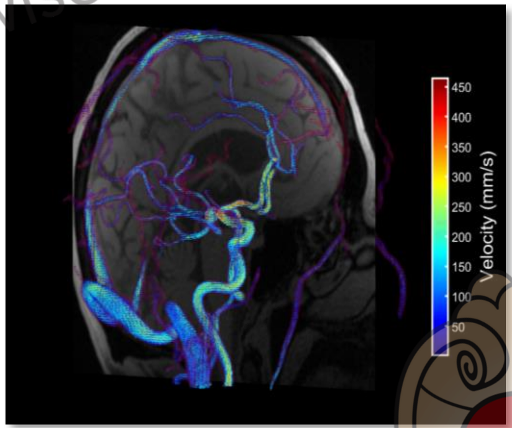
DEPARTMENT OF
Medical Physics
University of Wisconsin - Madison School of Medicine and Public Health

Advancing Functional Assessment with Flow-Sensitive Magnetic Resonance Imaging

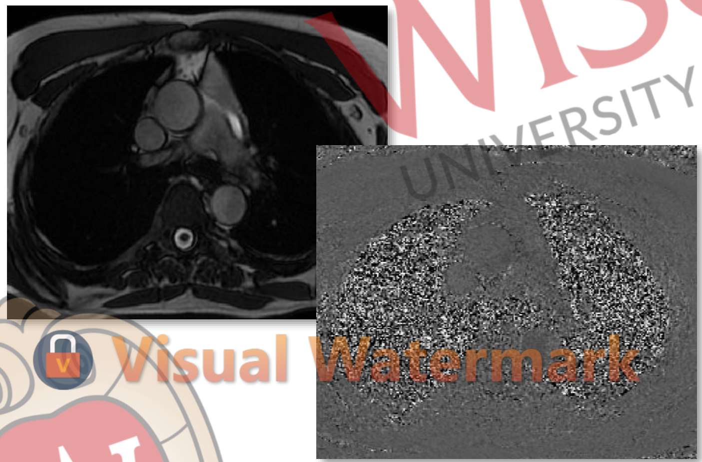
Grant S. Roberts, MSc

PhD dissertation defense in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Medical Physics



<u>Thesis Committee</u>

Oliver Wieben, PhD (advisor)
Laura Eisenmenger, MD (co-advisor)
Kevin Johnson, PhD
Diego Hernando, PhD
Ozioma Okonkwo, PhD



About Me

2014 – BS, Radiological Sciences
- X-ray and CT Tech

2017 – BS, Physics
2020 – MSc, Medical Physics

Work I've Done

- Abdominal 4D Flow MRI
  - Diagnosing chronic mesenteric ischemia with 4D flow MRI
  - 4D flow MRI in the portal vein
- Cranial 4D Flow MRI
  - 'Virtual Injections' with improved 4D flow streamlines
  - Relationship between cerebral hemodynamics and white matter (NODDI)
  - Cranial 4D flow MRI analysis Tool (QVT)
  - Establish normative intracranial flow/pulsatility in 759 older adults
- Cardiac 2D Phase Contrast MRI
  - Free-breathing MRI sequence to measure aortic stiffness
  - Accelerated free-breathing sequence using simultaneous multislice
- Other Projects
  - Brain MR elastography
  - Cardiac function in pre-term birth

Check out my website for more info! https://gsroberts1.github.io/

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Thesis

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Defense

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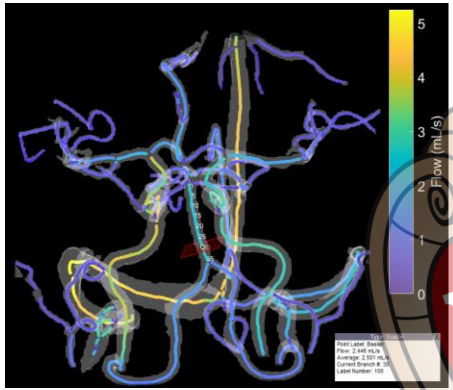
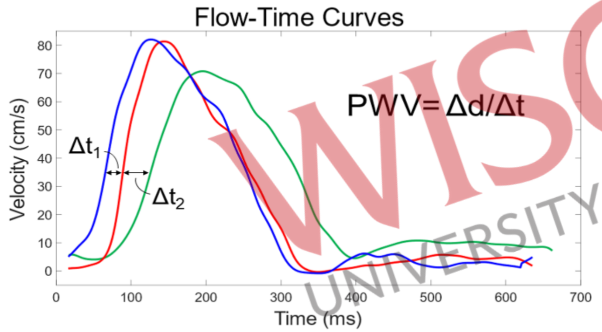
Outline



- **Background**
- **Part 1:** Cranial 4D Flow MRI
  - <u>Aim 1</u>: Develop 4D flow MRI tool for efficient flow analysis in the brain
  - <u>Aim 2</u>: Establish "normal" intracranial blood flow and pulsatility in 759 older adults
- **Part 2:** Aortic Pulse Wave Velocity
  - <u>Aim 3</u>: Implement a free-breathing, radial 2D phase contrast sequence to assess aortic pulse wave velocity
  - <u>Aim 4</u>: Develop a simultaneous multislice sequence for aortic pulse wave velocity assessment



- **Summary**

Outline

- **Background**
- **Part 1:** Cranial 4D Flow MRI
  - Aim 1: Develop 4D flow MRI tool for efficient flow analysis in the brain
  - Aim 2: Establish "normal" intracranial blood flow and pulsatility in 759 older adults
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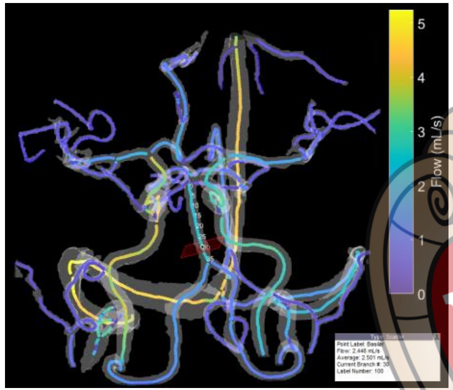
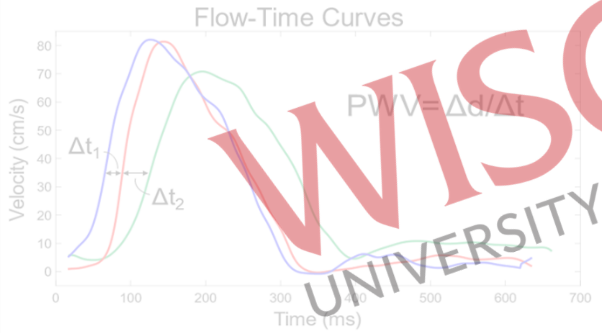
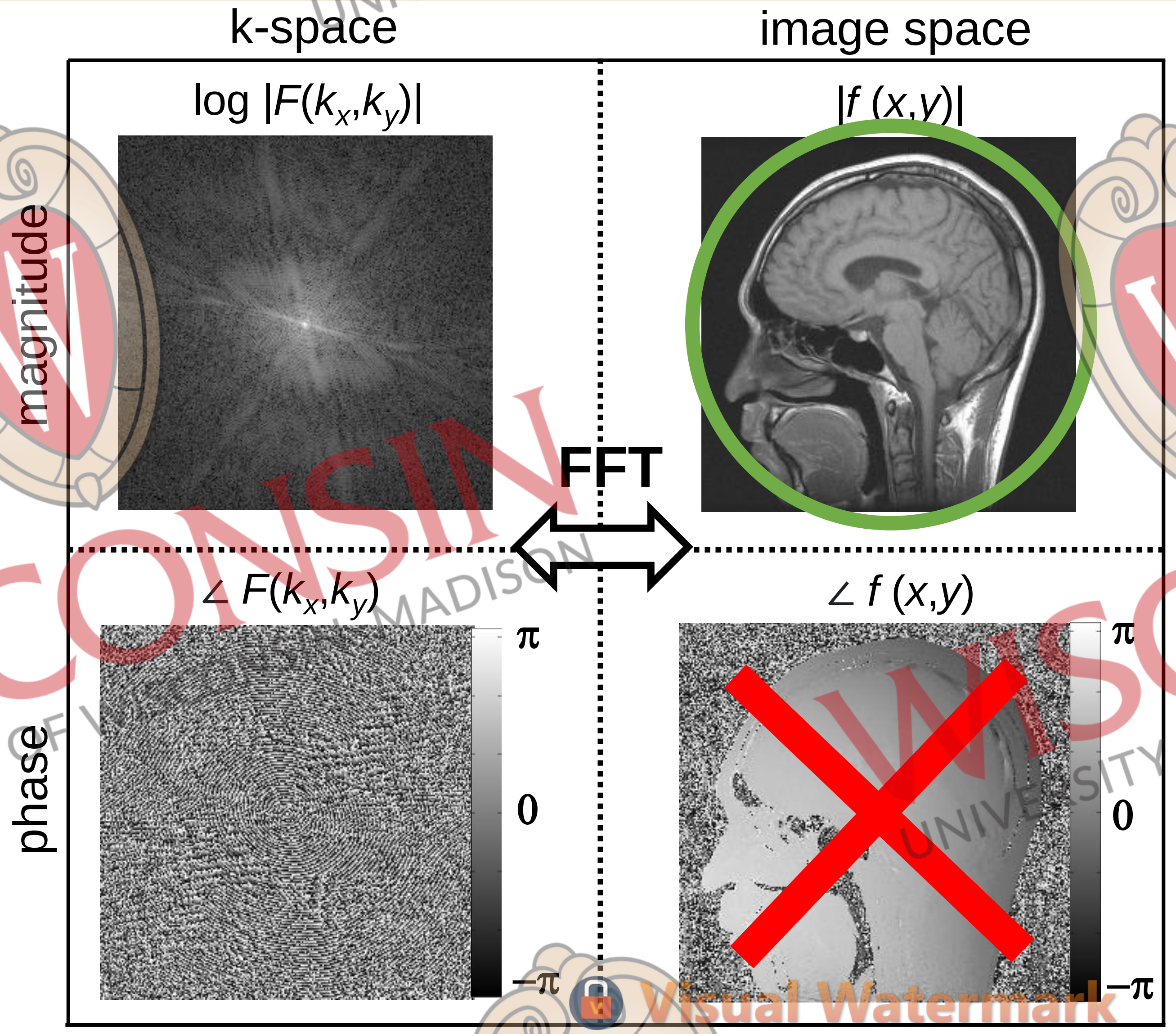
- **Summary**





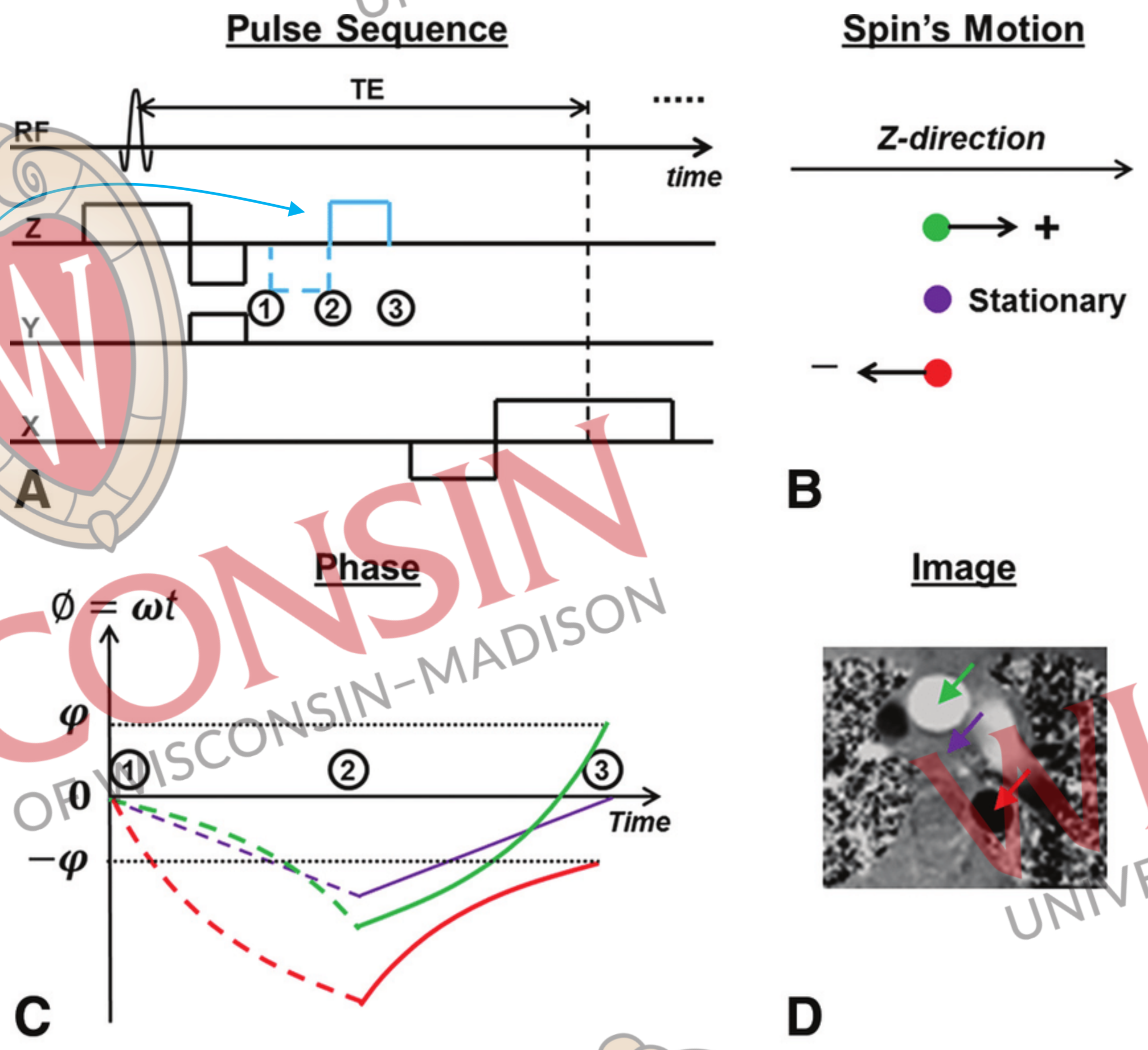
Background – MR Images are Complex!

- Acquired data is complex-valued
  - Phase and magnitude
  - Phase maps often discarded



Background – Phase Contrast MRI

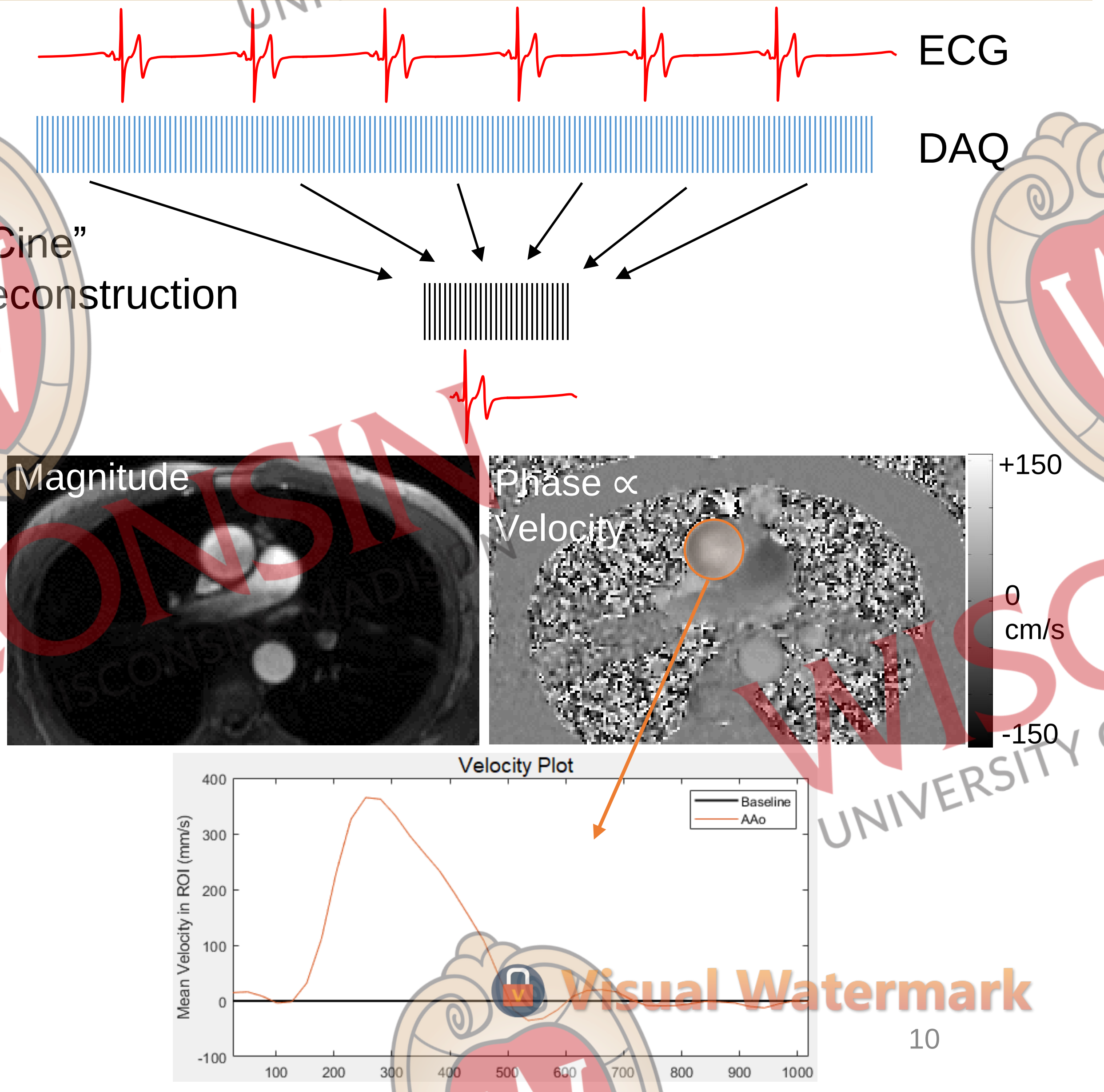
- Acquired data is complex-valued
  - Phase and magnitude
  - Phase maps often discarded
- **Can encode velocity into phase**
  - Bipolar gradients
  - Phase contrast MRI



Alves T, et al (2017). *Neurographics.* 7(3):199-210.

Background – 2DPC MRI

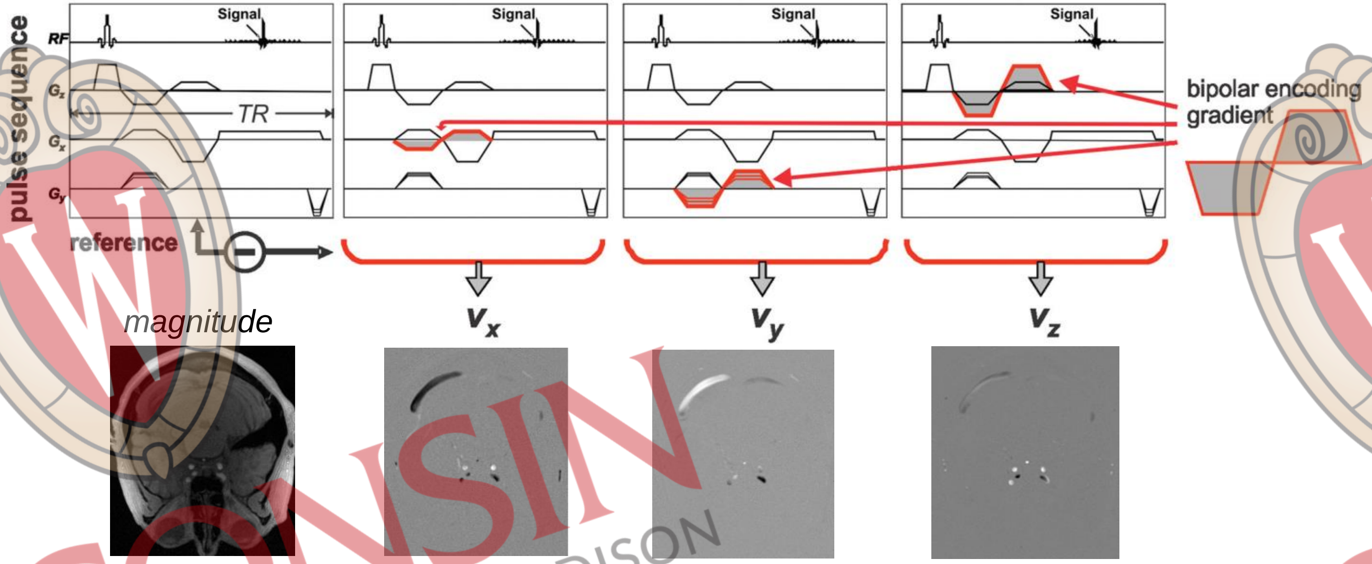
- Acquired data is complex-valued
  - Phase and magnitude
  - Phase maps often discarded
- Can encode velocity into phase
  - Bipolar gradients
  - Phase contrast MRI
- <u>2D Phase Contrast MRI</u>
  - Velocity encoded “through-plane”
  - “Gated” over multiple heartbeats
    - Time-resolved over cardiac cycle

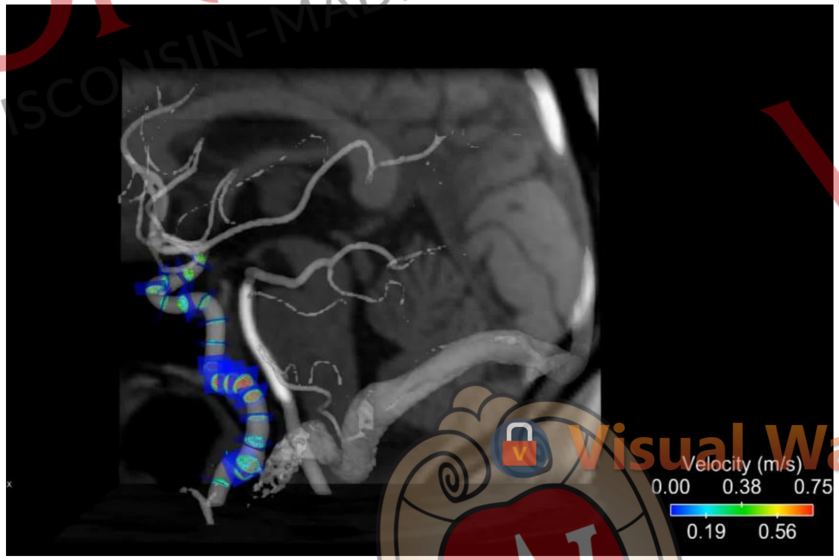


Background – 4D Flow MRI

- Acquired data is complex-valued
  - Phase and magnitude
  - Phase maps often discarded
- Can encode velocity into phase
  - Bipolar gradients
  - Phase contrast MRI
- 2D Phase Contrast MRI
  - Velocity encoded “through-plane”
  - “Gated” over multiple heartbeats
    - Time-resolved over cardiac cycle
- 4D Flow MRI
  - 4D? → 3D Space + 1D Time
  - 3D velocity fields

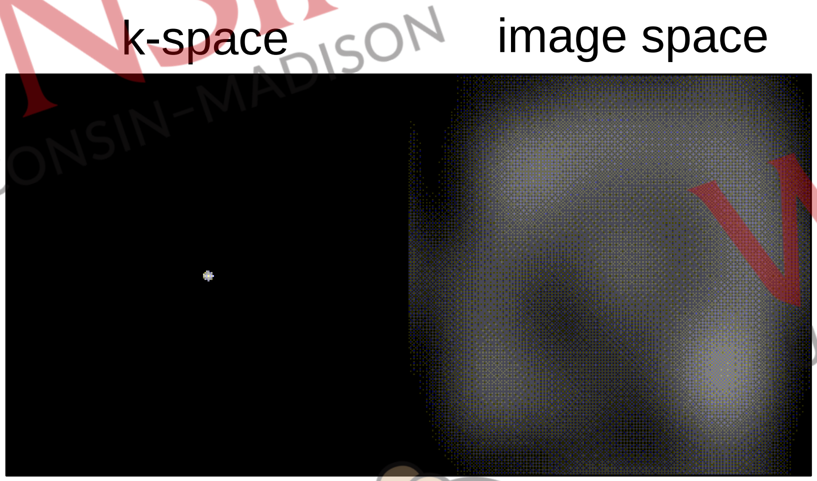
Markl M, et al (2012). *JMRI*. 36(5):1015-1036



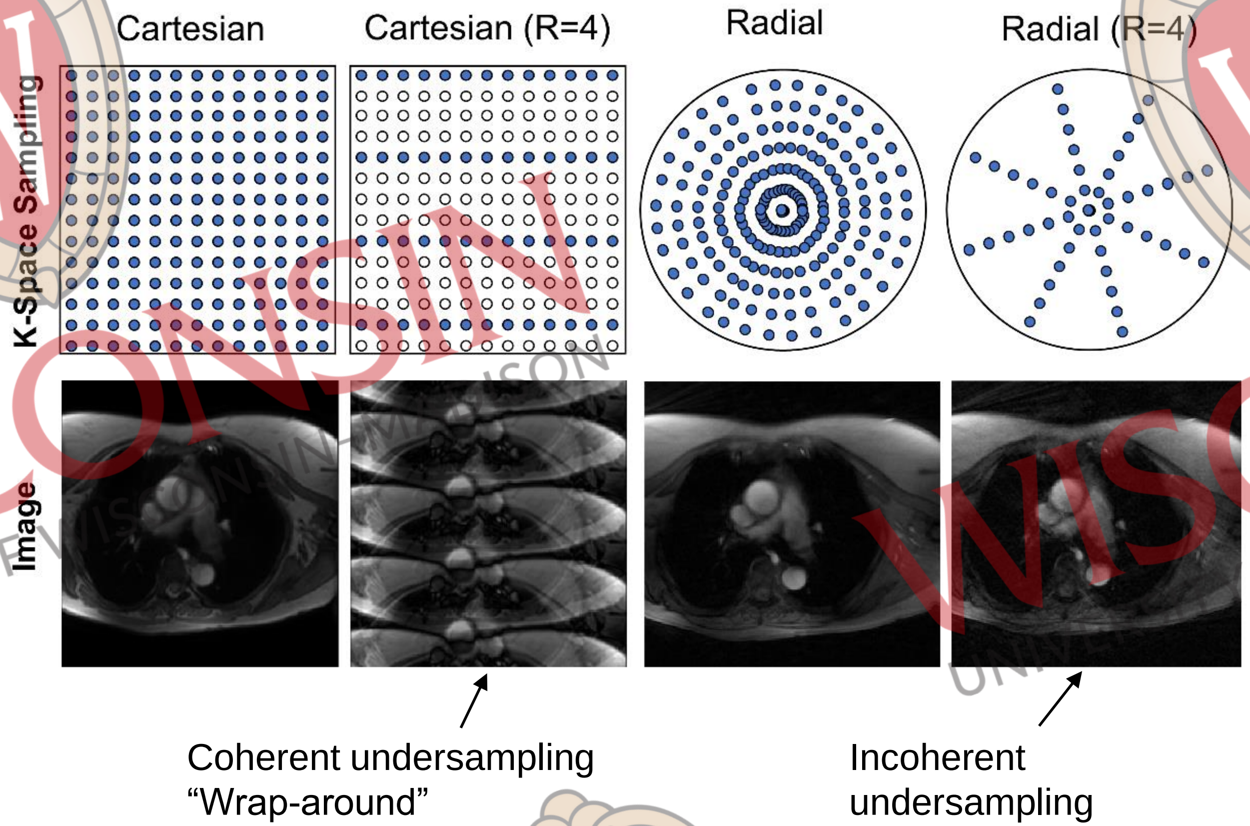


Background – Radial Sampling

- Raw data energy focused in center of k-space
- Noise-like undersampling artifacts
  - Incoherent aliasing
  - Ideal for regularized reconstructions
- Robust to motion
- Flexibility in cardiac/respiratory gating



http://mriquestions.com/k-space-trajectories.html

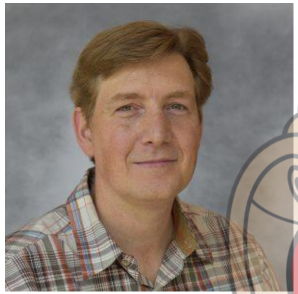


Background – PCVIPR

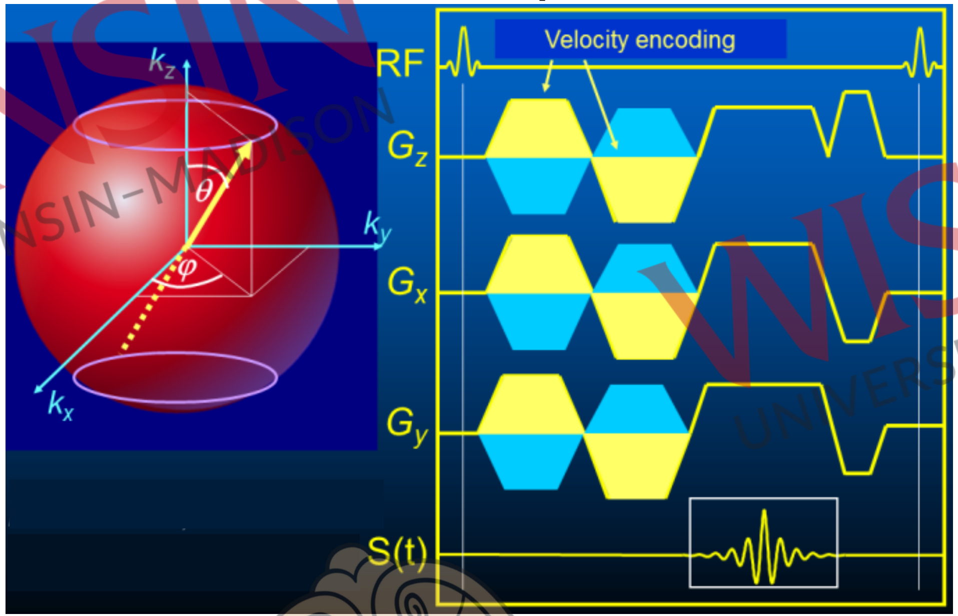
- PCVIPR – Phase Contrast Vastly Undersampled Isotropic Projection Reconstruction[1,2]
  - Radial 4D Flow MRI acquisition
  - Sample center of k-space with every TR
  - Clinically feasible scan times (5-10 minutes)

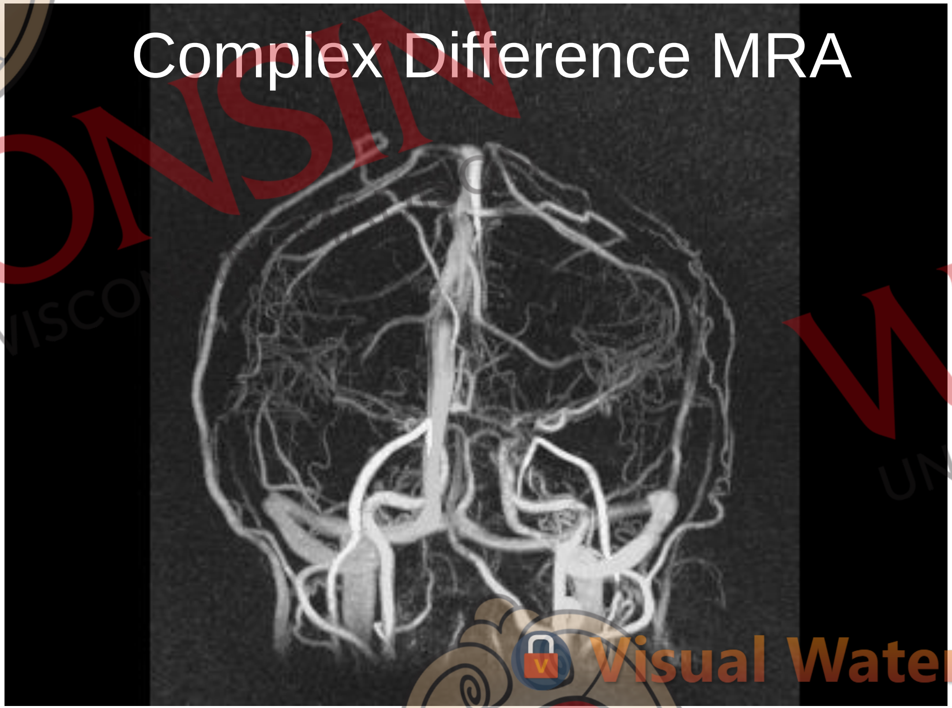

Chuck Mistretta


Kevin Johnson


Oliver Wieben

PCVIPR Sequence

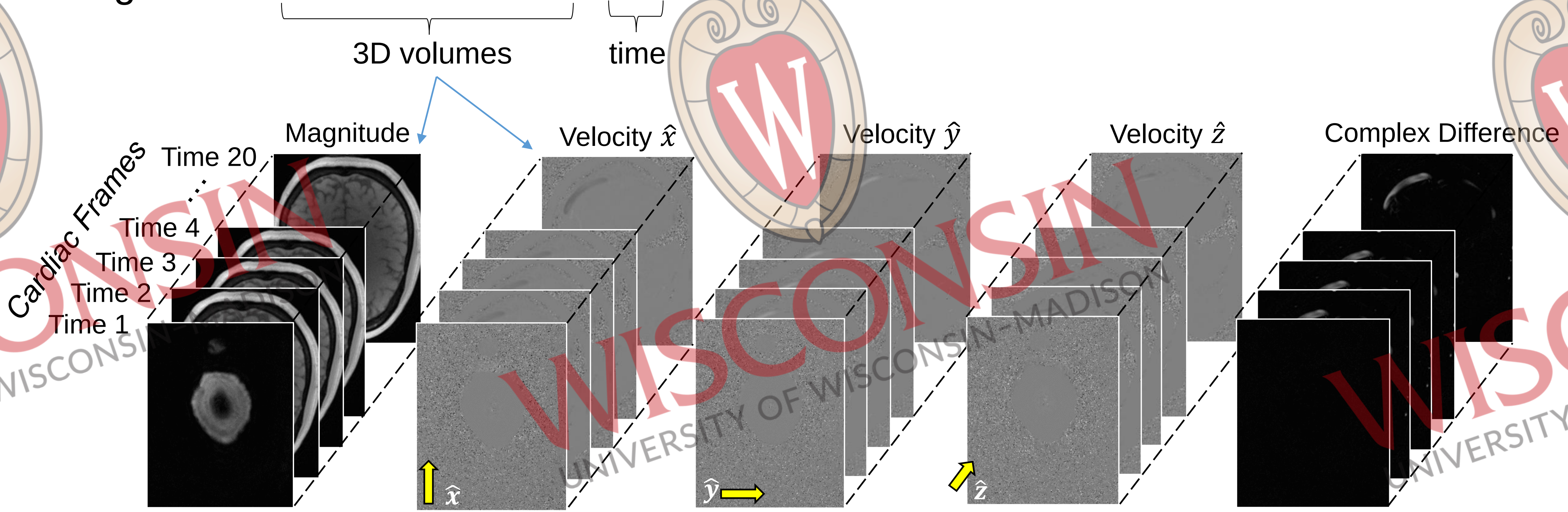




[1]Gu TL, et al (2005). *AJNR*. 26(4):743–9
[2]Johnson KM, et al (2008). *MRM*. 60(6):1329-36

Background – 4D Flow MRI Data

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



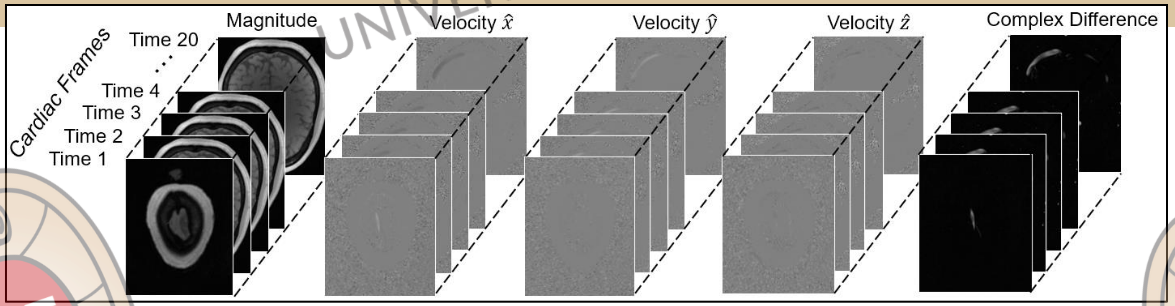
$$CD = M\left|\sin\left(\frac{\|\vec{V}\|/V_{enc}}{2}\right)\right|$$

Background – Post-Processing

1. Boil down large amount of data
2. Extract hemodynamic measures
   - Vessel area
   - Vessel length
   - Flow tracking
   - Blood velocity
   - Blood flow
   - Pulsatility index
   - Resistivity index
   - Pressure maps
   - Wall-shear stress
   - Kinetic energy
   - Pulse wave velocity

Structural (Vessel area, Vessel length, Flow tracking)

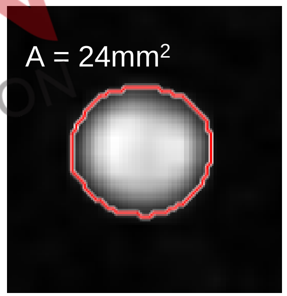
Functional (Flow tracking through Pulse wave velocity)



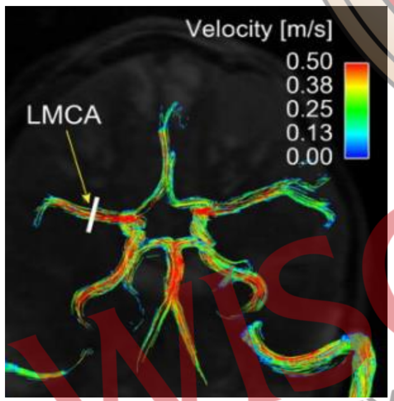
Flow Tracking

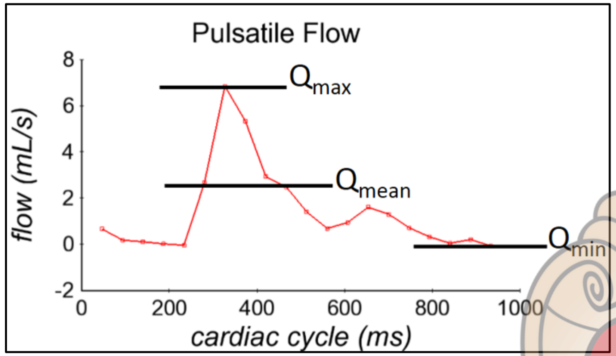
Wall Shear Stress

Vessel Area

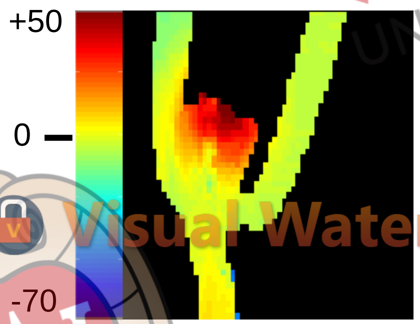


Blood Velocity





Pressure



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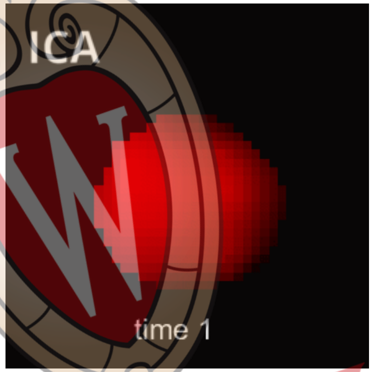
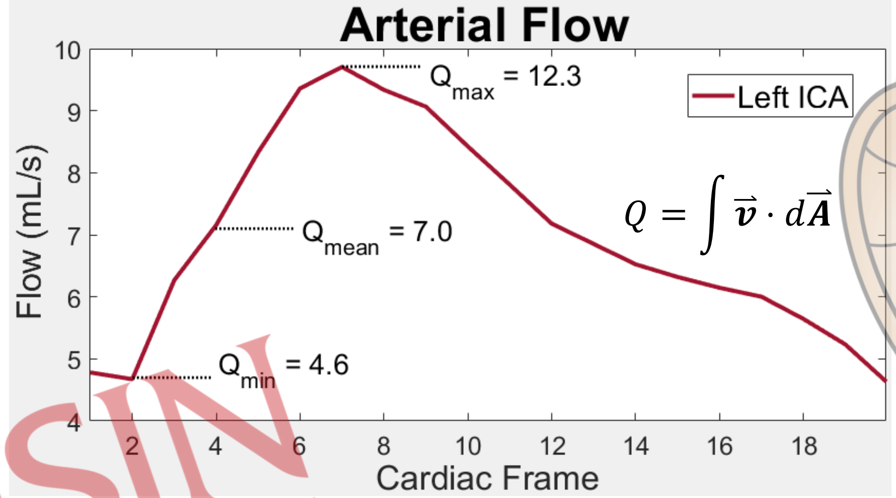
   - Pulse wave velocity

Aims 1-2

Aims 3-4





$$\text{Blood Flow} = Q_{mean}$$

$$\text{Pulsatility Index} = \frac{Q_{max} - Q_{min}}{Q_{mean}}$$

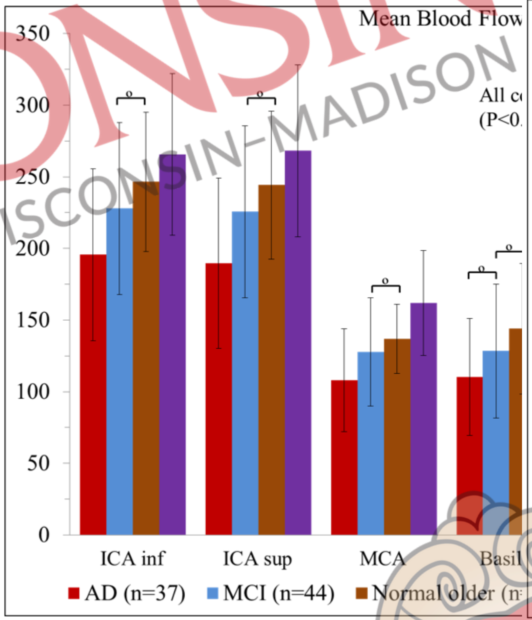
Background – Intracranial Flow and Pulsatility

- Vascular alterations in Alzheimer's Disease using 4D Flow MRI
  - ↓ cerebral blood flow
  - ↑ arterial "pulsatility"
  - ↑ ICA stiffness
  - Relationship with AD biomarkers

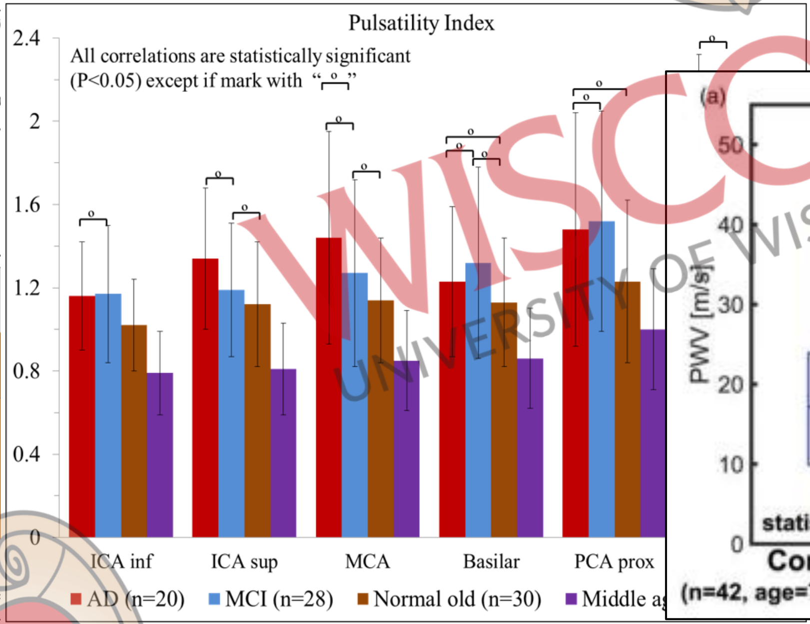
Sara Berman

Leonardo Rivera-Rivera

Blood Flow (mL/min)

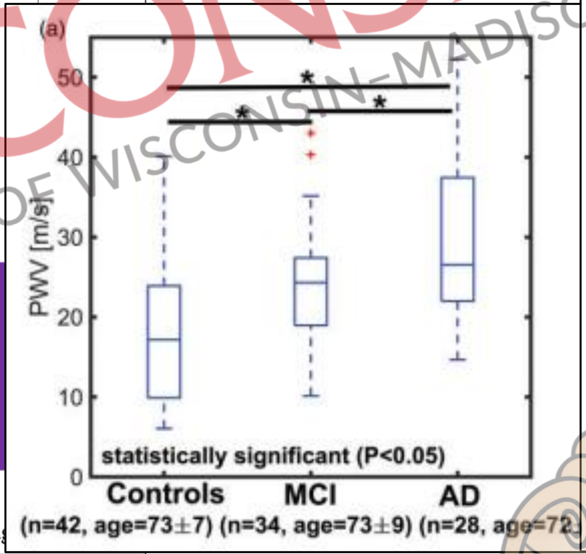


Pulsatility Index



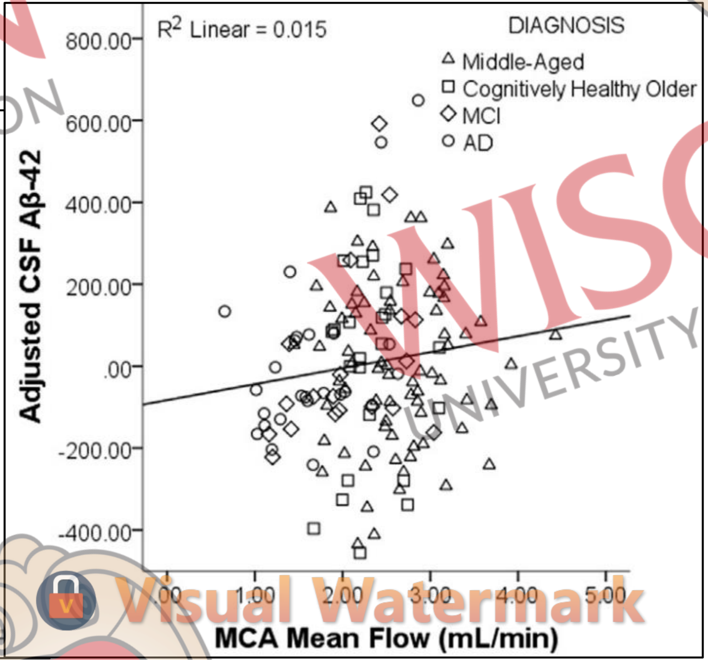
Rivera-Rivera LA, et al (2016). *JCBFM*. 36(1):1718-1730

