High AIS Grade Conversion Rate Following Neuro-Spinal Scaffold Implantation in Acute Thoracic Complete AIS A Spinal Cord Injury (SCI): Potential Mechanisms

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Introduction

In pre-clinical animal models, a neuro-spinal scaffold (NSS) implantation following SCI promotes neural sparing and regeneration through internal decompression and tissue remodeling. Rather than common post-injury cyst formation, the NSS acts through appositional healing to form remodeled tissue which supports endogenous neural sprouting. A pilot clinical study of the investigational NSS enrolled 6 patients with acute complete thoracic SCI. Four patients converted to incomplete injuries at 1 month or later. Sustained or delayed patterns of recovery compared to natural history were observed in select patients. Longitudinal MRI scans and the extended time course of neurological recovery suggest that reduced cyst formation and potential neural regeneration may contribute to these clinical findings.

Methods

The neuro-spinal scaffold is a highly porous, cylindrical device composed of a synthetic, biocompatible, and biodegradable polymer. This device will naturally degrade within 4-8 weeks and be cleared via established pathways.

Implantation procedure: The device is implanted acutely following injury within the intraparenchymal lesion.

Clinical trial pilot study: Pilot Study of Clinical Safety and Feasibility of the PLGA Poly-L-Lysine Scaffold for the Treatment of Complete (AIS A) Traumatic Acute Spinal Cord Injury (NCT 02138110).

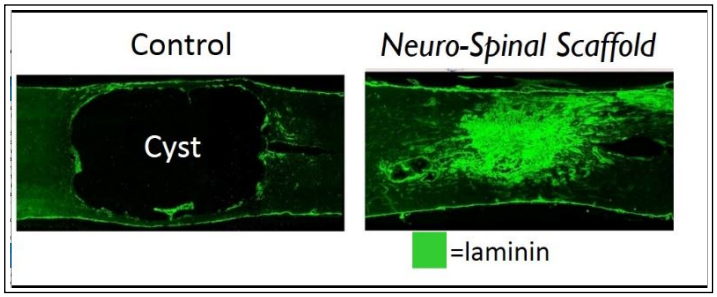
Key Inclusion Criteria:
- AIS A (T3-T12/L1) ? 16-70 years of age ? Non-penetrating injury ? within 96 hours of injury ?

Key Exclusion Criteria:
- Incomplete SCI ? SCI associated with TBI ?

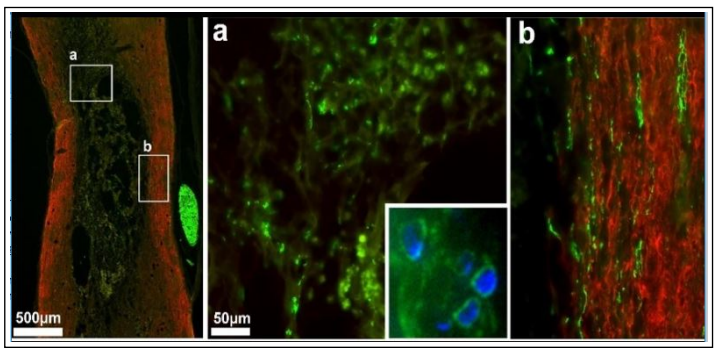
Results

Pre-Clinical

Acute implantation of the NSS in a rat contusion model results in a significant increase in the deposition of laminin



The remodeled tissue (laminin) at the injury epicenter is permissive to endogenous axonal sprouting and Schwann cell remyelination.



Schwann cell myelin (green) is observed ensheathing the sprouting axons (blue) in the injury epicenter (a) and in the spared peripheral white matter tracts (b) alongside native oligodendrocytes (red).

Clinical

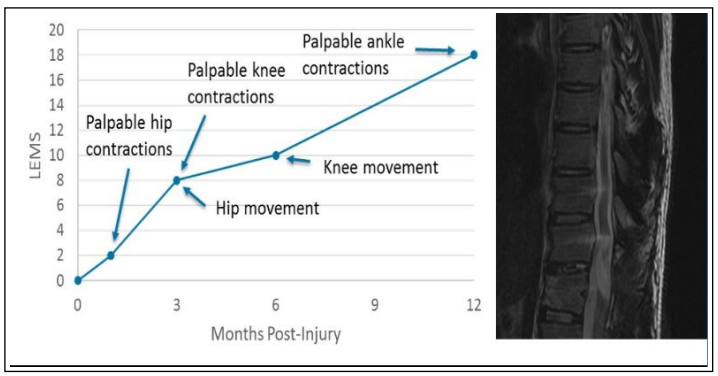
Pilot Study Patients

Patient	Gender	Age	NLI	Time to Implant (hr)
1	M	25	T11	9
2	F	22	T7	46
3	M	55	T4	83
4	M	28	T3	53
5	F	18	T8	69
6	M	21	T10	9

Historical benchmarks report 14-16% AIS conversion at 6-12 months in baseline thoracic AIS A's. Although a small sample size, 4/6 (67%) of subjects in the Pilot study converted to incomplete injuries by 6 months post-injury

Patient	NLI	Neurologic Outcome to Date
1	T11	Converted to AIS C at 1 month Δ LEMS = +18 at 12 months
2	T7	Remains AIS A but with marked bowel and bladder improvement by 12 months
3	T4	Converted to AIS B at 1 month
4	T3	Remains AIS A at 6 months
5	T8	Converted to AIS B at 6 months
6	T10	Converted to AIS B at 2 months

Neurologic recovery was sustained beyond 12 months in Patient 1 and delayed by 6 months in Patient 5. Below illustrates Patient 1's continuous lower extremity motor score (LEMS) improvement out to 12 months. The 12 month MRI demonstrates myelomalacia with internal architecture observed within the lesion epicenter.



Conclusion

A pilot clinical study to assess the safety and preliminary effectiveness of neuro-spinal scaffold implantation in acute SCI was conducted. An increased proportion of patients converted to incomplete AIS grades compared to natural history. Further, possible clinical mechanisms of action of cyst reduction and neural regeneration are hypothesized based on pre-clinical findings. Significant future work including advanced MRI techniques is needed to support these claims.