What's new in neuroimaging?

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IV Congreso Nacional de Ictus - RICORS – ICTUS

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RICORS - ICTUS

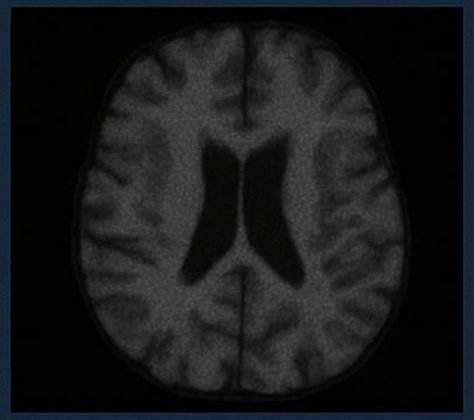
No conflictos de interés para esta presentación

Clinical perspective from a neurologist

Imaging insights into SVD mechanisms

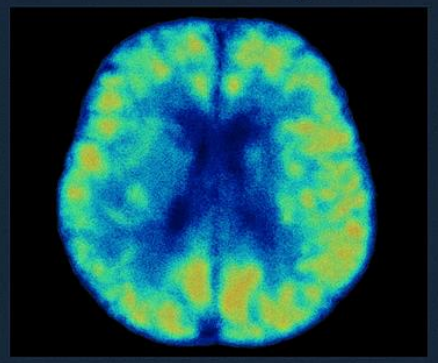
MRI techniques for studying:

Parenchyma

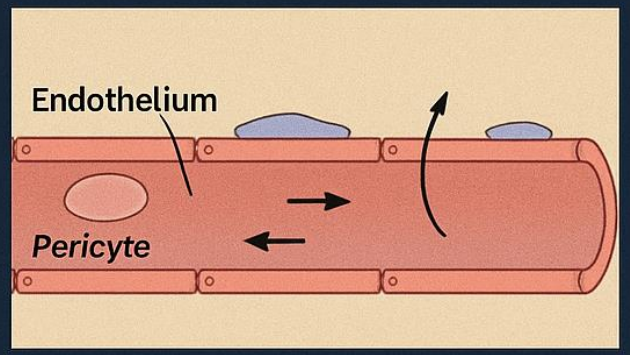


Vessels

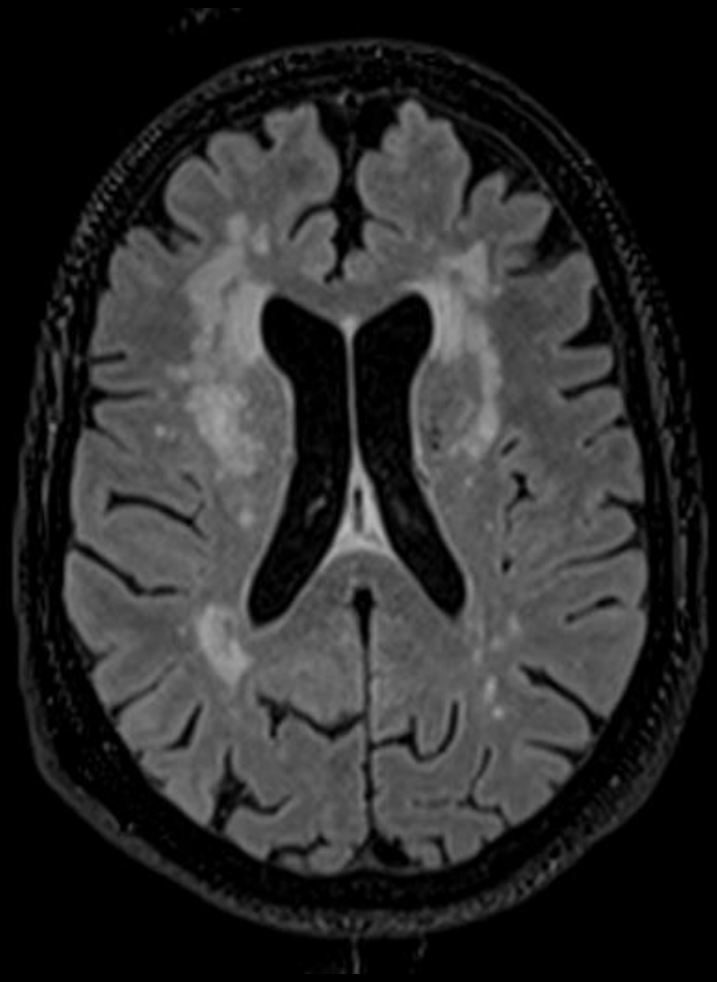
Brain fluid dynamics



Vascular function

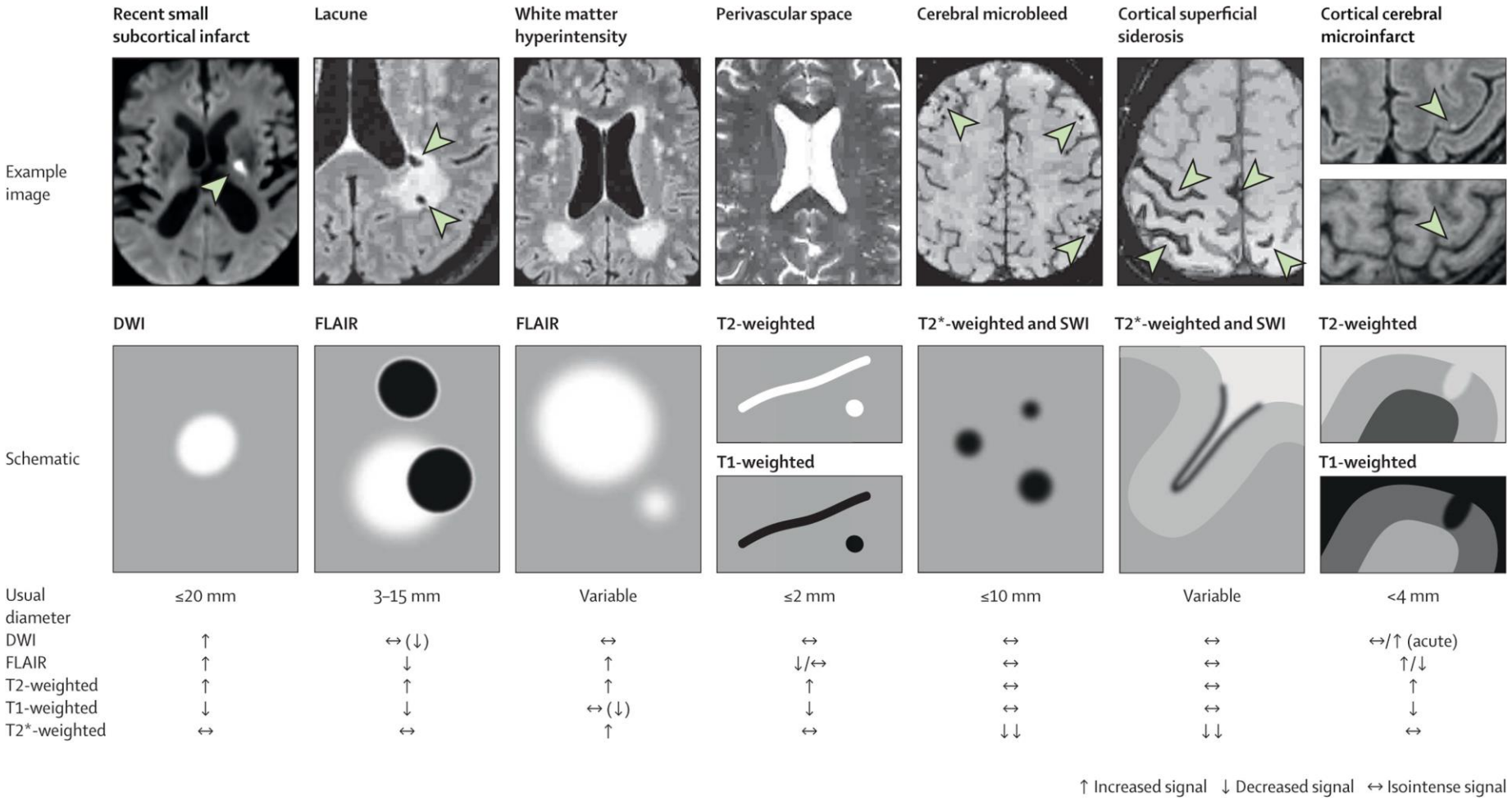


Brain tissular assessment



STandards for ReportIng Vascular changes on nEuroimaging (STRIVE-2)

A new spectrum of SVD lesions on MRI



Duering M et al. Lancet Neurology 2023

Incidental DWI-positive lesions

Clinically **covert** lesions

Location may be:

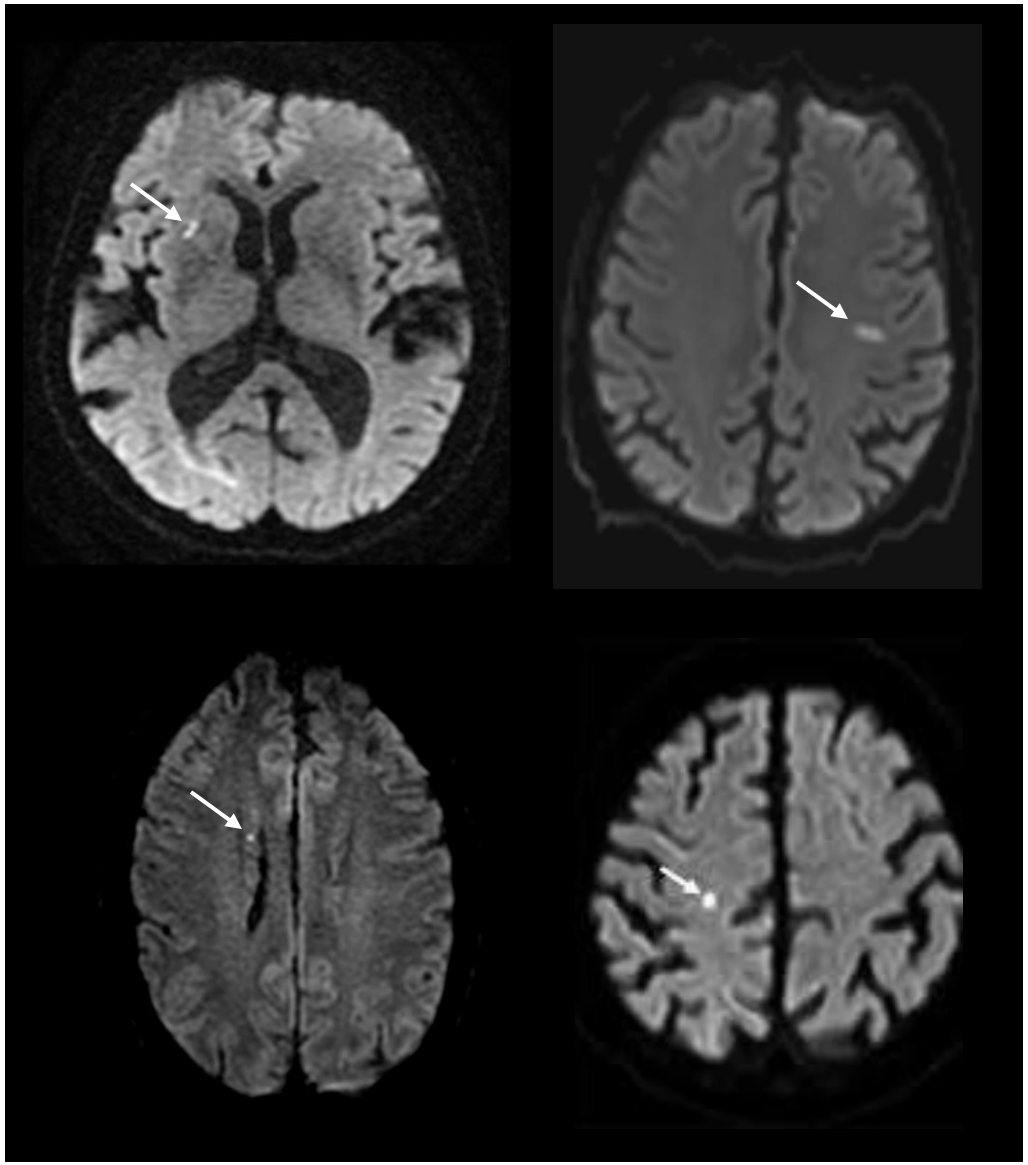
1. **Cortical** (overlap with **cortical cerebral microinfarcts** when size <5mm)
2. **Subcortical** (overlap with **recent small subcortical infarcts** when size ≤20mm)

Different fates (WMH, lacunes, CMB, disappear)

Contribute to **SVD progression**

Multiple **etiology** (SVD, embolism, pro-thrombotic state)

The clinical management for covert brain infarction is uncertain



Duering M et al. Lancet Neurol. 2023; Ter Telgte A et al. Ann Neurol. 2019; Clancy U et al. Neurology. 2024; Naftali J et al. Neurology. 2024

Tissue characteristics

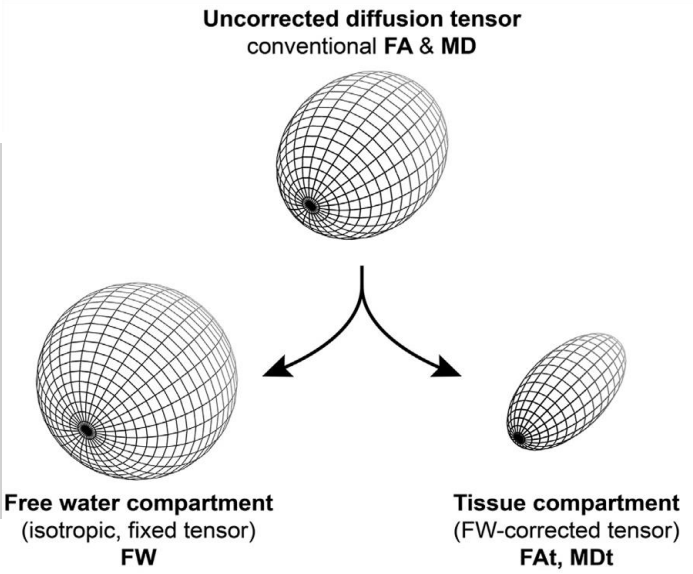
WMH represent only the **visible portion** of a more extended microstructural WM injury

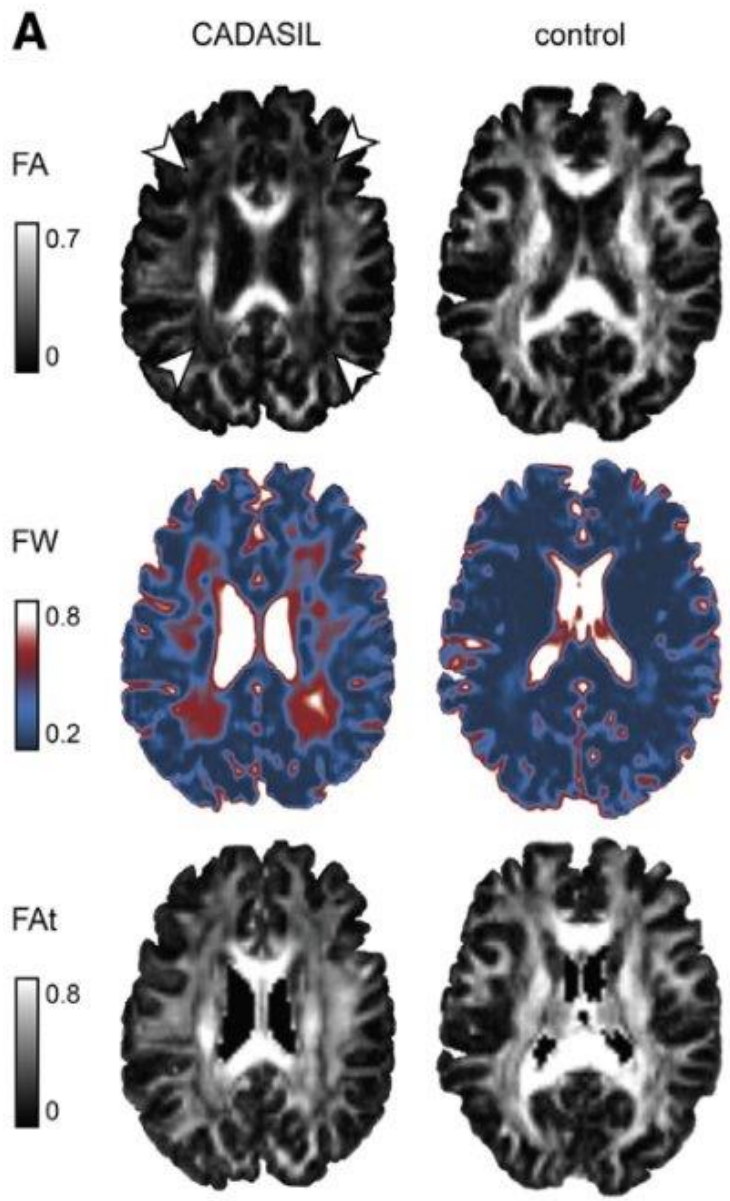
Diffusion Tensor Imaging (DTI) measures directionality and magnitude of water diffusion in brain tissue, providing quantitative metrics to assess:

- **fiber tracts integrity** beyond visible lesions (normal appearing white matter)
- Extracellular **free water** component

PROS: non-invasive, sensitive to microstructural damage, quantitative metrics, regional or specific tracts analysis, surrogate marker for clinical cognitive outcomes

CONS: lacks pathological specificity, complex interpretation, limited direct clinical utility