ICA Stiffness



Rivera-Rivera LA, et al (2021), *JCBFM*. *41*(2)

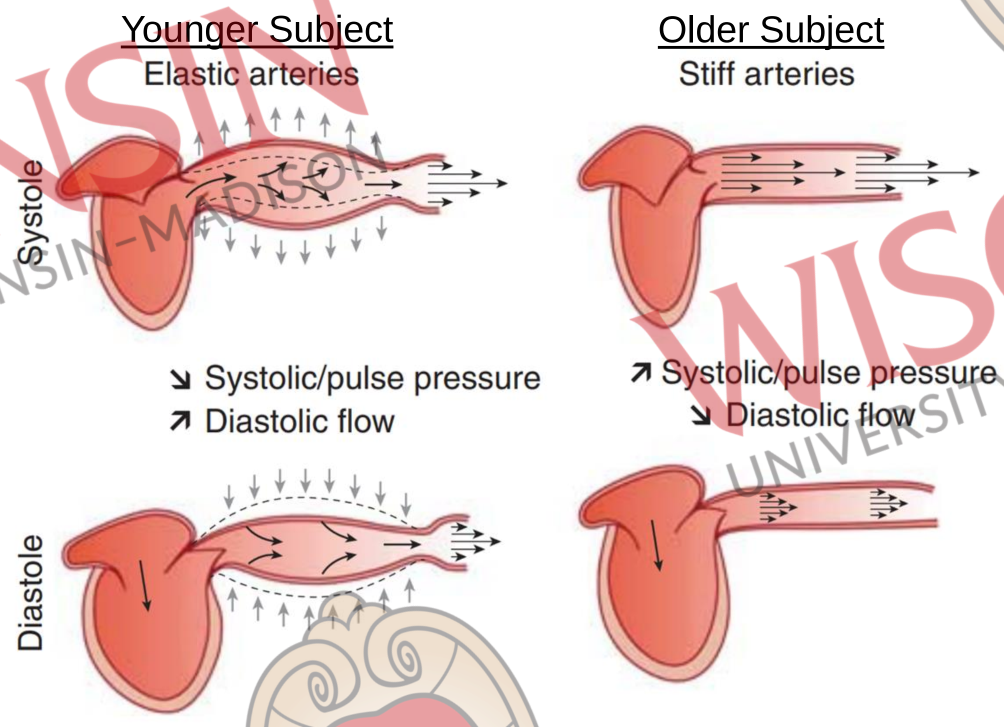
Flow vs. Aβ



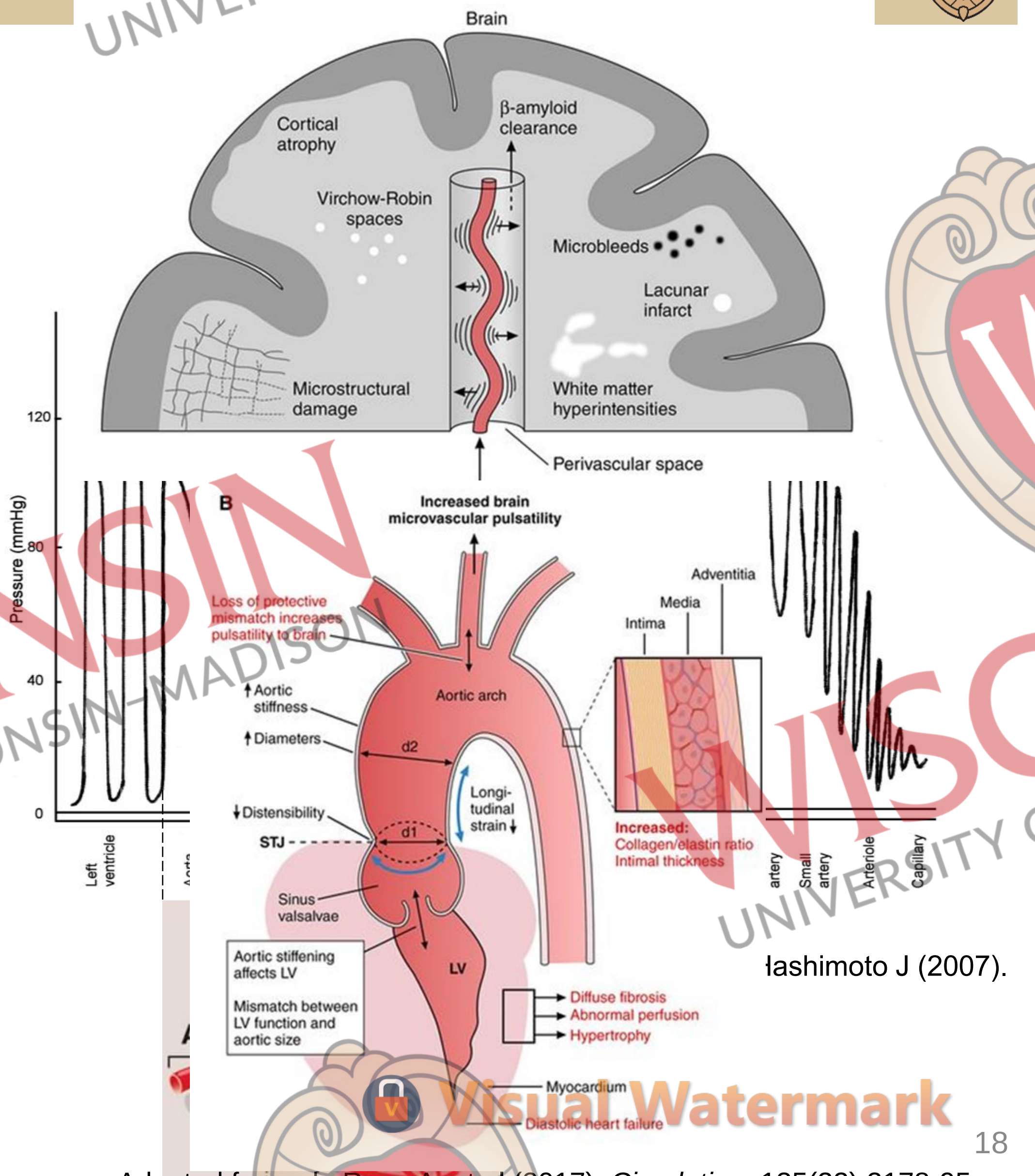
Berman SE, et al (2015). *Alzheimers Dement* 1(4)

Background – Aortic Stiffness

- Aorta also impacts intracranial hemodynamics!
  - Highly elastic and sets compliance for arterial system
  - "Buffers" contractions from the heart
  - Stiffening leads to increased transmitted pulsatility
    - **Can damage brain's microvasculature**



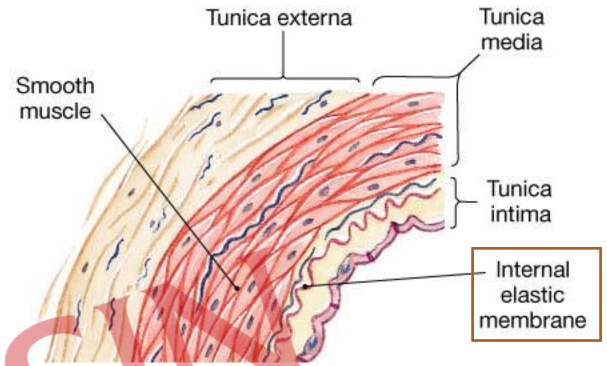
Briet M, et al (2012). *Kidney International.* 82(4):388-400

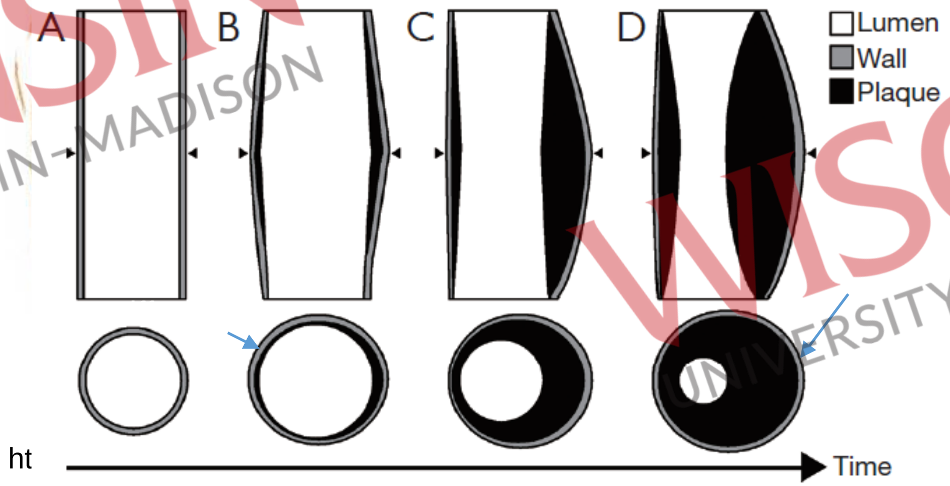


Adapted from: de Roos A, et al (2017). *Circulation.* 135(22):2178-95

Background – Aortic Stiffness

- Aortic stiffness impacts intracranial hemodynamics!
  - Highly elastic and sets compliance for arterial system
  - "Buffers" contractions from the heart
  - Stiffening leads to increased transmitted pulsatility
    - **Can damage brain's microvasculature**
- Age-Related Stiffening[1]
  - Elastin fibers fatigue/fracture
  - Increased collagen deposition
  - Increased calcium deposition
- Cardiovascular Disease-Related Stiffening[1]
  - Aortic stiffness is accelerated by CVD
    - One of the earliest manifestations





Wentland AL, et al (2014). *Cardiovasc Diagn Ther*. 4(2):193-206

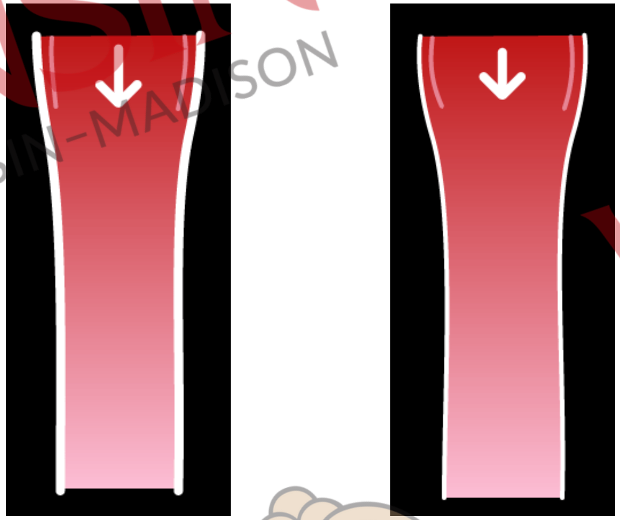
[1]Calvacante JL, et al (2011). *J Am Coll Cardiol*. 57:1511–22

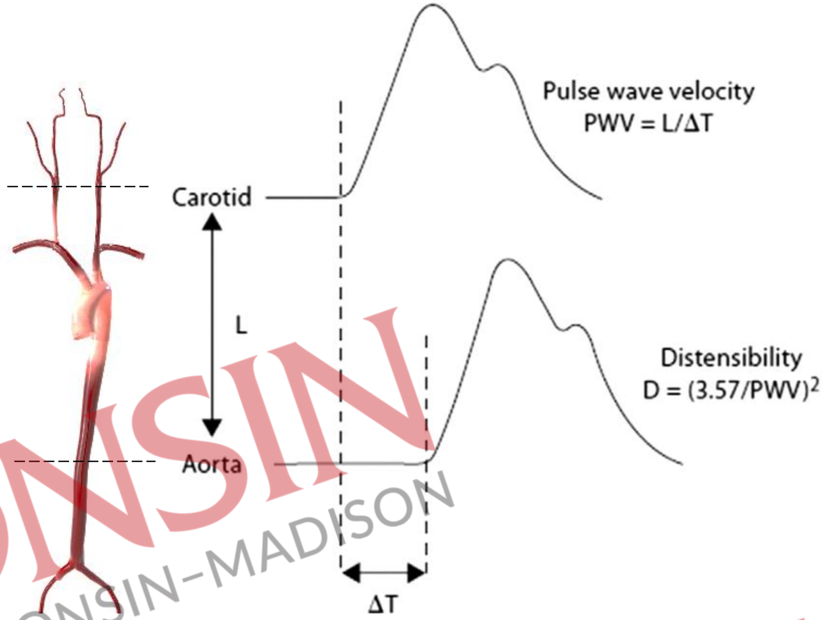
Background – Pulse Wave Velocity (PWV)

- Rate of pulse pressure propagation through vessel
- **PWV indirectly related to vessel stiffness**
  - Moens-Korteweg Equation
  - Bramwell-Hill Equation

Stiff artery
↑ PWV (fast)

Elastic artery
↓ PWV (slow)





Calvacante JL, et al (2011). *J Am Coll Cardiol*. 57:1511–22

Moens-Korteweg & Bramwell-Hill Equations

$$PWV = \sqrt{\frac{Eh}{2r\rho}} = \frac{1}{\sqrt{\rho D}}$$

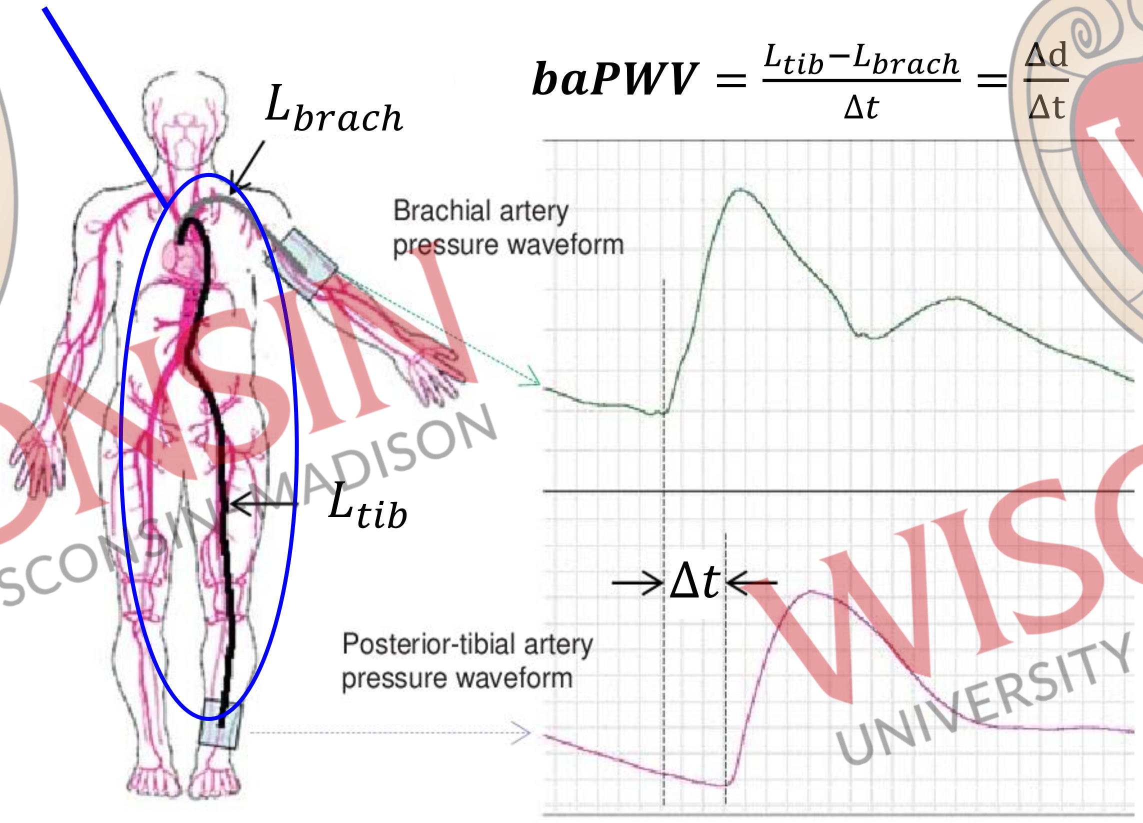
PWV = pulse wave velocity (m/s)
E = Young's modulus (N/m^2)
h = vessel wall thickness (m)
r = vessel radius (m)
ρ = blood density (N s^2/m^4)
D = distensibility

Background – Measuring PWV

- Applanation tonometry PWV
  - Clinical standard
    - Carotid-femoral (cf-PWV) or brachial-ankle (ba-PWV)
  - Easy, inexpensive, non-invasive
    - Large body of literature
  - **Distances are approximated**
    - Leads to PWV error[2]

How can we determine vessel distances accurately?

$$\boldsymbol{baPWV} = \frac{L_{tib} - L_{brach}}{\Delta t} = \frac{\Delta d}{\Delta t}$$

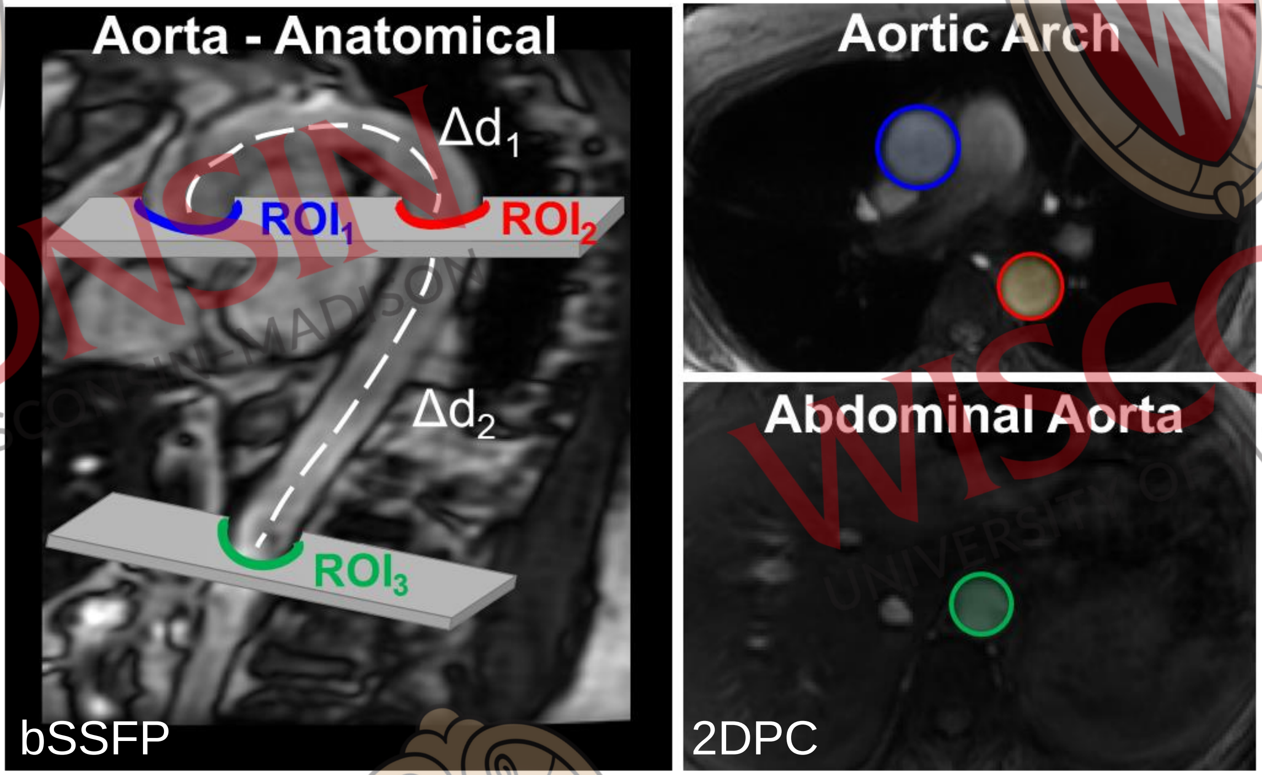


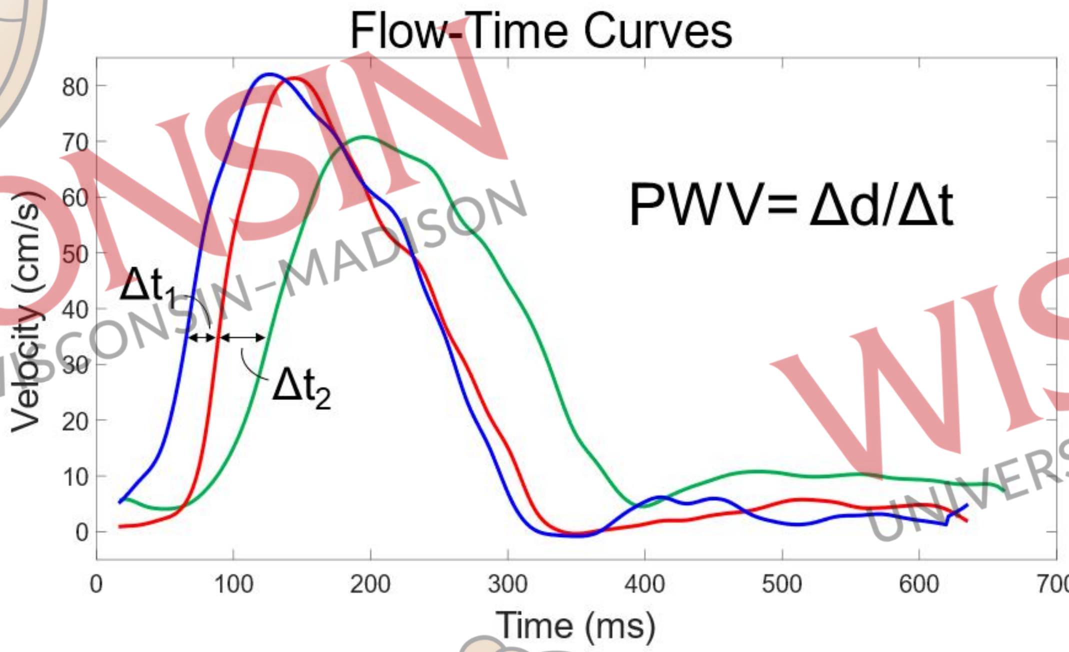
Sugawara J and Tanaka H (2015). *Pulse (Basel)*. 3(2):106-13

[1]Wentland AL, et al (2014). *Cardiovasc Diagn Ther*. 4(2):193-206
[2]Rajzer MW, et al (2008). *J Hypertens*. 26(10):2001-07

Background – PWV with MRI

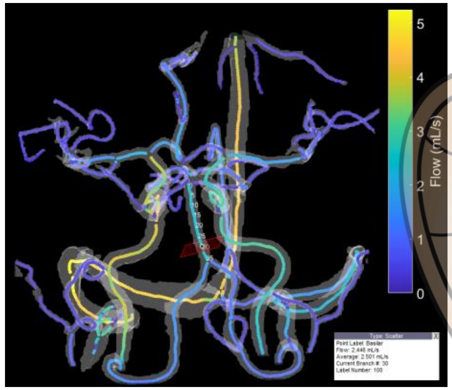
1. Measure vascular distance (Δd) with angiography
2. Draw ROIs in 2D phase contrast slices
3. Measure time shifts (Δt) between waveforms



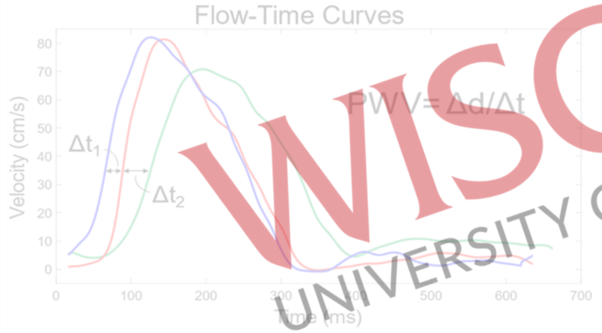


Outline

- **Background**
- **Part 1:** Cranial 4D Flow MRI
  - Aim 1: Develop 4D flow MRI tool for efficient flow analysis in the brain
  - Aim 2: Establish "normal" intracranial blood flow and pulsatility in 759 older adults



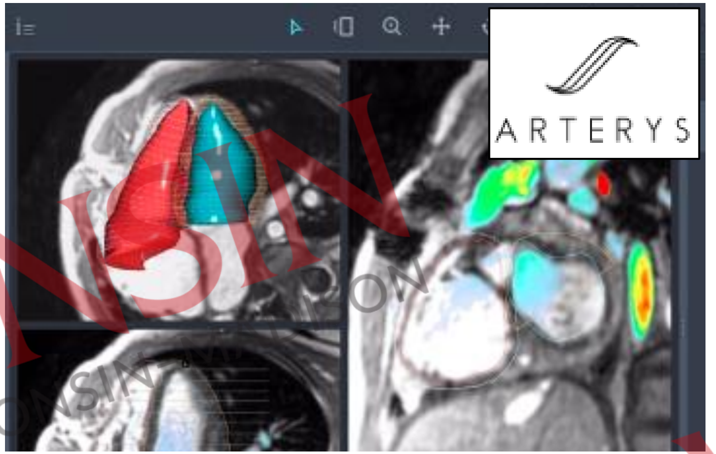
- **Part 2:** Aortic Pulse Wave Velocity
  - Aim 3: Implement a free-breathing, radial 2D phase contrast sequence to assess aortic pulse wave velocity
  - Aim 4: Develop a simultaneous multislice sequence for aortic pulse wave velocity assessment

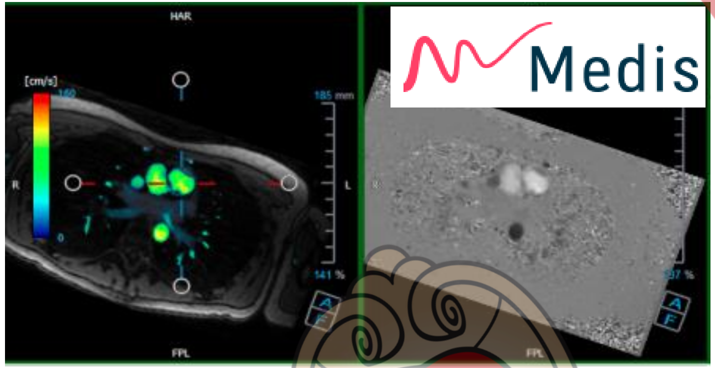


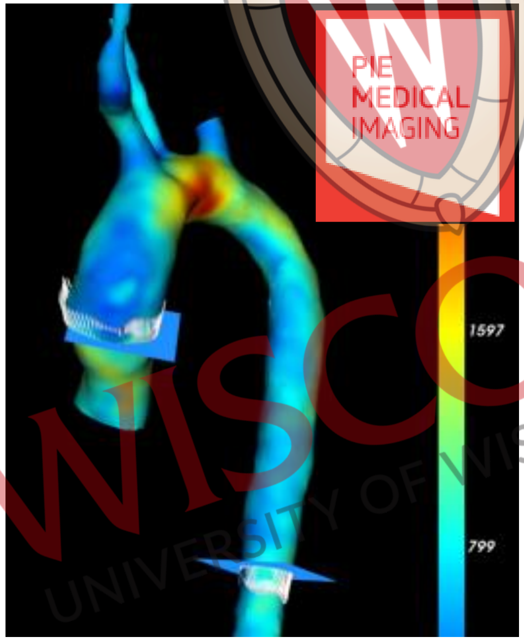
- **Summary**

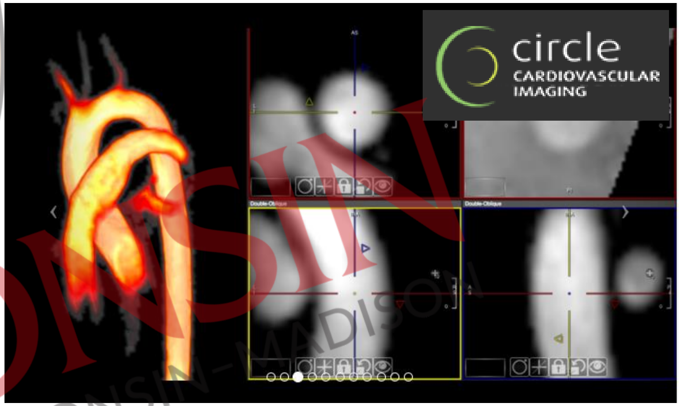
Aim 1 – Motivation

- Limited post-processing software tools for flow analysis in brain
  - Cerebral vessels – tortuous and small
  - Easy-to-use software required for efficient analysis





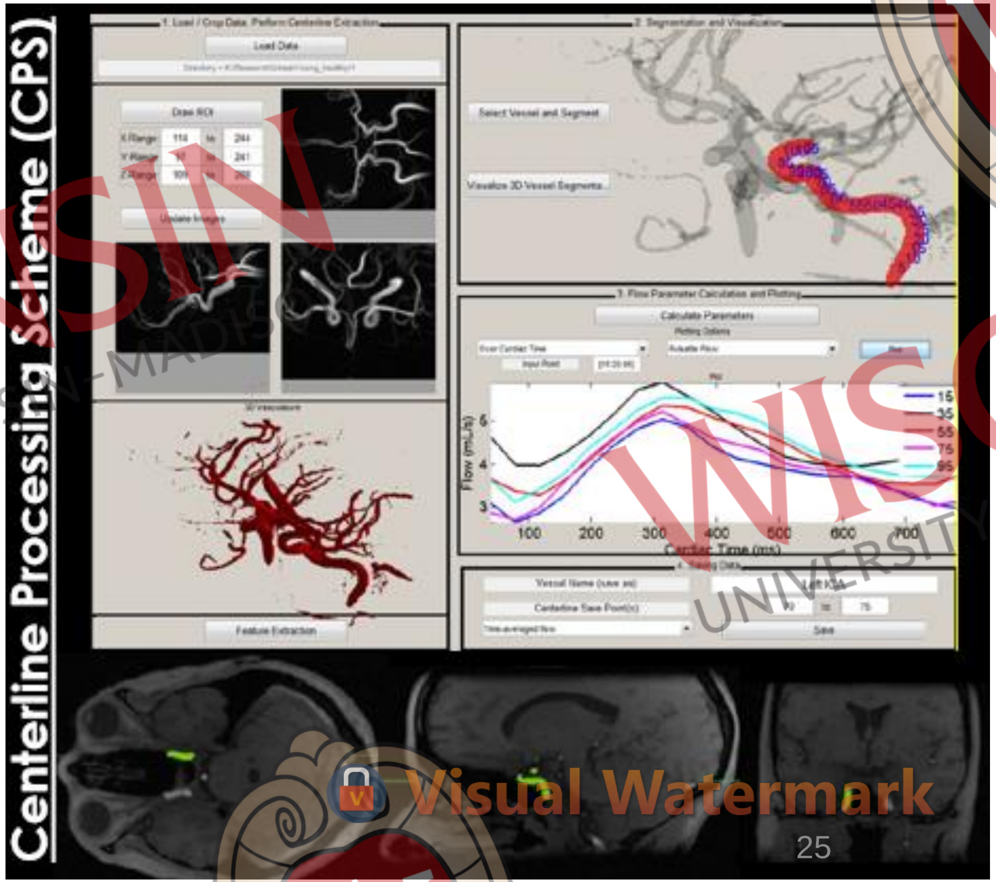




Aim 1 – Motivation

- Limited software tools for flow analysis in brain
  - Cerebral vessels – tortuous and small
  - Easy-to-use software required for efficient analysis
- Previous cranial 4D flow analysis tool (CPS)[1]
  - Eric Schrauben + Umea Sweden (2015)
  - Automated segmentation

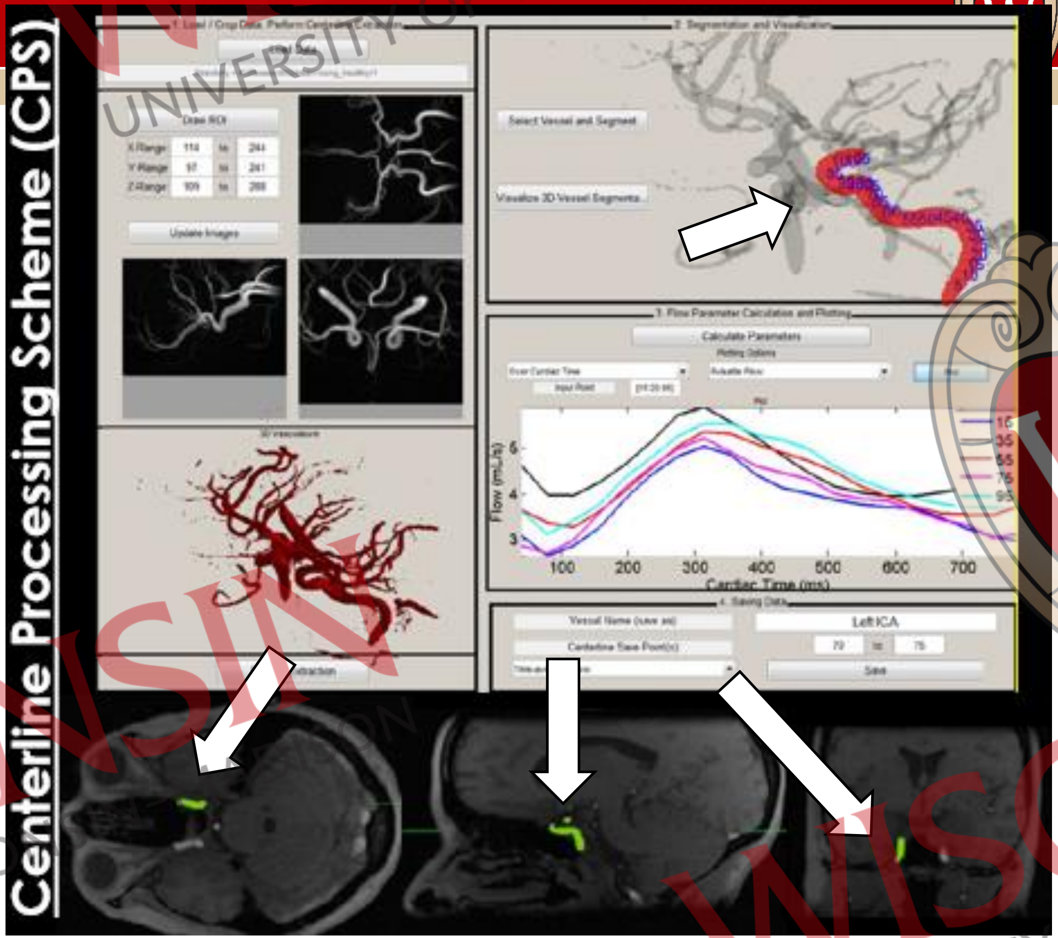
Eric Schrauben

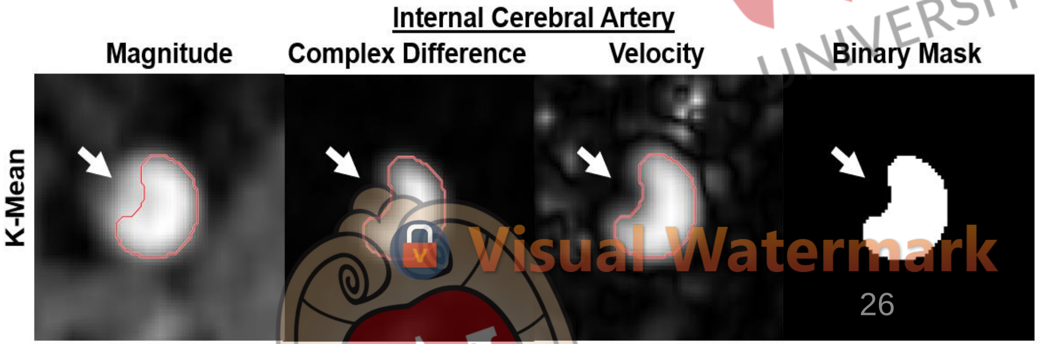


[1]Schrauben E, et al (2015). *JMRI*. 42(5):1458-64

Aim 1 – Motivation

- Limited software tools for flow analysis in brain
  - Cerebral vessels – tortuous and small
  - Easy-to-use software required for efficient analysis
- Previous cranial 4D flow analysis tool (CPS)[1]
  - Eric Schrauben + Umea Sweden (2015)
  - Automated segmentation
- There were several limitations with this tool
  - Difficult to select vessels of interest
  - Poor angiogram/flow visualizations
  - Lengthy processing times (>15 minutes)
  - K-means segmentation underestimates[2]



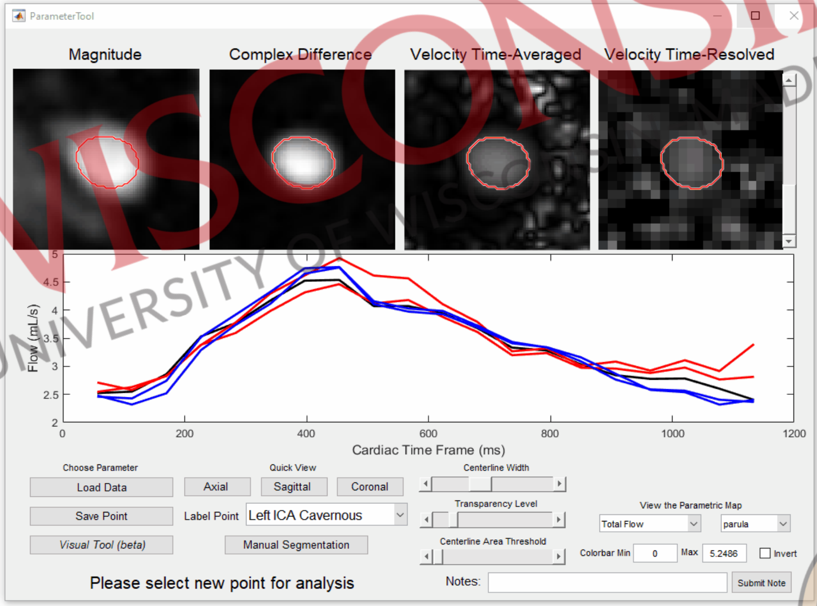


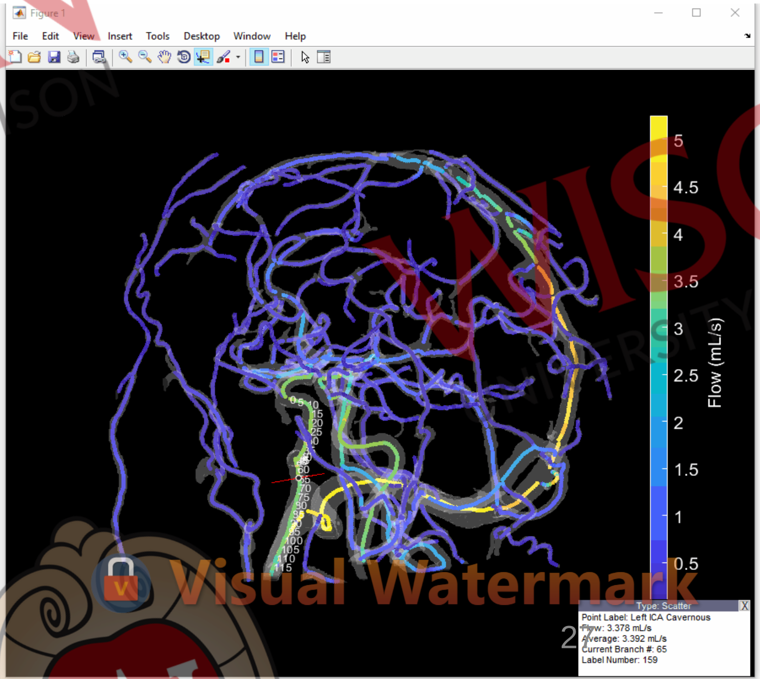
[1]Schrauben E, et al (2015). *JMRI.* 42(5):1458-64
[2]Dunas T, et al (2019). *JMRI.* 50(2):511-8

Aim 1

- Develop an improved "quantitative velocity tool"(QVT)[1,2]
  - Interactive 3D vessel selection
  - Improve vessel segmentation
    - Automated threshold-based method
  - **Reduce processing times** (faster flow quantification)
  - Publicly available: https://github.com/uwmri/QVT
- Validate Tool
  - In vitro (flow phantom)
  - In vivo (10 healthy volunteers)
  - **Compare CPS and QVT head-to-head**

Carson Hoffman



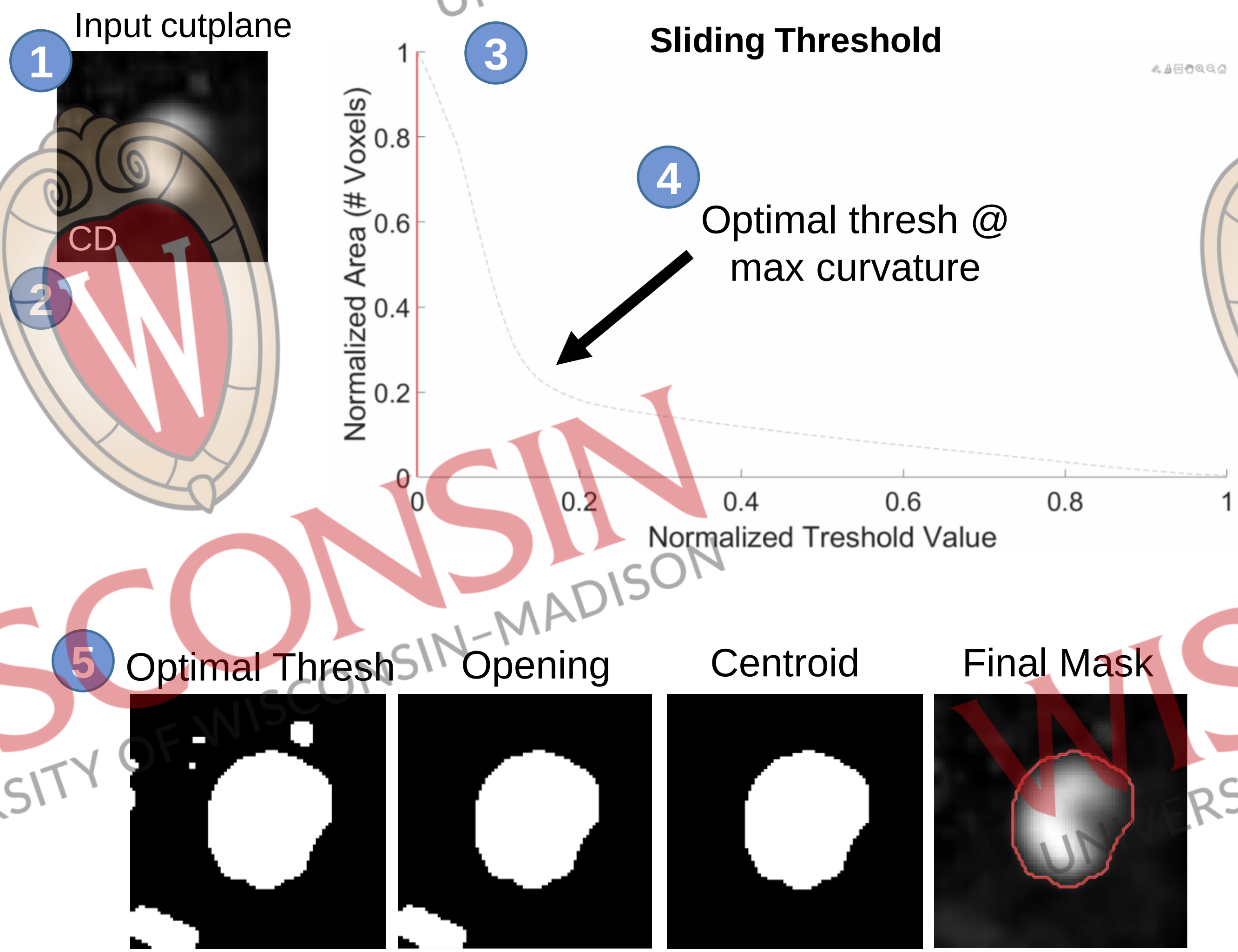


[1]Hoffman CA, et al (2019). *SMRA.* p.80
[2]Roberts and Hoffman, et al (2022). *MRI.* 97:46-55

Methods – Sliding Threshold Segmentation

- In-Plane Segmentation
  - “Sliding threshold” method

1. Take initial cut-plane
2. Segment image over large range of threshold values
3. Plot sum of non-zero voxels as a function of threshold value
4. Set threshold as point of max curvature
5. Clean binarized image



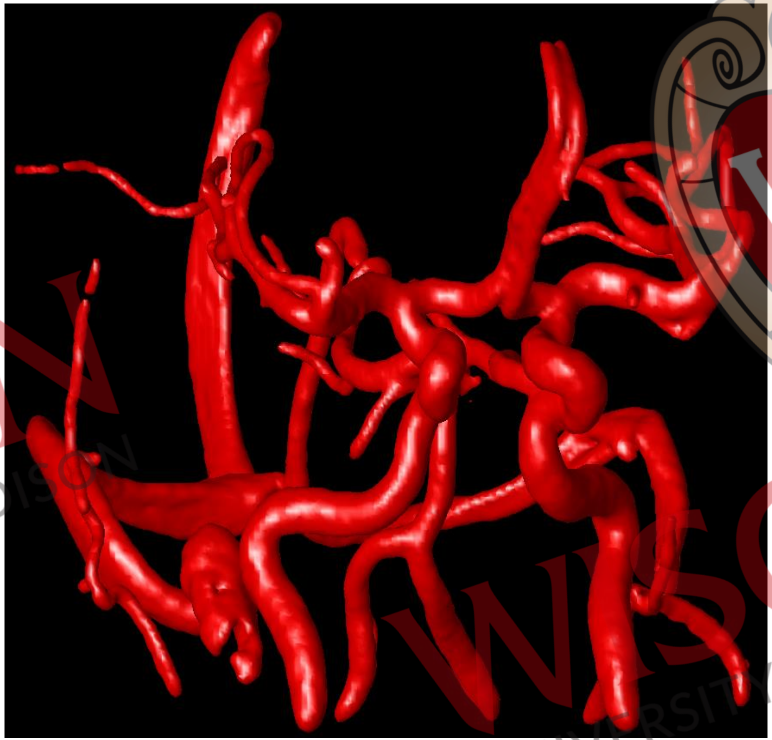
Methods – MRI Parameters

- ADRC Scan Protocol
  - 3T MR750 (GE Healthcare)
  - 4D Flow MRI
    - Radial acquisition (PCVIPR[1,2])
  - Spatial resolution: 0.68 mm
  - V_{enc} = 80 cm/s
  - Scan Duration: 7 min
  - 5-point velocity encoding
- Reconstruction
  - Retrospective cardiac gating
  - 20 cardiac phases

