

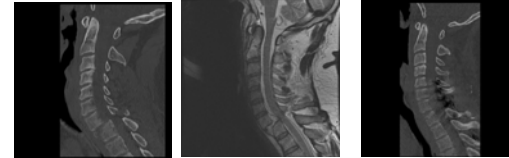
## Spinal Cord Injury: The Benefits of Functional Restoration

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## Index Case I



29 Year Old Male in Rollover MVA

Quadriparetic at Scene

Densely Quadriparetic in ER

Large Body Habitus (380 lb)  
Emergent OR

ORIF, Posterior Approach

ASIA E at 6 month Follow Up



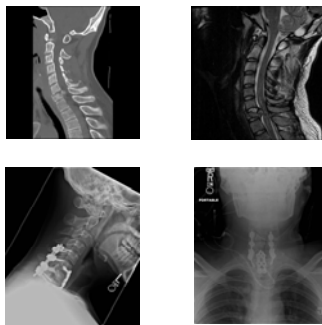
## Index Case II

24 Year Old Male  
Medical Student

Diving Accident

Quadriplegic at Scene  
and in ER

ASIA A at 1 year



[Spine \(Phila Pa 1976\)](#). 2010 Oct 1;35(21 Suppl):S166-73.  
Current practice in the timing of surgical intervention in spinal cord injury.  
[Fehlings MG](#)<sup>1</sup>, [Rabin D](#), [Sears W](#), [Cadotte DW](#), [Aarabi B](#).



## 21 Year Old Future Computer Programmer May 2016

- College Student
- Driving on county road on errand for grandmother
- MVA Car vs Pole
- C5 Quadriplegia
- Able to shrug shoulders and twitch biceps
- Cannot transfer, No Hand and Finger Function

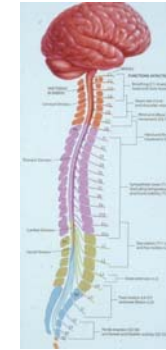
## Now What??

- Education and Prevention
- Early Surgery
- Neuroprotective Strategies
- Neuroregenerative Strategies



## Spinal Cord Injury Facts and Figures

If you drive a car...Or ride a motorcycle



- **Incidence**
- 3-5/100,000 in the US
- **New cases**
- 12,000/year in the US, 250,000 total
- with deficits
- **Survival**
- 90%, near-normal life span
- **Costs**
- > \$ 6 billion/year in the US
- **Age**
- Average: 33.4 years
- most common age: 19 years



## What is the Spinal Cord?

- A structure as big as your index finger essentially built like a fiberoptic cable.
- Individual components of this cable (neurons) carry vital information to impart sensation and motor function to the arms, trunk and legs
- Consists of nerve cells, supporting cells (**oligodendrocytes**) and blood vessels



## Edwin Smith Papyrus (2500-1700 BC)

- Five Cases reported
- Crushed vertebra- "He is unconscious of neck and arms, speechless and urine dribbles". **An ailment not to be treated**
- Sprained vertebra- Treat with application of fresh meat and honey



## What Has Been Available?

- Early Diagnosis
- Intravenous Medication (Methylprednisolone)
- Surgical Reconstruction of the Spine (if indicated)
- Long Term Rehabilitation



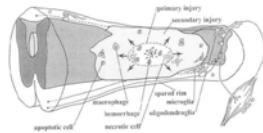
## What Do We Do?



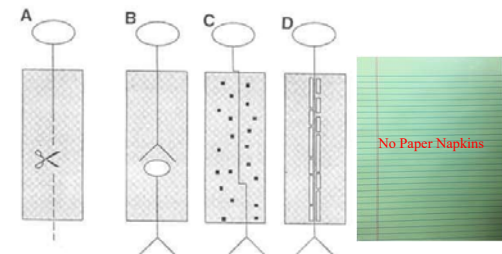
- Plus Long Term Rehabilitation and Re-integration

