# Quantitative Measurements of magnetic resonance Angiography Decrease with Aging and Cognitive Decline in the ACT cohort.

Robert Ritchie[1], Max Kobiesa[2], Gador Canton[1] PhD, Kaiyu Zhang[2], Thomas Hatsukami[3] MD, Jalal Andre[1] MD, Esther Yuh[4] MD, Mahmud Mossa-Basha[1] MD, Paul Crane[5] MD, Christine McDonald[6] PhD, Chun Yuan[1,7] PhD, Cecilia Lee[8] MD, Niranjan Balu[1] PhD

[1]Radiology, University of Washington

[2]Bioengineering, University of Washington

[3]Vascular Surgery, University of Washington

[4]Radiology, University of California San Francisco

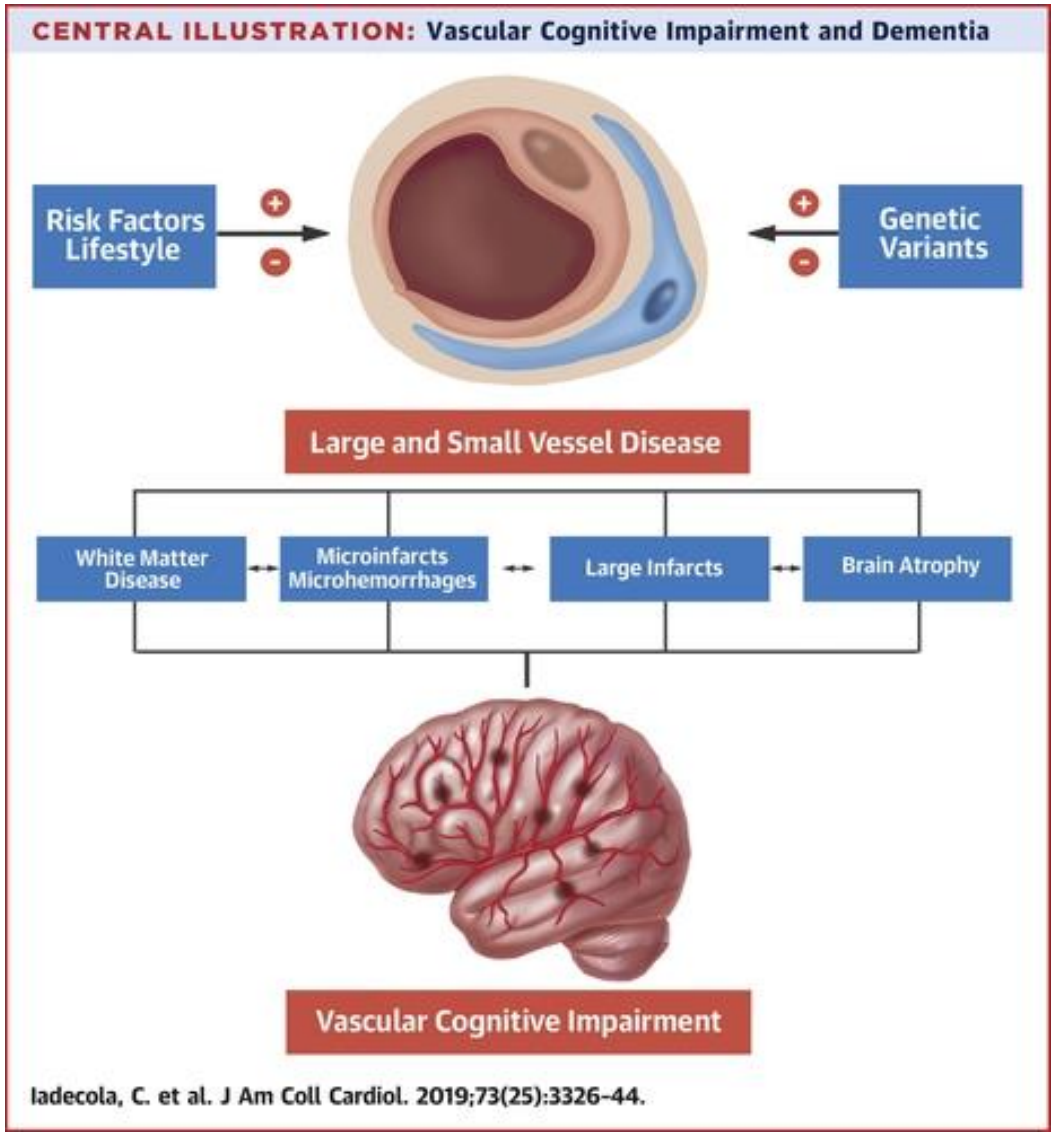
[5]Internal Medicine, University of Washington

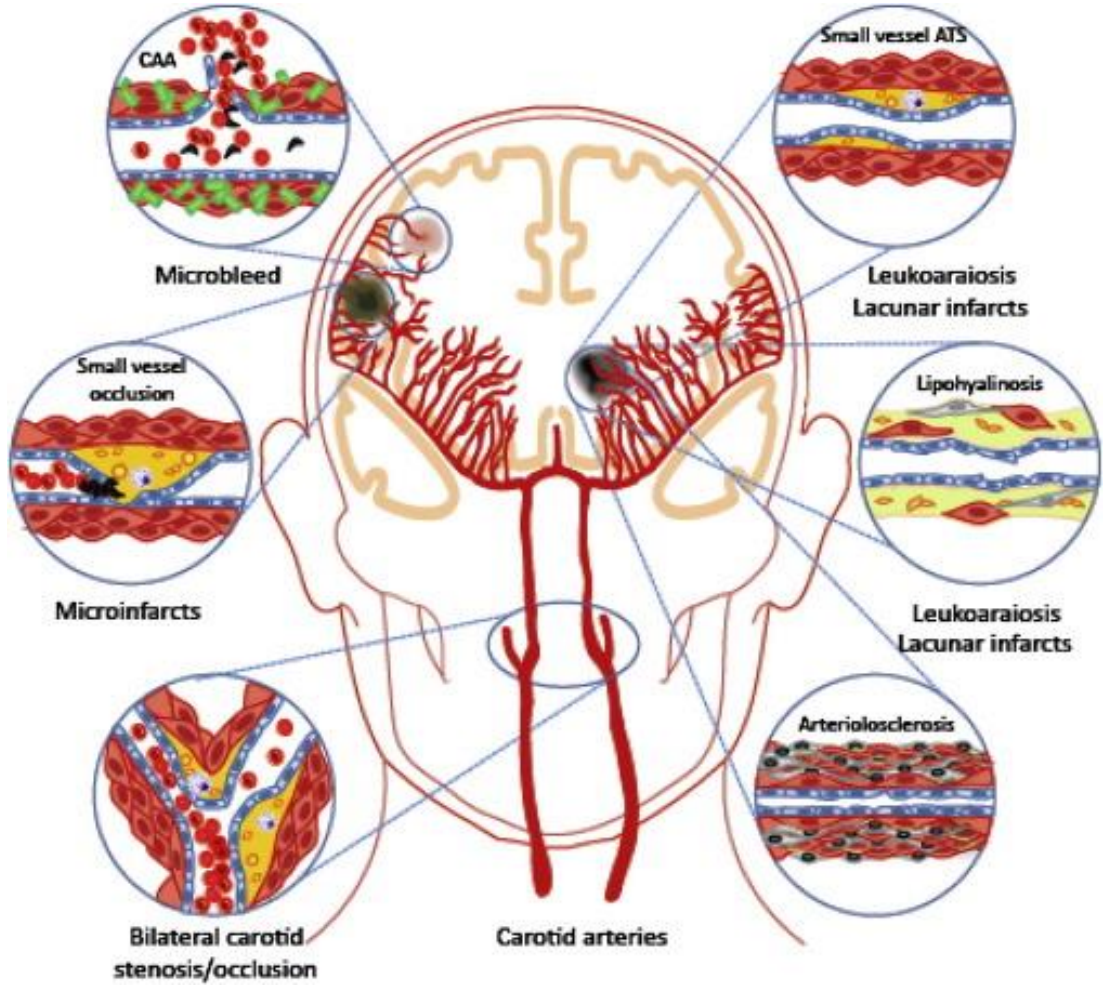
[6]Neurosurgery, University of Washington

[7]Radiology, University of Utah

[8]Opthalmology, University of Washington

# Vascular causes of dementia

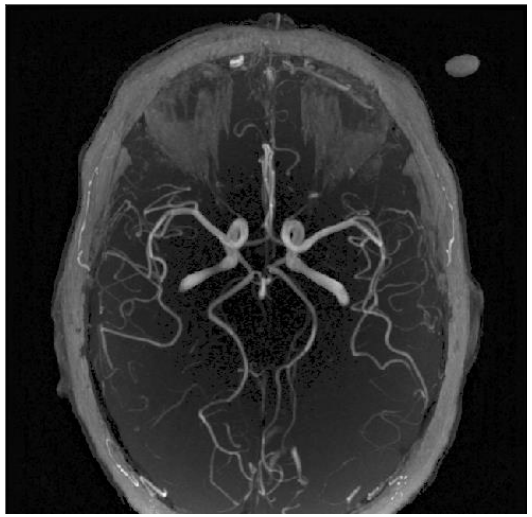


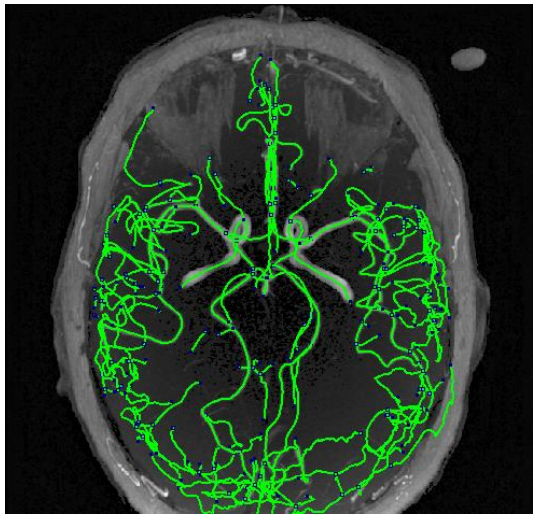



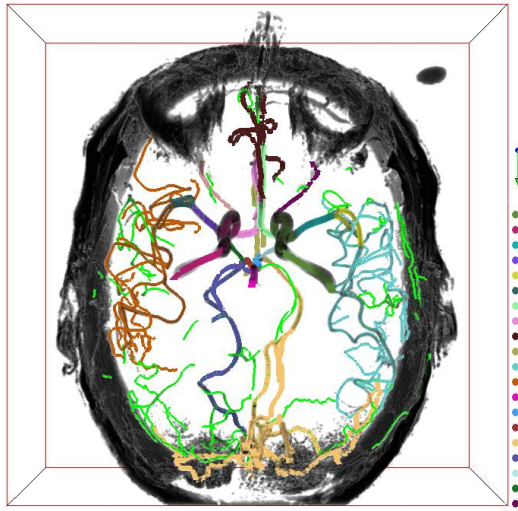

Iadecola C. et al, Neuron 2013

# Intracranial Feature Extraction Tool (iCafe)

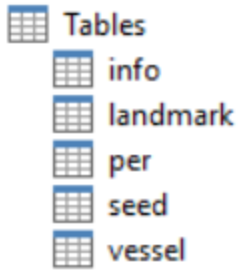
- Enables large vessel perfusion assessment from MR angiography (MRA)
- Features measured: Artery length, tortuosity, branch number, intensity

