

# **DOHaD Summer Course 2023: First Principles and Future Directions**

## **Monitoring the Effect of Intrauterine Environment on Fetal Brain Development in Rhesus Macaques with In Utero MRI**

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*Advanced Imaging Research Center,*

*ONPRC Division of Neuroscience*

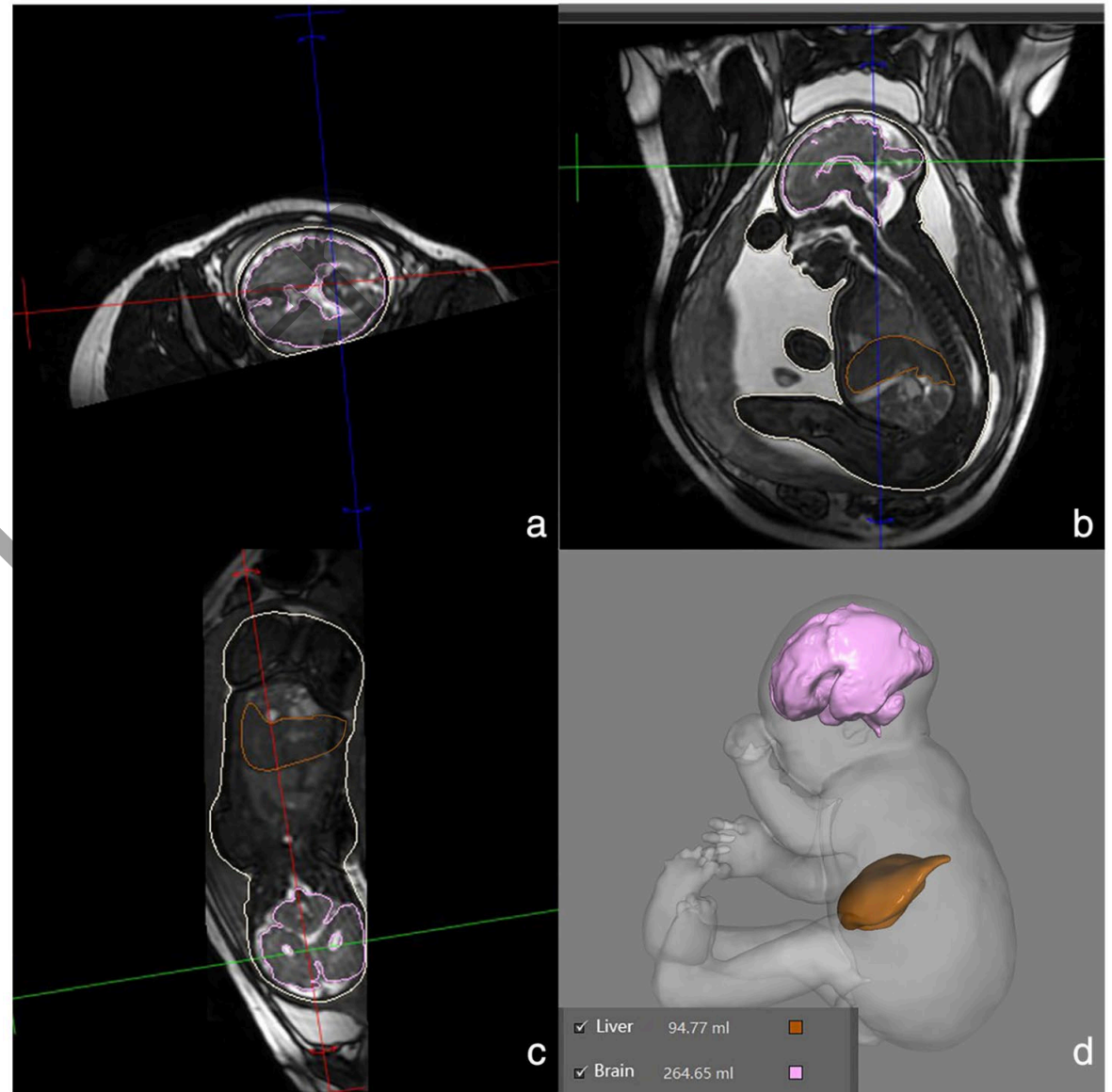
**August 8, 2023**

## *New plan for this presentation*

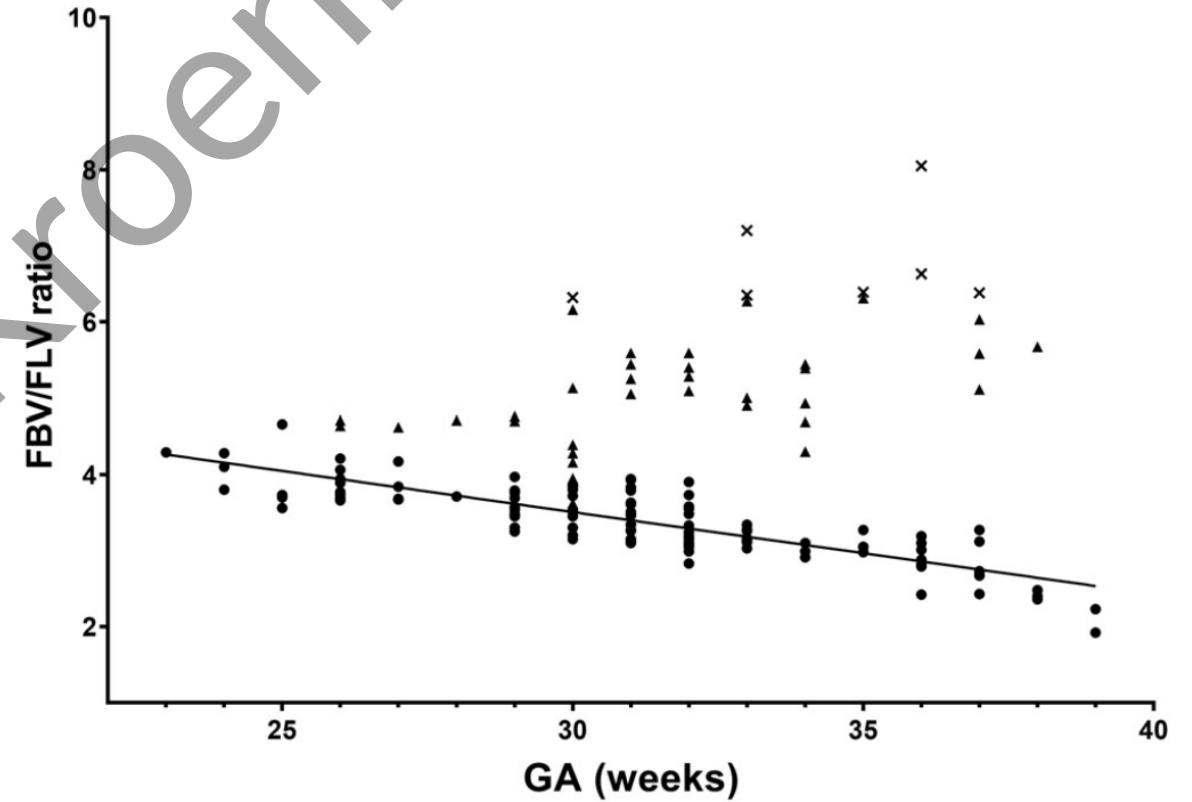
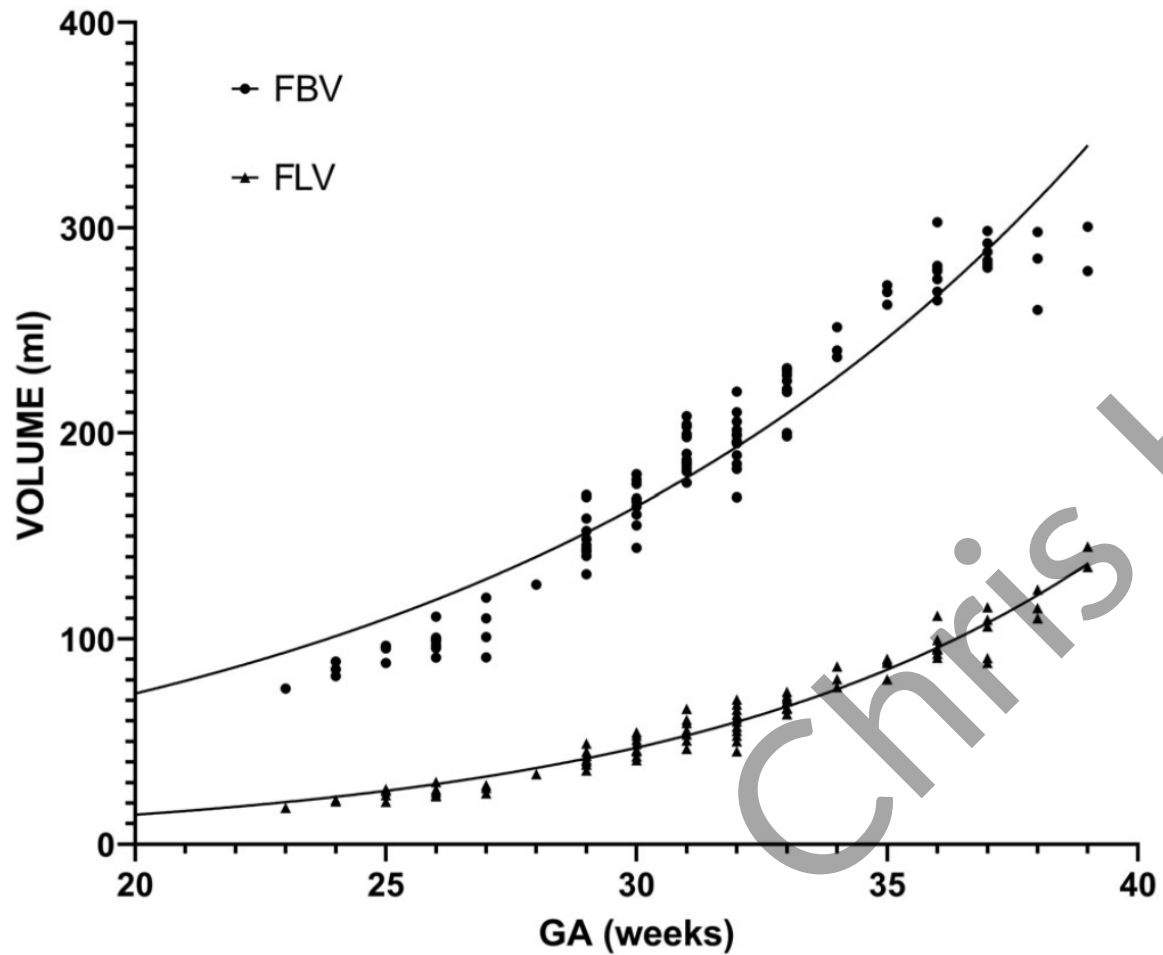
- Survey of fetal MRI capabilities of potential relevance to DOHaD
- Fetal rhesus brain development