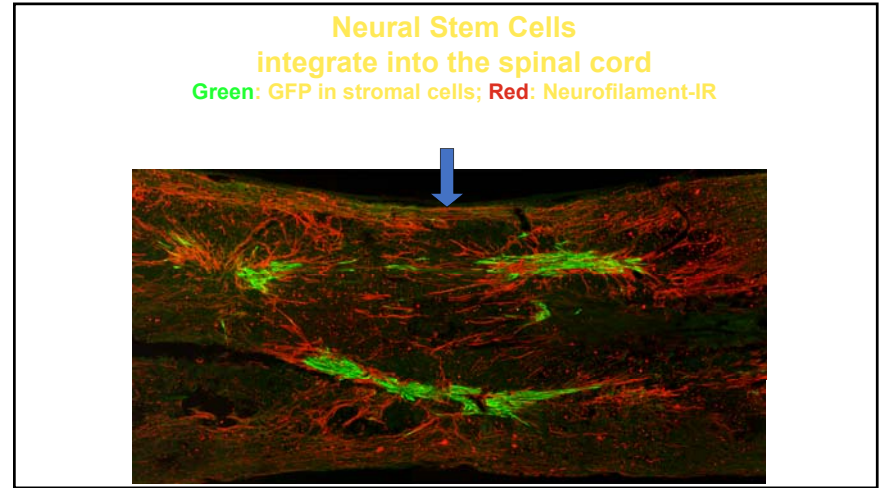
## What Happens after Spinal Cord Injury?

- Tissue Swelling from Inflammation
- Release of toxic substances into the zone of injury
- Loss of normal tissue
- Disruption of normal nerve connections
- Scar Formation
- Creation of environment hostile to regrowth of nerves



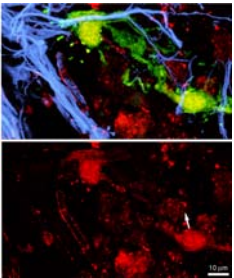
## Strategies for Spinal Cord Repair Karolinska Institutet 2001



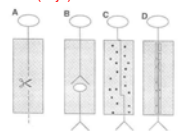


**Grafting Ngn-2 transduced neuronal stem cells  
into the injured spinal cord**

GFP / MBP / TuJ1

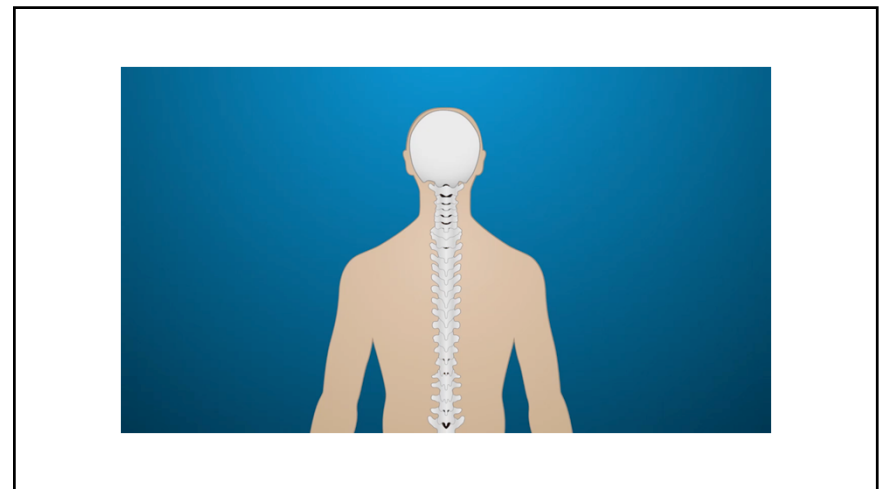


Ng-2 stem cells (GFP) have become oligos (MBP) ensheathing host nerve fiber (TuJ1)



*Nature Neuroscience* 2005 Mar;8(3):346-53. Allodynia limits the usefulness of intraspinal neural stem cell grafts; directed differentiation improves outcome.  
 Hofstetter CP, Holmstrom NA, Lillja JA, Schweinhardt P, Hao J, Spenger C, Wiesenfeld-Hallin Z, Finsen J, Olson L, Kurpad SN

Pain with no Gain: Allodynia following Neural Stem Cell Transplantation Following Spinal Cord Injury  
 Macias MY, Syring MB, Pizzi MA, Crowe MJ, Alexanian AR, Kurpad SN.  
*Exp Neurol.* 2006 Oct;201(2):335-48.



