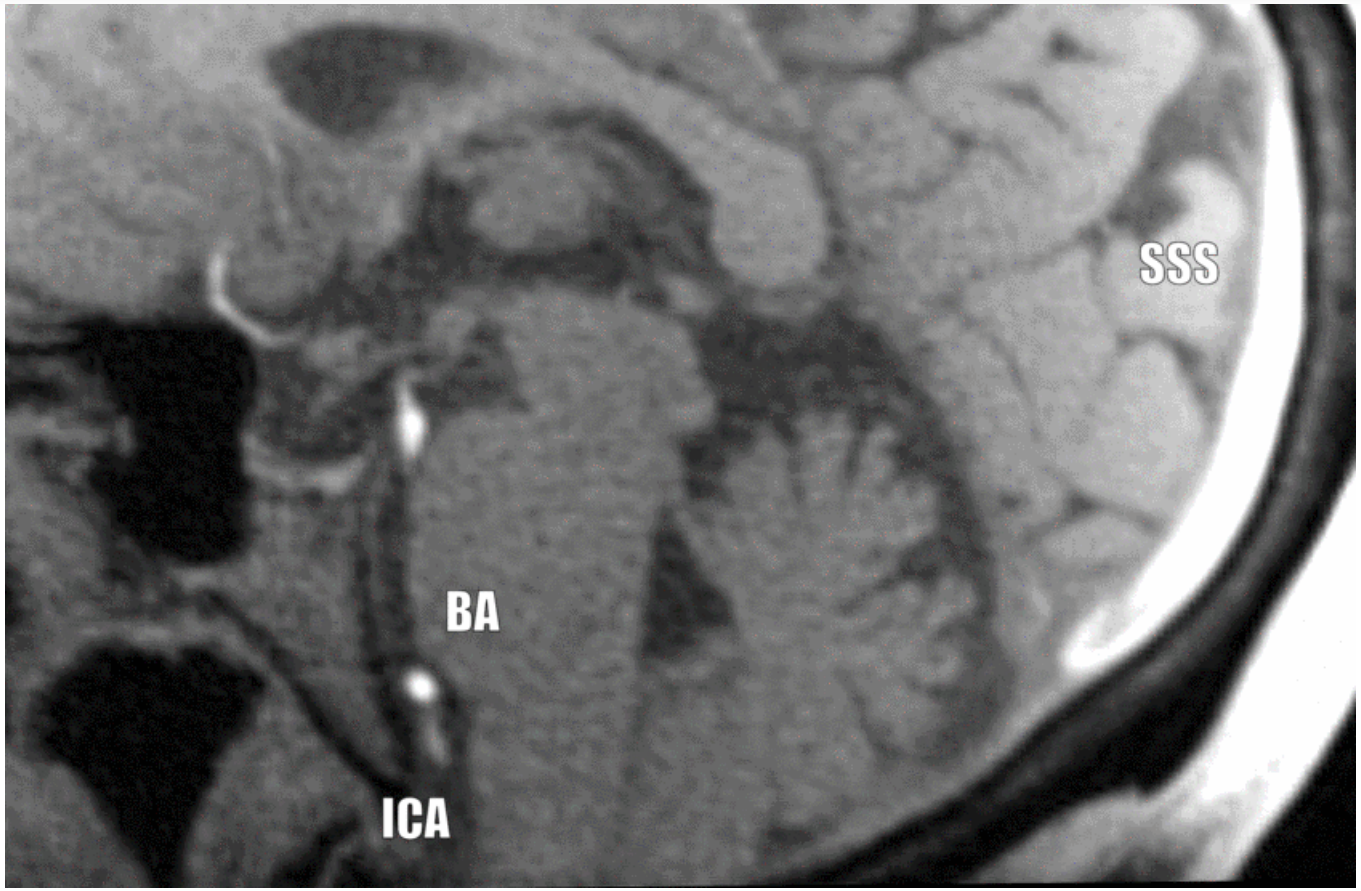
Cerebrovascular Markers in Alzheimer's Disease Quantifiable with 4D Flow MRI



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Alzheimer's disease and cerebrovascular disease

