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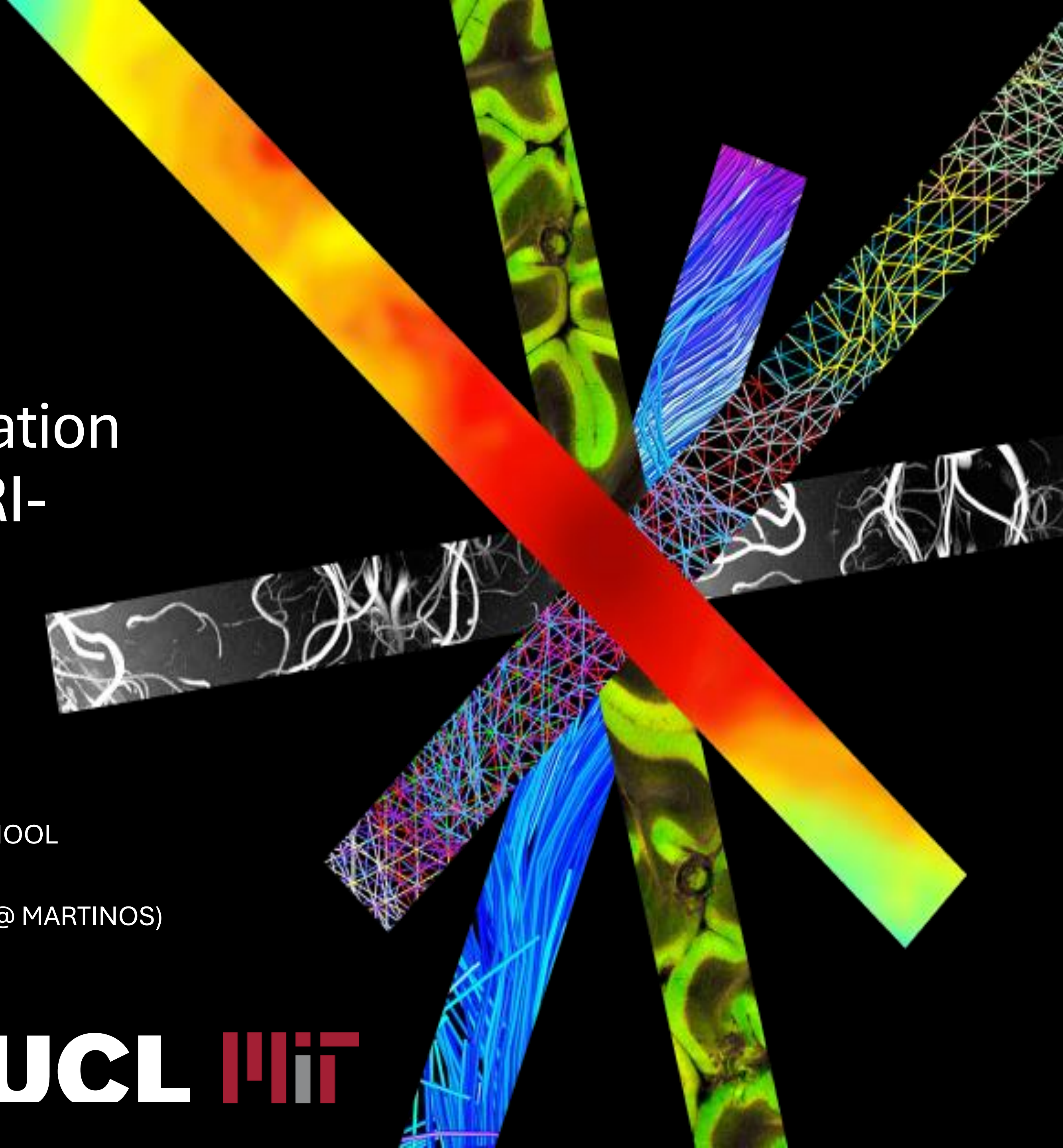

3D Reconstruction and Segmentation of Dissection Photographs for MRI-Free “Neuropathometry”

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ACT RESEARCH SYMPOSIUM, SEATTLE, MAY 14TH, 2025

UCL

Outline

- Introduction
- Data acquisition and preprocessing
- Data processing
- Discussion

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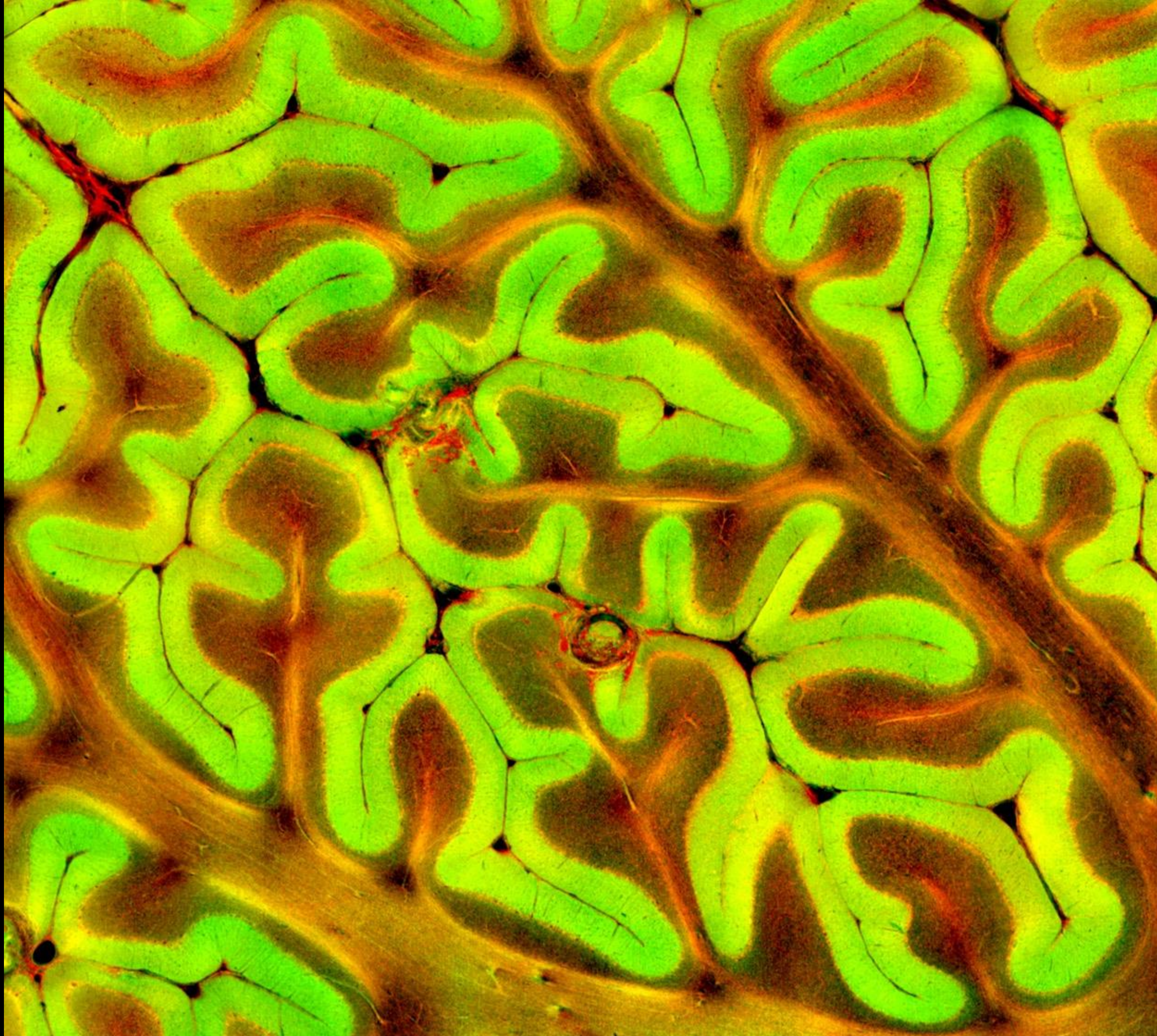
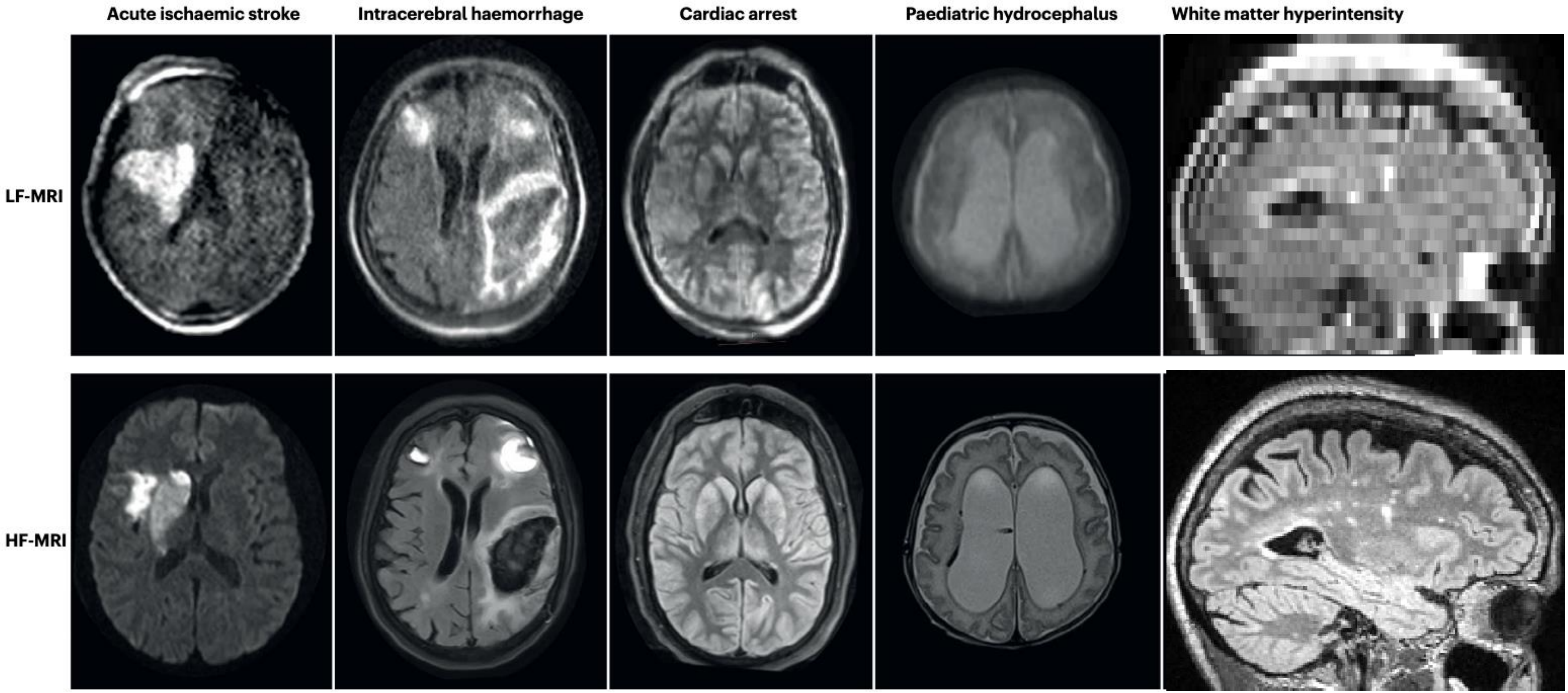
INTRODUCTION



3D characterization of postmortem brains

- In vivo MRI (if you are lucky!)
- Cadaveric MRI
  - Relatively easy, especially if body is still warm.
  - Requires fast access to MRI scanner
- Ex vivo MRI
  - Requires niche expertise
  - Tissue must be fixed
- Portable MRI (e.g., Hyperfine)
  - Cheap, accessible, no special shielding/power requirements.
  - If you time it right, you can scan fresh!
  - You get what you pay for (64 mT, 1.5 x 1.5 x 5.0 mm)

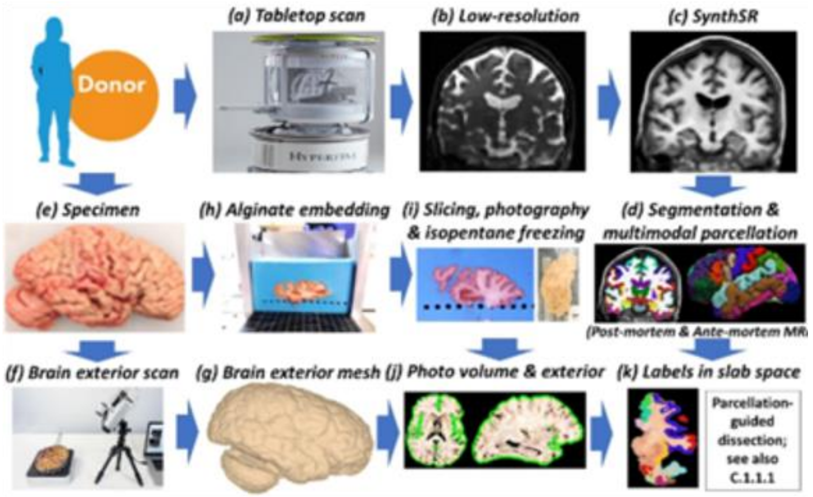
3D characterization of postmortem brains