***In Vitro*: Intracranial Flow Phantom**

Scans: 7 pulsatile flow rates (0.8-1.2 L/min)

***In Vivo*: Healthy Controls**



Scans: 10 healthy volunteers

[1]Gu TL, et al (2005). *AJNR*. 26(4):743–9
[2]Johnson KM, et al (2008). *MRM*. 60(6):1329-36

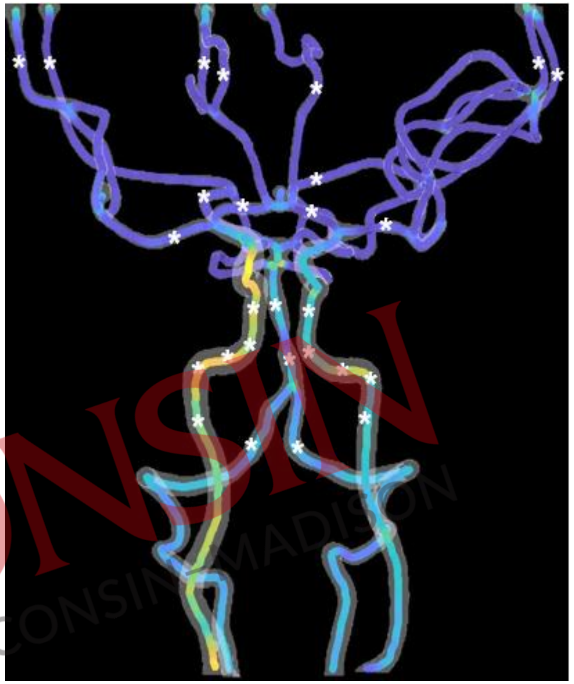
Methods – Segmentation Validation

- 4D Flow MRI
  - QVT (new tool)
    - Threshold segmentation
  - CPS (old tool)
    - K-means segmentation

- *In Vitro*
  - **Reference: Hi-Res CT**
  - Vessel areas
    - 27 locations x 7 flow rates

Cone Beam CT

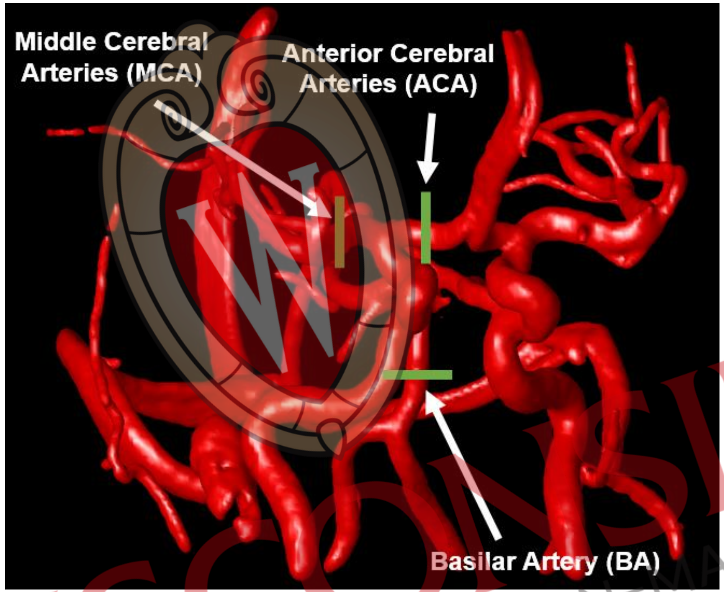
Measurement Locations (*)

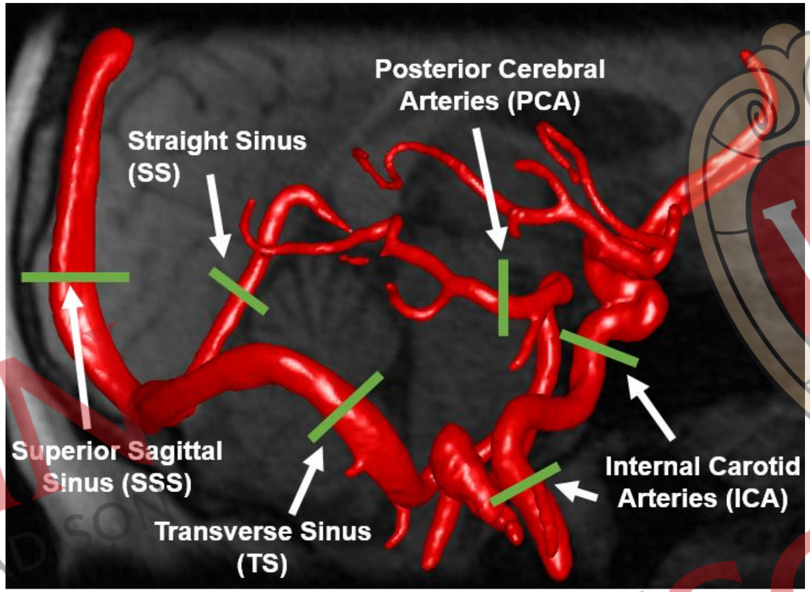


Co-Registered CT-MRI

Methods – Segmentation Validation

- 4D Flow MRI
  - QVT (new tool)
    - Threshold segmentation
  - CPS (old tool)
    - K-means segmentation





- *In Vitro*
  - **Reference: Hi-Res CT**
  - Vessel areas
    - 27 locations x 7 flow rates
- *In Vivo*
  - **Reference: Manual Segmentation**
  - Vessel areas and Dice coefficients
    - 13 locations x 5 neighboring planes x 10 subjects

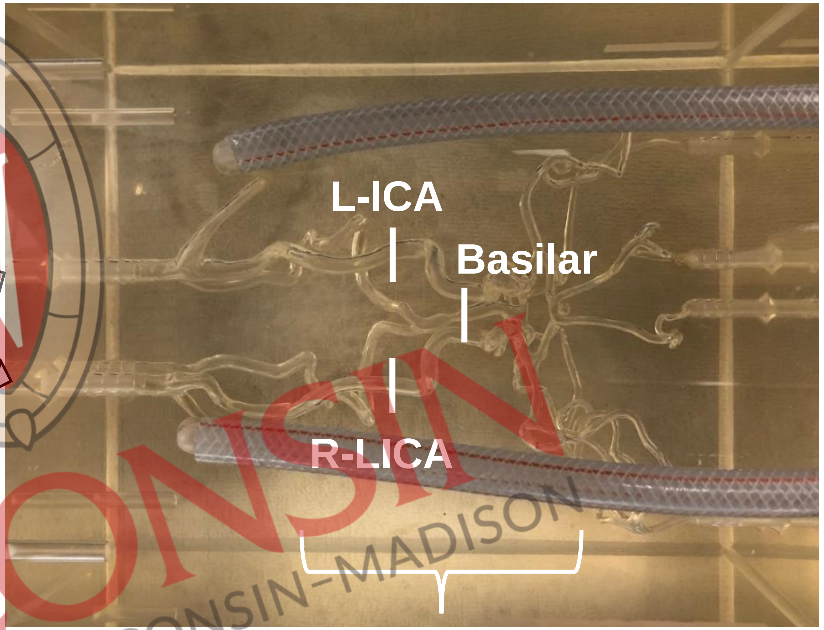
Methods – Flow Validation

- 4D Flow MRI
  - QVT – Flow Rates

- *In Vitro*
  - **Reference: Ultrasound**
  - Inlet/Outlet flow
    - 7 flow rates

US Flow
Pump Outlet

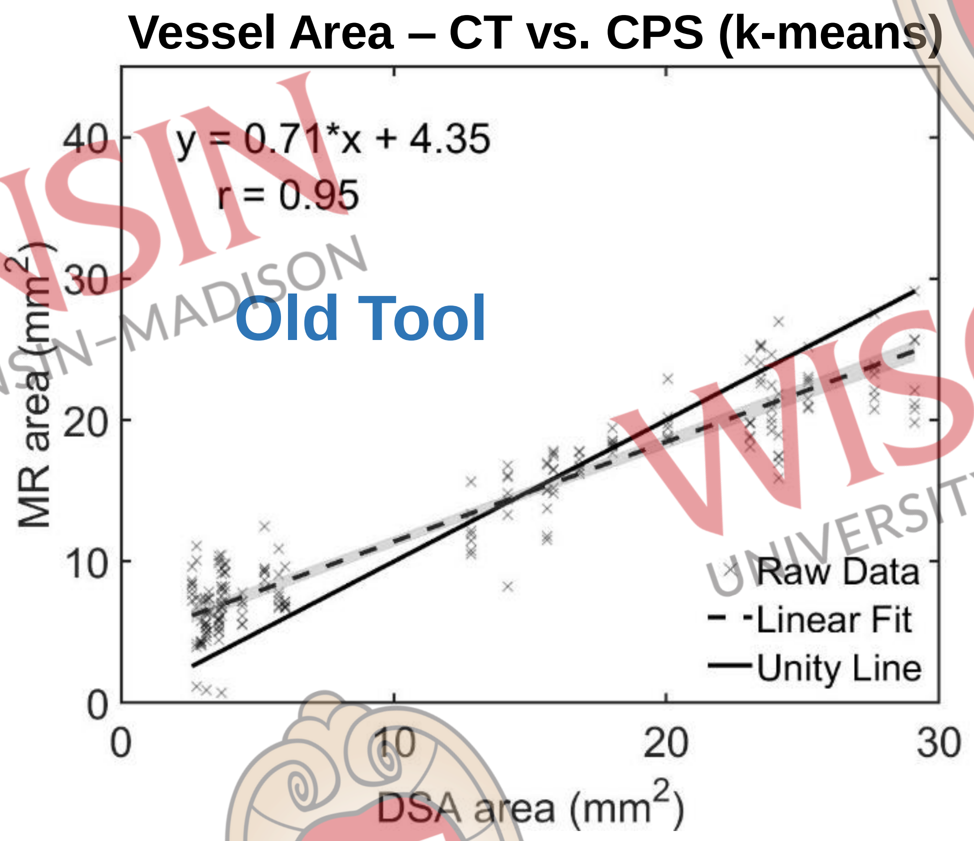
Silicon Phantom

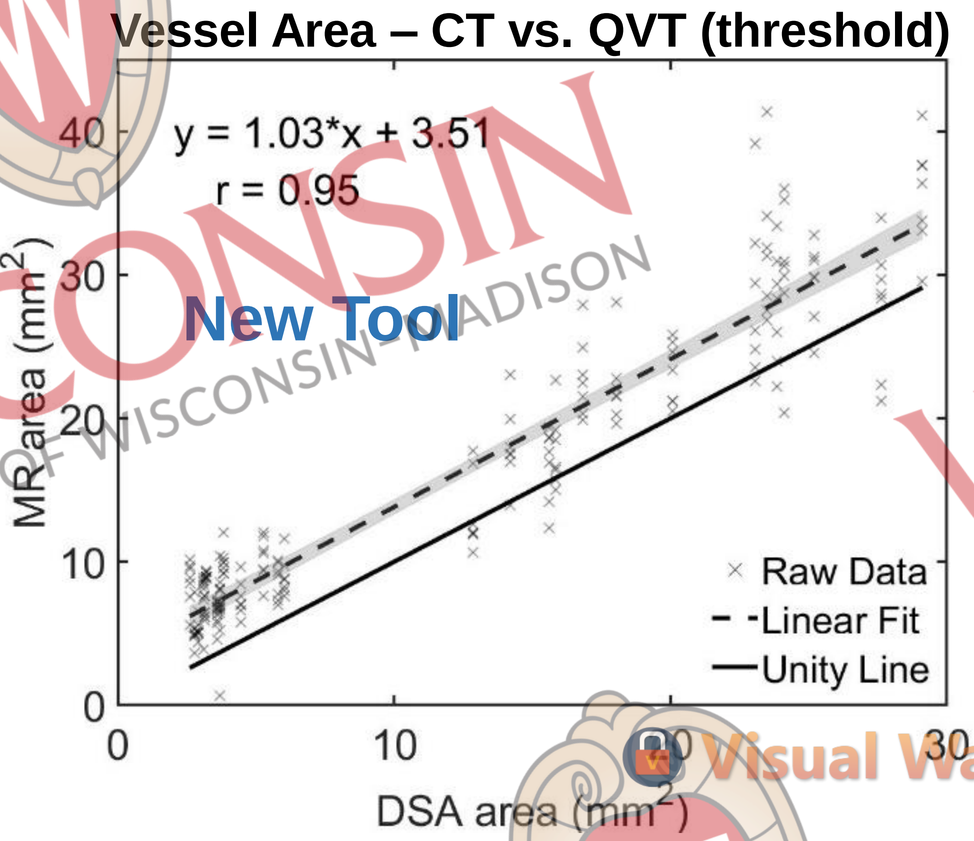


MRI Flow
Phantom Inlet

Results – Segmentation In Vitro

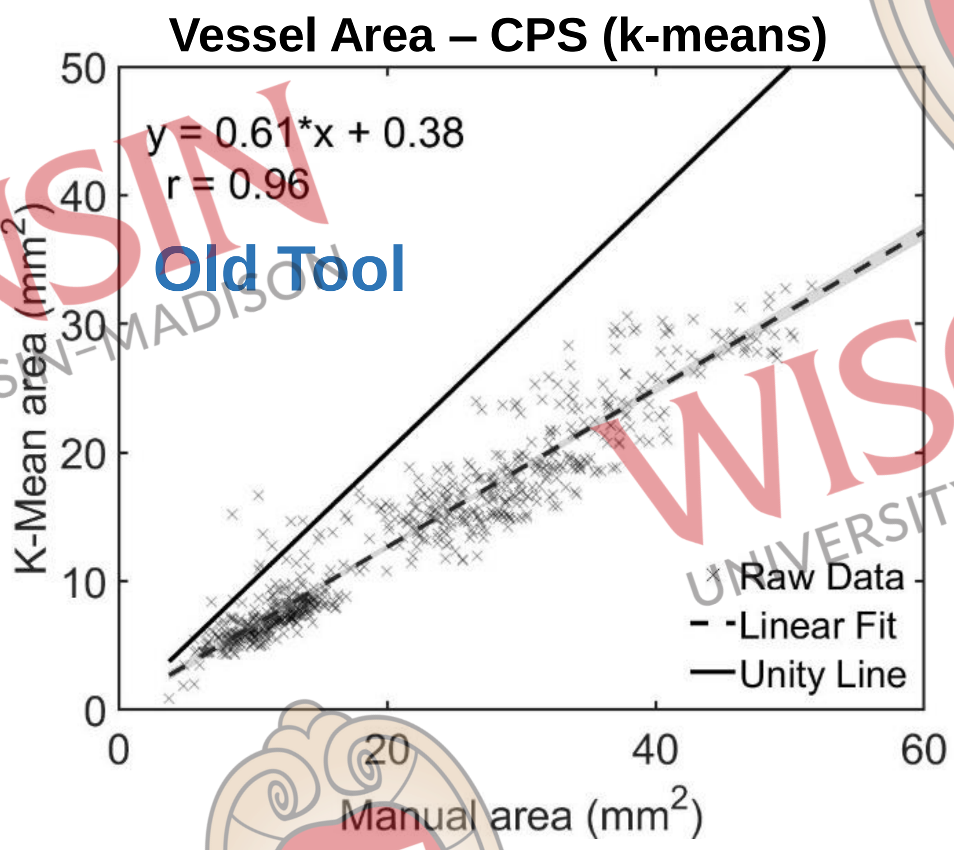
- **Reference: Hi-Res CT**
- Vessel areas
  - 29 vessel locations x 7 flow rates

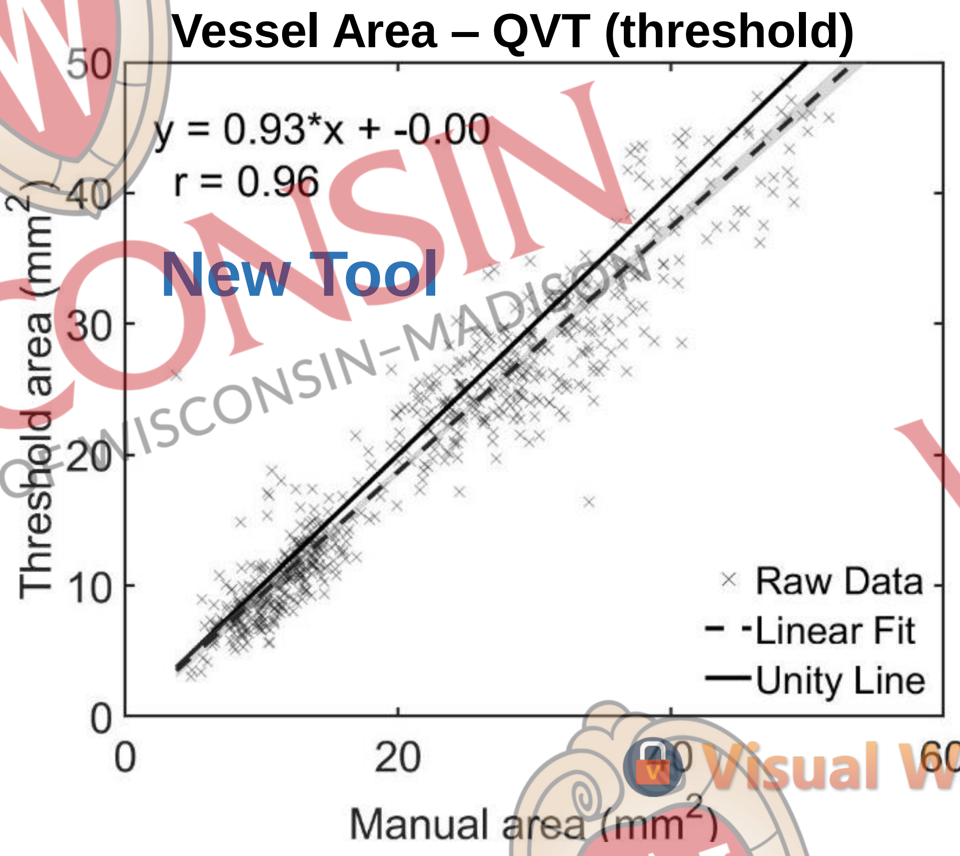




Results – Segmentation In Vivo

- **Reference: Manual Segmentation**
- Vessel areas
  - 13 locations x 5 neighboring planes x 10 subjects

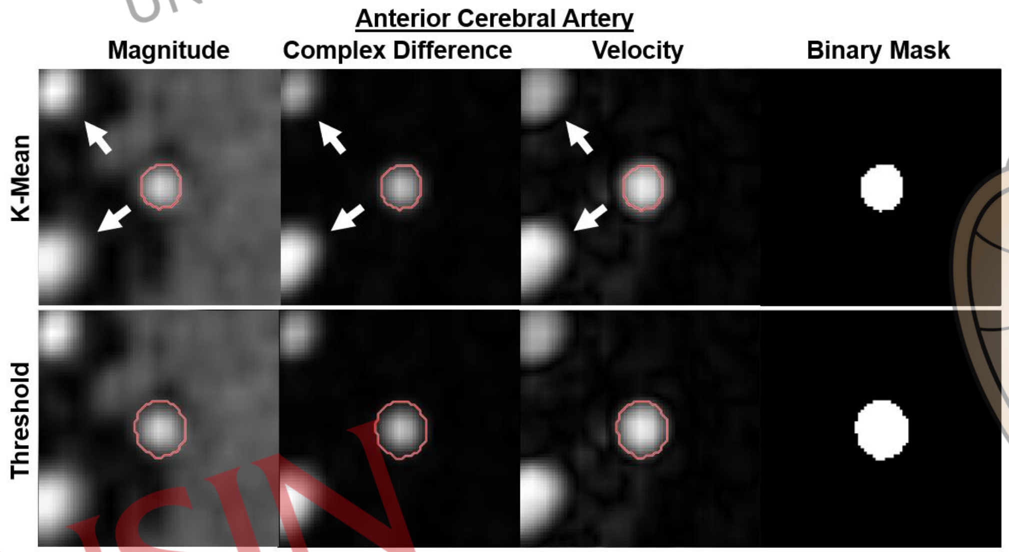


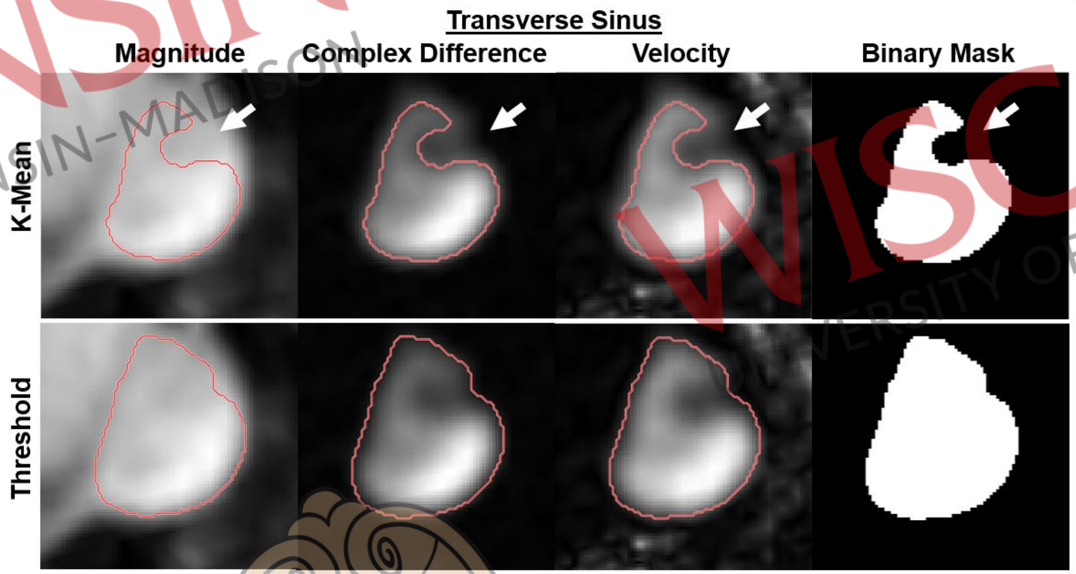


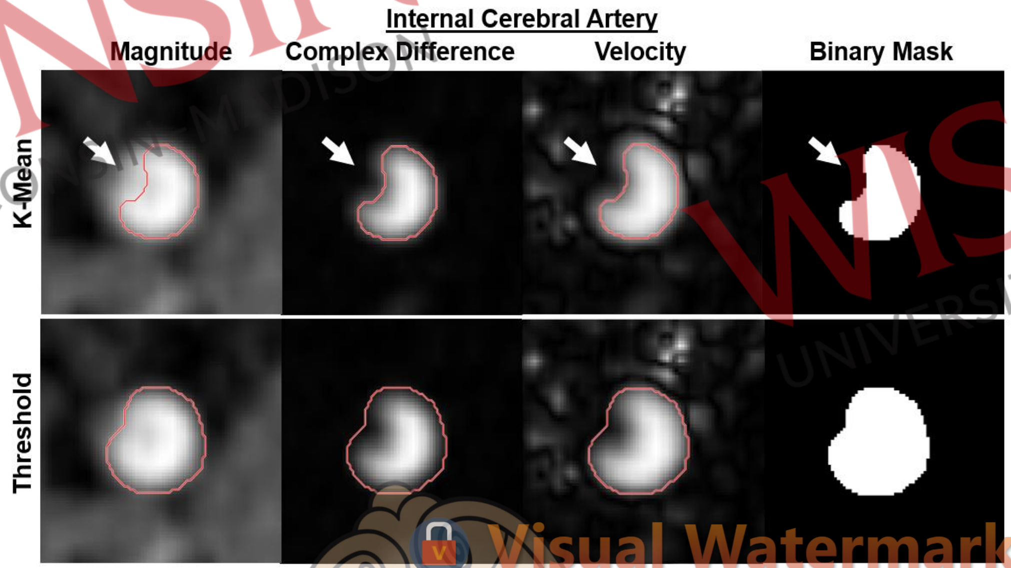
Results – Segmentation In Vivo

- **Reference: Manual Segmentation**
- Dice coefficients
  - 13 locations x 5 neighboring planes x 10 subjects

K-means vs. Manual = **0.77** ± 0.07
Threshold vs. Manual = **0.91** ± 0.06



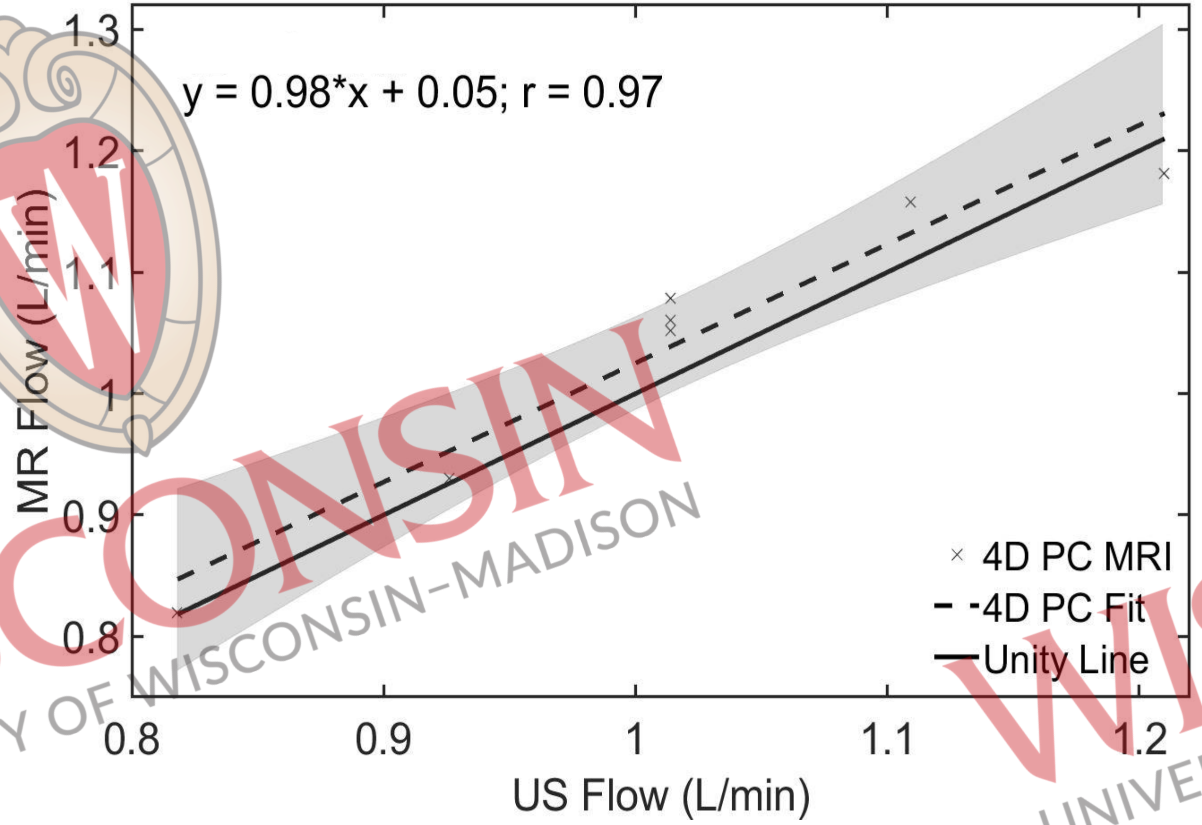




Results – Flow In Vitro

- **Reference: Ultrasound**
- Inlet vs. Outlet Flow
  - 7 flow rates (0.8 – 1.2 mL/min)

Flow Rates – US vs. QVT

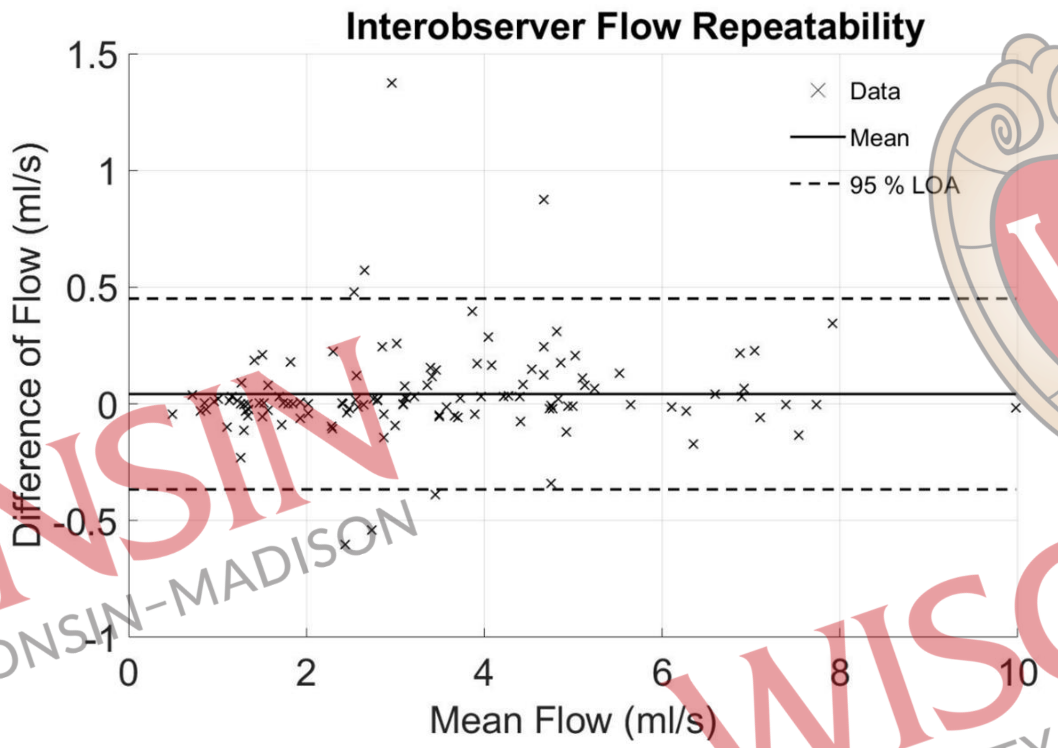


Results – Flow In Vivo

- Flow measures repeatable between observers
- Processing times reduced by >2x

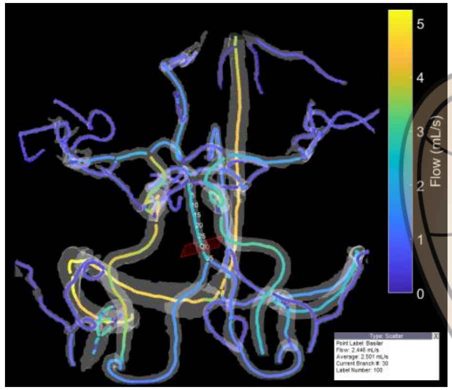
Table 1: Post-Processing Times for CPS and QVT Methods					
Method	Angiogram (min)	Load Data* (min)	Vessel Select (min)	Total Case (min)	Per Plane (min)
CPS	0.8 ± 0.1	1.0 ± 0.2	15.6 ± 3.4	17.5 ± 3.4	1.2 ± 3.2
QVT	0.2 ± 0.02	2.3 ± 0.4	4.7 ± 0.9	7.94 ± 1.0	0.4 ± 1.0

*Data loading for QVT included saving reloadable MATLAB file structures.

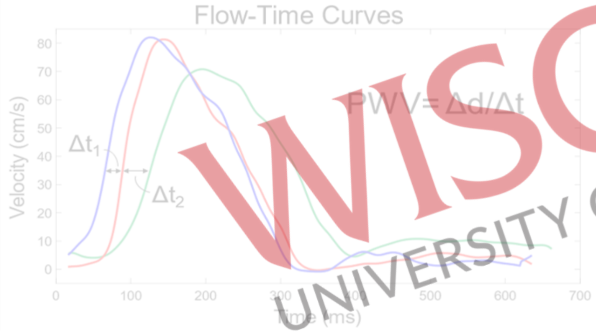


Outline

- **Background**
- **Part 1:** Cranial 4D Flow MRI
  - Aim 1: Develop 4D flow MRI tool for efficient flow analysis in the brain
  - Aim 2: Establish “normal” intracranial blood flow and pulsatility in 759 older adults



- **Part 2:** Aortic Pulse Wave Velocity
  - Aim 3: Implement a free-breathing, radial 2D phase contrast sequence to assess aortic pulse wave velocity
  - Aim 4: Develop a simultaneous multislice sequence for aortic pulse wave velocity assessment

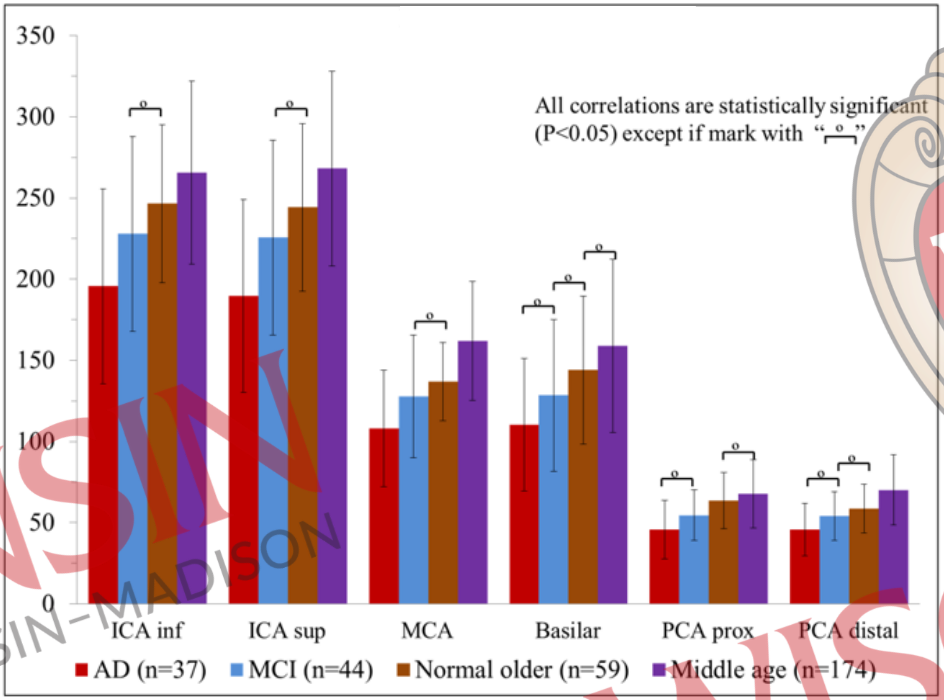


- **Summary**

Aim 2 – Motivation

- Relationship with Alzheimer's disease (AD)
  - Macrovascular changes[1-3]
  - Microvascular (perfusion) changes[4]
  - Normative data is still lacking
- Important to determine normal cerebrovascular hemodynamics in older adults

Blood Flow (mL/min)

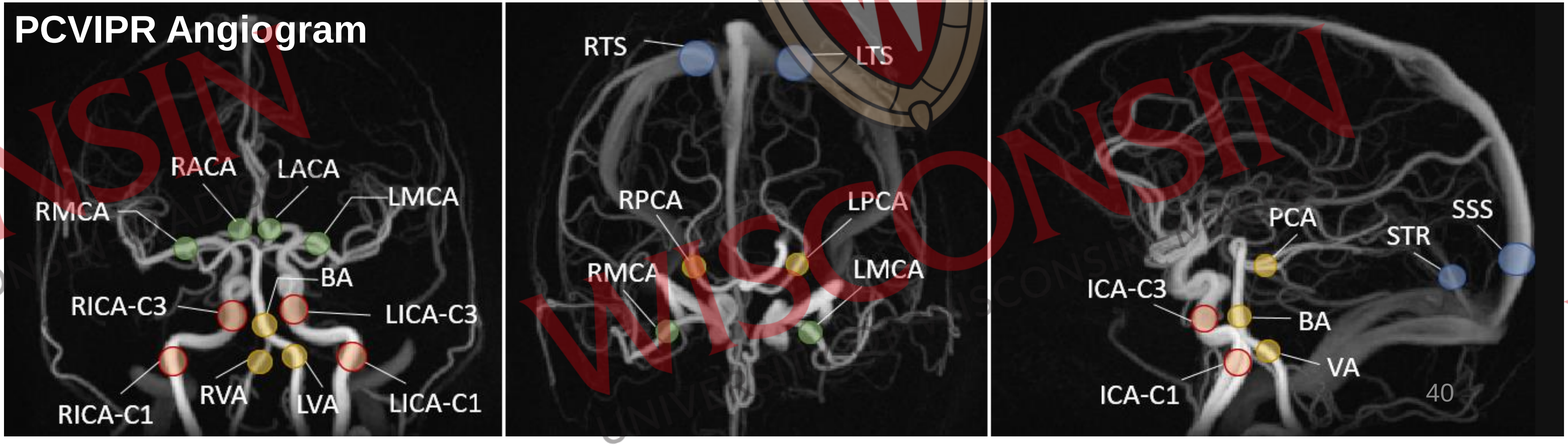


Courtesy: Leonardo Rivera-Rivera, PhD

[1]Rivera-Rivera LA, et al (2016). *JCBFM.* 36(10):1718-30
[2]Rivera-Rivera LA, et al (2017). *JCBFM.* 37(6):2149-58
[3]Rivera-Rivera LA, et al (2020). *NeuroImage Clin.* 28
[4]Clark LR, et al (2017). *Alzheimers Dement.* 7:48-55

Aim 2

- Use QVT to analyze 4D flow MRI data from 759 older adults
  - Establish reference blood flow rates and pulsatility indices in 13 major cerebral arteries and 4 major sinuses
  - Assess the relationship between age and sex on blood flow and pulsatility



Methods – Study Population

- Subjects retrospectively recruited from:
  - Wisconsin Alzheimer's Disease Research Center (ADRC)
  - Wisconsin Registry for Alzheimer's Prevention (WRAP)
  - Between March 2010 – March 2020
- Exclusion criteria:
  - Abnormal cognitive status
  - PiB index > 1.19[1]
  - Image quality and cardiac gating quality
- **759 subjects (mean age 65 years)**
  - Some measures deviate from "normal"
    - Sex (67% females)
    - APOE4 carriers
    - Parental history of dementia

Subject demographics

	Count (n)	Percent (%)	N*
Sex			759
Female	506	66.7	
Male	253	33.3	
Race			757
White	645	85.3	
Black or African American	82	10.7	
American Indian	24	3.2	
Asian	2	0.3	
Other	4	0.5	
Diabetes	63	9.1	689
Smoker	29	4.2	689
On Anti-hypertensive Meds	240	34.8	689
Parental history of dementia	500	67.6	740
APOE ε4 carrier**	247	35.6	694

	Mean	SD	N*
Age (years)	64.7	7.7	759
Systolic Blood Press. (mmHg)	125.1	16.4	751
Diastolic Blood Press. (mmHg)	76.9	8.3	751
Total Cholesterol (mg/dL)	199.0	39.4	744
Triglycerides (mg/dL)	106.4	56.7	744

***Total number of measured data points over all subjects (759 total).**
****APOE ε4 carrier defined as presence of at least one APOE ε4 allele.**

[1]Tudorascu DL, et al (2018). *Alzheimers Dement.* 10:332-9

Methods – Acquisition, Reconstruction, Analysis

- Scan Protocol
  - 3T on 3 different GE scanners
  - Radially-undersampled PCVIPR
    - Scan time: 5-7 minutes
- Reconstruction
  - 20 cardiac frames
  - Temporal view sharing
- Analysis
  - Two observers analyzed 759 cases
    - Observer 1 = 302 cases (40%)
    - Observer 2 = 457 cases (60%)
  - Multiple linear regression
  - Linear mixed effects modelling


Anthony Peret


Erin Jonaitis


Rebecca Koscik

MRI Scanners and Coils

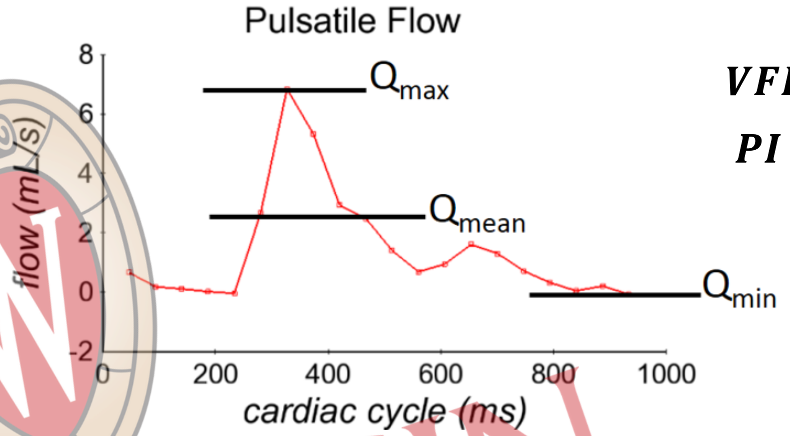
MRI Coil Type	Discovery MR750 (N=611)	Signa PET/MR (N=8)	Signa Premier (N=140)
48 channel	-	-	140
32 channel	565	-	-
8 channel	46	8	-

MRI Acquisition Parameters

Characteristic	Value
TR (ms)	7.71
TE (ms)	2.63
Flip Angle (degrees)	8
Matrix Size	320
Resolution Size (mm)	0.69
Radial Projections	11000
VENC (cm/s)	80
Encoding Scheme	4-point (58%)
	5-point (42%)
Scan Time (min)	5.6 (58%)
	7.1 (42%)

Methods – Post-Processing

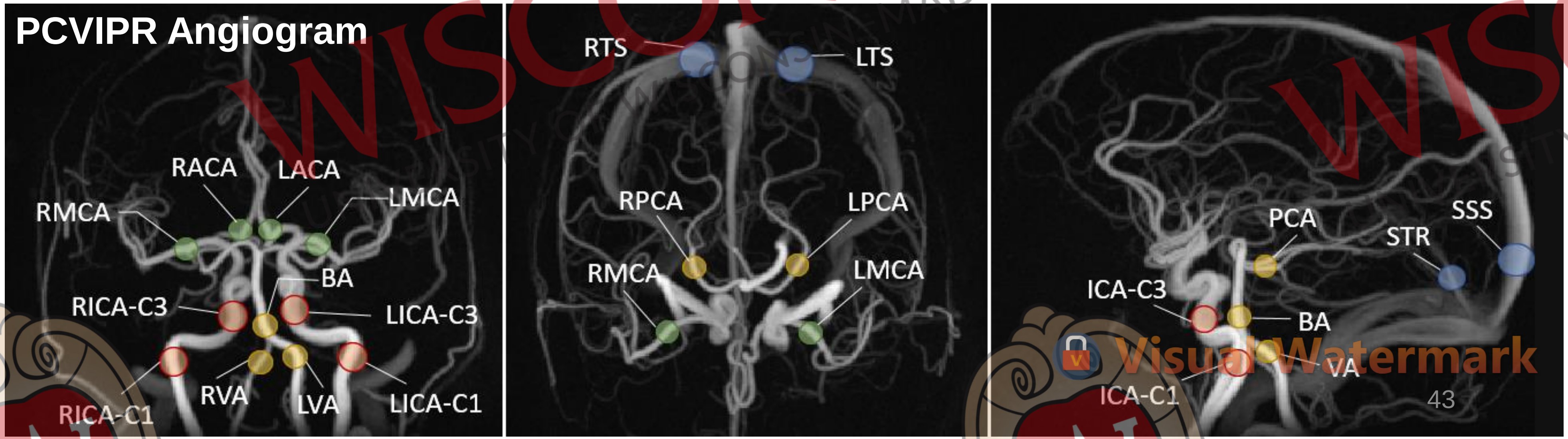
- Hemodynamic Measures
  - **Volumetric Flow Rates** (mL/min)
  - **Pulsatility Indices** (a.u.)
  - **Total Cerebral Blood Flow** (mL/min)
    - $TCBF = Q_{LICA} + Q_{RICA} + Q_{BA}$
- Vessel Segment Locations
  - 13 arteries + 4 veins