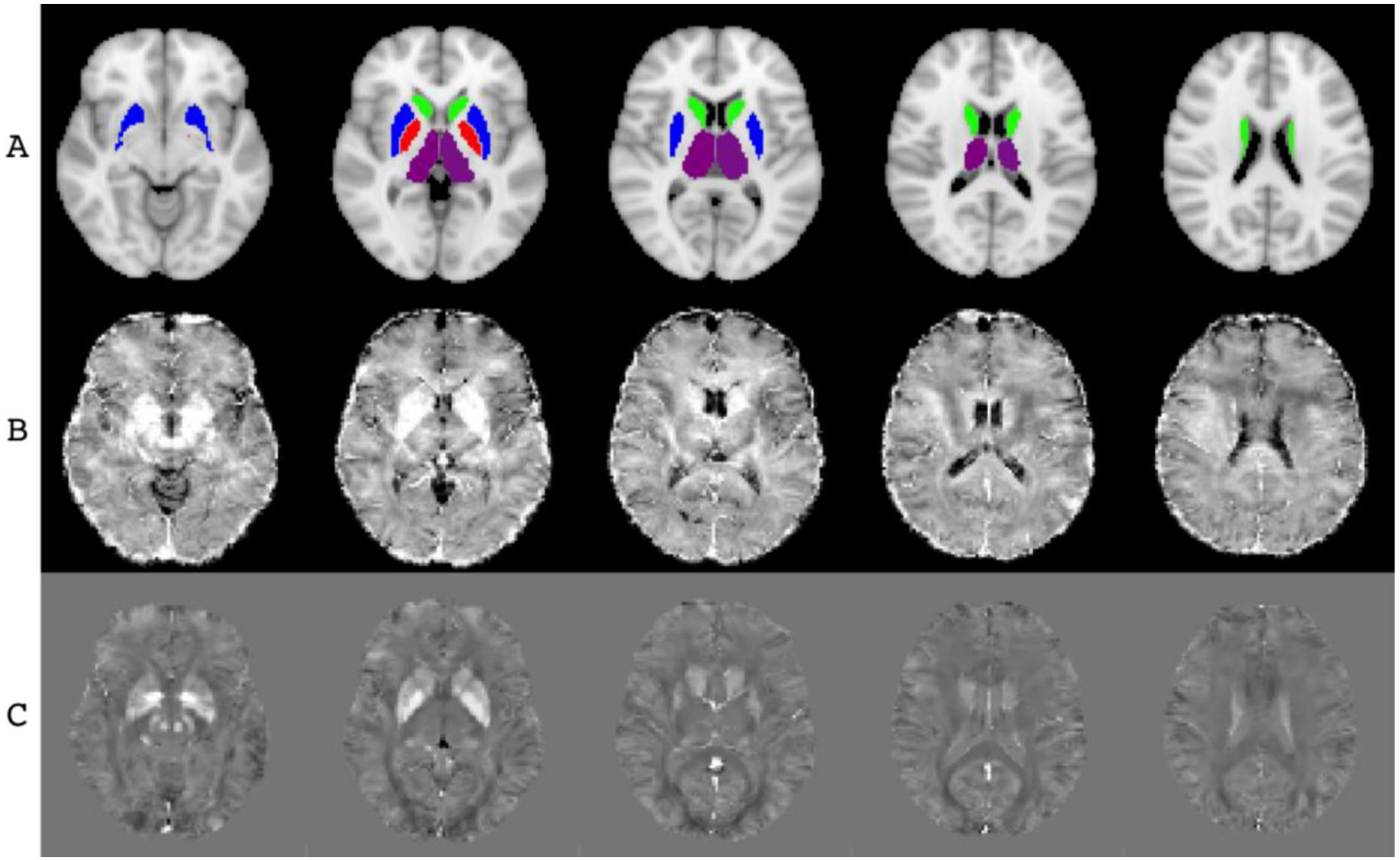




Alghamdi AJ. Brain Sci. 2023; Duering M, et al. Alzheimers Dement. 2018

Quantitative susceptibility mapping (QSM)

Sensitive to paramagnetic substances like iron, calcium, and deoxygenated blood



Iron deposition due to microvascular injury in SVD

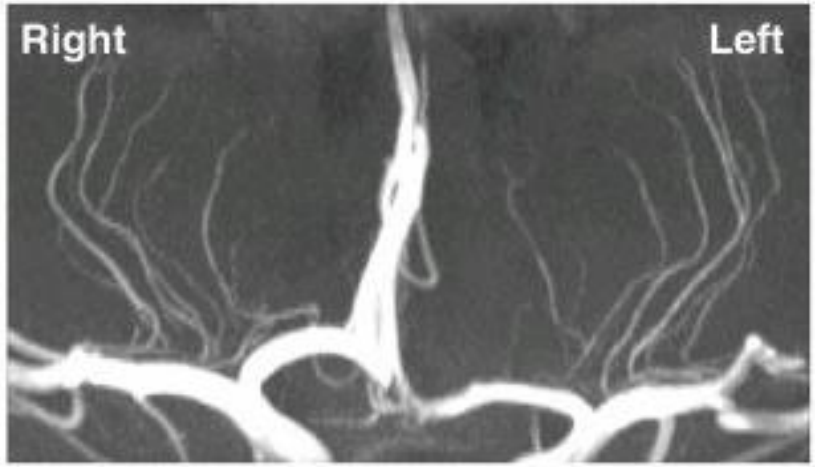
PROS: non-invasive, quantitative, sensitive to iron (differentiate from calcium)

CONS: lack of standardization, requires high-field MRI

Murray KD et al. Magn Reson Imaging. 2023

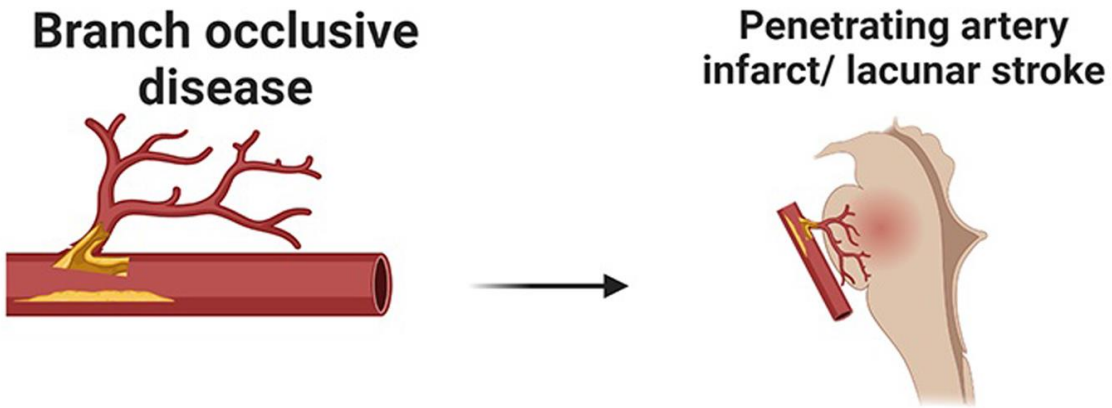
Vessel imaging

Vessel imaging

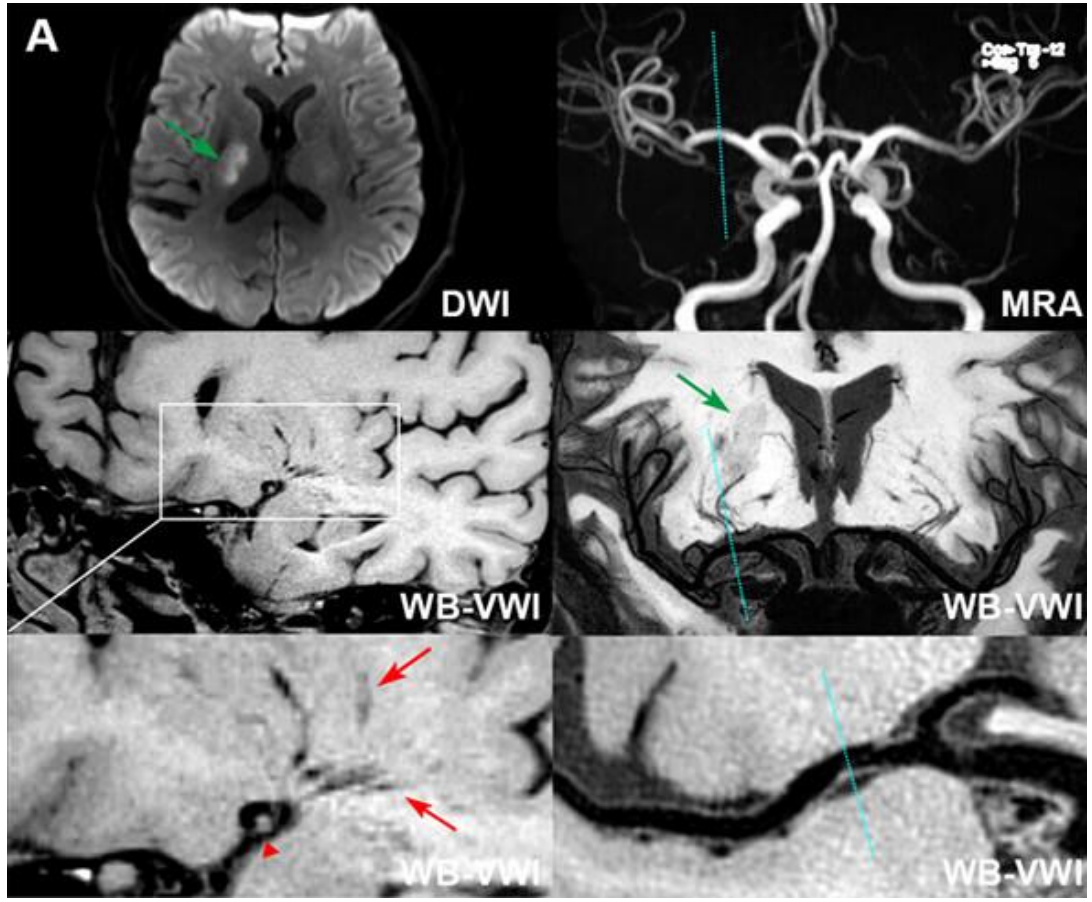


7T MRI

Branch atheromatous disease



High resolution **vessel wall imaging** (3T MRI)