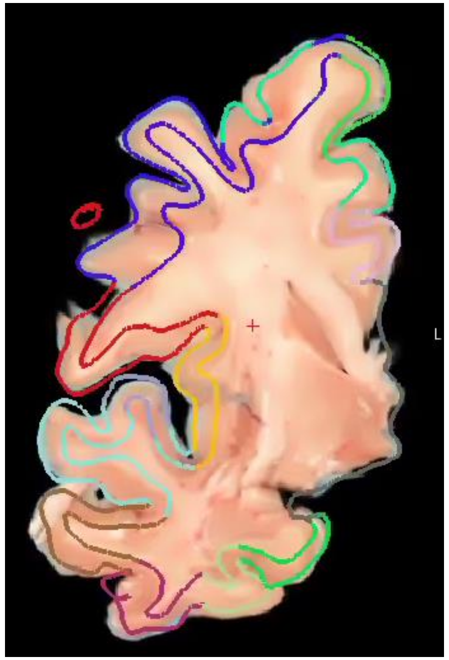
Kimberly et al., Nat Rev Bioeng, 2023

3D characterization of postmortem brains

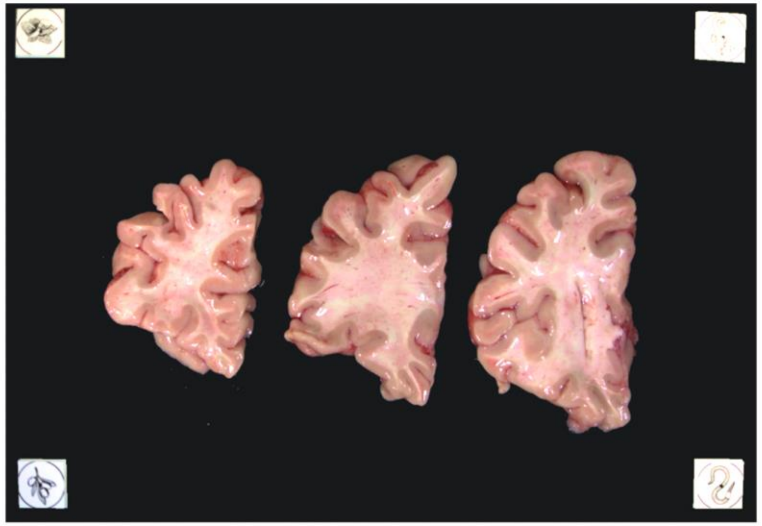
- Dissection photography of coronal slabs.
  - Routine, cheap.
  - 2D: hard to obtain 3D segmentations, cortical parcellation, volumes, etc.
- Why not assembling the photographs into a 3D volume, ala 2D MRI?
  - Potential for 3D morphometry (segmentation, parcellation, etc).
  - Computationally guided dissection (useful even if MRI is available).



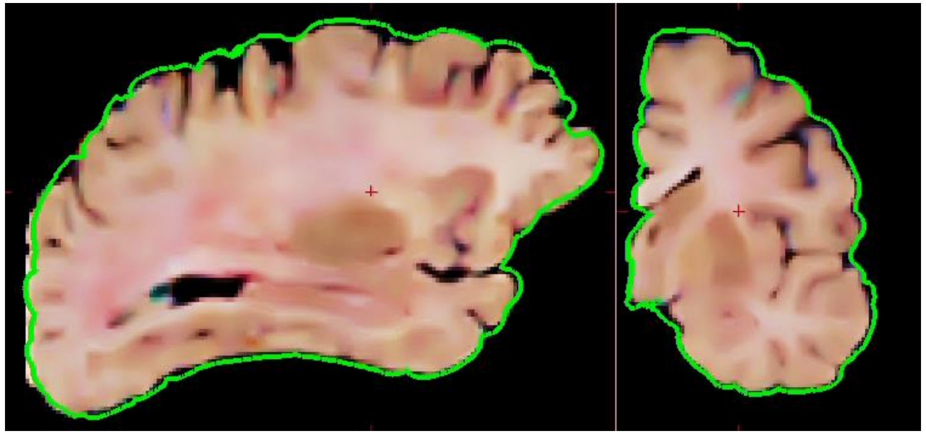
BRAIN Initiative 1UM1MH130981: “Functionally guided adult whole brain cell atlas in human and non-human primates”

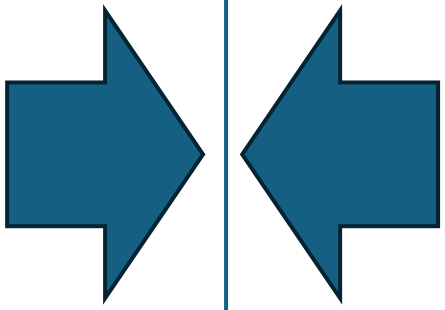


General idea: data and objectives

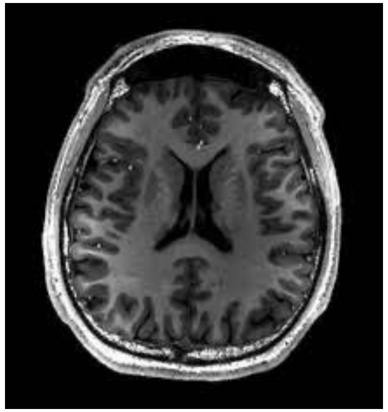


Dissection photos (fixed or fresh tissue)

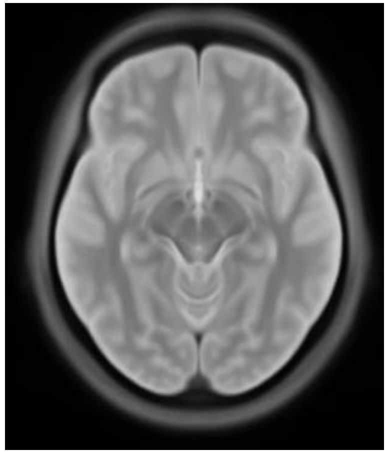




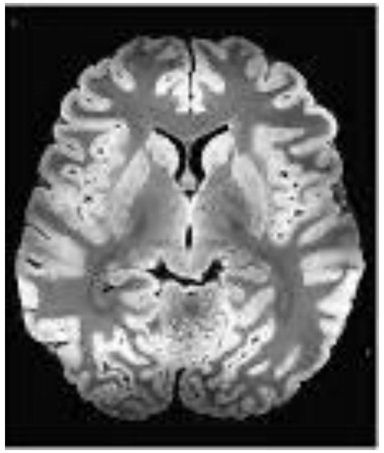
Surface scan



Brain MRI (pre-mortem, cadaveric)



Brain atlas



Brain MRI (ex vivo)

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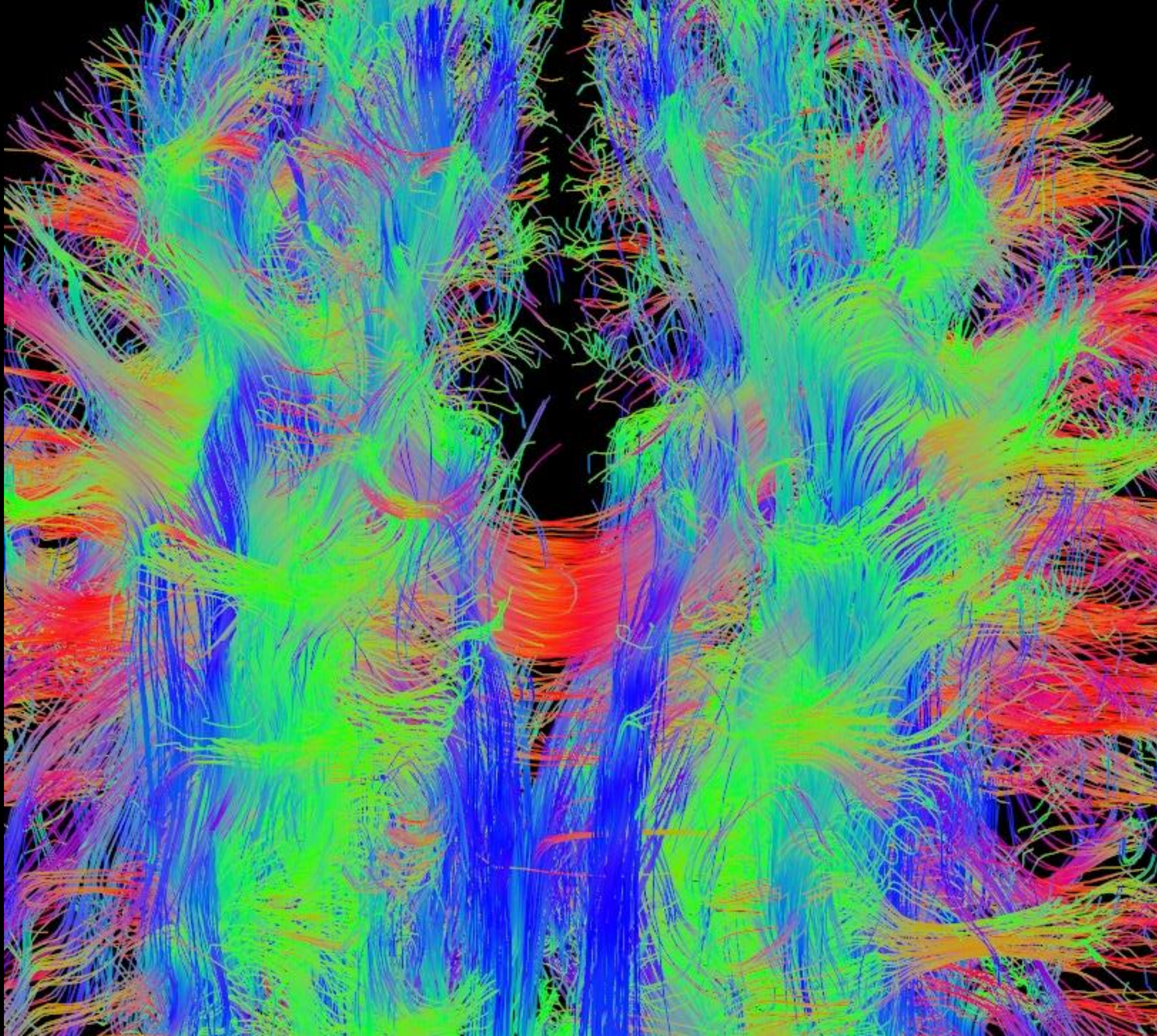
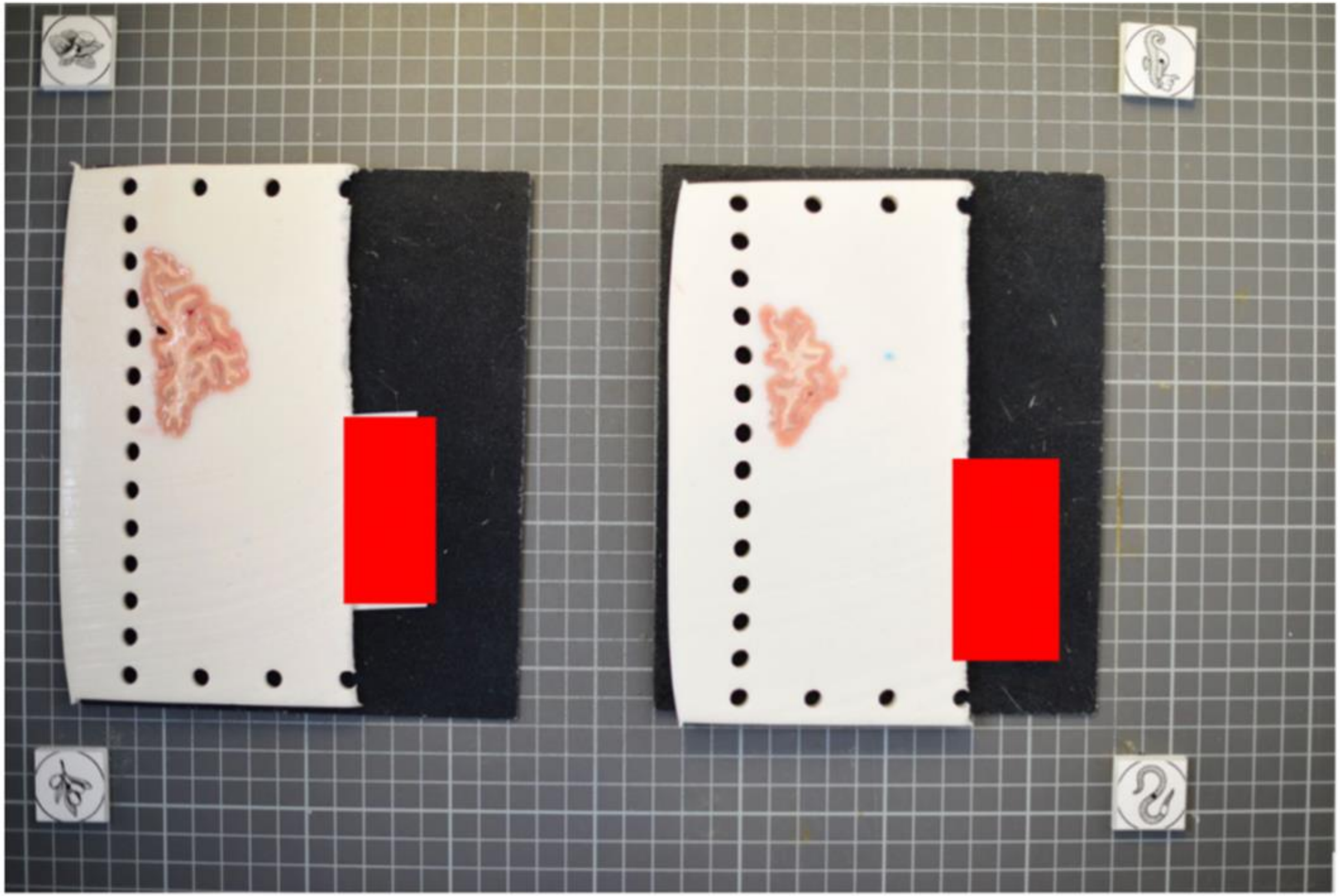
DATA ACQUISITION AND PREPROCESSING