## Timeline (Stem Cell Strategies)

- 2005-2008: Application of concept to Human Stem Cells to generate Transplantable Myelin Making Cells
- 2009: GERON Stem Cell Study Starts. Terminated in 2011 (FUNDING Shortages!)
- 2015: Asterias Stem Cell Study Starts
  - Human Embryonic Stem Cells
  - Genetically Engineered to form Oligodendrocytes



## AST-OPC1: hESC-Derived Oligodendrocyte Progenitor Cells (OPCs)



### AST-OPC1 (formerly GRNOPC1)

- Cryopreserved Allogeneic Cell Population
- Derived from Human Embryonic Stem Cells (hESCs)
- Characterized Composition of Cells:
  - Oligodendrocyte progenitors
  - Neural progenitors
  - Infrequent mature neural cells and Rare other characterized cell types
- Three identified functions
  - Produces neurotrophic factors
  - Induces remyelination
  - Induces vascularization
- "Off the shelf" administration
- First indication: spinal cord injury
- Potential line extensions in other neurodegenerative diseases



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### Summary of Phase 1 Thoracic Safety Study of AST-OPC1 (F/MCW had a patient in 2011)

- |  |  |
|--|--|
| <div style="background-color: #90EE90; padding: 5px; margin-bottom: 5px;">Well Tolerated</div> <div style="background-color: #90EE90; padding: 5px; margin-bottom: 5px;">No Immune Responses</div> <div style="background-color: #90EE90; padding: 5px; margin-bottom: 5px;">Activity</div> <div style="background-color: #90EE90; padding: 5px;">No Changes Neurological Function</div> | <ul style="list-style-type: none"> <li>• AST-OPC1 well tolerated, with no SAEs to date deemed related to the cells, delivery method, or immunosuppressive regimen</li> <li>• No evidence of immune responses to AST-OPC1, even 10 months after removal of all immunosuppression           <ul style="list-style-type: none"> <li>-Despite significant HLA mismatches between AST-OPC1 and subjects</li> </ul> </li> <li>• MRI results consistent with activity in injection site in 4 of 5 subjects at 4-5 years post-transplant</li> <li>• No evidence of significant changes in neurological function           <ul style="list-style-type: none"> <li>-No evidence for ascending loss of function from cells or delivery</li> <li>-Efficacy not anticipated in this study due to low dose (5-10x below predicted efficacious range) and suboptimal patient population (complete thoracic injuries)</li> </ul> </li> </ul> |
|--|--|



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## Evaluation of AST-OPC1 in Subacute Cervical SCI

### A Phase 1/2a Dose Escalation Study of AST-OPC1 in Subjects With Subacute Cervical Spinal Cord Injury

Six Sites Currently Enrolling


ClinicalTrials.gov: [NCT02302157](https://clinicaltrials.gov/ct2/show/study/NCT02302157)




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### AST-OPC1 Injection Procedure

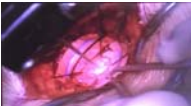

**Shepherd Center**



**Rush**





- Injections performed using a table-mounted syringe positioning device (SPD)
- Direct intra-parenchymal injection into the spinal cord lesion
- Single 50µL injection for both the 2M & 10M doses
- No intraoperative complications to date

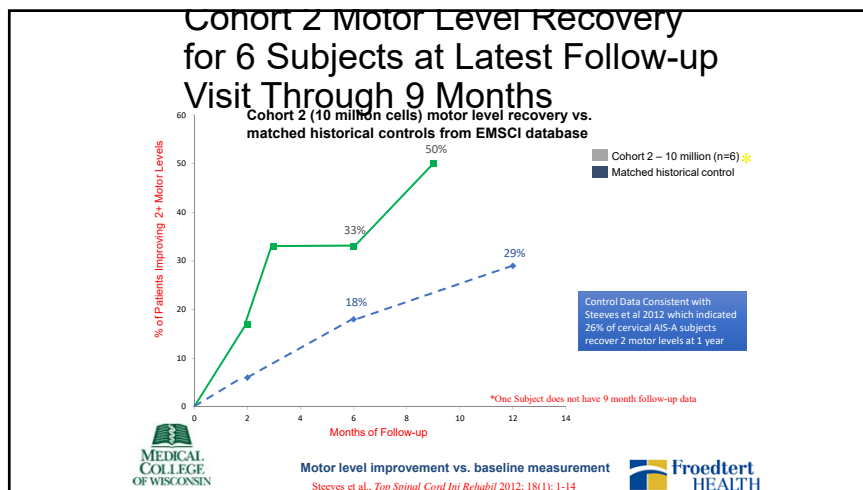
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### Safety Profile Remains Positive

- Safety profile from all AST-OPC1 patients enrolled to date remains positive through 6-12 months of follow up
- No SAE's associated with injection procedure
- Immunosuppression with tacrolimus has been well tolerated
- Safety profile of AST-OPC1 cells has been favorable, including no SAEs related to AST-OPC1 and no adverse findings on MRI scans to date

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### Where are we NOW?

