

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



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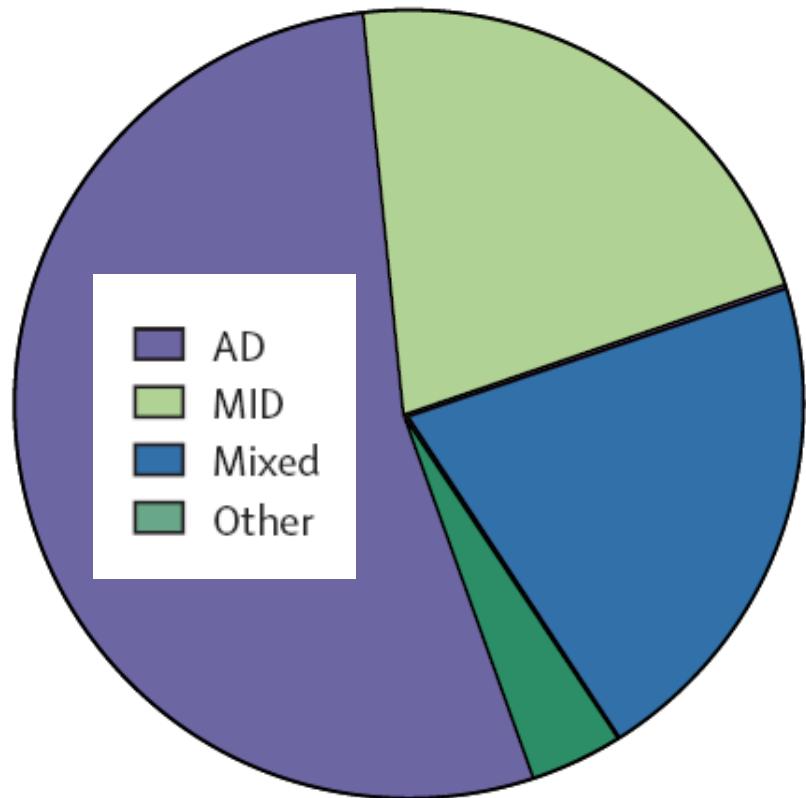


**Oliver Wieben, PhD**  
Professor  
Medical Physics  
Radiology  
Biomed. Eng.  
Vice Chair -  
Research

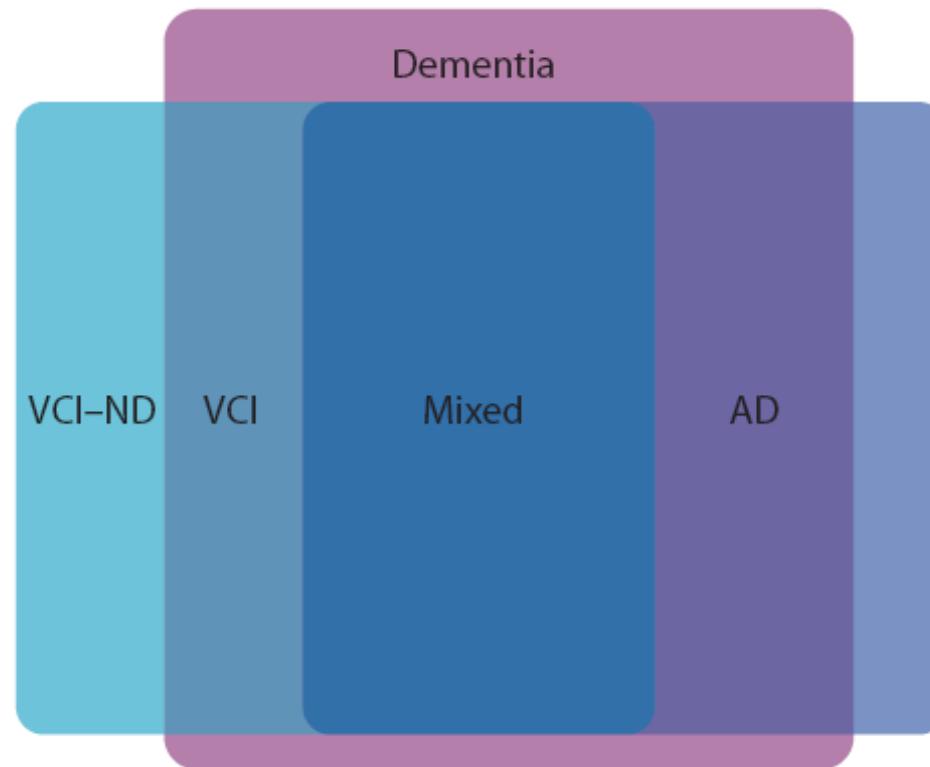
[owieben@wisc.edu](mailto:owieben@wisc.edu)

# Contribution of Vascular Disease to Dementia

**Traditional**



**Revised**



# Vascular Disease Markers

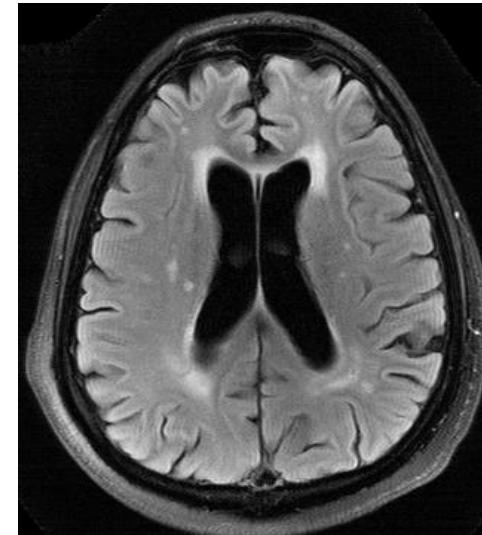
## Systemic Markers

*Blood Pressure*  
*Cholesterol*  
*Genetics*



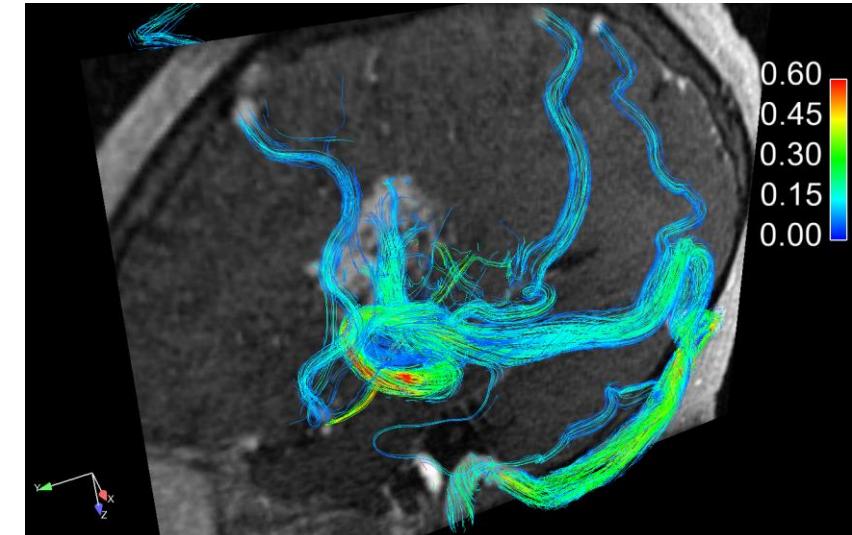
## Structural Imaging

*White Matter Lesions*  
*Microbleeds*  
*Diffusion*



## Functional Vascular Imaging

*Perfusion*  
***Flow imaging***



## Overview

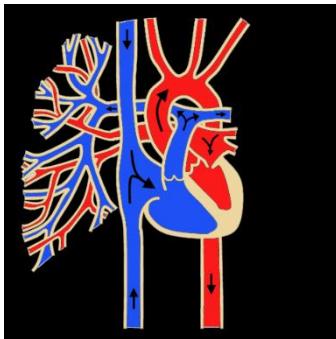
- **Introduction to Blood Flow Measures with MRI**
  - Kevin Johnson, Assistant Professor, Medical Physics and Radiology
- **What can we measure** and how we measure it
  - Grant Roberts, PhD Candidate, Medical Physics
- **Results** in studies of ADRD
  - Leonardo Rivera-Rivera, Postdoctoral Fellow

## Overview

- **Introduction to Blood Flow Measures with MRI**
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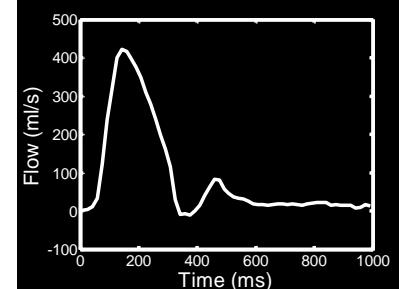
# Vascular System

*Waste / Nutrient Exchange  
(lung/liver/kidneys)*



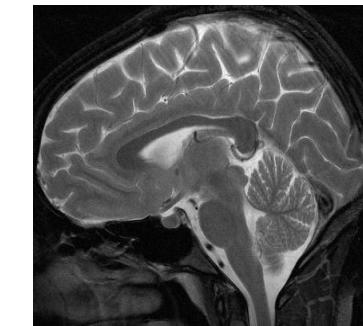
**Arterial Network**

*transport +*

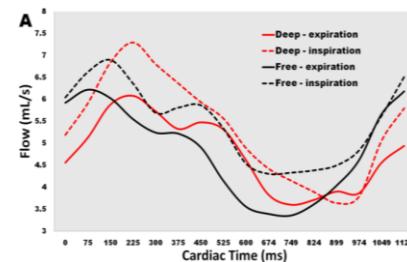


***Brain Tissue***

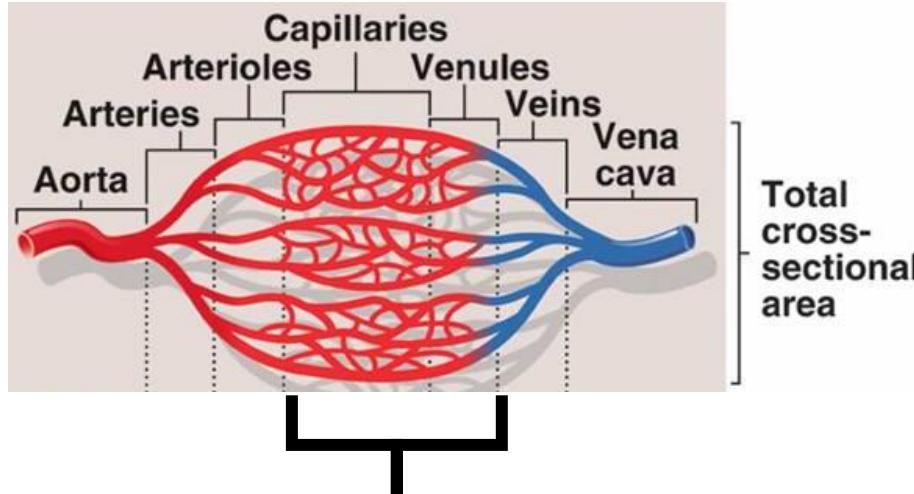
*Capillary Bed  
exchange + regulation*



**Venous Network**  
*transport (waste clearance)*



# Vascular Imaging Landscape



## Tissue Perfusion

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

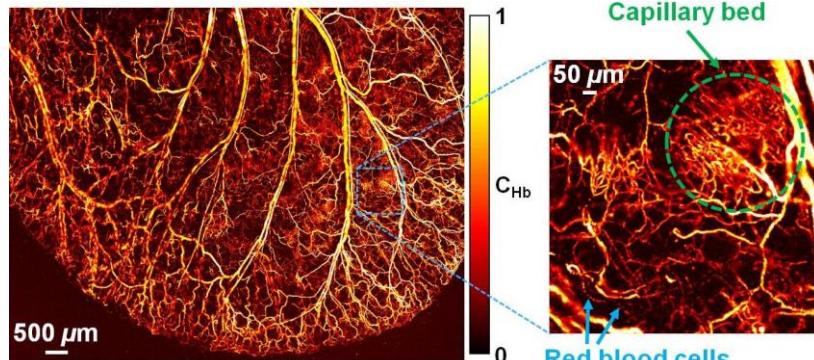


Photo acoustic Microscopy: Yeh,C et al. J  
Biomed Optics 14', 19(9):96011

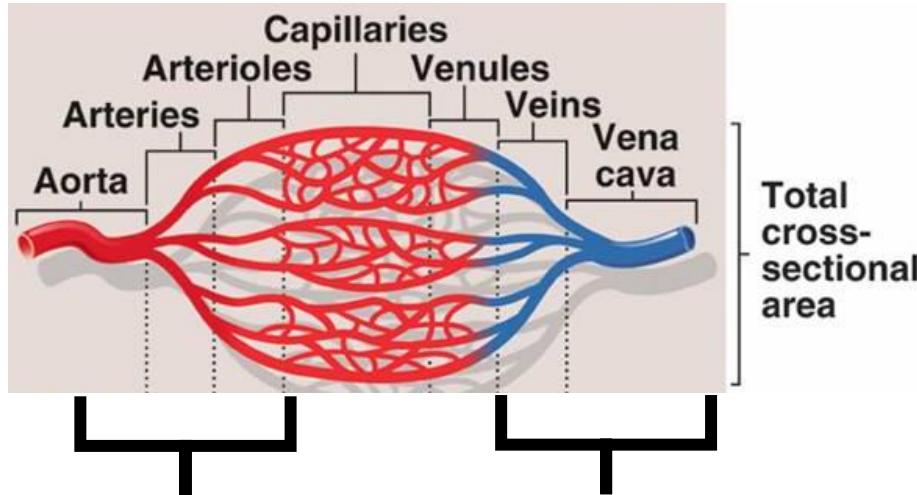
CT: Iodine, Xenon

$^{15}\text{O}$  PET

MRI:  
Arterial Spin Labeling (ASL),  
Contrast Media

***To be covered in future lecture***

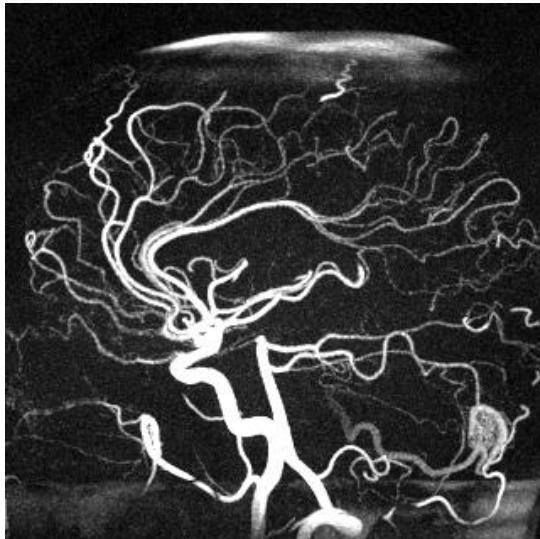
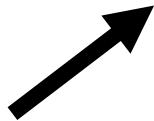
# Vascular Imaging Landscape



Arteries

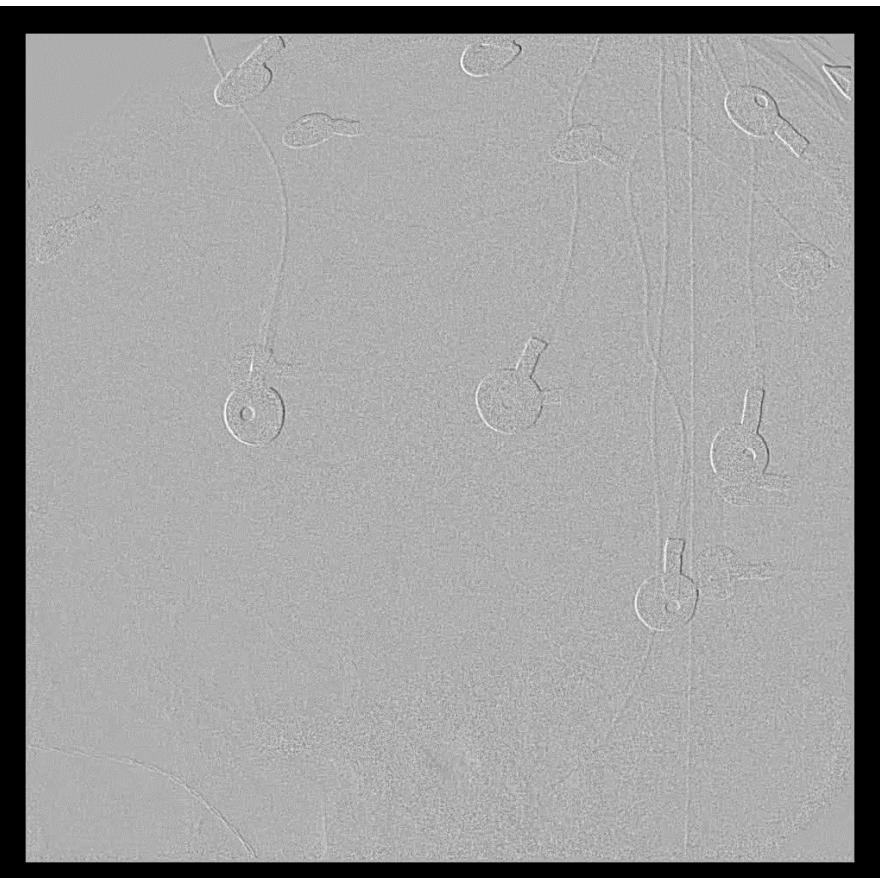
Veins

CT / DSA Angiography



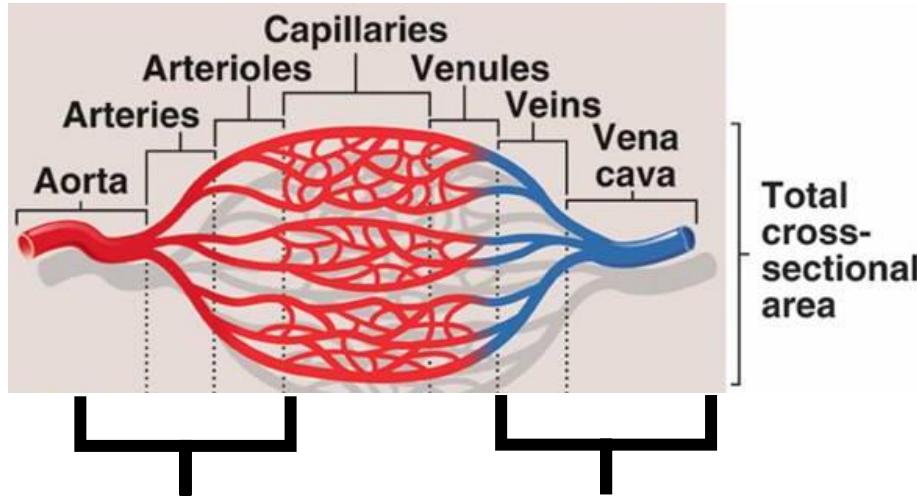
# Quantifying Intracranial Hemodynamics

- 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*

# Vascular Imaging Landscape



Arteries

Veins



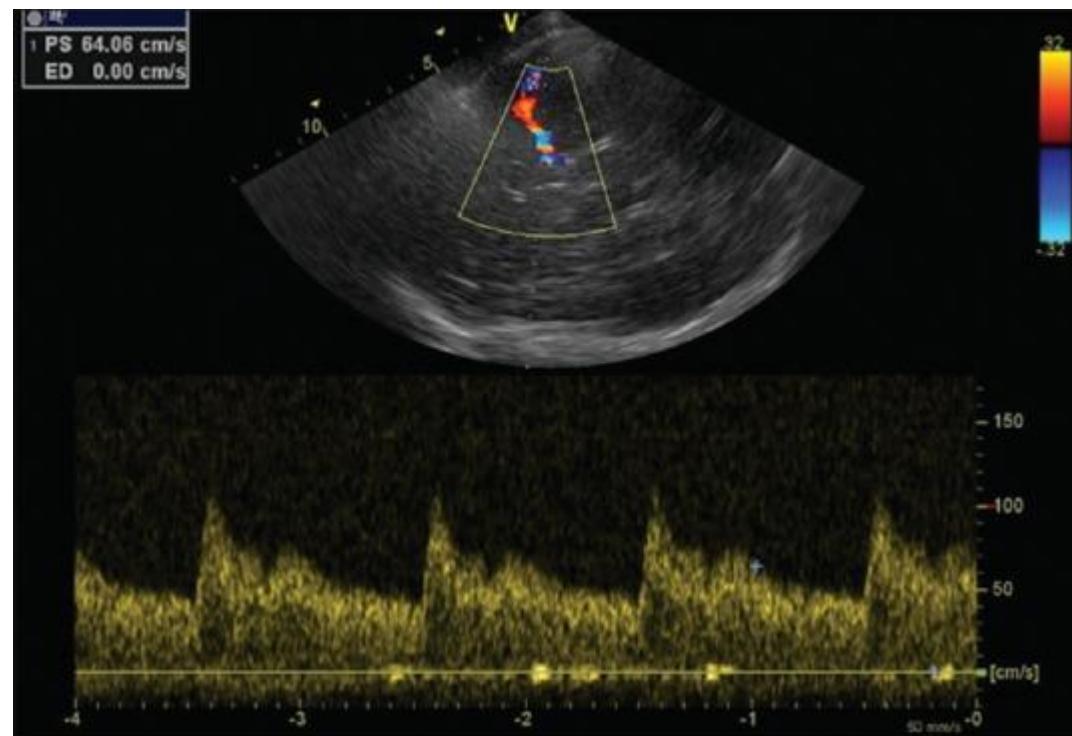
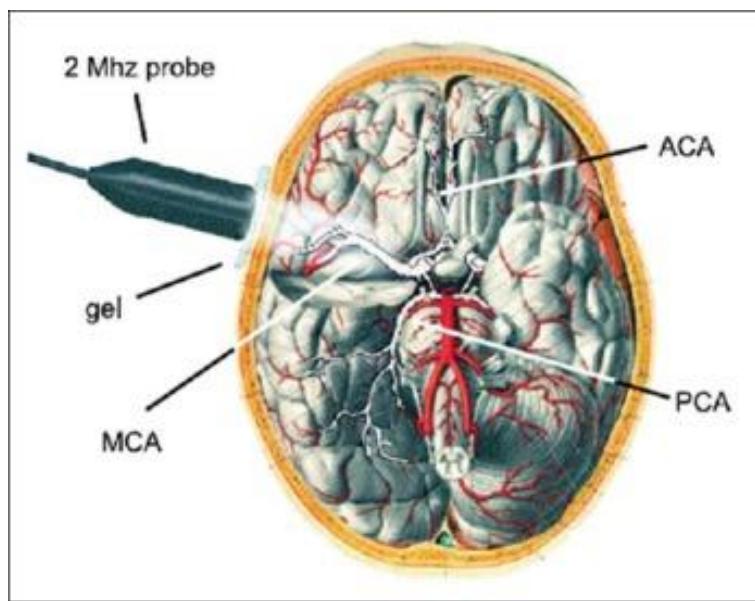
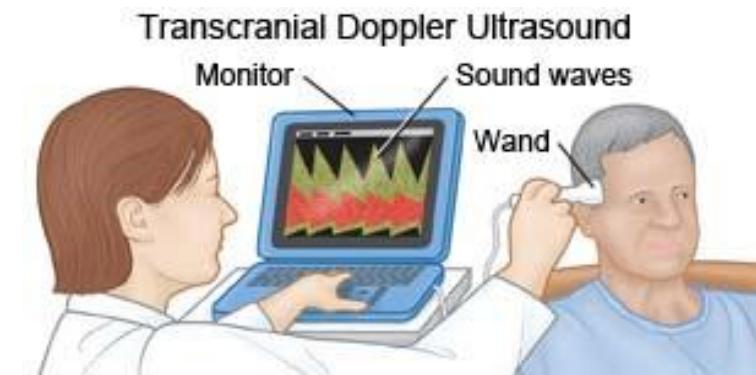
**CT / DSA Angiography**

**Doppler Ultrasound**

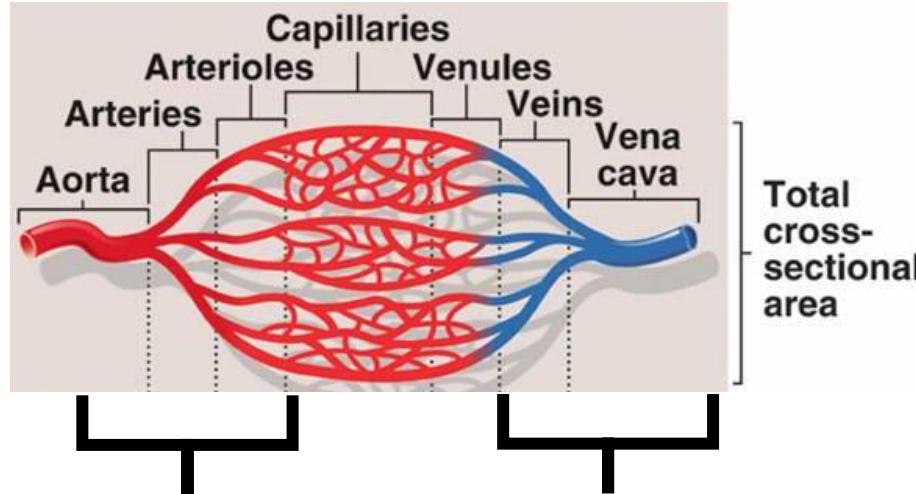
# Quantifying Intracranial Hemodynamics

- 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



# Vascular Imaging Landscape



Arteries

Veins



**CT / DSA Angiography**

**Doppler Ultrasound**

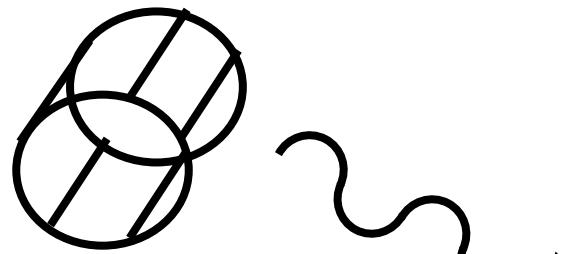
**MRI:**

**MR Angiography**

***Phase Contrast Flow Imaging***

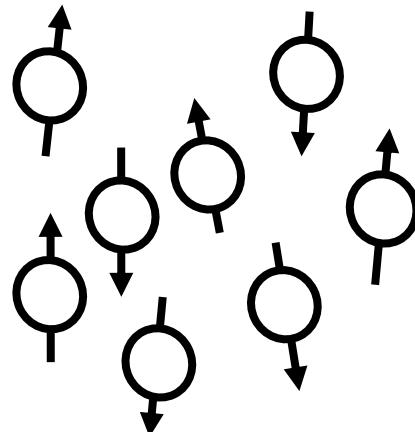
# MRI : Excitation

## RF Transmitter



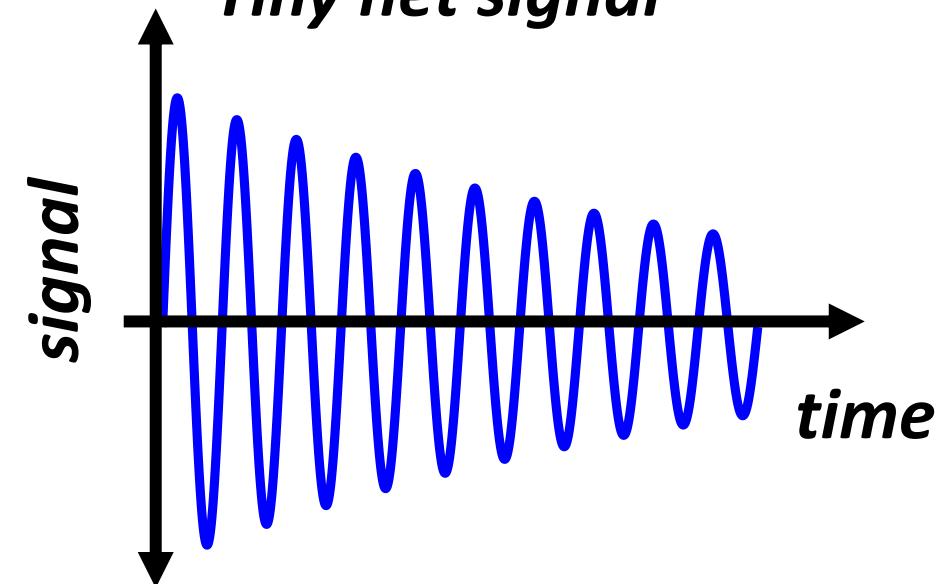
High Power  
RF Wave

Hydrogen Atoms  
(each like a little magnet)