# *In utero MRI*

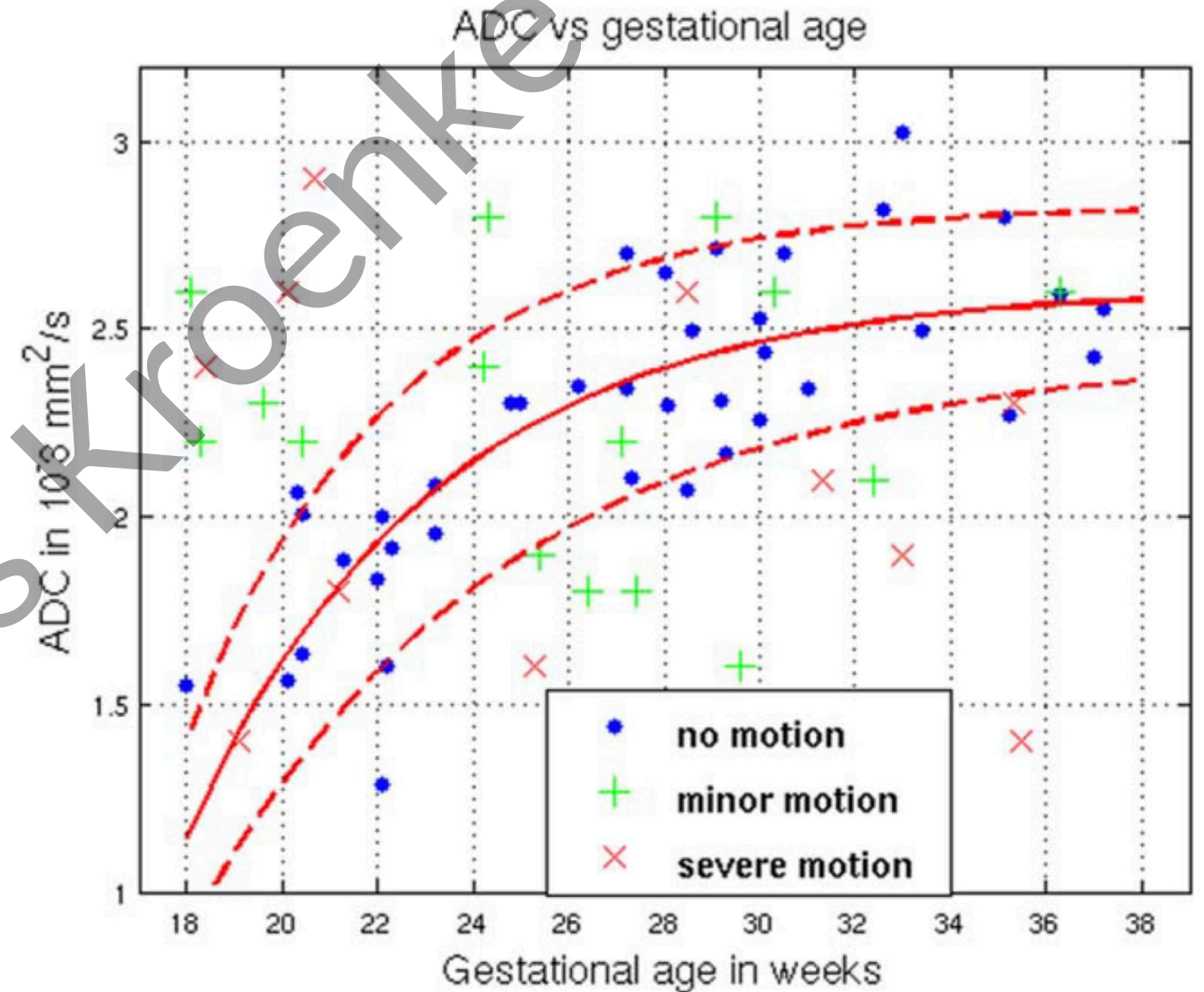
- Is safe – performed in studies of healthy human volunteers
- Entire fetus frequently within the field of view
- Facilitates structural and functional characterization of a novel stage of development



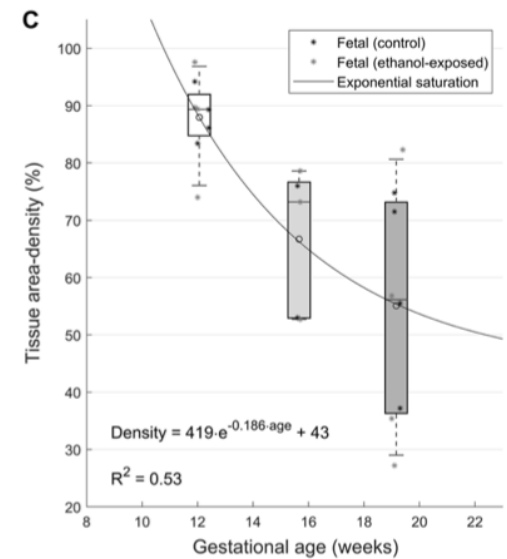
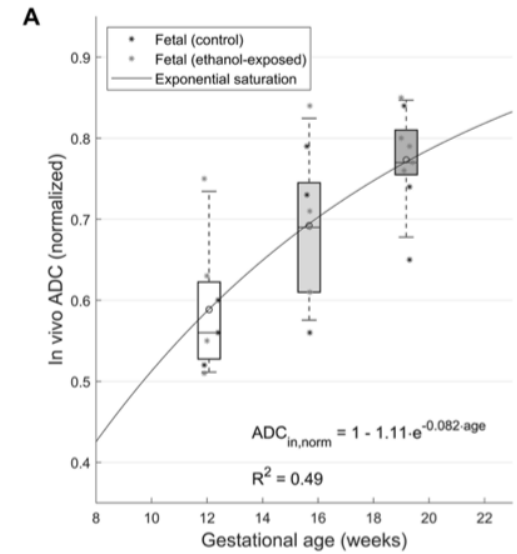
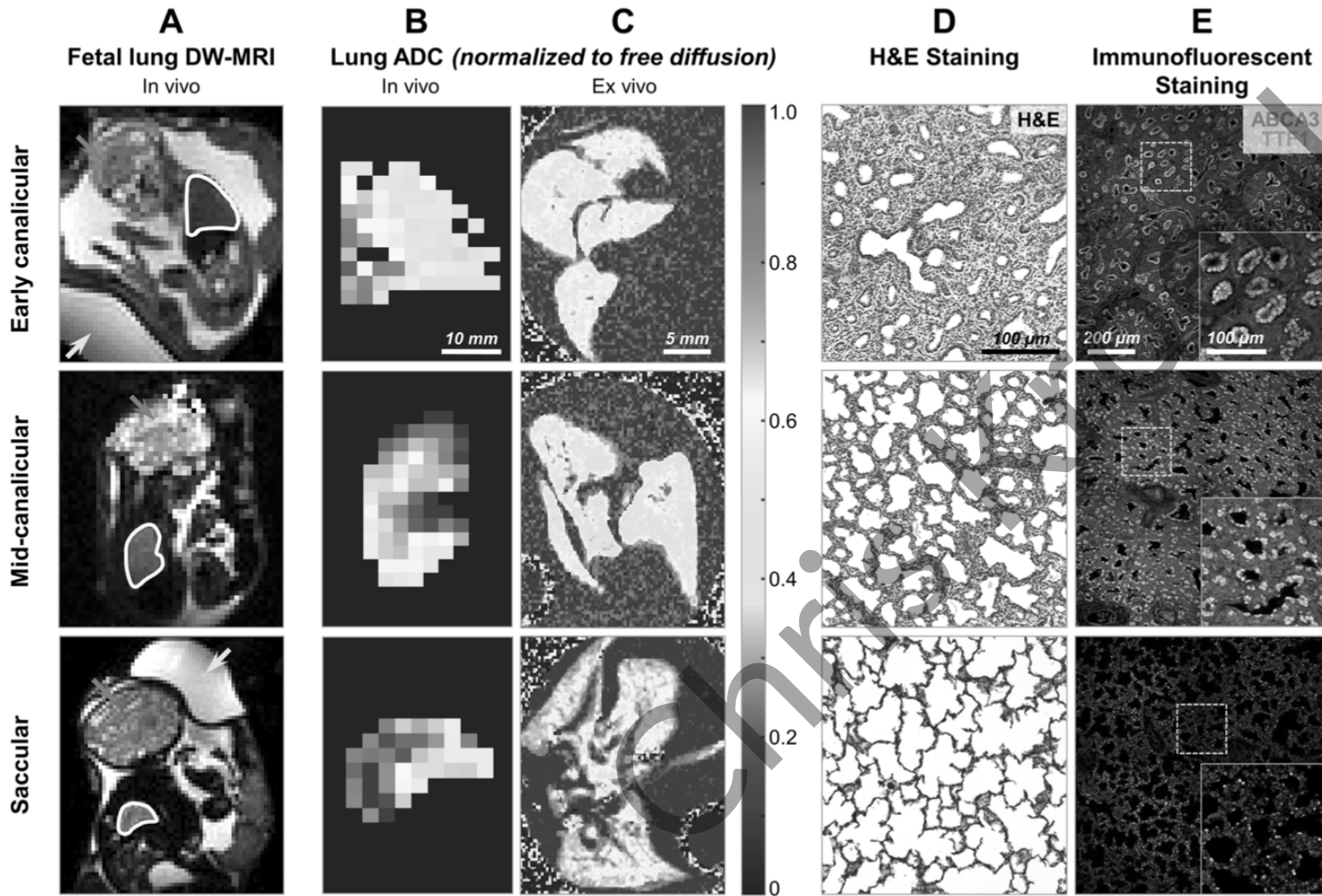
# Quantification of Brain and Liver Volumes