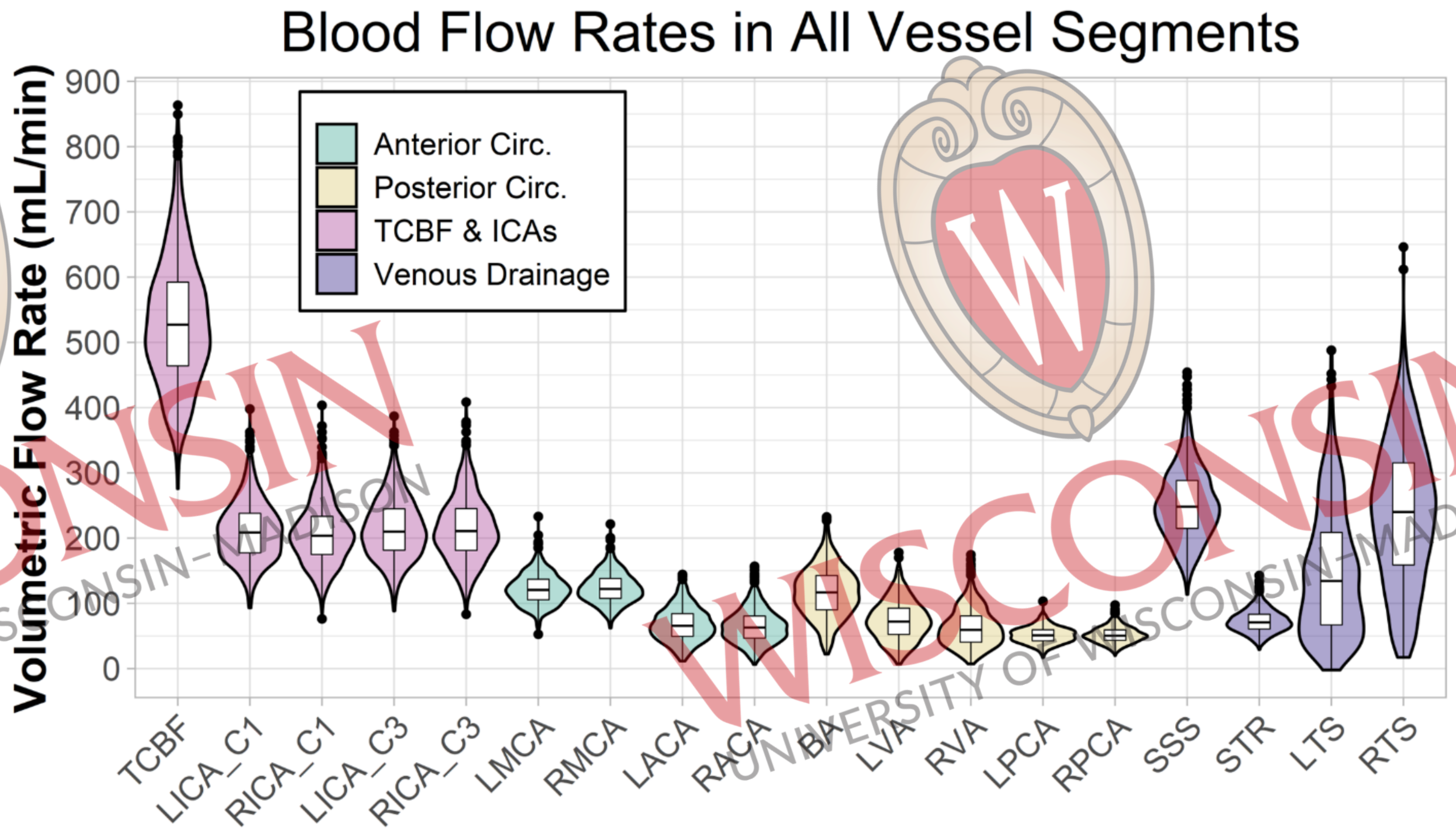
$$VFR = Q_{mean}$$

$$PI = (Q_{max} - Q_{min})/Q_{mean}$$

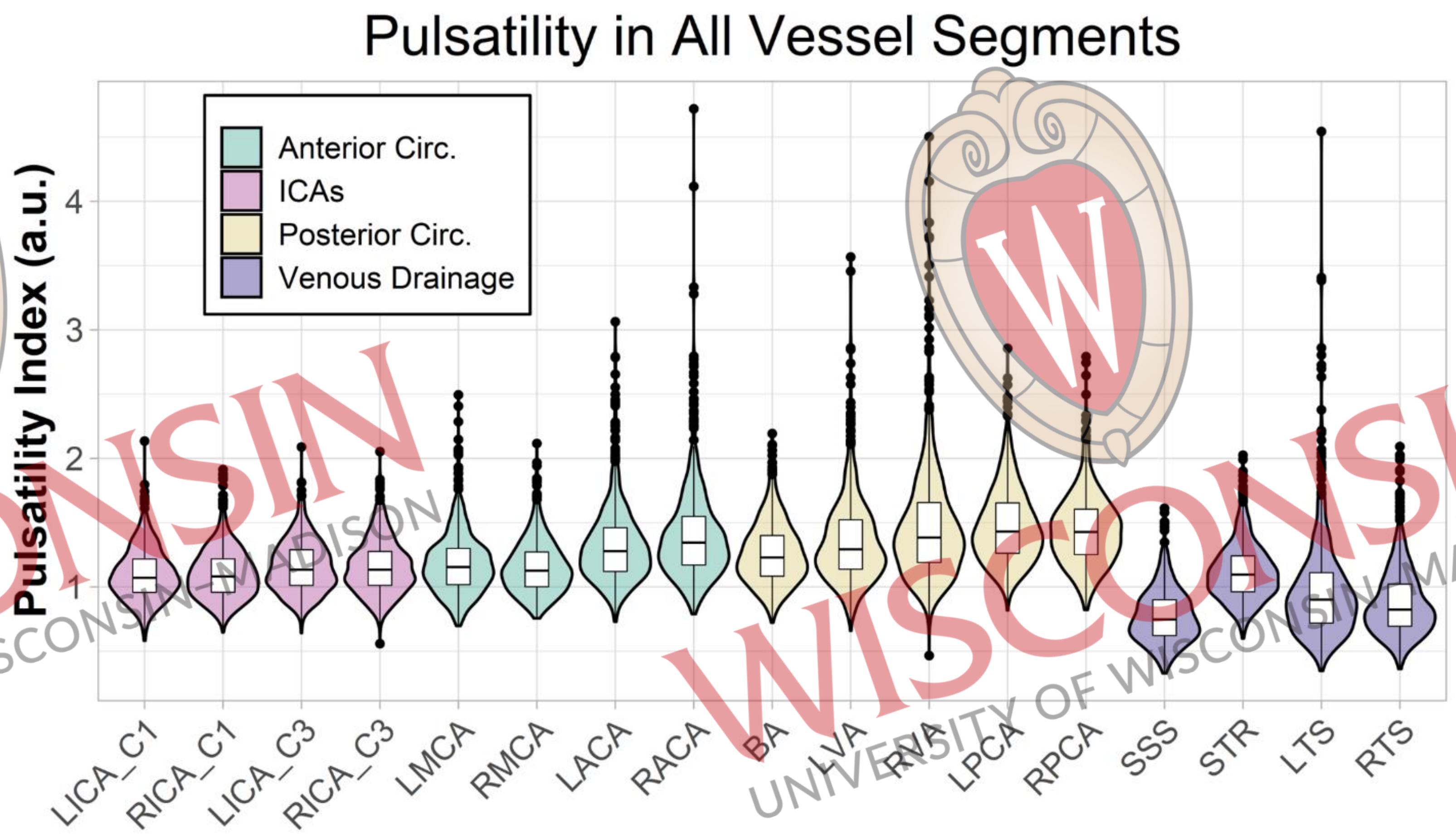
Vessel
Total Cerebral Blood Flow (TCBF)
Cervical ICA (RICA-C1)
Cavernous ICA (RICA-C3)
Middle Cerebral Artery (MCA)
Anterior Cerebral Artery (ACA)
Basilar Artery (BA)
Vertebral Artery (VA)
Posterior Cerebral Artery (PCA)
Superior Sagittal Sinus (SSS)
Straight Sinus (STR)
Transverse Sinus (TS)



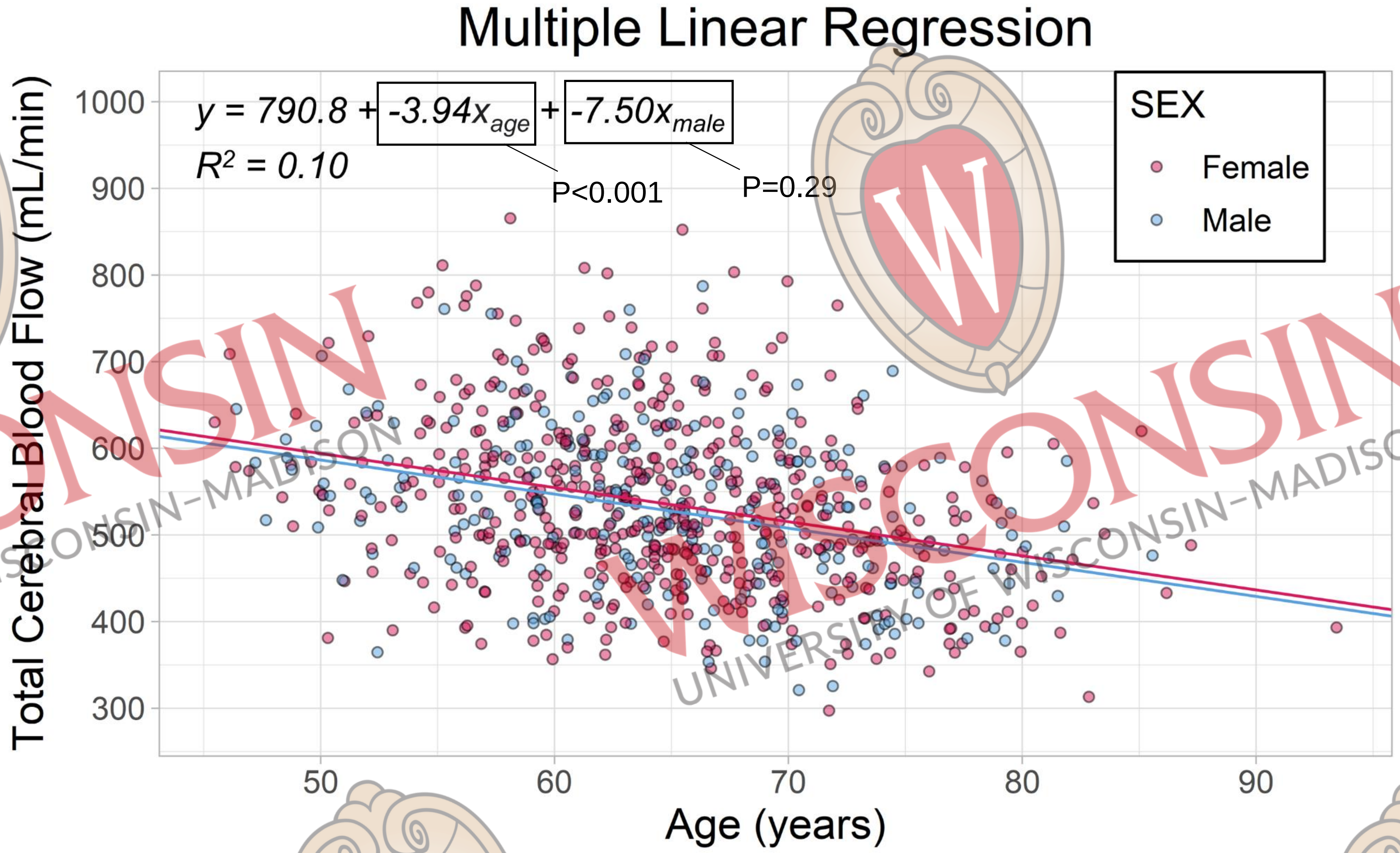
Results – Blood Flow Rates



Results – Pulsatility



Results – Total Flow vs. Age/Sex

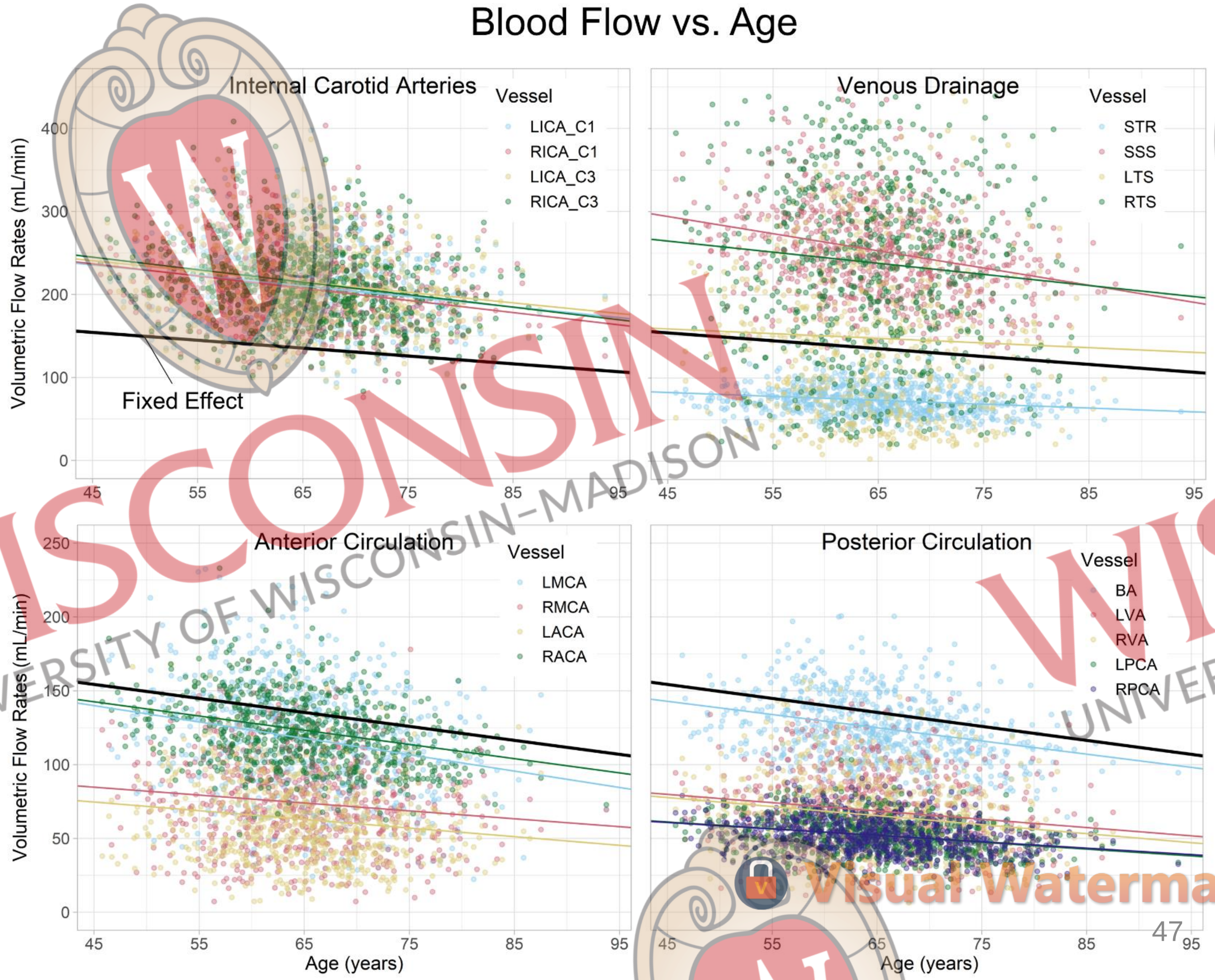


Results – Flow vs. Age/Sex

Mixed Effects Regression: Flow ~ Age + Sex + (1 + Age | Vessel) + (1 | Participant)

	β (coefficients)		
	Intercept	Age	Sex (male)
FIXED EFFECT	**135.4*** **	**-0.95*** **	-1.60
ICA_C1	295.4	-1.33	
ICA_C3	305.4	-1.38	
MCA	188.4	-0.98	
ACA	115.9	-0.72	
BA	198.4	-1.23	
VA	117.6	-0.72	
PCA	88.5	-0.55	
TS	247.0	-0.47	
STR	111.7	-0.58	
SSS	386.0	-2.04	

T-Tests using Satterthwaite's Method
*p<0.05
**p<0.01
***p<0.001

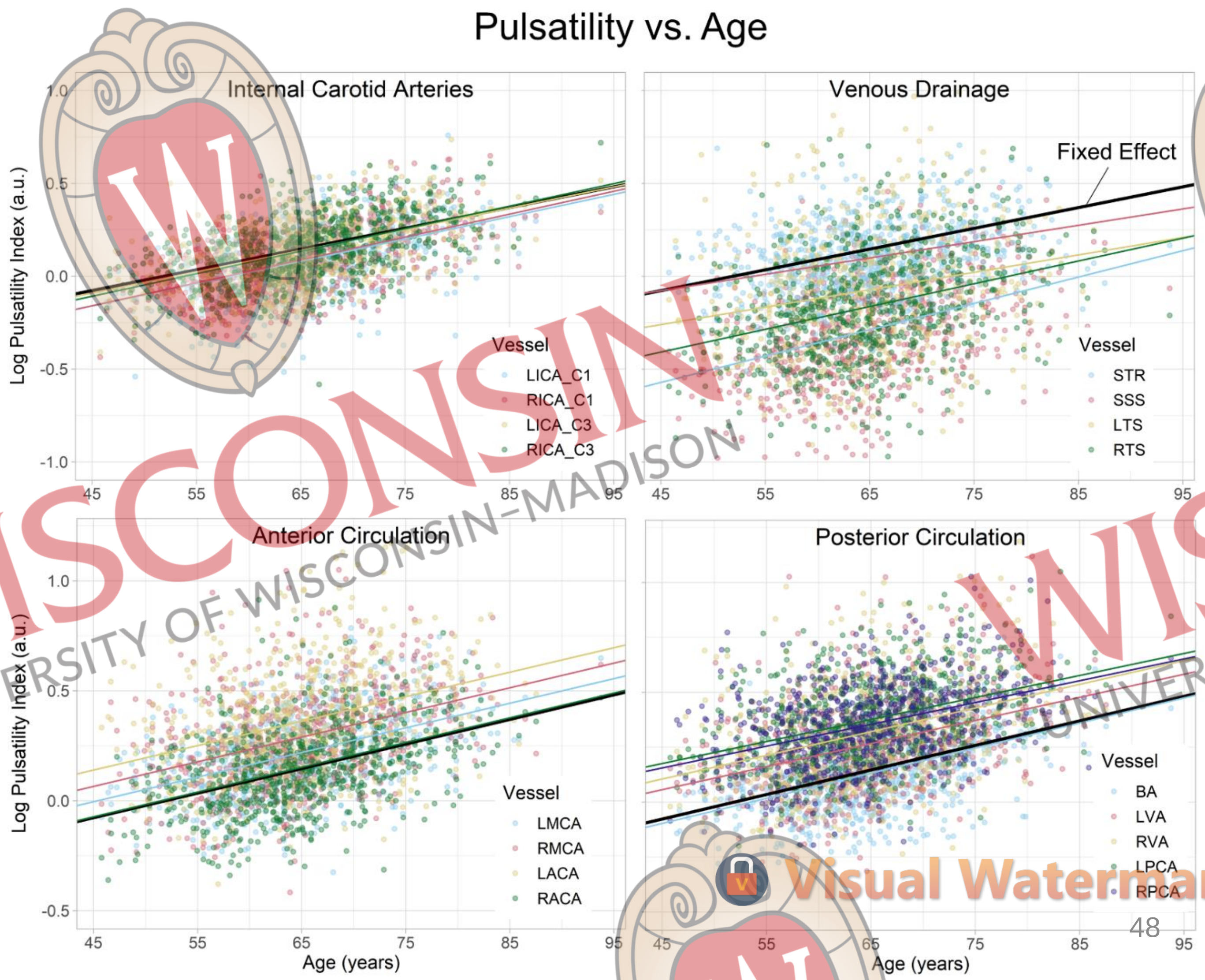


Results – Pulsatility vs. Age/Sex

Mixed Effects Regression: PI ~ Age + Sex + (1 + Age | Vessel) + (1|Participant)

	β (coefficients)		
	Intercept	Age	Sex (male)
FIXED EFFECT	**0.146****	**0.011*****	**-0.018***
ICA_C1	0.174	0.014	
ICA_C3	0.227	0.014	
MCA	0.271	0.014	
ACA	0.333	0.016	
BA	0.286	0.015	
VA	0.329	0.017	
PCA	0.441	0.016	
TS	0.211	0.011	
STR	0.405	0.011	
SSS	0.069	0.011	

T-tests using Satterthwaite's method
*p<0.05
**p<0.01
***p<0.001



Outline

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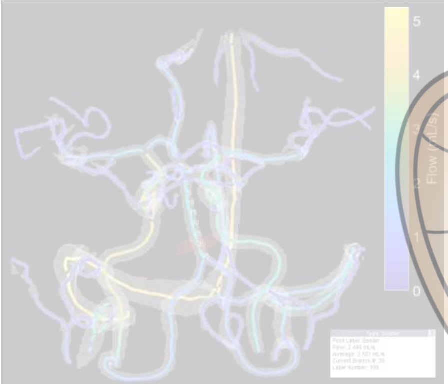
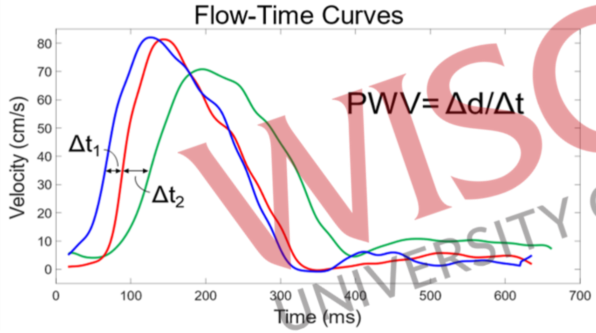
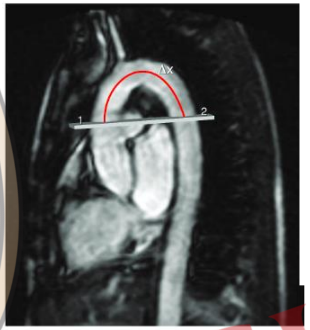
- Summary



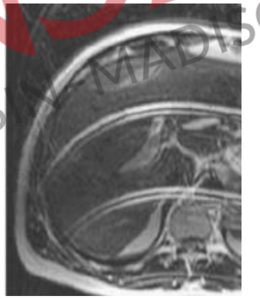


Aim 3 – Motivation

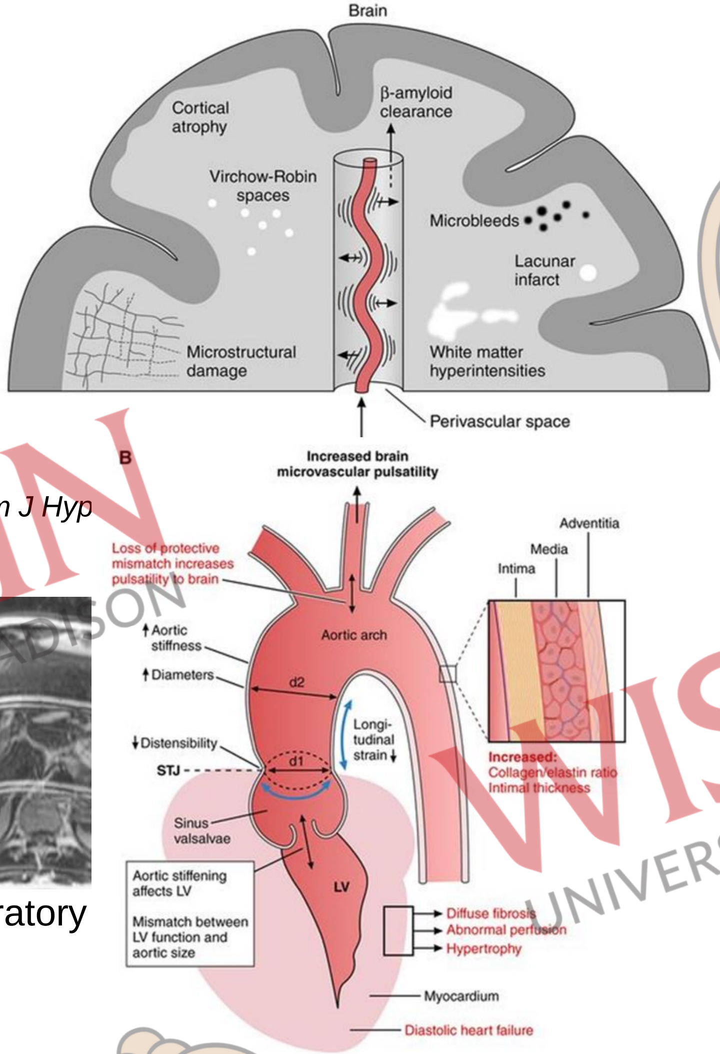
- Previously discussed clinical relevance aortic stiffness
  - Aortic stiffening propagates pulsatile energy
    - Gets transmitted to brain's microvasculature
- Aortic PWV has been measured with MRI[1]
  - Usually 1-2 imaging planes along aorta
  - Requires breath-holds ~10-20s
    - Reduce respiratory motion artifact
- Some subjects may have breath-hold difficulties
  - Elderly, dementia, or respiratory issues
  - Need free-breathing methodology for these subjects
    - Radial 2DPC MRI allows for this
- Older individuals may have higher PWV
  - May require higher temporal resolution[2]



Sala M, et al (2015). *Am J Hyp*



Respiratory

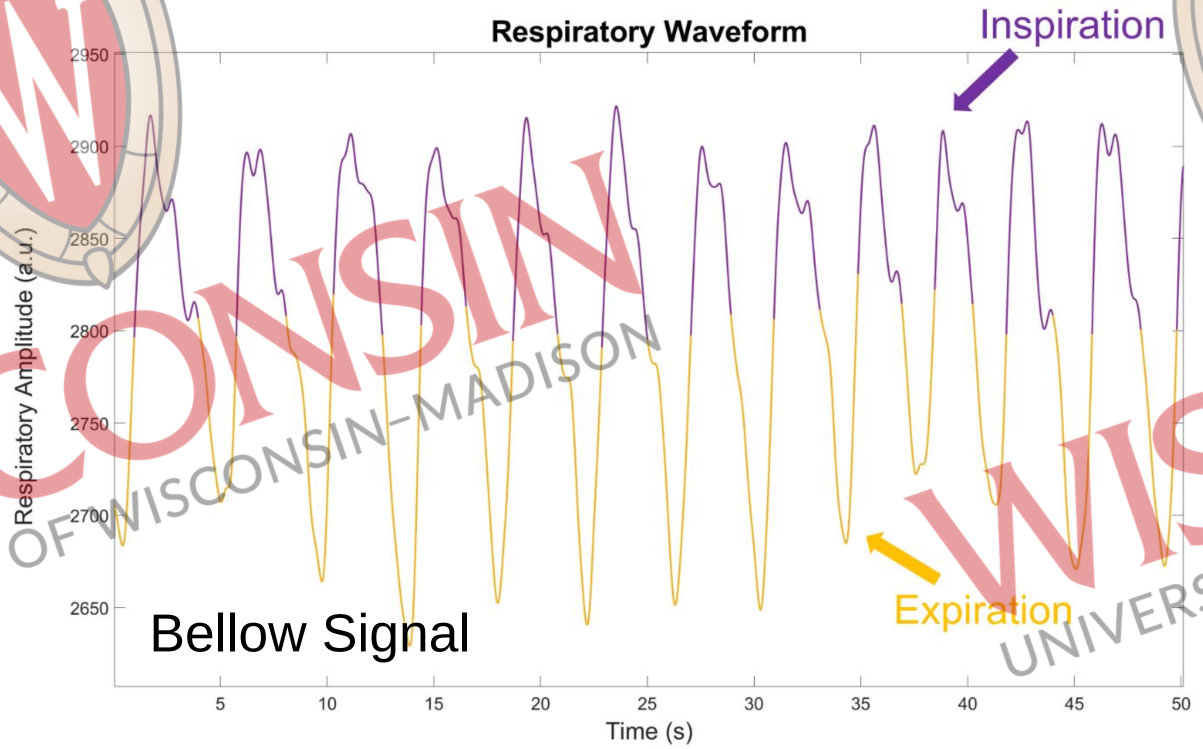


de Roos A, et al (2017). *Circulation*. 135(22):2178-95

[1]Wentland AL, et al (2014). *Cardiovasc Diagn Ther*. 4(2):193-206
[2]Dorniak K, et al (2016). *BMC Cardiovasc Disord*. 16(1):110

Aim 3

- Implement a novel free-breathing, radial 2DPC sequence to measure aortic pulse wave velocity (PWV) using retrospective respiratory gating
  - Compare to standard breath-hold Cartesian 2DPC sequence



Aim 3

- Implement a novel free-breathing, radial 2DPC sequence to measure aortic pulse wave velocity (PWV) using retrospective respiratory gating
  - Compare to standard breath-hold Cartesian 2DPC sequence
- Utilize local low rank (LLR) reconstruction[1,2] to improve temporal resolution

$$\hat{\mathbf{x}} = min_{\mathbf{x}} \left[\|\mathbf{Ax} - \mathbf{k}\|_2^2 + \sum \lambda_b \|\mathbf{R}_b \mathbf{x}\|_* \right]$$

Data fidelity term

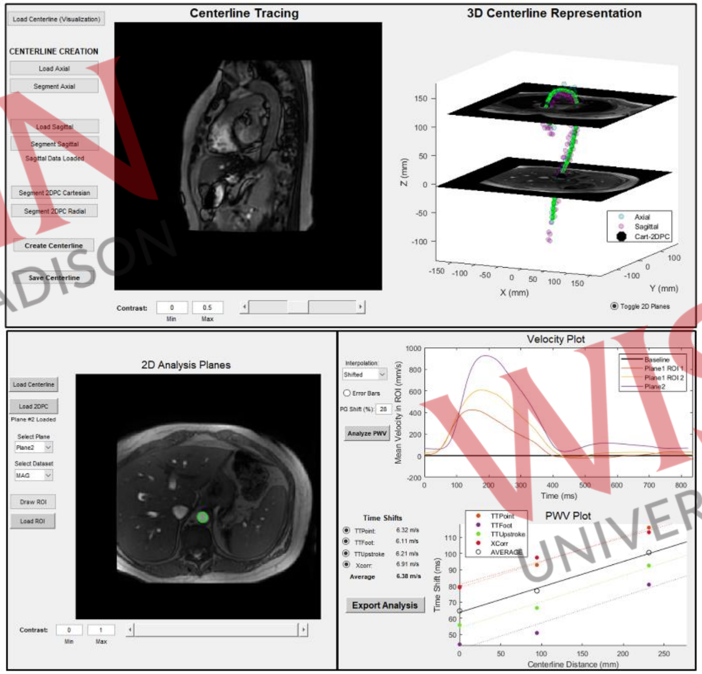
Temporospatial sparsity (low rank)

- $\hat{x}$ = optimized image
- **x** = image variable
- **A** = coil-sensitivity, FT, and sampling operator
- **k** = acquired k-space data
- || || = norm operator
- * = nuclear norm
- $\mathbf{R_b}$ = low rank operator acting on b_{th} local block
- λ_b = rank weighting coefficient

[1] Jimenez JE, et al (2018). *MRM*. 80(4):1452-66
[2] Rivera-Rivera LA, et al (2021). *JCBFM*. 41(2):298-311

Aim 3

- Implement a novel free-breathing, radial 2DPC sequence to measure aortic pulse wave velocity (PWV) using retrospective respiratory gating
  - Compare to standard breath-hold Cartesian 2DPC sequence
- Utilize local low rank (LLR) reconstruction[1,2] to improve temporal resolution
- Develop PWV post-processing package
  - Publicly available: https://github.com/gsroberts1/PWV_2DPC



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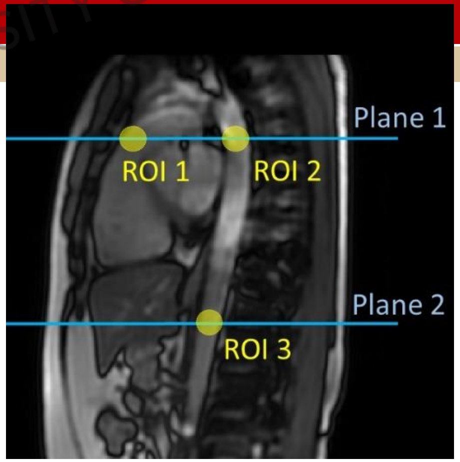
- Develop PWV post-processing package
  - Publicly available: https://github.com/gsroberts1/PWV_2DPC
- Validate our free-breathing PWV measures in an aorta flow phantom
- Measure aortic PWV in 150 older subjects from LIFE study
  - Assess intra/interobserver repeatability
  - Assess correlations PWV with age

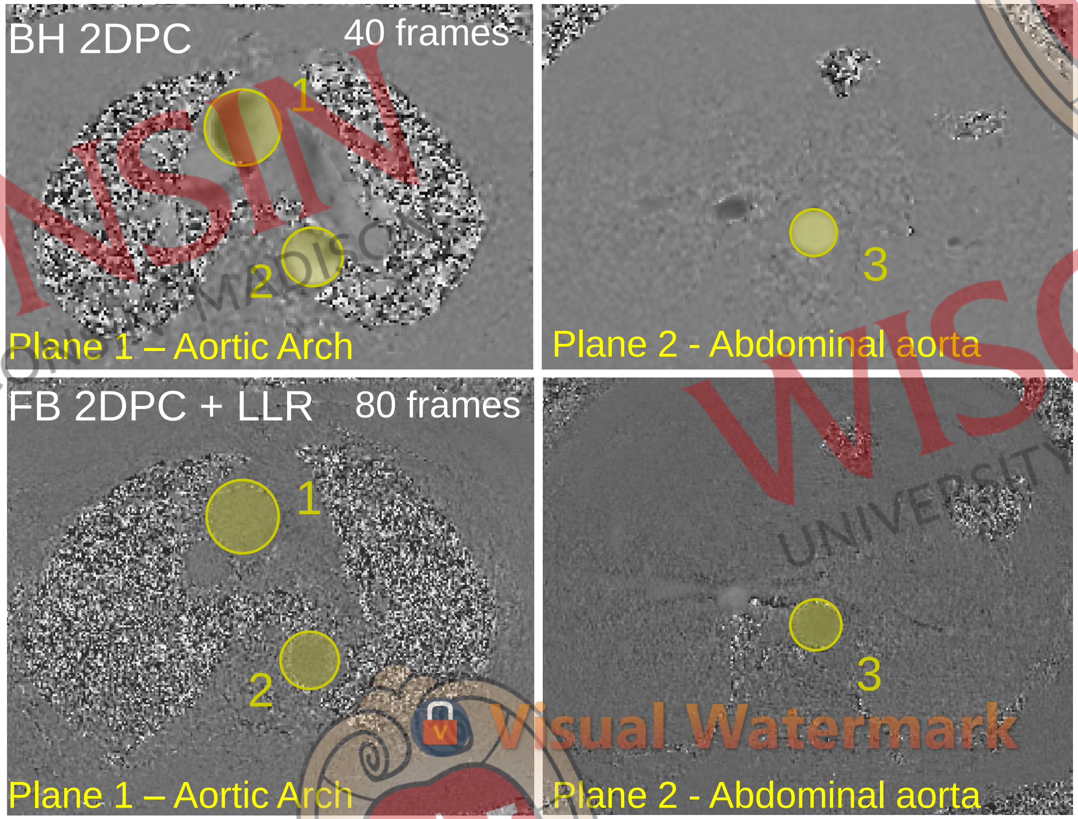
Methods – LIFE Study

- LIFE Study
  - Longitudinal Impact of Fitness and Exercise
    - Aerobic fitness on AD biomarkers
- Aortic PWV as metric of cardiovascular integrity

Ozioma Okonkwo



- MRI Protocol Overview
  - Anatomical bSSFP scan
    - Aorta structure
    - Scan time = 0:18
  - Breath-hold Cartesian 2DPC scan
    - 2 planes → aortic arch + abdominal aorta
    - Scan time = 0:15
  - Free-breathing radial 2DPC scan
    - 2 planes → aortic arch + abdominal aorta
    - Scan time = 2:29, projections = 10,000



Methods – 2DPC Protocol

- Participant demographics
  - **150 subjects (mean age 64 years)**
  - Demographics similar to normative study

Participant demographics		
Age (years)		64 ± 7 (48-74)
Sex		
	Female	84 (72%)
	Male	33 (28%)
Race*		
	Hispanic	1 (<1%)
	Black or African American	5 (4%)
	White	111 (95%)
Education (years)		16 ± 2 (12-20)
Parental history of dementia		
	Yes	31 (26%)
	No	68 (58%)
	Unknown	18 (15%)
APOE4 carrier**		46 (39%)

Methods – 2DPC Protocol

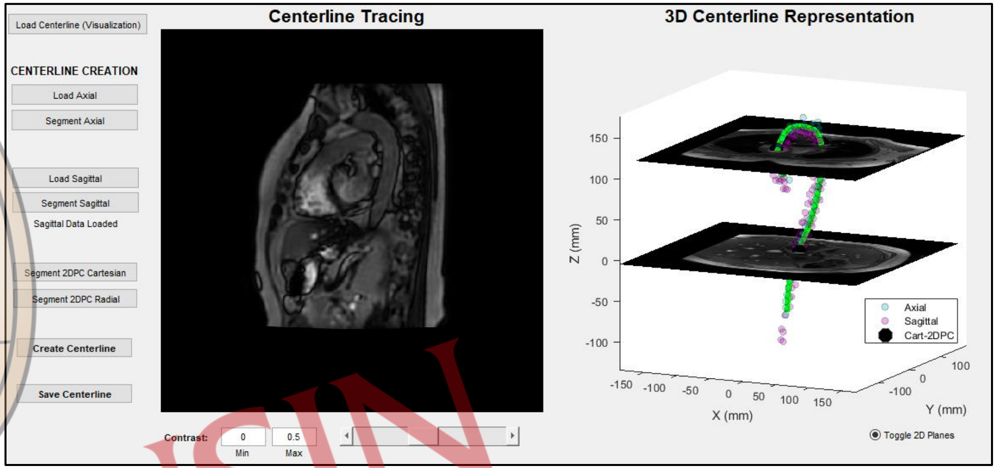
- **Two** acquisitions, **three** reconstructed datasets
  - Breath-Hold Cartesian 2DPC
    1. Online Reconstruction: GE DICOMs – 40 frames
  - Free-Breathing Radial 2DPC
    2. Offline Reconstruction: Low temporal resolution (matched to Cartesian) – 40 frames
    3. Offline Reconstruction: High temporal resolution reconstruction (LLR) – 80 frames

[1]CART [2]RAD-LR [3]RAD-HR

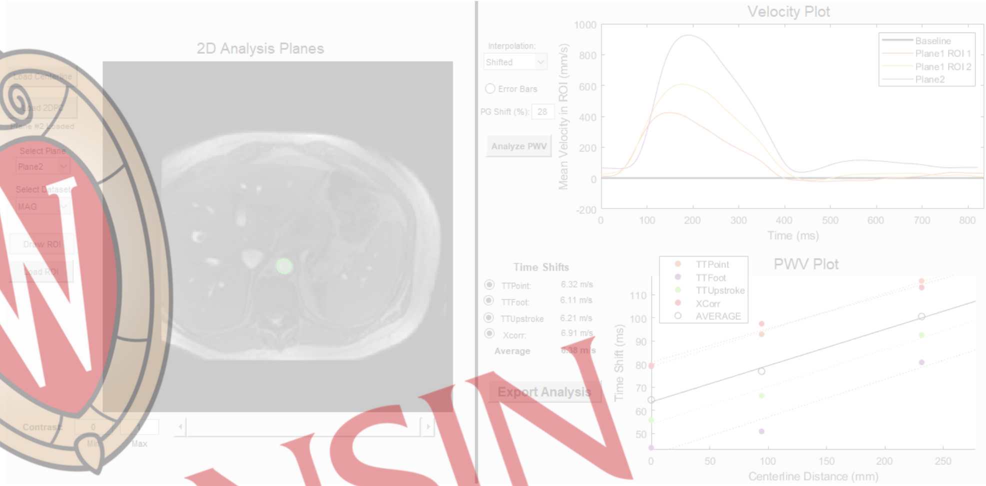
Parameter	Breath-Held Cartesian	Free-Breathing Radial	
		Low-Res	High-Res
Scan time	0:15	2:27	2:27
Projections	N/A	10,000	10,000
Slice Thickness	6 mm	6 mm	6 mm
V_{enc}	150 cm/s	150 cm/s	150 cm/s
Cardiac Gating	Prosp. PG	Retrosp. PG	Retrosp. PG
Resp. Gating	N/A	Retrosp. Bellows	Retrosp. Bellows
Spatial Res.	1.41 mm^2	1.40 mm^2	1.00 mm^2
# Frames	40	40	80
Temporal Res.	~25 ms	~25 ms	~13 ms

Methods – Graphical User Interface

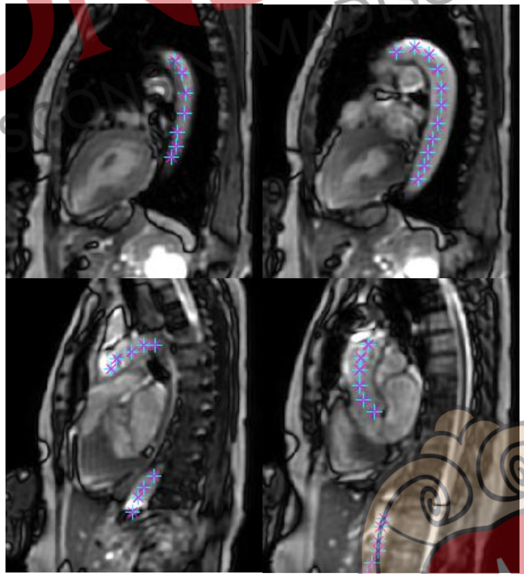
Aorta Distance Measurements



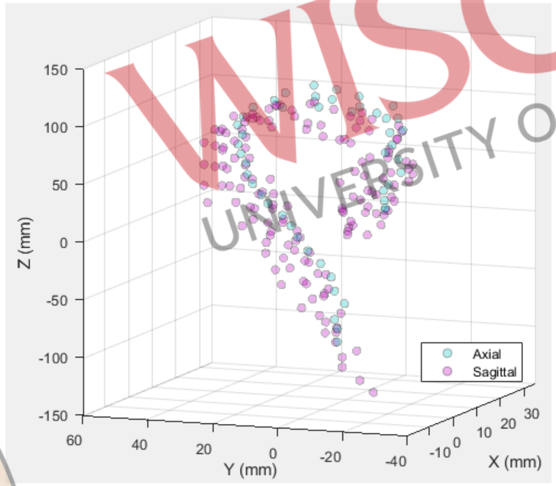
Waveform Time Shifts, PWV Calculation



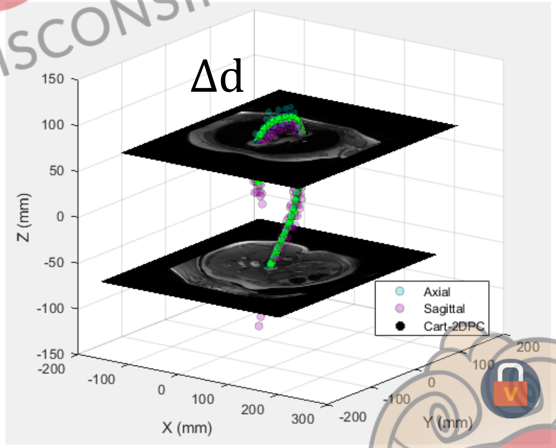
Sagittal bSSFP



Spatial Localization of Points

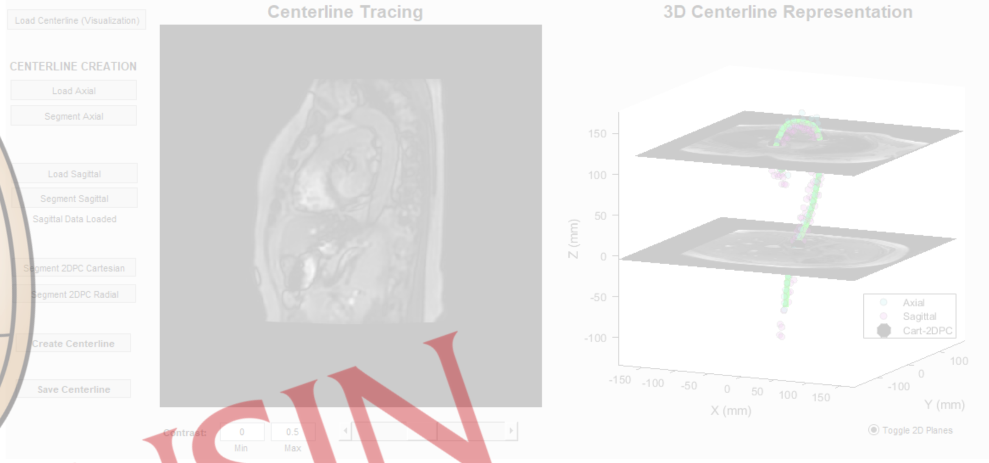


3D Centerline Representation

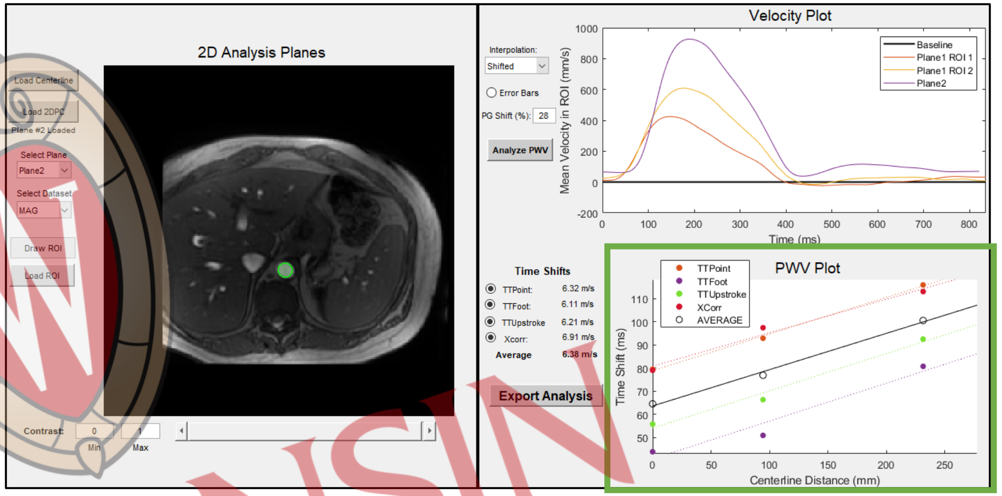


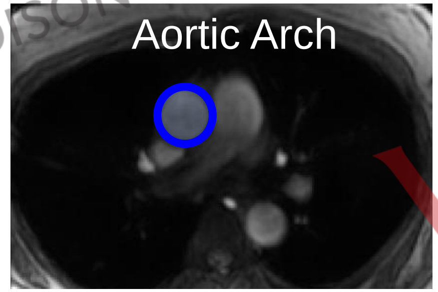
Methods – Graphical User Interface

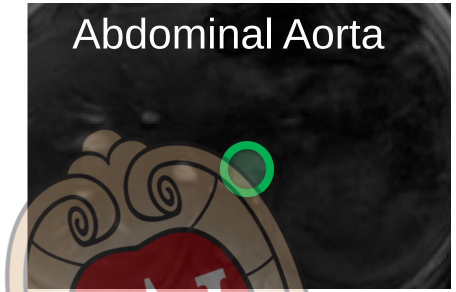
Aorta Distance Measurements

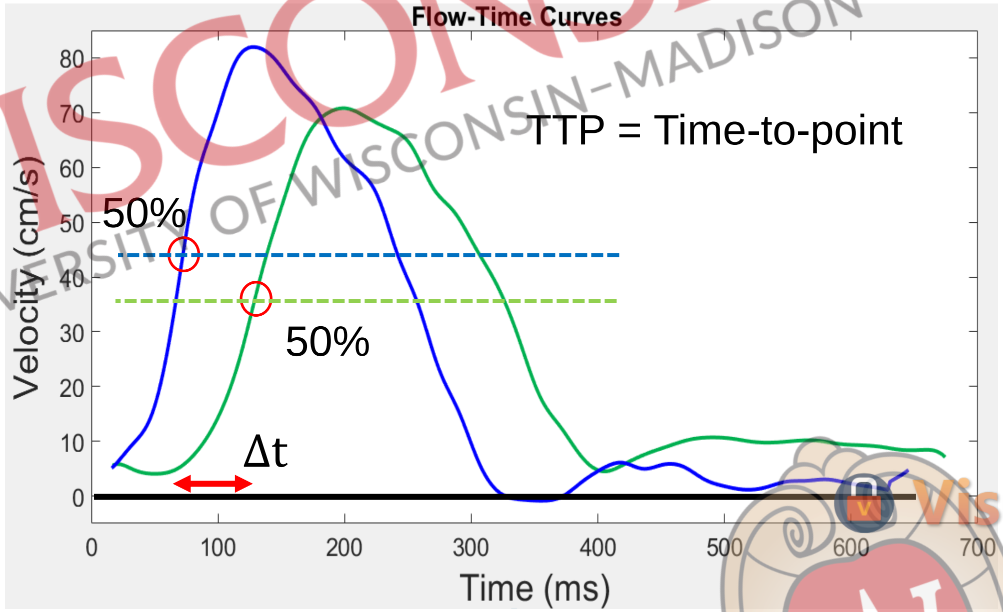


Waveform Time Shifts, PWV Calculation









$$PWV = \frac{\Delta d}{\Delta t}$$

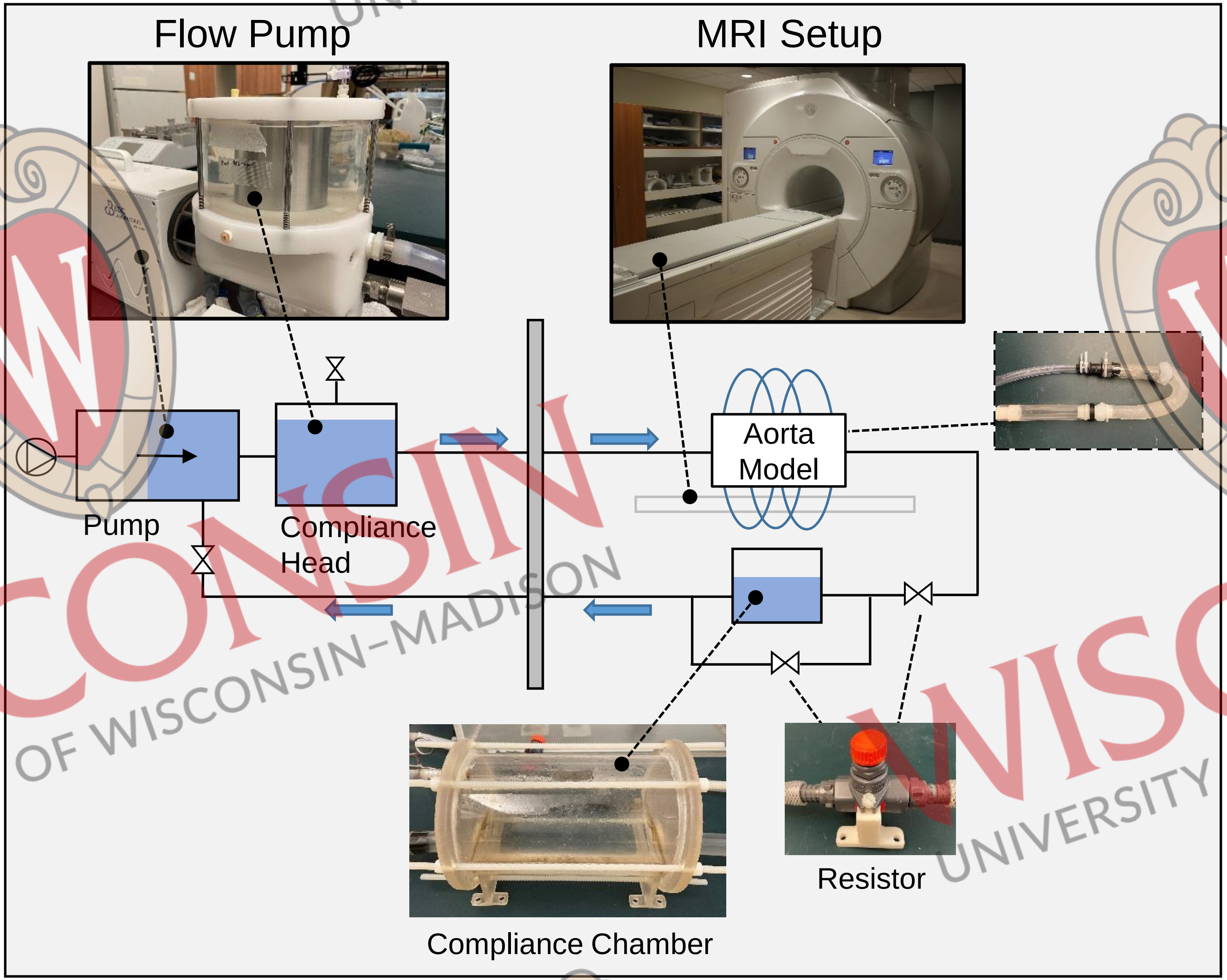
Methods – Flow Phantom

- Aorta model
  - MRA from 25 y.o. male volunteer
  - 3D-printed w/ Elastic 50A™ resin
  - Tygon tubing for ultrasound
  - **Reference: Ultrasound**