## RF Receiver

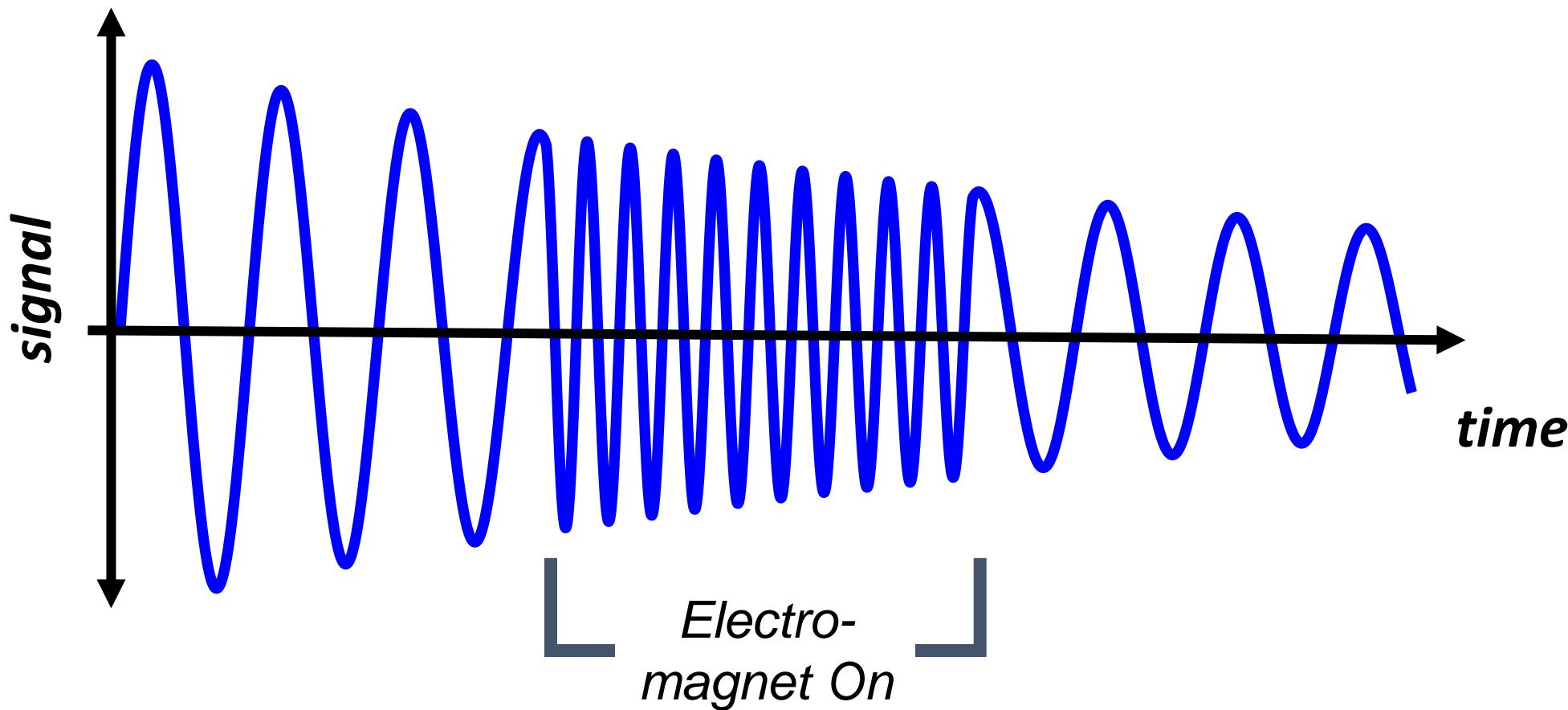
*Tiny net signal*



Lasts ~1-100ms

## MRI : Spatial Encoding

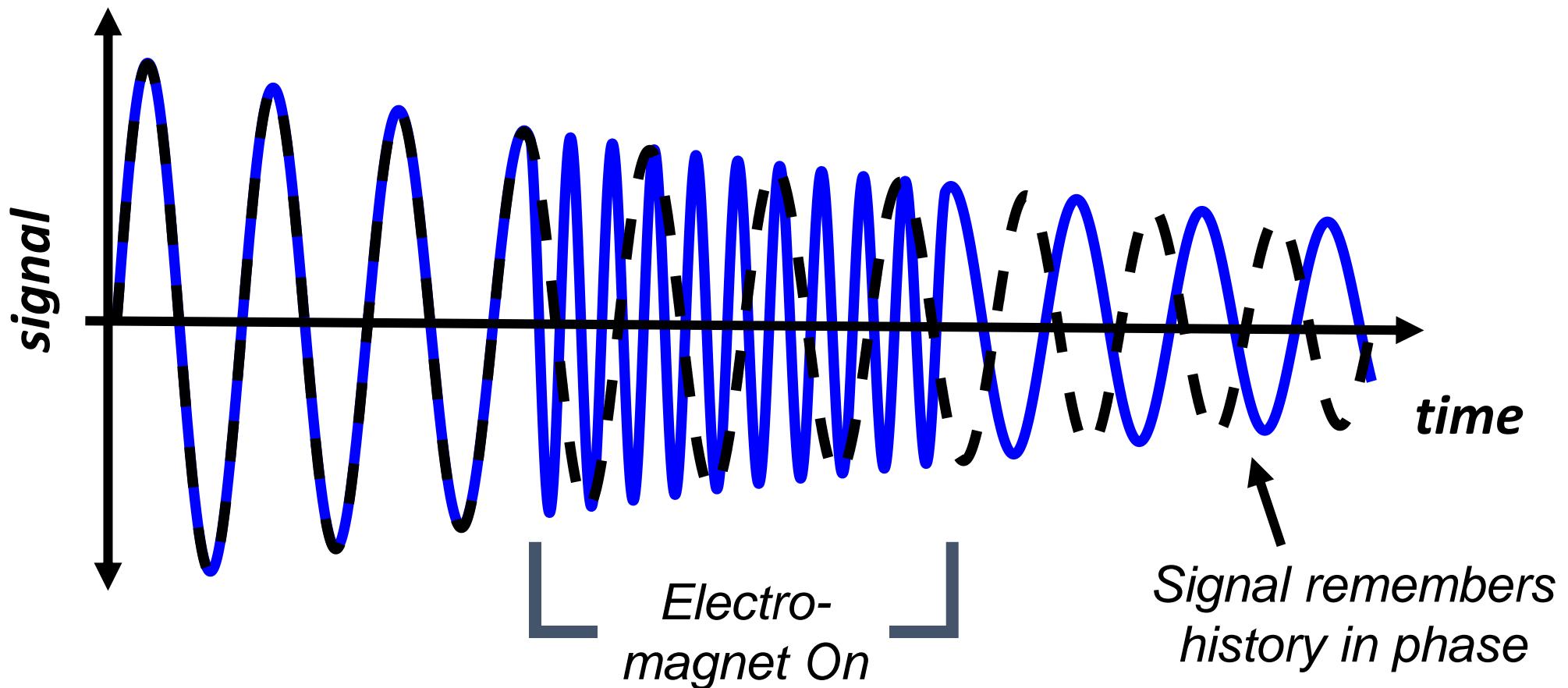
- The signal can be modified after excitation and has memory!



**Dynamic Electromagnets encode Position**  
(Also make scans loud)

## MRI : Spatial Encoding

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



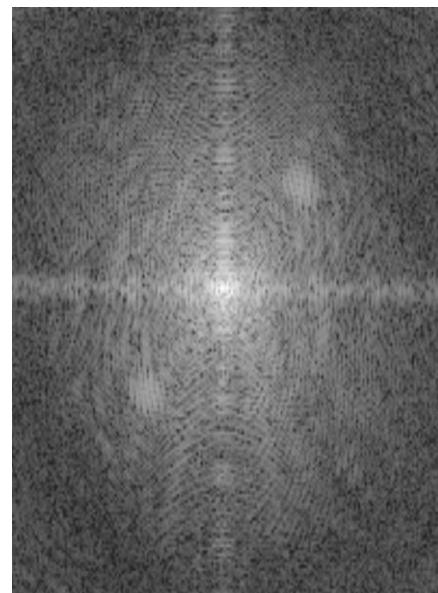
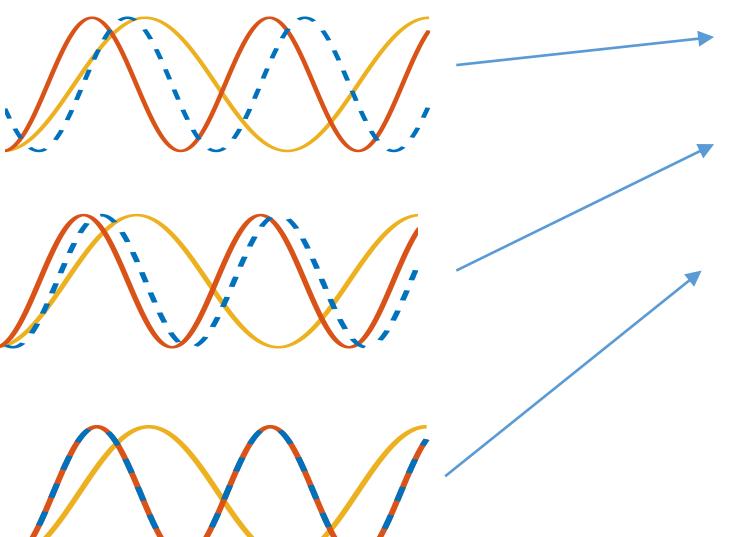
**Dynamic Electromagnets encode Position**

(Also make scans loud)

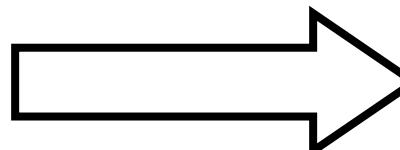
# MRI : Spatial Encoding

Raw Data

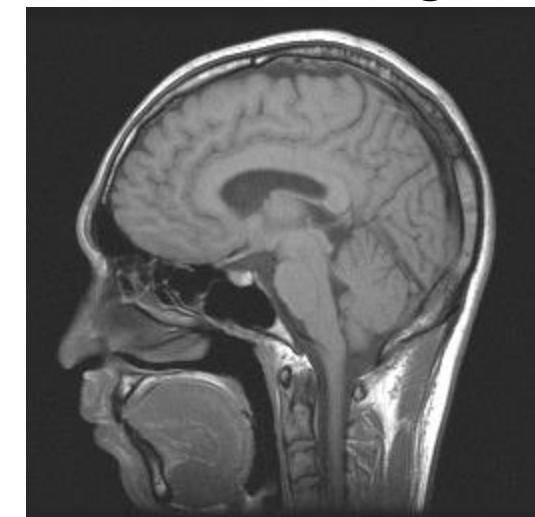
*(Mixed Frequencies)*



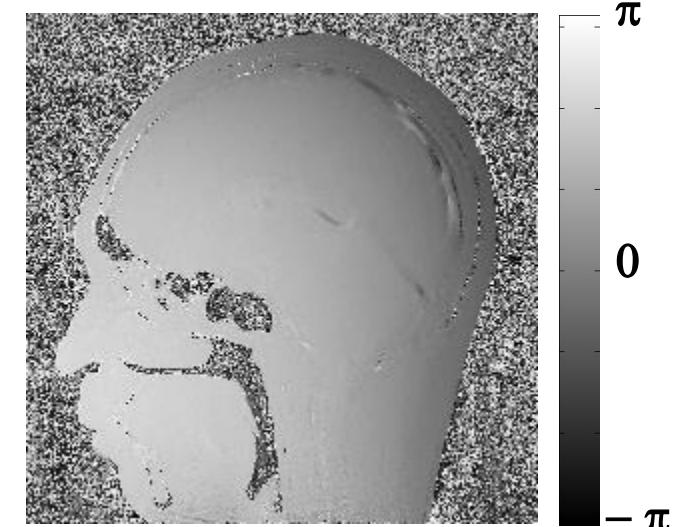
*Signal Separator  
(~Fourier transform)*



