Histopathology of Necrotic Spinal Cord Tissue Exudate Collected During Surgical Implantation of a Biodegradable Scaffold Following Acute Spinal Cord Injury: Pre-clinical and Clinical Findings

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CNS 2017 ANNUAL MEETING BOSTON, MASSACHUSETTS OCTOBER 7–11, 2017

INTRODUCTION

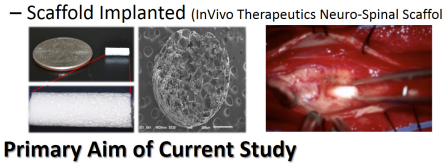
- Acute implantation of biodegradable scaffolds following spinal cord injury (SCI) has been shown pre-clinically to reduce chronic cavitation, increase white matter sparing, and increase the deposition of neuropermissive remodeled tissue.
- The surgical procedure of scaffold implantation allows for the gentle removal of acutely necrotic tissue resulting in a cavity in which the scaffold is placed.
- Here we report for the first time on the histopathological findings in both animal and human tissue specimens.

METHODS

Pre-clinically, experimental spinal cord contusion injuries were performed as previously reported in pigs[1]. Clinically, the ongoing INSPIRE study (NCT02138110) is enrolling baseline T2-T12/L1 subjects with neurologically complete (American Spinal Injury Association Impairment Scale (AIS) A) SCI within 96 hours of injury. The surgical procedure for implantation consists of durotomy and sometimes myelotomy. Commonly, damaged spinal cord tissue under pressure spontaneously extrudes after piotomy. This tissue sample is collected and submitted for histopathologic analysis.

INSPIRE Study (NCT02138110)

- **Surgical Procedure**
  - Laminotomy/ Durotomy +/- Piotomy or Myelotomy
  - Damaged spinal cord tissue exudes from site (+/-)
  - **Sample collected : submitted for evaluation**
  - Scaffold Implanted (InVivo Therapeutics Neuro-Spinal Scaffold™)



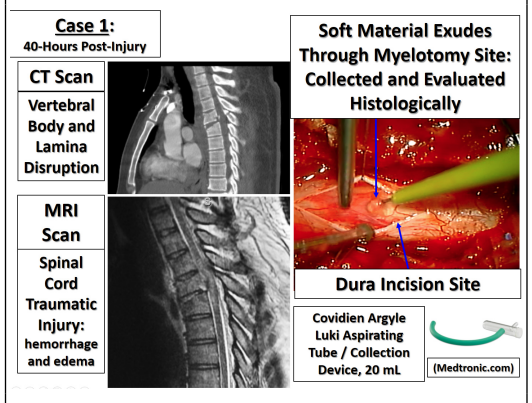
- **Primary Aim of Current Study**
  - Characterize histopathologic features of tissue at site of scaffold implantation in 2 patients

RESULTS

- **Pig Model**:
- 24-hours post-severe contusion/compression injury in a pig model, hematoxylin and eosin-stained (H&E) paraffin sections revealed myelin and axonal degeneration along with numerous scattered spheroids (swollen axons) with hemorrhage and acute inflammation at the wound site.

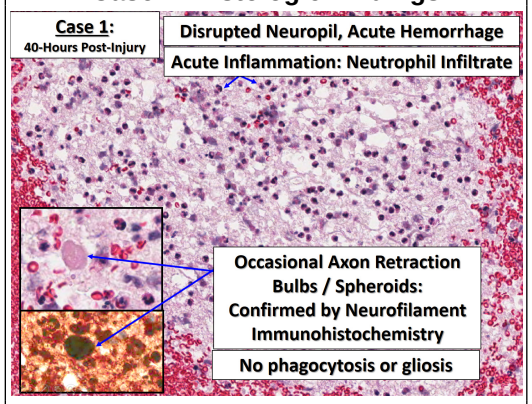
- **Human Subjects**:
- A total of 19 patients have had a Neuro-Spinal Scaffold implanted as of 08/04/2017: 16 currently in follow-up; 3 died with cause of death deemed unrelated to the scaffold or implantation.
- Histologic and immunohistochemical characterization of tissue extruded from damaged cord at the time of surgery to place a scaffold from 2 patients revealed disrupted and devitalized neuropil. There was an acute inflammatory cell infiltrate and axonal retraction bulbs / spheroids, as evaluated at both 40 and 82 hours post-injury.

Case 1: Clinical Information



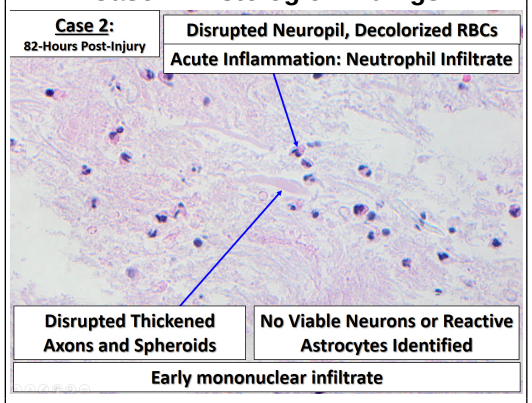
Imaging, intraoperative, and specimen device information.

Case 1: Histologic Findings



Histologic Findings: Hematoxylin and eosin stain and neurofilament immunohistochemistry.

Case 2: Histologic Findings



Histologic Findings: Hematoxylin and eosin stained section.

CLINICAL PROGRESS

- **Case 1**: 1-Year Post-Implantation
  - AIS Impairment: Original: A; Current: C
  - Rectal sensation present; anal sphincter tone regained
  - Urinary sphincter control regained; still requires catheterization

- **Case 2**: 3-Months-Post Implantation
  - AIS Impairment: Original: A; Current: A

CONCLUSIONS

- Severe spinal cord injury leads to irreversibly damaged parenchyma: this injured tissue can exude from the injured spinal cord under pressure following piotomy / myelotomy.
- Histopathologic findings in human cases parallel those seen in porcine injury model.
- Our findings in both animal samples (24-hours post-injury) and human tissue samples (40- and 82-hours post-injury) revealed acute tissue disruption and devitalization.
- The initial response to the injury is acute inflammation.
- This time frame was too short to appreciate phagocytosis, gliosis, or axon sprouts.
- Future patient enrollment and tissue collection in the ongoing clinical study will continue to build upon these initial observations.
- This study provides insight about the state of the injured spinal cord in region into which scaffold is inserted.

LEARNING OBJECTIVES

By the conclusion of this session, participants should be able to:

- Understand the histopathological findings following severe SCI in animals and in humans as part of the ongoing INSPIRE study.
- Be aware of the clinical study (INSPIRE) to evaluate the use of scaffolds following acute SCI.
- Be updated on the clinical results of the ongoing INSPIRE study.

REFERENCE

1. Lee JH et al. J Neurotrauma. 2013;30(3):142.