Diffusion Kurtosis – a Sensitive Marker For Traumatic Brain Injury

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Declaration of Relevant Financial Interests or Relationships

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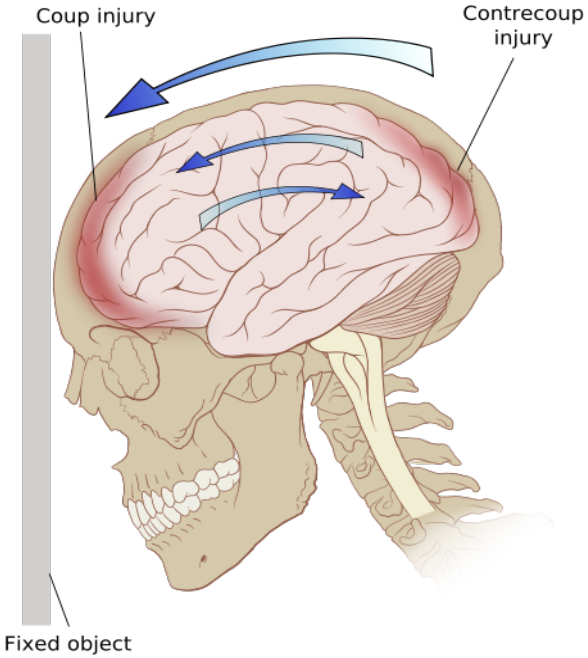
I have no relevant financial interest or relationship to disclose with regard to the subject matter of this presentation.

Traumatic Brain Injury

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



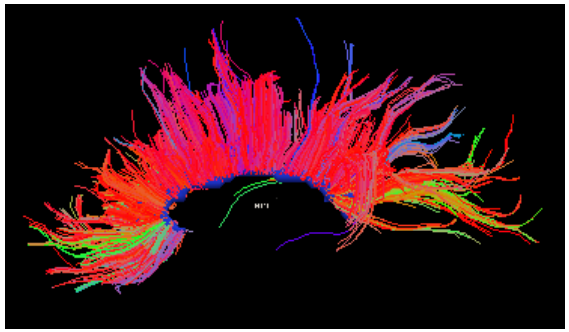
- **Primary injury:**
  Structural changes due to mechanical forces
- **Secondary injury:**
  Widespread degeneration of neurons, gial cells, axons
- **Patient outcome is hard to predict!**

- The major focus of TBI management:

