Advanced diffusion modeling characterizes FLAIR white matter hyperintensities in the ACT prospective neuroimaging cohort

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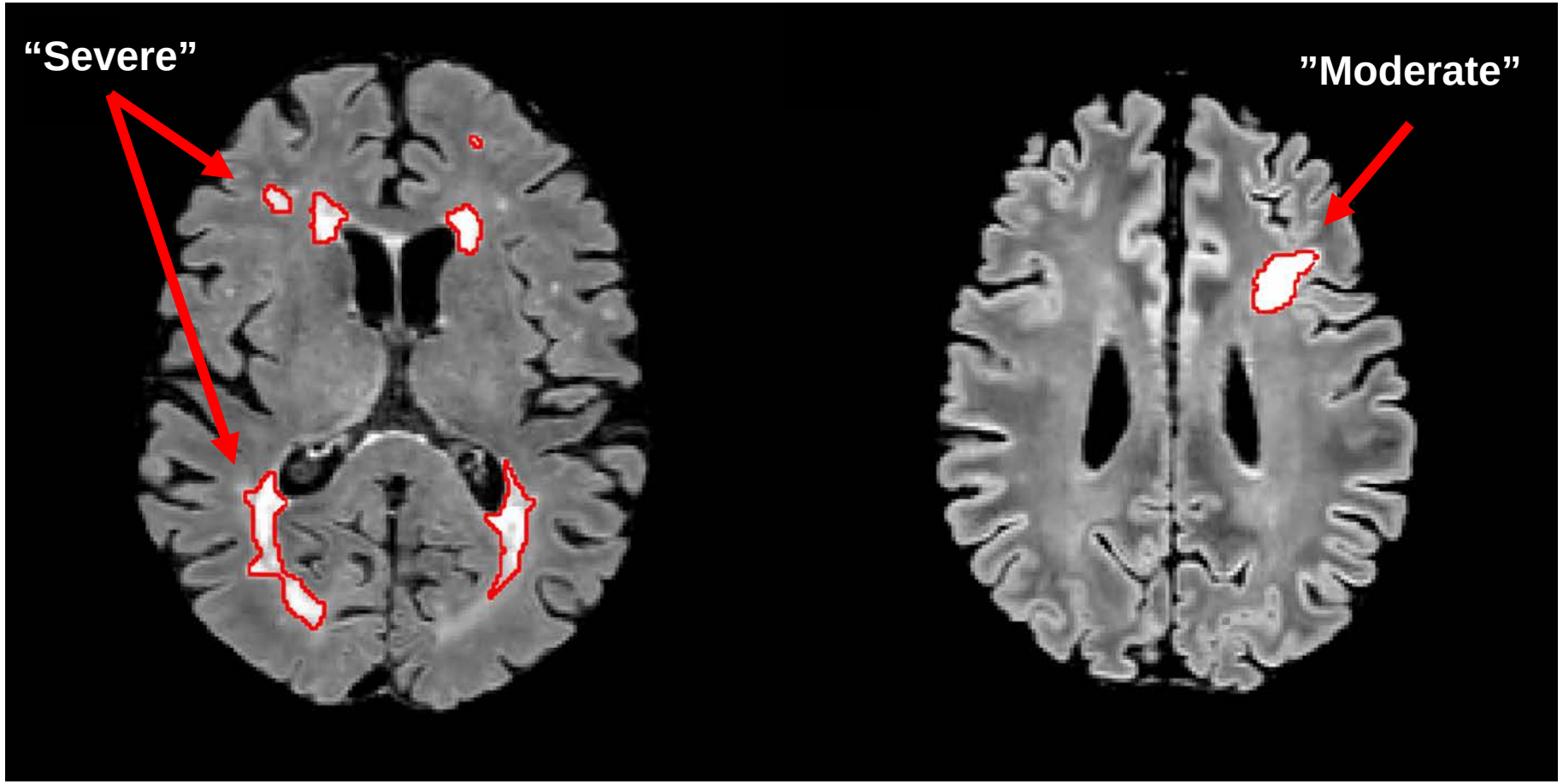
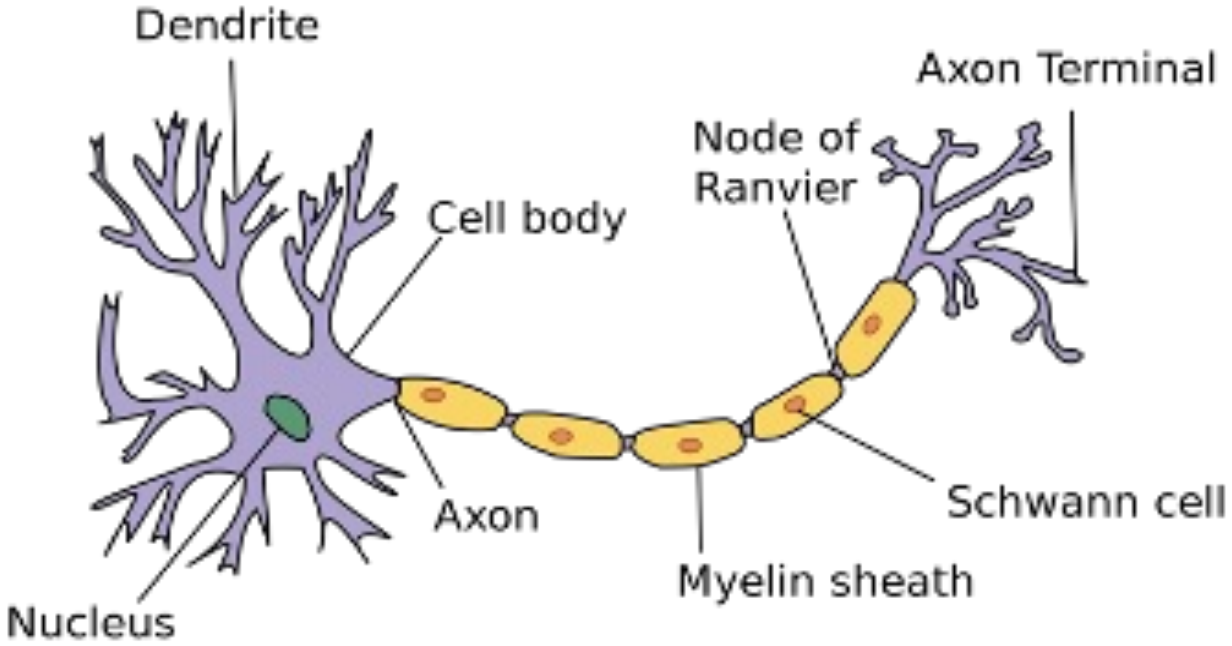
Fluid-attenuated inversion recovery (FLAIR) white matter hyperintensities are associated with aging and cognitive decline

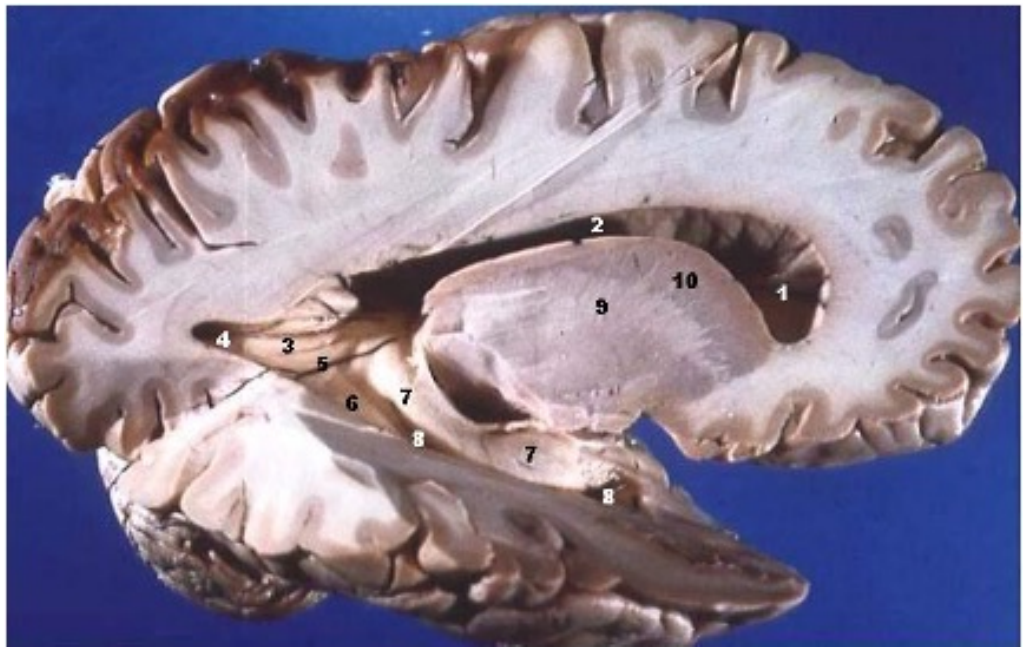


Periventricular WMH

Deep WMH

Diffusion imaging and modeling produce biophysically interpretable metrics





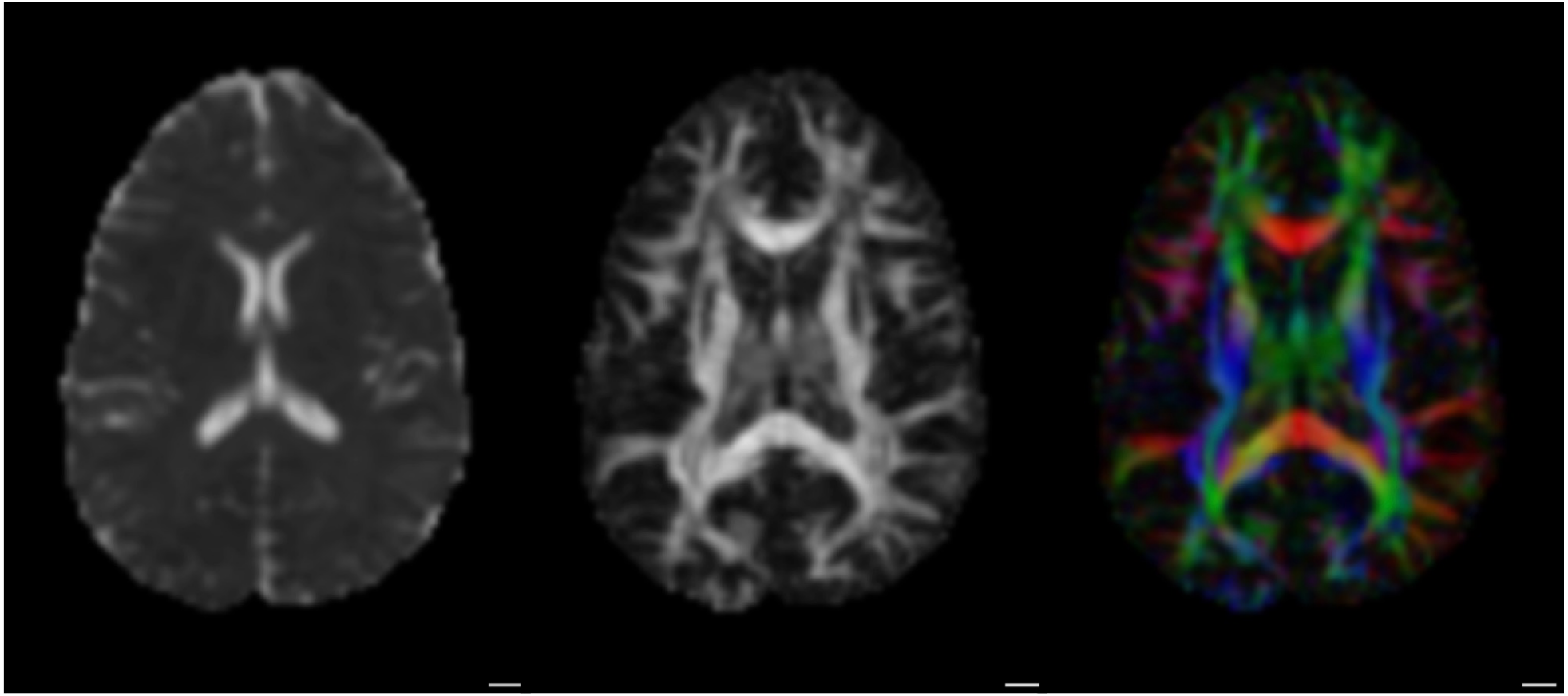
https://en.wikipedia.org/wiki/Axon

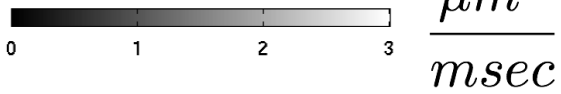
Diffusion-derived tissue properties

Mean diffusivity

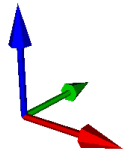
Fractional anisotropy

Principal diffusion direction





$$\frac{\mu m^2}{msec}$$



Basser et al. (1994), Basser and Pierpaoli (1996)