James Rice

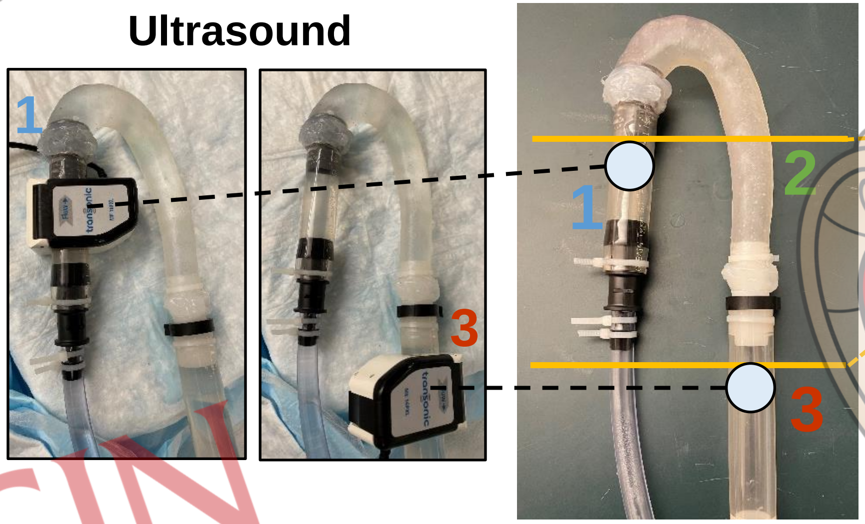
Methods – Flow Phantom

- Aorta model
  - MRA from 25 y.o. male volunteer
  - 3D-printed w/ Elastic 50A^TM resin
  - Tygon tubing for ultrasound
  - **Reference: Ultrasound**
- Flow phantom experiment
  - Flow rate: 3 L/min
  - Heart rate: 60 bpm
  - Added compliance/resistance
- Ultrasound validation
  - Obtained immediately before MRI scan
- MRI Protocol
  - Same as LIFE study
    - Anatomical bSSFP scan
    - Breath-hold Cartesian scan
    - Free-breathing radial scan

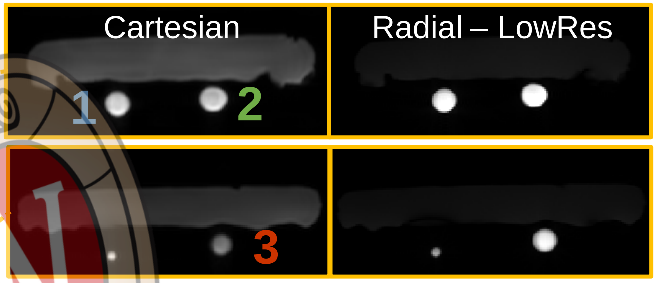


Results – Flow Phantom

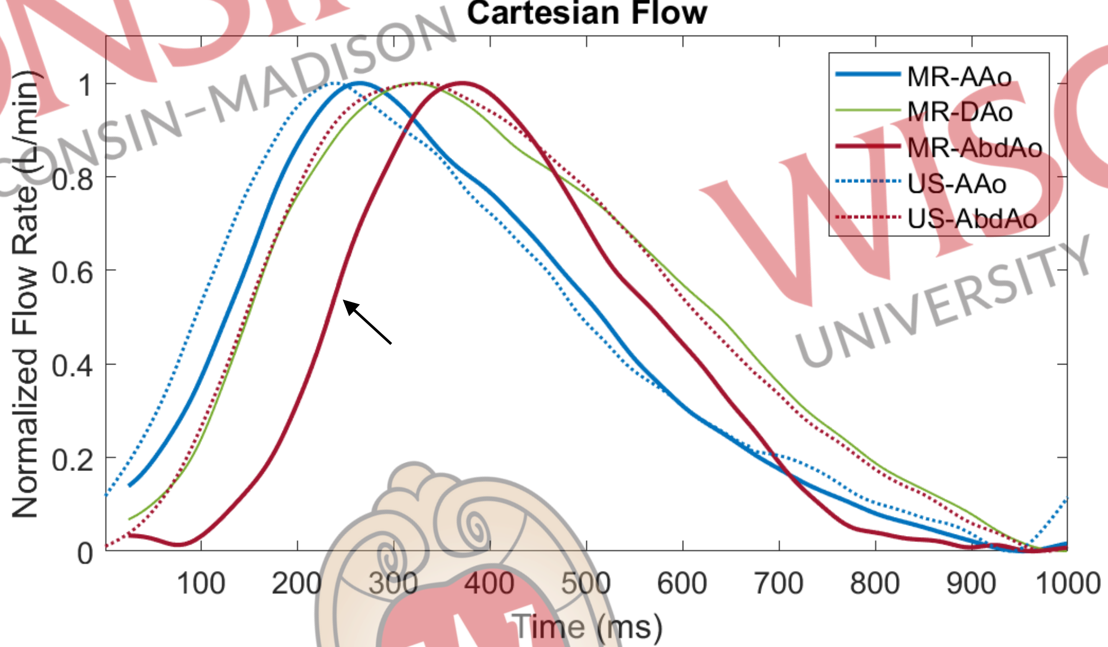
Ultrasound

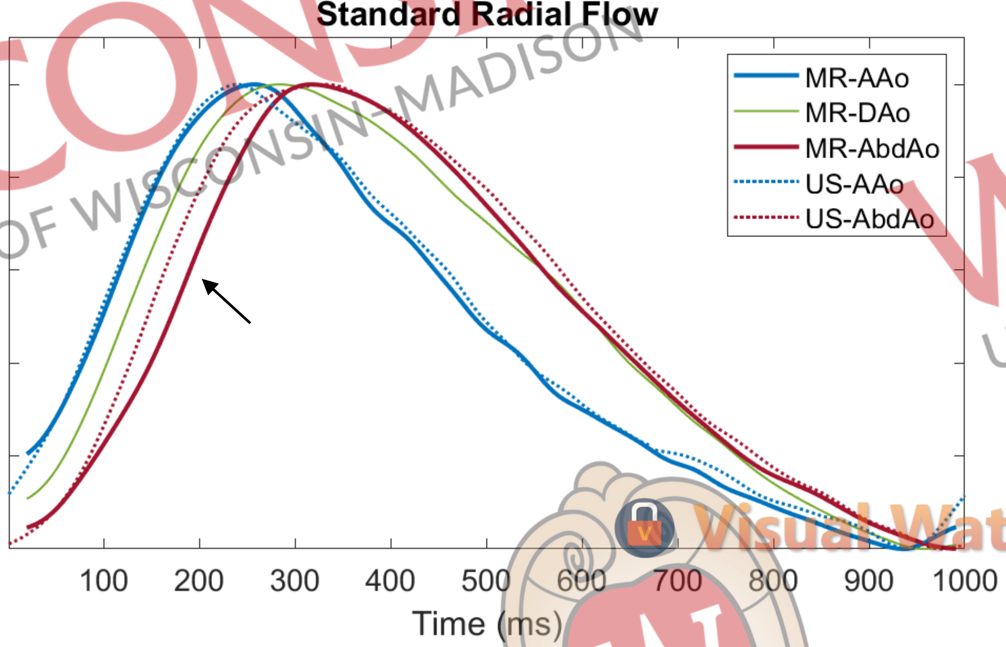


MRI



Locations: 1 = Ascending Aorta (AAo)
2 = Descending Aorta (DAo)
3 = Abdominal Aorta (AbdAo)





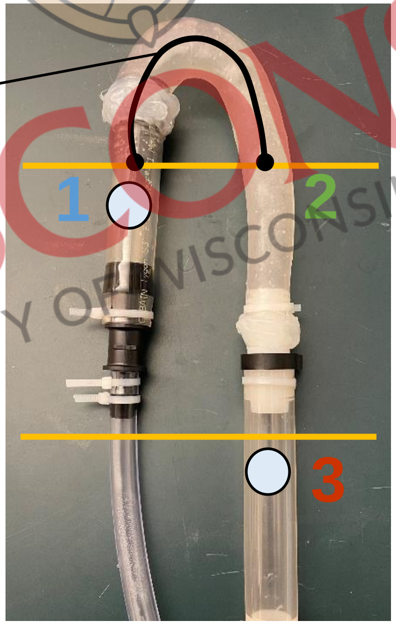
Results – Flow Phantom

- AAo – DAo PWV
  - Bias
    - Cartesian: 4 m/s
    - Radial Low-Res: -1 m/s
    - Radial High-Res: -1 m/s

In Vitro Results

Location	Acquisition	Length	PWV
AAo – DAo	CART	169	12.1 ± 2.41
	RAD-LR	169	7.0 ± 0.19
	RAD-HR	169	6.6 ± 1.66
AAo – AbdAo	**US**	**332**	**8.0 ± 1.09**
	CART	291	1.4 ± 0.07
	RAD-LR	291	2.2 ± 0.08
	RAD-HR	291	2.2 ± 0.11
AAo – DAo – AbdAo	CART	291	2.8 ± 0.04
	RAD-LR	291	3.7 ± 0.08
	RAD-HR	291	3.6 ± 0.04

Values reported as mean ± standard deviation
AAo = ascending aorta, DAo = descending aorta, AbdAo = abdominal aorta, CART = Cartesian, RAD-LR = low temporal resolution radial reconstruction, RAD-HR = high temporal resolution radial reconstruction, US = ultrasound



Results – Flow Phantom

- AAo – AbdAo PWV
  - Bias
    - Cartesian: -7 m/s
    - Radial Low-Res: -6 m/s
    - Radial High-Res: -6 m/s

In Vitro Results

Location	Acquisition	Length	PWV
AAo – DAo	CART	169	12.1 ± 2.41
	RAD-LR	169	7.0 ± 0.19
	RAD-HR	169	6.6 ± 1.66
AAo – AbdAo	**US**	**332**	**8.0 ± 1.09**
	CART	291	1.4 ± 0.07
	RAD-LR	291	2.2 ± 0.08
	RAD-HR	291	2.2 ± 0.11
AAo – DAo – AbdAo	CART	291	2.8 ± 0.04
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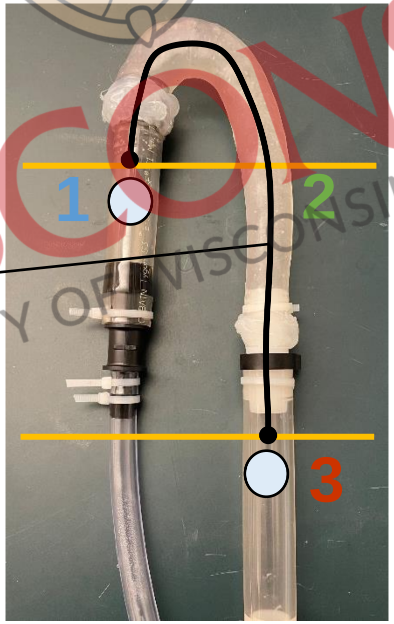
	RAD-HR	291	3.6 ± 0.04

Values reported as mean ± standard deviation
AAo = ascending aorta, DAo = descending aorta, AbdAo = abdominal aorta, CART = Cartesian, RAD-LR = low temporal resolution radial reconstruction, RAD-HR = high temporal resolution radial reconstruction, US = ultrasound



Results – Flow Phantom

- PWV using all 3 points
  - Bias
    - Cartesian: -5 m/s
    - Radial Low-Res: -4 m/s
    - Radial High-Res: -4 m/s

In Vitro Results

Location	Acquisition	Length	PWV
AAo – DAo	CART	169	12.1 ± 2.41
	RAD-LR	169	7.0 ± 0.19
	RAD-HR	169	6.6 ± 1.66
AAo – AbdAo	**US**	**332**	**8.0 ± 1.09**
	CART	291	1.4 ± 0.07
	RAD-LR	291	2.2 ± 0.08
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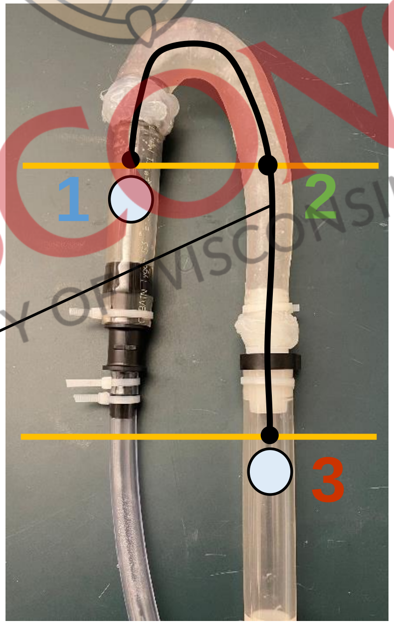
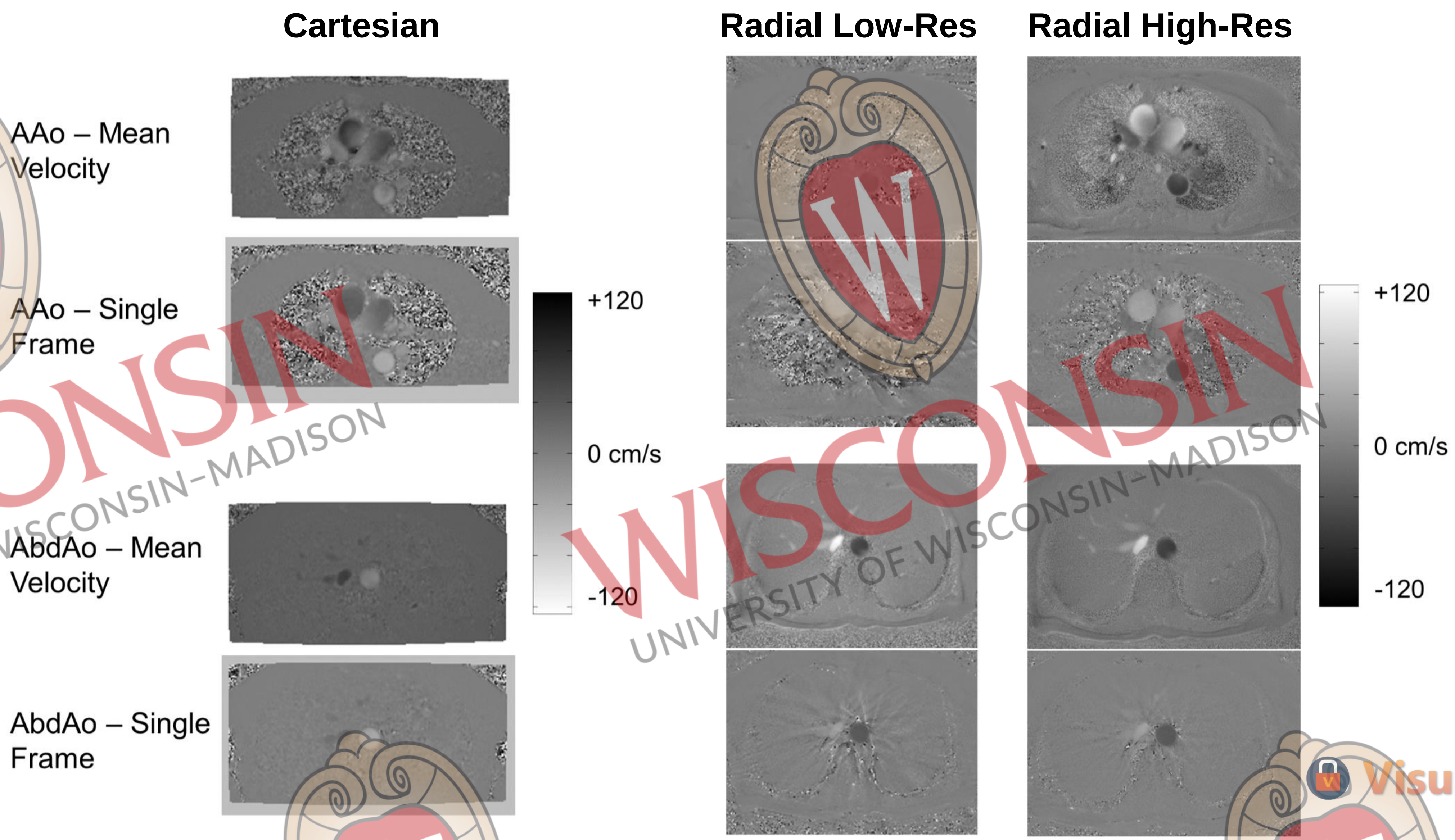
Values reported as mean ± standard deviation
AAo = ascending aorta, DAo = descending aorta, AbdAo = abdominal aorta, CART = Cartesian, RAD-LR = low temporal resolution radial reconstruction, RAD-HR = high temporal resolution radial reconstruction, US = ultrasound



Results – In Vivo

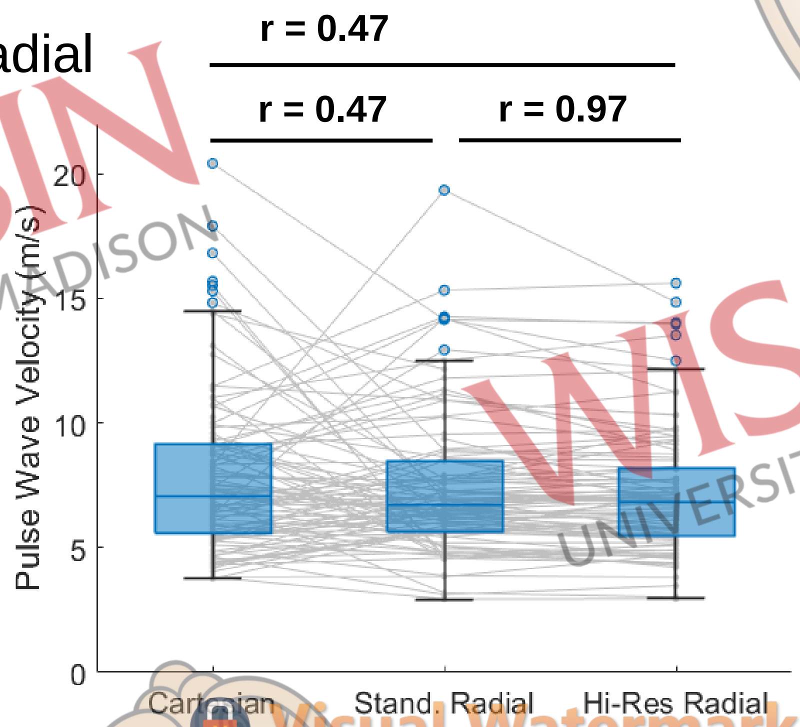


Results – LIFE PWV

- Good external agreement for all datasets
  - Our study: **7.9 m/s** [60-69 years], N=64
  - van Hout et al[1]: **6.8 m/s** [60-65 years], N=397
  - Nethononda et al[2]: **9 m/s** [60-69 years], N=777
- Comparison between radial and Cartesian methods
  - Relatively poor pairwise correlation between Cartesian and radial
  - PWV from both radial datasets highly correlated

Parameter	Overall	Age (years)			Sex	
		45-59	*60-69*	*70-79*	*Female*	*Male*
Aorta Length (mm)	**241** ± 25 (117)	235 ± 26 (26)	242 ± 22 (66)	246 ± 32 (25)	236 ± 23 (85)	257 ± 23 (32)
Cartesian PWV (m/s)	**7.9** ± 3.3 (114)	7.0 ± 3.2 (25)	7.9 ± 3.4 (64)	8.7 ± 2.9 (25)	7.8 ± 3.5 (82)	8.0 ± 2.6 (32)
Radial – LowRes PWV (m/s)	**7.8** ± 3.9 (103)	6.0 ± 1.4 (23)	8.3 ± 4.6 (60)	8.5 ± 2.8 (20)	7.5 ± 3.4 (74)	8.7 ± 4.9 (29)
Radial – HighRes PWV (m/s)	**7.5** ± 3.3 (102)	5.8 ± 1.5 (23)	7.9 ± 3.8 (59)	8.4 ± 2.6 (20)	7.2 ± 2.8 (73)	8.3 ± 4.3 (29)

Values reported as mean ± standard deviation (N)



[1]van Hout MJ, et al (2021). *JCMR*. 23(1):46
[2]Nethononda RM, et al (2015). *JCMR*. 17(1):20

Results – Reproducibility

- Repeatability in subset of 16/150 subjects
- ICC show excellent reproducibility
  - Both distance and PWV measurements
  - Both intraobserver and interobserver ≥0.95


Bri Breidenbach


Jennifer Fondakowski


Mackenzie Jarchow

Intraobserver Agreement

Variable	Measure (Time 1)	Measure (Time 2)	Bias	ICC*
Aorta Distance (mm)				
AscAo – DescAo	103.88	105.95	2.07	0.97
DescAo – AbdAo	140.68	141.55	0.87	0.99
AscAo – AbdAo	244.57	247.50	2.93	0.99
Cartesian PWV (m/s)	7.31	7.51	0.20	0.99
Standard Radial PWV (m/s)	7.57	7.67	0.11	1.00
High-Resolution Radial PWV (m/s)	7.69	7.59	-0.10	1.00

*ICC(3,k) – Two-way mixed effects model, consistency, mean of 2 observers

AscAo = Ascending aorta; DescAo = Descending Aorta; AbdAo = Abdominal aorta; PWV = pulse wave velocity; ICC = intraclass correlation coefficient

Interobserver Agreement

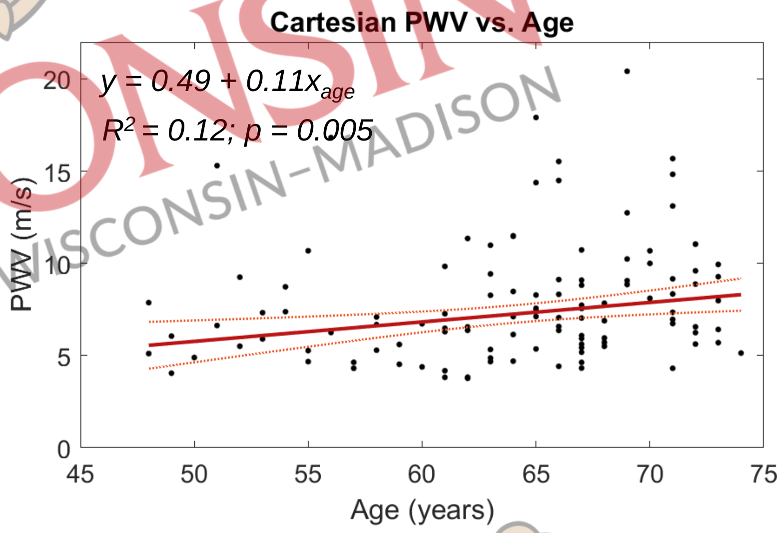
Variable	Measure (Obs 1)*	Measure (Obs 2)*	Measure (Obs 3)	ICC**
Aorta Distance (mm)				
AscAo – DescAo	110.64	99.21	107.03	0.97
DescAo – AbdAo	141.14	141.32	142.96	1.00
AscAo – AbdAo	251.78	240.53	249.99	0.99
Cartesian PWV (m/s)	7.27	7.85	7.77	0.95
Standard Radial PWV (m/s)	7.61	7.62	7.79	1.00
High-Resolution Radial PWV (m/s)	7.71	7.68	7.85	1.00

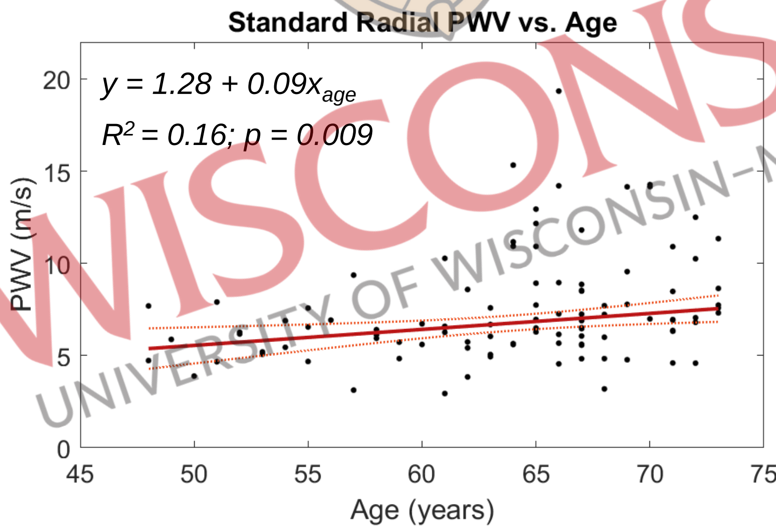
*Reported measures from second analysis time point

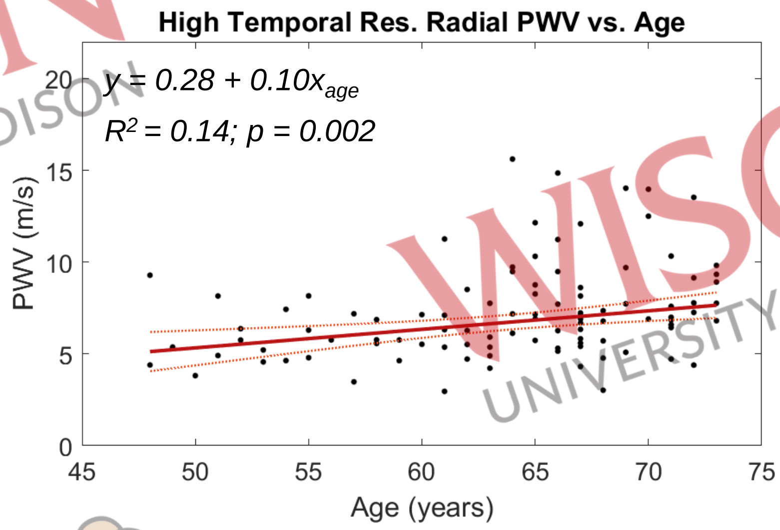
**ICC(3,k) – Two-way mixed effects model, consistency, mean of 2 observers

Results – PWV vs. Age

- PWV significantly correlated with age
  - For both breath-hold and free-breathing sequences
  - Regression suggests ~1.0 m/s increase in PWV every decade
    - van Hout et al: 1.0 [0.8-1.3] m/s (N=397)[1]



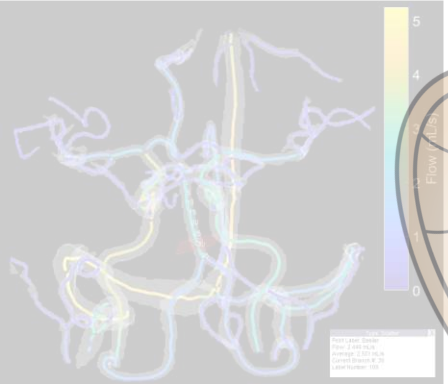




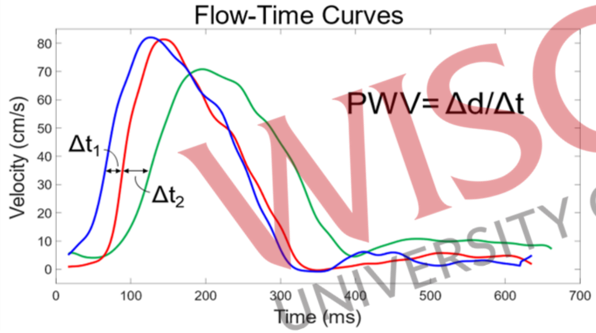
[1]van Hout MJ, et al (2021). *JCMR*. 23(1):46

Outline

- **Background**
- **Part 1:** Cranial 4D Flow MRI
  - Aim 1: Develop 4D flow MRI tool for efficient flow analysis in the brain
  - Aim 2: Establish “normal” intracranial blood flow and pulsatility in 759 older adults



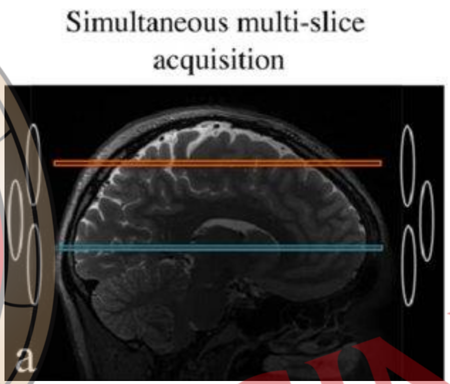
- **Part 2:** Aortic Pulse Wave Velocity
  - Aim 3: Implement a free-breathing, radial 2D phase contrast sequence to assess aortic pulse wave velocity in 150 older adults
  - Aim 4: Develop a simultaneous multislice sequence for aortic pulse wave velocity assessment



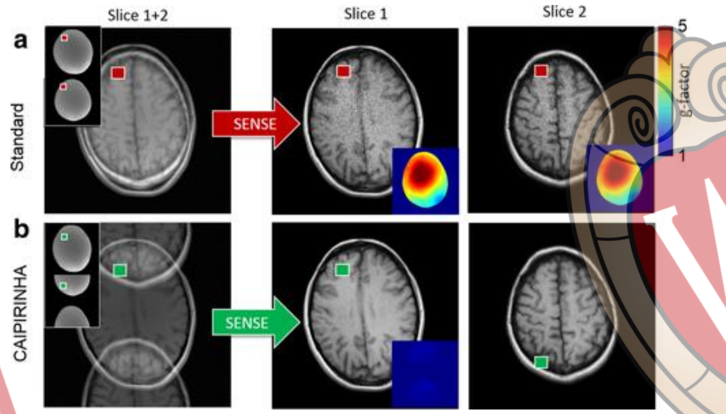
- **Summary**

Aim 4 – Motivation

- Simultaneous multislice (SMS) is compelling approach for aortic PWV assessment
  - Allows for imaging 2 slices at once
    - Need multiple receiver coils
- Key benefits:
  - Reduce scan time
    - Slight SNR penalty[1]
  - Increase physiological consistence
    - Single acquisition
    - Heart rate differences between scans?
    - Gating timing/delays differences between scans?



Wu W, et al (2017). *JMRI*. 46(3):646-62



Barth M, et al (2016). *MRM*. 75(1):63-81

In Vitro Results

Location	Acquisition	Length	PWV
AAo – DAo	CART	169	12.1 ± 2.41
	RAD-LR	169	7.0 ± 0.19
	RAD-HR	169	6.6 ± 1.66
AAo – AbdAo	**US**	**332**	**8.0 ± 1.09**
	CART	291	1.4 ± 0.07
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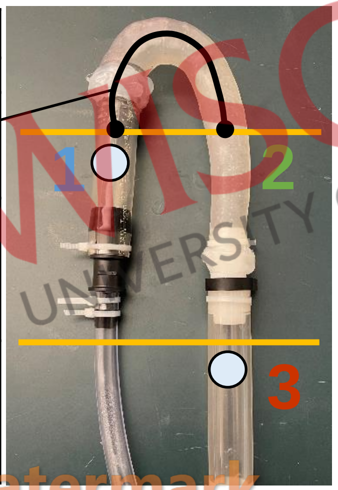
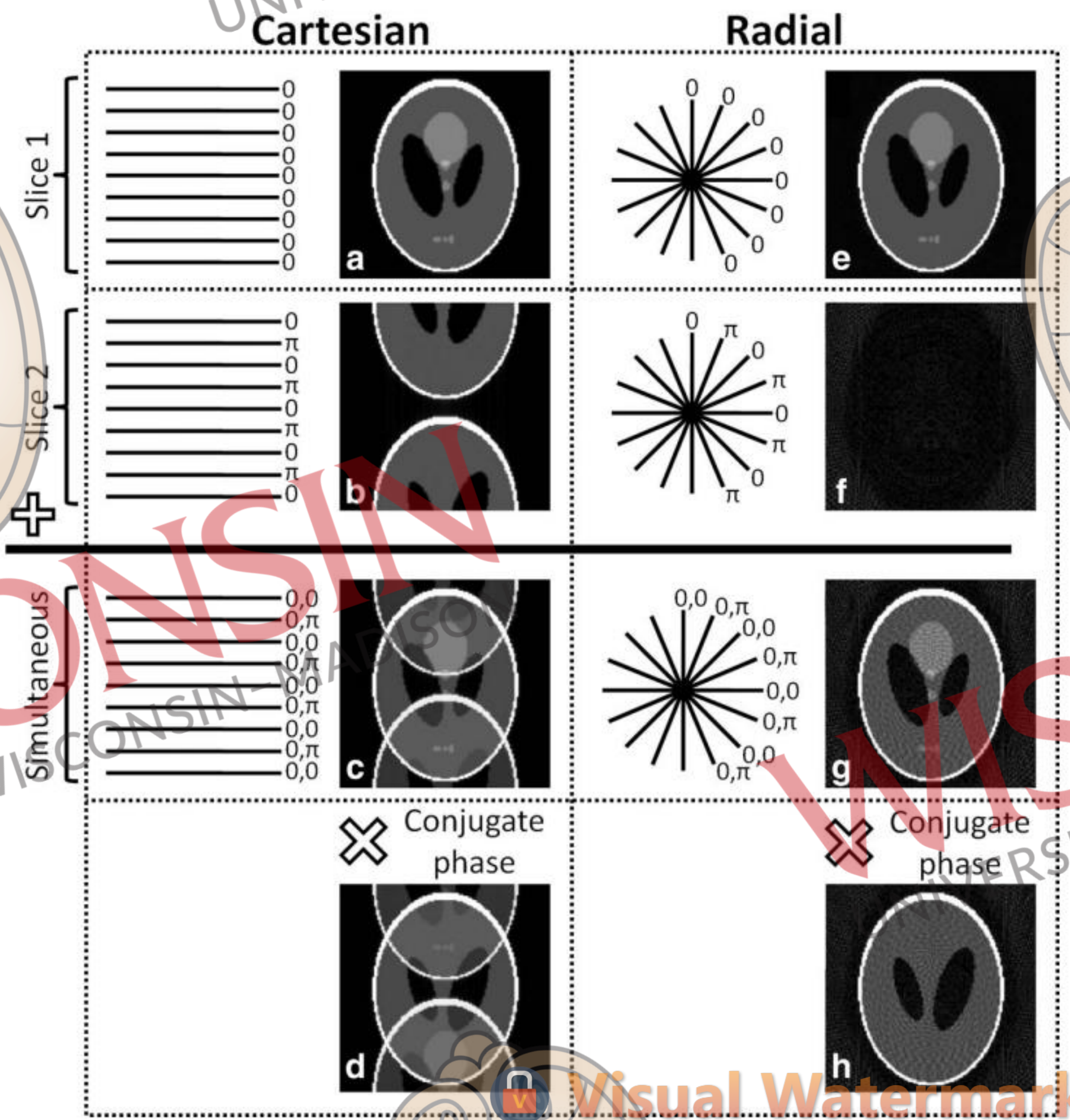
	RAD-LR	291	3.7 ± 0.08
	RAD-HR	291	3.6 ± 0.04



[1]Barth M, et al (2016). *MRM*. 75(1):63-81

Aim 4 – Motivation

- Cartesian SMS
  - Phase "blips" with each alternating phase encode line
    - Intentional shifting
    - Use parallel imaging to recover slices
- Can also be used with radial imaging
  - Introduced by Lutzy et al[1]
  - Apply "blips" along sequential radial spokes
    - One slice is either in-phase or out-of-phase
  - Apply conjugate phase pattern to recover phase modulated slices



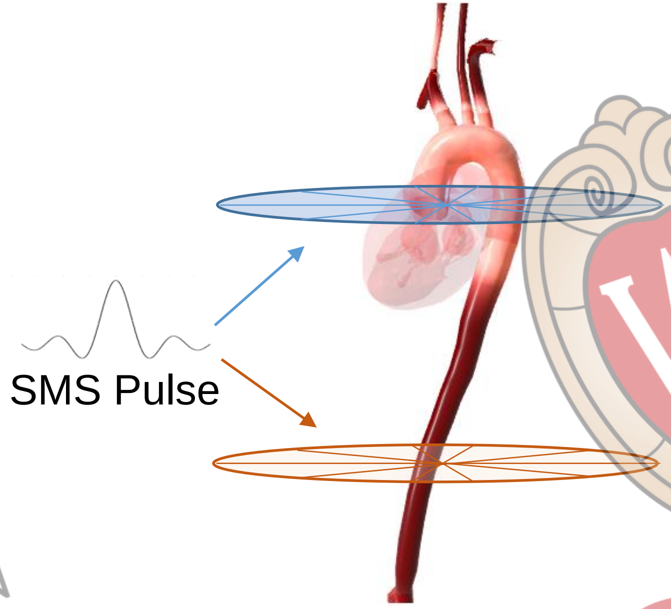
Lutzy SR, et al (2011). *MRM*. 65(6):1631

[1]Lutzy SR, et al (2011). *MRM*. 65(6):1631

Aim 4

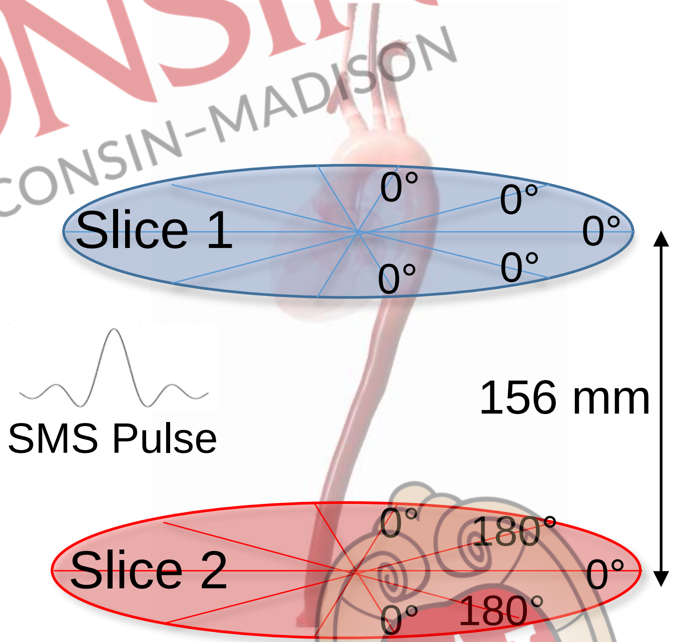
- Implement a free-breathing, radial simultaneous multislice 2DPC sequence
  - Would be the first study to apply this method to study aortic PWV

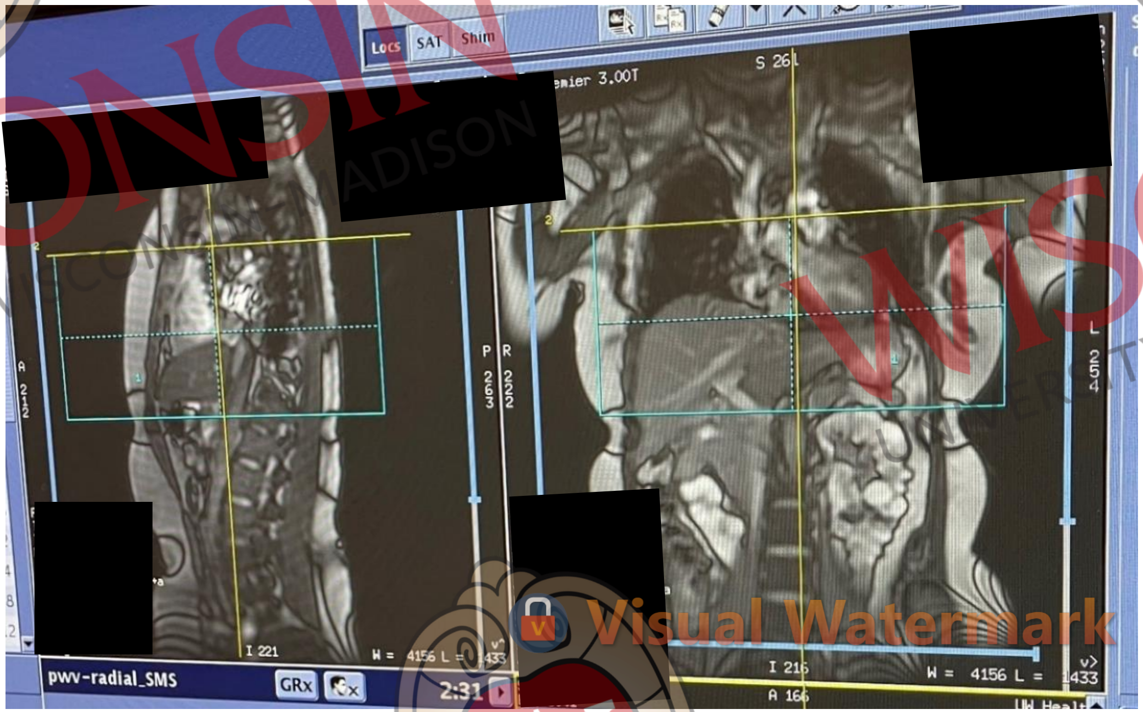
- Simulation study
  - Assess feasibility of SMS reconstruction
- Validation *in vitro*
  - Identical flow phantom setup as before
- Small *in vivo* pilot study
  - 3 young volunteers
  - 3 LIFE subjects
    - Recently added onto LIFE protocol (December 2022)



