protective cap at the time of amputation or revision procedures may assist in the prevention of nerve-end neuromas. New nerve capping techniques, such as with novel porcine small intestine submucosa (SIS) nerve caps, may lead to improved neuroma management strategies. This study evaluated the local effects of two Nerve Caps (NC) with internal chambering (Partition or Spiral) on a terminal nerve end.

Methods & Materials

The tibial nerves of fifty-seven (57) male Sprague Dawley rats were dissected, ligated, transected and trans-positioned to the lateral hindleg. The nerves were either treated with a Nerve Cap Spiral (NCs), Nerve Cap Partition (NCp) or Open-End Tube (OT), alternatively surgical control (SC) nerve stumps were non-treated. The nerve caps contained internal chambering within an enclosed structure. The animals were euthanized at 8 and 12 weeks. Tissues samples were explanted, sectioned longitudinally, and stained with Hematoxylin and Eosin (HE), Masson's Trichrome (MT), or Neurofilament 200 (NF 200). Slides were analyzed for axonal swirling, nerve width, cap remodeling and overall tissue response.

Surgical Model

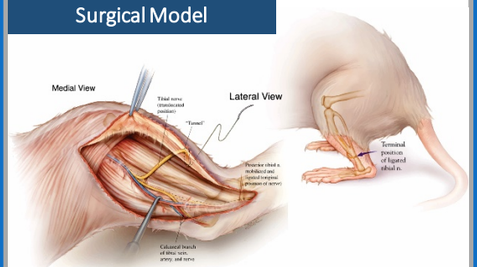


Figure 1. Rat surgical procedures (Dorsi et al. 2008).

Study Design

*1 One animal was inadvertently euthanized early.
*2 Six animals were euthanized early due to device erosion through the skin

Figure 2. Experimental Design

Histological Analysis

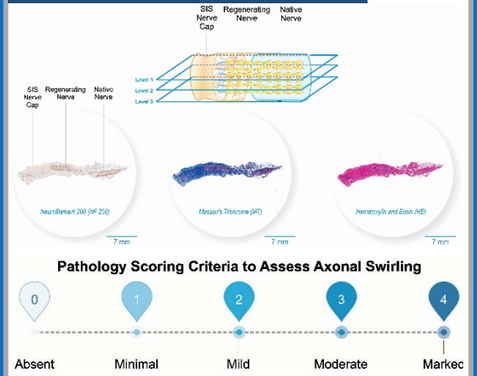
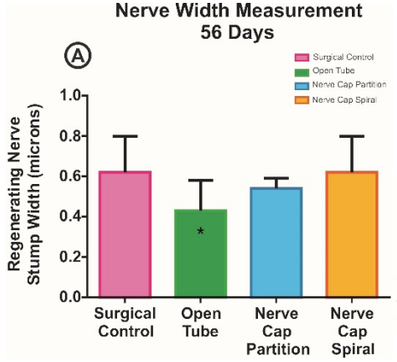
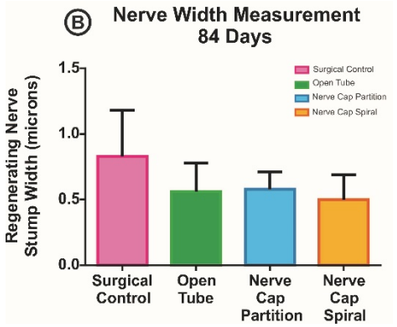


Figure 3. Histological Analysis. Samples were sectioned at 3 levels with three serial sections per level for a total of 9 sections. Sections were stained with Hematoxylin & Eosin (H&E), Masson's Trichrome (MT), and Neurofilament 200 (NF200). Sections were scored using a 0-4 semi-quantitative scale for pathology evaluations for axonal swirling.