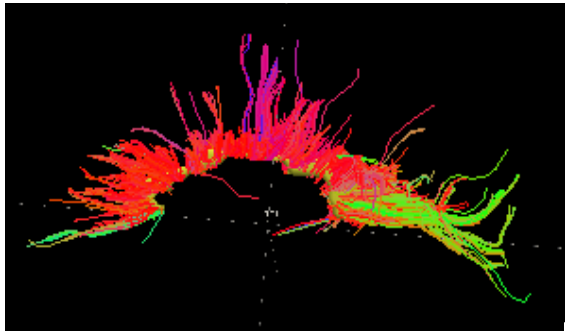
Prevention of secondary injuries

Diffusion Tensor Imaging in Evaluating TBI

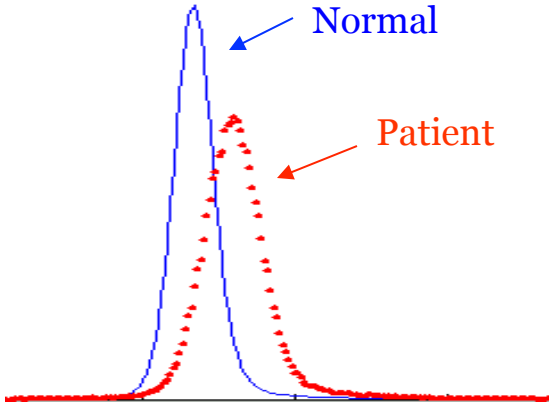
Normal



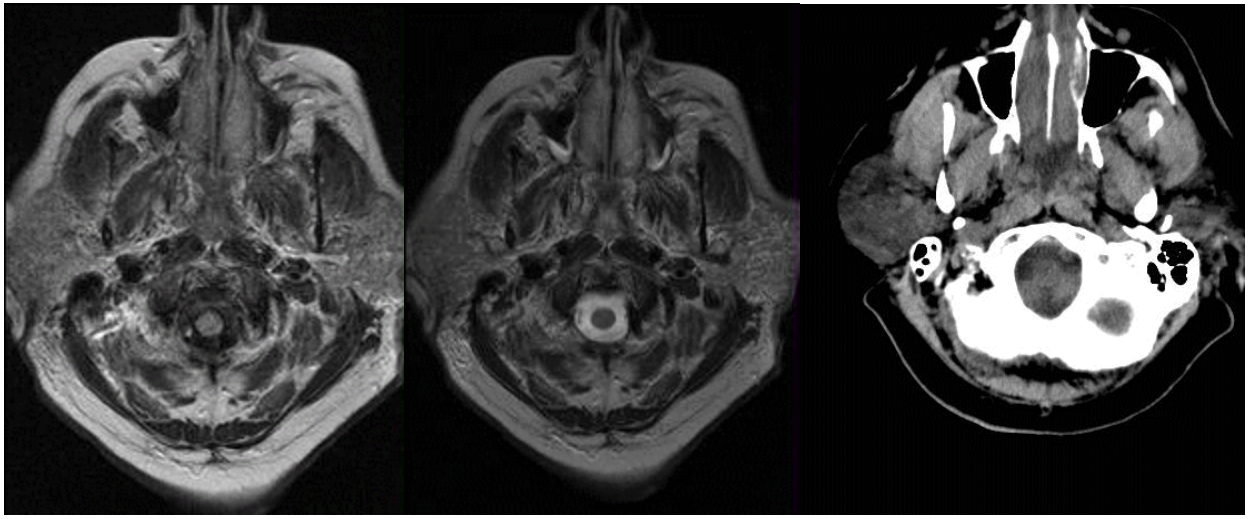
Patient



Whole brain ADC histogram



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*

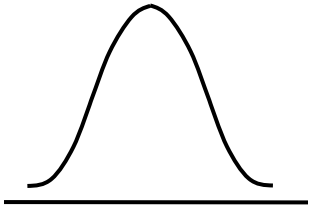
  Possible cause: edema, cellular destruction, axonal degeneration, etc.
- At sub-acute stage, DTI parameters may undergo pseudo-normalization[1,2].
- Does this mean there is no injury?

[1]MacDonald et al., 2007. [2]Mayer et al, 2010

Beyond DTI: Diffusion Kurtosis

– the Non-Gaussian property of water diffusion

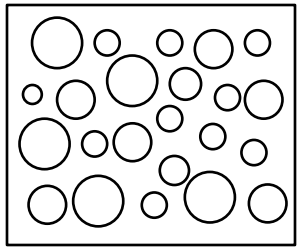
Uniform water diffusion



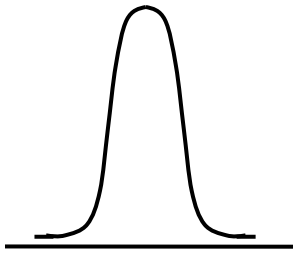
K=0

Gaussian
(**DTI**)

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



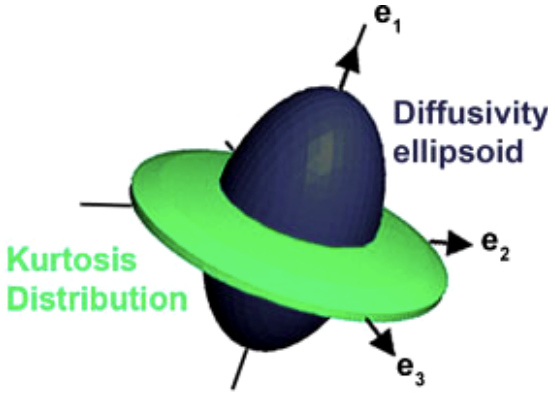
Non-uniform water diffusion



K>0

Non-Gaussian
(**DKI**[*])