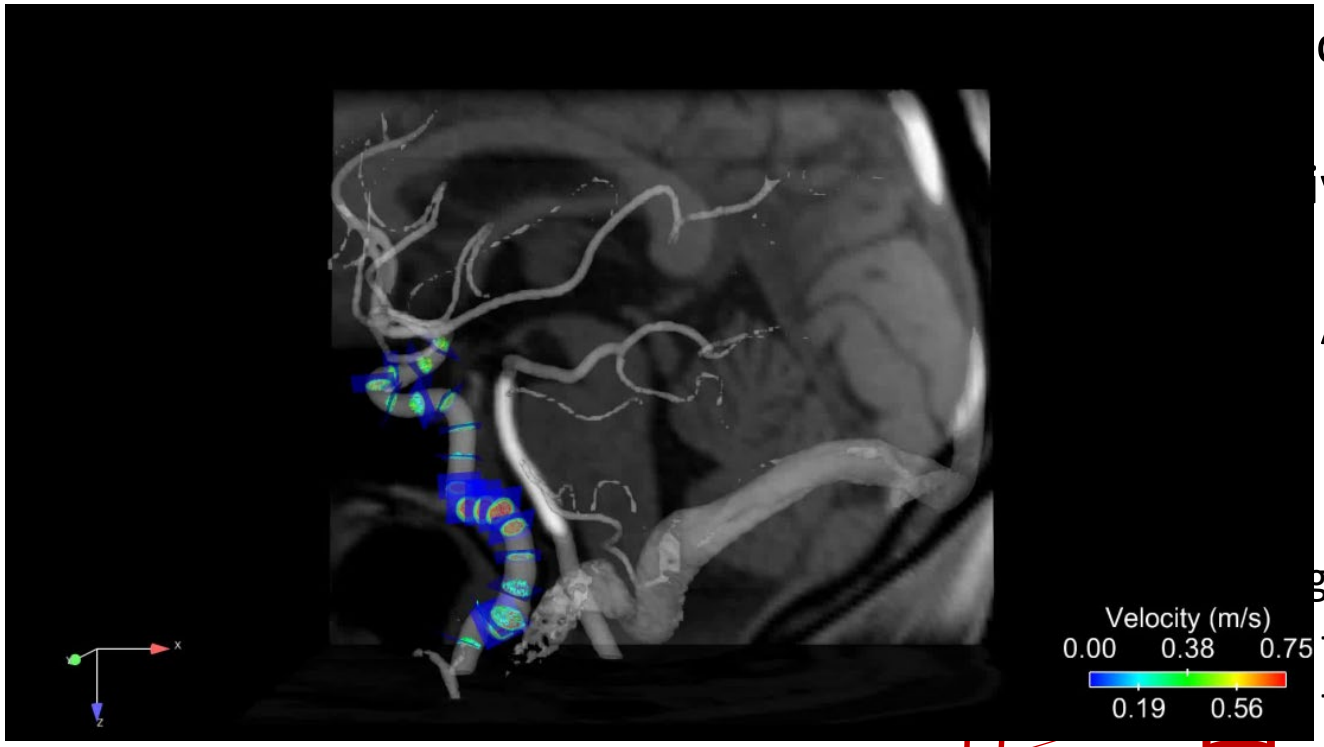
- **Cerebrovascular disease manifests in AD but is also an independent cause of dementia**

