Advanced Diffusion MRI as a Prognostic Marker of Acute Spinal Cord Trauma: Preclinical Studies

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Spinal Cord Injury (SCI)

**Functional assessment (AIS grade) has only modest prognostic ability.**

**ASIA Impairment Scale Grade**

**A:** Complete lack of motor and sensory function below the level of injury

**B:** Some sensation below the level of the injury

**C:** Some muscle movement is spared below the level of injury, but most of the muscles below the level of injury cannot move against gravity.

**D:** Most of the muscles that are spared below the level of injury are strong enough to move against gravity.

**E:** All neurologic function has returned.

MRI of Spinal Cord Injury

Conventional MRI improves diagnosis, but prognostic ability is limited.

6-month improvement in AIS grade
Spinal Cord Injury Pathology

Axonal sparing is the greatest predictor of functional outcome.

**Functional Outcome**
Number of spared axons

**Acute**
- ✔ Microscopic
- ❌ Macroscopic

**Chronic**
- ✔ Microscopic
- ✔ Macroscopic

1 Hour Post Injury

60 Days Post Injury

Adapted from:
Acute Axonal Injury In Vivo in SCI

Williams PR, et al. 2014. Nature Communications 5,
Diffusion Weighted Imaging: A biomarker for SCI?

Sensitive.
Reliable.
Clinically Useful.

Double Diffusion Encoding MRI

High sensitivity to axonal injury without contamination from edema & CSF.

Parallel

<table>
<thead>
<tr>
<th>b = 0</th>
<th>b₁ = 500</th>
<th>b₁ = 1000</th>
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ADC₁ (AD)

Axial Diffusivity
Axonal injury
Edema/CSF

Perpendicular

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<thead>
<tr>
<th>b = 0</th>
<th>b₁ = 500</th>
<th>b₁ = 2000</th>
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ADC₁ (RD)

Radial Diffusivity
Edema/CSF

Parallel with Perpendicular “Filter”

<table>
<thead>
<tr>
<th>b₁ = 2000</th>
<th>b₁ = 2000; b₁ = 100</th>
<th>b₁ = 2000; b₁ = 250</th>
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</thead>
</table>

fADC₁

Filtered Axial Diffusivity
Detect axonal injury
Suppress edema/CSF
## DDE in Spinal Cord Injury Model

<table>
<thead>
<tr>
<th>Acute (48 hrs)</th>
<th>Chronic (30 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T₂w</strong></td>
<td><strong>T₂w</strong></td>
</tr>
<tr>
<td><strong>Composite</strong></td>
<td><strong>Composite</strong></td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td><strong>Histology</strong></td>
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</tbody>
</table>

**Severe**
- T₂w
- Composite
- Histology: SMI31 :Axons

**Mild**
- T₂w
- Composite
- Histology

**Sham**
- T₂w
- Composite
- Histology

Legend:
- Healthy
- Injured
- None
Predicting Functional Outcome

Acute MRI

- **2 Day DDE f_R**: $R^2=0.80$, $p<0.001$
- **2 Day DTI FA**: $R^2=0.06$, $p=0.38$

Chronic MRI

- **30 Day DDE f_R**: $R^2=0.04$, $p=0.47$
- **30 Day DTI FA**: $R^2=0.77$, $p<0.001$
Metal Artifacts

Pre-Surgical  Post

Precludes followup MRI in patients with surgical instrumentation.

Courtesy Shekar Kurpad, MD PhD
DDE Whole Cord Spectroscopy

Rapid, quantitative, and robust method to detect injury severity.

<3 min, automated analysis integrated into scanner, largely insensitive to magnetic field inhomogeneity.
DDE in Healthy Cervical Cord

3T GE 750 Discovery; 12 channel spine array, rFOV-DWI-EPI (FOCUS)
TR/TE: 2000/80 ms; slices: 10; slice thick: 5mm; NEX: 6; 5:30 min each

**DTI**

B-values: 1000 & 2000 s/mm², 15Dirs

**DDE**

B-values: 2000 s/mm² filter (0-1000 probe)
Degenerative Cervical Myelopathy

Neurological and radiographic exams are modest predictors of outcome.

*Modified Japanese Orthopedic Association (mJOA):* 18-point scale assessing motor function, sensation, and micturition (normal=18)

![Graph showing pre-operative versus 6-month post-operative mJOA scores](image)

![Images of normal, myelopathic, and asymptomatic cervical spinal cords](image)

Courtesy Marjorie Wang, MD MPH
DDE in Chronic Compression Model

Day 2
Compression

Day 30
Compression

Sham

Composite
DDE in Chronic Compression

- **CSA**: p=0.00034
- **fADC||**: p=0.028
- **AD_{DTI}**: p=0.014
- **FWHM**: p=0.0085
- **CoV**: p=0.024
- **BBB 28d**: p=0.0028
Summary and Future Directions

Double diffusion encoding MRI is:
- Sensitive to axonal injury.
- Minimizes contamination from edema/CSF.
- Easy to visualize pattern of acute injury.

DDE Spectroscopy is:
- Rapid, automated, quantitative, and robust.

Animals studies demonstrate high prognostic value.

Human studies in acute SCI and Cervical Myelopathy are in development.
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