# Water diffusion in the fetal lung becomes less restricted with alveolar development

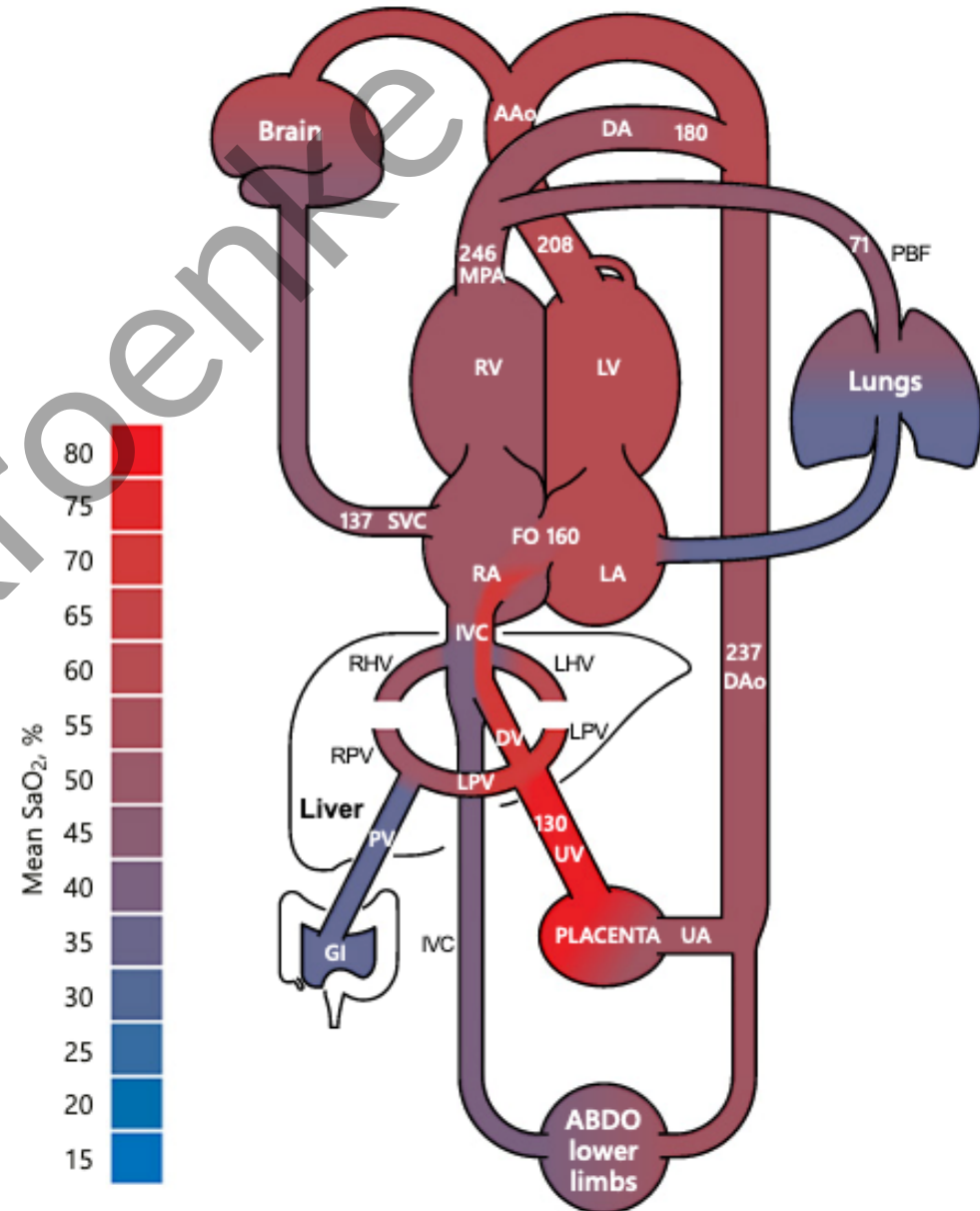


# Validation of fetal lung approach in rhesus animals



# Fetal Circulation

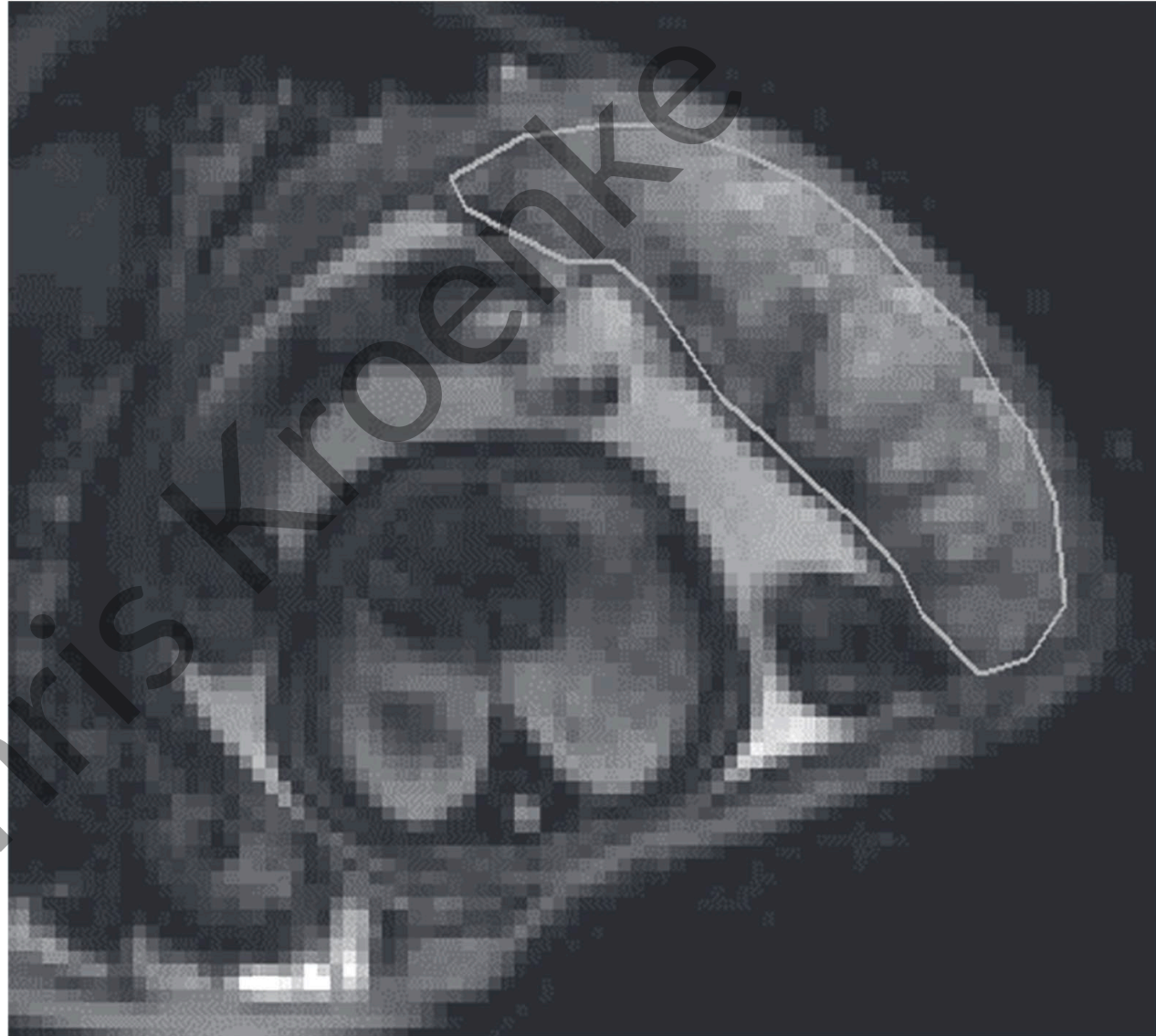
- Blood flow measured via phase contrast MRI
- Vessel blood oxygen saturation via T1 and T2 mapping
- Methods applied in human studies validated with instrumented sheep



# Opinion

**T2\*-weighted placental MRI: basic research tool or emerging clinical test for placental dysfunction?**

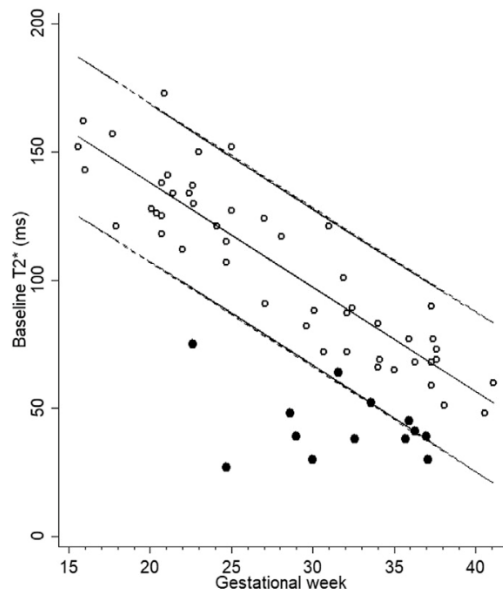
A. SØRENSEN<sup>1\*</sup> , J. HUTTER<sup>2</sup>, M. SEED<sup>3</sup>,  
P. E. GRANT<sup>4</sup> and P. GOWLAND<sup>5</sup>





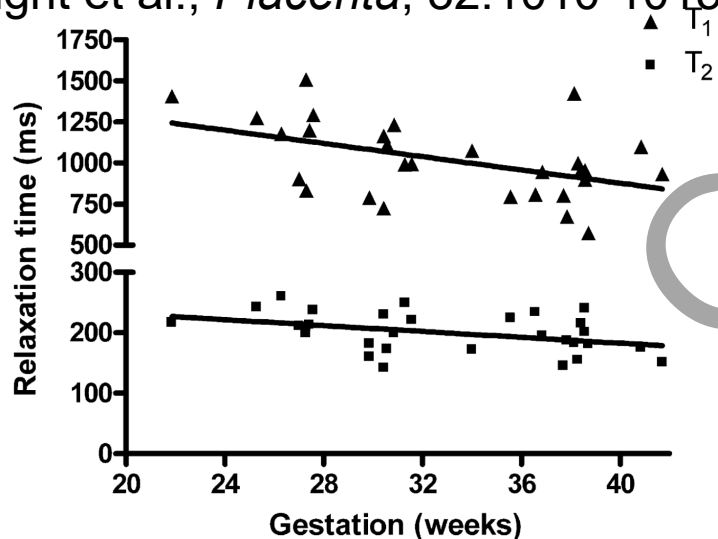
Aalborg University Hospital

Sinding et al., *Placenta*, 61:17-23 (2018)



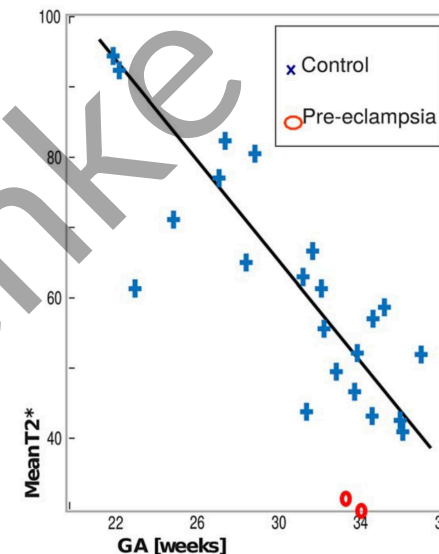
Manchester/Nottingham

Wright et al., *Placenta*, 32:1010-1015 (2011)



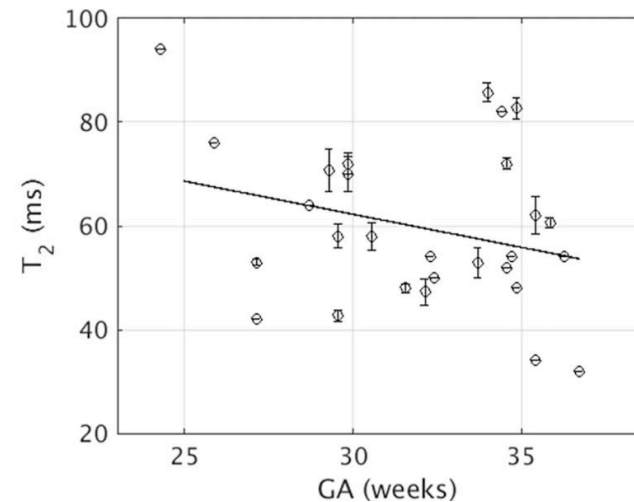
Kings College London

Hutter et al., *Magn. Reson. Med*, 81:1191-1204 (2019)

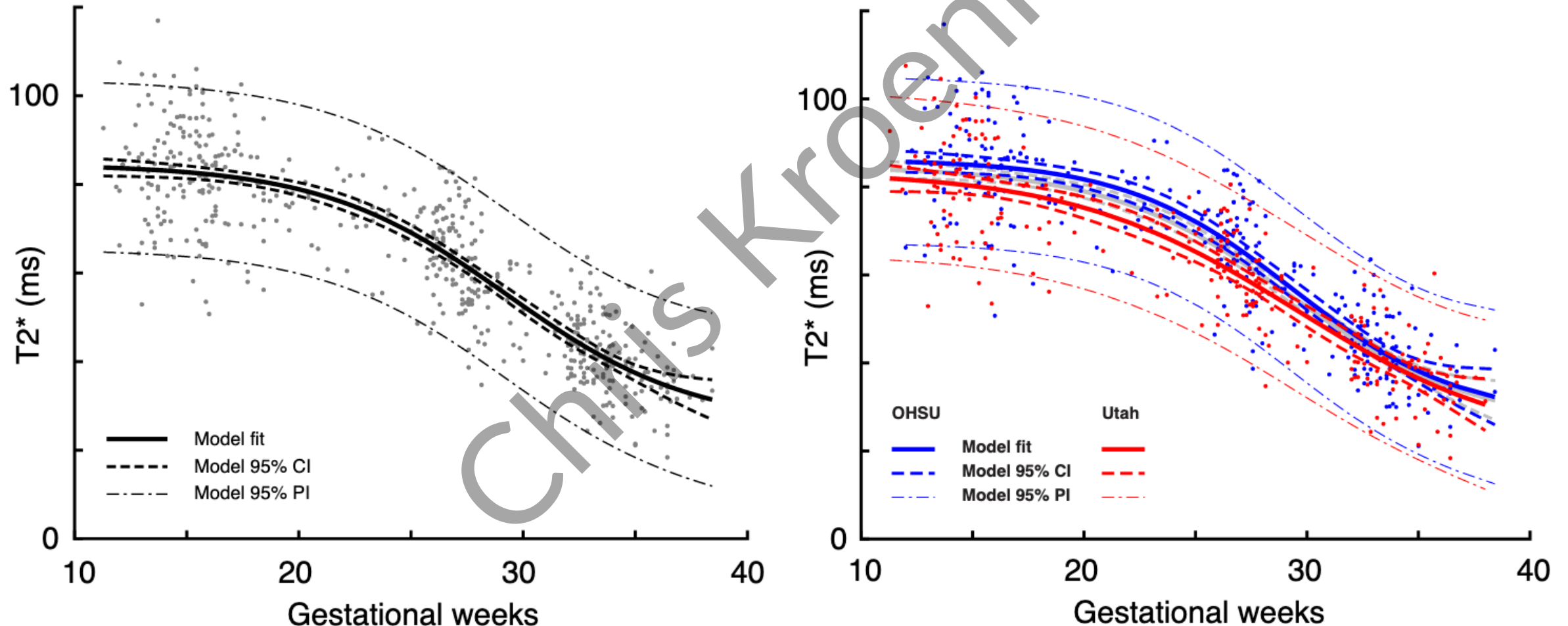


Mass. General/MIT

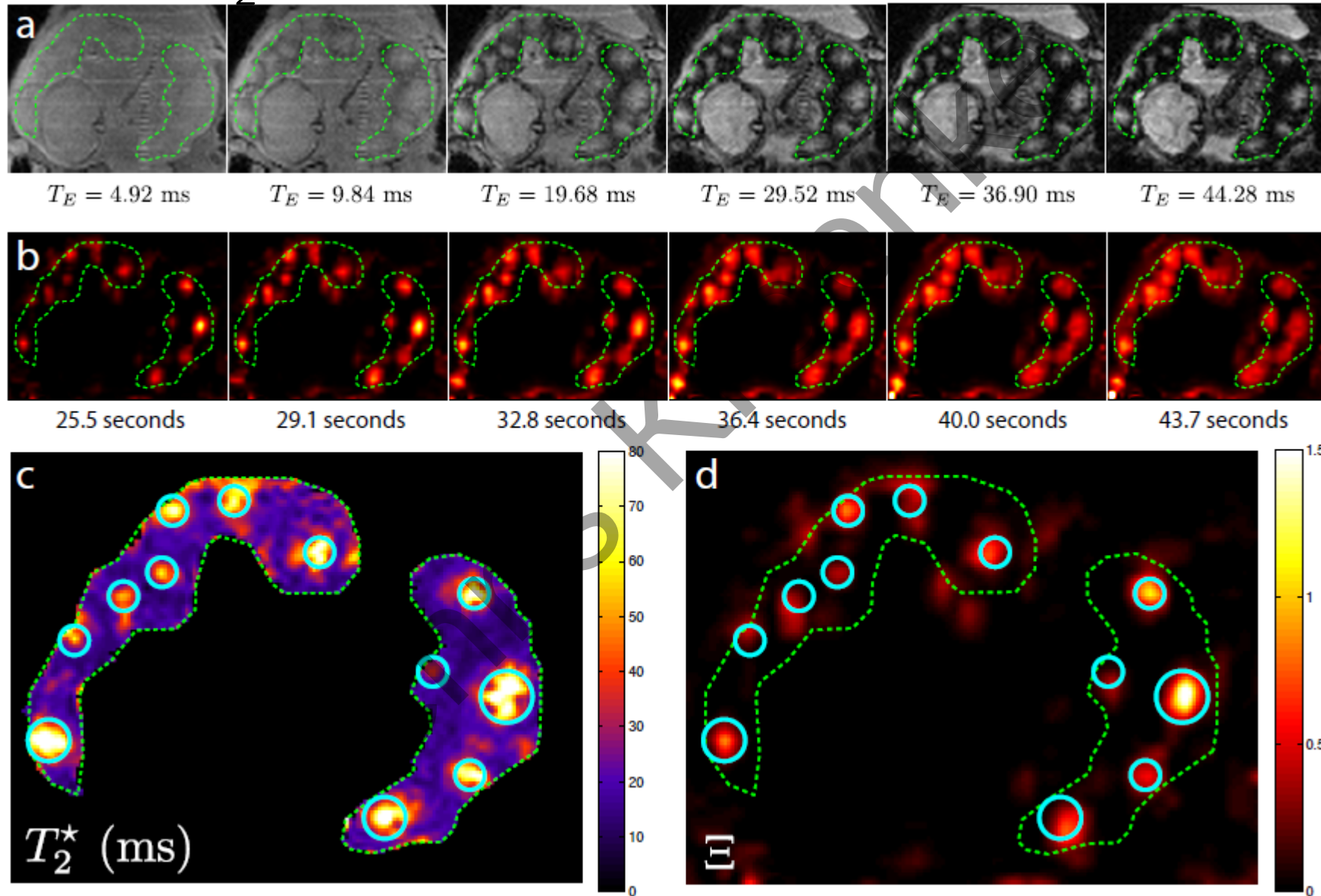
Stout et al., *Placenta*, 114:124-132 (2021)



