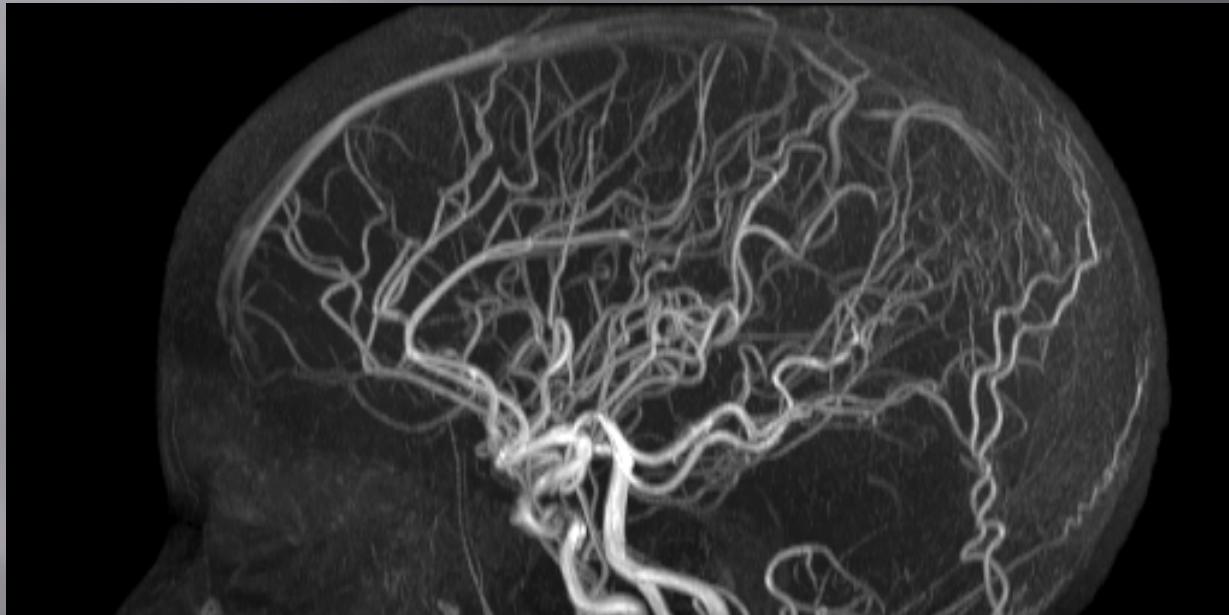


DEVELOPMENT OF MRI BIOMARKERS FOR IMPROVED DIAGNOSIS OF TBI



E. Mark Haacke, PhD, nmrimage@aol.com
Director, MR Research Facility, Wayne State University
Detroit, Michigan

Conflicts of Interest

- ❑ Research support from the DoD for TBI
- ❑ President of MR Innovations, Inc
- ❑ NIH support for research into flow and iron deposition using MRA and SWI methods

Acknowledgements

- Xia Shuang, Tianjin, stroke
- Meng Li, MS, for perfusion TSM data
- Jaladhar Neelavalli, PhD for SWIM support
- Sagar Buch, MS, for SWIM support
- Saifeng Liu, for SWIM support
- Yongquan Ye, PhD, for MRA support

Goals and Outcomes

Aim 1: Compare advanced MRI methods to conventional imaging methods in their ability to detect mTBI in the acute setting.

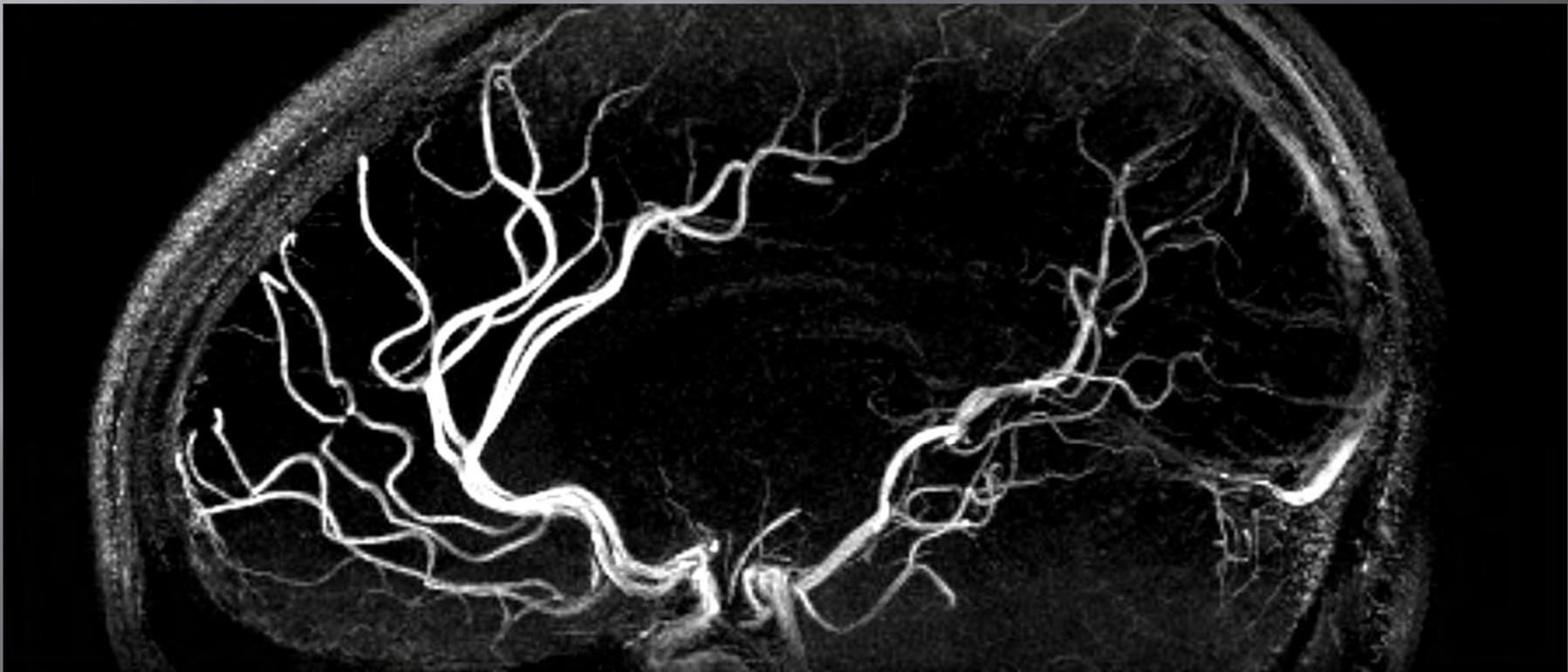
Aim 2: Apply susceptibility weighted imaging and mapping (SWIM) to quantify and monitor evolution of pathological changes in mTBI.

Aim 3: Explore the role of perfusion weighted imaging as a means to diagnose hemodynamic abnormalities.

Outcomes: The major findings presented here is that SWI is a means to detect microvascular damage, and this is particularly the case in the venous system for mild TBI.

High resolution MR angiography

Small arteries around 250 microns are beginning to become visible even without a contrast agent (0.5mm isotropic resolution).



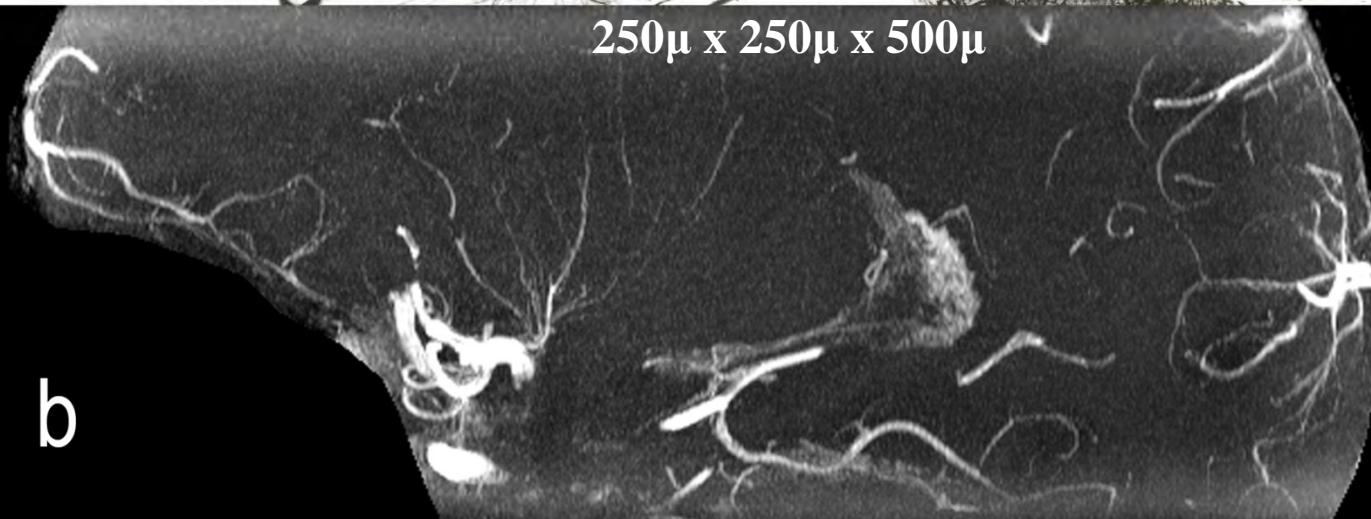
11) Salamon, G., 1971. Atlas of the arteries of the human brain. Sandoz, Paris.

