Cranial Hemodynamics assessed with MRI: An introduction with relevance to AD

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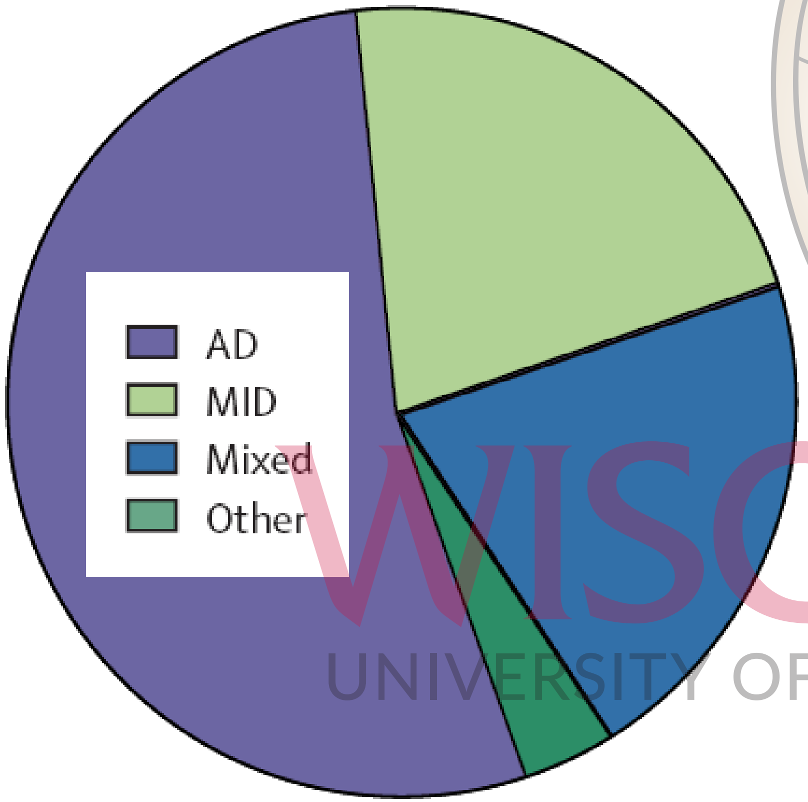
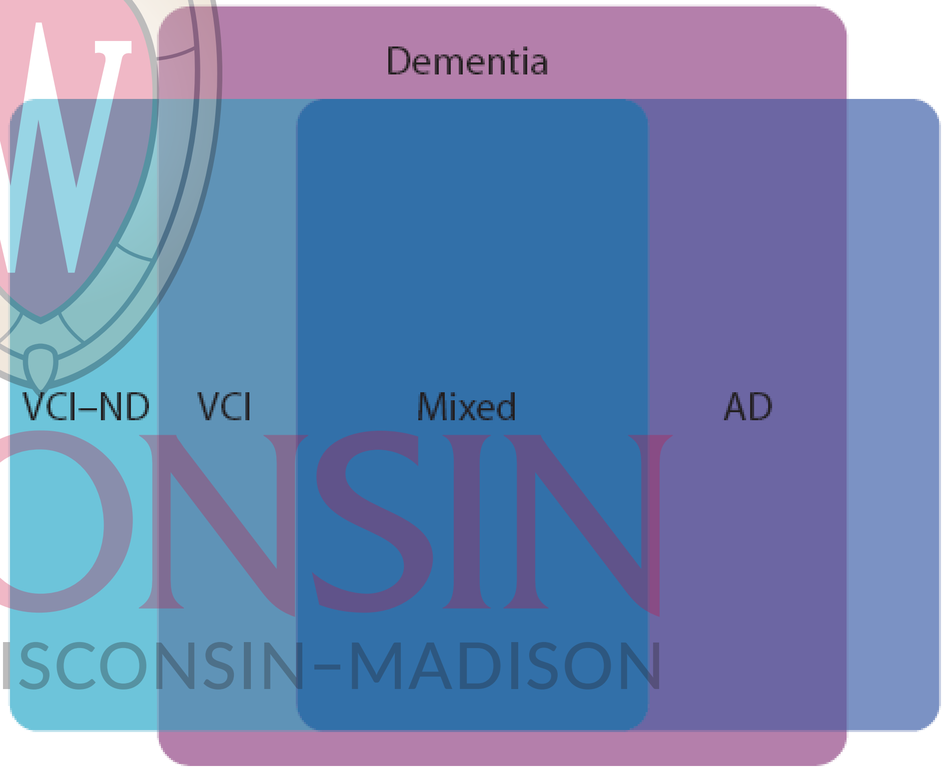
Contribution of Vascular Disease to Dementia

Traditional



Revised



Moorhouse, P Lancet Neurol 2008; 7: 246–55

Vascular Disease Markers

<u>Systemic Markers</u>

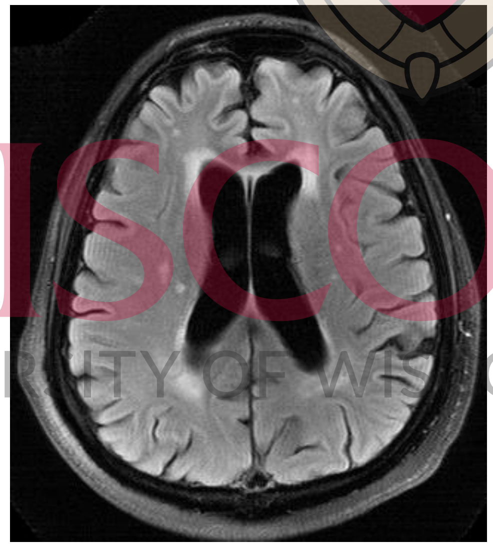
Blood Pressure
Cholesterol
Genetics

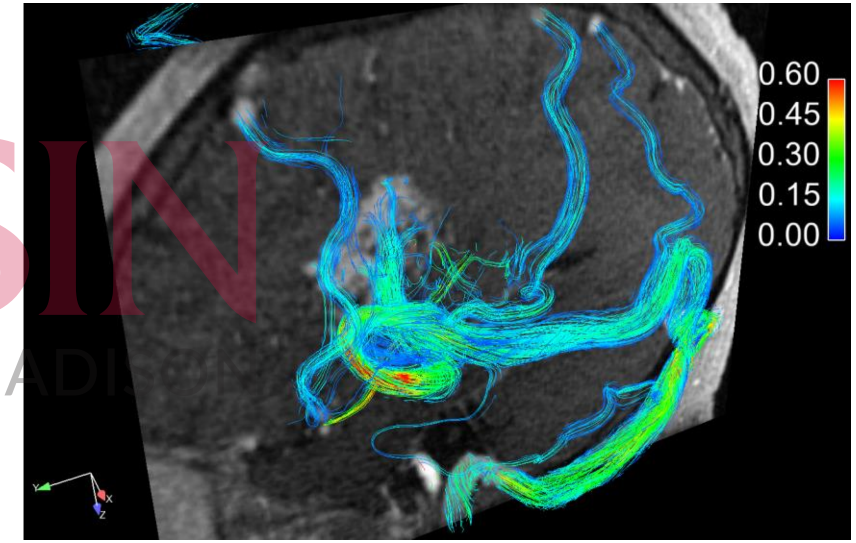
<u>Structural Imaging</u>

White Matter Lesions
Microbleeds
Diffusion

<u>Functional Vascular Imaging</u>

Perfusion
Flow imaging





Overview

- **Introduction** to Blood Flow Measures with MRI
  - —Kevin Johnson, Assistant Professor, Medical Physics and Radiology
- **What can we measure** and how we measure it
  - —Grant Roberts, PhD Candidate, Medical Physics
- **Results** in studies of ADRD
  - —Leonardo Rivera-Rivera, Postdoctoral Fellow

WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON

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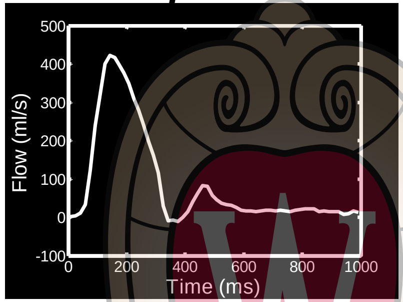
Arterial Network

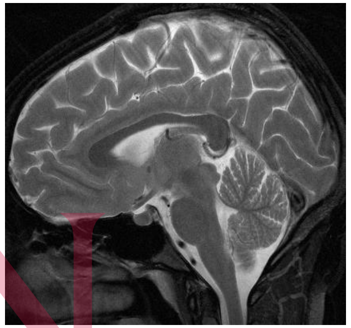
transport +



Brain Tissue

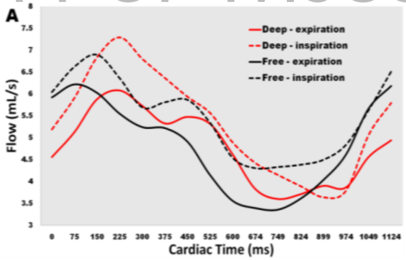
Capillary Bed

exchange + regulation

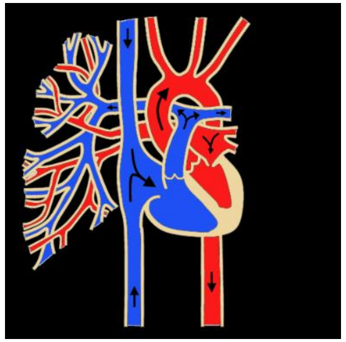


Venous Network

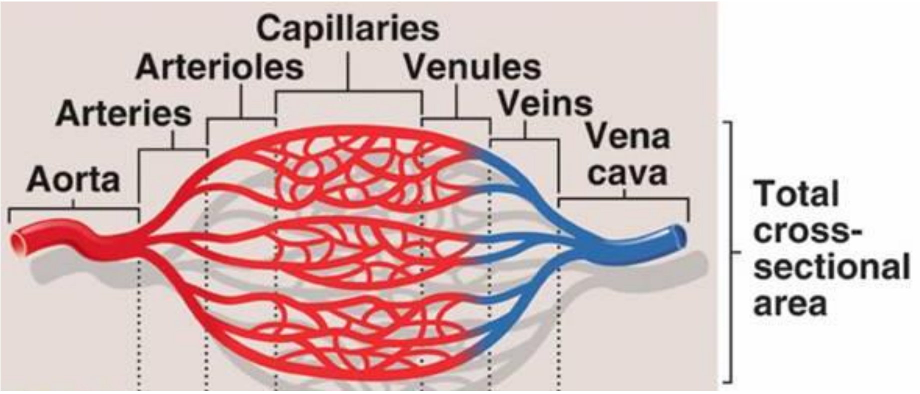
transport (waste clearance)



Waste / Nutrient Exchange (lung/liver/kidneys)



Vascular Imaging Landscape



Tissue Perfusion

Cerebral Blood Flow CBF [ml/100g/min]

Cerebral Blood Volume CBV [ml/100g]

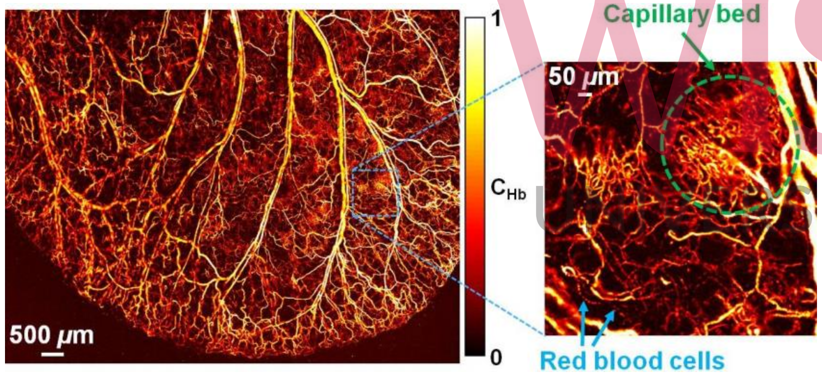


Photo acoustic Microscopy: Yeh,C et al. J Biomed Optics 14', 19(9):96011

CT: Iodine, Xenon

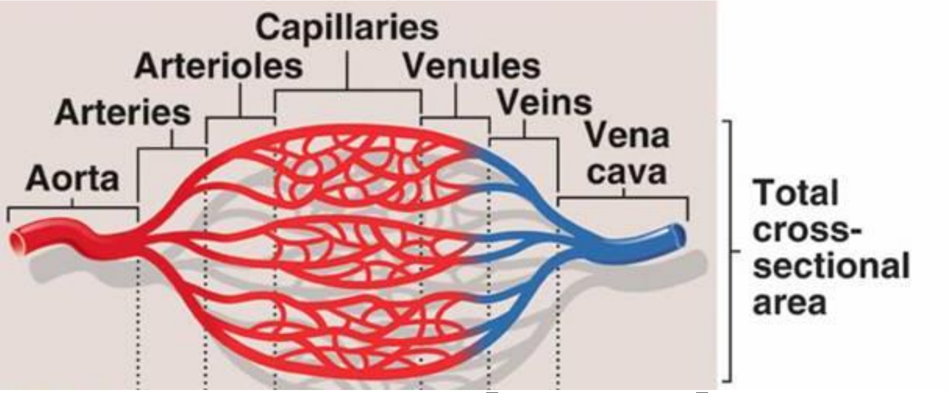
^{15}O PET

MRI:

Arterial Spin Labeling (ASL), Contrast Media

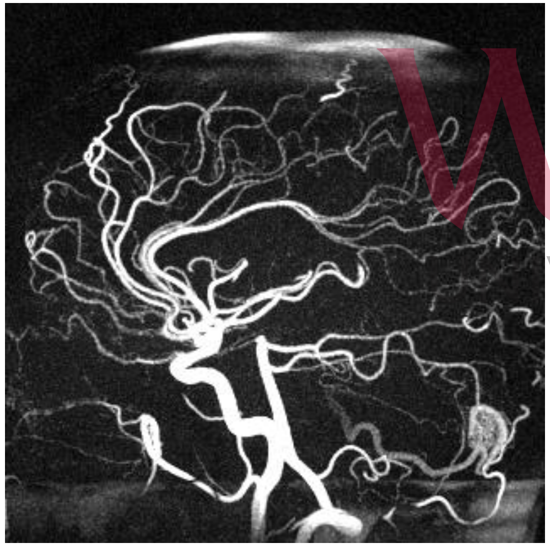
To be covered in future lecture

Vascular Imaging Landscape



Arteries

Veins



CT / DSA Angiography

Quantifying Intracranial Hemodynamics

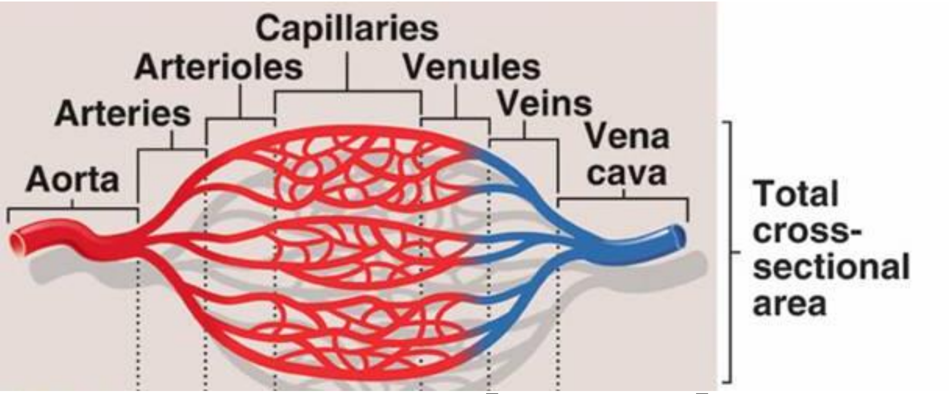
- X-Ray Digital Subtraction Angiography
  - (+) High spatial and temporal resolution
  - (−) Radiation, intra-arterial injections of contrast agent
  - (−) Extracting velocities / flow is challenging

Intracranial Aneurysm – DSA

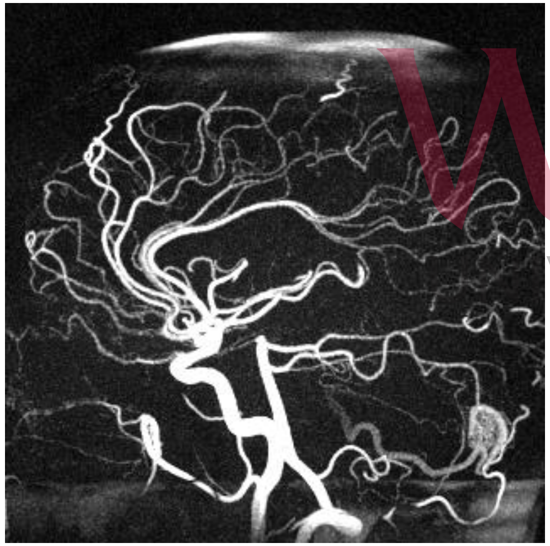
2D projection
1024x1024 matrix,
30 frames per second

S Shpilfoygel et al., Med Phys. 2000 Sep;27(9):2008-23.

Vascular Imaging Landscape



Arteries **Veins**

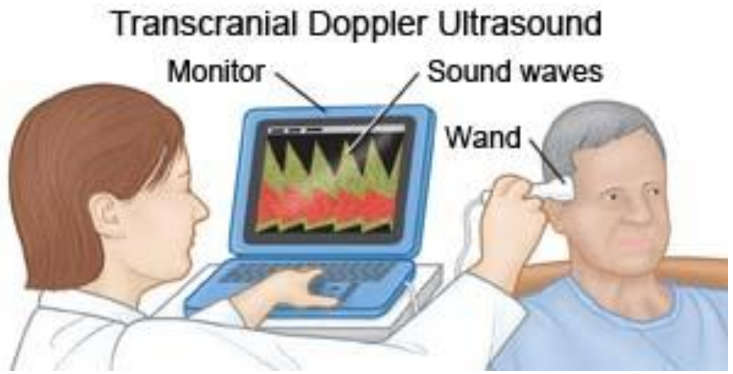


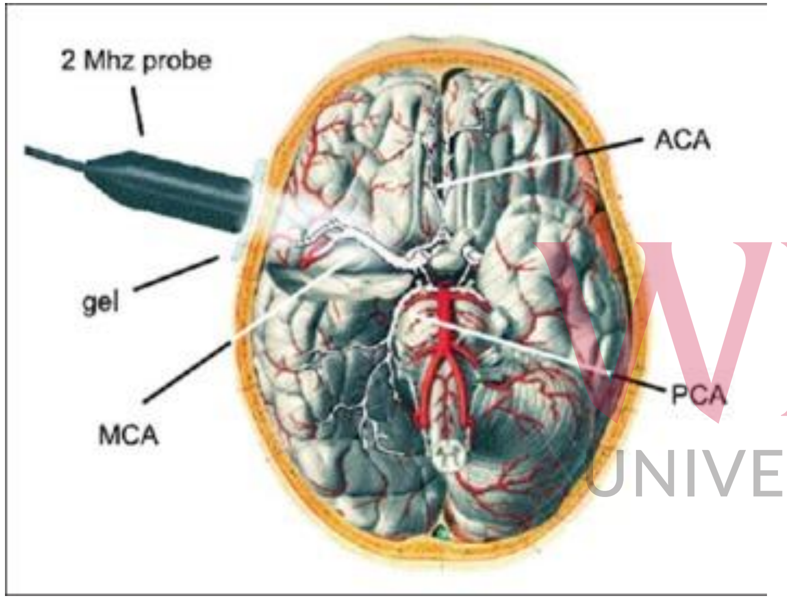
CT / DSA Angiography

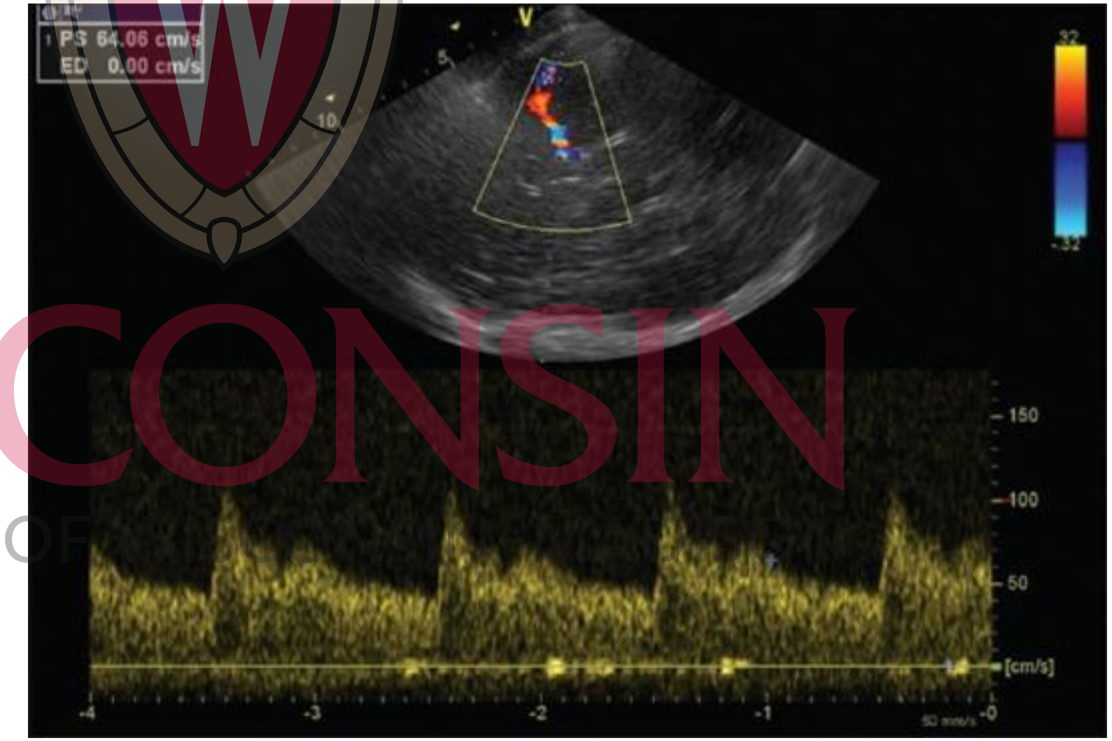
Doppler Ultrasound

Quantifying Intracranial Hemodynamics

- Transcranial Doppler ultrasound (TCD)
  - (+) Inexpensive, high frame rates
  - (−) Dependent on sonographer skill
  - (−) Limited by beam penetration of the bone window
  - (−) Flow estimated from velocity profile and area estimate

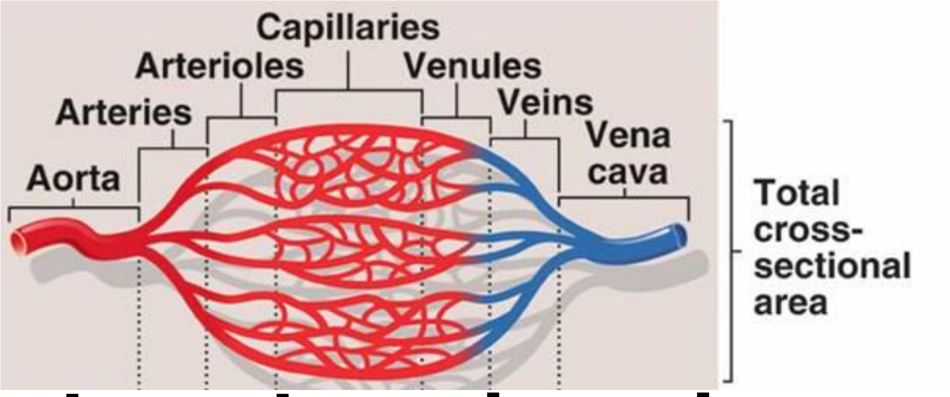




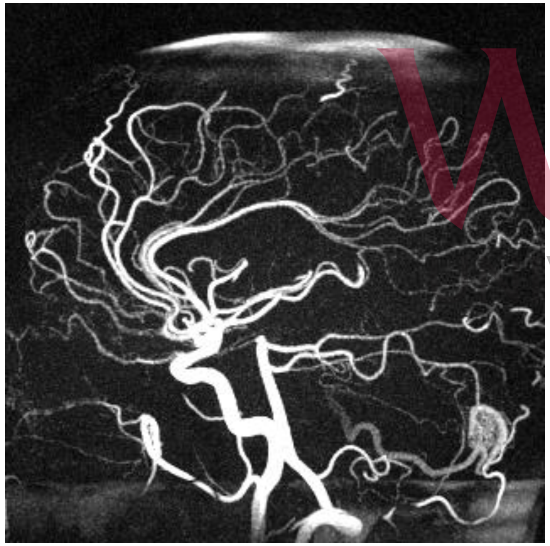


D'Andrea et al., J Cardiovasc Ecogr. 2016 Apr-Jun; 26(2)