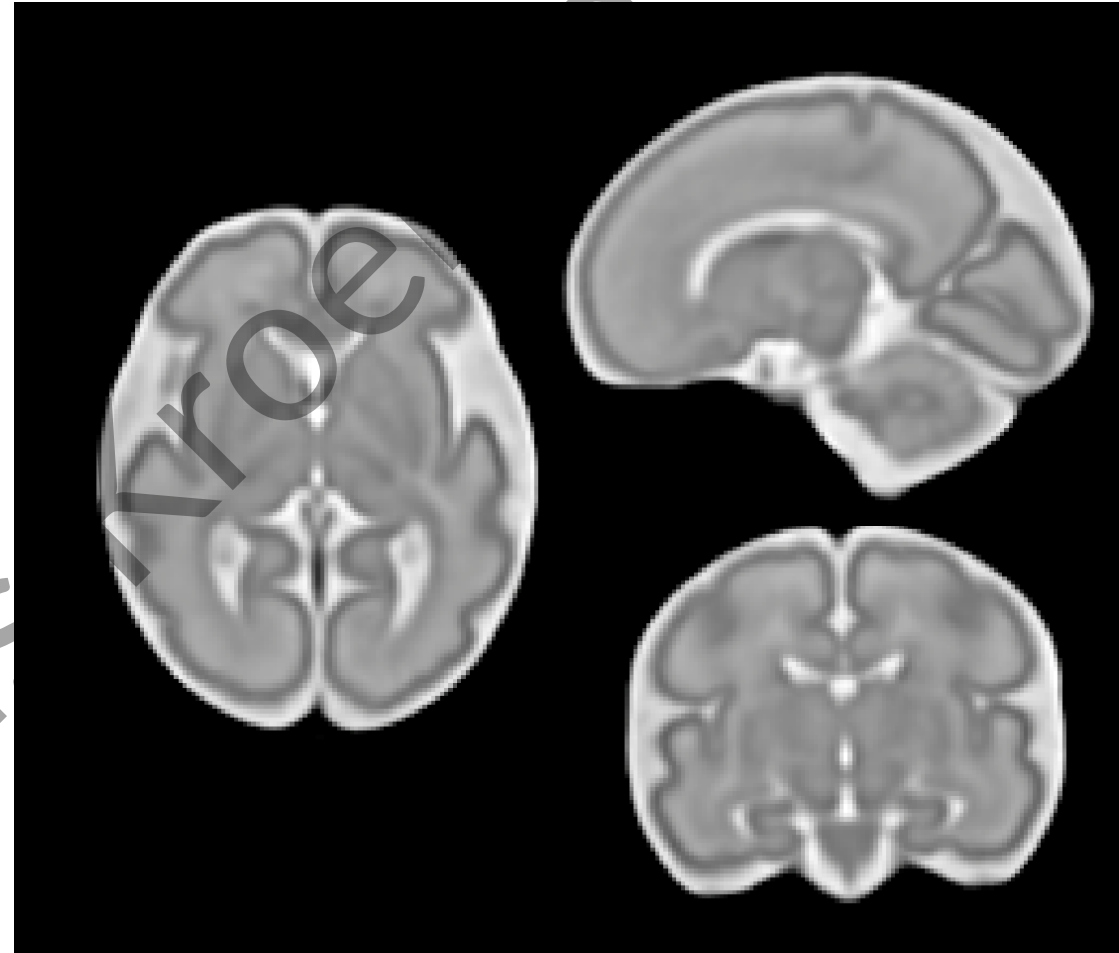
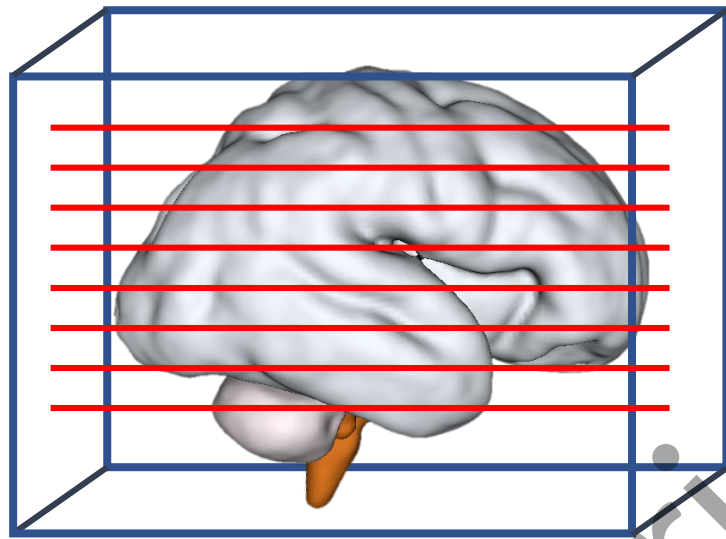
“Future multicenter trials with a consistent MRI protocol performed at specific gestational ages in clinically well-defined population should be the next step to determine the clinical potential of T2\* weighted placental MRI.” –Sorensen, Hutter, Grant, Seed, Gowland (2020)



# Validation in rhesus: Large $T_2^*$ corresponds to spiral artery location



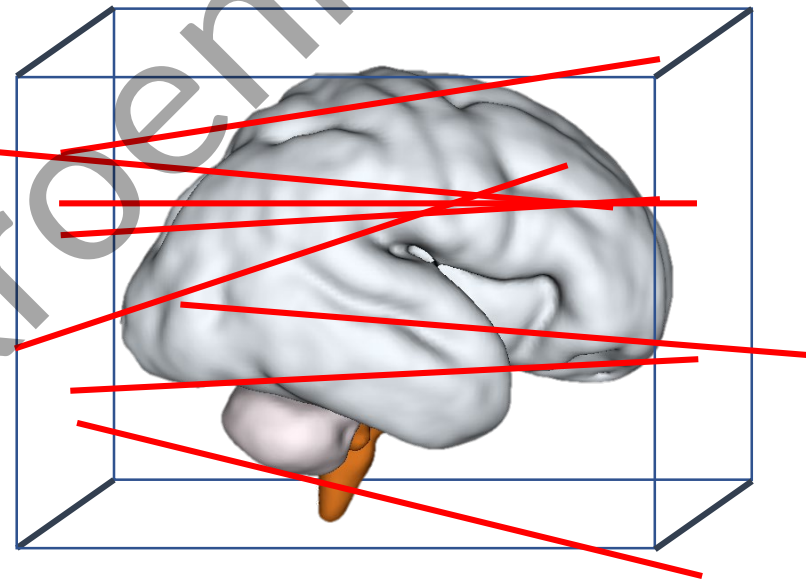
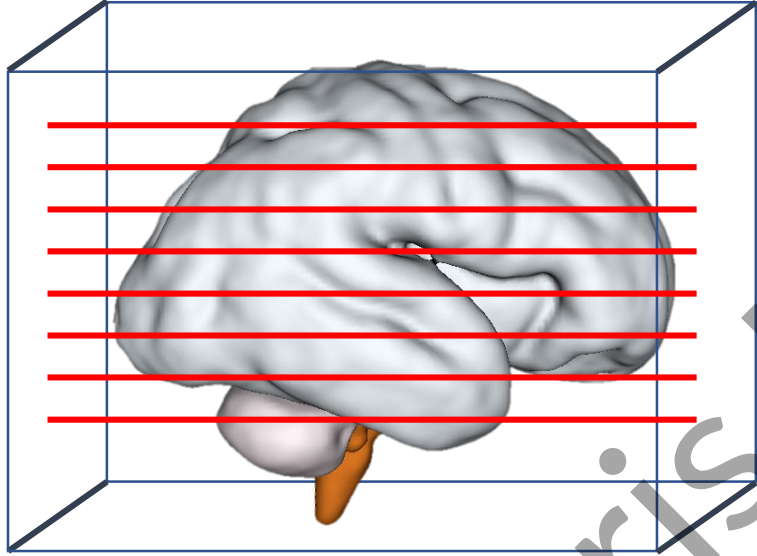




Gholipour et al., *Sci. Rep.*, 7:476 (2017)

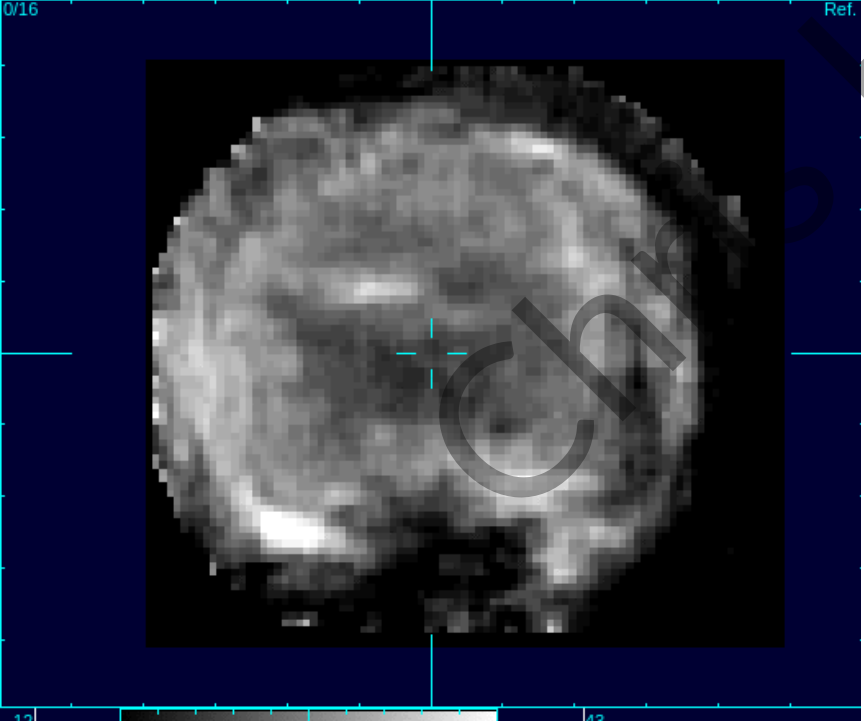
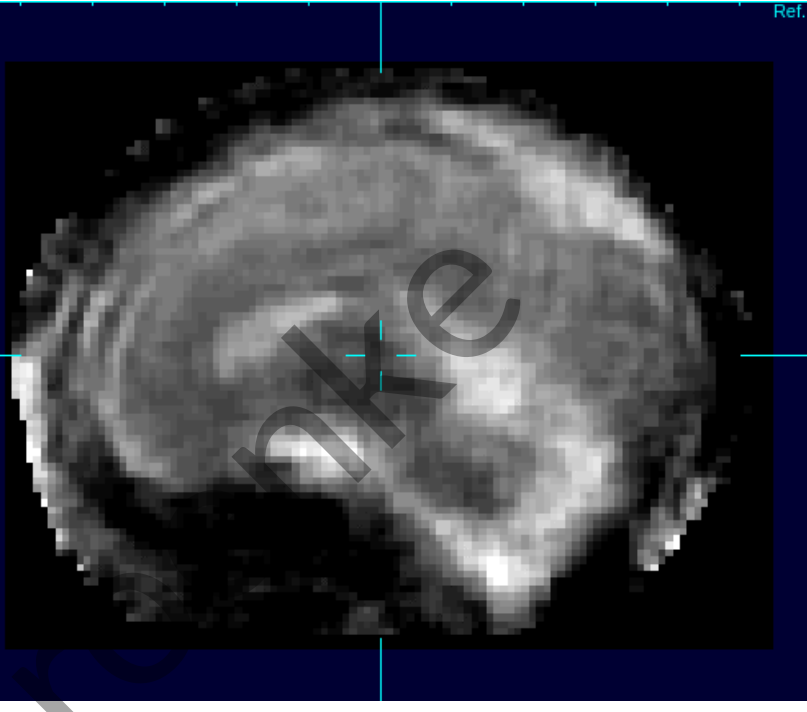
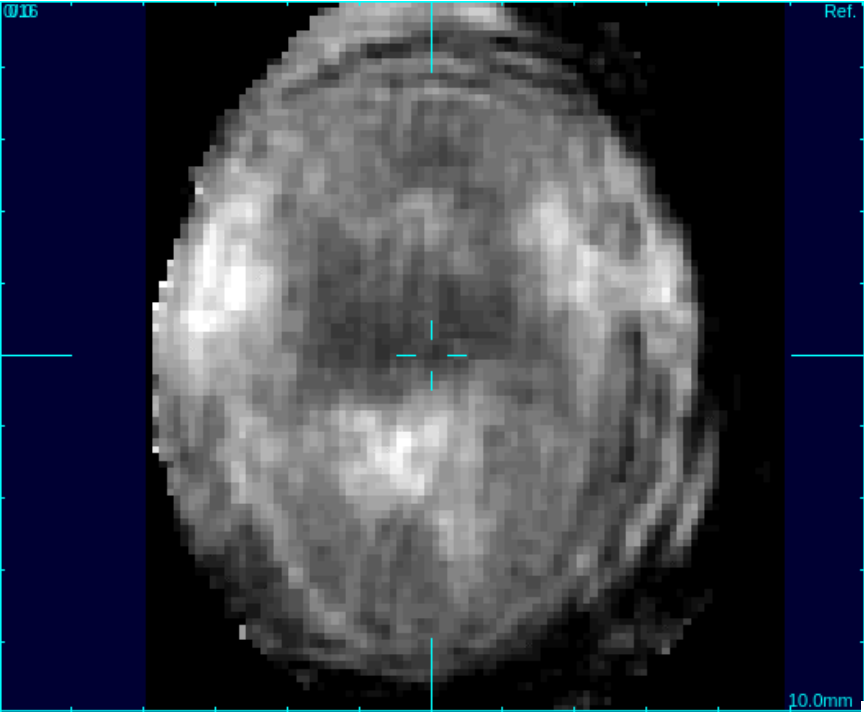