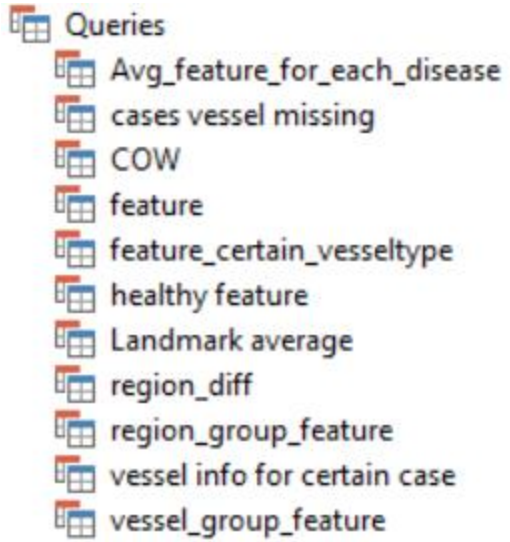








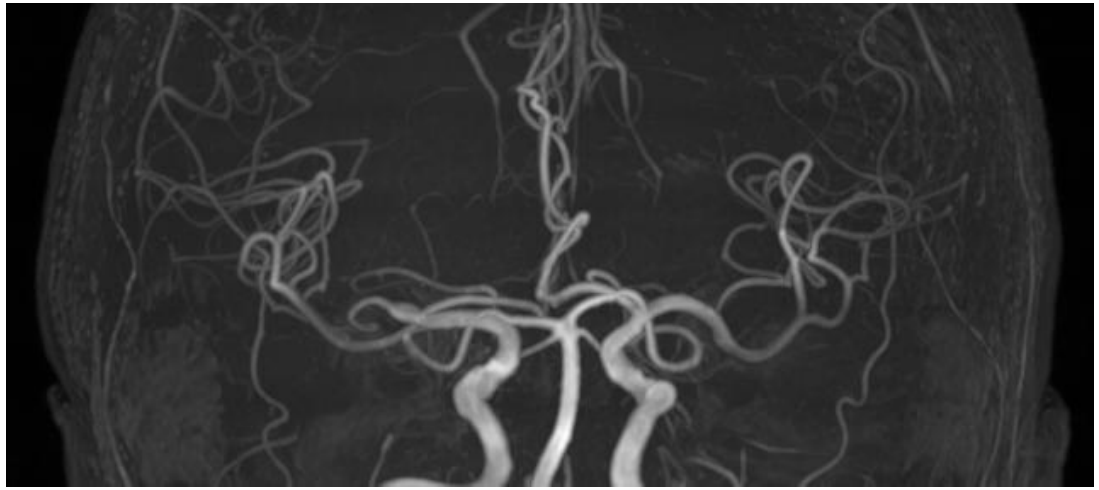


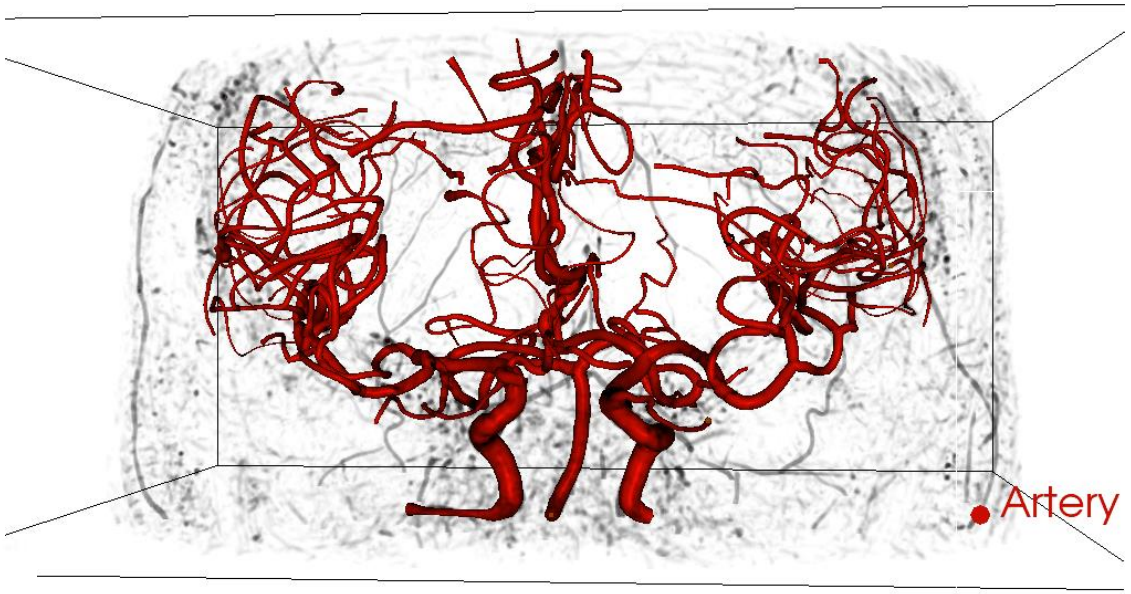



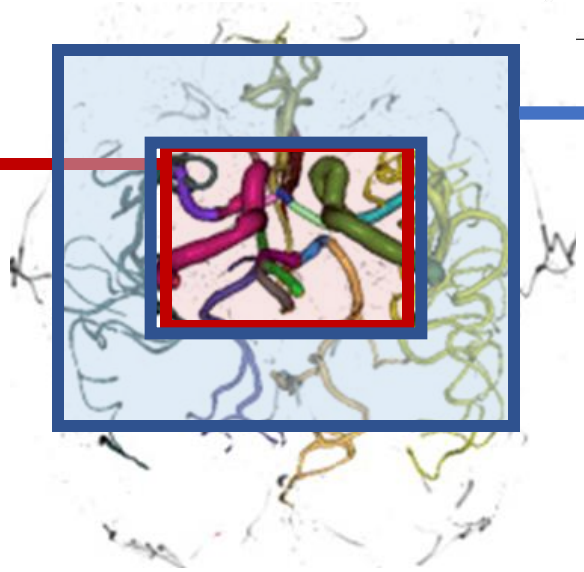

Raw MRA image → Artery tracing → Artery labeling → Feature extraction → Output and Analysis

Chen L. et al, MRM 2018

# Distal artery blood flow





**Proximal Arteries**

**Geometrical measurements**

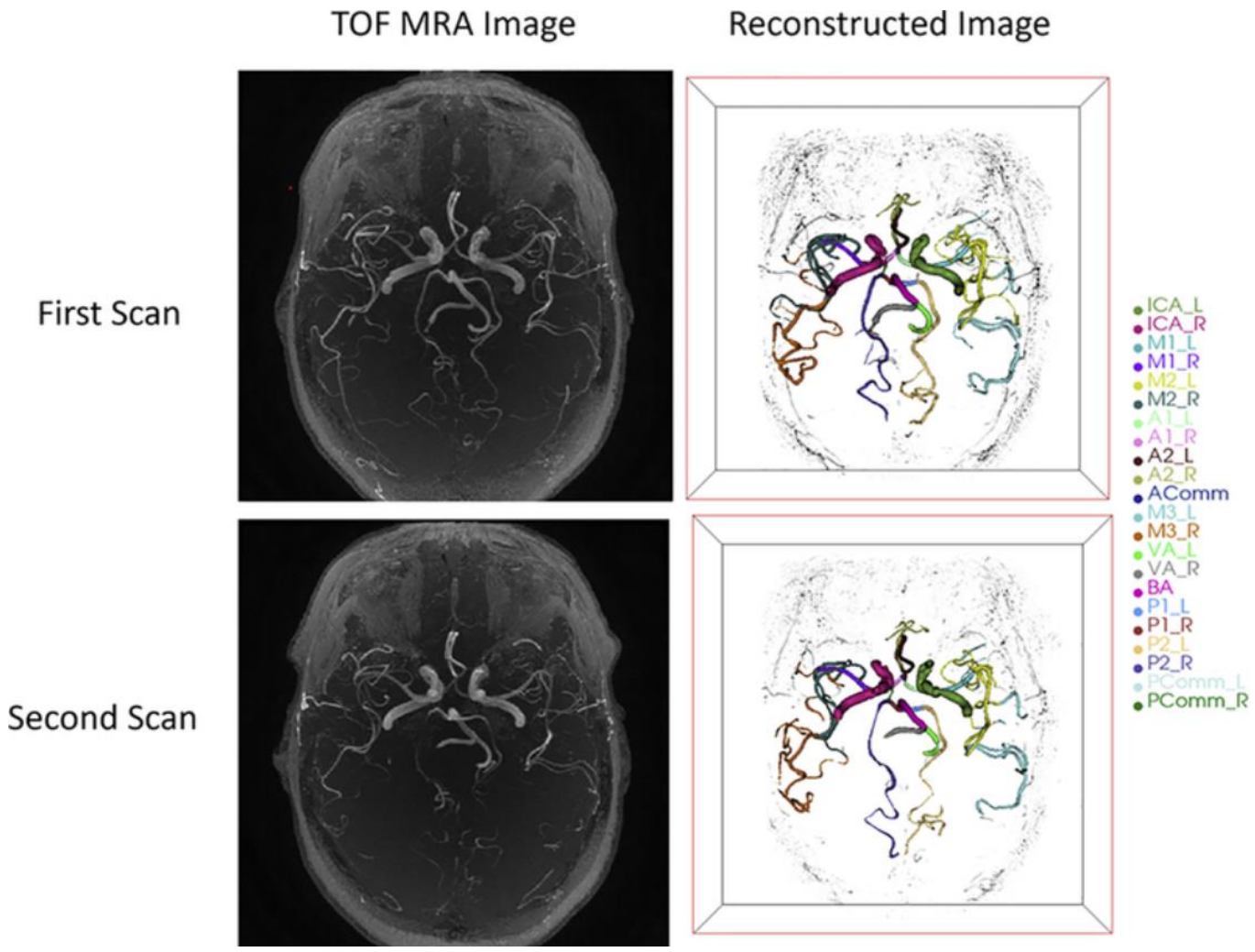
- Stenosis
- Radius
- Tortuosity

**Distal Arteries**

**Flow related measures**

- Distal artery length
- Number of branches
- Branch order

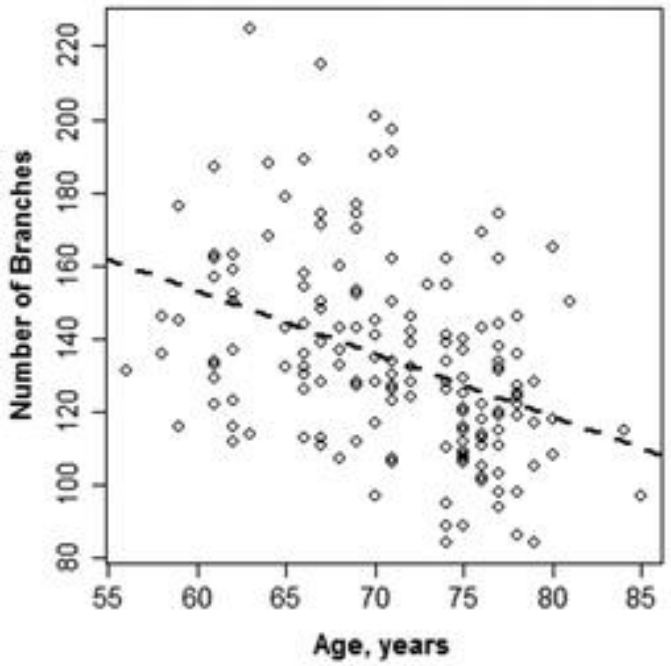
# iCafe Measurements using TOF are reproducible

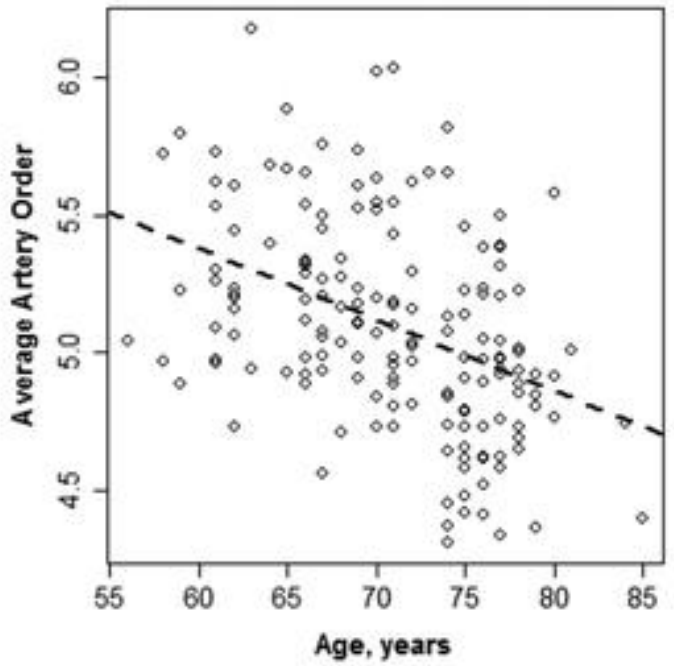


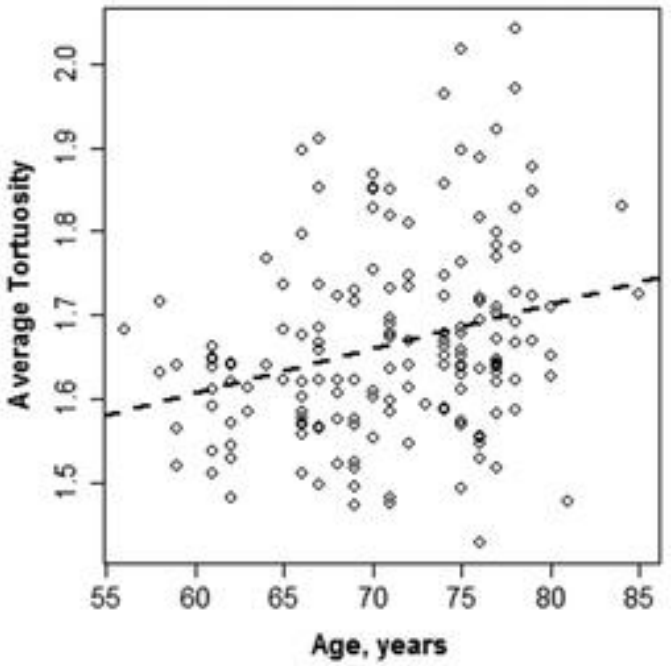

| Features | Inter-scan | | | |
|---|---|---|---|---|
| | Mean+-SD | ICC | 95% CI | CV |
| Total Length (mm) | 2639.7+-636.2 | 0.97 | 0.94-0.99 | 4.03% |
| Total Volume (mm3) | 7597.2+-2259.6 | 0.92 | 0.82-0.96 | 8.78% |
| Proximal Length (mm) | 98.8+-16.9 | 0.96 | 0.91-0.98 | 3.29% |
| Distal Length (mm) | 2469.5+-625.5 | 0.97 | 0.93-0.99 | 4.39% |
| Total Branches | 126.3+-30.4 | 0.92 | 0.83-0.97 | 6.81% |
| Average M1 Radius | 1.7+-0.2 | 0.91 | 0.81-0.96 | 4.12% |
| Average Normalized Intensity | 880.8+-215.2 | 0.96 | 0.91-0.98 | 4.96% |
| Average Normalized Intensity for large arteries | 1535.2+-598 | 0.97 | 0.92-0.99 | 6.85% |

Chen et al, MRI, 2019

# iCafe measurements track aging




163 normal participants (56–85 years) from Cardiovascular Risk of Older Population (CROP) Study
iCafe indicates decreasing brain blood flow with age

- Decrease in distal vessel length
- Decrease in number of distal branches and branch order
- Increase in vessel tortuosity

