High ASIA Impairment Scale Conversion Rate Following Scaffold Implantation in Acute Thoracic Complete AIS A Spinal Cord Injury (SCI): Potential Mechanisms

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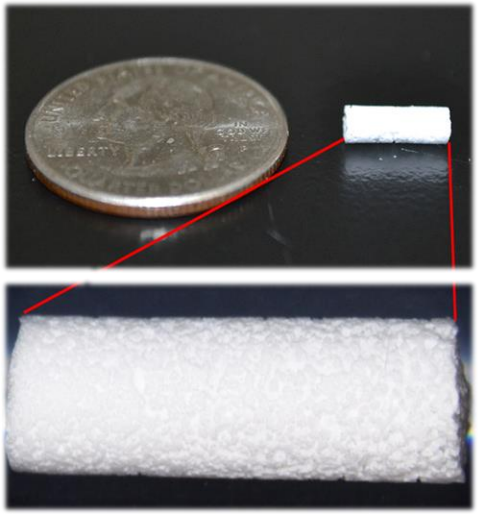
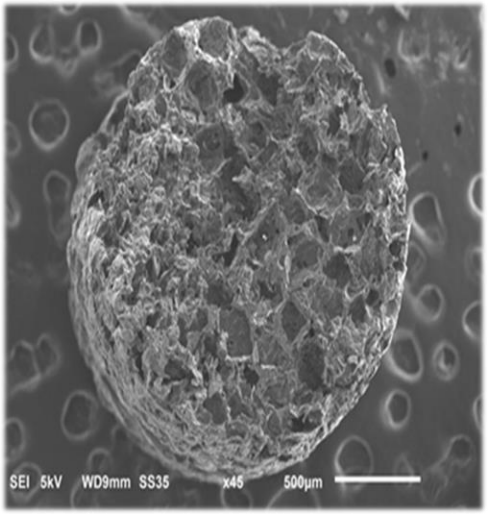
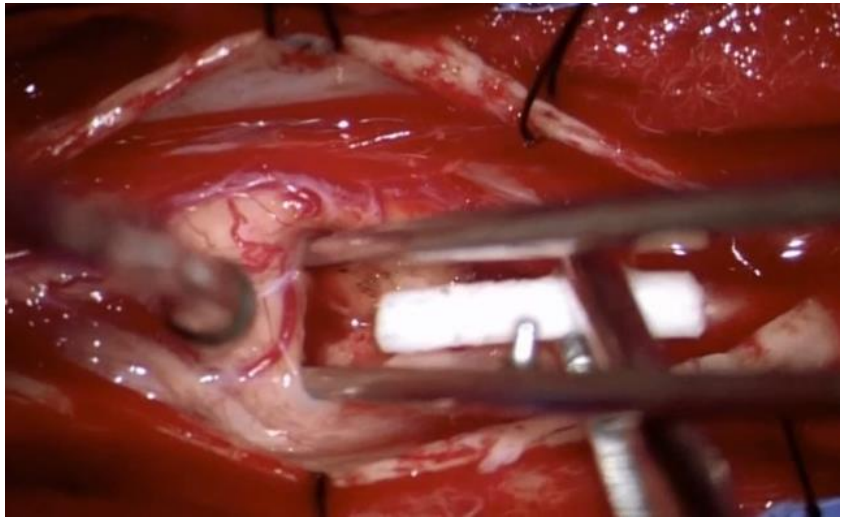
Novel Clinical Approach for Acute SCI Treatment: Intraparenchymal Scaffold Implantation

- Designed to act as a physical substrate to promote neural repair
  - Porous, bioresorbable device
  - *In vivo* residence time ~4-8 weeks
- Intraparenchymal implantation within acute cavity following durotomy and often myelotomy
- Investigational device currently being evaluated in INSPIRE clinical trial: **NCT02138110** – Currently enrolling baseline T2-T12/L1 AIS A injuries <96hrs



