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Validated Sex-Specific Brain Models Reveal Structural Differences and Distinct Strain Responses in Traumatic Brain Injury

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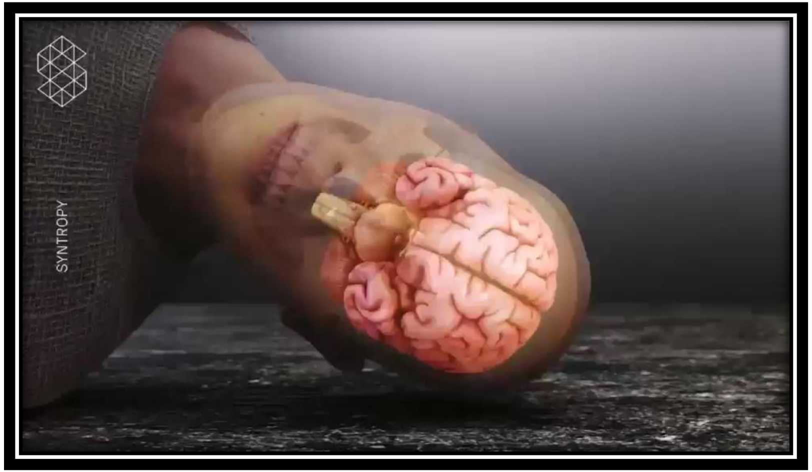
Disclosure

Marzieh Memar has no conflicts to report. Marzieh Memar has no relevant, real, or apparent personal or professional financial relationships with proprietary entities that produce healthcare goods and services.

Background

- TBI is a major public health burden with
- ~50millions cases and ~$400 Billions Cost yearly
- Tissue deformation (axonal & brain) under mechanical loading



Sex Differences

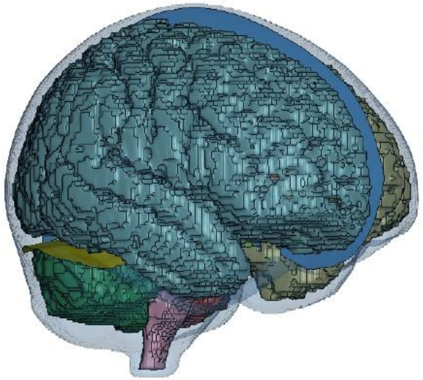
- Higher TBI exposures and incidences in Males
- Higher incidence of TBI in females in female-male comparable settings
- Worse affective outcomes (e.g., anxiety, depression) in females
- More structural damage in some regions reported in females and in some other regions reported in males
- More prolonged symptom in females
- …

Background & Mission

Sex-varied Contributors

- Brain Structure ✓
- Head Kinematics ✓
- Hormonal ✓
- Functional
- Neurochemical

Population level, sex specific brain finite element (FE) models

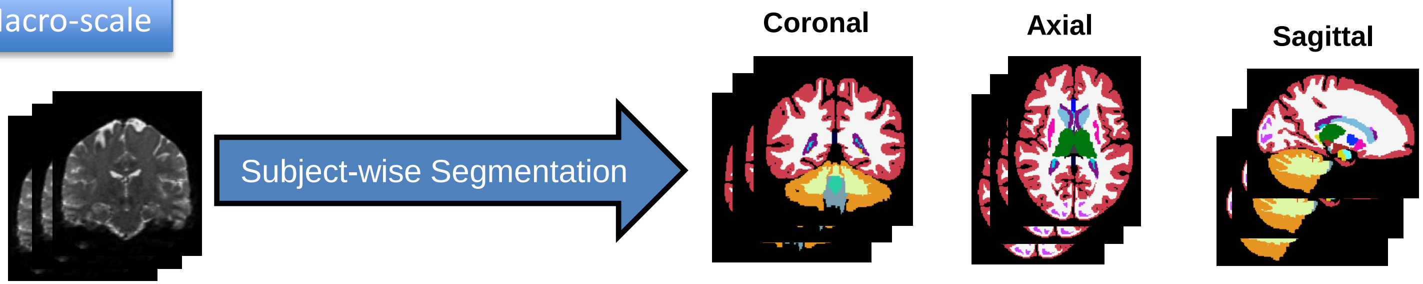


Gaps

- Lack of population level, sex-specific brain imaging templates
- Lack of population level, sex-specific FEMs
- Limited anatomical fidelity in FEMs

Sex-Based Differences in Brain Structure- Macroscale/Anatomical Features

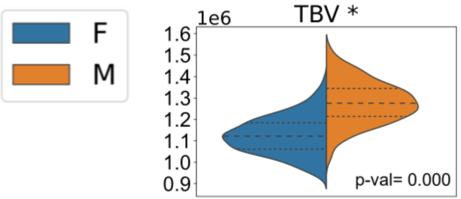
Macro-scale



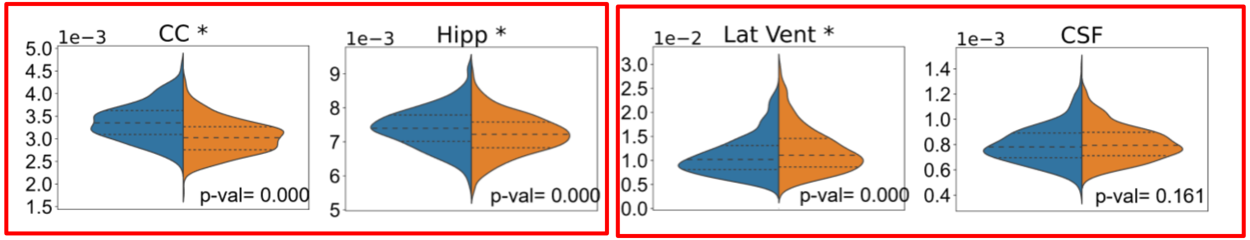
500 female & 500 male T1-MRIs (20-40 year-old)