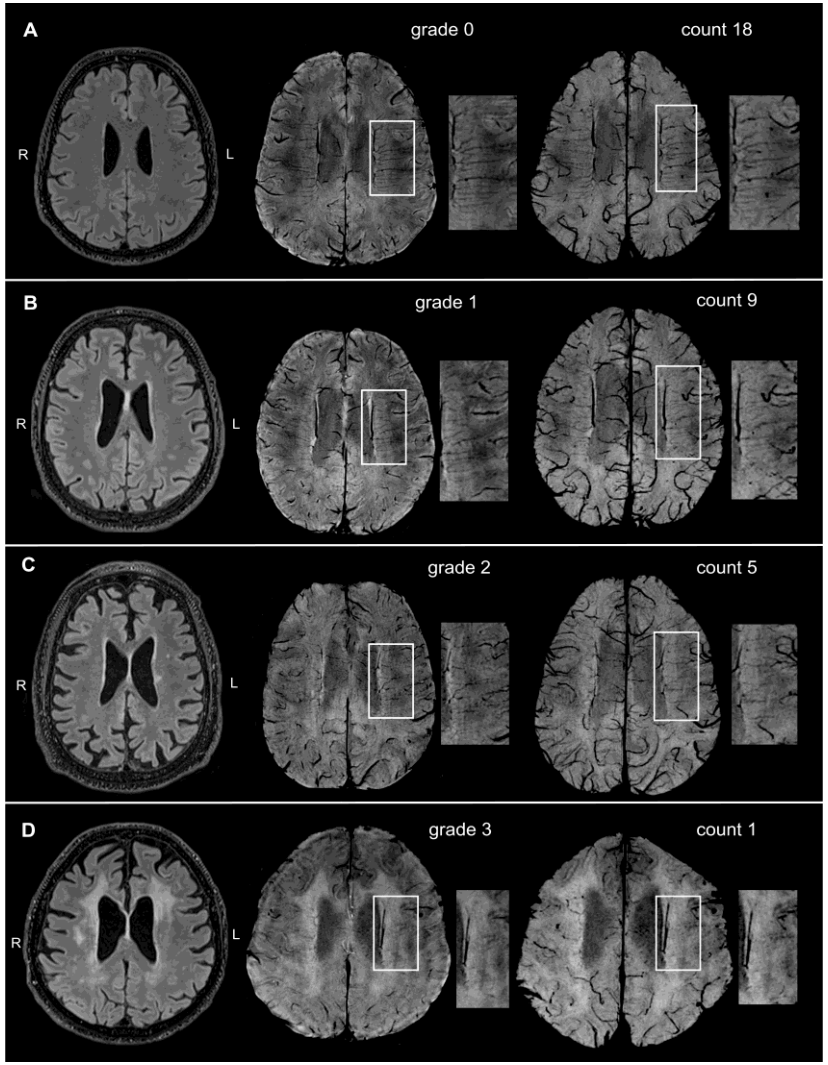
PROS: direct imaging, etiological study

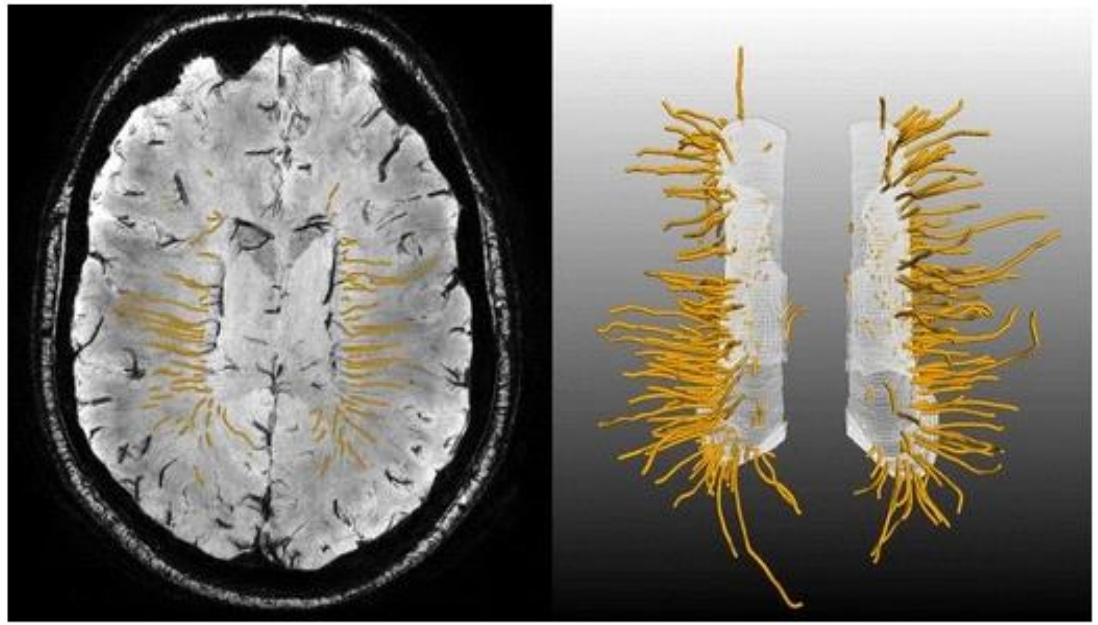
CONS: limited resolution, requires contrast, long acquisition, and expertise

Chen LH et al. Stroke. 2024; Jiang S, et al. Stroke. 2020

Deep medullary vein disruption in SVD
(venous collagenosis)

DMV visual scales on SWI (3T-MRI)





DMV segmentation on 7T MRI

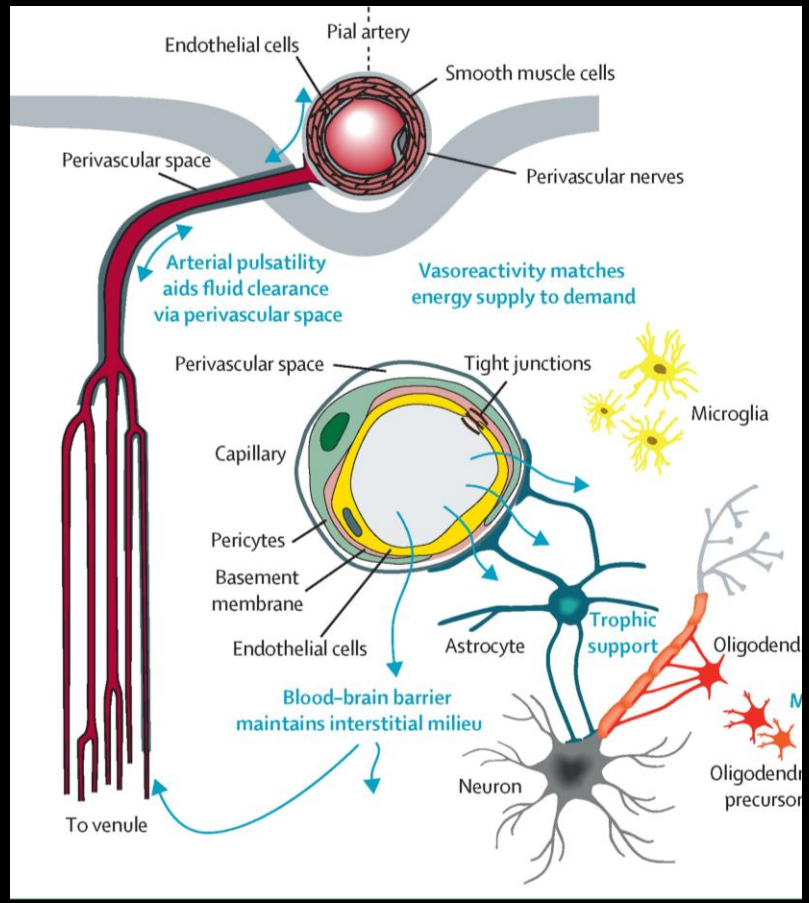
Quantitative assessment: number, density, tortuosity, length, diameter

PROS: morphologic assessment, no invasive

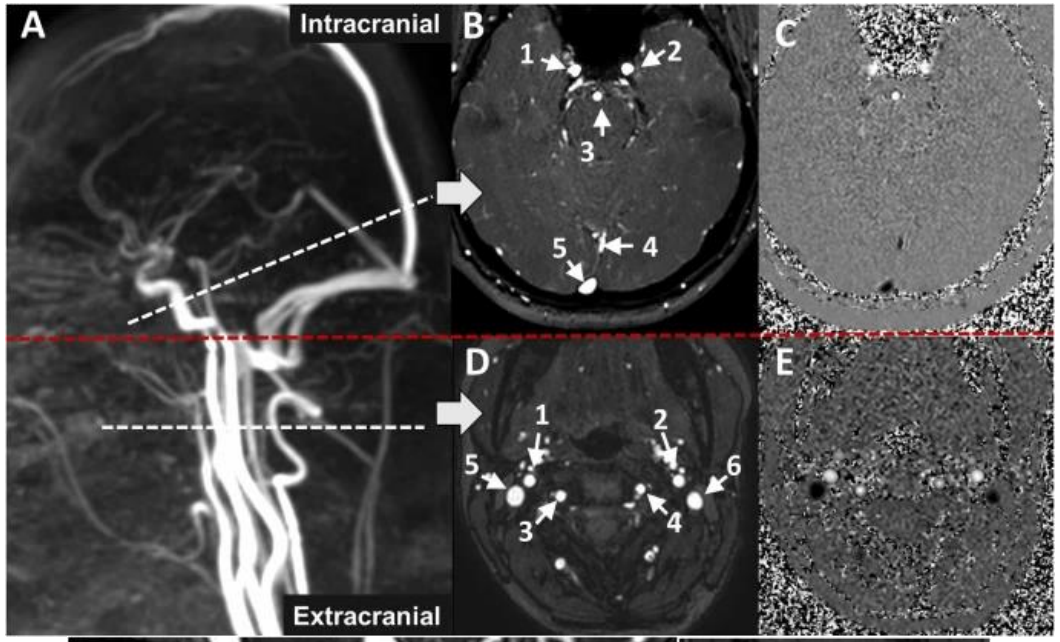
CONS: need of high magnetic field, non-specific changes (e.g., blood flow, hematocrit, deoxyhemoglobin), uncertain clinical interpretation