Methods – SMS Pulse Sequence Development

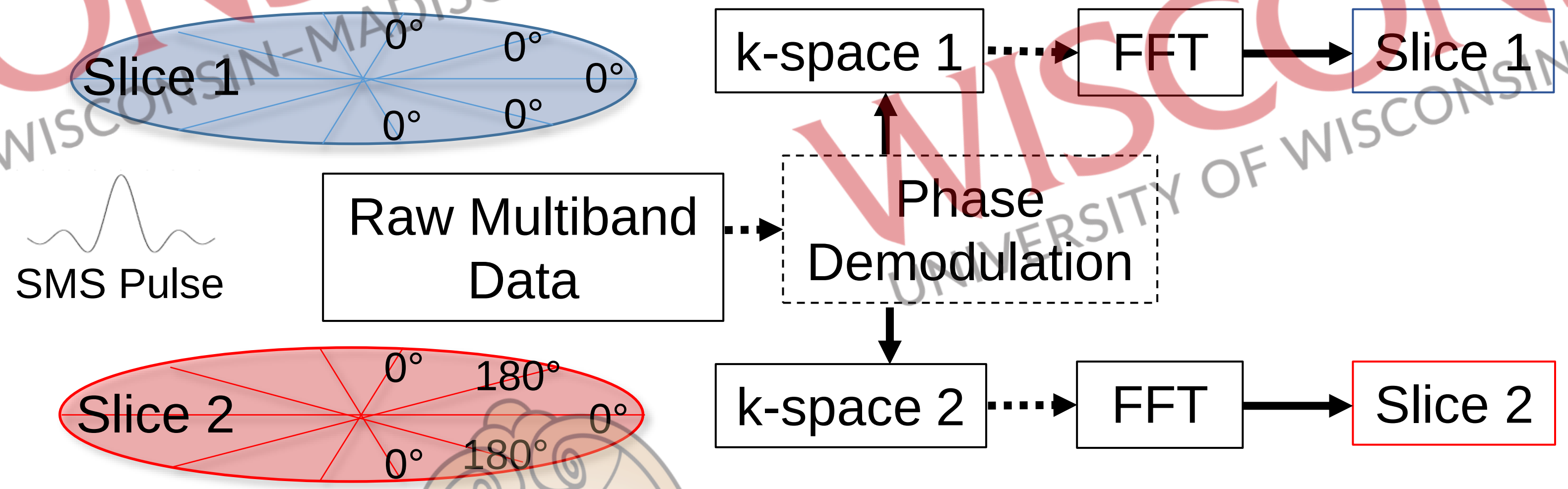
- Pulse sequence implemented in EPIC
  - Built on the ‘pcvipr’ pulse sequence
  - Phase modulation applied in z-direction (alternating spokes)
    - Golden-angle sampling for cardiac/respiratory gating
- Acceleration factor of 2 used (only 2 slices excited)
- Operated in 3D mode to localize slices
  - Slice separation set at 156 mm



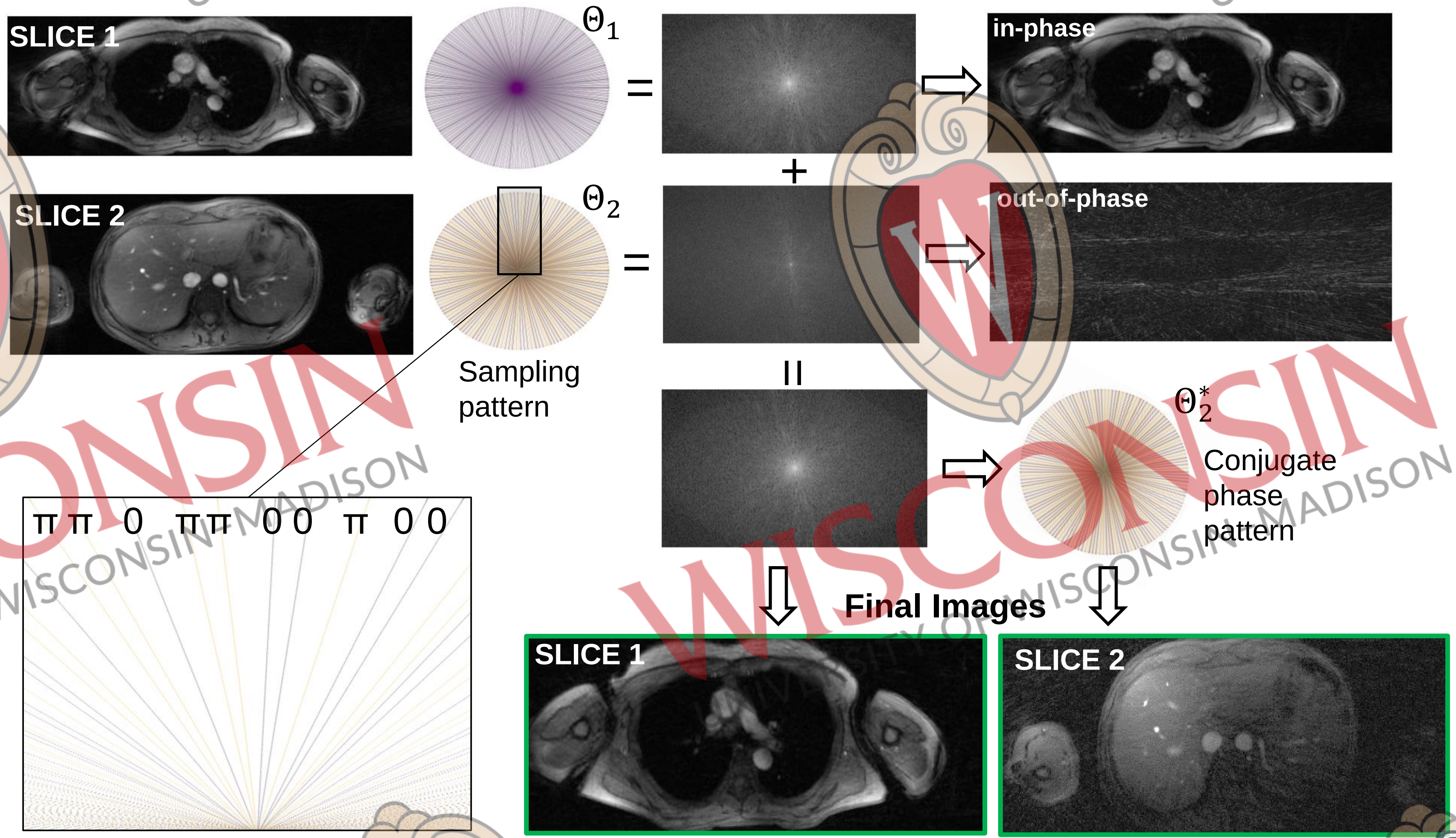


Methods – SMS Reconstruction

- SMS recon functionality added to our Python reconstruction code
  - https://github.com/uwmri/flow_recon/tree/sms
- Runs two separate recons
  - Different phase demodulation pattern for each reconstruction
  - Parallel Imaging with localized sensitivities (PILS)
  - Coil sensitivity maps obtained from low-resolution, low-pass filtered images
  - 40 time frames



Results – SMS Simulation



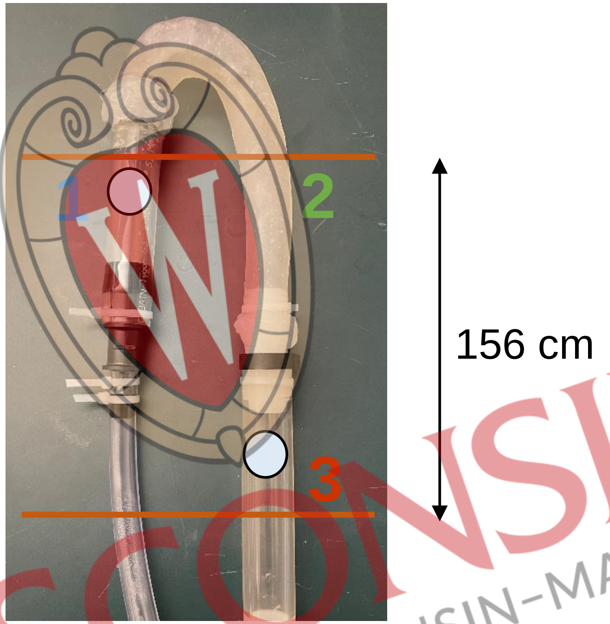
Results – Phantom Study

In Vitro Results

Location	Acquisition	Length	PWV
AAo – DAo	CART	169	12.1 ± 2.41
	RAD-LR	169	7.0 ± 0.19
	RAD-HR	169	6.6 ± 1.66
	SMS	**166**	**6.0 ± 0.47**
AAo – AbdAo	**US**	**332**	**8.0 ± 1.09**
	CART	291	1.4 ± 0.07
	RAD-LR	291	2.2 ± 0.08
	RAD-HR	291	2.2 ± 0.11
	SMS	**340**	**8.1 ± 1.19**
AAo – DAo – AbdAo	CART	291	2.8 ± 0.04
	RAD-LR	291	3.7 ± 0.08
	RAD-HR	291	3.6 ± 0.04
	SMS	**340**	**6.9 ± 0.12**

Values reported as mean ± standard deviation

AAo = ascending aorta, DAo = descending aorta, AbdAo = abdominal aorta, CART = Cartesian, RAD-LR = standard radial reconstruction, RAD-HR = high temporal resolution radial reconstruction, US = ultrasound



Results – SMS Image Quality

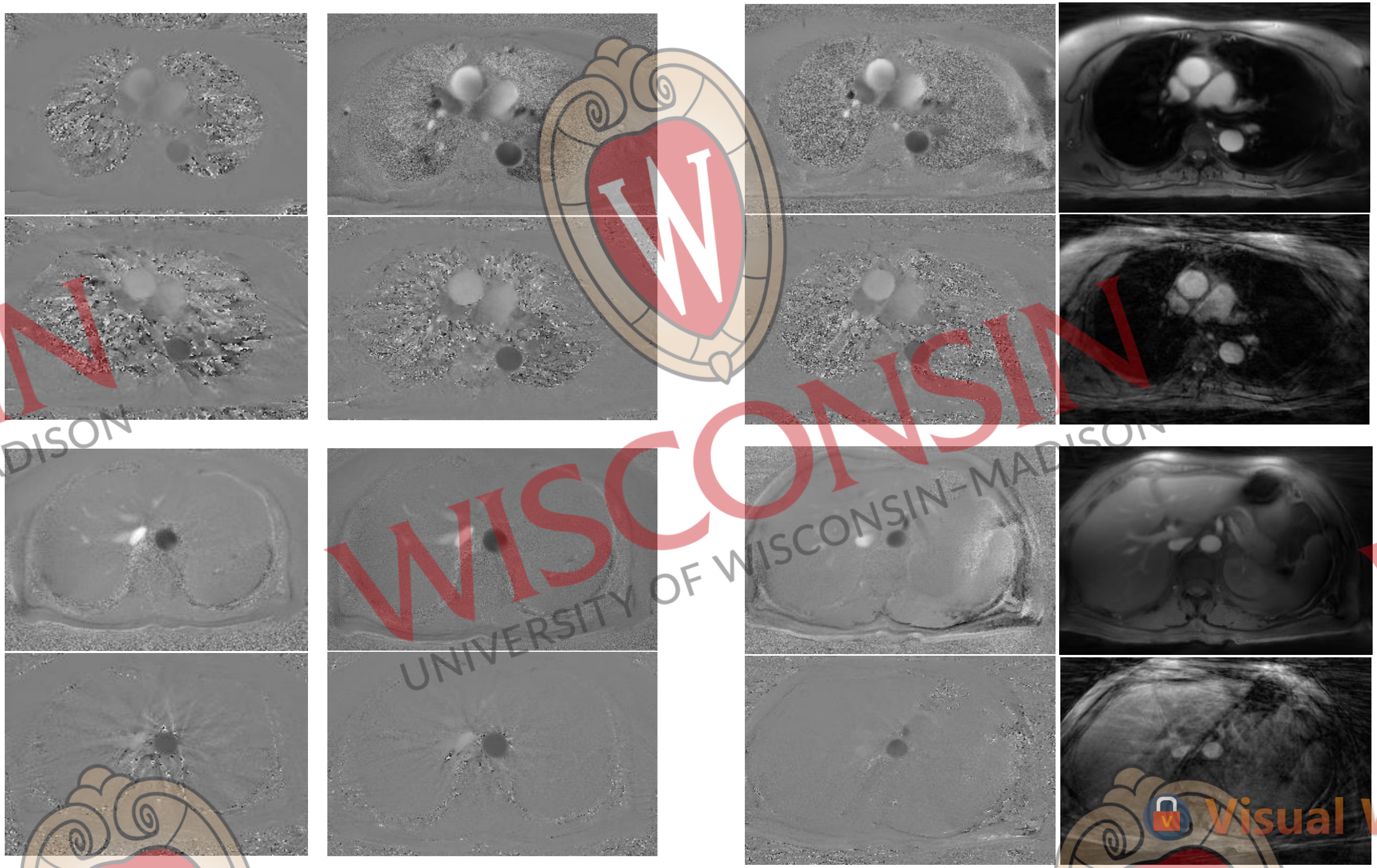
Low-Res Radial | Hi-Res Radial | SMS Velocity | SMS Magnitude

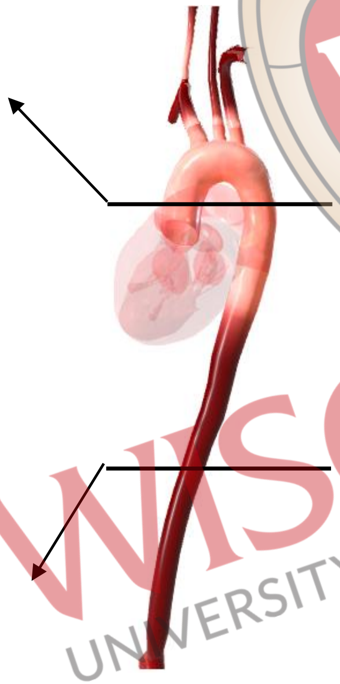
AAo – Mean Velocity

AAo – Single Frame

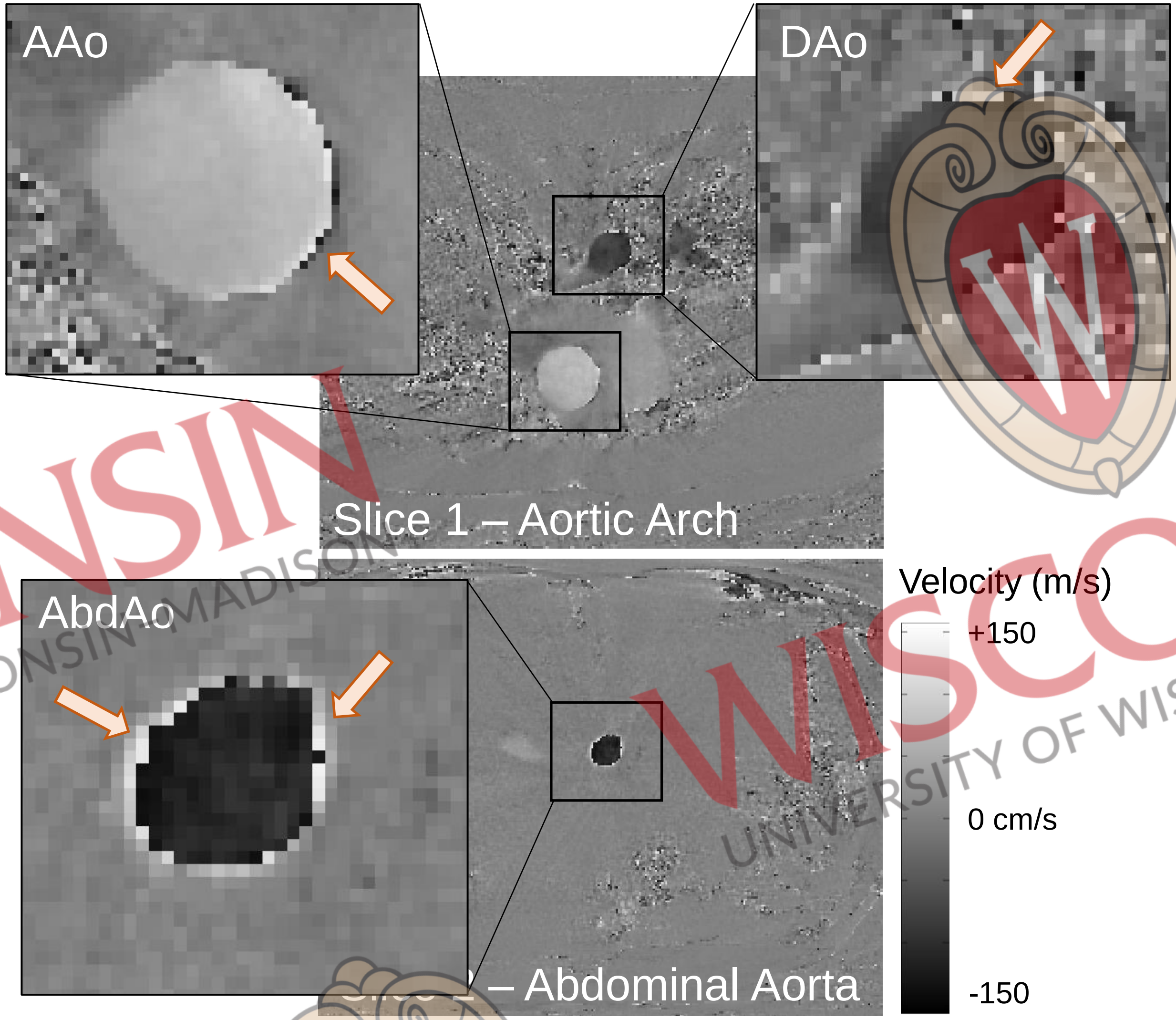
AbdAo – Mean Velocity

AbdAo – Single Frame





Results – SMS Image Quality



Results – SMS Pilot Study

- Results consistent between acquisitions
  - One outlier Cartesian data point
- PWV lower in younger volunteers

In Vivo Pilot Study						
Participant	**Age**	**Sex**	**Cartesian**	**Radial Low-Res**	**Radial Hi-Res**	**SMS**
VOL001	25	F	8.1	4.5	4.7	**4.9**
VOL002	19	F	4.2	4.0	3.8	**4.6**
VOL003	26	M	5.0	4.4	4.2	**4.2**
life00134	56	F	6.3	-	-	**5.7**
life00039	64	F	8.1	7.3	7.6	**8.9**
life00028	68	F	8.6	8.8	8.3	**8.8**

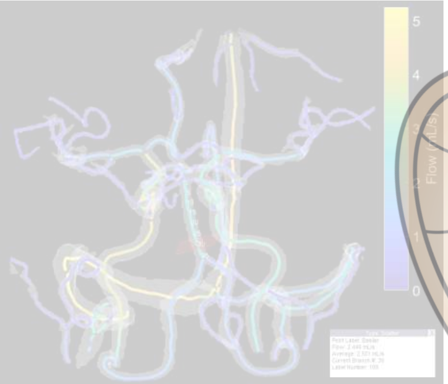
F = female, M = male, SMS = simultaneous multislice

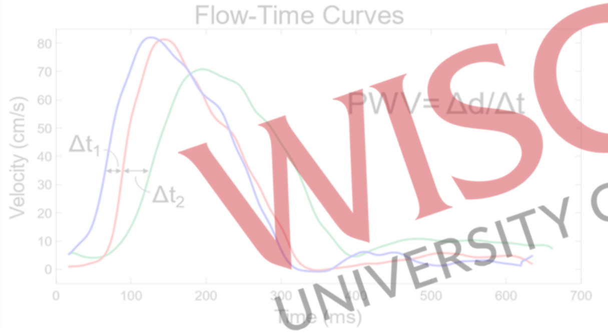
younger (VOL001–VOL003)

older (life00134, life00039, life00028)

Outline

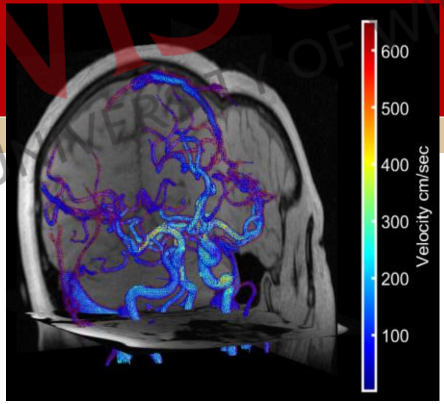
- **Background**
- **Part 1:** Cranial 4D Flow MRI
  - Aim 1: Develop 4D flow MRI tool for efficient flow analysis in the brain
  - Aim 2: Establish “normal” intracranial blood flow and pulsatility in 759 older adults
- **Part 2:** Aortic Pulse Wave Velocity
  - Aim 3: Implement a free-breathing, radial 2D phase contrast sequence to assess aortic pulse wave velocity in 150 older adults
  - Aim 4: Develop a simultaneous multislice sequence for aortic pulse wave velocity assessment
- **Summary**



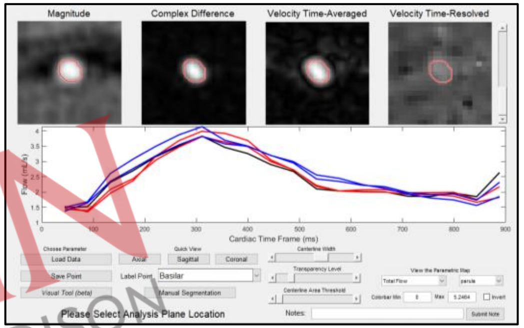


Summary

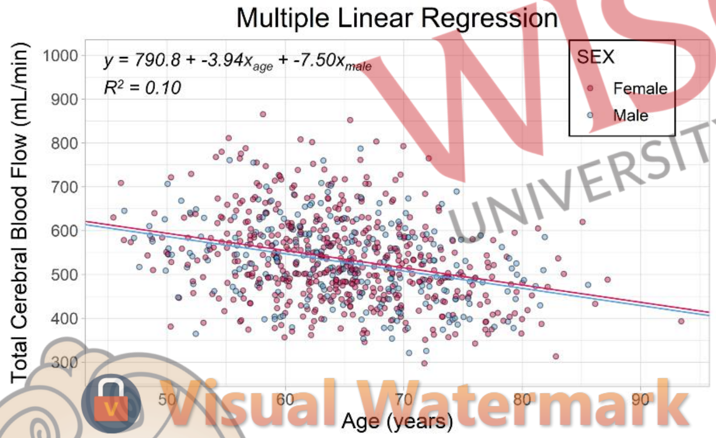
- **4D flow MRI**
  - Powerful method for obtaining 3D velocity fields in vivo
  - Blood velocities, blood flow rates, pulsatility index, etc.



- Aim 1: Developed cranial 4D flow MRI analysis tool
  - Interactive 3D vessel selection and visualization
  - **Accurate segmentation** and flow quantification
  - Flow measures **repeatable** and **internally consistent**
  - **Fast flow analysis** in brain

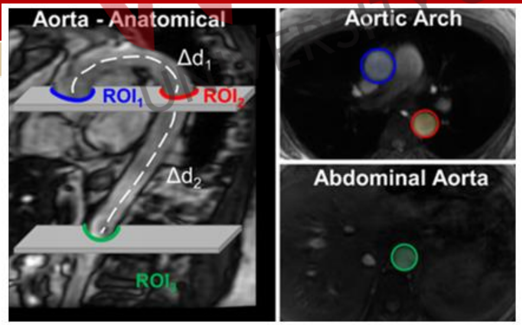


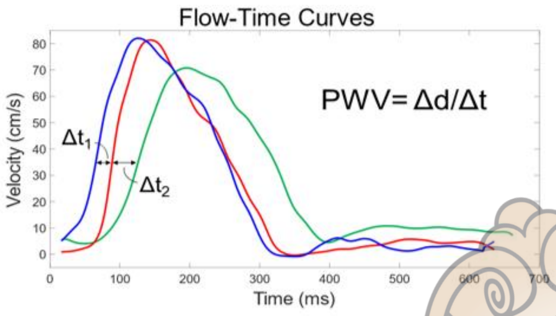
- Aim 2: Established "normative" intracranial flow and pulsatility in 759 cognitively healthy older adults
  - One of the largest 4D flow MRI studies to date
  - **Strong age dependence** on flow and pulsatility



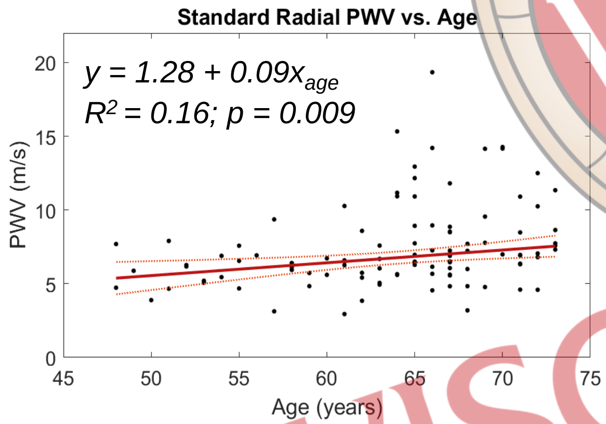
Summary

- **2D Phase Contrast (2DPC) MRI**
  - Can be used to assess aortic pulse wave velocity as a measure of aortic stiffness

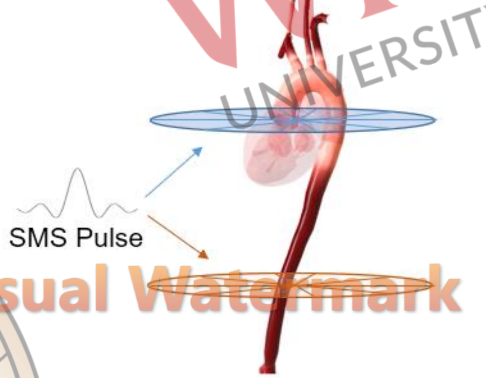




- Aim 3: Implemented a free-breathing radial 2DPC sequence for assessing aortic stiffness
  - LLR recon increased temp. resolution while maintaining image quality
  - Radial and Cartesian acquisitions didn't align well with US
  - Poor pairwise correlation between Cartesian and radial in vivo
  - PWV measures **correlated with age,** were **repeatable,** and were **consistent with previous studies**



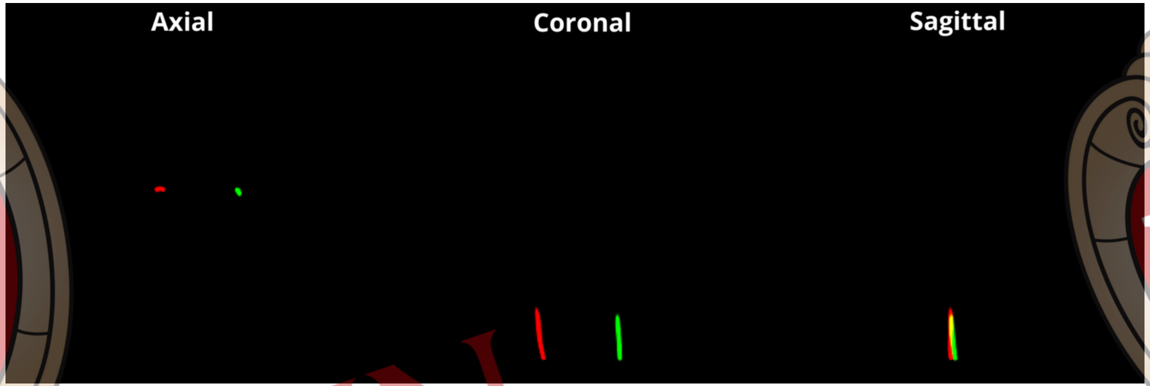
- Aim 4: Developed a simultaneous multislice sequence for aortic pulse wave velocity assessment
  - **Reduced scan time by half** with excellent image quality
  - **Better agreement with ground truth ultrasound PWV**
  - Acquiring data in single scan **improves physiological consistency**



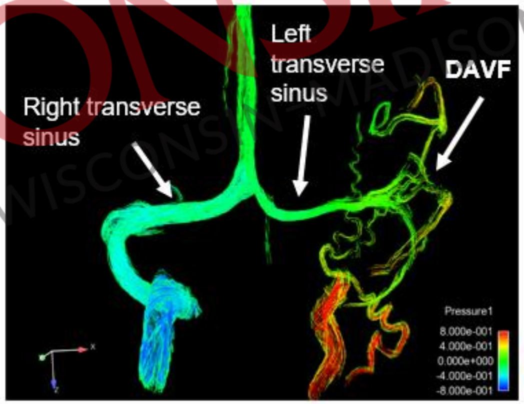
Other Projects – Virtual Injection

Mike Loecher

Healthy Volunteer

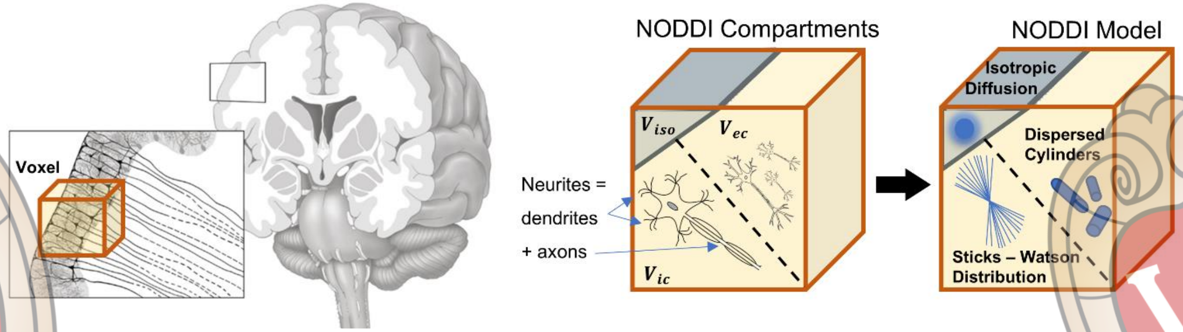


Dural Arteriovenous Malformation



Roberts GS and Loecher MW, et al (2022) *MRM*. 87(5):2495-511

Other Projects – NODDI vs. 4D Flow MRI

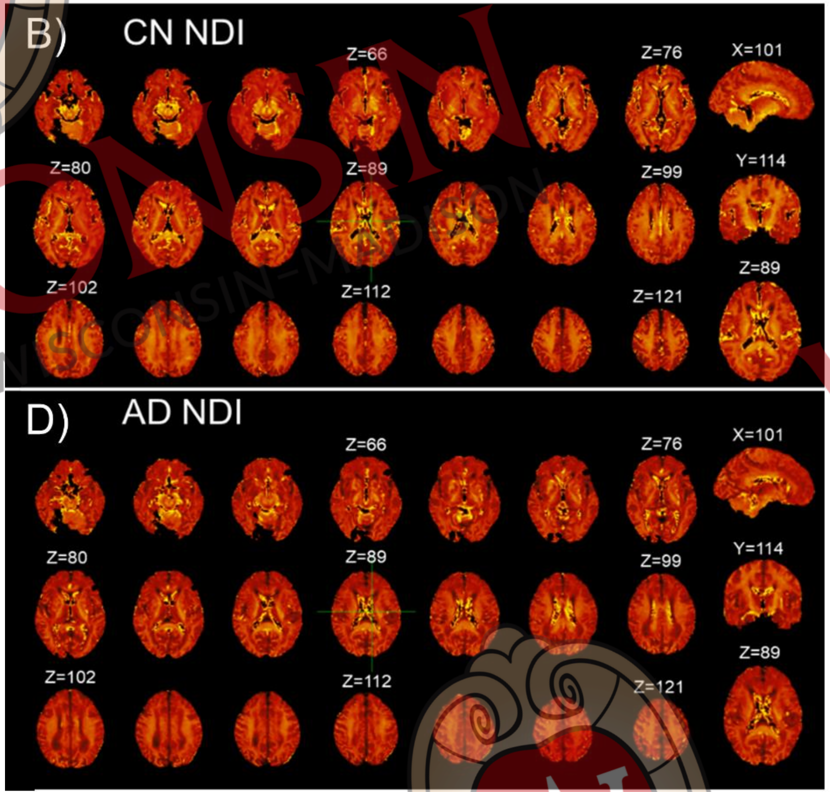


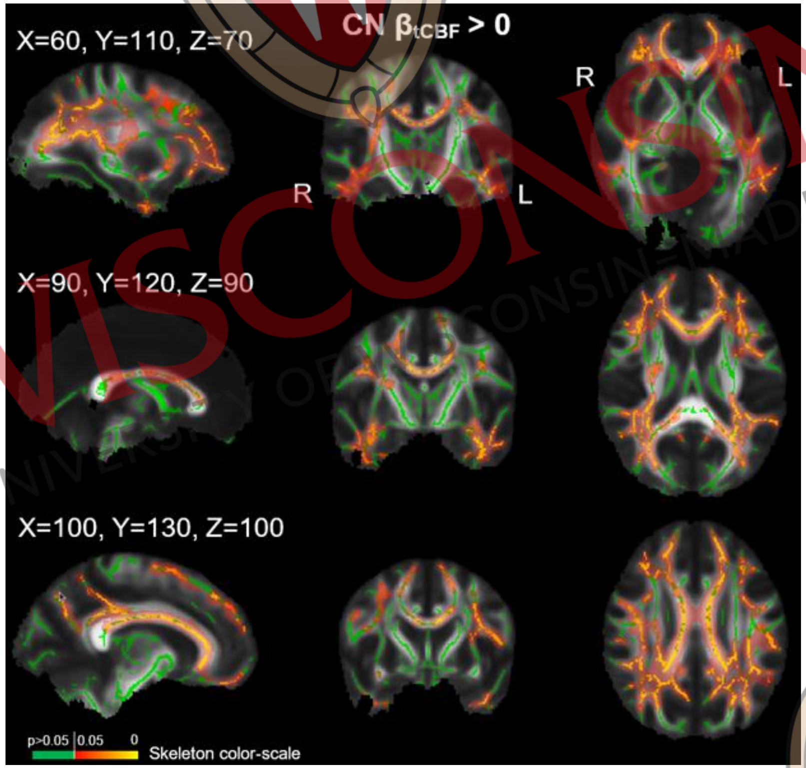

Doug Dean III

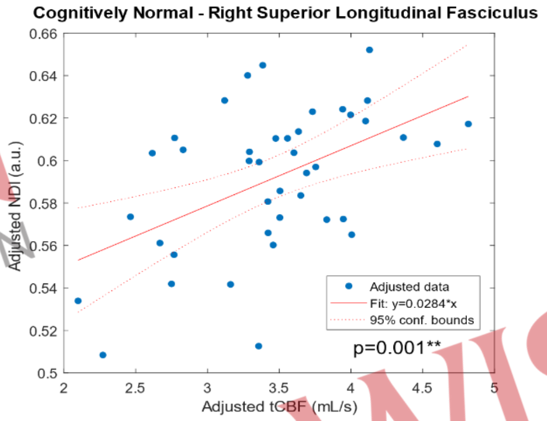

Andy Alexander

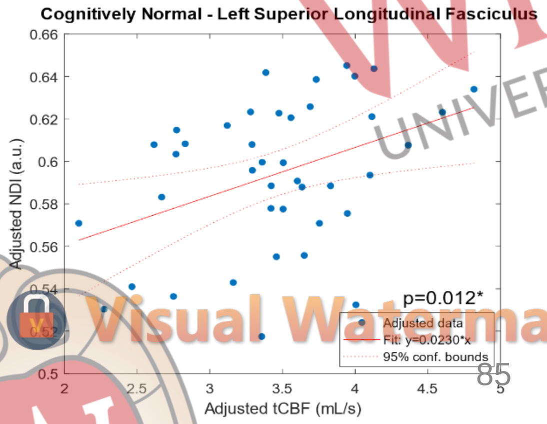

Jason Moody


Alma Spahic



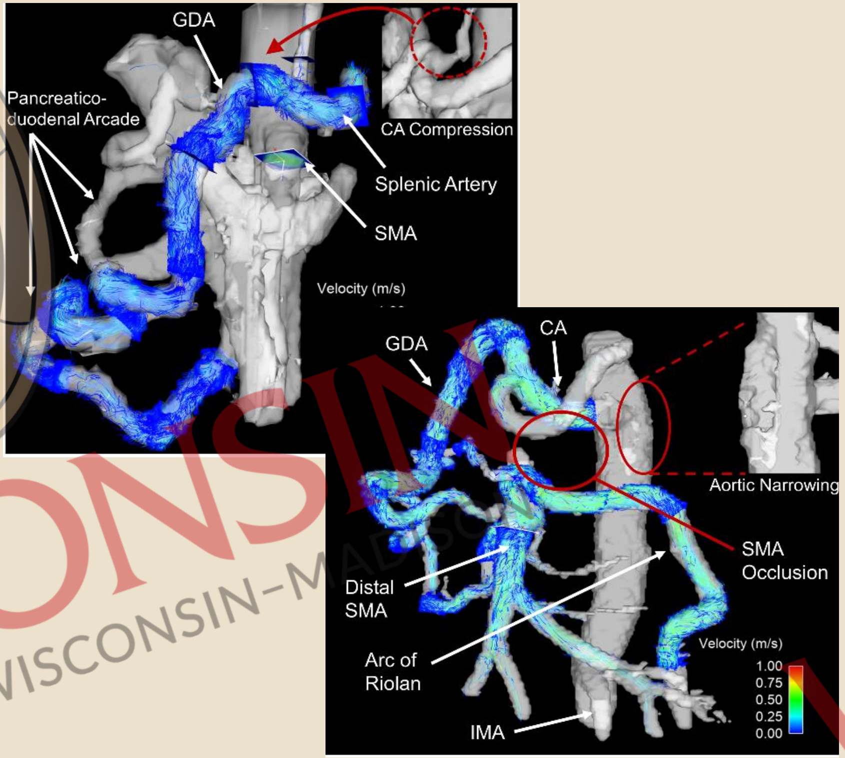






Other Projects Not Covered

Chronic Mesenteric Ischemia




Alejandro Roldan


Chris Francois

Roberts GS, et al (2021). *Abdominal Radiology*. 47(5):1684-98

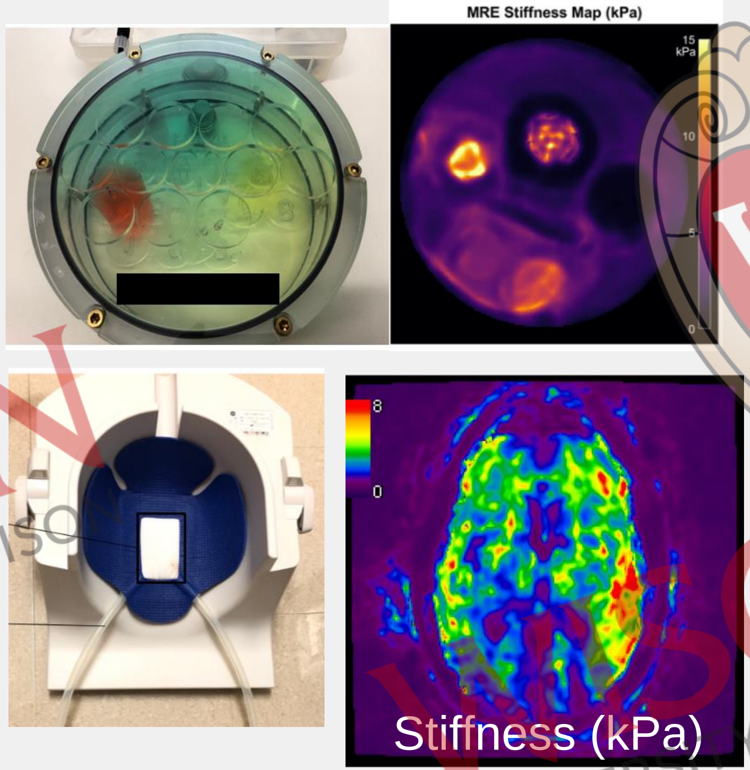
Abdominal 4D Flow MRI


Scott Reeder


Thekla Oechtering

1. Oechtering TH, **Roberts GS**, et al (2022). *Magn Reson Med Sci.* 21(3):340-53
2. Oechtering, TH, **Roberts GS**, et al (2022). *Abdom Radiol*. 47(9):3229-3250

Brain MR Elastography




David Rutkowski


Leonardo Rivera-Rivera

Manuscripts, Funding, and Abstracts

Published and Accepted Manuscripts

1. **Roberts, G. S.*,** Hoffman, C. A.*, Rivera-Rivera, L. A., Berman, S. E., Eisenmenger, L. B., & Wieben, O (2023). "Automated Hemodynamic Assessment for Cranial 4D Flow MRI". *Magnetic Resonance Imaging*. 10.1016/j.mri.2022.12.016.
2. **Roberts, G. S.**, Peret, A., Hoffman, C. A., Koscik, R. L., Jonaitis, E. M., Rivera-Rivera, L. A., Cody, K. A., Rowley, H. A., Johnson, S. C., Wieben, O., Johnson, K. M., & Eisenmenger, L. B (2023). "Normative Cerebral Blood Flow and Pulsatility in Cognitively Unimpaired Older Adults using 4D Flow MRI". *Accepted to Radiology*.
3. **Roberts, G. S.***, Loecher, M. W.*, Spahic, A., Johnson, K. M., Turski, P. A., Eisenmenger, L. B., & Wieben, O. (2022). "Virtual Injections Using 4D Flow MRI with Displacement Corrections and Constrained Probabilistic Streamlines". *Magnetic Resonance in Medicine*. 10.1002/mrm.29134.
4. **Roberts, G. S.,** François, C. J., Starekova, J., Roldán-Alzate, A., & Wieben, O. (2021). Non-invasive assessment of mesenteric hemodynamics in patients with suspected chronic mesenteric ischemia using 4D flow MRI. *Abdominal Radiology (New York)*, 10.1007/s00261-020-02900-0.
5. Oechtering, T. H., **Roberts, G. S.**, Panagiotopoulos, N., Wieben, O., Reeder, S.B., & Roldan-Alzate, A. (2022). Clinical Applications of 4D Flow MRI in the Portal Venous System. *Magnetic Resonance in Medical Sciences.* 10.2463/mrms.rev.2021-0105
6. Oechtering, T. H., **Roberts, G. S.**, Panagiotopoulos, N., Wieben, O., Roldan-Alzate, A., & Reeder, S. B. (2021). Abdominal Applications of Quantitative 4D Flow MRI. *Abdominal Radiology*. 10.1007/s00261-021-03352-w.
7. Macdonald, J. A., **Roberts, G. S.**, Corrado, P. A., Beshish, A. G., Barton, G. P., Goss, K. N., Eldridge, M. W., Francois, C. J., & Wieben, O. (2021). Irregular Right Heart Flow Dynamics in Children and Young Adults Born Preterm. *Journal of Cardiovascular Magnetic Resonance*, 10.1186/s12968-021-00816-2.
8. Capel, K. W., **Roberts, G. S.**, Kuner, A. D., Manunga, J., Chang, W., Spahic, A., Peret, A., Wieben, O., Johnson, K. M., & Eisenmenger, L. B. Beyond Time-of-Flight MRA: Review of Flow Imaging Techniques. *Accepted to Neurographics.*
9. Eisenmenger, L. B.*, Peret, A.*, **Roberts, G. S.**, Spahic, A., Tang, C., Kuner, A., Grayev, A., Field, A., Rowley, H. A., & Kennedy, T. When Less is More: FAST MR Protocols for Neuroradiology. *Accepted in Radiographics.*
10. Eisenmenger, L. B.*, Peret, A.*, Famakin, B. M., Spahic, A., **Roberts, G. S.**, Bockholt, H. J., Johnson, K. M., & Paulsen, J. S. (2022). Vascular Contributions to Alzheimer's Disease. *Translation Research,* 10.1016/j.trsl.2022.12.003.

Independent Funding

2021–2023 National Institute on Aging F31 Predoctoral Fellowship: "Multi-Parametric Imaging of Systemic Cardiovascular and Cerebrovascular Health in Alzheimer's Disease", NIA F31AG071183

Manuscripts, Funding, and Abstracts

Manuscripts Under Review or In Preparation

1. Huang, A., **Roberts, G. S.**, Reeder, S. B., & Oechtering, T. H. Reference Values for 4D Flow Magnetic Resonance Imaging of the Portal Venous System. *Submitted to Abdominal Radiology.*
2. Carter, K. J., Ward, A. T., Kellawan, J. M., Harrell, J. W., Peltonen, G. L., **Roberts, G. S.**, Al-Subu, A., Hagen, S. A., Serlin, R. C., Eldridge, M., Wieben, O., & Schrage, W. G. Reduced Resting Macrovascular and Microvascular Cerebral Blood Flow in Young Adults with Metabolic Syndrome: Exploring Mechanisms. *Submitted to JCBFM.*
3. Spahic, A*, **Roberts, GS***, Peret, A, Rivera-Rivera, LA, Moody, JF, Dean III, DC, Alexander, AL, Johnson, KM, Johnson, SC, Wieben, O, & Eisenmenger, LB. Assessment of Cerebrovascular Disease and White Matter Neurite Density in Alzheimer's Disease. *To Submit to Journal of Alzheimer's Disease.*
4. Peret, A., **Roberts, G. S.**, Hoffman, C. A., Koscik, R. L., Jonaitis, E. M., Rivera-Rivera, L. A., Cody, K. A., Rowley, H. A., Johnson, S. C., Wieben, O., Johnson, K. M., & Eisenmenger, L. B. 4D Flow Magnetic Resonance Imaging for the Study of Normal Cerebrovascular Aging in a Large Cohort of Cognitively Normal Older Adults. *To submit to JAMA Neurology*.
5. **Roberts, G. S.,** Rice, J., Breidenbach, B. M., Naren, T., Bernhardt, Z. S., Fondakowski, J. F., Jarchow, M., Lose, S., Pandos, A., Kecskemeti, S., Eisenmenger, L. B., Johnson, K. M., Okonkwo, O., & Wieben, O. Feasibility of Free-Breathing 2D Phase Contrast MRI for Aortic Pulse Wave Velocity Measurements. *Under Consideration for Submission to JCMR.*

Manuscripts, Funding, and Abstracts

Abstracts Selected for Oral Presentation or Award

1. **Roberts, G. S.**, Peret, A., Rivera-Rivera, L. A., Cody, K. A., Rowley, H. A., Wieben, O., Johnson, S. C., Johnson, K. M., & Eisenmenger, L. B. Defining Normative Cerebral Hemodynamics in Cognitively Healthy Older Adults with 4D Flow MRI. Joint Annual Meeting ISMRM-ESMRMB & SMRT 31st Annual Meeting. 2022 May 7.
2. **Roberts, G. S.**, Rivera-Rivera, L. A., Johnson, K. M., Johnson, S. C., Dean III, D. C., Alexander, A. L., Wieben, O., & Eisenmenger, L. B. Assessment of Cerebrovascular Disease and White Matter Neurite Density in Alzheimer's Disease. 2021 ISMRM & SMRT Annual Meeting & Exhibition; 2021 May 15.
3. **Roberts, G. S.**, Johnson, K. M., Rivera-Rivera, L. A., Kecskemeti, S. R., Okonkwo, O. C., Eisenmenger, L. B., & Wieben, O. Free-Breathing Radial 2D Phase Contrast MRI for Aortic Pulse Wave Velocity Measurements in Healthy Older Adults. Society for Magnetic Resonance Angiography (SMRA) 32nd Annual International Conference; 2020 September 18.
4. **Roberts, G. S.**, Loecher, M. W., Rivera-Rivera, L. A., Turski, P. A., Johnson, K. M., Wieben, O., & Eisenmenger, L. B. Venous Mapping of Vascular Malformations using Cranial 4D Flow MRI. ASNR 58th Annual Meeting of the American Society of Neuroradiology; 2020 May 30.
5. **Roberts, G. S.**, Johnson, K. M., Hoffman, C. A., Eisenmenger, L. B., & Wieben, O. Automating Background Phase Correction in Cranial 4D Flow MRI. Society for Magnetic Resonance Angiography (SMRA) 31st Annual International Conference; 2019 August 27.
6. **Roberts, G. S.**, Francois, C. J., Roldan-Alzate, A., & Wieben, O. Pulsatility and Resistivity Indices in Mesenteric Vasculature in Patients Suspected of Chronic Mesenteric Ischemia using 4D Flow MRI. ISMRM 27th Annual Meeting & Exhibition; 2019 May 11; Montreal, QC, Canada.
7. **Roberts, G. S.**, Roldan-Alzate, A., Francois, C. J., & Wieben, O. Non-Invasive Assessment of Mesenteric Hemodynamics with 4D Flow MRI. Joint Annual Meeting ISMRM-ESMRMB; 2018 June 16; Paris, France.