- AST-OPC1 cells are safe.
- No serious adverse effects so far
- Early recovery of **meaningful** function






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### Clinical Translation of Two Level Motor Improvement

- Improved Arm and Hand Function
- Greater Independence in Self-care
- Greater Independence in Transfers and Transport
- Greater Independence in Activities of Daily Living

### Summary

- Safety Profile of Injection Procedure and AST-OPC1 Excellent with No Associated SAEs
- Immunosuppression with tacrolimus has been well tolerated
- UEMS improvement in Cohort 1 (2 million cells) was similar to matched controls which is indicative of safety in this low dose safety cohort
- Subjects in Cohort 2 have also shown a greater degree of motor score and motor level recovery than matched historical controls in the EMSCI database
- Improvements in motor function reported for Cohort 2 (10 million cells) have been maintained or further increased through last date of follow up at 9 months
- 2 motor level improvement translates into increased arm and hand function along with improved independence in activities of daily living.

### Implications and Impact on Quality of Life

- Lucas was very young at the time of the subject accident. He was a college student and working as a manager at McDonald's. The vocational implications of his improvement will be discussed later;
- As noted by Dr. Kurpad, the accident rendered Lucas a quadriplegic, at the level of C4. Lucas had very limited range of motion, primarily only able to shrug his shoulders;
- Following the stem cell transplant, Lucas regained several levels of function to the C7-T1 level. That is three levels of improvement;
- As noted in the video, Lucas is able to independently eat, use a computer and operate his wheelchair;
- He is able to manipulate small items and type on a keyboard;
- He is able to transfer himself from his wheelchair independently;

### Implications and Impact on Quality of Life - Continued

- Physically, he is now able to lift upwards of 65 pounds in each hand;
- Lucas is more likely than not, able to undergo a driver's evaluation and would probably be found capable of operating a motor vehicle via hand controls.
- THESE THINGS WOULD NOT BE POSSIBLE AT THE ORIGINAL LEVEL OF INJURY

**How Function & Independence Differ at Each Level:**

As noted in Blackwell, T. L., Krause, J. S., Winkler, T., & Stiens, S. A. (2001). *Spinal Cord Injury Desk Reference: Guidelines for Life Care Planning and Case Management*. New York, NY: Demos Medical Publishing, Inc.

- **LEVEL C4:**
  - Power recline/tilt wheelchair with head, chin, or breath control; manual recliner; vent tray; pressure relief cushion; postural support and head control devices as indicated.
  - Full electric hospital bed; specialty or pressure relief mattress may be indicated; power or mechanical lift with sling; transfer board;
  - Padded/reclining shower/commode chair; handheld shower;
  - If ventilator free – hydraulic standing table; mouth stick, high-tech computer access, ECU, hand splints may be indicated;
  - Unable to manage bowel and bladder program independently;

**How Function & Independence Differ at Each Level:**

As noted in Blackwell, T. L., Krause, J. S., Winkler, T., & Stiens, S. A. (2001). *Spinal Cord Injury Desk Reference: Guidelines for Life Care Planning and Case Management*. New York, NY: Demos Medical Publishing, Inc.

- **LEVEL C7-T1:**
  - Lightweight manual (rigid or folding) wheelchair;
  - Full electric hospital bed or full to king standard bed; pressure relief mattress or overlay may be indicated; may or may not require transfer board;
  - Padded or elevated tub bench with commode cutout. Handheld shower;
  - Hydraulic or standard standing frame;
  - Should be able to manage bladder (and probably bowel program) independently;