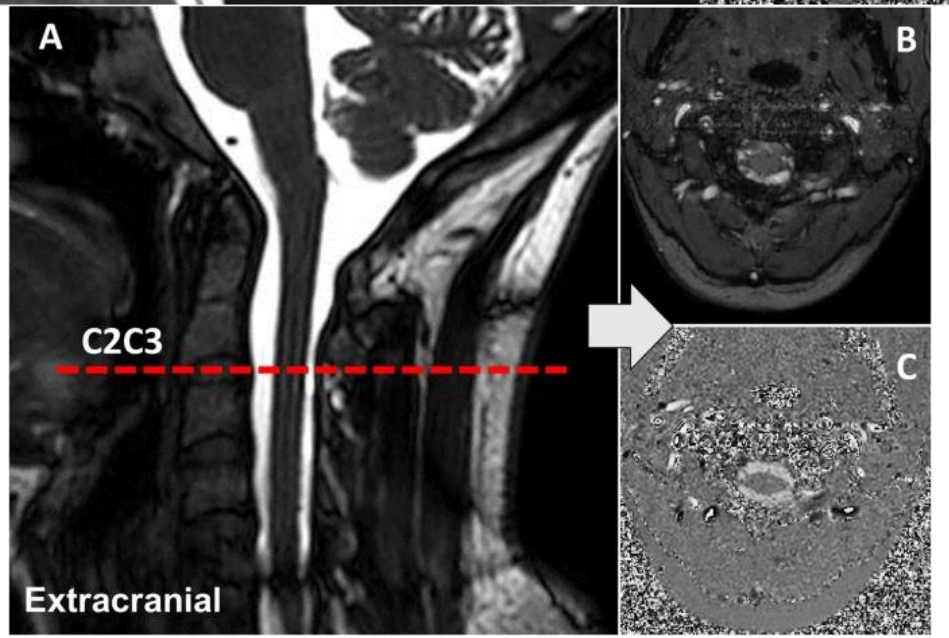
Brenlla C et al. AJNR 2024; Kuijf HJ et al. Eur Radiol. 2016

Vascular dysfunction



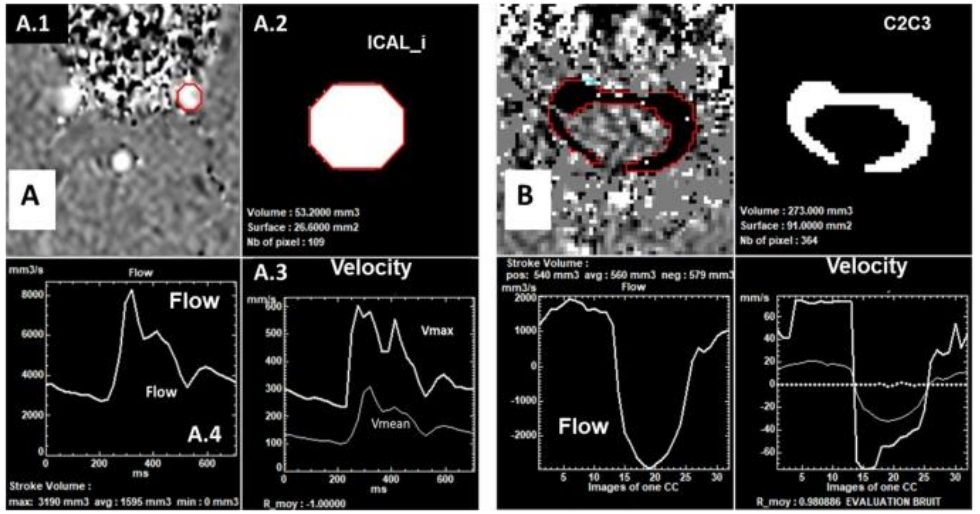
Phase-contrast MRI: cerebral blood and CSF flow





Velocity and flow of moving fluids (like blood or cerebrospinal fluid) based on phase shifts of the MRI signal caused by motion across the cardiac cycle

- **Arterial pulsatility**
- **Venous pulsatility**
- **CSF pulsatility**

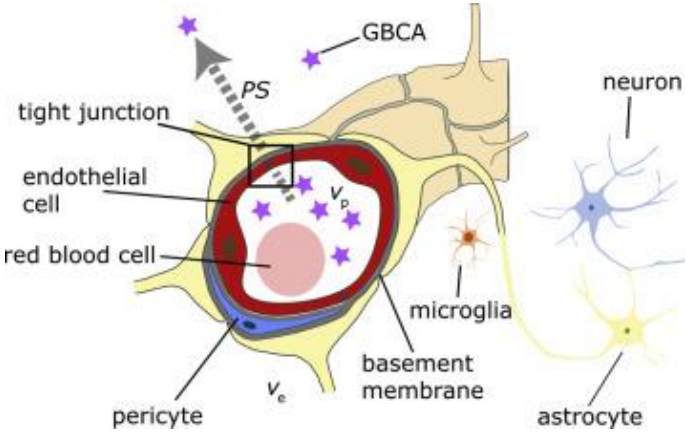


PROS: no contrast agent, regional specificity, different measures at a time

CONS: challenging setup (cardiac gating), lack of standardization

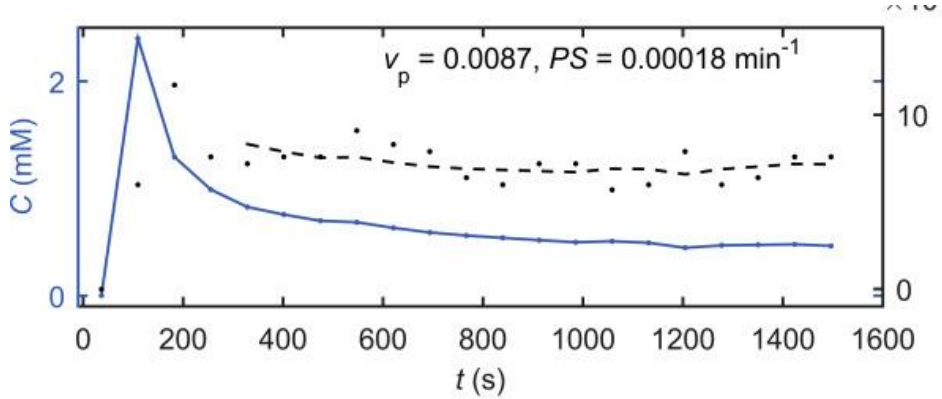
Owashi KP et al. Fluids Barriers CNS. 2024

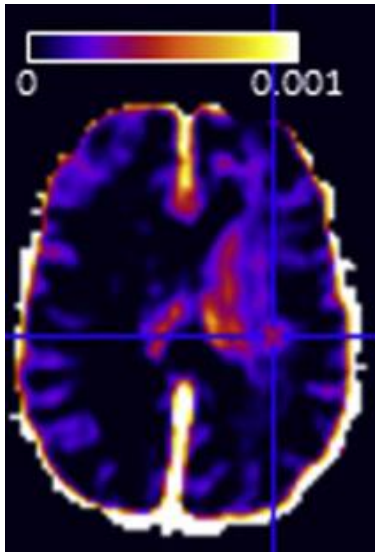
Dynamic contrast-enhanced MRI (DCE-MRI) for the assessment of BBB permeability:

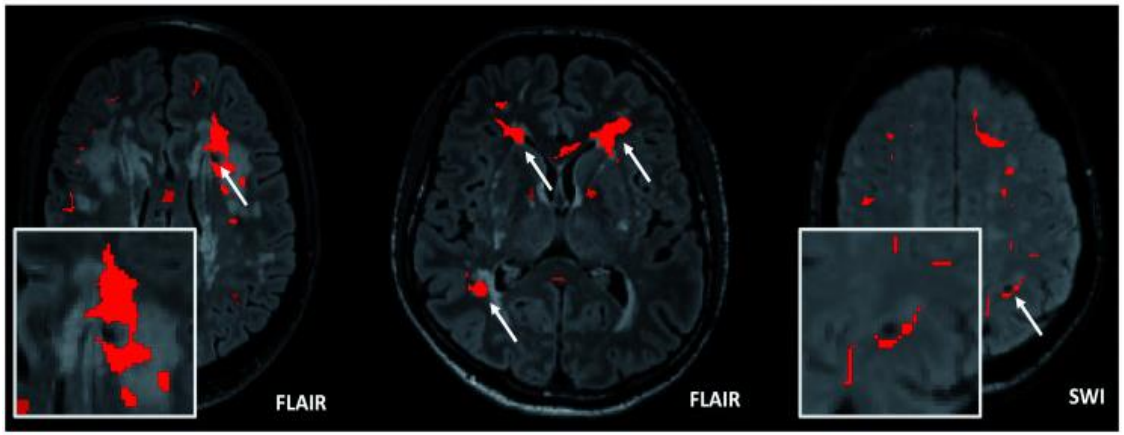


Tracks the passage of **gadolinium** from the intravascular to the brain tissue providing metrics of **BBB permeability**

