Case Study: Cumulative Head Impact Trauma Over a Season of Collegiate Women's Soccer

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Acknowledgements

Head Impact Injuries

Concussions: just the tip of the iceberg!

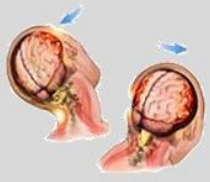
Extensive studies published since 2010:

- Cumulative small impacts cause significant physiological changes in brain, even without concussion symptoms
- Can lead to permanent neurological injuries and long-term degenerative neural disorders such as CTE
- Incidence, costs may exceed diagnosed concussions.

Complex Problem → Simple Physics

PROTX

Typical "sub-concussive" head impacts:

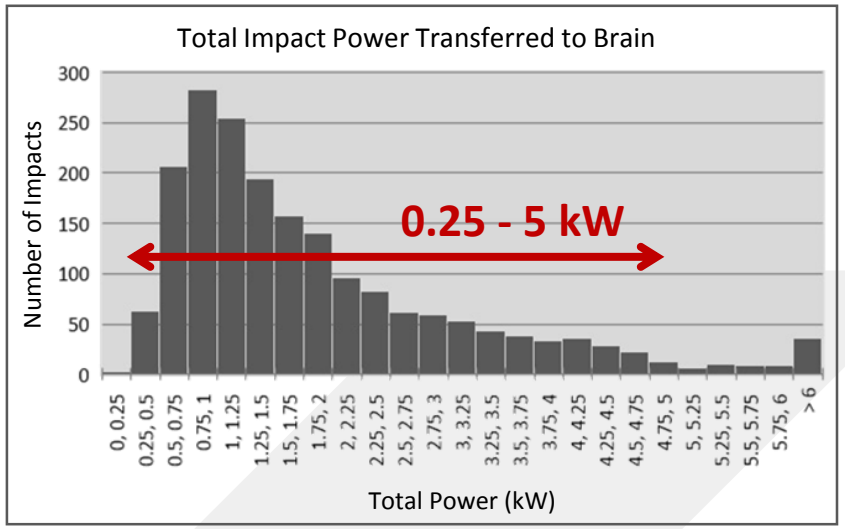


$$m_B = 1.2kg$$
$$I_B = 0.004kg \cdot m^2$$
$$a_{lin} = 10g$$
$$a_{rot} = 3500rad/s^2$$
$$\Delta d_{lin} = 10cm$$
$$\Delta\theta_{rot} = 0.79rad\ (45°)$$
$$\Delta t = 10msec$$

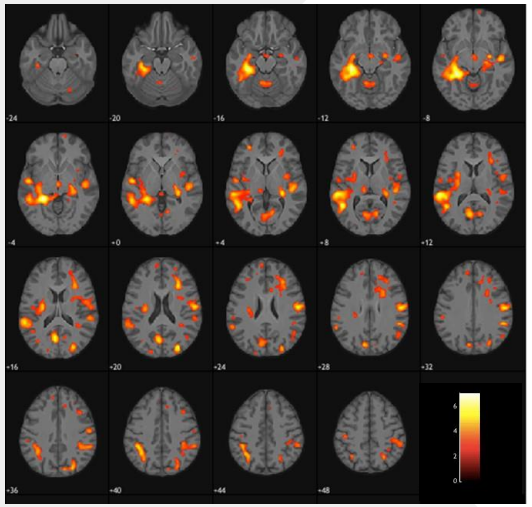
$$\Delta P_{lin} = \frac{m_B \times a_{lin} \times \Delta d_{lin}}{\Delta t} = 1.2 \text{ kilowatts}$$

$$\Delta P_{rot} = \frac{I_B \times a_{rot} \times \Delta\theta_{rot}}{\Delta t} = 1.1 \text{ kilowatts}$$

$$\Delta P_{total} = 2.3 \text{ kilowatts}$$

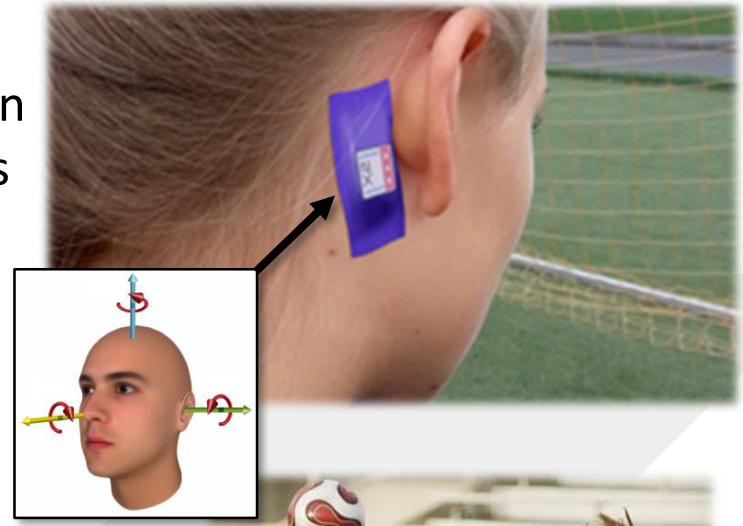


- "Routine" impacts in youth sports transfer 0.25-5 kW to athlete's brain
- Well below observed concussion thresholds, but sufficient to cause diffuse axonal injury
- Can observe these microscopic changes in DSI/MRI, correlate with measured impact biomechanics