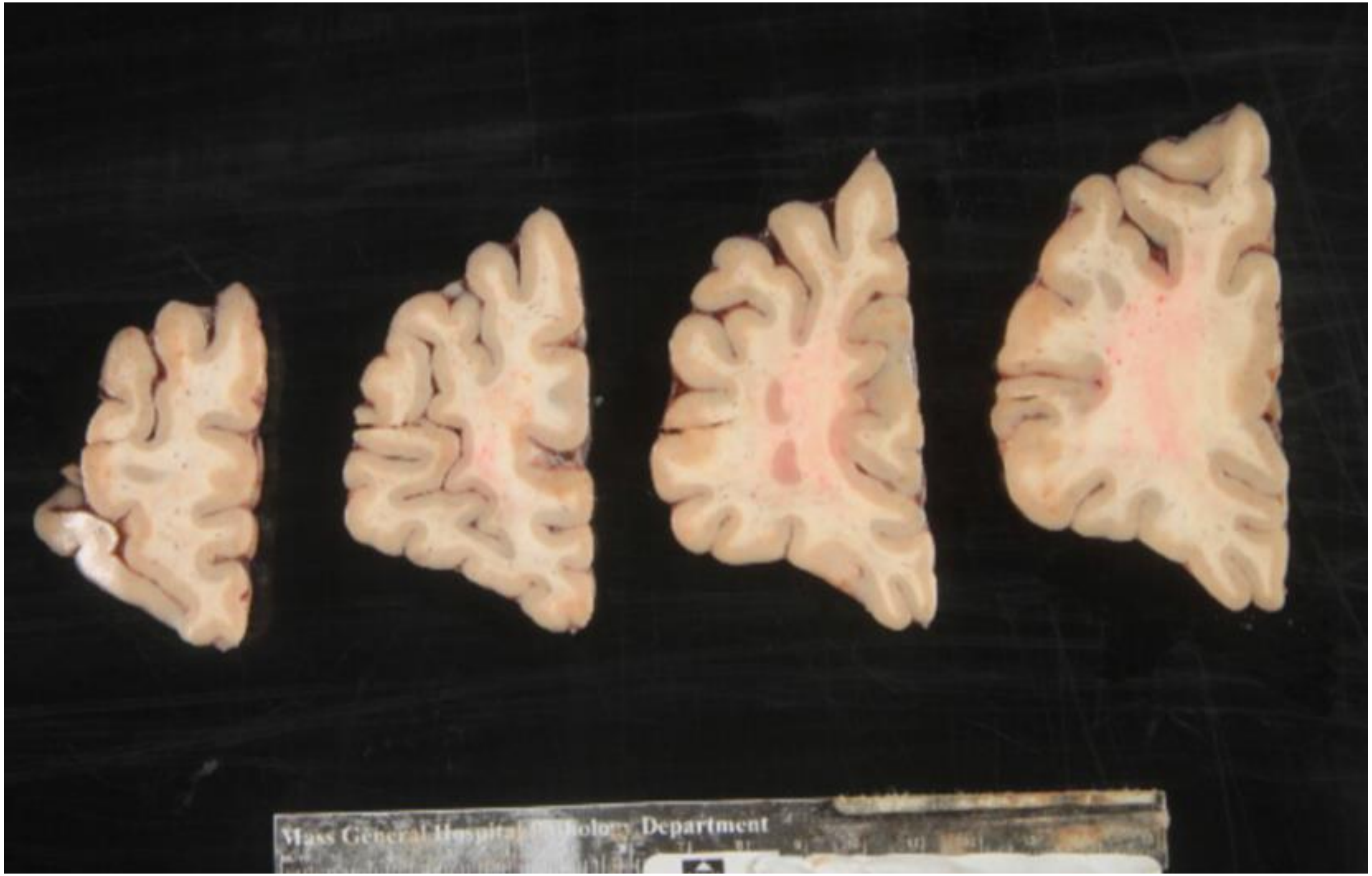
Slab photos requirements

- Minimum requirements: no occlusions, presence of ruler.
- Only anterior or posterior photos required.
- Make your life easier!
  - Use fiducials (enable automated correction mode).
  - Use a high-contrast background and avoid reflections.
  - If a slab comprises multiple chunks or is deformed, try to preserve its original shape.