Patlak model







Areas of high permeability **(hotspots)** corresponding to tissue surrounding WMH, lacunes and cerebral microbleeds

PROS: quantitative BBB permeability assessment, early detection of the disease, regional specificity, standardized for SVD studies (HARNESS initiative)

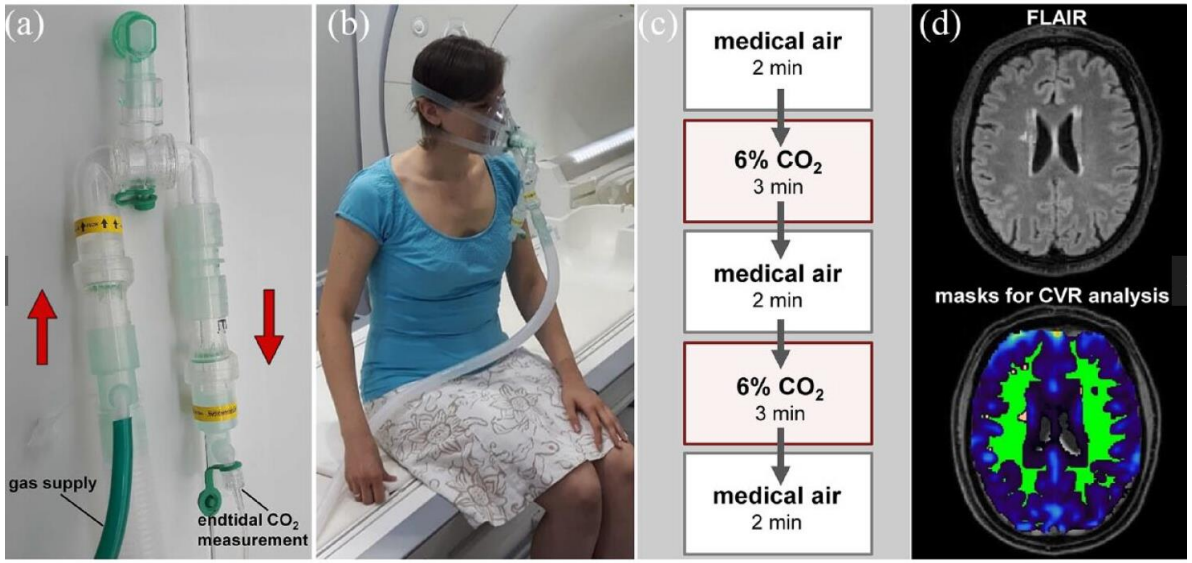
CONS: contrast agent required, long acquisition time, complex modelling

Thrippleton MJ, et al. Alzheimers Dement. 2019
Rudilosso S et al. JCBFM 2023

Cerebrovascular reactivity (CVR)

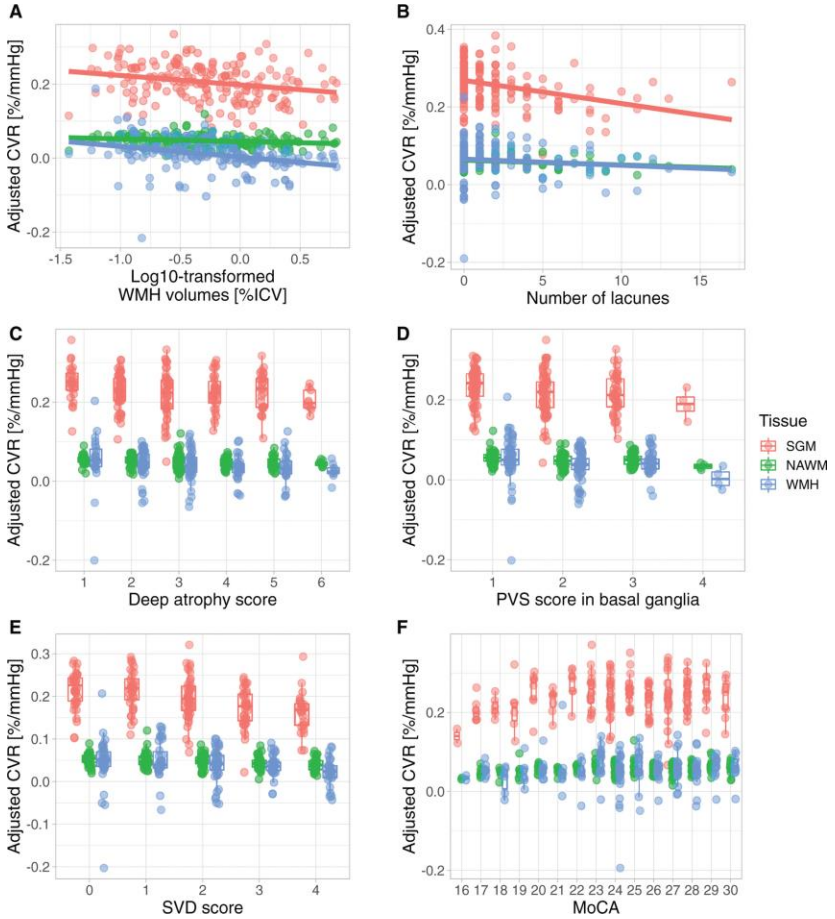
BOLD-CVR MRI: Reflects the capacity of cerebral blood vessels to adjust blood flow in response to **stimuli** (hypercapnic air)

In SVD CVR is reduced due to **vessel stiffening** and endothelial dysfunction



PROS: direct quantitative measure, early detection of the disease, regional specificity

CONS: challenging stimulus delivery and patient compliance, specialized hardware, high cost



"Lower CVR in patients with SVD was related to more severe SVD burden and worse cognition."

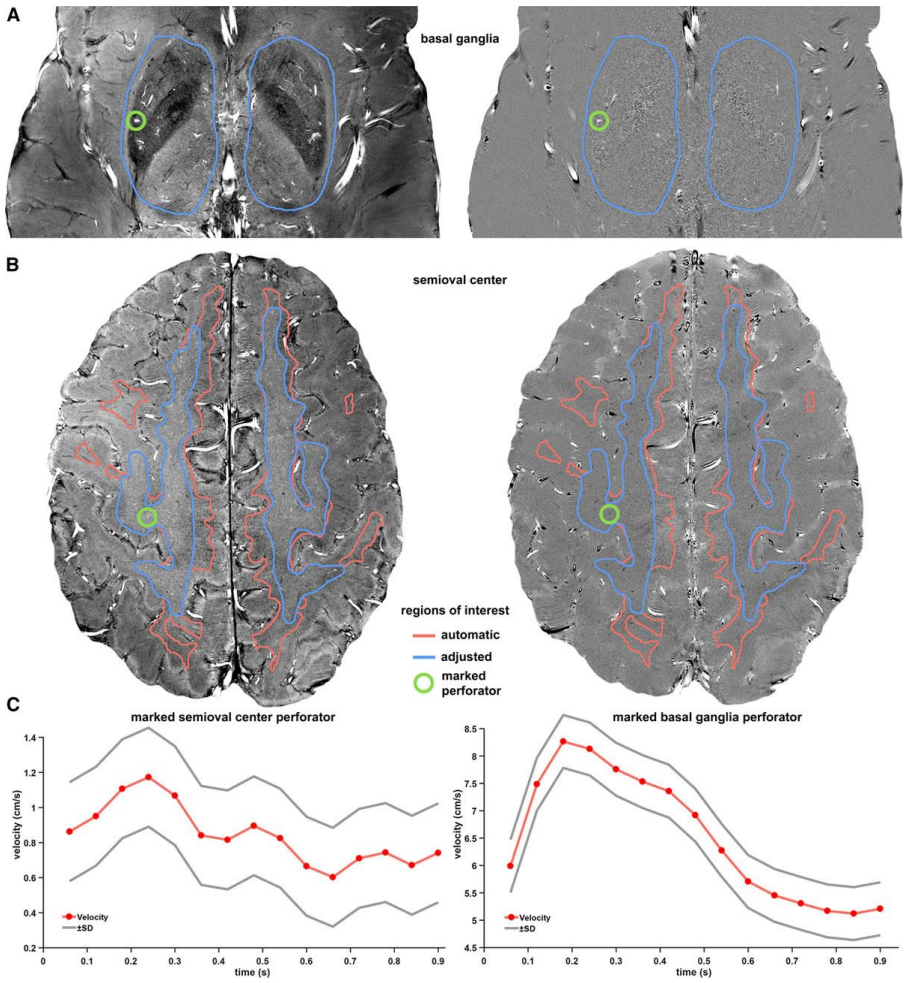
Effect of blood pressure-lowering agents on microvascular function in people with small vessel diseases (TREAT-SVDs): a multicentre, open-label, randomised, crossover trial