Vascular Imaging Landscape



Arteries **Veins**



CT / DSA Angiography

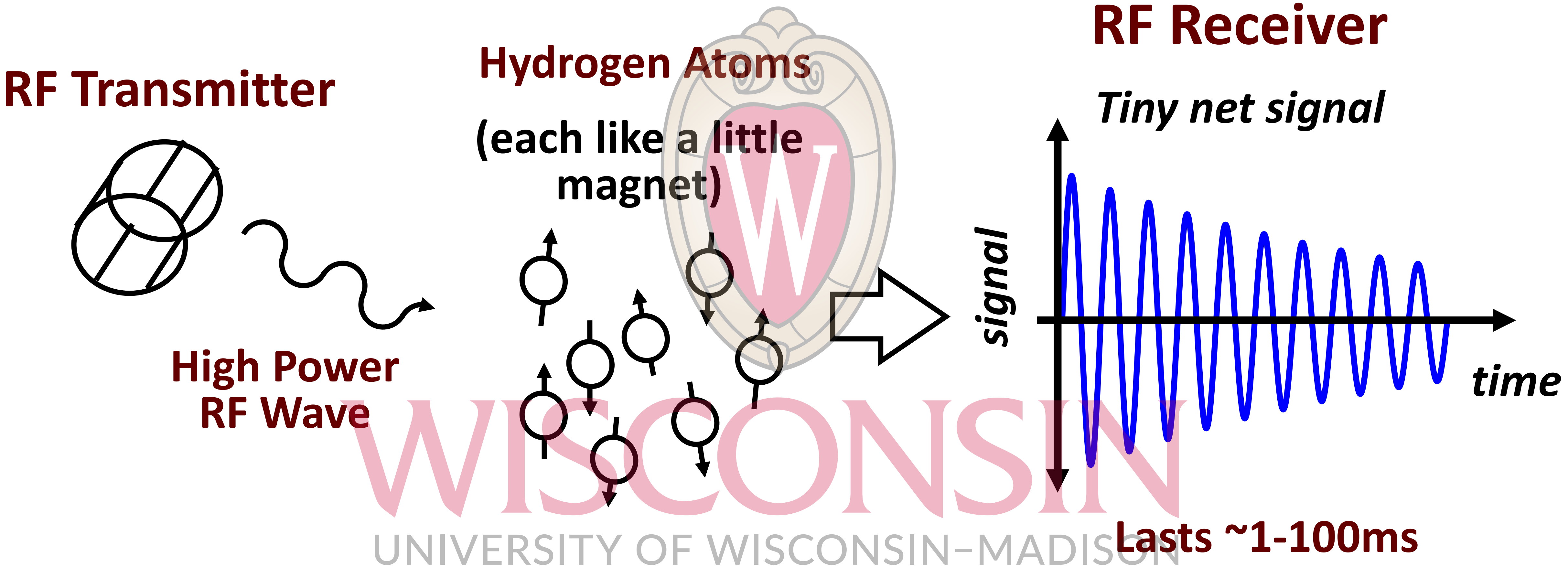
Doppler Ultrasound

MRI:

MR Angiography

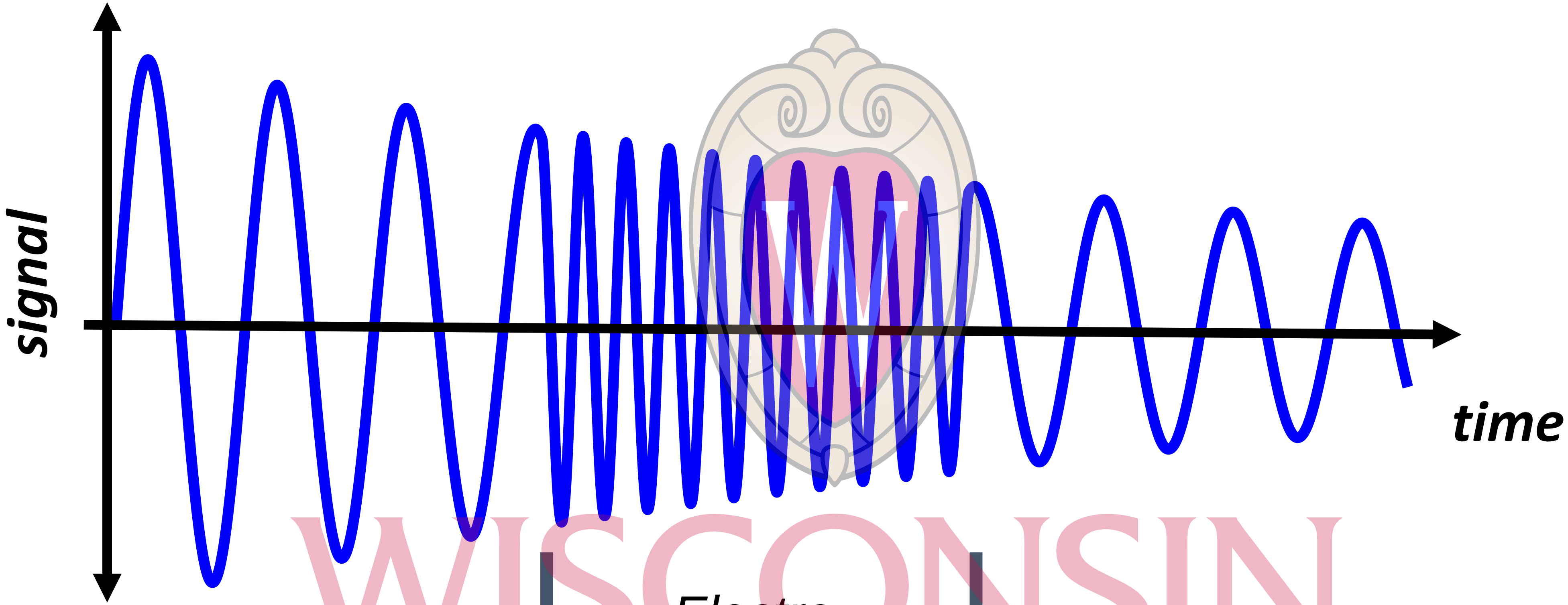
Phase Contrast Flow Imaging

MRI : Excitation



MRI : Spatial Encoding

- The signal can be modified after excitation and has memory!

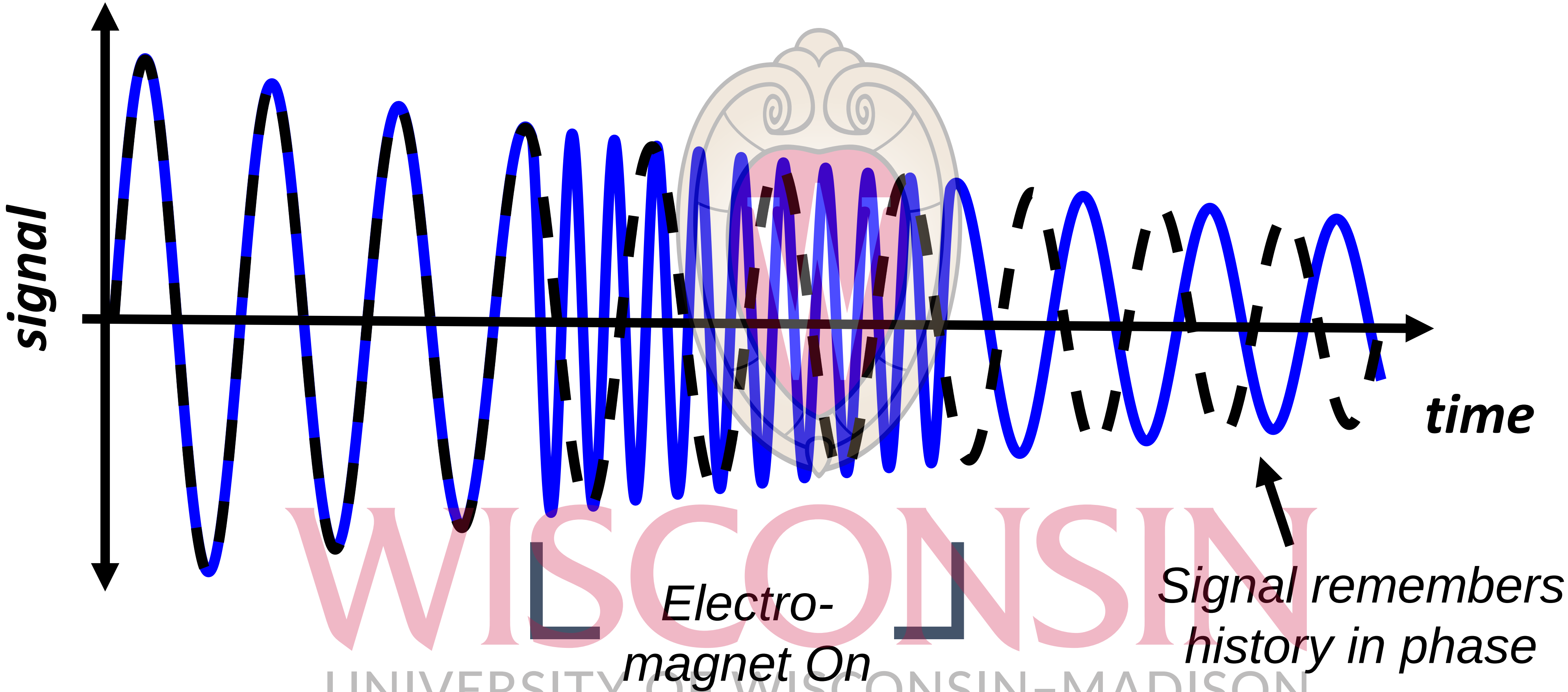


<u>Dynamic Electromagnets encode Position</u>

(Also make scans loud)

MRI : Spatial Encoding

- The signal can be modified after excitation and has memory!



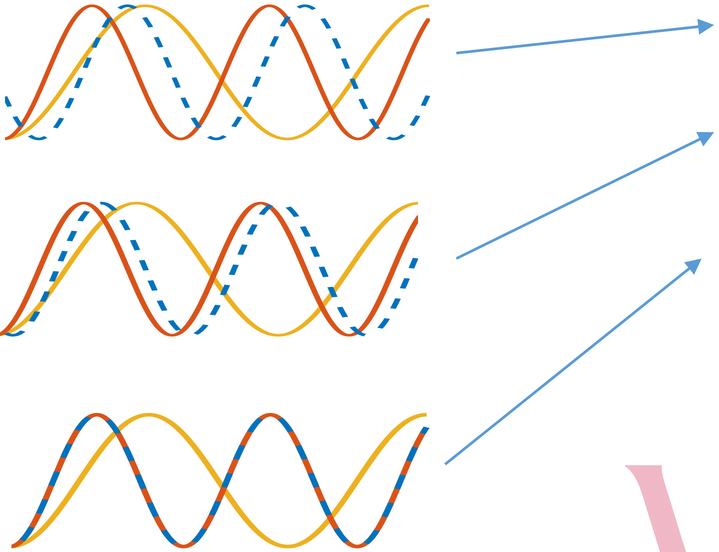
<u>Dynamic Electromagnets encode Position</u>

(Also make scans loud)

MRI : Spatial Encoding

Raw Data

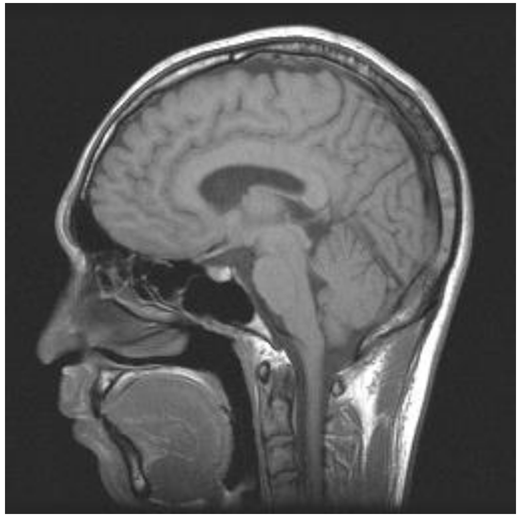
(Mixed Frequencies)

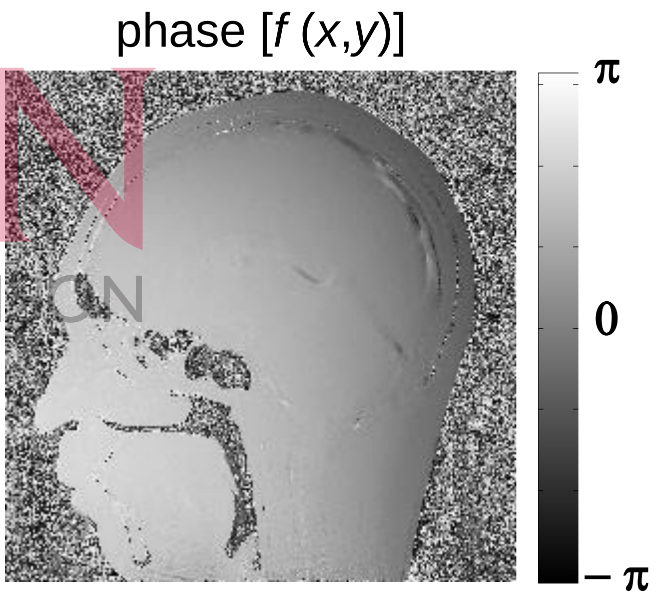


Signal Separator

(~Fourier transform)

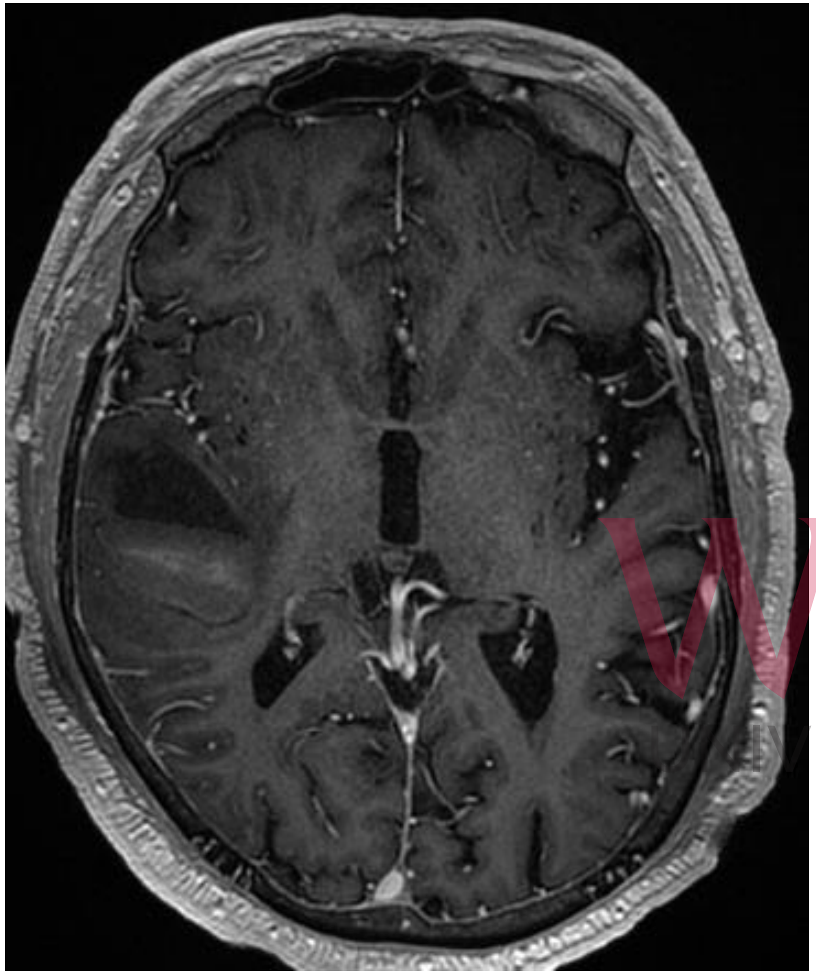
MRI Image





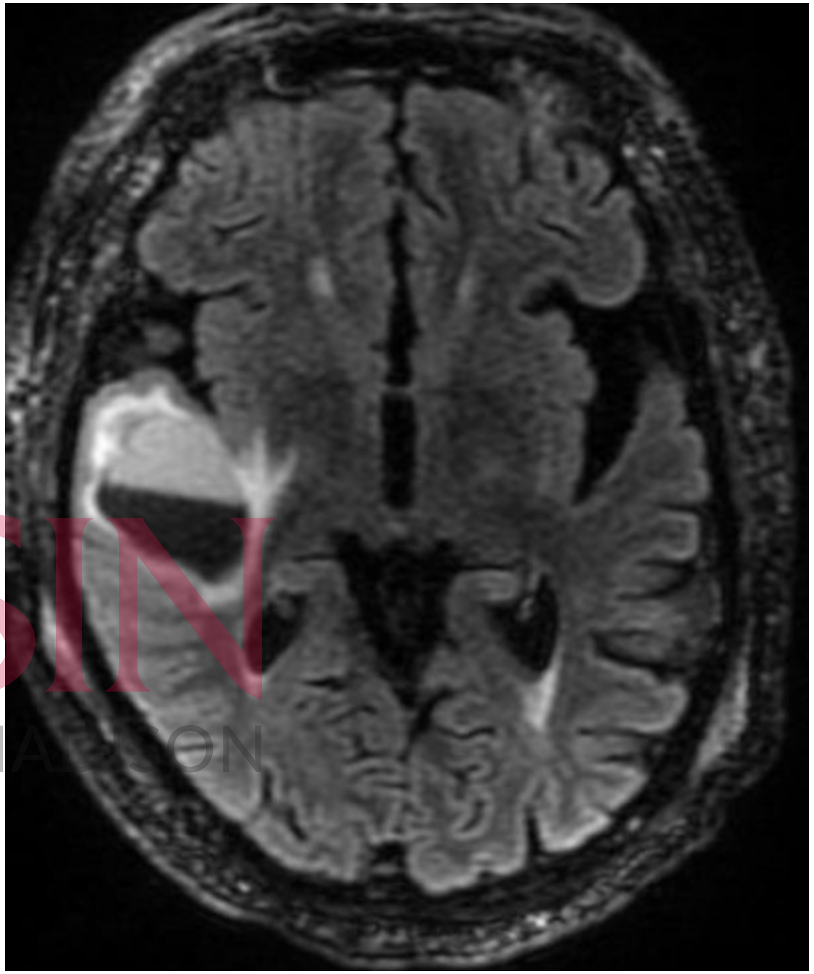
MRI Provides Opportunities to Manipulate Contrast

Bright Blood

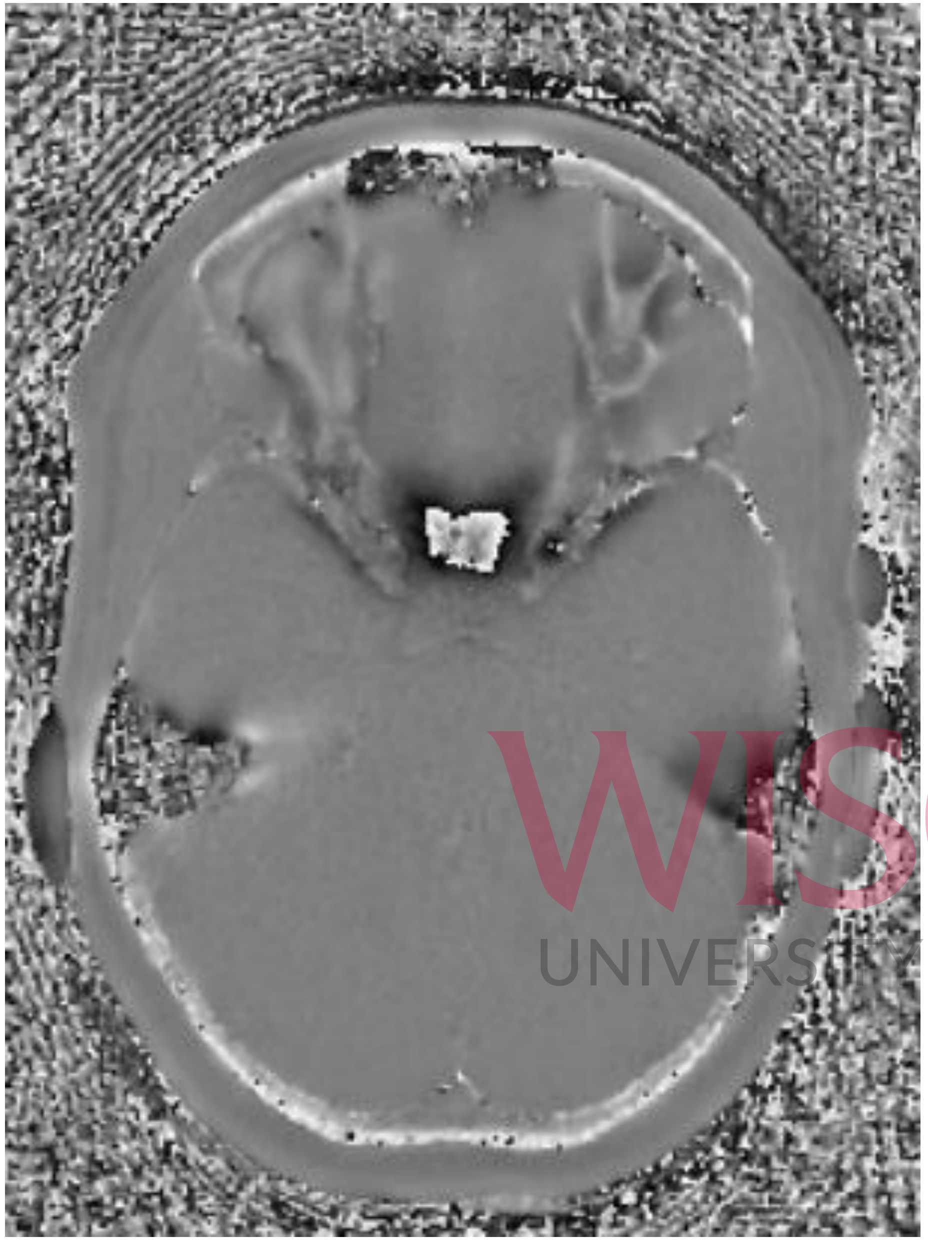


Bright Fluid

Dark Fluid



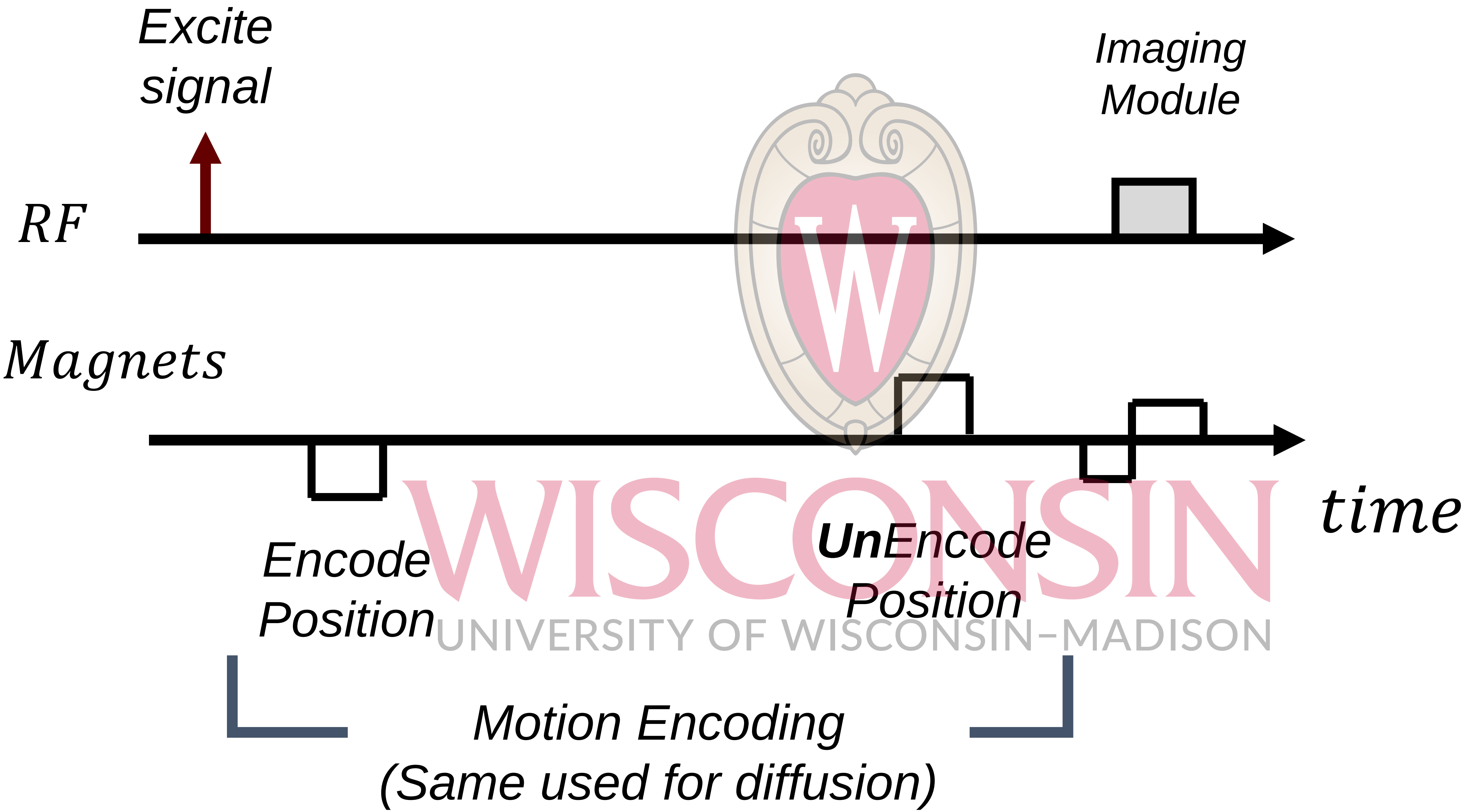
The image phase is often uninteresting



Phase image has limited contrast

(QSM) Susceptibility Mapping does use this phase

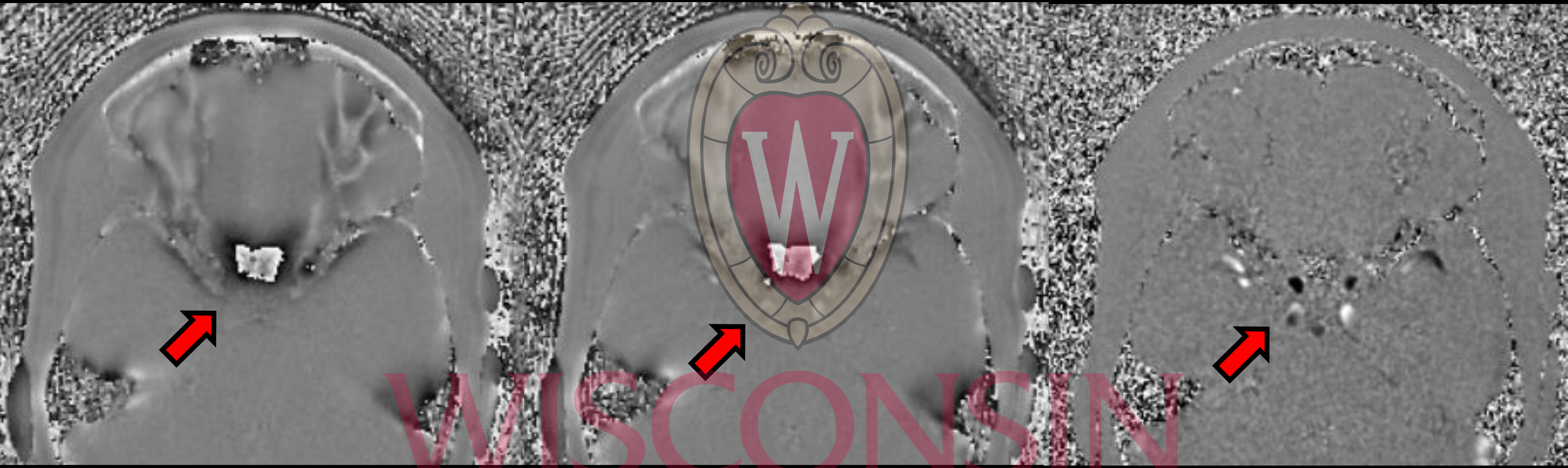
Motion Sensitization with MRI



Without Motion Encoding | With Motion Encoding

Phase images change based on velocity

Without Motion Encoding - With Motion Encoding = Difference (Velocity)