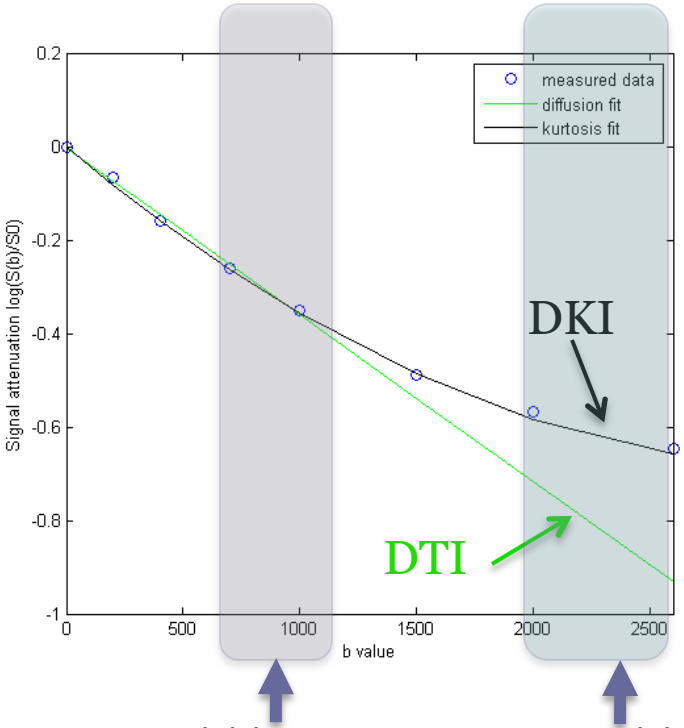
$$\ln\frac{S(b)}{S(0)} = -bD + \frac{1}{6}b^2D^2K$$



* Jensen JH, et al. Magn Reson Med. 2005; 53:1432-40.

Diffusion Kurtosis

- the Non-Gaussian property of water diffusion



Gaussian (**DTI**)

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

Non-Gaussian (**DKI***)

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

- Diffusion kurtosis
  - tissue complexity (heterogeneity)[1]
  - higher sensitivity in characterizing tissue microstructure[2,3]

[1] Jensen JH, Helpern JA, 2010. [2] Falangola MF et al, 2008. [3] Hui ES et al., 2008.