Adult Changes in Thought (ACT) Neuroimaging Dataset

- The ACT study conducts research with aging adults to understand factors that contribute to Alzheimer's Disease and related dementia

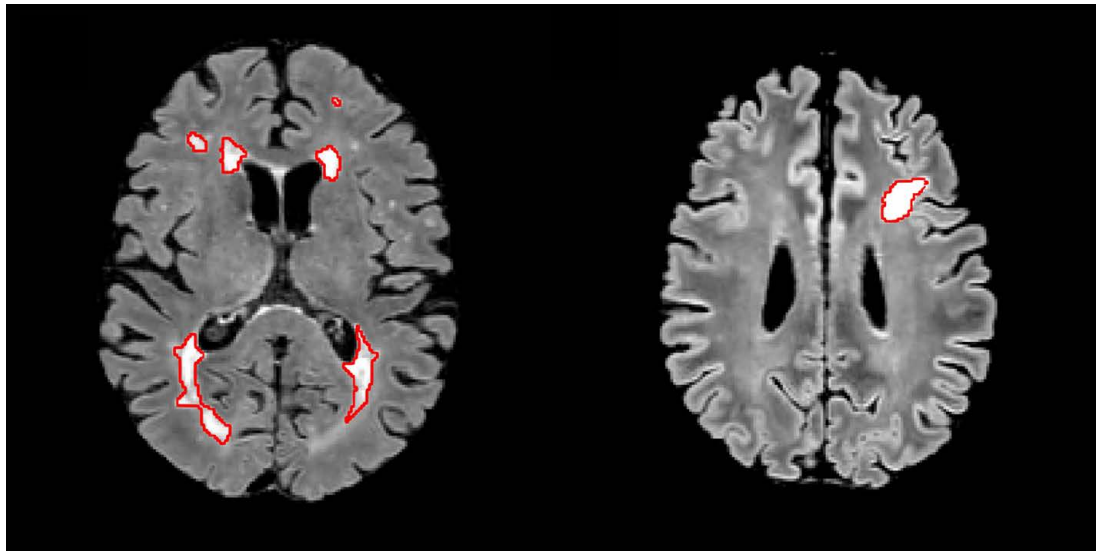
- FLAIR and multi-shell, high angular resolution diffusion MRI (dMRI) images were collected from 282 participants

- **Goal**: Use diffusion modeling to characterize the underlying biophysical properties of FLAIR white matter hyperintensities

Kukull et al. (2002)

FLAIR processing

- A deep learning convolutional neural network, HyperMapp3r, was used to segment FLAIR WMH regions of interest (Forooshani et al., 2022) and classified as either periventricular or deep.
- FLAIR values were standardized within each participant's white matter volume and registered to their diffusion images.



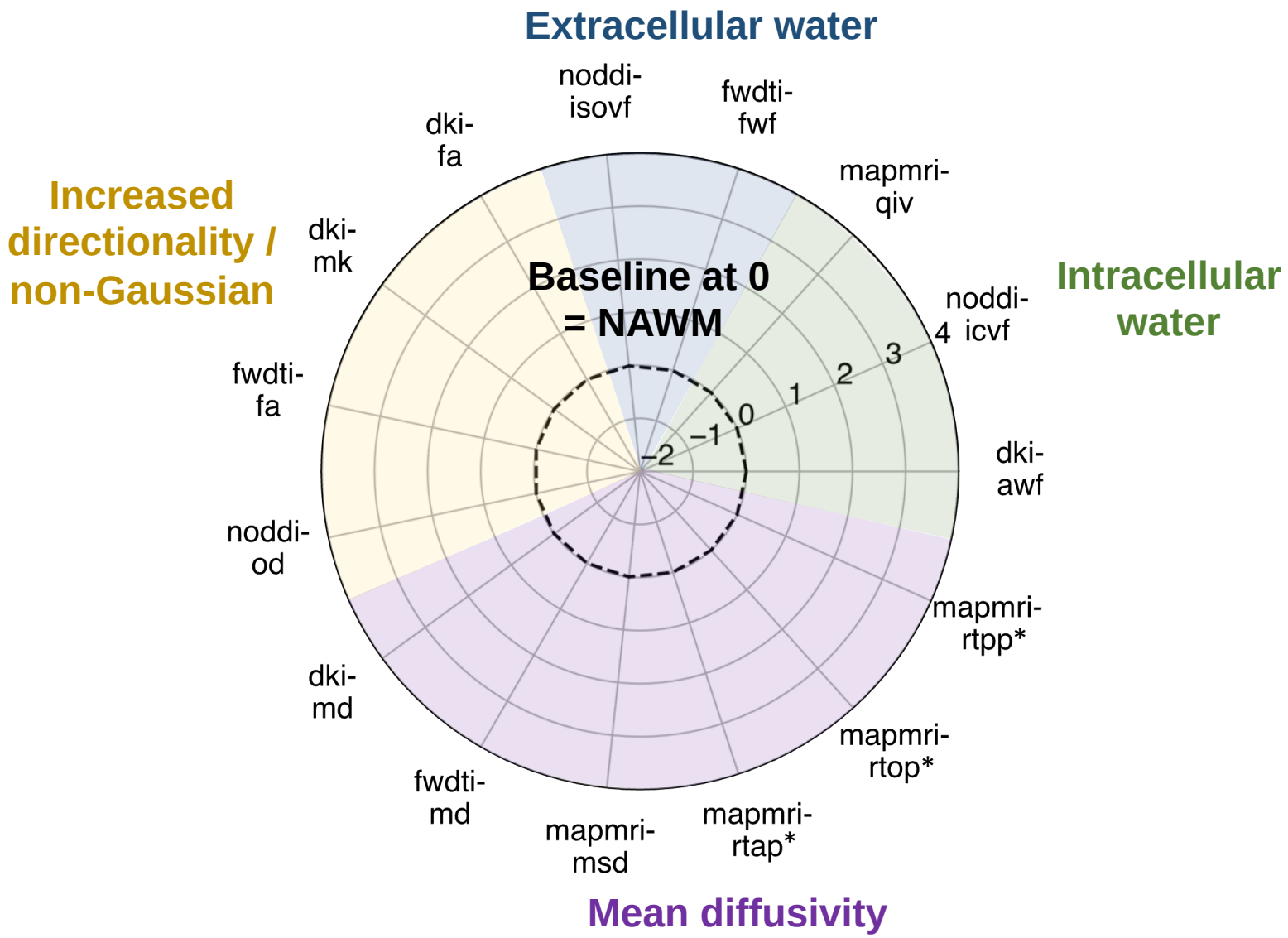
Periventricular WMH

Deep WMH

Diffusion MRI (dMRI) Models and Metrics

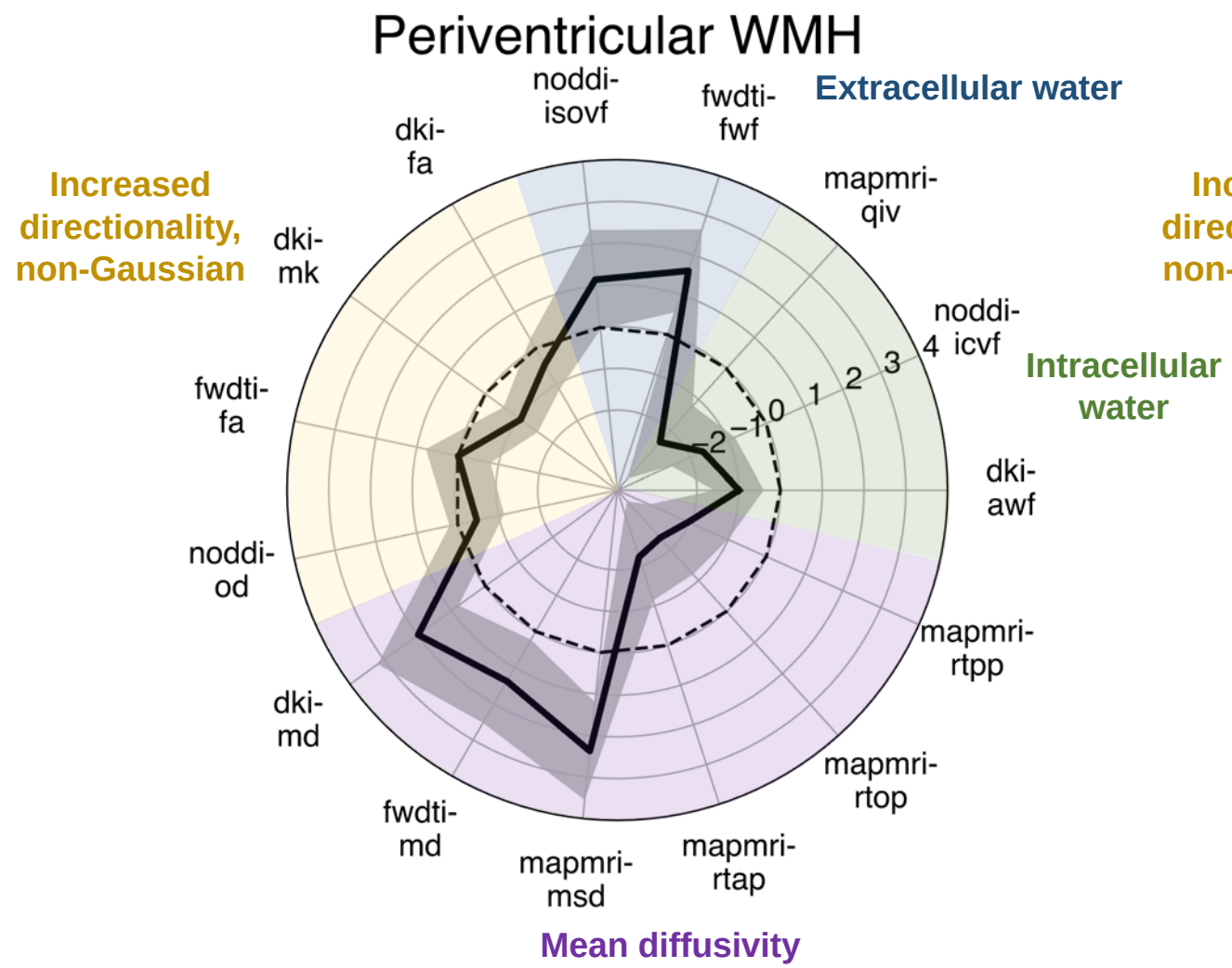
- Diffusional kurtosis imaging (DKI) and its White Matter Tract Integrity model extension (Fieremans et al., 2011)
  - Axonal water fraction (AWF), fractional anisotropy (FA), mean diffusivity (MD), mean kurtosis (MK)
- Free-water diffusion tensor imaging (FWDTI) model (Hoy et al., 2014)
  - FA, free-water fraction (FWF), MD
- Mean apparent propagator MRI (MAPMRI) model (Ozarslan et al., 2013)
  - Mean square displacement (MSD), Q-space inverse variance (QIV), return-to-axis/origin/plane probability (RTAP, RTOP, RTPP)
- Neurite orientation dispersion and density imaging (NODDI) model (Zhang et al., 2012)
  - Intra-cellular volume fraction (ICVF), isotropic volume fraction (ISOVF), orientation dispersion (OD)

