



Seeing is Believing: Ultra-high field MRI in Vascular and Neurodegeneration Research

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Outline

- ❑ Ultra-high-field MR potentials & challenges
- ❑ Susceptibility-sensitive imaging on 7T
- ❑ Seeing is believing & what we can see
- ❑ The role of ultra-high field MRI in aging and dementia



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7T MR at NYU

- **Human whole body MR system (MAGNETOM, Siemens)**
 - Gradients: 45 mT/m (maximum 72 mT/m effective) and a slew rate of 200 T/m/s (346 T/m/s effective)
- **7T magnet offers 32 independent RF channels, enabling parallel imaging with radio frequency (RF) coil arrays of up to 32 elements**
- **A 32-element head coil array (Nova Medical, Inc. MA)**
 - Two separate components: a birdcage like circularly polarized transmit coil and a 32 element phased array positioned on a close-fitting helmet-like former to maximize SNR



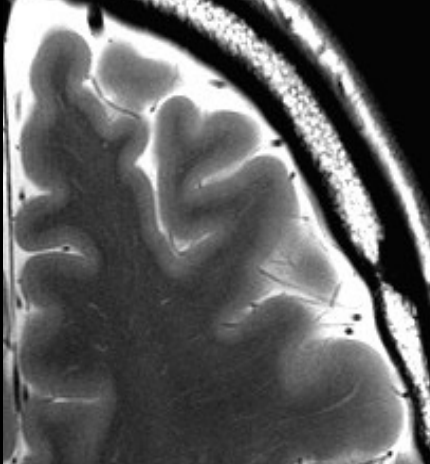





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Ultra-High-Field MR Potentials

Technical drive: it is all about signal or SNR
 Clinical drive: disease pathophysiology and diagnostic value

- *One Tesla is equal to 30,000 times the strength of the Earth's magnetic field; therefore a 7 Tesla is 210,000 times stronger*
- *Allow a 2- to 3-fold improvement in image SNR over 3.0 T systems.*
- *Novel multichannel coil technology provides an additional 2- to 6-fold increase in SNR in certain brain regions.*
- *The combined advantages of these techniques allow reduction of the voxel volume to <math><0.1 \text{ mm}^3</math> just because of the magnitude of increase in SNR*



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Characteristics of higher field MRI

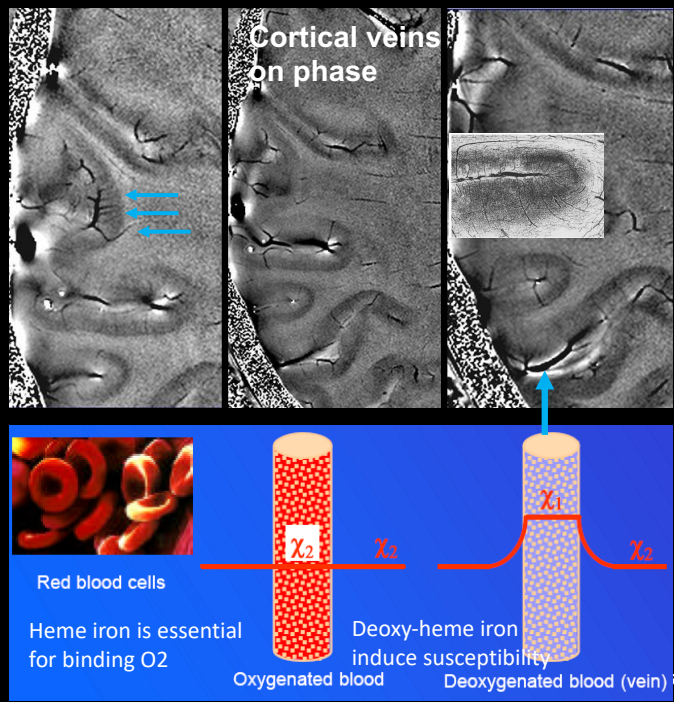
Characteristics	↑ or ↓	Strength	Challenges
SNR	↑↑	Benefit in all aspects in image quality especially in high resolution imaging	None noted
T1	↑	Benefit in Artery Spin Labeling Technique, TOF MR angiography. ↓ doses of Gd.	↑ TR to keep the same tissue contrast.
T2	↓	Allow shorter TE	T2 signal drop
SAR	↑	None noted	Due to RF energy deposition, limit the optimization in many protocols such as slice number, flip angle etc
Susceptibility	↑↑	Benefit in susceptibility-sensitive imaging	Reduced image quality by susceptibility artifacts
Dielectric effect	↑	None noted	↑ image heterogeneities. Can be improved with optimization and parallel RF transmission.
Chemical shift	↑	Benefit in MRS for ↑ differences in resonance frequency	↑ chemical shift artifacts



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Susceptibility-sensitive Imaging

- Susceptibility-sensitive imaging
 - ✓ 2D or 3D gradient echo imaging
 - ✓ SWI
 - ✓ Hypointensity or signal drop
- Higher field MRI has unique susceptibility contrast
 - ✓ BOLD-fMRI
 - ✓ Deoxyhemoglobin
 - ✓ Iron content (heme, non-heme)
 - ✓ Anisotropic fiber

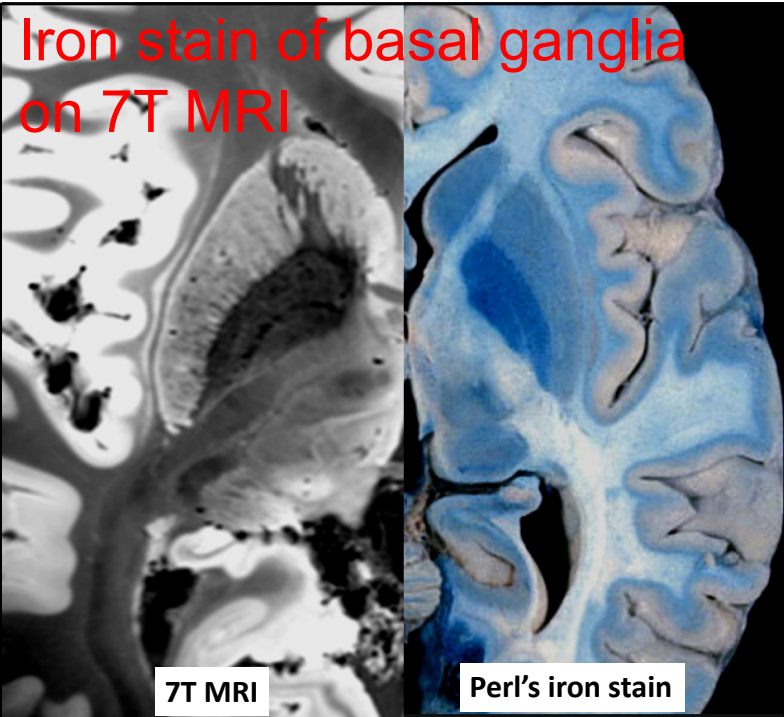


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- Iron plays a paradoxical role in aging
 - Vital role to normal neuronal functions
 - Strong oxidizer that promotes neurodegeneration
- Non-heme iron on MRI may be a biomarker of neurodegenerative diseases for metabolic dysfunction and oxidative stress

