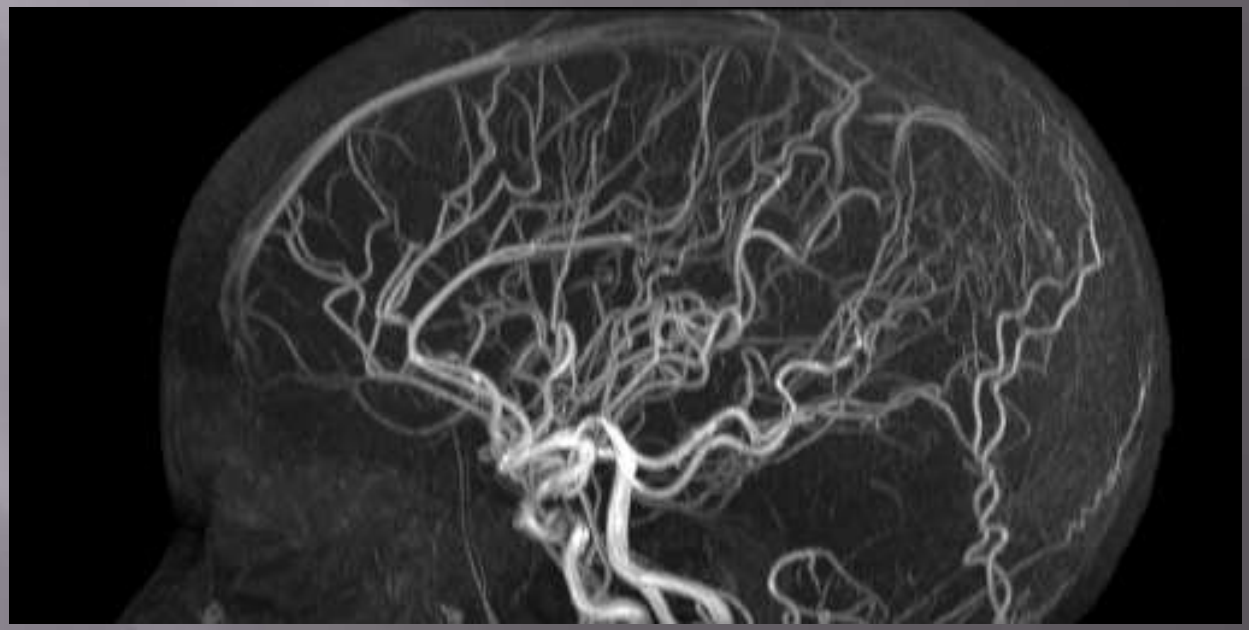
THE ROLE OF SWI IN NEURODEGENERATIVE DISEASE: FROM PERINATAL TO AGING APPLICATIONS



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Detroit, Michigan

Acknowledgements

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- David Utriainen, for image analysis
- Meng Li, MS, for perfusion TSM data
- Jaladhar Neelavalli, PhD for SWIM support
- Zhifeng Kou, PhD for TBI data