Overall & Regional Volumes

Steps: Non-Uniform Intensity Correction, Alignment to the Talairach atlas, Skull Stripping, Brain Subcortical Segmentation
Absolute and Fractional Volume Comparison for 40 Regions

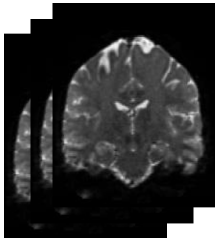


Female > Male **Fractional Regional Volumes** **Male >= Female**



[1] M. Ramzanpour, B. Jafari, J. Smith, J. Allen, **M. Memar**, Brain Multiphysics, 100077, 2023.

Sex-Specific MRI Template Development



500 female & 500 male
T1-MRIs (20-40 year-old)

Template Construction

Nonlinear registration to T_{i-1}

Nonlinear registration to T_0

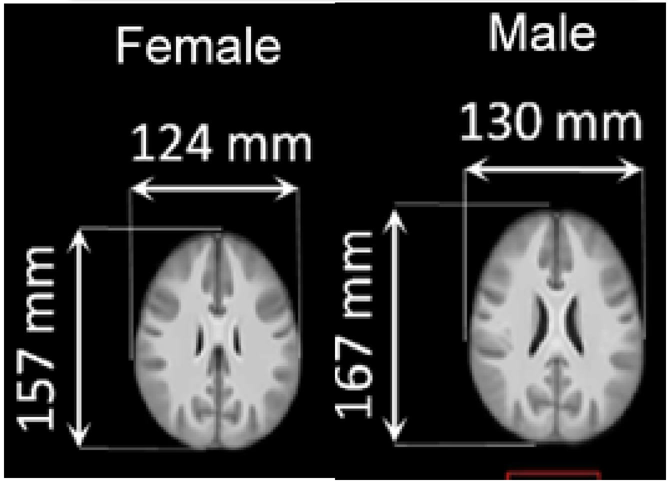
Rigid registration to image 1

T_1 T_1 : T_1

T_0 T_1 T_i

Converged after
4 iterations

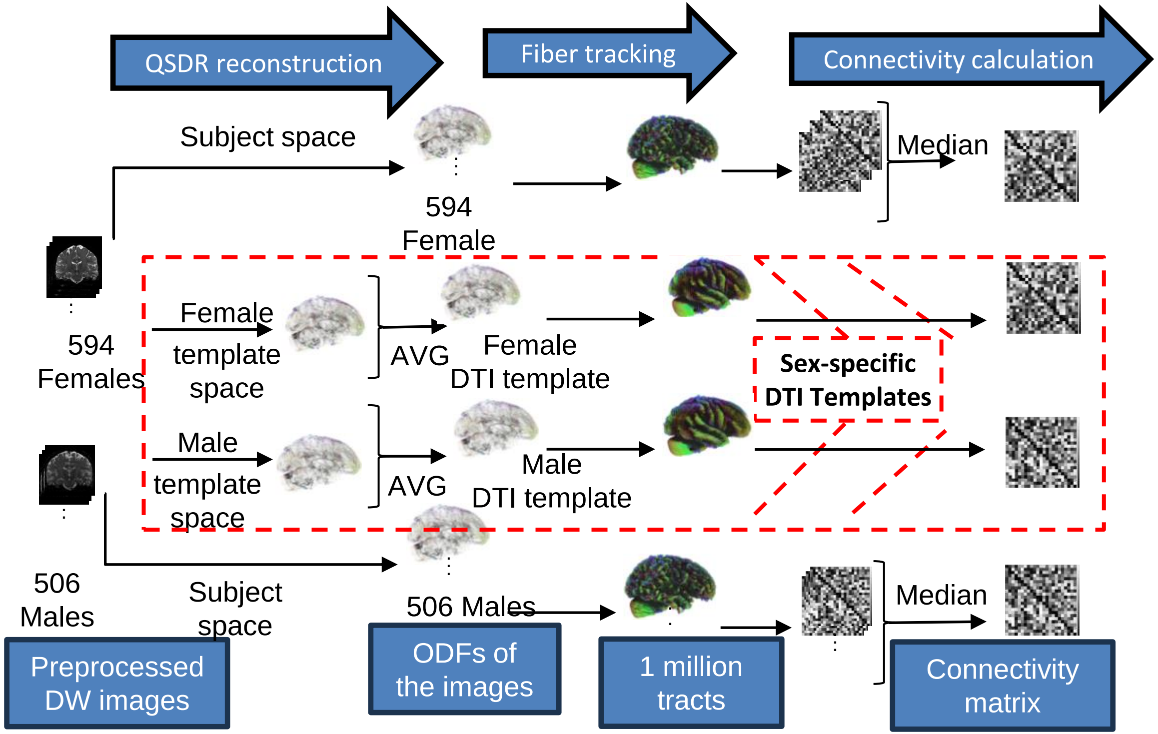
Representativeness

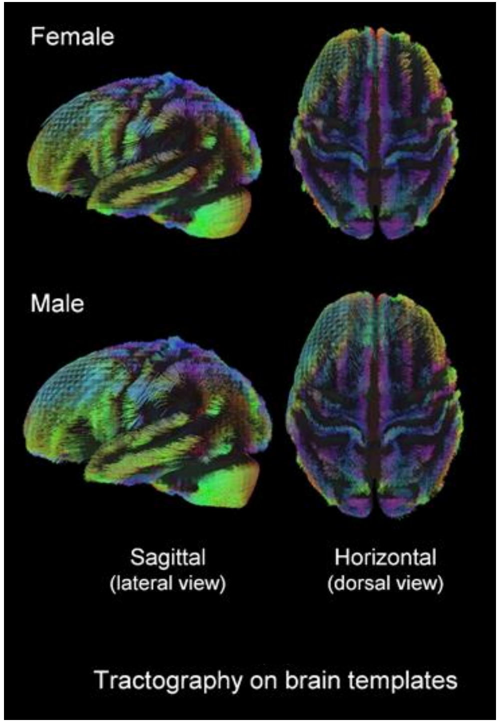


For female & male on average 6-7% regional differences between template and median of population,