Chen L et al, Neurobiol Aging, 2019

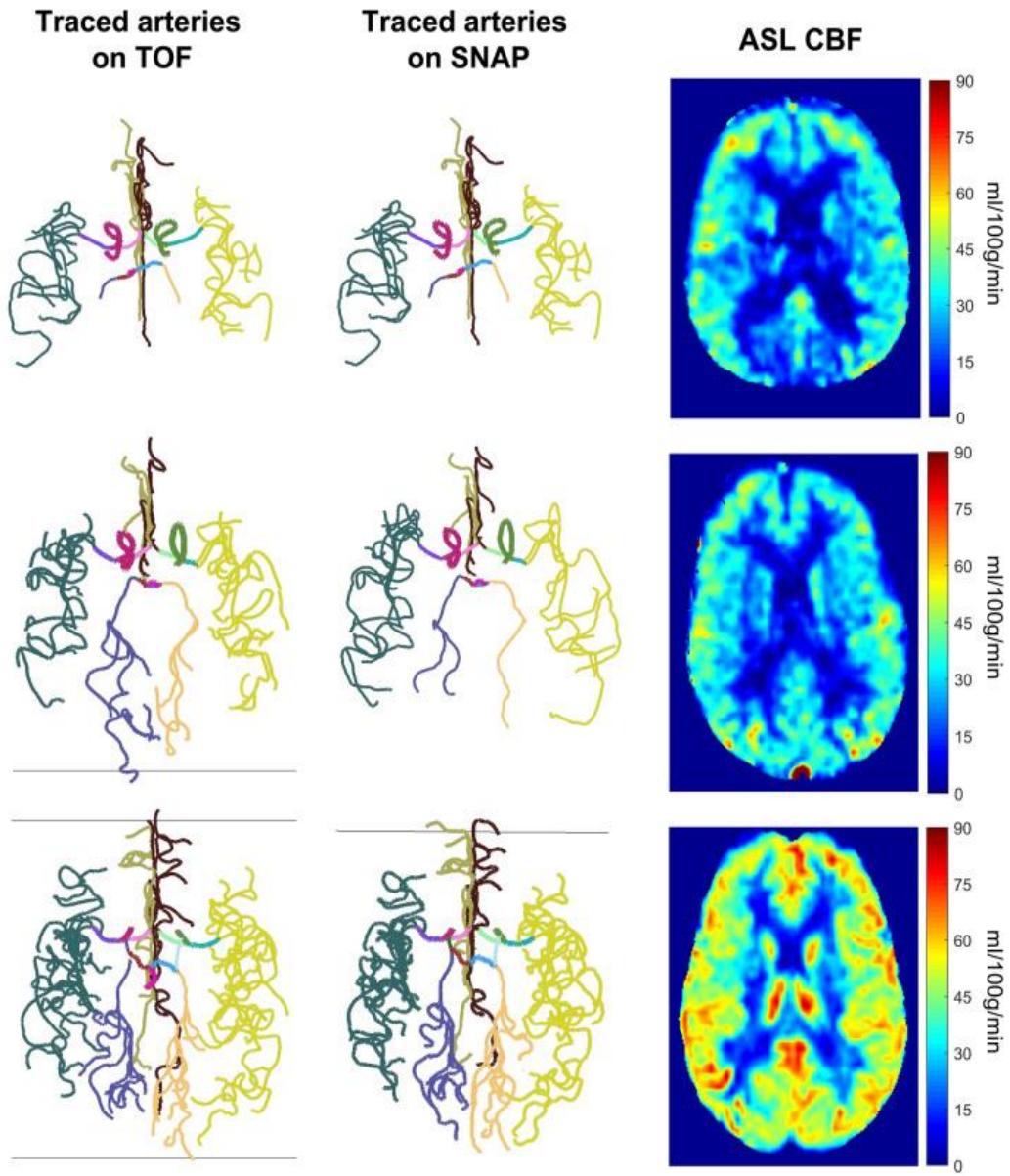
# iCafe measures are indicative of cognitive function

Subjects with asymptomatic carotid disease

## Association of iCafe measures with MoCA

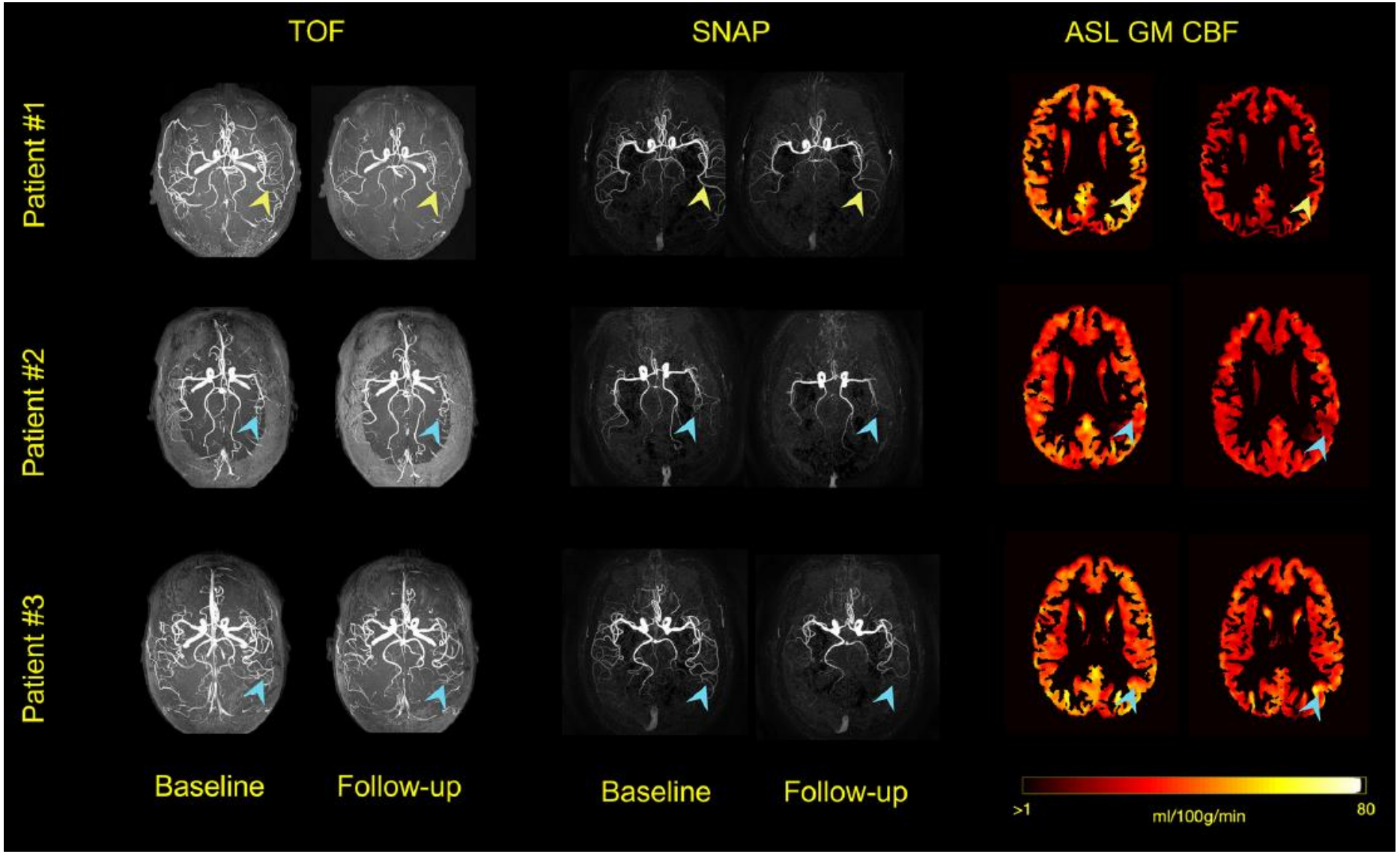
| | Adjusted for ASL CBF | | | Adjusted for PC CBF | | |
|---|---|---|---|---|---|---|
| | $\beta$ | $P$ | Adjusted $R^2$ | $\beta$ | $P$ | Adjusted $R^2$ |
| TOF, artery length | 0.484 | **0.018** | 0.452 | 0.441 | **0.014** | 0.492 |
| SNAP, artery length | 0.366 | 0.220 | 0.331 | 0.329 | 0.129 | 0.392 |
| TOF, number of branches | 0.527 | **0.007** | 0.493 | 0.496 | **0.012** | 0.502 |
| SNAP, number of branches | 0.600 | **0.047** | 0.406 | 0.441 | 0.056 | 0.431 |
| TOF, average tortuosity | −0.182 | 0.283 | 0.319 | −0.164 | 0.318 | 0.352 |
| SNAP, average tortuosity | −0.046 | 0.792 | 0.282 | −0.037 | 0.830 | 0.321 |

Also adjusted for age, carotid stenosis, use of hypertensives, systolic bp



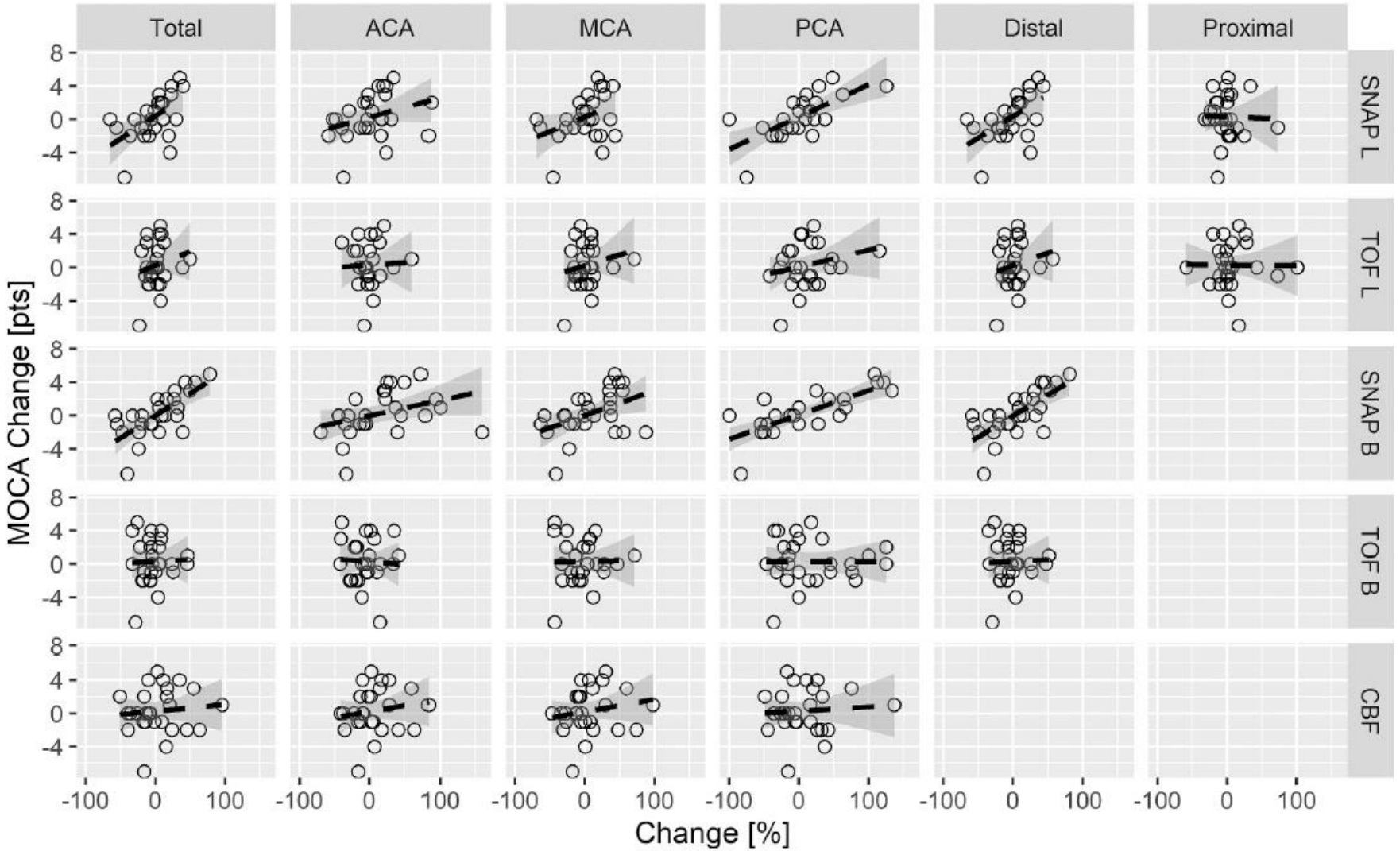

Chen Z et al, Sci Reports, 2021

# iCafe measures are indicative of cognitive decline




Zhang K et al, MRI, 2023

# iCafe measures are indicative of cognitive decline




Zhang K et al, MRI, 2023

ACT
ADULT CHANGES IN THOUGHT STUDY

Kaiser Permanente Washington
Health Research Institute

Study population and creation of the ACT cohort

ABOUT COLLABORATION DATA RESOURCES NEWS & RESULTS

The Adult Changes in Thought (ACT) Study recruits participants from random samples of Kaiser Permanente Washington (previously Group Health) health plan members who meet the following criteria:

