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Ultra-High-Performance 3T MR in mTBI

James Kevin DeMarco, MD

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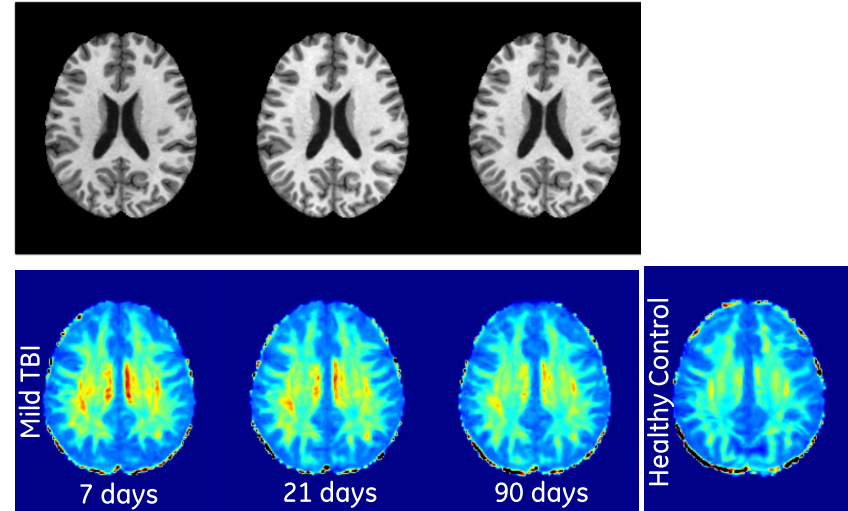
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- I have no disclosures



Mild TBI: Unmet imaging needs

- Today, CT is the only urgent care gold standard available for TBI cleared by FDA. It is highly effective to detect life-threatening bleeds, but are often negative.
- MRI can detect more mTBI pathology than CT, although many structural images are negative.
- Clinicians have limited ability to predict how long symptoms in individual patients will persist.
- Return-to-learn/Return-to-play/Return-to-active-duty decisions are based on clinical observation, not on objective measures of brain physiology.



This patient exited the study still symptomatic, three months after injury. Structural MRI was normal at every time point.

Courtesy of Luca Marinelli



TRACK-TBI

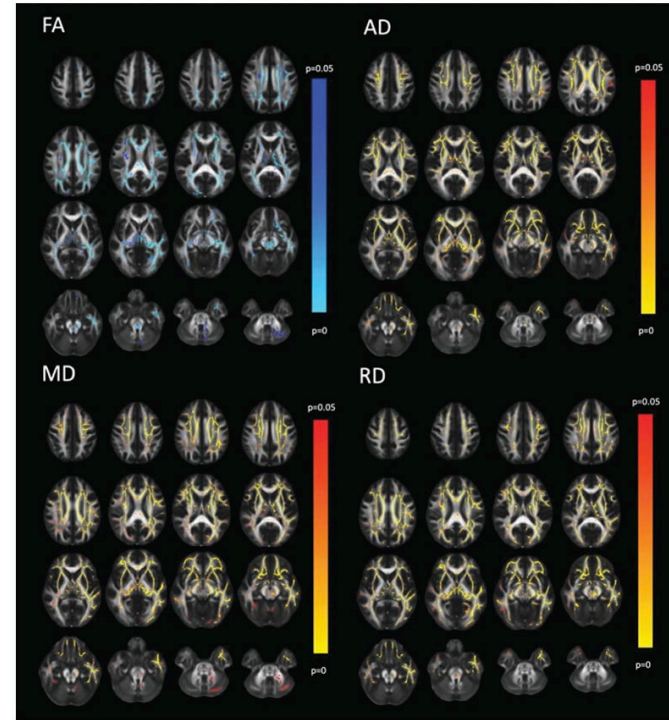
- Enrollment
 - ✧ Enriched population by design
 - ⑩ Enrolling mTBI patients sent for clinical head CT at 11 academic level 1 trauma center
 - Of 367 mTBI patients, 28% CT+ and 47% MR+ in TRACK-TBI cohort with imaging at 2 time points
- 3T brain MRI with diffusion imaging
 - ✧ Diffusion tensor imaging (DTI) is a simplified model to describe anisotropic Brownian motion of water molecules in the brain
 - ✧ Key assumption of DTI is Gaussian diffusion process, ie no restrictions or barriers



TRACK-TBI – Group level analysis

- DTI of mTBI patients (n=391) at two weeks post-injury versus demographically matched controls (n=148) showed:
- Elevated global white matter axial diffusivity (AD) and mean diffusivity (MD) were independently associated with a six-month incomplete recovery.

