Diffusion Kurtosis - a Sensitive Marker For Traumatic Brain Injury

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Declaration of Relevant Financial Interests or Relationships

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I have no relevant financial interest or relationship to disclose with regard to the subject matter of this presentation.
Traumatic Brain Injury

- Traumatic injuries remain the leading cause of death in children and in adults aged 45 years or younger.

  - **Primary injury:** Structural changes due to mechanical forces

  - **Secondary injury:** Widespread degeneration of neurons, glial cells, axons

  - Patient outcome is hard to predict!

- The major focus of TBI management:
  Prevention of secondary injuries
Diffusion Tensor Imaging in Evaluating TBI

Abnormal DTI despite negative conventional MRI and CT findings!
Does normal DTI mean no injury?

- **Acutely post injury:**
  - Increased $FA$
  - Reduced $MD$
  Possible cause: cytotoxic edema, reduced extracellular space, etc.

- **Chronic stage:**
  - Reduced $FA$
  - Increased $MD$
  Possible cause: edema, cellular destruction, axonal degeneration, etc.

- At sub-acute stage, DTI parameters may undergo pseudo-normalization$^{1,2}$.

- Does this mean there is no injury?

$^1$MacDonald et al., 2007.  $^2$Mayer et al, 2010
Beyond DTI: Diffusion Kurtosis
- the Non-Gaussian property of water diffusion

Uniform water diffusion

Non-uniform water diffusion

\[ \ln \frac{S(b)}{S(0)} = -bD \]

Non-Gaussian (DKI*)

\[ \ln \frac{S(b)}{S(0)} = -bD + \frac{1}{6} b^2 D^2 K \]

Diffusion Kurtosis
- the Non-Gaussian property of water diffusion

\[
\ln \frac{S(b)}{S(0)} = -bD
\]

\[
\ln \frac{S(b)}{S(0)} = -bD + \frac{1}{6} b^2 D^2 K
\]

• Diffusion kurtosis
  ▪ tissue complexity (heterogeneity)\(^1\)
  ▪ higher sensitivity in characterizing tissue microstructure\(^2,3\)

Our Goal

• To investigate whether diffusion kurtosis parameters provide information over and beyond that available from DTI parameters regarding tissue damage following TBI

• Whether DKI is sensitive to microstructure changes in grey matter
Animal Preparation

Controlled Cortical Impact (CCI) injury model*

- Velocity: 5 m/sec
- Depth: 2.5 mm

- Rats (Adult male Sprague-Dawley): n = 12
- Imaging (Bruker 7T):
  - baseline (1 day before injury)
  - acute stage (2 hours post injury)
  - sub-acute stage (7 days post injury, n = 7)
- Histology: 7 days post injury after imaging

DKI protocol:
- 30 directions
- 2 b-values (b=1000 and 2000 s/mm²)
- 2 averages
- TR/TE = 6000/50 ms

Parametric maps of a representative rat base

2 hour

7 day

$FA$  $MD$  $MK$  $T_2$-weighted
Regional evolution of DKI parameters

Injured site

\[ \begin{align*}
\text{MD} (\times 10^{-3}\text{ mm}^2/\text{s}) & \\
\text{HC-ips} & < \text{CTX-ips} & > \text{HC-con} & < \text{CTX-con}
\end{align*} \]

\[ \begin{align*}
\text{FA} & \\
\text{HC-ips} & < \text{CTX-ips} & > \text{HC-con} & = \text{CTX-con}
\end{align*} \]

* : \( p < 0.05 \)  
*** : \( p < 0.0005 \)
Tissue microstructure & kurtosis

a Astrocytes in healthy CNS tissue
- Not all astrocytes express detectable levels of GFAP
- Astrocytes have non-overlapping domains
- Little or no proliferation

b Mild to moderate reactive astroglia
- Most astrocytes are GFAP+
- Preservation of individual domains
- Little or no proliferation

c Severe diffuse reactive astroglia
- Most astrocytes are GFAP+
- Disruption of individual domains
- Proliferation

d Severe astroglia with compact glial scar formation
- Compact Glial Scar
- Bordering along regions of tissue damage & inflammation due to:
  - Trauma
  - Ischemia
  - Cytotoxicity
  - Infection
  - Autoimmune
  - Inflammation
  - Neoplasm
- Inflammatory cells, infectious agents, Non-CNS cells etc.

Increased severity of injury

MK ↑

Sofroniew & Vinters, Acta Neuropathol 2010
Diffusion Kurtosis - Imaging Marker for Astrogliosis?

Sham

Rat A

Rat B

Pair-wise cluster plot

Blue: baseline  Red: 7 day post injury

* Baseline  ○ 7 day post injury
Correlation between histology & MK

Contralateral Cortex

- **Baseline**: MK value around 0.6
- **Mild**: MK value around 0.7
- **Severe**: MK value around 0.85
Conclusion

- We observe a clear association of mean kurtosis with increased GFAP immunoreactivity.

- Mean Kurtosis is increased despite the fact that DTI parameters such as $MD$ and $FA$ were normal.

- Mean Kurtosis appears to be a sensitive marker for mild inflammatory responses, even in grey matter regions and may help in the management of secondary injury.

- Other biological factors (processes associated with neuro-degeneration, microglia, etc.) can also affect mean kurtosis.

- Future studies will focus on understanding how these factors affect diffusion and kurtosis parameters.
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