Chronic Response of the Cat Sciatic, Median, and Ulnar Nerves to a Compliant, Composite Flat Interface Nerve Electrode (C-FINE)

Max J Freeberg, Matthew A. Stone, Dustin J. Tyler, and Ronald J. Triolo

THE flat interface nerve electrode (FINE) was designed to improve stimulation and recording selectivity from peripheral nerves by gently reshaping them to move fascicles closer to contacts [1]. Many nerves are not circular in cross section *in-situ* and the FINE also better conforms to their shape compared to circular electrode designs. A compliant, composite FINE (C-FINE) was designed to minimize structural material, implement a space-efficient closure, and allow for regionally patterned stiffness that reshapes the nerve at the contacts while minimizing pressures along its length. This should allow for similarly designed electrodes to be placed in tightly-confined areas and those prone to movement around the nerve [2].

In order to verify the safety of chronically implanting the C-FINE in tightly-confined spaces, 3 cats were implanted with un-instrumented C-FINE cuffs for 90, 84, and 88 days bilaterally on the distal sciatic nerves (6 total) and either the median (4 total) or ulnar (2 total) nerves, depending on the safety of surgical access, for a grand total of 12 cuffs. All procedures were performed in accordance with the Case Western Reserve University Institutional Animal Care and Use Committees.

Cats recovered from implantation surgery and, immediately after anesthesia recovery—4-8 hours postoperatively—showed no signs of pain, weakness, or lameness. These same behavioral signs were monitored 3 times weekly. From the period hours after surgery and during the entire period while the cats were implanted, there were no signs of any ill effects from the cuffs in terms of any difficulty trotting, gait abnormalities, weakness, decreased toe or claw movement, or decreased sensation.

Nerve conduction velocities (NCVs) were measured through the cuffs at implant and explant by stimulating approximately 1 cm proximal and distal to the nerve and recording muscle twitch responses (EMG). NCV averaged 71.5 ± 12.2 m/s for sciatic nerves, and 59.4 ± 5.9 m/s for median and ulnar nerves, within normal limits. Moreover, a one-tailed, paired samples t-test showed no significant difference in NCV at implant compared to explant for any grouping of nerves ($p>0.1$).

Encapsulation at explant appeared minimal for cuffs on the sciatic nerves and unremarkable for cuffs implanted on the median and ulnar nerves, given the amount of movement and many major vessels and nerves in the very tight space in the forelimb. This finding was reaffirmed by histology and with magnified images taken during nerve dissection. Morphological examination confirmed that the C-FINE had reshaped the nerves to a more oblong cross-section. Embedded blocks of nerve were sectioned at 1μm and stained with Toluidine Blue [1] for examination under light microscopy for any indications of damage. Changes in axon density, axon diameter distribution, and ratio of inner axon to outer fiber diameter (d/D ratio) are characteristic of nerve damage and regeneration [3]. Sections from near the center of and the distal edge of the cuff, and as far distal to the cuffs as possible were compared to sections 2-5cm proximal to the cuff. Histological analysis showed healthy nerve with densely packed axons with diameters following an expected bimodal distribution and well myelinated. The d/D ratio was consistently between 0.75 and 0.92 with a linear fit to myelin sheath thickness vs. axon diameter with $R^2 > 0.8$ for fibers >1μm in diameter. This was consistent underneath, distal to, and proximal to the cuff, indicating no injury occurred.

These results all indicate there was never any damage caused by chronic implantation of these C-FINE cuffs. This is especially impressive in the forelimb where the C-FINE replicated reshaping properties of the FINE and made it even more amenable to placement around nerves in tightly-confined areas near joint spaces, sensitive structures, and prone to movement.

REFERENCES

[1] D. J. Tyler and D. M. Durand, "Chronic Response of the Rat Sciatic Nerve to the Flat Interface Nerve Electrode," *Ann. Biomed. Eng.*, vol. 31, no. 6, pp. 633–642, 2003.

[2] M. Stone, L. Fisher, N. Brill, D. Tyler, and R. Triolo, "Multilayer Microfabrication-Compatible Nerve Cuff Electrode with Regionally Patterned Stiffness," presented at the Neural Interfaces Conference, Salt Lake City, UT, 2012.

[3] J. M. Schröder, "Altered ratio between axon diameter and myelin sheath thickness in regenerated nerve fibers," *Brain Res.*, vol. 45, no. 1, pp. 49–65, Oct. 1972.

This work supported in part by the National Institutes of Health under grants 5-R01-EB001889-07, 5-T32EB004314-15, and TL1-RR024991-05.

M. J. Freeberg, *Student Member IEEE,* is with the Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH 44106 USA and with the Louis Stokes Department of Veterans Affairs Medical Center, Cleveland, OH 44106 (phone: (610) 291-2140; e-mail: mxf218@case.edu).

M. A. Stone is with the Louis Stokes Department of Veterans Affairs Medical Center, Cleveland, OH 44106 USA (e-mail: mstone@aptcenter.org).

D. J. Tyler, *Member IEEE,* is with the Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH 44106 USA and also with the Louis Stokes Department of Veterans Affairs Medical Center, Cleveland, OH 44106 USA (e-mail: dustin.tyler@case.edu).

R. J. Triolo, *Member IEEE,* is with the Departments of Orthopaedics and Biomedical Engineering, Case Western Reserve University, Cleveland, OH 44106 USA and also with the Louis Stokes Department of Veterans Affairs Medical Center, Cleveland, OH 44106 USA (e-mail: ronald.triolo@case.edu).