[1] M. Ramzanpour, B. Jafari, J. Smith, J. Allen, **M. Memar**, Brain Multiphysics, 100077, 2023.

Methods: Sex-Based Differences in Meso-Scale Brain Structure and DTI Template Development: Tractography & Brain Connectivity

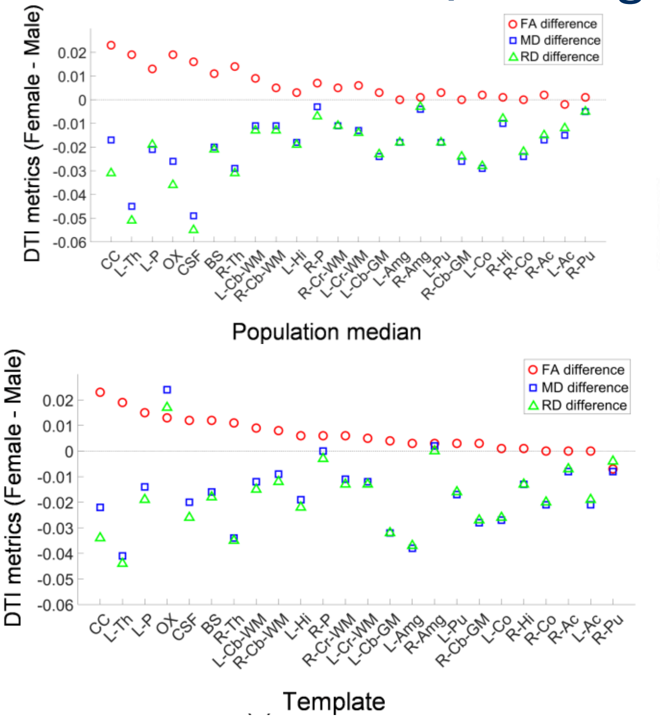




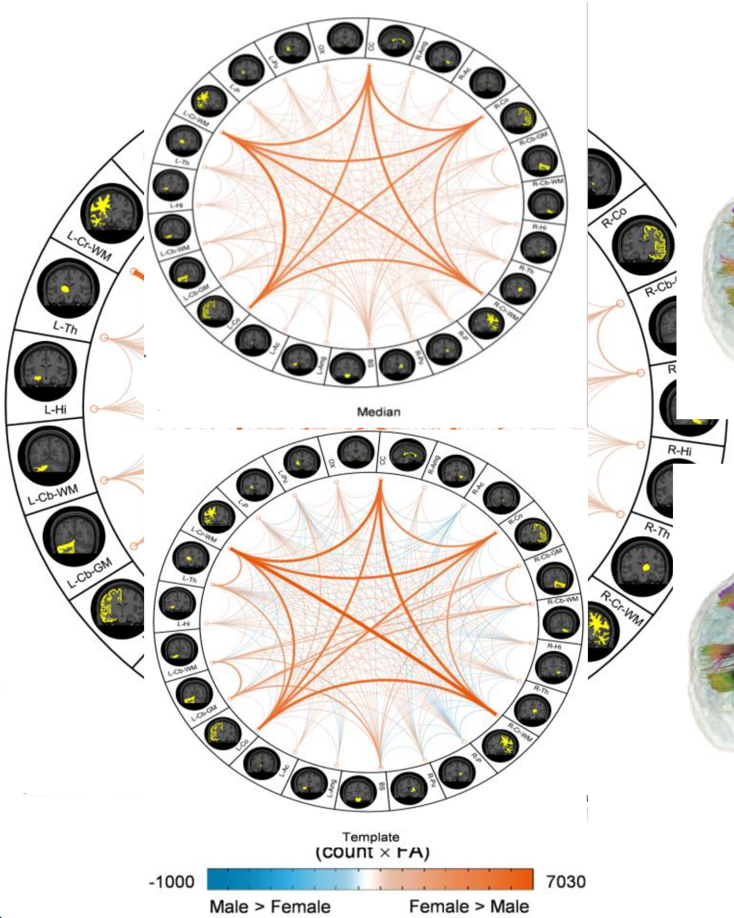
[2] Jafari, B. and **M. Memar**, Exploring mesoscale brain connectivity variations and developing sex-specific tractography templates. NeuroImage, 2025: p. 121545.