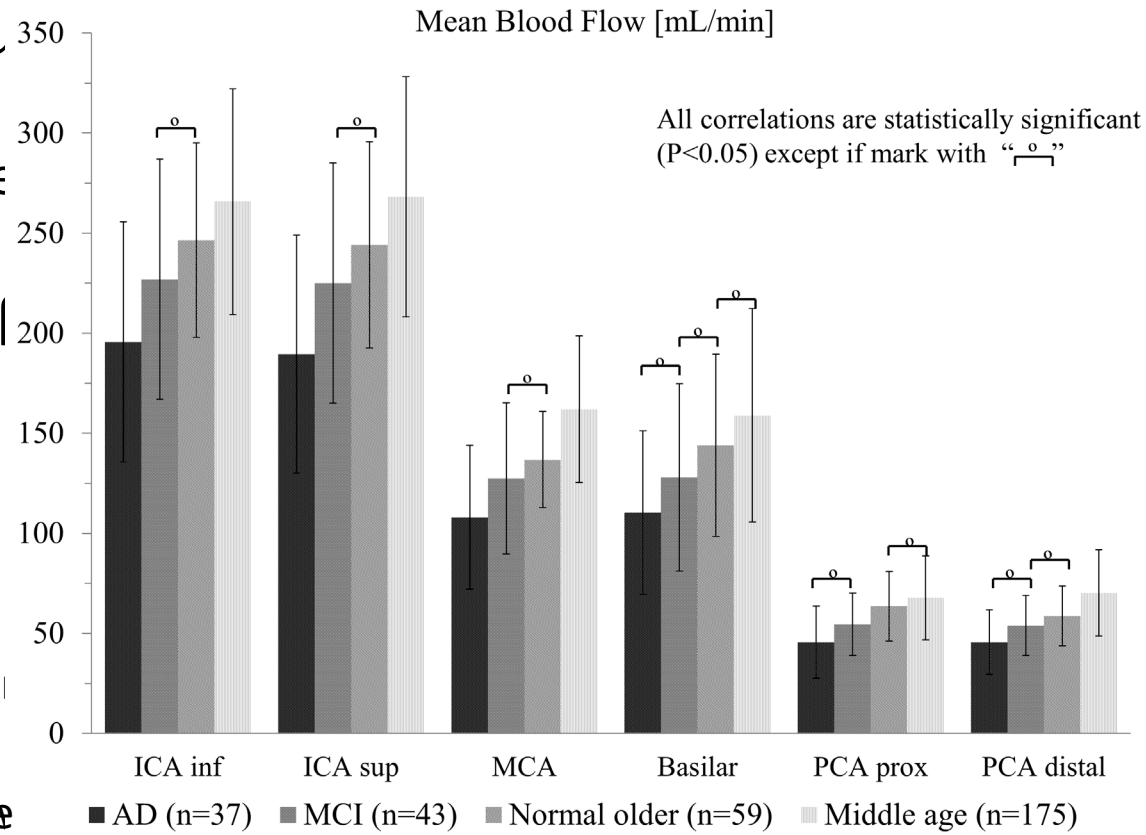
- **AD – CVD hypotheses need testing:**
  - Additive, causative, AND/OR combinatorial effects ?
  - Will CVD biomarkers improve early diagnosis ?

- **Need for CVD biomarkers in longitudinal studies of subjects at risk of AD**
  - Push to incorporate vascular dysfunction into the AT(N) biomarker system (Responses to the 2018 NIA-AA Research Framework [1,2])
  - Potential for MRI biomarkers of CVD

[1] Jack CR Jr. et al. Alzheimer's & Dementia 14 (2018) 535-562
[2] Sweeney et al. Alzheimer's & Dementia 15 (2019) 158-167

Neuroimaging of cerebrovascular disease using 4D flow MRI





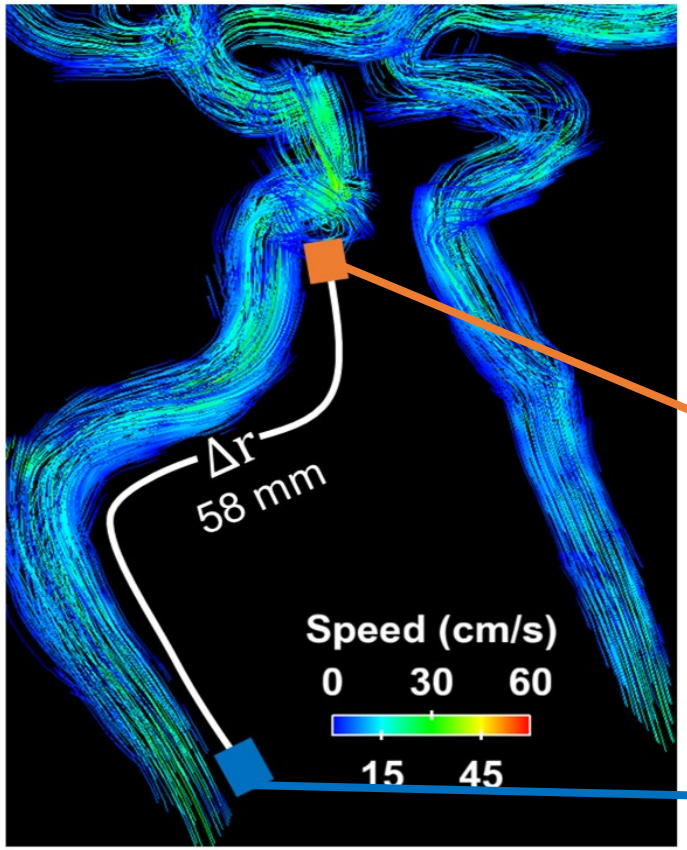
- 4D flow MRI enables both volumetric angiographic and quantitative assessment of blood flow velocities in a single acquisition
- AD patients showed decreased blood flow
  - neuron loss -> decreased metabolism

