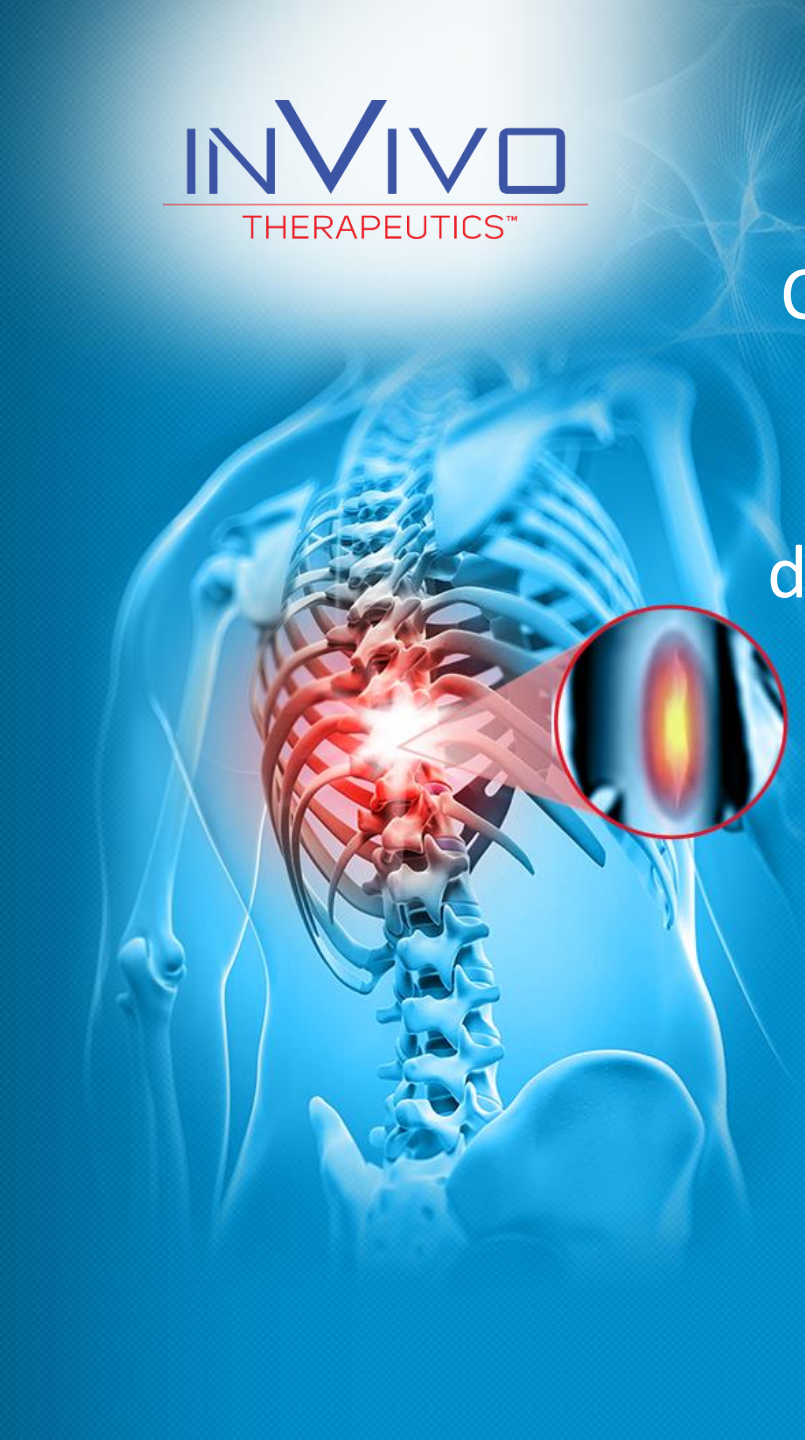
INVIVO THERAPEUTICS™



Clinical-Pathological Assessment of Severe (AIS A) Traumatic Acute Thoracic Spinal Cord Injury: Post-durotomy/myelotomy Observations from the INSPIRE Trial