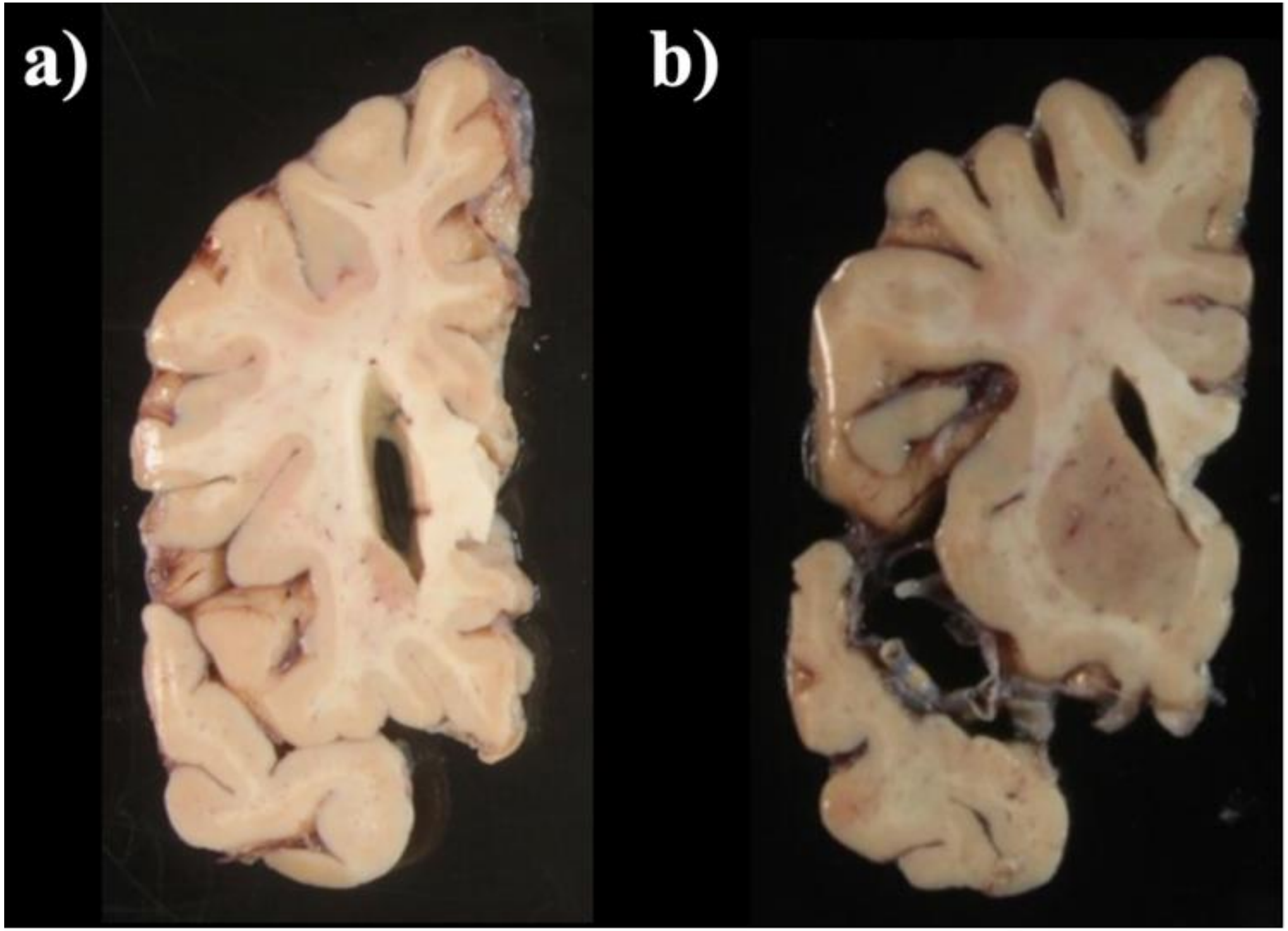
Slab photo requirements



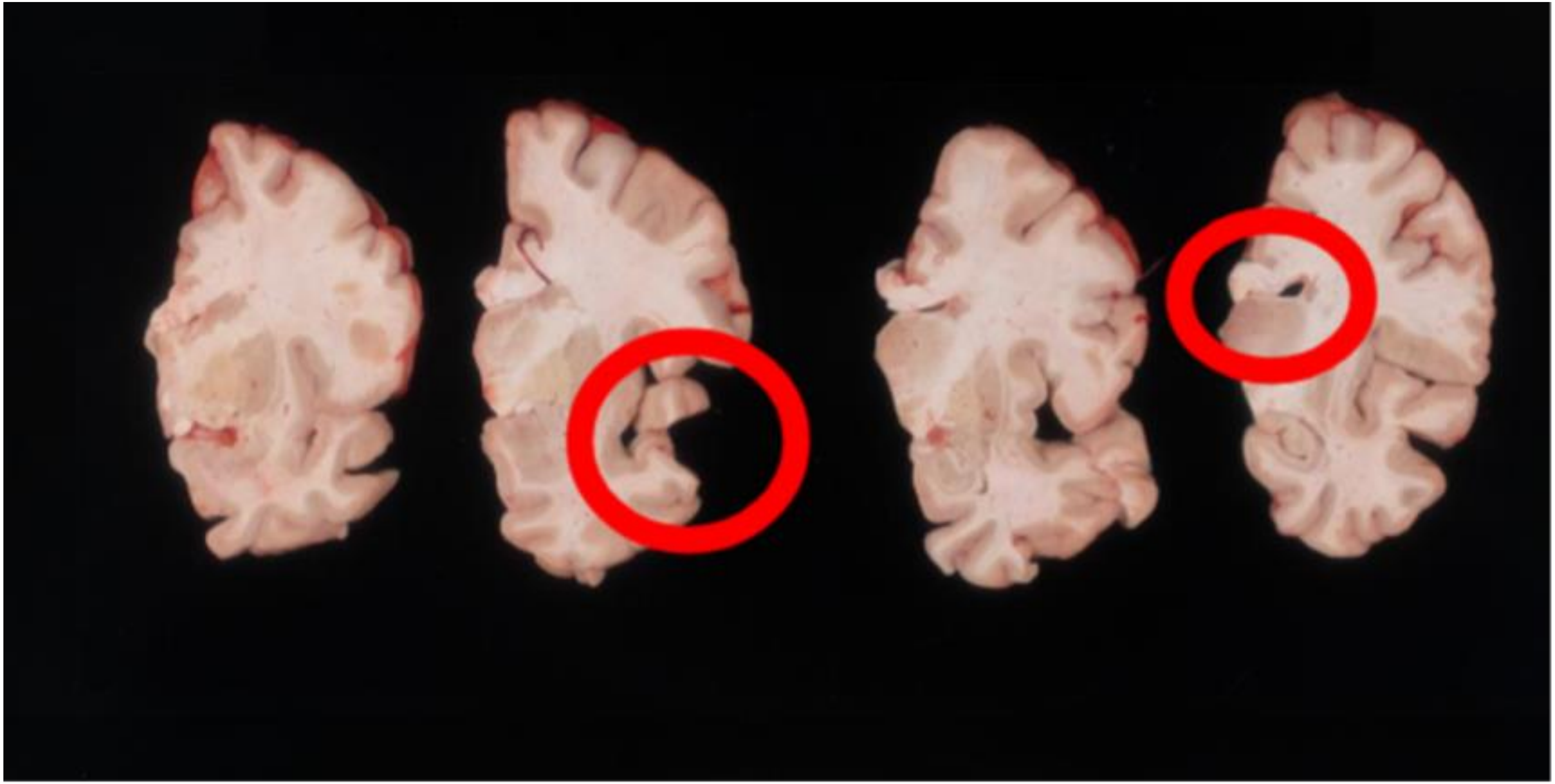
Slab photo requirements



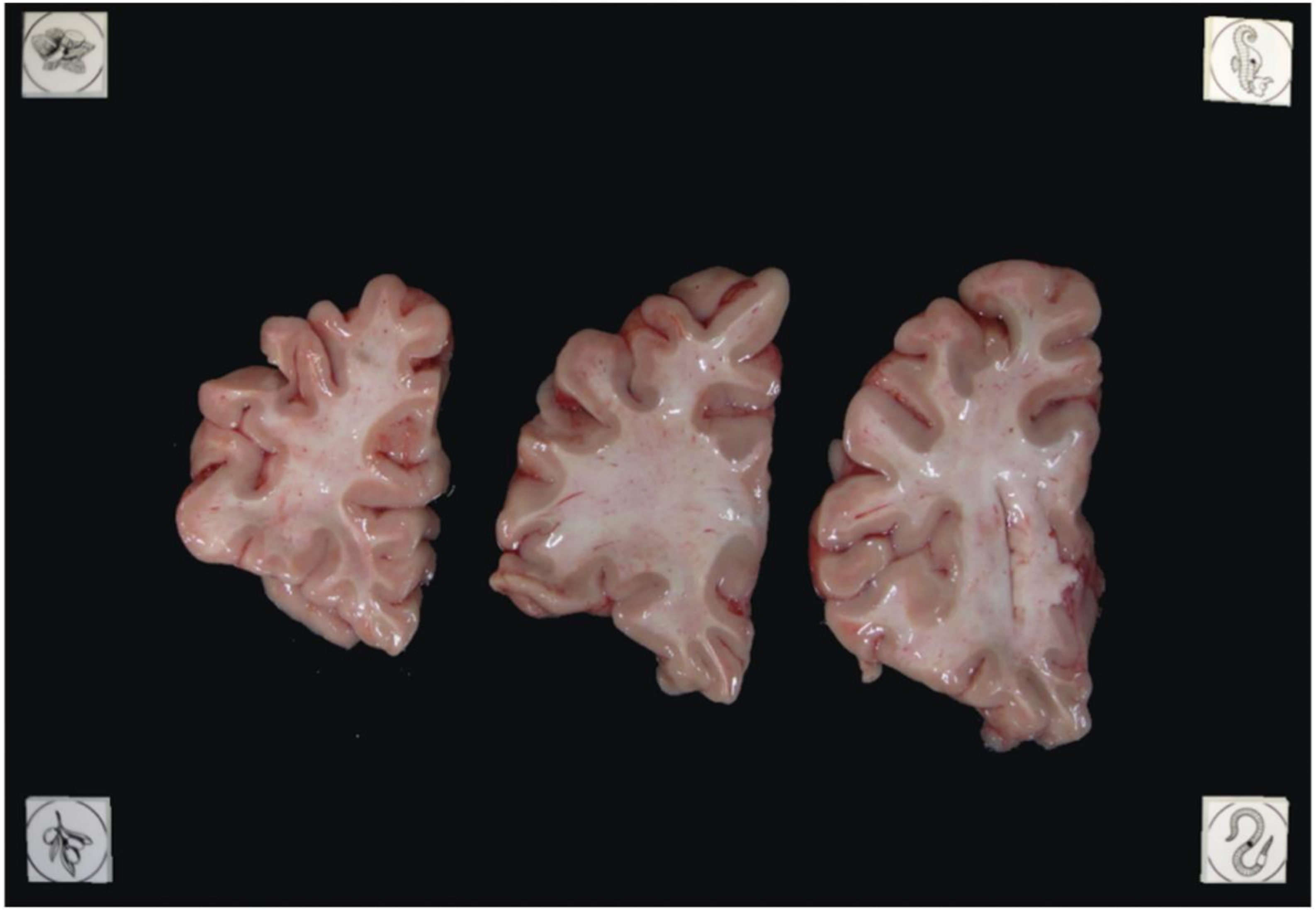
Slab photo requirements



Slab photo requirements

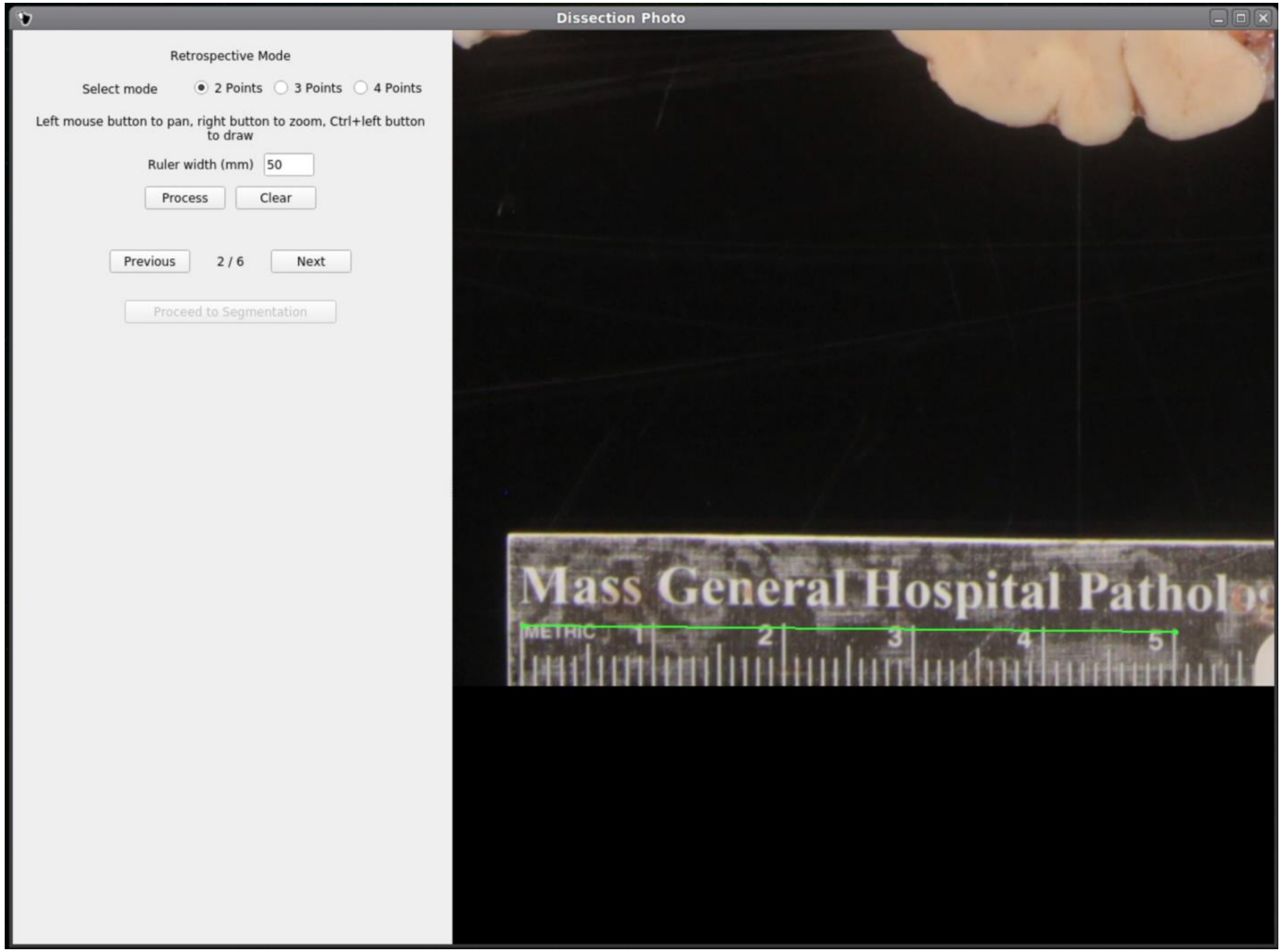


Slab photo requirements



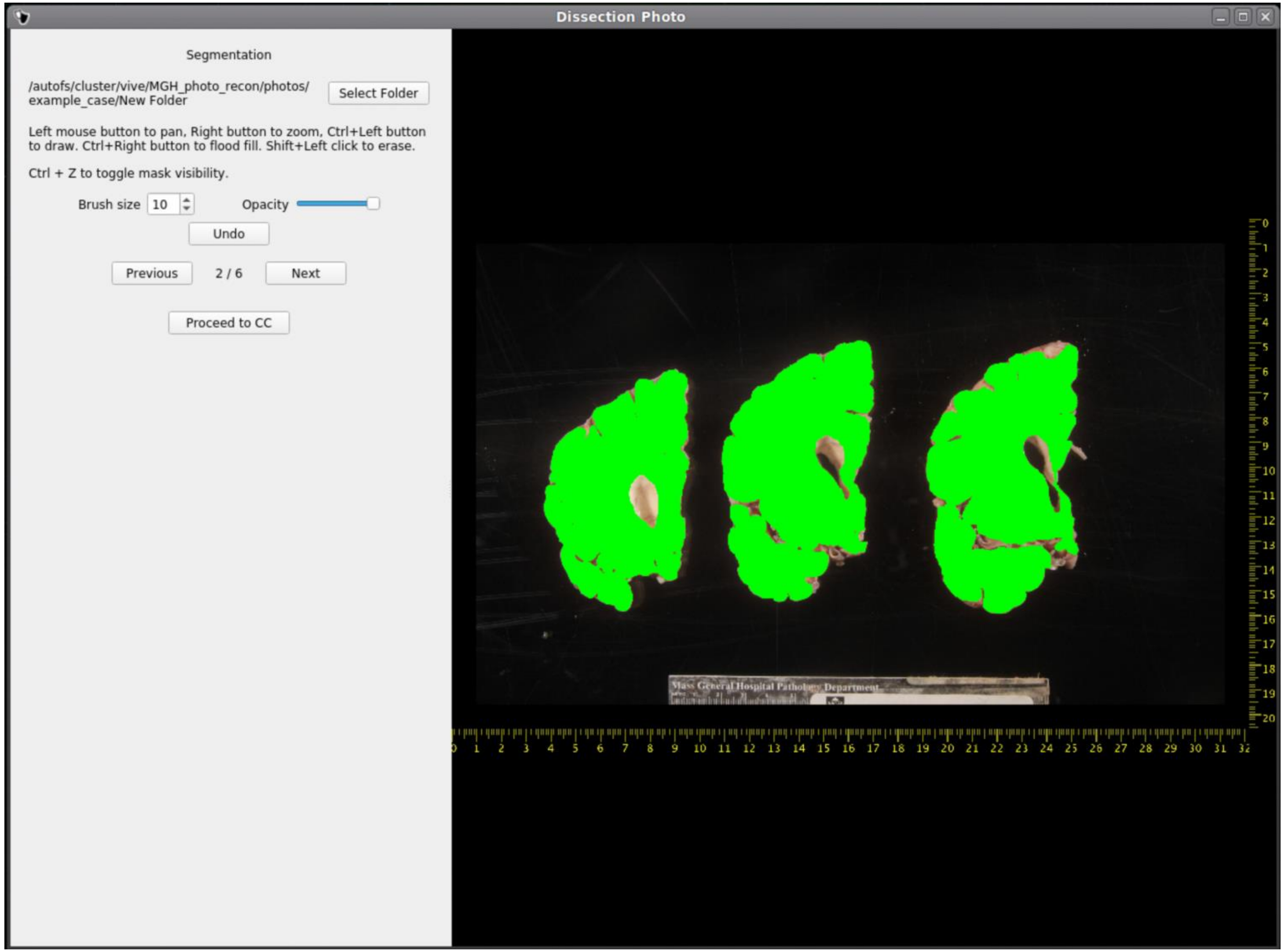
Slab photo processing with GUI

- Correction for pixel size and perspective:
  - Ruler (2 clicks)
  - Grid (3 or 4 clicks), or fiducial (no clicks).