Methods – Impact Measurements

- Division 1 female soccer athletes
- Skin-affixed wearable accelerometers worn on mastoid of each player during practices and games (Aug – Nov, 11 weeks)
- Linear and rotational head accelerations recorded for all impact events
- 12 players, 12 age-matched controls
- Data used to calculate cumulative impact power transferred to brain (modelled as 3D ellipsoid)
  - mass = 1.2 kg, volume = 1120 cm^3
  - radii = 8.3 cm (L), 7.0 cm (W), 4.6 cm (H)
  - moment of inertia I=0.004 kg • m^2 (assume rotation about axes through base of brain/neck)

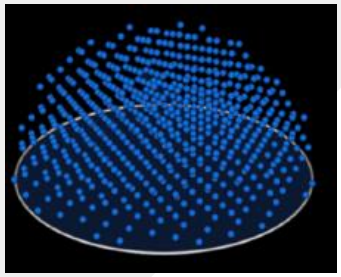


Methods – MRI

- Each player and control scanned 4 times using high angular resolution diffusion spectrum MRI (DSI) scans

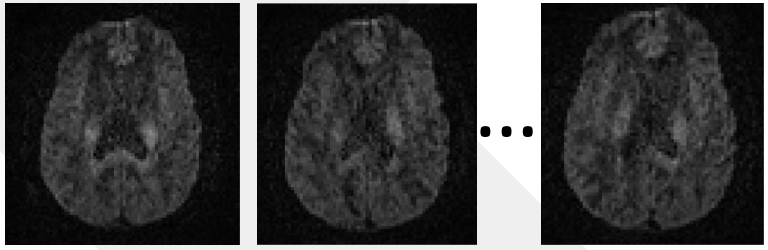
- MRI images acquired for 257 diffusion directions in each session
  - One hemisphere in **q**-space
  - 2.0 x 2.0 x 2.0 mm^3 resolution per voxel

Siemens Prisma 3T



q-space sampling scheme

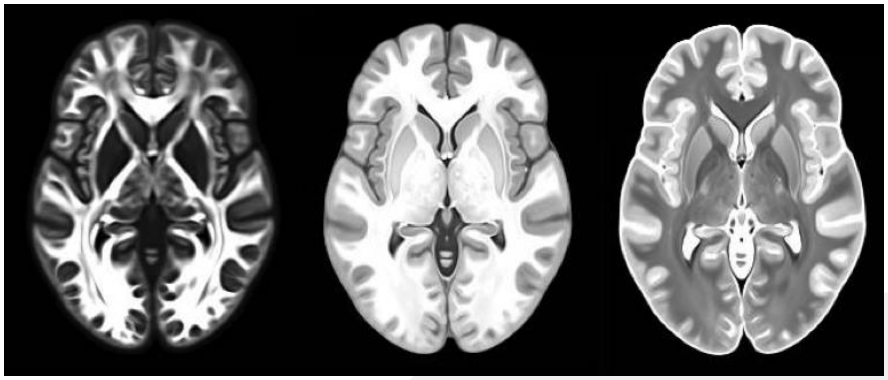
- Spatial diffusion images reconstructed using generalized q-ball imaging algorithm (DSI-Studio)



Spatial diffusion image reconstruction

Methods – MRI

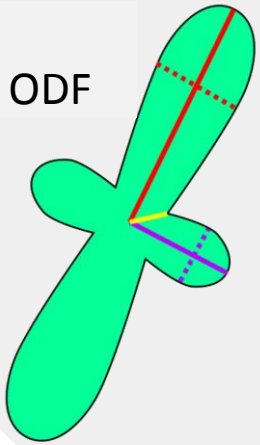
- Scans for athlete/control cohorts spatially normalized, aligned, combined into composite scan sequence using ANTs (Advanced Neuroimaging Tools)



Scans combined using ANTs

- Multi-directional orientation distribution function (ODF) calculated for each voxel
  - ODF used to estimate two strongest directions of diffusion anisotropy, MDA_0 and MDA_1
  - allows detection of changes in brain physiology even with multiple neural fiber directions present in voxel
- Differences in MDA_0 and MDA_1 between 4 MRI scanning sessions used to assess # of voxels evidencing changes in brain physiology as a function of cumulative head impact exposure.