Palacios et al, J. Neurotrauma 2022



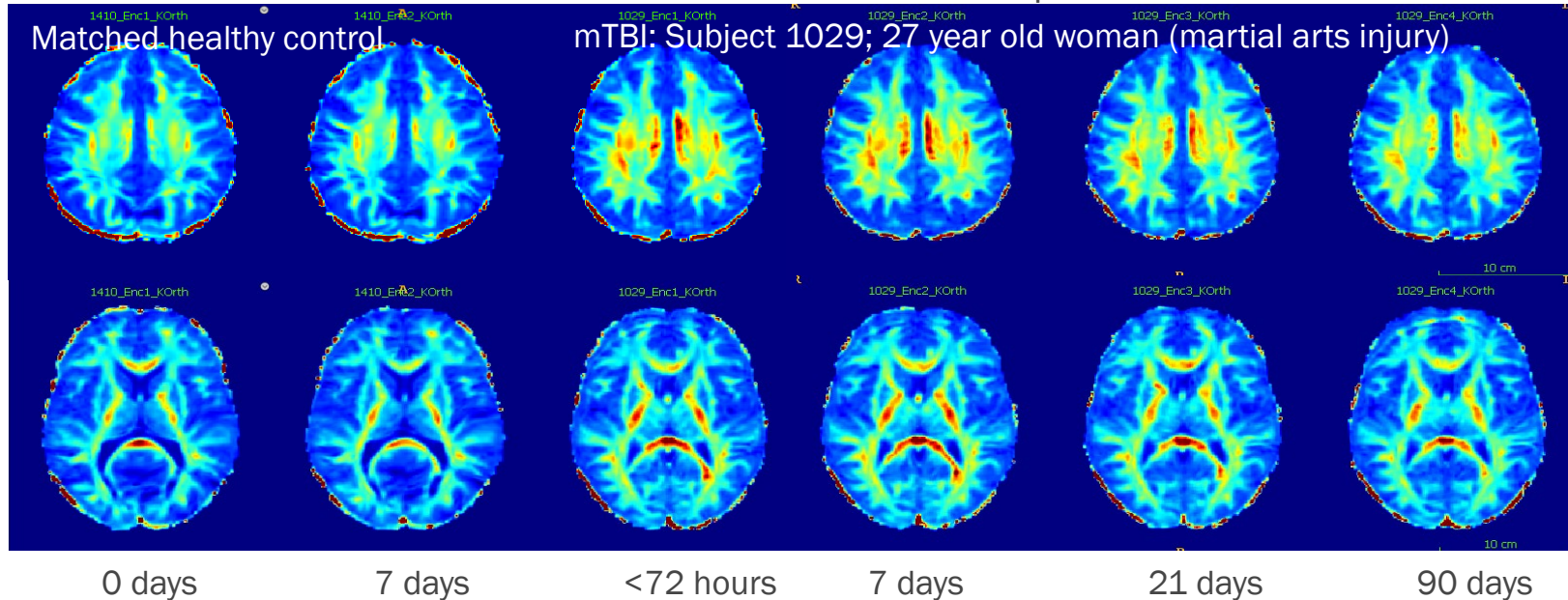
Higher-order diffusion MRI metrics

- DKI (diffusion kurtosis imaging)
 - DTI assumes Gaussian diffusion of water in a single microstructural compartment
 - DKI estimated both Gaussian and non-Gaussian components of the diffusion signal by acquiring diffusion-weighted images with multiple b-values
 - DKI is sensitive to boundaries and restriction in white matter, not just direction of fiber tracts
 - Multiple studies demonstrate DKI abnormalities in mTBI not recruited from ER and less anatomical abnormalities



Multi-shell Diffusion MRI using DKI

Radial Diffusional Kurtosis: Measure of restriction of diffusion process



Structural MRI for mTBI subject was normal at all time points. The patient exited the study not recovered and still symptomatic.

SSS = SCAT2 symptom severity score

Courtesy of Luca Marinelli

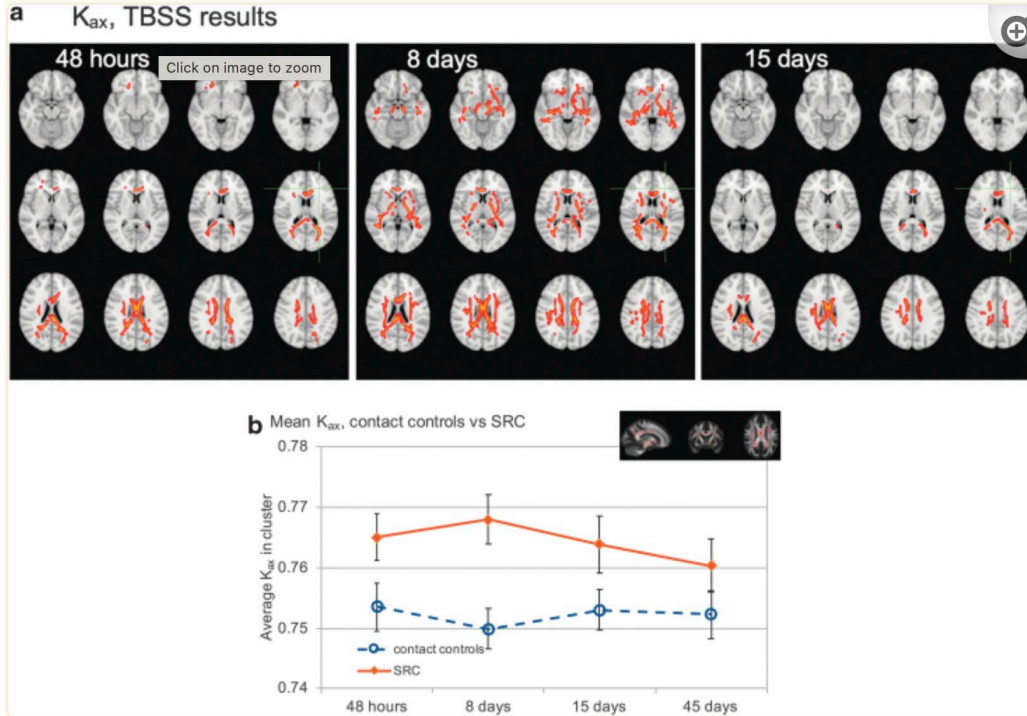


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DKI is sensitive to axonal injury and recovery