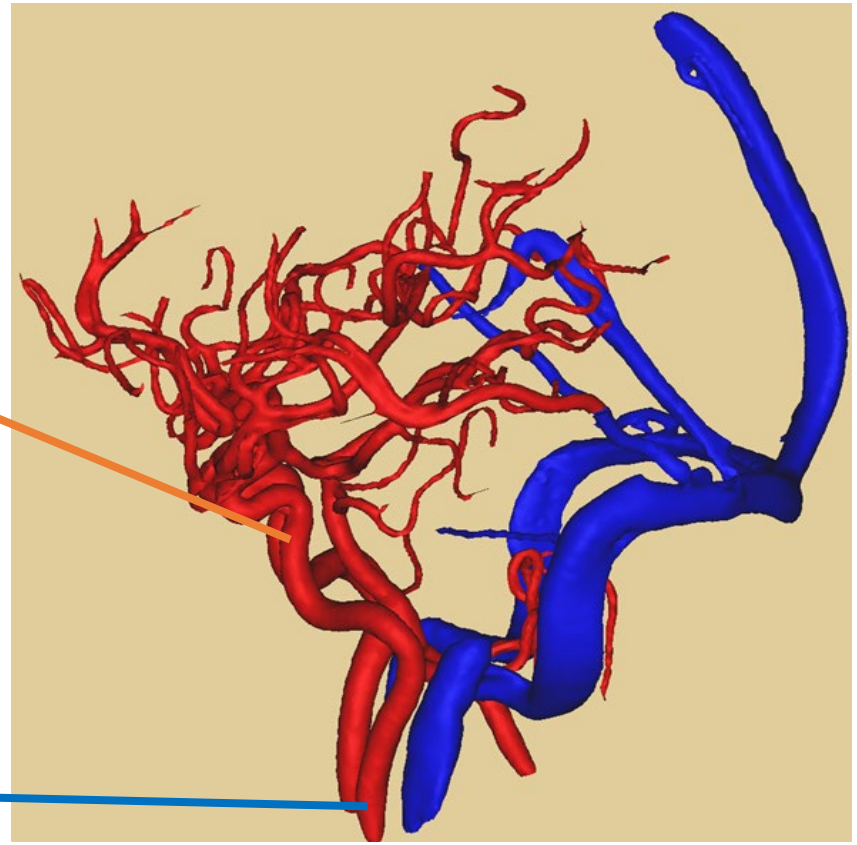
[1] Laurent S, et al. Eur Heart J 2006; 27:2588–2605.
[2] Hughes TM, et al. JAMA Neurol. 2014;71(5):562-568.

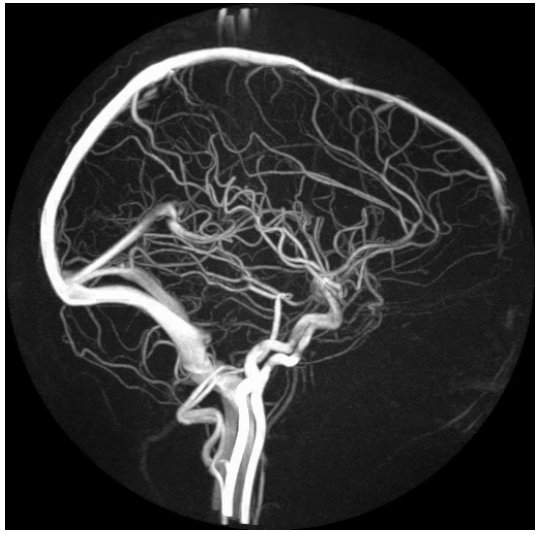
Berman SE, et al. Alzheimers Dement (Amst). 2015 Dec; 1(4): 420–428.
Rivera-Rivera LA, et al. J Cereb Blood Flow Metab. 2016 Oct;36(10):1718-1730.
Berman SE, et al. J Alzheimers Dis. 2017;60(1):243-252.
Rivera-Rivera LA, et al. J Cereb Blood Flow Metab. 2017 Jun; 37(6): 2149–2158.