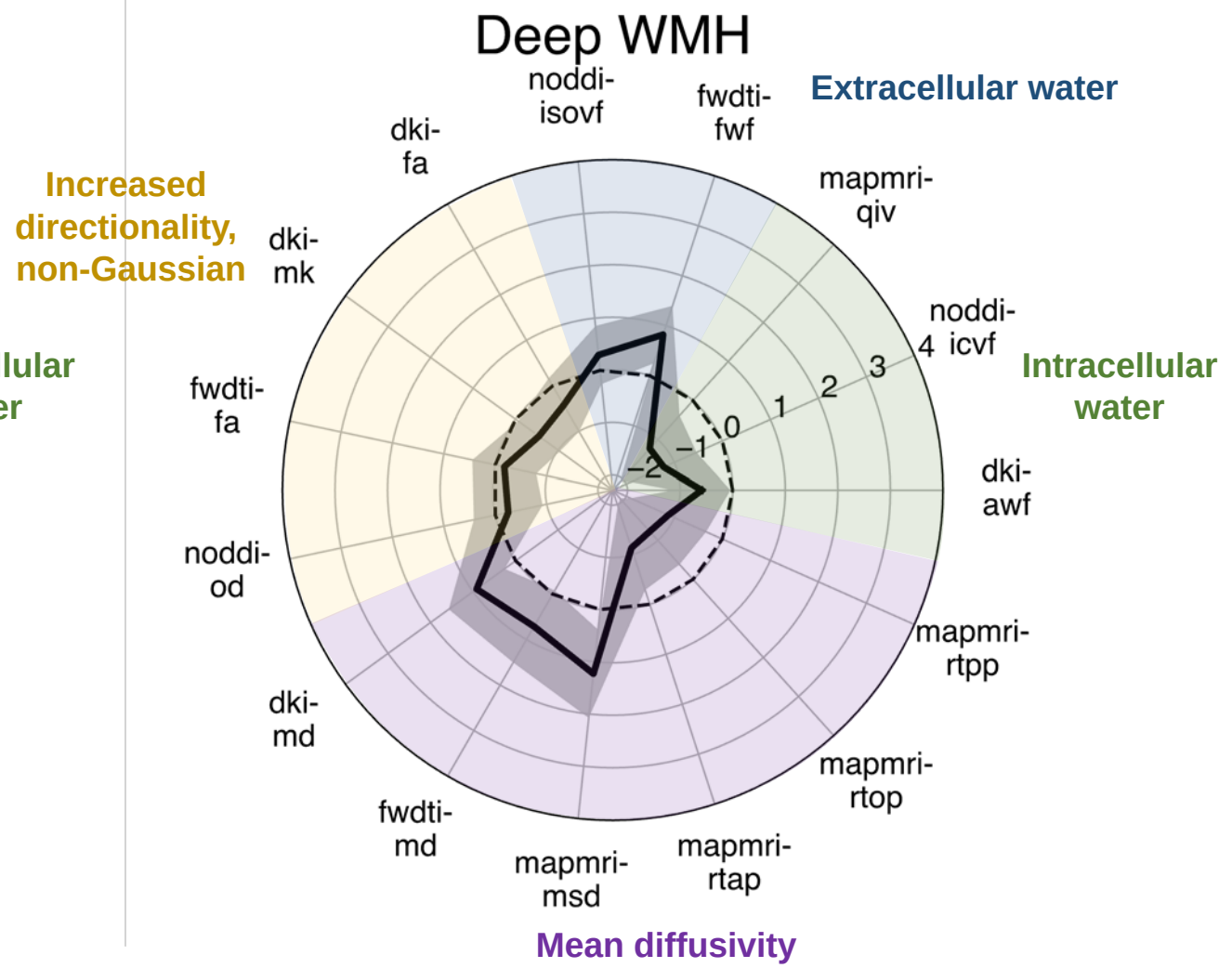
Diffusion MRI (dMRI) Models and Metrics



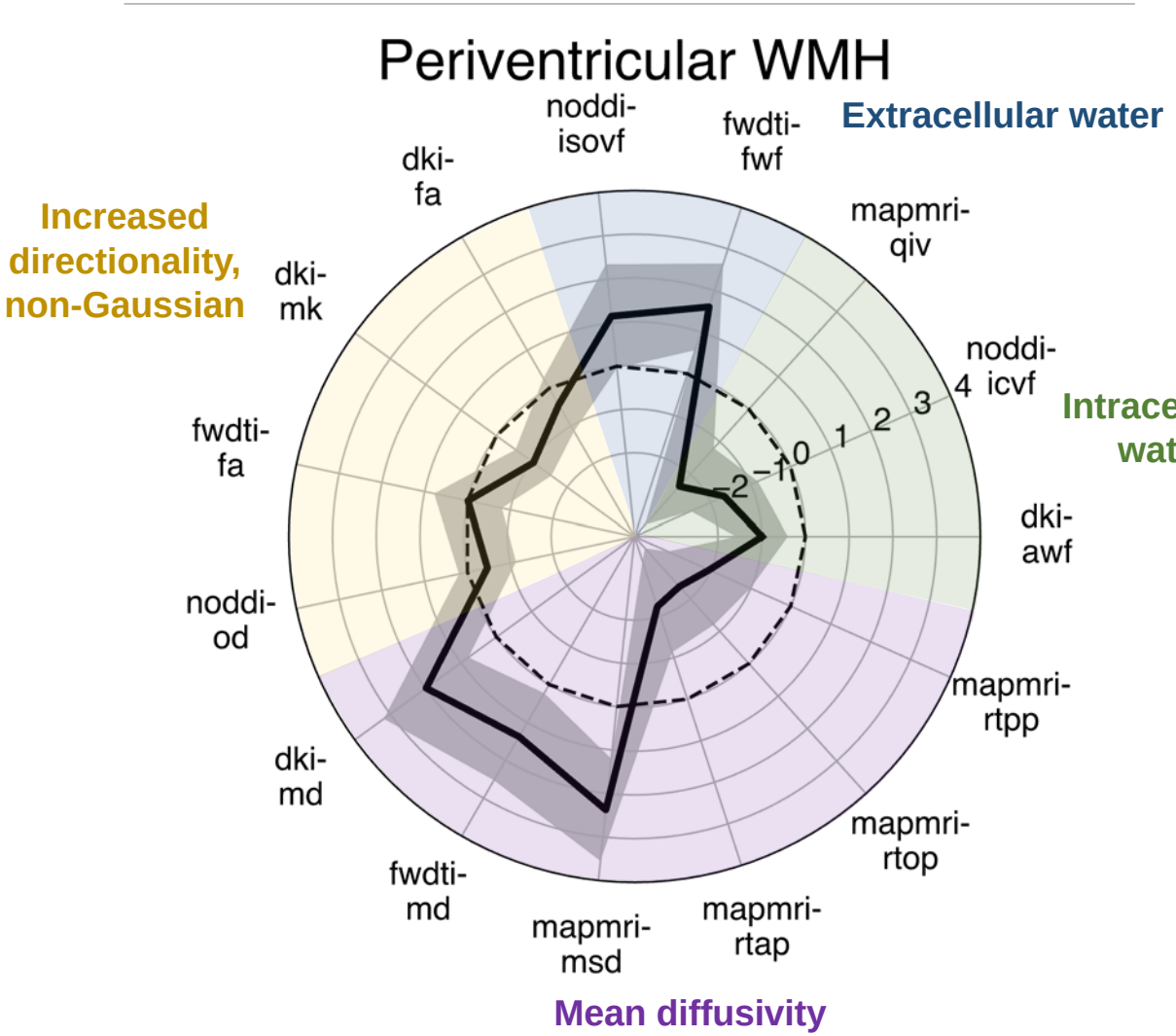
* Inverse relationship

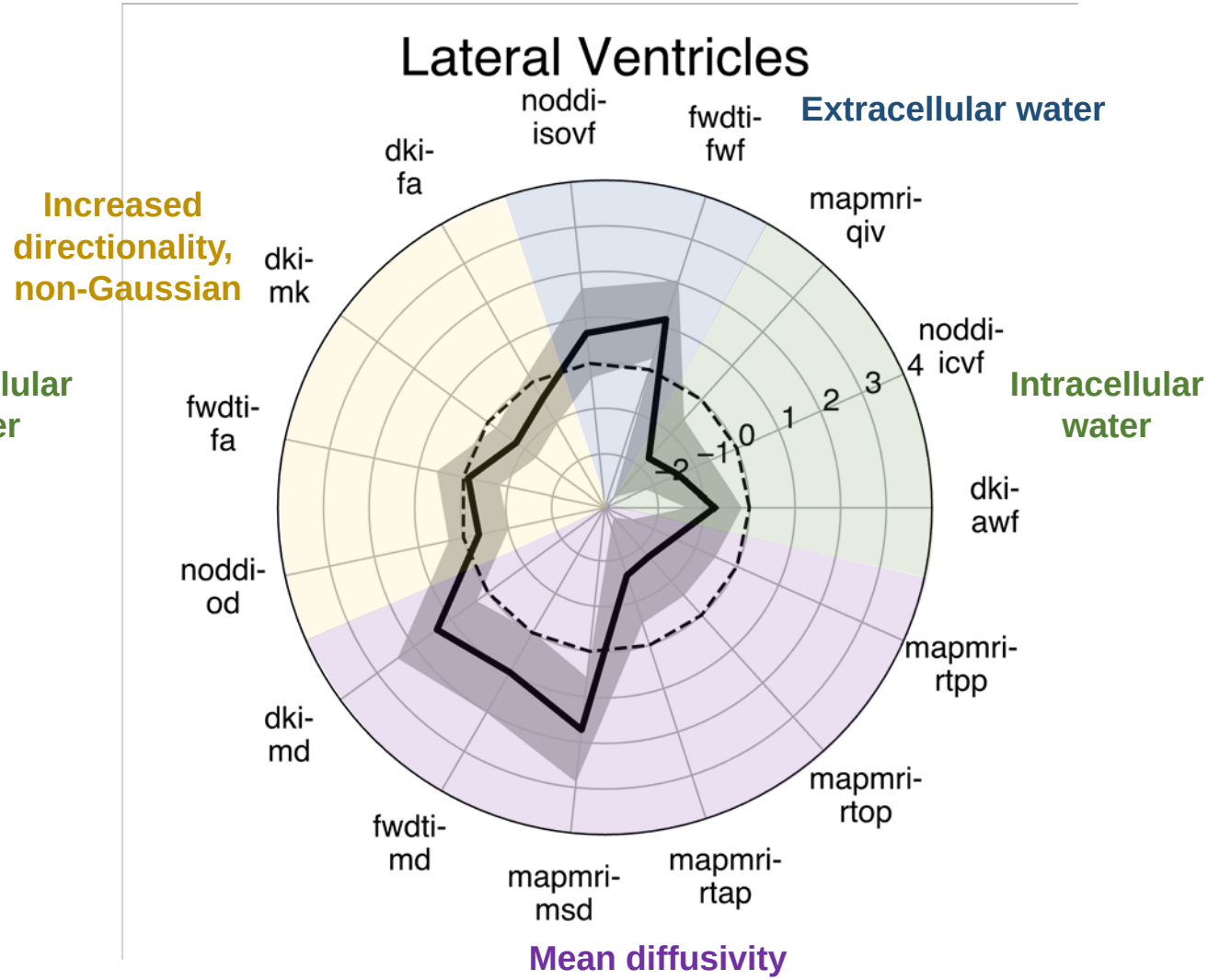
WMHs are characterized by increased mean diffusivity and extracellular water, especially in periventricular WMH