American football study in high school and college athletes



Clinical Assessment of Participants

	Concussed	Control	
	(n = 96)	(n = 82)	
	mean (SE)	mean (SE)	p
SCAT3 Symptom Severity			
Baseline	3.7 (0.91)	2.2 (1.02)	0.267
48 h	23.5 (0.92)	1.7 (1.02)	< 0.001
8 days	5.7 (0.94)	1.1 (1.05)	0.01
15 days	1.7(0.97)	0.93(1.07)	0.58
45 days	1.01(1.01)	1.13(1.11)	0.94

Muftuler, McCrea et al, J. Neurotrauma 2020



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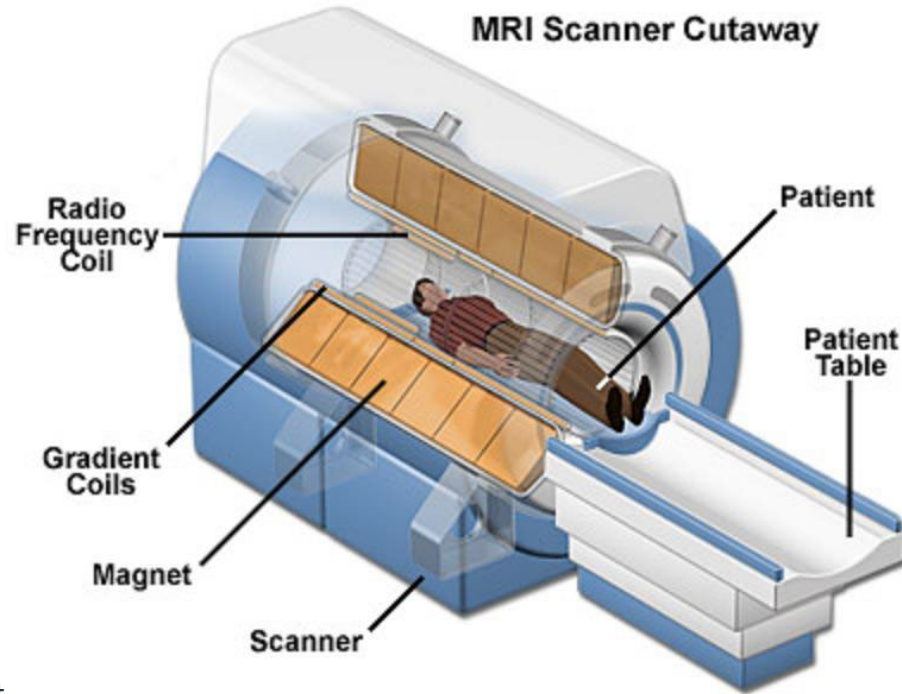


New Trend towards Dedicated Neuro MR scanners

- Business is recognizing role of dedicated ultra-high-performance neuro MRI
 - Move away from large bore whole body MR that can scan everything, but not optimally
 - Dedicated head-only gradients 3T systems for exceptional brain MR at busy imaging centers
- Dedicated head-only ultra-high-performance 3T MR allows us to be sensitive to intra-axonal water using ultra-high-b-value DW with high SNR for direct measurement of axonal properties such as diameter
 - Higher max gradient amplitude for ultra-high-b-value DW
 - Higher slew rate for less artifacts and higher SNR



What is a gradient coil?



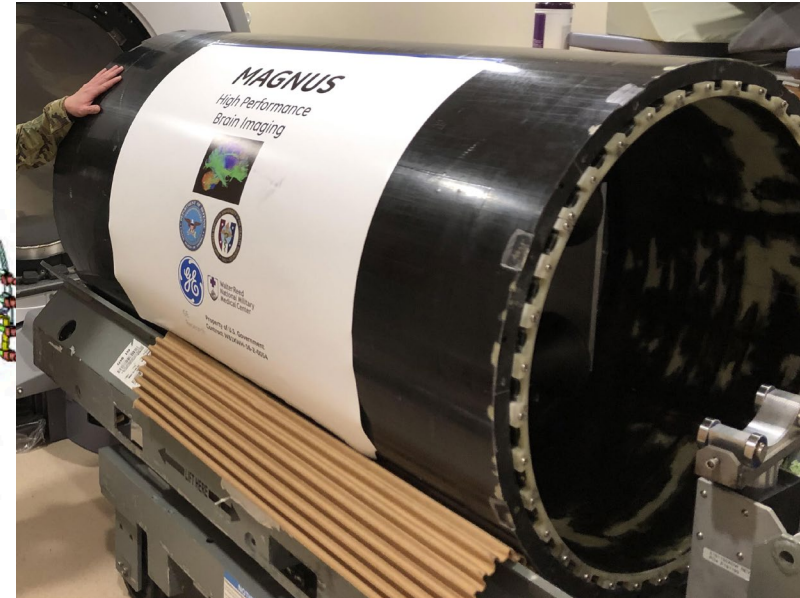
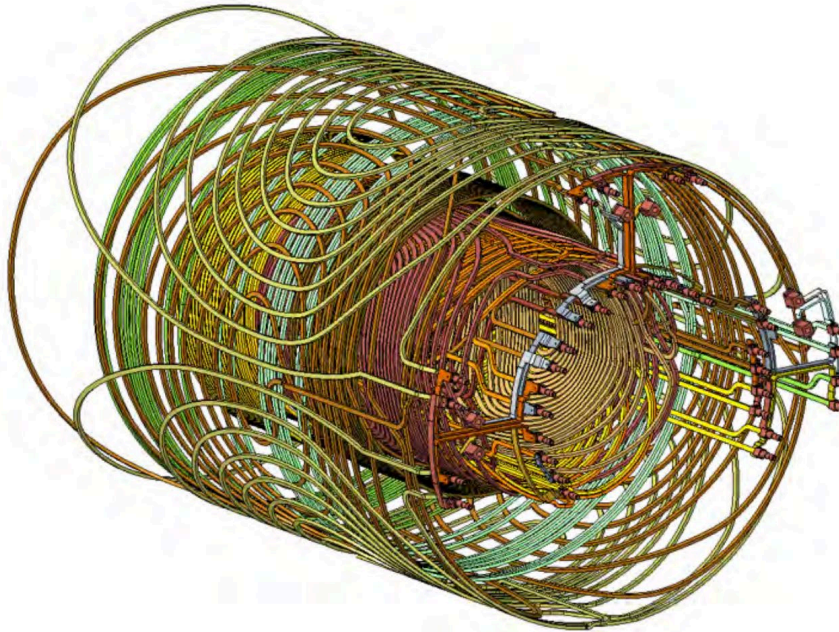
Source: Slideshare.net