MRI Image

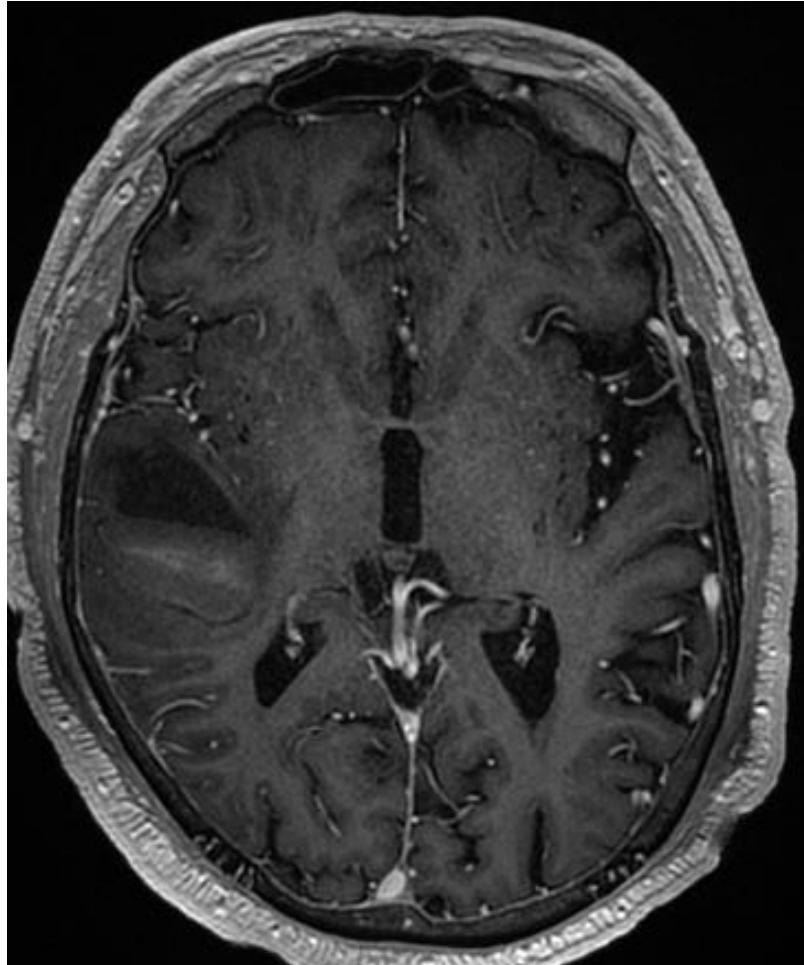


*phase [ $f(x,y)$ ]*

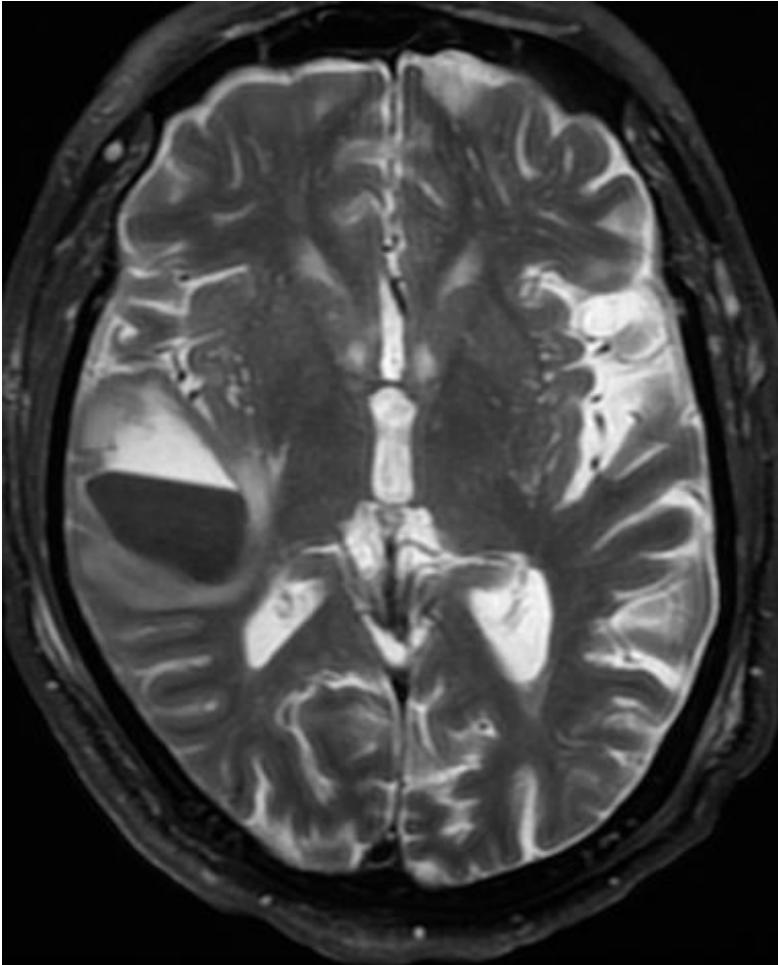


# MRI Provides Opportunities to Manipulate Contrast

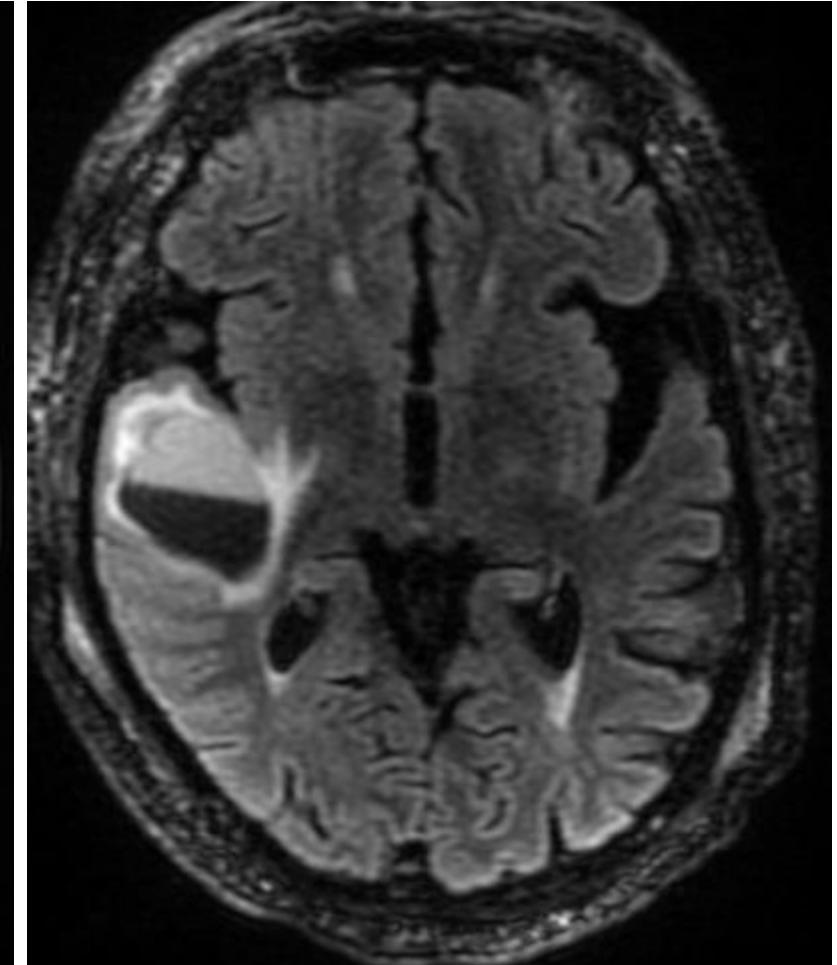
*Bright Blood*



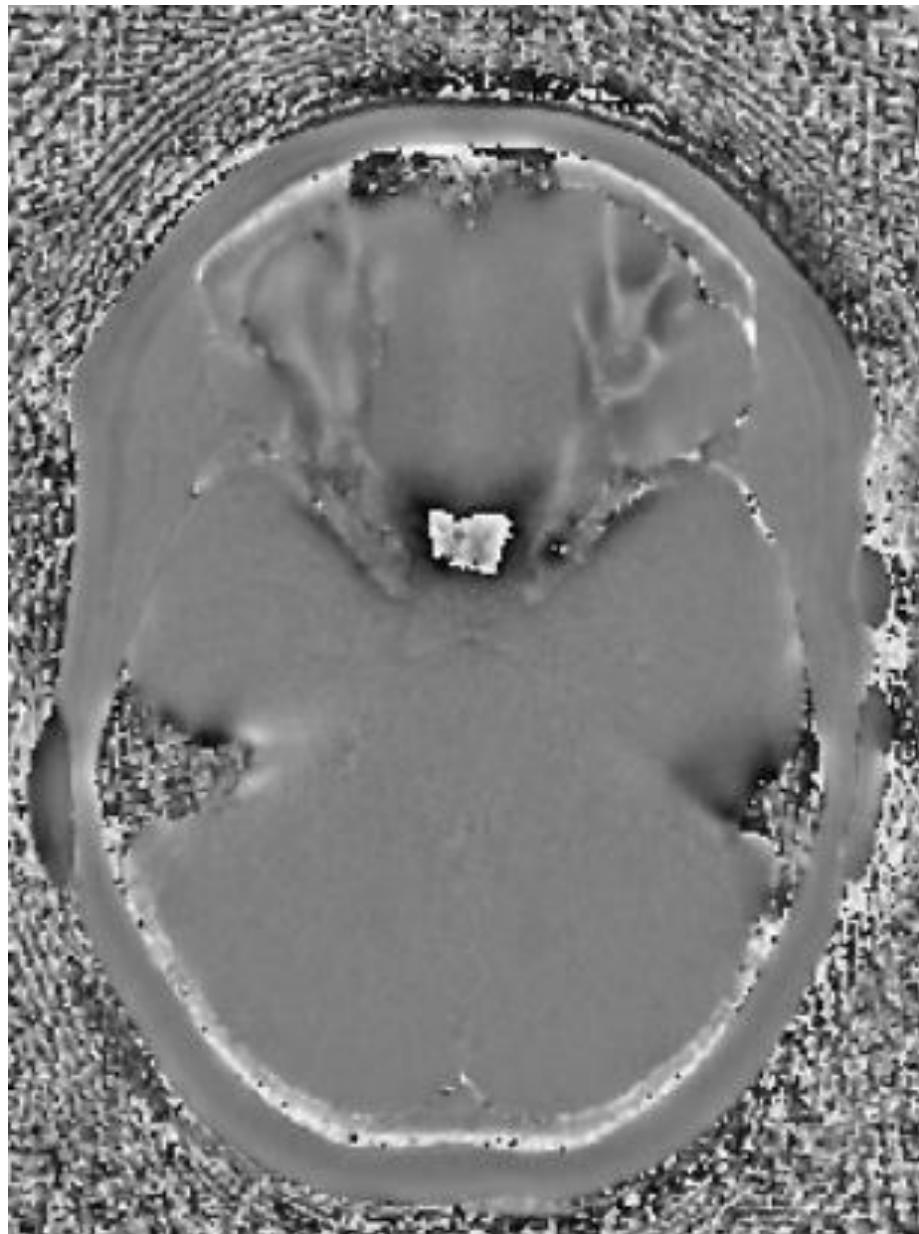
*Bright Fluid*



*Dark Fluid*



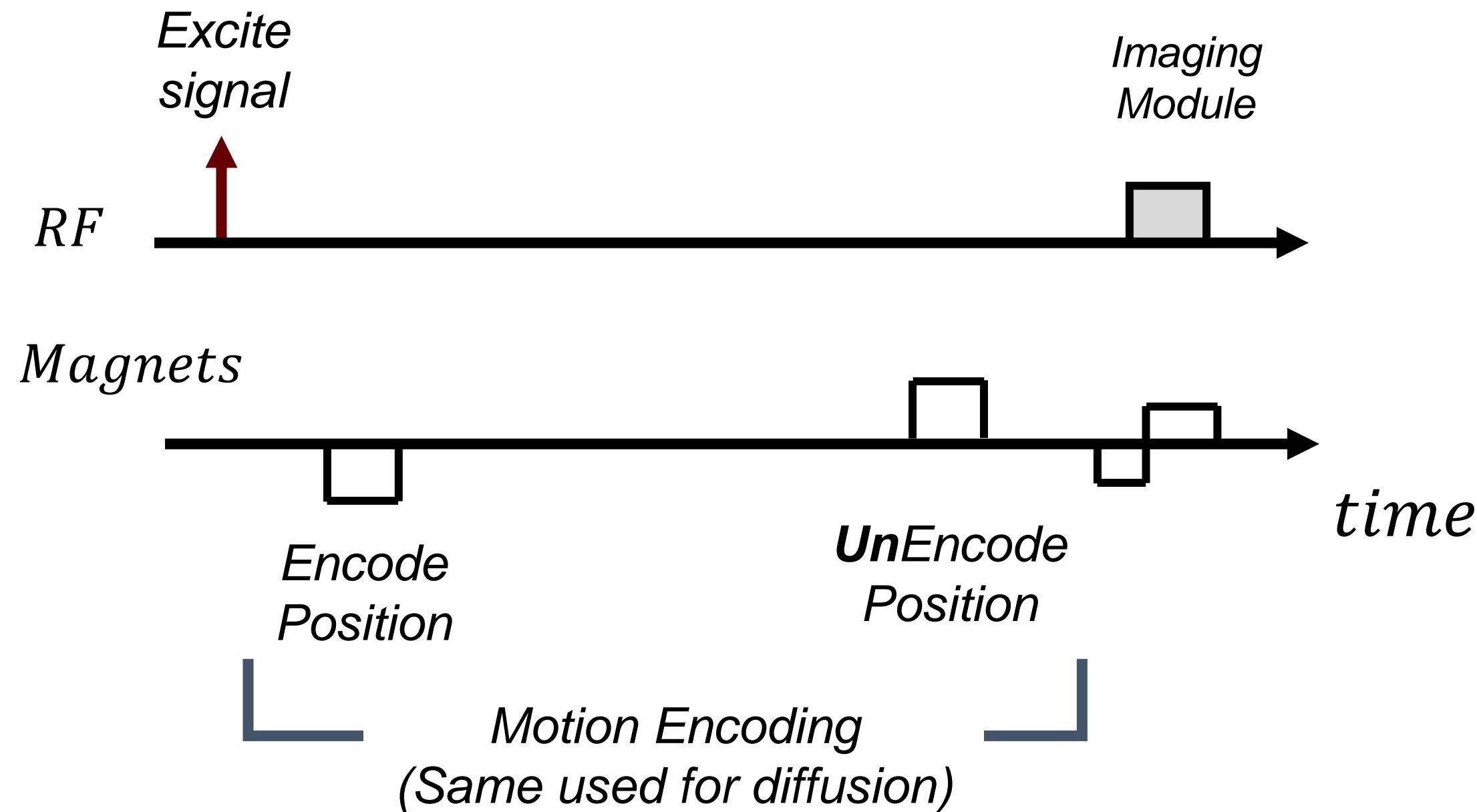
The image phase is often uninteresting



*Phase image has  
limited contrast*

*(QSM) Susceptibility  
Mapping does use this  
phase*

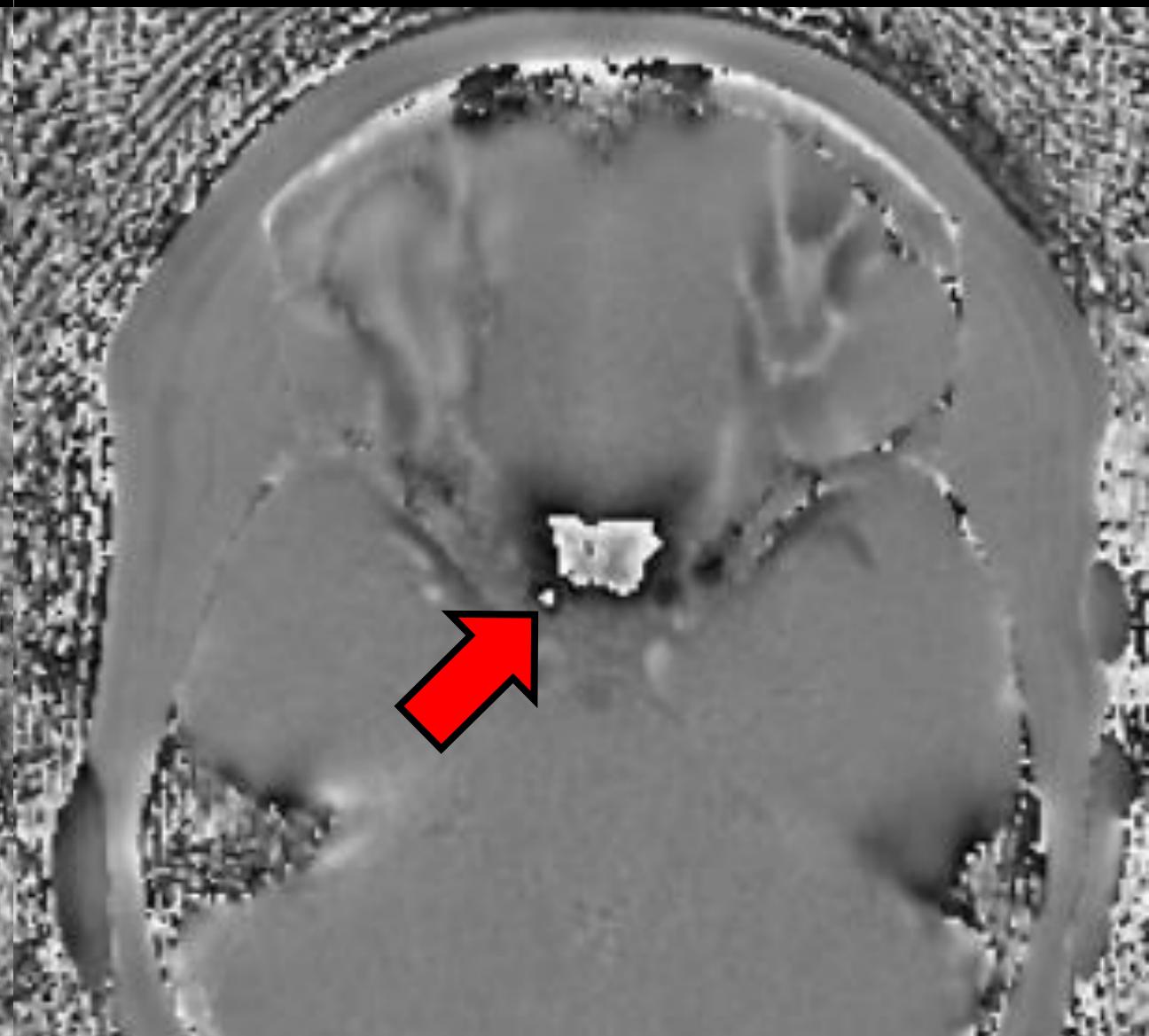
# Motion Sensitization with MRI



Without Motion Encoding



With Motion Encoding

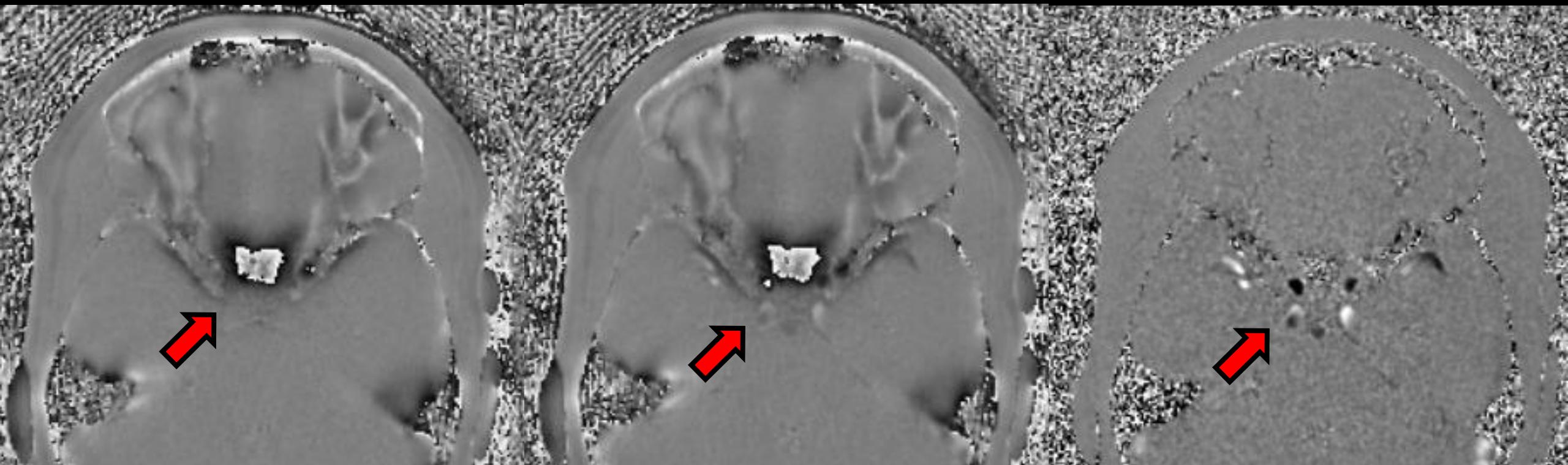


*Phase images change based on velocity*

Without Motion  
Encoding

With Motion  
Encoding

Difference  
(Velocity)

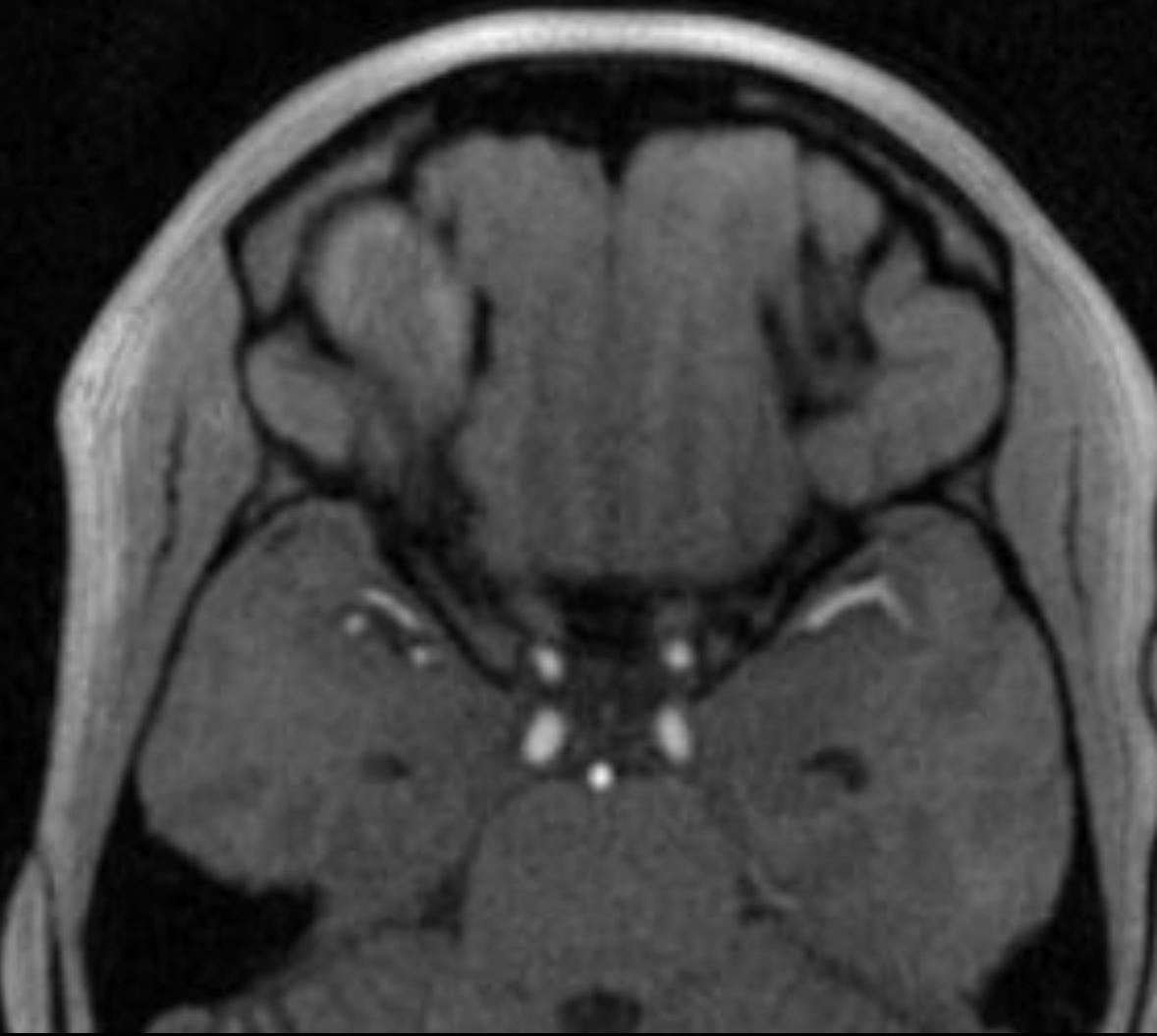


$\phi$

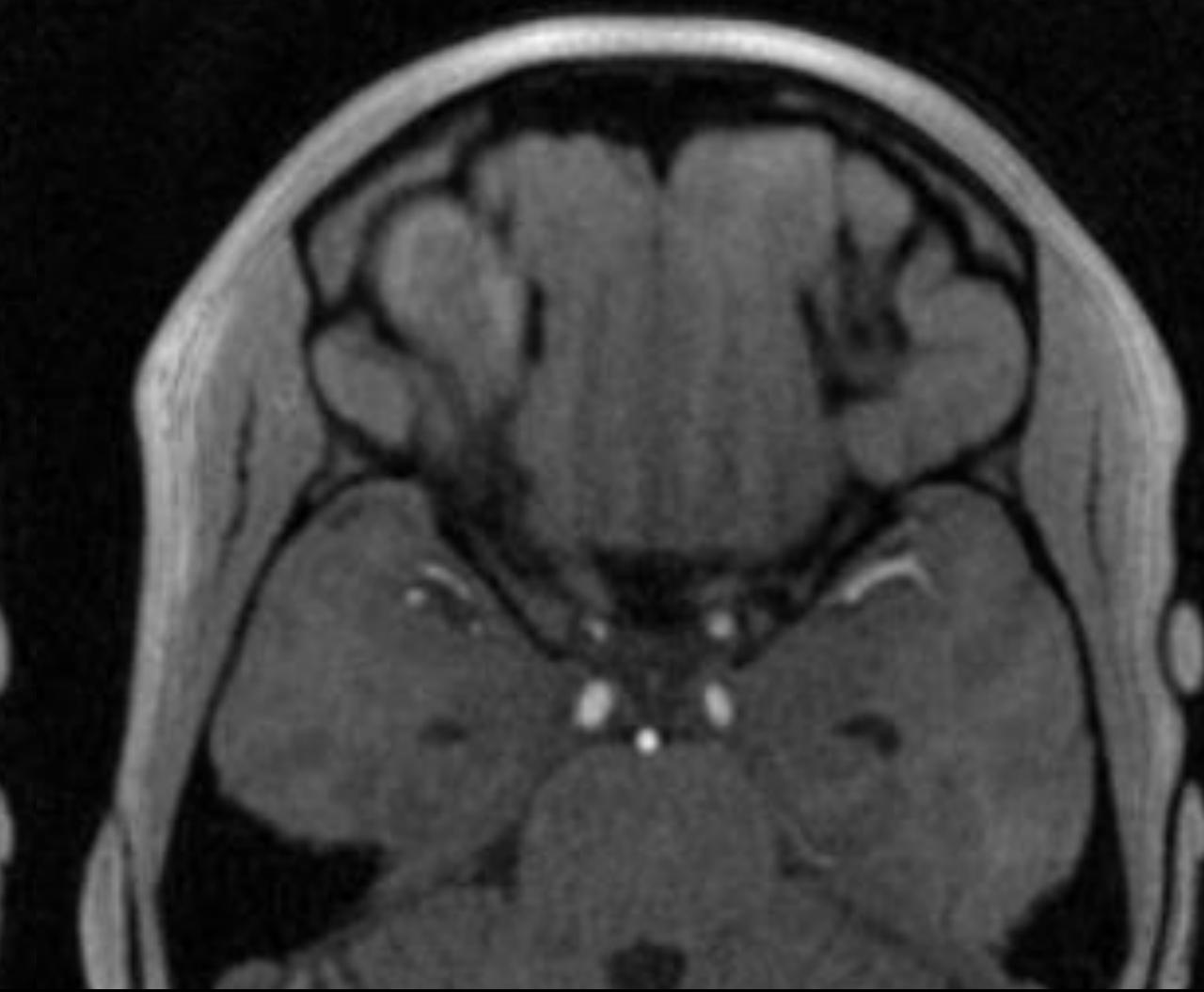
$\phi + v$

$v$

Without Motion Encoding

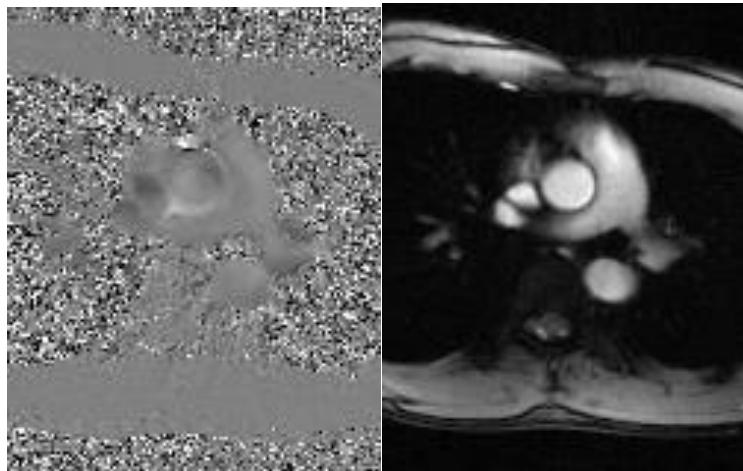
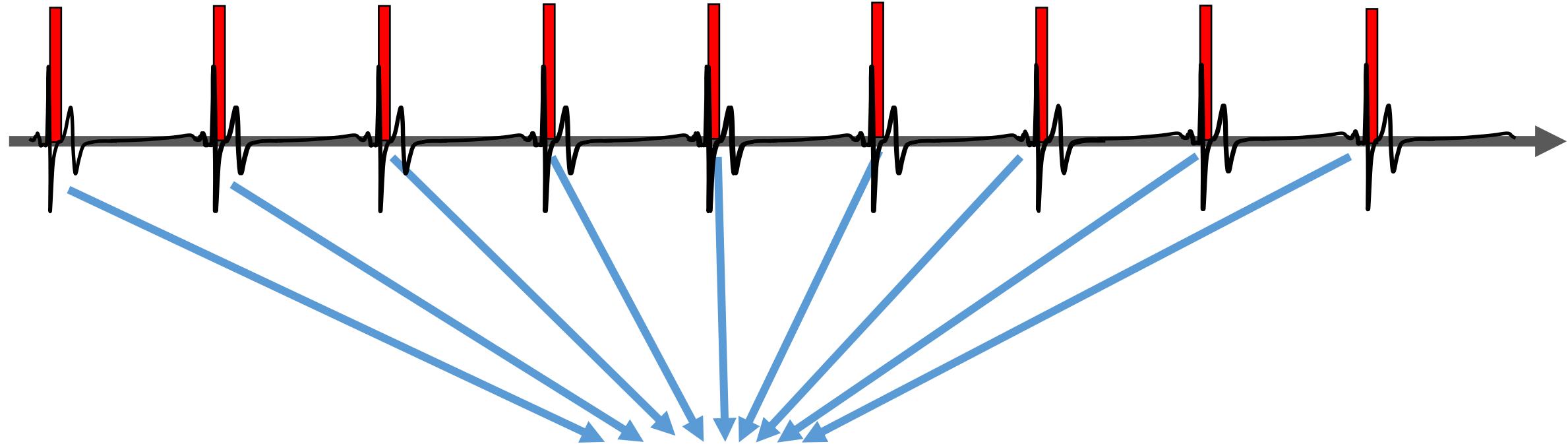


With Motion Encoding



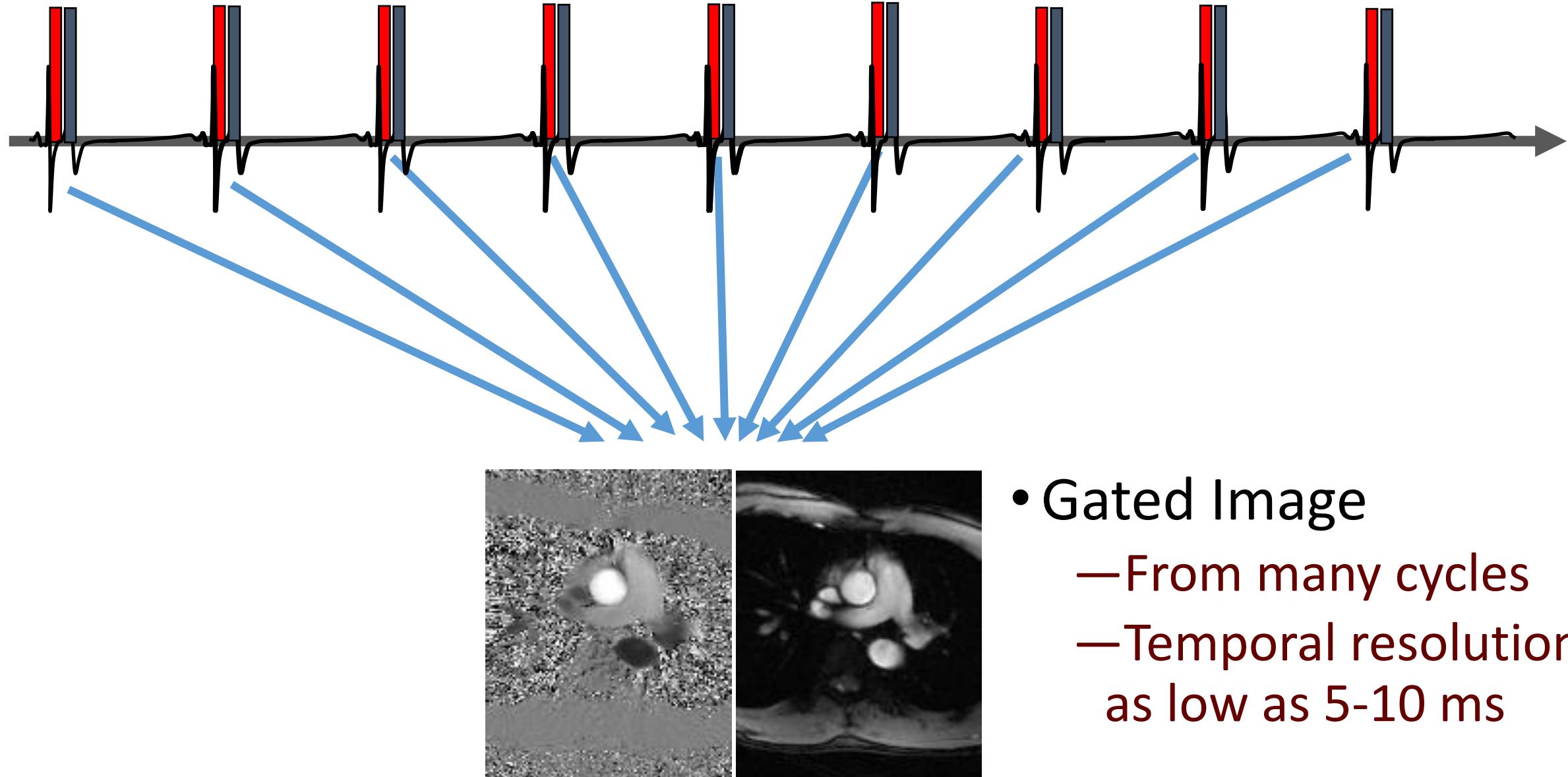
*Magnitude images unaffected unless we use strong gradients (diffusion imaging!)*

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



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

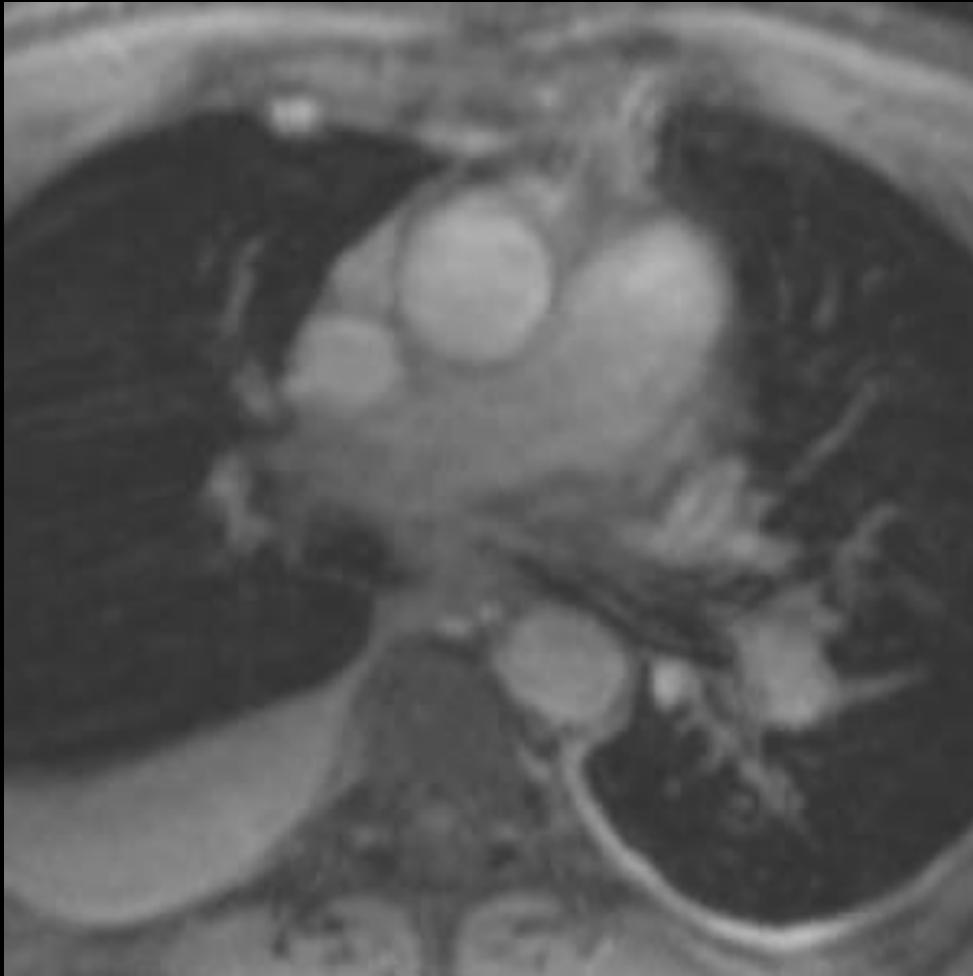
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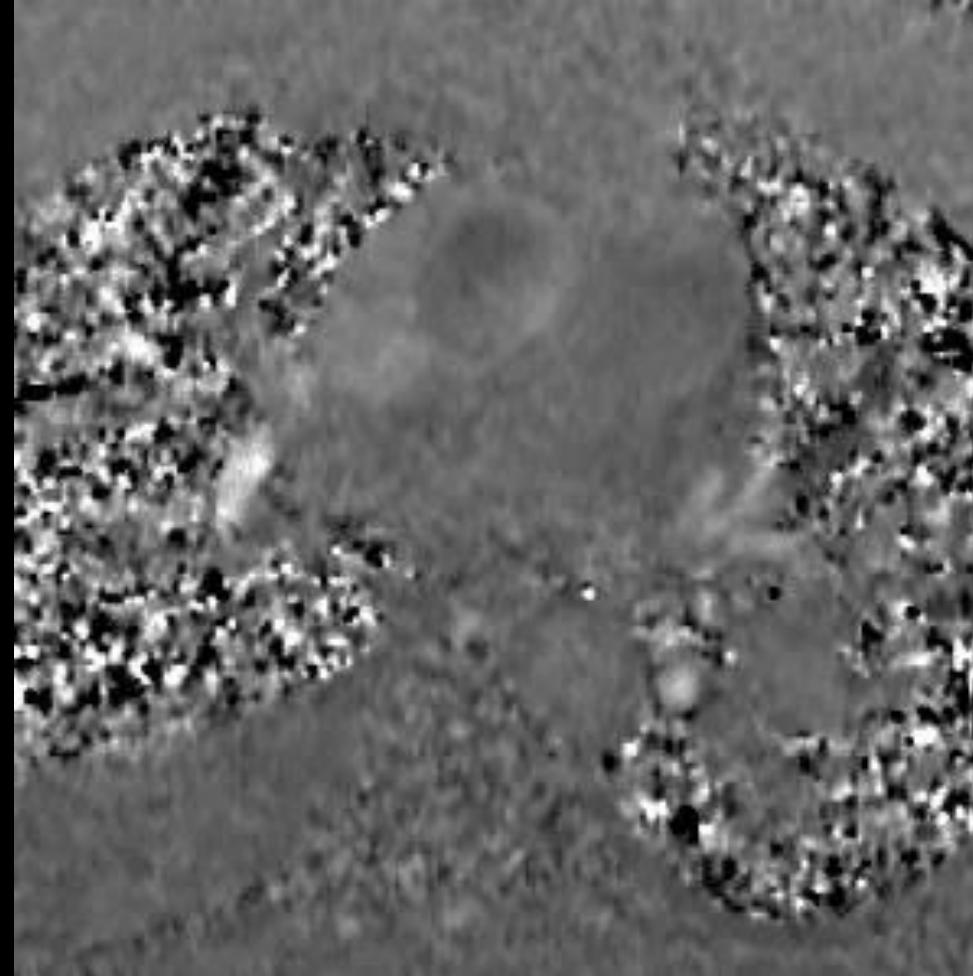
- Gated Image
  - From many cycles
  - Temporal resolution as low as 5-10 ms