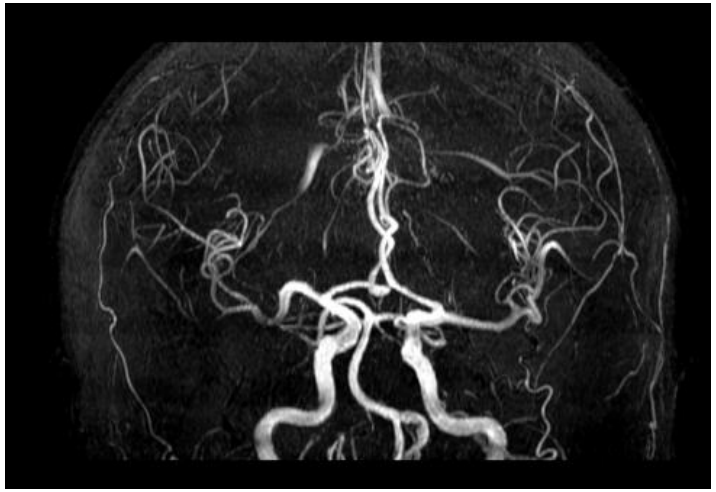
- At least 65 years of age
- Do not have dementia
- Do not reside in a nursing home
- Enrolled in the health plan for at least 2 years
- Primary health care clinic is in the greater Seattle area of King County

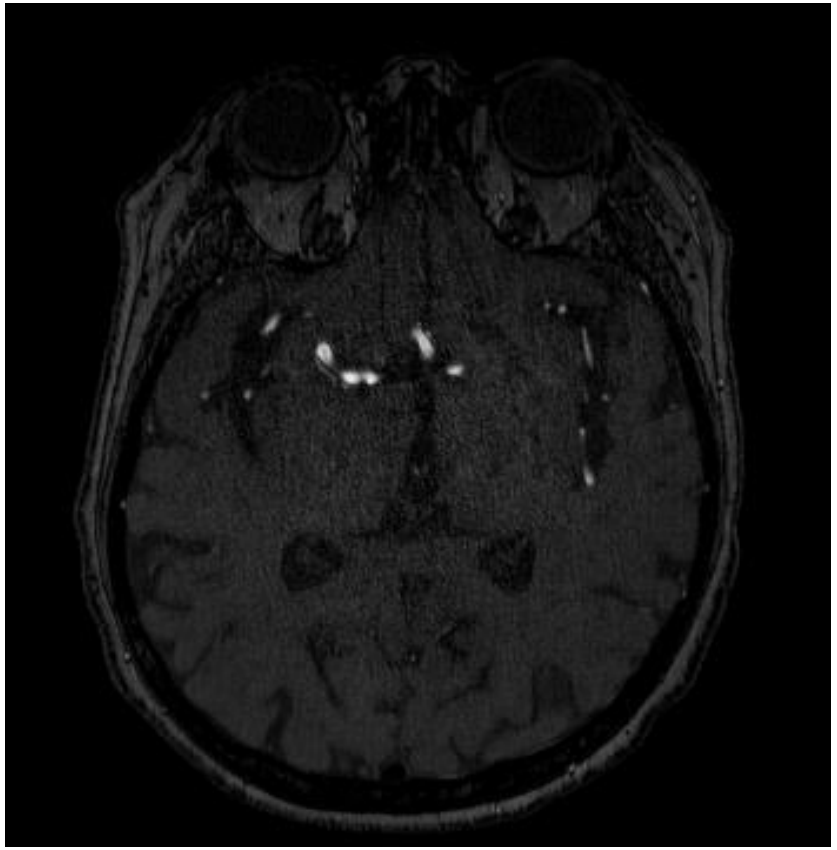
Since its inception in 1994, the ACT Study has recruited an Original Cohort (2,581 participants recruited from 1994 to 1996), an Expansion Cohort (811 participants recruited from 2000 to 2003), and a Replacement Cohort (2,371 participants recruited from 2004 to the present). The ongoing recruitment of new participants into the ACT Study as part of the Replacement Cohort is designed to maintain a study cohort of ~2,000 participants without dementia who are actively undergoing biennial follow-up.

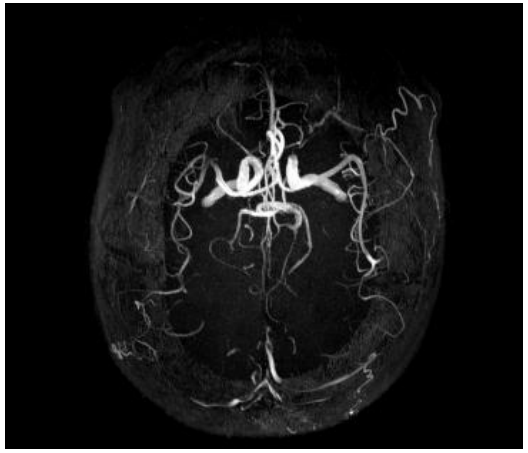
| Characteristic | N = 128[1] |
|---|---|
| age | 80 (75, 84) |
| male | |
| Female | 69 (54%) |
| Male | 59 (46%) |
| education | 16.0 (13.0, 18.0) |
| casi_irt | -0.01 (-0.56, 0.76) |
| Unknown | 3 |
| length | 1,057 (909, 1,266) |
| tortuosity | 1.51 (1.43, 1.61) |
| leuk_arwmc_total | 5.0 (2.0, 7.0) |
| acute_infarct | |
| 1 | 18 (14%) |
| 2 | 2 (1.6%) |
| 3 | 105 (82%) |
| 4 | 3 (2.3%) |
| chronic_infarct_present | 26 (20%) |

[1] Median (IQR); n (%)

# ACT TOF MRA from Clinical Scans



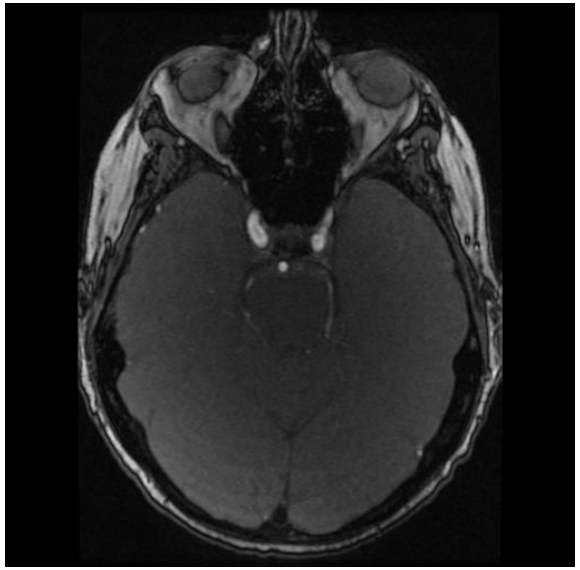


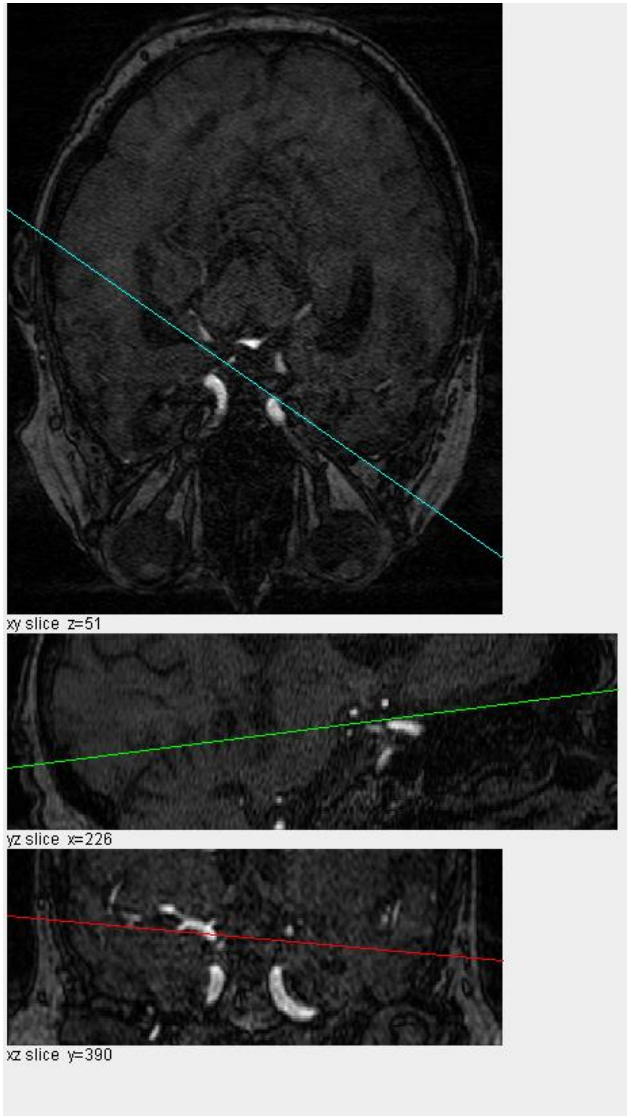


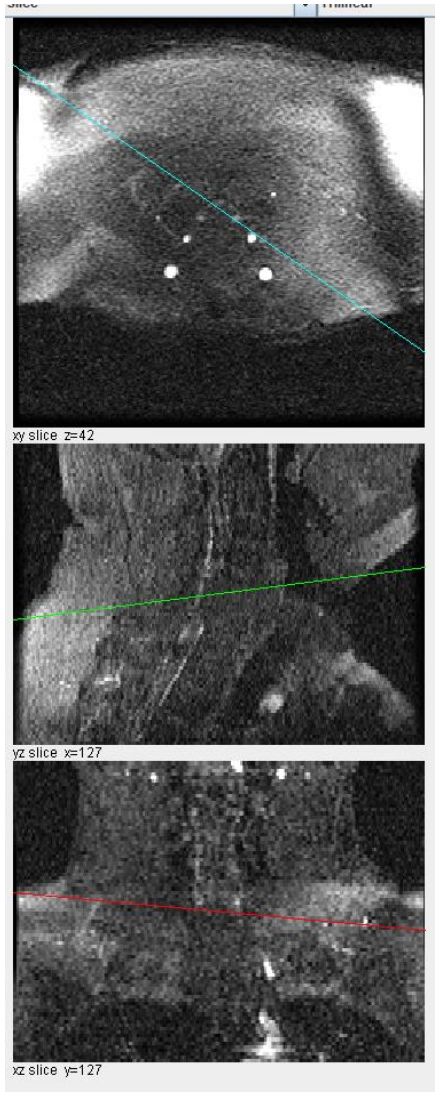
Clinical MRI at different hospitals, different scanners and different MRI protocols

# ACT TOF MRA Challenges

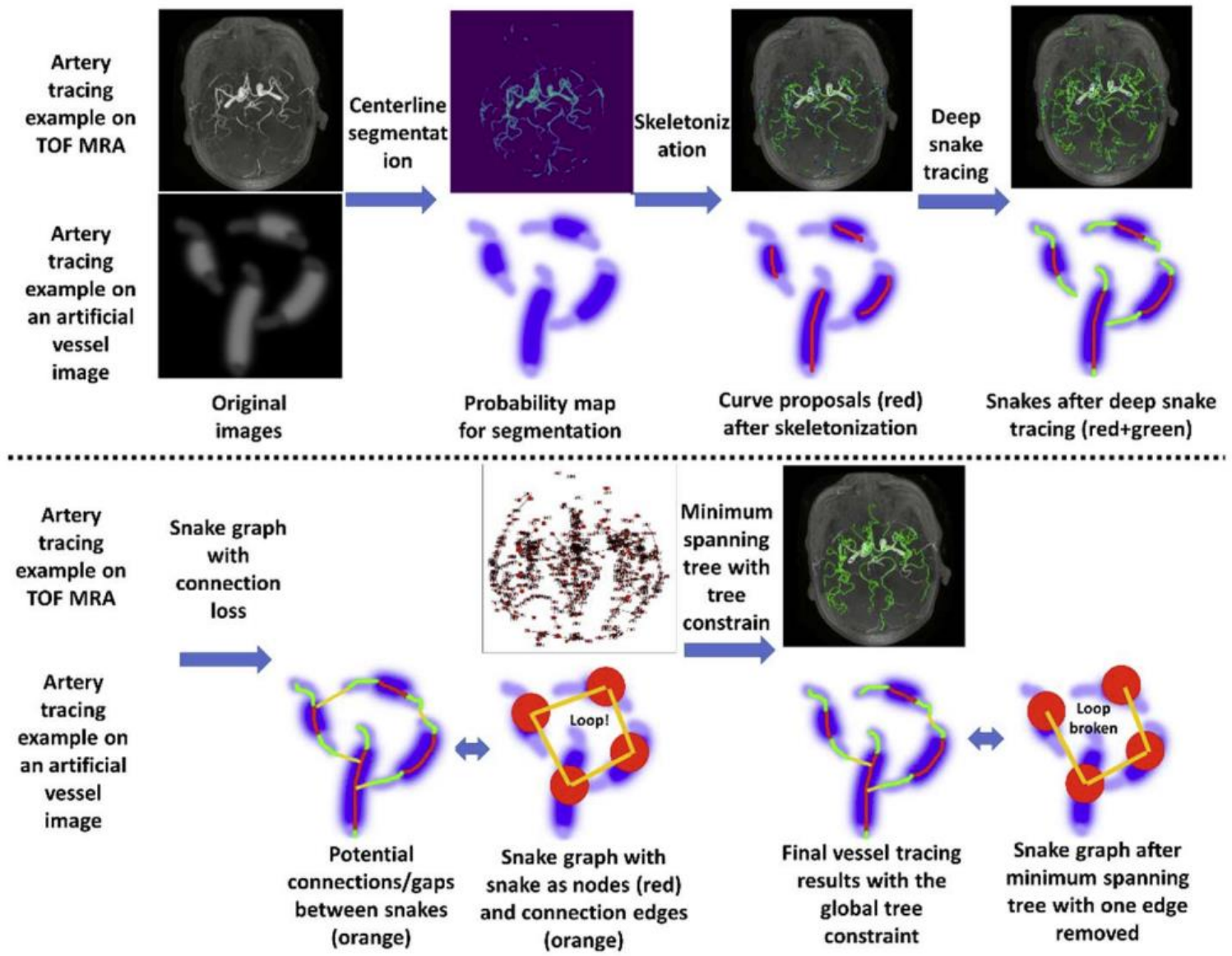
- Differences in
  - FOV
  - Resolution
  - Fat suppression
  - Sequence parameters