a



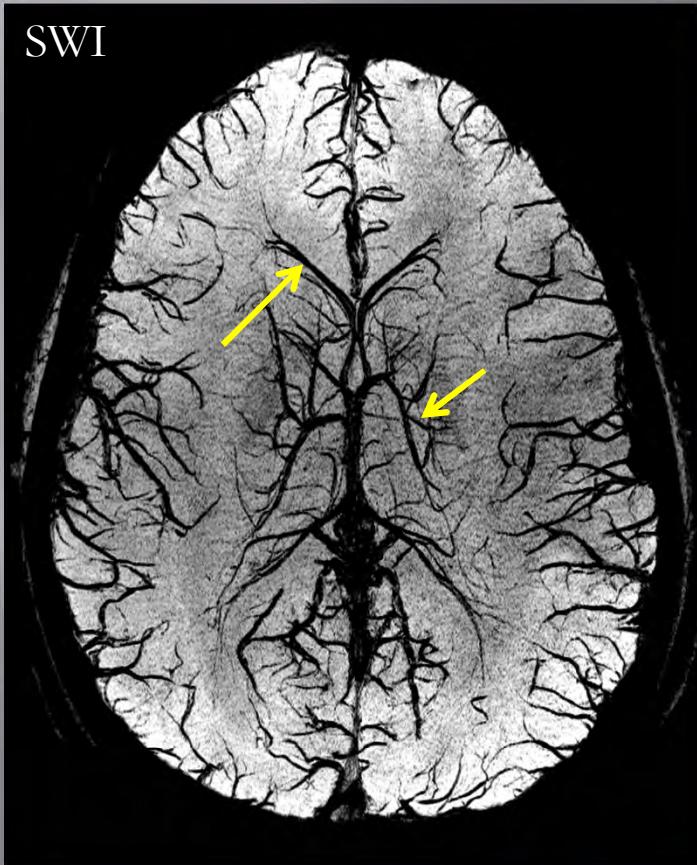
$250\mu \times 250\mu \times 500\mu$

b





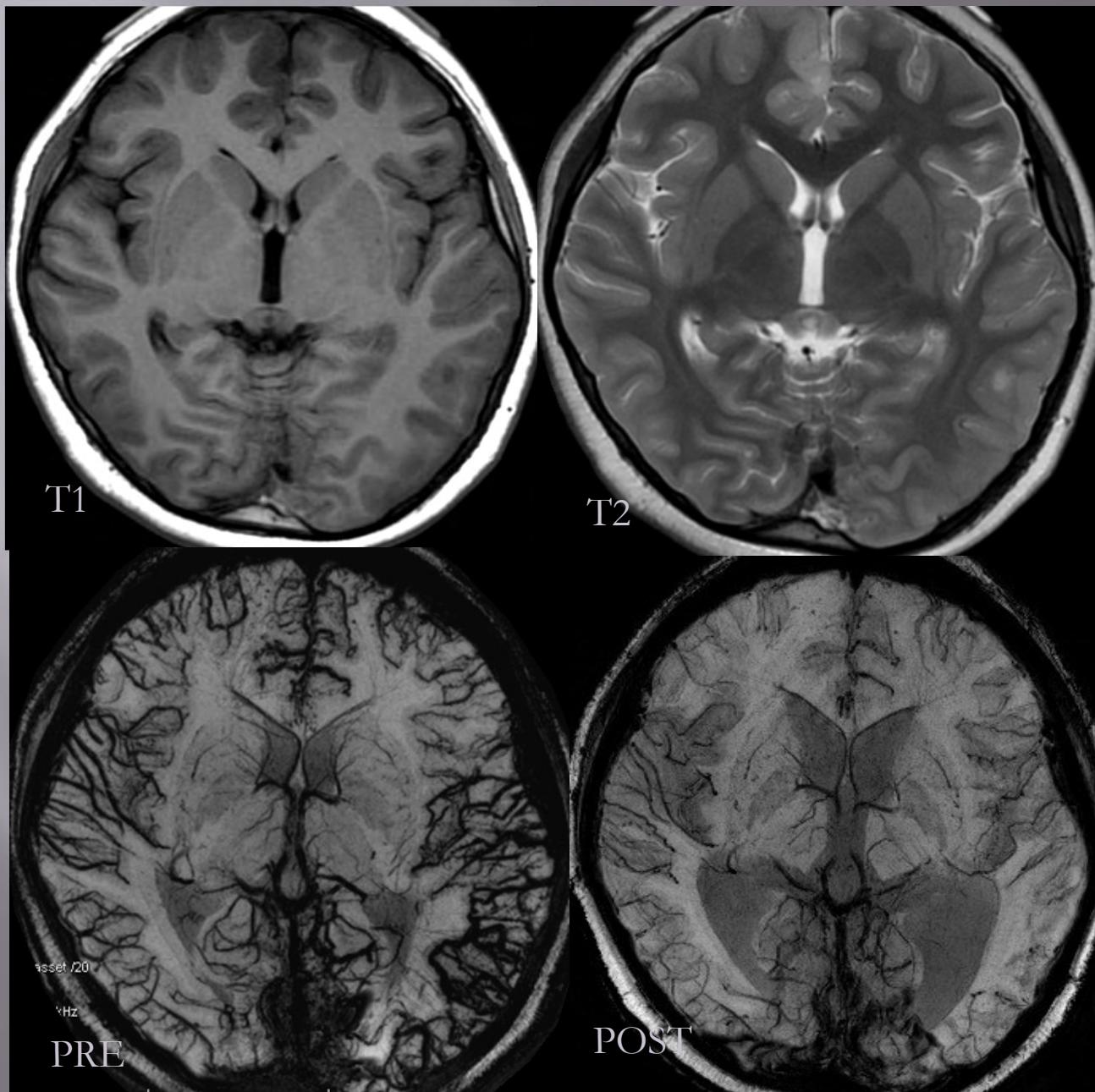
Susceptibility Weighted Imaging



- Enhances the presence of ferritin, hemosiderin and deoxyhemoglobin
- Exquisite images from which brain damage, microbleeding and increases in deoxyhemoglobin can be diagnosed