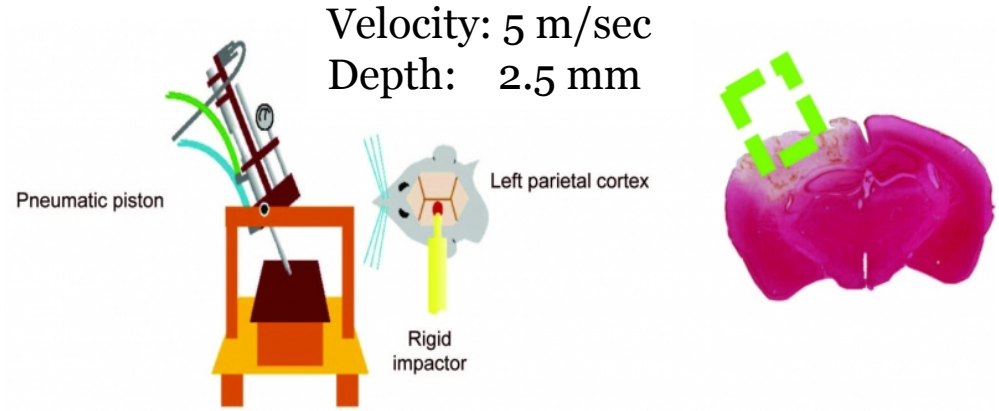
Our Goal

- 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*



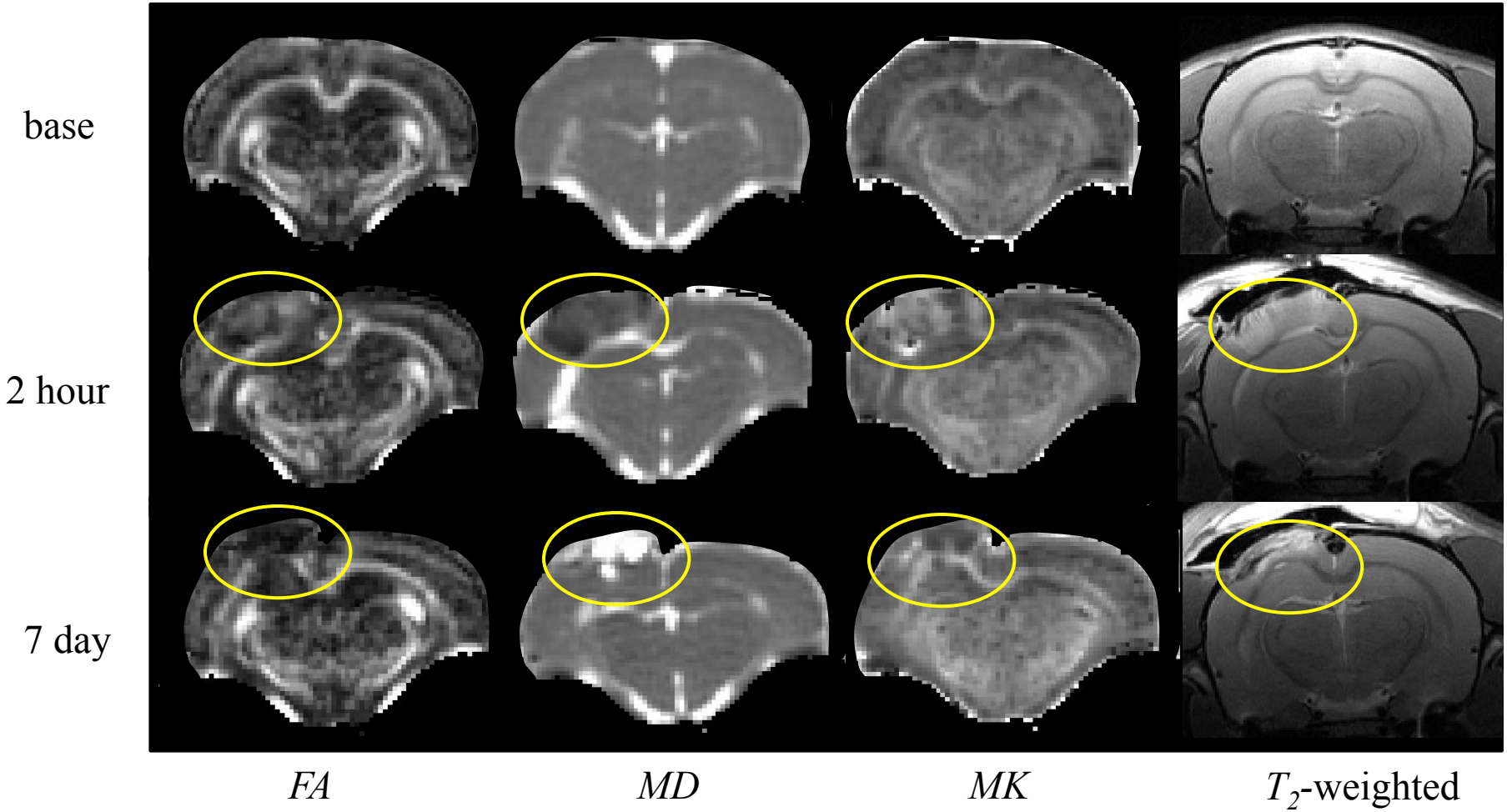
DKI protocol:

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

- 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

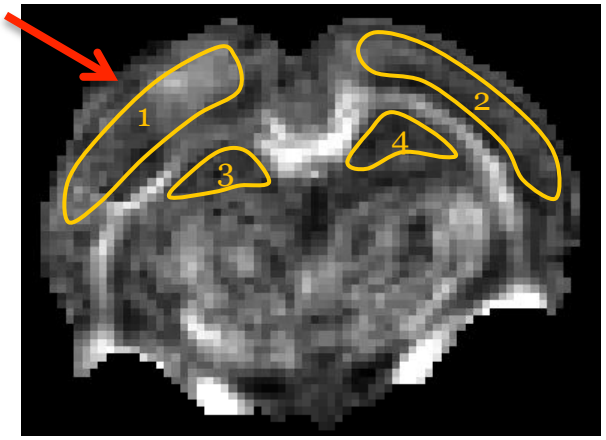
* Dixon et al., J Neurosci Methods. 1991; 39:253-62.