# RESULTING IMAGES – CARDIAC RESOLVED

*Magnitude*



*Velocity*



150 cm/s

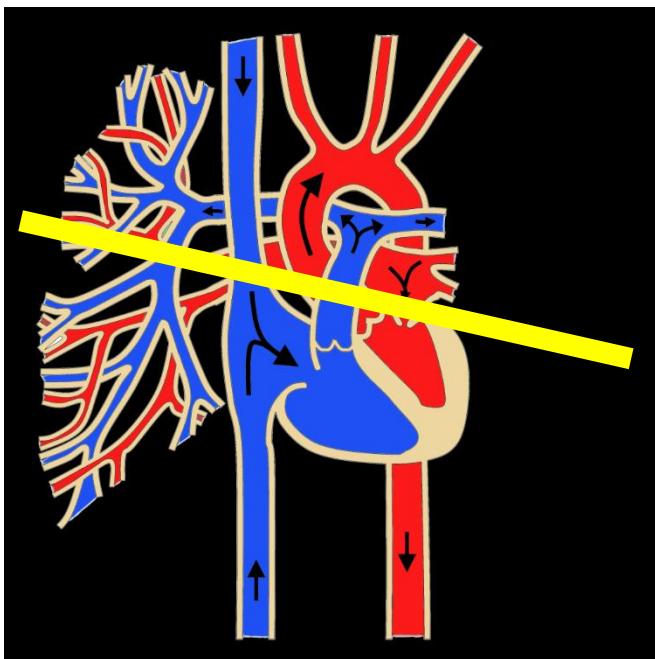
0 cm/s

- 150 cm/s

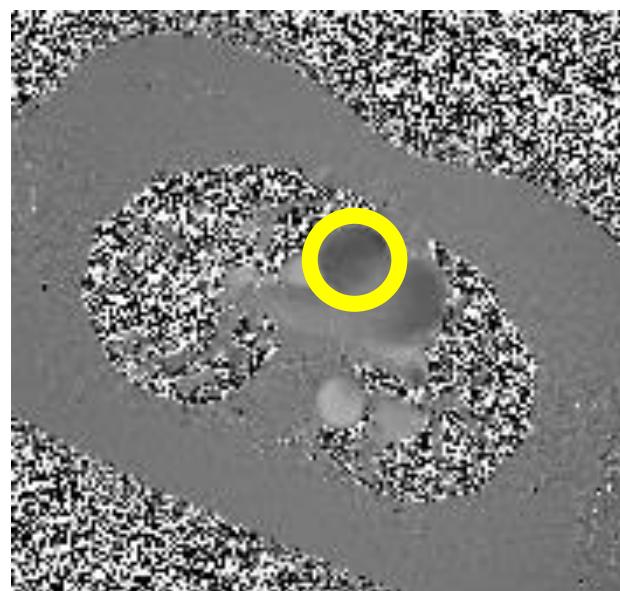
## 2D Phase Contrast MRI

- Common flow techniques use 2D MRI planes

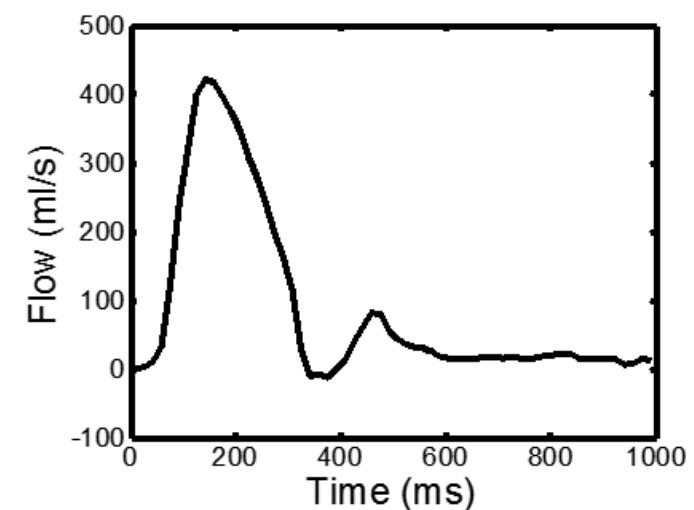
Plan Target Plane  
(cross section of artery)



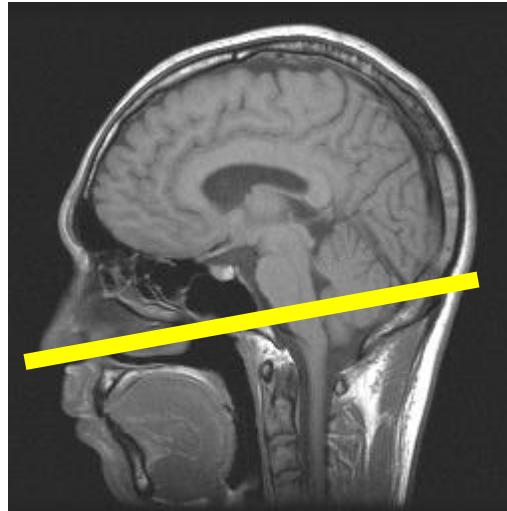
Acquire Images



Analyze Locally  
(e.g. flow)

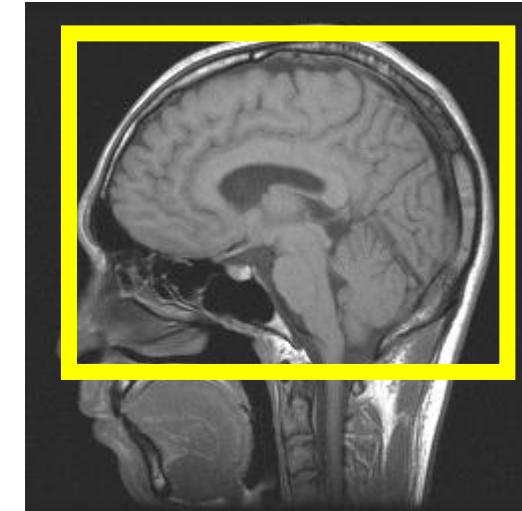


## 2D PC MRI



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

## 4D Flow



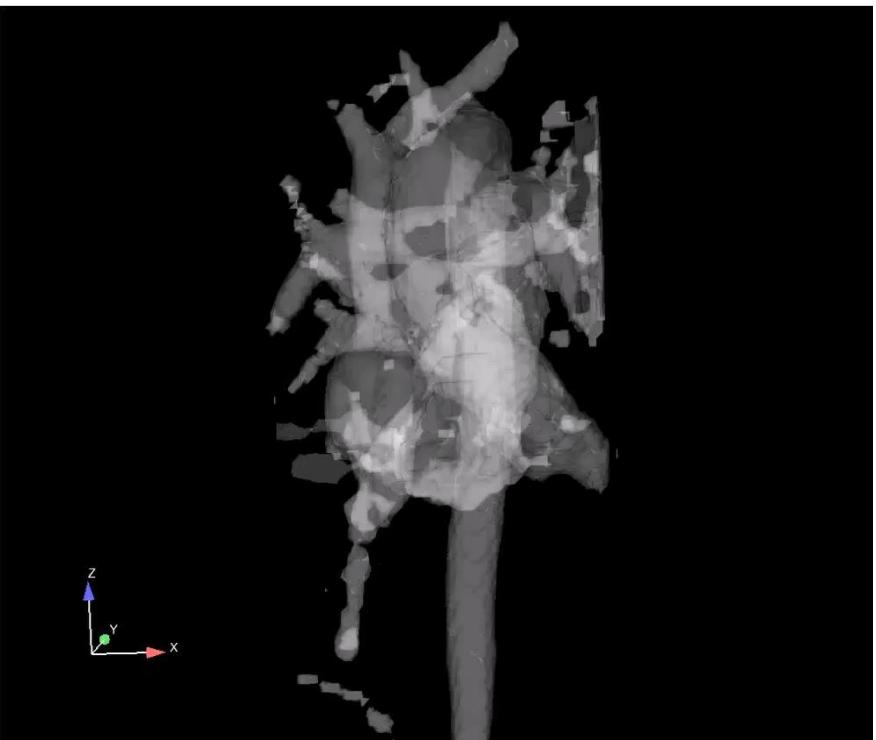
- *Volumetric acquisition*
- *All vessels simultaneously*
- *All 3 velocity directions*
- *Retrospective analysis*

## 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)*



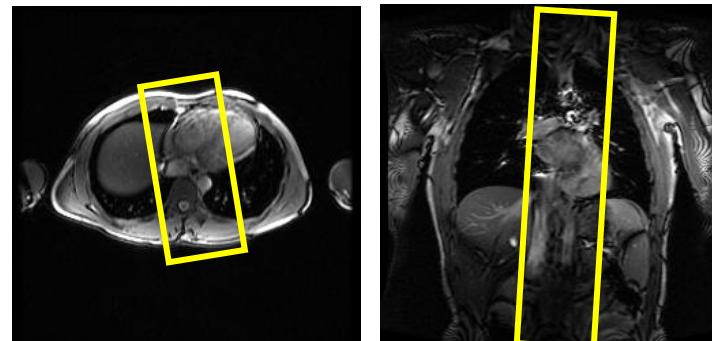
## Blood Flow Origin

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

## Aorta

Large vessels  
(10+mm)

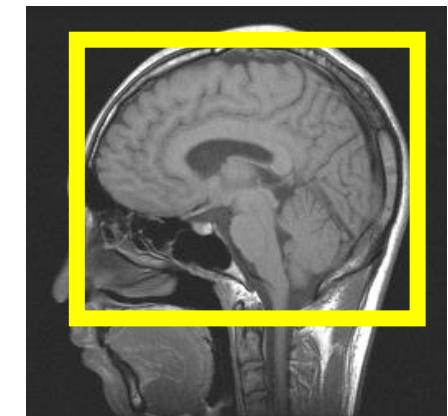
Tailored geometry



## Brain

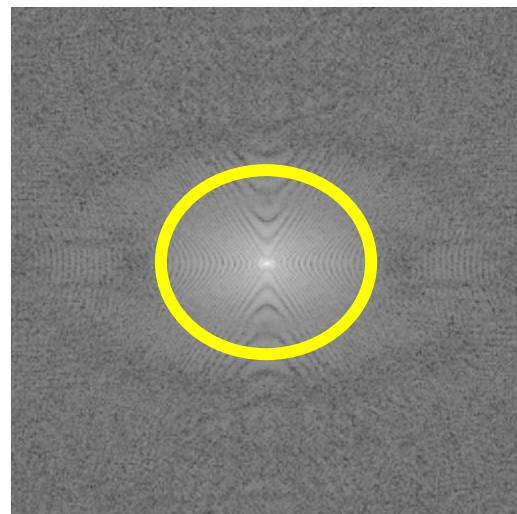
Smaller vessels  
(1-7 mm)

Large volume of  
interest



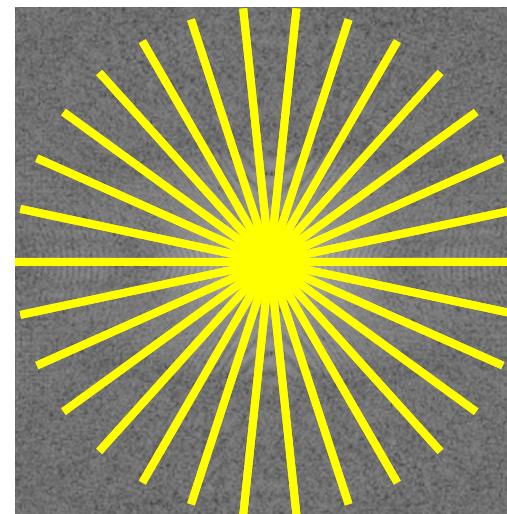
# PC VIPR (Accelerated 4D-Flow) Principle

Raw Data energy  
is focused



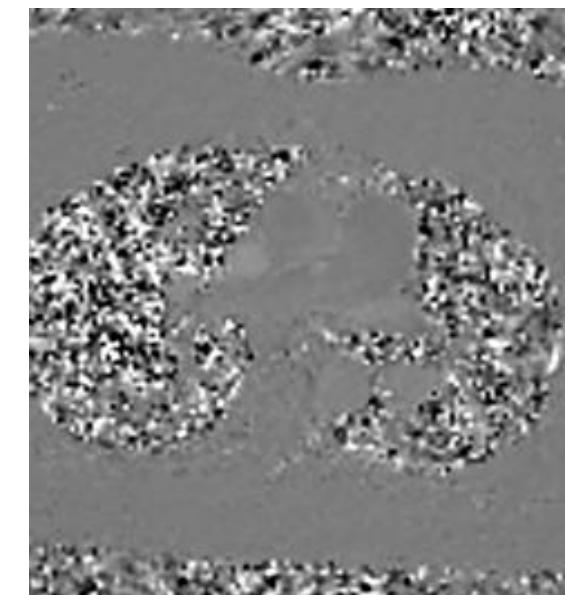
(center most  
needed)

*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'

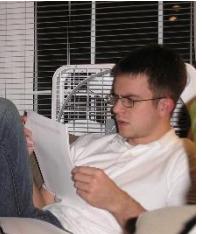
## Initial Idea

Chuck Mistretta  
TL Gu



## Core Technical Methods

Kevin Johnson



Steve Kecskemeti



Oliver Wieben



Eric Schrauben



Mike Loecher



Liz Nett



Leonardo Rivera-Rivera

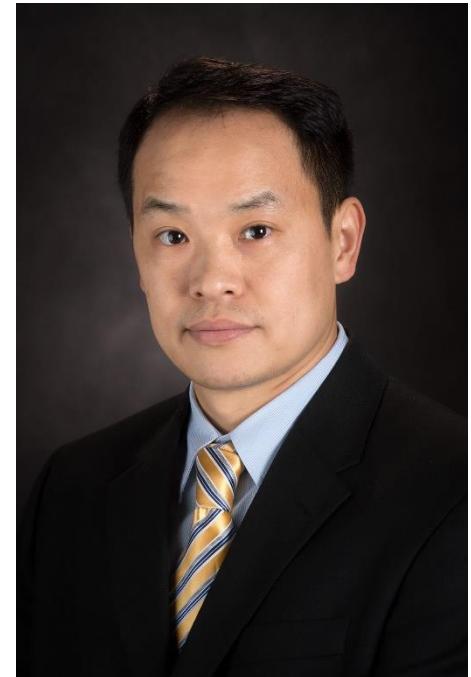


+ many more

## 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'**

## Initial Idea

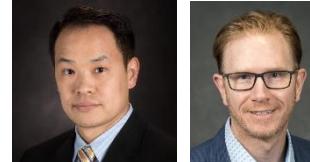
Chuck Mistretta  
TL Gu



**08' 09'**

## ADRC Scans

Guofan Xu,  
Sterling Johnson



**15'**

## First AD Papers

Sara Berman,  
Leonardo Rivera



## Validation (throughout)

Alex Frydrychowicz  
Alejandro Roldan  
Darren Lum



Thorsten Bley



Andrew Wendtland



+ many more

## Core Technical Methods

Kevin Johnson



Steve Kecskemeti



Oliver Wieben



Eric Schrauben



Mike Loecher



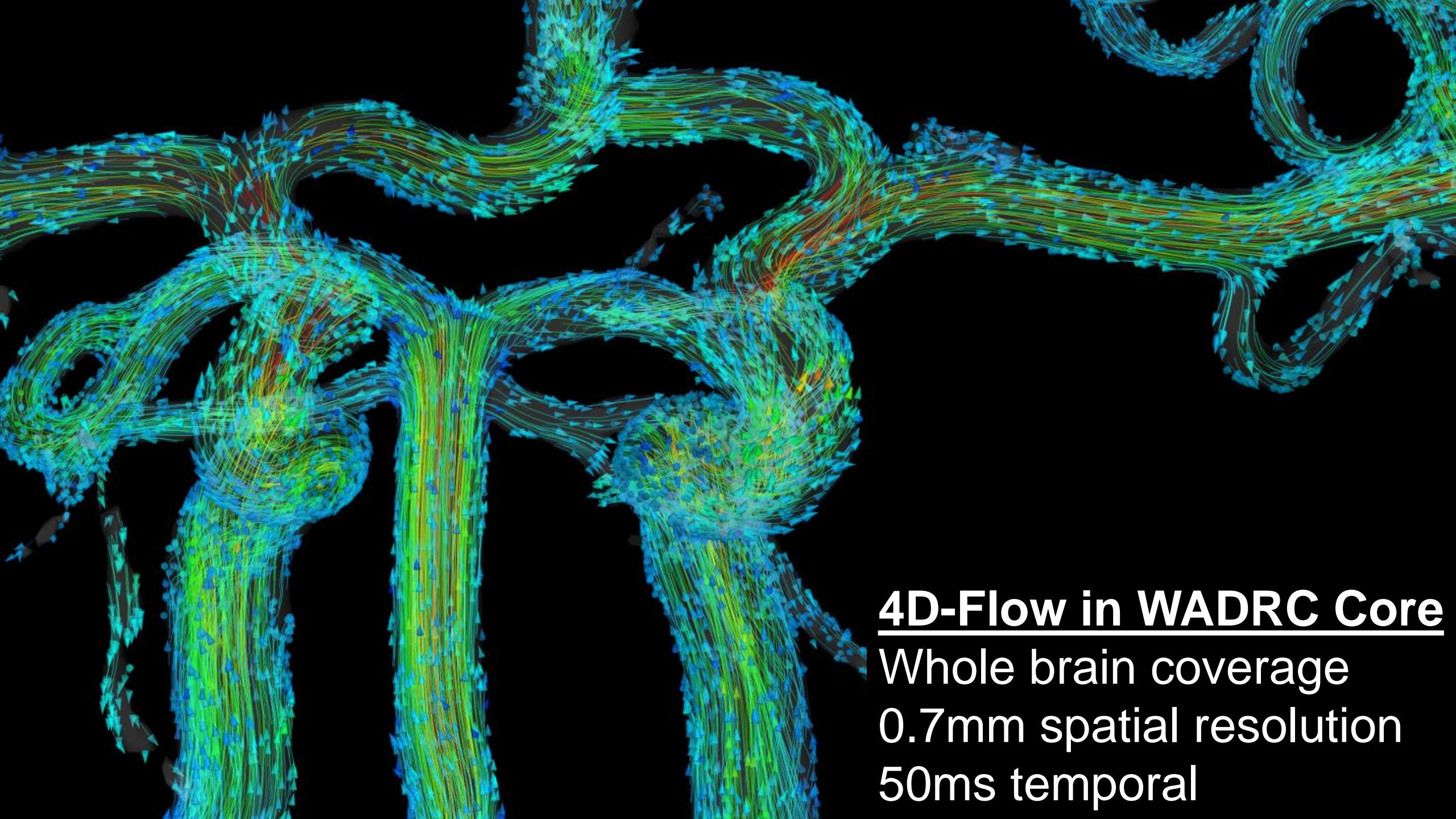
Liz Nett



Leonardo Rivera-Rivera



+ many more

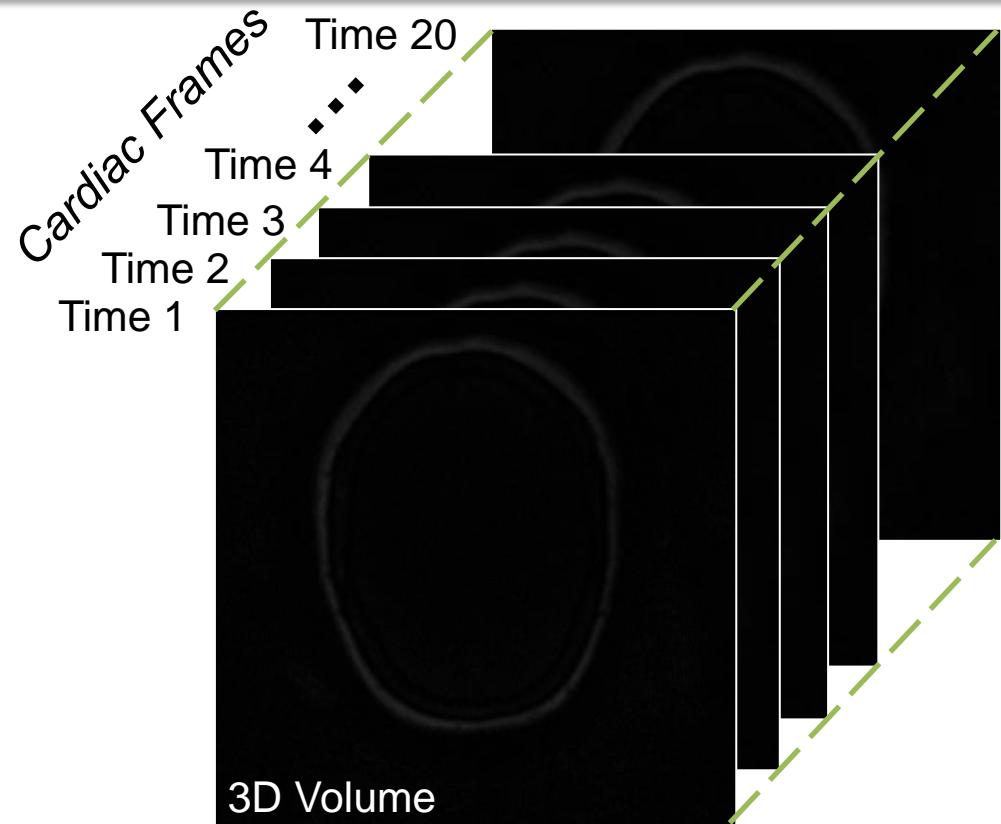


**4D-Flow in WADRC Core**  
Whole brain coverage  
0.7mm spatial resolution  
50ms temporal

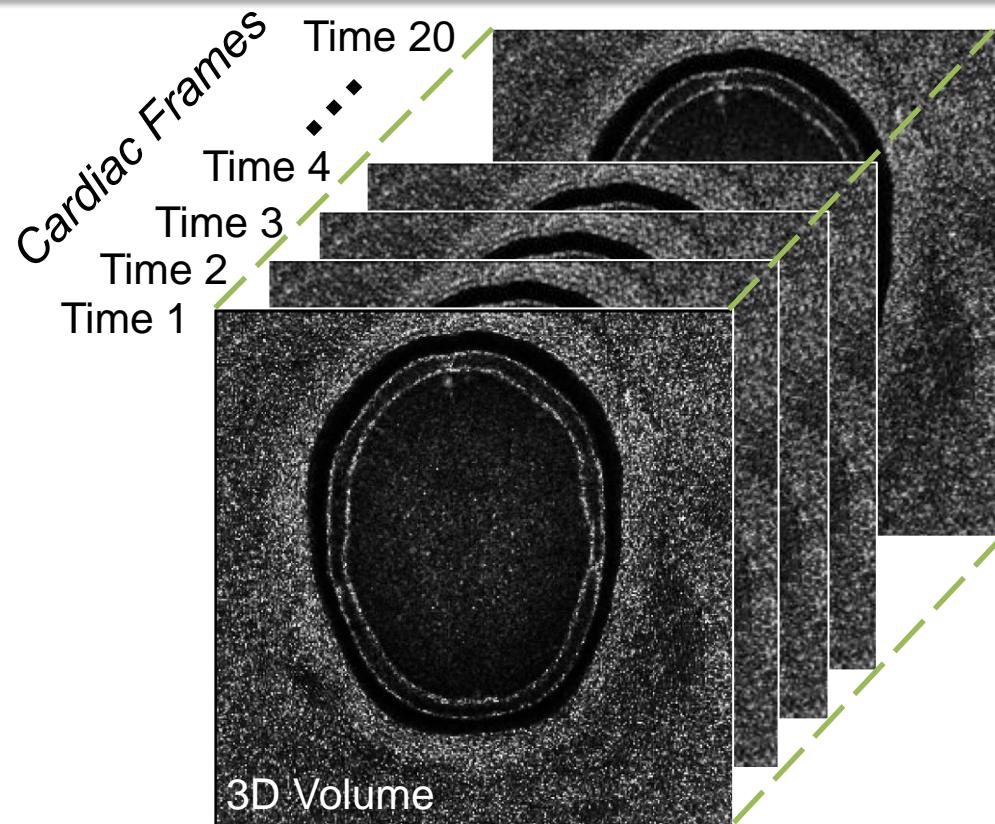
## Overview

- **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

# 4D Flow Post-Processing



**Magnitude Data**

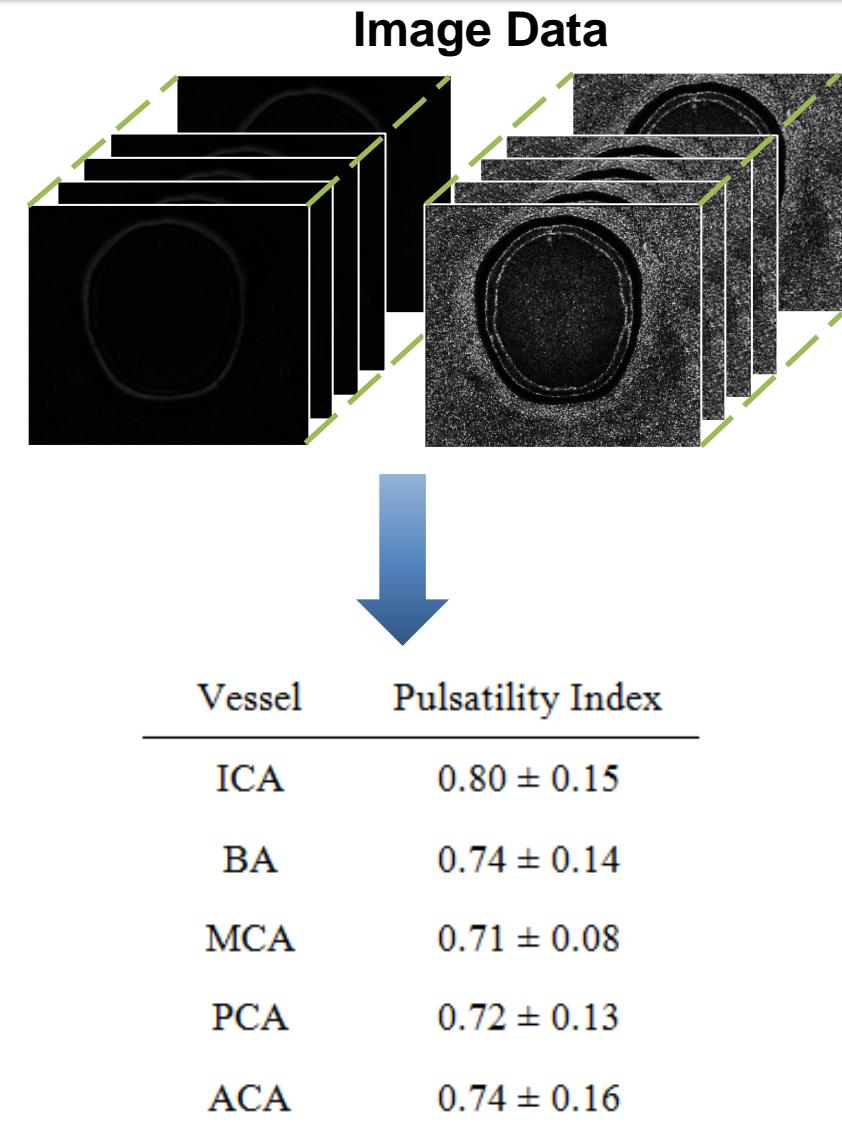


**Velocity Data**

- Image sizes:  $320 \times 320 \times 320 \times 20$
- **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**



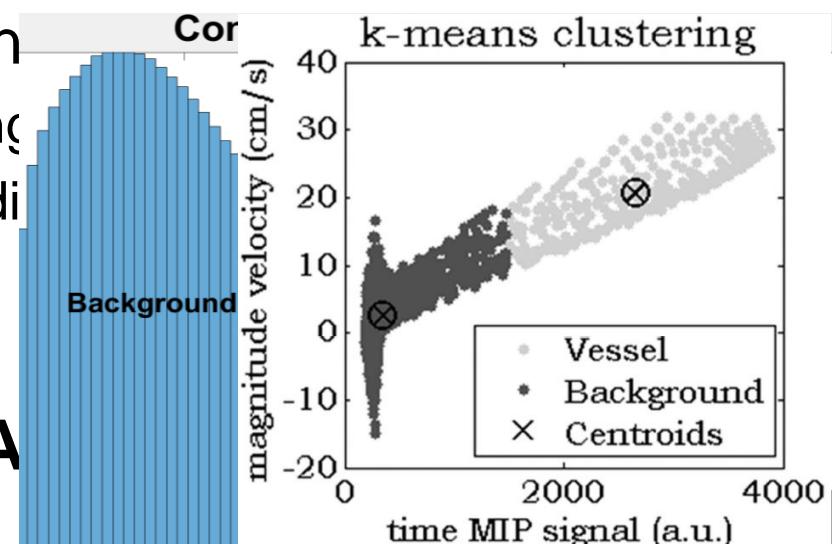
# Vessel Segmentation

Complex Difference

- Identify vessel vs. not vessel
  - Termed “angiogram”
  - Complex difference images delineate vessels well