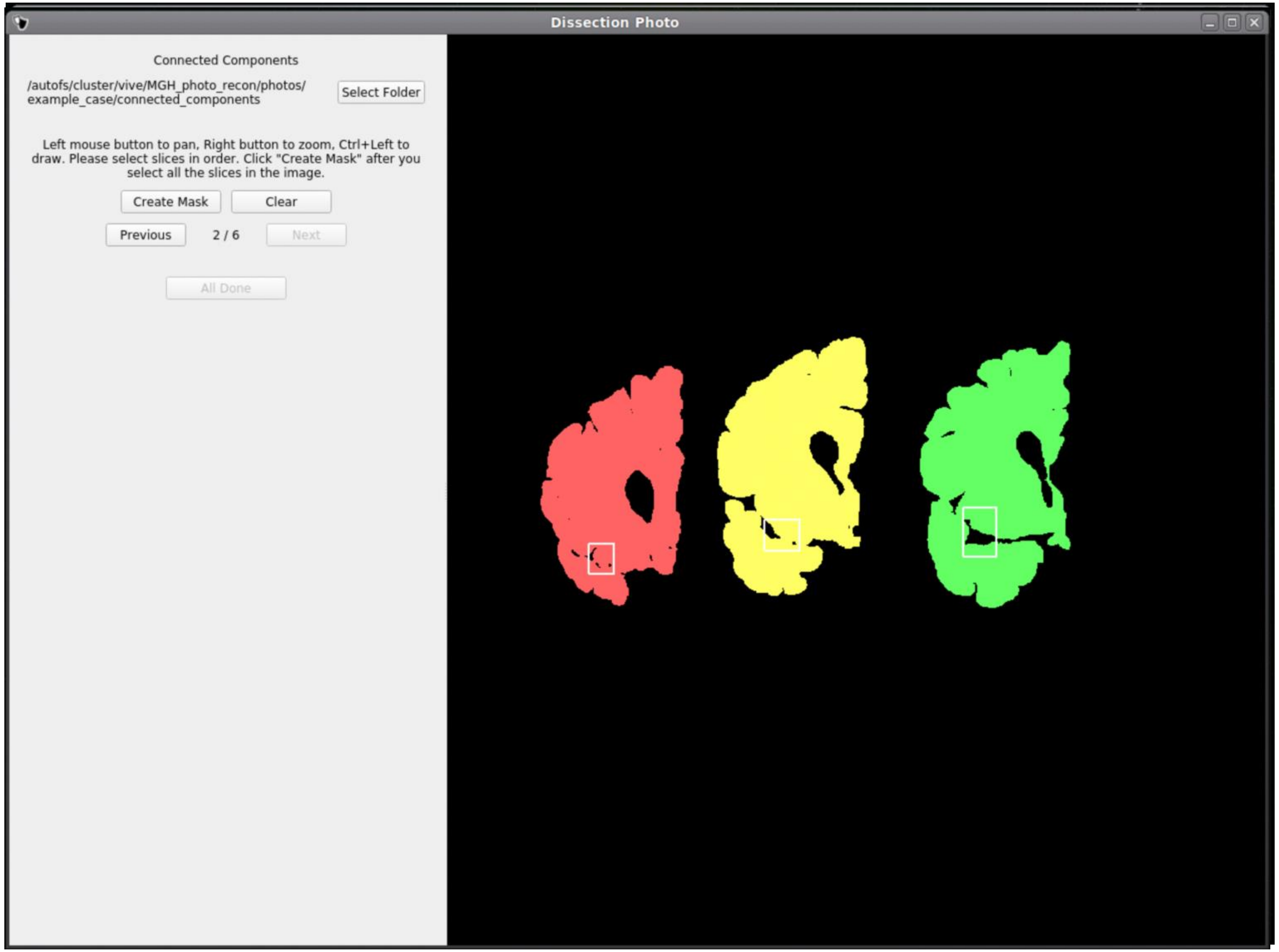
Slab photo processing with GUI

- Segmentation:
  - Automated with deep neural network.
  - Can be edited in the GUI

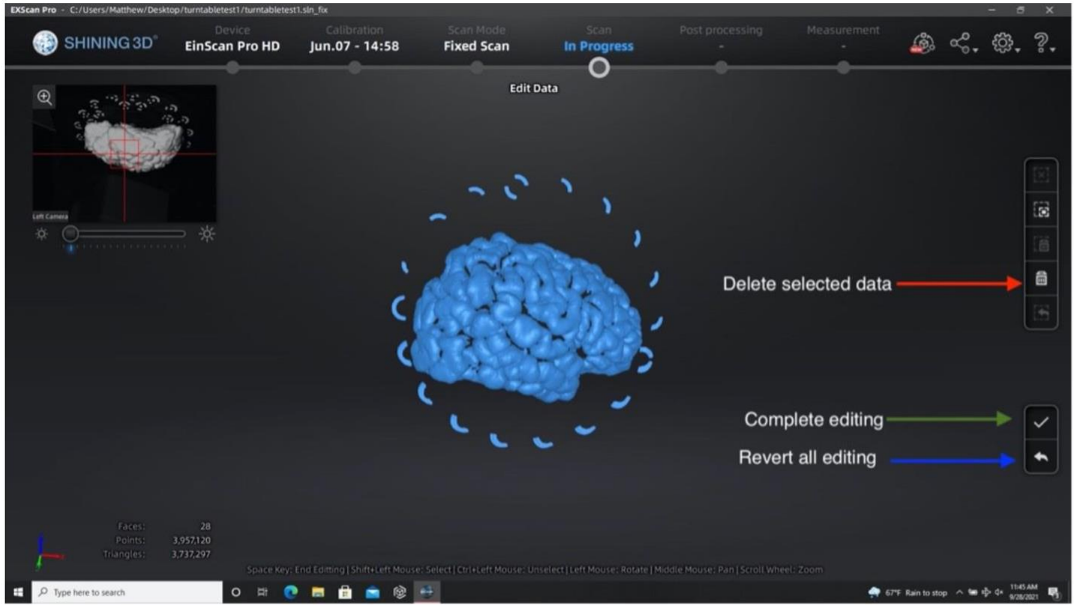


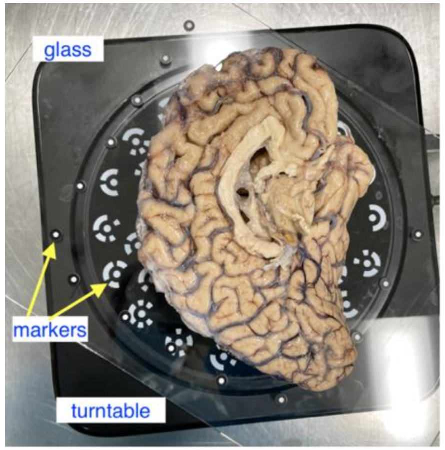
Slab photo processing with GUI

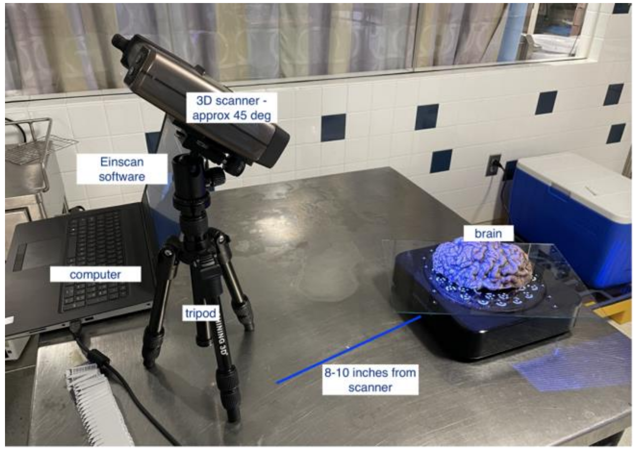
- Ordering and connected components:
  - Go over slabs, clicking on them in order.
  - Option to group disconnected components into single slabs.
  - Also serves as QC.



Acquisition of surface scan (optional)







https://surfer.nmr.mgh.harvard.edu/fswiki/PhotoTools

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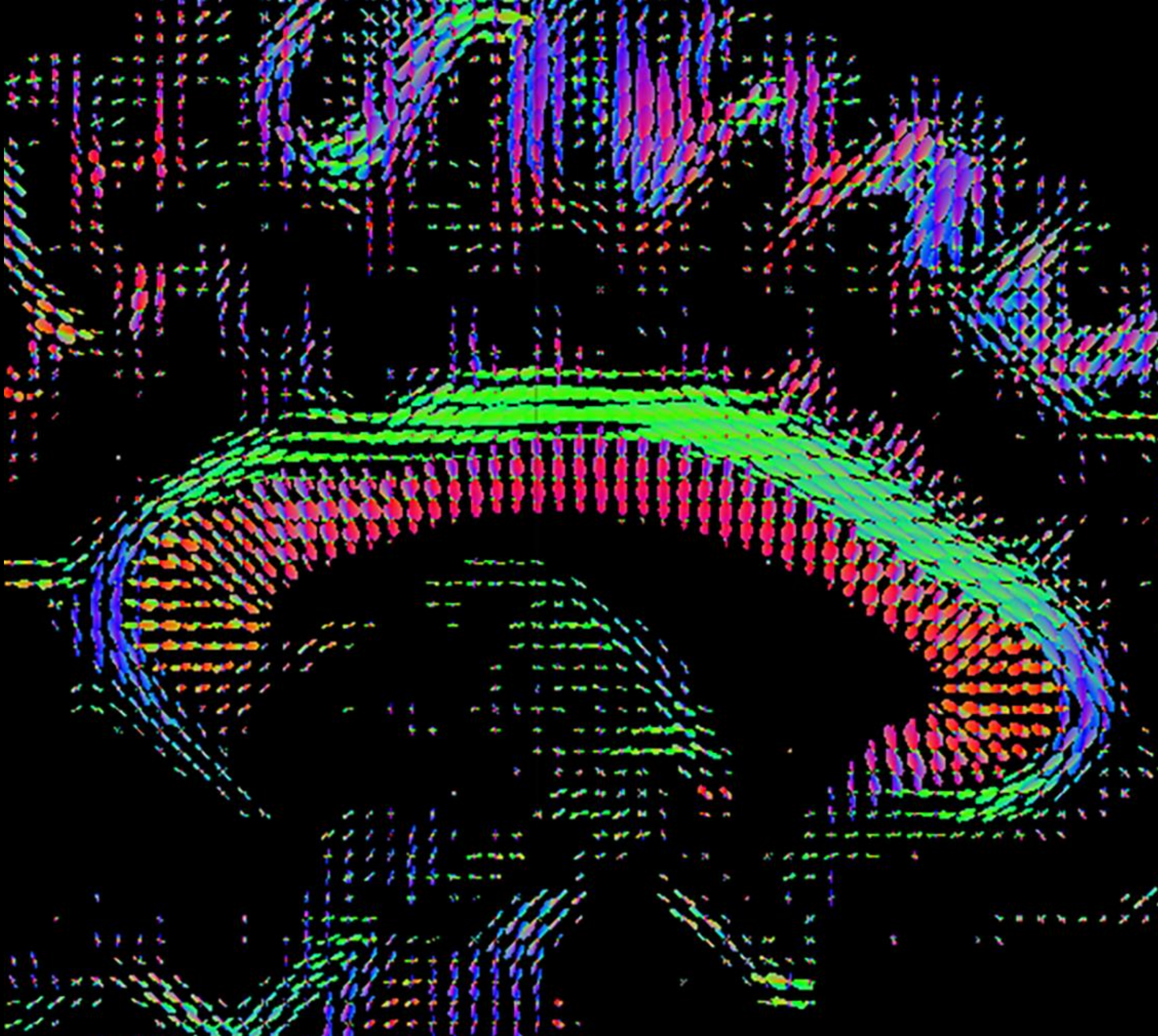
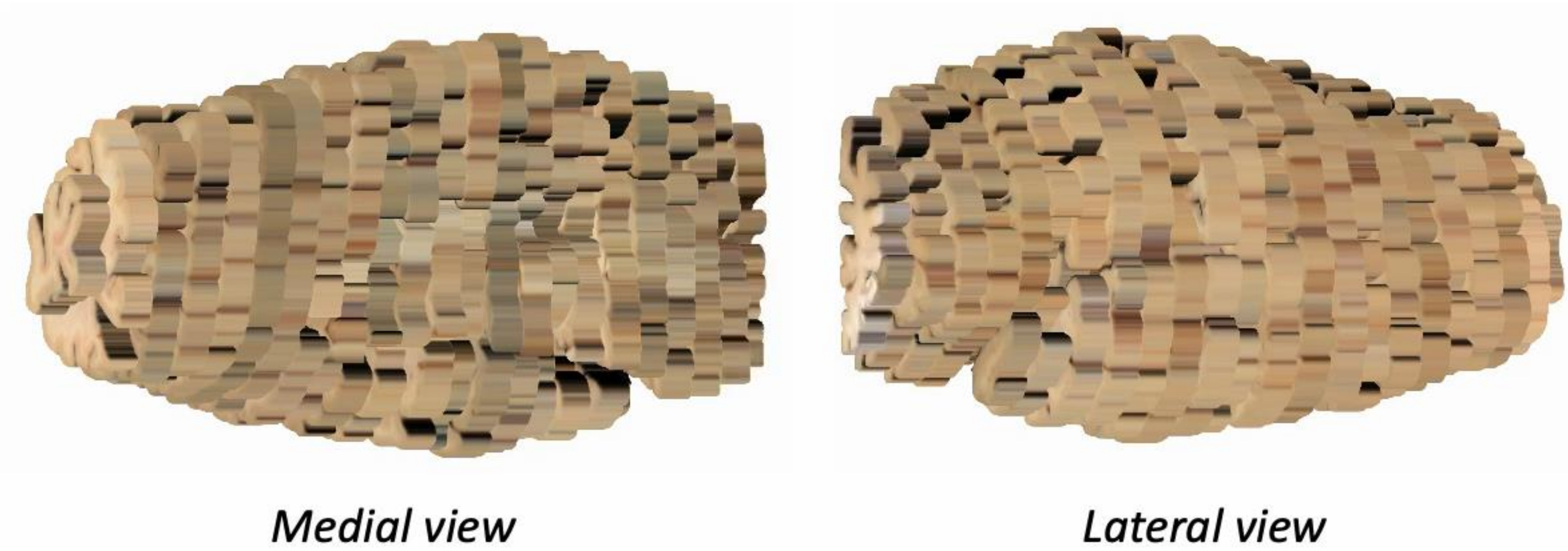
DATA PROCESSING