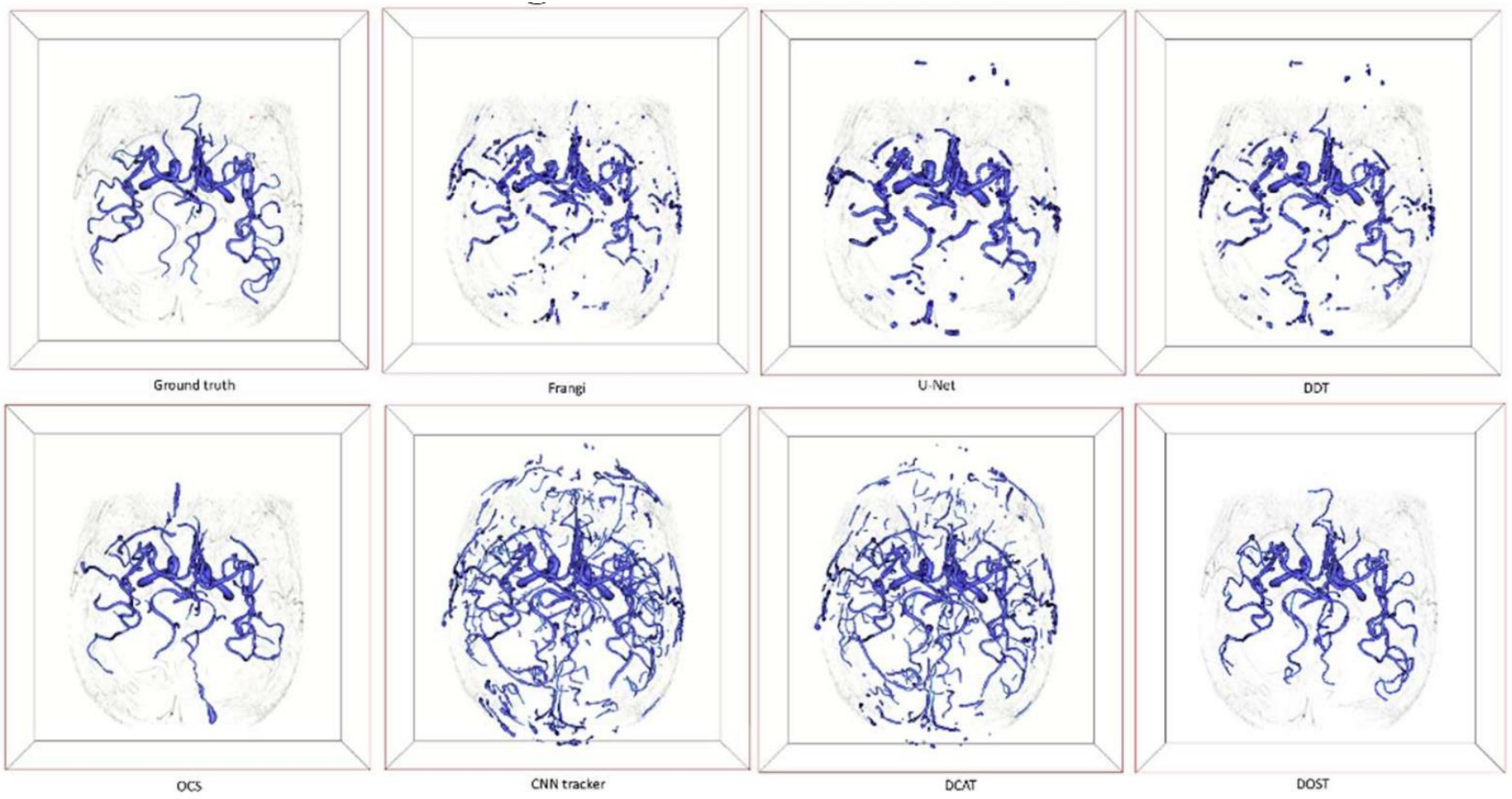



# AiCafe: Automatic centerline tracing




Chen L. et al, MICCAI 2021

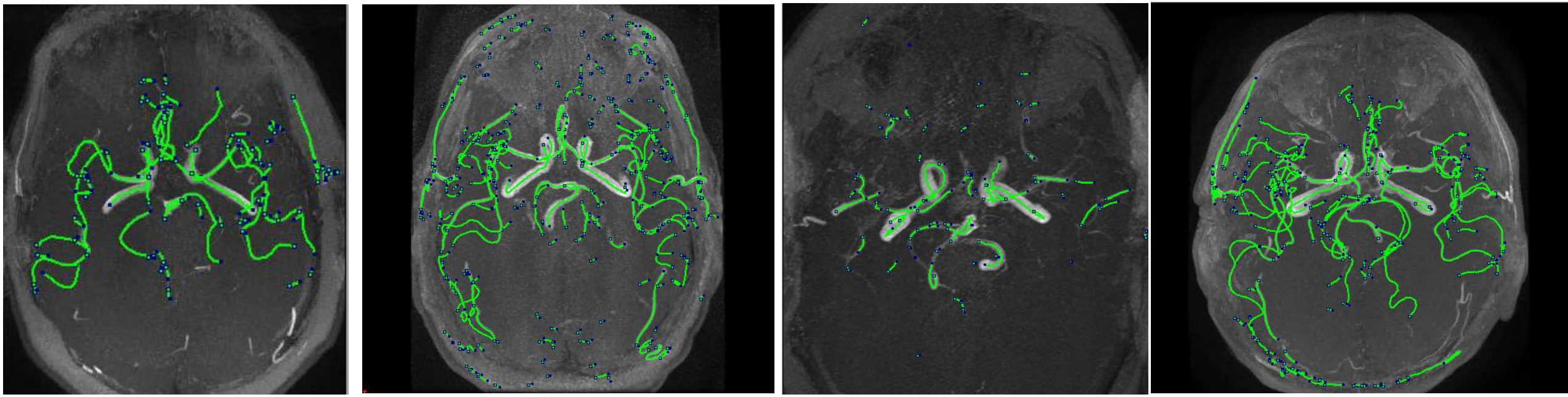
# AiCafe: Automatic centerline tracing




Chen L. et al, MICCAI 2021

# AiCafe on ACT-MRA

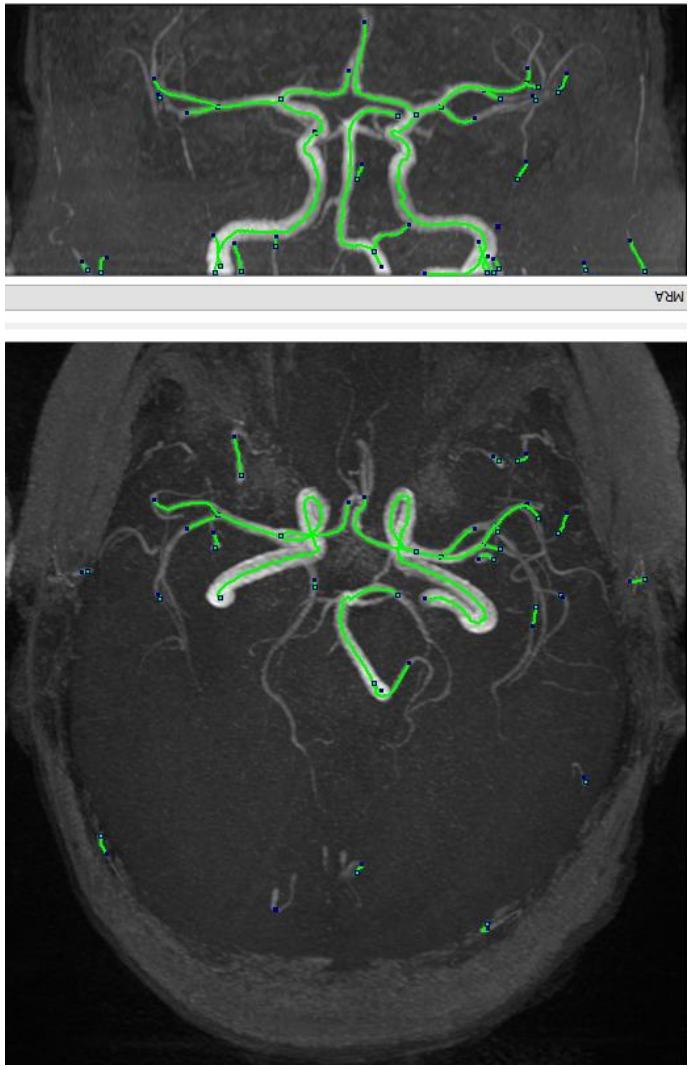
- Clinical MRA with different resolution, coverage and signal intensity
- Needed manual correction
- Two readers corrected traces and labeled all AiCafe tracings