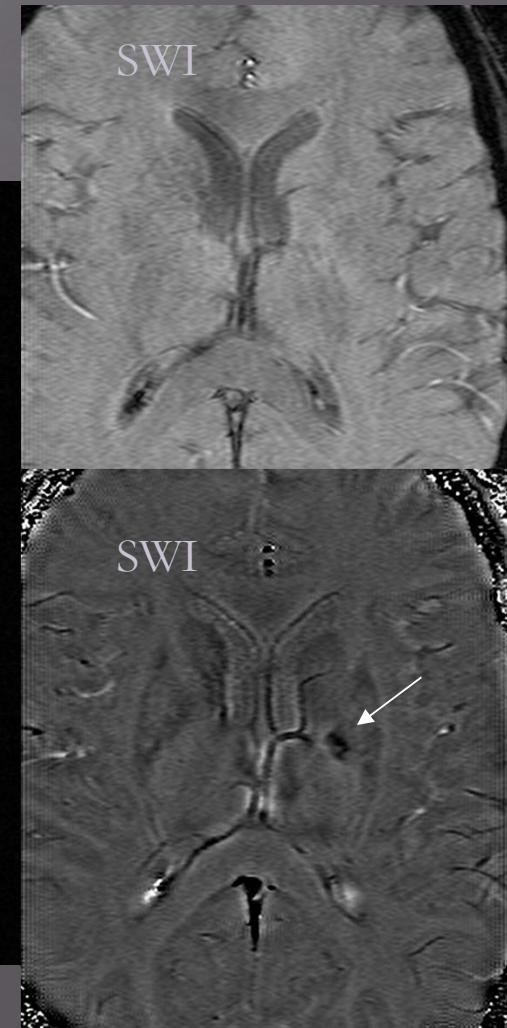
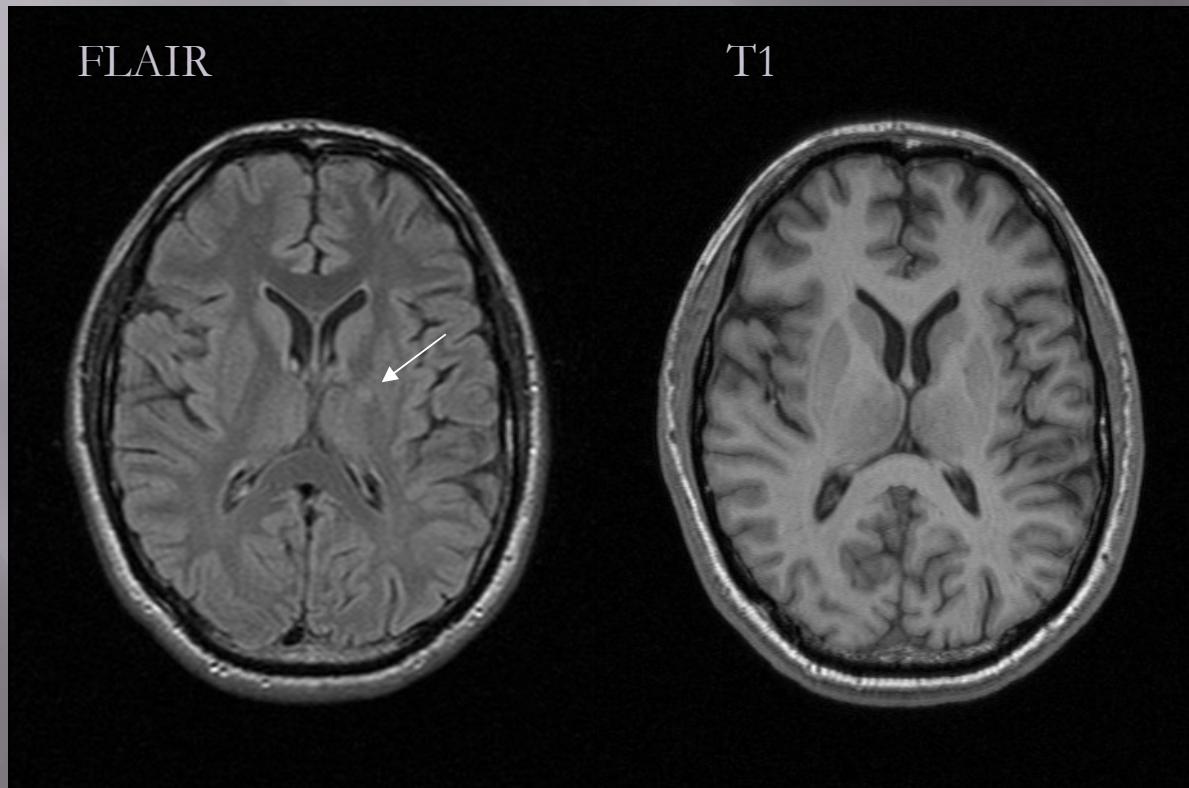
Haacke EM et al. Susceptibility weighted imaging. Magnetic Resonance in Medicine, 52: 612; 2004.

Venous
Thrombosis:
before
treatment and
after
thrombolysis

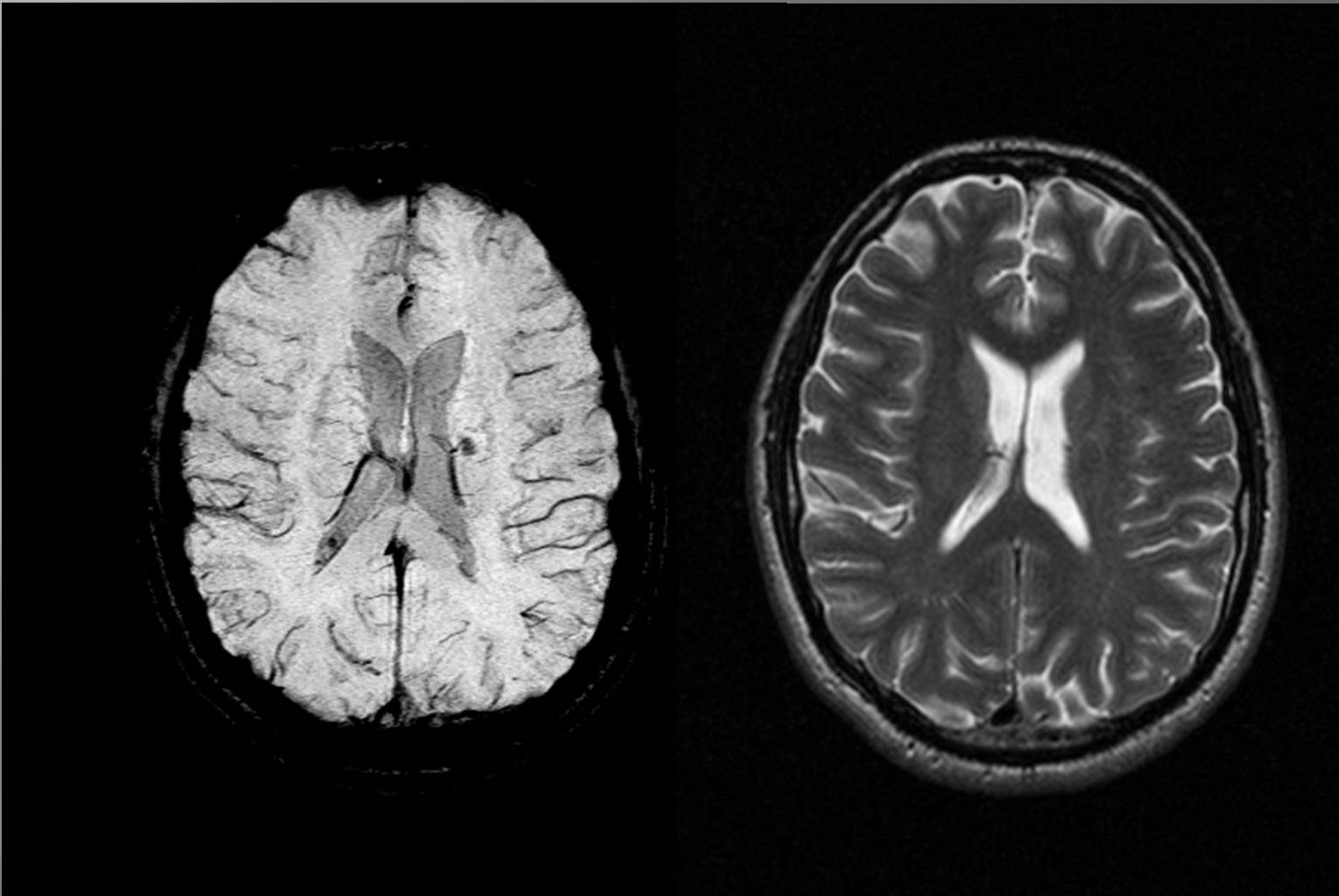


Guangbin Wang M.D.
Shandong Medical
Imaging Research
Institute

Low concentration iron is still seen on 7 slices with SWI and barely discernable on FLAIR!



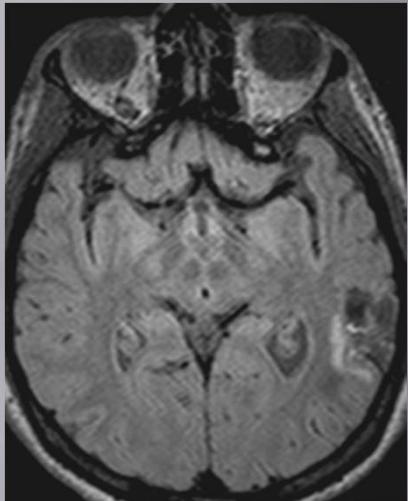
Stroke with almost imperceptible bleeding



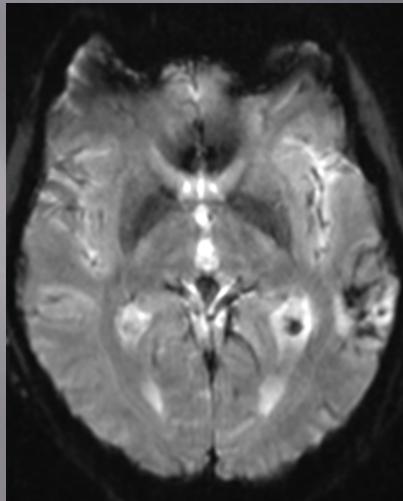
SWI shows the bleed

short TE GRE T1

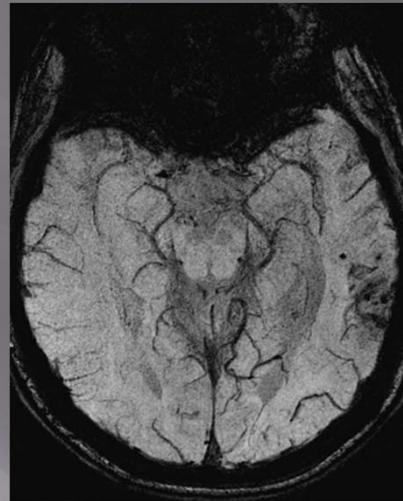
Stroke case for a young woman in her mid 30s