Intracranial PWV

- AD patients or at risk of AD will likely get an MRI
- 4D flow MRI:
  - blood flow, pulsatility, intracranial pulse wave velocity and other markers of vascular health





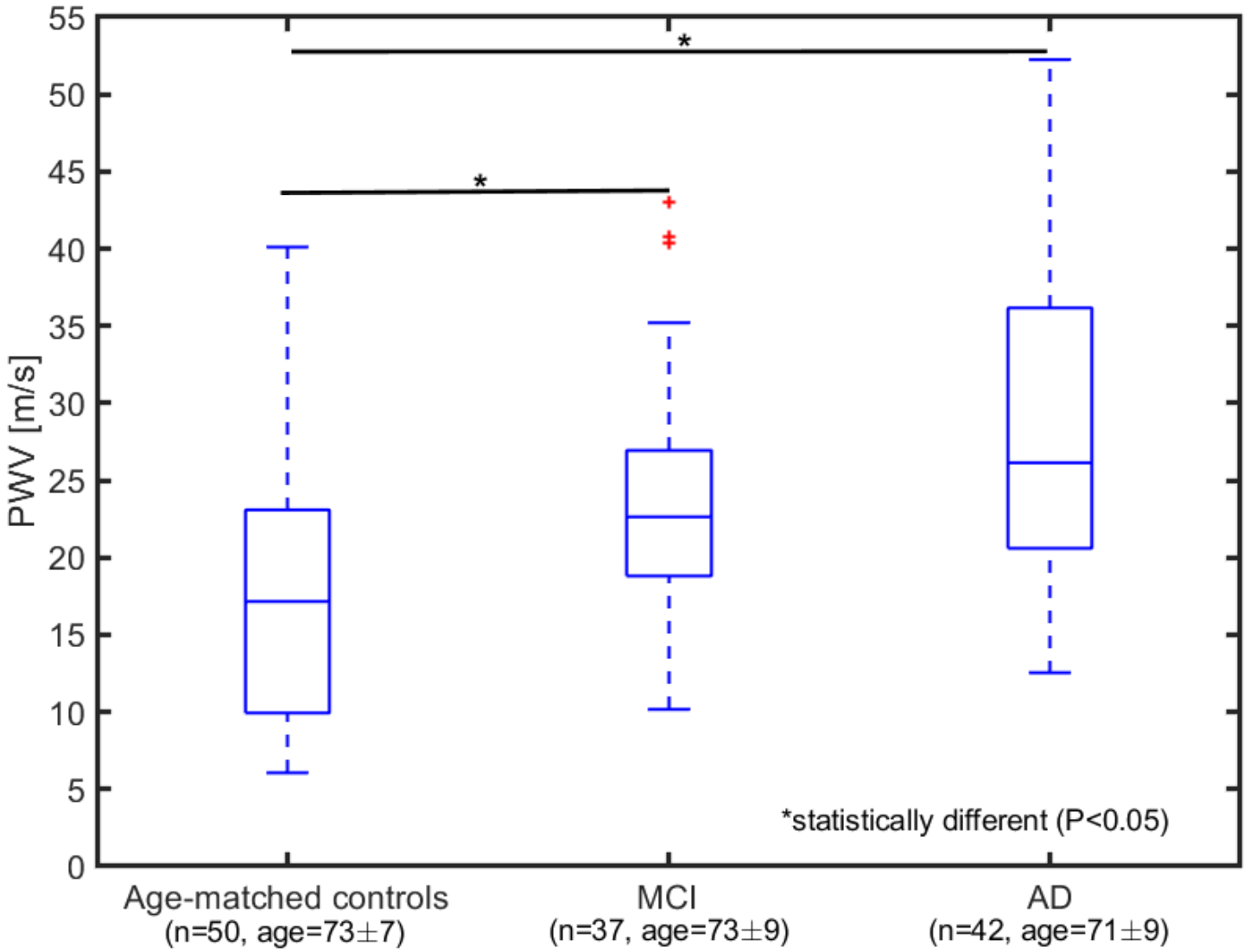


Study population recruited from WADRC clinical core

- Total number of subjects for this study = 192
- 5 groups

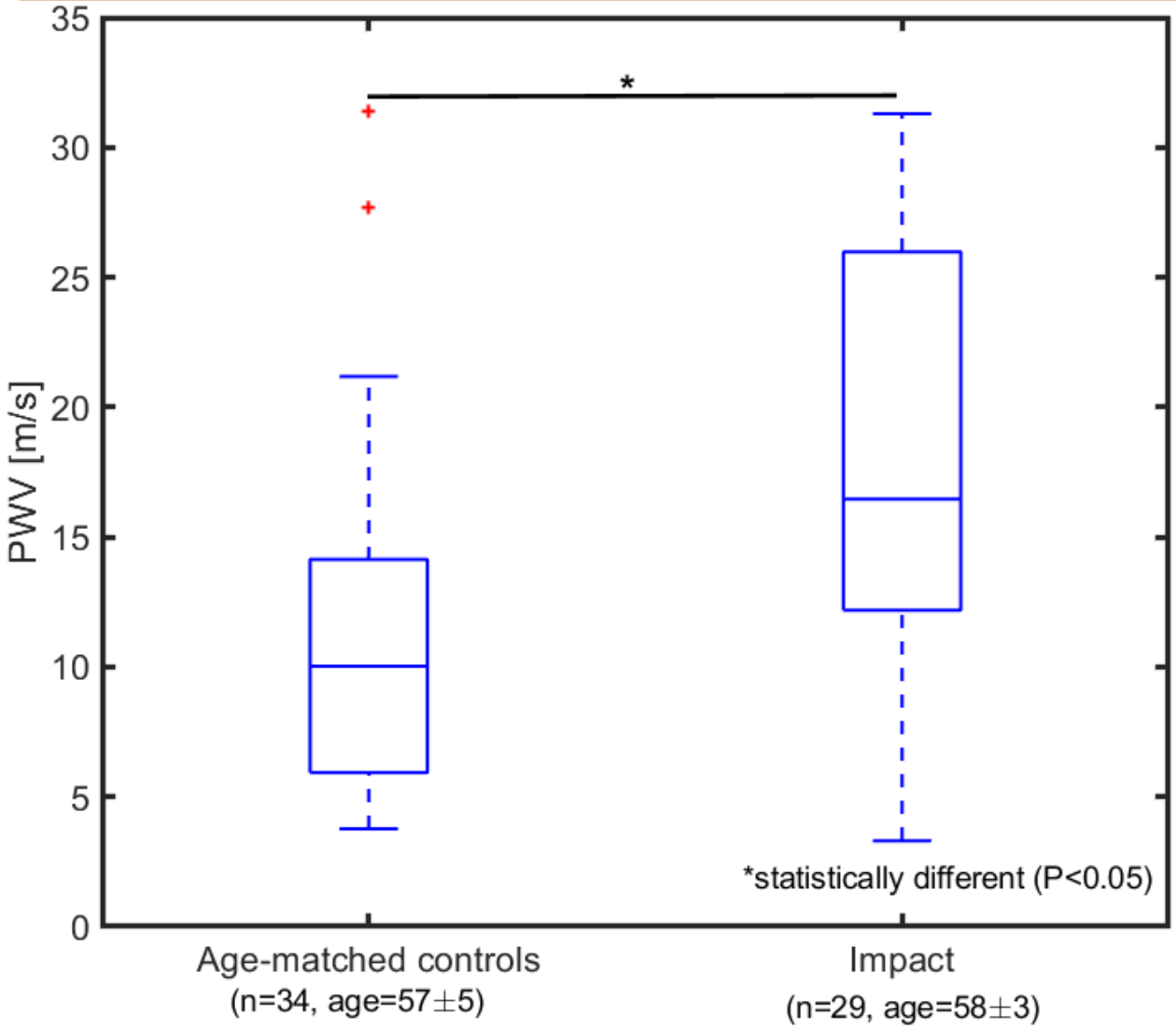
	AD (n=42)	MCI (n=37)	Older Cognitively healthy (n=50)	Impact (n=29)	Younger cognitively healthy (n=34)
Age in years	71 ± 9	73 ± 9	73 ± 7	58 ± 3	57 ± 5
Sex (# females, %)	25, 60	20, 54	28, 56	21, 72	26, 76
Parental dementia history positive (# positive, %)	18, 43	19, 51	3, 6	29, 100	0, 0
APOE ε4 postive (# postivie, %)*	16, 46	16, 57	0, 0	29, 100	0, 0