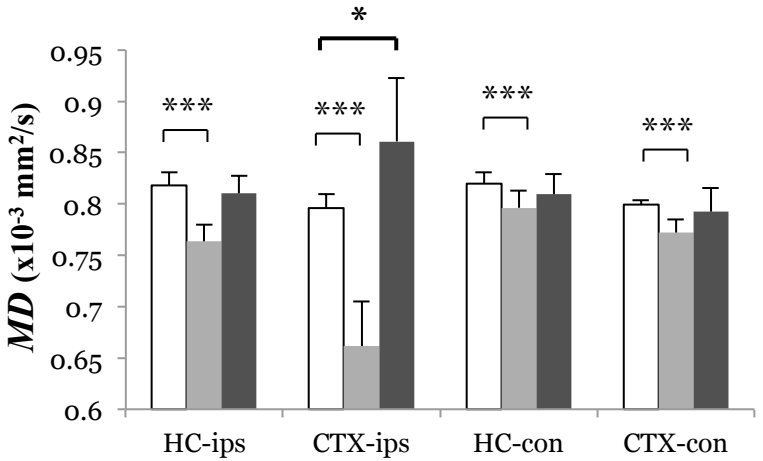
Parametric maps of a representative rat

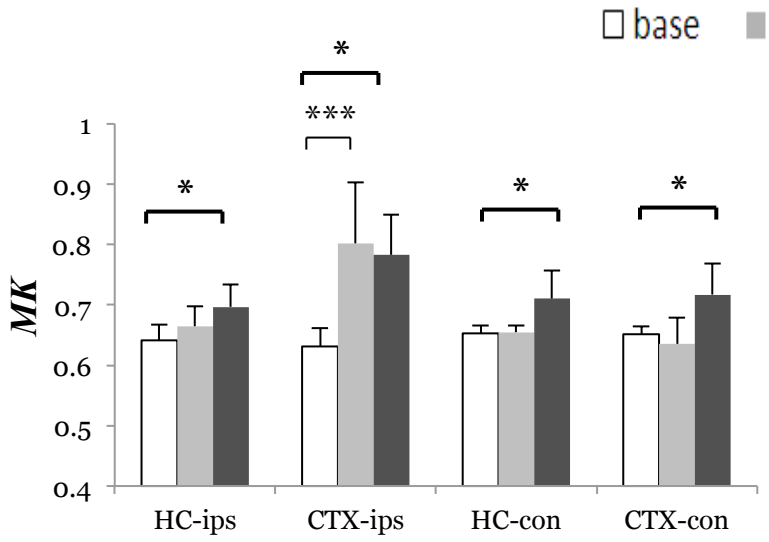


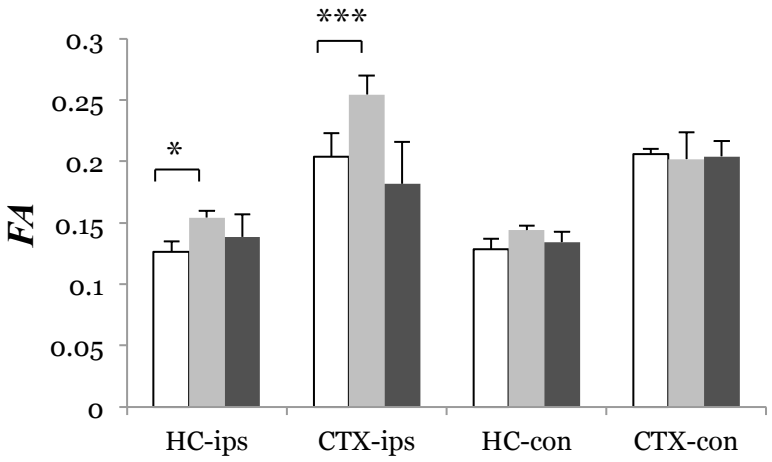
Regional evolution of DKI parameters

Injured site



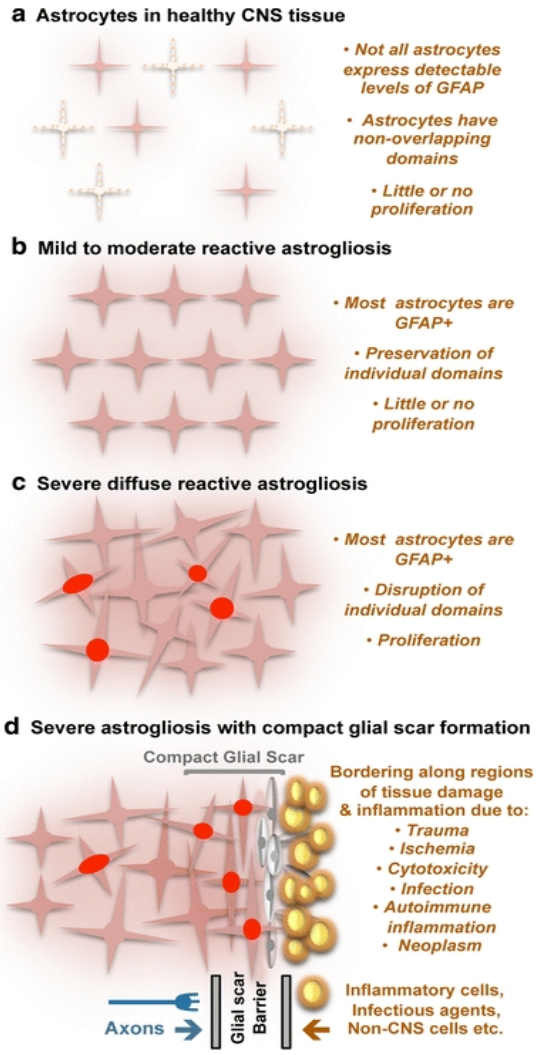