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Advanced gradient Subsystem Design



Courtesy of Tom Foo

Gradient = Linear change

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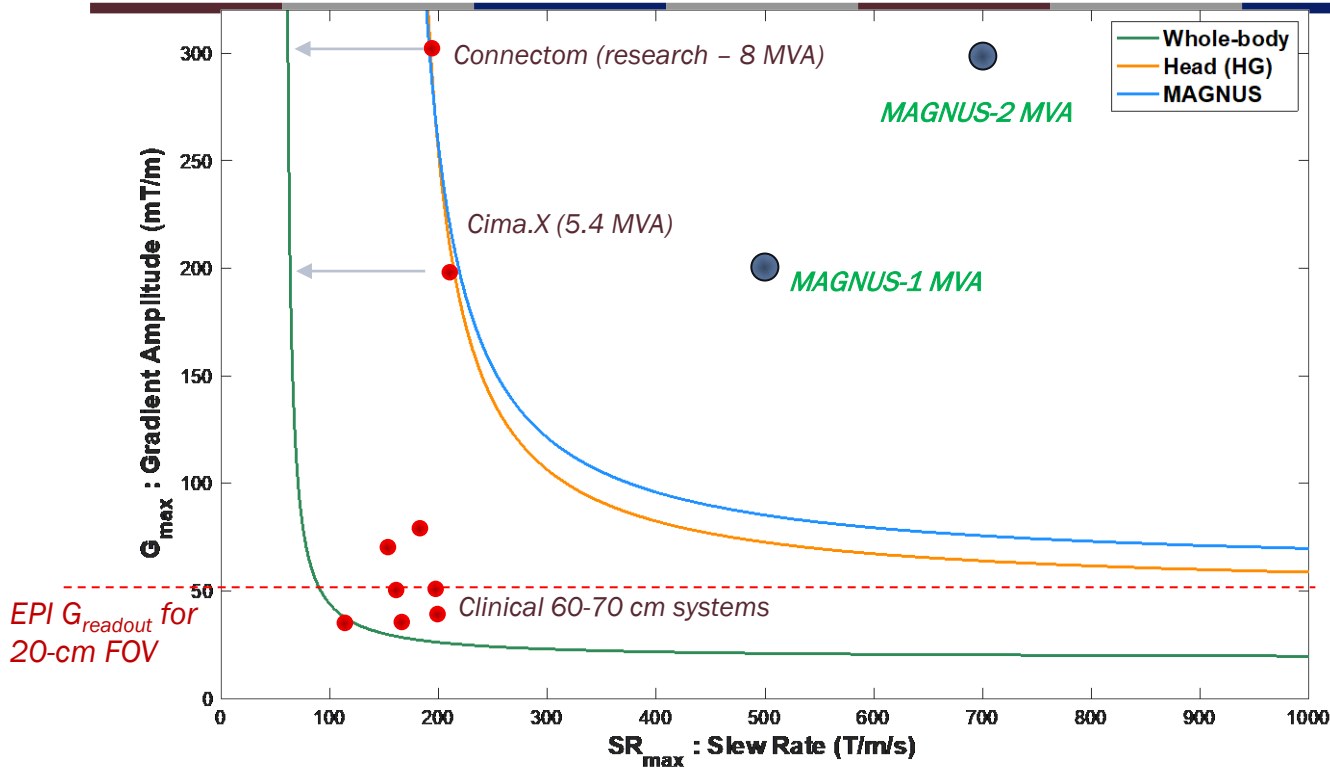
First MAGNUS gradient installation



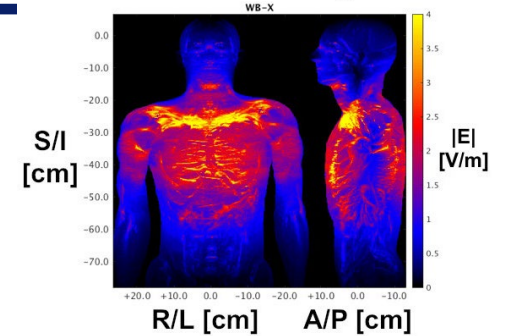
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Head-only gradient MR scanner