3D reconstruction code



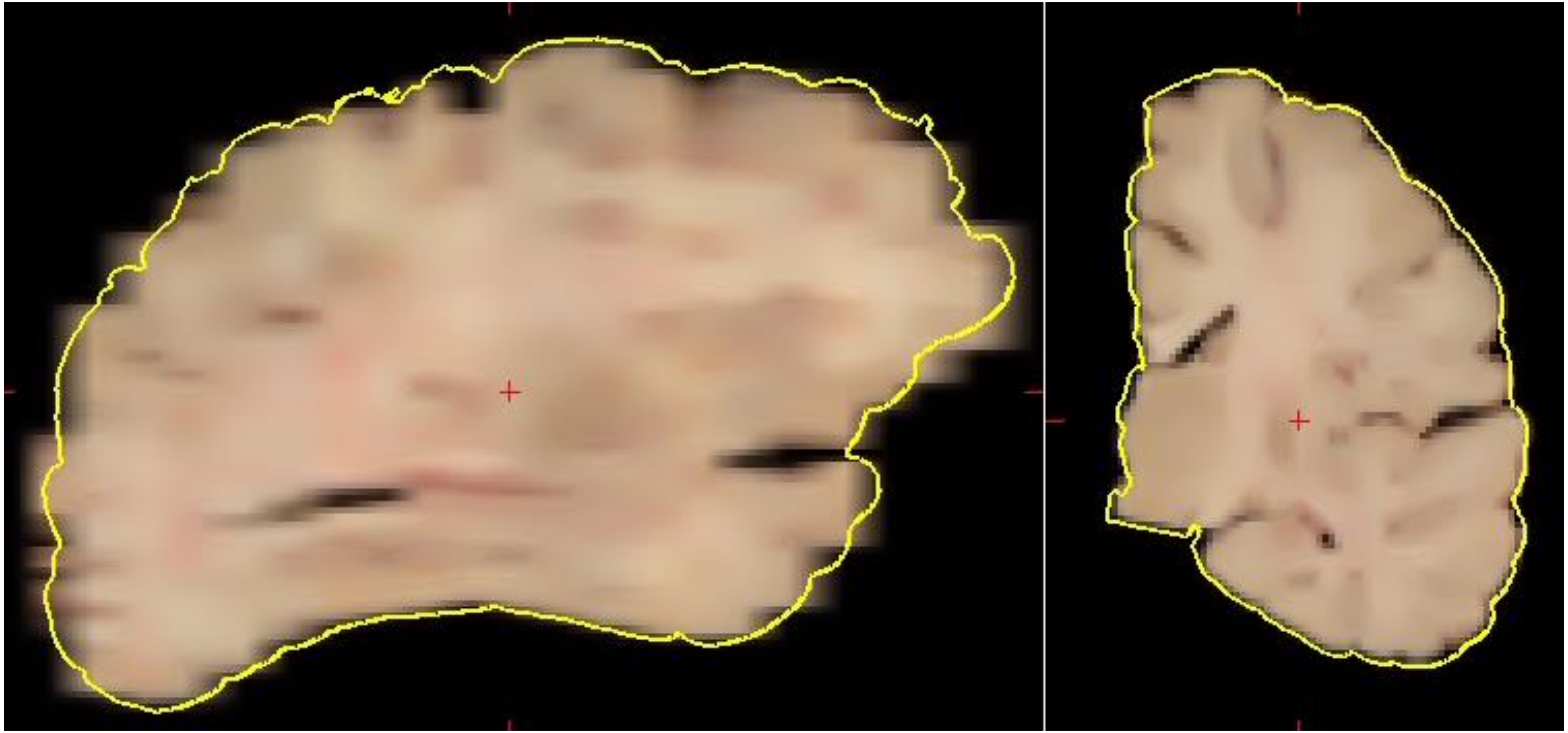
Kimberly et al., Nat Rev Bioeng, 2023

3D reconstruction code

- Recently made available on development version of FreeSurfer.
    - Documentation available in wiki: https://surfer.nmr.mgh.harvard.edu/fswiki/mri_3d_photo_recon
- Increased flexibility: uses one or multiple references in reconstruction.
    - MNI atlas / surface scan / MRI scan / combination thereof.
- Options are now self-configured, depending on type of reference and fresh/fixed.
- Faster processing.
- Supports slabs of variable thickness.
- New feature: machine learning imputation of data in between slices.
    - Greatly improves subsequent processing.

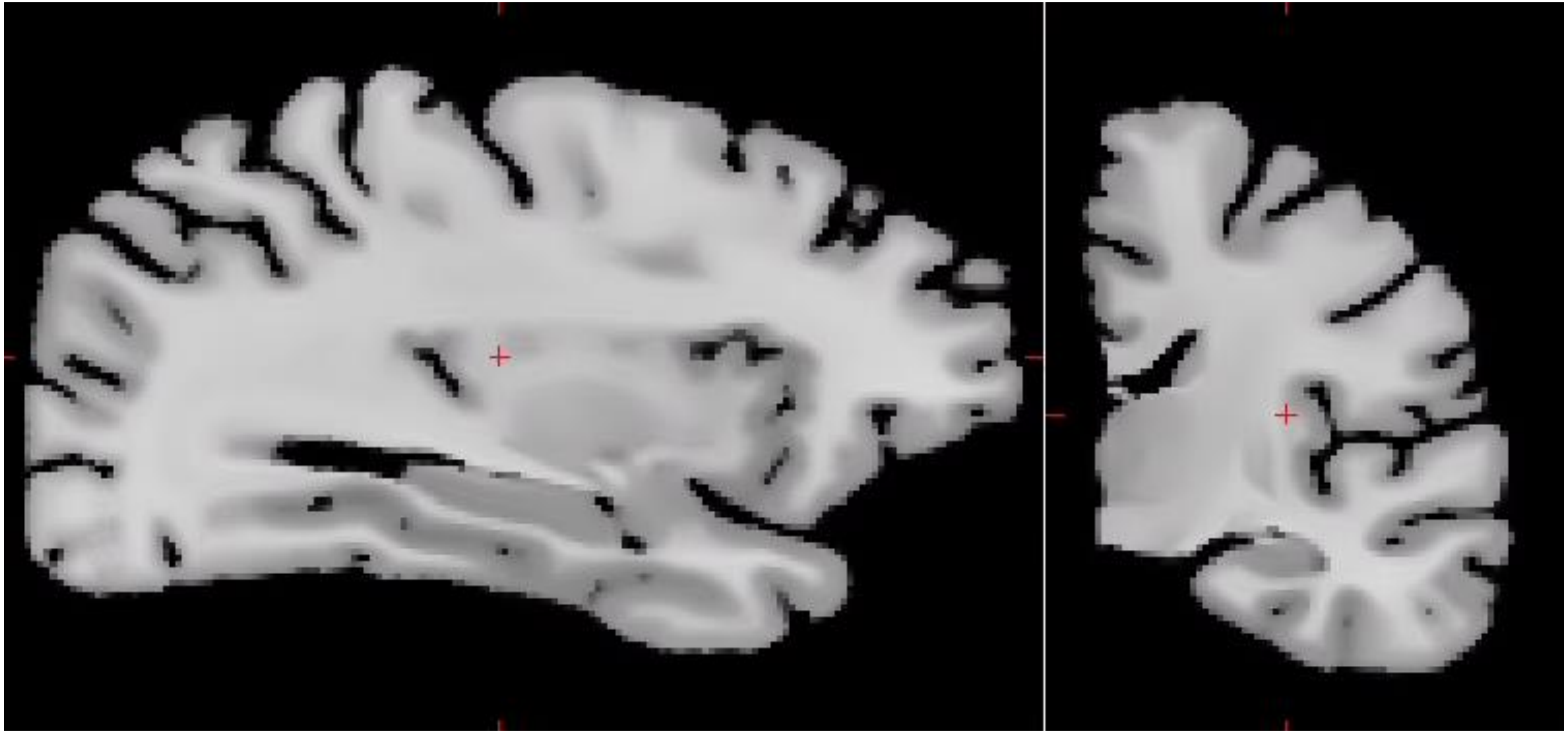
3D reconstruction code

- Reconstruction with 3D scanned surface.



3D reconstruction code

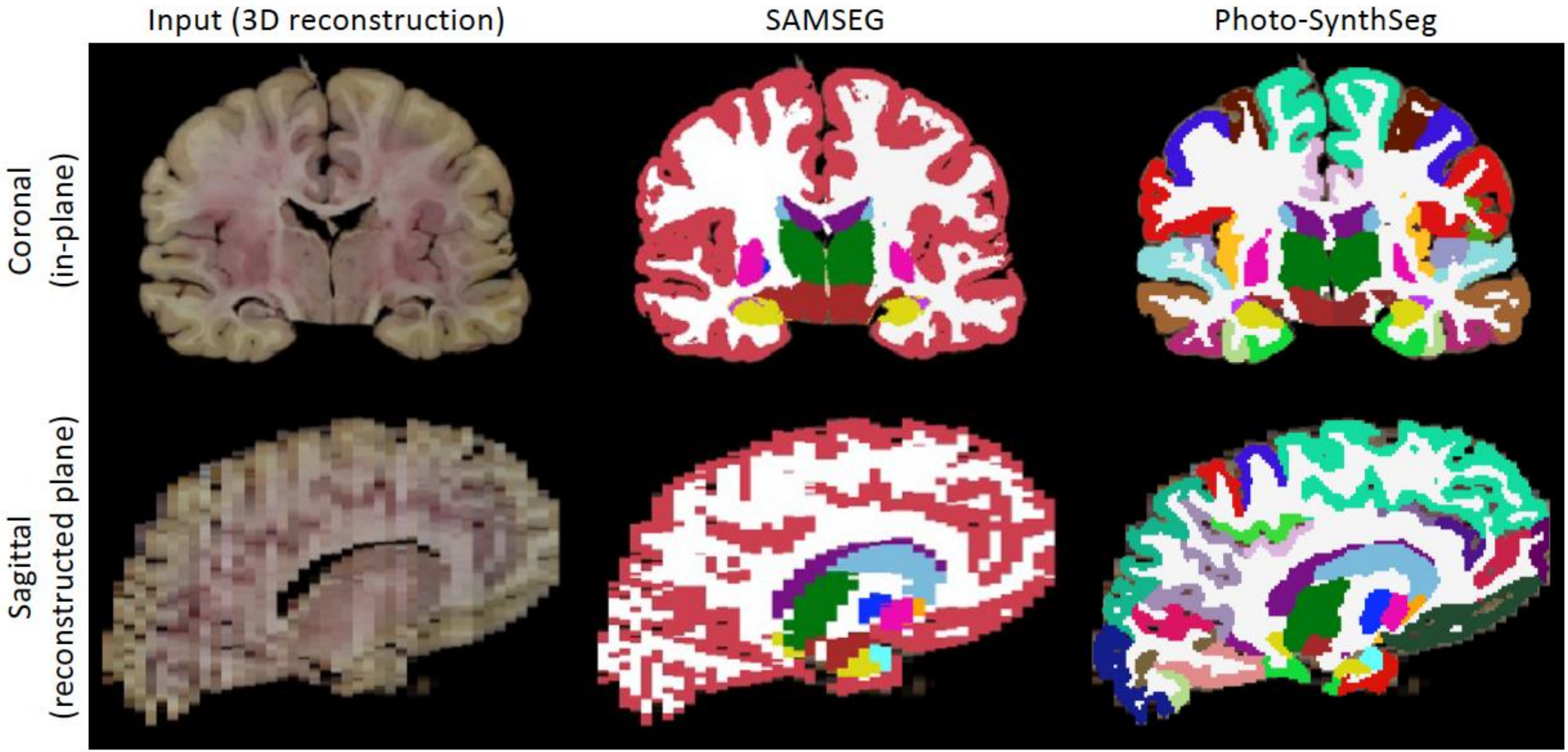
- Reconstruction with MNI atlas.