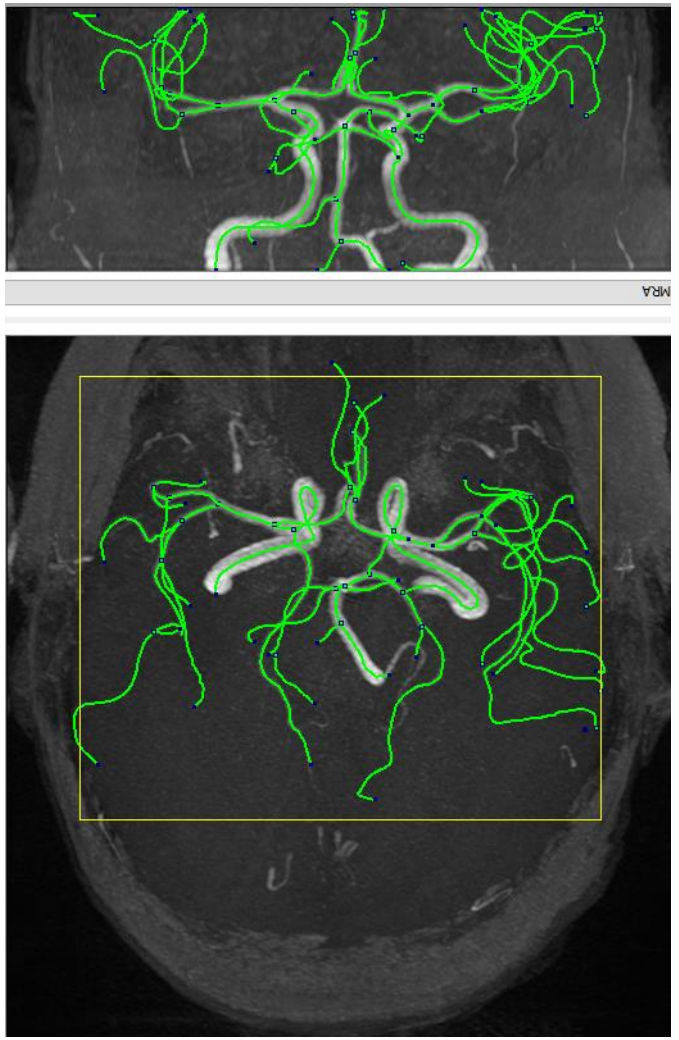
AiCafe tracings without correction

# Corrected MRA tracings

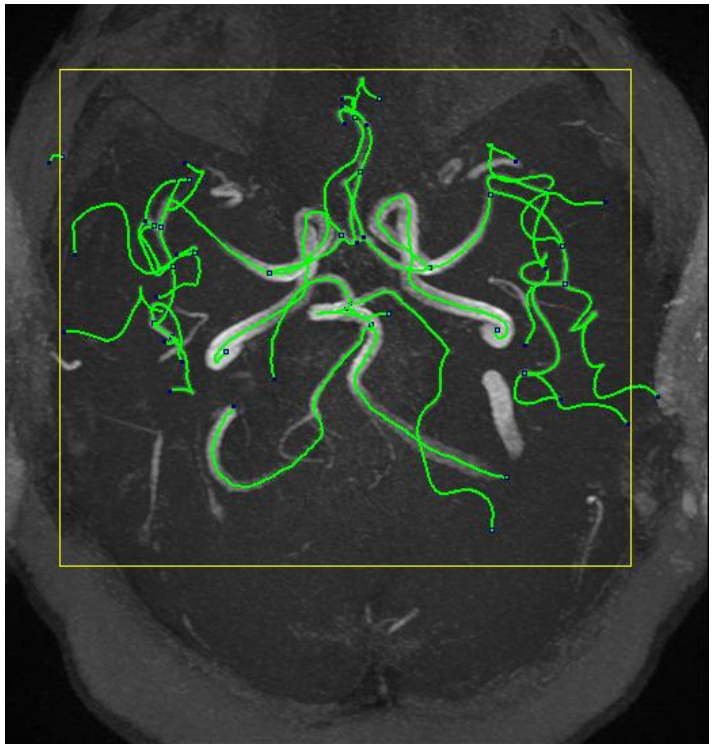
Uncorrected

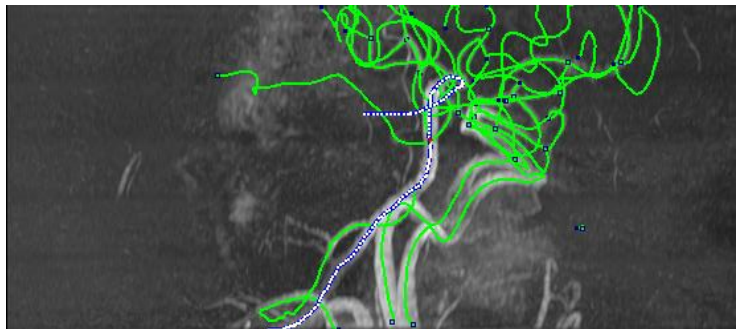


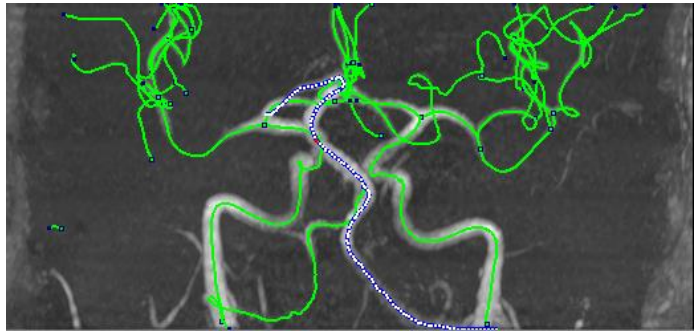
Corrected



# Results





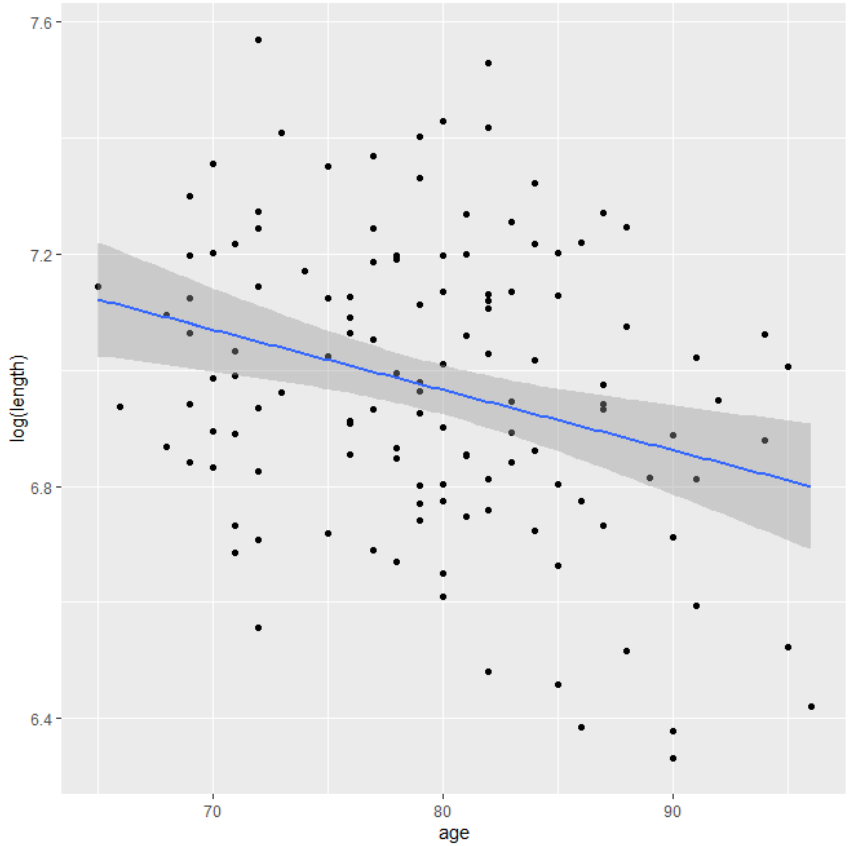


| Characteristic | N = 128[1] |
|---|---|
| age | 80 (75, 84) |
| male | |
| Female | 69 (54%) |
| Male | 59 (46%) |
| education | 16.0 (13.0, 18.0) |
| casi_irt | -0.01 (-0.56, 0.76) |
| Unknown | 3 |
| length | 1,057 (909, 1,266) |
| tortuosity | 1.51 (1.43, 1.61) |
| leuk_arwmc_total | 5.0 (2.0, 7.0) |
| acute_infarct | |
| 1 | 18 (14%) |
| 2 | 2 (1.6%) |
| 3 | 105 (82%) |
| 4 | 3 (2.3%) |
| chronic_infarct_present | 26 (20%) |

[1] Median (IQR); n (%)

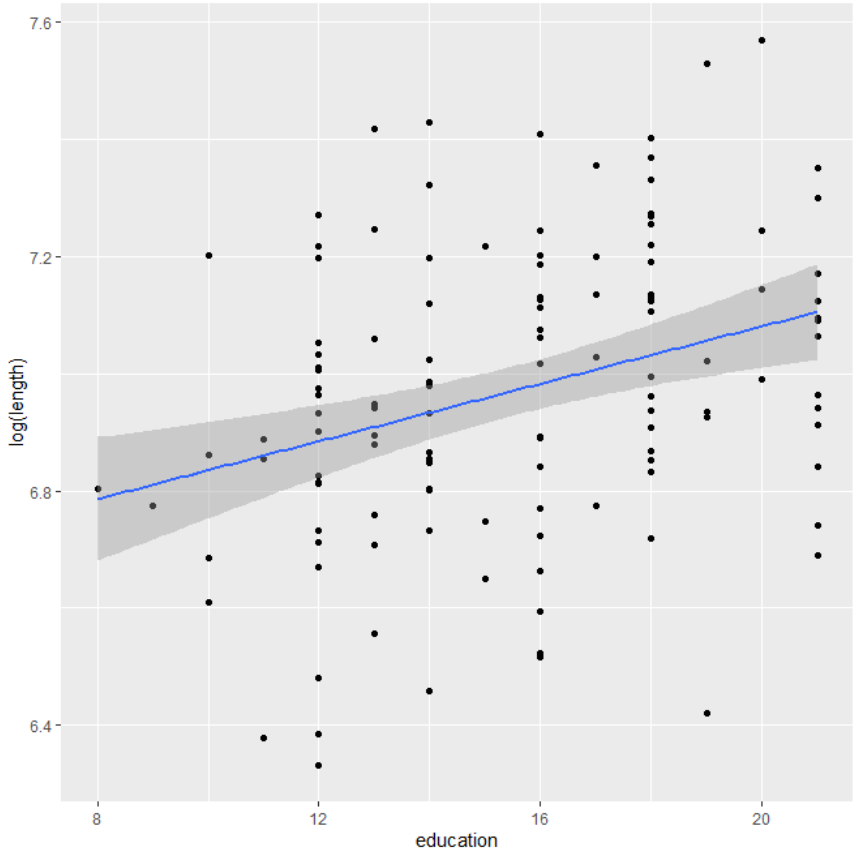
# Relationship of distal vessel length with age and education in ACT

Higher total cerebral artery length was associated with lower age




R=-0.24, P<0.01

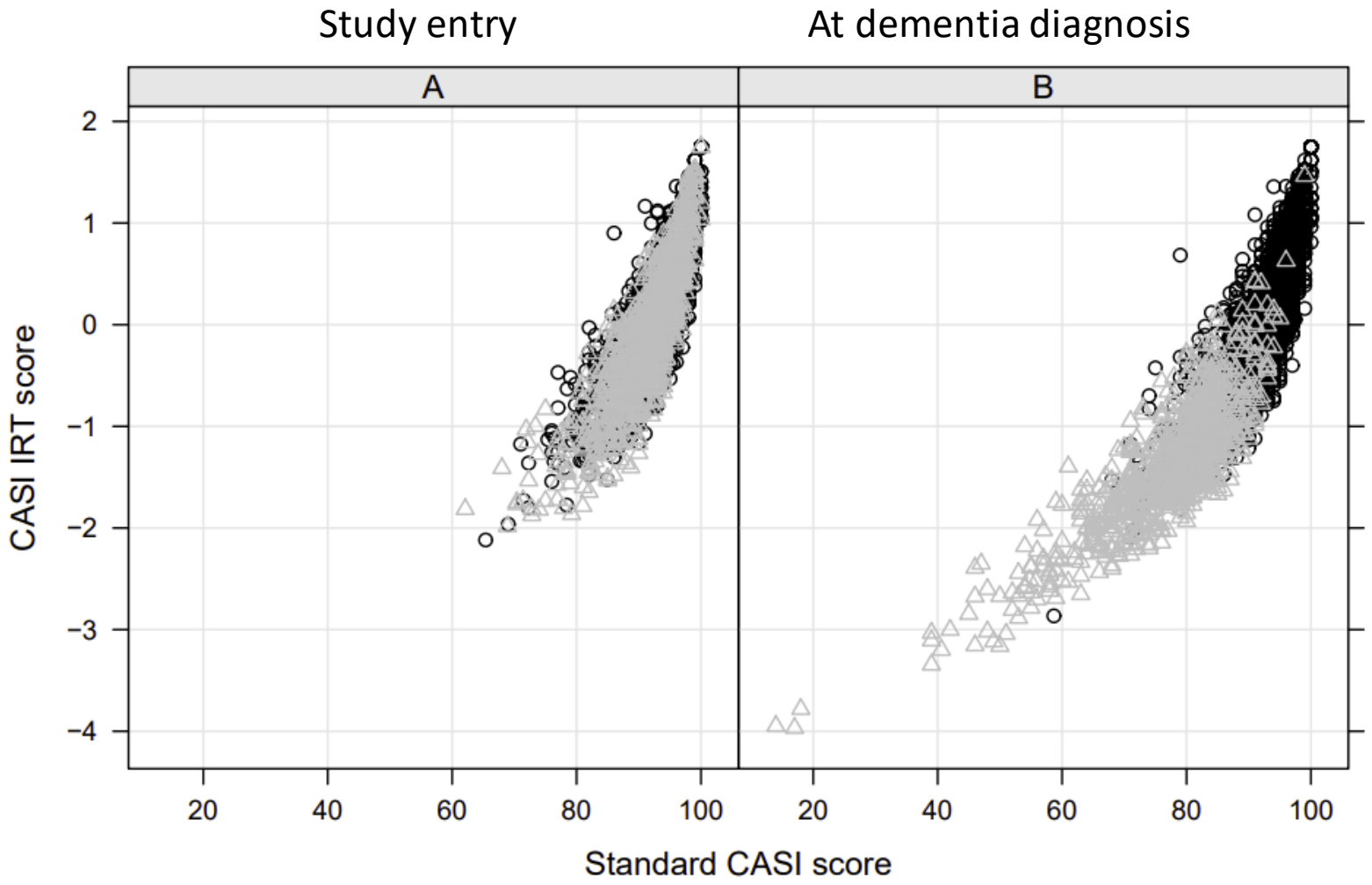
Higher total cerebral artery length was associated with higher number of years of education




R=0.33, P<0.001

# Cognitive scoring in ACT: CASI IRT score

- Measure of cognition in ACT subjects
- CASI: 40-item global cognitive test, total score of 0 – 100
- CASI IRT: Scaled CASI, approximately mean 0 and standard deviation (SD) 1
- We used CASI score closest to the date of clinical MRI scan




Ge Li et al, J Am Geriatr Soc. 2017 Dec; 65(12): 2627–2633.

# Distal PCA Length is related to Cognitive impairment

- Total distal artery length was not associated with cognition
- Our prior studies have also shown distal PCA length to be associated with cognition[1]

