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The Effects of Exercise and an Enhanced Nerve Conduit on Peripheral Nerve Injury

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The effects of exercise and an enhanced nerve conduit on peripheral nerve injury

College of Engineering

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Biomedical Engineering

Opportunity and Significance

Induced regeneration and reinnervation of peripheral neurons post injury remains a challenge [1]. This study examines the effects of exercise combined with a multimodal scaffold on recovery from peripheral nerve injury. Currently, the gold standard is the autograft in which a nerve is severed elsewhere in the body and used as a replacement segment for the damaged nerve of interest [1]. This study examines a hypothesized alternative to this current standard that does not involve harvesting a preexisting nerve segment.

Technical Objectives

The primary objective of this effort is to quantify peripheral nerve recovery as a result of exposure to a multimodal conduit in addition to exercise. Quantification was based on behavioral data collected from a rat sciatic nerve model.

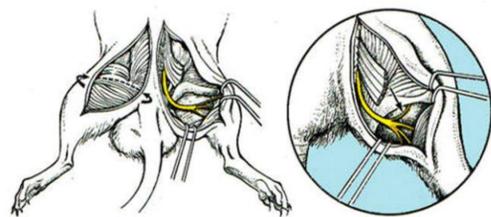


Figure 1: Rat sciatic nerve

Related Work and State of Practice

A multimodal scaffold incorporating:

- Topographical cues: aligned MeHA fibers
- Mechanical cues: soft material
- Adhesive cues: fibronectin
- Chemical cues: glial cell derived neurotrophic factor (GDNF).

Was developed in the Sundararaghavan lab and tested *in vitro* prior to this animal study. This *in vitro* study yielded promising results that were the impetus that led to the animal study

Technical Approach, Accomplishments

- This study utilized a rat sciatic nerve model in which a 10 mm section of the sciatic nerve was removed, and the gap bridged in various ways.
- Scaffold efficacy was measured by examining the following five groups:
 - Autograft with no exercise
 - Bare conduit (fibers only) with no exercise
 - Bare conduit with exercise
 - Multimodal conduit with no exercise
 - Multimodal conduit with exercise
- Weekly behavioral tests were conducted:
 - Footfall
 - Animals walk across a ladder and the number of footfalls is recorded
 - Static Sciatic Index (SSI)
 - Measurements taken from images of feet and functionality estimated based on SSI calculation
 - Von Frey Filament Test
 - Force required to elicit response is measured
- Data analysis is still in progress

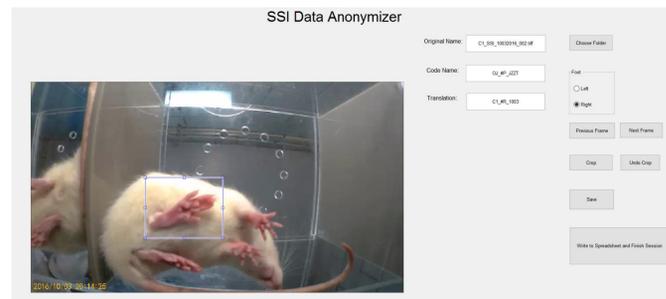


Figure 2: User interface based code developed for SSI data anonymizing –used to crop images and encrypt filenames to remove bias during measurement

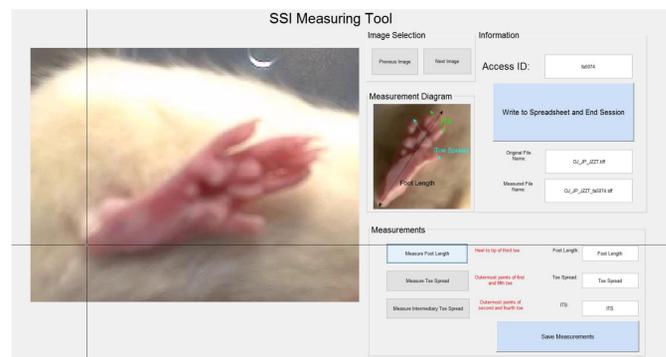


Figure 3: User interface based code developed for SSI measurements – used to take measurements of anonymized images for calculation of SSI

Results

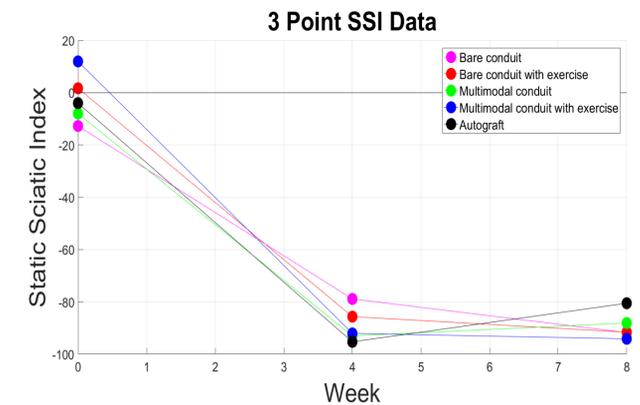


Figure 4: Preliminary 3 point SSI data – 0 represents normal and -100 represents complete impairment

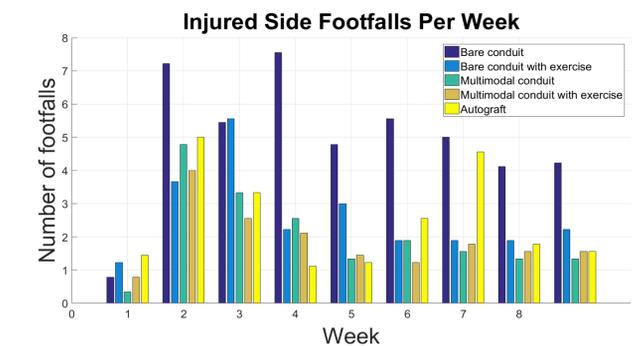


Figure 5: Footfall data, lower scores indicate higher functionality

Conclusion

The multimodal scaffold shows results that are competitive with the autograft gold standard. The benefits of exercise seem questionable, however this may be due to the gender of the animals chosen [2].

Next Steps for Development and Test

- Fine tune the microsphere growth factor delivery system
- Investigation of other growth factors (i.e. nerve growth factor (NGF) or brain-derived neurotrophic factor(BDNF))
- Investigation of the effects of scaffold stretching

References

- [1] Whitehead, T. J. and H. G. Sundararaghavan (2014). "Electrospinning growth factor releasing microspheres into fibrous scaffolds." J Vis Exp(90).
- [2] Thompson, N. J., Sengelau, D. R. & English, A. W. Enhancement of peripheral nerve regeneration due to treadmill training and electrical stimulation is dependent on androgen receptor signaling. Dev. Neurobiol. 74, 531–540 (2014).