Gradient PNS Threshold



Whole-Body



Courtesy of Tom Foo



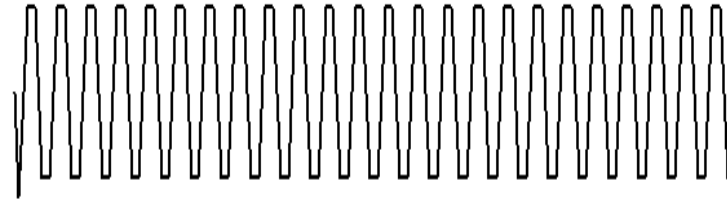
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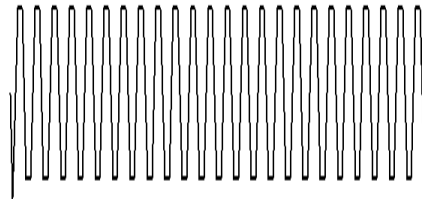
More SNR and less distortion with fast slew rate

Slew Rate (T/m/s)	ESP (μ s)
200*	724*
200	588
300	475
500	375
700	344

EPI readout echo spacing
Max $G_{\text{read}} \sim 50 \text{ mT/m}$

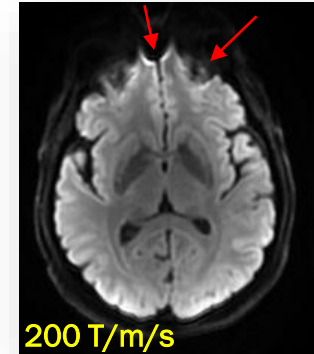


Whole-body : slew rate < 200 T/m/s

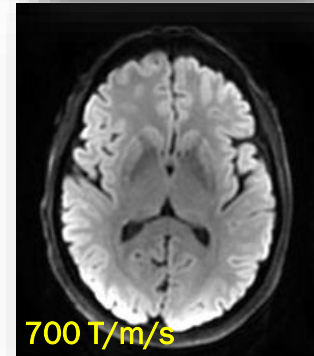


Head-only : slew rate > 500 T/m/s

Courtesy of Tom Foo

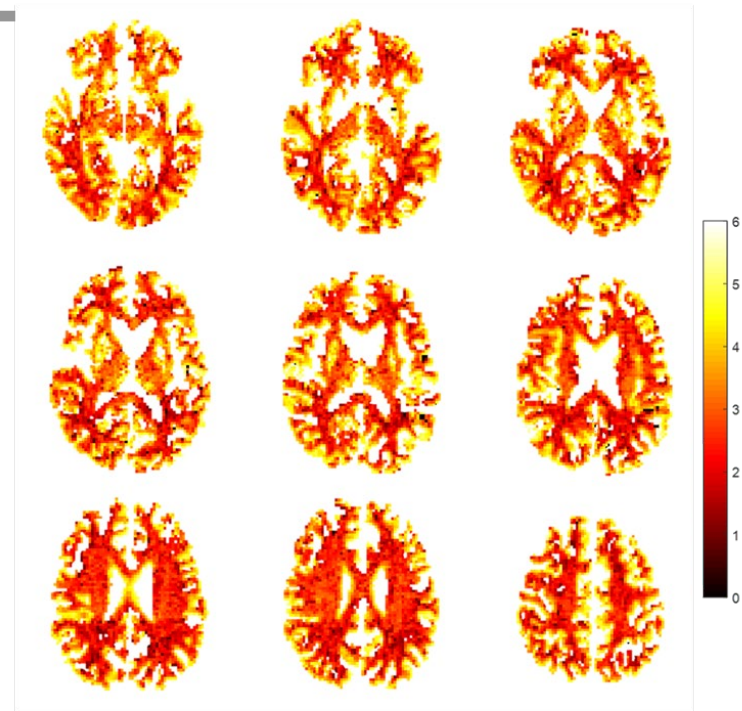
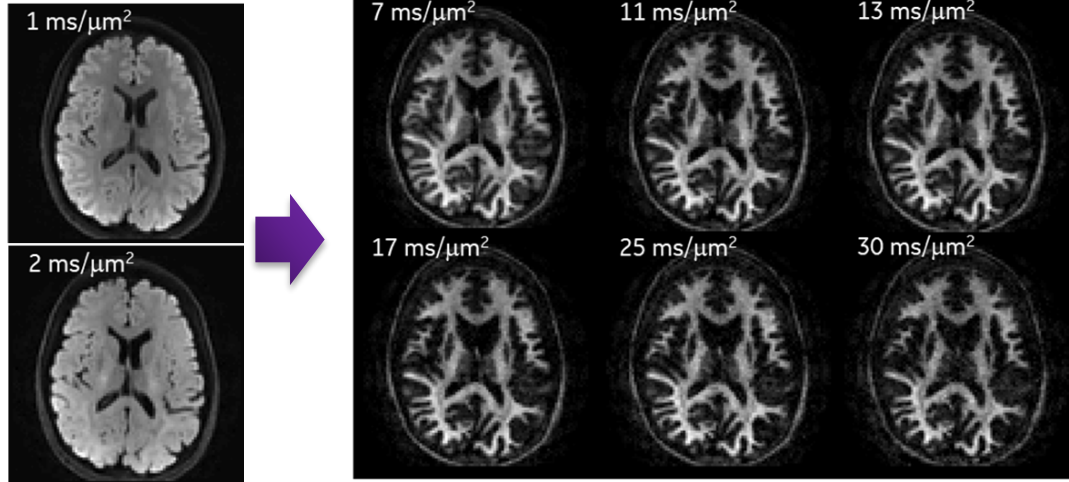