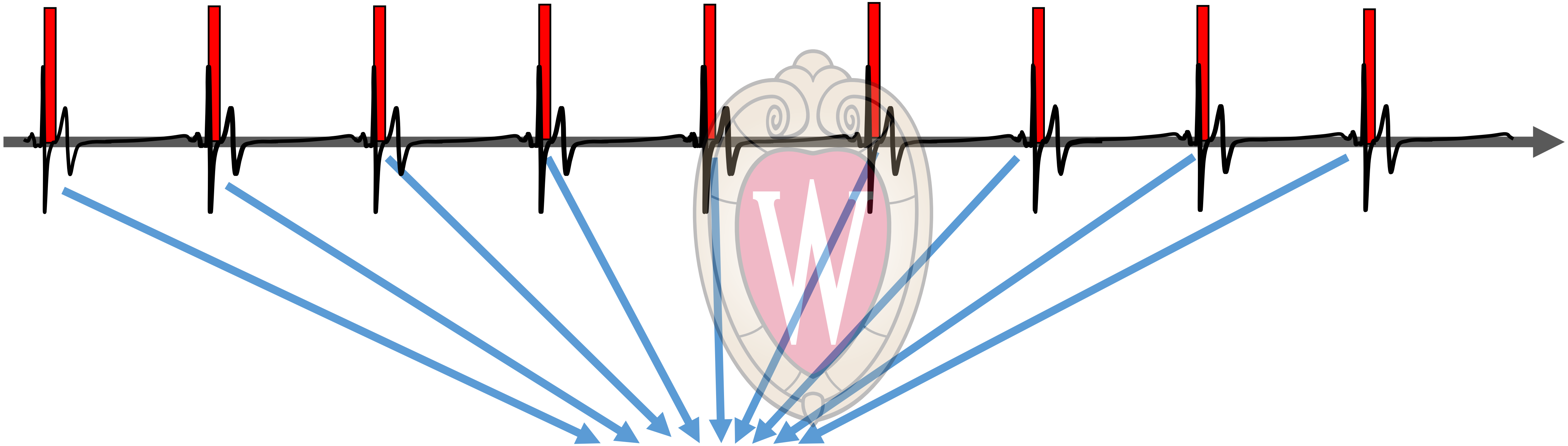
ϕ $\phi + v$ v

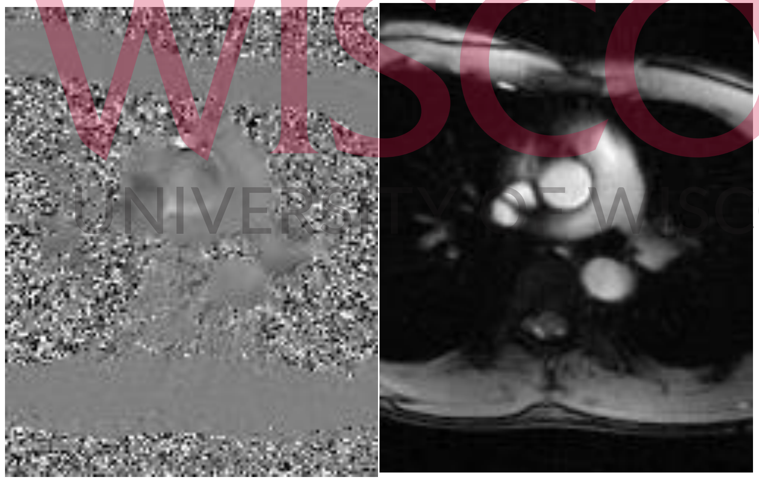
Without Motion Encoding

With Motion Encoding

Magnitude images unaffected unless we use strong gradients (diffusion imaging!)

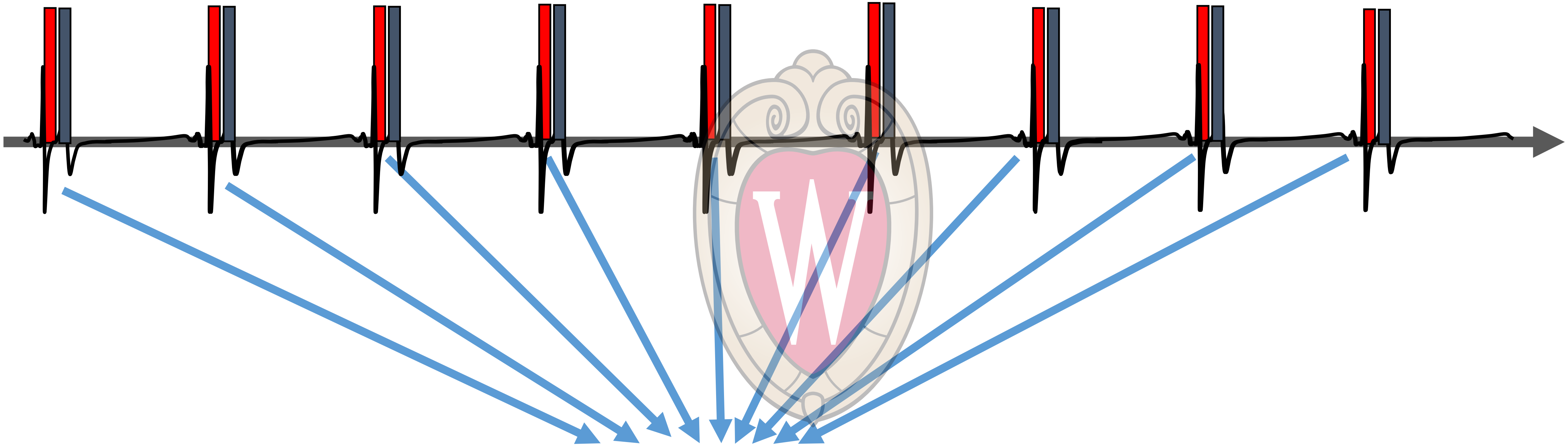
“Gating” allows part of image to be collected in each cycle

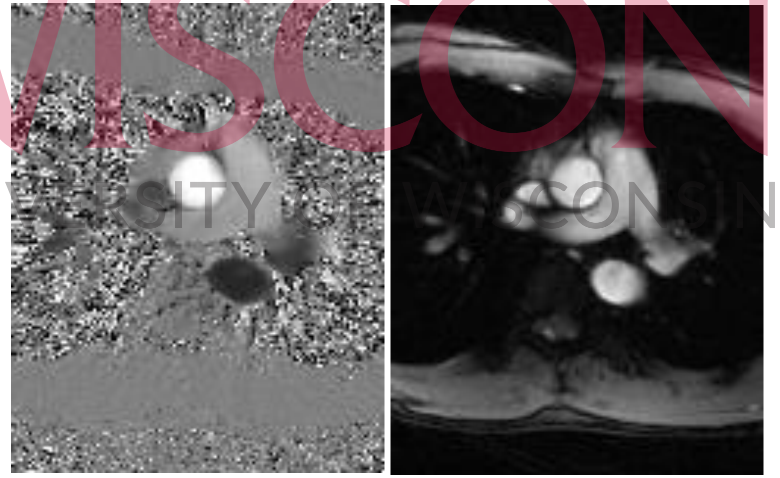




- Gated Image
  - From many cycles
  - Temporal resolution as low as 5-10 ms

"Gating" allows part of image to be collected in each cycle

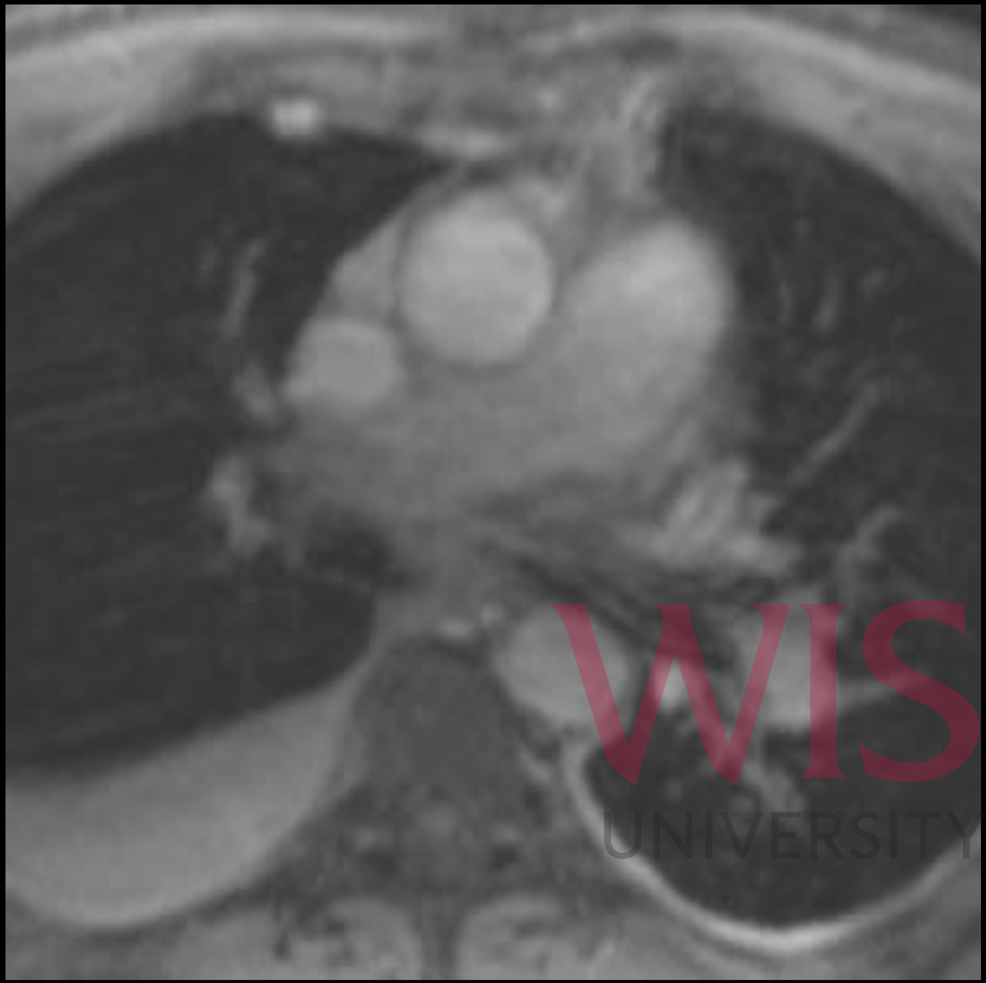




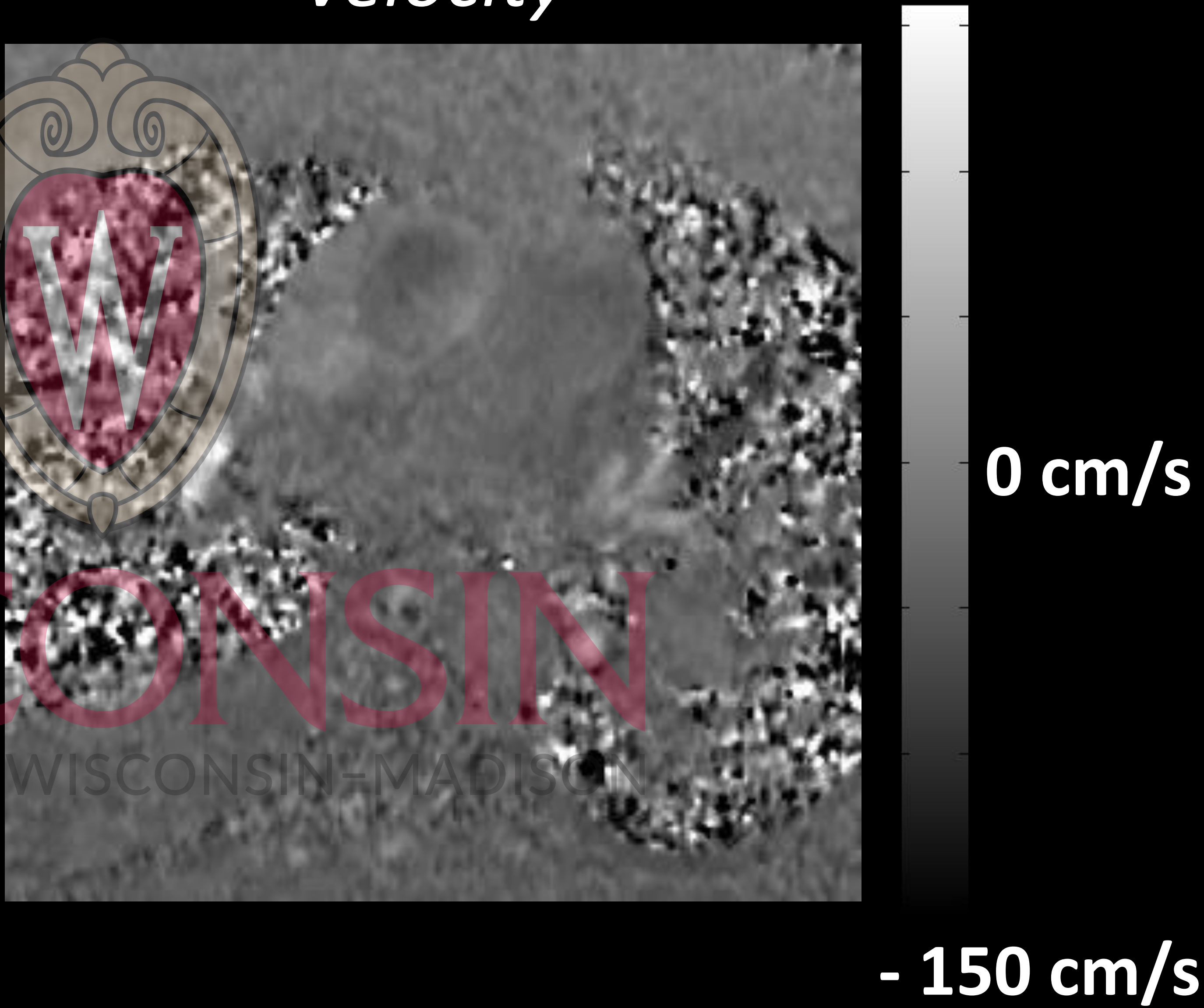
- Gated Image
  - From many cycles
  - Temporal resolution as low as 5-10 ms

RESULTING IMAGES – CARDIAC RESOLVED

Magnitude



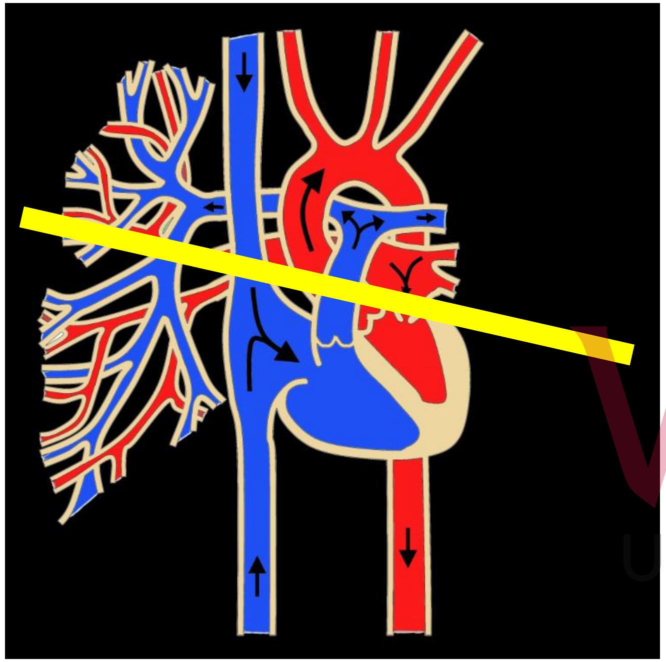
Velocity



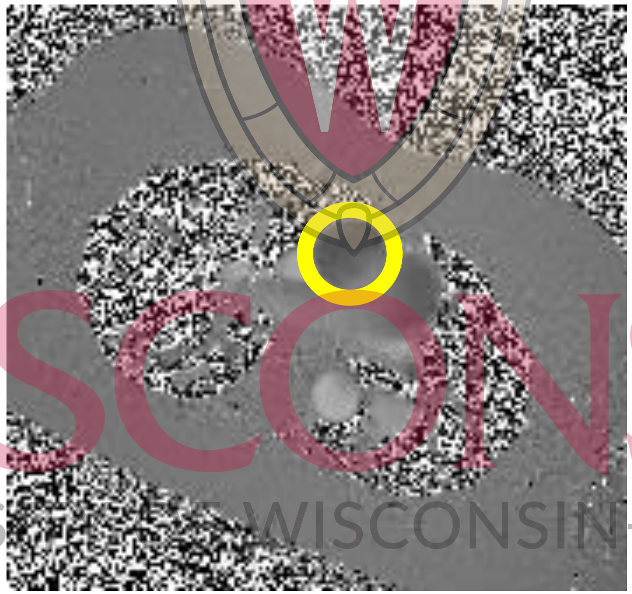
2D Phase Contrast MRI

- Common flow techniques use 2D MRI planes

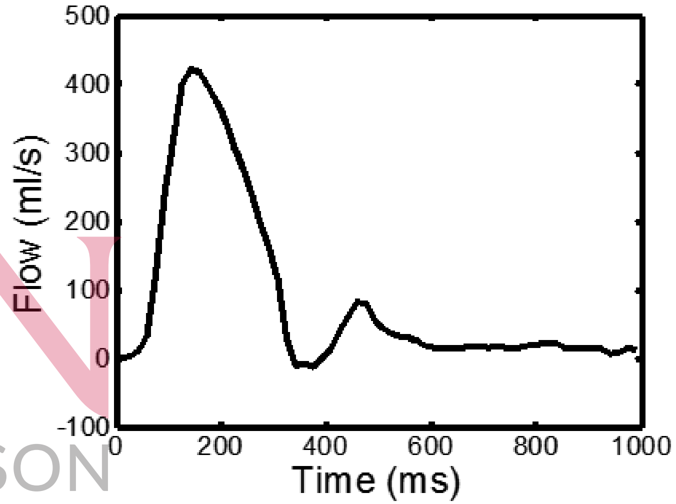
Plan Target Plane
(cross section of artery)



Acquire Images

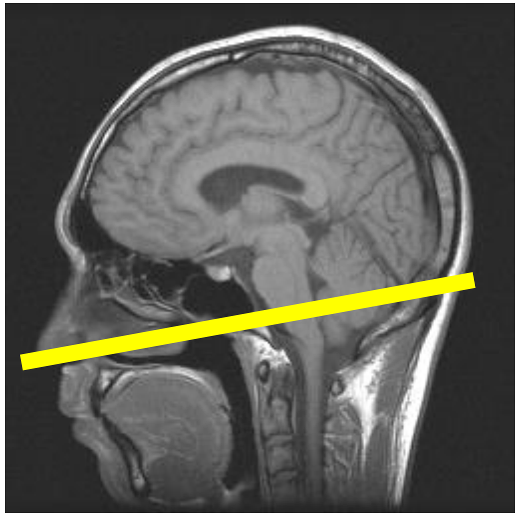


Analyze Locally
(e.g. flow)



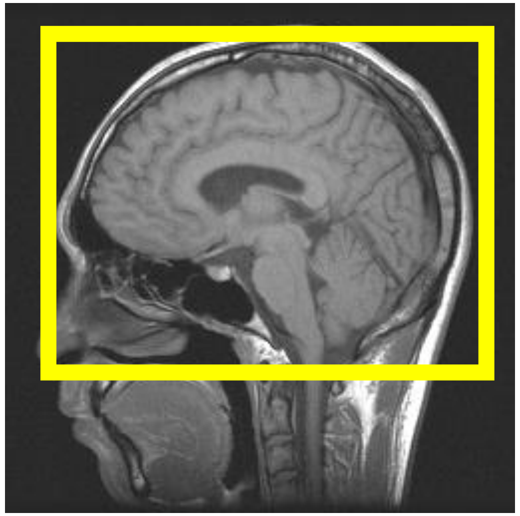
Extension to 4D Flow

<u>2D PC MRI</u>



- ***Prospectively Targeted plane(s)***
- ***Need vessel image to acquire***
- ***One vessel at a time***
- ***Usually 1 direction of velocity***

<u>4D Flow</u>



- ***Volumetric acquisition***
- ***All vessels simultaneously***
- ***All 3 velocity directions***
- ***<u>Retrospective analysis</u>***

Speed of MRI

- MR Imaging rate is ~50,000 voxels/pixels per second
  - HD Camera : 62,208,000 pixels/s (1200x faster)

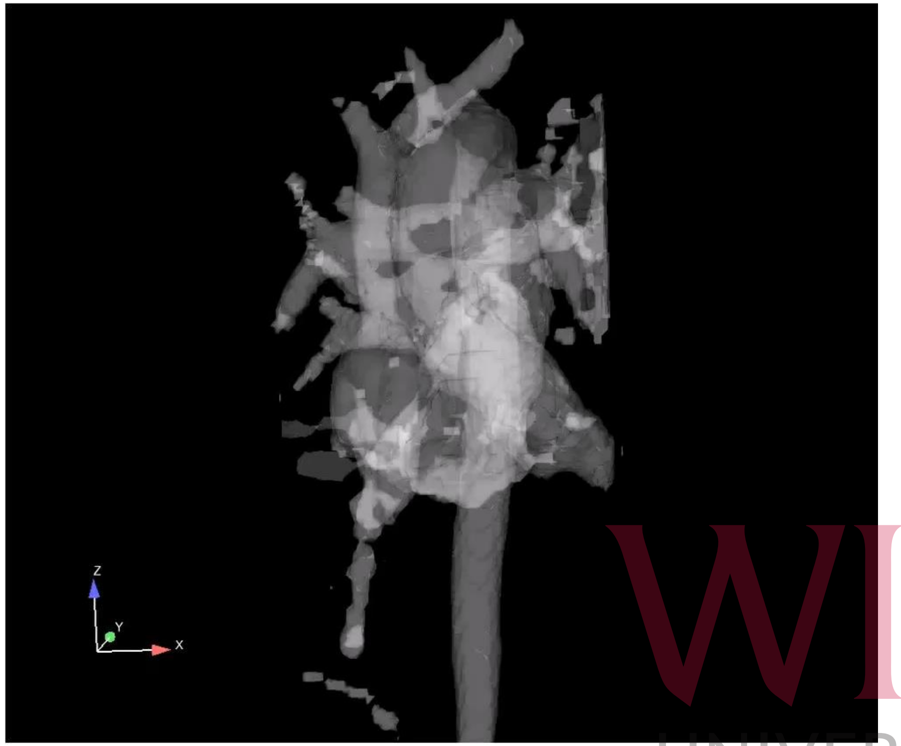
- 256x256 image: ~1 second to acquire
- 256^3 volume: ~4minutes to acquire
- 20 volumes: >1hr to acquire