**What are some of the cost SAVINGS?**

C-4 Quad	C7-T1
Power recline/tilt wheelchair - <b>\$20,000 to \$25,000</b>	Manual wheelchair - <b>\$1,500 to \$2,300</b>
Full electric hospital bed (with mattress) - <b>\$1,665</b>	Full to queen bed – possibly an additional <b>\$100 to \$400</b>
Hoyer lift for bed to wheelchair transfers - <b>\$2,650</b> ; Hoyer sling - <b>\$370</b>	Probable that no Hoyer lift is needed – <b>\$0.00</b>
Padded and reclining shower/commode chair - <b>\$950</b>	Shower/commode chair - <b>\$157</b>
Mouth stick, high-tech computer access, environmental control unit (ECU) - <b>\$2,100 to \$5,300</b>	ECU/mouth stick and high-tech computer access - <b>\$0.00</b>
Hydraulic standing frame - <b>\$4,900 to \$6,000</b>	Standard standing frame - <b>\$1,500 to \$2,000</b>
Personal care attendant*	Personal care attendant*

**\*Personal Assistance/Attendant Care Required:**

- C4 Quadriplegia
  - 24-hour care to include homemaking;
  - NSCISC\*\* Median: 24 hours/day
- C7-T1 Paraplegia
  - C7-C8: 6 hours per day of personal care; 2 hours of homemaking per day;
  - T1: 3 hours of homemaking per day
  - NSCISC Median: 3 to 9 hours/day

\*\*NSCISC = National Spinal Cord Injury Statistical Center - <https://www.nscisc.uab.edu/>



### Personal Assistance/Attendant Care Charges:

- C4 Quadriplegia
  - NSCISC Median: 24 hours/day;
  - 24 hours x \$27/hr. x 365.25 days per year = **\$236,682 per year**
- C7-T1 Paraplegia
  - NSCISC Median: 3 to 12 hours/day
  - 3 to 9 hrs. x \$27/hr. x 365.25 days per year = **\$29,585.25 - \$88,755.75/yr.**

A difference in cost savings of **\$147,926.25 - \$207,096.75 per year**

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**Table 14B. Life expectancy for SCI persons surviving at least 1 year post-injury**

Current Age	Neurologic Level					Ventilator Dependent
	No SCI	Any Level AIS-D	T1-S3	C5-C8	C1-C4	Any Level
10 years	69.4	63.0	55.6	50.5	44.1	24.5
15 years	64.5	58.1	50.8	45.7	39.4	20.7
20 years	59.6	53.4	46.4	41.3	35.3	18.1
25 years	54.9	48.9	42.4	37.3	31.9	17.3
30 years	50.1	44.4	38.3	33.3	28.5	17.0
35 years	45.4	39.9	34.3	29.5	25.3	15.1
40 years	40.7	35.6	30.3	25.8	22.2	13.0
45 years	36.1	31.3	26.6	22.3	19.5	11.5
50 years	31.6	27.2	22.9	19.1	16.7	9.6
55 years	27.3	23.4	19.5	16.3	14.2	8.2
60 years	23.2	19.8	16.5	14.1	12.5	7.9
65 years	19.3	16.2	13.4	11.3	10.0	6.4
70 years	15.5	12.8	10.3	8.6	7.5	4.6
75 years	12.2	9.8	7.6	6.2	5.3	3.1
80 years	9.1	7.1	5.4	4.2	3.6	1.9

*Footnote: Values for persons with no SCI are from the 2012 U.S. Life Tables for the general population.*

### Few words on Loss of Earning Capacity...

- Employment after spinal cord injury is always a challenge;
- The level of injury and level of function and independence have a significant impact on vocational options for the person with a SCI;
- In Lucas's case, his vocational goal is to work in IT. As a person with a C4 quadriplegia, the likelihood of ever achieving this goal would be minimal.
- However, as someone with C7-T1 paraplegia, and almost complete function/use of his hands, the likelihood of Lucas completing an academic training program and entering the workforce is much higher.
- While he will still have challenges as a person with paraplegia at the level he is at now, Lucas does not have to rely upon things such as assistive technology, more personal care, etc. to complete his education and enter the workforce.

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### Few words on Loss of Earning Capacity...

Per the 2016 *Occupational Employment Statistics, Milwaukee-Waukesha-West Allis, WI MSA*, published by the Bureau of Labor Statistics, the median earnings for those employed in the IT field are as follows:

- 15-1131 Computer Programmers - \$68,453/year
- 15-1142 Network and Computer Systems Administrators - \$ 71,926/year
- 15-1151 Computer User Support Specialists - \$52,666/year
- 15-1152 Computer Network Support Specialists - \$56,888/year

As compared to potentially zero earnings or minimal/part-time earnings living as person with C4 quadriplegia.

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