200 T/m/s



700 T/m/s

Effective axon radius maps enabled by ultra-high b-value dMRI



Multi-compartment model
 → combination of intra-
 and extra-axonal signal

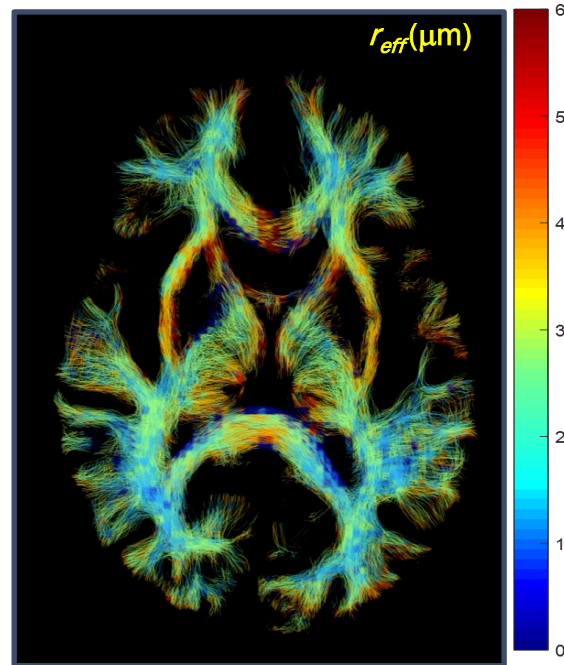
$$S_a = \beta \exp(-bD_a^\perp) b^{-1/2}$$