- Need acceleration methods for 4D Flow

4D Flow in the Heart vs Brain

Targeted Aorta Scan

(Markl et al)



Blood Flow Origin

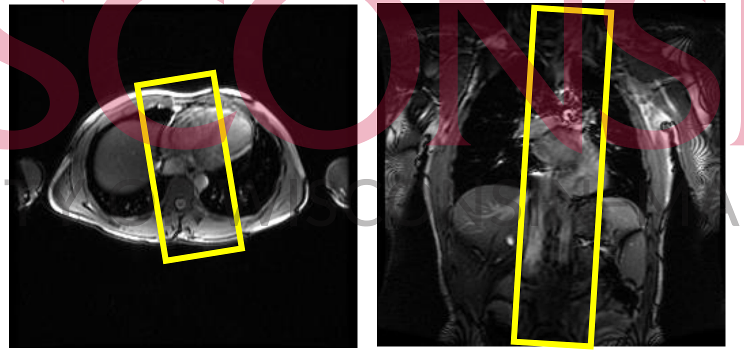
- Left ventricle (LV) & aorta (Ao)
- Left pulmonary vein (LPV)
- Right pulmonary vein (RPV)
- Inferior vena cava (IVC)
- Superior vena cava (SVC)

Brain poses challenges for 4D flow

Aorta

Large vessels (10+mm)

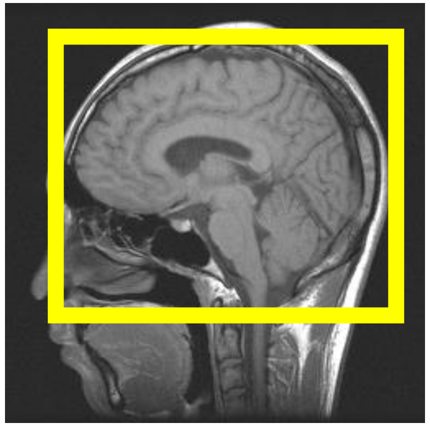
Tailored geometry



Brain

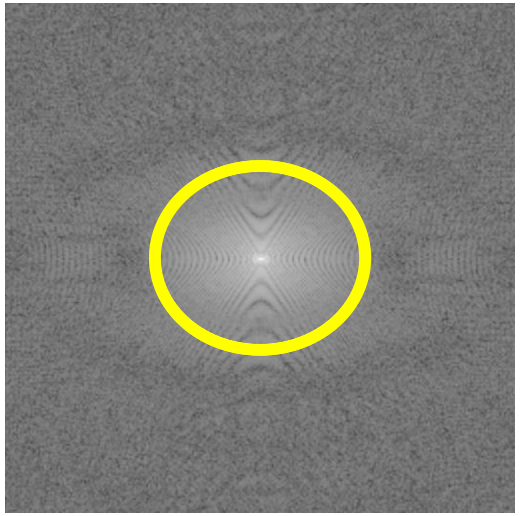
Smaller vessels (1-7 mm)

Large volume of interest



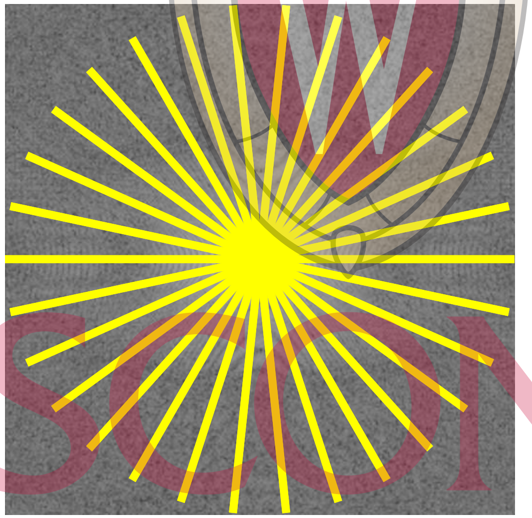
PC VIPR (Accelerated 4D-Flow) Principle

Raw Data energy is focused



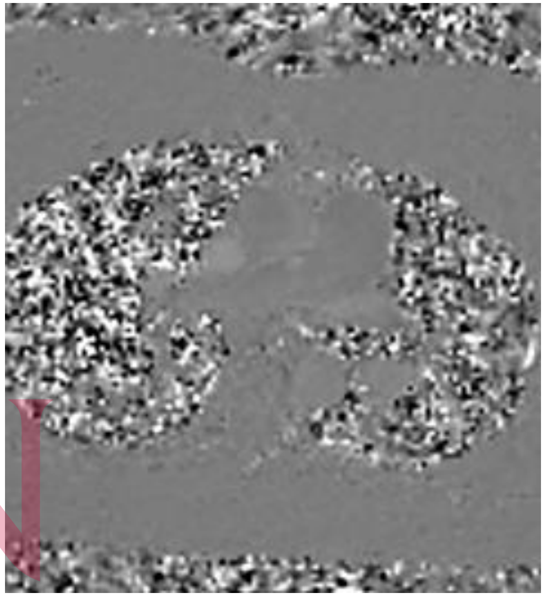
(center most needed)

Focus on collecting most important data



(3D radial sampling)

Accurate images with much less data (10-30x)



(when images sparse or compressible)

PCVIPR History

Core development	Refinement / Validation

05' ***08'***

Initial Idea

Chuck Mistretta
TL Gu

Core Technical Methods

Kevin Johnson

Steve Kecskemeti

Oliver Wieben

Eric Schrauben

Mike Loecher

Liz Nett

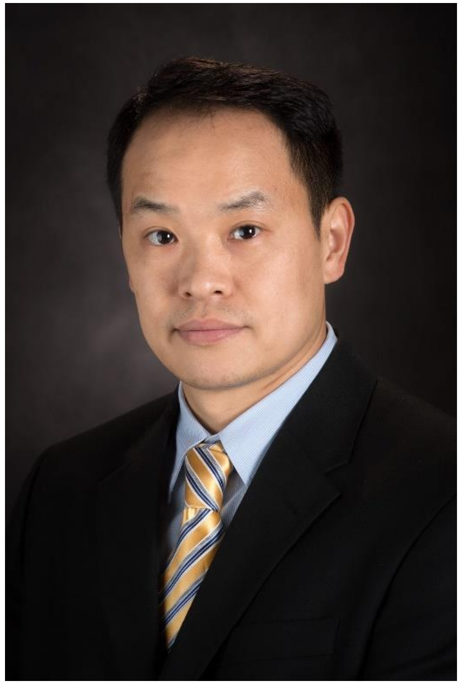
Leonardo Rivera-Rivera

+ many more

History of 4D Flow in the ADRC

March 2009

This is Guofan from Dept. of Medicine & Radiology. We currently start a new Alzheimer's disease research project with MR neuroimaging. **I am interested in the carotid artery flow speed measurement.** Dr. Rowley and Dr. Turski told me that I should use the PC-VIPR sequence and you are the best person to ask. I read that VIPR paper in 2005 AJNR. Is that sequence available on the new GE x750 system? If possible, could you give me some updates about this technique and data processing? Thanks!



PCVIPR History

Core development | Refinement / Validation

05' **08'** **09'** **15'**

Initial Idea

Chuck Mistretta
TL Gu

ADRC Scans

Guofan Xu,
Sterling Johnson


First AD Papers

Sara Berman,
Leonardo Rivera

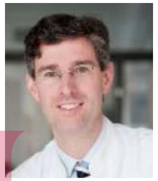
Validation (throughout)

Alex Frydrychowicz

Alejandro Roldan

Darren Lum

Thorsten Bley



Andrew Wendtland

+ many more

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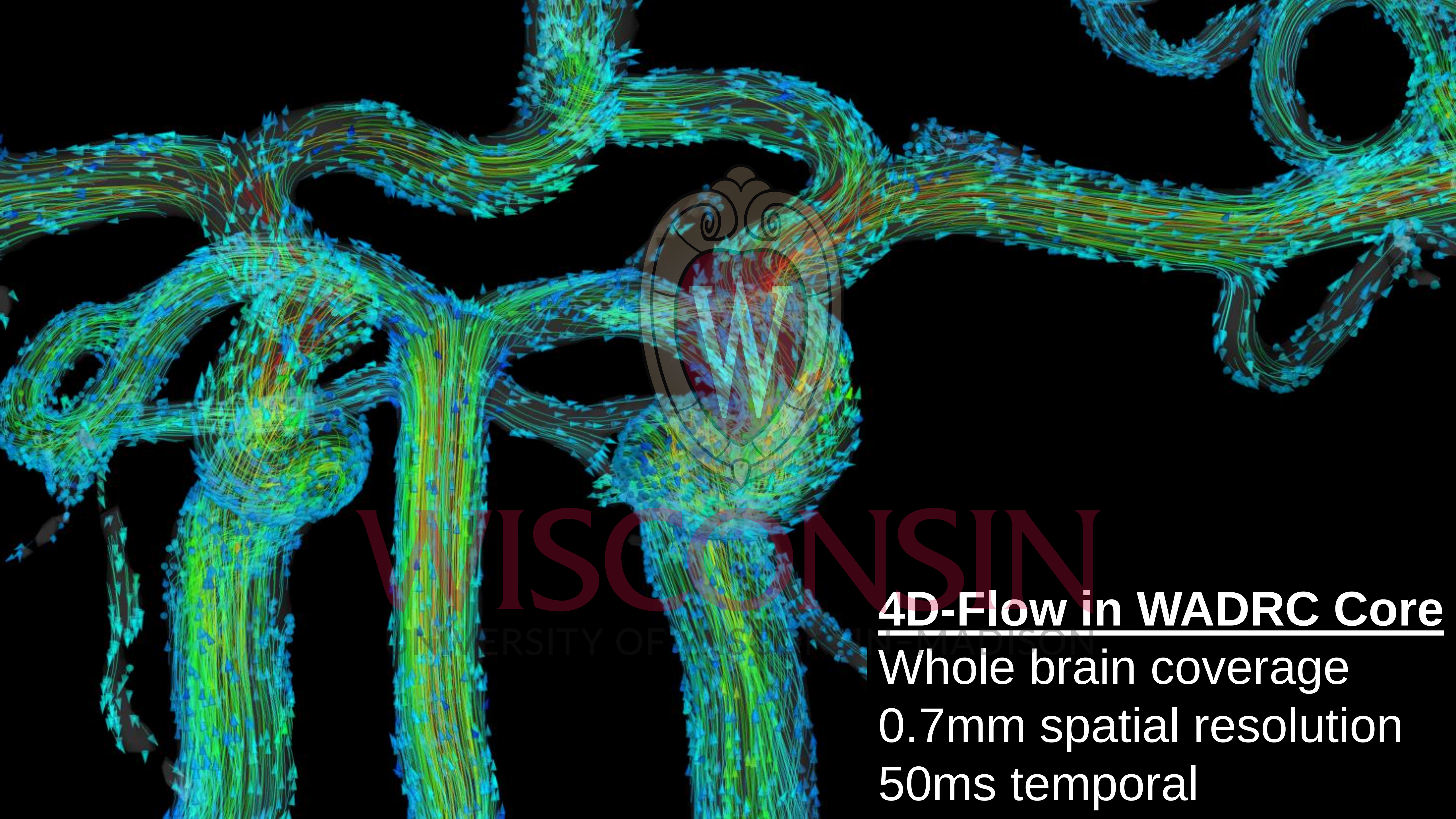
+ many more



4D-Flow in WADRC Core

Whole brain coverage

0.7mm spatial resolution

50ms temporal

Overview

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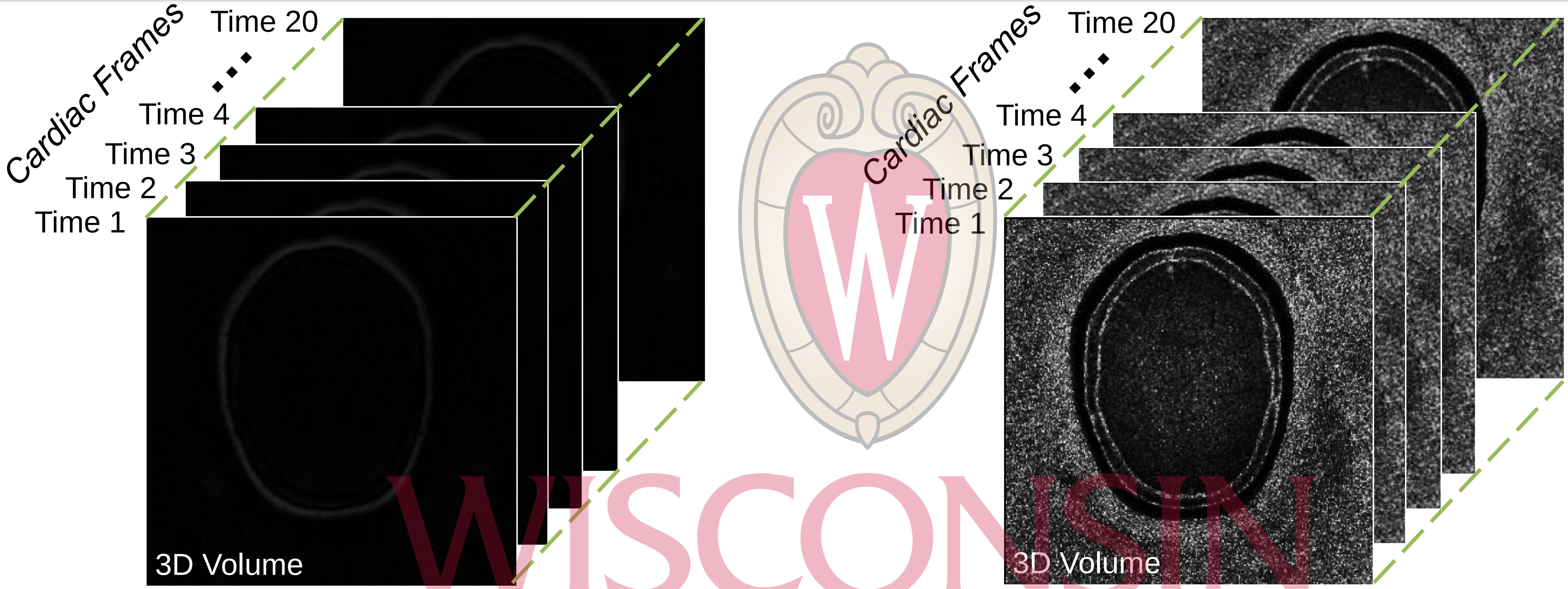
- **What can we measure** and how we measure it
  - —Grant Roberts, PhD Candidate, Medical Physics
- **Results** in studies of ADRD
  - —Leonardo Rivera-Rivera, Postdoctoral Fellow

4D Flow Post-Processing



Magnitude Data **Velocity Data**

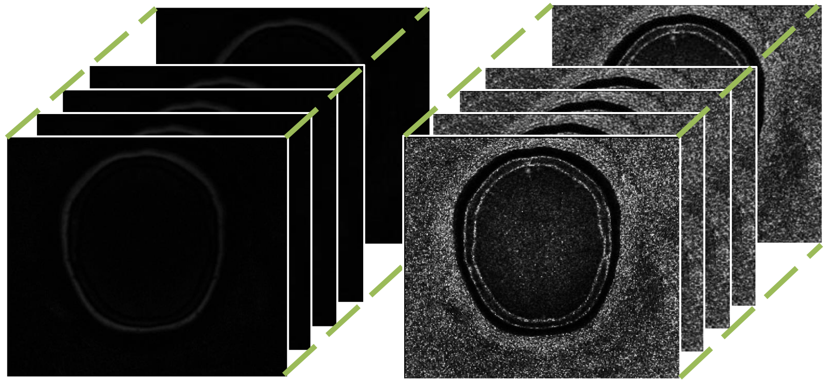
- Image sizes: 320 x 320 x 320 x 20
- **We have a lot of data!**

4D Flow Post-Processing

- Our goal now is to
    1. Boil down this large amount of 4D flow data
    2. Extract blood flow measurements
        - Vessel diameters
        - Blood flow rates
        - Pulsatility
        - Wall shear stress
        - … Many More!

- First Step: **Segmentation**

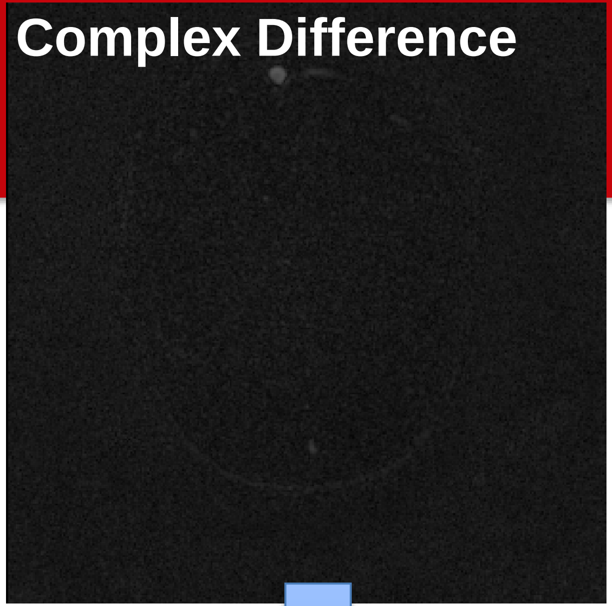
Image Data

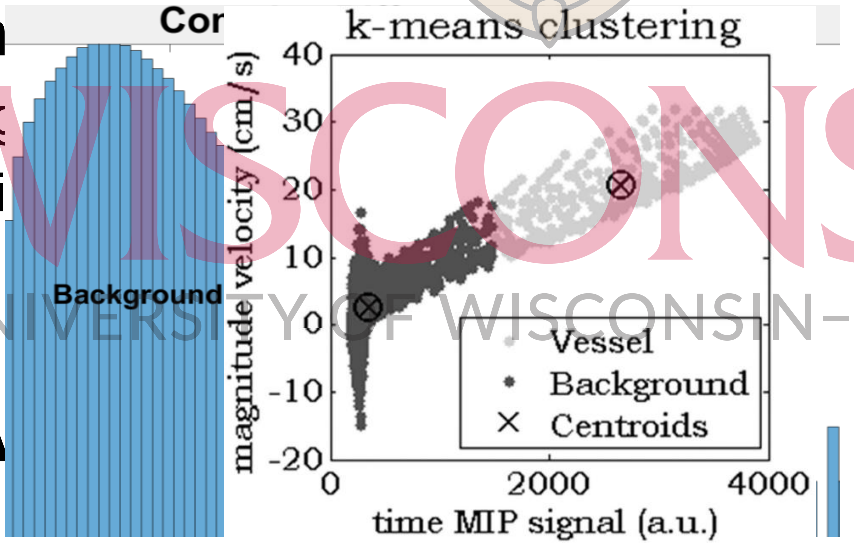


Vessel	Pulsatility Index
ICA	0.80 ± 0.15
BA	0.74 ± 0.14
MCA	0.71 ± 0.08
PCA	0.72 ± 0.13
ACA	0.74 ± 0.16

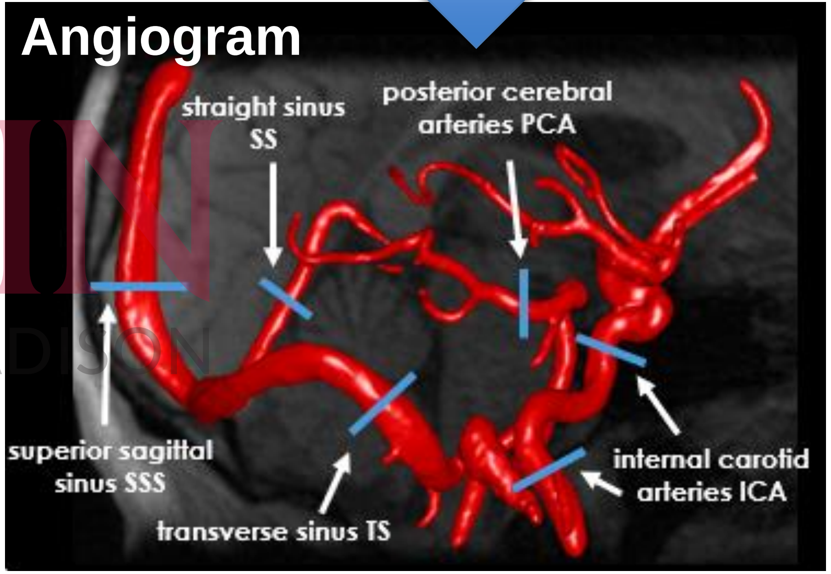
Vessel Segmentation

- Identify vessel vs. not vessel
  - Termed “angiogram”
  - Complex difference images delineate vessels well
- Segmentation techniques
  - Manual segmentation
    - Threshold-based
  - Automatic Segmen
    - K-Means Clusterin
    - Adaptive thresholdi
    - Sliding threshold
- Second Step: **ROI A**



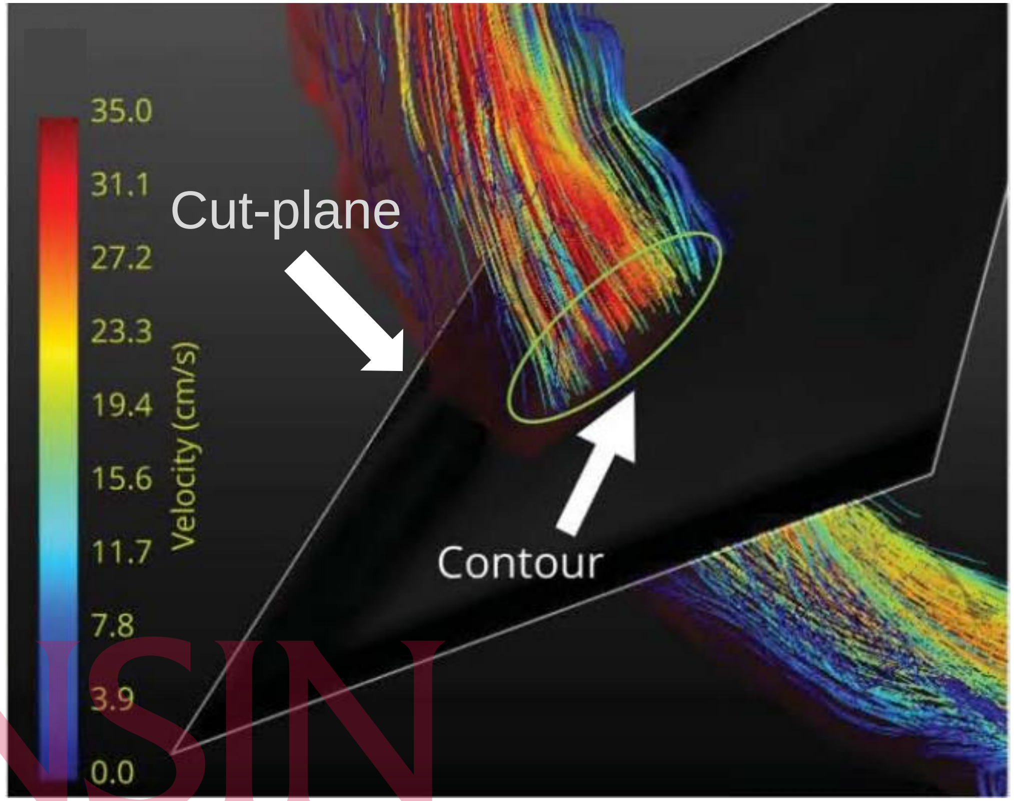


From: Schrauben E, et al. *JMRI* 2015 (42)



ROI Analysis

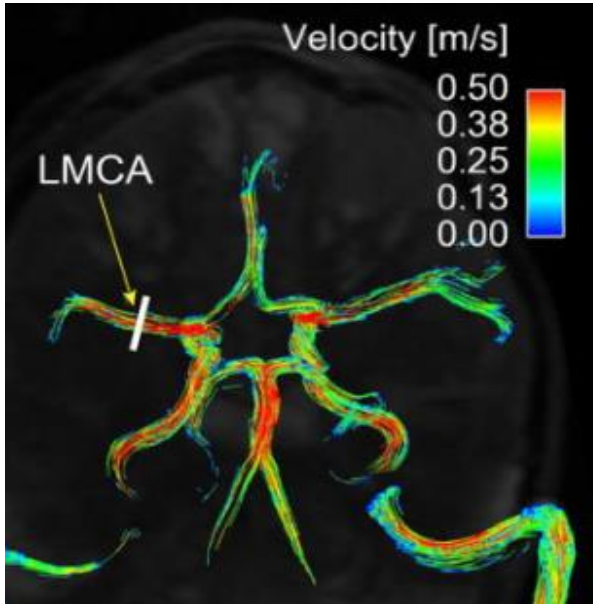
- Define vessel of interest
- Make cut-plane
  - Measure "through-plane" velocity
  - Analogous to 2DPC
  - Ideally perpendicular to length of vessel
- Segmentation defines vessel boundary
- Analyze velocities inside vessel
  - Allows for quantitative hemodynamic measures
    - Blood flow, velocity, pulsatility, etc.