ODF



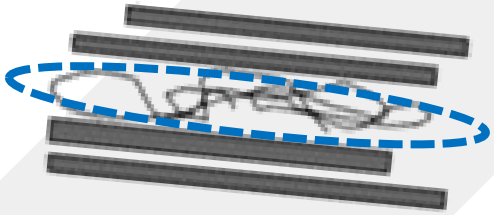
Multi-Dimensional Anisotropy

$$MDA_0 = \frac{\text{Peak}}{\text{Isotropic}}$$

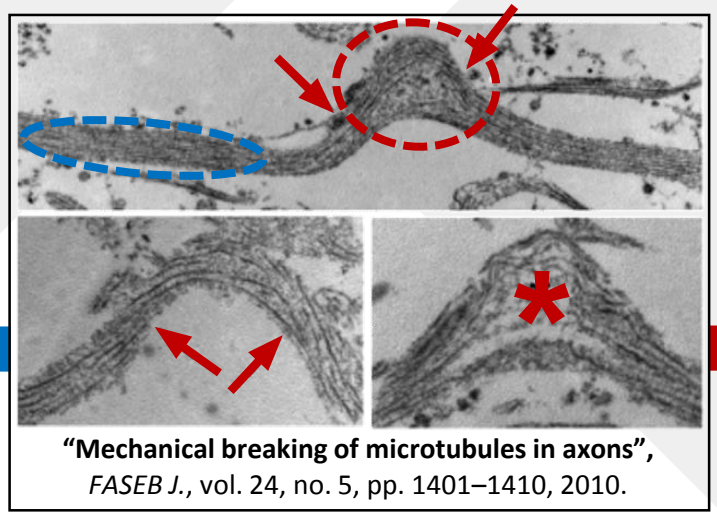
$$MDA_1 = \frac{\text{Peak}}{\text{Isotropic}}$$

What Will all of this Tell Us?

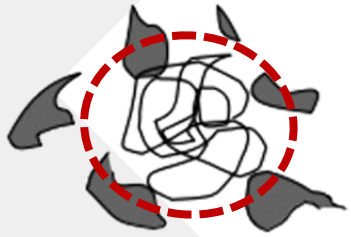
- Whole brain suffers dynamic tissue deformation during head impacts
- Axons suffer pronounced mechanical damage
  - internal microtubule structures break, cause varicose swellings along axons
- DSI scanning techniques enable very sensitive/high-resolution imaging of water diffusion within axons
- Axons healthy, intact → cell membranes constrain water → diffusion is highly anisotropic
- Axons damaged, membranes more permeable, varicose swellings present → water less constrained → diffusion anisotropy reduced