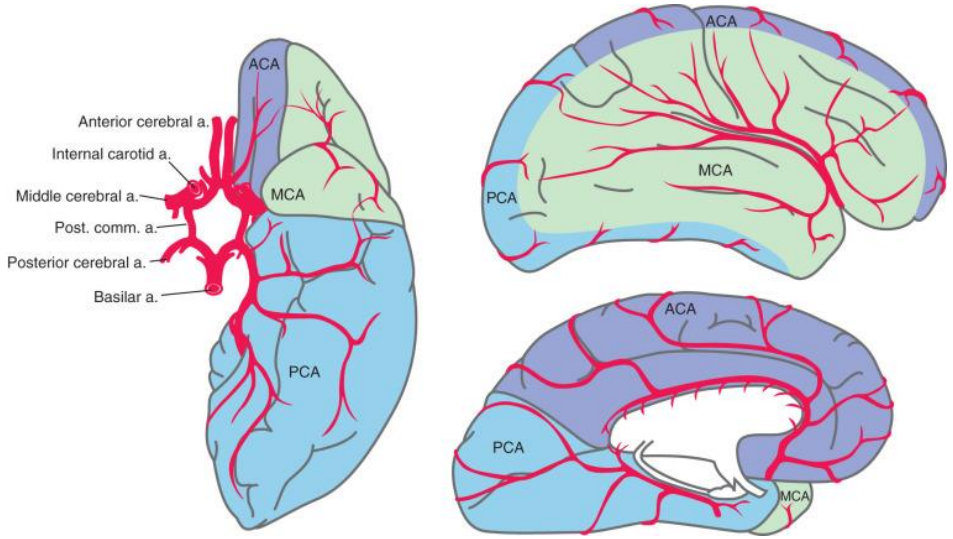
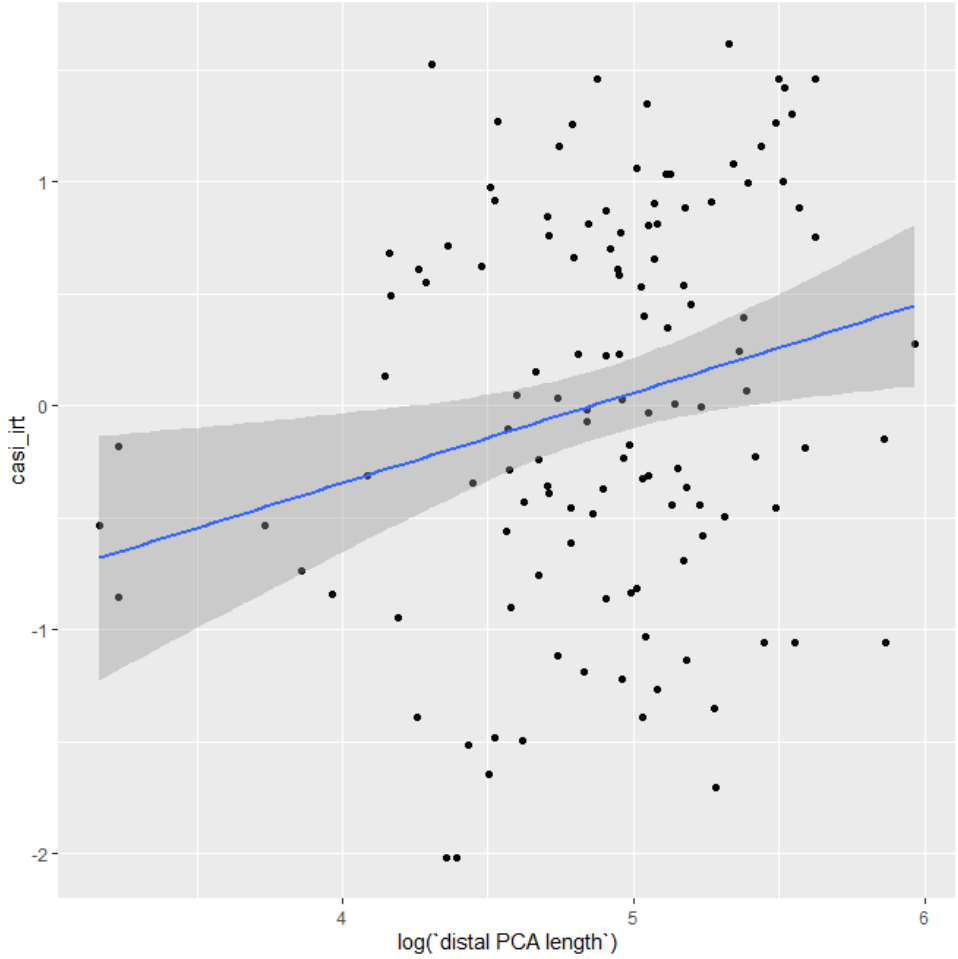


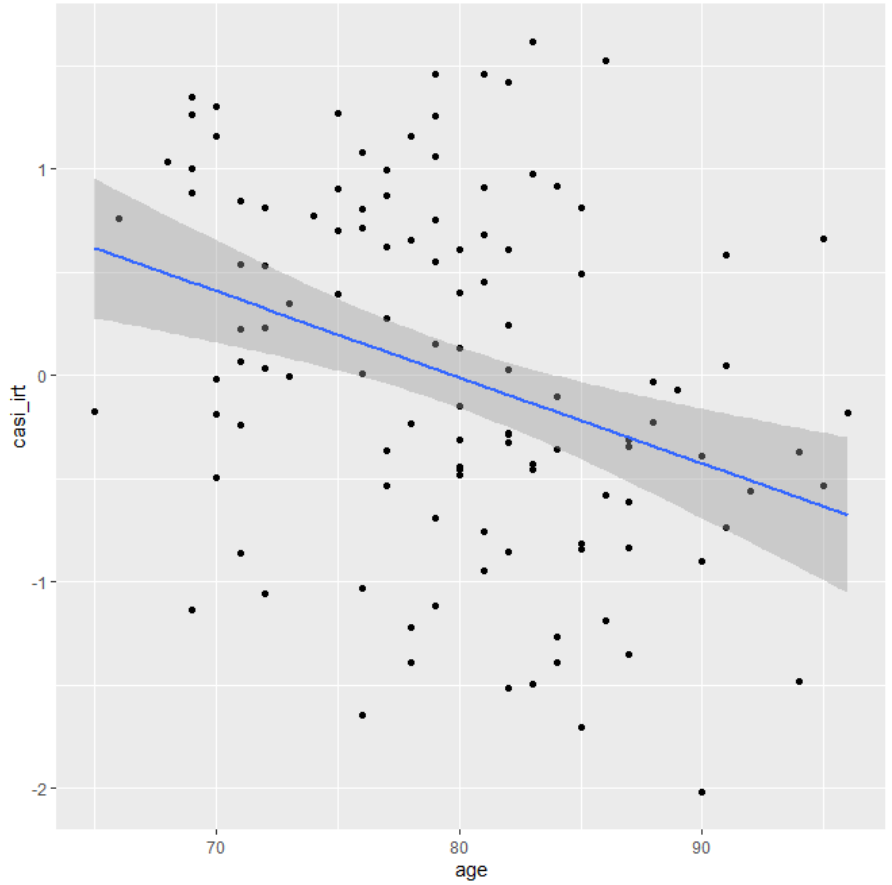

Image Source: NeupsyKey



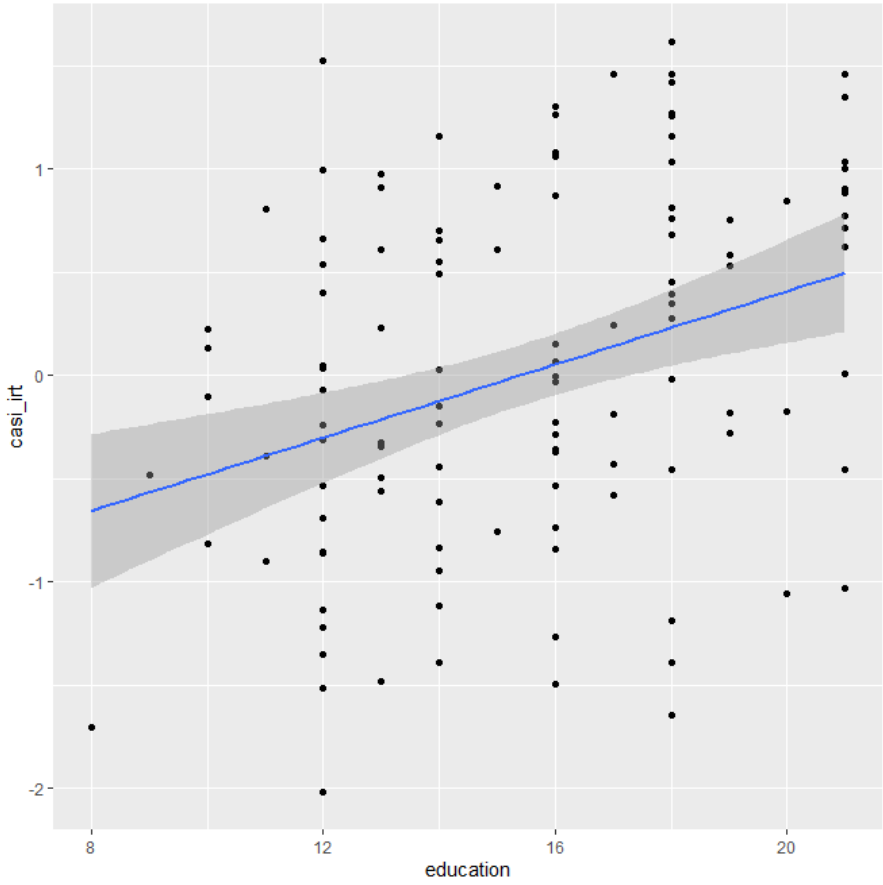

R=0.23, P<0.01

1. Zhang K et al, MRI, 2023

# Cognition is related to age and education




R=-0.35, P<0.001




R=0.33, P<0.001

- When examined in a multivariable regression, only age and education remained significant predictors of CASI scores.

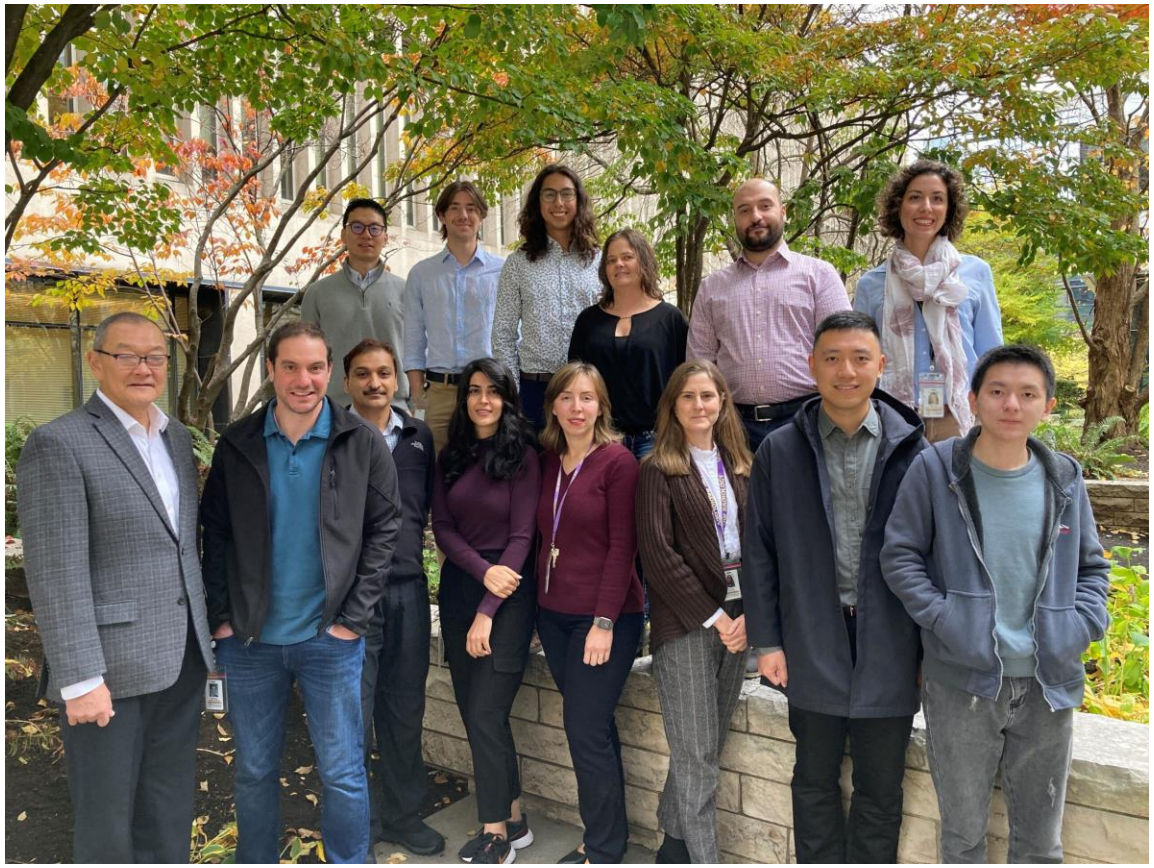
# Conclusions

- Distal vessel length is lower with higher age in ACT
  - Reduced blood flow to the brain
- Factors affecting cognition in ACT
  - Age
  - Education level
  - (Posterior cerebral artery length)
- Clinical MRA non-ideal for iCafe measures
  - Heterogenous protocols
- Research MRI scans ongoing
  - Neuroimaging Core

http://drleasure.com

# Acknowledgements


## Vascular Imaging Lab, University of Washington, Seattle



- Mahmud Mossa-Basha, MD
- Niranjan Balu, PhD
- Chun Yuan, PhD
- Thomas Hatsukami, MD

- Baocheng Chu, MD PhD
- Maria Gador Canton, PhD
- Daniel Hippe, MS
- Dongxiang Xu, PhD
- Duygu B Geleri, MD
- Mona Kharaji, MD
- Mohamed Mosi, MD
- Ahmed Safwat, MD
- Mohammed Dawood, MD
- Kristi Pimentel
- Tong Zhu

- Yin Guo
- Kaiyu Zhang
- Xin Wang
- Robert Ritchie
- Max Kobiesa

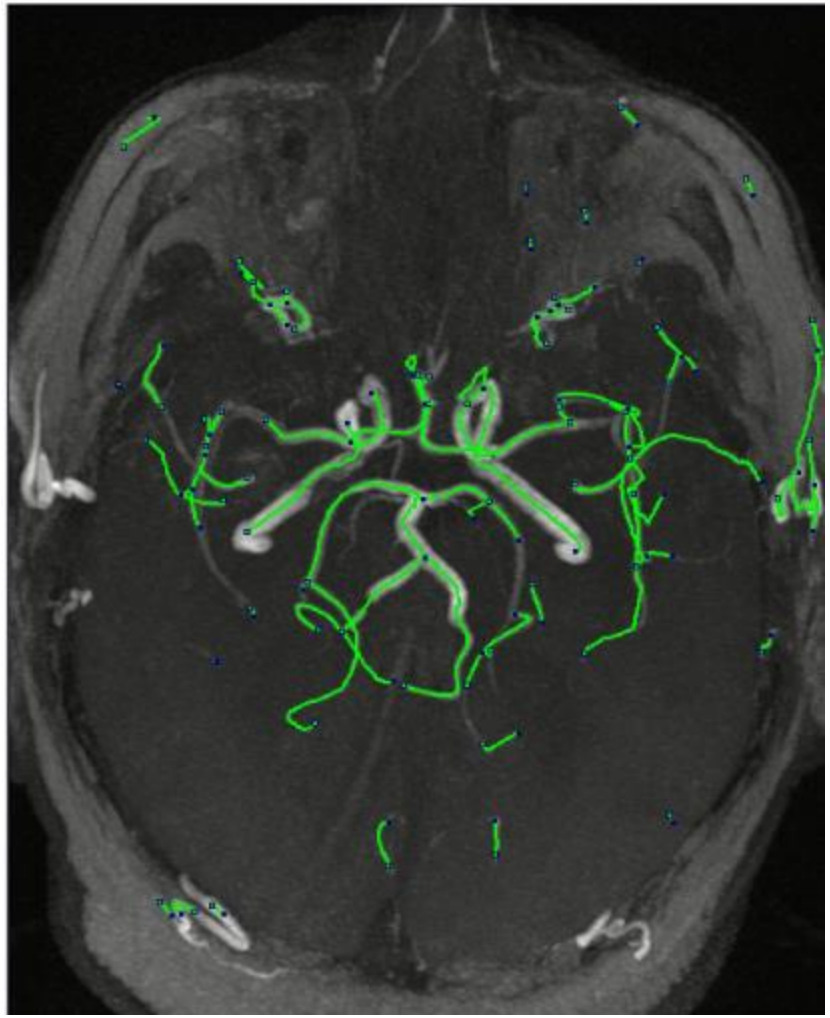
## ACT Neuroimaging

- Paul Crane, MD
- Cecilia Lee, MD
- Christine MacDonald, PhD
- Jalal Andre, MD
- David Hunt, PhD
- Missy Takahashi
- Ariel Rokem, PhD
- Kelly Chang, PhD
- James Ralston, MD
- Patti Curl, MD
- Margaret Dezelar, MS
- Luke Burke
- John Ewing
- Bradley Howlett
- Nina LaPiana
- Samantha Tuesta