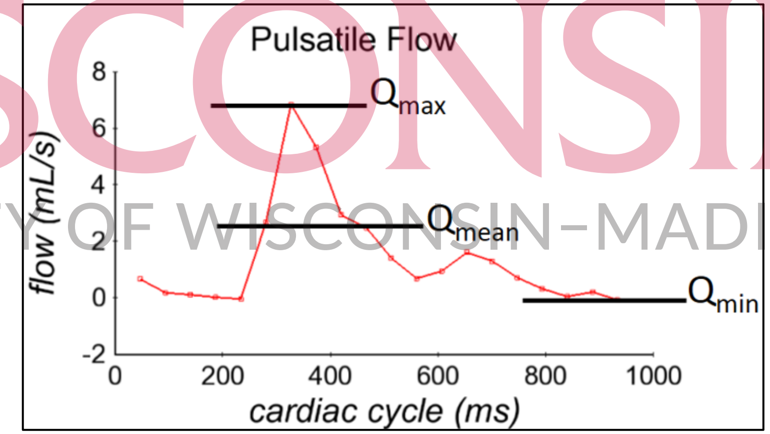


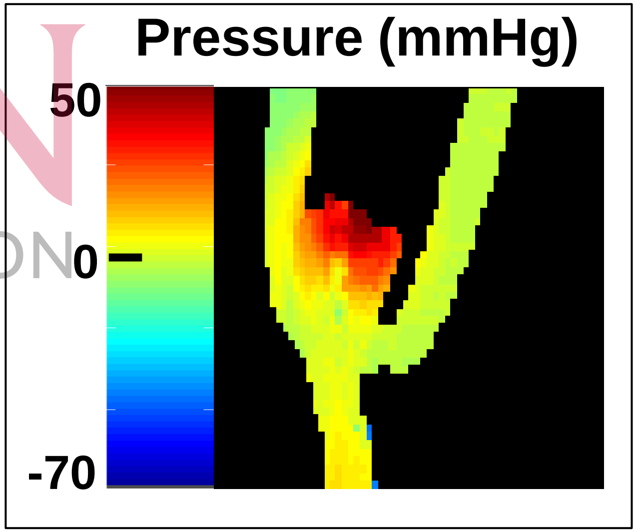
From: Yunduo Li et. al. *Neurology* 2018 (91)

Hemodynamic Parameters

- What can 4D flow measure?
  - Morphological
    - Vessel Areas
    - Vessel lengths
  - Functional
    - Blood flow
    - Blood velocities
    - Pulsatility Index
    - Resistivity Index
    - Pressure maps
    - Wall-shear stress
    - Pulse wave velocity
    - Kinetic energy



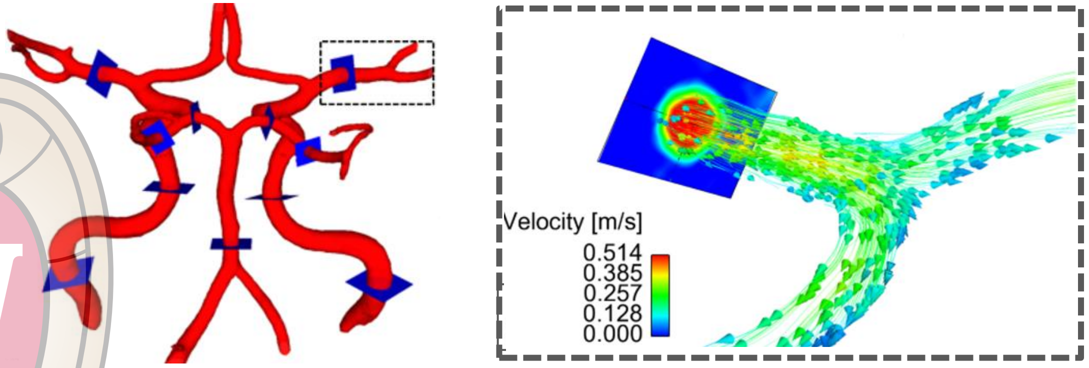




Velocity and Blood Flow

Blood velocity

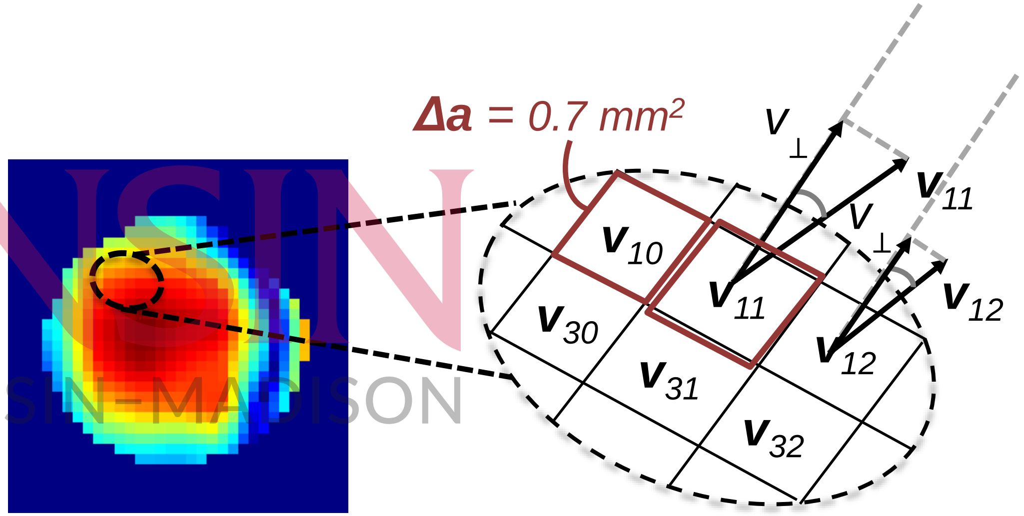
- After defining ROI in cut-plane, we can measure velocity in vessel.
  - Peak systolic velocity
  - Mean velocity over cardiac cycle



From: Rivera-Rivera LA et al. *JCBFM* 2016 (36)

Blood flow

- Instantaneous volumetric flow rate (mL/s)
  - $Q = \sum (v_{\perp} \cdot \Delta a)$
- Average volumetric flow rage (mL/s)
  - Just average Q_f over all cardiac frames!



Cardiac frame 1

- $Q_1 = \cdots\ v_{\perp,10} \cdot \Delta a\ +\ v_{\perp,11} \cdot \Delta a\ +\ v_{\perp,12} \cdot \Delta a\ + \cdots$

Pulsatility and Resistivity Index

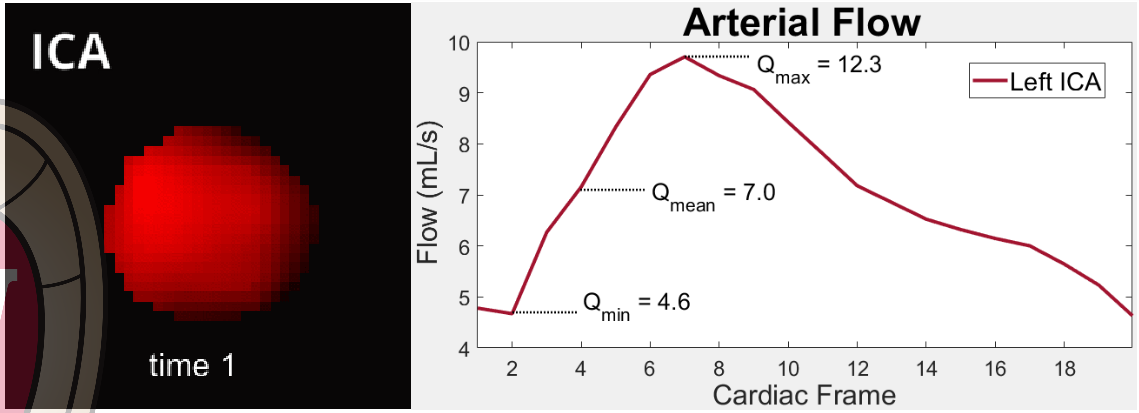
Pulsatility Index (PI)

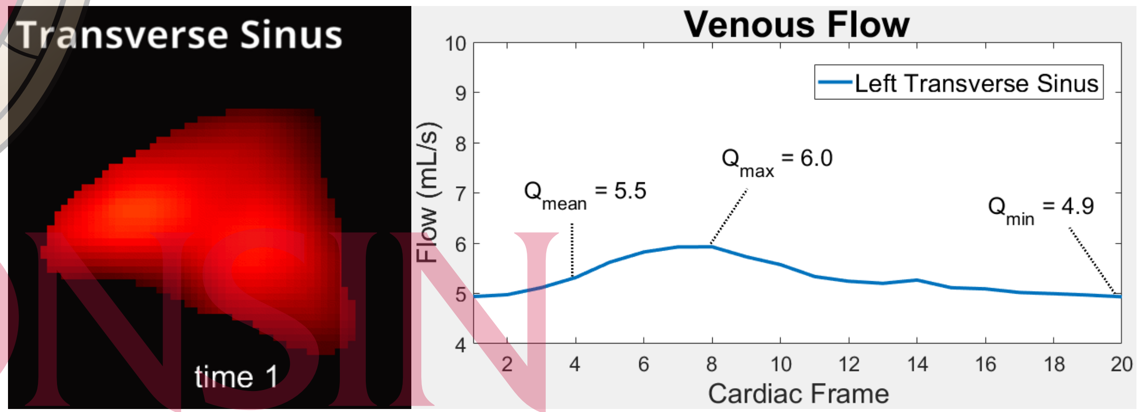
- $$PI = \frac{Flow_{max} - Flow_{min}}{Flow_{mean}}$$

Resistivity Index (RI)

- $$RI = \frac{Flow_{max} - Flow_{min}}{Flow_{max}}$$

- Clinical importance
  - Both are measures of downstream vascular resistance and intracranial compliance.
  - Affected in diseases like TBI, hydrocephalus, and AD.

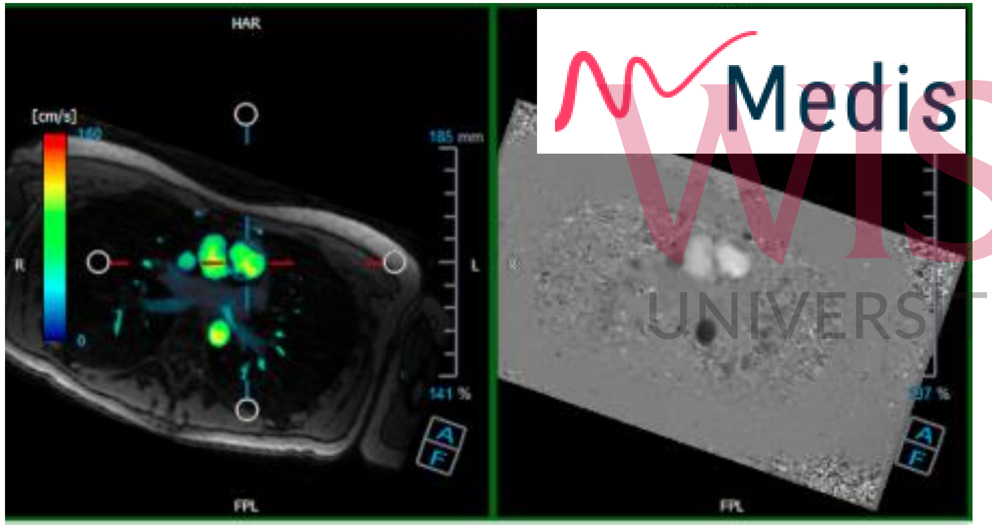


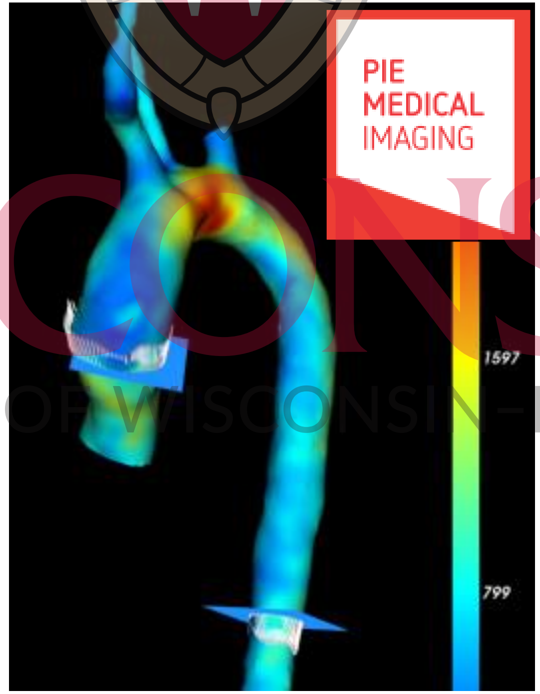


Vessel	Pulsatility Index	Resistivity Index
Arterial → Left ICA	1.10	0.63
Venous → Left Trans. Sinus	0.20	0.18

Commercial 4D Flow Software

- Commercial 4D flow post-processing software already exist.
  - However, applications are primarily cardiac
- **No software dedicated to cranial 4D flow**



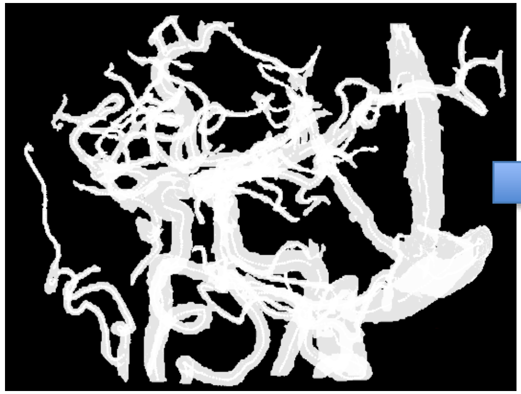


Automated Tool

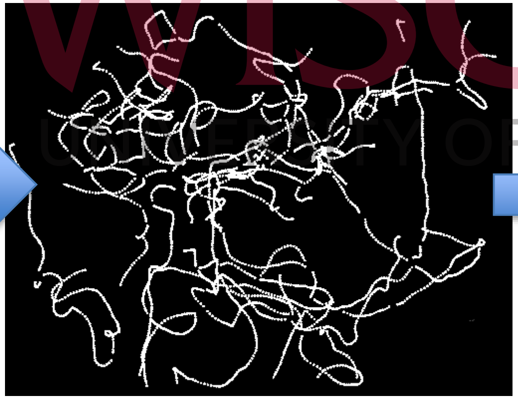
- UW pioneers in cranial 4D flow post-processing software
  - Initial work done by Eric Schrauben in 2014.
- Allows for automatic flow analysis along all cranial vessels.
  - Automatically segments
  - Creating "centerlines"
  - Calculate orthogonal cut-planes (tangent planes)
  - Calculate in-plane hemodynamics

Eric Schrauben

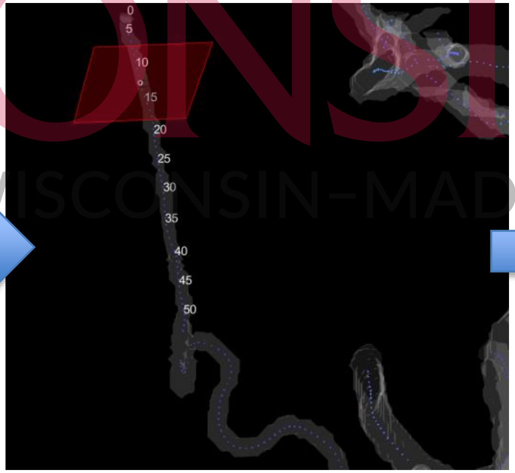
Automatic Segmentation



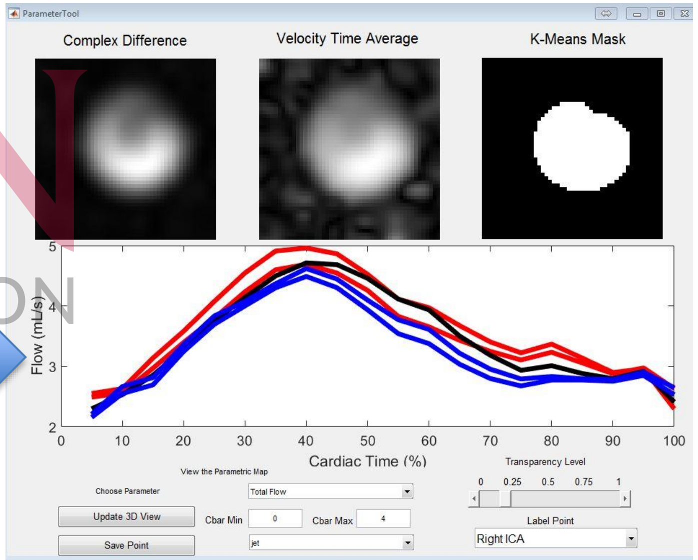
Create Centerlines



Automatic Tangent Planes



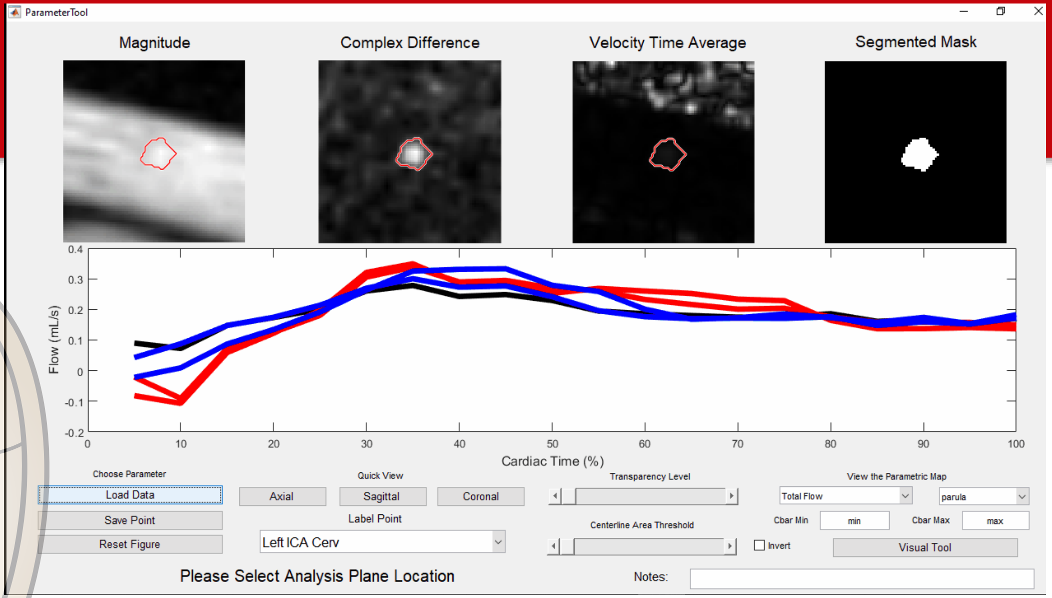
Flow Analysis



Automated Tool

- Nearly finalized a major update to this tool
  - Interactive 3D display
  - Visualize in-plane magnitude, velocity, complex difference data in real-time.
  - Overlay centerlines on angiogram
  - Color-coding of 4D flow parameters
  - Streamlined code
    - Faster with less memory usage
  - Saves user-state

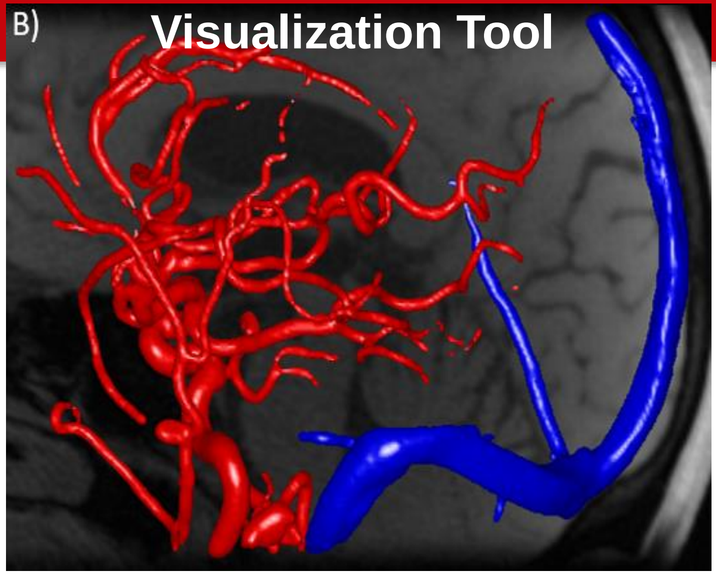
Control Window

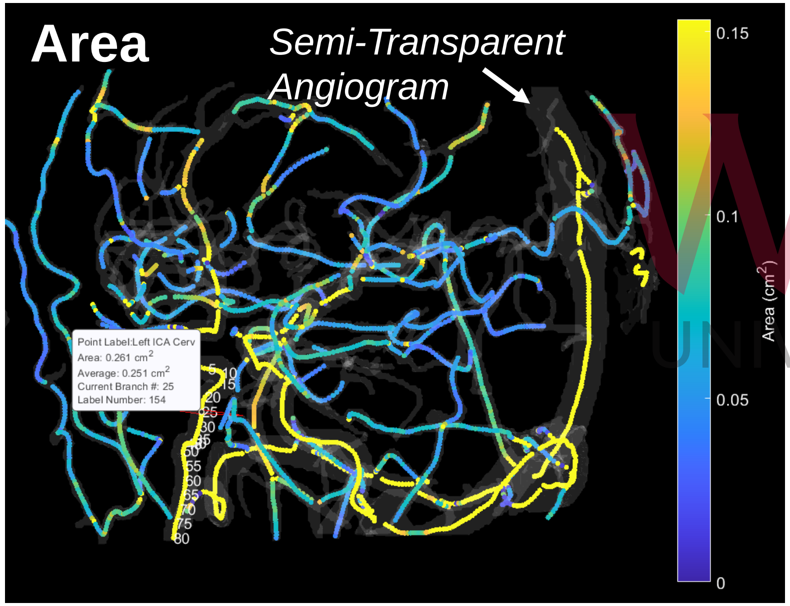


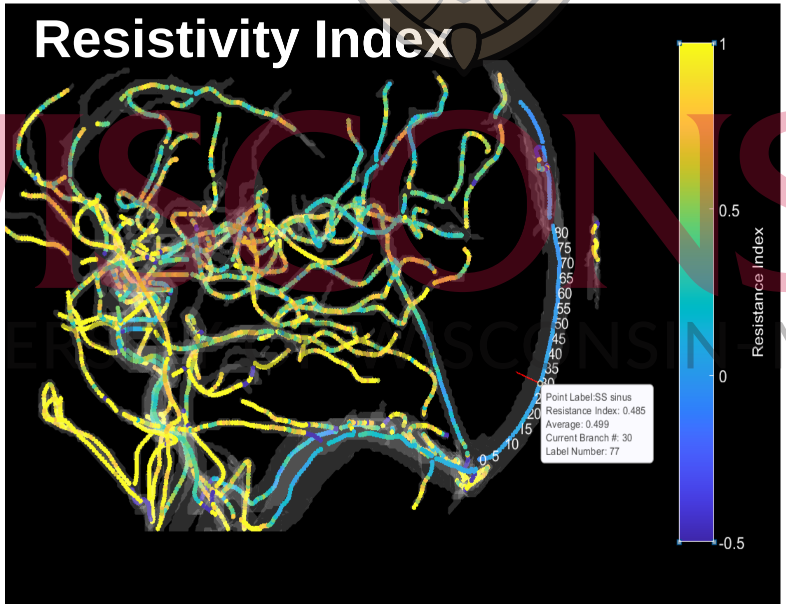
Carson Hoffman

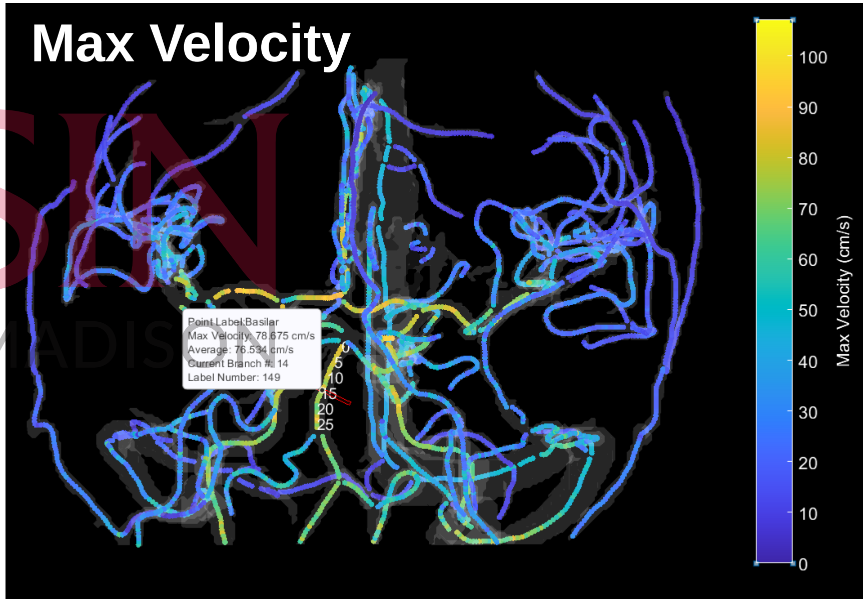
Automated Tool

- Examples of visualization
  - Display angiogram (right)
  - Color-coded hemodynamics (below)
    - Can display: area, pulsatility index, resistivity index, mean velocity, max velocity, consistency of flow along vessel, and more.









