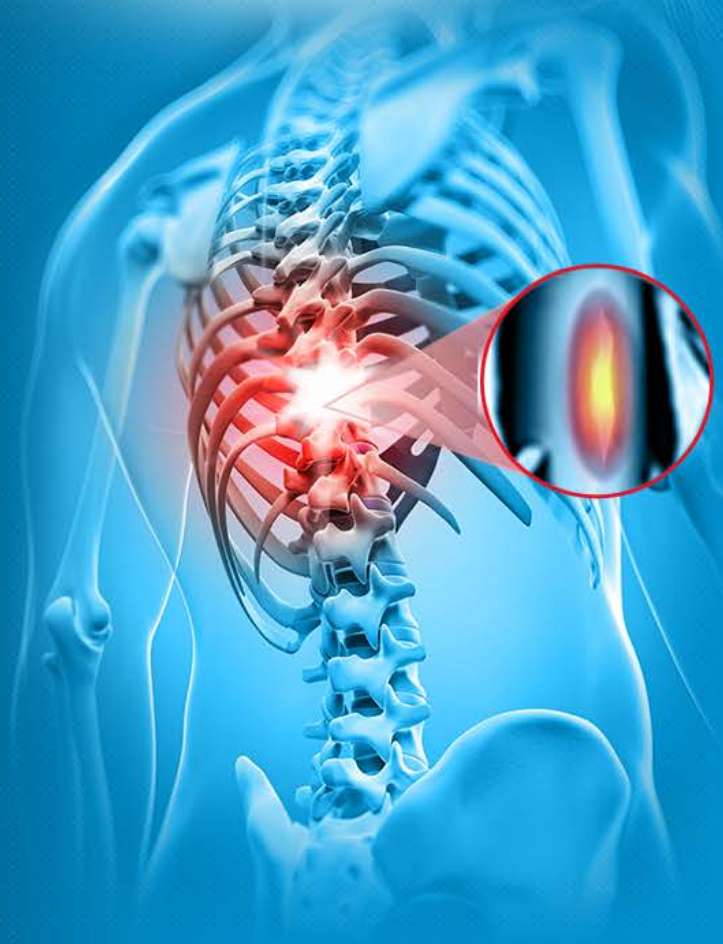
INVIVO THERAPEUTICS™



Translation of Biomaterial-based Therapies for the Treatment of Spinal Cord Injury: The *Neuro-Spinal Scaffold*™ and Bioengineered Neural Trails™

Alex A. Aimetti, PhD

Sr. Director, Medical Education

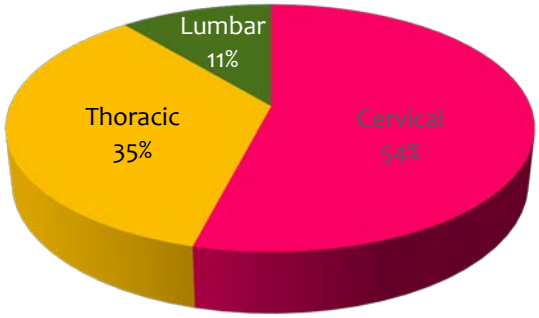
October 25, 2016

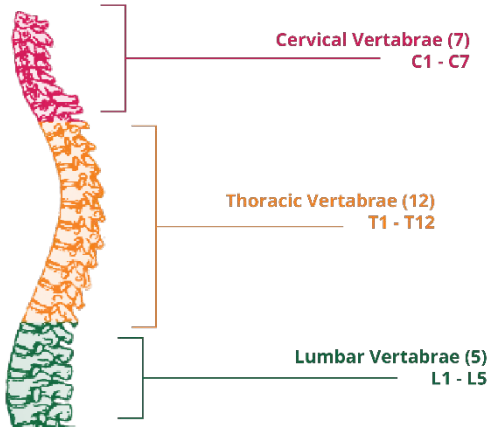
Agenda

- Spinal cord injury background
  - Science of natural progression & modern day standard of care
- *Neuro-Spinal Scaffold*™: Our approach to acute SCI
  - Technology & mechanism of action
  - Translation to the clinic
  - Clinical results to date and future clinical development plans
- Bioengineered Neural Trails: Our approach to chronic SCI
  - Rationale
  - Pre-clinical development and results to date

Spinal Cord Injury: An Unmet Clinical Need

- Unserved patient population
  - 12,500 new cases of acute SCI per year in US[1]
  - 276,000 currently live with chronic SCI in US[1]

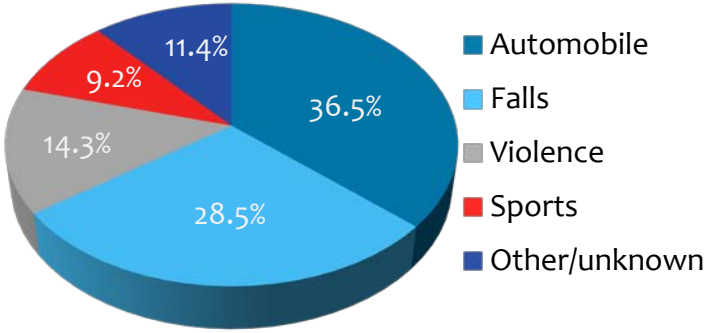




  - Only small percentage of patients ever regain function[2]

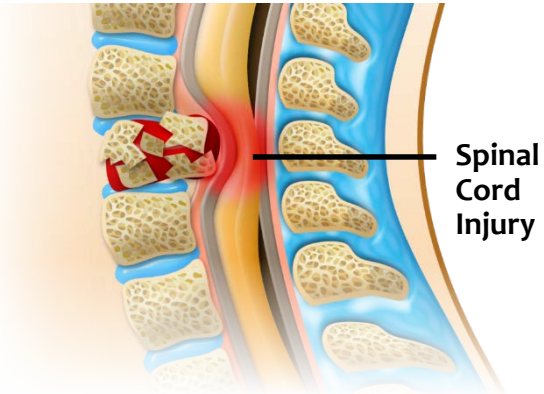
- Acute SCI clinical trials using drugs/biologics/cells have all been unsuccessful in showing clinically meaningful improvement

Causes of Spinal Cord Injury[1]



1. National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance. Birmingham, AL: University of Alabama at Birmingham, February 2015.
2. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal cord (2007).*

Progression of Acute SCI to Post-Traumatic Cavity in Contusion Injuries



Hemorrhage & Spinal Cord Swelling

Reduced Blood Flow & Ischemic Necrosis

Cavity Development & White Matter Reduction

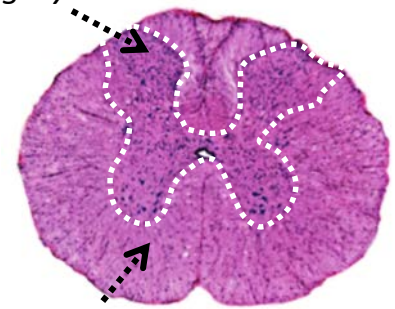
Chronic injury and mature cavity formation