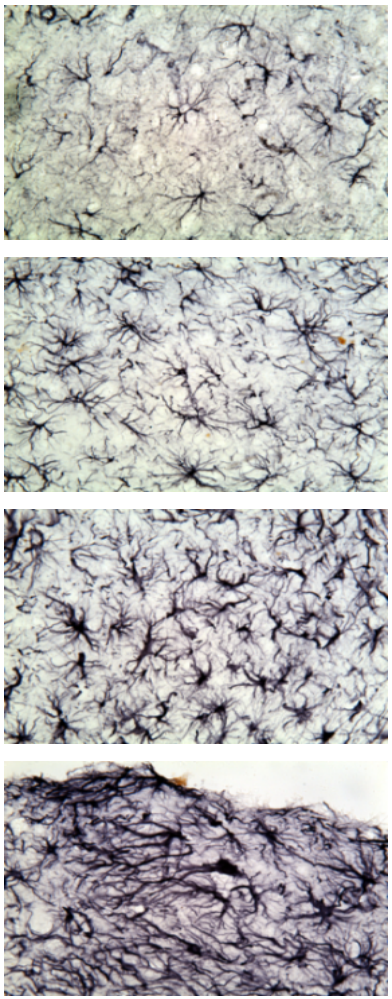




* : $p < 0.05$ *** : $p < 0.0005$

Tissue microstructure & kurtosis



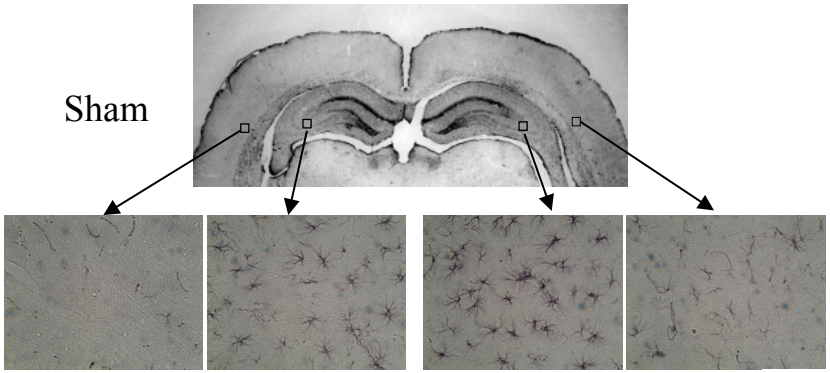


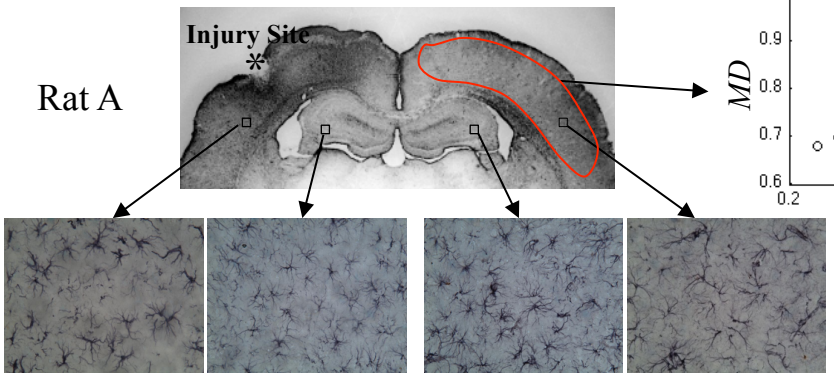
Increased severity of injury