*Anna Kopczak, Michael S Stringer, Hilde van den Brink, Danielle Kerkhofs, Gordon W Blair, Maud van Dinther, Carmen Arteaga Reyes, Daniela Jaime Garcia, Laurien Onkenhout, Karolina A Wartolowska, Michael J Thrippleton, Agniete Kampaite, Marco Duering, Julie Staals, Saskia Lesnik-Oberstein, Keith W Muir, Martin Middeke, Bo Norrving, Marie-Germaine Bousser, Ulrich Mansmann, Peter M Rothwell, Fergus N Doubal, Robert van Oostenbrugge, Geert Jan Biessels, Alastair J S Webb, Joanna M Wardlaw, Martin Dichgans, on behalf of the TREAT-SVDs collaborators**

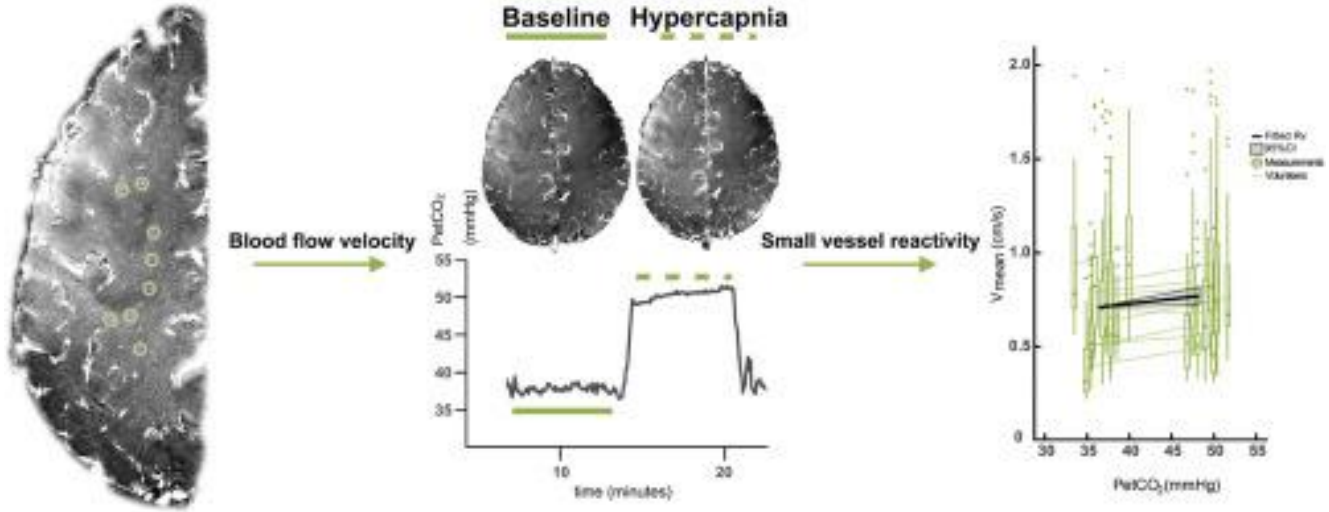
Kopczak A,et al. Eur Stroke J. 2023; Sleight E et al. Stroke 2023; Kopczak A et al. Lancet Neurol. 2023.

Vascular function measured at single vessel level (7T MRI)

Arterial pulsatility



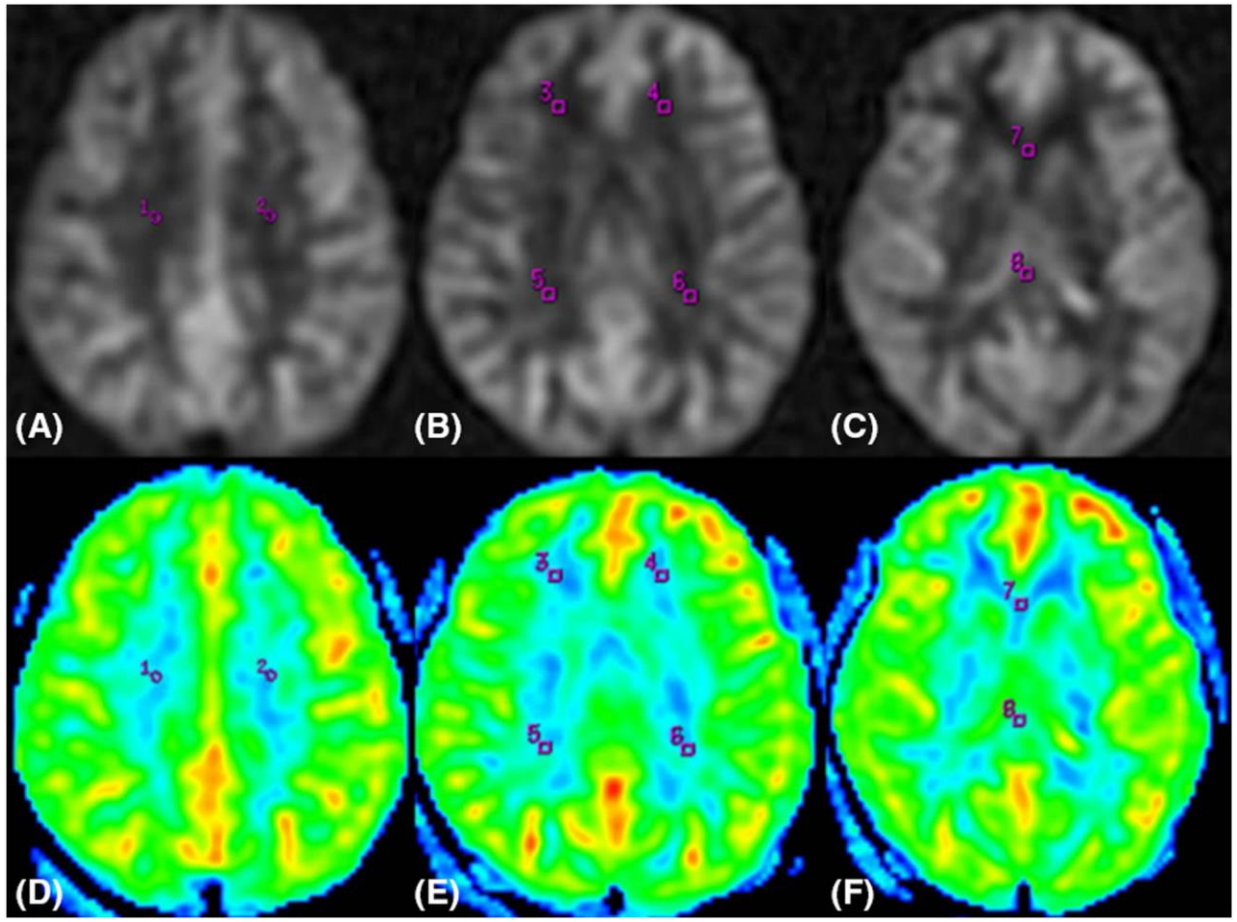
CVR to hypercapnic challenge (or brief visual stimulation)



Increased arteriolar stiffness and decreased reactivity. Worse small vessel function correlated with **increased disease burden.**

Geurts LJ et al. Stroke. 2018; Geurts LJ et al. Neuroimage. 2018; Van Den Brink H et al. Neurology. 2024

Brain perfusion



Arterial Spin Labelling (ASL): non-contrast perfusion methods using magnetically labeled arterial blood water