FLAIR



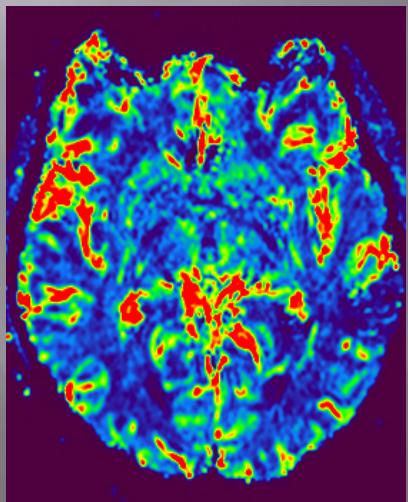
PWI (1st)



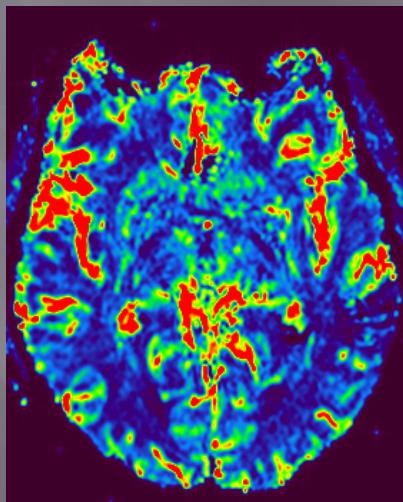
SWI mIP



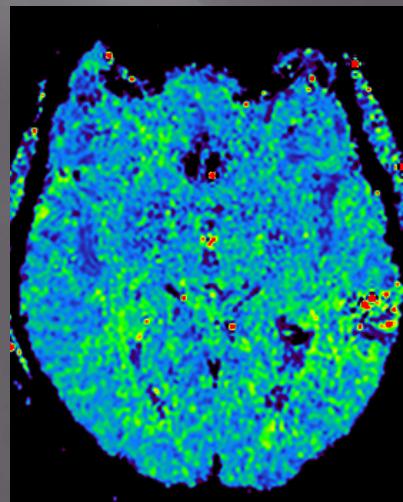
MRA



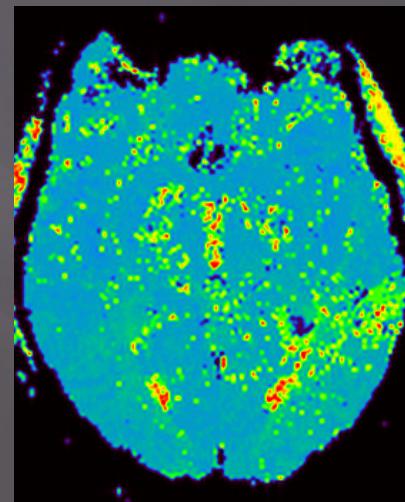
CBV



CBF



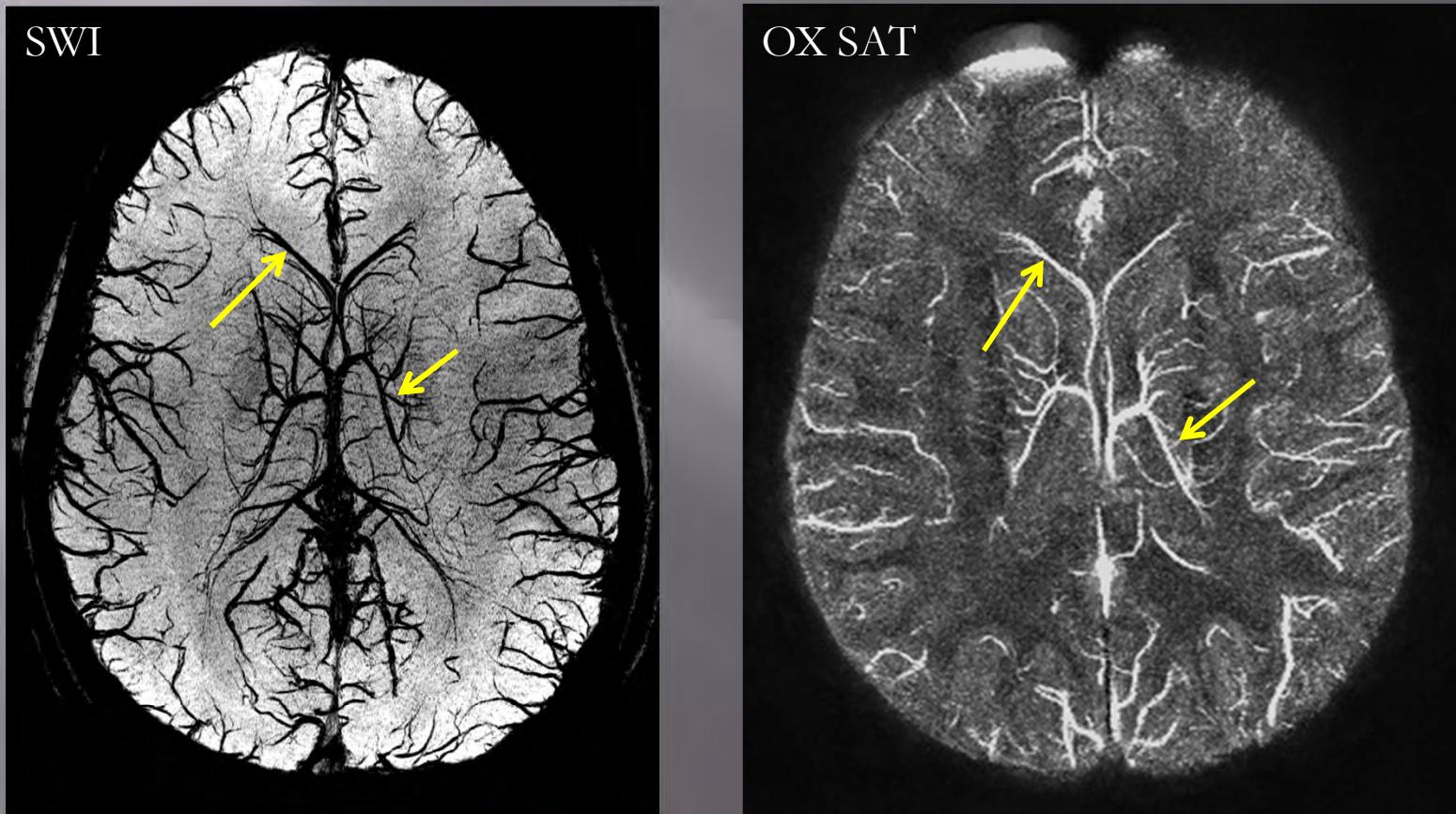
MTT



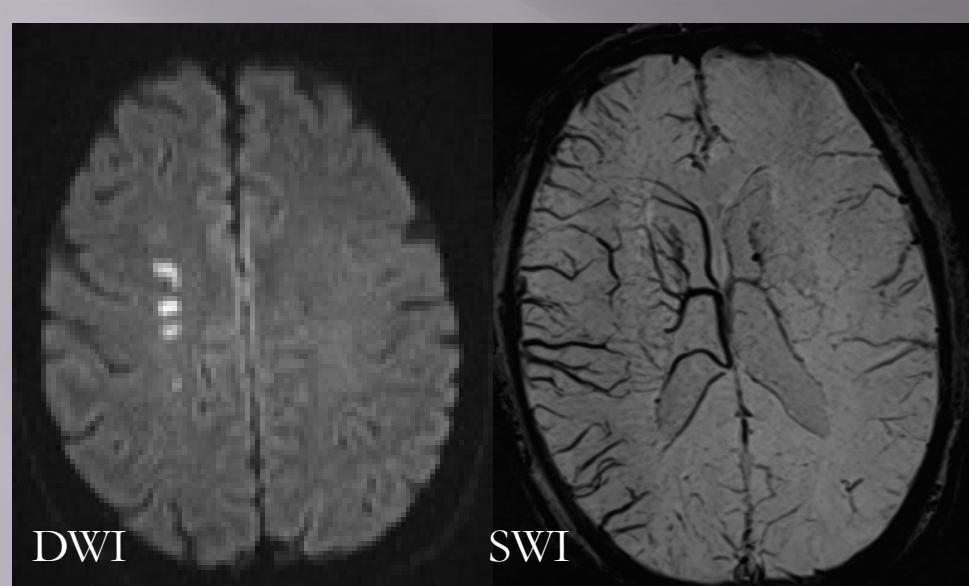
TTP



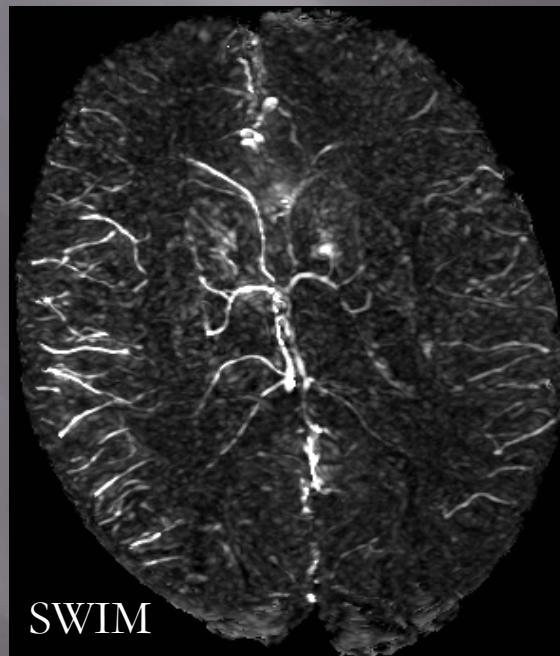
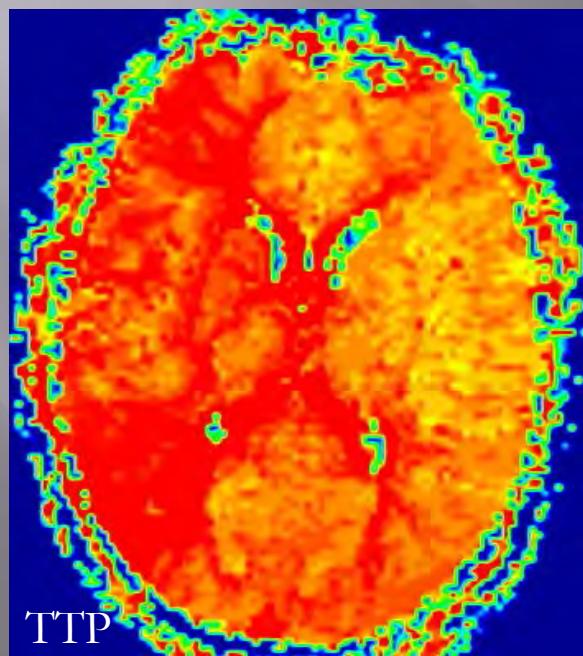
The data collected for SWI can also be reprocessed to produce whole brain maps of oxygen saturation.



Haacke EM et al. Susceptibility mapping as a means to visualize veins and quantify oxygen saturation. JMRI 2010;32:663-76.



A 57 year old male patient with left limb weakness was scanned 144 hours after onset.