First generation of segmentation code

- In *Gazula et al. (2024)* we adapted two methods from in vivo MRI literature:
  - SAMSEG *(Puonti et al., 2016)*: Bayesian segmentation.
  - SynthSeg *(Billot et al., 2023)*: Machine learning / domain randomization.
    - ✓ Faster, more accurate, can handle “French fry” voxels.
  - Both available on FreeSurfer
  - Work well for very high quality data, but may falter otherwise.

First generation of segmentation code



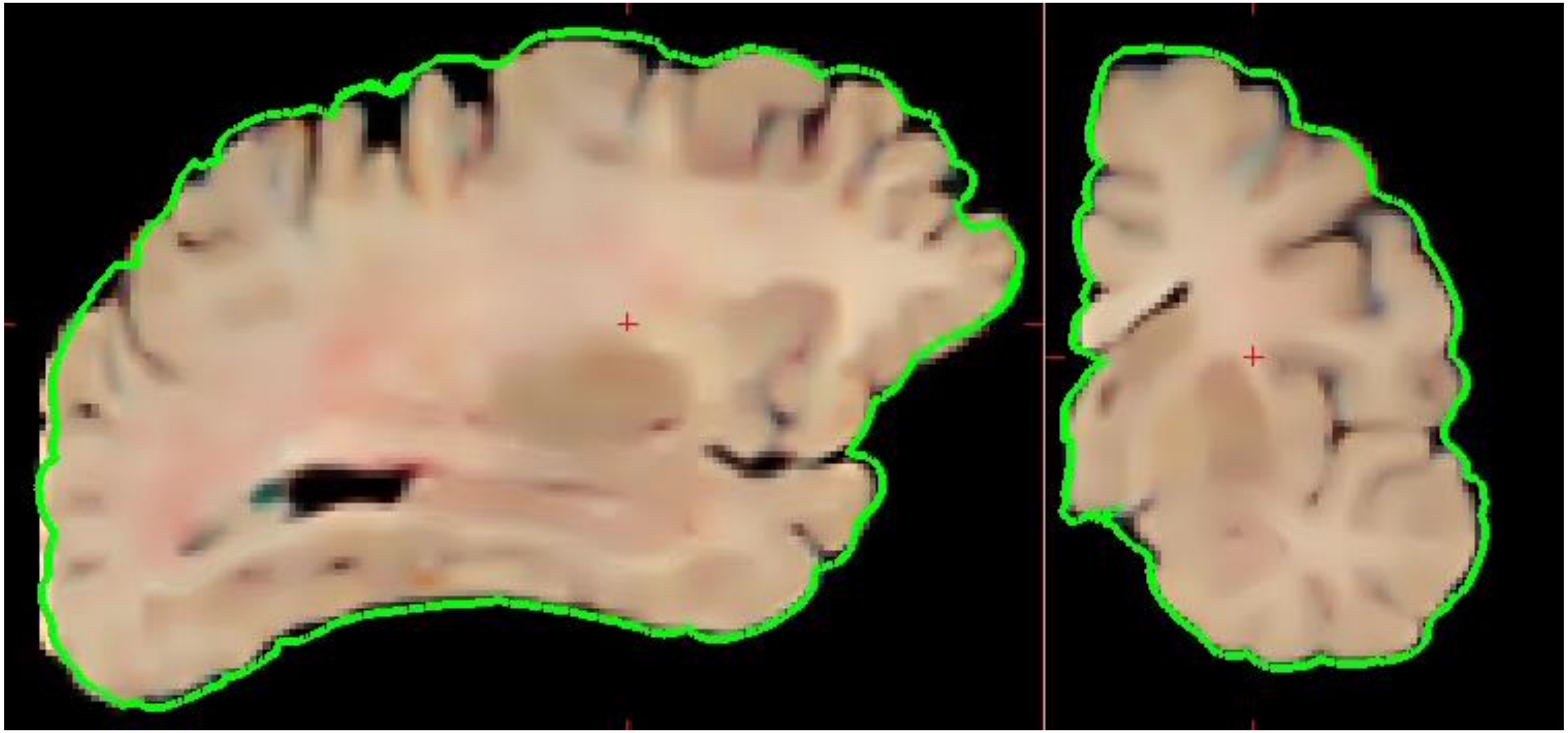
Data from CD Keene, CM MacDonald, M Montine, et al. (UW)

Improved 3D reconstruction: slice imputation

- Why limit ourselves to linear or nearest neighbor interpolation?
  - Trilinear -> $S(y) = \frac{y_2 - y}{y_2 - y_1} S_1 + \frac{y - y_1}{y_2 - y_1} S_2$
- Why not use a neural network to estimate a slice at a given A-P coordinate *y*?
  - $S(y) = f_\theta(y - y_1, y_2 - y, S_1, S_2)$ where f_θ is a comple neural network.
    - It depends on just 2 slabs.
    - Agnostic to spacing, by design – just change y-y_1, y_2-y.
    - Trained with boatloads of simulated data (similar to SynthSeg).
    - Unreasonably effective!

Machine learning imputation

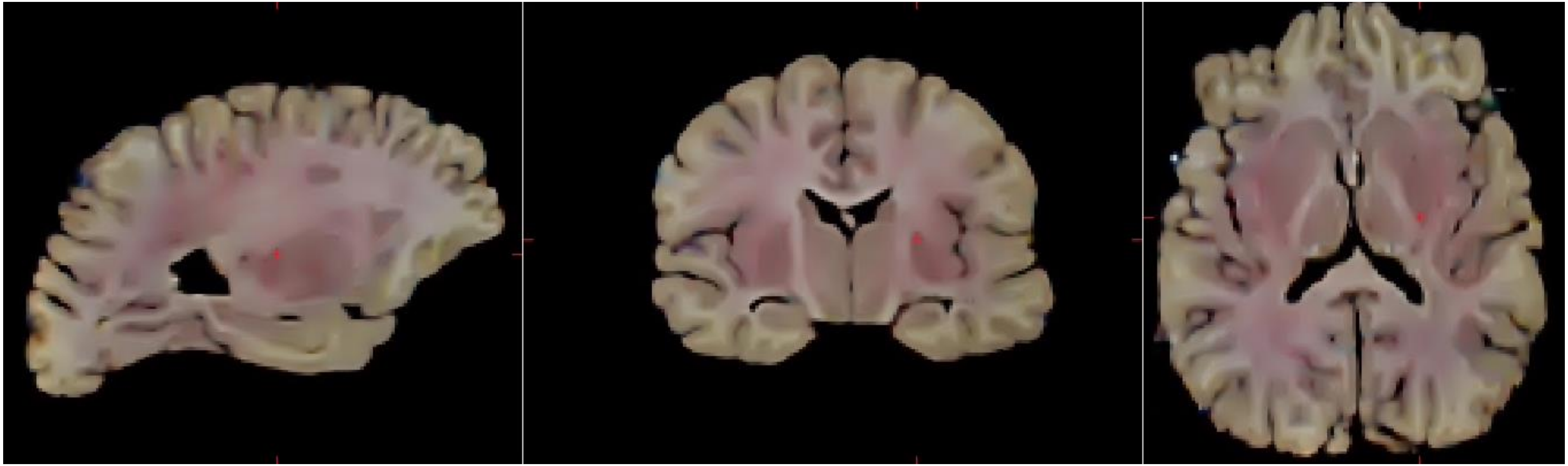
MGH dataset: ~8mm thickness on average (variable spacing)



Data from BT Hyman, D Oackley, T Connors, et al (MGH)