Simplified intra-axonal diffusion signal
 response at ultra-high b-values

Ultra-high b-values suppress extra-axonal water signal

Courtesy of Tom Foo

Effective axon radius tractography



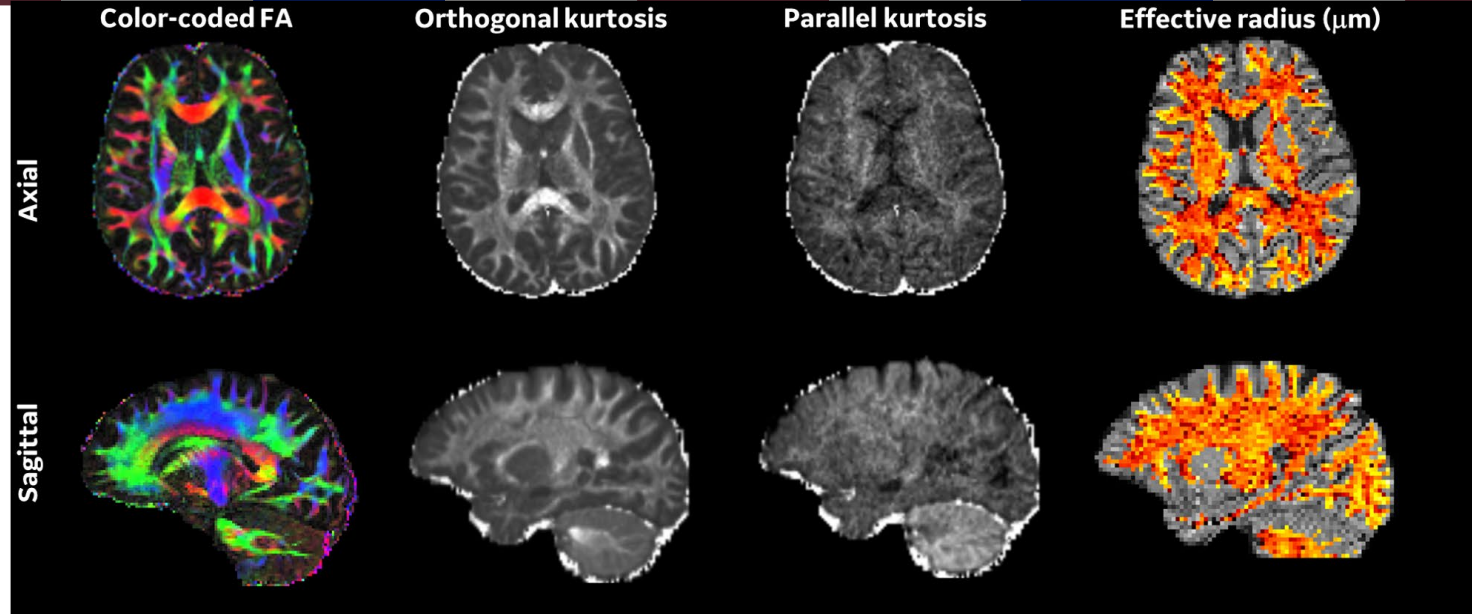
Courtesy of Nastaran Abad



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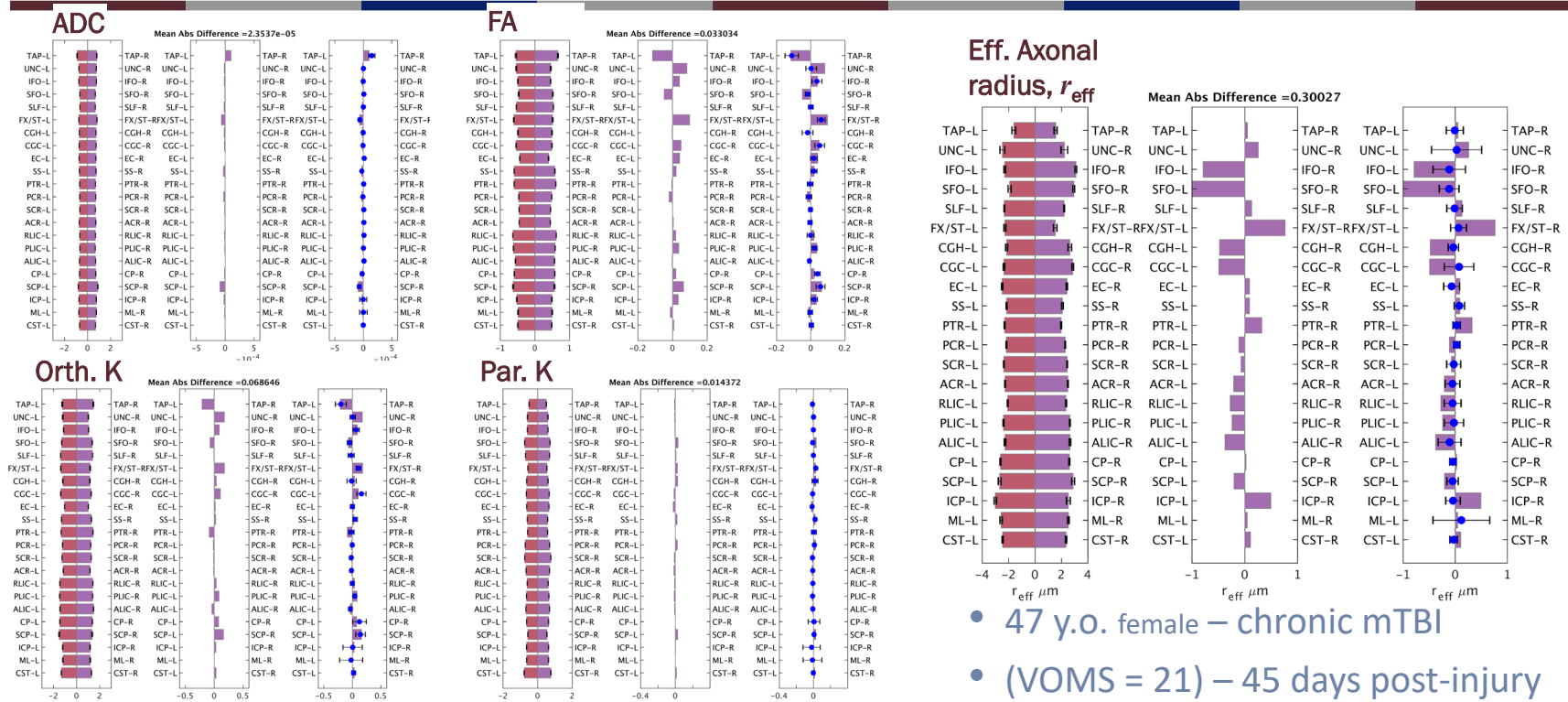