Acute SCI: *Neuro-Spinal Scaffold™*

Chronic SCI: Bioengineered Neural Trails™

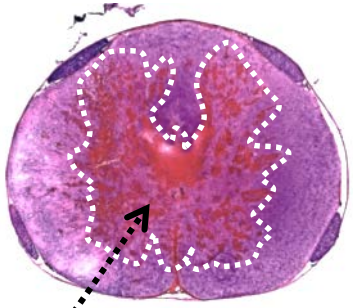
Normal

Highly vascularized gray matter



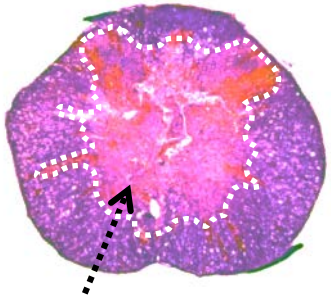
White matter

2 hours after SCI



Acute hemorrhage & necrosis

24 hours after SCI



Liquefactive necrosis

12 weeks after SCI

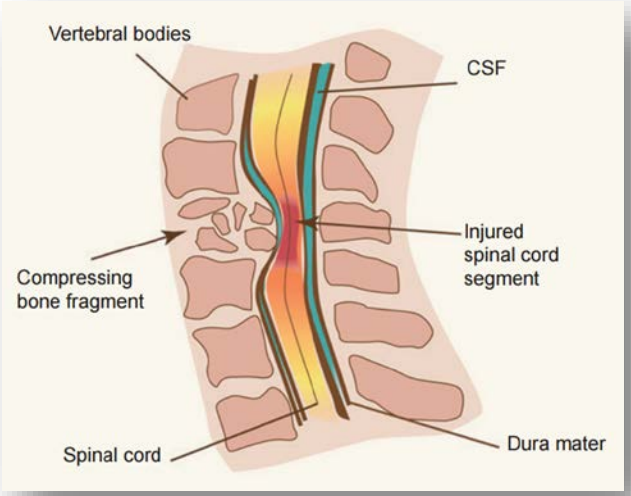
Mature cavity

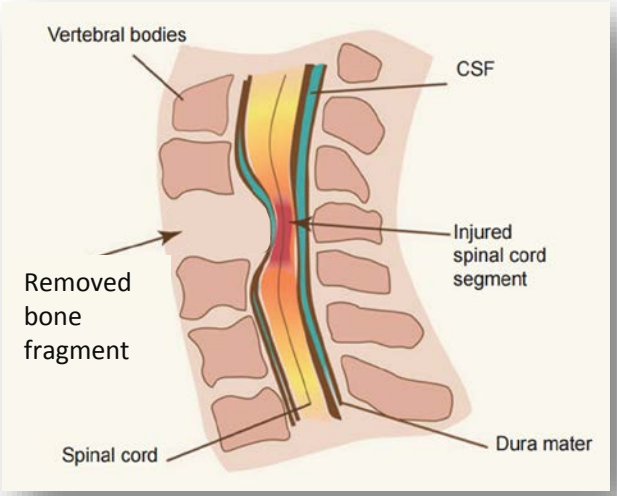
Histology from rat contusion model of SCI

Poster D8-06; National Neurotrauma Society 2015 Symposium; Santa Fe, NM.

Standard of Care Following Acute Injury

- Extradural bony decompression and spine stabilization using mechanical hardware





- Rehabilitation is recommended however no specific regimens are proven to improve neurologic recovery (i.e. no SOC rehab)
- Surgical access to the injured spinal cord (intradural/intraparenchymal) is **not** currently practiced

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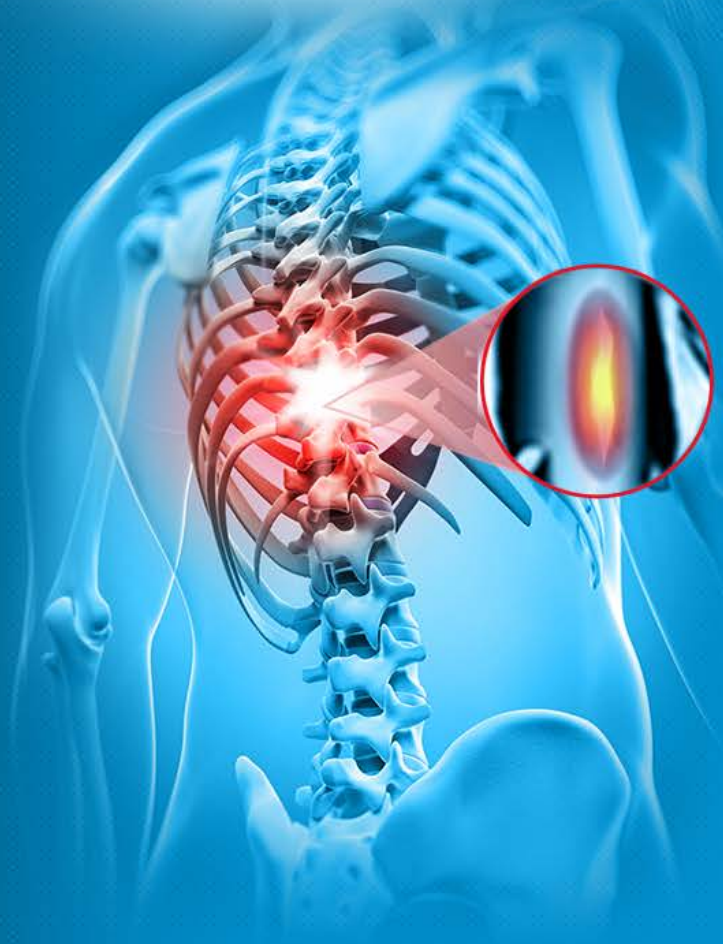
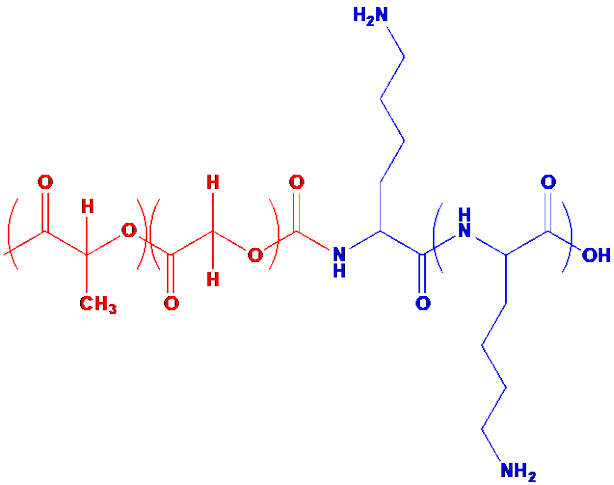