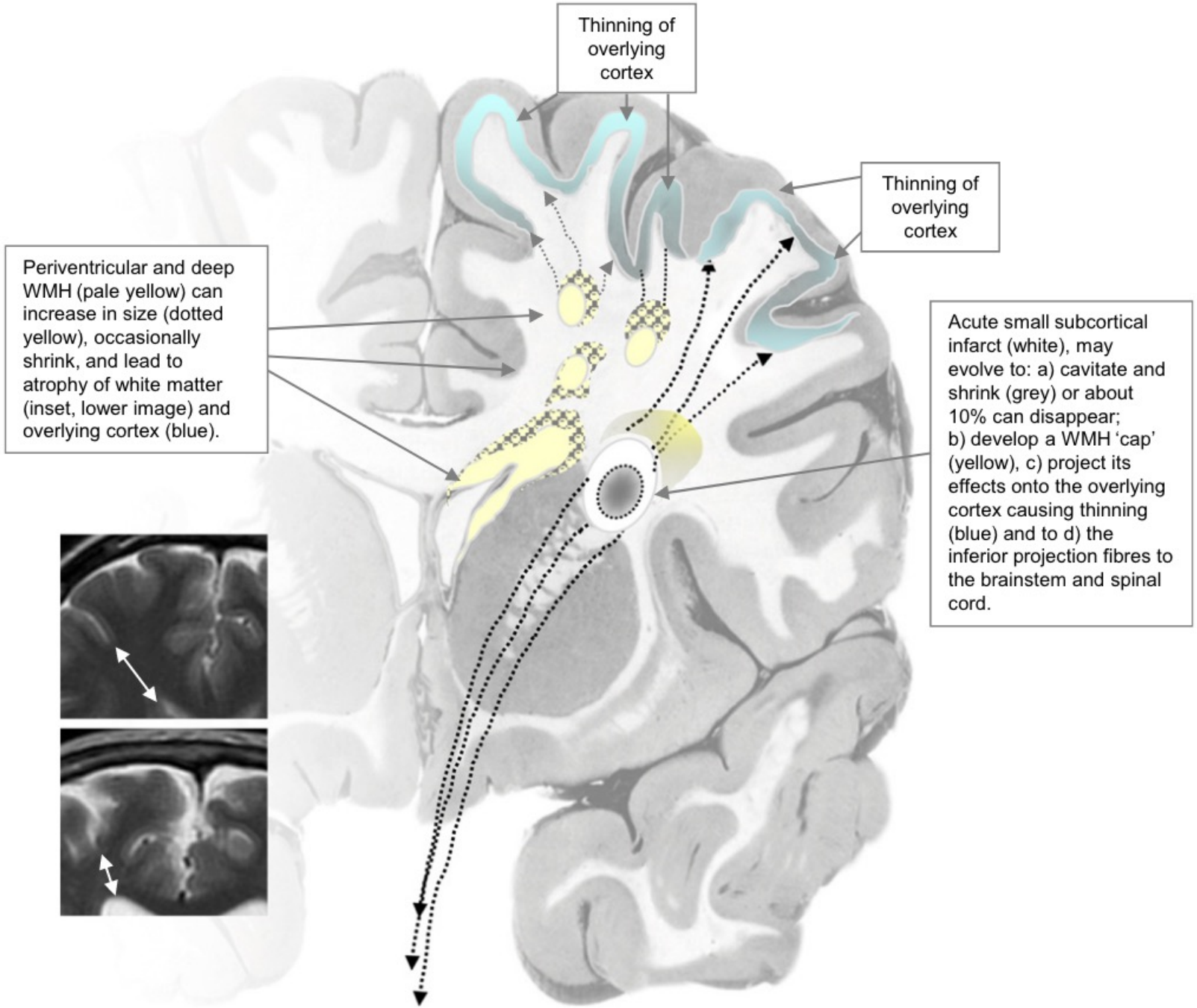


Periventricular WMH's dMRI metric pattern resembles those of the lateral ventricles



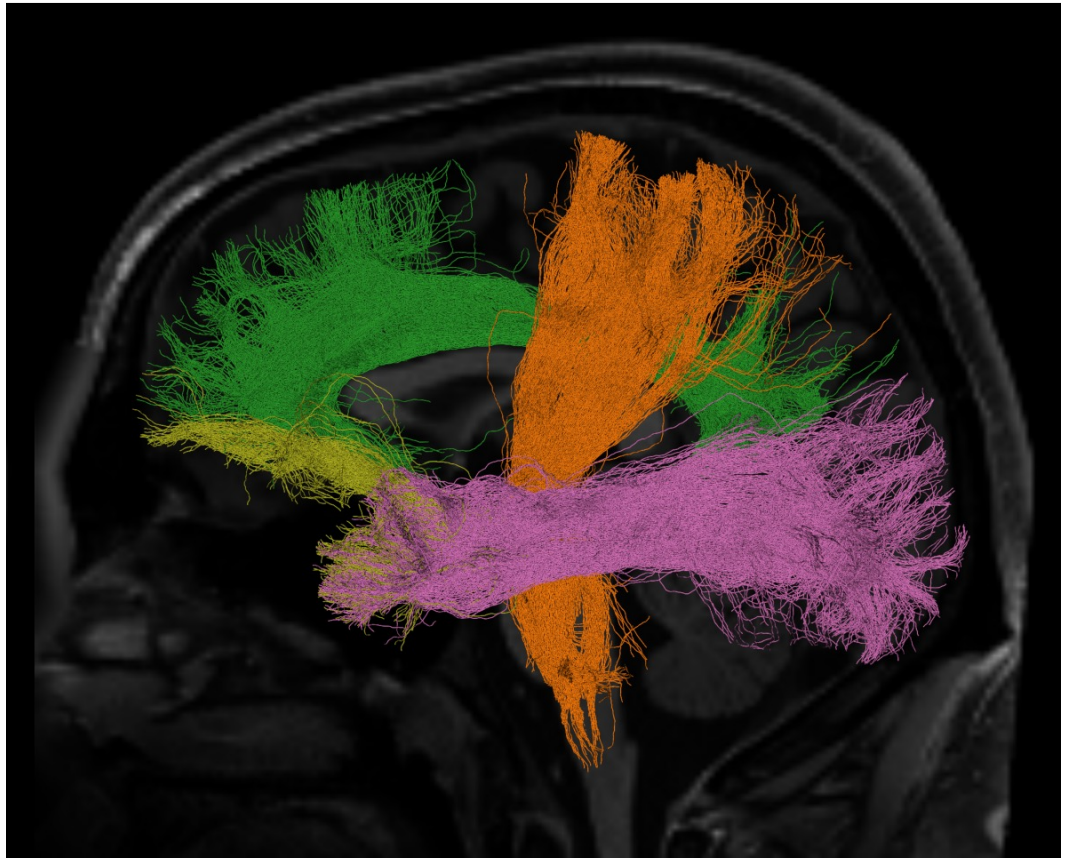


dMRI patterns are suggestive of different progression stages or underlying mechanisms that cause periventricular and deep WMH to arise



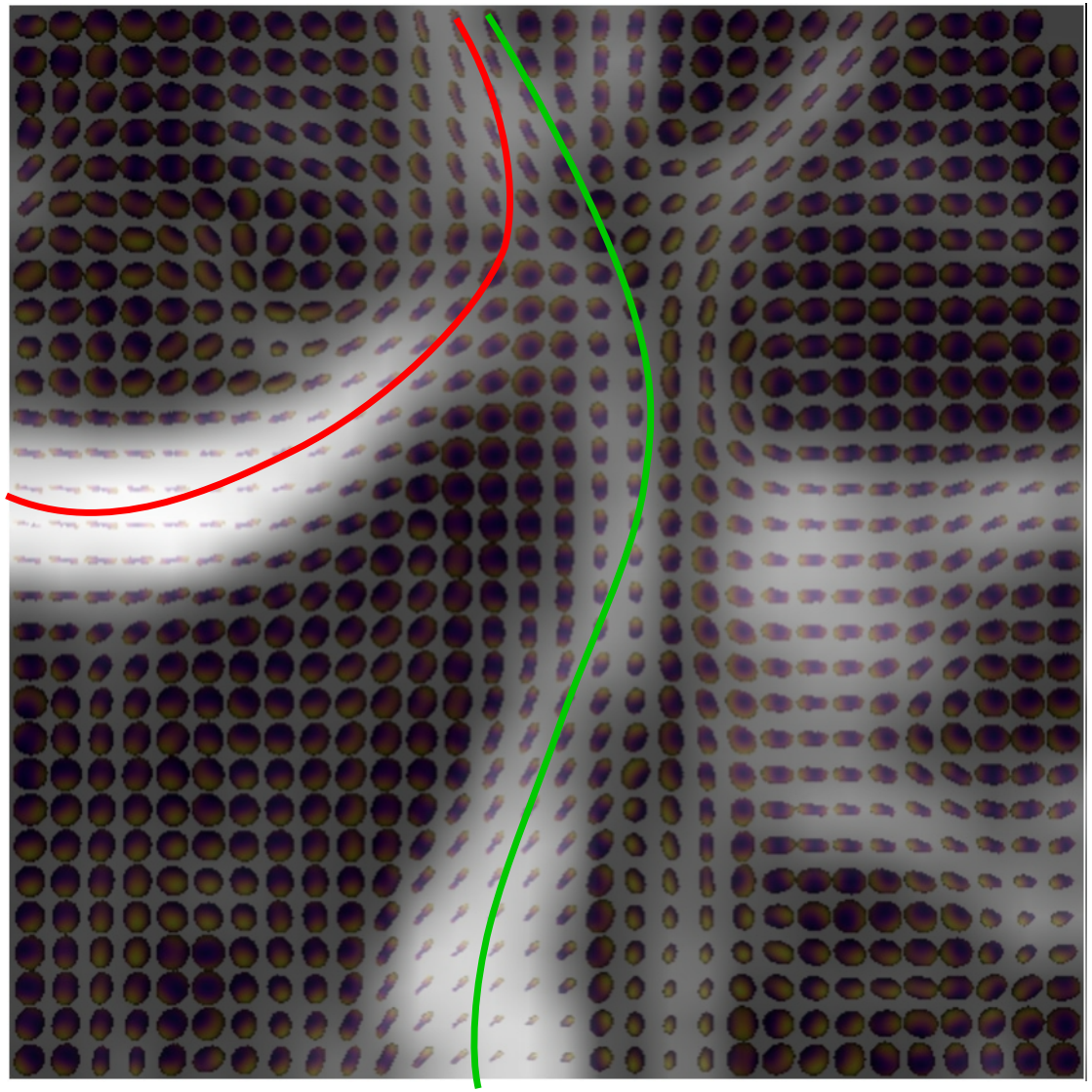
Wardlaw et al. (2015)

White matter can be spatially localized and segmented into known tracts



Kruper et al. (2024; in prep)

Computational tract-tracing (tractography)