Chris Kroenke





Colin Studholme  
University of Washington

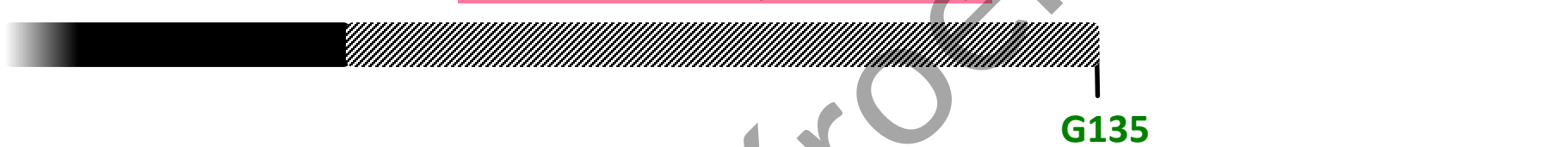
<https://bioe.uw.edu/new-technology-images-fetal-brain-activity-in-4d/>

# Fetal MRI in rhesus monkeys

## Maternal protein-restricted diet



## Zika virus infection



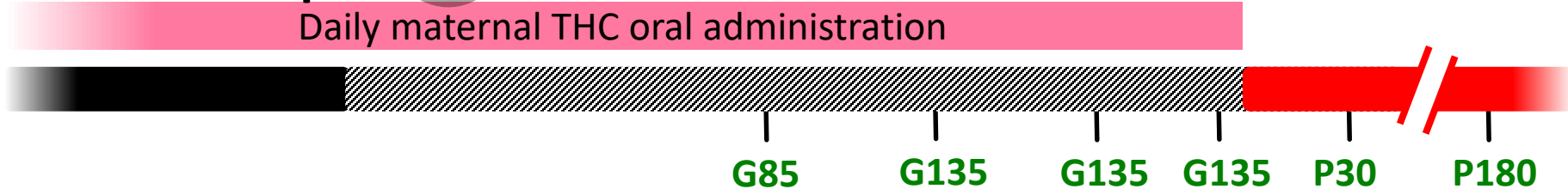
## Acute (within magnet) physiological manipulation



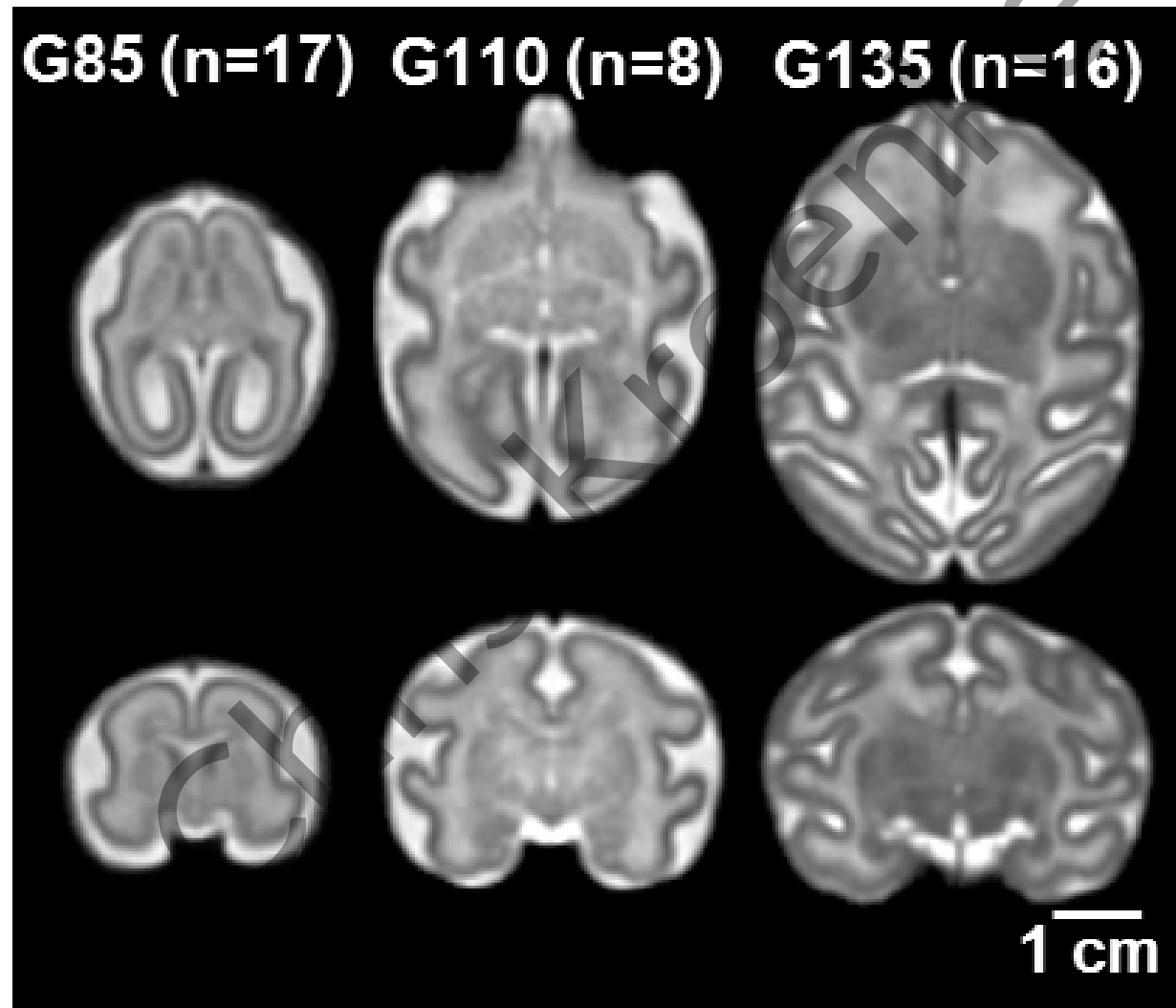
## Fetal alcohol spectrum disorders



## Fetal THC exposure

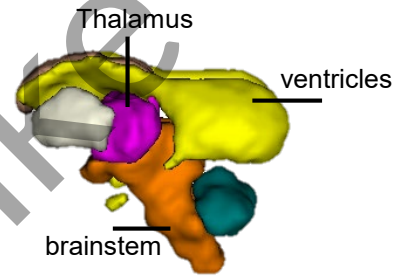
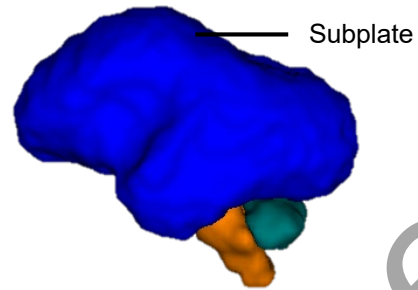
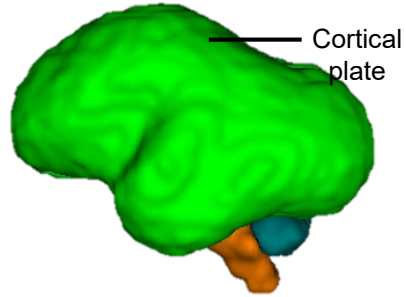


# *Fetal rhesus macaque brain templates*

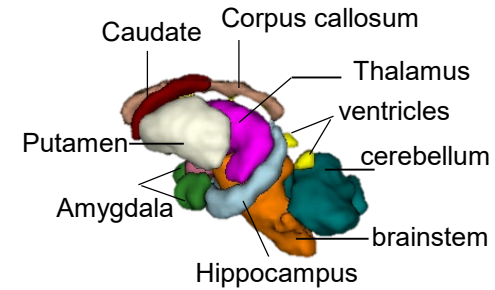
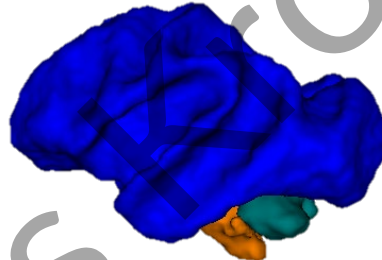
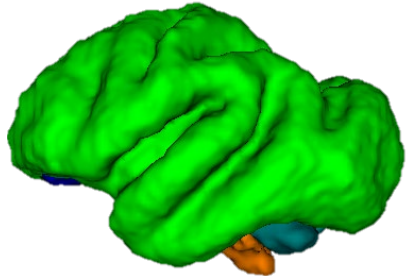


# Labelmaps for G85, G110, and G135 rhesus brains

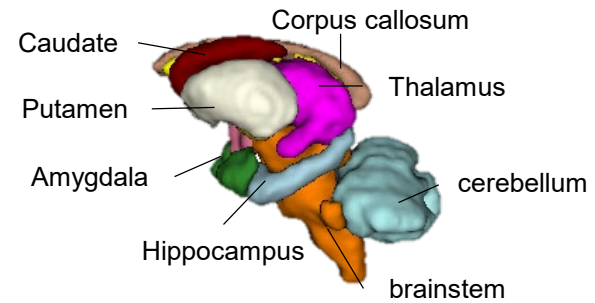
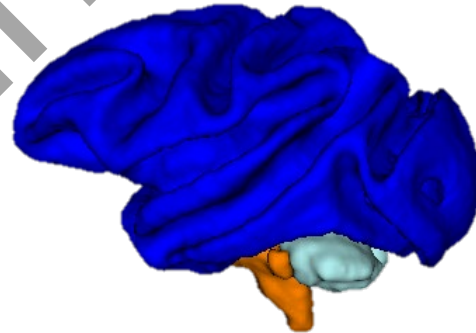
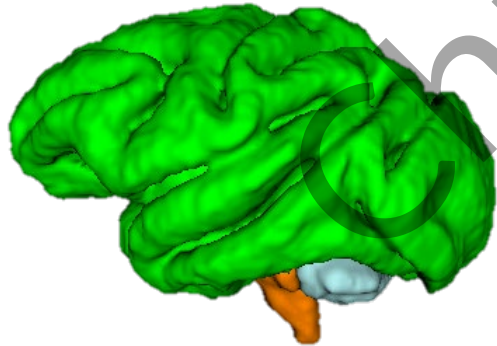
G85