Ultra-High-Performance-Gradient 3T MR in mTBI

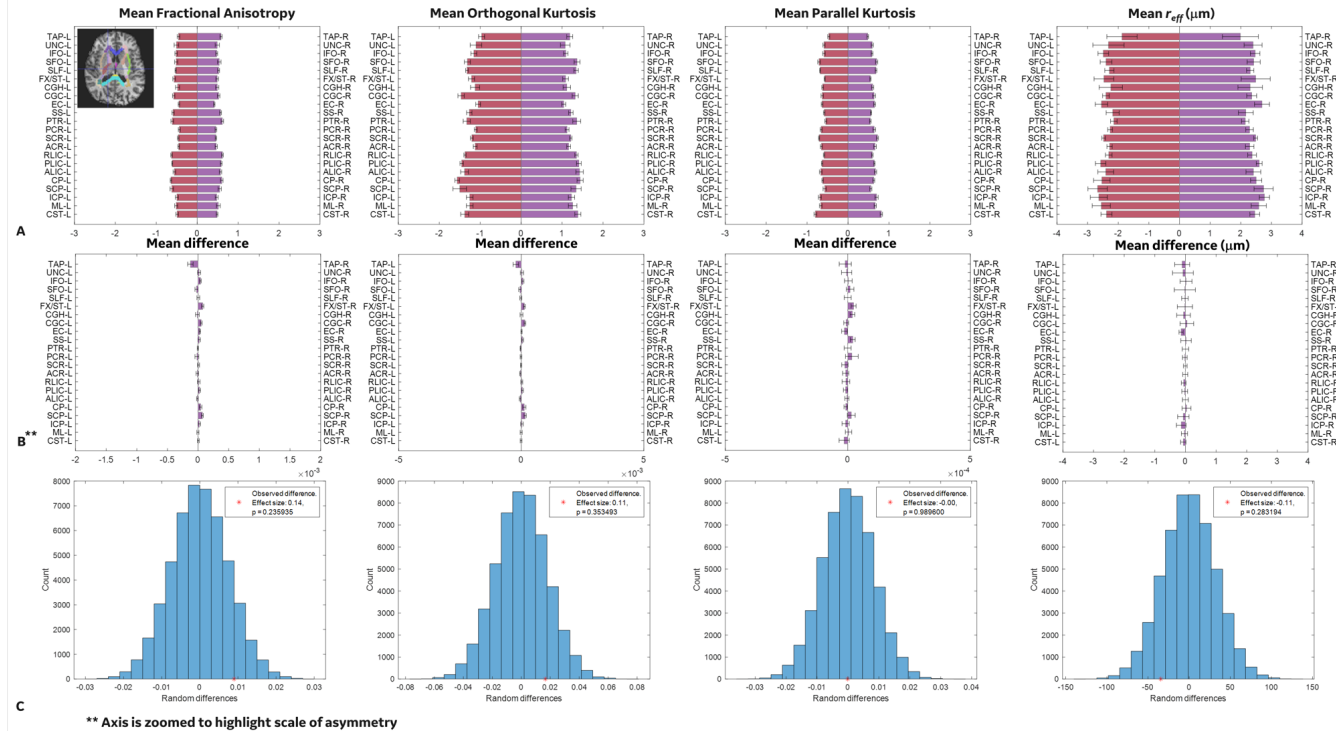


Representative axial and sagittal maps for DTI, DKI, and intra-axonal effective radius (r_{eff}) maps

Symmetry analysis - chronic mTBI



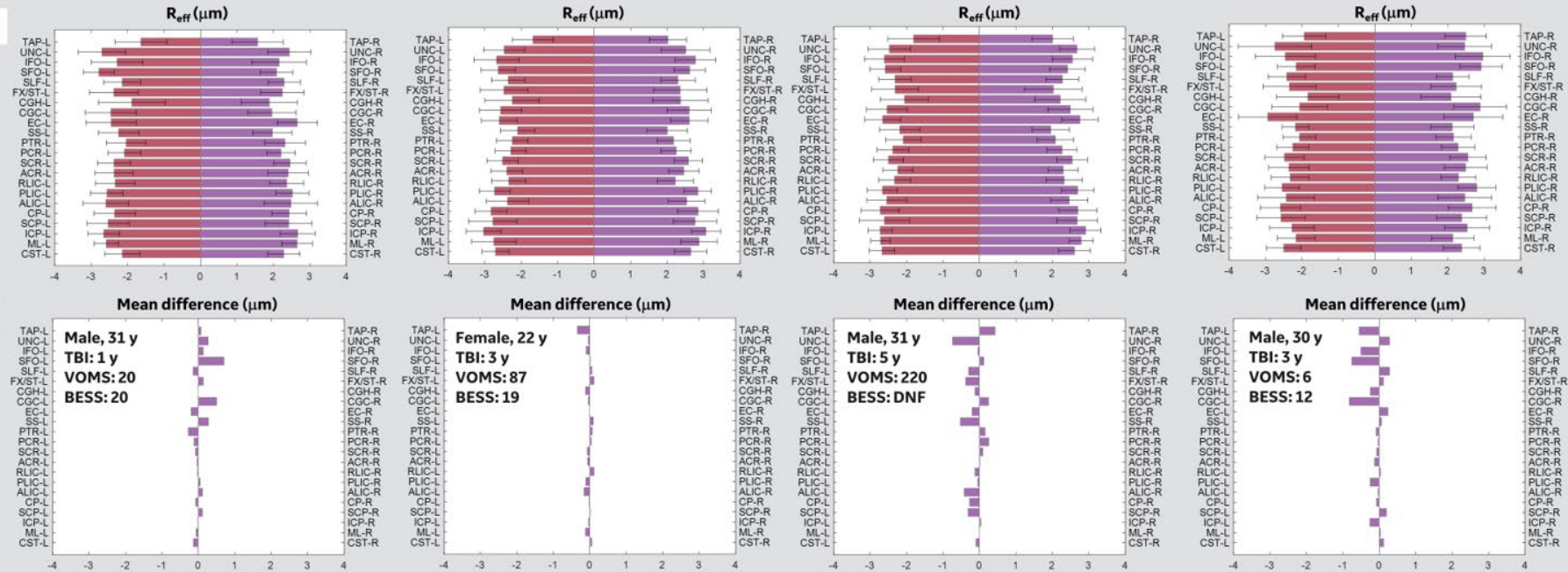
Bar plots show brain lateralization in health controls



Lateralization of r_{eff} highlight individual variability in chronic mTBI

B

Chronic symptomatic mTBI



Future work

- Ongoing analysis
 - Chronic mTBI
 - Evaluate the ability of other advanced diffusion techniques made possible by the high-performance gradients
 - OGSE evaluation of time-dependent parallel diffusivity to detect varicosities of axons
 - Evaluate the benefit of combined DTI/DKI/ r_{eff} /OGSE to identify new biomarkers of chronic mTBI
 - Acute mTBI
 - Similar analysis as chronic mTBI but with the added benefit of multiple time points
 - Correlate with symptomology over time
 - Decreased biological variance by restricting the analysis to the same subject over time



Summary

- Business is recognizing role of dedicated ultra-high-performance neuro imaging MR scanner
 - Dedicated head-only MR scanners will open the door to new brain MR biomarkers.
- Advanced diffusion MR with ultra-high-performance 3T MR
 - Multiple measures allow us to see trends in white matter damage
 - Ultra-high b-value dMRI r_{eff} has the sensitivity to pathology that neither DTI/DKI can reach in the same population. This new capability will allow properly powered studies to fully characterize axon size distributions in healthy and mTBI cohorts
- Future work
 - Expand population study size of mTBI
 - Proof-of-concept ultra-high-performance 3T MR funding by JPC-6 has resulted in 4 MAGNUS installations with 2 more to installed in 2024