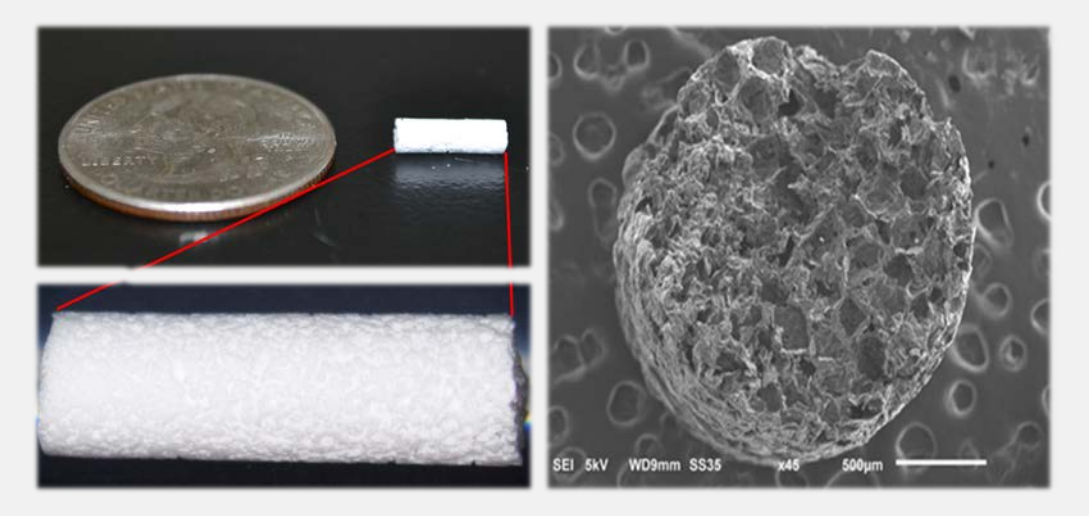
Neuro-Spinal Scaffold™ for Acute SCI

Designed to Promote Healing in Spinal Cord Injury

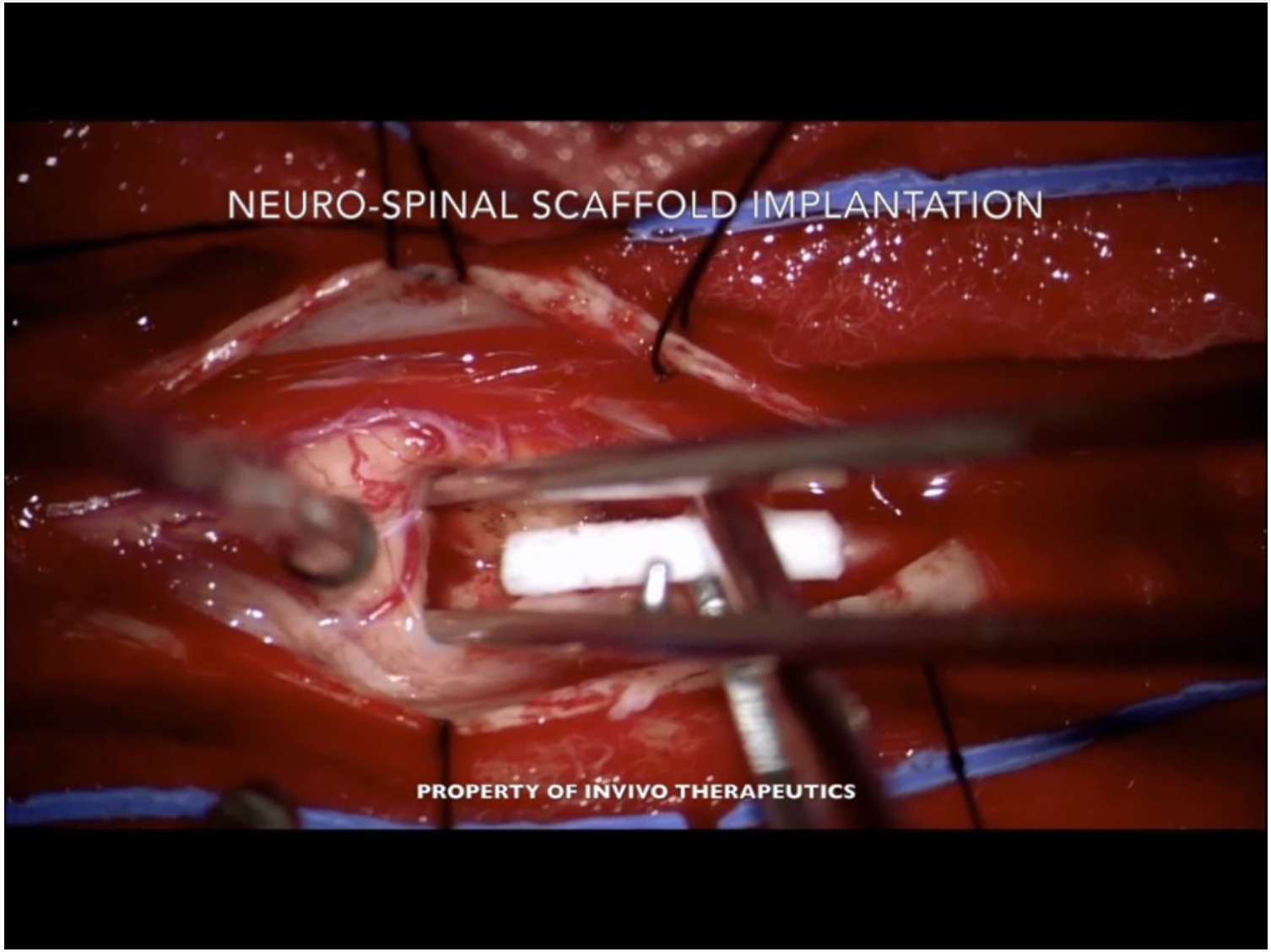
Novel Clinical Approach for Acute SCI: The *Neuro-Spinal Scaffold*™



poly(lactic-co-glycolic acid)-*b*-poly(L-lysine)

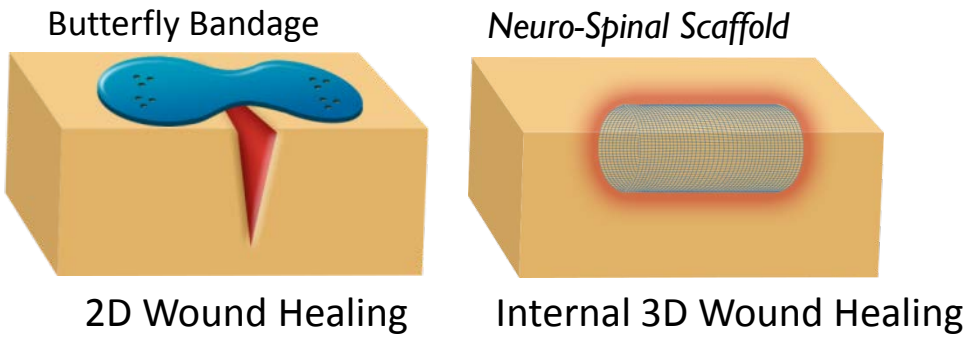


First *Neuro-Spinal Scaffold*™ Implantation in Human Contusion Injury



Neuro-Spinal Scaffold™ Mechanism of Action

- Promotes the formation of neuro-permissive remodeled tissue that supports neural regeneration
- Provides structural support to surrounding viable tissue
- Serves as a locus for 3-dimensional appositional healing

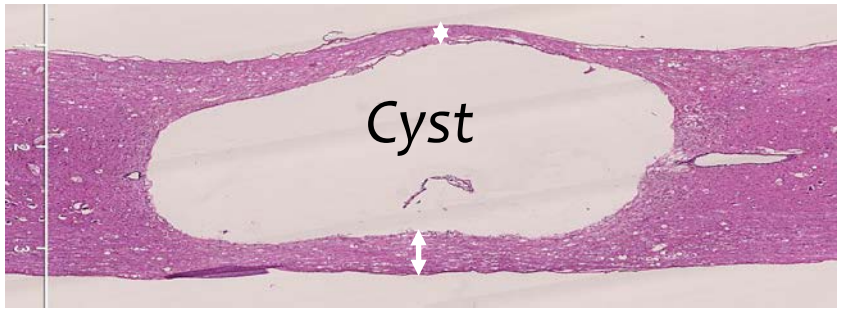


- Preserves macroscopic spinal cord architecture and decreases cyst volume
- Increases spared white matter and promotes remyelination of denuded axons