Constrained, highly anisotropic diffusion

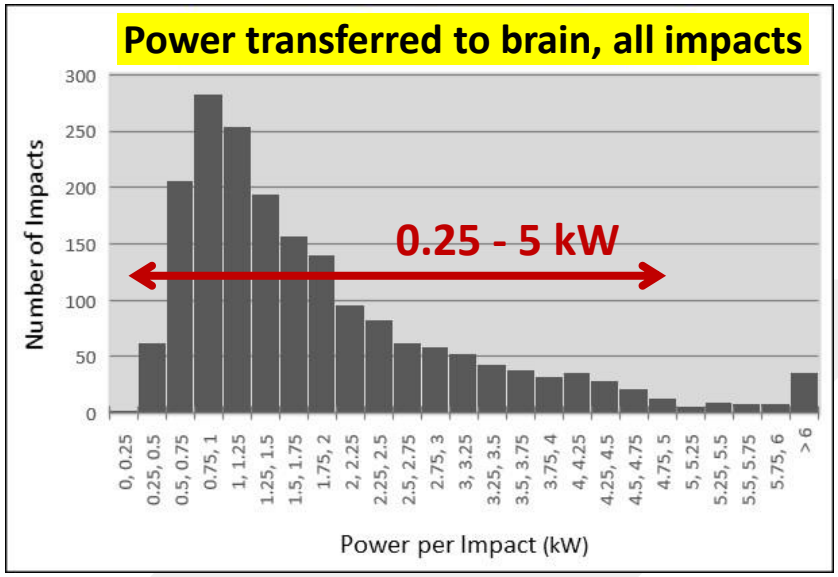


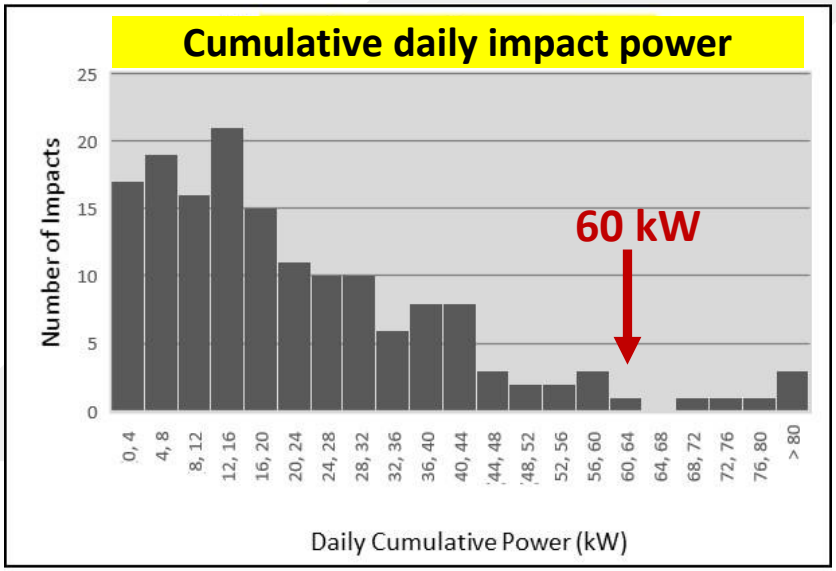
"Mechanical breaking of microtubules in axons", *FASEB J.*, vol. 24, no. 5, pp. 1401–1410, 2010.



