RELIABILITY AND ACUTE *IN VIVO* TESTING OF THE LYSE-AND-ATTRACT CUFF ELECTRODE

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Background: One of the major obstacles limiting clinical implementation of peripheral nerve (PN) interfaces is the dual requirement to maintain long-term health of the nerve while selectively targeting specific nerve fibers. It is difficult to isolate different sensory and motor signals from bundled PN fibers without damaging the nerves. Our approach integrates microfluidic channels into an extraneural PN cuff for targeted delivery of a lyse-and-attract drug regimen. First, collagenase is delivered to lyse the collagen-rich connective tissue layers, followed by delivery of a neurotrophic growth factor to induce collateral sprouting of the nerve fibers toward electrodes embedded in the cuff. The anticipated result is proximity of the nerve fibers to the electrodes, and thus increased selectivity and signal fidelity without invading the PN bundle. Design, fabrication, and benchtop characterization of this lyse-and-attract cuff electrode (LACE) were presented previously. We now present reliability tests of the LACE under simulated *in vivo* conditions and preliminary results from acute *in vivo* implantations on rat sciatic nerve, including, for the first time, localized lysing of epineurium on live nerve through an extraneural cuff.

Materials and Methods: LACE devices were soaked for one month in phosphate-buffered saline at 37 °C and periodically underwent electrochemical impedance spectroscopy and interelectrode cross-talk testing. For *in vivo* experiments, LACE devices were implanted on rat sciatic nerve. LACE was used to record compound action potentials (CAP), which were evoked by monophasic bipolar stimulation (200 µs duration, 5 to 150 µA amplitude) through needle electrodes inserted into the nerve 2 cm from the cuff. Lidocaine was then applied to the nerve to block action potential propagation, and the stimulation protocol was repeated. To perform lysing with the LACE, 1 µL of collagenase was delivered to the nerve through the microchannels at a rate of 100 µL/min. Each nerve was then explanted, frozen, sectioned, stained, and imaged.

Results: Electrode impedance at 1 kHz decreased over the soaking period from 2.5 to 2.1 kΩ after two weeks, and to 1.0 kΩ after one month. Average voltage signal leakage between electrodes remained below 10% for all devices up to two weeks and ranged from 10 to 63% by the end of one month, suggesting possible delamination of the electrical insulation. Electrical recordings of evoked nerve activity prior to lidocaine application captured increasing CAP amplitude with stimulus amplitude, but after lidocaine captured only the stimulus artifact. After acute collagenase delivery to rat sciatic nerve, histology sections near the microchannel outlets revealed lysed regions of the epineurium layer, while no evidence of lysing was seen in sections away from the microchannel outlets.

Conclusions: Reliability testing demonstrated suitability of the current LACE design for implantation experiments up to two weeks, but also called for strategies to increase long-term reliability of the electrical insulation *in vivo.* Acute *in vivo* experiments successfully demonstrated use of the LACE to record evoked neural signals and to focally deliver drug to the nerve for localized lysing of the epineurium.

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