Informational Websites

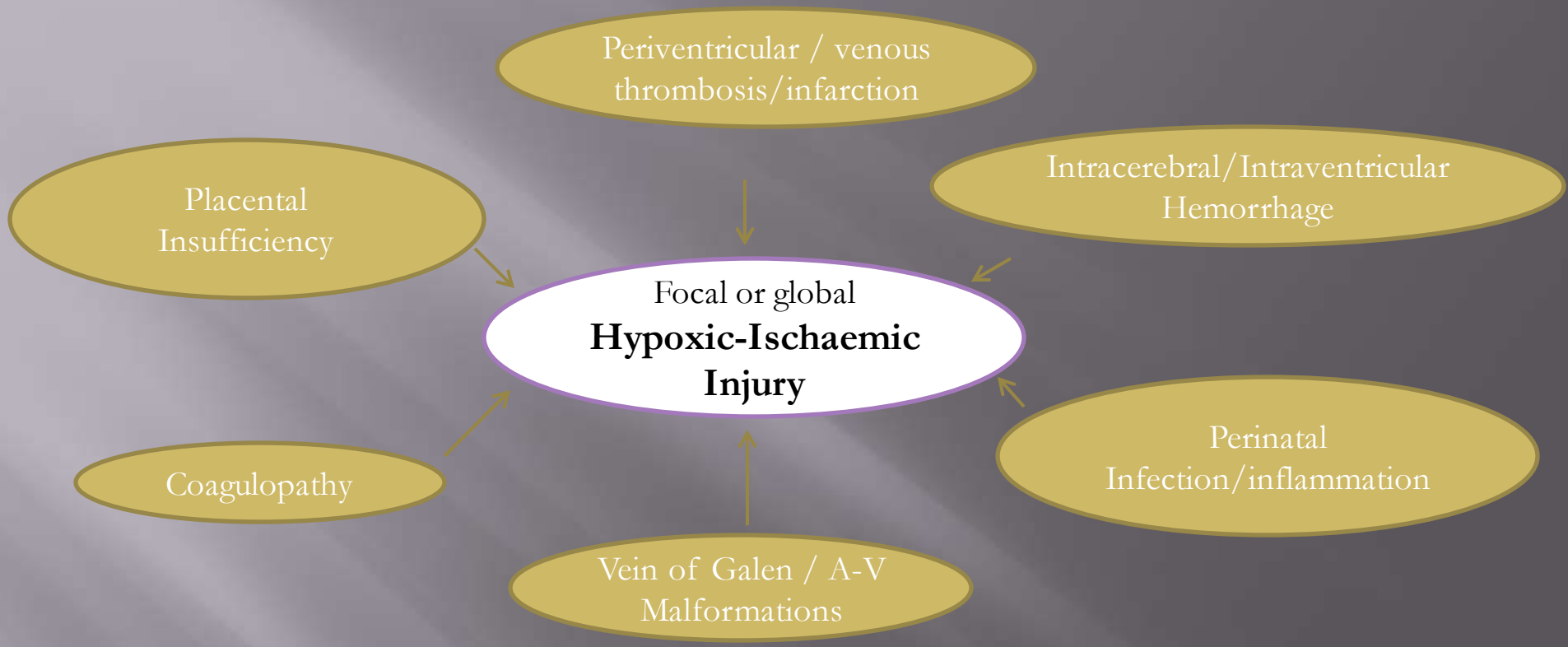
- Clinical applications of SWI and SWIM
- See www.swim-mri.com

- The role of abnormal venous flow in neurodegenerative diseases: MS as an example
- See www.ms-mri.com
- Our work in Detroit at Wayne State University
- See www.mrc.wayne.edu

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

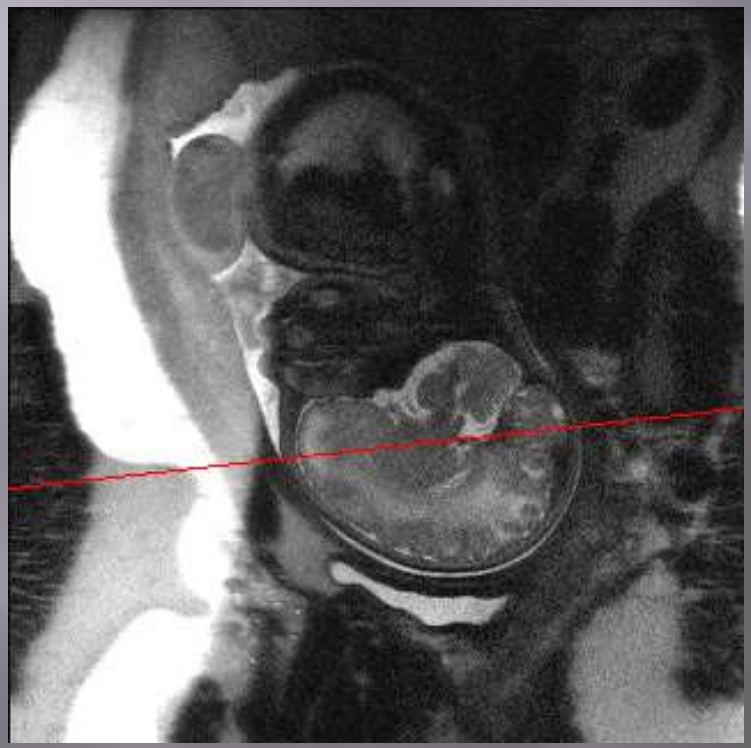
Haacke EM et al. Susceptibility weighted imaging. Magnetic Resonance in Medicine, 52: 612; 2004.