Less constrained, diffusion anisotropy reduced

Results – Impact Measurements

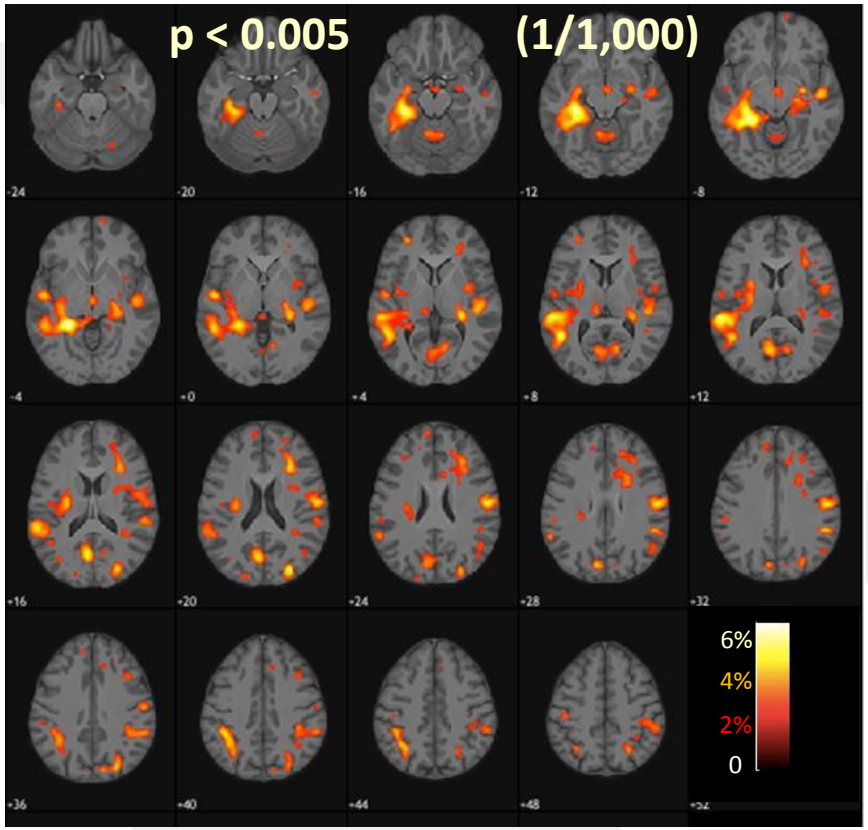


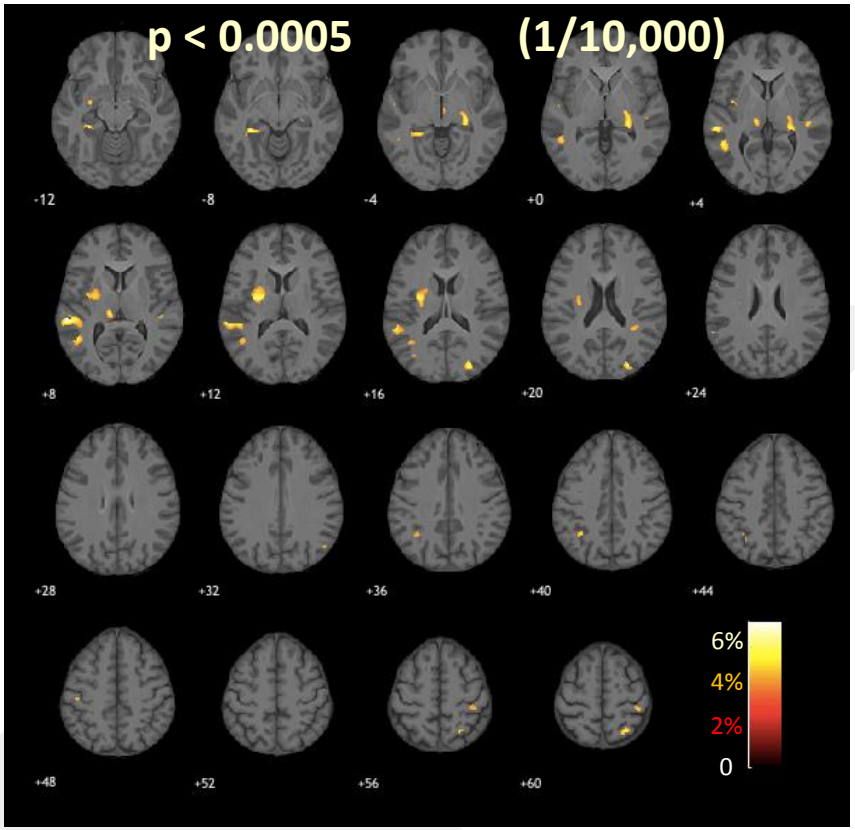


Routine head impacts transfer 0.25kW - 5kW per impact to athletes’ brains, dissipated via mechanical deformation of neural tissues

Cumulative daily impact power loads extend out to 60 kW, 6 players received daily loads 68kW - 110kW

DSI Results – Players vs. Controls



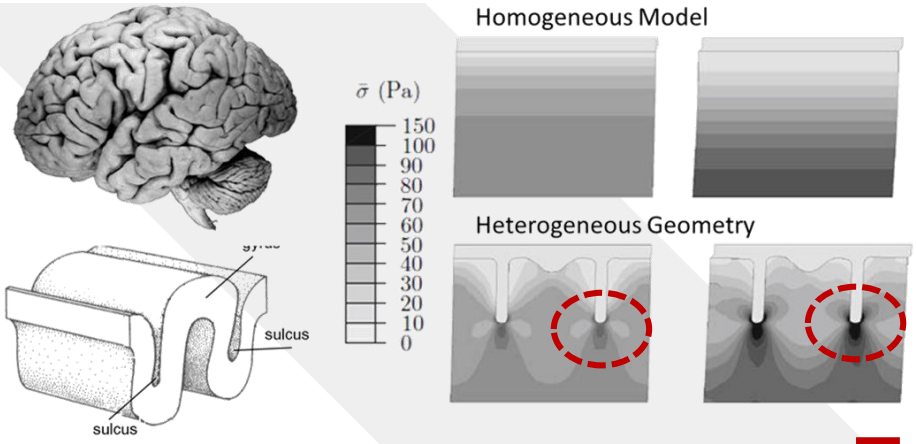


- Calculate end of season % change of MDA_0 = 100 * $MDA_{0,\ scan3}$/ $MDA_{0,baseline}$
- Plot difference in % change between players vs. controls
- Unpaired T-test, exploratory thresholds p < 0.005 (1/1,000), p < 0.0005 (1/10,000)

➢ Diffusion changes widely distributed (linear/rotational coupling)

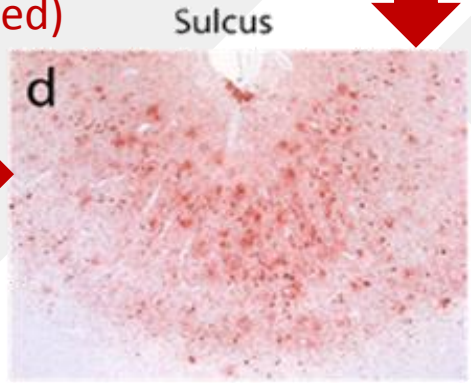
➢ Consistently observed at WM-cortical border and sulci

Spatially Localized DSI Changes



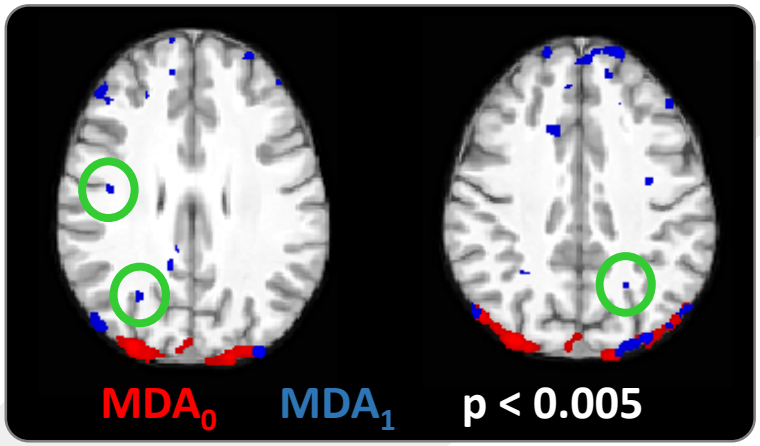
"Biomechanics of Traumatic Brain Injury: Influences of the Morphologic Heterogeneities of the Cerebral Cortex"
R.J.H. Cloots et al, Annals of Biomed Eng (2008)