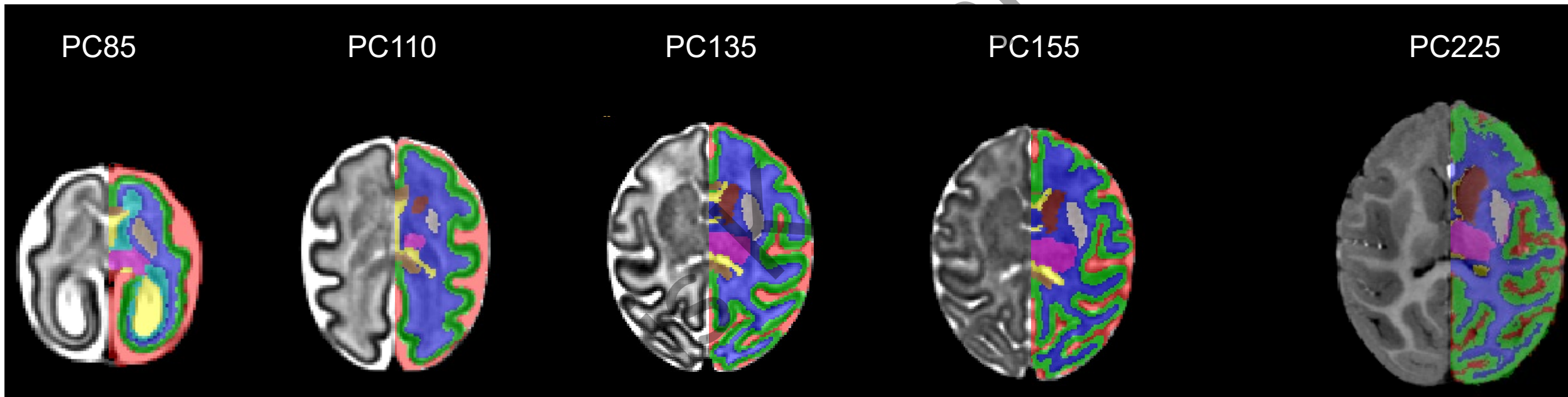
G110



G135

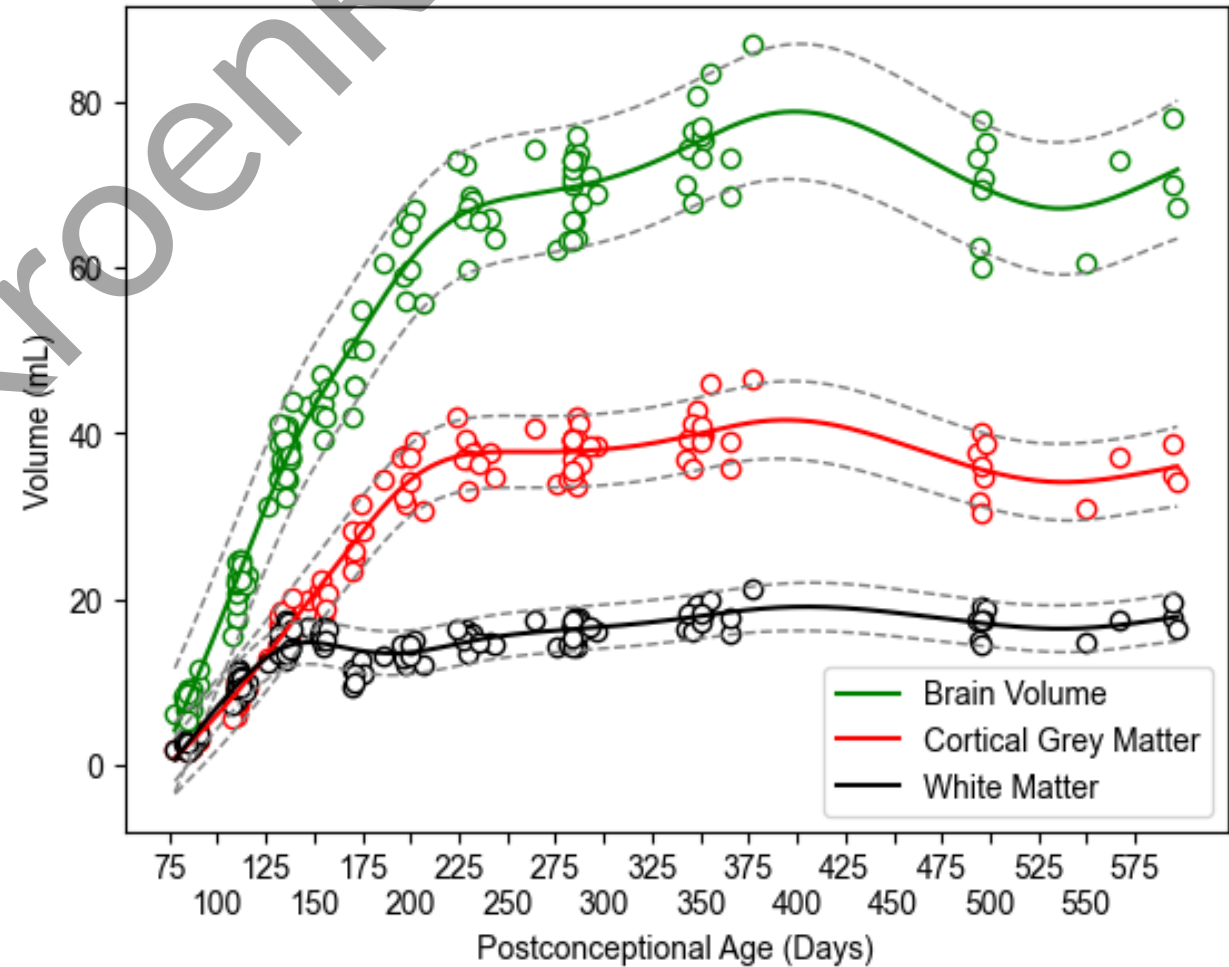
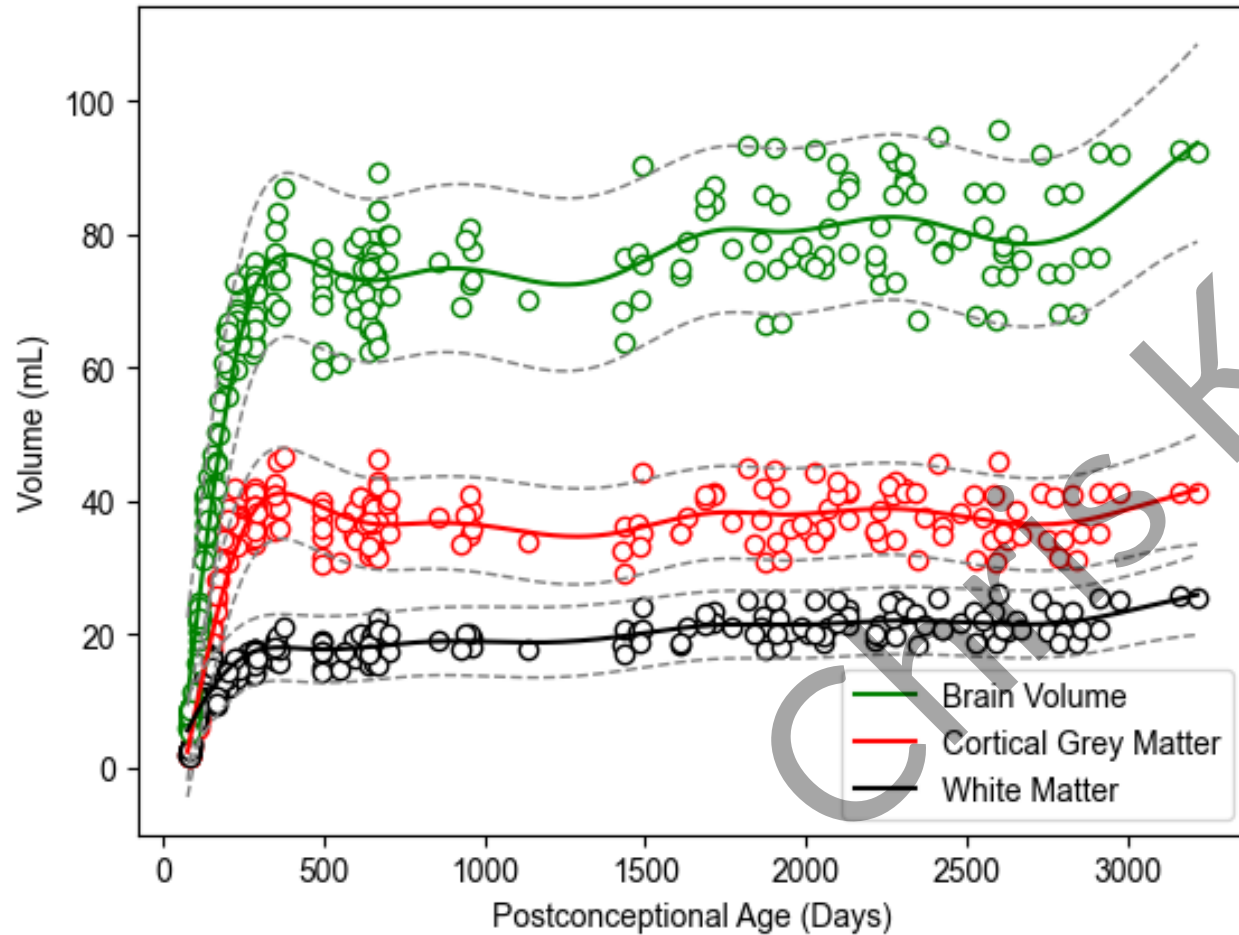


*Ongoing work to extend the number of time points  
and merge with postnatal templates*

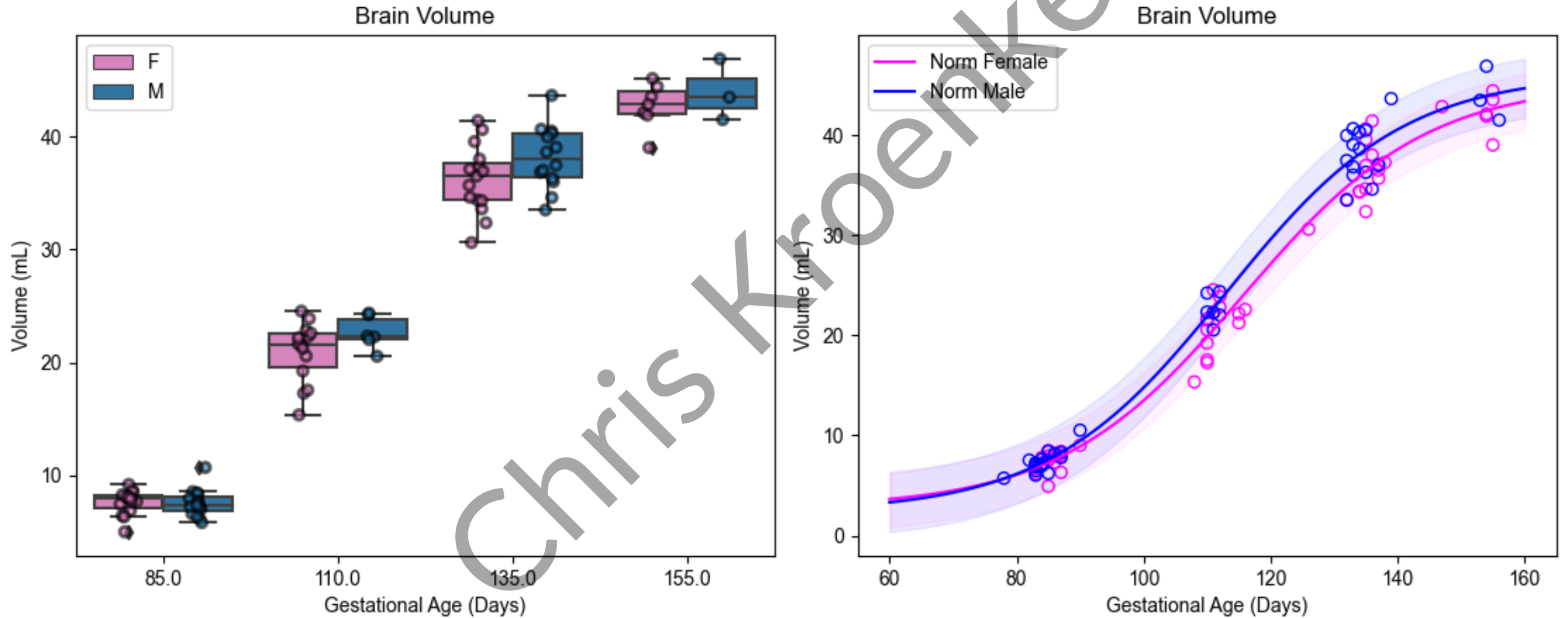


Joshua Karpf, OHSU, in preparation.