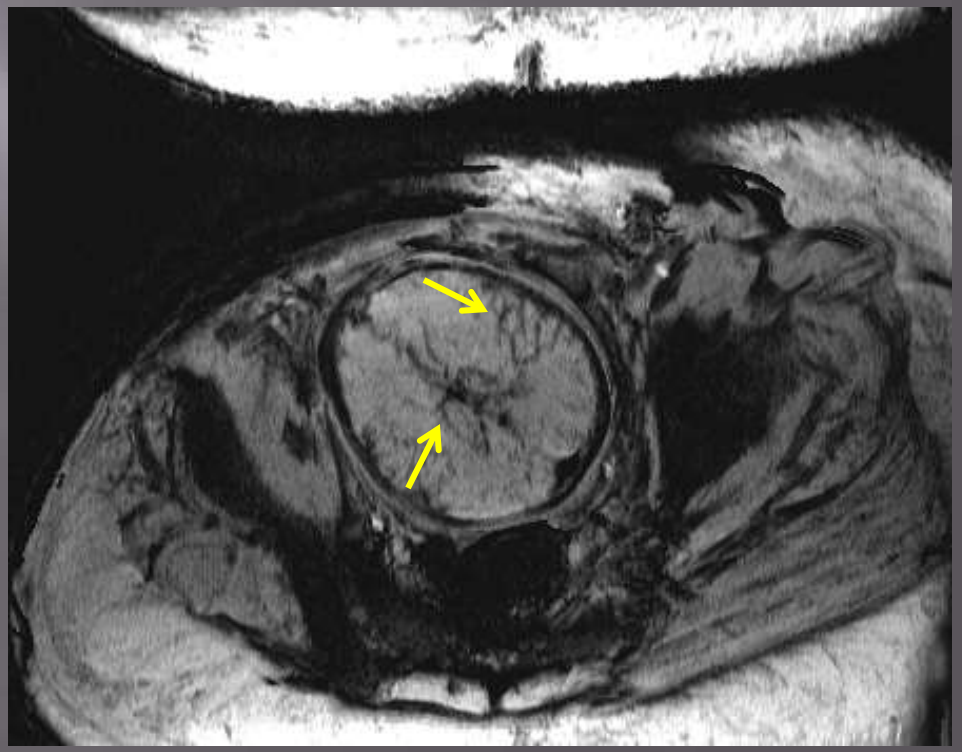


Fetal brain injury, due to Hypoxic-Ischaemic (HII) or hemorrhagic events, may be associated with debilitating neurological sequelae post partum. Early detection and possible quantification of HII in-utero may help predict outcome

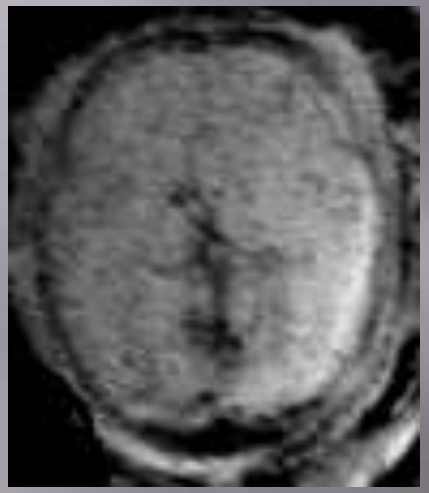
Volpe, J.J., 2009. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. Lancet Neurol. 8, 110–124.