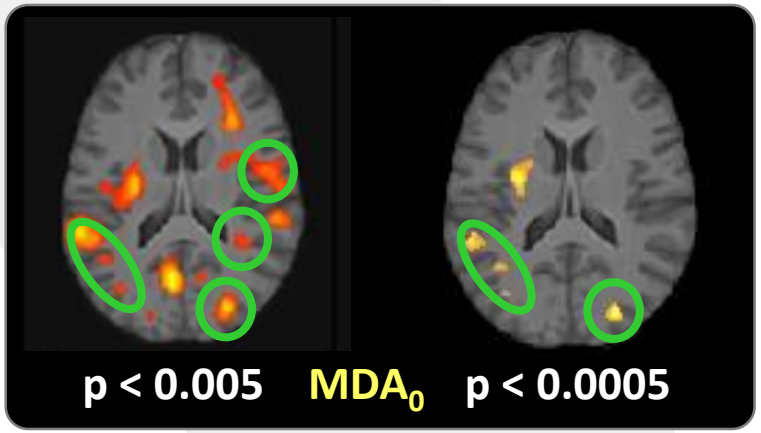
Spatially localized stress enhancement (predicted) possible explanation for spatially localized damage



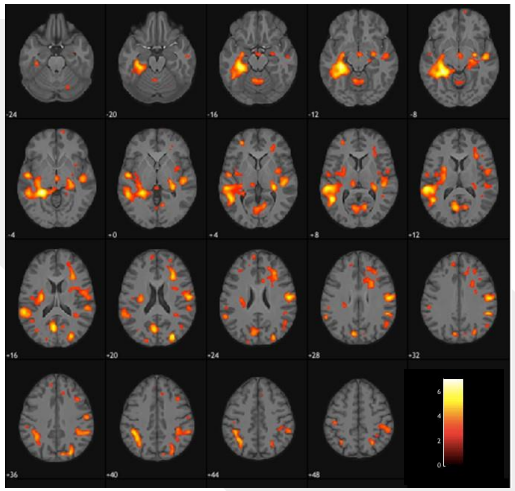
"Beta-amyloid deposition in CTE", T.D. Stein et al, Acta Neuropathology (2015)

In-vivo DSI observations of localized diffusion changes at cortical sulci, consistent with localized stress enhancement