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Wisconsin Alzheimer's Disease Research Center
GE Healthcare

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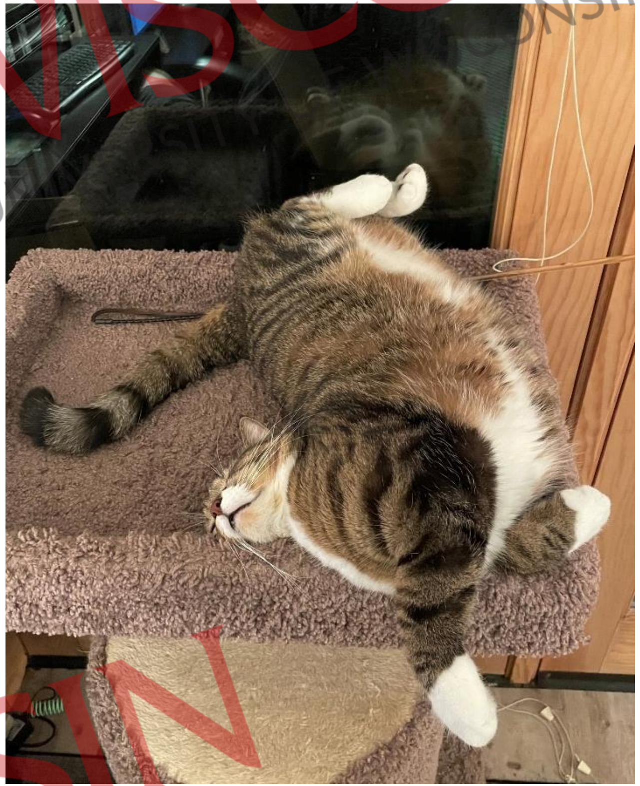
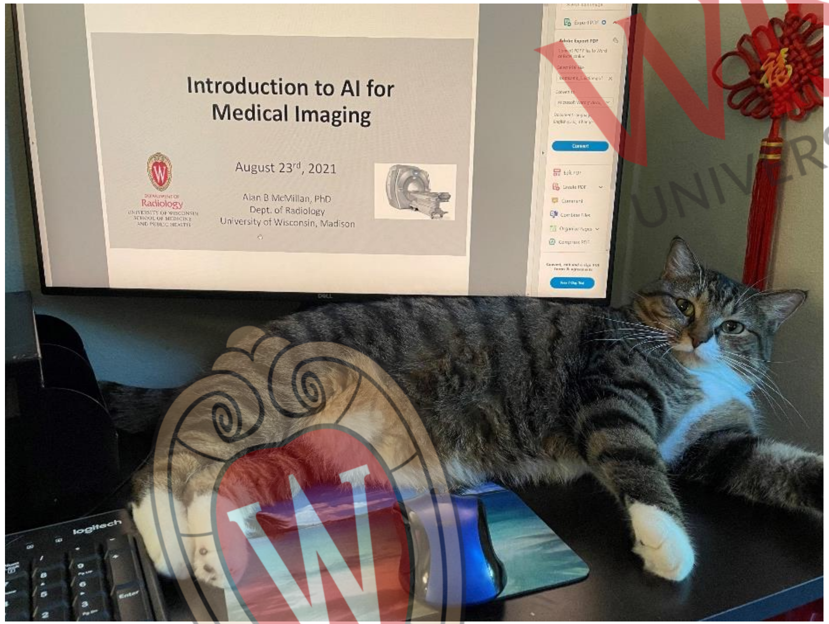
Happy Birthday
Lawrence!


WISCONSIN
TEAM GRANT
Visual Watermark





Introduction to AI for Medical Imaging
August 23rd, 2021
Alan B McMillan, PhD
Dept. of Radiology
University of Wisconsin, Madison
Radiology
logitech

Future

NeoSoft

Role: Data Scientist
Start: April 3rd

Thanks for listening!

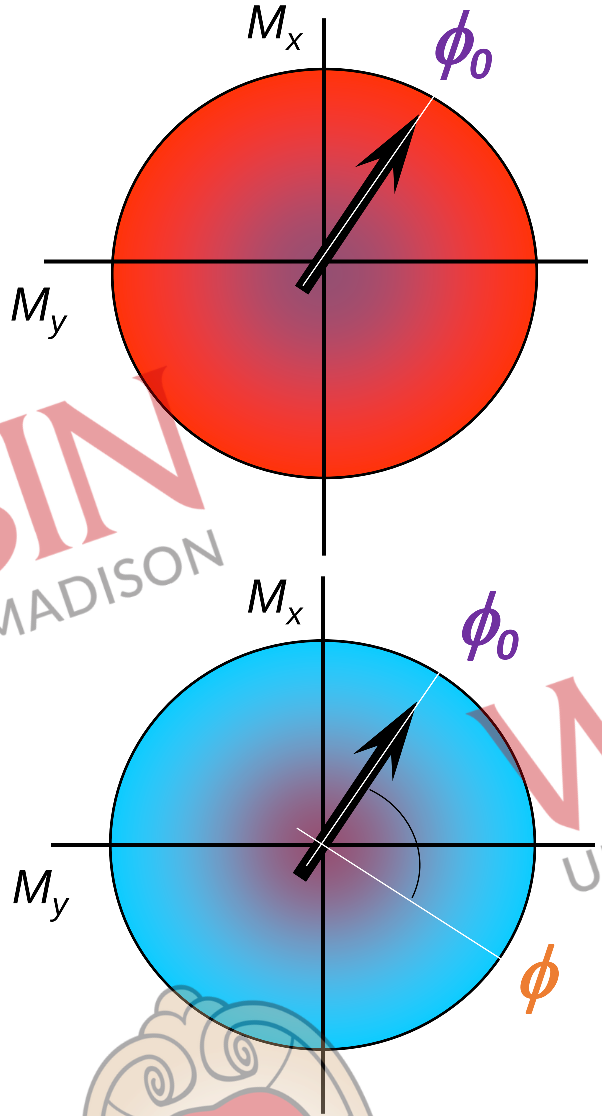
Questions?

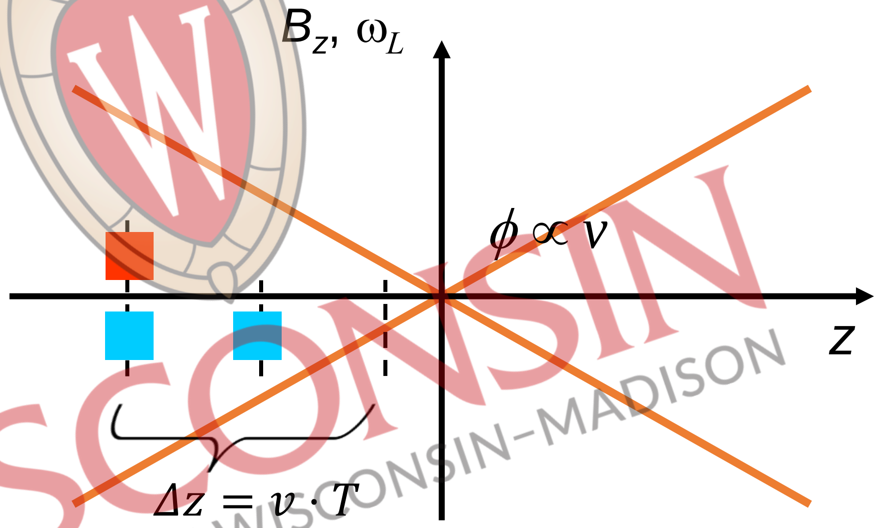
Extra Slides

Phase Contrast MRI

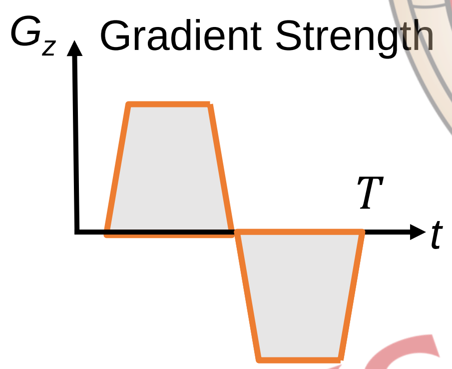
Static Spins

Moving Spins





Bipolar gradient



$$\omega_L = \gamma B_0 + \gamma \Delta B + \gamma(\vec{r}(t) \cdot G_z(t))$$

Main field

Local field

Local gradient and position

Background – Aortic Stiffness

- Aorta stiffness correlates with…
  - Intracranial pulsatility
  - Brain tissue changes
    - White matter hyperintensities
    - Gray matter
  - Alzheimer's disease and dementia
    - "Pulse Wave Encephalopathy"

Pulse wave encephalopathy: a spectrum hypothesis incorporating Alzheimer's disease, vascular dementia and normal pressure hydrocephalus

Grant A Bateman [1]

Arterial Pulse Wave Velocity and Cognition with Advancing Age

Merrill F. Elias, Michael A. Robbins, Marc M. Budge, Walter P. Abhayaratna, Gregory A. Dore, and Penelope K. Elias

Pulse Wave Velocity Is Associated With Greater Risk of Dementia in Mild Cognitive Impairment Patients

Laure Rouch, Philippe Cestac, Brigitte Sallerin, Sandrine Andrieu, Henri Bailly, Maëlle Beunardeau, Adrien Cohen, Delphine Dubail, Intza Hernandorena, Marie-Laure Seux, ... See all authors

The association between pulse wave velocity and cognitive function: the Sydney Memory and Ageing Study

Joel Singer [1], Julian N Trollor, John Crawford, Michael F O'Rourke, Bernhard T Baune, Henry Brodaty, Katherine Samaras, Nicole A Kochan, Lesley Campbell, Perminder S Sachdev, Evelyn Smith

Pulse wave velocity is associated with β-amyloid deposition in the brains of very elderly adults

Timothy M. Hughes, PhD, Lewis H. Kuller, MD, DrPH, Emma J.M. Barinas-Mitchell, PhD, Rachel H. Mackey, PhD, Eric M. McDade, DO, William E. Klunk, MD, PhD, Howard J. Aizenstein, MD, PhD, Ann D. Cohen, PhD, Beth E. Snitz, PhD, Chester A. Mathis, PhD, Steven T. DeKosky, MD, and Oscar L. Lopez, MD

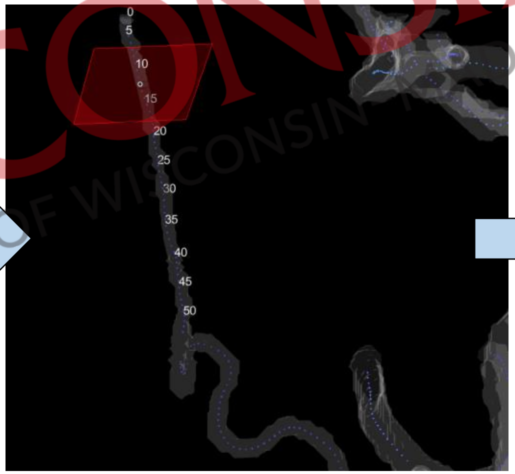
Methods – Automated Post-Processing

- Outline of automated post-processing steps:
  - Global segmentation
  - Create centerlines (skeletonization)
  - Cut-plane generation
  - In-plane segmentation
  - Calculate hemodynamics

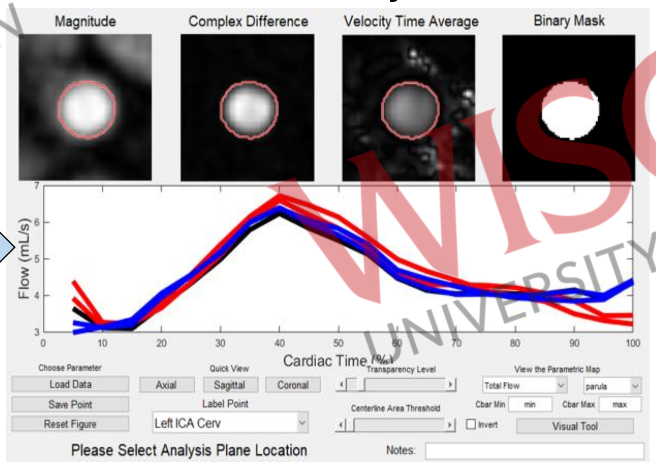
Global Segmentation

Create Centerlines

Automatic Cut-Planes

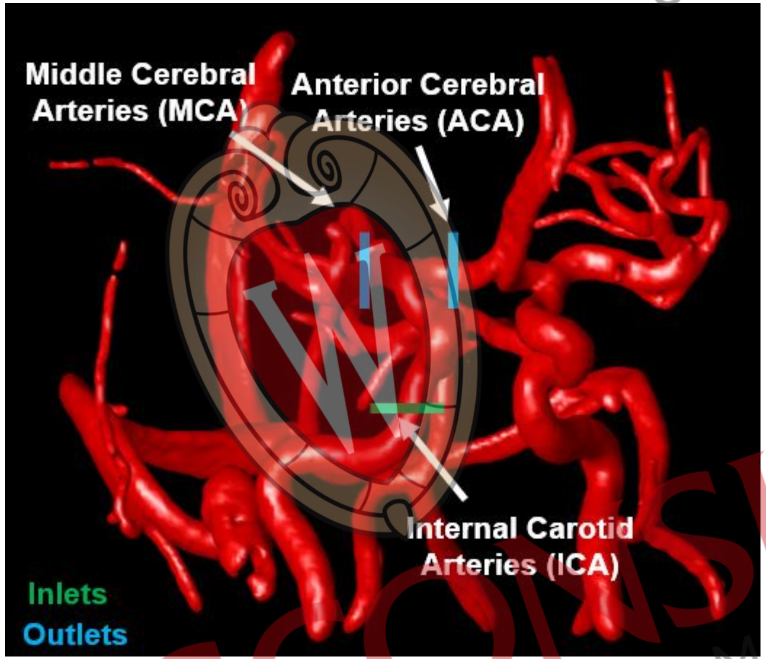


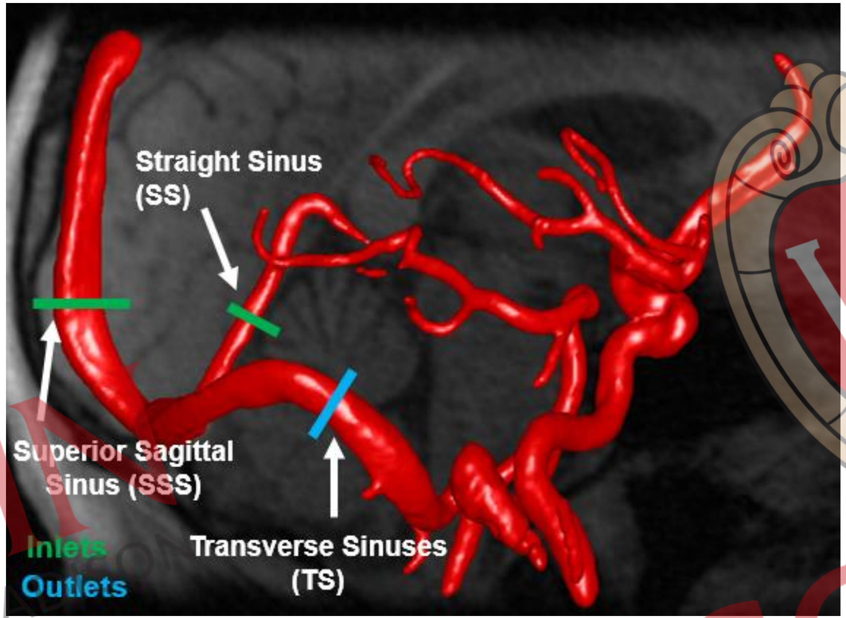
Flow Analysis



Methods – Flow Validation

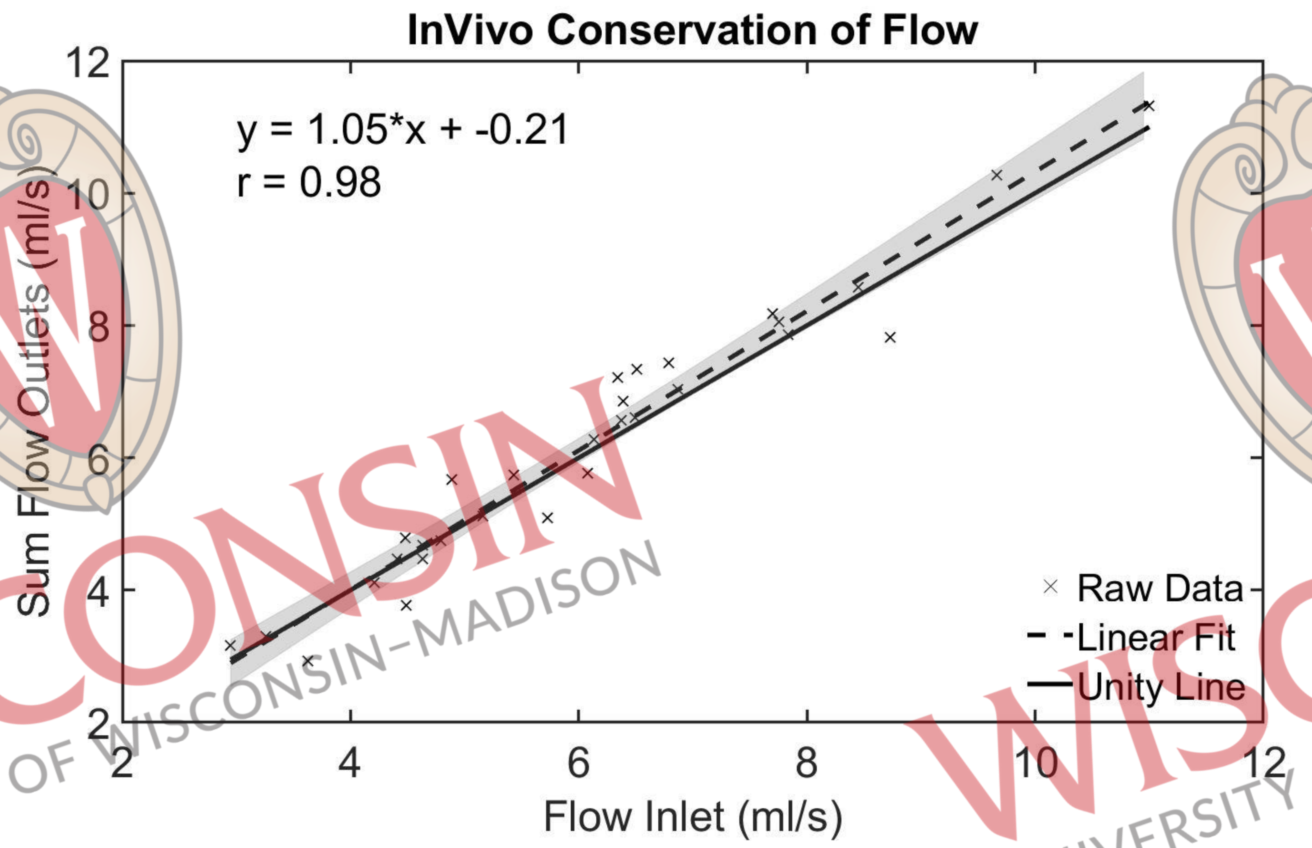
- 4D Flow MRI
  - QVT – Flow Rates
- *In Vitro*
  - **Reference: Ultrasound**
  - Inlet/Outlet flow
    - 7 flow rates
- *In Vivo*
  - **Internal Consistency**
  - Conservation of flow
    - 3 vessel junctions x 10 subjects
      - LICA = LMCA + LACA
      - RICA = RMCA + RACA
      - SSS + SS = LTS + RTS



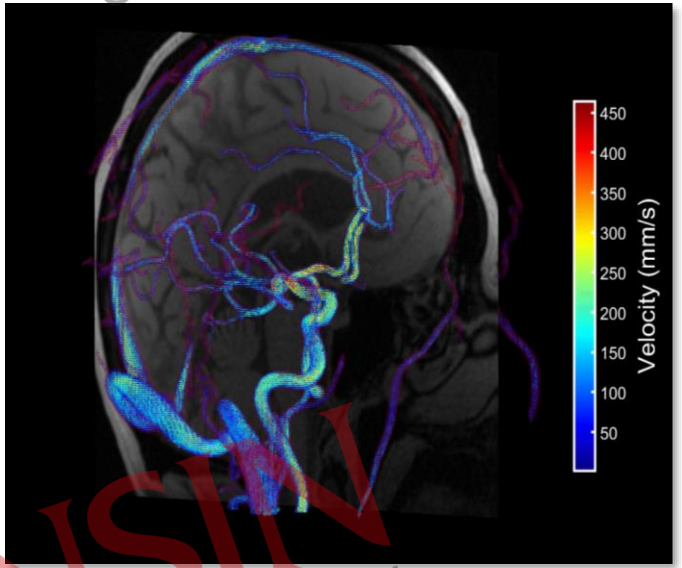


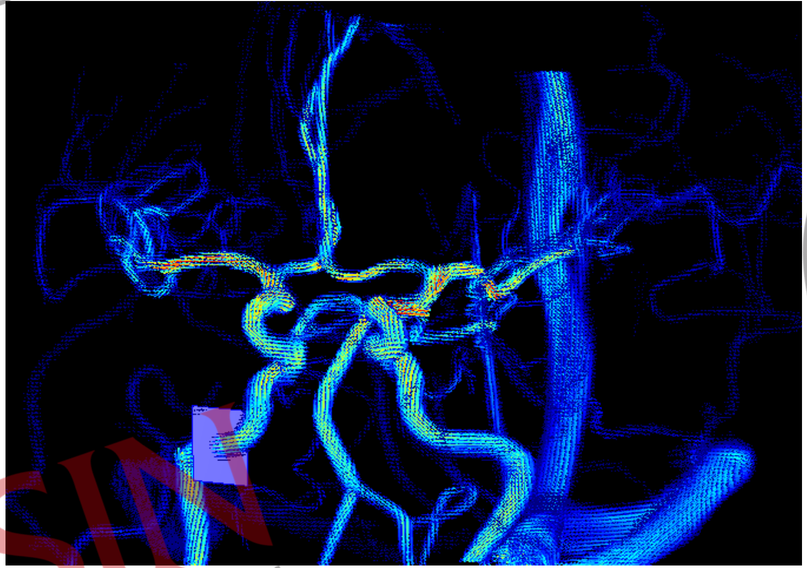
Results – Flow In Vivo

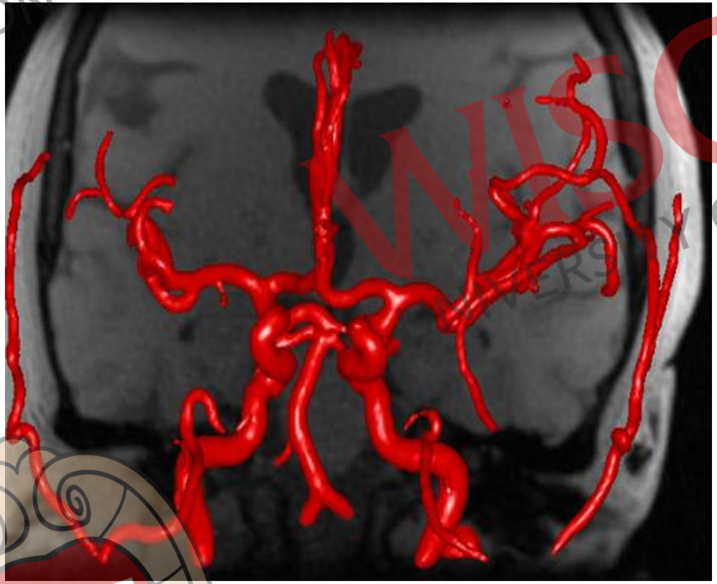
- **Reference: Internal Consistency**
  - Conservation of Flow
    - 3 vessel junctions
- Should validate against ground-truth for future studies

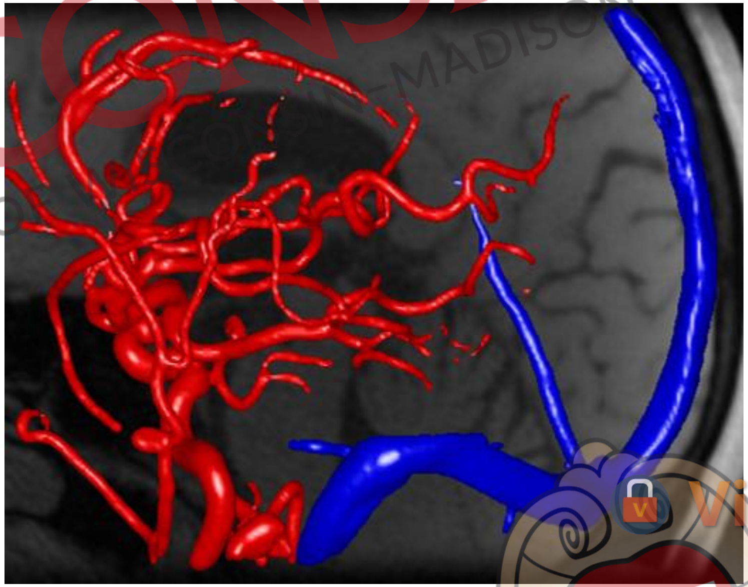


QVT Visualization Features



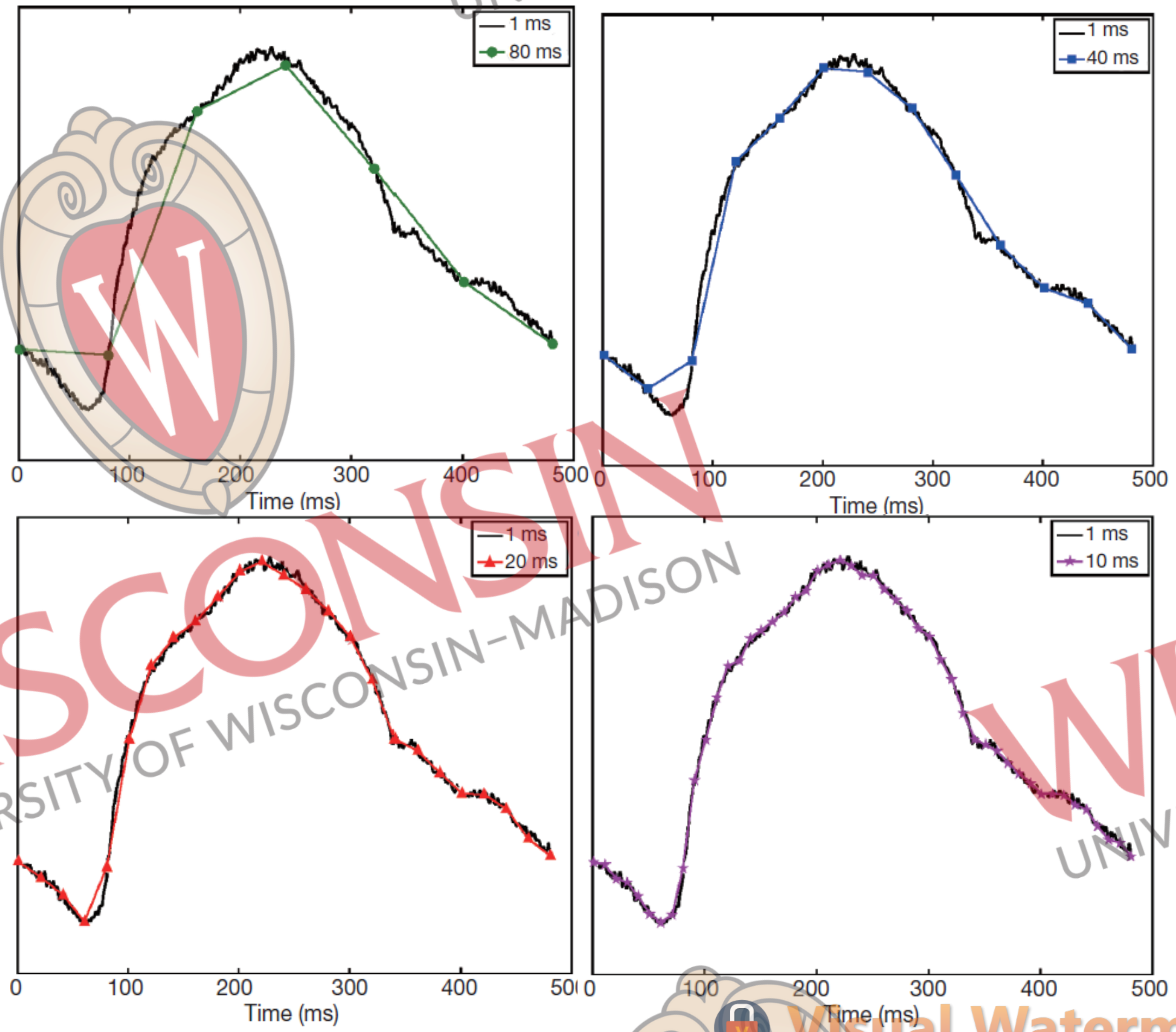






Background – Aortic PWV

- Desirable to have:
  - High temporal resolution[1]
    - Accurately depict waveforms
    - Capture high PWV



From: Wentland AL, et al (2014). *Cardiovasc Diagn Ther*. 4(2):193-206

[1]Wentland AL, et al (2014). *Cardiovasc Diagn Ther*. 4(2):193-206
[2]Kroner ESJ, et al (2012). *JMRI*. 36:1470-6

Methods – Local Low Rank Recon

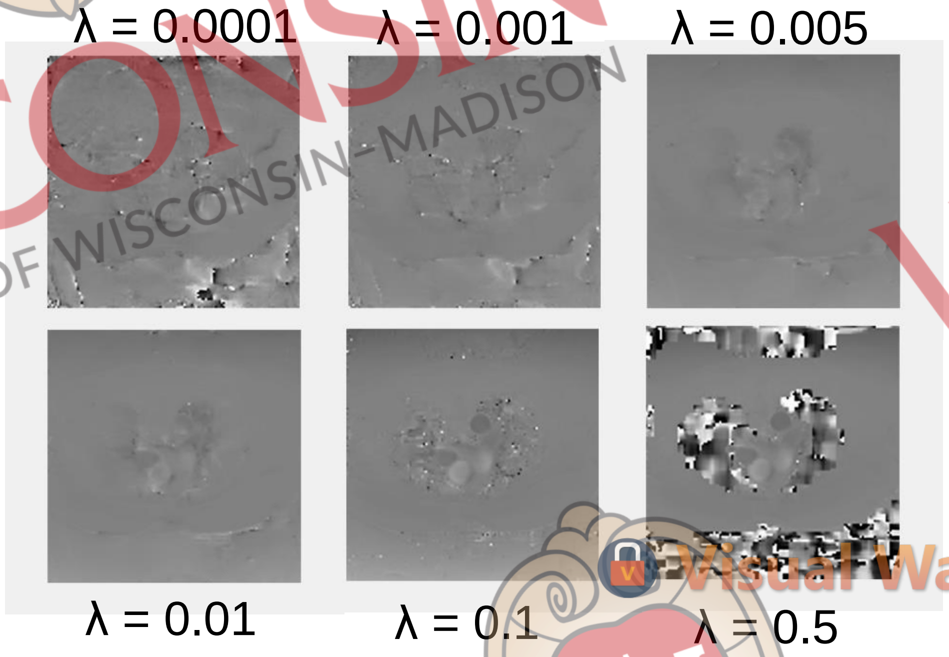
- Local Low Rank Reconstruction[1,2]

$$\hat{\mathbf{x}} = min_{\mathbf{x}} \left[\|\mathbf{Ax} - \mathbf{k}\|_2^2 + \sum \lambda_b \|\mathbf{R}_b\mathbf{x}\|_* \right]$$

Data fidelity term

Temporal sparsity (local low rank)

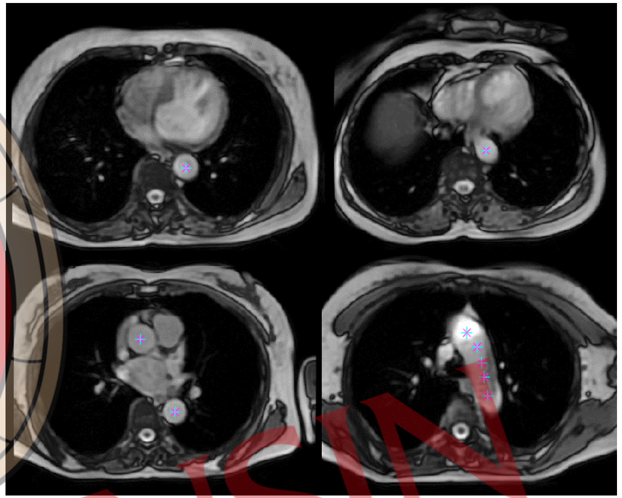
$\hat{x}$ = optimized image
x = image variable
A = coil-sensitivity, FT, and sampling operator
k = acquired k-space data
|| || = norm operator
* = nuclear norm
$\mathbf{R}_b$ = low rank operator acting on b_{th} local block
λ_b = rank weighting coefficient



[1] Jimenez JE, et al (2018). *MRM*. 80(4):1452-66
[2] Rivera-Rivera LA, et al (2021). *JCBFM*. 41(2):298-311

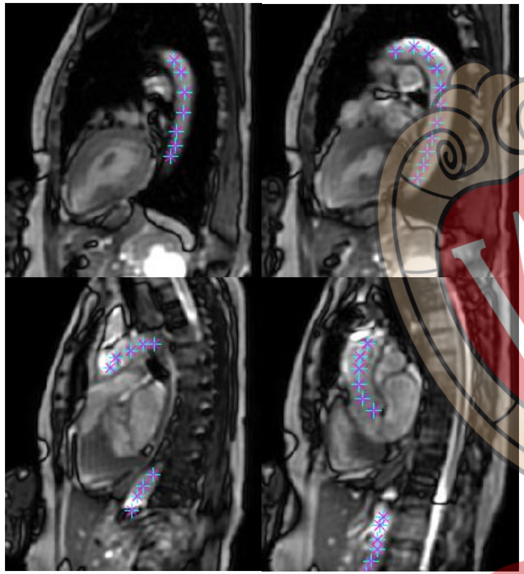
Methods – Graphical User Interface

Axial bSSFP – Aorta Point Selection

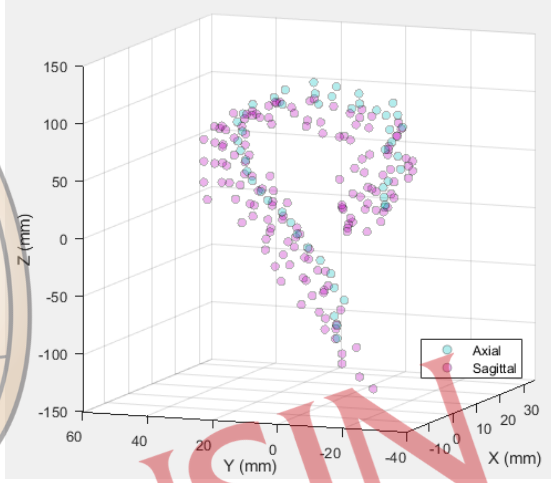


\+

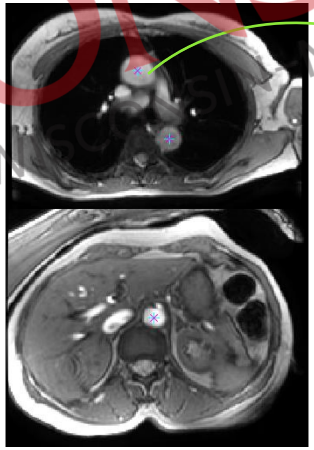
Sagittal bSSFP – Aorta Point Selection



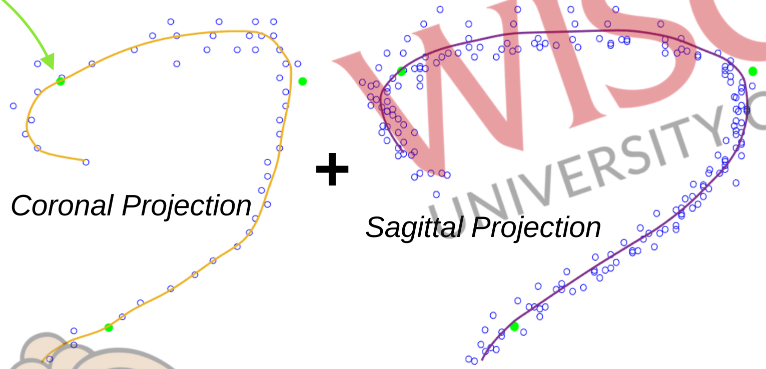
Spatial Localization of Points



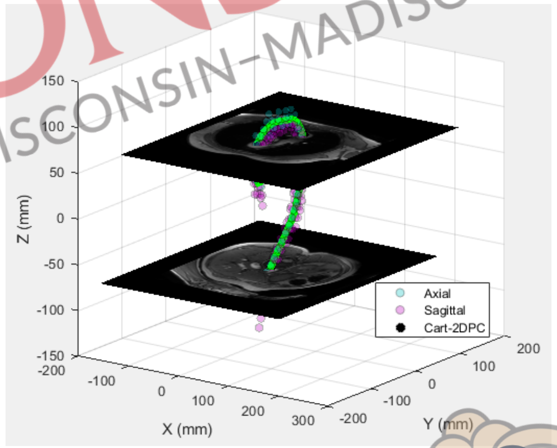
2DPC Point Selection



Aorta Centerline Tracing



3D Centerline Representation



Methods – Local Low Rank Recon

- Local Low Rank Reconstruction[1,2]

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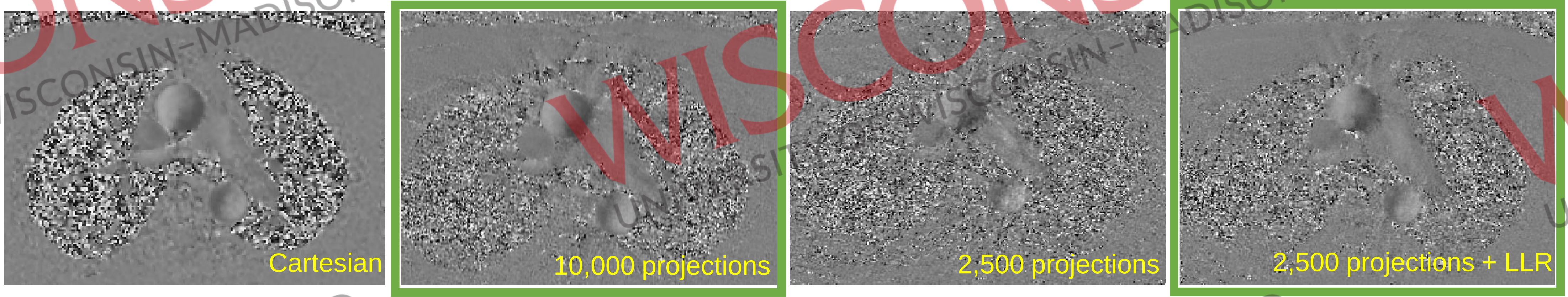
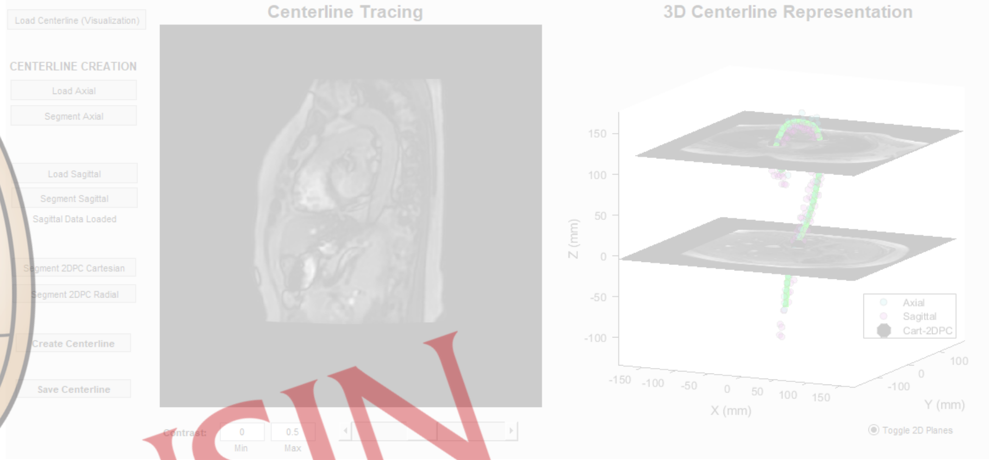


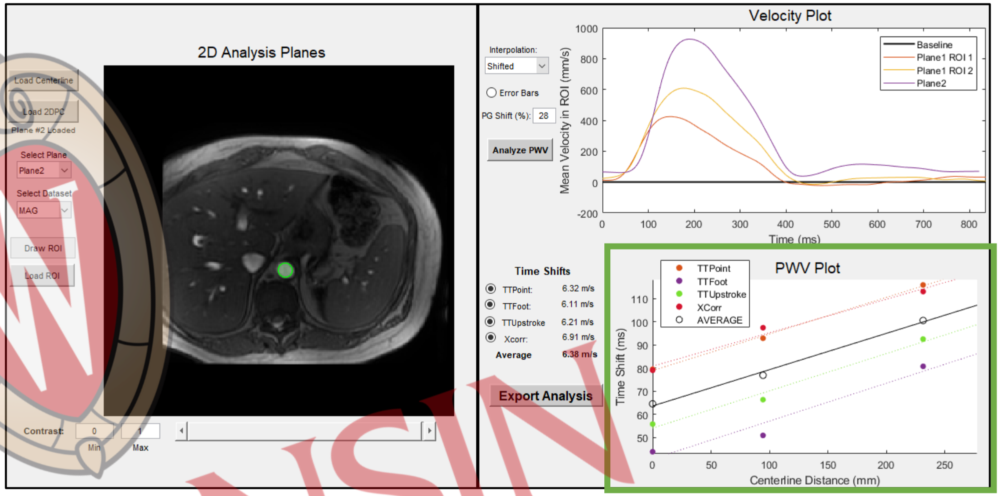
[1]Jimenez JE, et al (2018). *MRM*. 80(4):1452-66
[2] Rivera-Rivera LA, et al (2021). *JCBFM*. 41(2):298-311