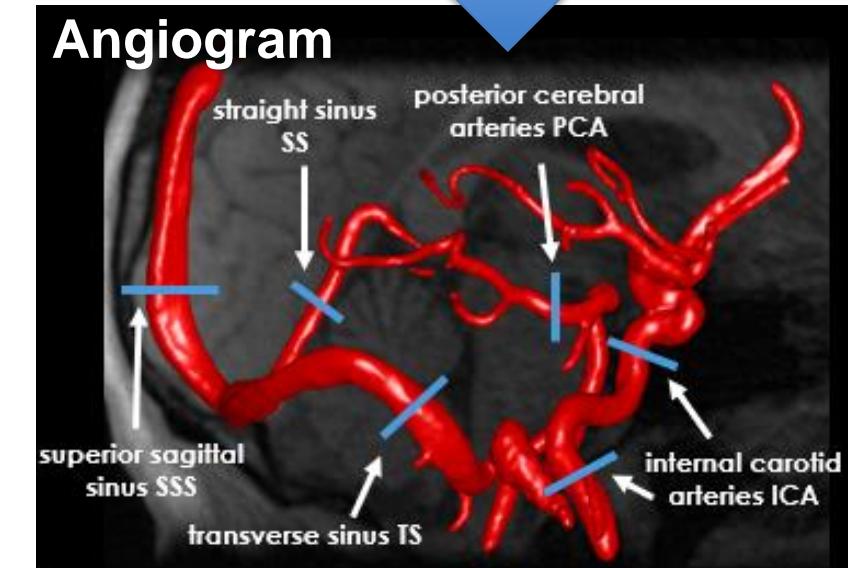
- Segmentation techniques

- Manual segmentation
  - Threshold-based
- Automatic Segmen
  - K-Means Clustering
  - Adaptive thresholding
  - Sliding threshold



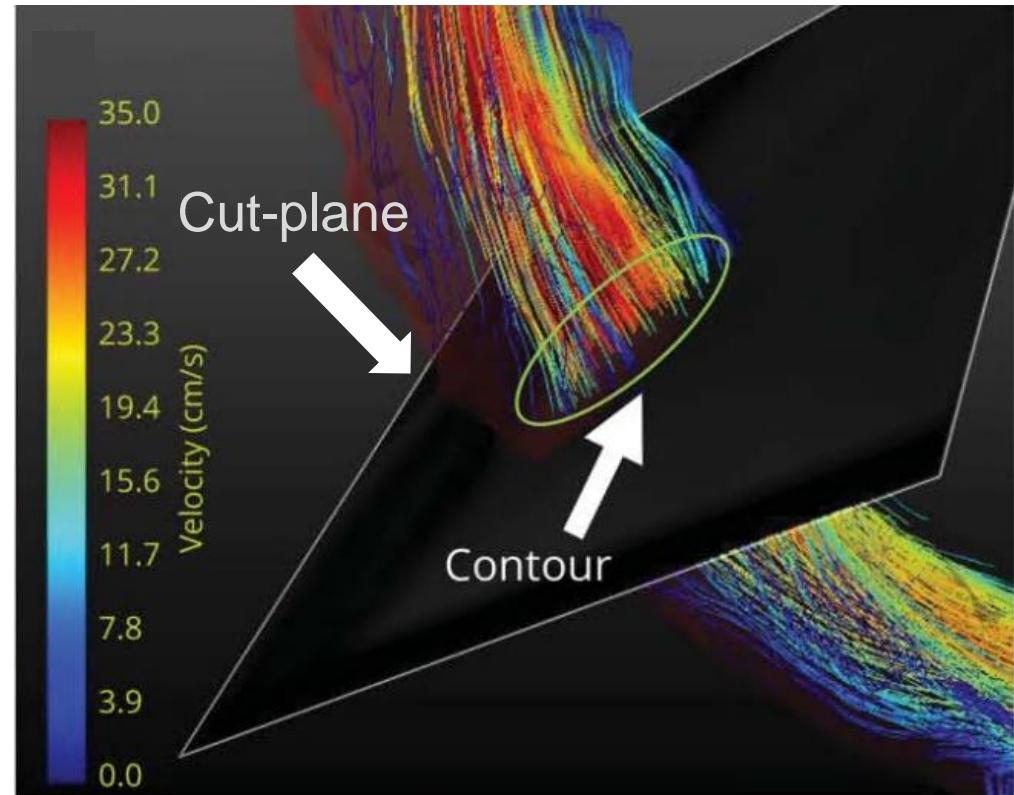
- Second Step: ROI A

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



# ROI Analysis

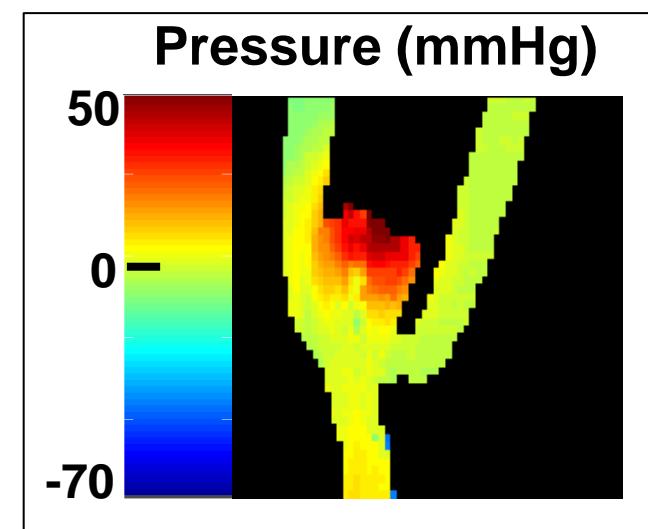
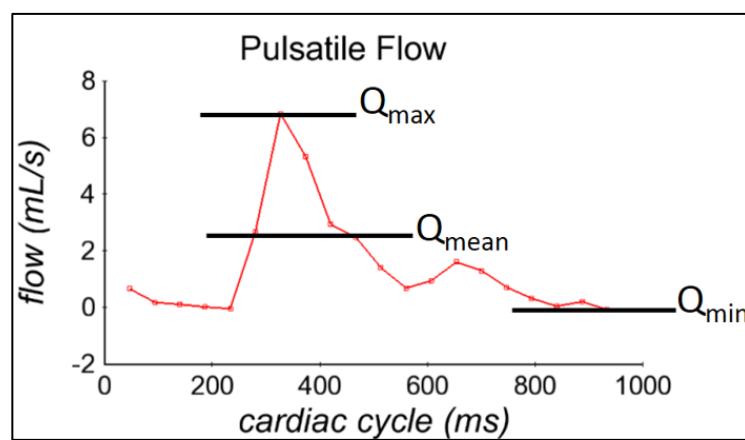
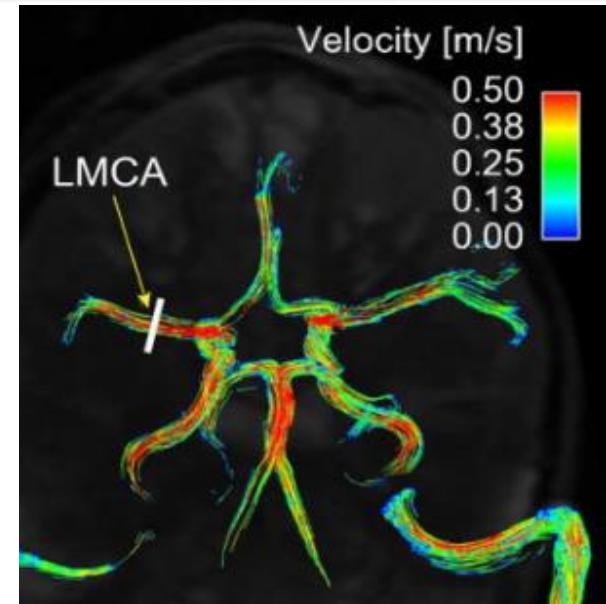
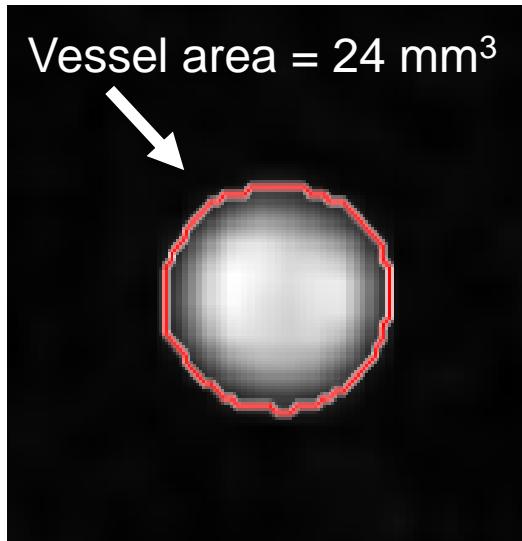
- Define vessel of interest
- Make cut-plane
  - Measure “through-plane” velocity
  - Analogous to 2DPC
  - Ideally perpendicular to length of vessel
- Segmentation defines vessel boundary
- Analyze velocities inside vessel
  - Allows for quantitative hemodynamic measures
    - Blood flow, velocity,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



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

# Hemodynamic Parameters

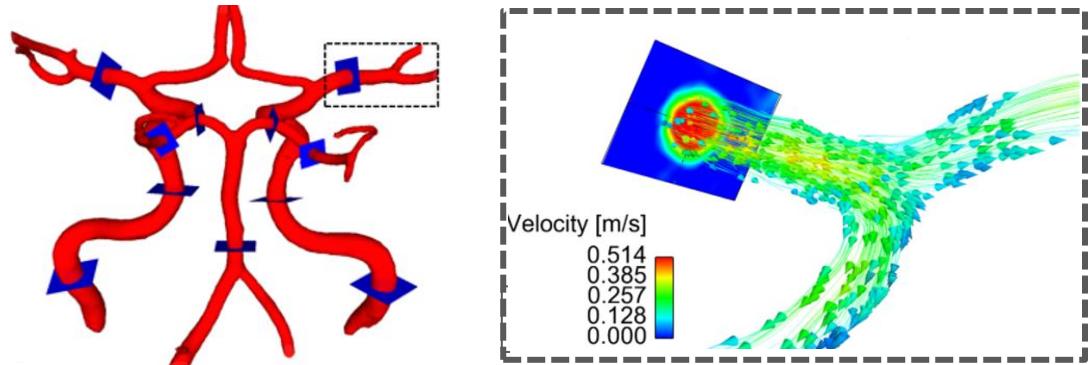
- What can 4D flow measure?
  - Morphological
    - Vessel Areas
    - Vessel lengths
  - Functional
    - Blood flow
    - Blood velocities
    - Pulsatility Index
    - Resistivity Index
    - Pressure maps
    - Wall-shear stress
    - Pulse wave velocity
    - Kinetic energy



# Velocity and Blood Flow

## Blood velocity

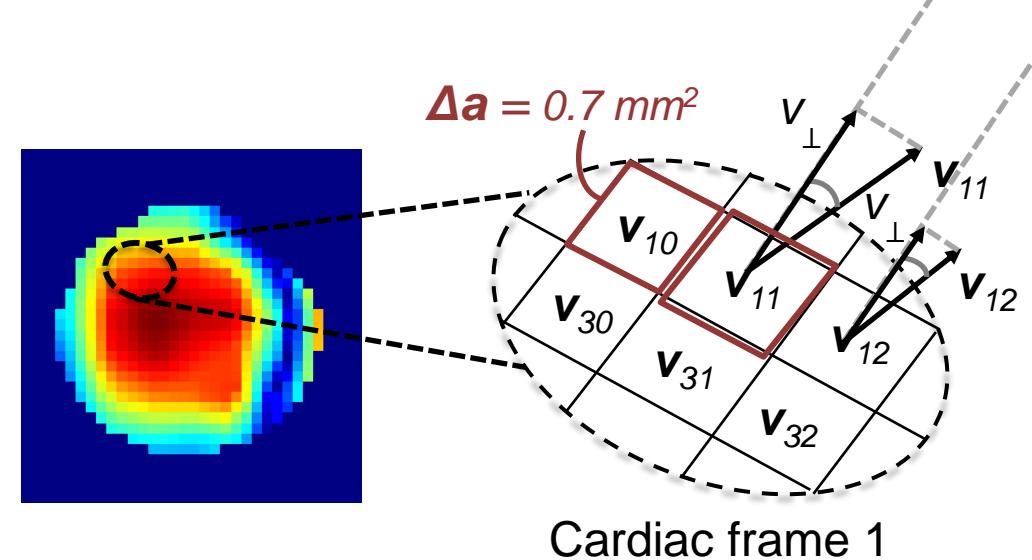
- After defining ROI in cut-plane, we can measure velocity in vessel.
  - Peak systolic velocity
  - Mean velocity over cardiac cycle



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 rate (mL/s)
  - Just average  $Q_f$  over all cardiac frames!



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

# Pulsatility and Resistivity Index

## Pulsatility Index (PI)

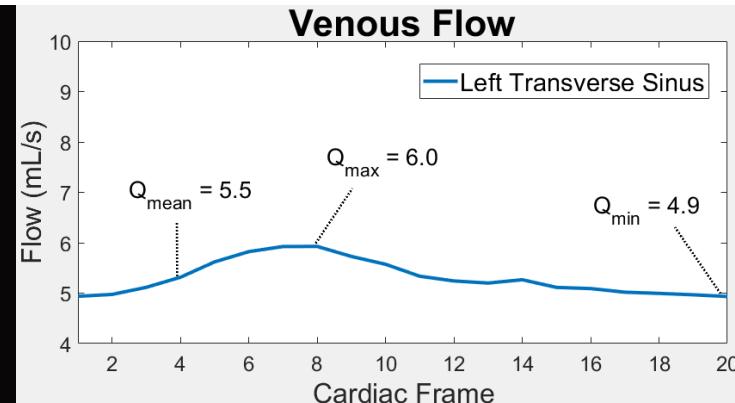
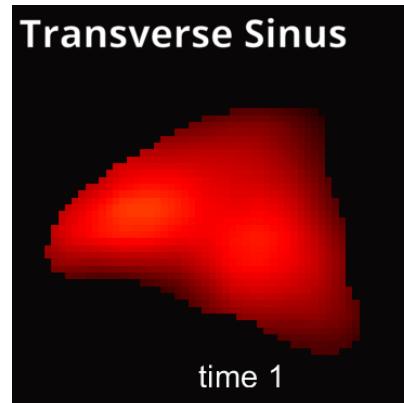
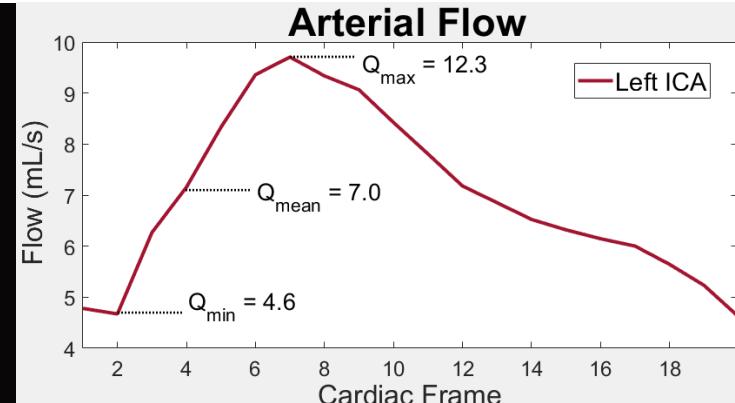
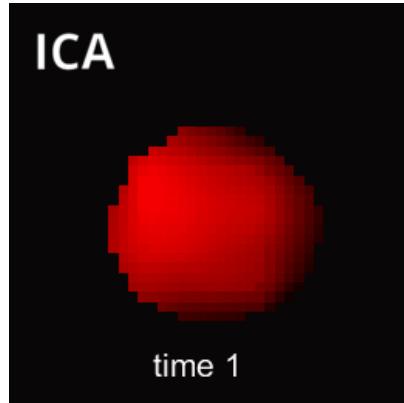
$$\bullet \quad PI = \frac{Flow_{max} - Flow_{min}}{Flow_{mean}}$$

## Resistivity Index (RI)

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

### Clinical importance

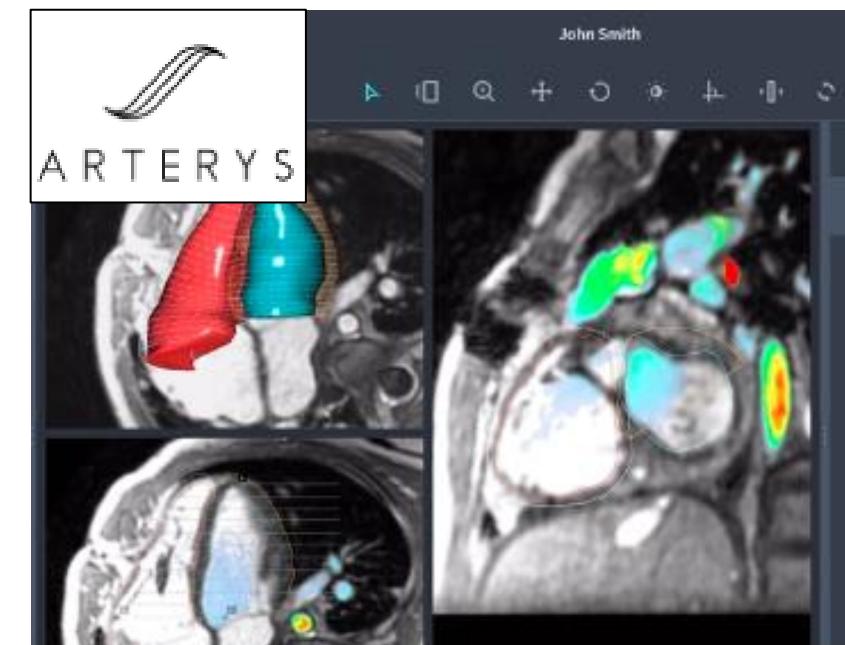
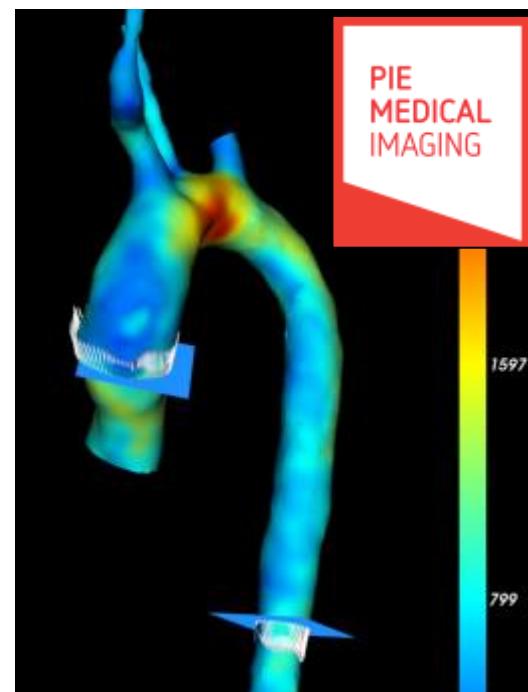
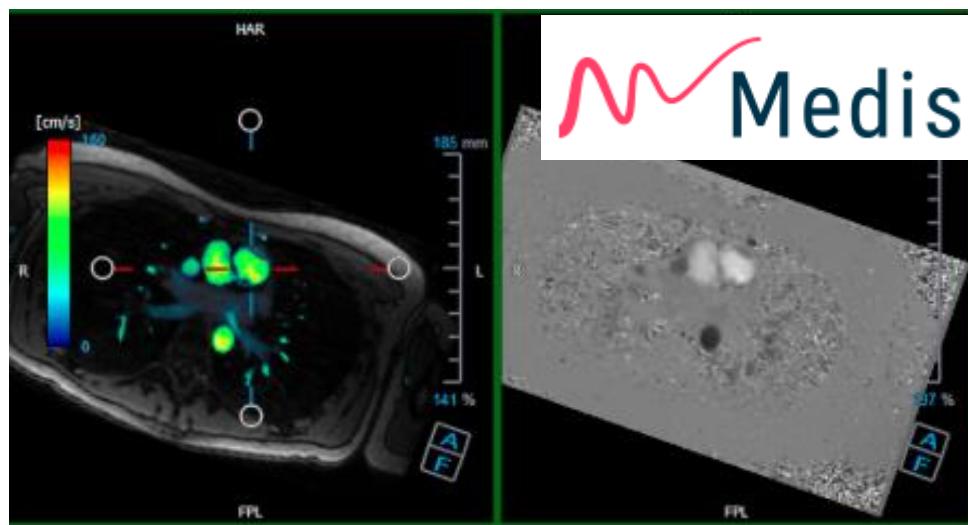
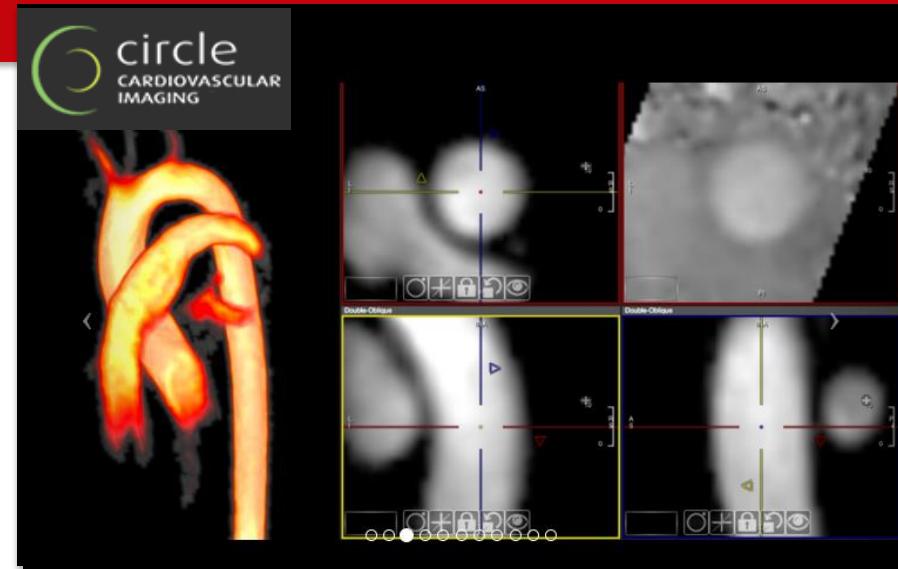
- Both are measures of downstream vascular resistance and intracranial compliance.
- Affected in diseases like TBI, hydrocephalus, and AD.