Daugherty AM, 2015

Iron stain of basal ganglia on 7T MRI

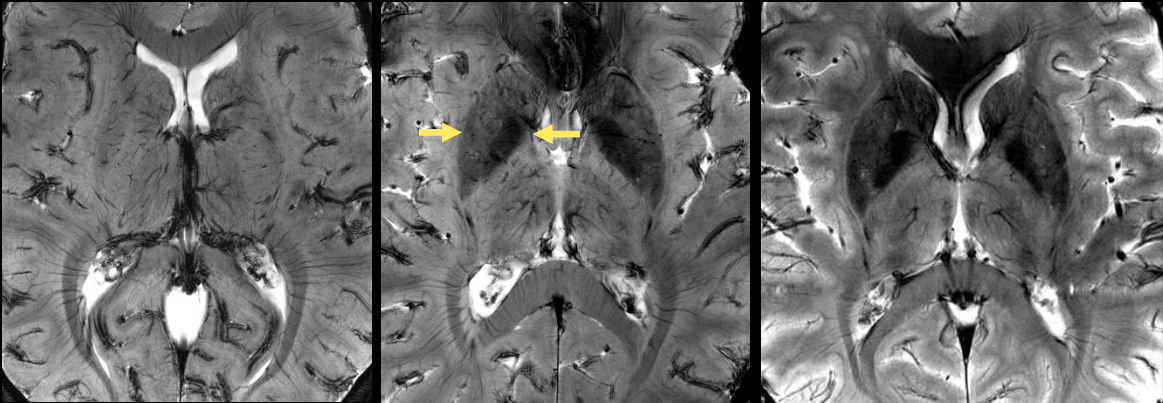


7T MRI

Perl's iron stain

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Iron deposition in healthy subjects



25yr male

35yr male

55yr male

- Clear evidence shows age-related iron increase in basal ganglia (not hippocampus in AD*)
- UHF MRI has advantage for early iron accumulation to predict cognitive impairment

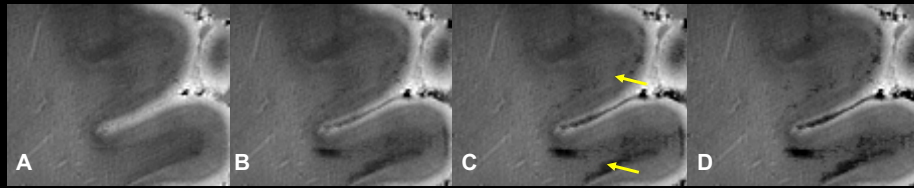
*van Rooden S, 2014

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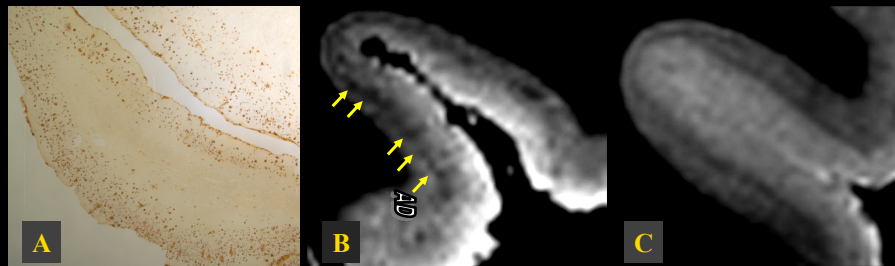
CAIPR

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Amyloid iron (postmortem) on 7T

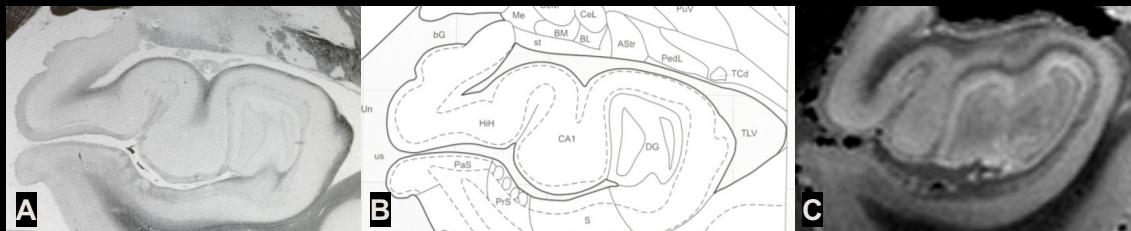


SWI images with phase multiplication factors of 0 (A), 4 (B), 6 (C), and 8 (D) in AD showing the detection of the iron deposition in the cortex

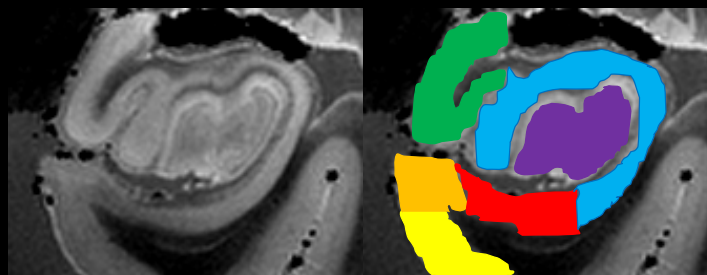


Ge Y et al, 2009  

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Atlas of the Human Brain by Mai, Assheuer & Paxinos