Pseudocontinuous arterial spin labeling (pCASL): better signal-to-noise ratio

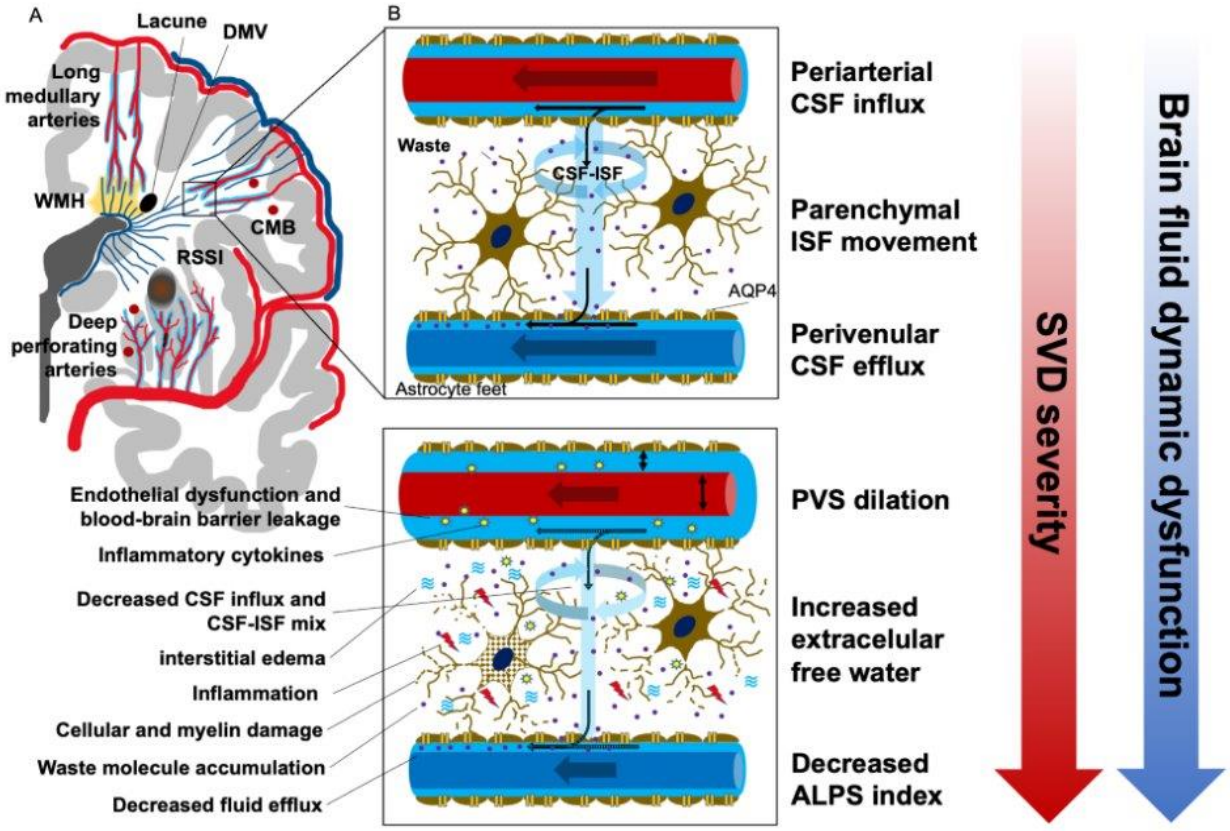
Hypoperfusion correlates with WMH load

PROS: Non-invasive, regional and global assessment

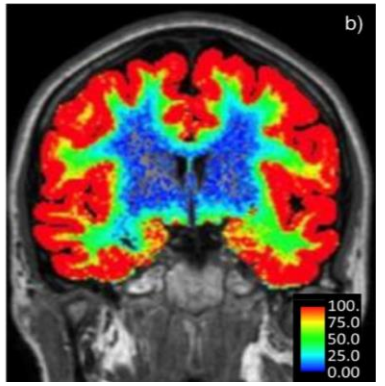
CONS: Low signal-to-noise ratio in white matter

Brain fluid clearance mechanisms

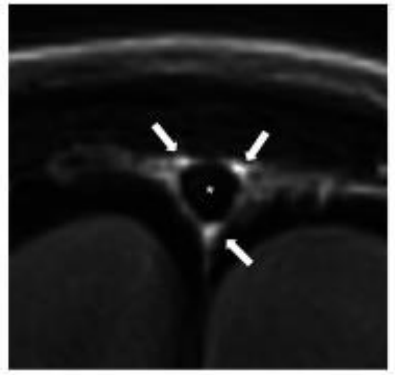
Brain fluid clearance impairment in SVD according to the **glymphatic model**



DCE- MRI (Gadobutrol)



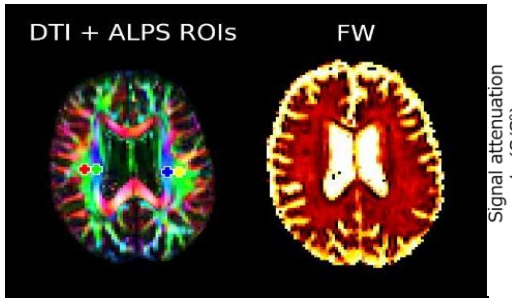
Intrathecal CSF tracer enrichment shows a centripetal pattern

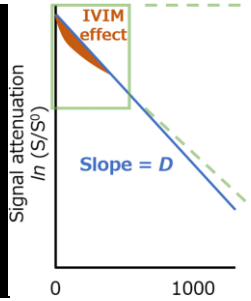


IV tracer shows dural meningeal lymphatic drainage

PROS: direct dynamic contrast tracing
CONS: invasive technique, requires multiple scans

Diffusion-based techniques (ALPS-DTI, FW, IVIM)



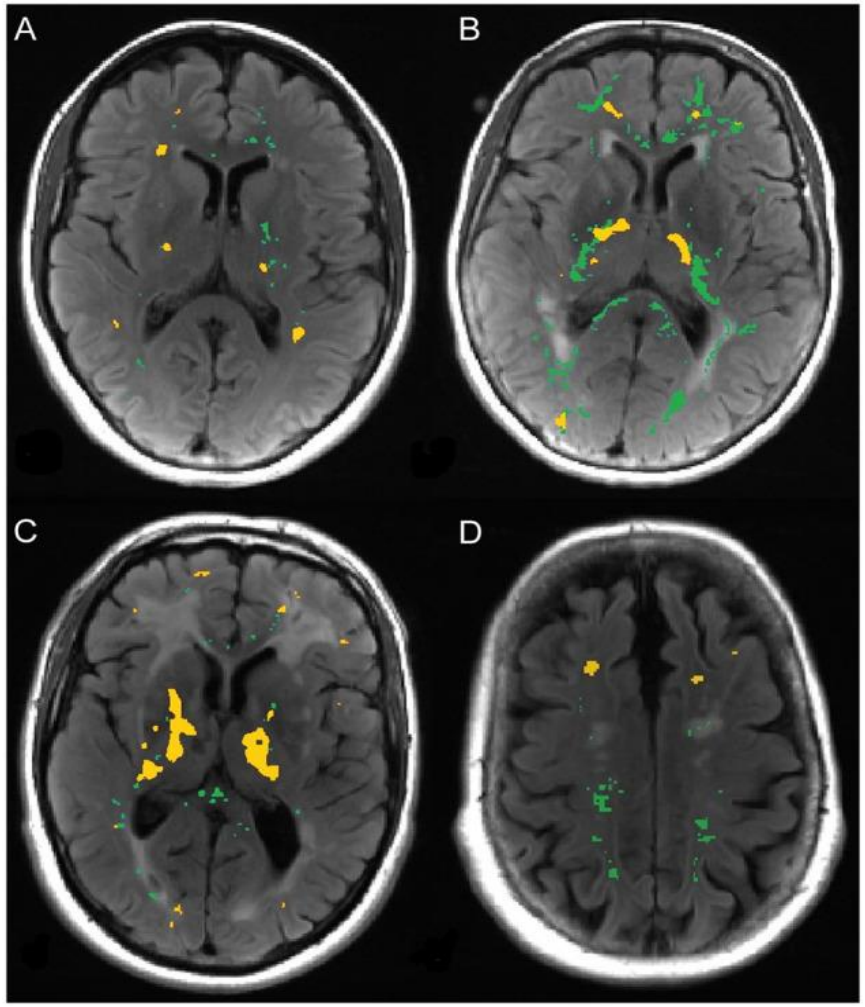


Evaluate water movement along perivascular spaces, extracellular diffusion, and microvascular perfusion

PROS: not invasive, highly available
CONS: indirect measures, low spatial resolution, unproven assumptions

Rudilosso et al.Neuroradiology 2025; Ringstad G, et al. JCI Insight. 2018; Sennfält S et al. J Cereb Blood Flow Metab. 2023; Kamagata J et al. JMRI. 2023

Neuroinflammation in SVD: TSPO-PET Imaging



PET imaging with radioligands targeting the **18 kDa translocator protein (TSPO)**

- in vivo detection of **activated microglia**, a marker of neuroinflammation.
- Increased microglial activation in normal-appearing white matter and periventricular regions of CSVD patients.

PROS: direct evidence of neuroinflammation, biomarker for treatment response,

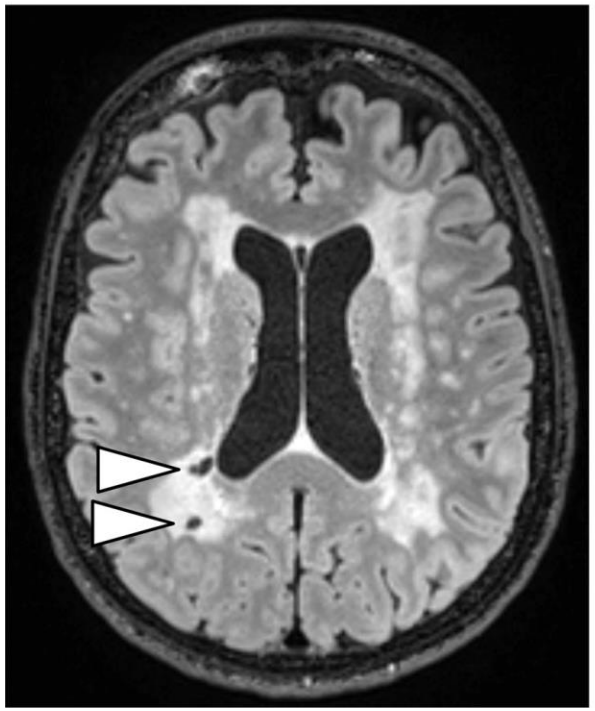
CONS: Limited availability, high cost, radiation exposure, complex interpretation

Walsh J, et al. Brain. 2021

Conclusions

Paradigm shifts in SVD neuroimaging study

Lesion-centric view



Paradigm shifts

Subcortical → Cortical 1
- Remote damage
- Cerebral microinfarcts

Lesion → Gradual damage 2
- Tissue microstructure
- Quantitative MRI

Tissue → Vessel 3
- Vascular function
- 7T small vessel imaging

Impact of neuroimaging advances in the last decade:

- Clinical practice
- Insights into pathophysiological mechanisms
- Potential surrogate markers for clinical trials

Ter Telgte A, Duering M. Stroke. 2024

Gracias por la atención