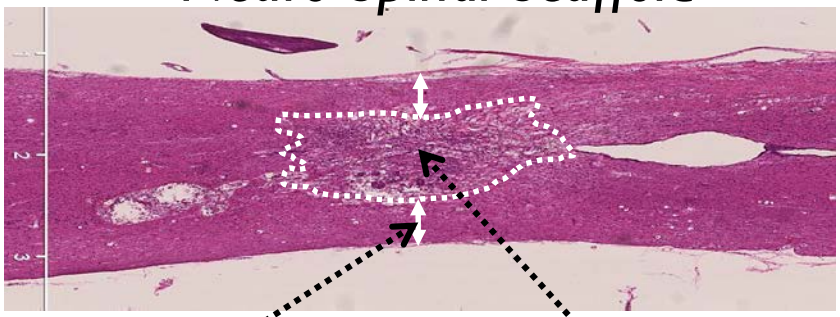
The *Neuro-Spinal Scaffold*™ Preserves Macroscopic Spinal Cord Architecture

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

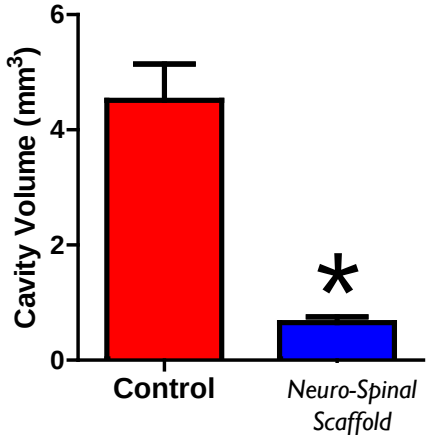
Control



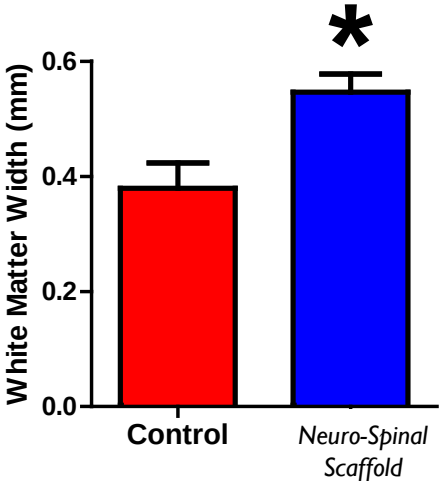
Neuro-Spinal Scaffold



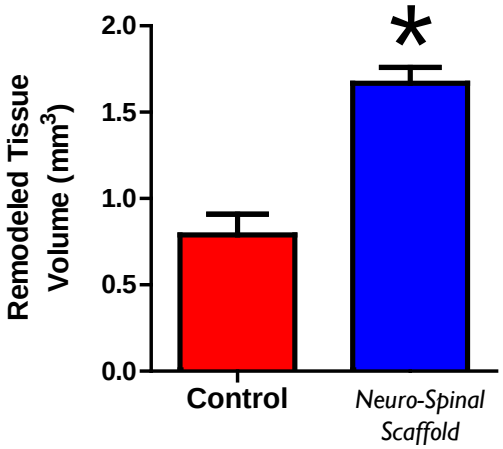
Cyst Reduction



White Matter Sparing



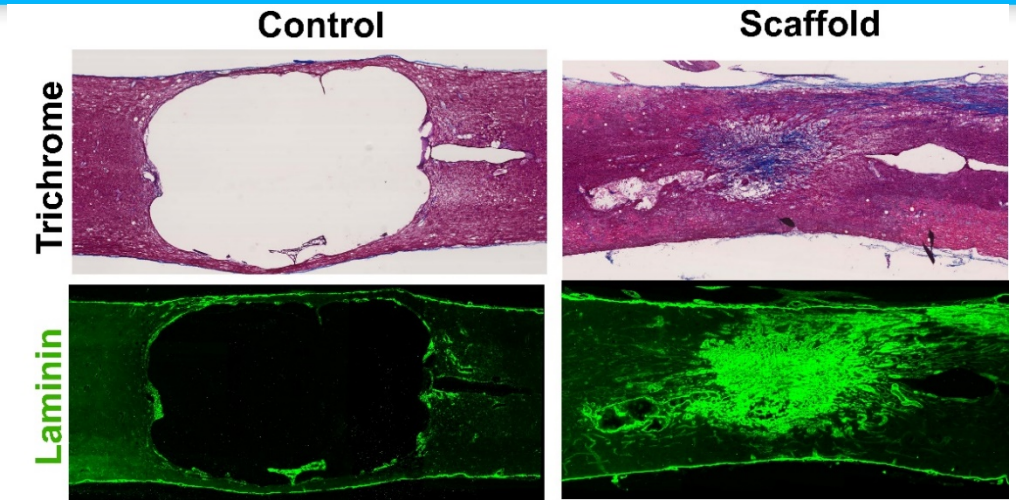
Remodeled Tissue



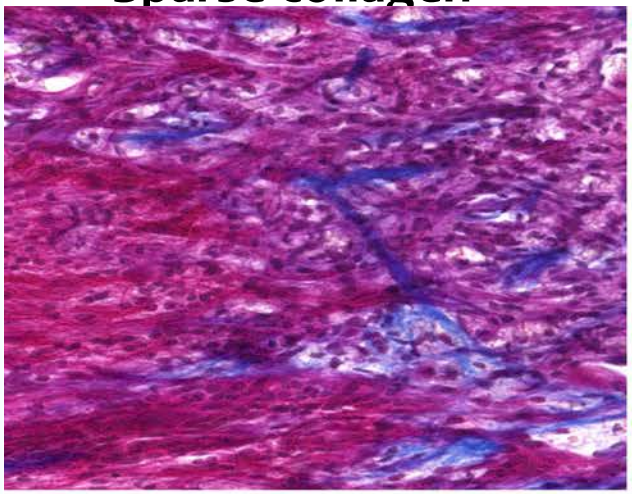
*P<0.05

Poster D8-06; National Neurotrauma Society 2015 Symposium; Santa Fe, NM.