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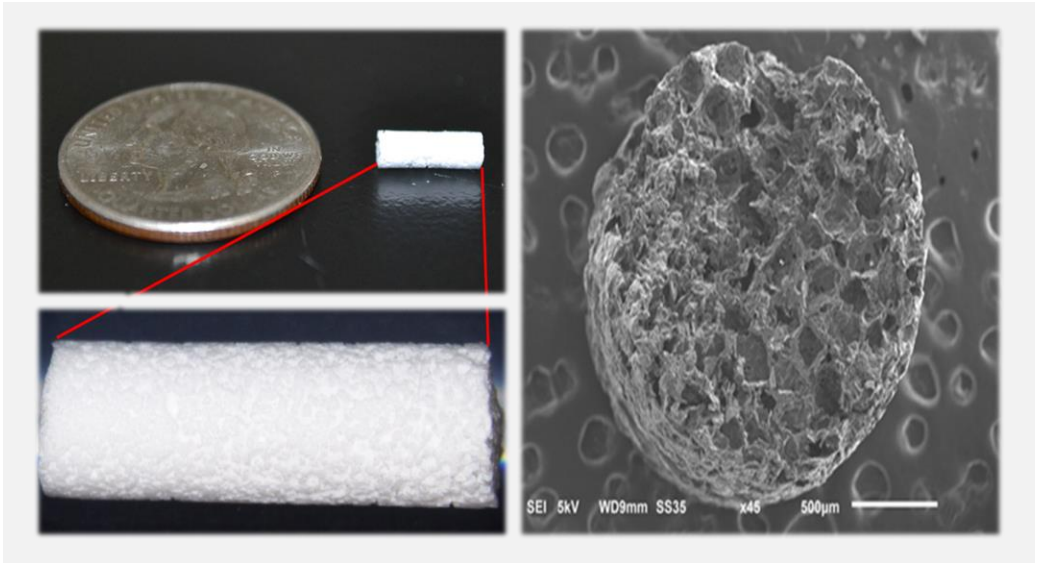
Disclosures and Acknowledgements

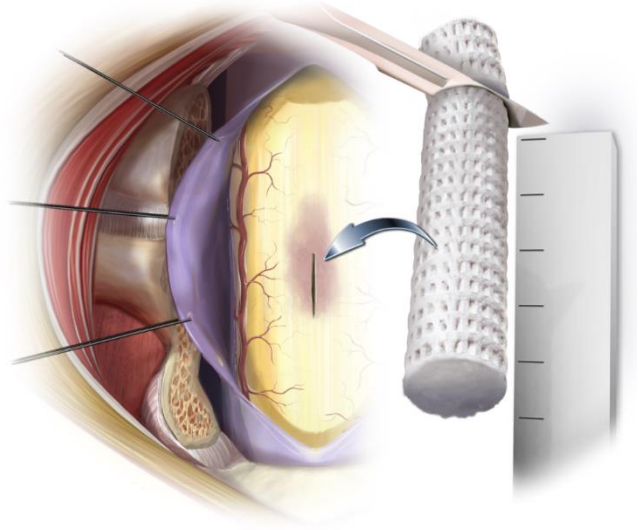
- Commercial disclosures
- RT Layer, T Ulich, KM Neff and LK Masuoka are employees of In Vivo Therapeutics

- Acknowledgements (co-authors)
- R. T. Layer; D. Coric; P Arnold; JD Guest; RH Heary; PC Hsieh; AL Jenkins; KD Kim; KL Lee; LK Masuoka; KM Neff; Z. Ray; T Ulich; N Theodore

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

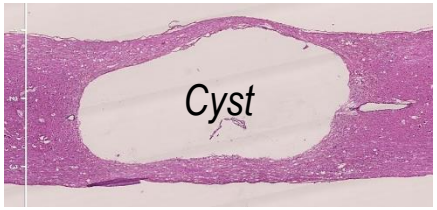


Porous, biodegradable device
In vivo residence time ~ 4-8 weeks

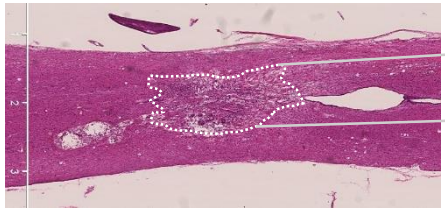


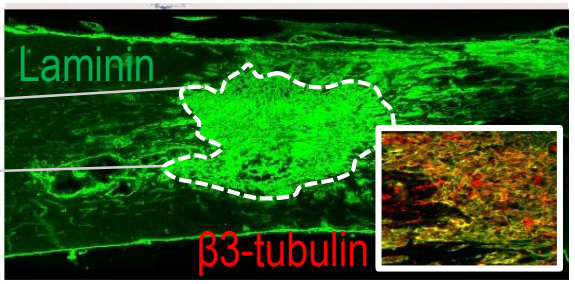
Intraparenchymal implantation within acute cavity following durotomy and often myelotomy