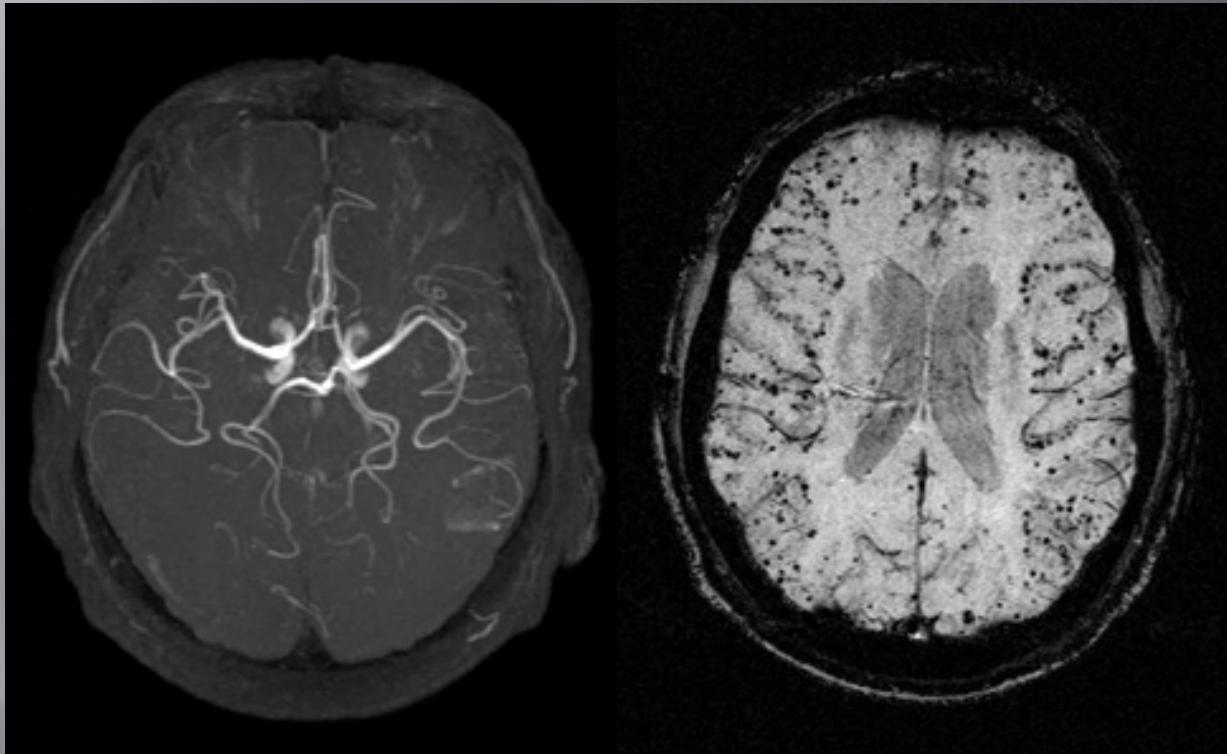


MR perfusion shows delayed TTP corresponding to the area of APCV, which can be associated with the penumbra of the right hemisphere.

Imaging Aging

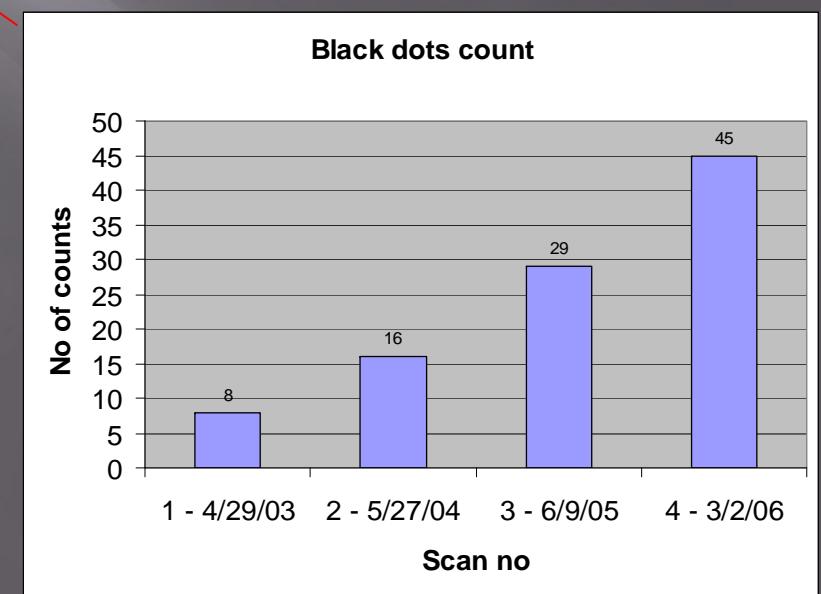
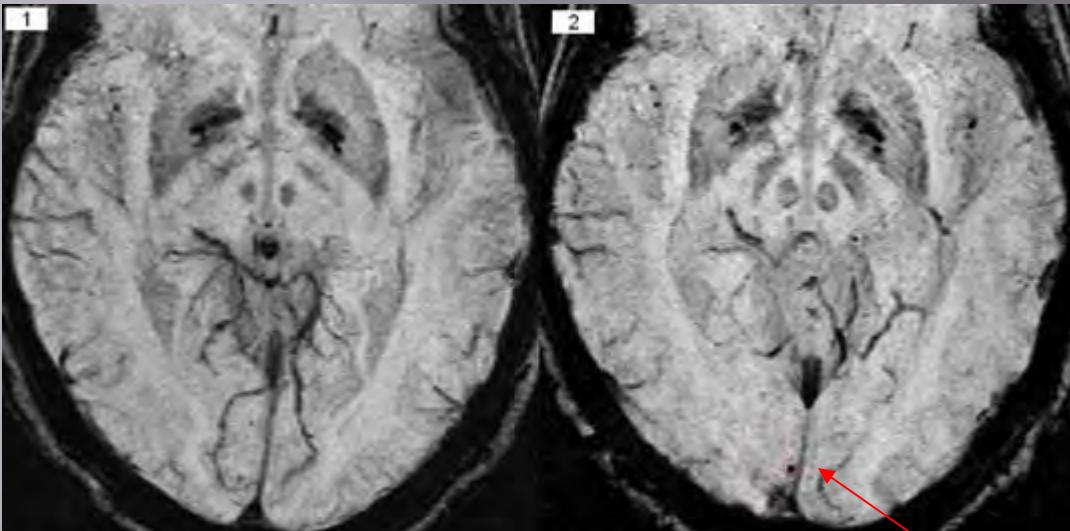
- ▶ It is now believed that up to 35% of dementia cases may be caused by vascular dementia.
- ▶ We see microhemorrhages as a means to predict who will get Alzheimer's disease.
- ▶ These may lead to “cognitive strokes”.
- ▶ Hopefully this work will lead to collaborations with the pharmaceutical industry to come up with neuroprotective drugs that will strengthen the vessel wall or help to prevent its degeneration.