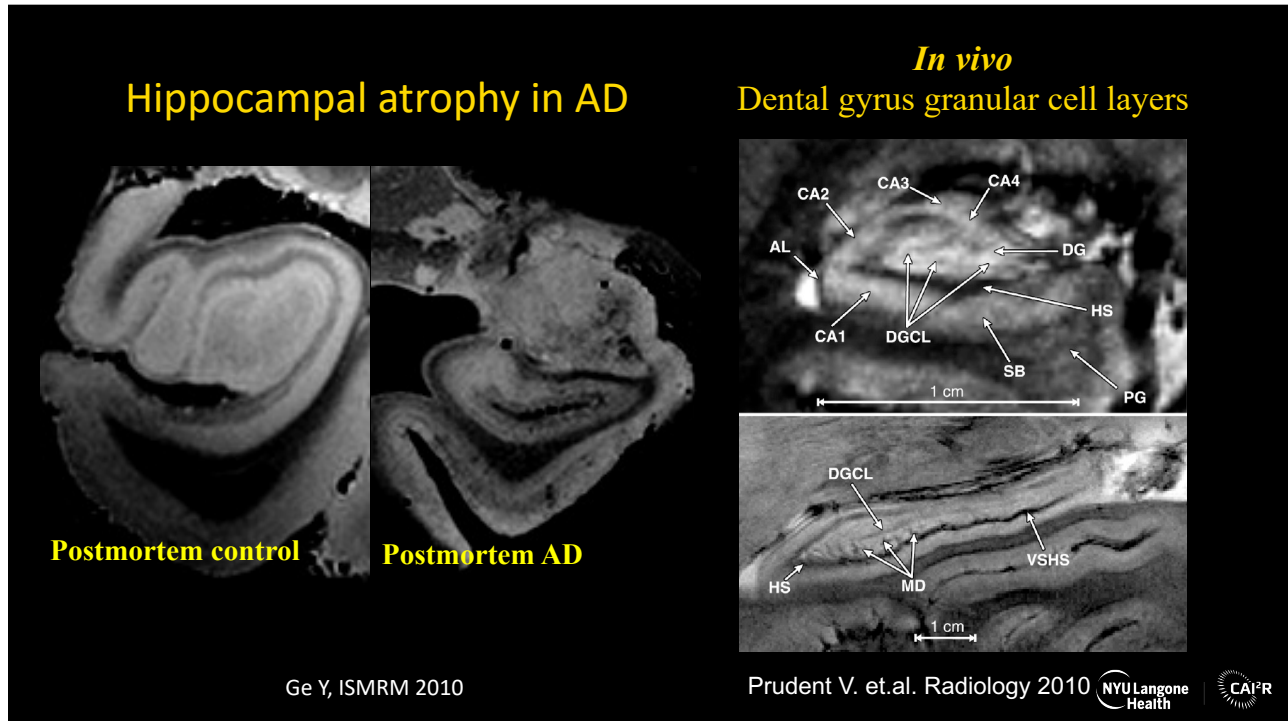


Hippocampal Head
 CA1~3
 Dentate Gyrus
 Pre - Subiculum /
 Subiculum
 Parasubiculum
 Entorhinal Cortex