Control



Neuro-Spinal Scaffold



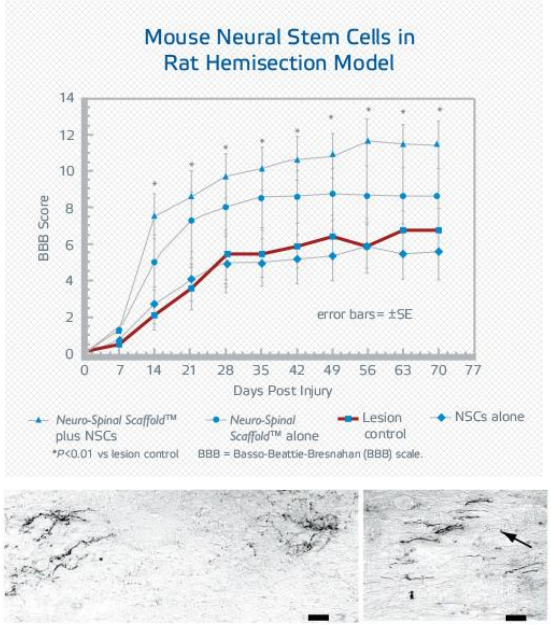


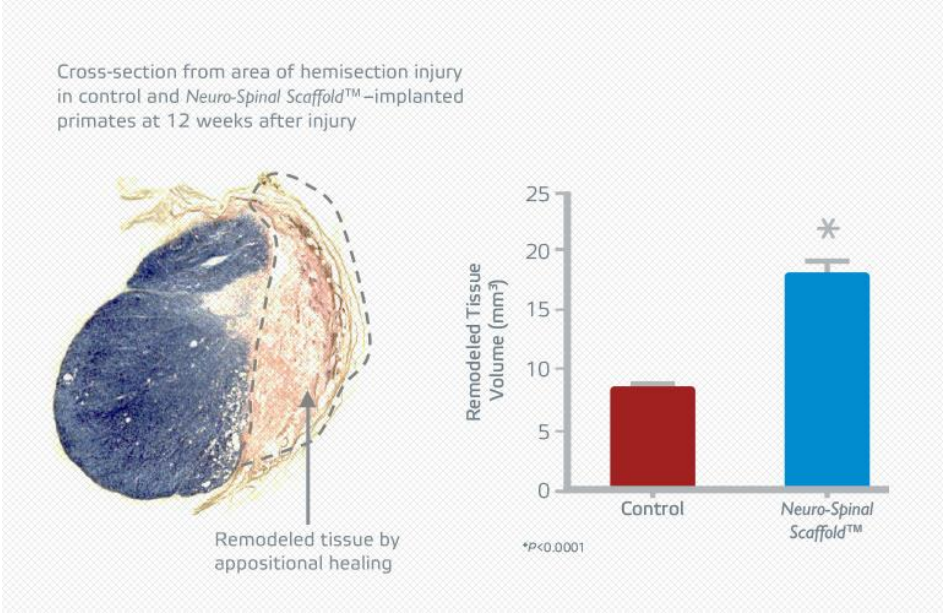
Reduces cyst volume, spares white matter, and promotes generation of remodeled tissue in rat contusion model

Remodeled tissue is rich in neuropermissive ECM and facilitates endogenous sprouting

Neuro-spinal scaffolds

- ✓ Neuro-spinal scaffolds + Neural stem cell treatment reduced tissue loss from secondary injury processes as well as in diminished glial scarring
- ✓ Enhanced regenerative axons and motor functional recovery in a rat and a monkey SCI





Teng YD et al., PNAS 2002 and InVivo Therapeutics (http://www.invivotherapeutics.com)