Cerebral amyloid angiopathy



50 μ objects can manifest as 1mm³ objects

time to go sailing



Using caffeine decreases blood flow to the brain

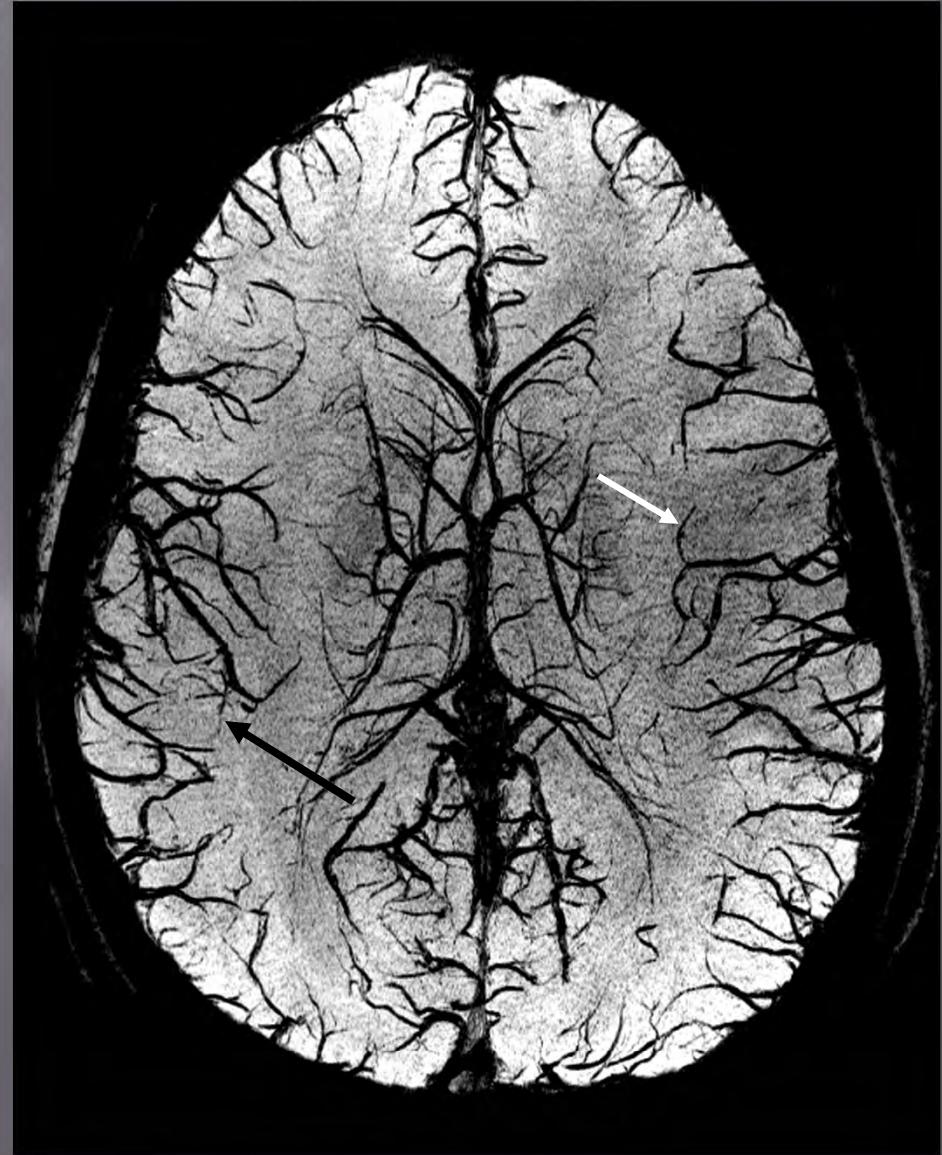
two cups of coffee and you will have a major
change of blood flow to the brain

maybe we should approach Starbucks for funding

at least it is a relatively harmless contrast agent to
use to study the brain and a heck of a lot cheaper