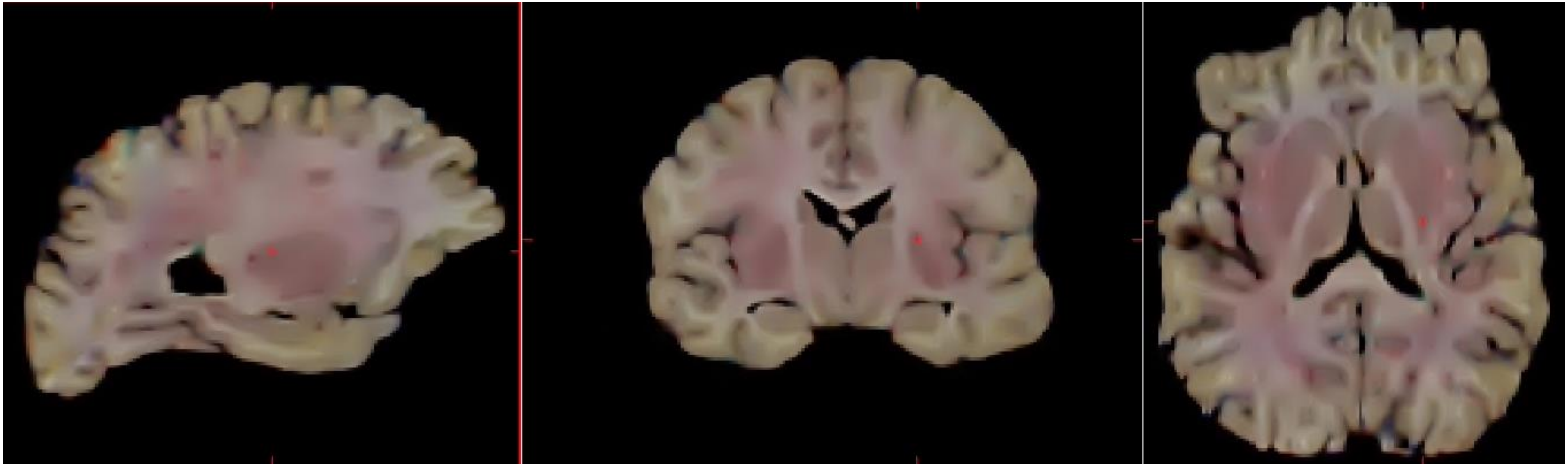
Machine learning imputation

UW dataset: ~4mm thickness (fixed) subsampled to 8 mm



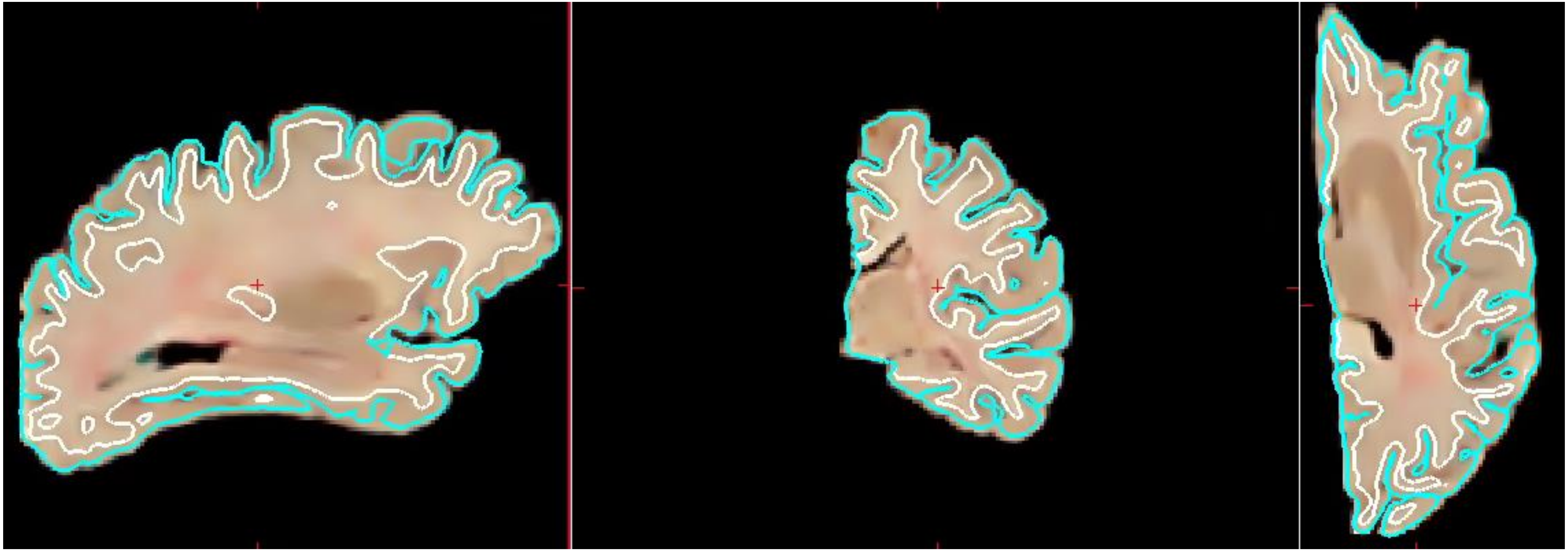
Machine learning imputation

UW dataset: ~4mm thickness (fixed) subsampled to 12 mm



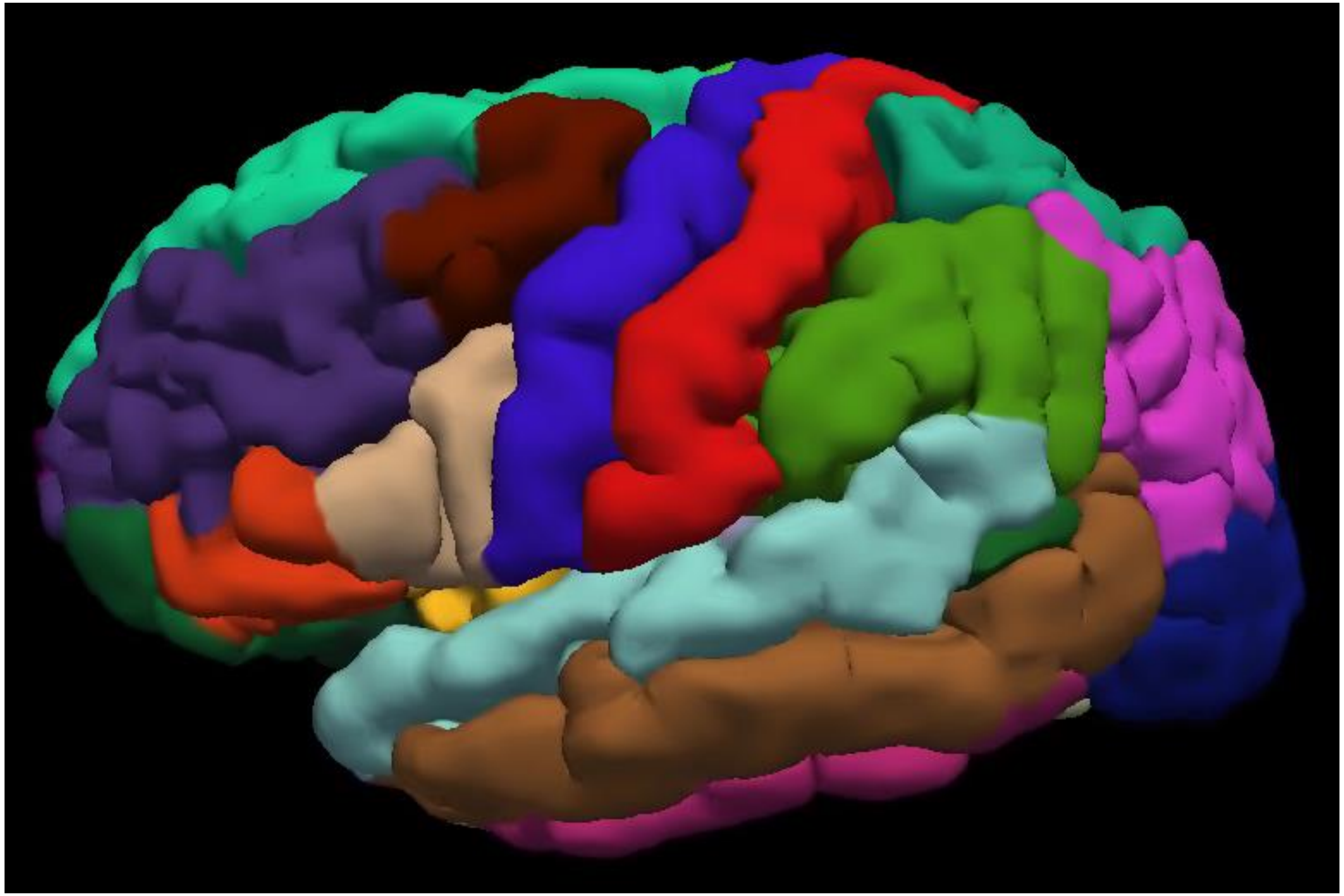
ML-powered image analysis

Super-resolved images work very well with our foundation model designed for MRI

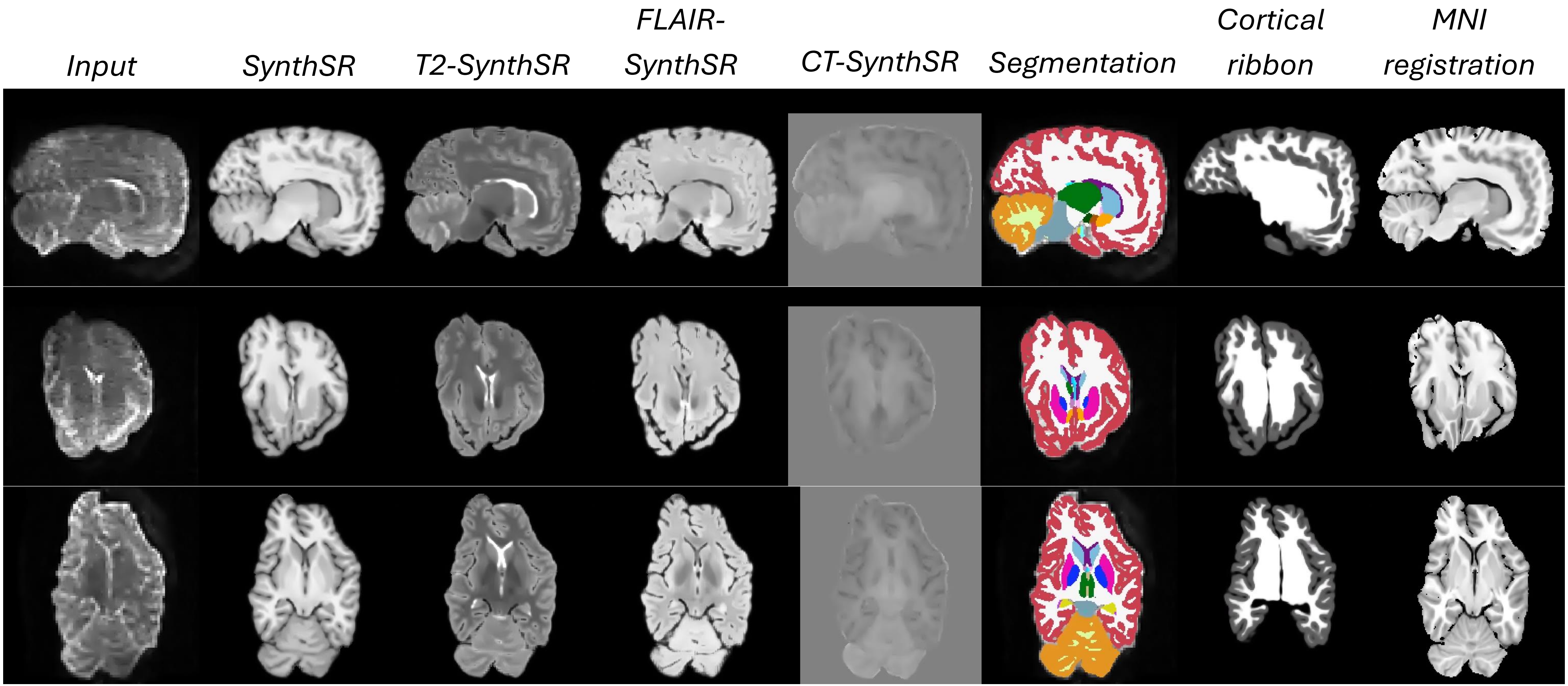


ML-powered image analysis

Super-resolved images work very well with our foundation model designed for MRI



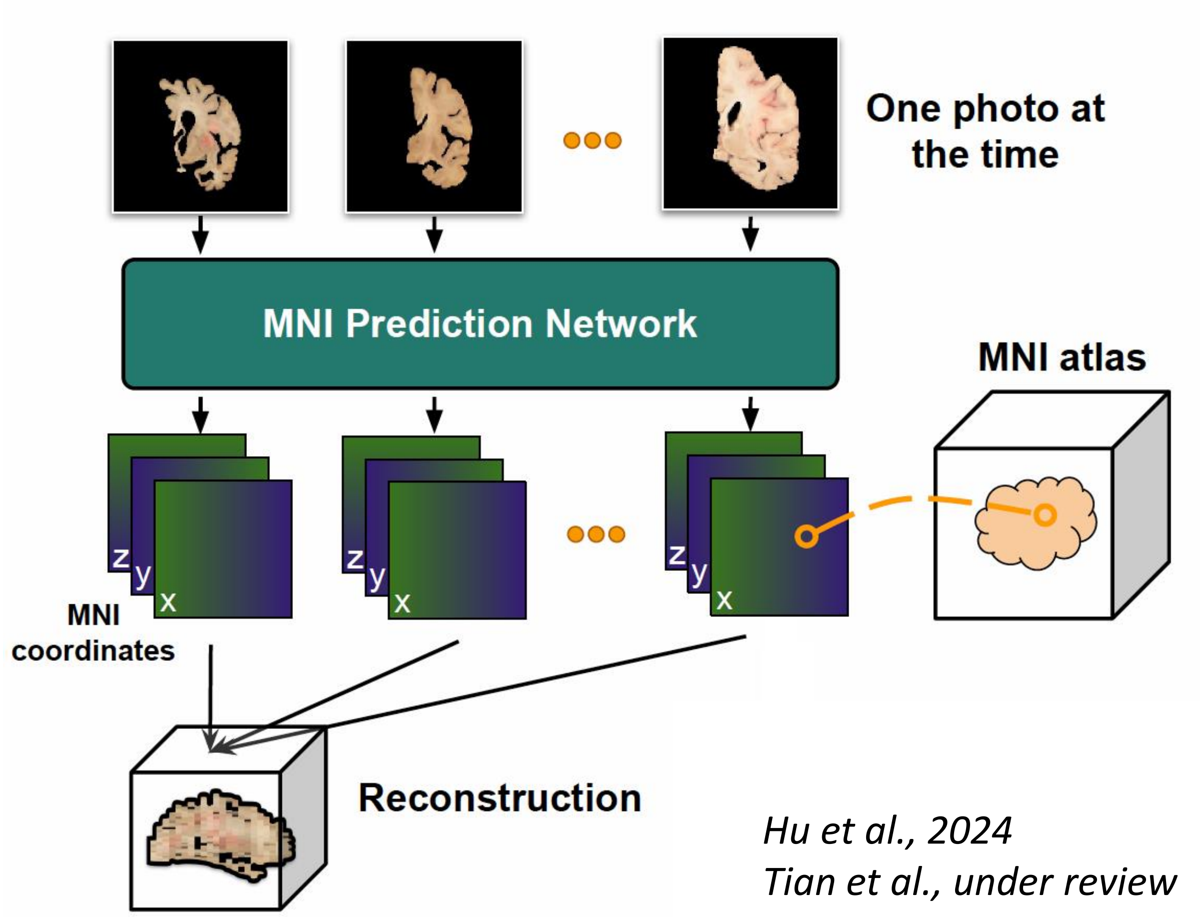
ML-powered image analysis: portable MRI



Iglesias et al., Radiology (2022), Science Advances (2023) *Liu et al., ECCV (2024), MICCAI (2024), CVPR (2025)* *Sorby-Adams et al., Nat Comms (2025)*

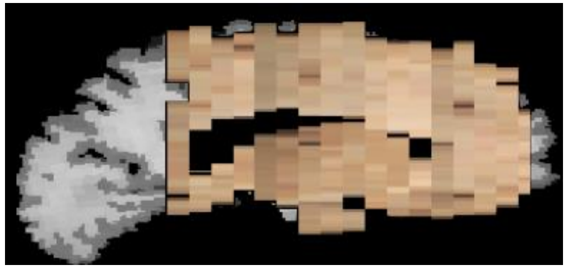
What about fresh tissue?

- The main problem is the geometric distortion between neighboring slabs.
- Again: machine learning to the rescue?



Hu et al., 2024
Tian et al., under review

- Can handle missing data (useful for eg.g., retrospective)



- Only linear for now – but will soon look into nonlinear (following *Hu et al., 2024*).
- Maybe invite me back next year for an update?

Ongoing and future work

- Fresh tissue
- Fancier models for the slice imputation, e.g., diffusion models.
- Suggestions?

Acknowledgment

Low-field MRI

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QUESTIONS / DISCUSSION