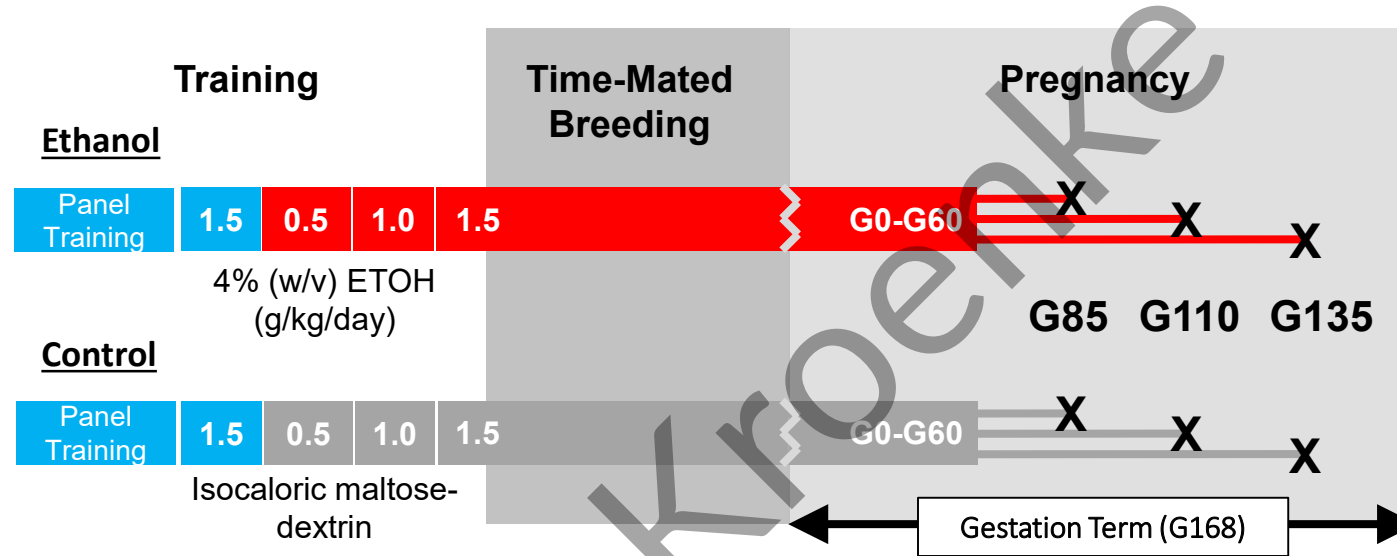
# Growth of cortical gray matter and developing white matter



# *Sex differences in brain growth*



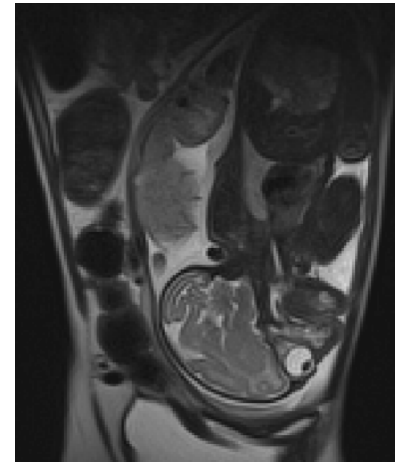
# Combining oral self administration with in utero MRI in a rhesus model of FASD



G85



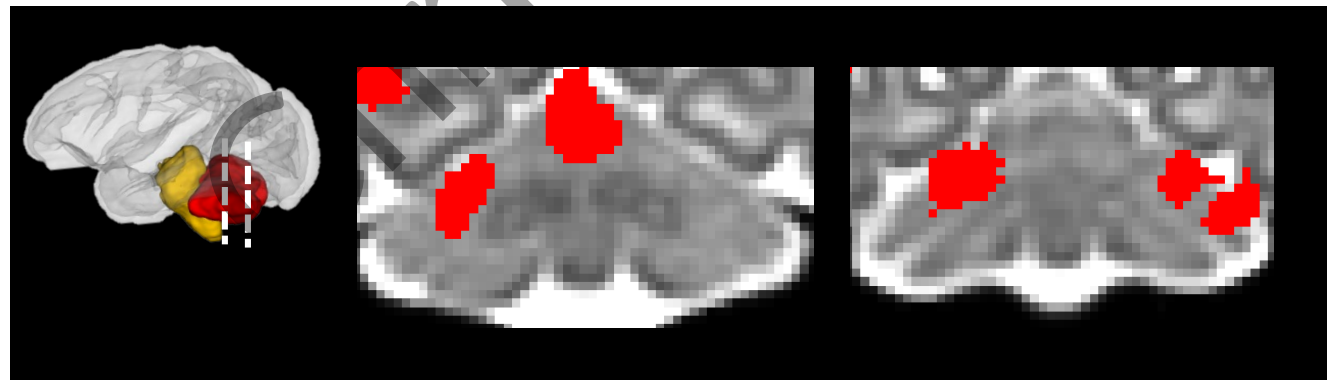
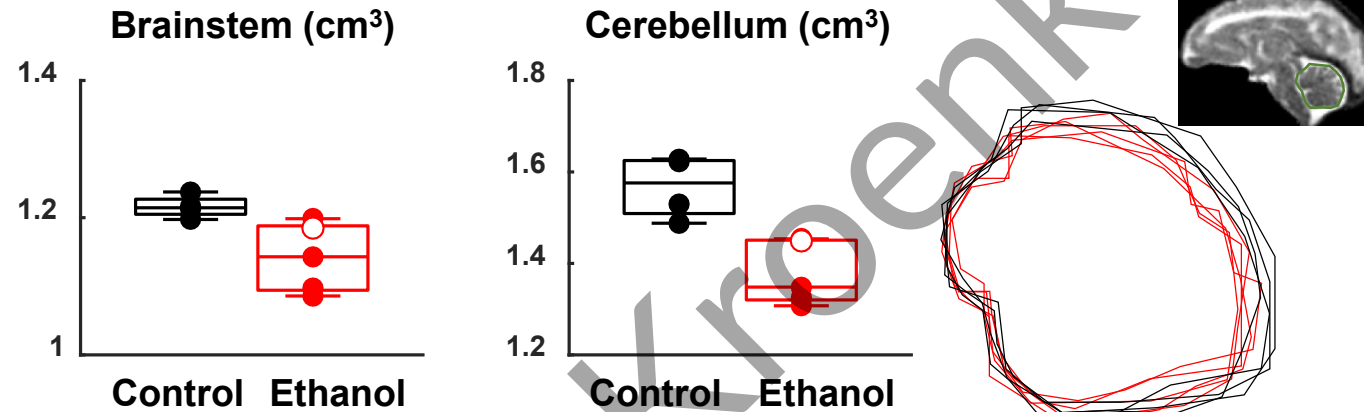
G110