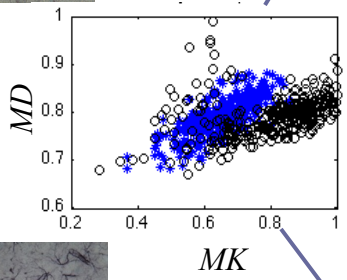
MK ↑

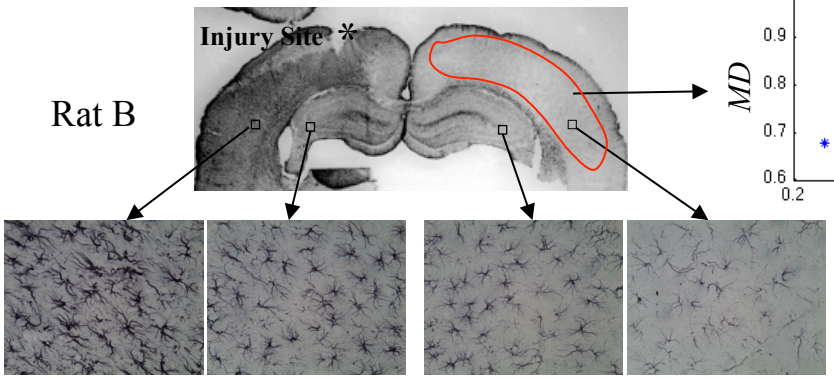
Sofroniew & Vinters, Acta Neuropathol 2010

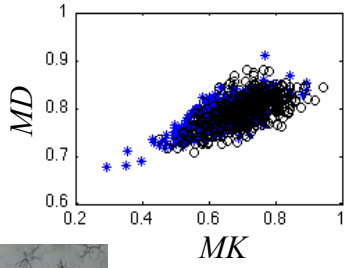
Diffusion Kurtosis – Imaging Marker for Astrogliosis?