Results

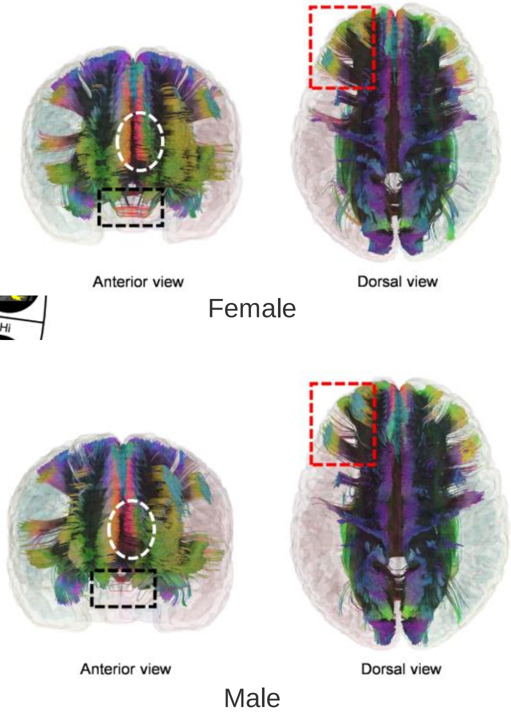
Meso-scale study findings



Sex differences (female - male) in DTI metrics across 24 regions

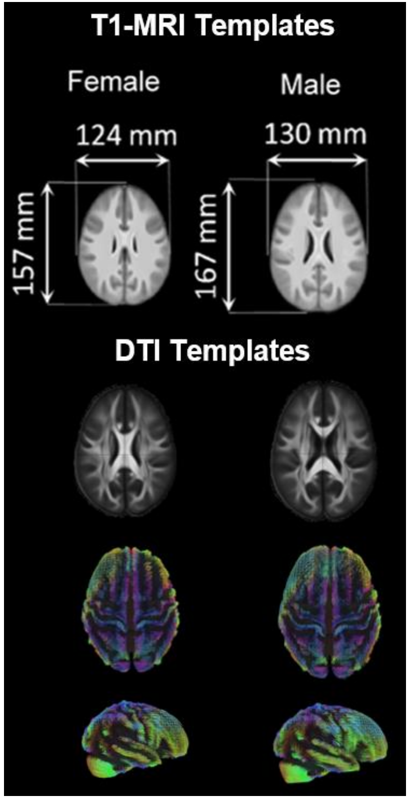


Connectivity strength (SoC) difference

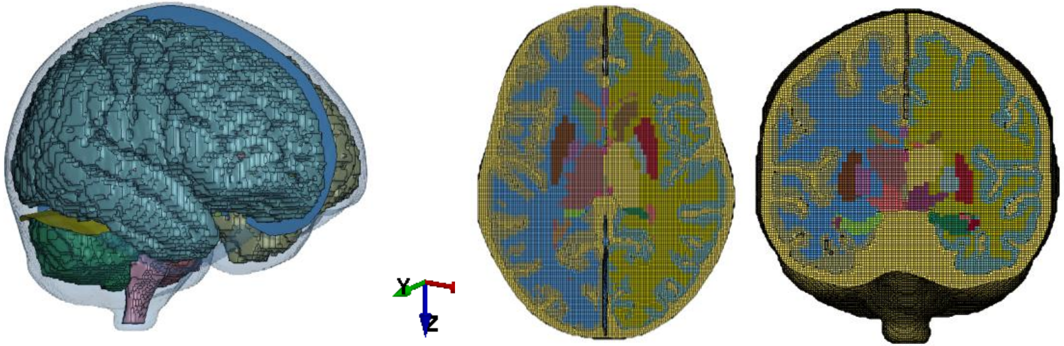


Left-right cortices connections

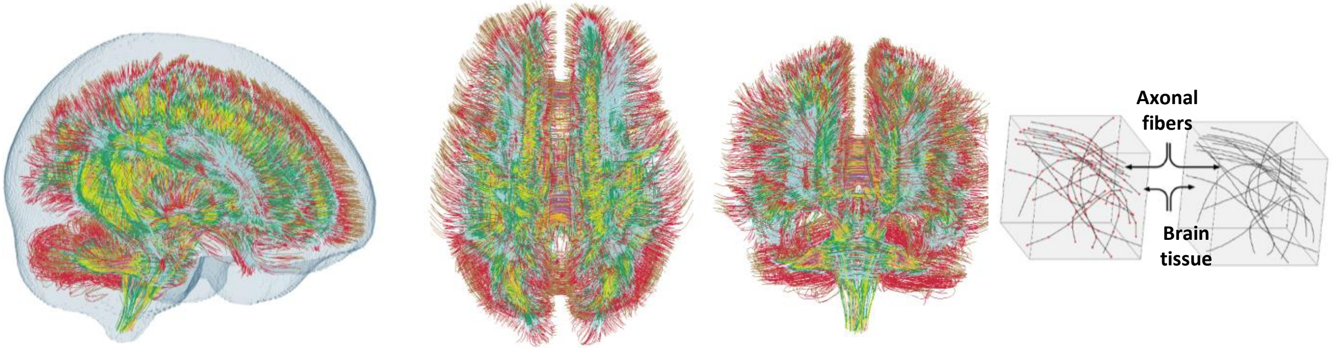
Mesh Generation and Model Development



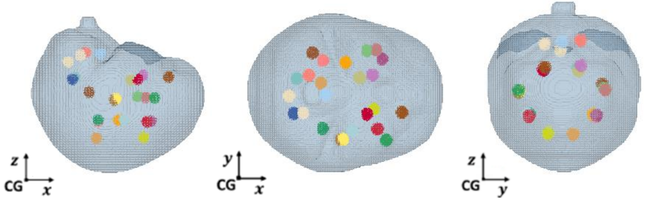
Brain regions and CSF: Automatic Voxel Based Meshing with a Laplacian Smoothing Approach, Hexa Elements, Skull, Falx, and Tentorium: Quad Shell Elements