| 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**



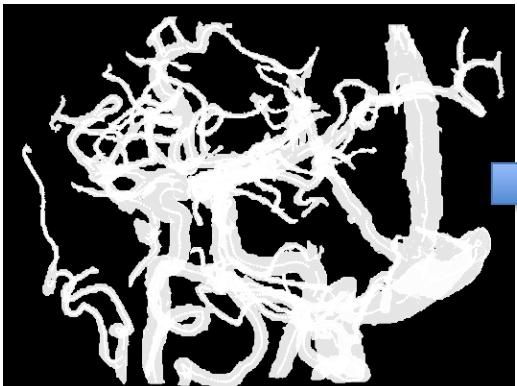
# Automated Tool

- 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

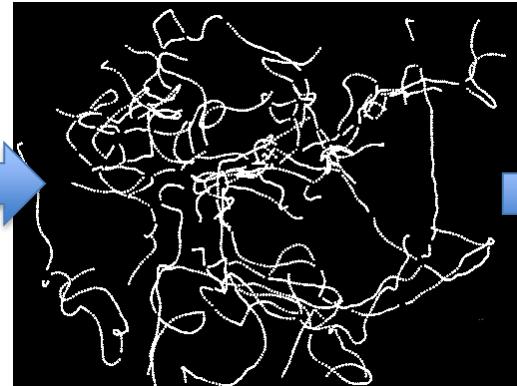


Eric Schrauben

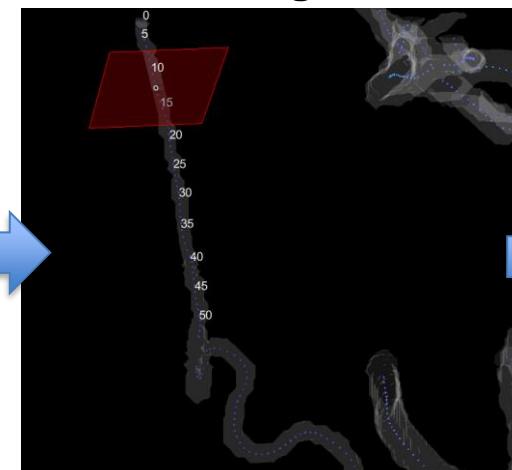
Automatic Segmentation



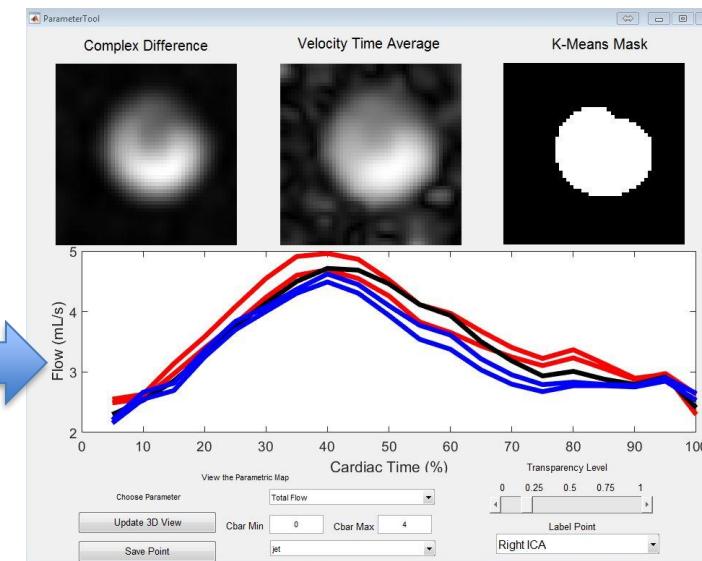
Create Centerlines



Automatic Tangent Planes



Flow Analysis



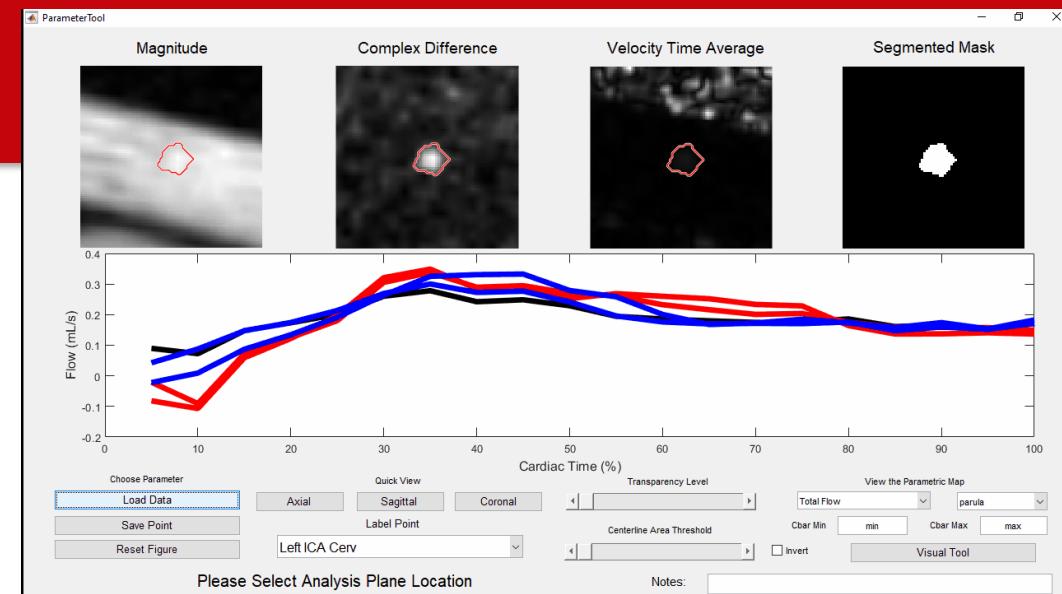
# Automated Tool

- 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

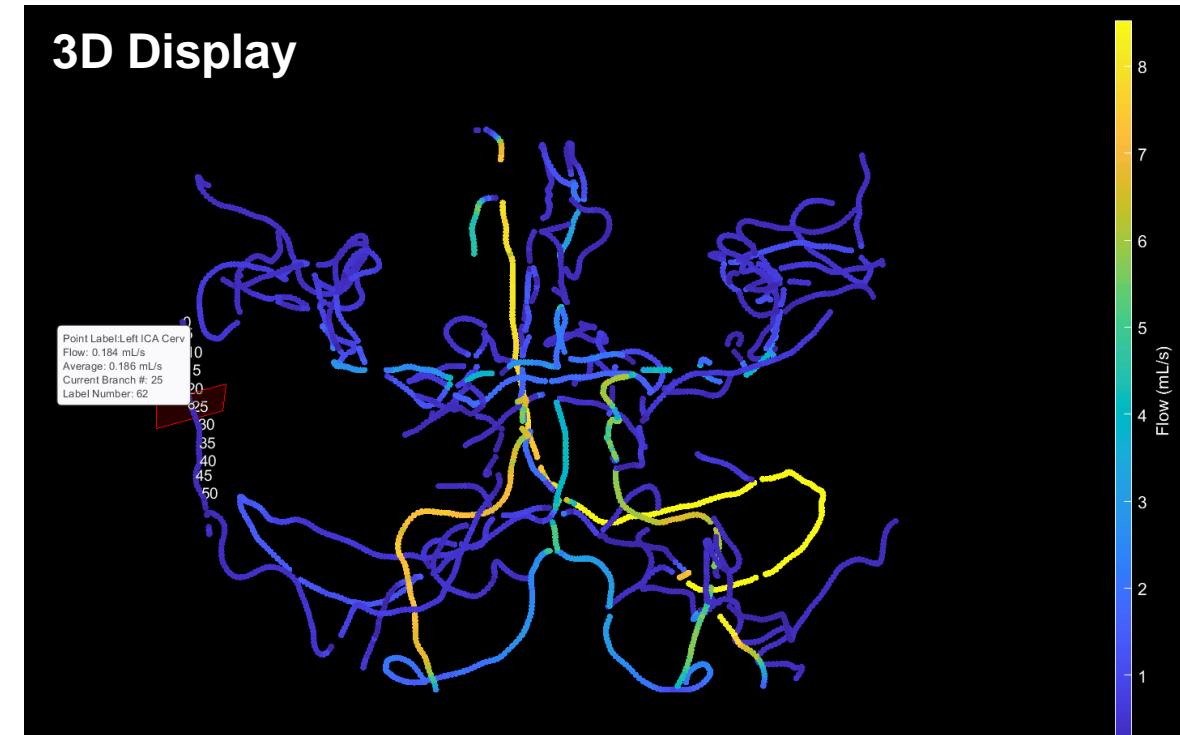


Carson Hoffman

## Control Window

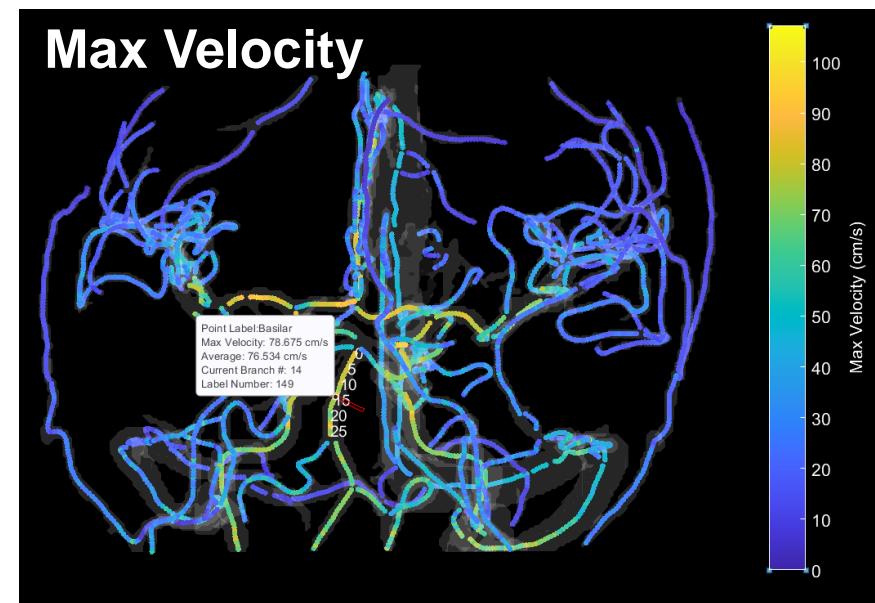
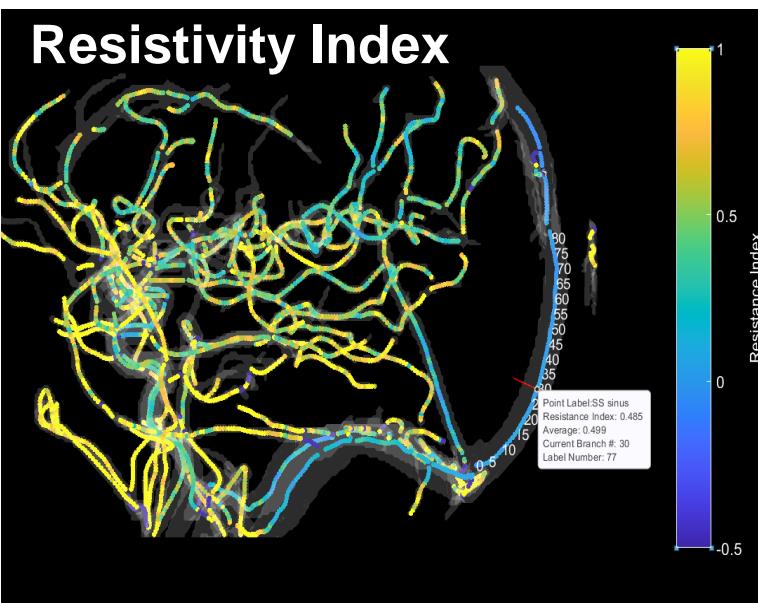
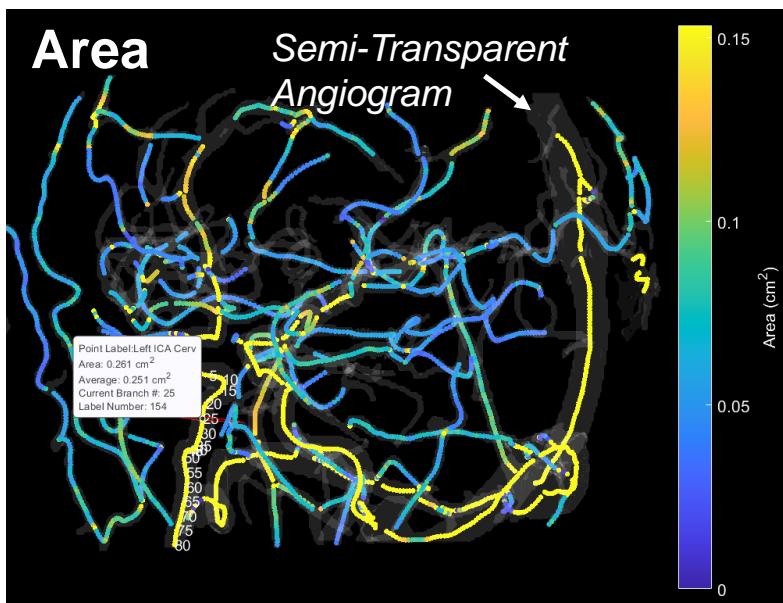
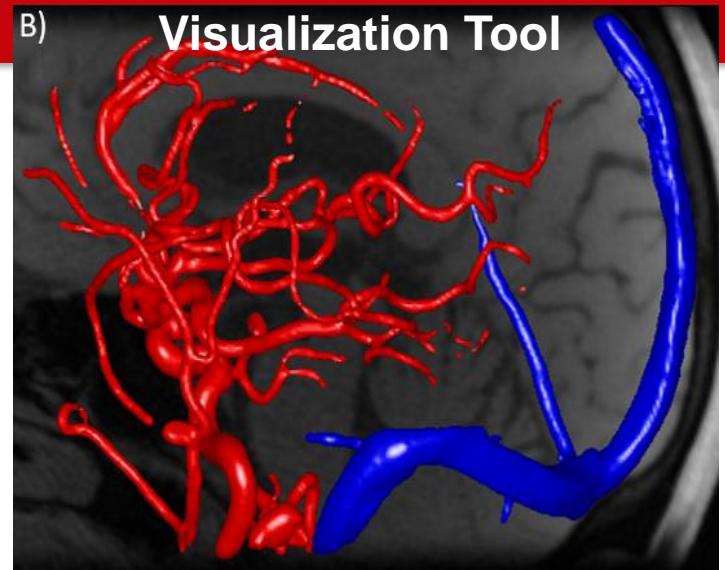


## 3D Display



# 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 equation

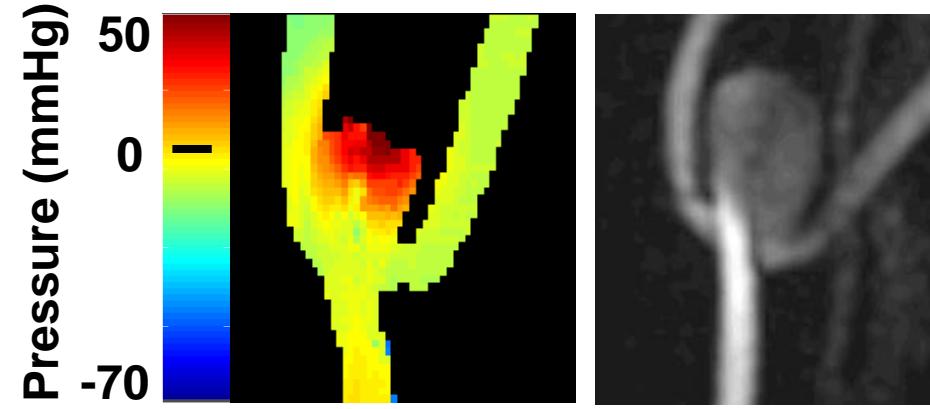
$$-\nabla P = -\rho \left( \frac{\partial \vec{v}}{\partial t} + \vec{v} \cdot \nabla \vec{v} - g \right) + \mu \nabla^2 \vec{v}$$

- May be useful in stratifying high risk aneurysms or DAVFs

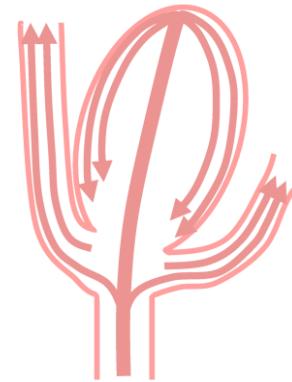
## Wall Shear Stress (WSS)

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

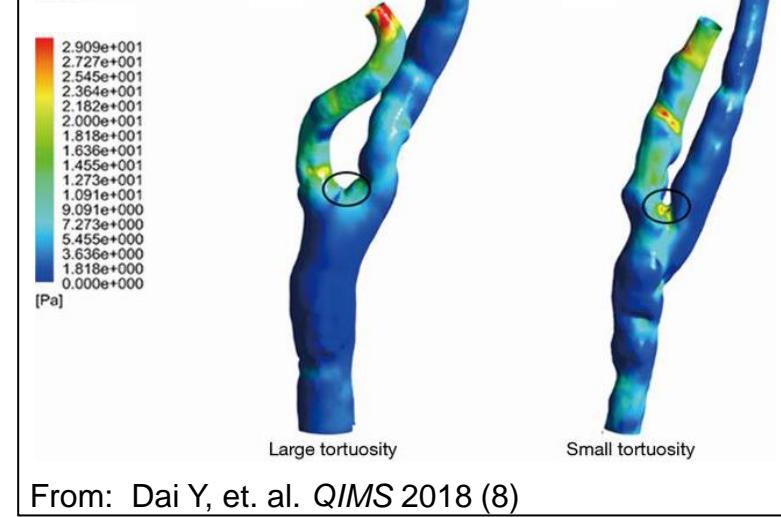
## Aneurysm Jet Pattern - High Dome Pressure



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



## Wall Shear Stress



From: Dai Y, et. al. Q/MS 2018 (8)

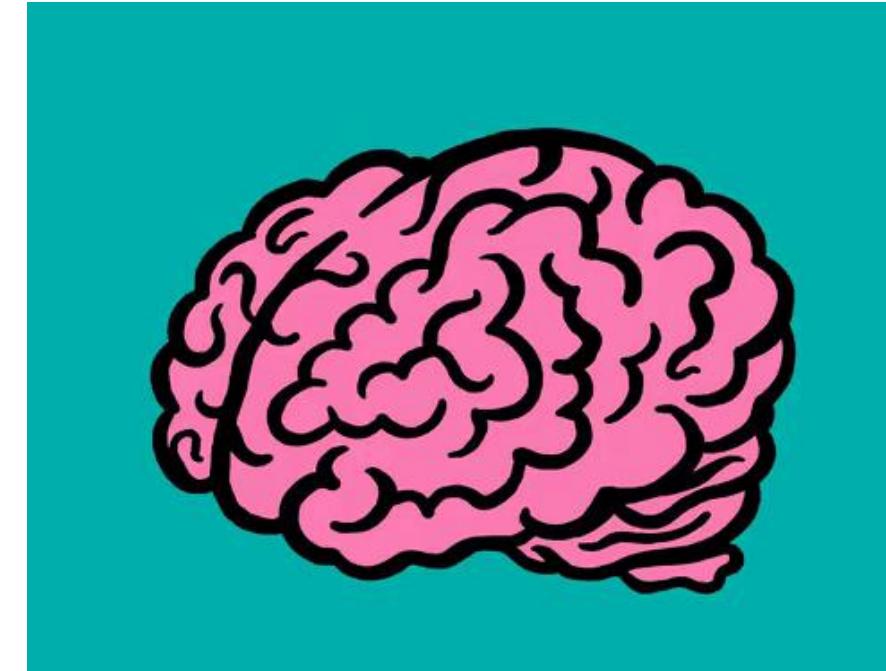
## Overview

- **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

# 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



# 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

Original Article

JCBFM  
Journal of Cerebral Blood Flow & Metabolism

Original Article

JCBFM  
Journal of Cerebral Blood Flow & Metabolism

## Macrovascular blood flow vs Microvascular brain perfusion (pcASL)

Insulin resistance

During hypercapnia challenges

Cerebrovascular reactivity

Intracranial arterial  
Cardiovascular risk factors and  
racial/ethnic disparities in AD dementia

Sara E. Berman<sup>a,b,c</sup>, **Macrovaska**  
Jon G. Keevil<sup>f,g</sup>,  
Howard A. Rowley<sup>a,f</sup>,

4D flow MR

Lindsay  
Siobhan M. Ho  
Cynthia M

Leonardo A River  
Patrick Turski<sup>1,2</sup>,  
Howard A Rowle  
Sterling C Johnson<sup>4,5,6</sup> and Oliver Wieben<sup>1</sup>

Alzheimer's assessment of vascular stiffness in



## 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<sup>a,b,c</sup>, Derek Norton<sup>d</sup>, Sara E. Berman<sup>e</sup>, Sterling C. Johnson<sup>a,b,c</sup>, Barbara B. Bendlin<sup>a,b</sup>, Oliver Wieben<sup>f,g</sup>, Patrick Turski<sup>f,g</sup>, Cynthia Carlsson<sup>a,b,c</sup>, Sanjay Asthana<sup>a,c</sup>, Carey E. Gleason<sup>a,c,\*</sup>, Heather M. Johnson<sup>h,\*</sup>

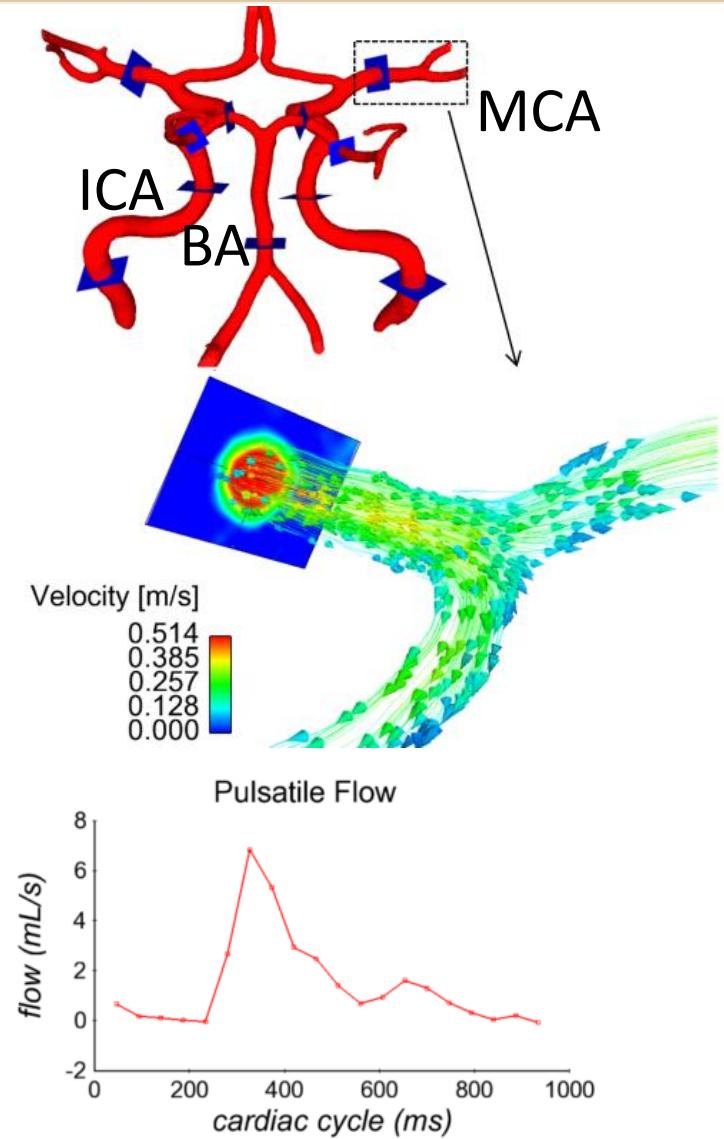
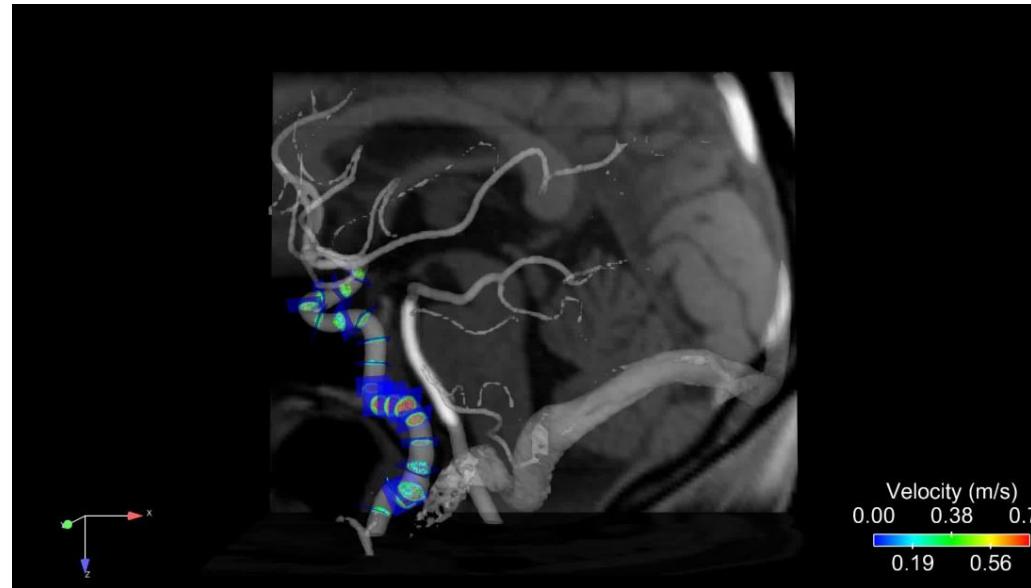
## 4D FLOW MRI

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

# Blood flow and Pulsatility Index in the circle of Willis



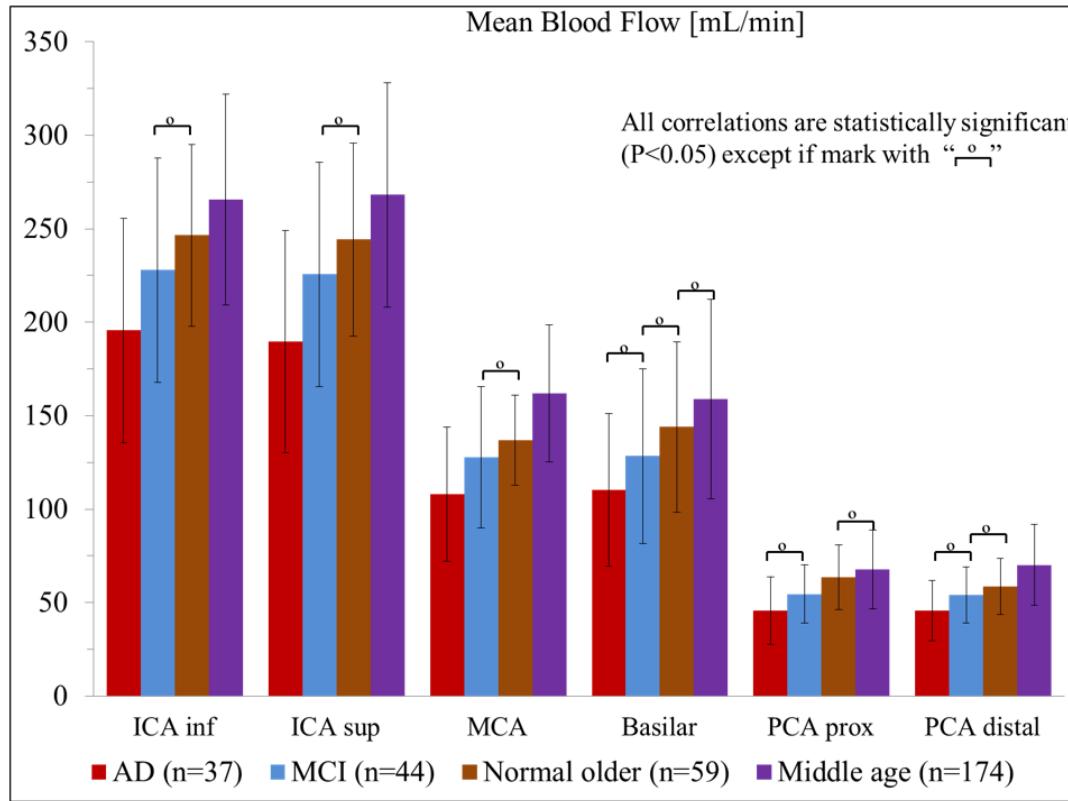
- Macrovascular hemodynamics
  - Vessel size  $\sim 4$  mm



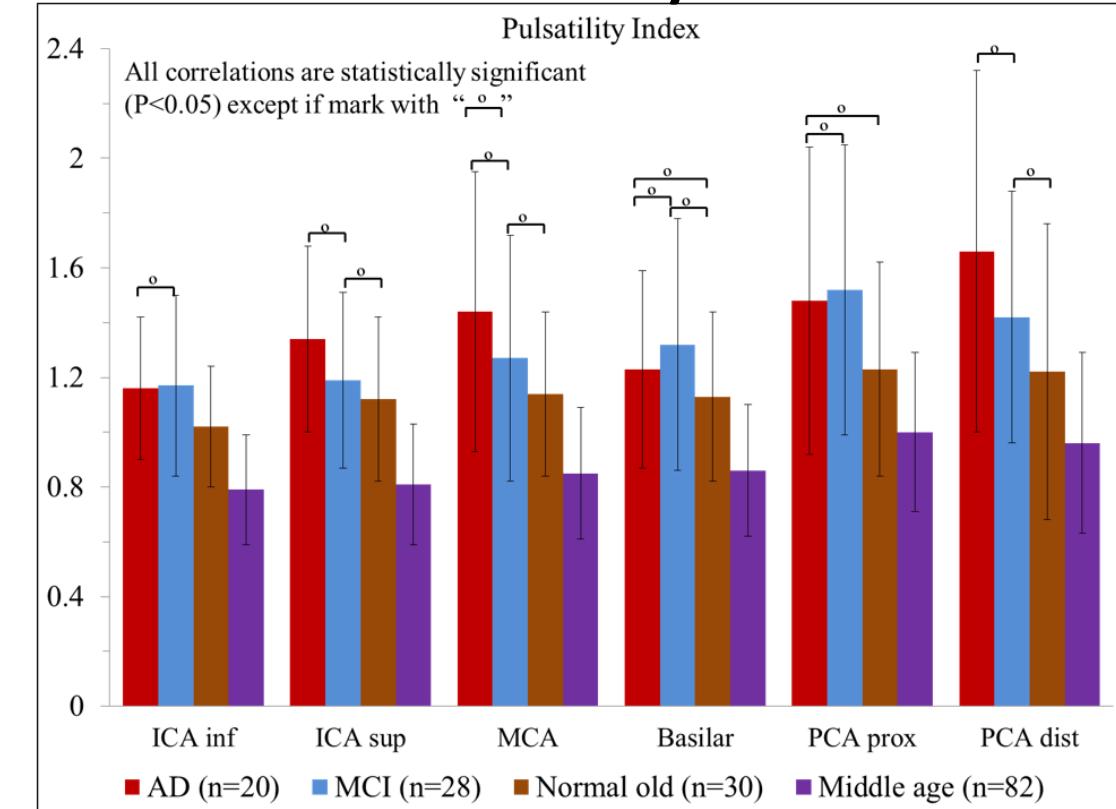
# Blood flow and Pulsatility Index in the circle of Willis