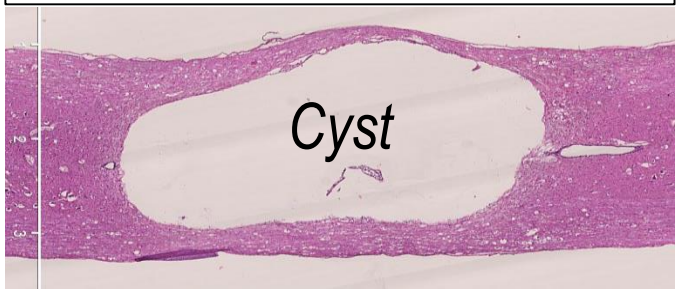




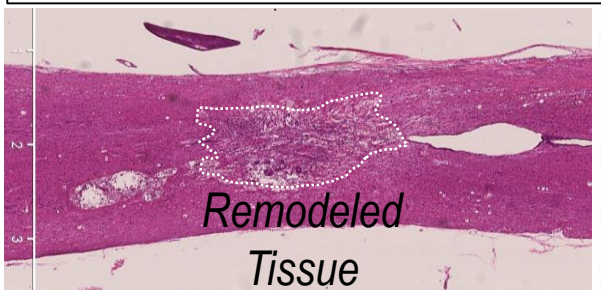
The Scaffold Preserves Spinal Cord Architecture in Pre-Clinical Models

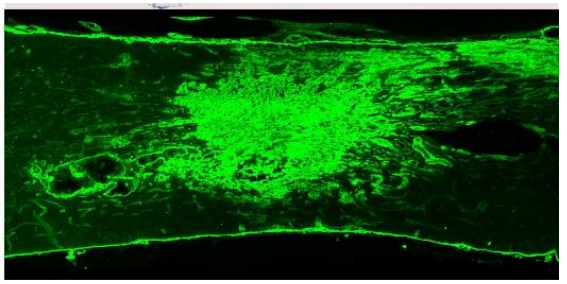
Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Control



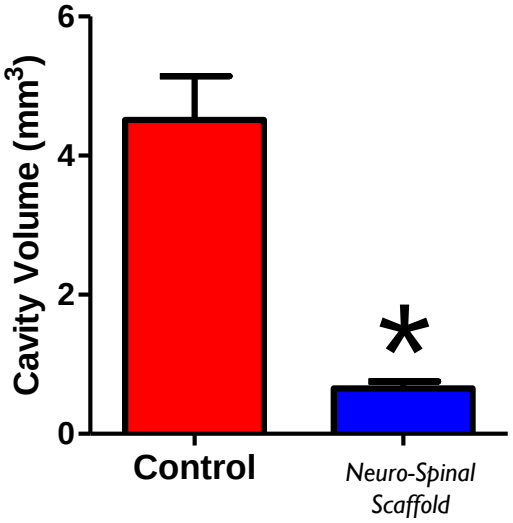
Neuro-Spinal Scaffold



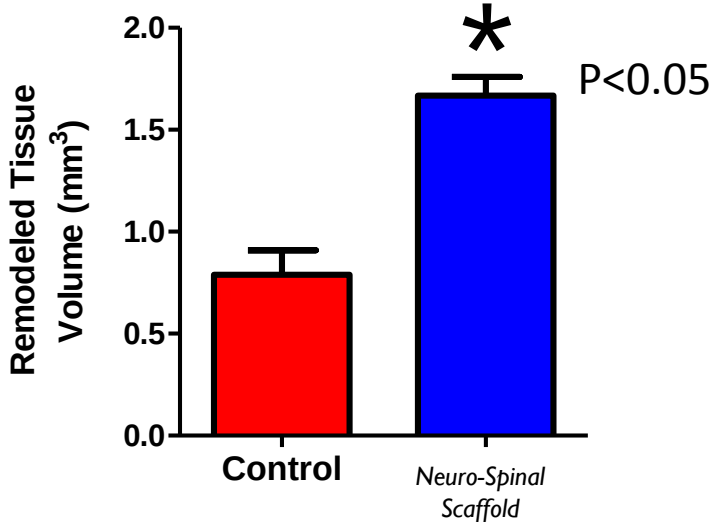


Laminin

Cyst Reduction



Remodeled Tissue



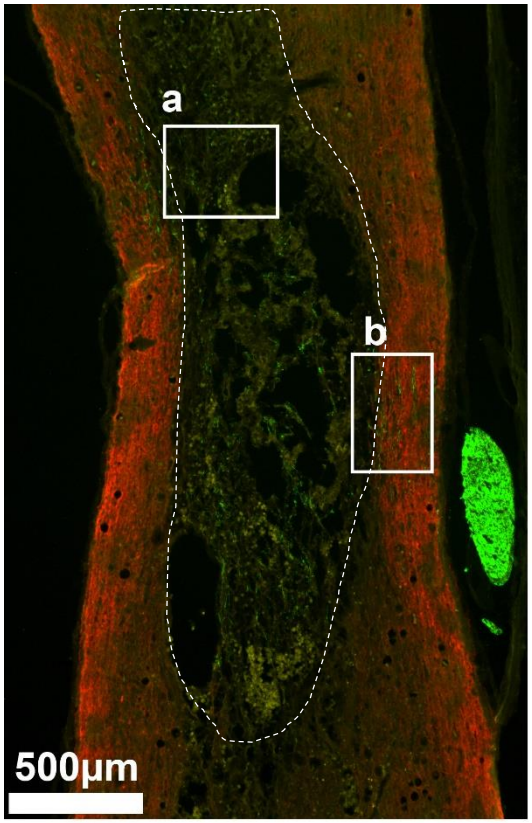
Neural Regeneration and Remyelination with Schwann Cells after Scaffold Implantation