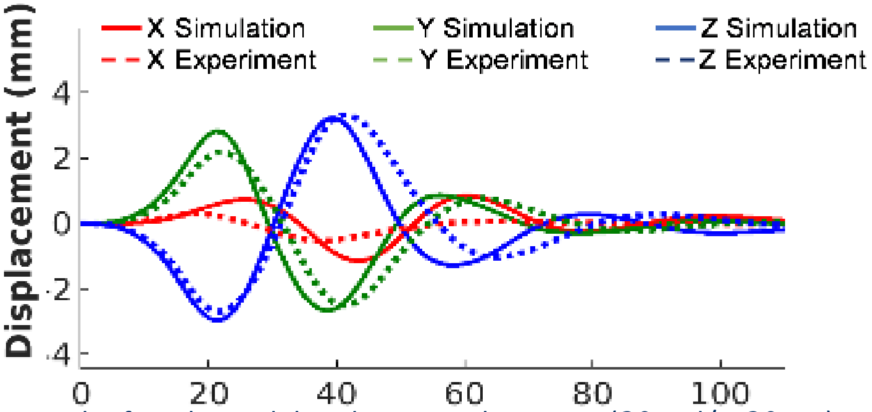
Axonal fibers: Automatic 1-D beam elements from tractography, 9 groups based on FA



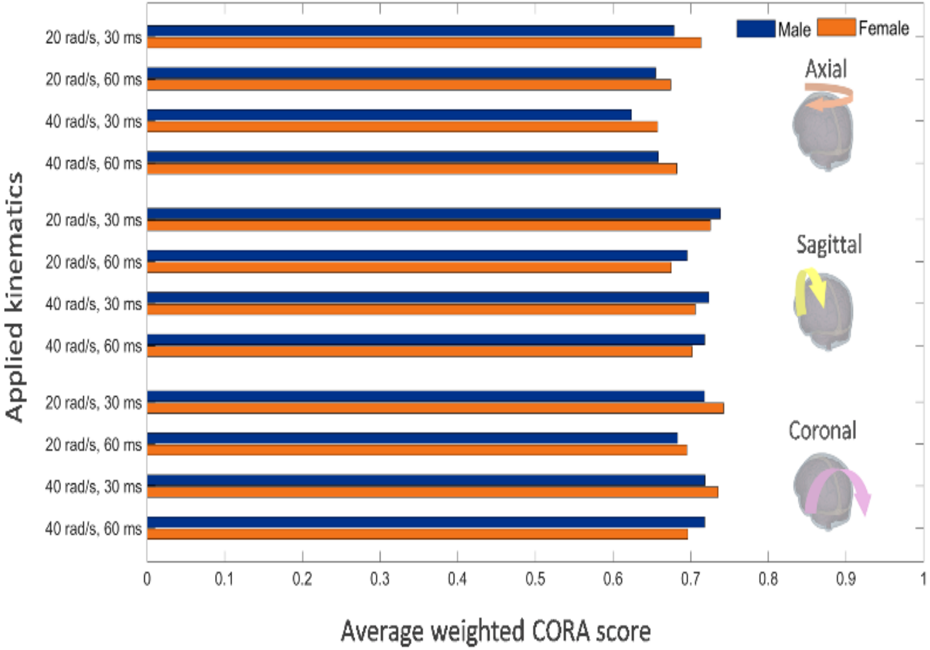
Model Validation against measured brain-skull relative displacement in cadaveric experiments



Intracranial locations used for model validation [3]



The female model under coronal rotation (20 rad/s, 30 ms)



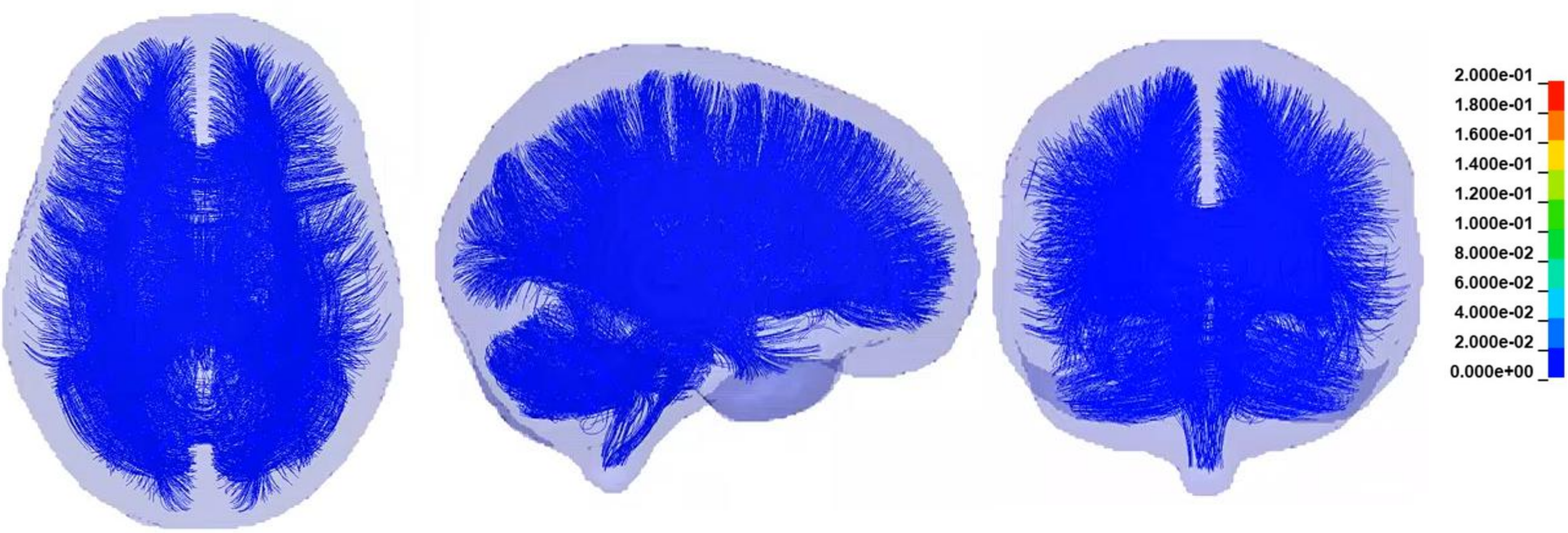
Average weighted CORA scores for the male and female finite element head models across all 24 reference points
CORA=0.71 on Avg