## Blood Flow (mL/min)

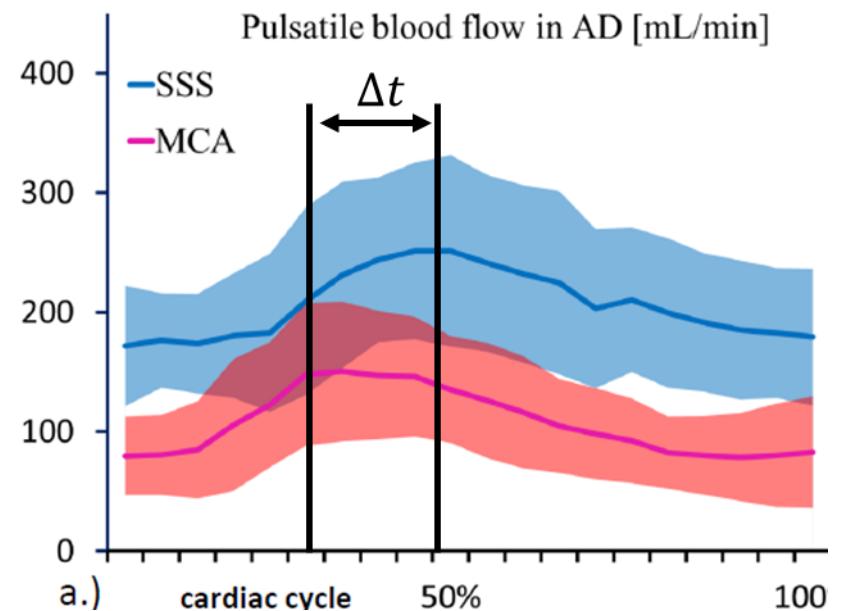


## Pulsatility index



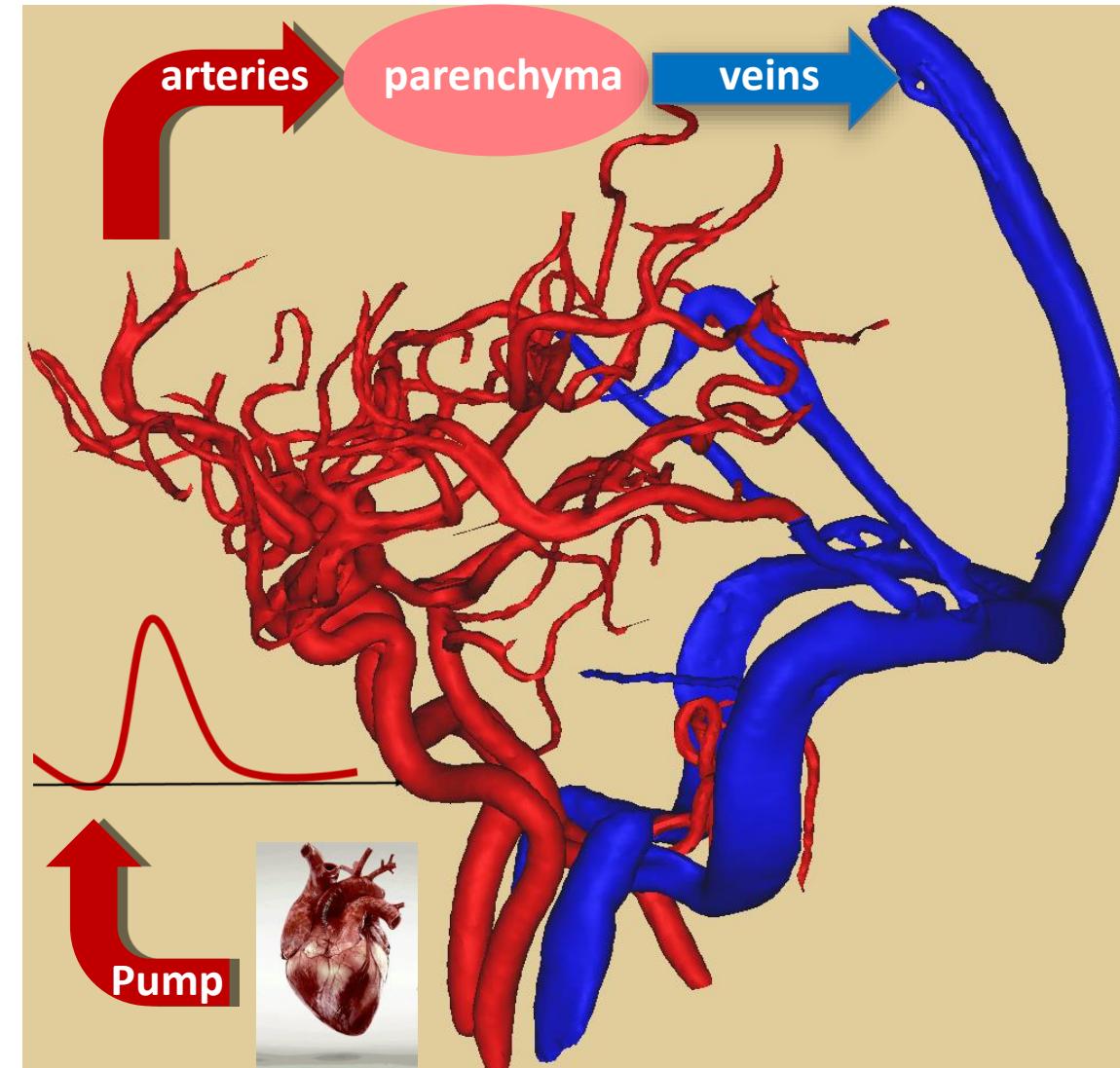
- Clinical AD: significant decrease in blood flow and increase in PI, suggesting decreased brain metabolism and vessel compliance

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



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

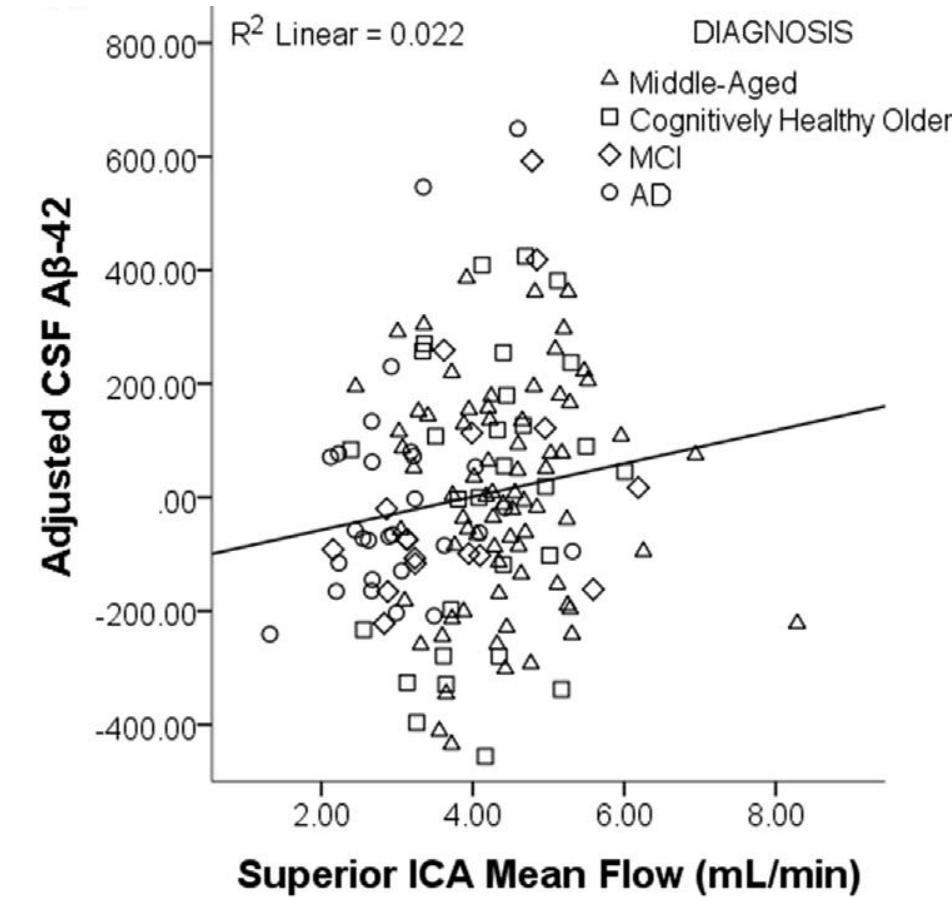
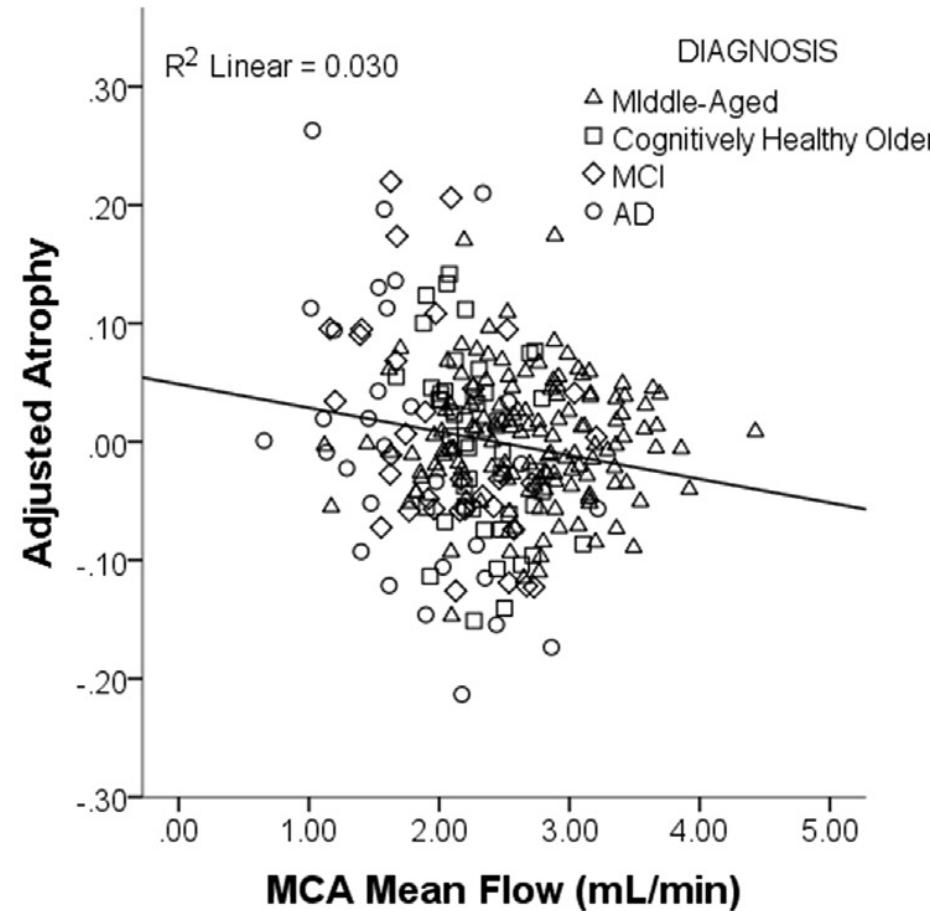
- Significantly shorter transit times in clinical AD
- Stiffer vessels, capillaries ? Reduced effective distance ?





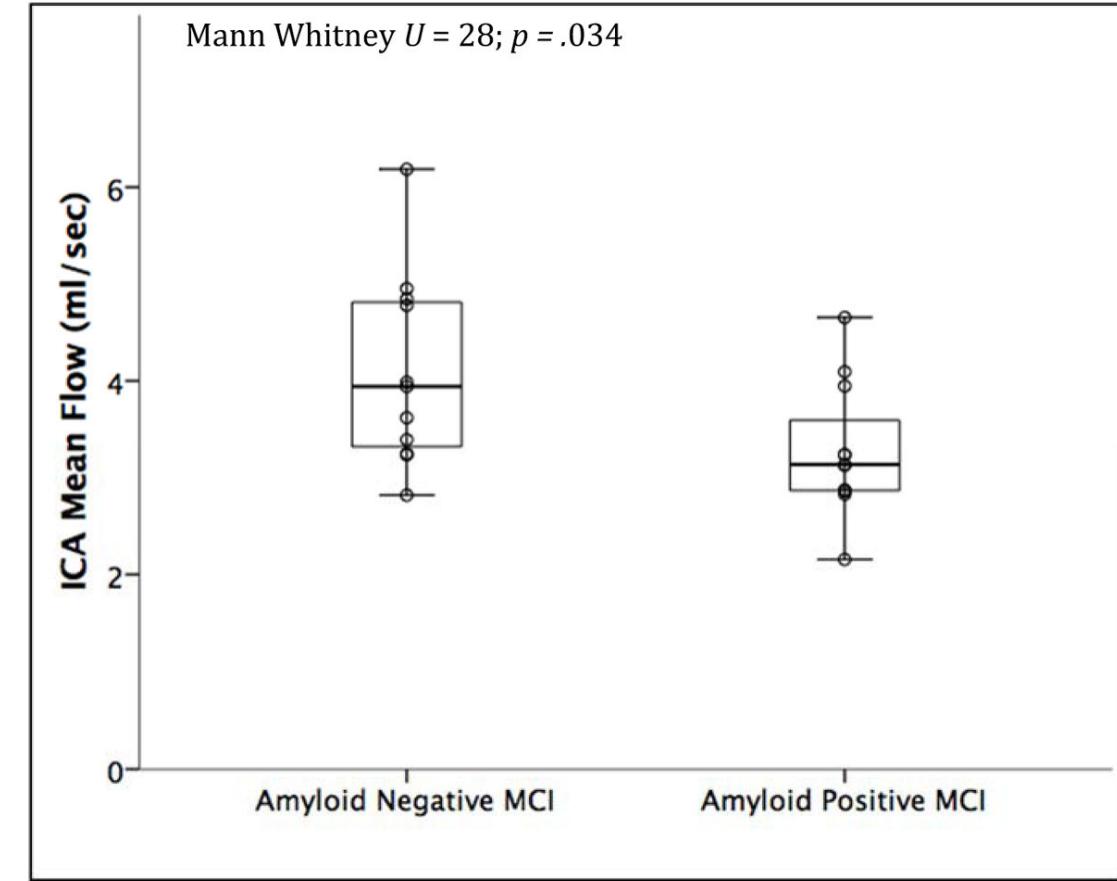
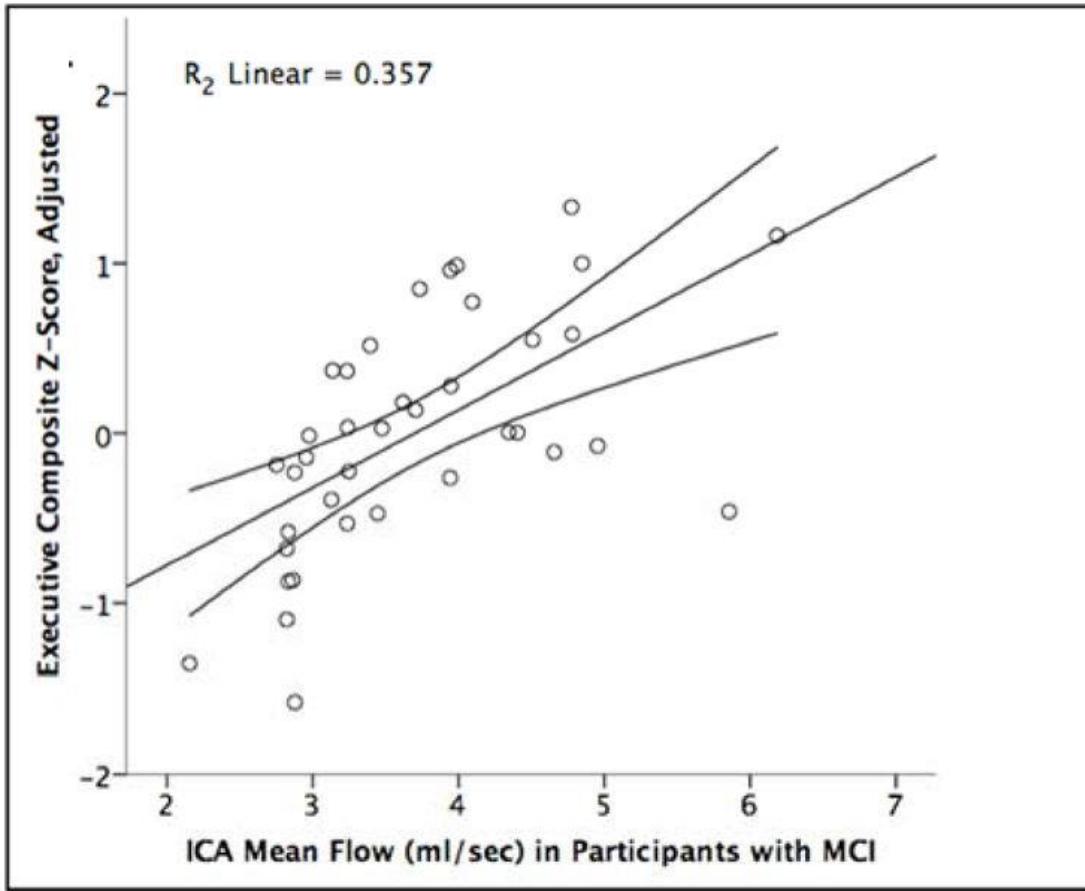
- Decreased brain blood flow and vessel compliance
- Correlation with AD markers ?
  - Brain atrophy
  - Amyloid pathology measured via CSF

# 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.

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



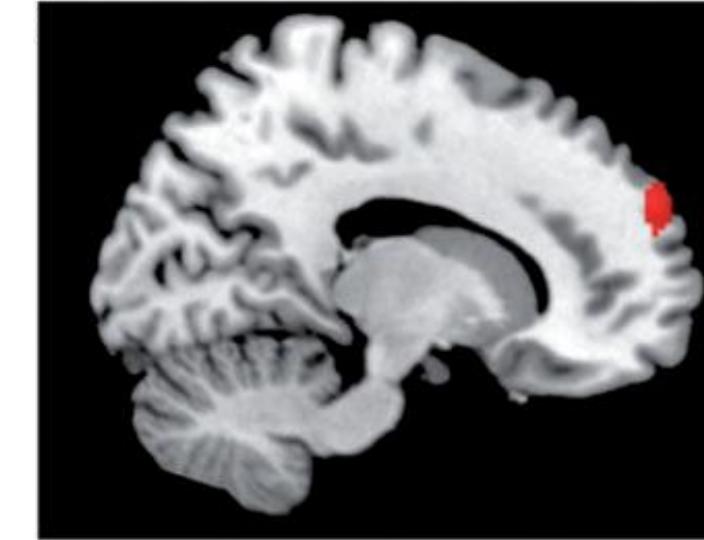
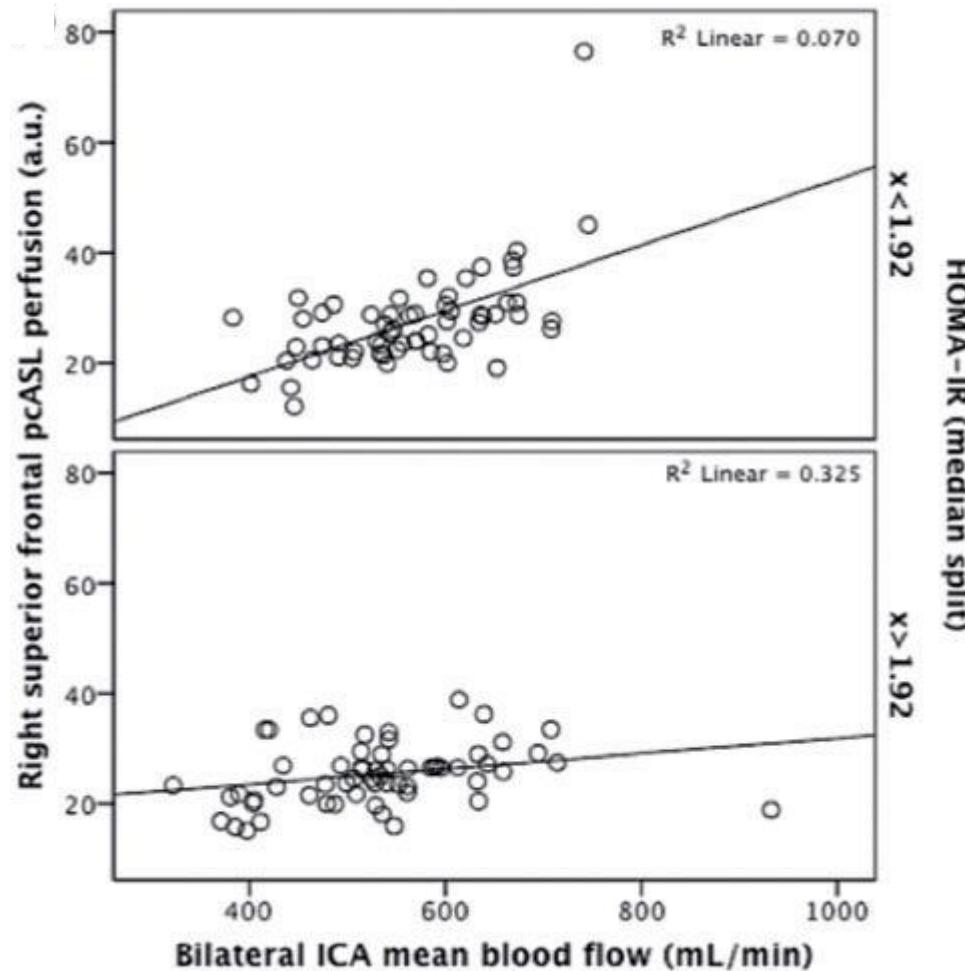
- Greater arterial flow correlates with better executive functioning performance.
- Participants with lower mean flow in the ICA were more likely to be amyloid positive.
- No relationships were observed in this sample between flow and tau positivity.

# Insulin resistance and cerebral blood flow



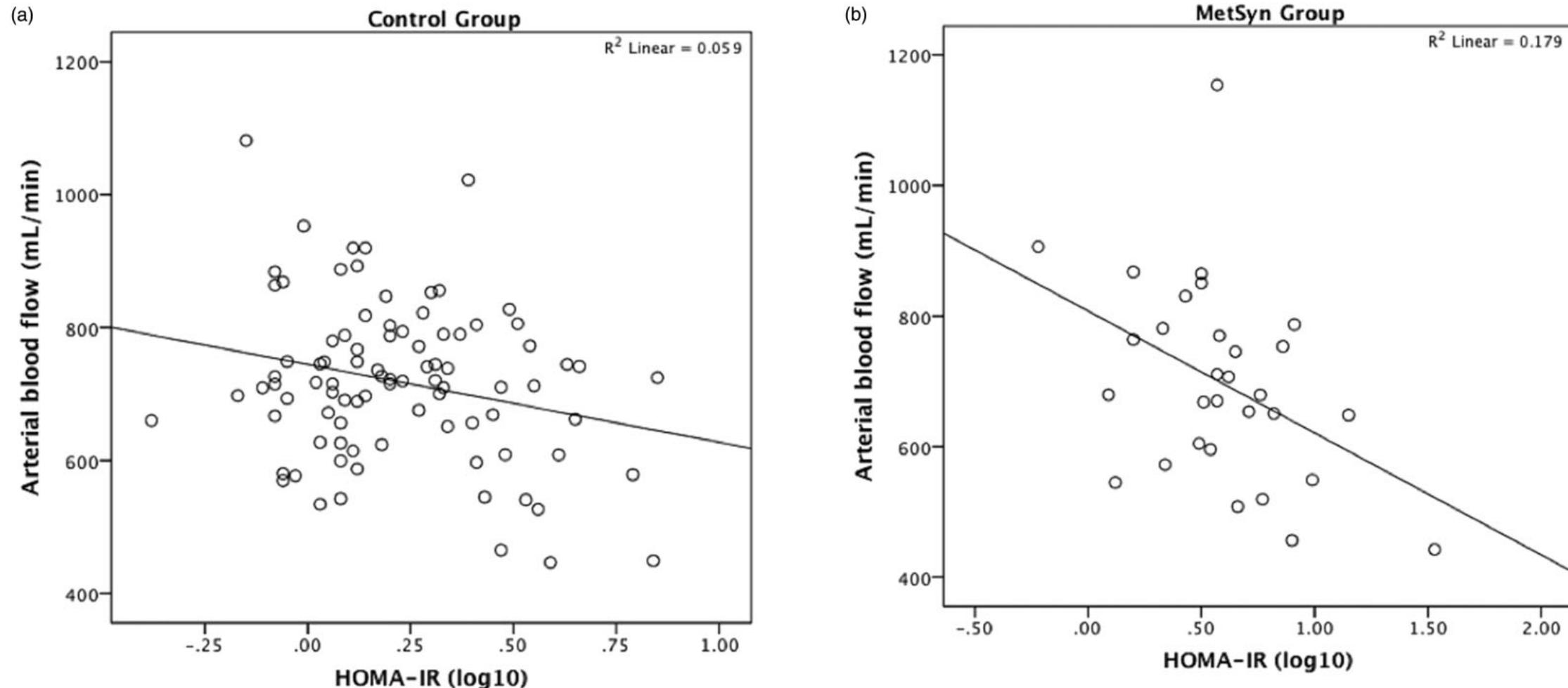
- IR is associated with cardiovascular disease and cognitive decline
- Metabolic syndrome
  - a cluster of cardiovascular risk factors characterized (IR, obesity, elevated levels)
  - linked to cognitive decline and decrease cortical perfusion
- **How do IR and cerebral macrovascular blood flow relate ?**

# 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 ( $x < 1.92$ ).

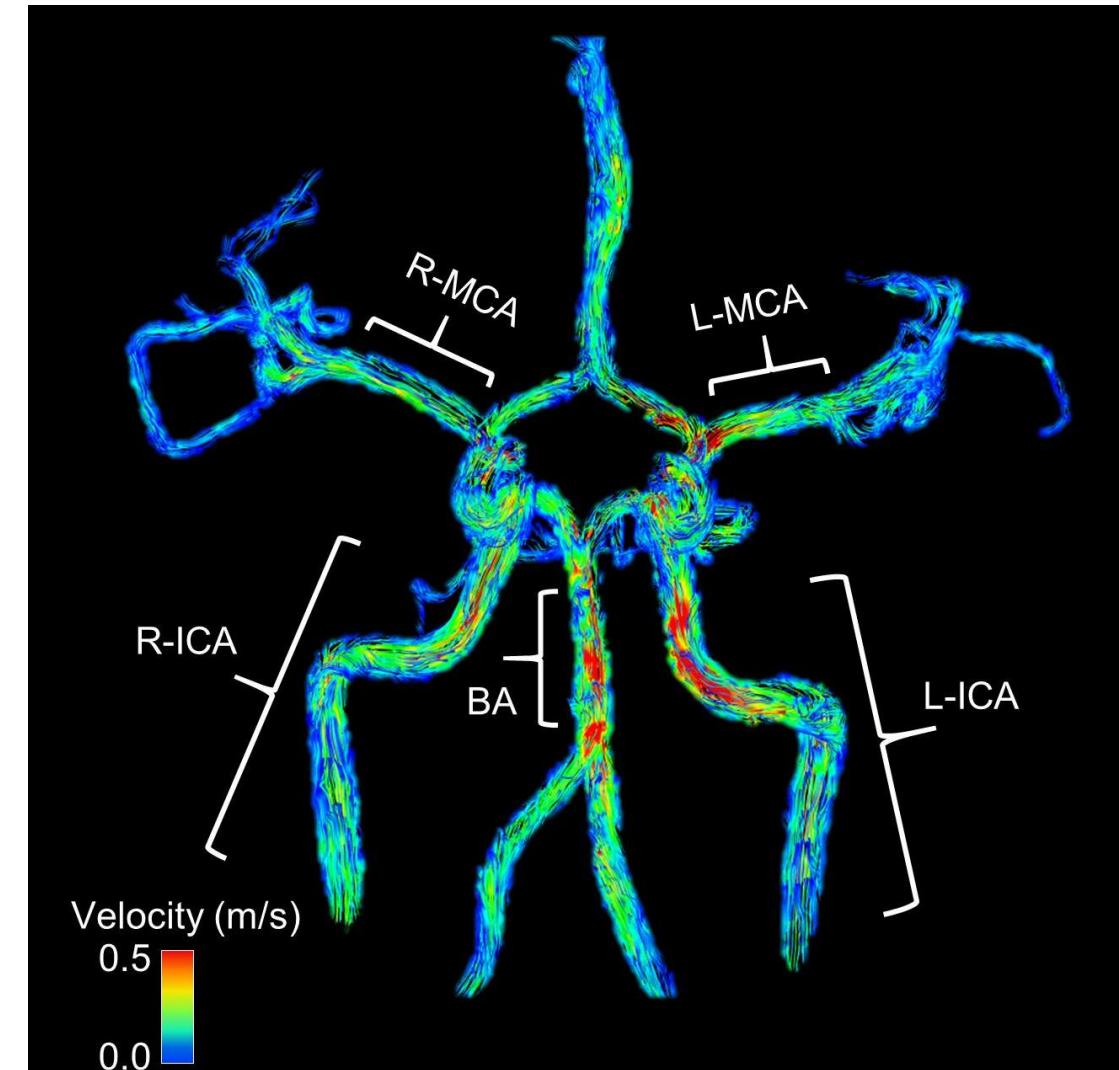
# Insulin resistance and cerebral blood flow