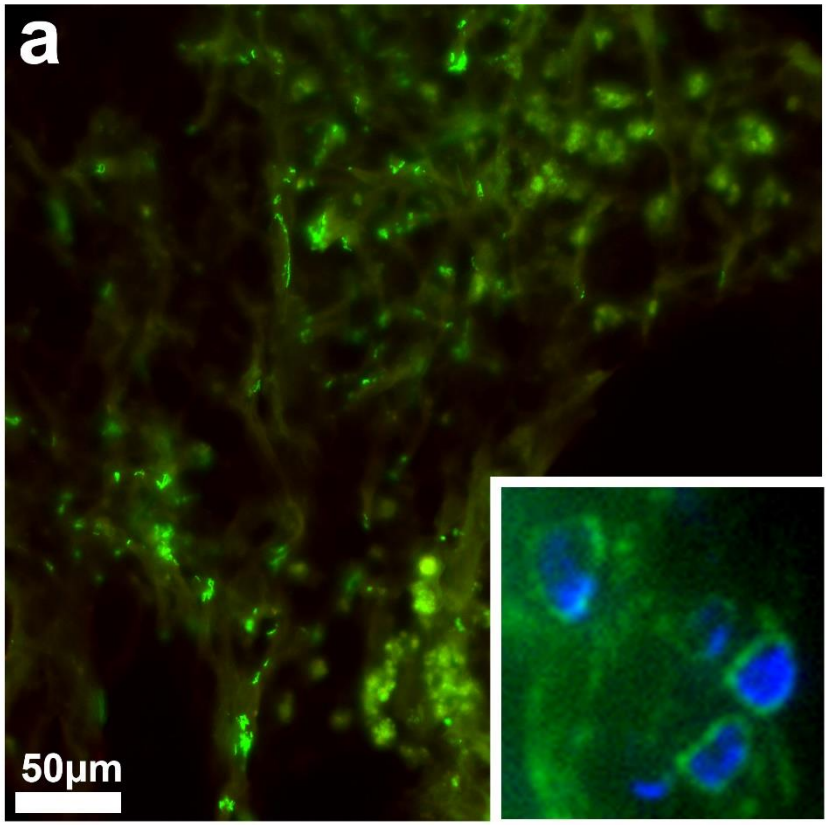
Contusion Injury

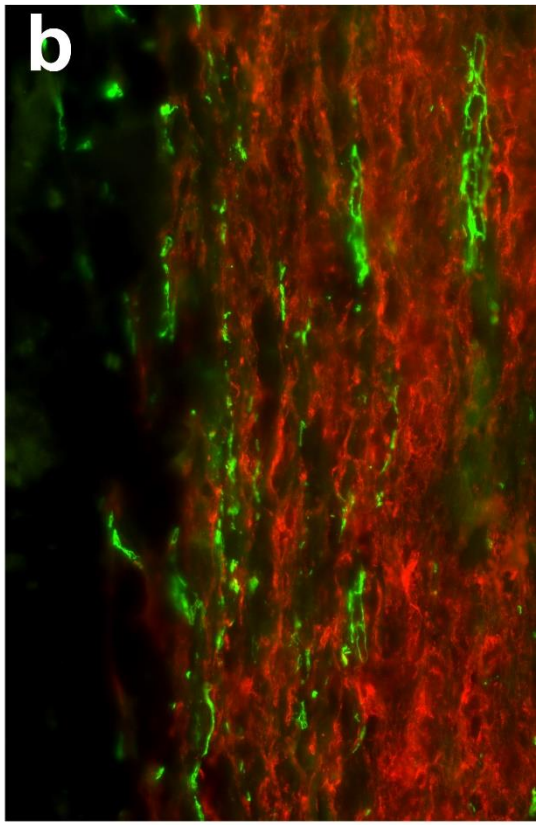
Central epicenter (a) and white matter (b)