PRESENTING THE FIRST VISUALIZATION OF THE FETAL VENOUS ANATOMY OF THE BRAIN USING SWI



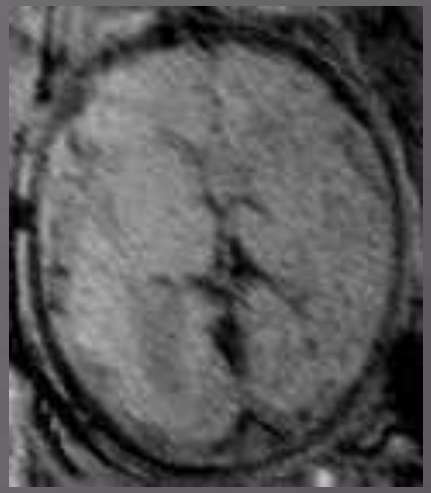


Pilot scan on the left, effective transverse SWI on the right: 37 weeks 1 day



GA – 24 5/7

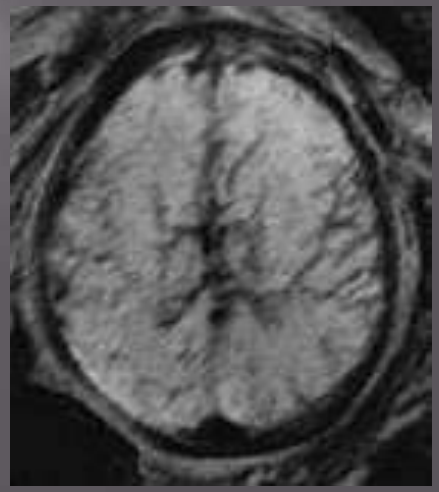
GA – 28 2/7



GA – 31 4/7