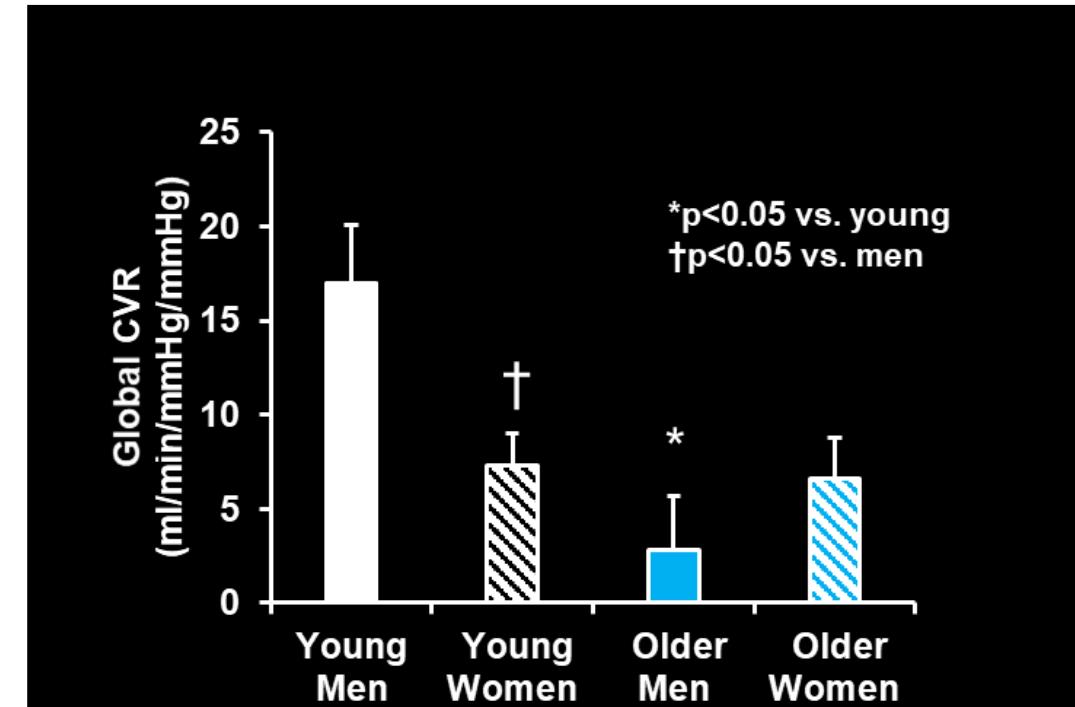
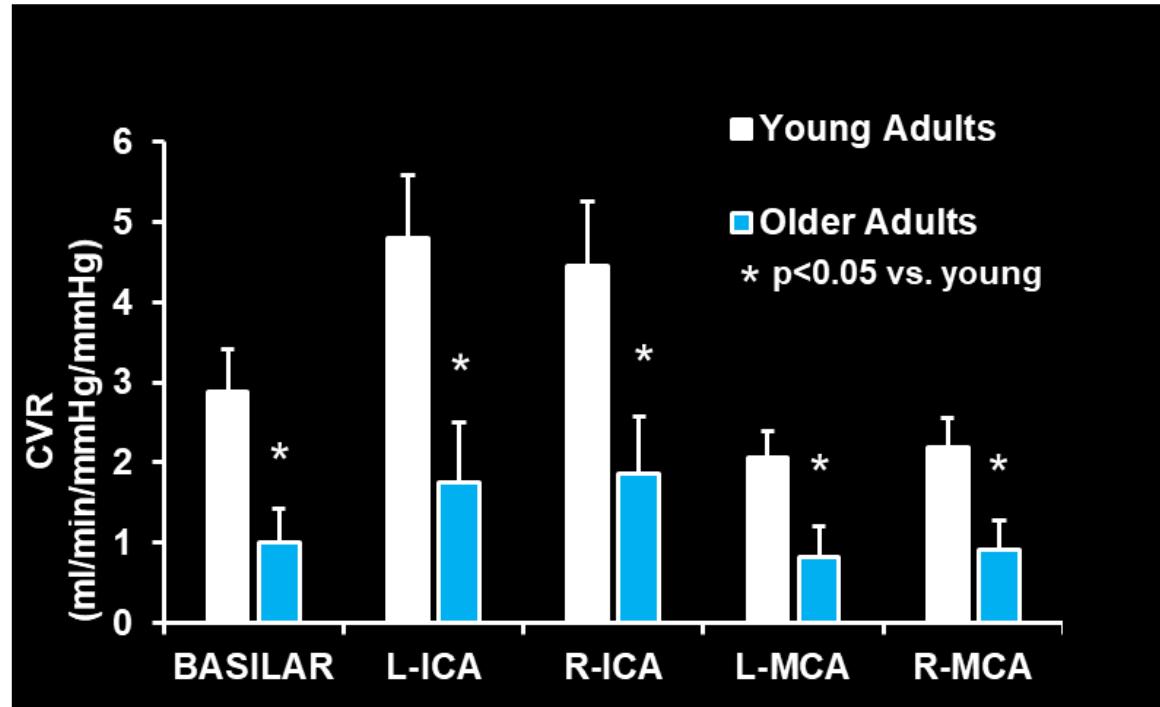
- Higher IR predicted lower arterial blood flow in Metabolic Syndrome subjects, but not in controls.

# Cerebrovascular reactivity (CVR) and aging

- CVR = response of brain blood vessels to vasoactive stimuli (e.g. neural activity, increases in CO<sub>2</sub>)
- 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 CO<sub>2</sub> inhalation.



# CVR to Hypercapnia



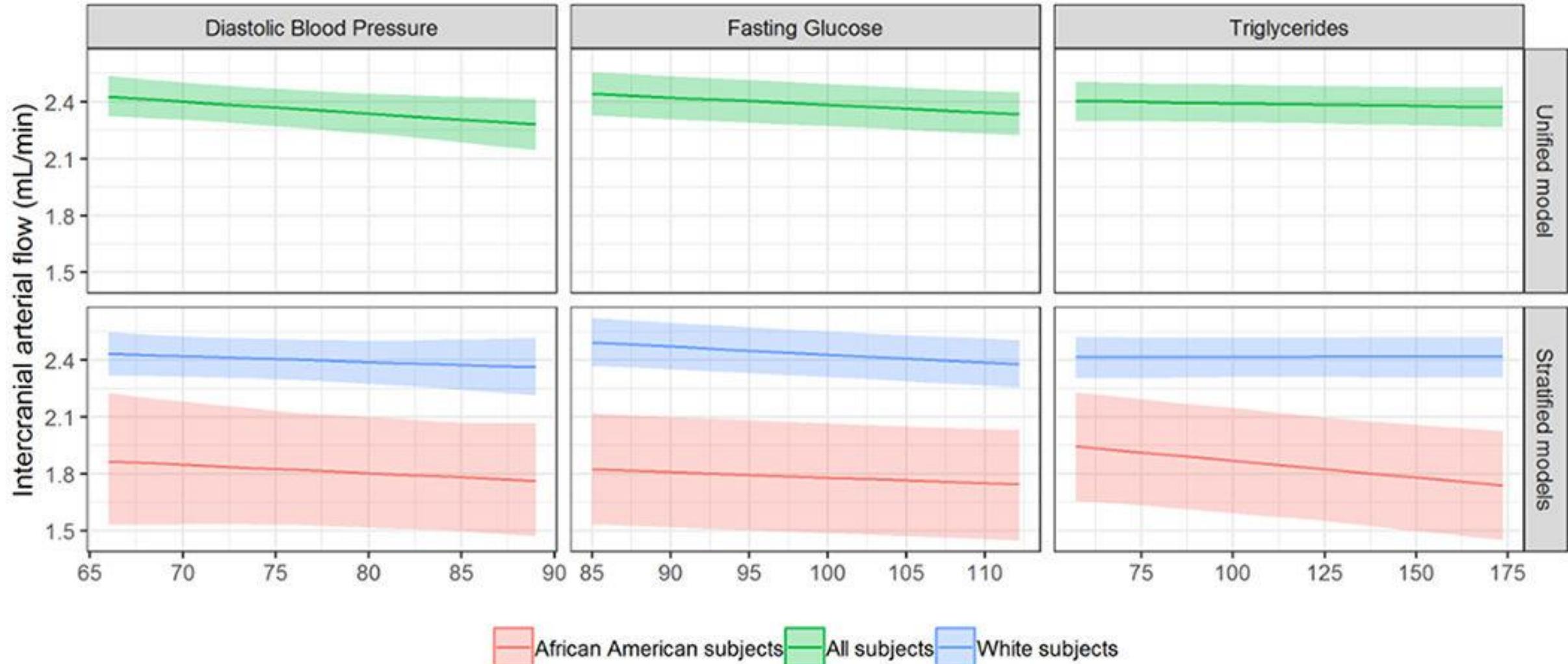
- The brain blood flow response to a vasodilatory stimulus (hypercapnia) was reduced in older adults.
- Findings may be sex-specific

# 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

# Cardiovascular risk factors and racial/ethnic disparities in AD





- 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.

# 4D flow MRI: Other vascular markers

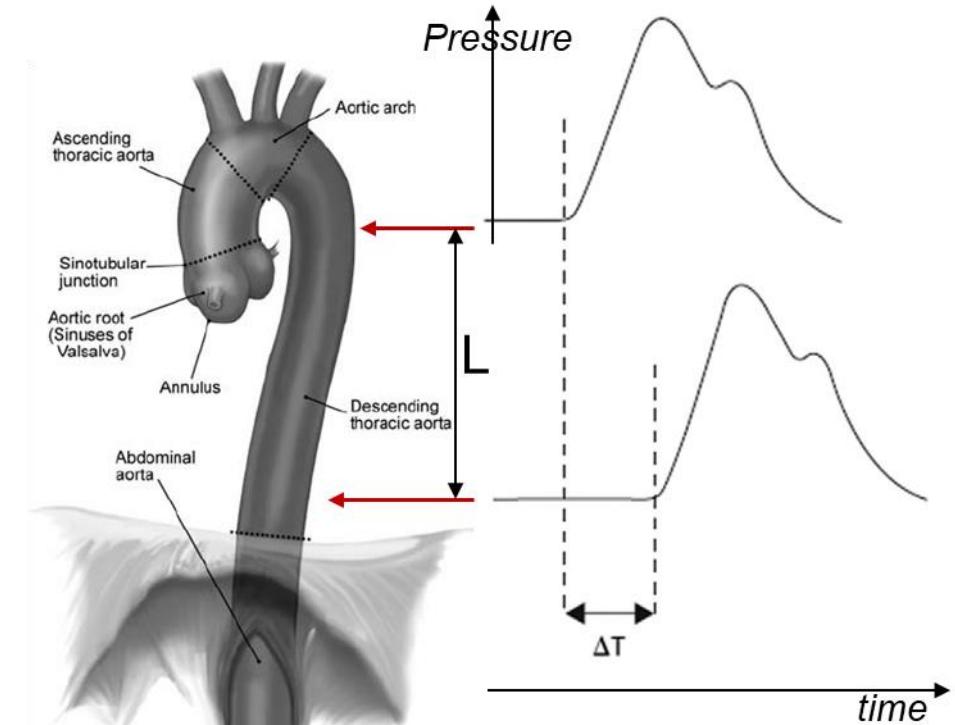
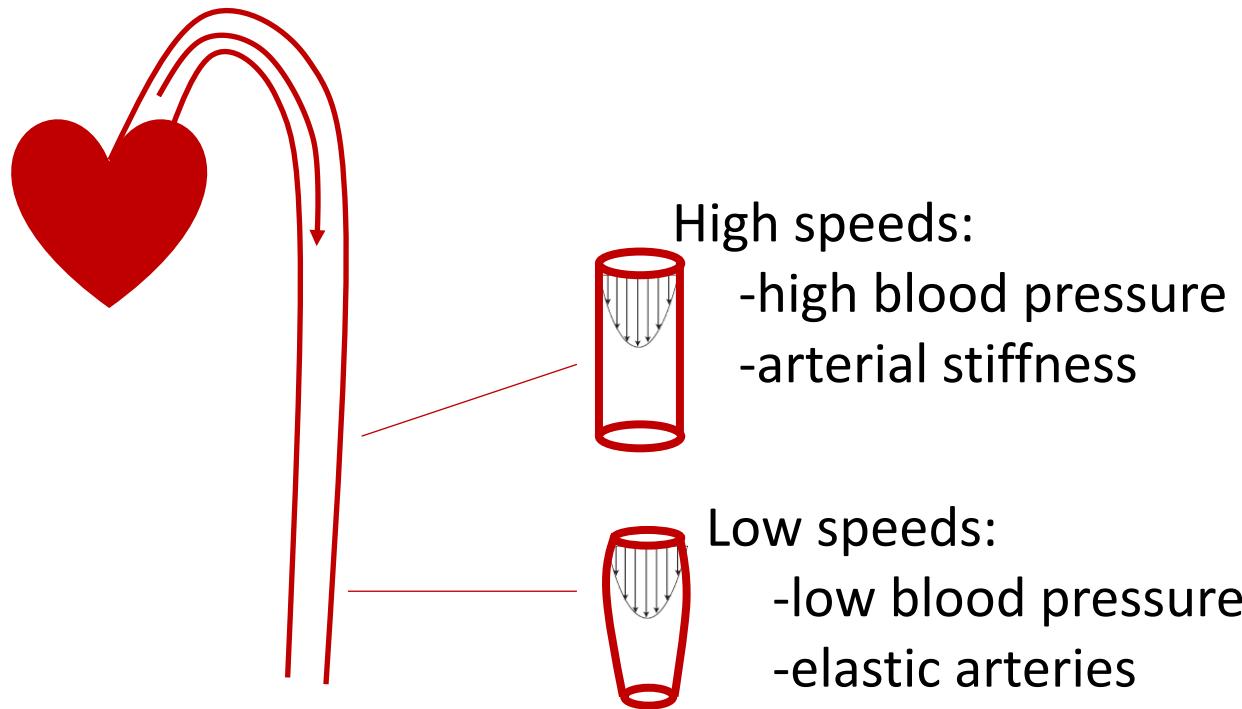


- What else besides flow and PI ?
- Clinical AD patients showed decreased blood flow and increased PI
  - neuron loss -> decreased metabolism -> decreased blood flow
  - increase cerebrovascular resistance -> increase PI
- What about a more local marker of vascular health ?

# 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]

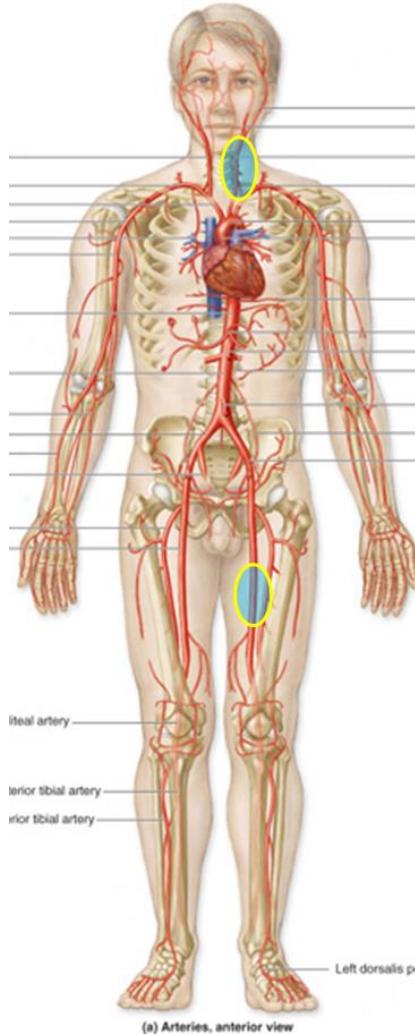


$$PWV = \frac{L}{\Delta T}$$

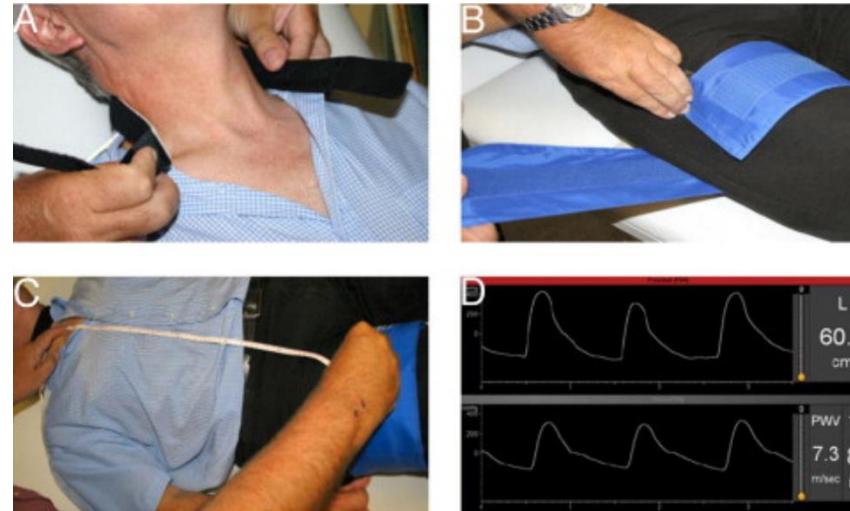
# 4D flow MRI: Other vascular markers



- carotid-femoral PWV associated with deposition of A $\beta$  in nondemented individuals [2]



- measured using applanation tonometry



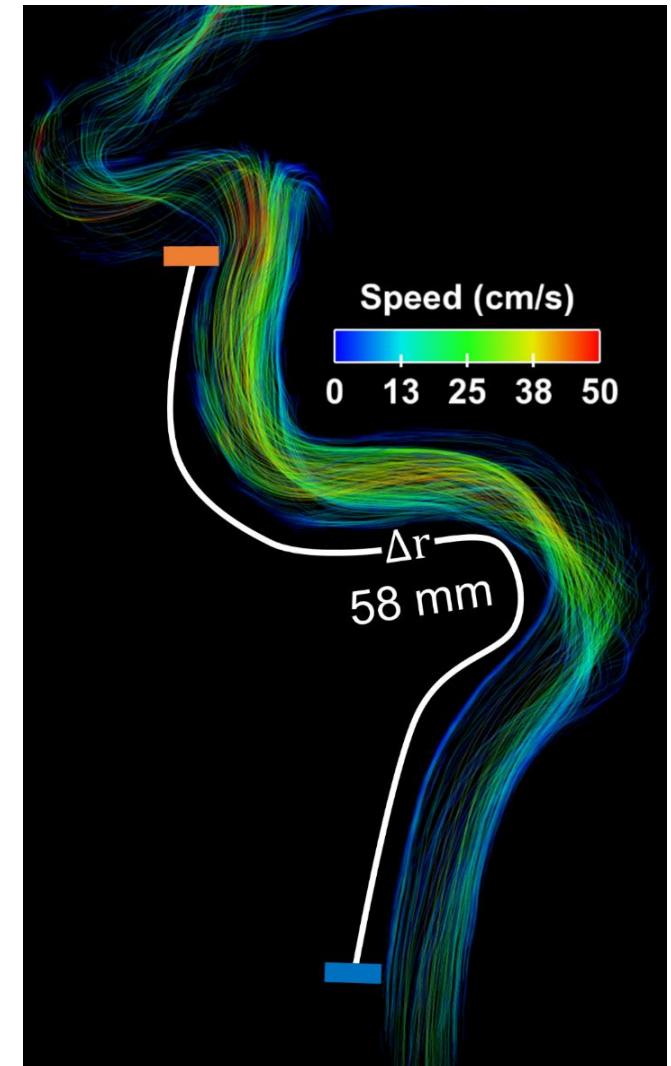
from Cavalcante et al. JACC. 2011;57(14):1511-22.

- + 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*

# 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

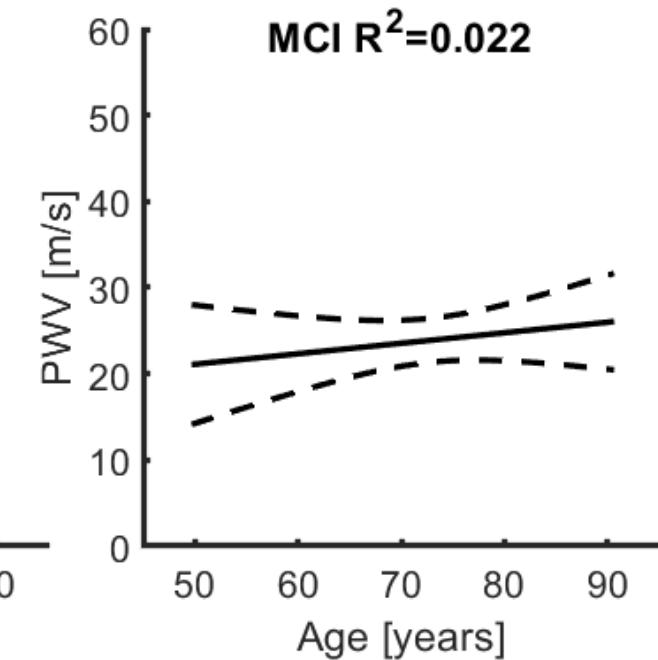
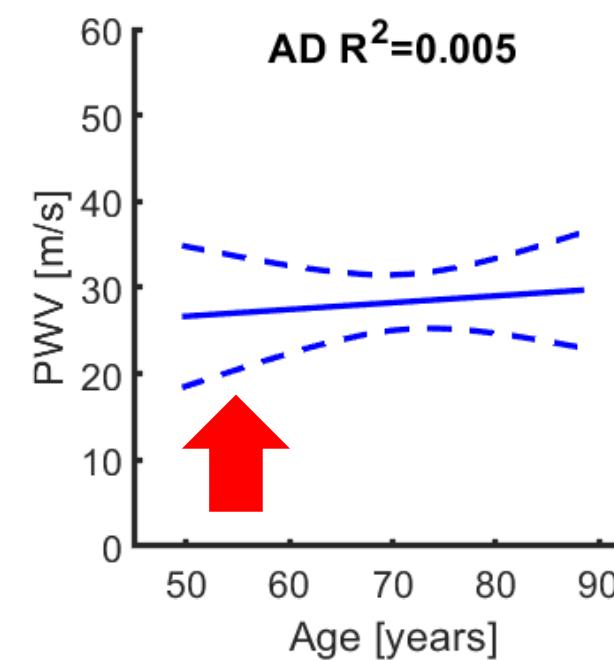
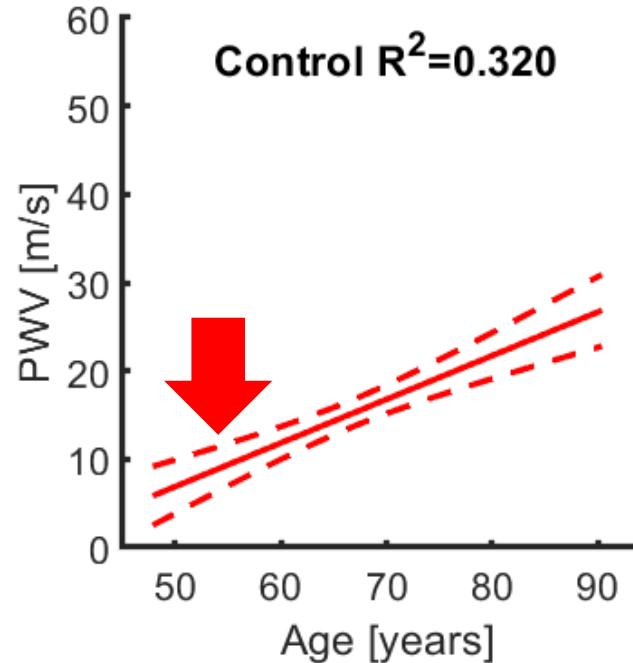


Sagittal view of ICA segment

# Pathology and age effects



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

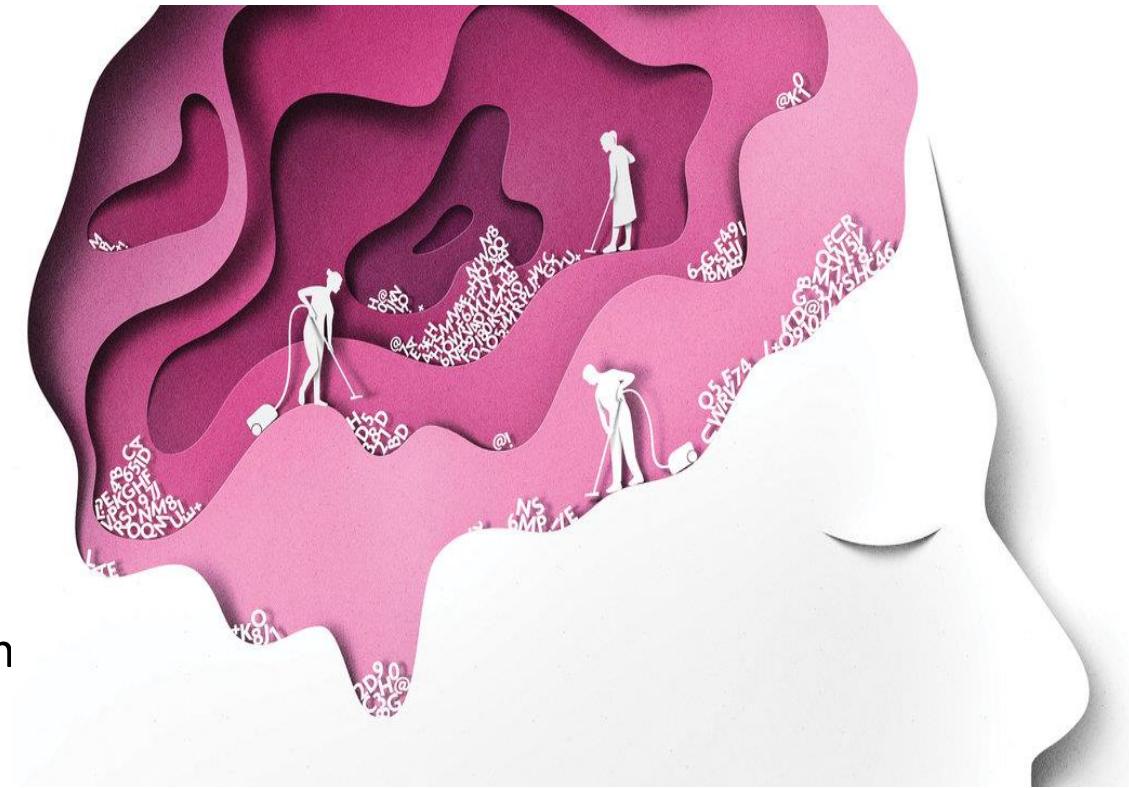
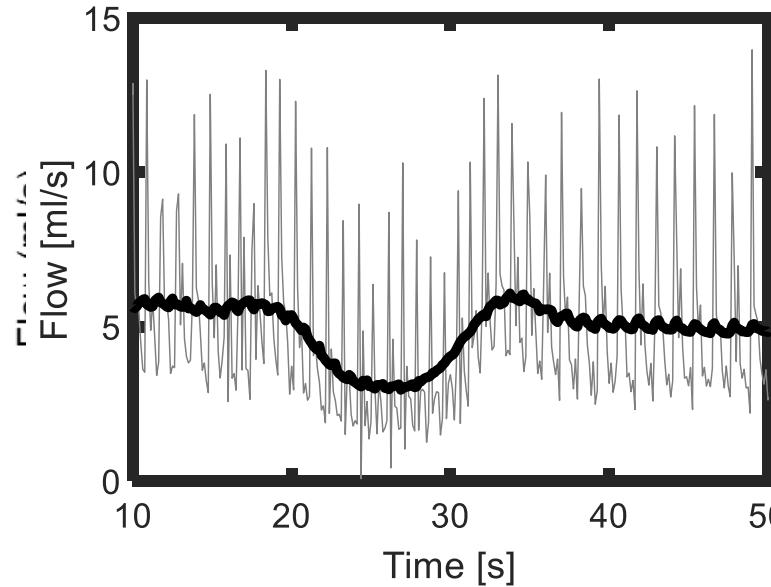


- AD appears to accelerate aging effect

# 4D Flow MRI (PCVIPR) Outlook



- Probe other components of macrovascular hemodynamics



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

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

# 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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**Thank You!**