The INSPIRE Study – Study Design

InVivo Study of Probable Benefit of the *Neuro-**Spi**nal Scaffold*™ for Safety and Neurologic **Re**covery in Subjects with Complete Thoracic AIS A Spinal Cord Injury

- Primary Objective: To evaluate whether the Scaffold is safe and demonstrates probable benefit for the treatment of AIS A T2-T12/L1 spinal cord injury (within 96 hrs of injury)
- Primary Endpoint: AIS conversion by 6 month follow-up visit
- Objective Performance Criterion: At least 25% of subjects convert from complete paraplegia (AIS A) to partial paralysis by 6 months
  - Large, multinational, natural history databases consistently indicate that only 12-16% of subjects with complete (AIS A) thoracic injury will convert to an improved AIS grade within 6 months after injury
- Additional Endpoints: Sensory and motor scores, bladder and bowel function, Spinal Cord Independence Measure, pain, quality of life
- Plan to enroll 20 subjects

The INSPIRE Study: Site Update

23 Active Sites in the US and Canada

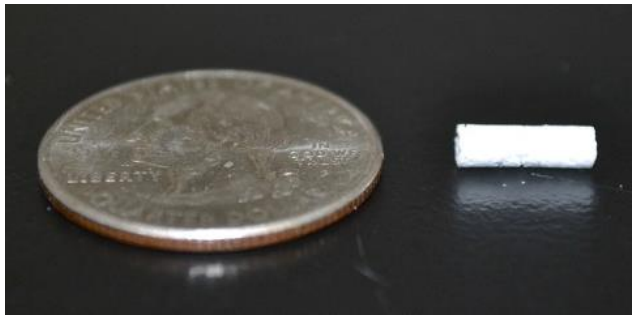
- Dr. Paul Arnold - KUMC
- Dr. Maxwell Boakye – Univ of Louisville
- Dr. Joseph Ciacci - UCSD
- Dr. Dom Coric, Dr. Bill Bockenek - CNSA
- Dr. Nadar Dahdaleh - Northwestern
- Dr. Travis Dumont – Univ of AZ Medical
- Dr. Michael Fehlings – Toronto Western
- Dr. James Harrop – Thomas Jefferson
- Dr. Bob Heary - Rutgers
- Dr. Eric Horn – Goodman Campbell
- Dr. Patrick Hsieh - USC
- Dr. Arthur Jenkins – Mount Sinai
- Dr. Kumar Kakarla – Barrow
- Dr. Kee Kim – UC Davis
- Dr. Shekar Kurpad – MC of WI
- Dr. Stuart Lee – Vidant Health
- Dr. Paul Okonkwo – UPMC
- Dr. Ahmed Raslan - OHSU
- Dr. Alex Ropper – Baylor
- Dr. Chris Shaffrey – UVA
- Dr. Paul Santiago, Dr. Zach Ray – WashU
- Dr. James Schuster – UPENN
- Dr. Steve Yocom – Cooper

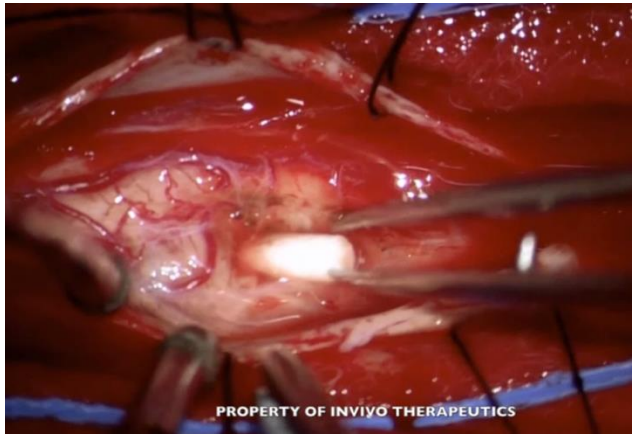
The INSPIRE Study: 23 Active Sites (22US, 1Canada)

The INSPIRE Study: An Opportunity to Observe the Acutely Injured Human Spinal Cord

InVivo Study of Probable Benefit of the *Neuro-**Spi**nal Scaffold*™ for Safety and Neurologic **Re**covery in Subjects with Complete Thoracic AIS A Spinal Cord Injury