Statistically higher PWV in AD and MCI compared to controls



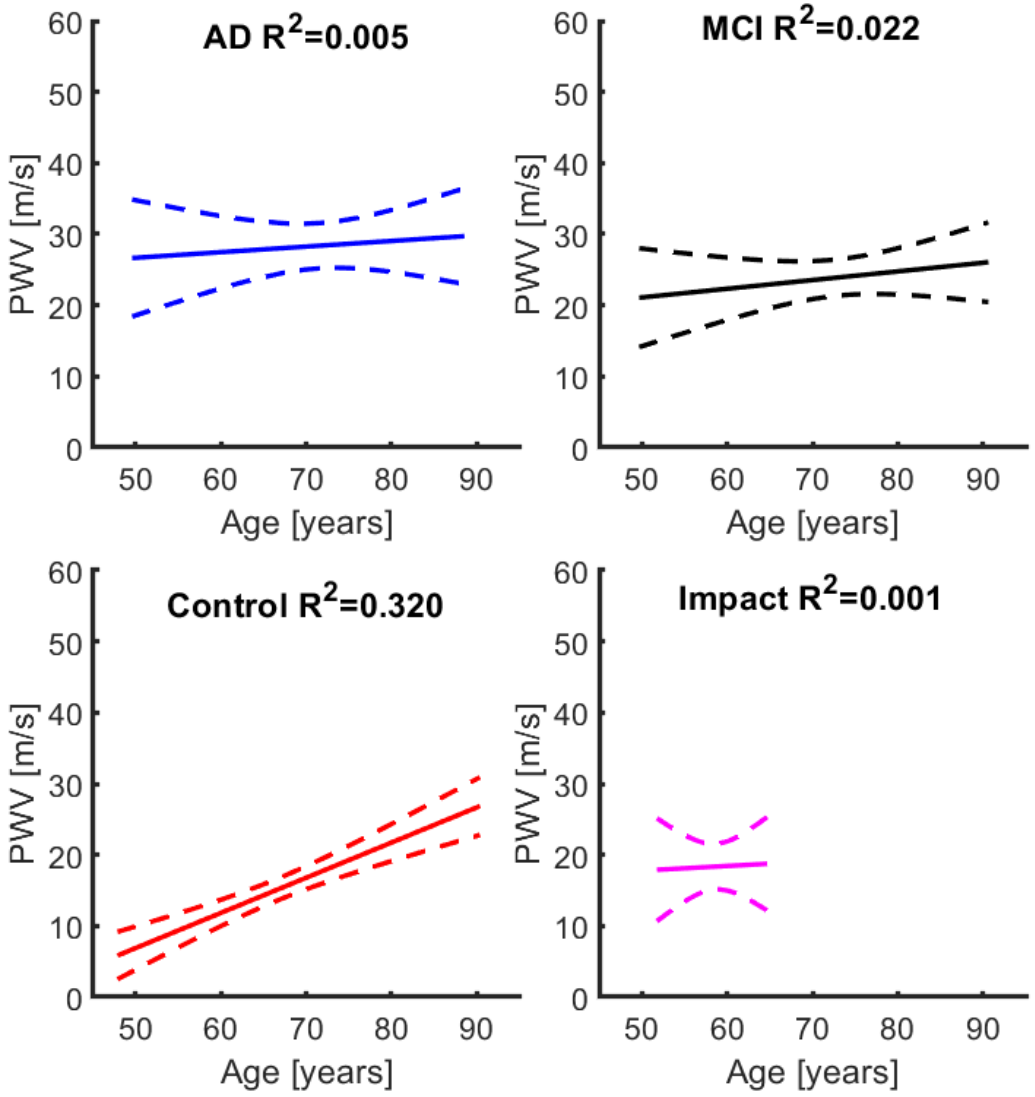
- Higher PWV in the AD group suggests arterial stiffening of the internal carotid arteries and macrovascular damage

Statistically higher PWV in *APOE* ε4 carriers healthy adults



- Higher PWV in the Impact group suggest vascular changes are occurring in a group of otherwise healthy individuals
  -need for longitudinal assessment

Pathology and age effects



- AD accelerates aging effect
- PWV increases with age in healthy adults
- PWV needs to be correlated pathologic biomarkers associated with AD such as:
  -amyloid burden,
  -tau pathology
  -brain atrophy

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