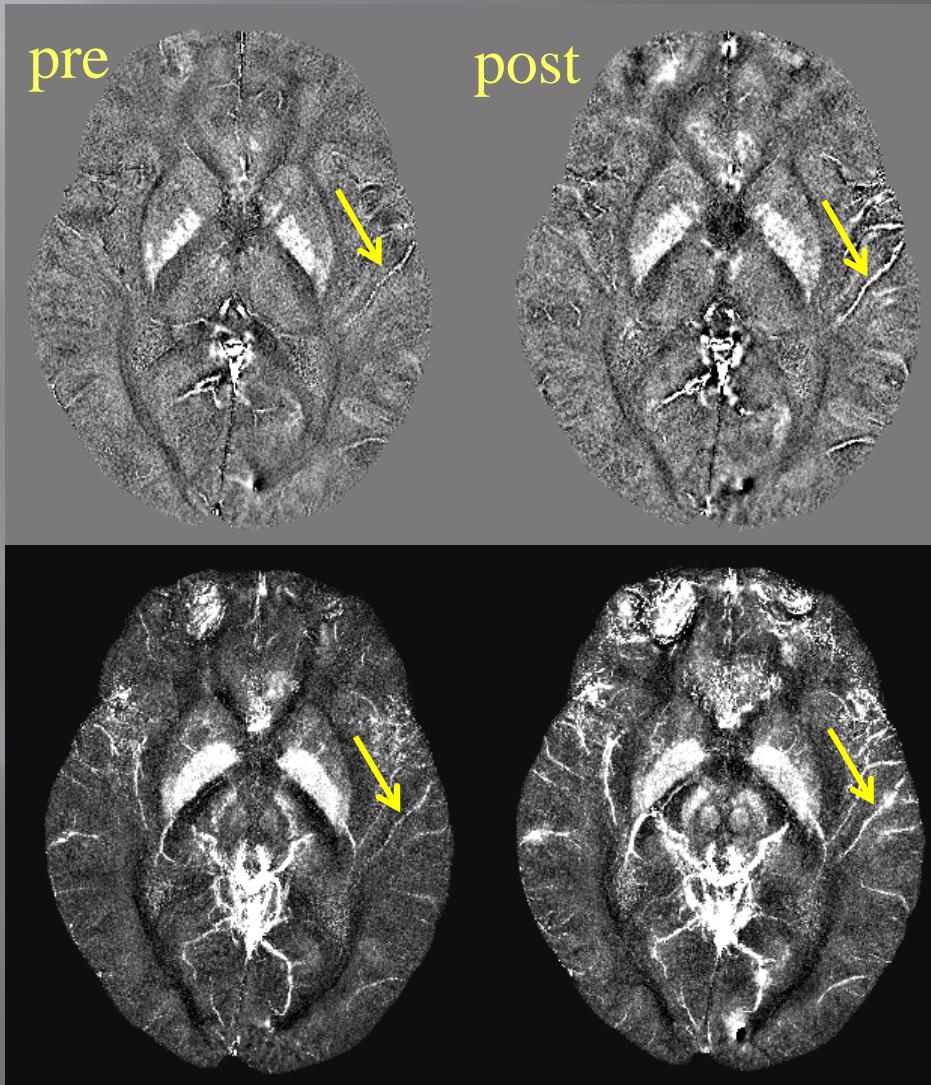
PRE



POST

MinIP of caffeine/Gd over 28 slices with 4 phase multiplications

SWIM images pre/post caffeine injection



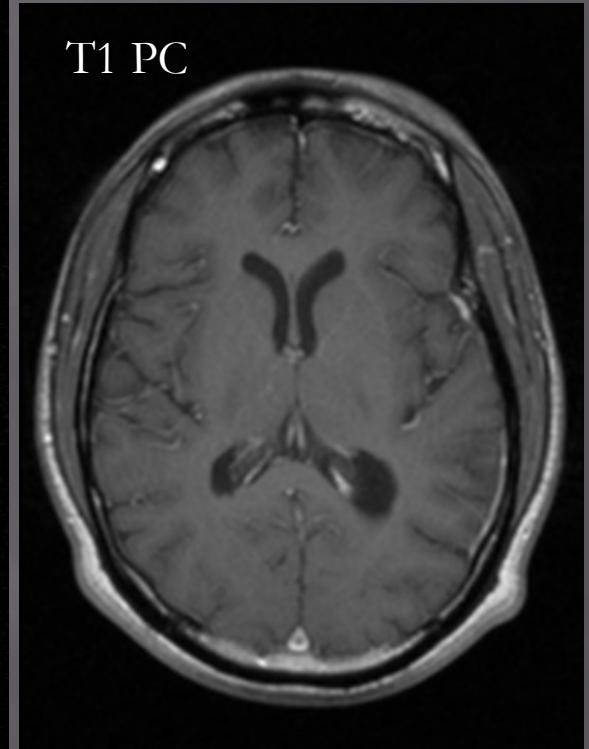
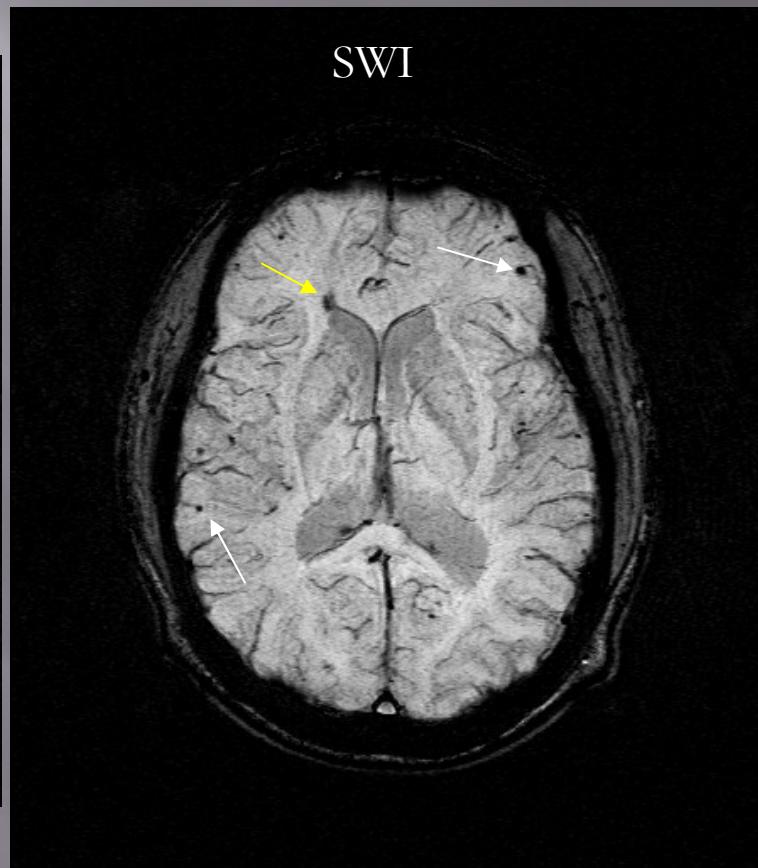
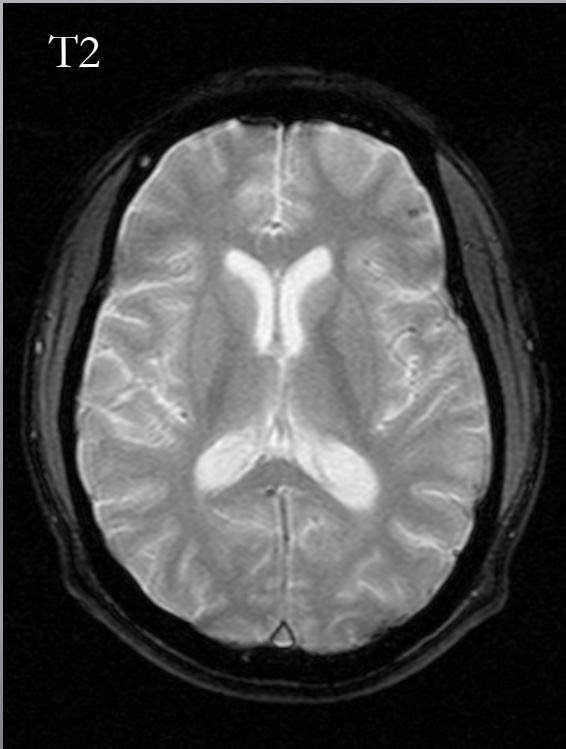
Increased
susceptibilities
indicated by
yellow arrows

Mipped over
8 slices
(16mm).

Approach to studying mTBI

- ❑ Conventional imaging (T1, T2, FLAIR, DWI)
- ❑ SWI for visualizing vascular abnormalities
- ❑ SWIM for quantifying oxygen saturation
- ❑ PWI for evaluating local tissue flow