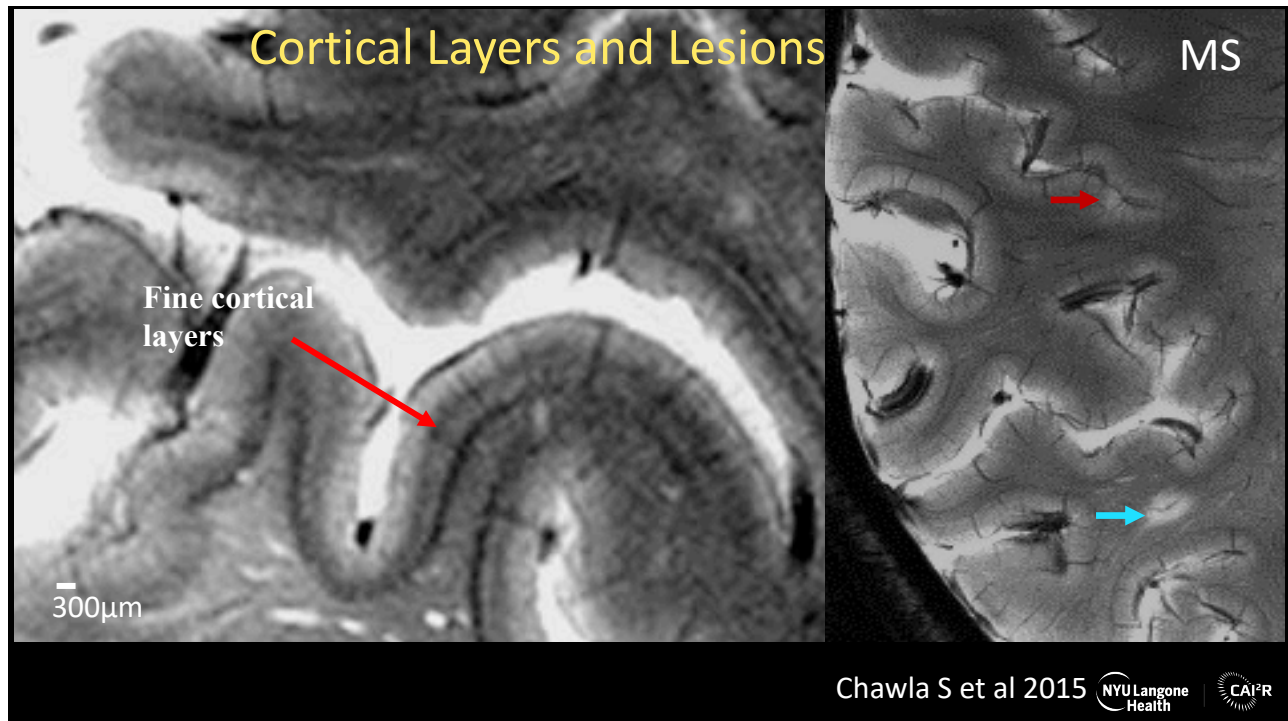
Hippocampus subcomponent @ 7T

Ge Y et al ISMRM 2010  

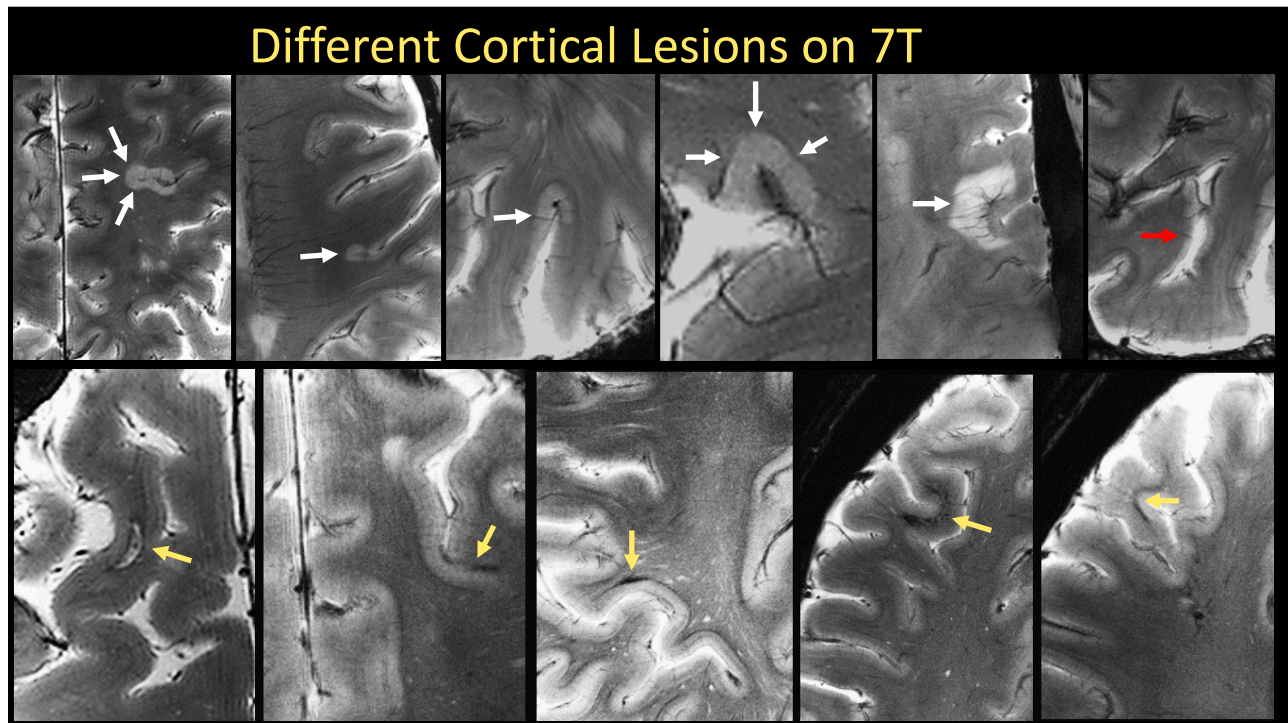
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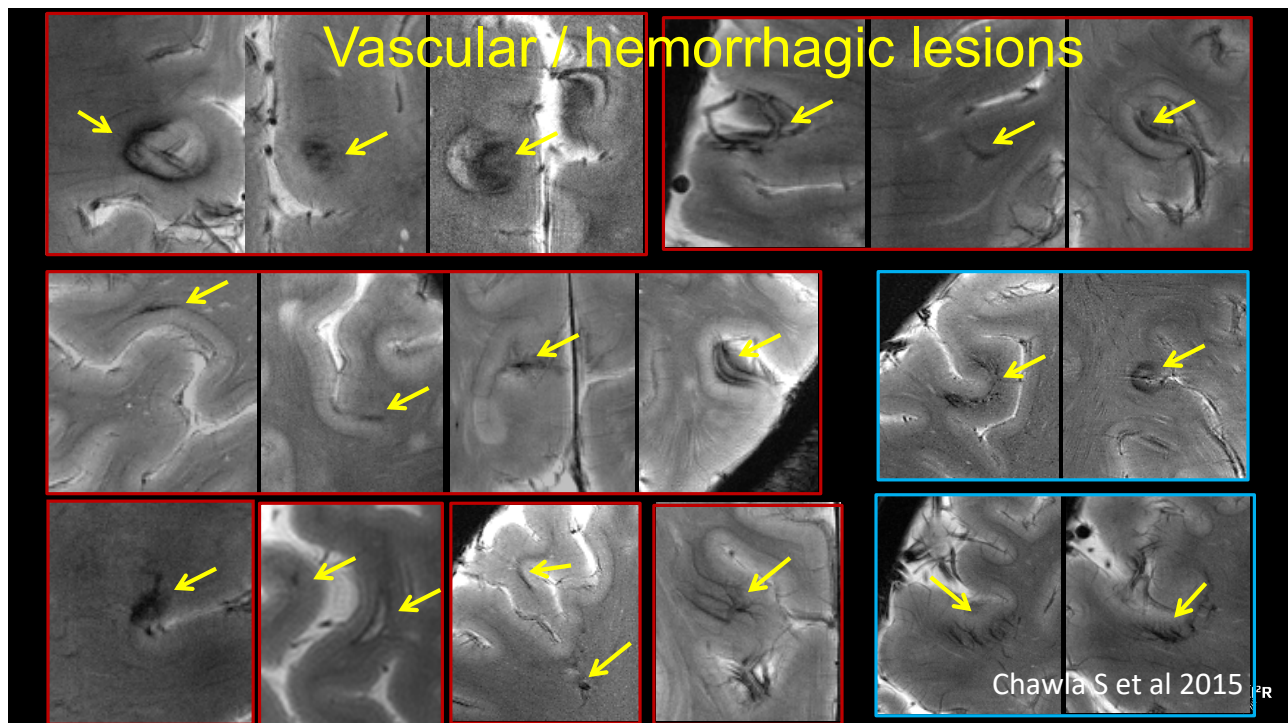
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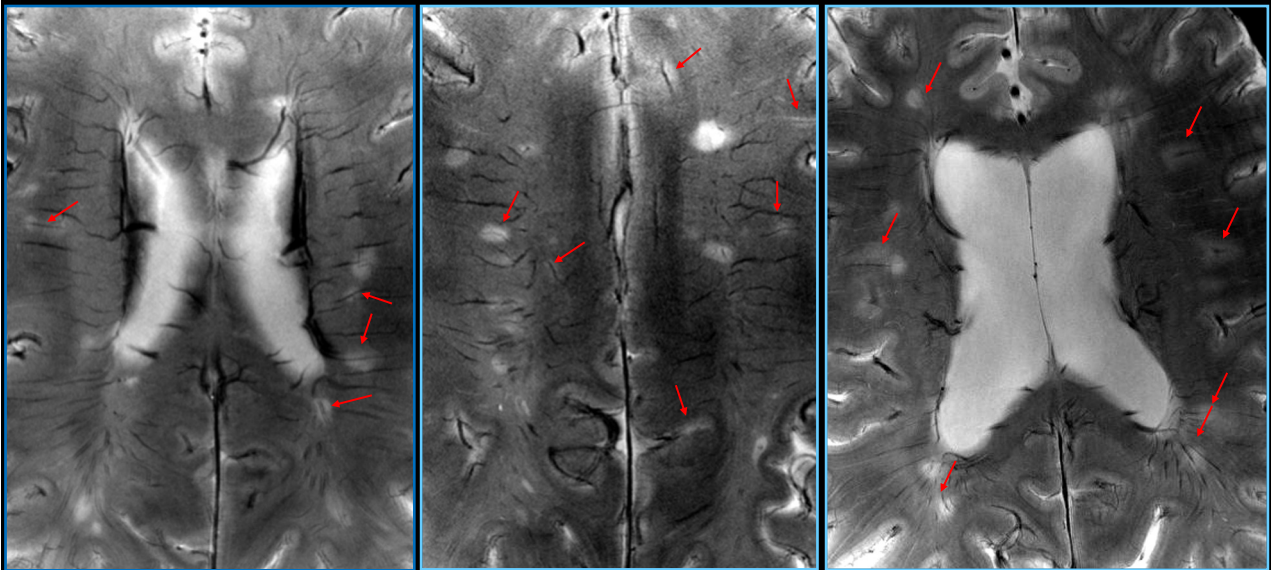
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Seeing the unseen on ultra-high field MRI