Other Exciting Hemodynamic Parameters

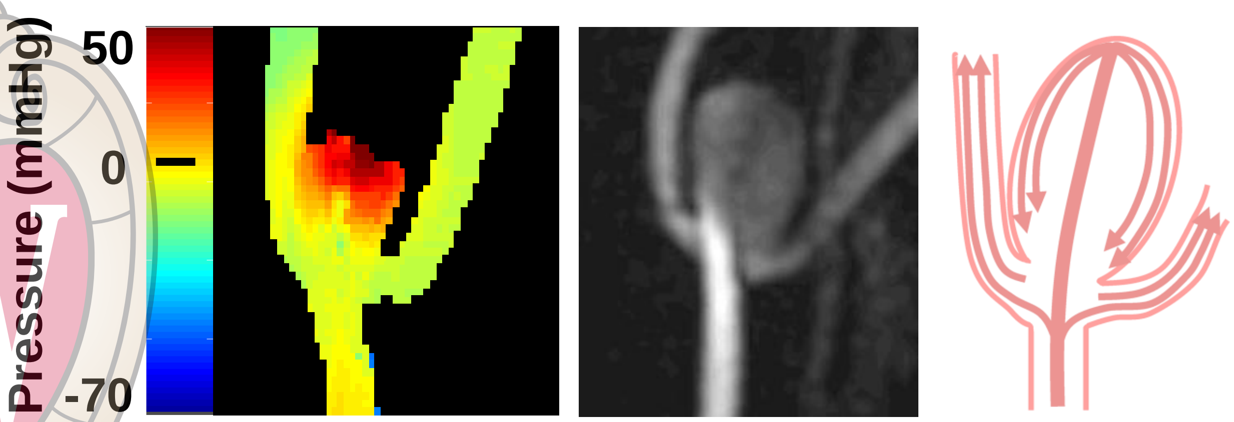
Intravascular Pressure

- Navier-Stokes equaation

$$-\nabla P = -\rho\left(\frac{\partial \vec{v}}{\partial t} + \vec{v}\cdot\nabla\vec{v} - g\right) + \mu\nabla^2\vec{v}$$

- May be useful in stratifying high risk aneurysms or DAVFs

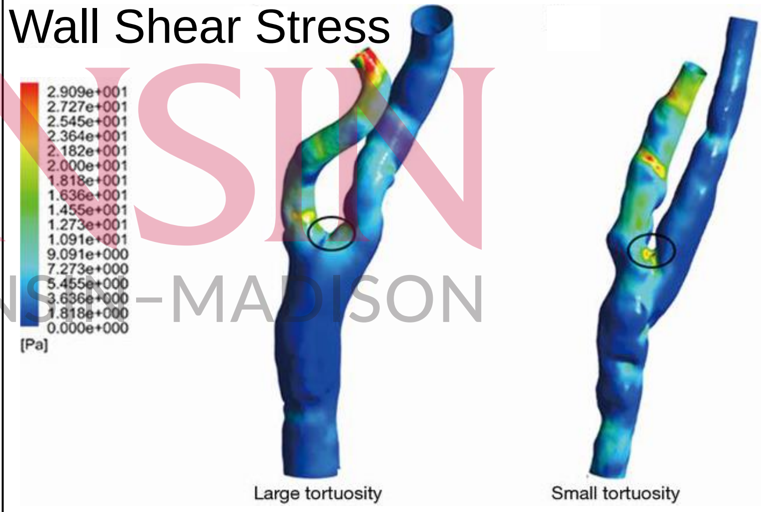
Aneurysm Jet Pattern - High Dome Pressure



From: R Moftakhar et al., *AJNR* 2007 (28)

Wall Shear Stress (WSS)

- Defined as the frictional force exerted on endothelium by pulsatile blood flow.
- Critical determinant of vessel diameter and vascular remodeling via atherogenesis



From: Dai Y, et. al. *QIMS* 2018 (8)

Overview

- **Introduction** to Blood Flow Measures with MRI
  - —Kevin Johnson, Assistant Professor, Medical Physics and Radiology
- **What can we measure** and how we measure it
  - —Grant Roberts, PhD Candidate, Medical Physics
- **Results** in studies of ADRD
  - —Leonardo Rivera-Rivera, Postdoctoral Fellow

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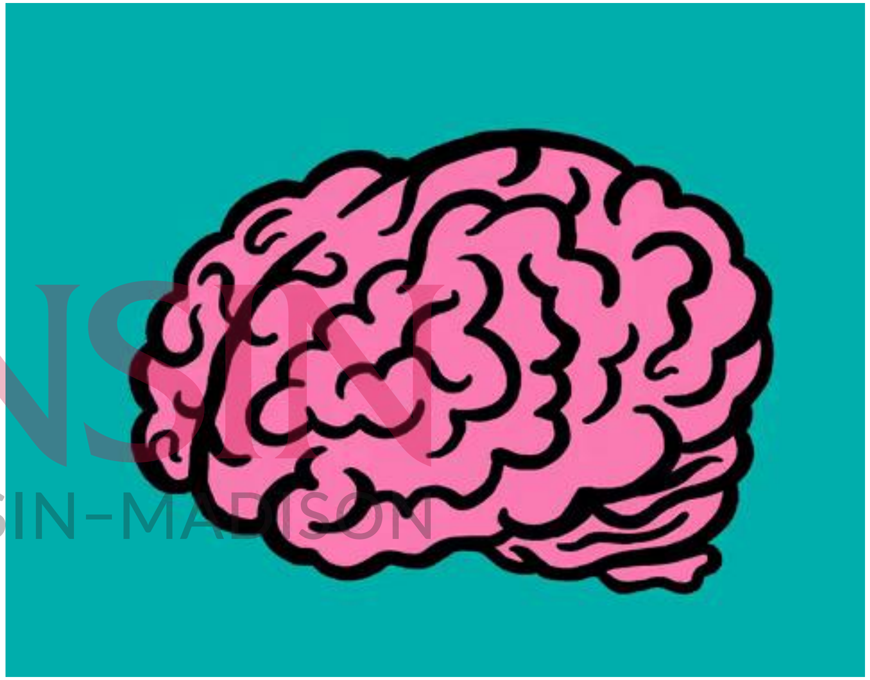
Alzheimer's disease and cerebrovascular disease

- **CVD manifests in AD but is also an independent cause of dementia**

- **AD – CVD hypotheses need testing:**
  - Additive, causative, AND/OR combinatorial effects ?
  - Will CVD biomarkers improve early diagnosis of dementia?

- **Potential for MRI biomarkers of CVD [1]**
  - Tissue Perfusion, ASL
  - Blood-brain barrier, DCE
  - Macrovascular flow, 4D flow



[1] Sweeney et al. Alzheimer's & Dementia 15 (2019) 158-167

Published Studies (n=9, 1st around 5 years ago)

- **Hemodynamics of the brain macrovasculature (from 4D flow)**
  - Clinically diagnosed AD, MCI, subjects at risk (FH+, APOE4+) and healthy controls
  - CSF bio markers, brain atrophy and cognitive performance
  - Macrovascular blood flow vs Microvascular brain perfusion (pcASL)
  - Insulin resistance
  - During hypercapnia challenges
    - Cerebrovascular reactivity
  - Cardiovascular risk factors and racial/ethnic disparities in AD dementia

Original Article

ELSEVIER

Intracranial arte

Sara E. Berman[a,b,c], Jon G. Keevil[f,g], Howard A. Rowley[a,f],

Macrovascula

4D flow MR

Leonardo A River
Patrick Turski[1,2],
Howard A Rowley
Sterling C Johnson[4,5,6] and Oliver Wieben[1]

Lindsay
Siobhan M. Ho
Cynthia M

CrossMark

Original Article

frontiers in Aging Neuroscience

JCBFM

Journal of Cerebral Blood Flow & Metabolism

Original Article

Alzheimer's

ssessment of vascular stiffness in

4D Flow MRI

Kathleen B. Miller[1], Anna J. Howery[1], Leonardo A. Rivera-Rivera[2], Sterling C. Johnson[3,4], Howard A. Rowley[2,3], Oliver Wieben[2] and Jill N. Barnes[1*]

JCBFM

Journal of Cerebral Blood Flow & Metabolism

HHS Public Access

Author manuscript

J Alzheimers Dis. Author manuscript; available in PMC 2020 March 19.

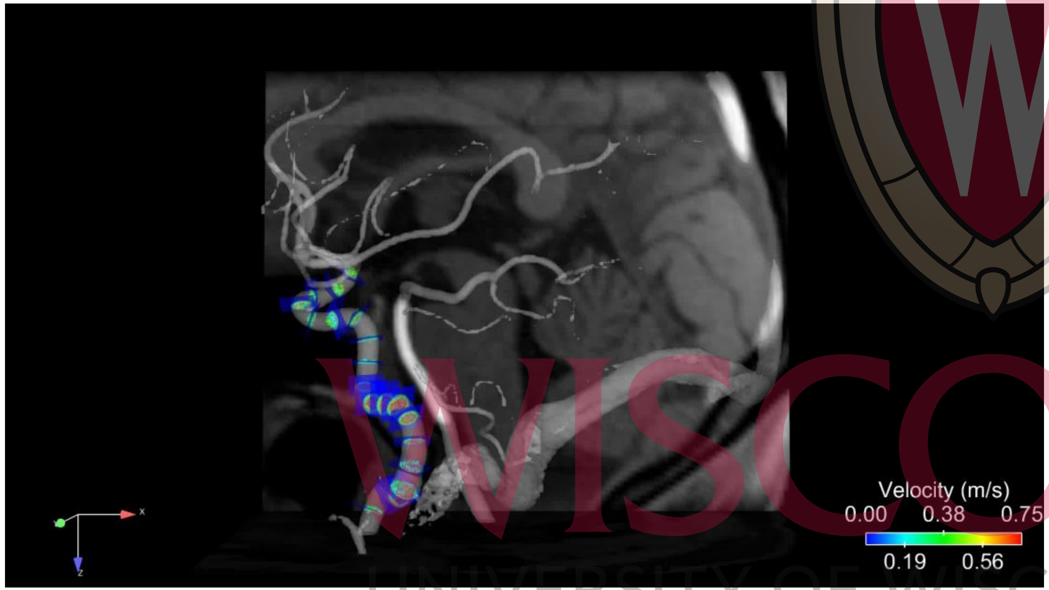
Published in final edited form as:
J Alzheimers Dis. 2019 ; 72(3): 919–929. doi:10.3233/JAD-190645.

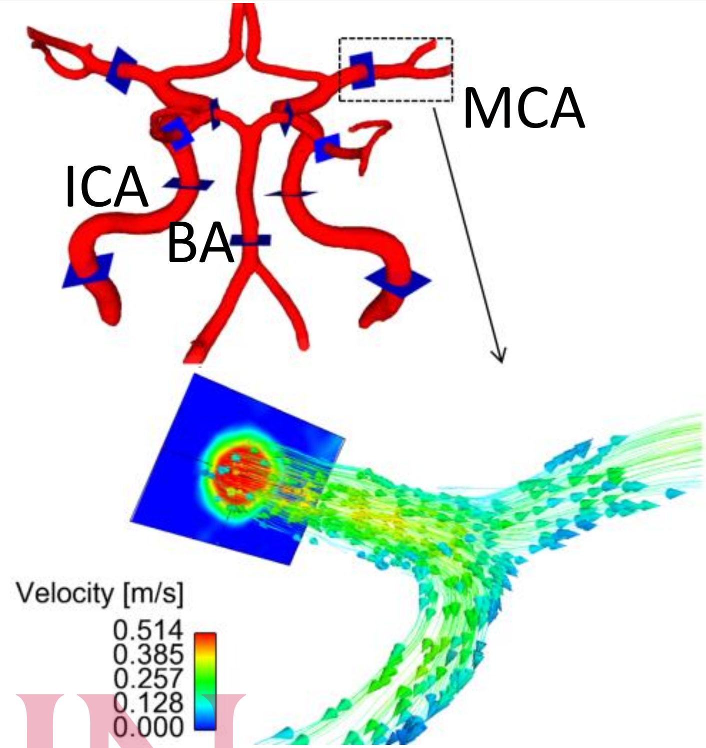
Association of Cardiovascular and Alzheimer's Disease Risk Factors with Intracranial Arterial Blood Flow in Whites and African Americans

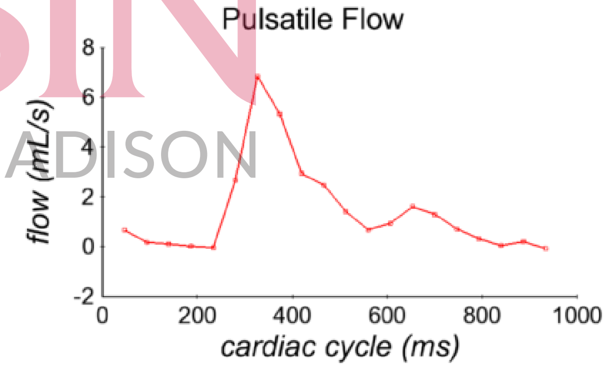
Lindsay R. Clark[a,b,c], Derek Norton[d], Sara E. Berman[e], Sterling C. Johnson[a,b,c], Barbara B. Bendlin[a,b], Oliver Wieben[f,g], Patrick Turski[f,g], Cynthia Carlsson[a,b,c], Sanjay Asthana[a,c], Carey E. Gleason[a,c,*], Heather M. Johnson[h,*]

Blood flow and Pulsatility Index in the circle of Willis

- Macrovascular hemodynamics
  - Vessel size ~ 4 mm



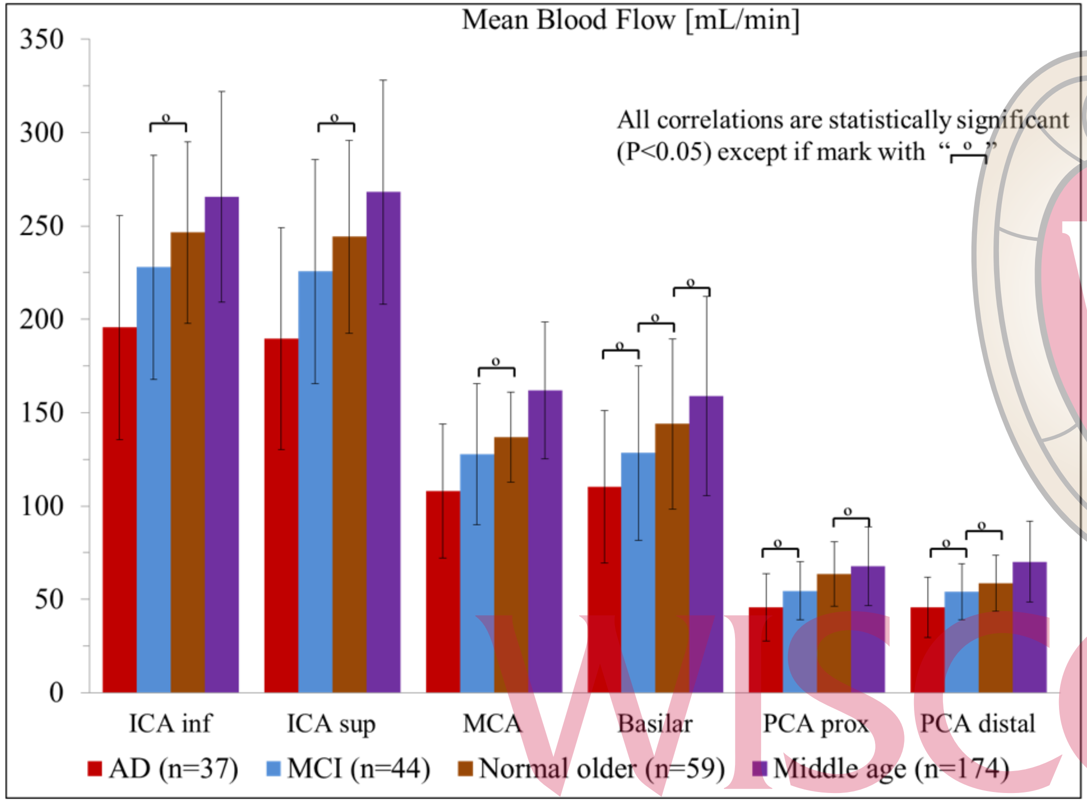




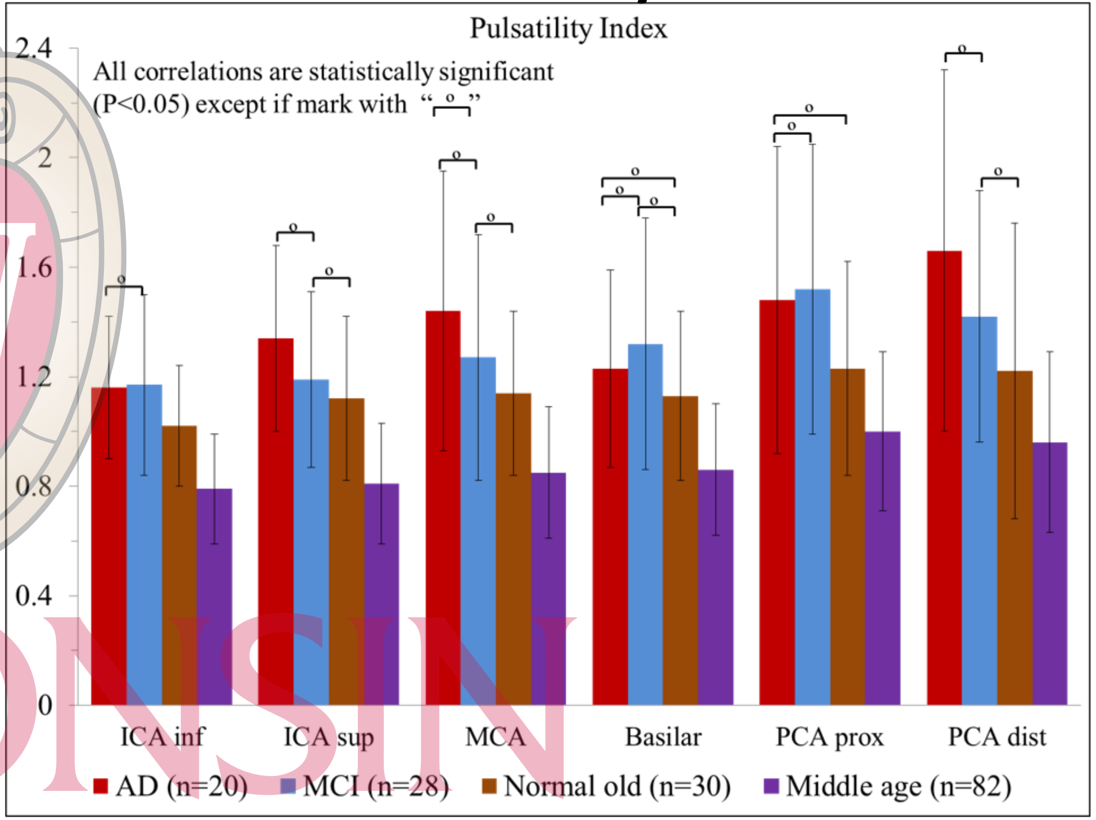
[1] Rivera-Rivera LA, et al. J Cereb Blood Flow Metab. 2016 Oct;36(10):1718-1730.

Blood flow and Pulsatility Index in the circle of Willis

Blood Flow (mL/min)



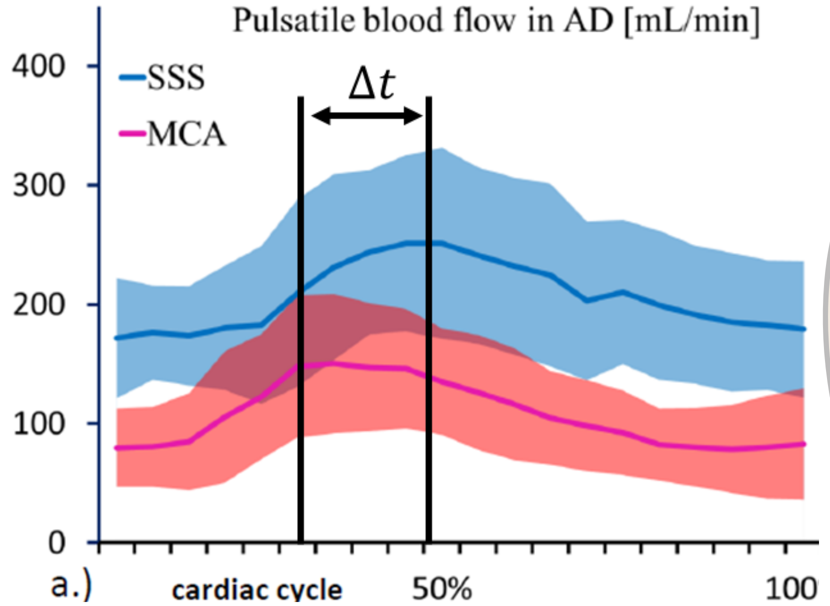
Pulsatility index



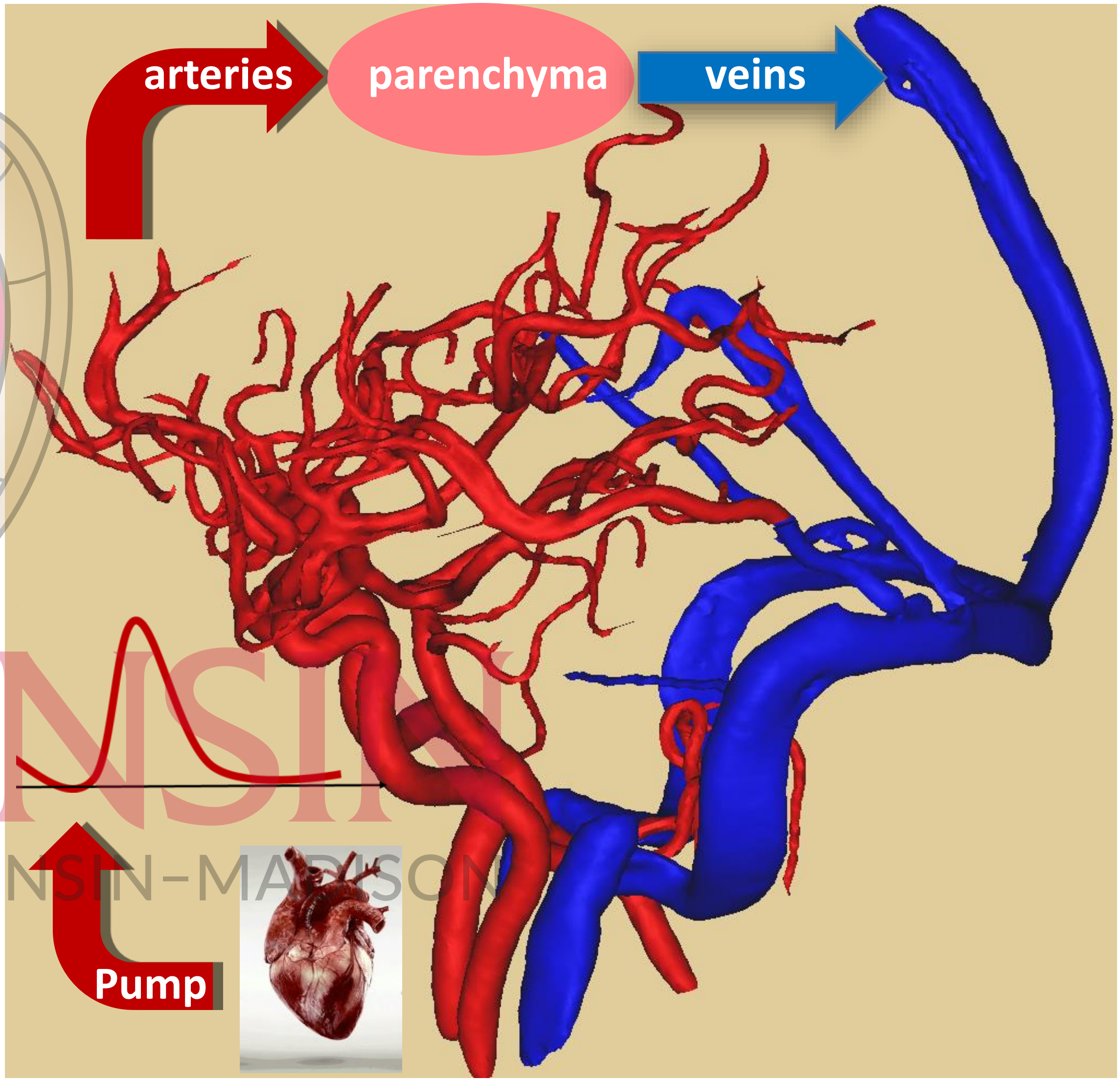
- **Clinical AD: significant decrease in blood flow and increase in PI, suggesting decreased brain metabolism and vessel compliance**

[1] Rivera-Rivera LA, et al. J Cereb Blood Flow Metab. 2016 Oct;36(10):1718-1730.

Cardiac Wave: How long it takes to traverse the brain ?