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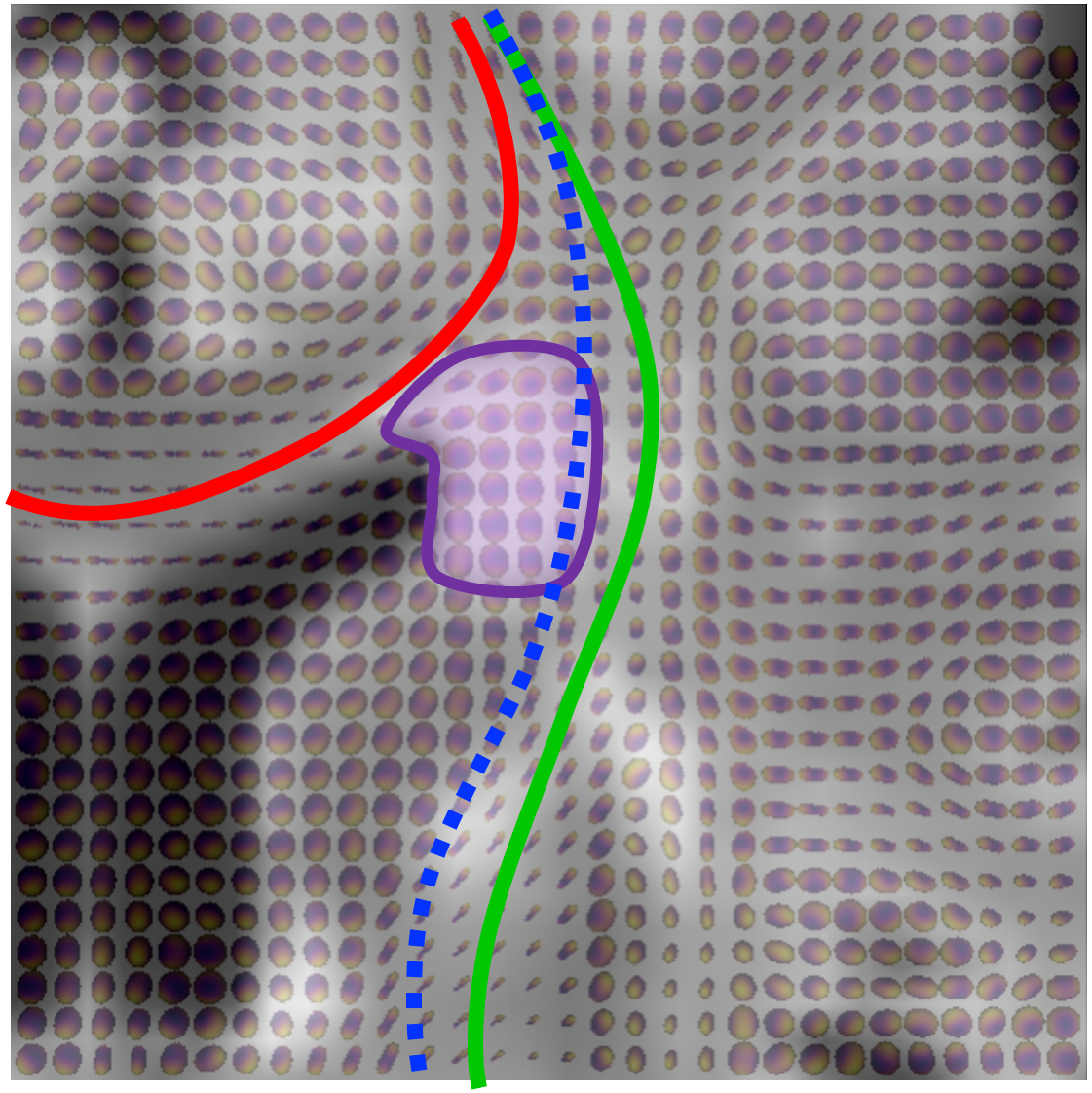
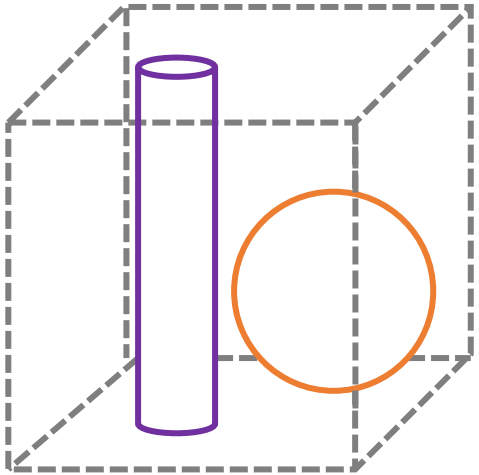


Free-water elimination (FWE) removes the free-water contamination from the diffusion signal

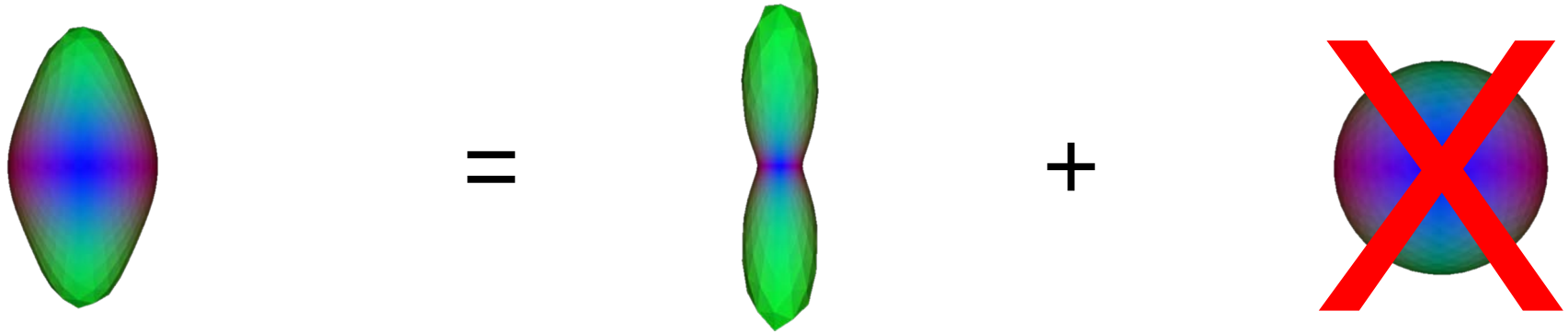


Suppose the measured **diffusion signal** can be split into two compartments:

1. Diffusion tensor compartment
2. Free-water compartment

Hoy et al. (2014)

Free-water elimination (FWE) removes the free-water contamination from the diffusion signal



Diffusion Tensor Compartment

Free-water Compartment

Suppose the measured **diffusion signal** can be split into two compartments:

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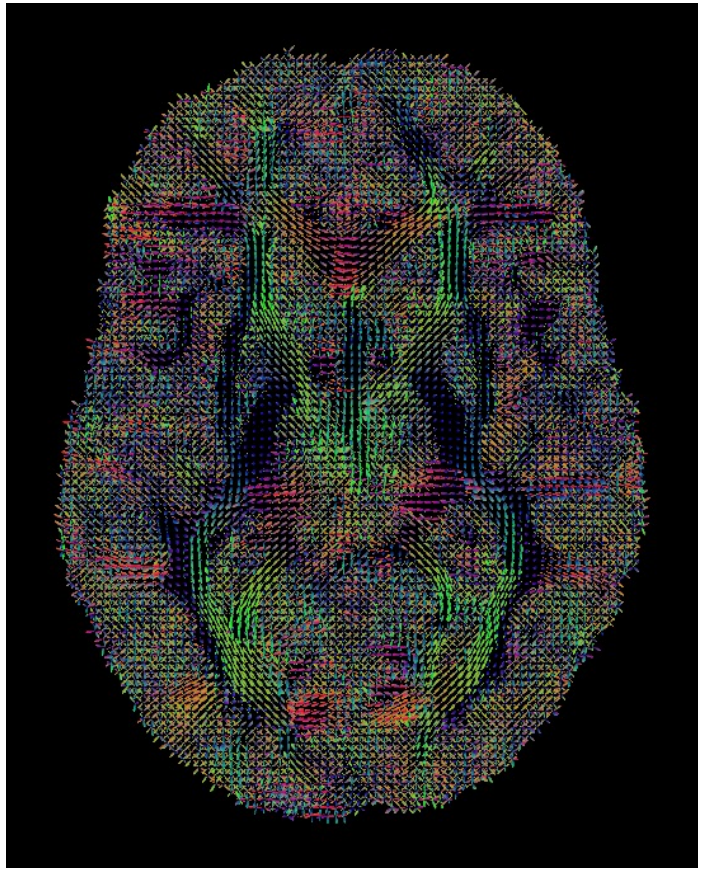
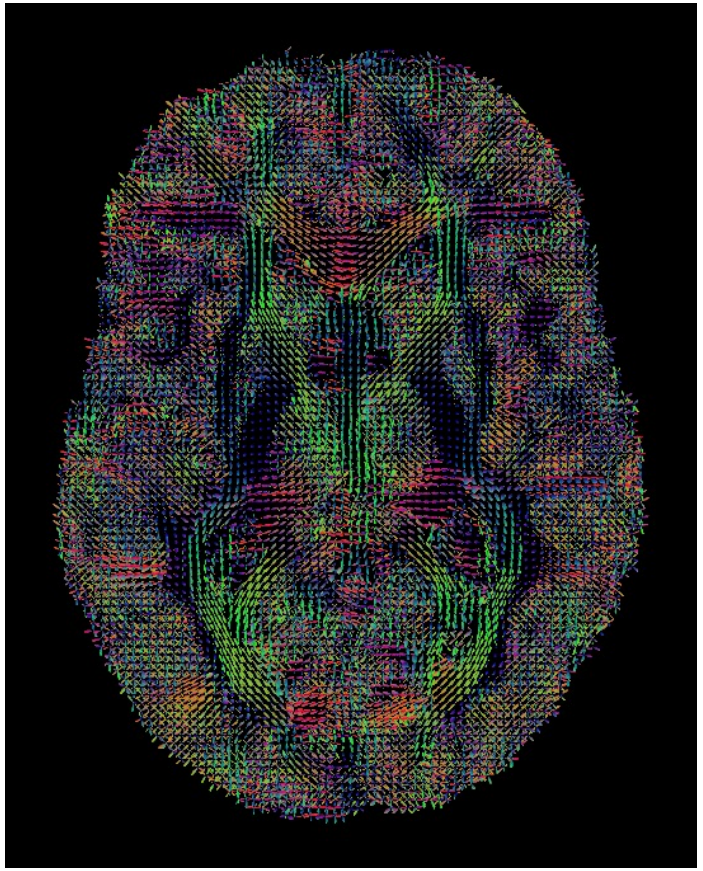
2. Free-water compartment

Hoy et al. (2014)

