nerve conduits would improve nerve regeneration and rodent extremity function by decreasing scar deposition at nerve co-apaptation sites.

METHODS: We utilized a novel, rat forelimb chronic denervation (CD) model to assess the effects of PCL conduits on: a) improving nerve regeneration; and b) improving upper extremity function. Three groups of rats were examined: (1) Group-1 (n = 5) underwent 8 weeks of median nerve CD injury followed by repair with no conduit; (2) Group-2 (experimental, n = 5) underwent 8 weeks of median nerve CD followed by repair and PCL nerve conduit wrapping of the nerve co-apaptation site; (3) Group-3 animals (n = 5) were naïve controls. All animals underwent nerve conduction studies on weeks 12 post-repair. All animals also underwent weekly muscle functional testing. At weeks 14 post-repair, the median nerve and flexor muscles were harvested for nerve histomorphometry and muscle weight. To enable the assessment of scarring at the nerve repair site, nerve samples were stained for collagen using direct red 80 sirius red stain. A student t-test was used to evaluate for statistical significance.

RESULTS: Histomorphometric analysis of regenerating nerve fibers in the median nerve demonstrated relatively robust axonal regeneration in Group 2, with higher total axon count, myelin thickness, axon diameter when compared to the Group 1. The difference in total axon count between Group 2 and 1 was statistically significant (Group 2 = 1769 ± 672 axons, Group 1 = 1072 ± 123.80 axons, p = 0.0468). Furthermore, the difference in flexor muscle mass weight between the group 2 and group 1 was statistically significant (Group 2 = 0.629 ± 0.054, Group 1 = 0.511 ± 0.07, p < 0.05). With regard to functional recovery, at 14 weeks post-repair, Group 2 had regained 34.9% of naïve baseline hand grip strength. In comparison, Group 1 regained only 25.4% of baseline hand grip strength. Between group 2 and 1, the difference in grip strength was statistically significant (Group 2 = 1.67 ± 0.04, Group 1 = 0.97 ± 0.39, p = 0.036). Sirius red staining revealed less collagen deposition at the nerve co-apaptation site of Group 2 animals when compared to group 1 animals (p < 0.05).

CONCLUSION: Biodegradable, PCL nanofiber nerve conduits can improve nerve regeneration and subsequent physiological extremity function in the setting of delayed nerve repair by decreasing the scar burden at nerve co-apaptation sites.

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The Osseointegrated Neural Interface (ONI): A Rabbit Model for Chronic Peripheral Nerve Interfacing in Bone with Percutaneous Osseointegrated Connectors

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PURPOSE: Peripheral nerve interfaces represent a paradigm shift in the treatment and prevention of amputation neuromas. Rather than simply bury a transected nerve in muscle or bone in an effort to prevent/treat painful neuromas, attention has shifted to exploiting the regenerative capacity of these nerves to carry the control signals needed to animate advanced robotic prostheses. Caveats to current interfacing technology are the motion artifact and long-term stability of these devices in dynamic soft tissue environments. The Osseointegrated Neural Interface (ONI) represents a novel approach to peripheral nerve interfacing- utilizing the medullary cavity of the amputated long bone to house and protect the amputated nerve/delicate electrode interfaces from motion artifact and damage. The ONI is based on the transposition of nerve in bone to treat amputation neuromas, first described by Edwin Boldrey in 1943 and relies on the premise that bone provides stability and protection from external stimuli that may cause neuropathic pain. These same principals of stability and protection are also key components of any technology seeking to achieve a robust, chronic interface with the peripheral nervous system.

Objective: To evaluate the stability and longevity of chronically implanted ONI devices.

METHODS: We have developed a novel dual cuff electrode implant with a percutaneous, osseointegrated connector that
enables chronic electrophysiological evaluation of the ONI. The device consists of two, bipolar cuff electrodes with percutaneous connectors secured to a stainless steel intramedullary rod. Transfemoral amputation was performed in New Zealand white rabbits. The terminal end of the transected sciatic was passed through a proximal corticotomy in the femur, threaded into the medullary cavity and out the end of the bone. The terminal end of the nerve was secured in one cuff electrode and inserted back into the medullary cavity, followed by the intramedullary rod, which was then secured with bone cement. The second cuff electrode was attached to the nerve external to the bone, proximal to the corticotomy. Stimulation (monophasic, cathodal pulses- 30µs duration, 100µA-8mA) evoked afferent and efferent compound nerve action potentials (CNAPs) were recorded 3 and 5 weeks post implant with cortical somatosensory evoked potentials (SSEPs) recorded at 5 weeks. Differences in peak CNAP amplitude were investigated with one-way ANOVA.

RESULTS: Efferent (motor) CNAPs are present at 3 weeks and improve by 5 weeks, as indicated by a significantly greater peak CNAP response from a smaller stimulus (n=6, p≤0.05). There were no obvious afferent (sensory) CNAPs recorded at the same time points; however, afferent SSEPs were measured. The ability to record afferent SSEPs demonstrates that there is still a connection between the distal end of the amputated nerve and the cortex, indicating that the ability to transmit sensory information through the ONI is not lost. Future work will investigate if the ability to record afferent signals improves with longer implant duration.

CONCLUSIONS: This is the first evidence that physiological activity of nerves transposed and interfaced within bone can be harnessed chronically, towards future prosthesis control via an ONI.

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A Novel Animal Model of Optic Nerve Transection with Preservation of the Retinal Viability

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PURPOSE: Poor optic nerve regeneration still remains one of the major challenges preventing successful eye transplantation. The purpose of this study was to establish an optic nerve transection model that would allow evaluation of the axonal regeneration of retinal ganglion cells.

METHODS: Lewis rats were dissected, optic nerves were exposed and transected to create a clean-cut injury. An incision along the superior orbital rim and extending to the lateral temporal area with partial excision of temporalis muscle provided adequate exposure of the optic nerve. The levator palpebrae superioris and superior rectus muscles were transected, the Harderian and lacrimal glands were retracted and preserved. A superior-temporal minimal transverse incision was made on dura mater that provided enough space for optic nerve transection and allowed to retain the integrity of the ophthalmic artery and posterior ciliary artery, which is localized along the posterior nasal side of the optic nerve. Spectral domain optical coherence tomography (SD-OCT), electroretinography (ERG) and confocal scanning laser ophthalmoscopy (cSLO) were used to evaluate morphology, electrical activity and vascular integrity of the retina.

RESULTS: SD-OCT detected progressive atrophy of the retinal nerve fiber layer (RNFL) over the post-operative 12 weeks follow up period. Starting from week 4 there was a noticeable (19.1%) reduction of the RNFL, however, it was not statistically significant (p>0.05) compared to the control side. The difference became statistically significant (p<0.05) at week 6 and by post-operative 12-week RNFL on operated side was reduced by 54.3%. However, the total retinal thickness on the operated side was reduced only by 21.8% (p<0.05). SLO fluorescein and indocyanine green angiography revealed preservation of retinal and choroidal vasculature. Positive peaks were detected on the ERGs of operated eyes in response to flashlight stimulation. However, the amplitudes of the waves were decreased in operated eyes compared to control side.

CONCLUSION: We developed optic nerve complete transection model that maintains the integrity of the ophthalmic artery and retinal perfusion, which is essential for the preservation of the viability of the retina and evaluation of the optic nerve regeneration.