- Technical question
 - How 240 μ m resolution can see 100 μ m structure?
 - ✓ Susceptibility blooming effect with largely increased SNR
 - Can they be quantitative?
 - ✓ Yes, but not quite there yet
- Clinical question
 - Are they clinically useful (e.g. diagnosis)?
 - ✓ Yes (especially with FDA approved 7T MRI)

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Microvascular abnormalities on 7T



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Neuromyelitis optica (NMO)

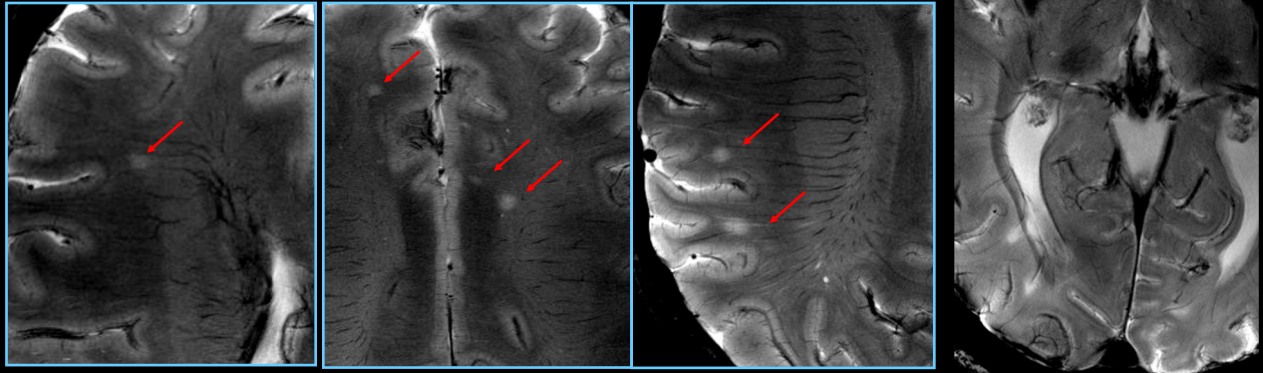
Kister I, et al Mult Scler Int.2013

OPEN

Sati P et al Nature Reviews 2016

EXPERT CONSENSUS DOCUMENT

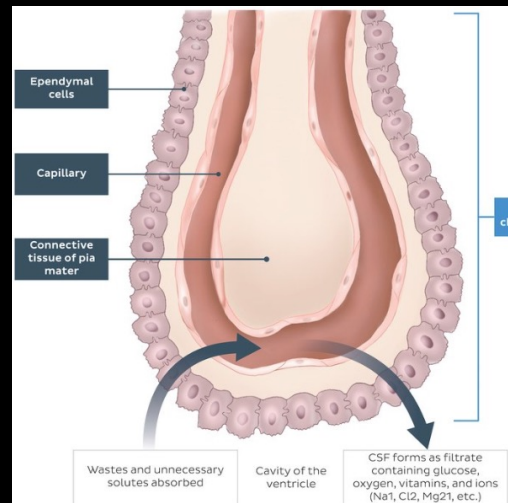
The central vein sign and its clinical evaluation for the diagnosis of multiple sclerosis: a consensus statement from the North American Imaging in Multiple Sclerosis Cooperative



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Choroid Plexus

- An epithelial tissue mass highly vascularized with fenestrated blood vessels
 - ✓ Waste absorption
 - ✓ CSF production
 - ✓ Ion exchange
- Blood-CSF barrier
 - ✓ Allows substances (e.g., Amino acids, peptide hormones, immune cells) to pass through into CSF



Hubert V et al Front Mol Neurosci. (2019)

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Age-related volume increase

- Stroma fibrosis
- Inflammation
- Vessel wall thickening

AD: upregulated receptors of fibroblast growth factor (FGF)

22Y 37Y 45-55Y 45-55Y
60's 70 80's

CONTROL ALZHEIMER'S

Age

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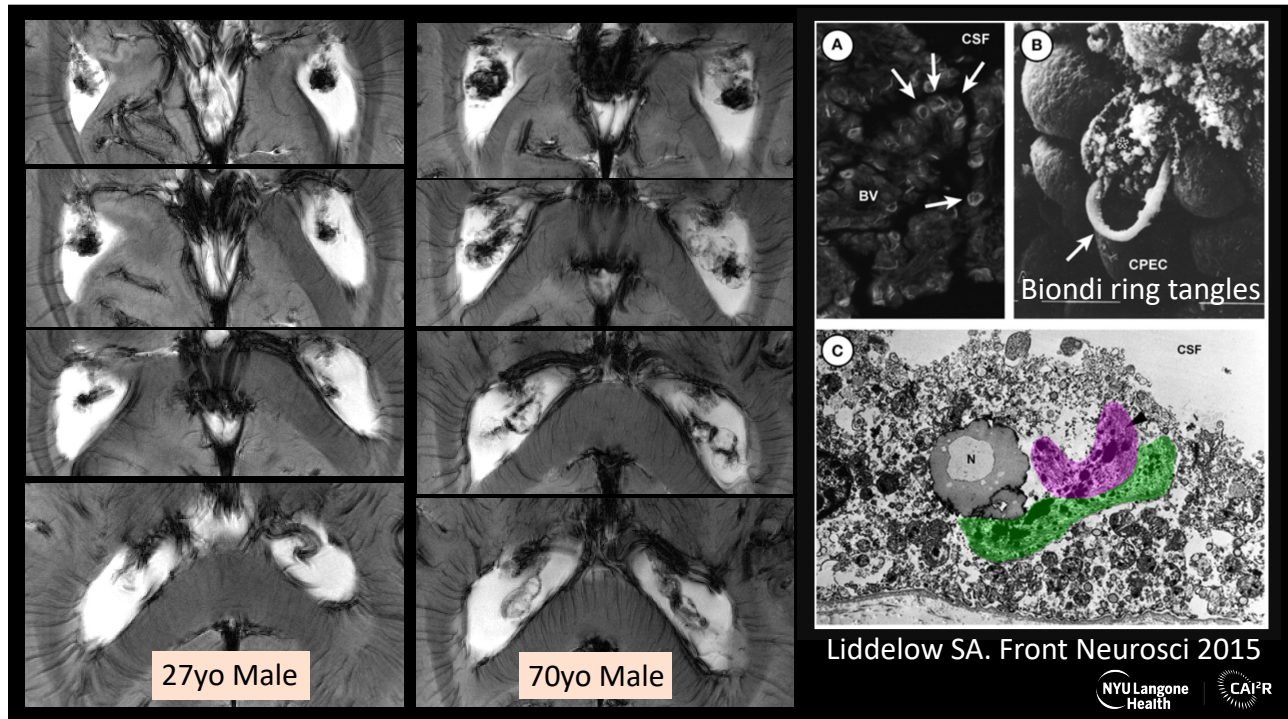
27yo Male 60yo Female