Epicenter

White Matter







Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Inset: Schwann cells ensheathing axons

Oligodendrocytes Schwann Cells

The INSPIRE Study - Promising Neurologic Outcomes and Favorable Safety Profile

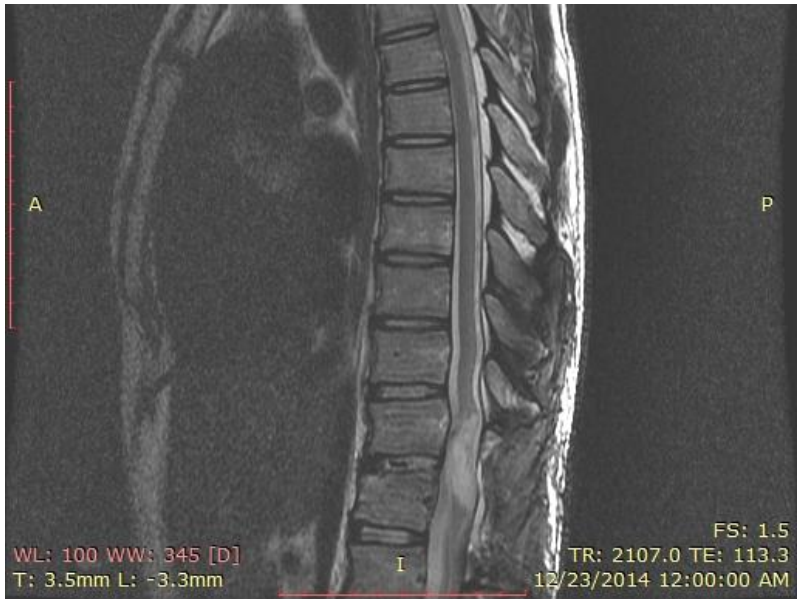
*All Subjects were AIS A at Baseline

Subject	Age Sex	NLI	Time to Implant (hr)	Neurologic Outcome to Date
1	25 M	T11	9.2	**Converted to AIS C at 1 month**
2	22 F	T7	45.6	Remains AIS A at 12 months
3	56 M	T4	82.6	**Converted to AIS B at 1 month**
4	28 M	T3	52.9	Remains AIS A at 12 months
5	18 F	T8	69.1	**Converted to AIS B at 6 months**
6	21 M	T10	8.8	**Converted to AIS B at 2 months**
7	25 M	T4	21.3	Remains AIS A at 3 months
9	37 M	T3	40.4	**Converted to AIS B at 3 months**

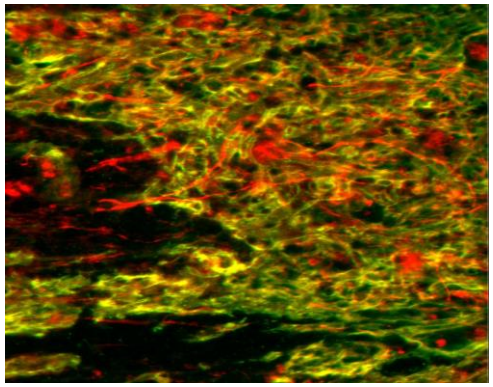
- 5 of 8 evaluable subjects converted from complete to incomplete injuries within 6 months
- Natural history reports ~14-16% conversion rate in this patient population

Clinical Benefit of Scaffold Implantation: Potential Mechanisms

- Scaffold implantation permits:
  - Intra-dural decompression
  - Evacuation of necro-hemorrhagic tissue
- Scaffold promotes endogenous tissue remodeling:
  - Potential cyst reduction – Follow-up MRI's being assessed *(clinical)*
  - Neural regeneration *(pre-clinical)*
  - Promotion of remyelination by Schwann cells *(pre-clinical)*



Patient 1: 6 month MRI



Rat Contusion Model

Laminin
β3-Tubulin

Conclusion and Future Clinical Plans for Scaffold Device

- **Conclusion**
  - The Scaffold device has demonstrated a favorable safety profile to date in the limited subject population
  - Preliminary neurological recovery is promising and warrants further clinical investigation
  - Various clinical mechanisms of action are presented and future advanced studies would be needed to confirm these hypotheses

- **Future Plans**
  - Continue to enroll acute T2-T12/L1 AIS A to reach 20 evaluable subjects (12 more needed)
    - 23 clinical sites throughout the U.S. and Canada are currently open
  - Plan to initiate acute cervical AIS A trial in coming months

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