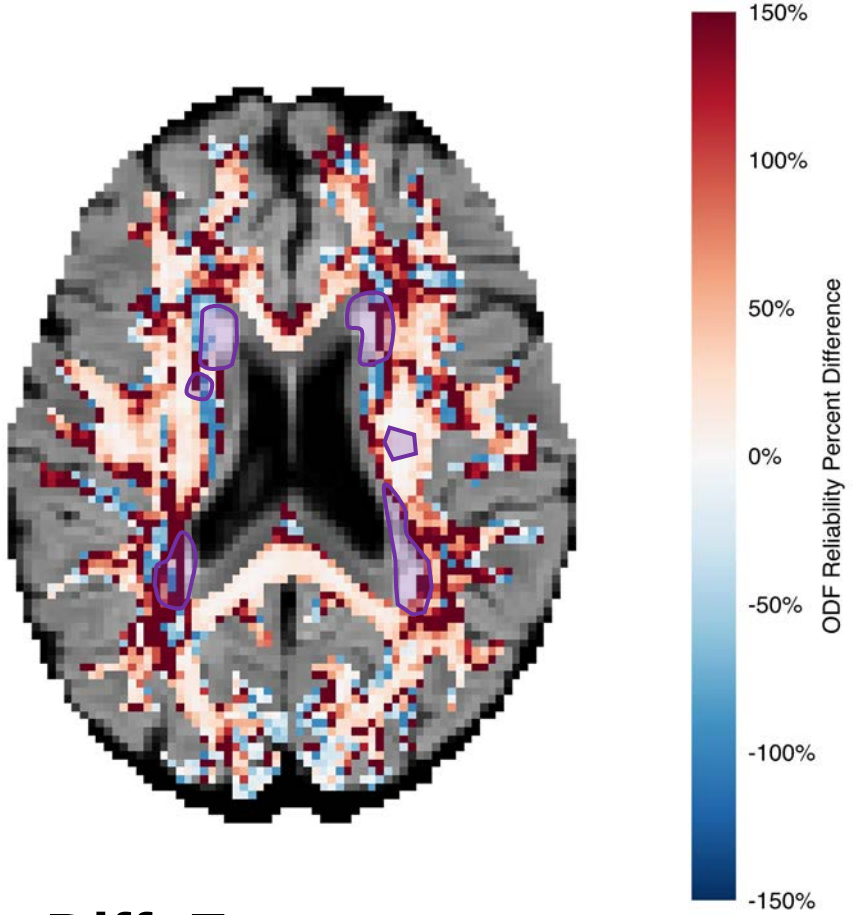
FWE produced more reliable orientation distribution functions (ODFs), especially in WMH regions



Original

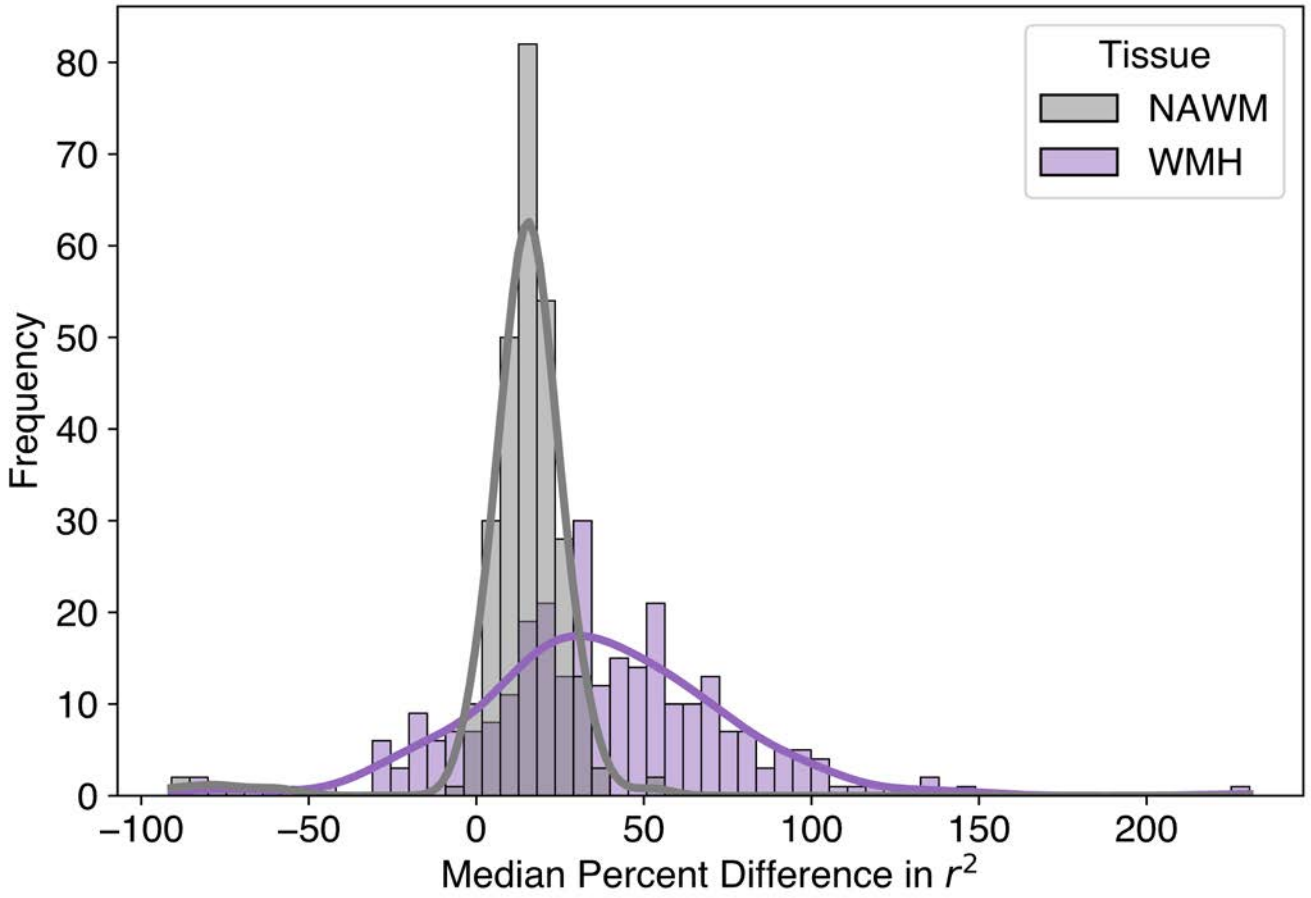


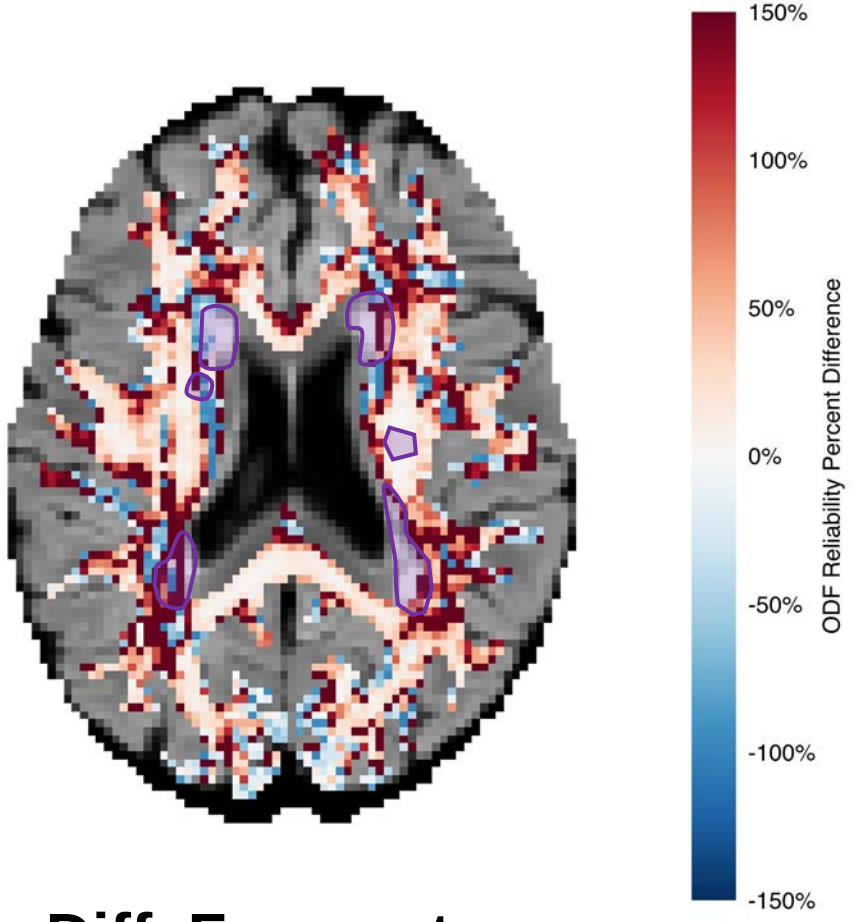
Free-water Eliminated (FWE)



Diff. Free-water – Original Reliability

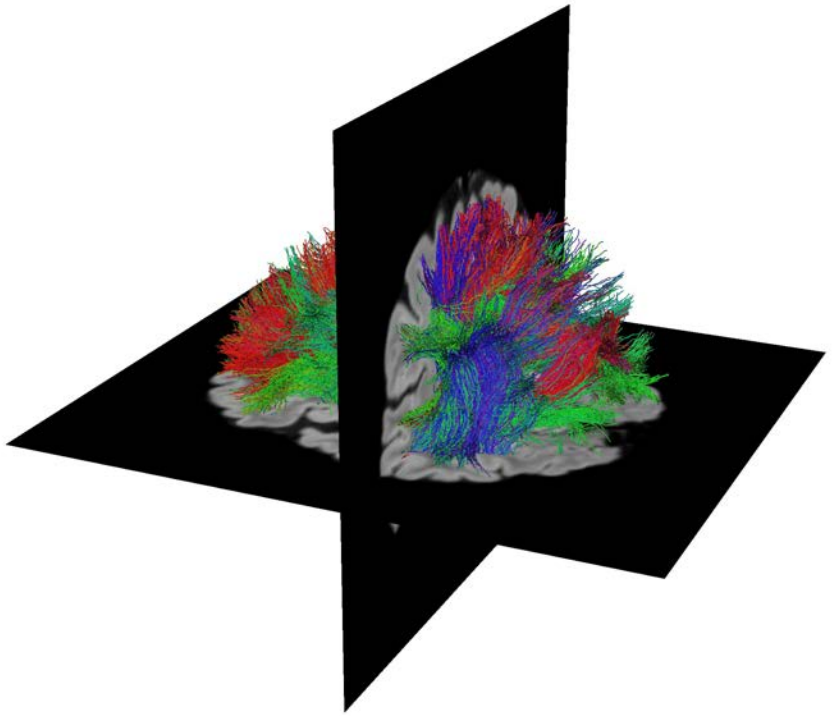
FWE produced more reliable orientation distribution functions (ODFs), especially in WMH regions





Diff. Free-water – Original Reliability

Tractometry produced from the original and FWE diffusion signal (Whole brain)