[3] Alshareef, A.A., et al., IEEE Transactions on Biomedical Engineering, 2025

Results

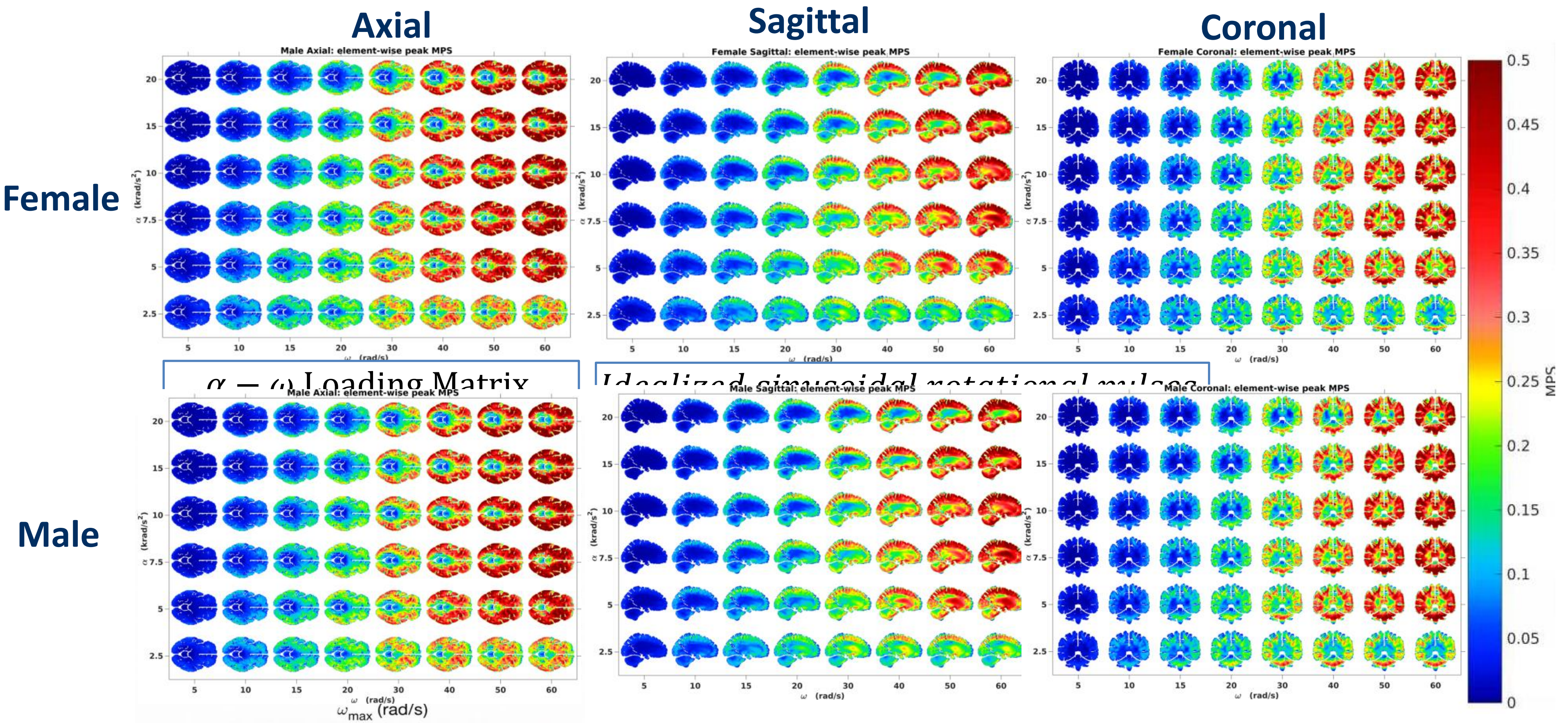
Sample of axonal deformations in different rotational planes

Axial **Sagittal** **Coronal**



Results

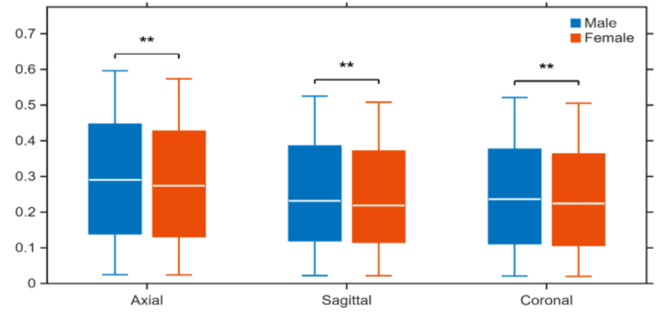
Spatial distribution of MPS across the α-ω loading matrix