CONTROL ALZHEIMER'S
GRP 94 GRP 94

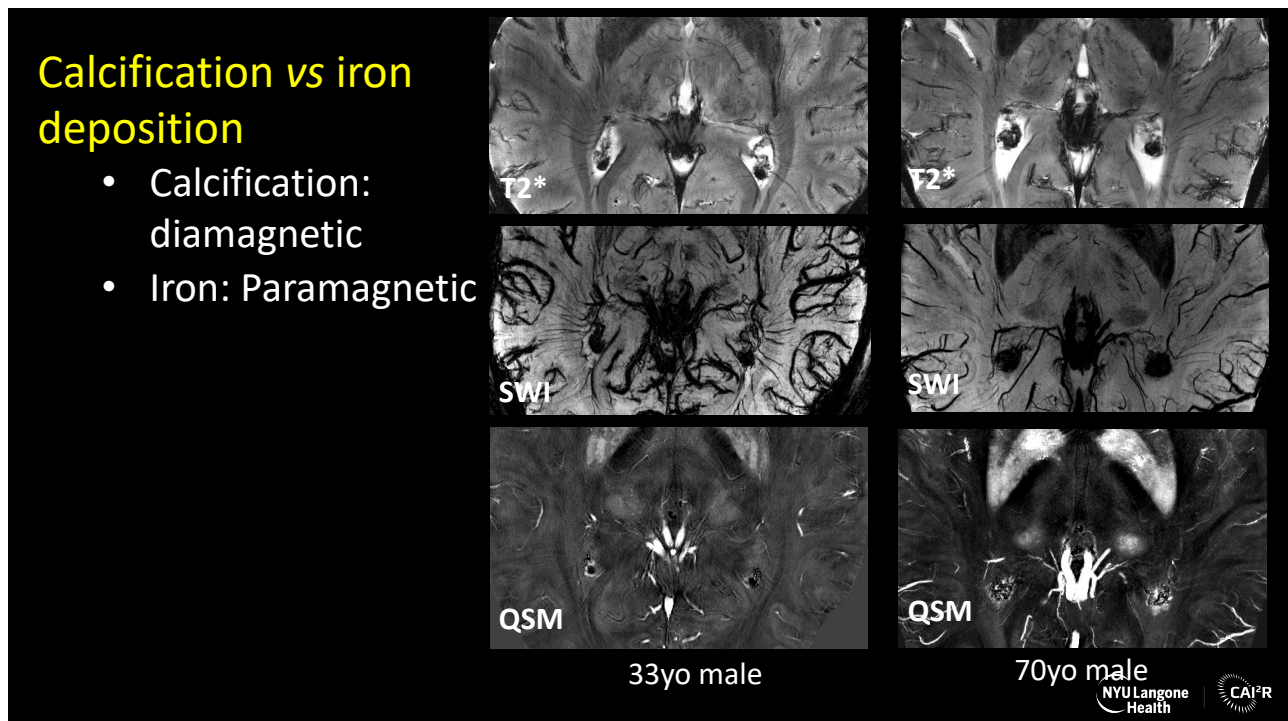
Vacuolation and loose contexture

Johanson C et al. 2004 NYU Langone Health CAIPR

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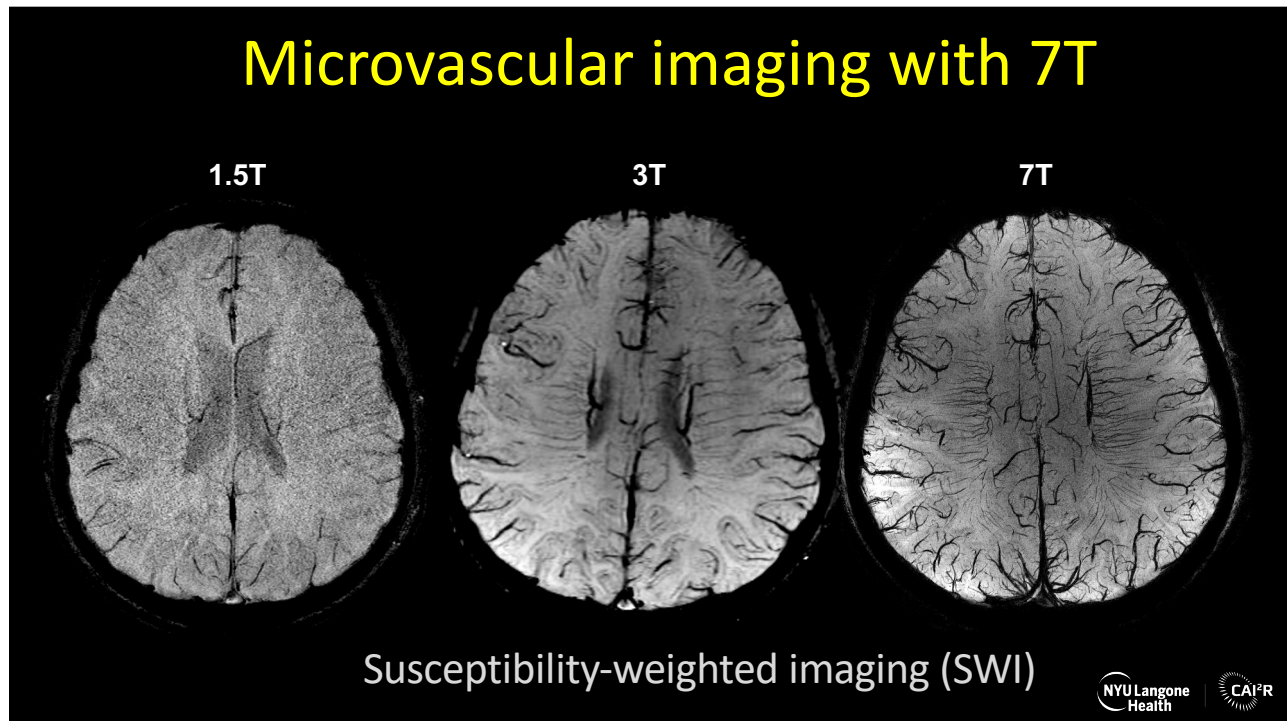


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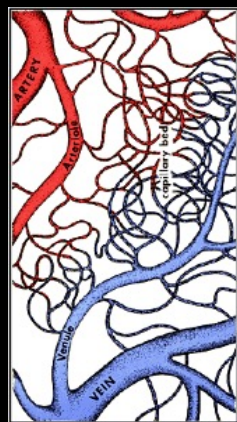
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Microvascular imaging with 7T



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Unmet need: *in vivo* detection of small vessel
in particular **small arteries**, where vasculogenic
neuropathology often begin



Diagrammatic
MRV



MR Arteriogram
MRA



SWI Venogram
MRV

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Ferumoxytol (Feraheme)

Feraheme
ferumoxytol
injection

USPIO – Ultrasmall Superparamagnetic Iron Oxide

THE FASTEST-GROWING IV IRON IN THE US MARKET*

Effective. Flexible.