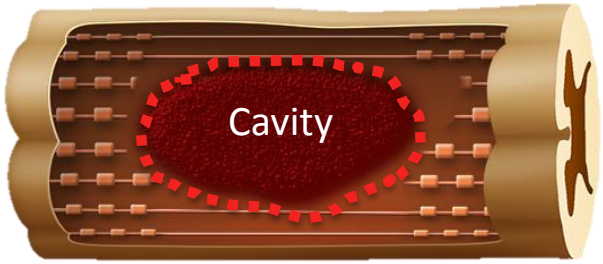
- Primary Objective: To evaluate whether the Neuro-Spinal Scaffold, a biodegradable investigational device, is safe and demonstrates probable benefit for the treatment of complete T2-T12/L1 spinal cord injury.
- The Neuro-Spinal Scaffold is implanted via durotomy and often myelotomy into acutely injured (within 96 hours) spinal cord parenchyma to facilitate healing and possibly neural regeneration.
- The procedure provides a unique opportunity to classify injury types and correlate visible cord pathology with neurologic outcome following Scaffold implantation.
- Prior anatomic injury classifications have been performed following autopsy and tissue fixation (Bunge et al., 1993; Kakulas and Bedbrook, 1969).





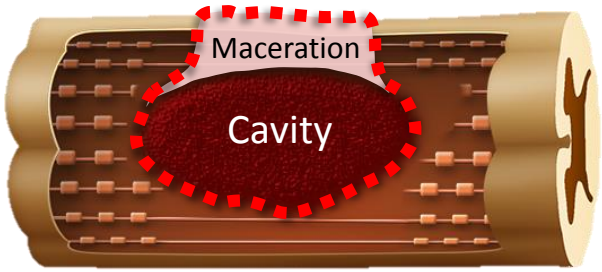
Classification of Sub-Dural Injury Types

‘Contusion-Type’ Injury



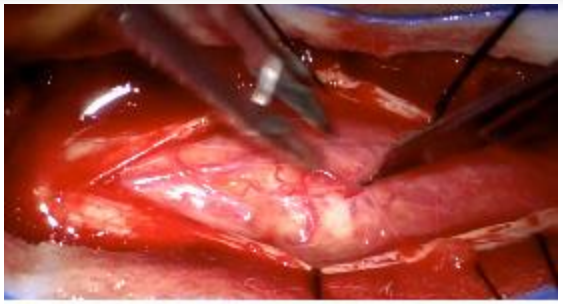
- ‘Contusion-type’ injuries (5 subjects) displayed intact pial surface and peripheral white matter.
- Following dorsal myelotomy, gentle irrigation of loose necrotic debris revealed an intra-medullary cavity.
- Scaffolds implanted into the cavity were generally not visible but could be identified using ultrasound.

‘Compound-Type’ Injury

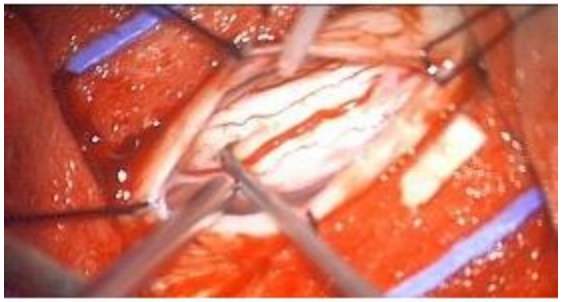


- ‘Compound-type’ injuries (3 subjects) displayed elements of contusion, pial-disruption, laceration, maceration, and damaged peripheral white matter but preserved cord continuity.
- Scaffolds implanted into compound-type injuries remained visible.