Results

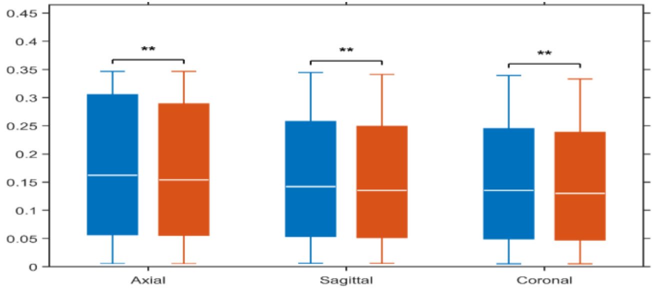
Peak 95th percentile of max principal strain of brain tissue elements (**MPS95 or MPS**)

MPS



Peak 95th percentile of max longitudinal strain of axonal fibers (**MAS95 or MAS**)

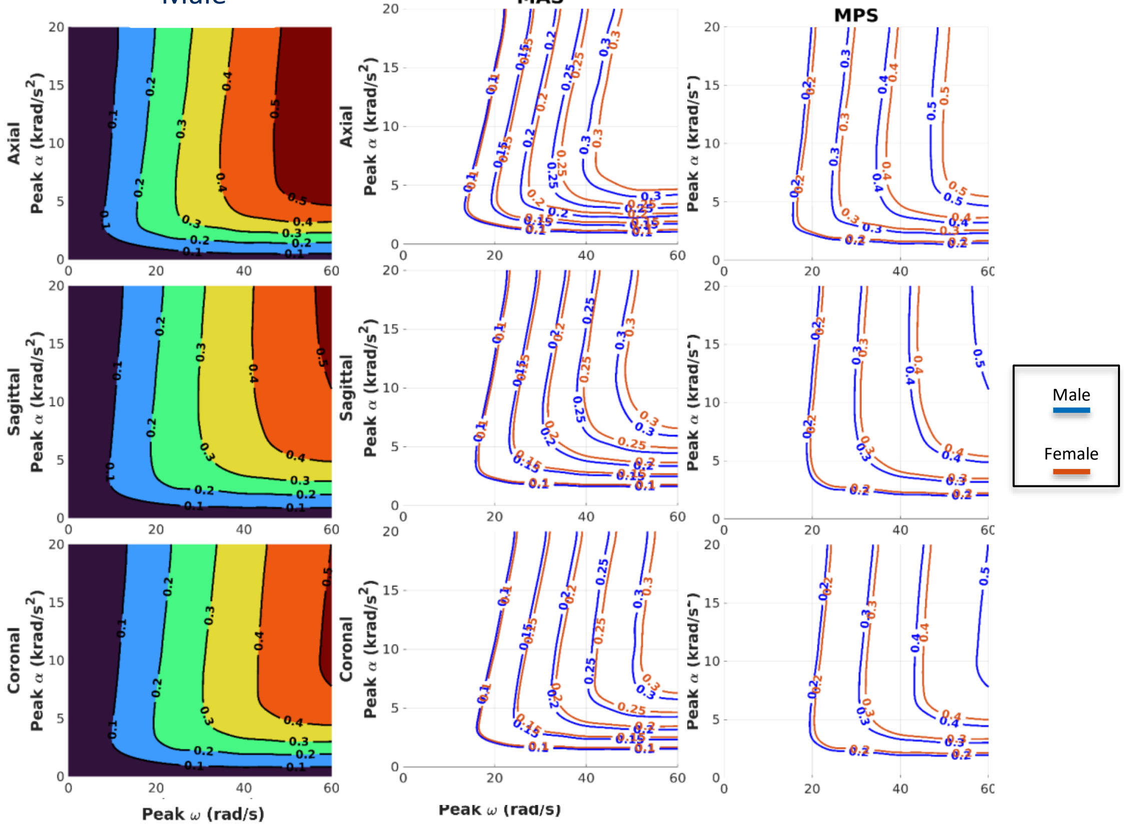
MAS



Iso-response maps of brain tissue deformation (MPS95)