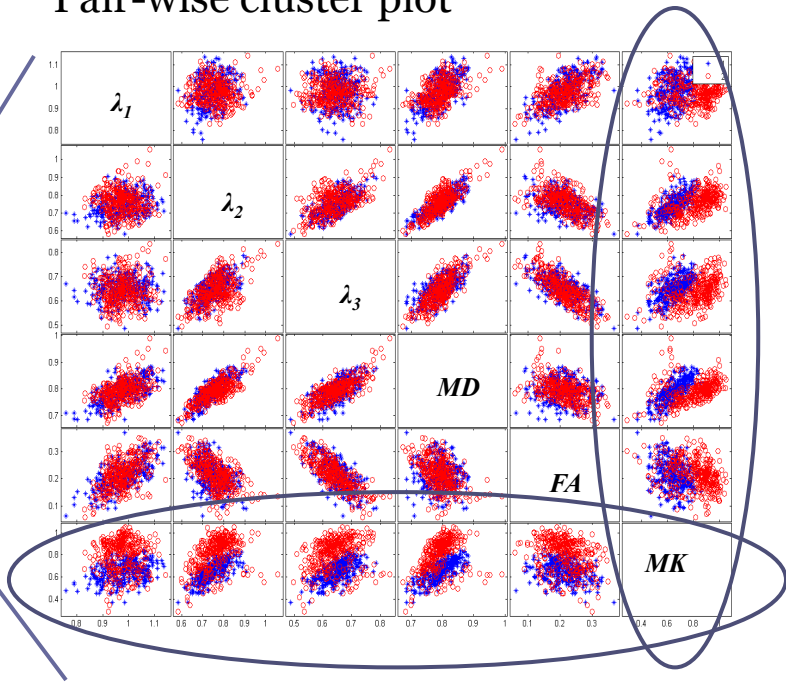






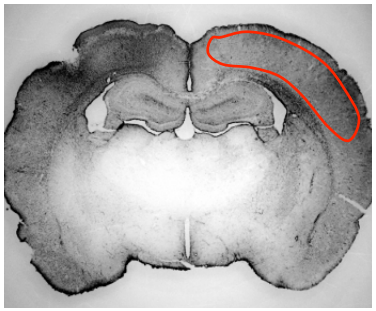
* Baseline
○ 7 day post injury

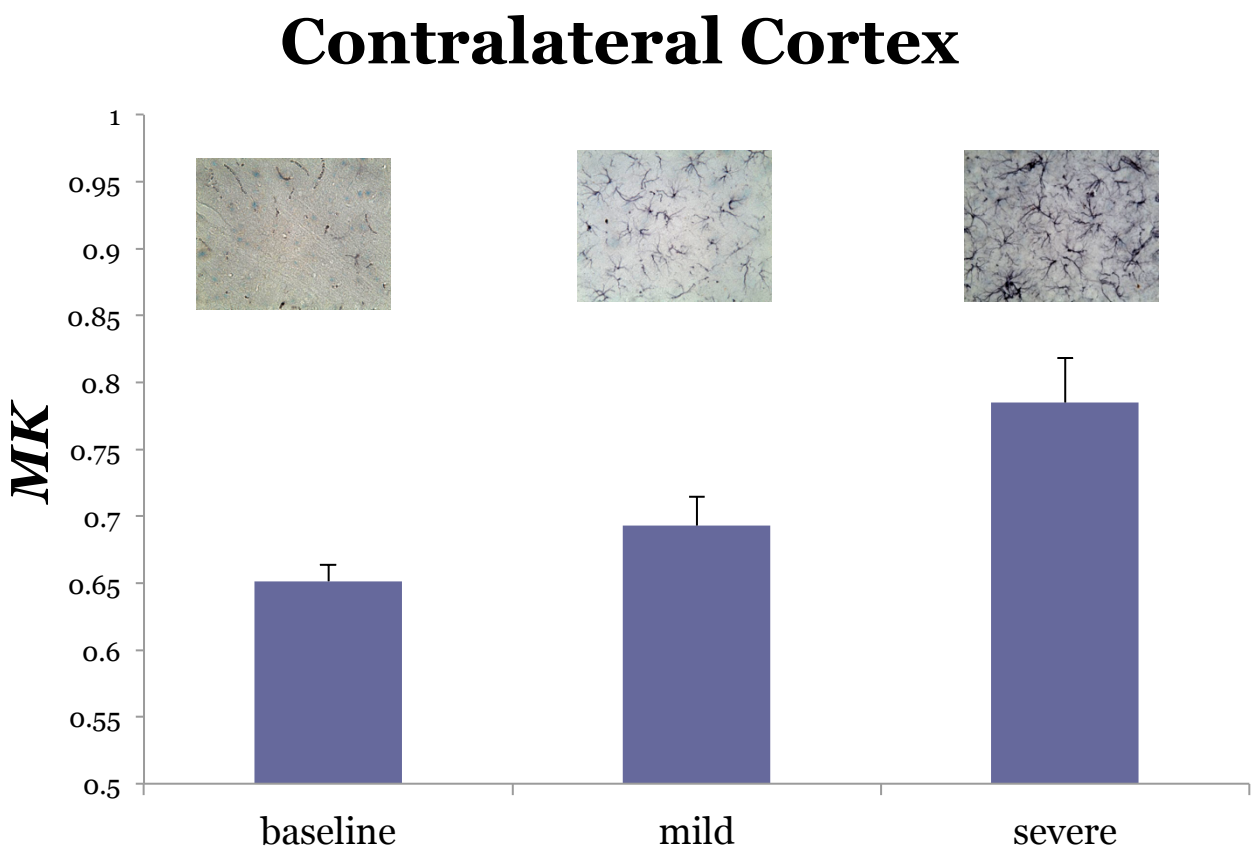
Pair-wise cluster plot



Blue: base line Red: 7 day post injury

Correlation between histology & MK





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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