Results

1 SIS Nerve Cap decreases width of regenerating nerve stump





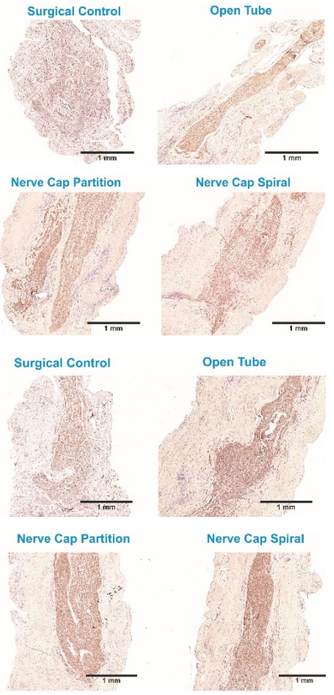
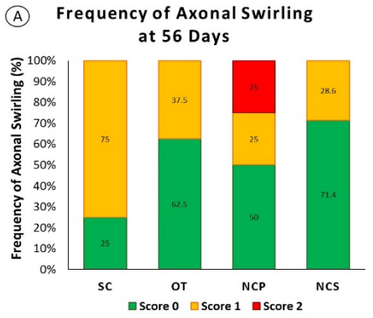
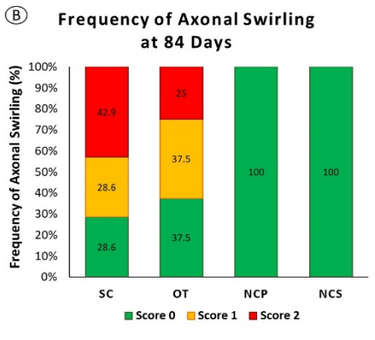


Figure 4. Nerve width measurement of the regenerating nerve stump at **A)** 56 days, **B)** 84 days. Statistically, at 56 days, the SIS Open-End Tube had decreased nerve width compared to the SC and NCs groups (* t-test p-value = 0.03 and 0.045, respectively). At 84 days, there were no statistical differences between the nerve widths of any group; however, the SC group showed an appreciably increased nerve width compared to the SIS Nerve Caps and the SIS Open-End Tube. (Mean +/- SD).

2 SIS Nerve Cap significantly decreases axonal swirling





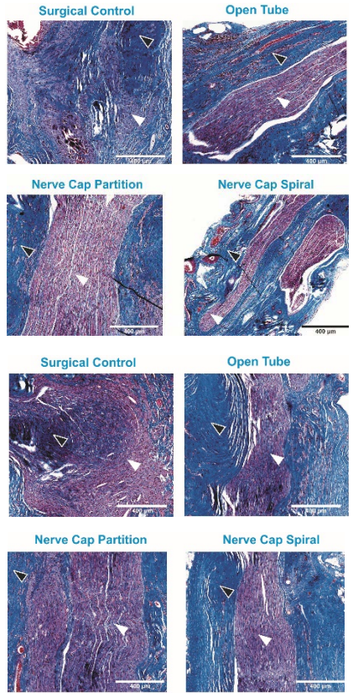


Figure 5. Axonal swirling analysis at **A)** 56 days, **B)** 84 days. The axonal swirling can be observed by axonal growth patterns (white arrows) through the collagen matrix (black arrows). At 56 days, the frequency of axonal swirling was similar across all four groups, with more than 75% of scores between 0 and 1. At 84 days, axonal swirling in the SIS Nerve Cap groups was scored at 0 in all animals. The SC and the SIS Open-End Tube showed significantly higher axonal swirling compared to the SIS Nerve Caps (NCp and NCs) at 84 days (* Fisher's Exact Test, p value = 0.02 and 0.03, respectively).

Conclusions

The investigational porcine SIS nerve caps effectively decreased axonal swirling and distal nerve diameters within a rodent neuroma model. The internal chambering within the nerve caps allowed axons to be dispersed, aligned, and mitigated in an enclosed microenvironment. This study suggests that nerve caps with internal chambering for axonal outgrowth may leverage the limitations of conduits and improve axonal alignment, therefore reducing the likelihood of symptomatic neuroma formation.

REFERENCES

Dorsi, M.J. et al. (2008) Pain 134, 320-334.

DISCLOSURE

Funding of this project was provided by AxoGen Corporation.