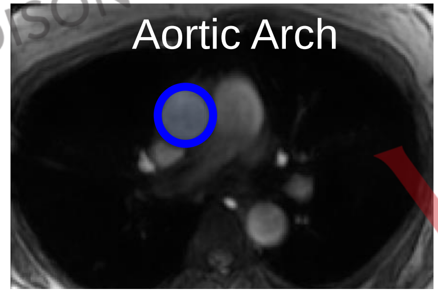
Methods – Graphical User Interface

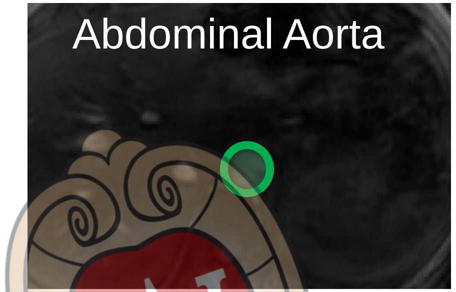
Aorta Distance Measurements

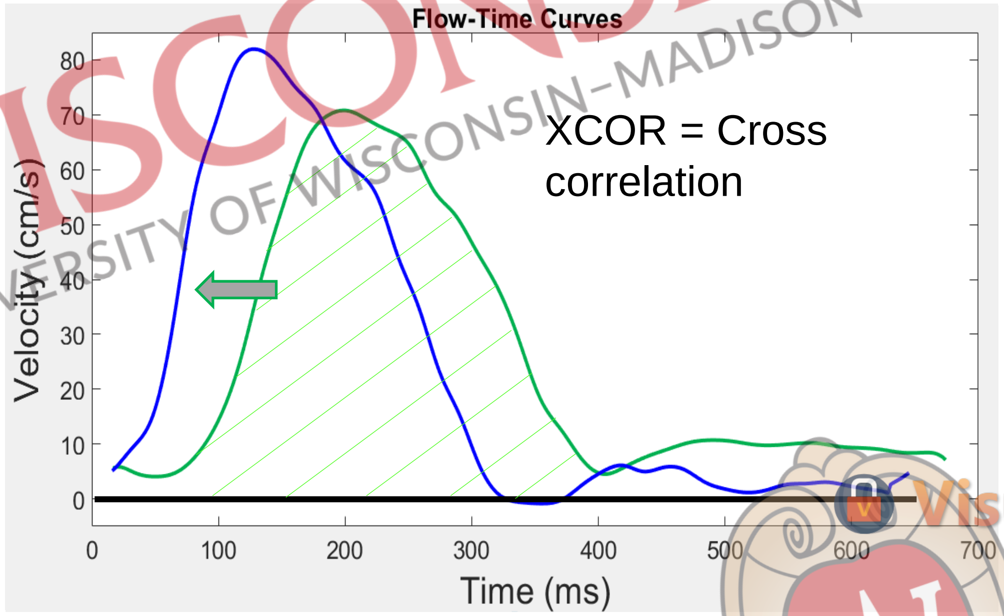


Waveform Time Shifts, PWV Calculation









XCOR = Cross correlation

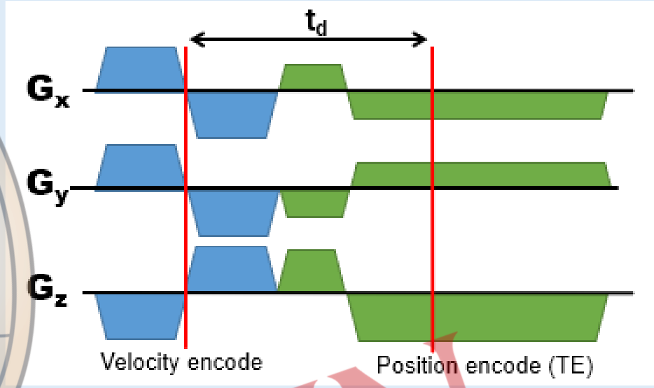
Methods – Flow Phantom

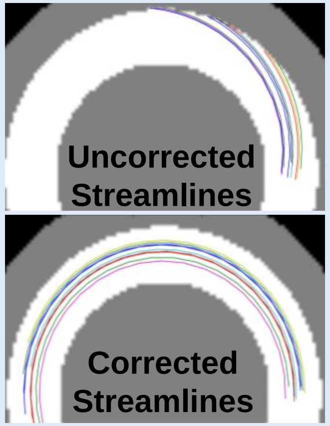
- Aorta model
  - MRA from 25 y.o. male volunteer
  - 3D-printed w/ Elastic 50A™ resin
  - Tygon tubing for ultrasound
  - **Reference: Ultrasound**

Pulse pressure too high

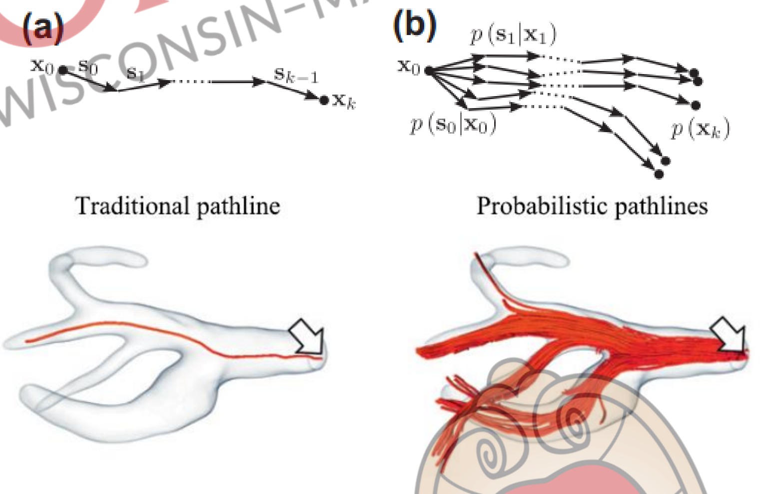
Other Projects – Virtual Injection

Displacement Correction





Probabilistic Streamlines (Monte Carlo)

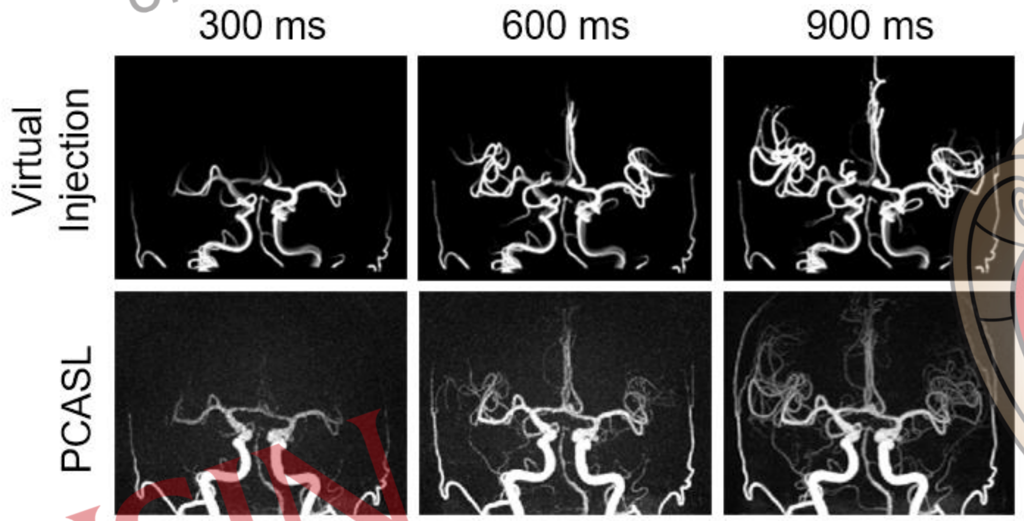


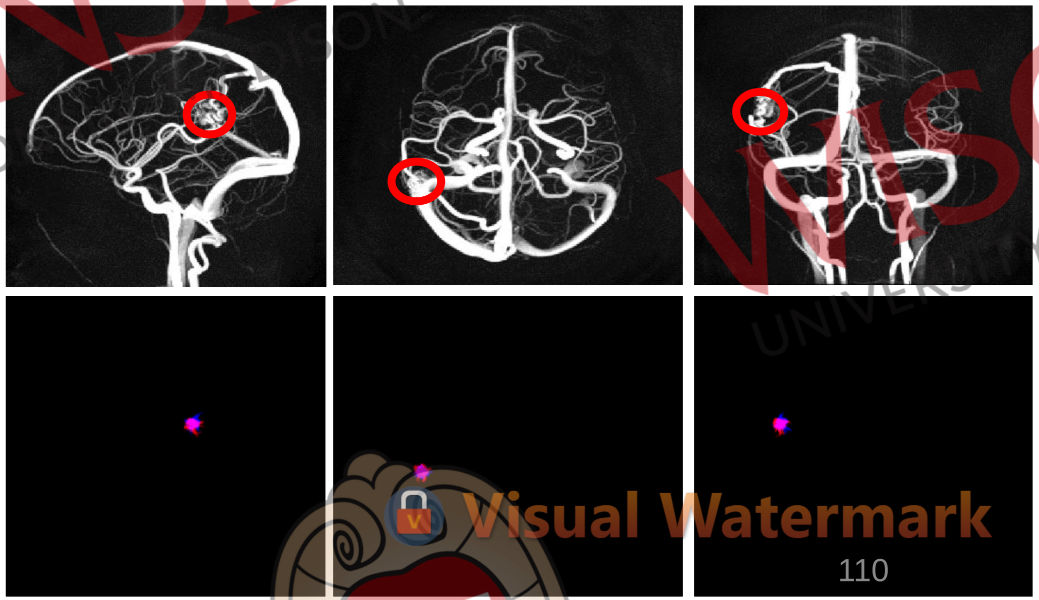
Friman, O et al. *Med Image Anal.* 2011 October; 15(5)

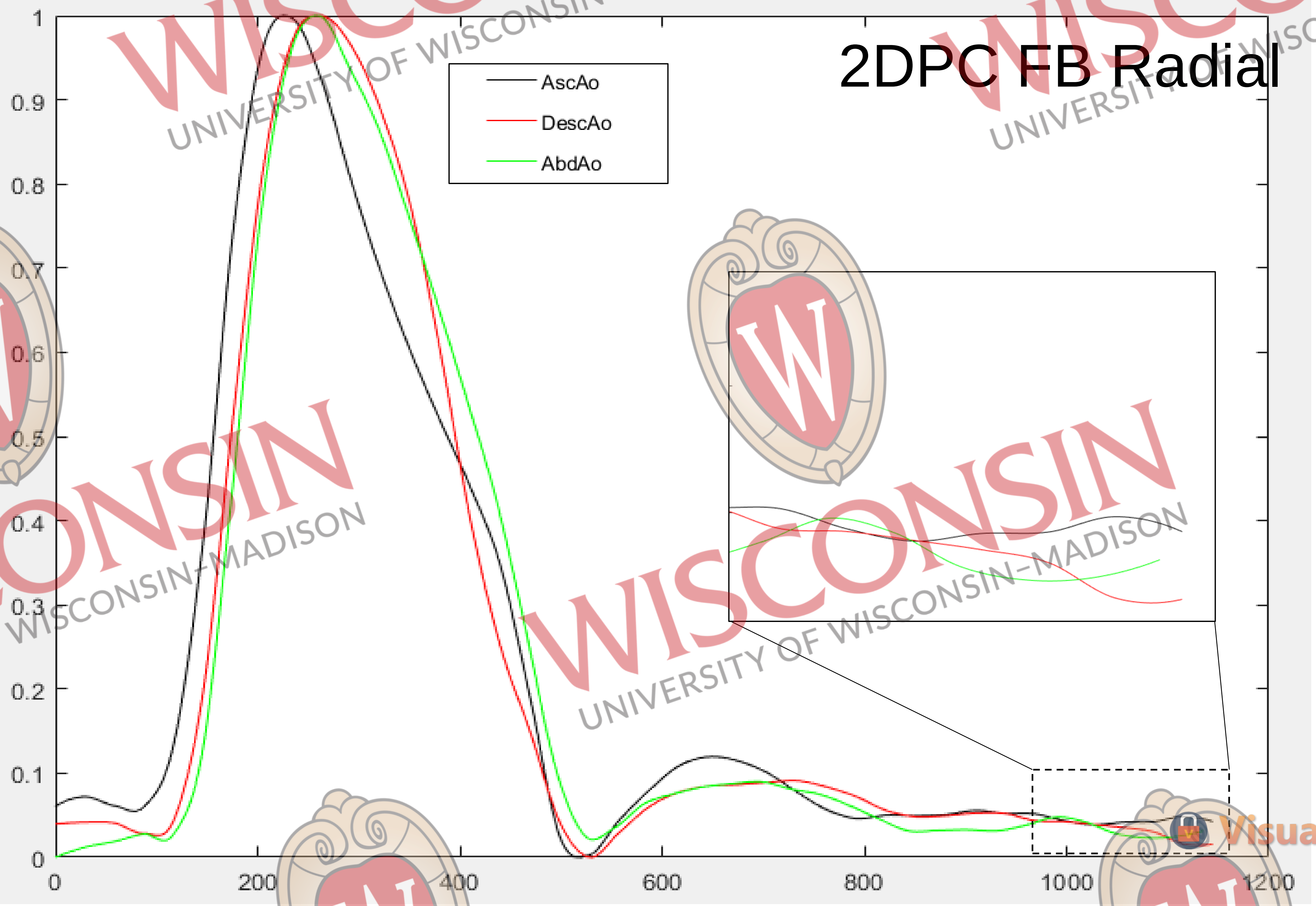
Fluid Constraints

$$p_{CD} = \widehat{CD}(\boldsymbol{r}_j + \tilde{\boldsymbol{s}}_j)$$

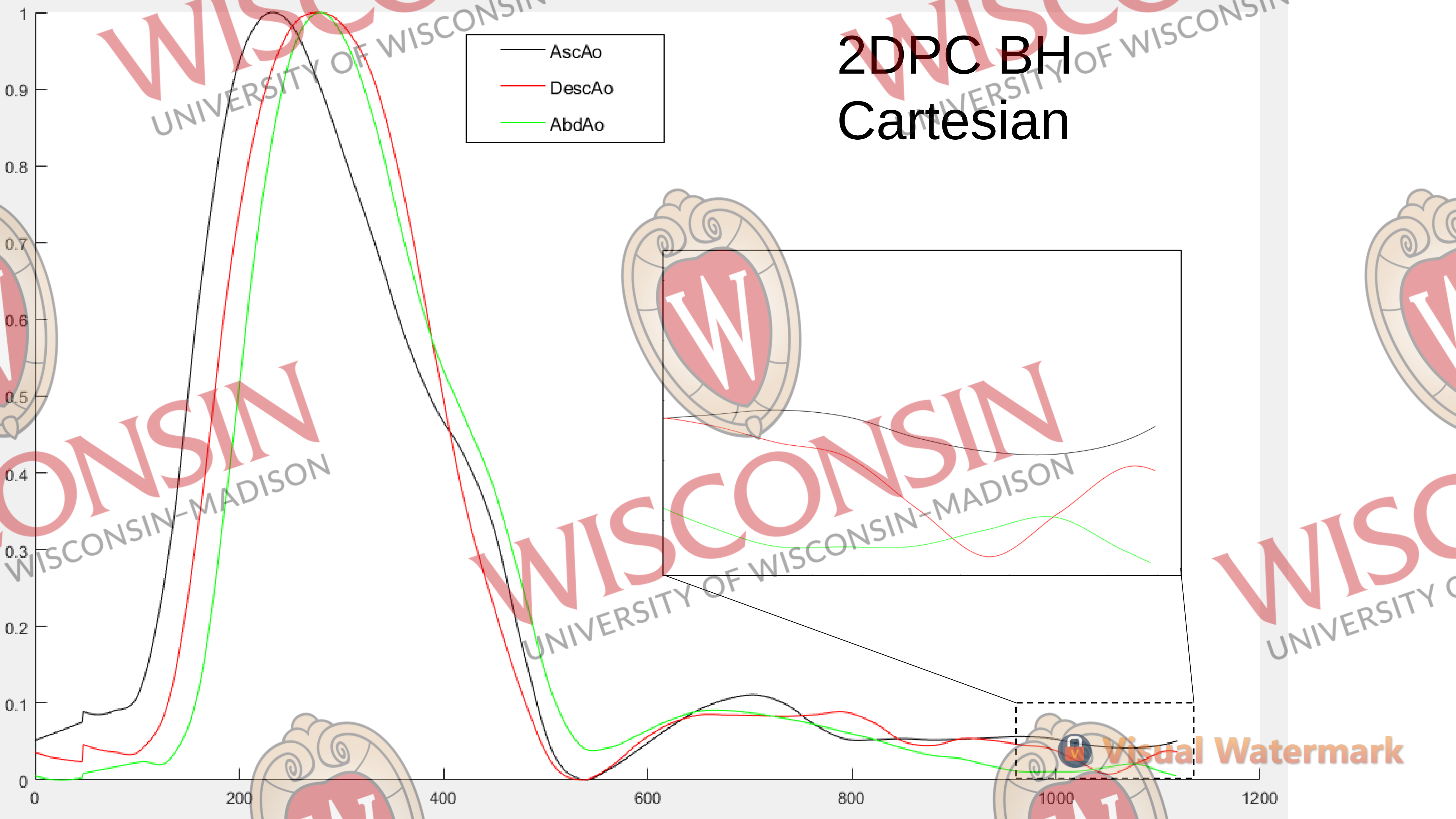
$$p_{KE} = 1 - \frac{|\tilde{\boldsymbol{s}}_j^2 - \boldsymbol{s}_{j-1}^2|}{|\tilde{\boldsymbol{s}}_j^2 + \boldsymbol{s}_{j-1}^2|}$$



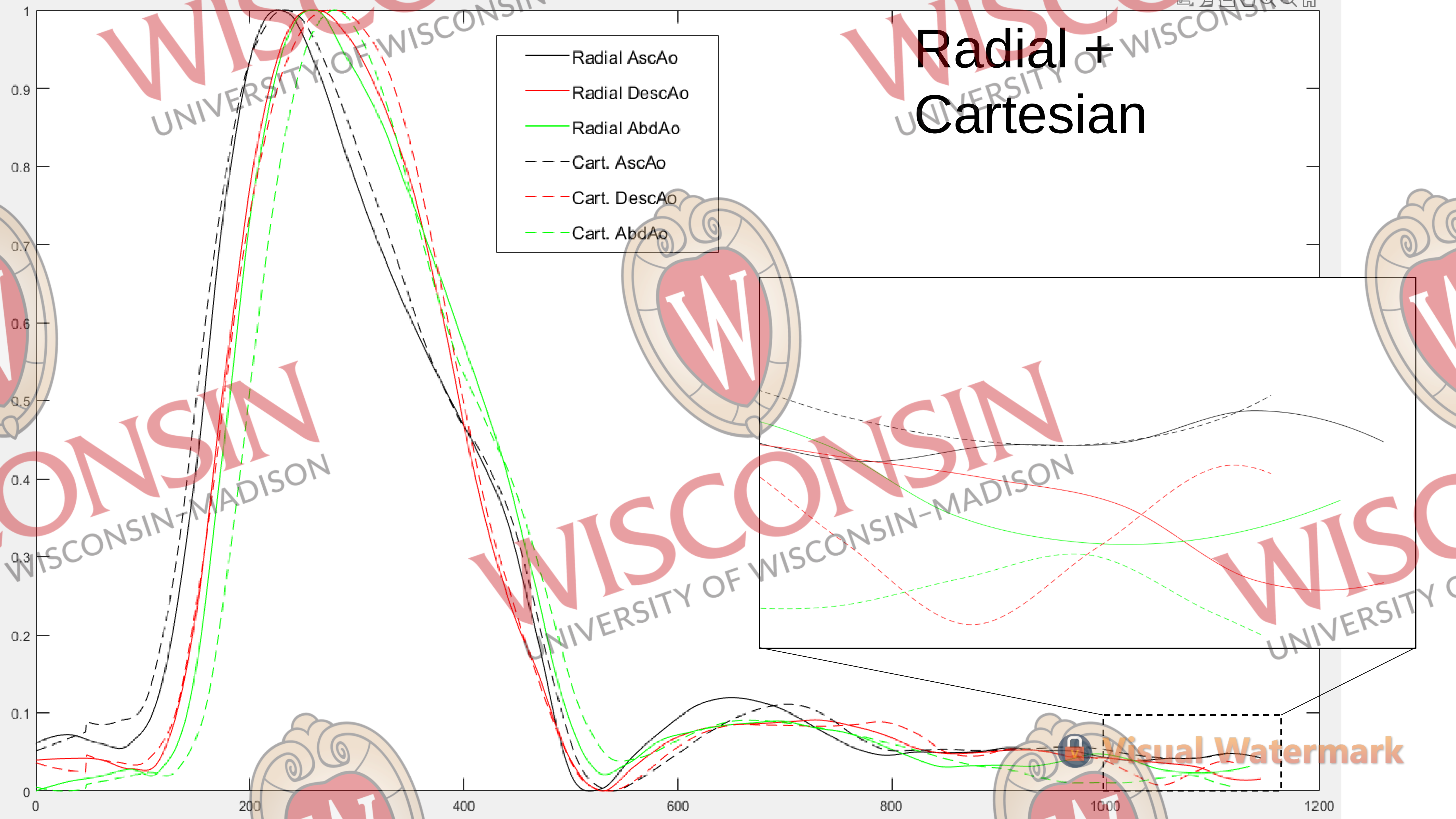




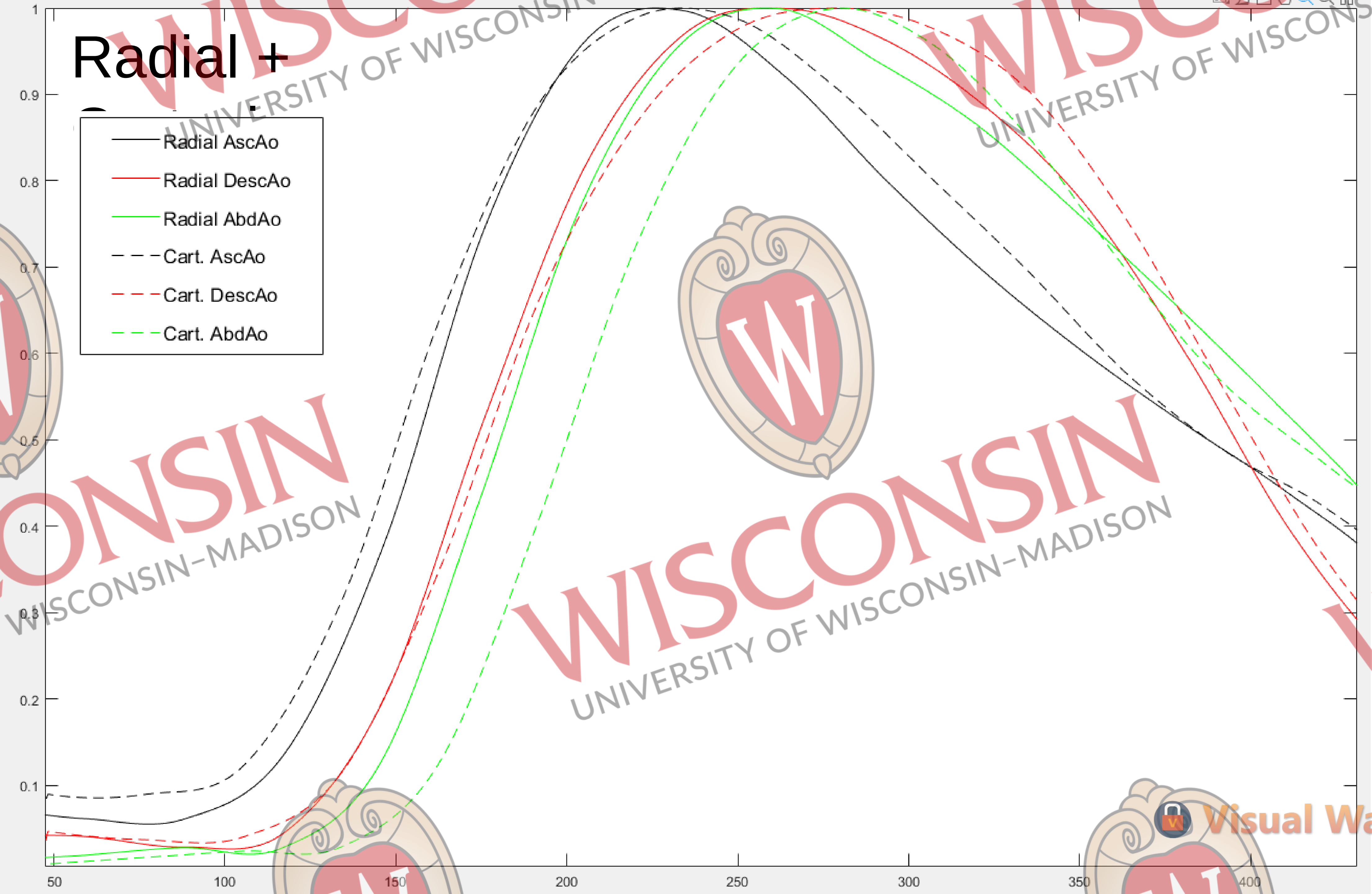
2DPC FB Radial
AscAo
DescAo
AbdAo
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
200
400
600
800
1000
1200

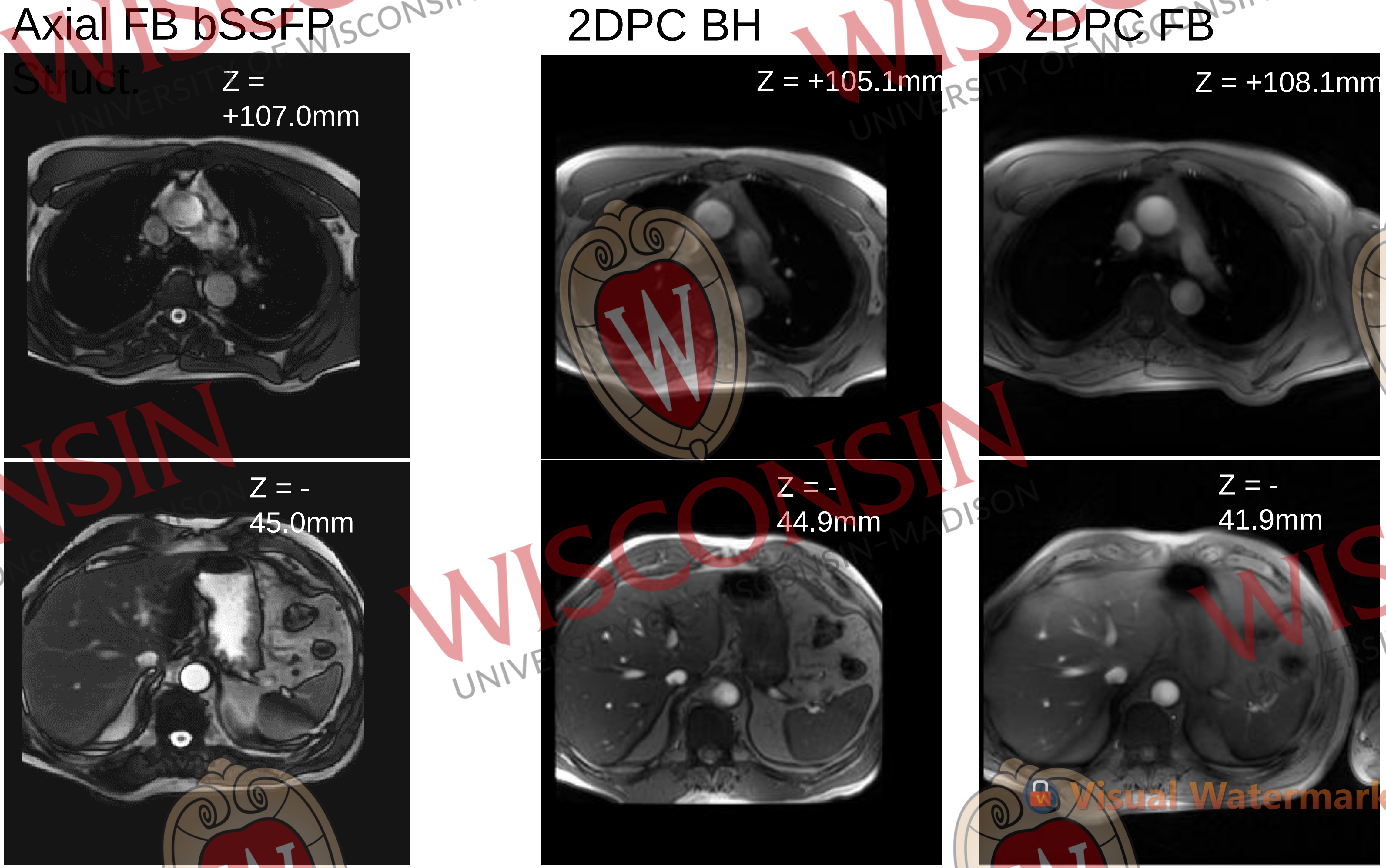


2DPC BH
Cartesian
AscAo
DescAo
AbdAo
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
200
400
600
800
1000
1200



Radial + Cartesian
Radial AscAo
Radial DescAo
Radial AbdAo
Cart. AscAo
Cart. DescAo
Cart. AbdAo
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
200
400
600
800
1000
1200


Radial +
Radial AscAo
Radial DescAo
Radial AbdAo
Cart. AscAo
Cart. DescAo
Cart. AbdAo
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
50
100
150
200
250
300
350
400



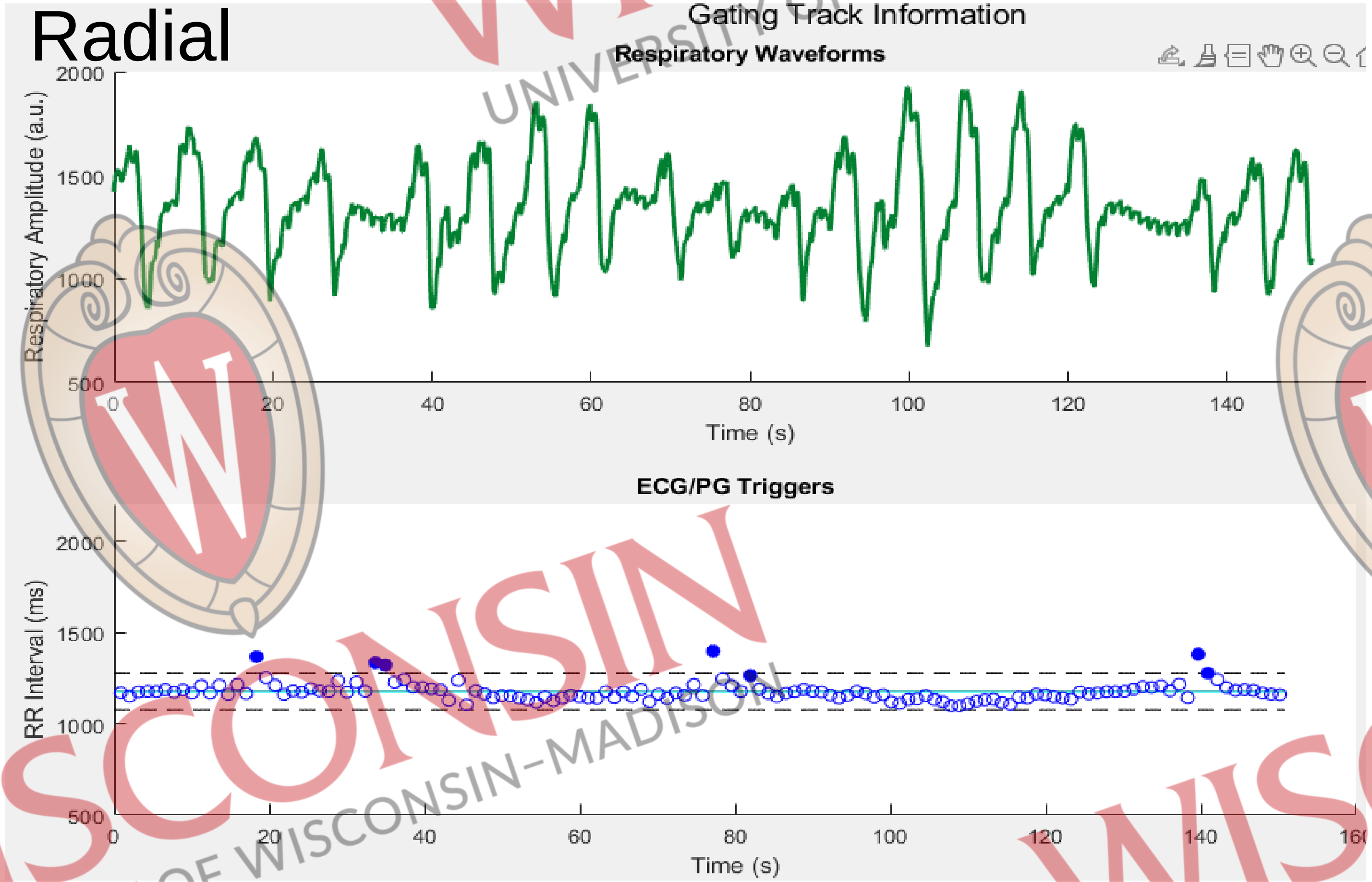
Axial FB bSSFP Struct.
2DPC BH
2DPC FB
Z = +107.0mm
Z = +105.1mm
Z = +108.1mm
Z = -45.0mm
Z = -44.9mm
Z = -41.9mm

2DPC BH Cartesian

Field	Value
DeviceSerialNumber	'0000000608WAISMR'
SoftwareVersions	'27\LX\MR Software release:DV26.0_R03_1831.b'
ProtocolName	'LIFE_20191024b'
TriggerTime	1
NominalInterval	1148
BeatRejectionFlag	'Y'
LowRRValue	1102
HighRRValue	1172
IntervalsAcquired	14
IntervalsRejected	0
HeartRate	52
CardiacNumberOfImages	40
TriggerWindow	20
ReconstructionDiameter	360
ReceiveCoilName	'8US TORSOPA'
AcquisitionMatrix	[192;0;0;160]
InPlanePhaseEncodingDirection	'COL'
FlipAngle	25

TR = 5 ms
VPS = 4
Encode = 2-pt
True temporal res. = 40 ms
Trigger window = 20 ms
Temporal res. = 28.7 ms (40 frames)
Prospectively gated (forced expiration)
Breath-hold

2DPC FB Radial



TR = 7.5 ms
Encode = 2-pt
Temporal res. = 29.4 ms (40 frames)
Retrospectively gated (expiration 0-50%)
Free-breathing

2DPC BH Cartesian

Field	Value
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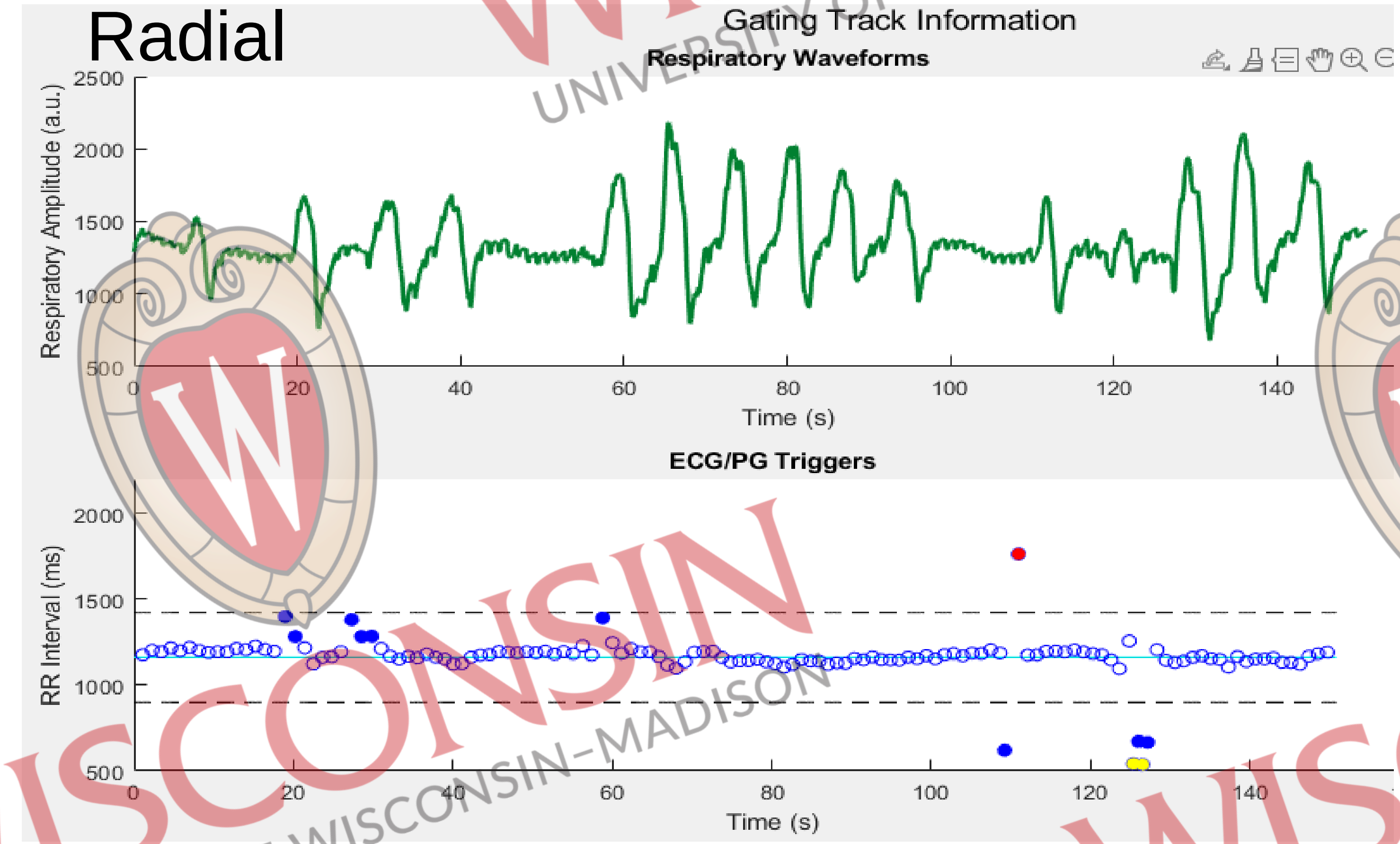
SoftwareVersions	'27\LX\MR Software release:DV26.0_R03_1831.b'
ProtocolName	'LIFE_20191024b'
TriggerTime	1
NominalInterval	1146
BeatRejectionFlag	'Y'
LowRRValue	1112
HighRRValue	1182
IntervalsAcquired	14
IntervalsRejected	0
HeartRate	52
CardiacNumberOfImages	40
TriggerWindow	20
ReconstructionDiameter	360
ReceiveCoilName	'8US TORSOPA'
AcquisitionMatrix	[192;0;0;160]
InPlanePhaseEncodingDirection	'COL'
FlipAngle	25

Temporal res. = **28.7 ms** (40 frames)
Prospectively gated (forced expiration)
Breath-hold

2DPC FB Radial



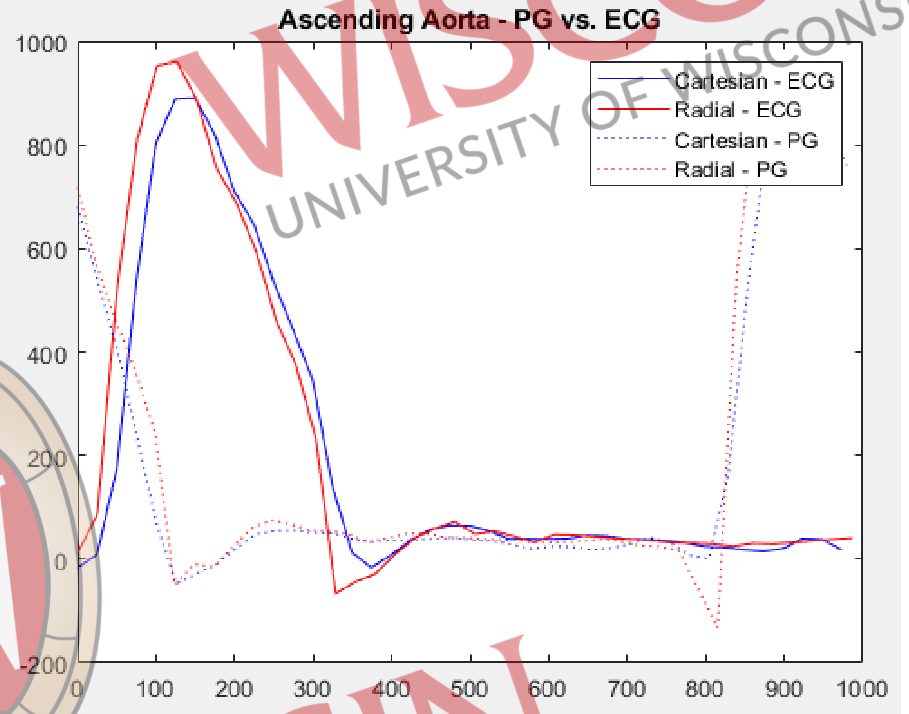
Temporal res. = **29.1 ms** (40 frames)
Retrospectively gated (expiration 0-50%)
Free-breathing

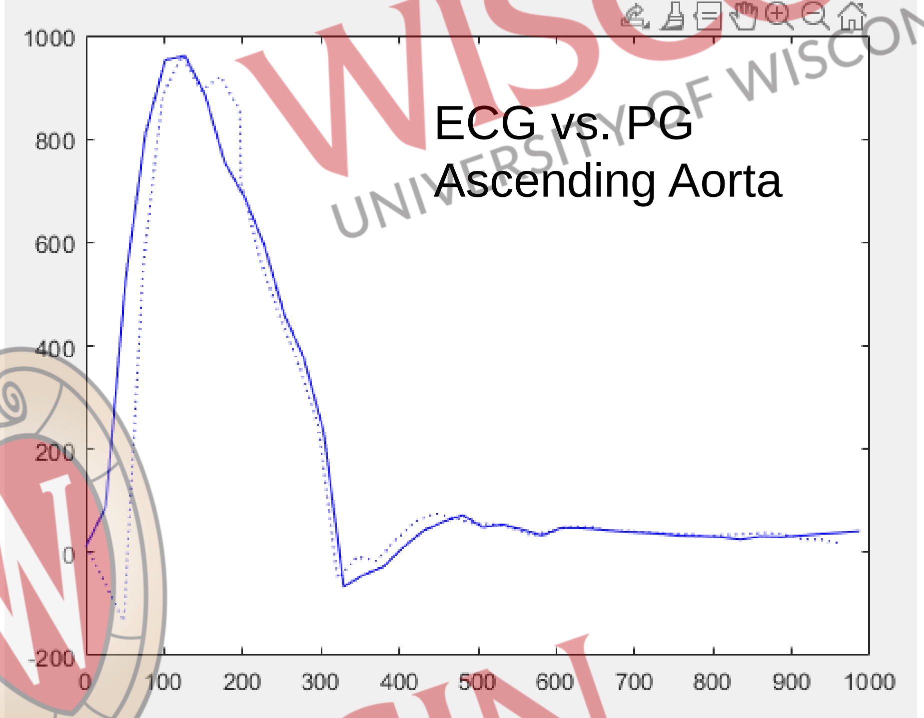
Checked:

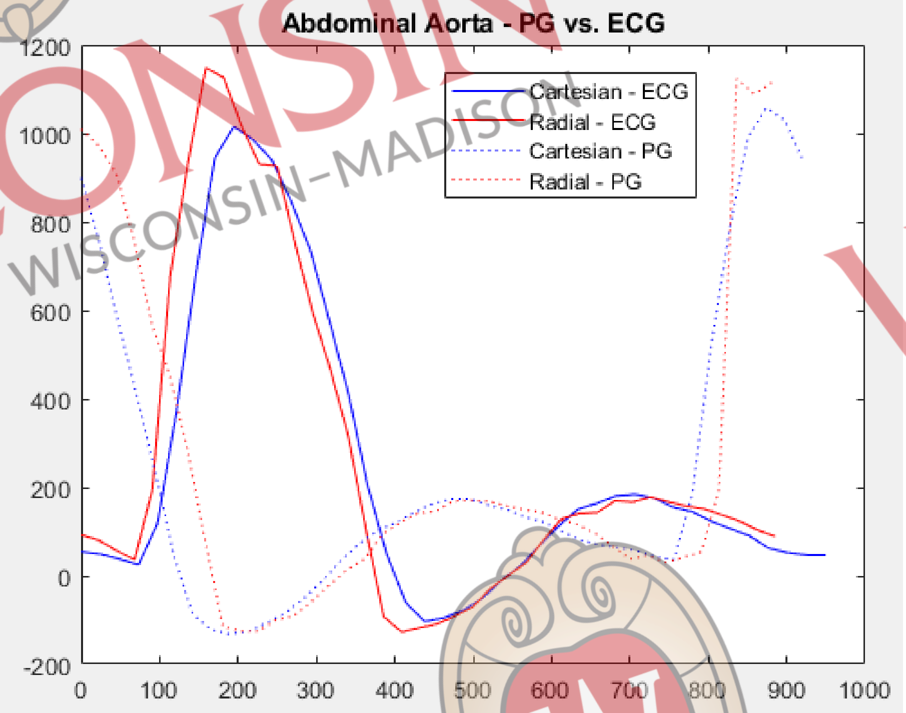
- Radial and Cartesian planes are approximately in the same location
- Timestamps in DICOM aren't offset (due to trigger window)
- Cardiac/Respiratory gating signals
- Differing temporal resolutions between AAo and AbdAo scans
  - Tool uses absolute time, not frames, to calculate PWV
- Waveform normalization
- Centerline distances are same between Radial/Cartesian
- Re-checked TTU/TTF/TTP/XCORR time shift methods

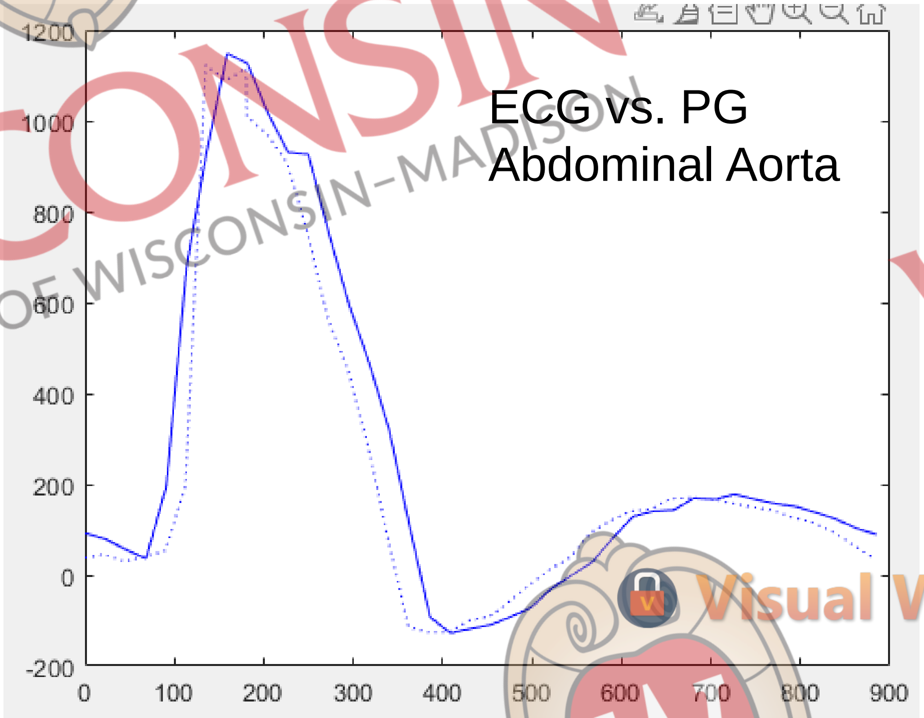
To Test:

- Reconstruct with constant temporal resolution (differing frames)
- Volunteer scans with forced expiration/inspiration
- PG vs. ECG (seeing differences in AscAo and DescAo flow waveforms)


Ascending Aorta - PG vs. ECG
Cartesian - ECG
Radial - ECG
Cartesian - PG
Radial - PG


ECG vs. PG
Ascending Aorta


Abdominal Aorta - PG vs. ECG
Cartesian - ECG
Radial - ECG
Cartesian - PG
Radial - PG


ECG vs. PG
Abdominal Aorta