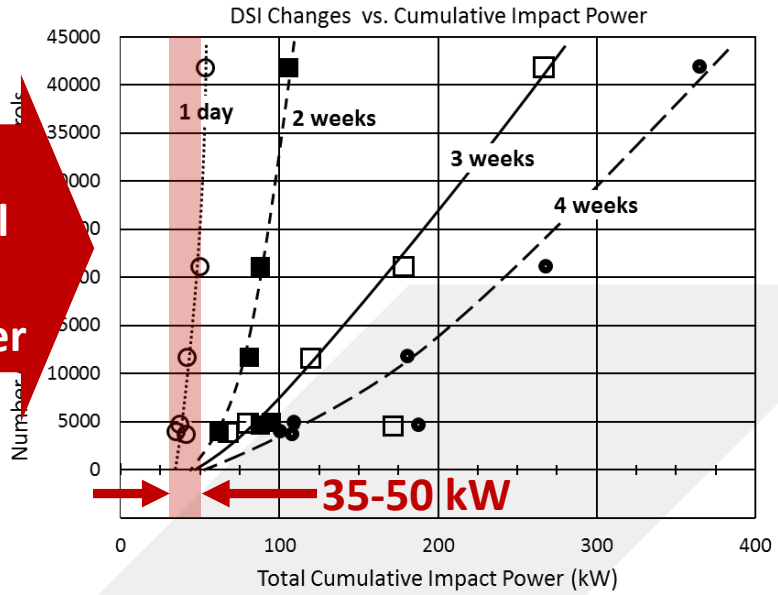


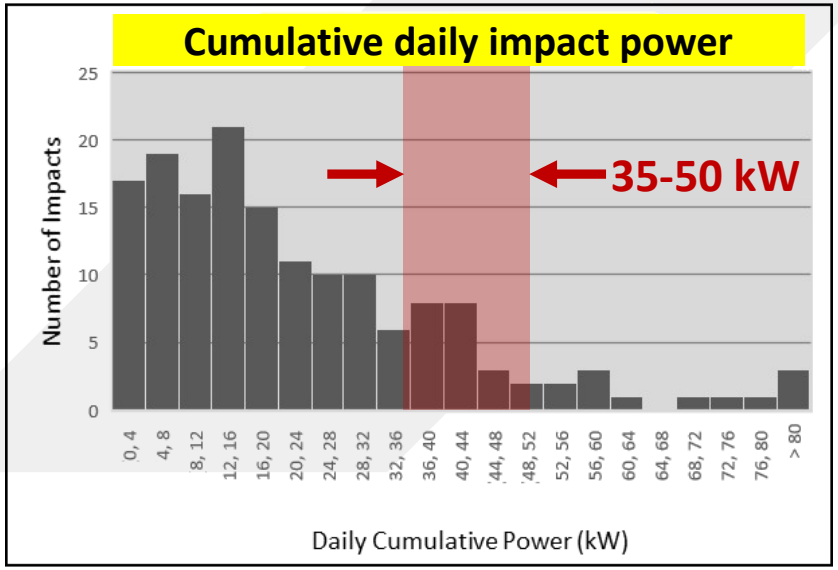


Cumulative Damage Threshold



Neuro-mechanical biomarker → dosimeter

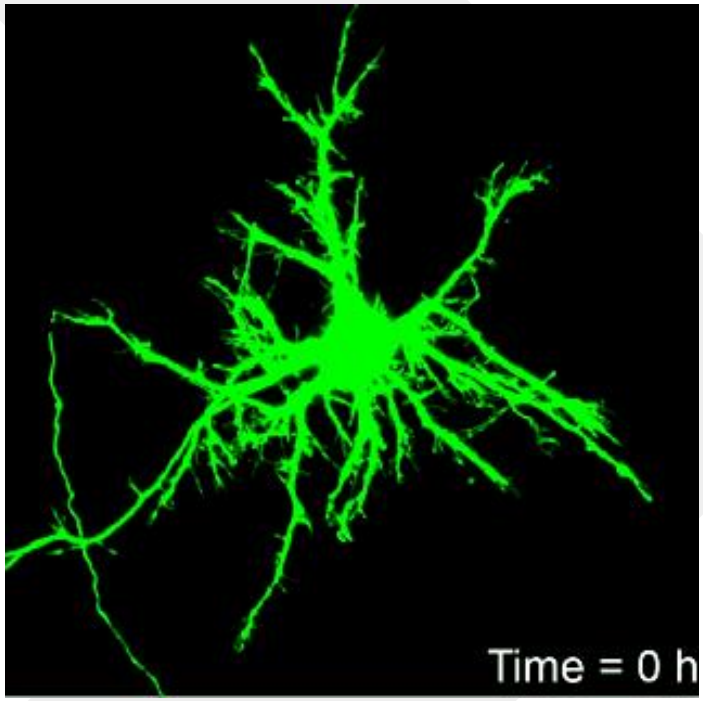




- Accumulated daily doses **35-50 kW** triggered **transient changes** (observed for in-season scans, but not in post-season washout scan). **All 12 players**
- Accumulated daily doses **>100 kW** triggered **persistent changes** (observed for in-season and post-season washout scans). **3 players**

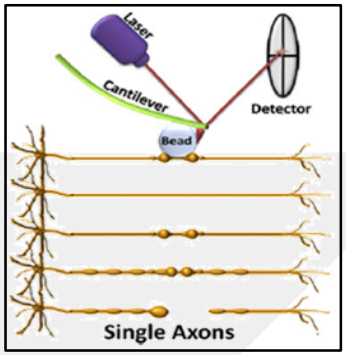
Axonal Damage Threshold

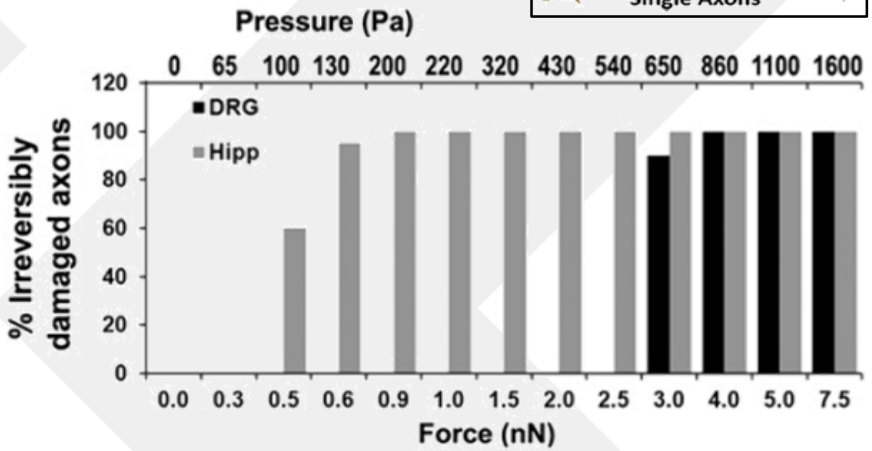
1. Impact-induced damage can now be studied directly in live cultured neurons.



"*Strain and rate-dependent neuronal injury in a 3D in vitro compression model of traumatic brain injury*", E. Bar-Kochba et al, Nature Scientific Reports, Aug 2, 2016. doi:10.1038/srep30550, http://www.nature.com/articles/srep30550.pdf

2. AFM → Initial threshold observed for transient local deformation of axons, followed by more abrupt higher threshold above which irrecoverable axon damage occurs.