Neural Sprouting Within Remodeled Tissue Contains Laminin and Sparse Collagen

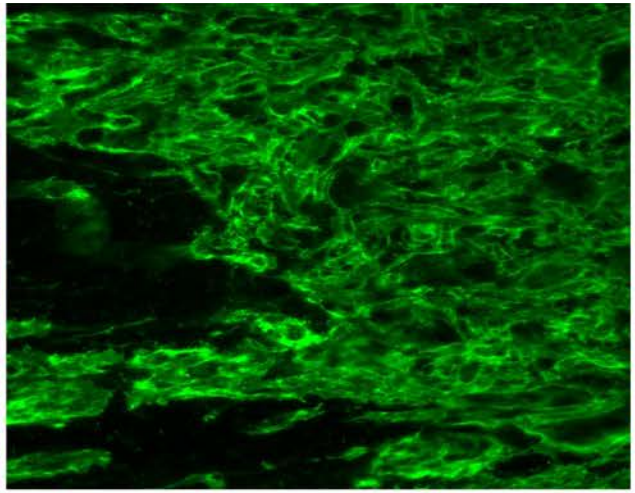


Sparse collagen



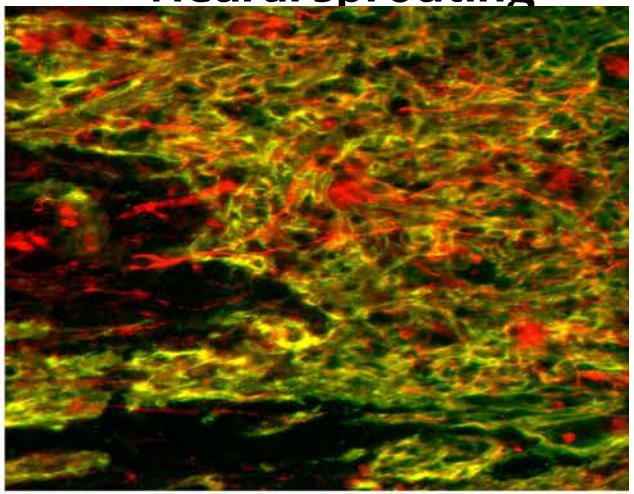
Masson's Trichrome

Abundant laminin



Laminin

Neural sprouting

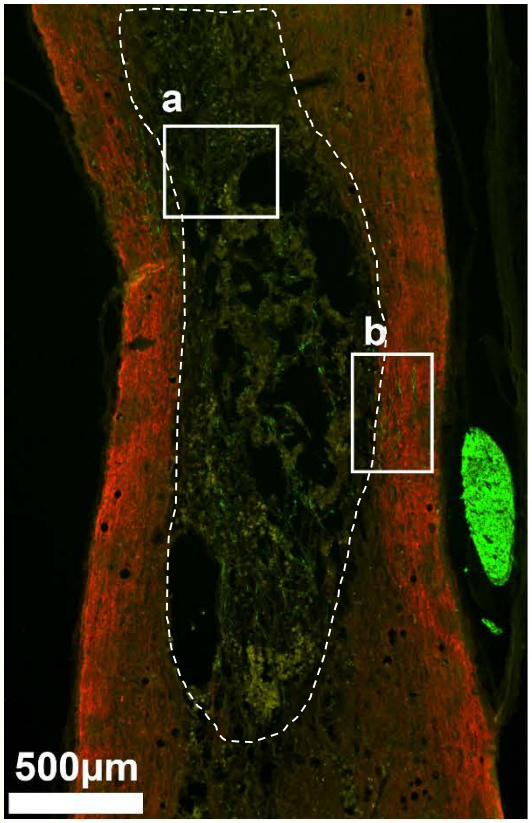


ß3-Tubulin/Laminin

Neural Regeneration and Remyelination with Schwann Cells after *Neuro-Spinal Scaffold*™ Implantation

Contusion Injury

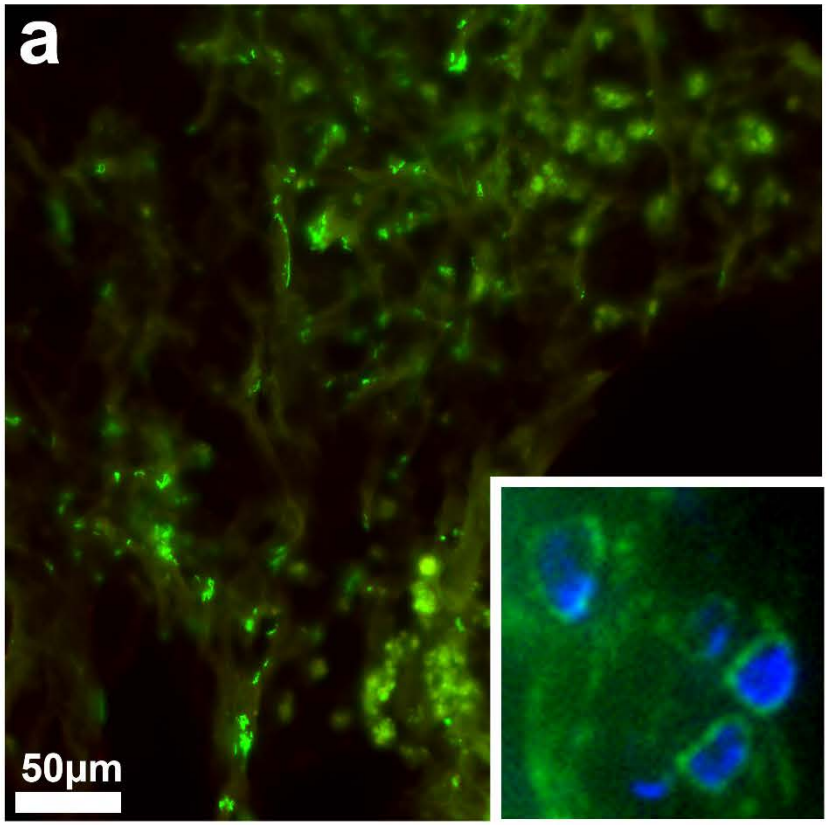
Central epicenter (a) and white matter (b)



Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Epicenter

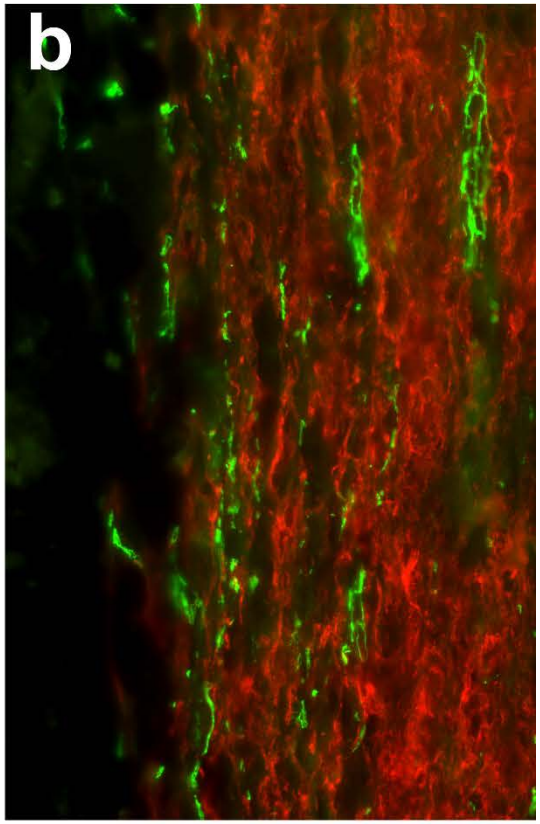
Schwann Cells aid neural regeneration



Inset: Schwann cells ensheathing axons

White Matter

Schwann Cells restore signal transduction



Oligodendrocytes Schwann Cells

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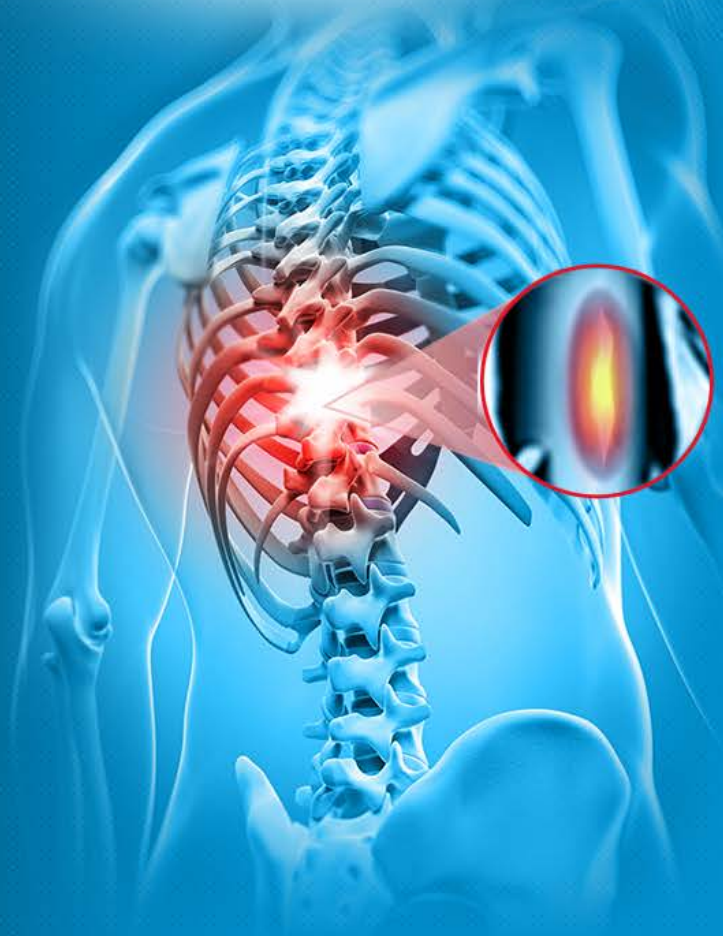
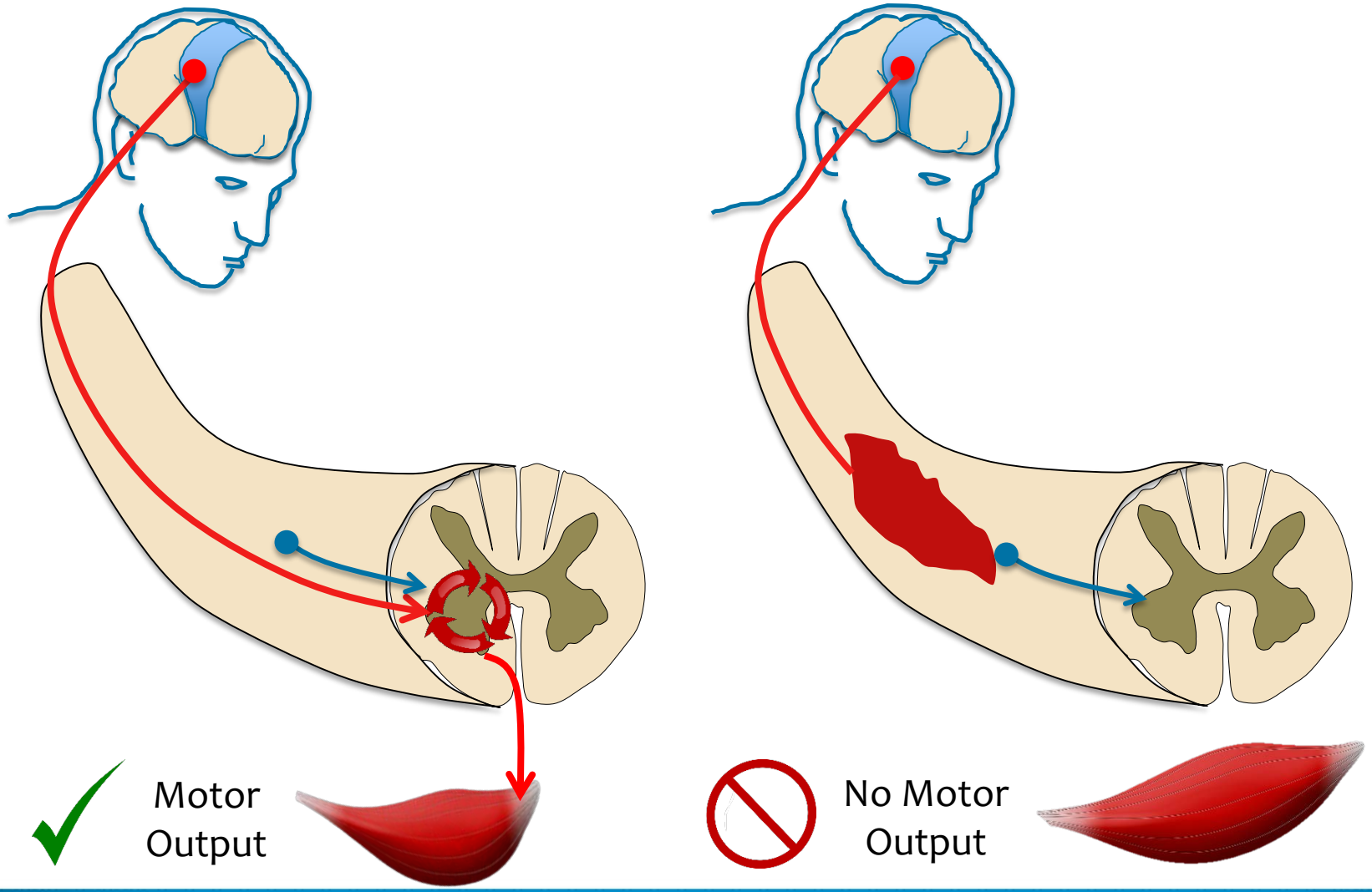


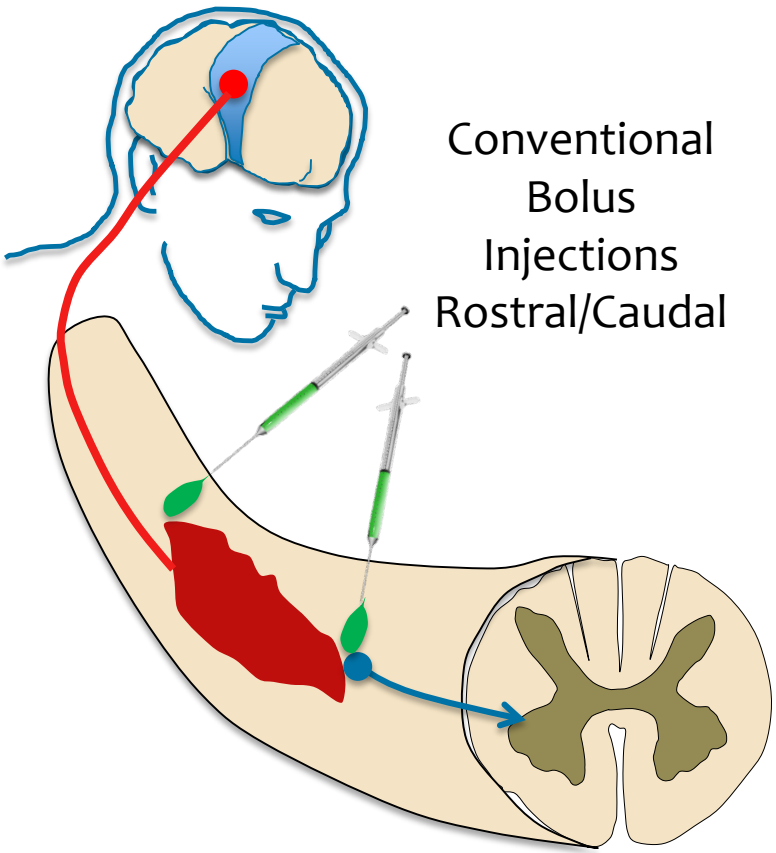
InVivo's Chronic SCI Product: Bioengineered Neural Trails™