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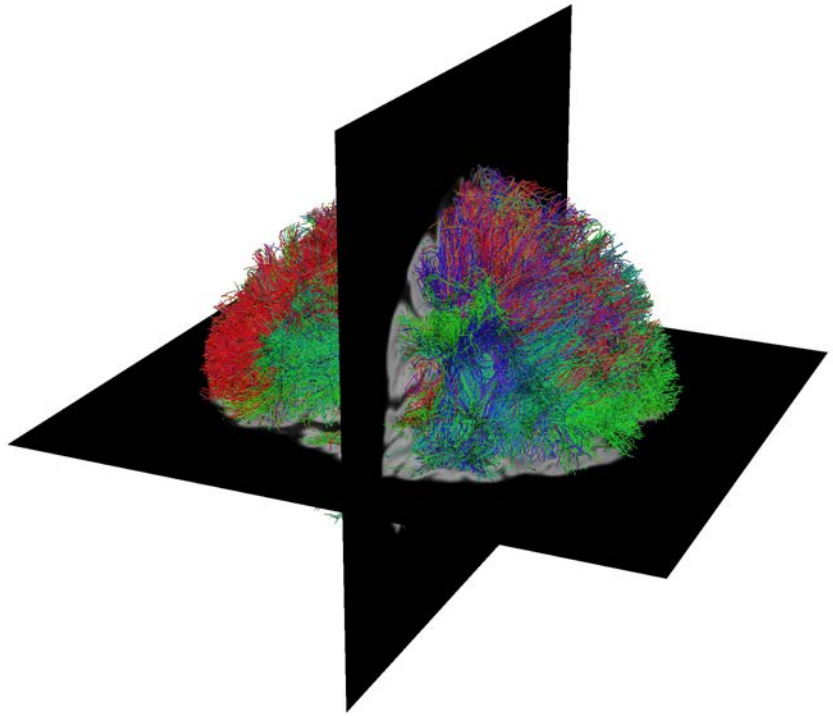
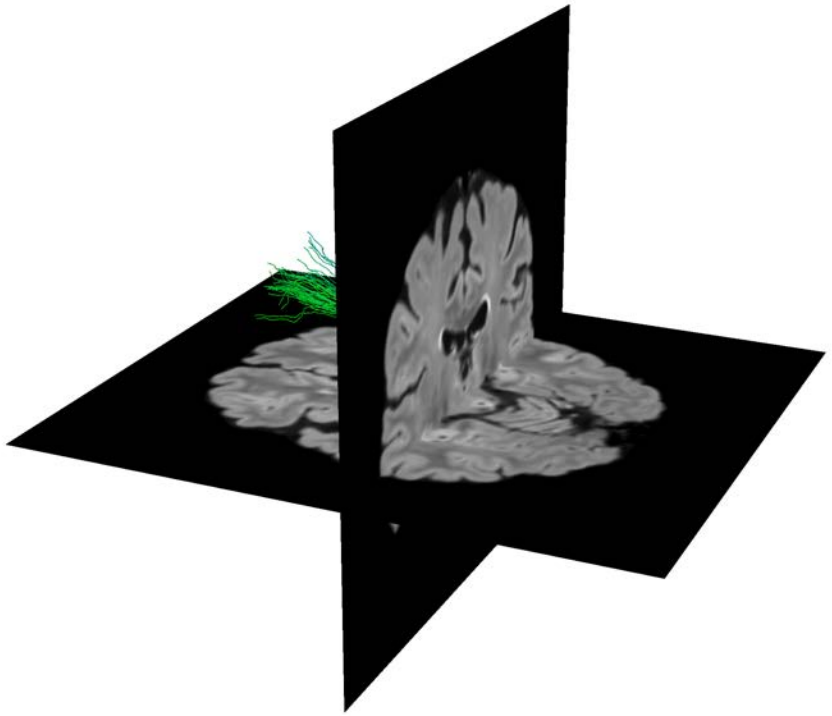


Free-water Eliminated (FWE)

Tractometry algorithm (Kruper et al., 2021)

Tractometry produced from the original and FWE diffusion signal (Right Anterior Thalamic Radiation)



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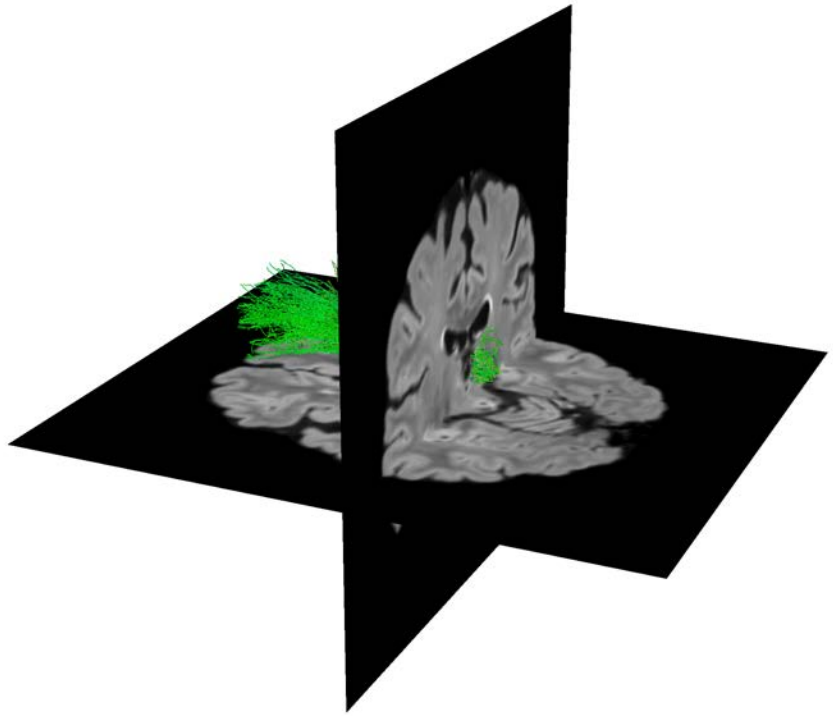
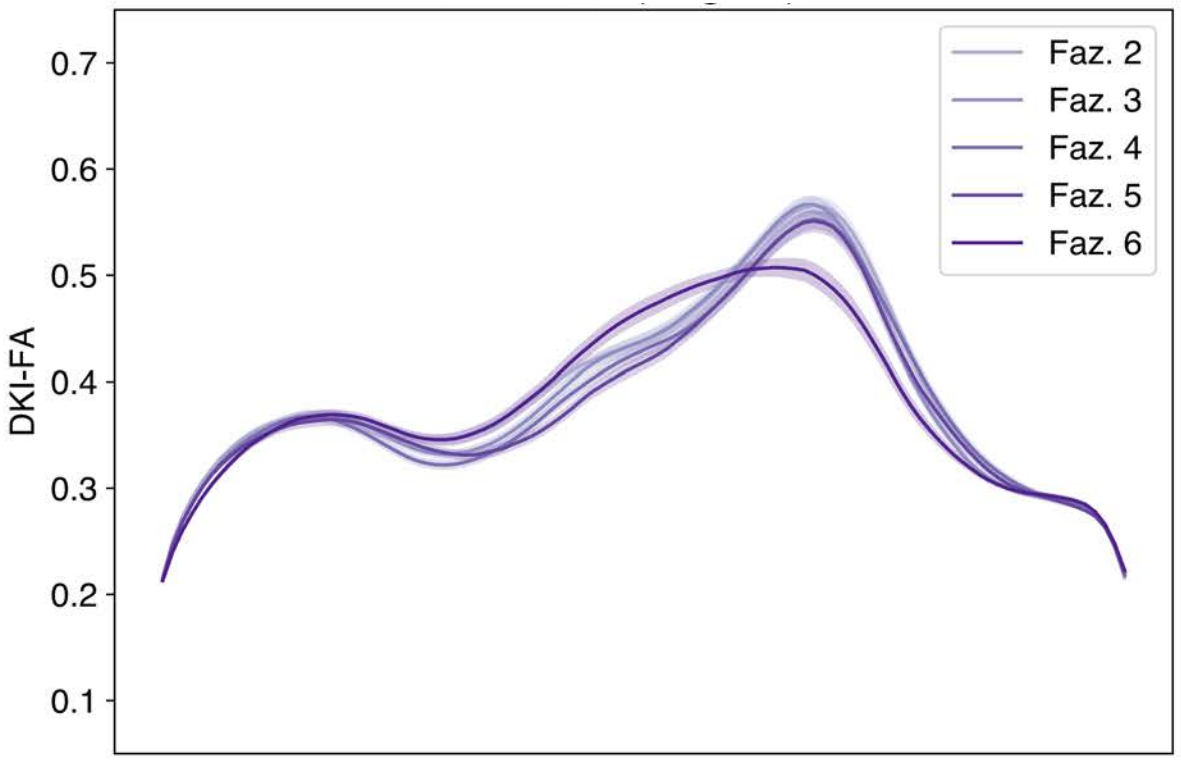


Free-water Eliminated (FWE)

Tractometry algorithm (Kruper et al., 2021)

FWE tract profiles better represent Fazekas scores (Right Anterior Thalamic Radiation)