Feraheme
ferumoxytol
injection

See IDA head-to-head trials ▶

**FERAHEME approved for second indication:
iron deficiency anemia**
The only IV iron demonstrating effective treatment for iron deficiency anemia (IDA) in adult patients with just one gram of iron across 2 fifteen-minute infusions 3 to 6 days apart.*

Fe₃O₄

2.1 million patient exposures**



510mg elemental iron per 17 mL (30mg/mL)

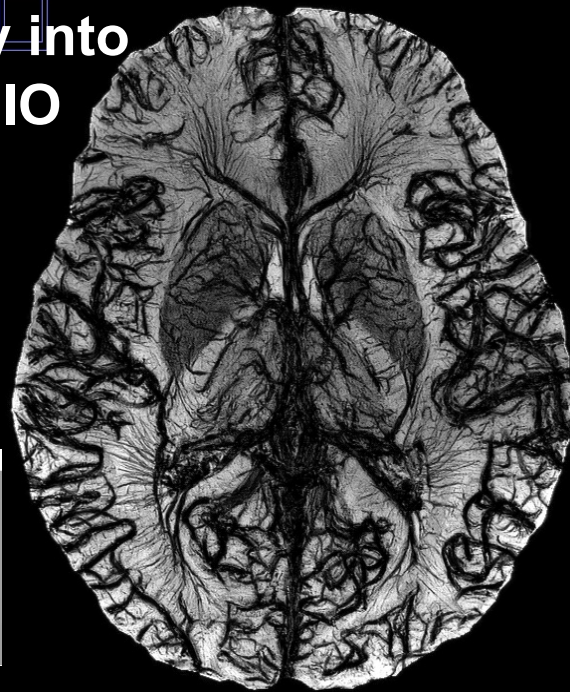
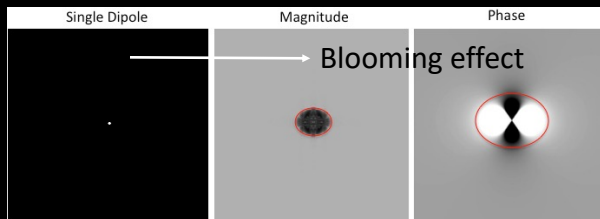
- First FDA-approved USPIO for human use in 2009 to treat iron deficiency anemia



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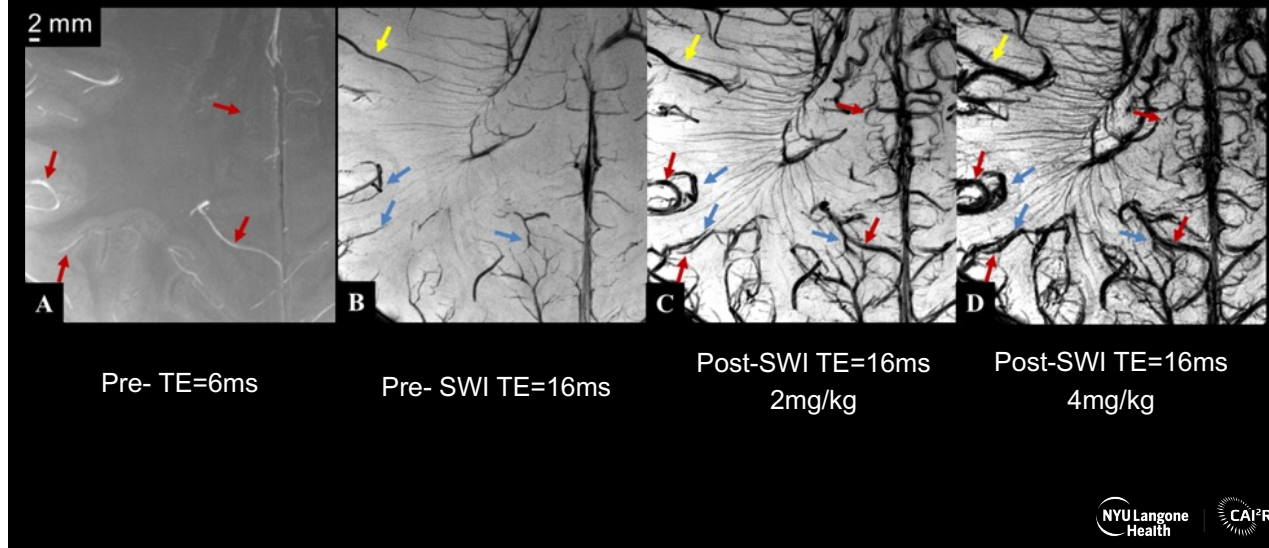
Introduce susceptibility into small vessels with USPIO

- Susceptibility induced blooming effect
- Significantly increases the detection of small vessels of both arterioles and veins