Neural Stem Cells Incorporated into an Injectable Scaffold for Minimally-Invasive Delivery

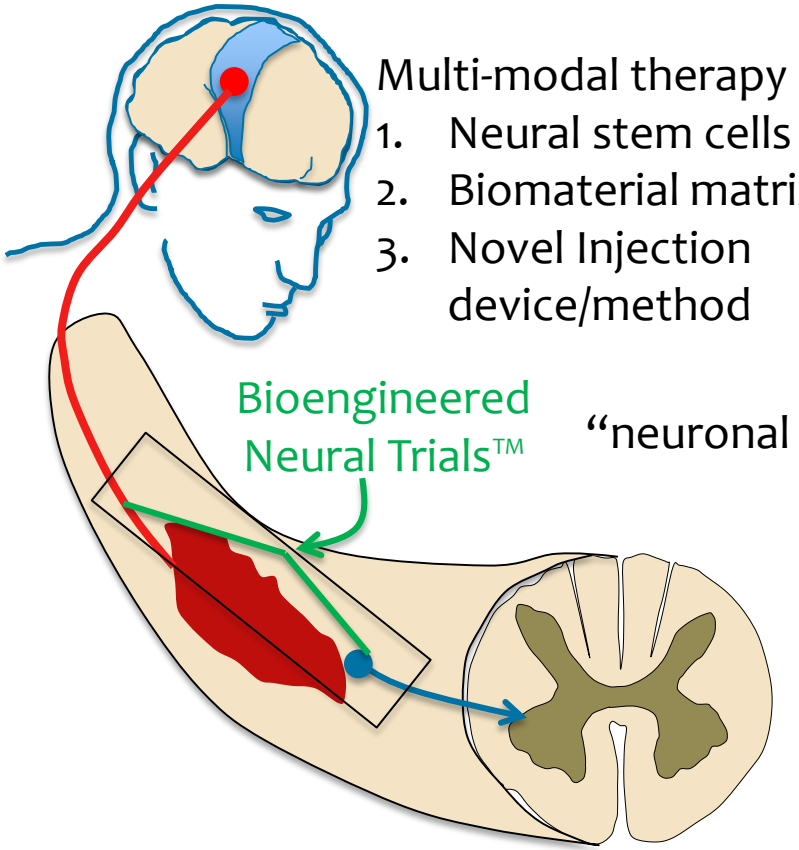
Disruption of Motor Control within the Spinal Cord Following Injury



Trails of Transplanted Cells May Provide a Preferred Delivery Approach to Bridge the Injury



Conventional
Bolus
Injections
Rostral/Caudal



Multi-modal therapy includes:

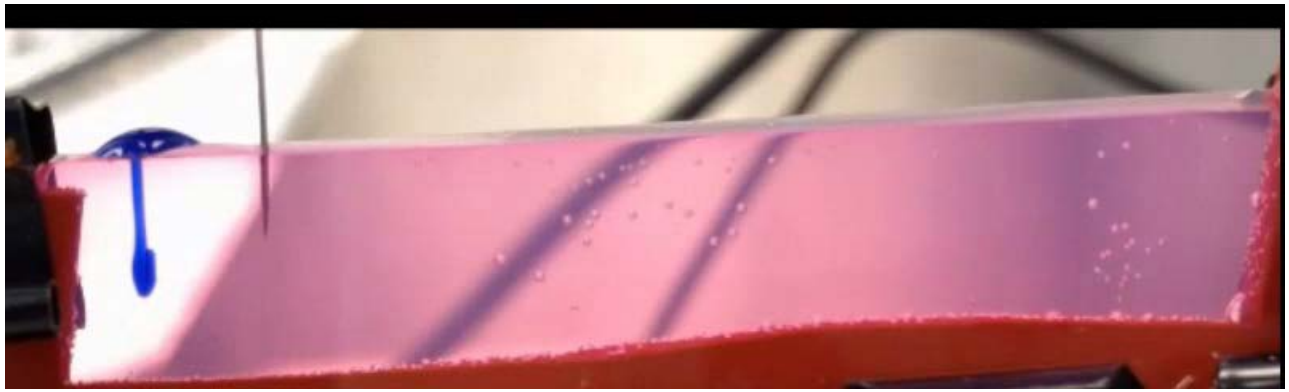
1. Neural stem cells
2. Biomaterial matrix
3. Novel Injection device/method

"neuronal relay"

Bioengineered Neural Trails™ Provide Many Advantages Over Conventional Bolus Injections

Bolus approach

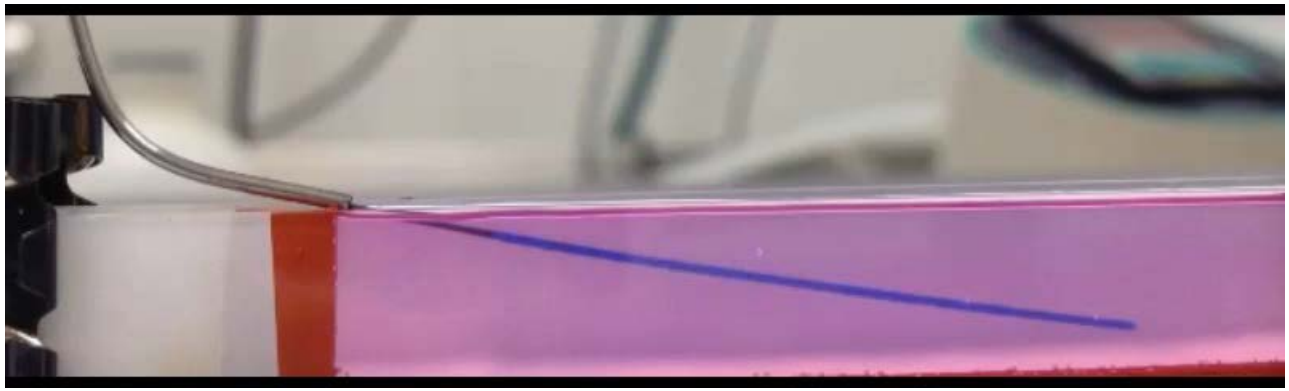
- Reflux at multiple injection sites
- Sub-optimal cell distribution
- No longitudinal connectivity



Collagen matrix to simulate spinal cord

Trail approach

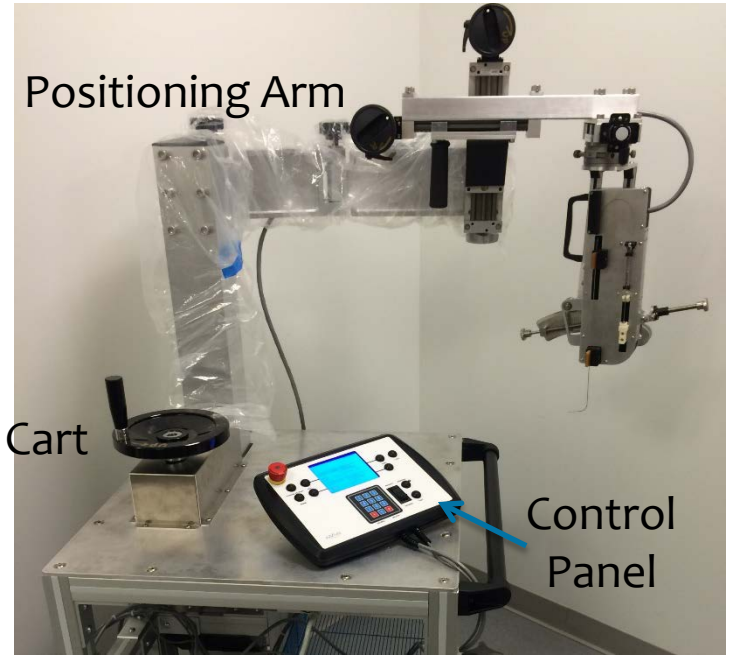
- No reflux at single injection site
- Homogeneous cellular suspension
- Immediate longitudinal connectivity