Development of the Venous System as a Function of Gestational Age

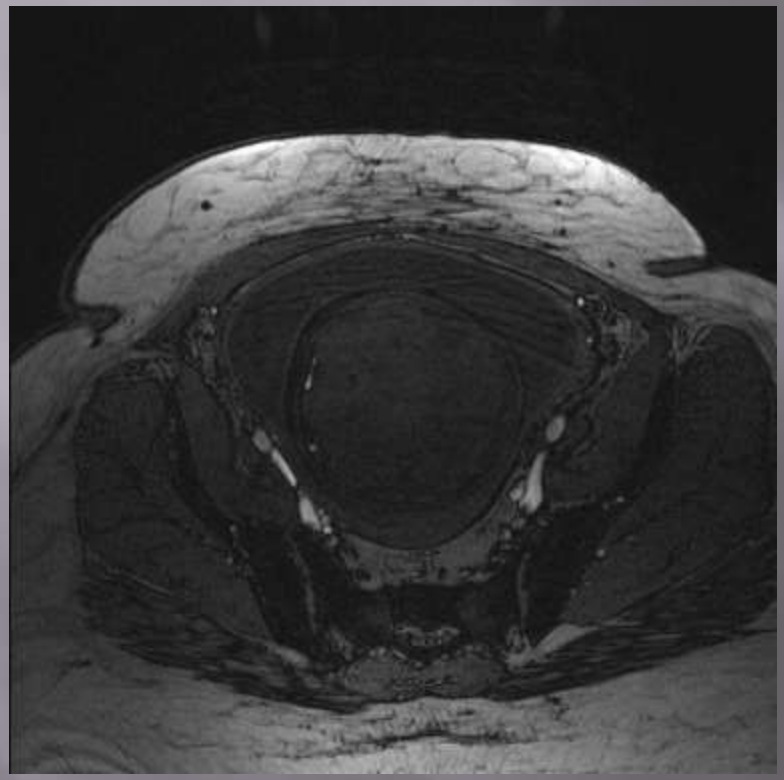
GA – 34 4/7



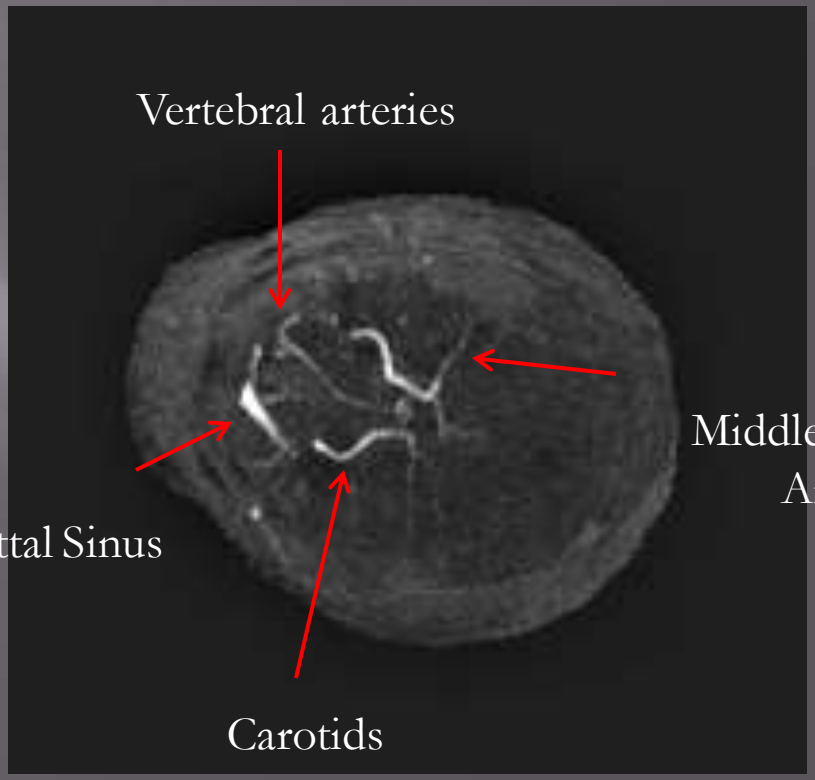
GA – 37 1/7

MRA – 3D - Time of Flight Angiography

Resolution – 0.8 x 0.8 x 1.6 mm^3



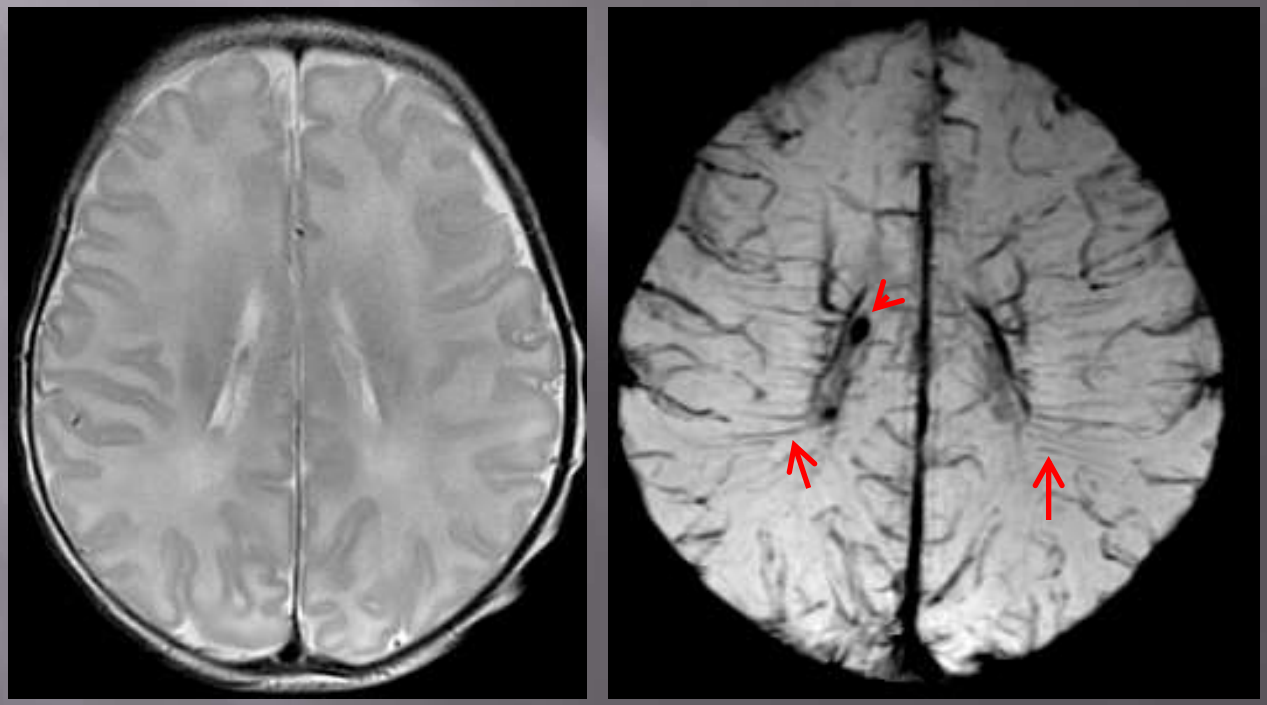
Animation of the original time of flight MRA data