Motorcycle trauma: medullary vein involvement

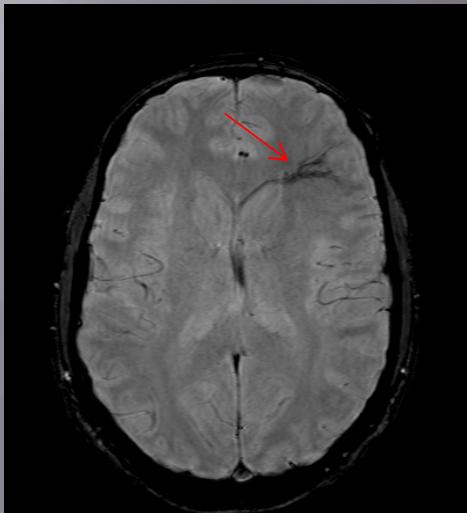


Major venous and medullary vein involvement

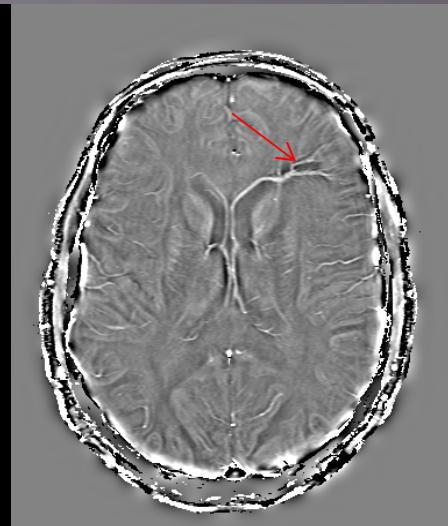


SWI reveals MVD

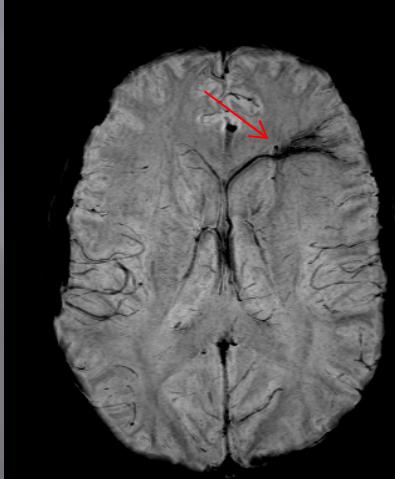
SWI-Magnitude



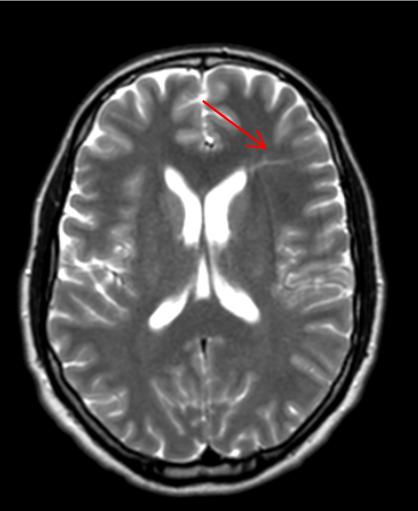
SWI-Phase



SWI-mIP

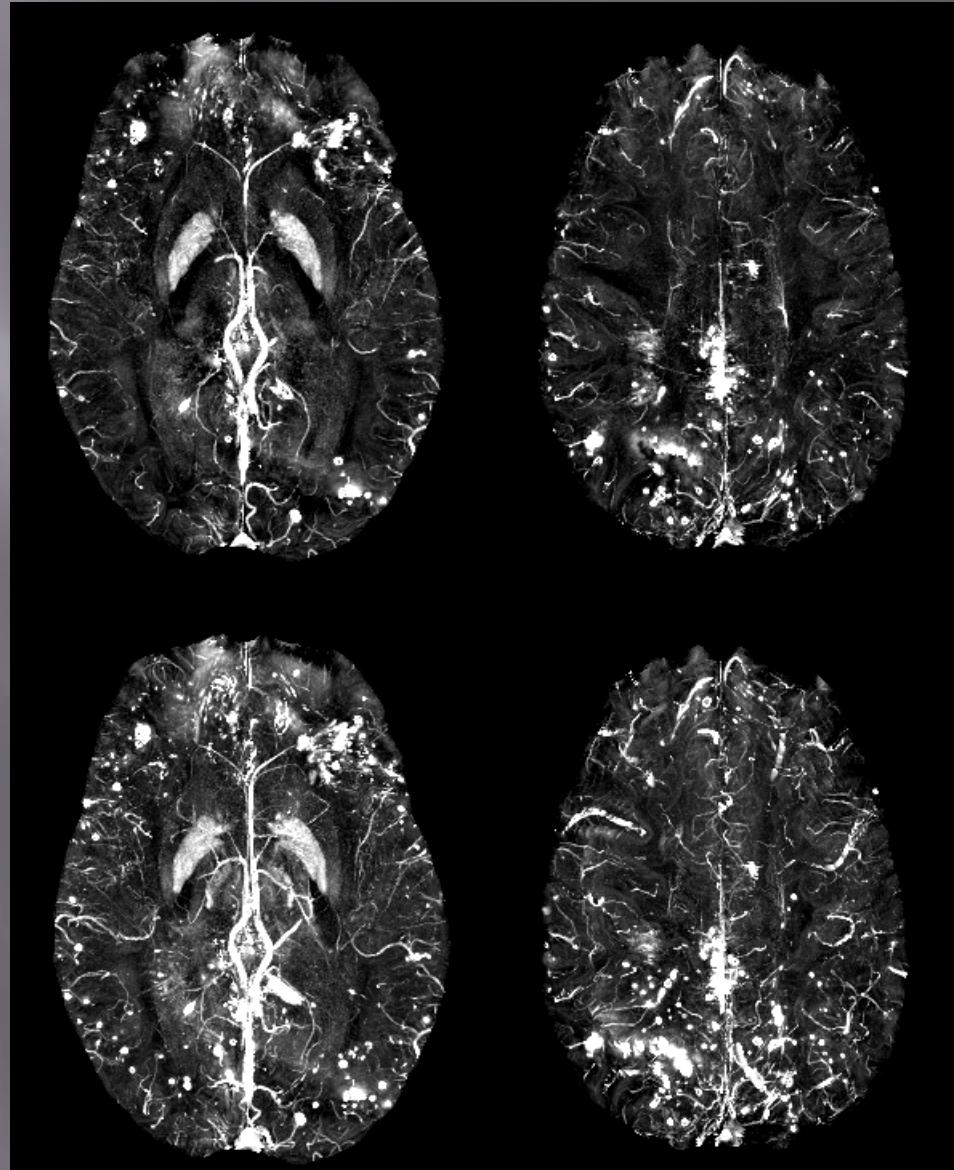


T2



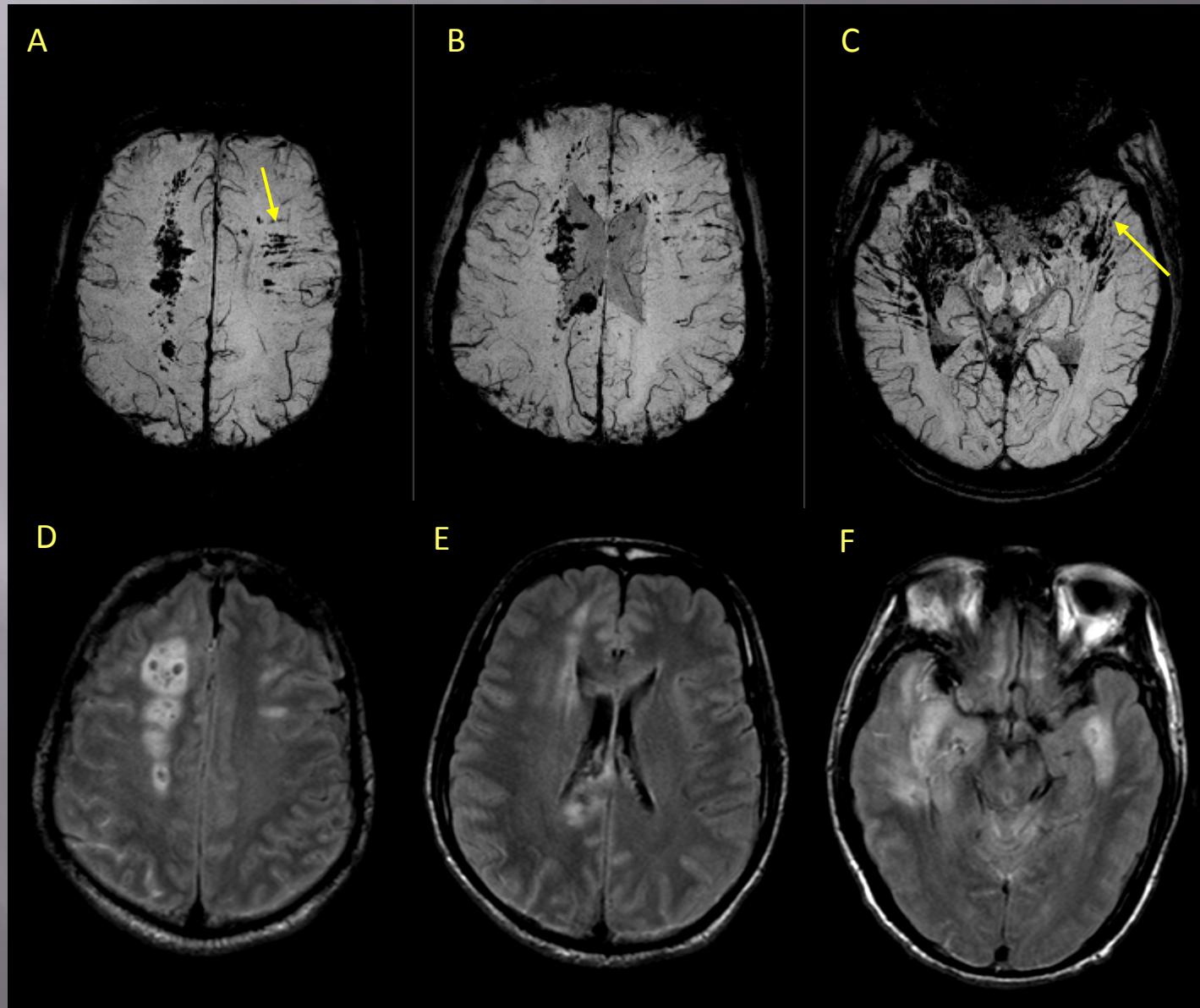
SWIM of cerebral microbleeds in TBI

Maximal
Intensity
Projection (MIP)
over 8mm



Maximal
Intensity
Projection (MIP)
over 32mm

Medullary vein involvement (severe TBI)



mTBI studies to date

- Abnormal Transmedullary Veins
 - 3/22 patients – mTBI
 - 11/62 patients – mTBI
- Microvascular damage and particularly medullary vein and pial vein damage may take place in roughly 15% of mTBI cases
- These findings could help understand why some mTBI cases continue to have long term problems and at least represents direct evidence that there was brain damage

To Treat or not to Treat?

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© Mary Ann Liebert, Inc.
DOI: 10.1089/neu.2012.2584

Review

Safety and Efficacy of Early Pharmacological Thromboprophylaxis in Traumatic Brain Injury: Systematic Review and Meta-Analysis

Aimun A.B. Jamjoom¹ and Abdulhakim B. Jamjoom²

- Patients with traumatic brain injury (TBI) are at an increased risk of developing venous thromboembolic events (VTE).
- Pharmacological thromboprophylaxis (PTP) is routinely delayed because of concerns of exacerbating intracranial hemorrhage (ICH).
- Based on the available literature, we can tentatively conclude that early PTP (< 72 h) reduces the risk of VTE without affecting progression of ICH.
- However, much work is yet to be done to better clarify ICH subtypes at risk of progression and the implementation of evidence-based guidelines backed up with randomized control trial level evidence.

Conclusions

Venous flow abnormalities are an important aspect of neurodegenerative disease.

SWI and SWIM are important methods for assessing venous abnormalities and microbleeds.

Perfusion should be part and parcel of studying neurodegenerative disease including TBI.

These observations call for more studies in this direction and could lead to improved treatment for patients with venous thrombosis.