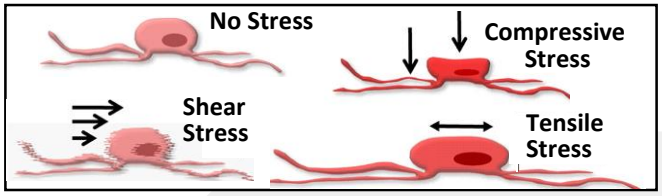


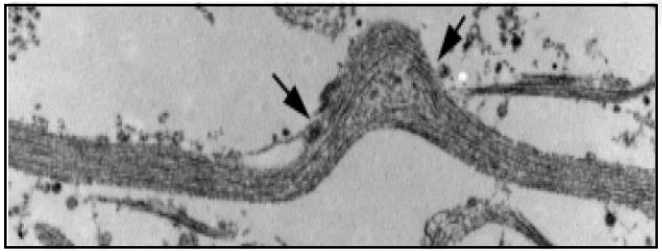
"Atomic Force Microscopy Reveals Important Differences in Axonal Resistance to Injury", M.H. Magdesian et al, Biophysical Journal, vol. 103. pp. 405-414, Aug 2012.

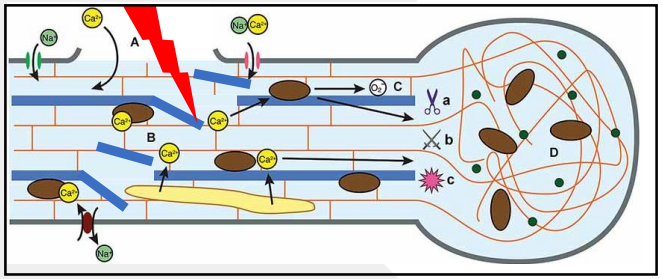
Head Impact Injuries Revisited

- Head impacts trigger wide and continuous spectrum of morphological and physiological changes, both transient and permanent

- Common hallmarks:
  1. **morphological deformation of axons**
     - small/slow deformations are transient
     - large/rapid deformations persist, accumulate
  2. **breakage of microtubules, axonal swelling**
  3. **axonal degeneration, biochemical cascade**



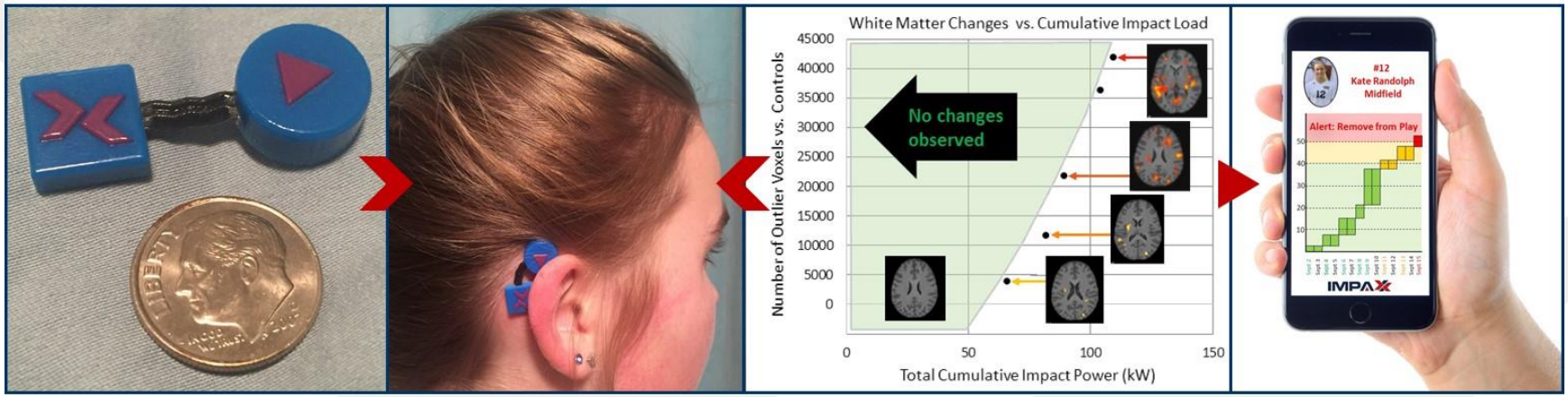




- More severe impacts can trigger wide range of immediate/delayed symptoms

- **Even without any near-term symptoms, cumulative head impacts can lead to serious degenerative consequences in long term.**

Future Efforts



- Improvements in the design of wearable sensors for impact monitoring
- Study of mechanical damage thresholds as a function of height, weight, gender, brain physiology, athletic activity, other relevant variables
- Investigation of the temporal evolution of impact-induced physiological, biochemical, and neuropsychological manifestations
- **Reduced head impact exposure → performance enhancements?**

Thank you!

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