Time(ms)	AD (n = 26)	Age-matched control (n = 26)
Time to peak (SSS-MCA)	99 ± 93	171 ± 77



- **Significantly shorter transit times in clinical AD**
- **Stiffer vessels, capillaries ? Reduced effective distance ?**

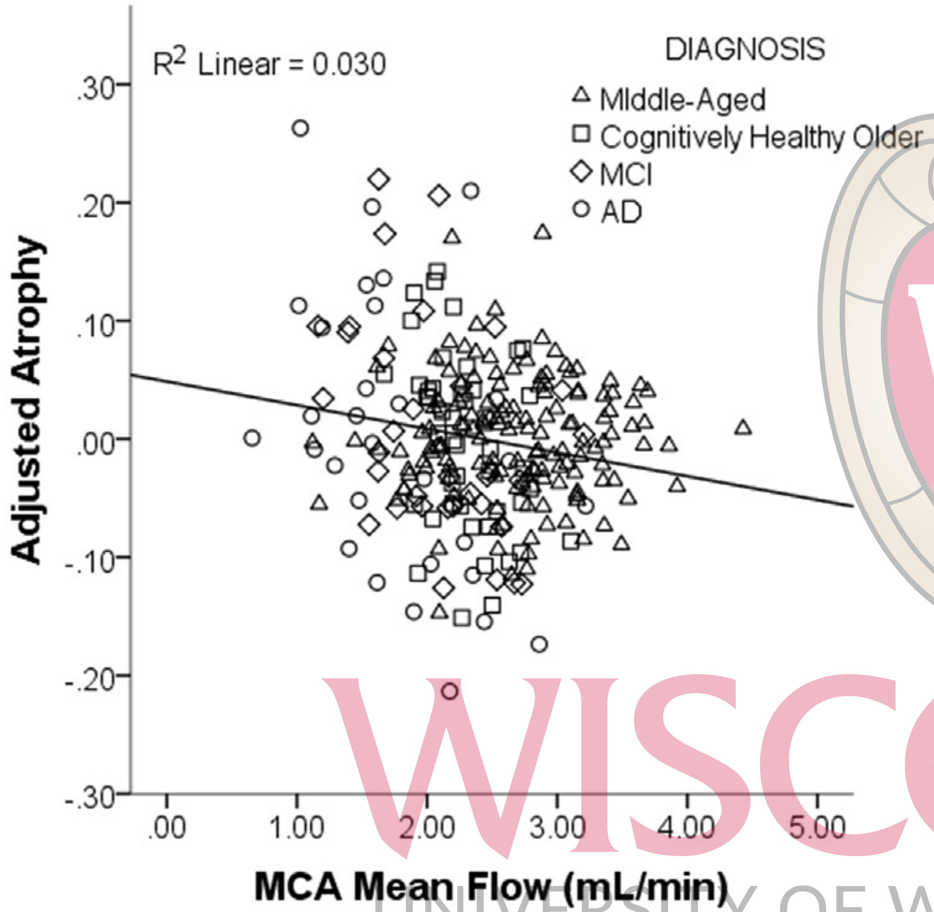
[2] Rivera-Rivera LA, et al. J Cereb Blood Flow Metab. 2017 Jun; 37(6): 2149–2158.

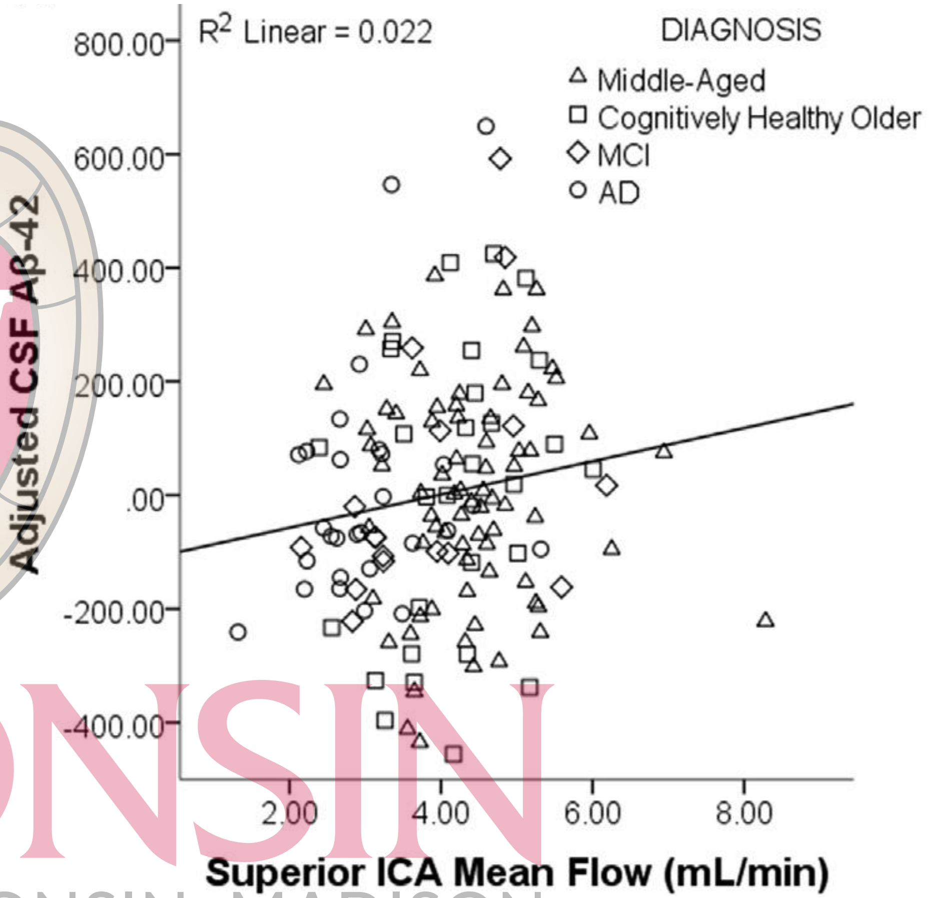
So far in clinical AD

- Decreased brain blood flow and vessel compliance

- Correlation with AD markers ?
  - Brain atrophy
  - Amyloid pathology measured via CSF

Blood flow, brain atrophy, and $A\beta_{42}$ levels in CSF

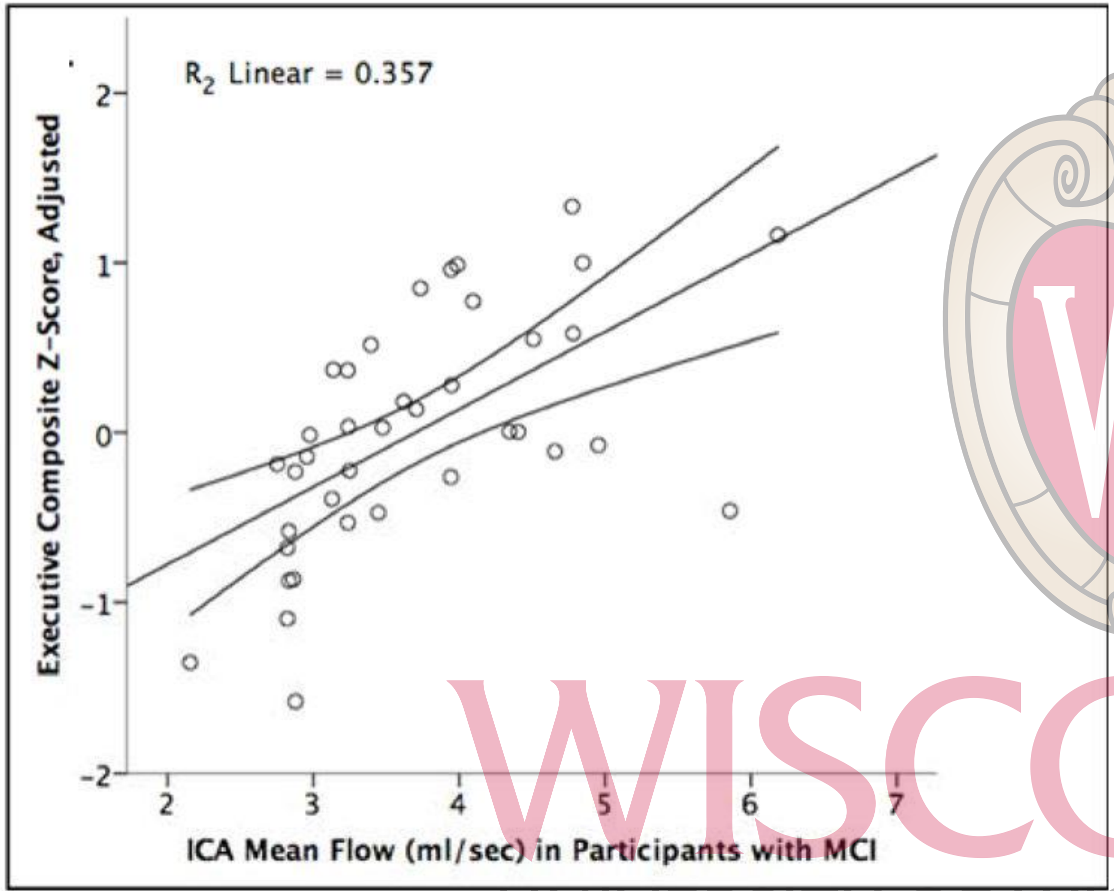


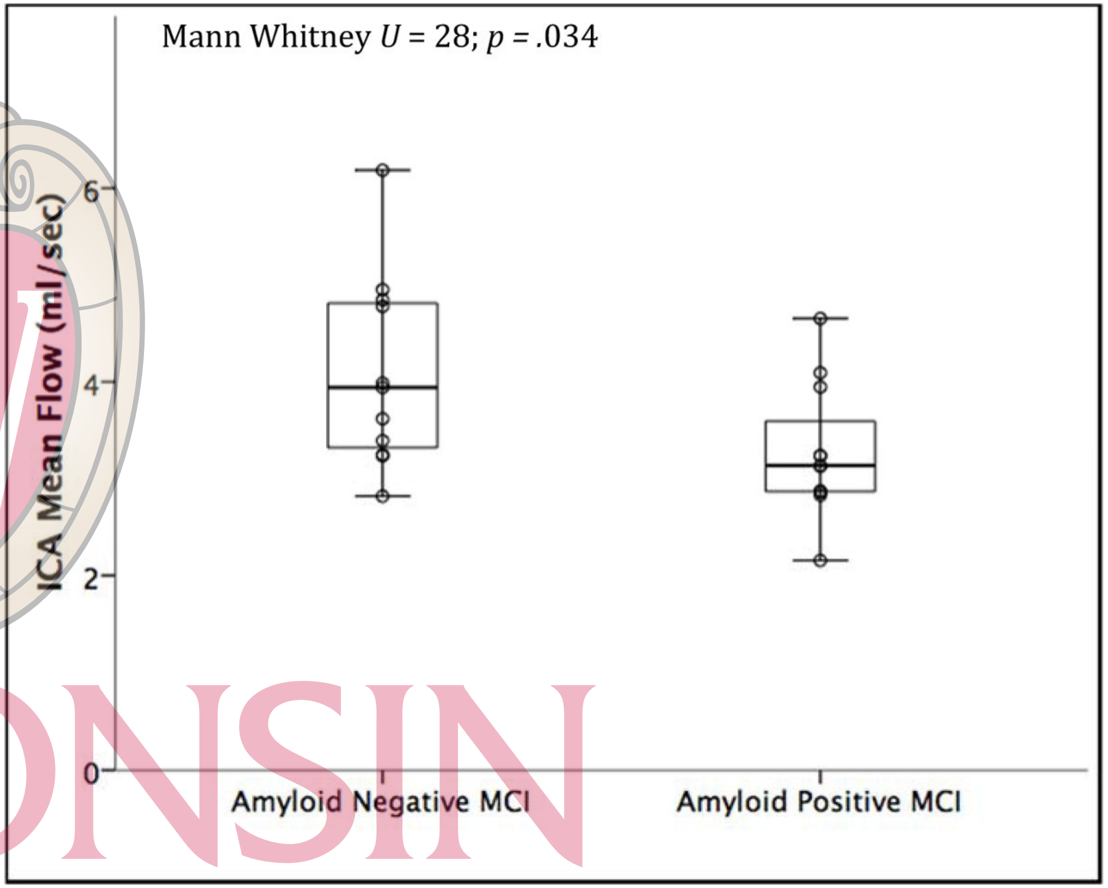


- **Subjects with lower blood flow had greater degree of atrophy.**
- **Lower flow was associated with lower levels of $A\beta_{42}$ in the CSF.**
- **4D flow adds information beyond that acquired using standard vascular risk scores.**

[3] Berman SE, et al. Alzheimers Dement (Amst). 2015 Dec; 1(4): 420–428.

Blood flow, executive function, $A\beta_{42}$ positivity in MCI





- **Greater arterial flow correlates with better executive functioning performance.**
- **Participants with lower mean flow in the ICA were more likely to be amyloid positive.**
- **No relationships were observed in this sample between flow and tau positivity.**

[4] Berman SE, et al. J Alzheimers Dis. 2017 ; 60(1): 243–252.

Insulin resistance and cerebral blood flow

- IR is associated with cardiovascular disease and cognitive decline

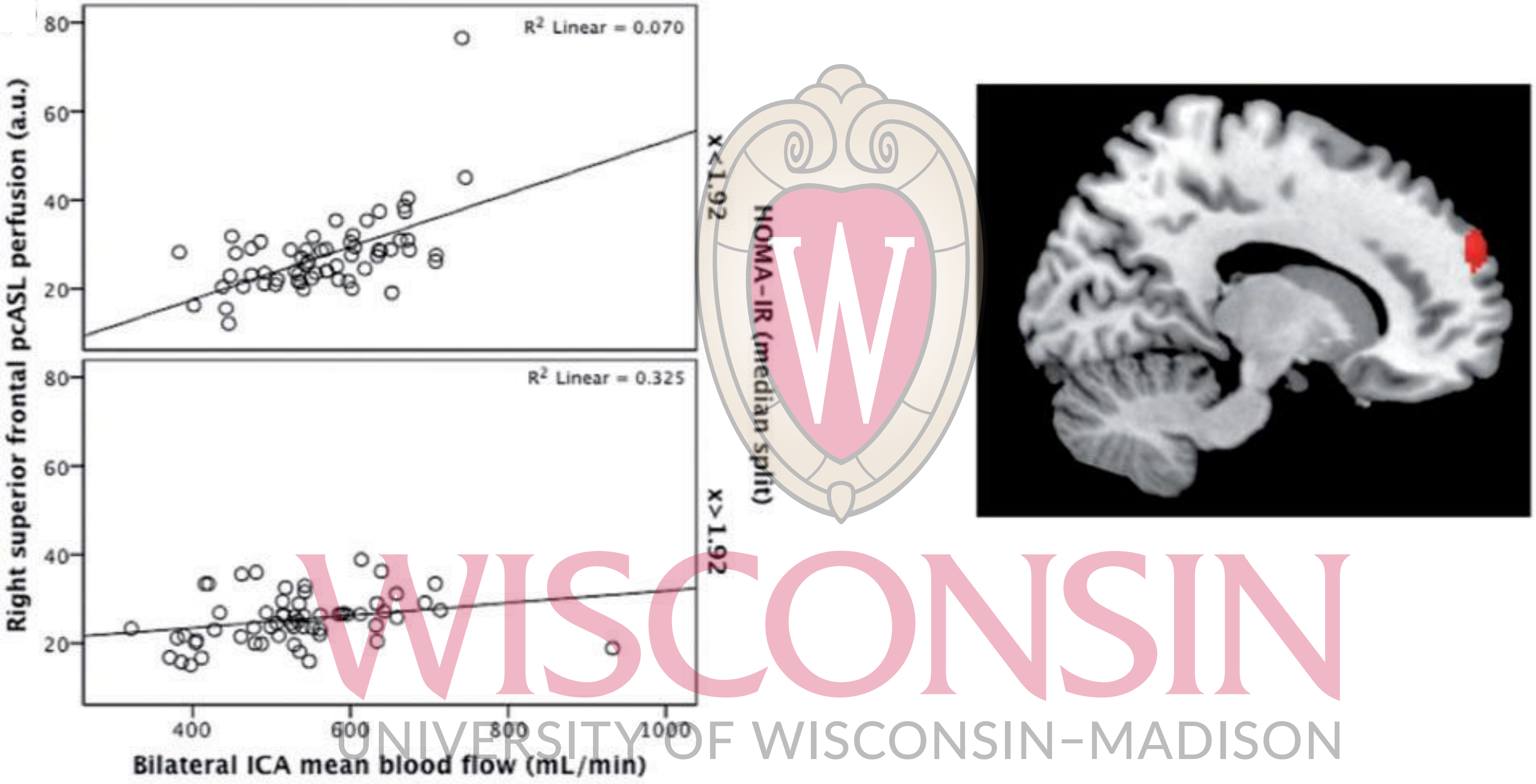
- Metabolic syndrome
  - a cluster of cardiovascular risk factors characterized (IR, obesity, elevated levels)

  - linked to cognitive decline and decrease cortical perfusion

- **How do IR and cerebral macrovascular blood flow relate ?**

[5] Hoscheidt SM, et al. J Cereb Blood Flow Metab. 2017 Jun; 37(6): 2249–2261.

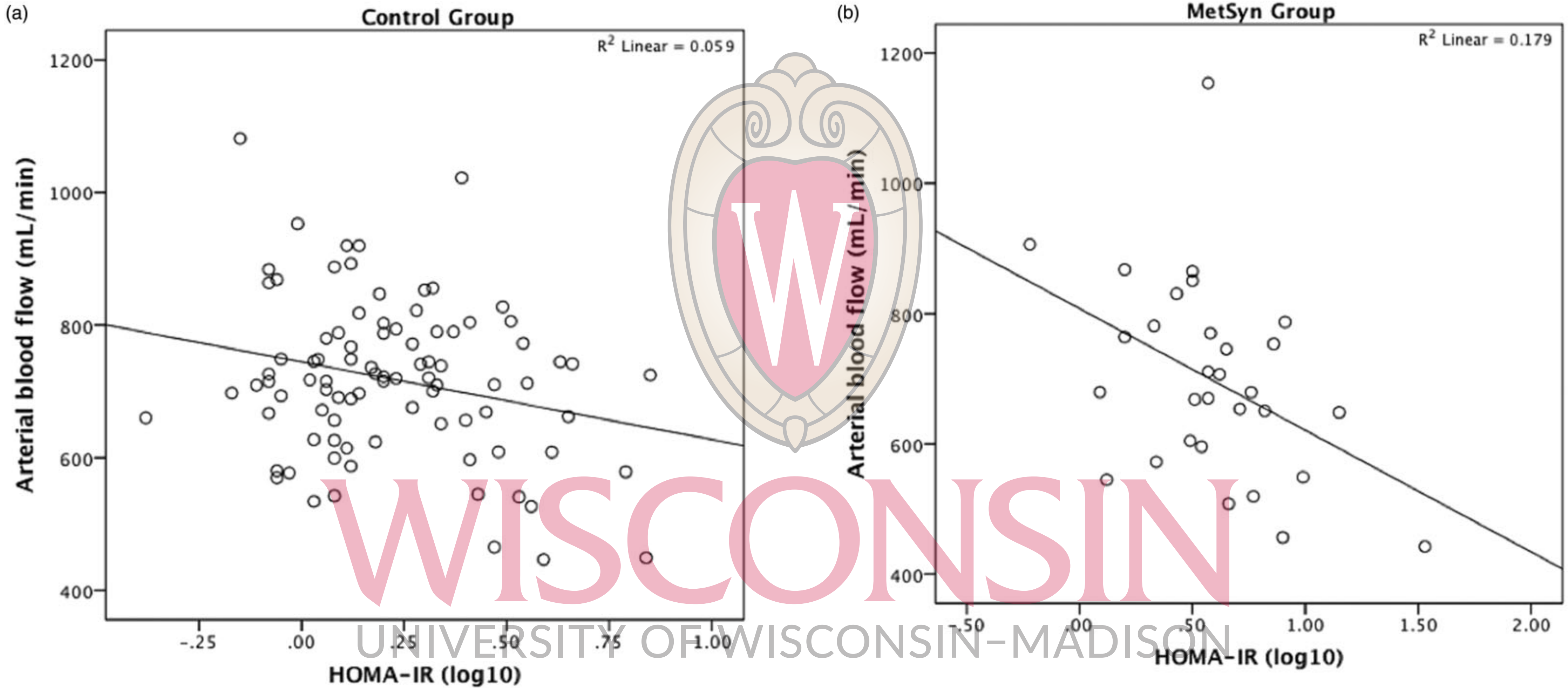
Insulin resistance and cerebral blood flow



- **Higher mean blood flow was associated with greater perfusion in the right superior frontal gyrus in individuals with lower IR index (x < 1.92).**

[5] Hoscheidt SM, et al. J Cereb Blood Flow Metab. 2017 Jun; 37(6): 2249–2261.

Insulin resistance and cerebral blood flow

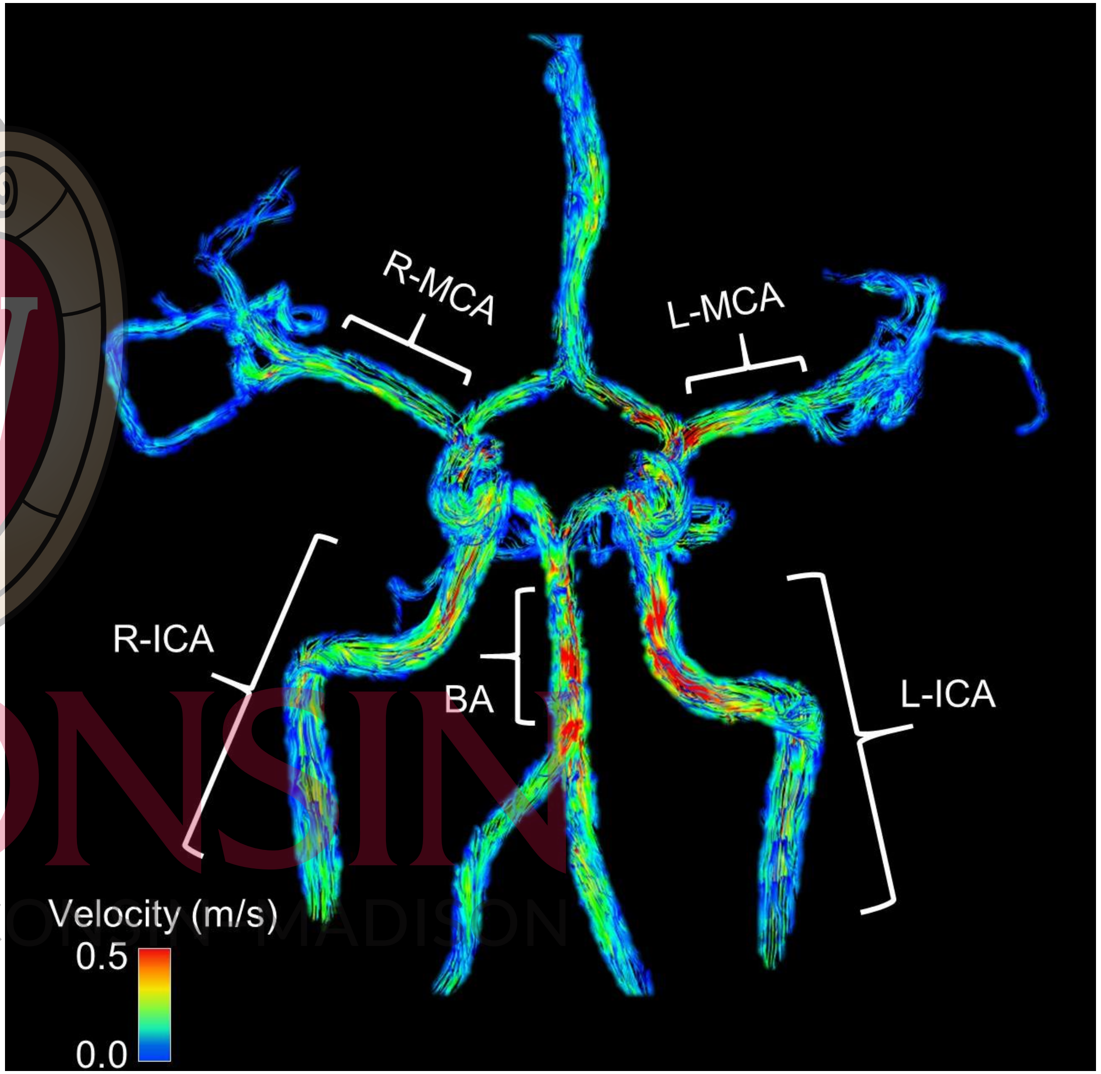


- **Higher IR predicted lower arterial blood flow in Metabolic Syndrome subjects, but not in controls.**

[5] Hoscheidt SM, et al. J Cereb Blood Flow Metab. 2017 Jun; 37(6): 2249–2261.