Maximum Intensity Projection Image

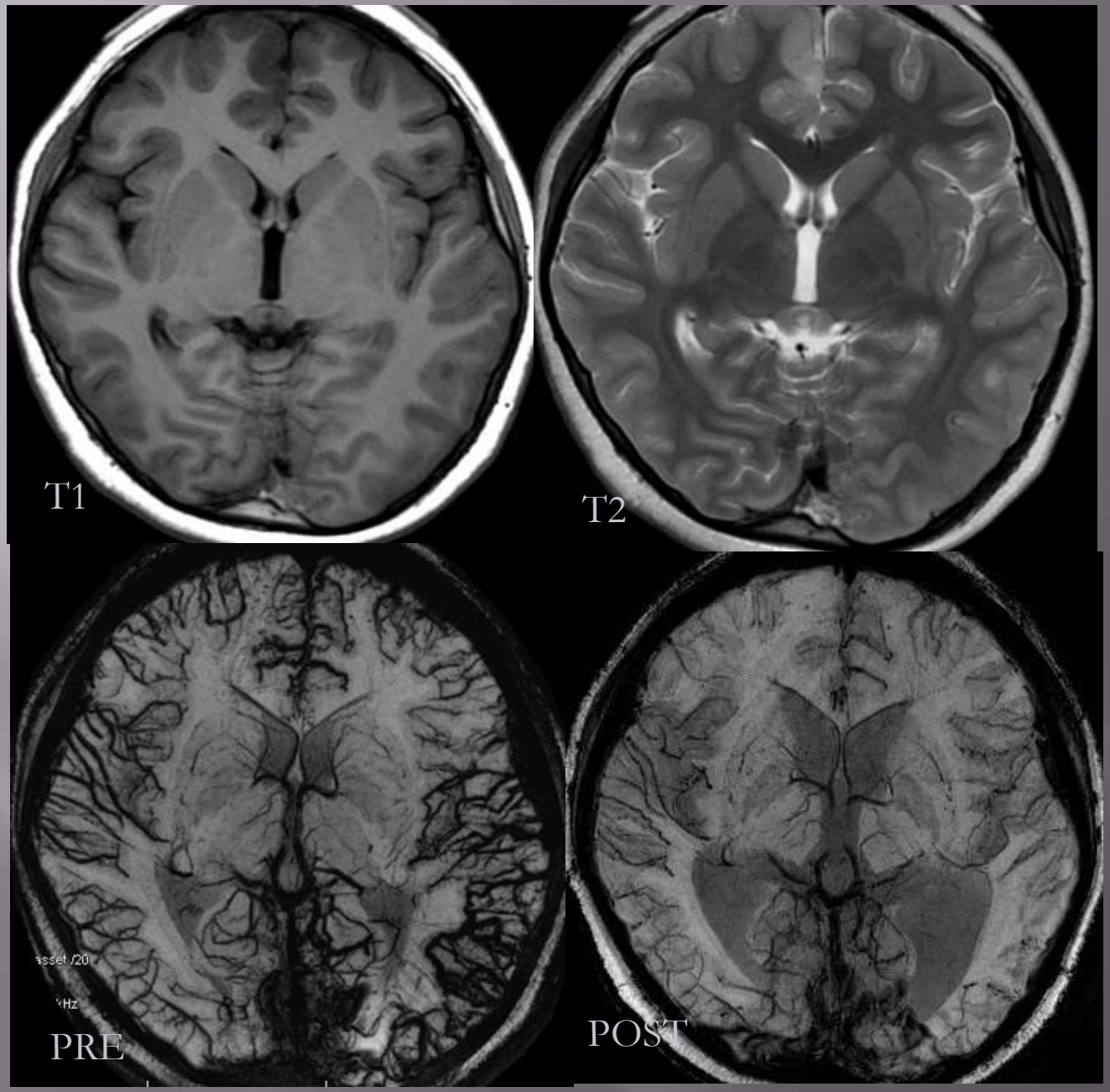
SWI- Venography in Pediatric Population

2 day old infant



T2 SWI

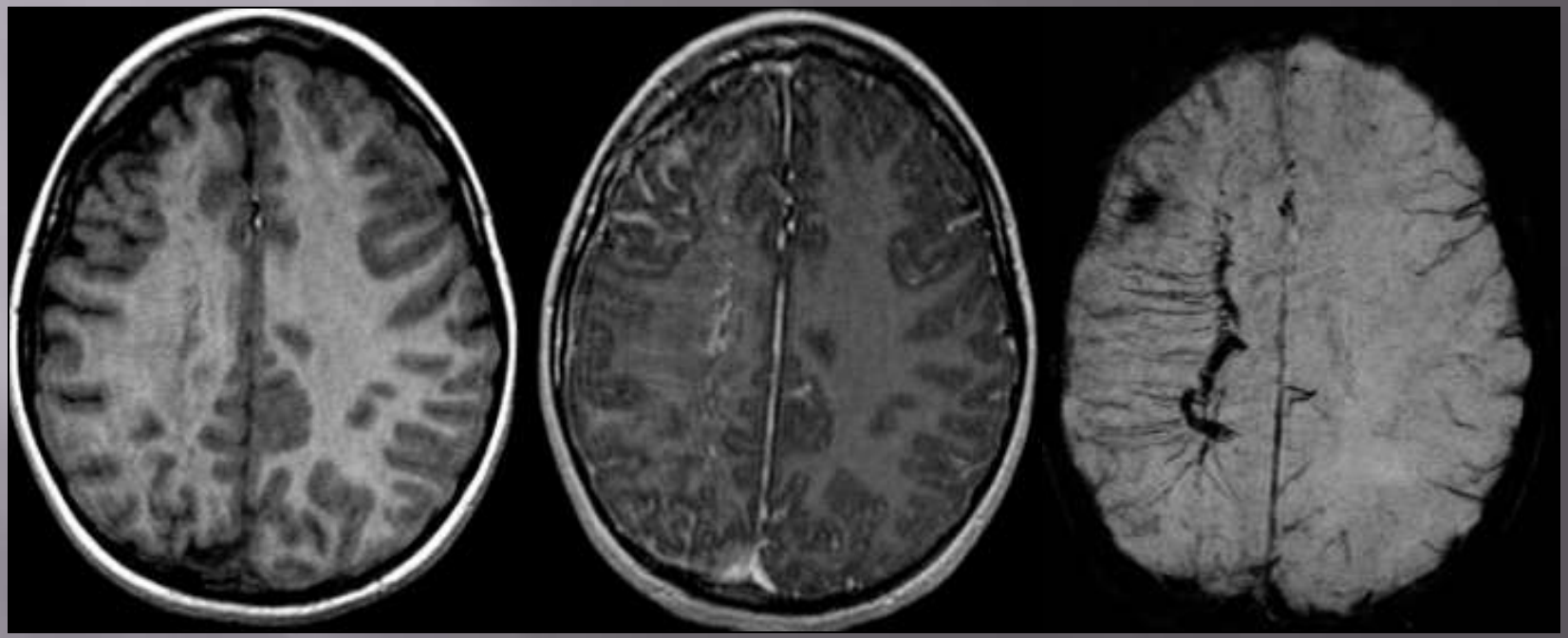
Neonatal encephalopathy