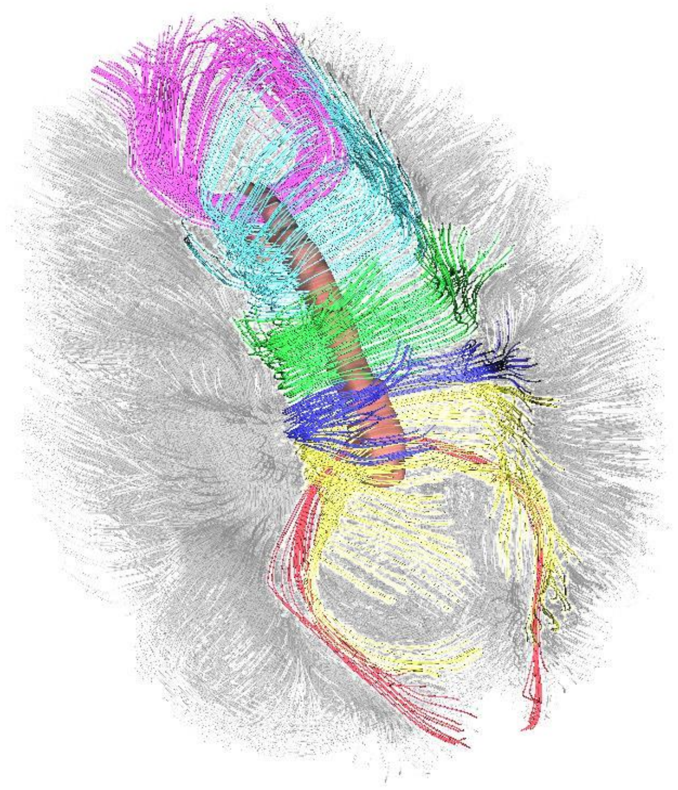
Male

Female

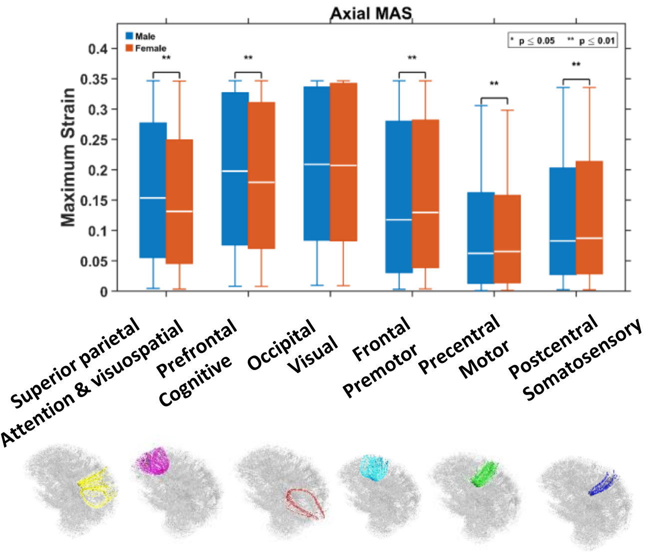


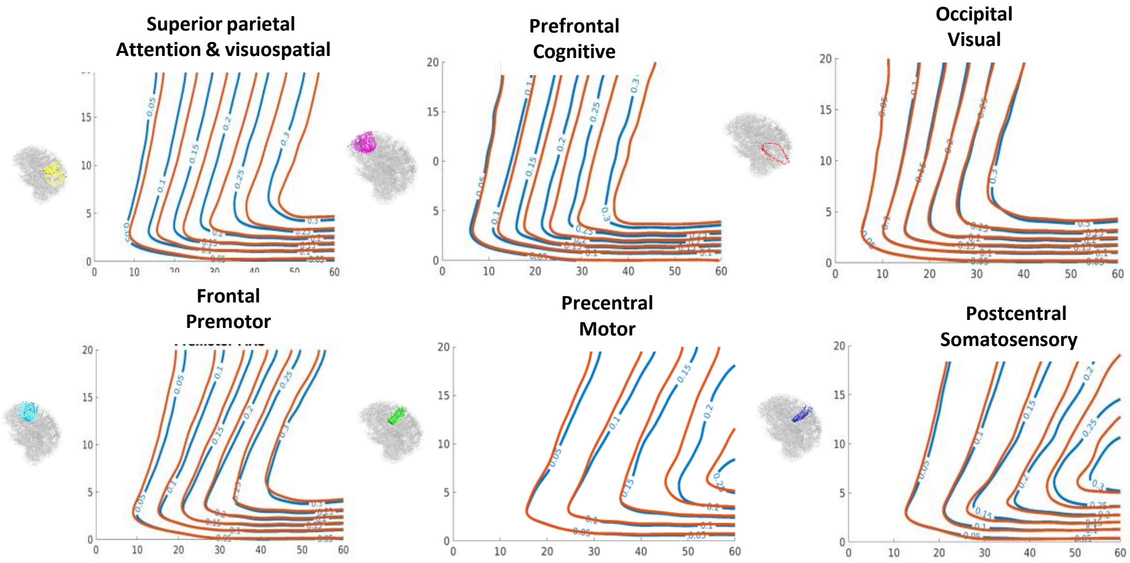
Projection-defined callosal pathways

Pathway	Bilateral cortical endpoints	Interhemispheric functional role
Prefrontal/ cognitive	Rostral middle frontal and superior frontal gyri	Working memory, inhibitory control, emotion regulation, and higher-order cognitive integration between hemispheres.
Frontal/ Premotor & executive-motor	Caudal middle frontal and superior frontal gyri	Movement preparation and planning, motor selection, and coordination of complex actions across hemispheres.
Precentral/ Primary motor	Precentral gyrus (primary motor cortex)	Coordination and modulation of primary motor cortices responsible for voluntary movement.
Postcentral/ Somatosensory	Postcentral gyrus (primary somatosensory cortex)	Transfer and integration of tactile and somatosensory information (touch, pain, temperature, proprioception) between body sides.
Superior parietal/– Attention and visuospatial	Superior parietal and precuneus	Bilateral integration of spatial attention, orienting, visuospatial processing, visuospatial memory, and self-awareness.
Occipital/ visual	Pericalcarine cortex and lingual gyrus	Interhemispheric integration of visual information across the two hemifields, including early visual, visual-motion, and visual memory processes.



Axonal Deformation Along Callosal Pathway in Axial Rotation





Take a Home Message

✓**Findings from our MRI and DTI studies showed sex structural differences that** Larger fractional volume of CC and smaller fractional volume of ventricles Larger FA values in most regions and stronger brain connectivity in females may **give a structural advantage to female brain under trauma relevant mechanical loadings**

✓Under **identical** rotational kinematics, **males generally showed higher whole-brain tissue and axonal deformation but results along the pathways were mixed** and Callosal response was pathway-, direction- and sex-dependent

✓**Sex differences in TBI biomechanics are multiscale: anatomy, white matter architecture, loading direction, and pathway organization all shape brain deformation**.

✓**Brain FEMs** provide the opportunity to evaluate global and regional tissue-level brain and axonal responses, as well as biomechanical responses along structurally and functionally meaningful axonal pathways, **providing a mechanistic framework for investigating brain susceptibility to TBI**.

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- Zade Pederson, BS
- Mohammadreza Ramzanpour, PhD

Memar Lab Members:

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