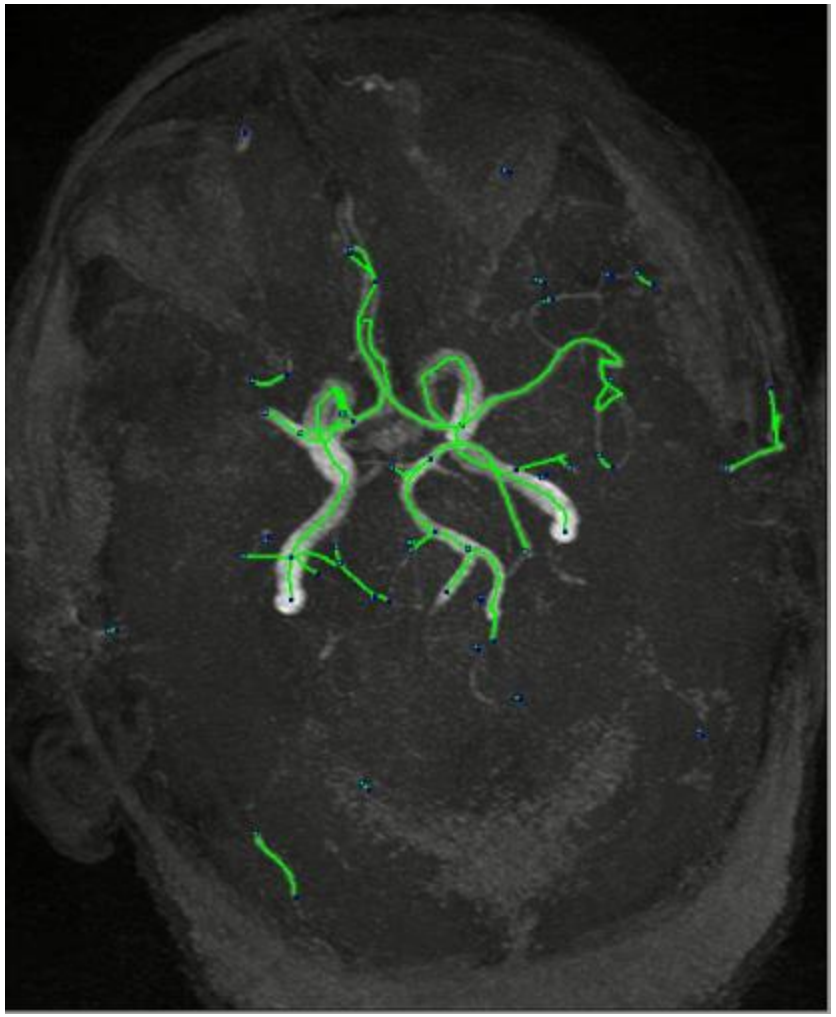
R01HL103609
R01NS125635
R01NS127317

# Additonal Slides

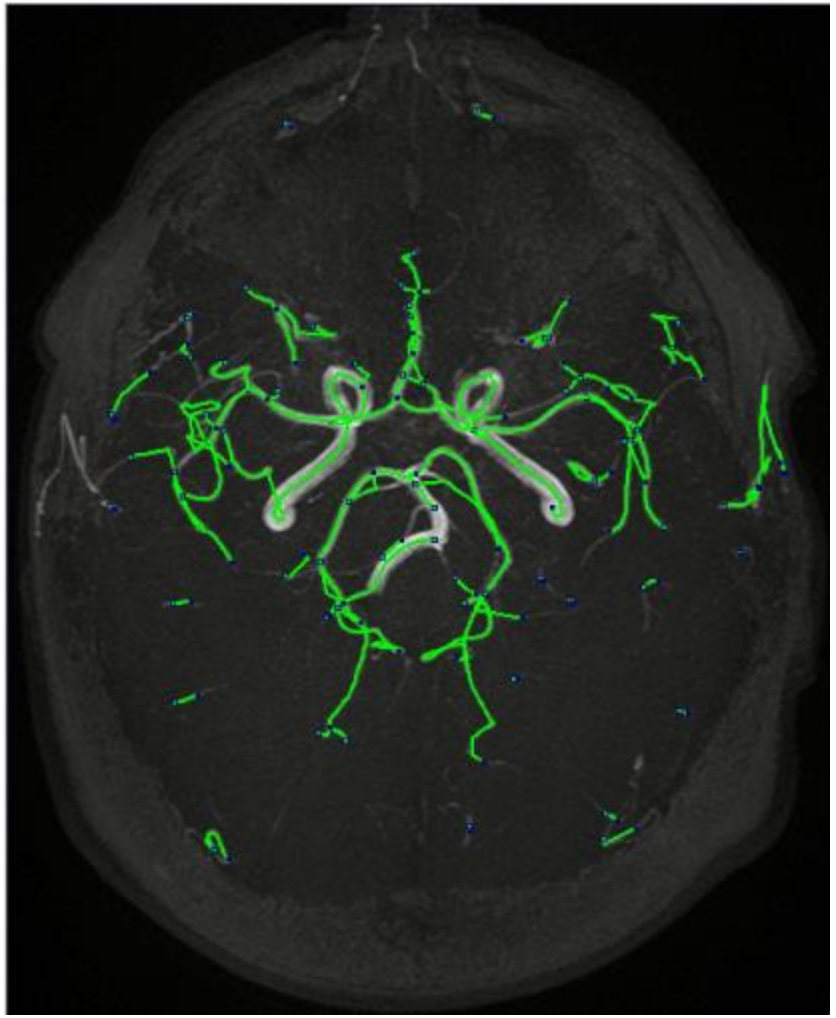
# Group 1



39014917

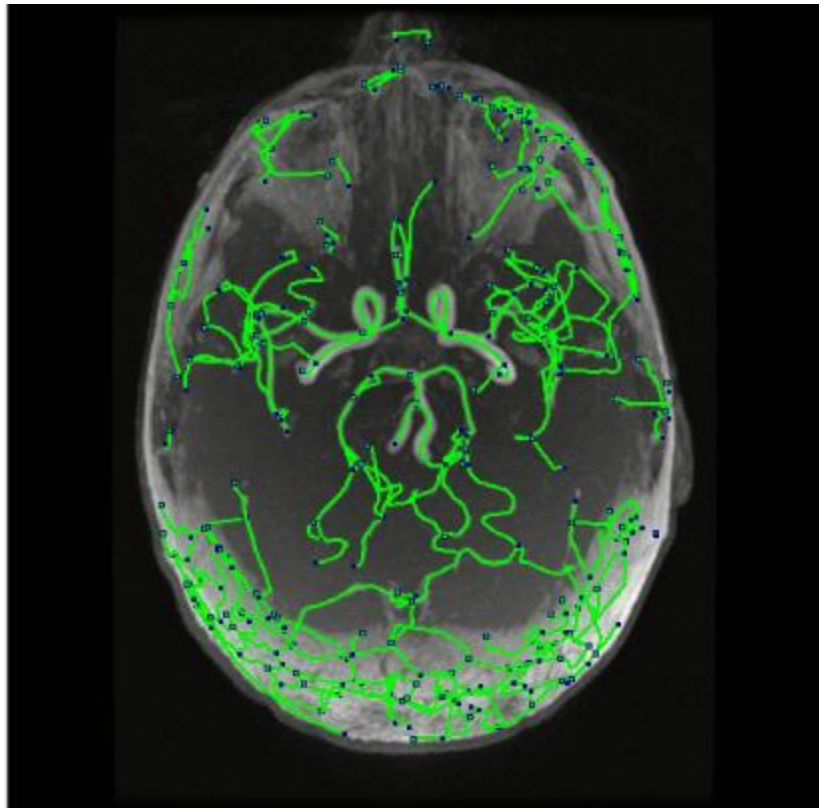


38557868

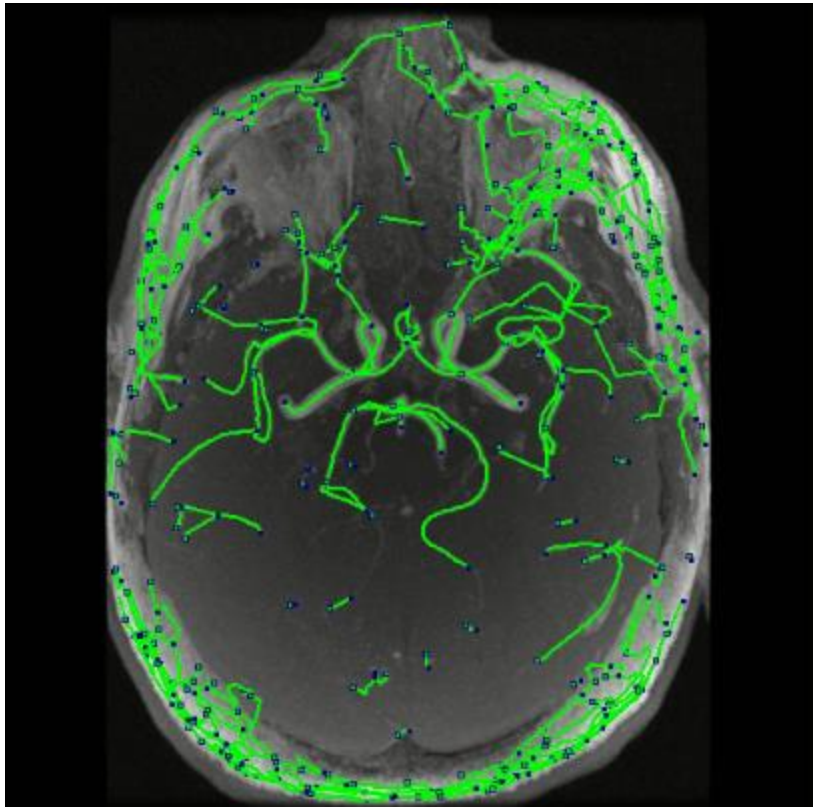


35894201

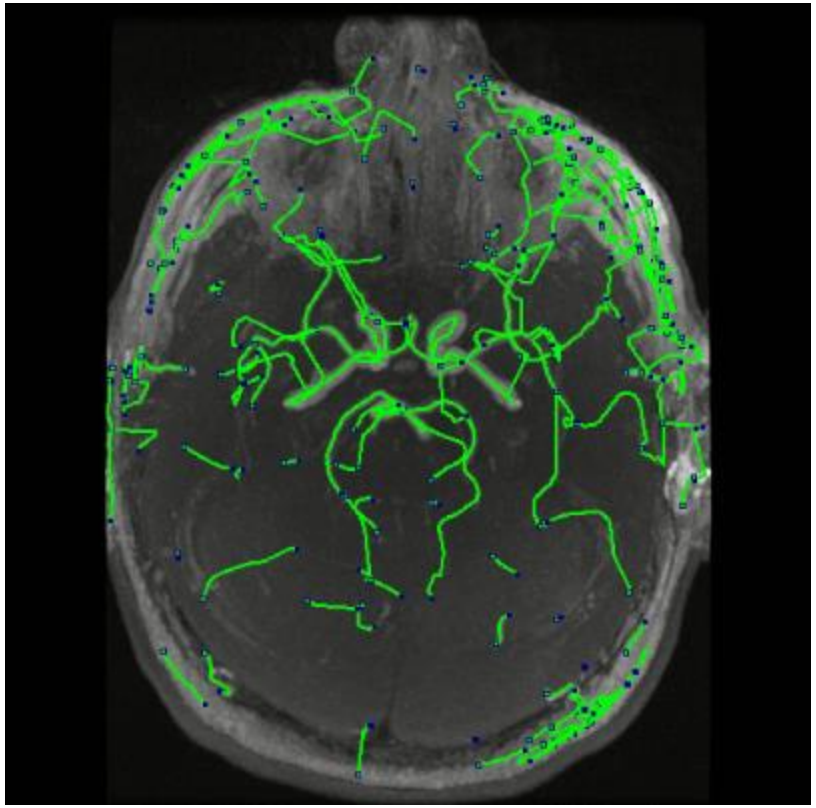
# Group 2



36089095



39944489



39523124