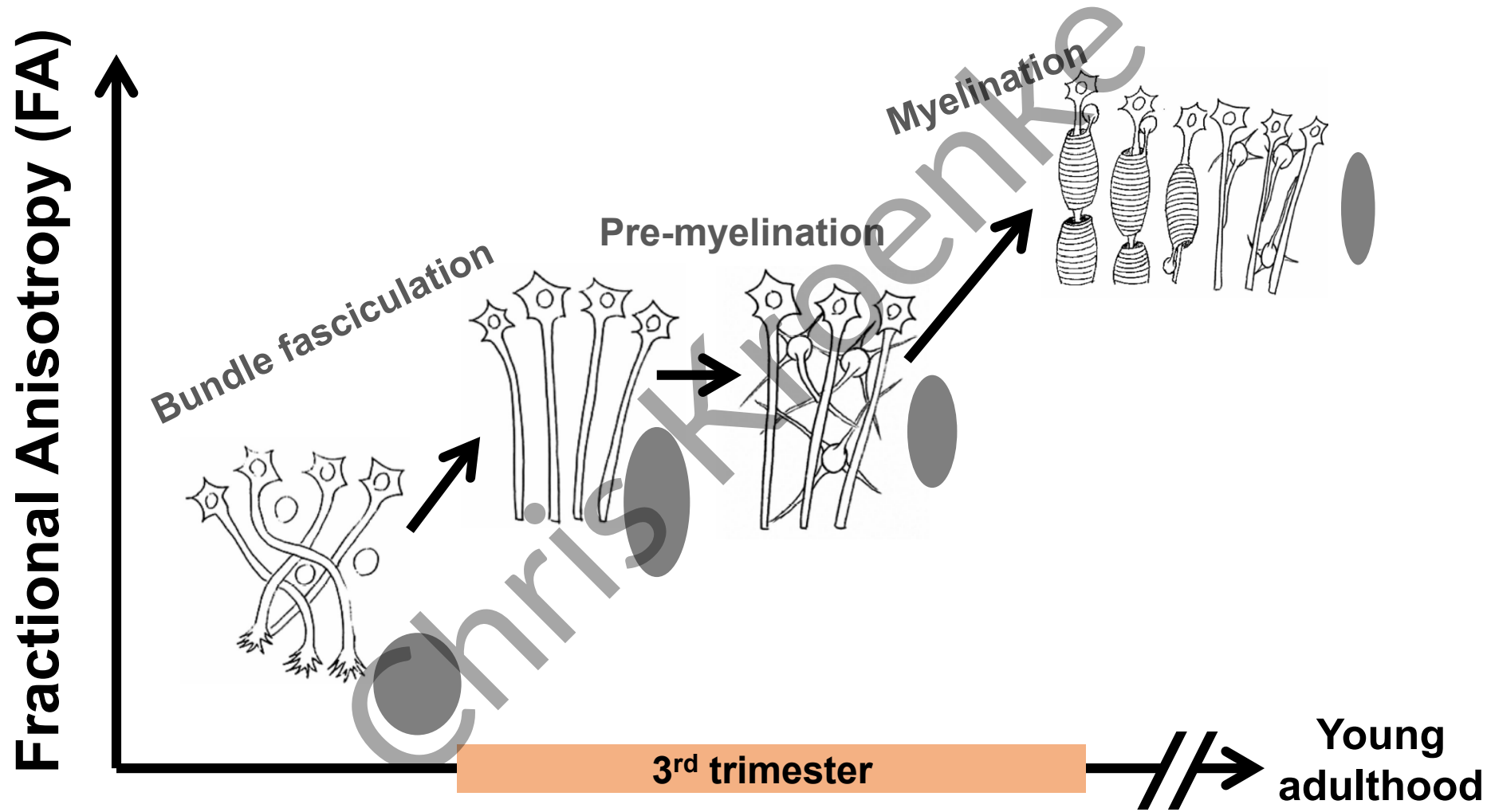
G135



# The cerebellum and brainstem are smaller in ethanol-exposed G135 fetal brains



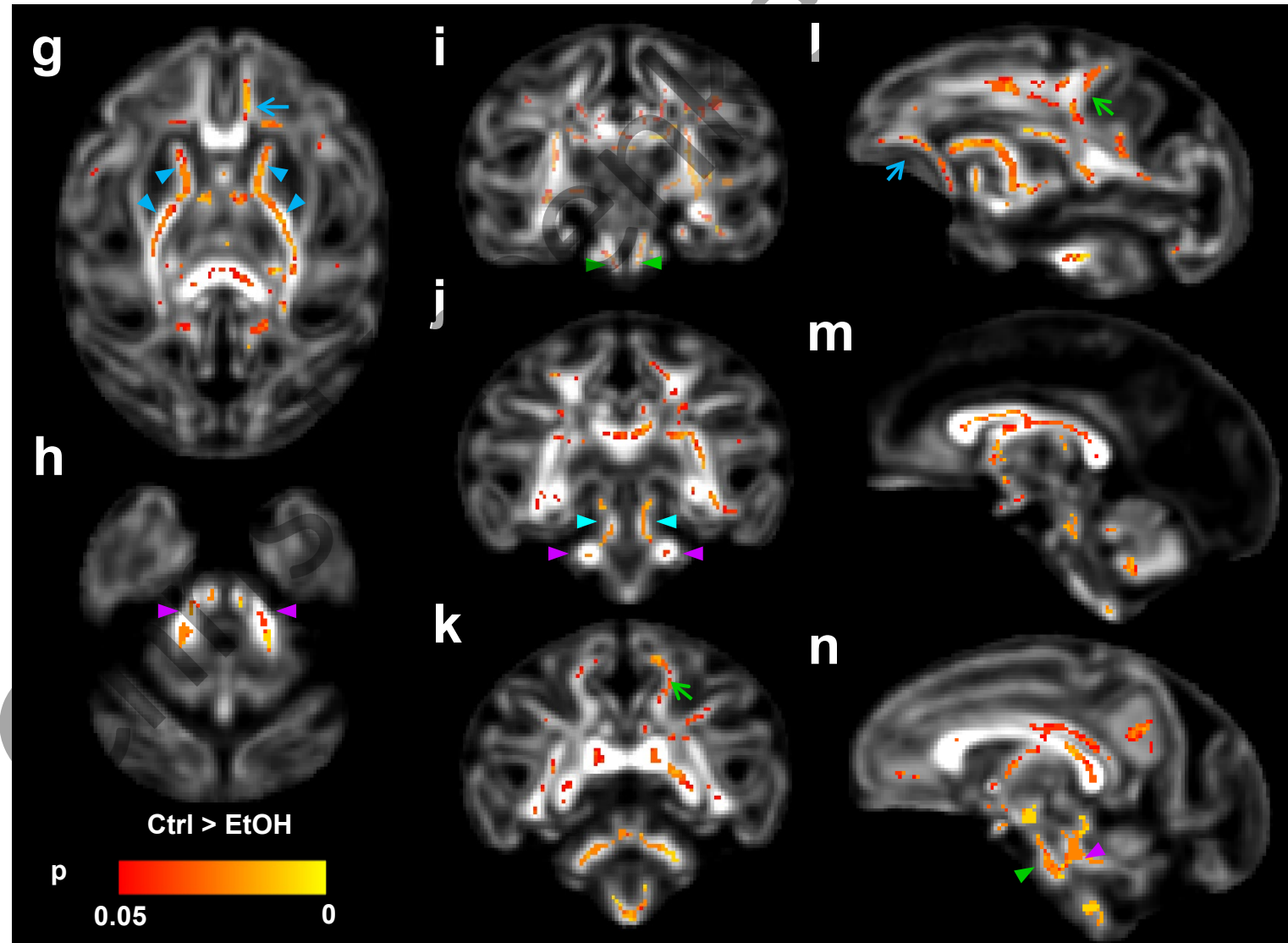
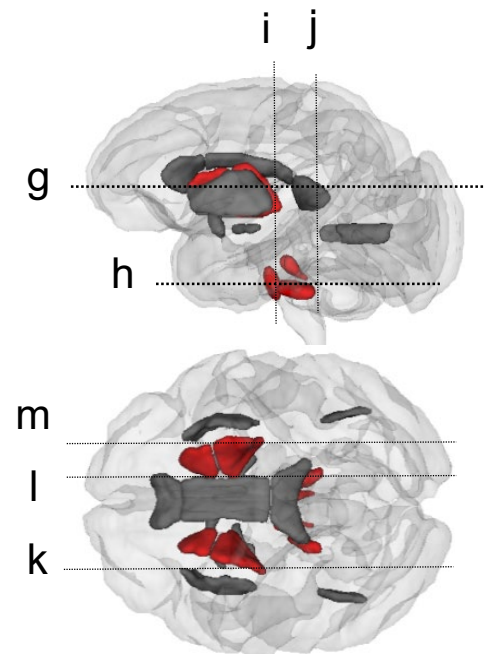
# Water diffusion anisotropy and WM maturation



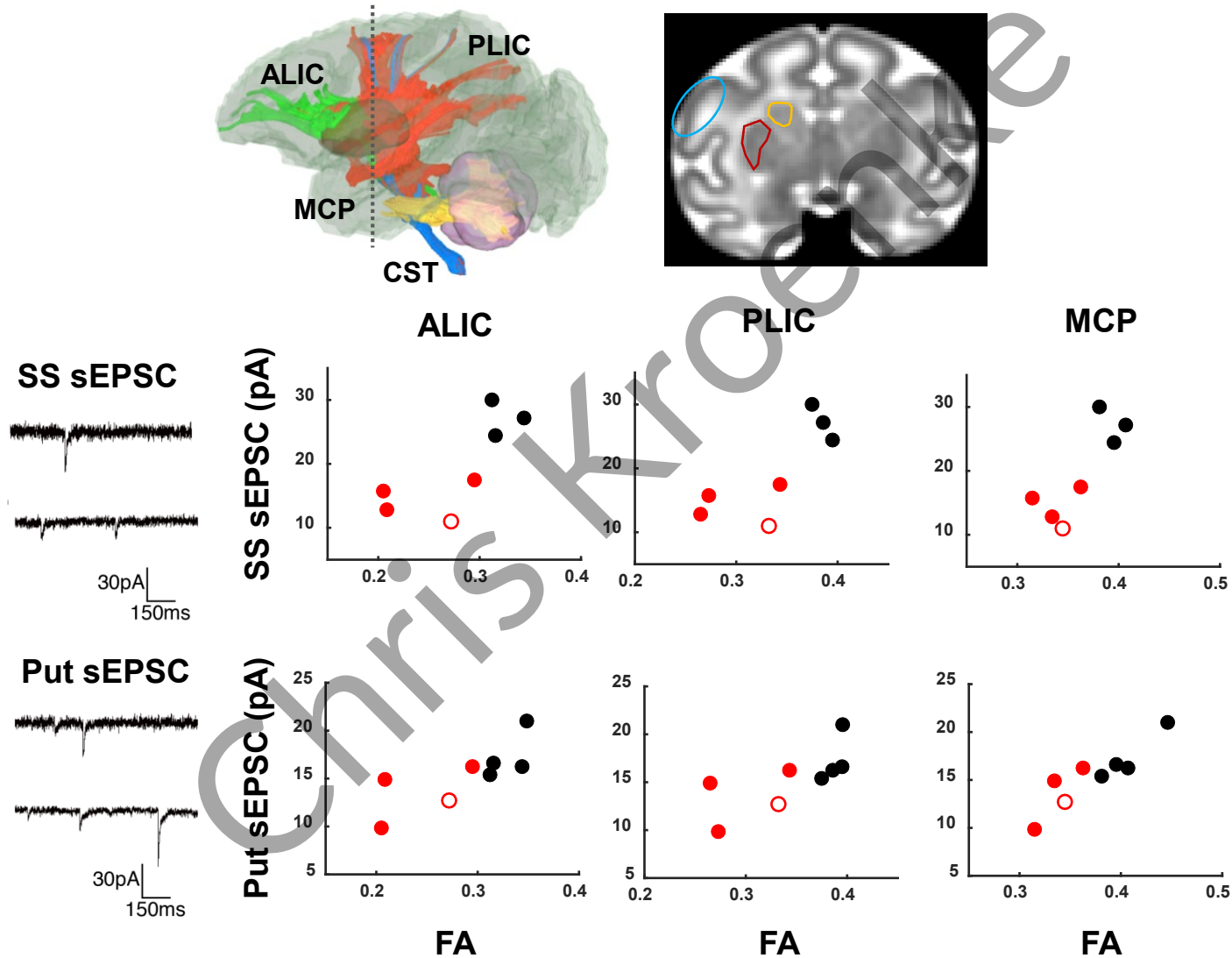
Dubois et al., *Hum. Brain Mapp.* 29:14-27 (2008)

ZaninE et al., *Brain. Behav.* 2:95-108 (2012)

# Voxel-wise analysis of regions with reduced FA due to ethanol exposure



# Reduced FA is associated with functional abnormalities



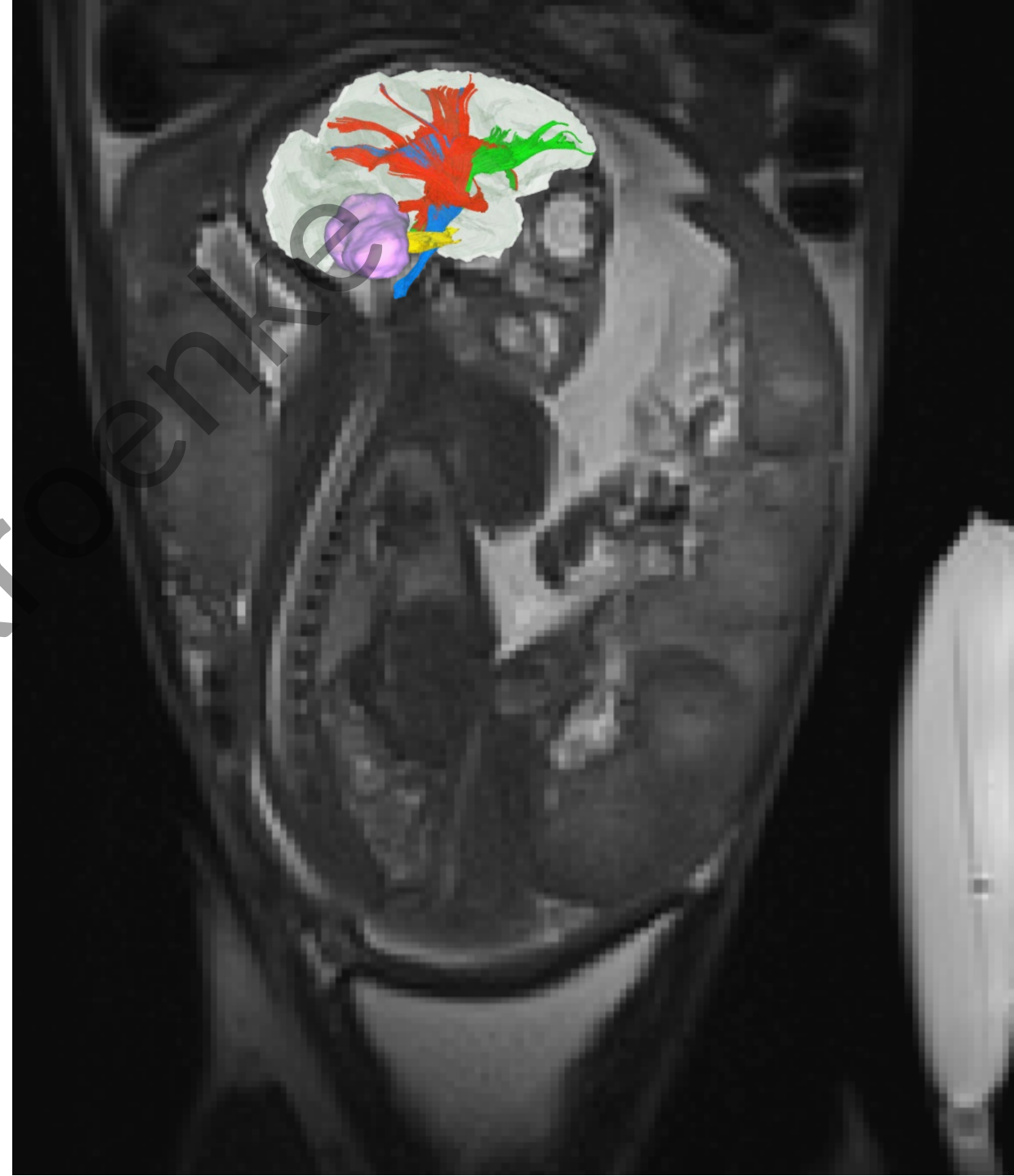
# Summary

Survey of fetal MRI capabilities  
(and validation with rhesus monkeys)

- Growth: volume vs. age
- Lung maturation
- Fetal cardiac
- Placental function

Rhesus brain development

- Retrospective motion correction
- Precise experimental control relative to gestational timing
- Template images available
- Fetal alcohol exposure affect motor-related growth and maturation



# Acknowledgements



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Eric Baetscher

Connor Hiltz



*Eunice Kennedy Shriver* National Institute of Child Health and Human Development



National Institute of Neurological Disorders and Stroke



National Institute on Alcohol Abuse and Alcoholism



International Society for Magnetic Resonance in Medicine  
Workshop (Denver, Colorado, USA, September 2024)

# Unlocking the Potential of Prenatal MRI: Advances in Fetal Brain, Heart, & Placenta Imaging

Mehdi H. Moghari, Ph.D., University of Colorado

David Lloyd, Ph.D., Kings College London

Christopher Macgowan, Ph.D., University of Toronto

Chris Kroenke, Ph.D., Oregon Health & Science University

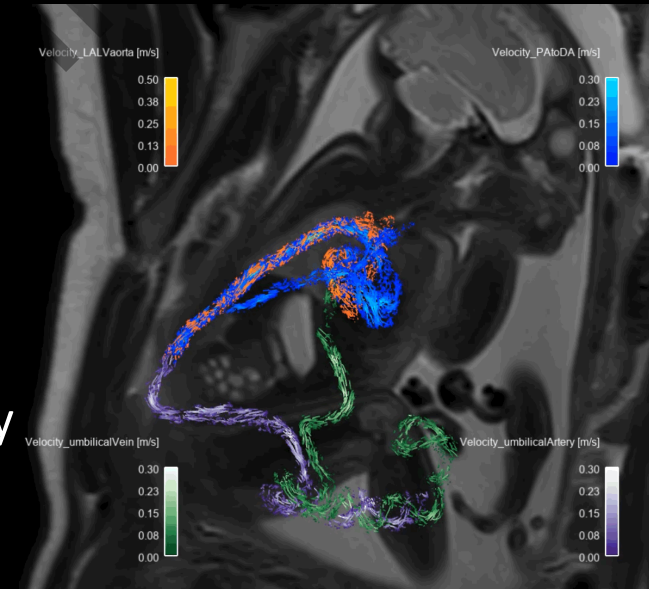


Image Courtesy of Dr. Erin Englund



Children's Hospital Colorado  
University of Colorado  
Aurora, CO, USA