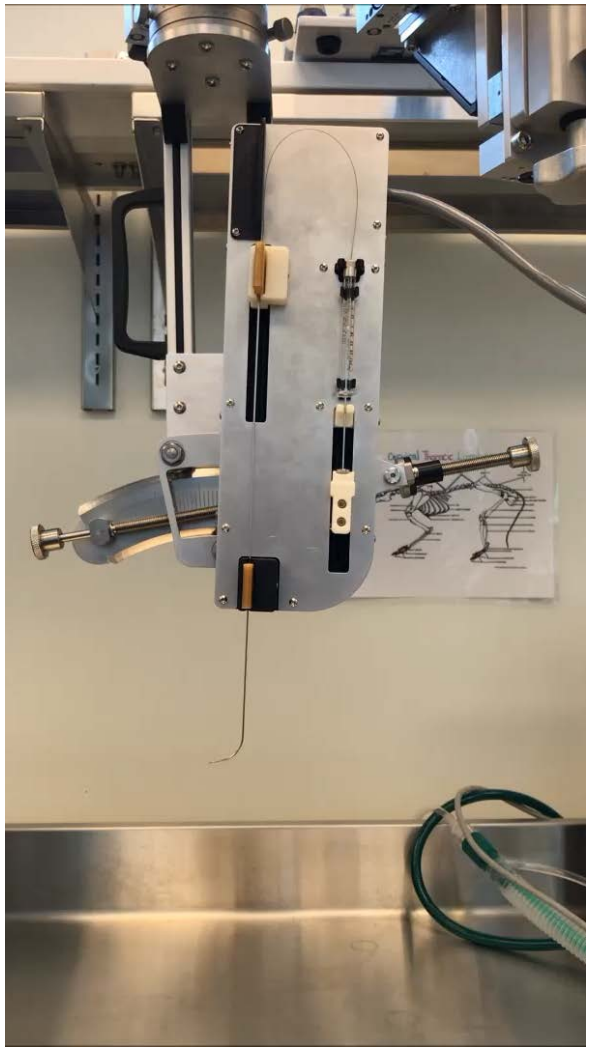


Company videos/images

Development of a Novel Device to Inject Therapeutic Trails within the Spinal Cord

The TrailMaker™ Injection Device

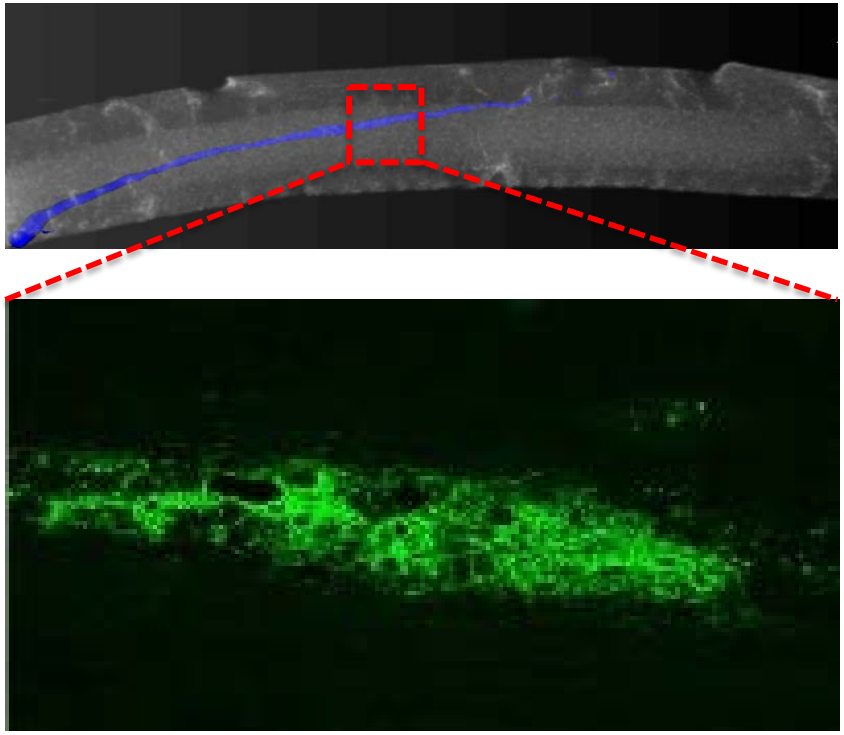




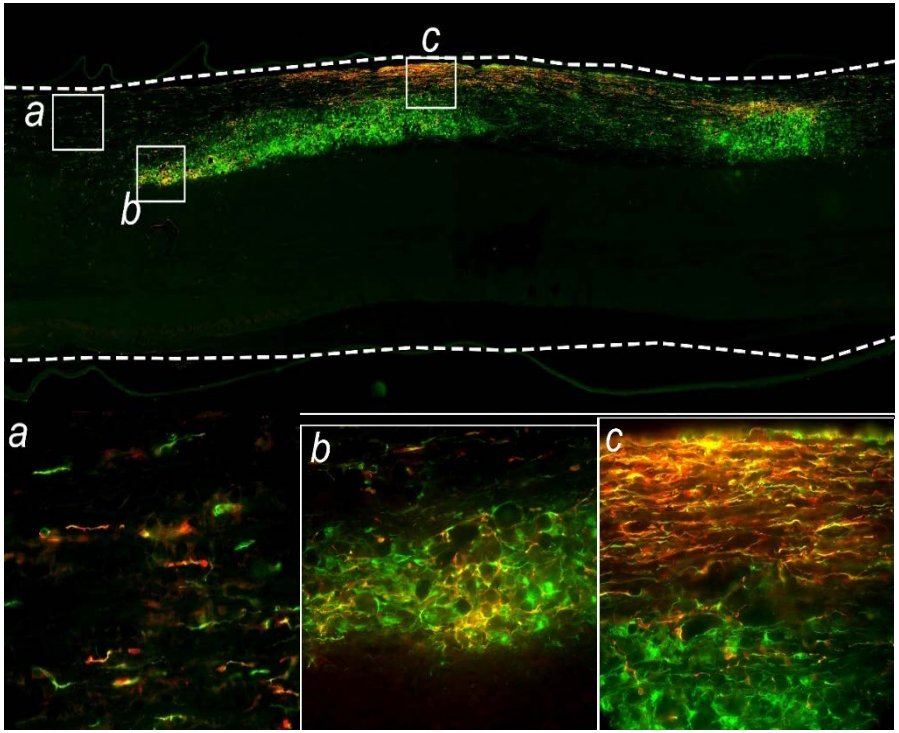
Bioengineered Neural Trails™: InVivo's Novel Neural Stem Cell Product for Chronic SCI

Porcine Model (1 week after injection)

3D MRI of Bioengineered Neural Trail



Rat Model (1 month after injection)



Histology demonstrating interconnected human cells (STEM121) and neural precursors (rat only) (DCX)