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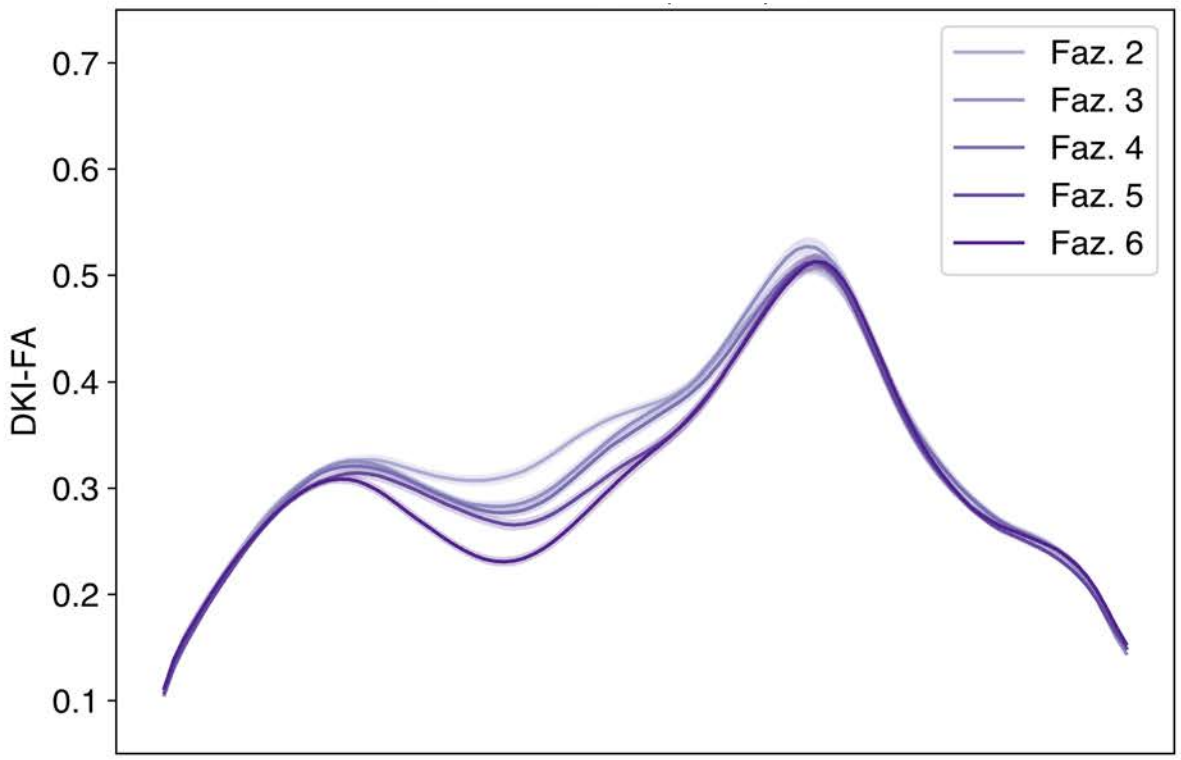
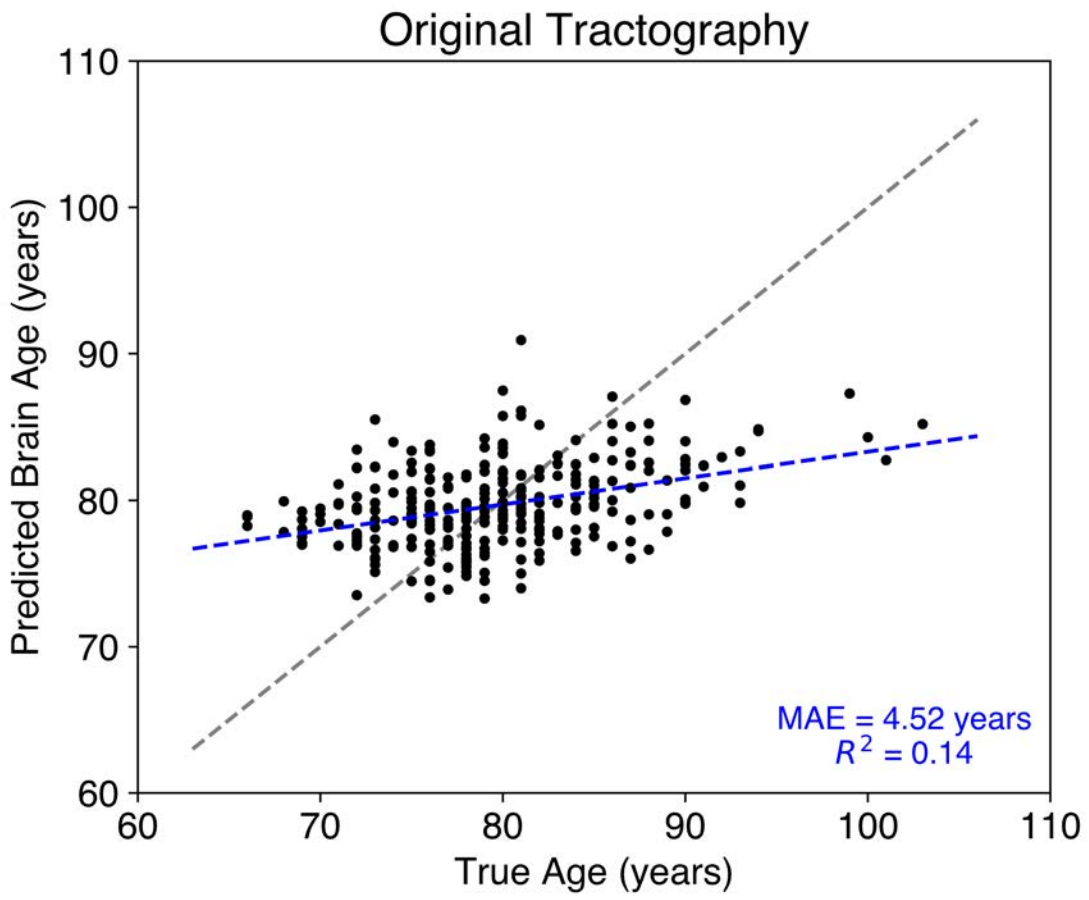
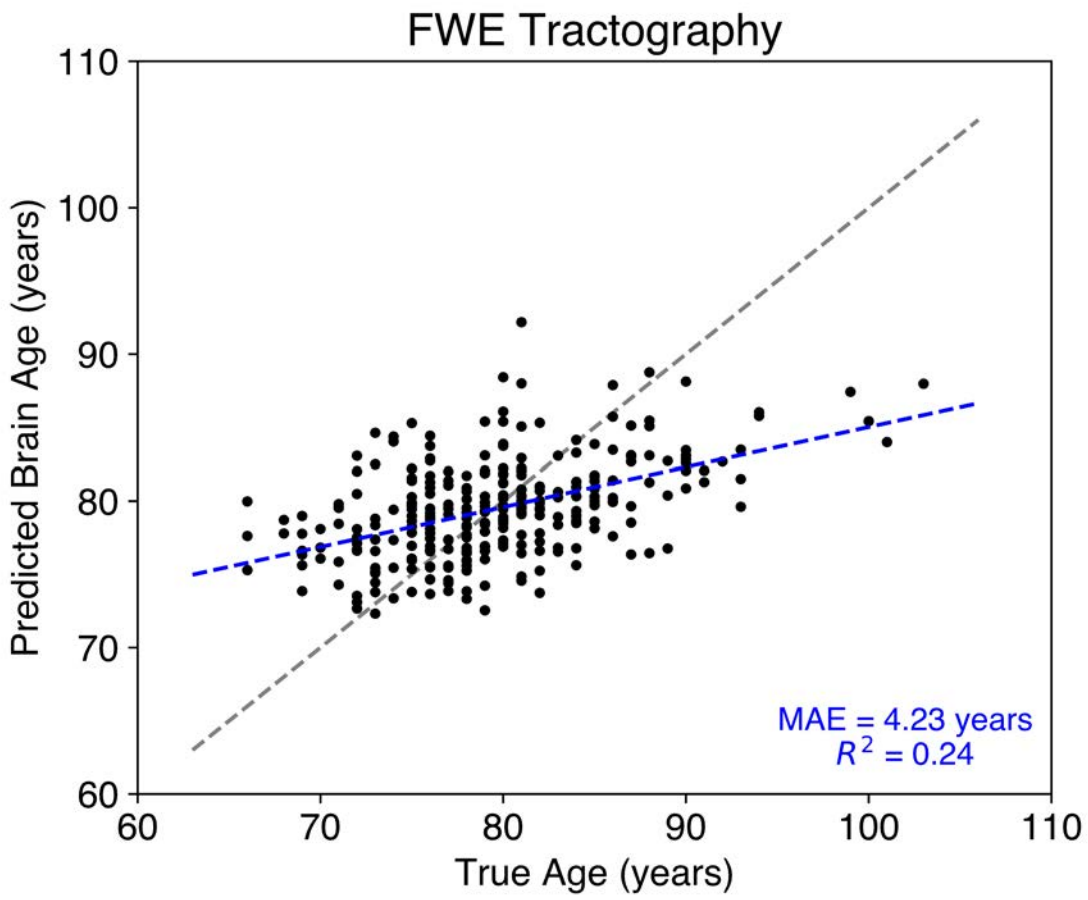


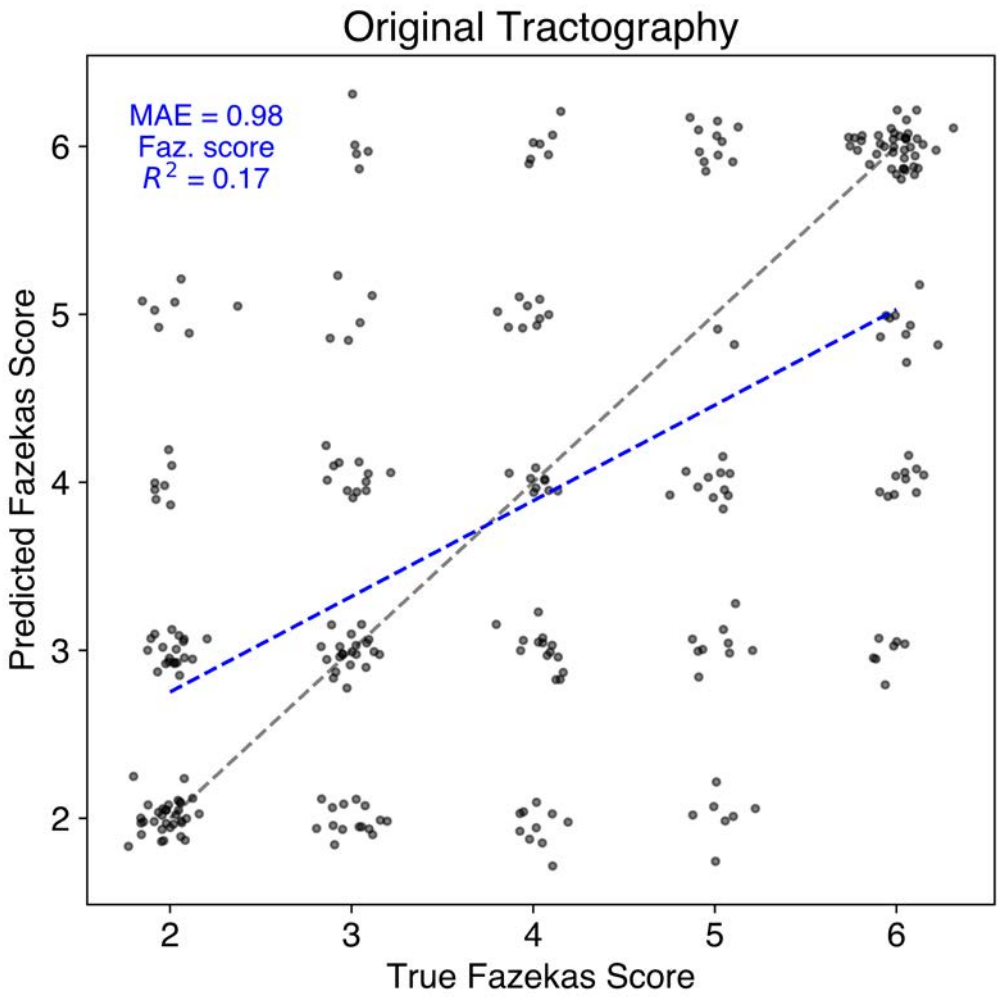
Free-water Eliminated (FWE)

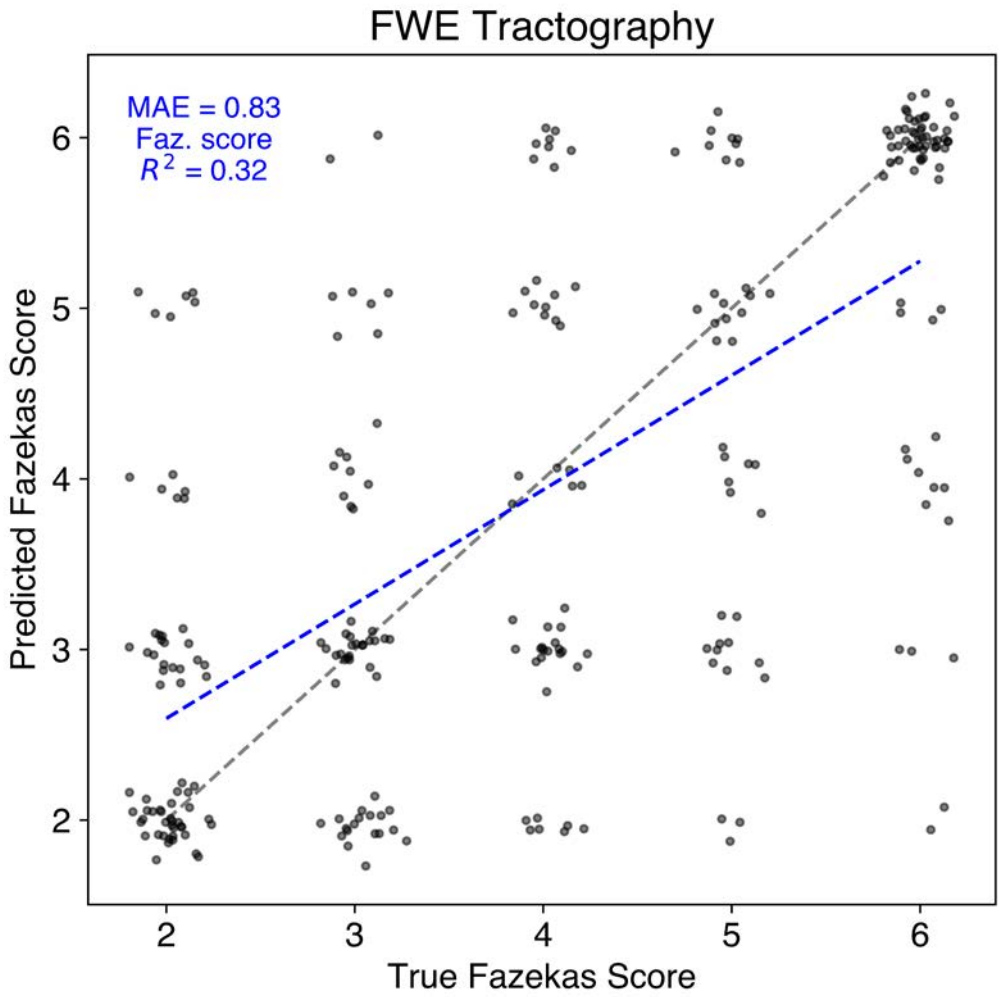
FWE improves brain age predictions from tract profiles





FWE improves Fazekas score predictions from tract profiles





Conclusions

- WMH are characterized by increased mean diffusivity and extracellular water content.

- The patterns observed indicate that periventricular and deep WMH tissue begins to resemble ventricles more than NAWM, particularly in the case of periventricular WMH.

- FWE improves tractometry at each stage (ODF and tract reliability), especially in WMH regions.

- FWE tract profiles predicted brain age and Fazekas scores more accurately than the tract profiles produced without free-water elimination.

Thank you!

Principal Investigators

Ariel Rokem

Christine Mac Donald

Acknowledgments

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