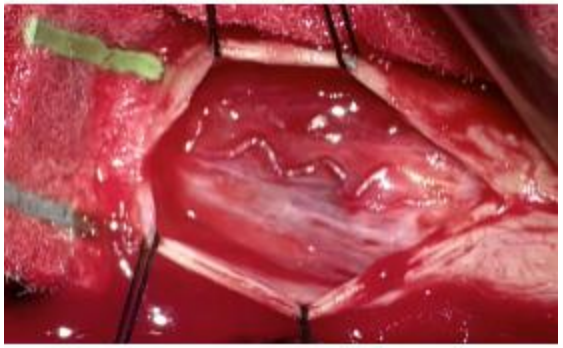
‘Contusion-Type’ Injuries



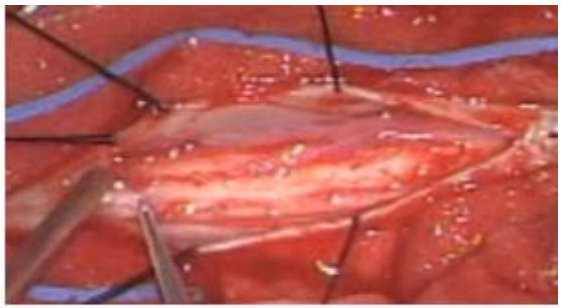
Subject 1 (102001) 9.2 hours post-injury, A→C



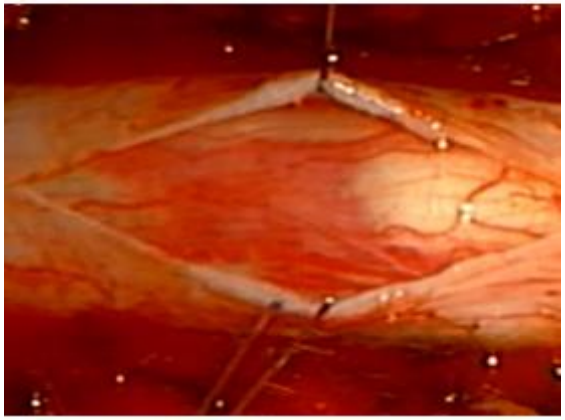
Subject 3 (103002) 82.6 hours post-injury, A→B



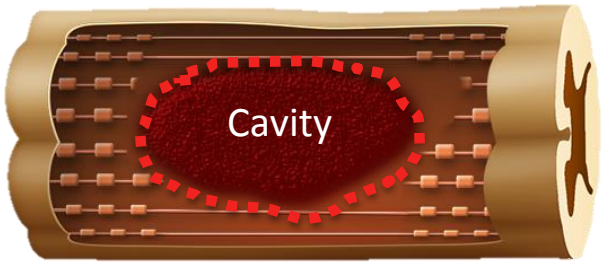
Subject 4 (113001) 52.9 hours post-injury, A→A



Subject 7 (103004) 21.3 hours post-injury, A→A



Subject 9 (117001) 40.4 hours post-injury, A→B



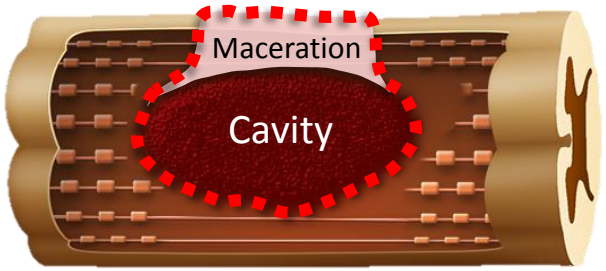
In ‘Contusion-Type’ injuries, the dorsal cord surface is intact.

‘Compound-Type’ Injuries

Subject 2 (103001) 45.6 hours post-injury, A→A

Subject 5 (109001) 69.1 hours post-injury, A→B

Subject 6 (104001) 8.8 hours post-injury, A→B



In ‘Compound-Type’ injury, the pia is breached and there is visible but incomplete cord parenchymal separation.

The INSPIRE Study - Injury Type Is Not Predictive of AIS Conversion

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

NOTE: Subjects 8 and 10 passed away with the cause of death deemed unrelated to Neuro-Spinal Scaffold™ or implantation

Conclusions

- We observed either 'Contusion-type' injury with central necrosis and peripheral tissue sparing, or 'Compound-type' injury with focal laceration and pial-disruption.
  - Both injury types could be successfully implanted with the scaffold
- Neurological outcome has been assessed in 6 males and 2 females (aged 18-55) implanted with Scaffolds 9-83 hours after injury.
- Injury type was not predictive of AIS conversion.
  - Of 5 patients with contusion-type injury, one converted to AIS C by 1 month and two to AIS B by 1 and 3 months. Of 3 patients with compound-type injury, two converted to AIS B by 2 and 6 months.
- This work could provide the basis of a novel clinical-pathological classification system for severe blunt injury of the human spinal cord