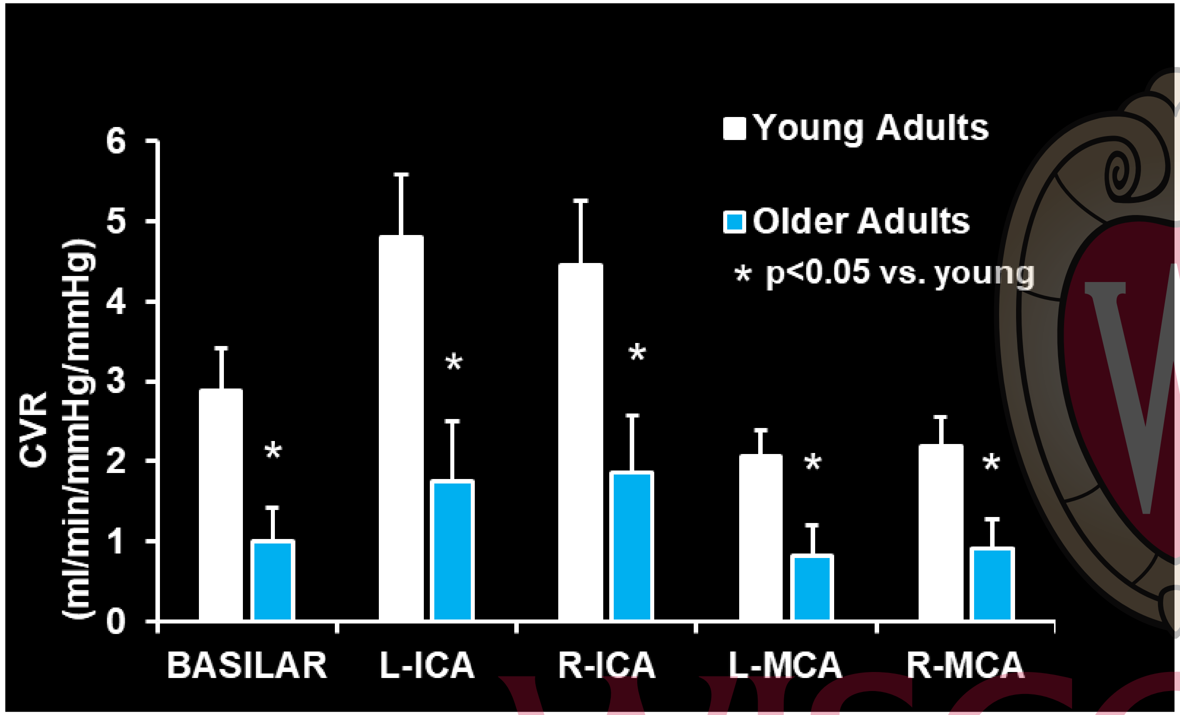
Cerebrovascular reactivity (CVR) and aging

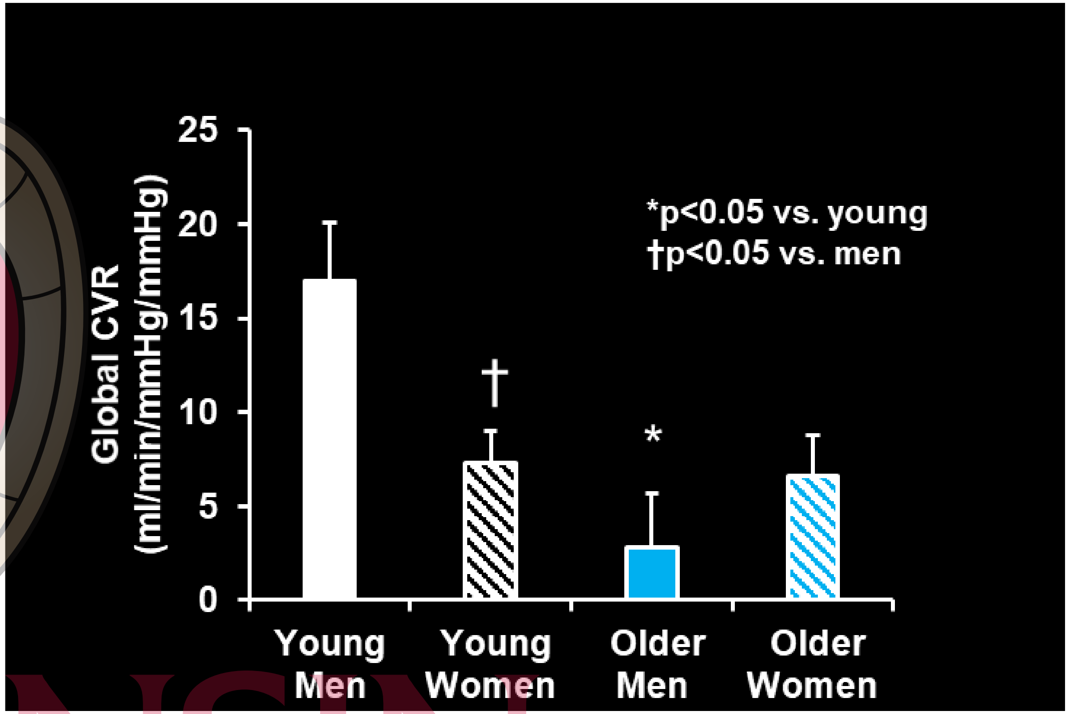
- CVR = response of brain blood vessels to vasoactive stimuli (e.g. neural activity, increases in CO2)
- CVR relates to future risk of CVD and is lower in patients with AD compared with cognitively normal
- Estimated from linear relationship between cerebrovascular conductance (flow/mean arterial pressure) and end-tidal carbon dioxide during CO2 inhalation.



[6] Miller KB, et al. Age-Related Reductions in Cerebrovascular Reactivity Using 4D Flow MRI. Front Aging Neurosci. 2019 Oct 17;11:281

CVR to Hypercapnia





- The brain blood flow response to a vasodilatory stimulus (hypercapnia) was reduced in older adults.
- Findings may be sex-specific

[6] Miller KB, et al. Age-Related Reductions in Cerebrovascular Reactivity Using 4D Flow MRI. Front Aging Neurosci. 2019 Oct 17;11:281

Cardiovascular risk factors and racial/ethnic disparities in AD

- AD has a higher prevalence among African Americans.
- Is there a relationship among **cardiovascular and metabolic risk factors** and **brain blood flow in Whites and African Americans** enriched for AD risk ?
- 399 cognitively unimpaired adults from the WADRC

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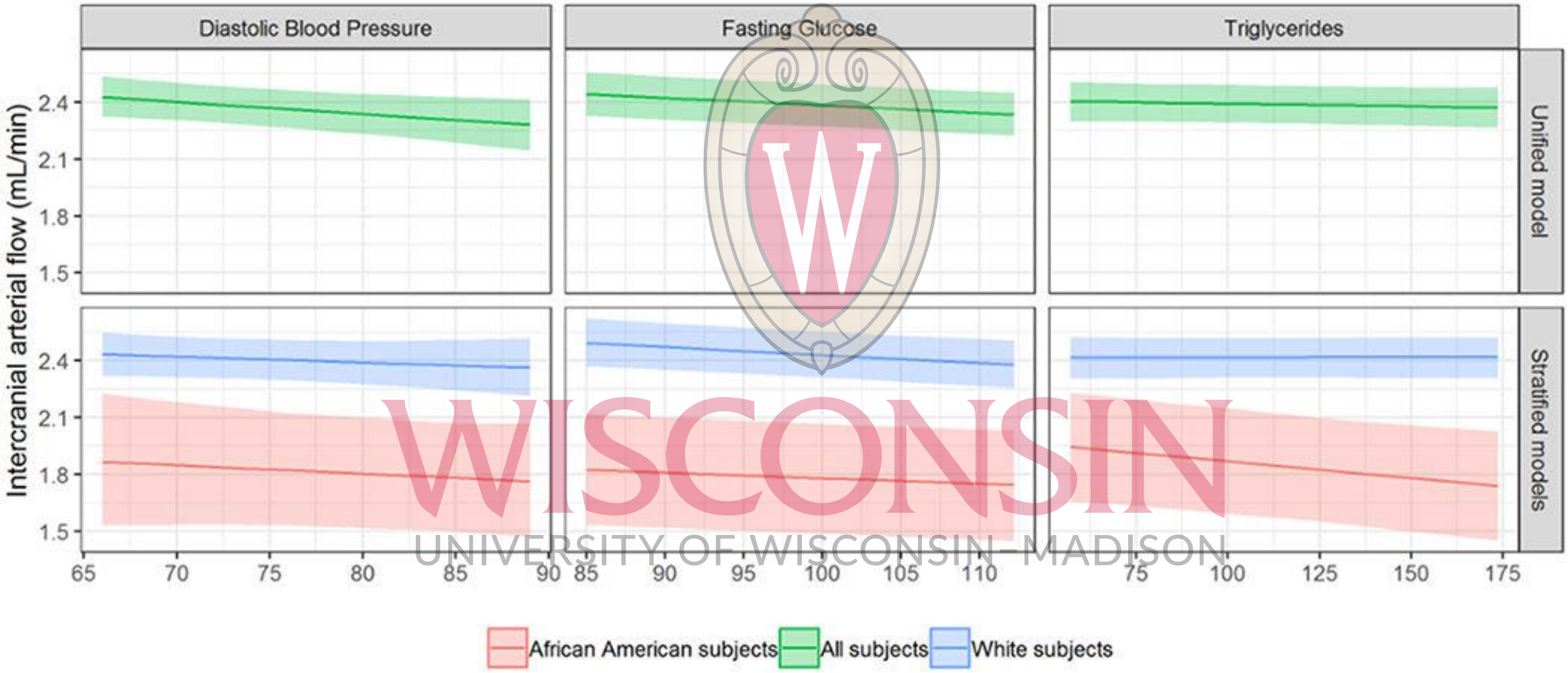
[7] Clark LR, et al. J Alzheimers Dis. 2019 ; 72(3): 919–929.

Cardiovascular risk factors and racial/ethnic disparities in AD



[7] Clark LR, et al. J Alzheimers Dis. 2019 ; 72(3): 919–929.

CV and AD Risk Factors and cerebral blood flow in Whites and African Americans

- **Elevated fasting glucose and triglycerides were associated with lower intracranial arterial flow**

- **These relationships were more prominent in African Americans.**

- **Targeting metabolic risk factors may impact intracranial arterial health.**

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[7] Clark LR, et al. J Alzheimers Dis. 2019 ; 72(3): 919–929.

4D flow MRI: Other vascular markers

- **What else besides flow and PI ?**

- **Clinical AD patients showed decreased blood flow and increased PI**
  - **neuron loss -> decreased metabolism -> decreased blood flow**
  - **increase cerebrovascular resistance -> increase PI**

- **What about a more local marker of vascular health ?**

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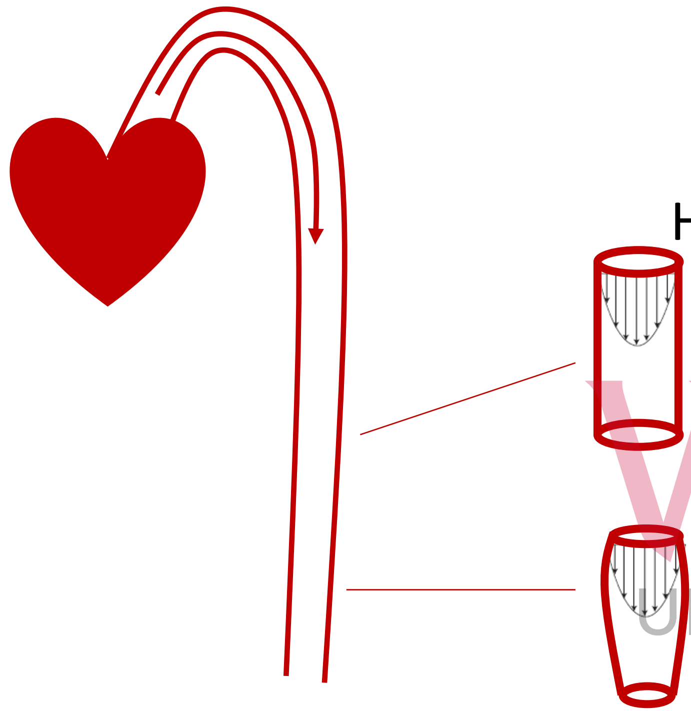
[1] Sweeney et al. Alzheimer's & Dementia 15 (2019) 158-167

4D flow MRI: Other vascular markers

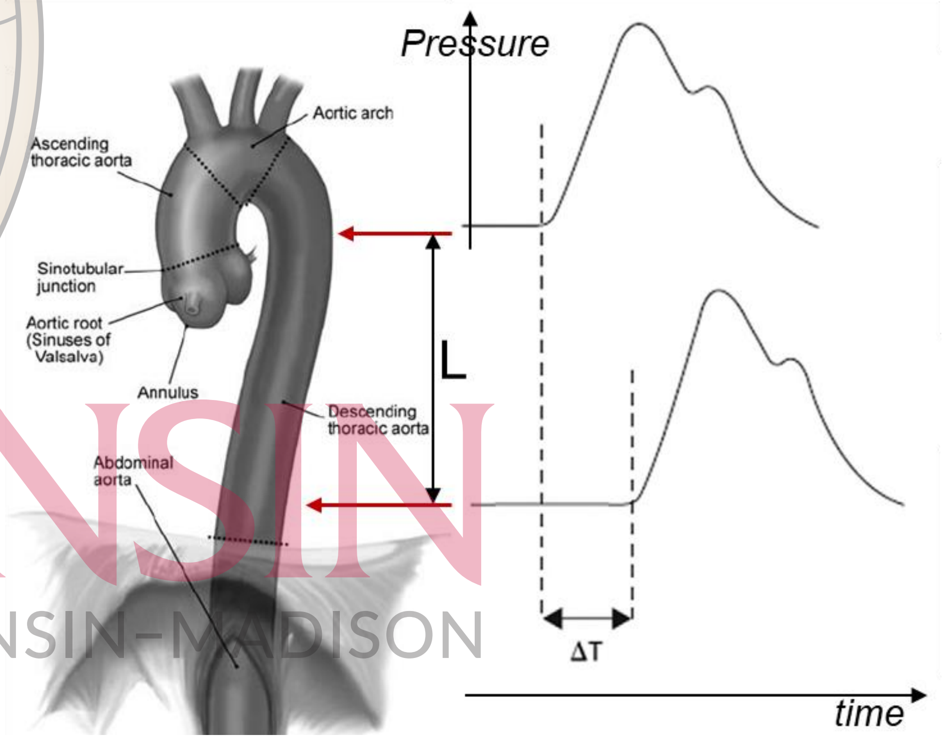
- **Pulse wave velocity (PWV)** gold standard noninvasive biomarker for arterial stiffness

- Arterial stiffness is a significant risk factor for cardiovascular disease and mortality [1]



High speeds:
-high blood pressure
-arterial stiffness

Low speeds:
-low blood pressure
-elastic arteries

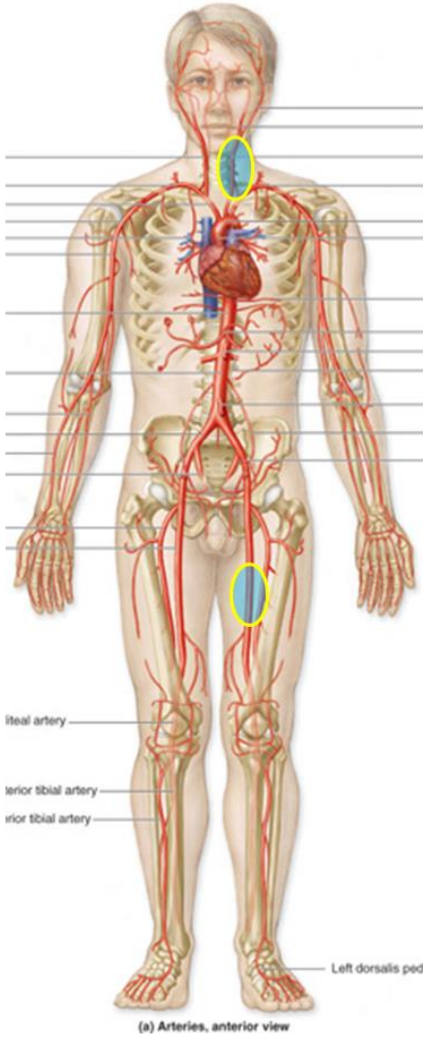


$$\text{PWV} = \frac{L}{\Delta T}$$

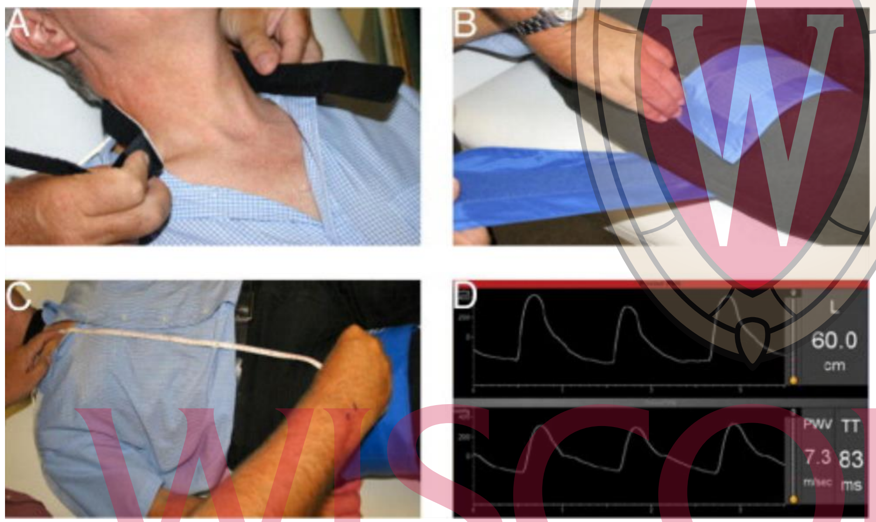
[1] Laurent S, et al. Eur Heart J 2006; 27:2588–2605.

4D flow MRI: Other vascular markers

- **carotid-femoral PWV associated with deposition of Aβ in nondemented individuals [2]**



- **measured using applanation tonometry**



from Cavalcante et al. *JACC*. 2011;57(14):1511-22.

+ Easy & inexpensive, accessible

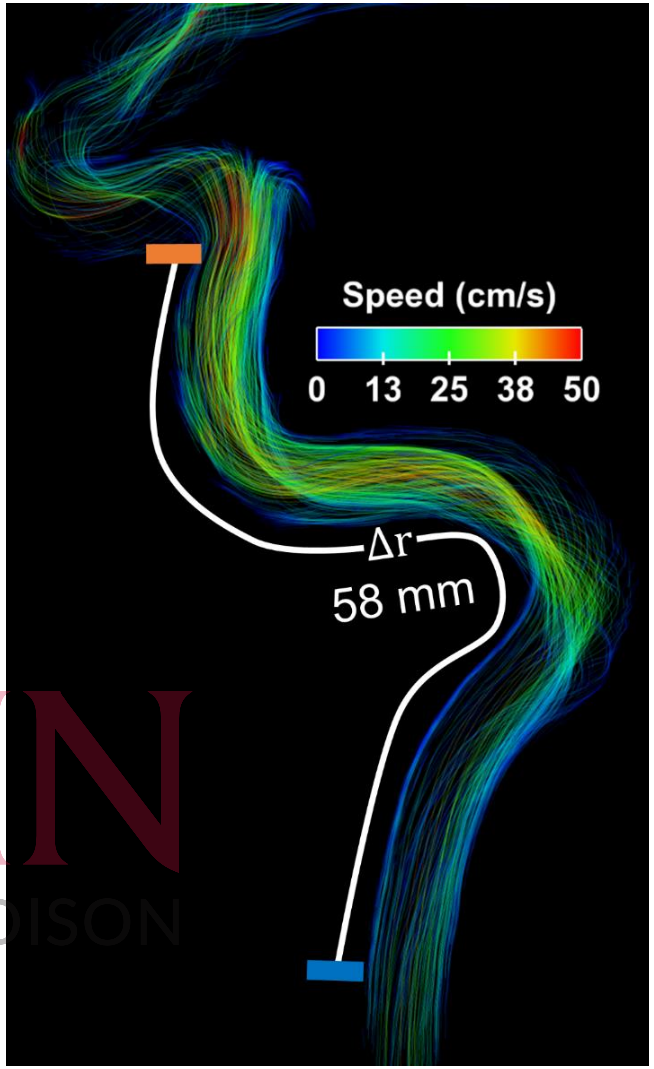
- Includes aorta + peripheral arteries
  - *Stiffness and effect of CVD varies*
  - *Increased wave reflections from peripheral arteries*
  - *Flow in opposite directions*

- Inaccurate distance measure
  - *Estimated from body surface area*
  - *No 3D considerations*
  - *Vessels are not always straight*

[2] Hughes TM, et al. JAMA Neurol. 2014;71(5):562-568.

4D flow MRI: intracranial PWV

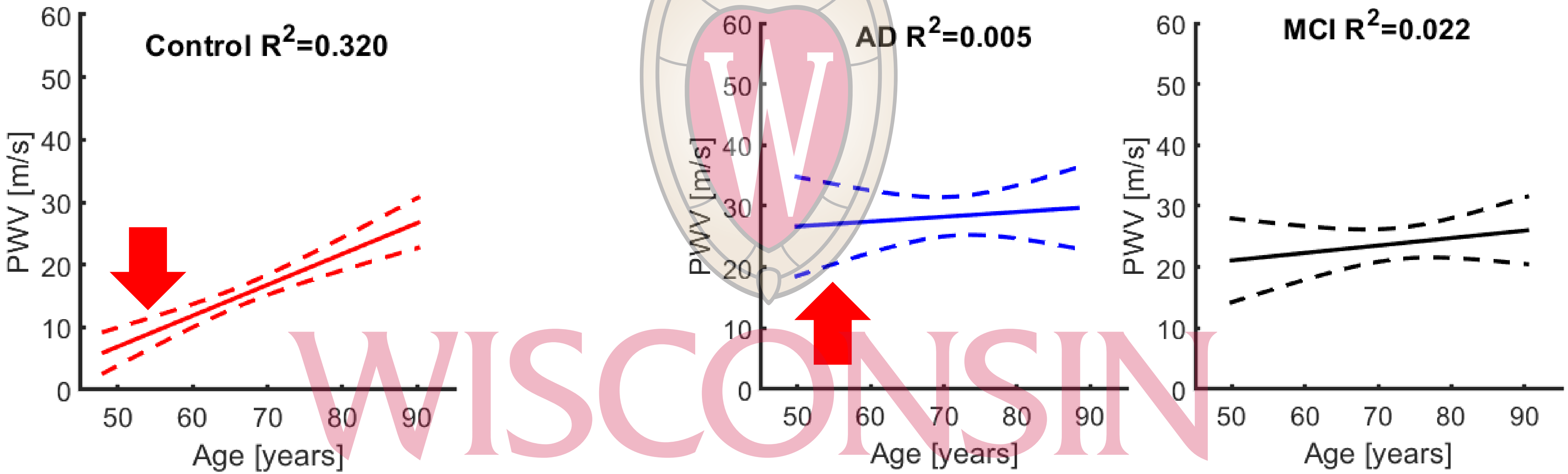
- Estimate intracranial PWV using 4D flow MRI
  - Technical challenges
    - High temporal resolution
  - Iterative reconstructions
  - AD, MCI, subjects at risk of AD and controls



Sagittal view of ICA segment

Pathology and age effects

- PWV increases with age in healthy
- Higher PWV suggests arterial stiffness in AD

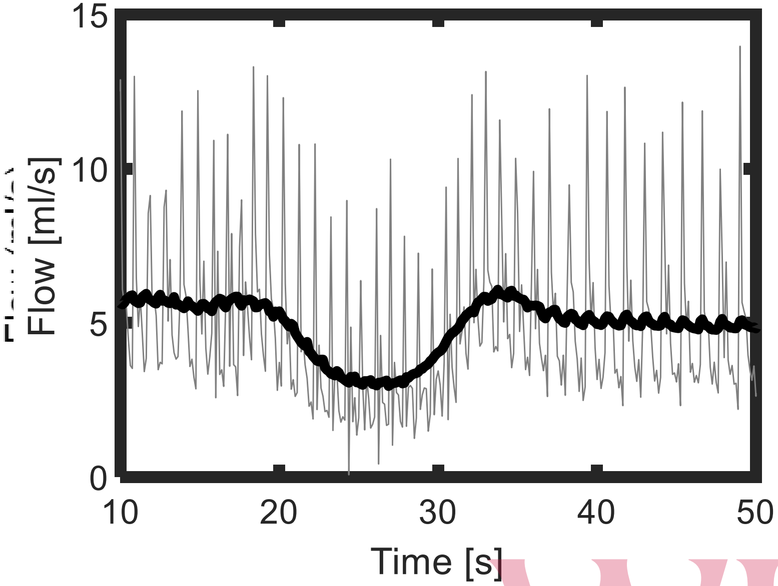


- AD appears to accelerate aging effect

[8] Rivera-Rivera LA, et al. J Cereb Blood Flow Metab. 2020 Mar 13; Online ahead of print.

4D Flow MRI (PCVIPR) Outlook

- Probe other components of macrovascular hemodynamics



http://www.nytimes.com/2014/01/12/opinion/sunday/goodnight-sleep-clean.html

- How about flow variations throughout the scan ?
- 1 cardiac waveform average throughout ~5min scannin
  - Blood flow, PI, PWV
  - Low frequency oscillations
  - high frequency
- Clearance mechanism hypothesis
  - glymphatic flow
  - cardiac, smooth muscle cells driven

4D Flow MRI (PCVIPR) Outlook

- Explore potential relations
  - 4D flow MRI and PET imaging markers

- Next lecture:
  - finish studies overview

  - clinical motivation for probing multiple compartments
    - advances in ASL techniques
    - tissue strain (DENSE) & stiffness (MRE)

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