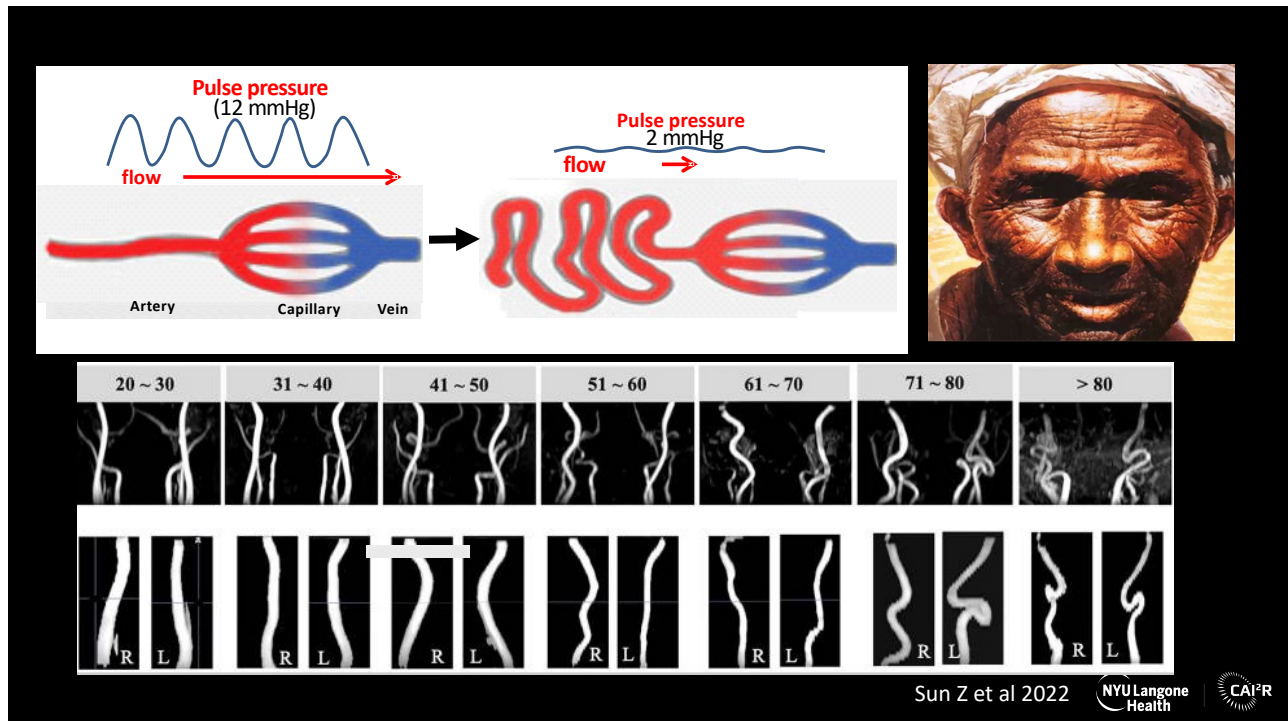


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Pre- vs Post-USPIO scans

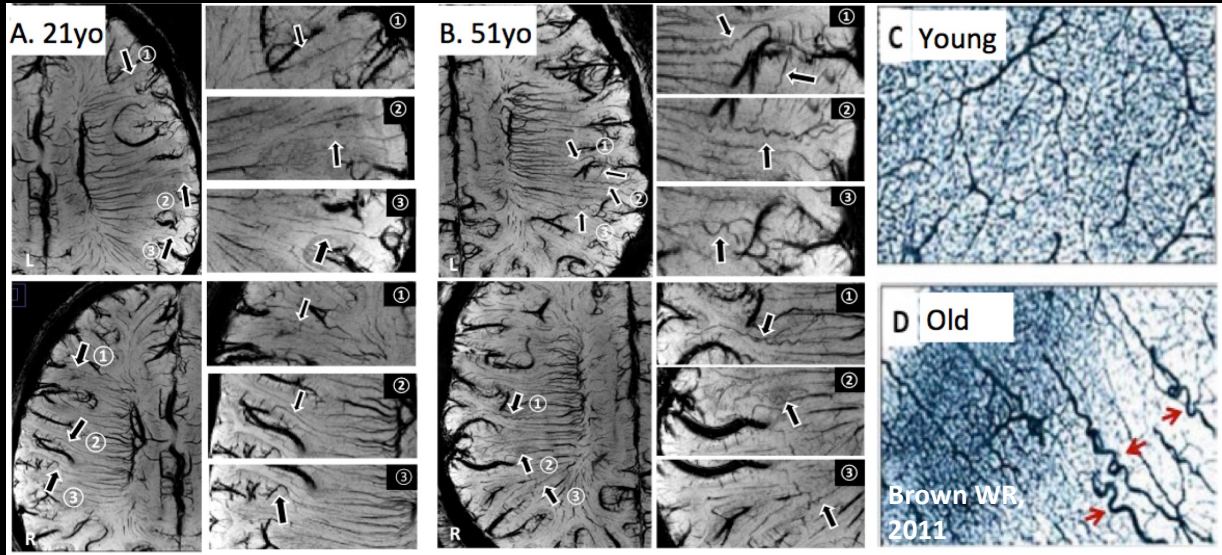


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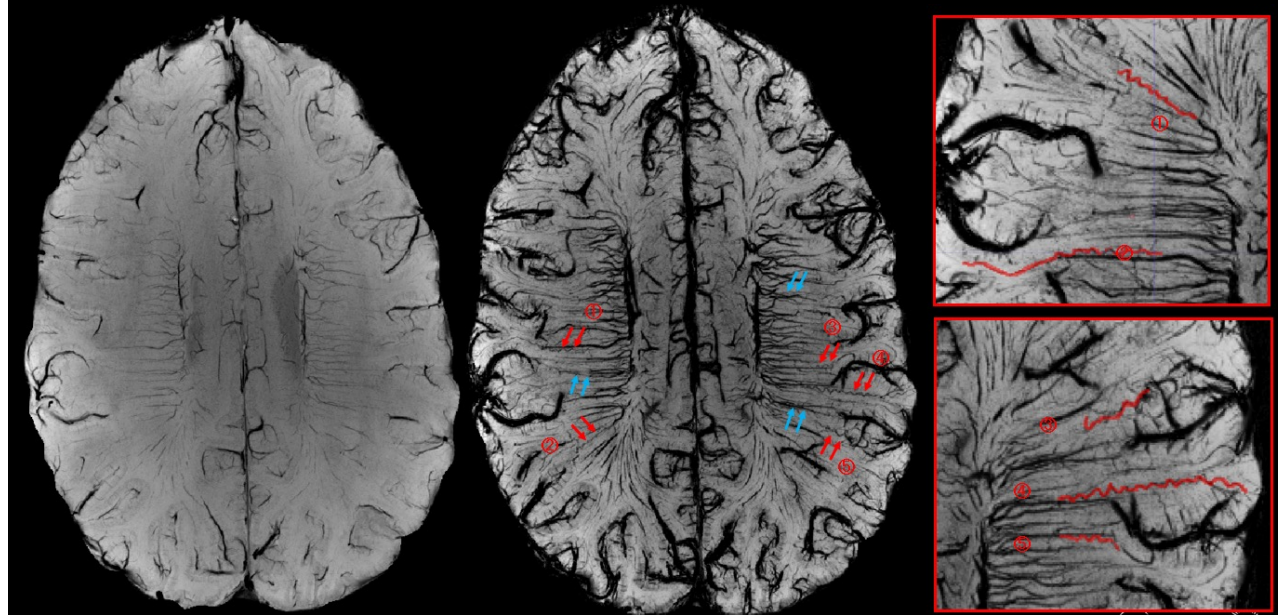
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Wrinkles of small vessels (corkscrew) in brain on USPIO-MRI



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Corkscrew appearance of small arteries



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USPIO-enhanced MRI

- Cerebral microvascular architecture print (cMAP)
- Vessel density (VD)
- Capillary density (CD)

Chenyang Li, S12 – 14:40
Zhe Sun, S13 -16:38
Sagar Buch (WSU) – S15 -10:10

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Summary

Seeing is believing: Being an imager or radiologist, we always tend to only believe what we actually see.

Ultra-high field MRI allows

- Macro- to micro-scope lesions (<math><50\mu\text{m}</math>) that are not seen on conventional imaging.
- Discovery of new *in vivo* pathology (iron, inflammation, microbleeds, cell edema, etc)
- Early changes to make early diagnosis and early treatment with better outcome.

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