Venous Thrombosis: before treatment and after thrombolysis

Guangbin Wang M.D.
Shandong Medical Imaging Research Institute

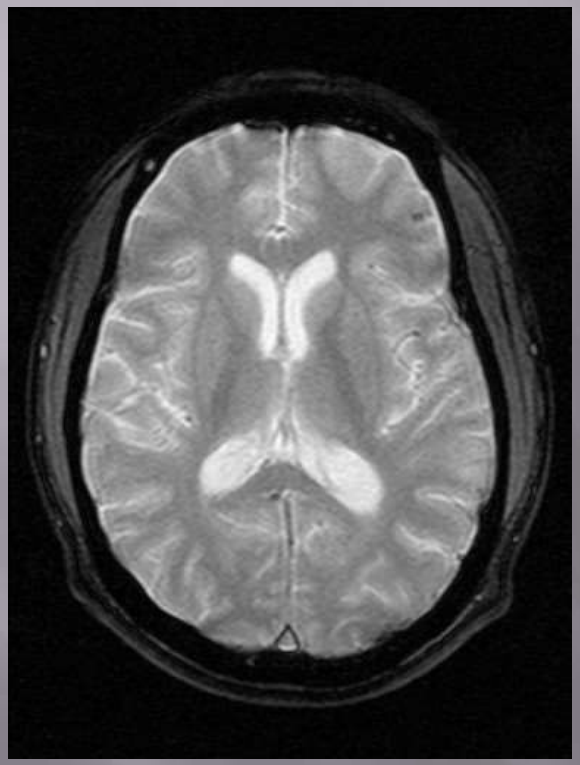
Sturge Weber Syndrome

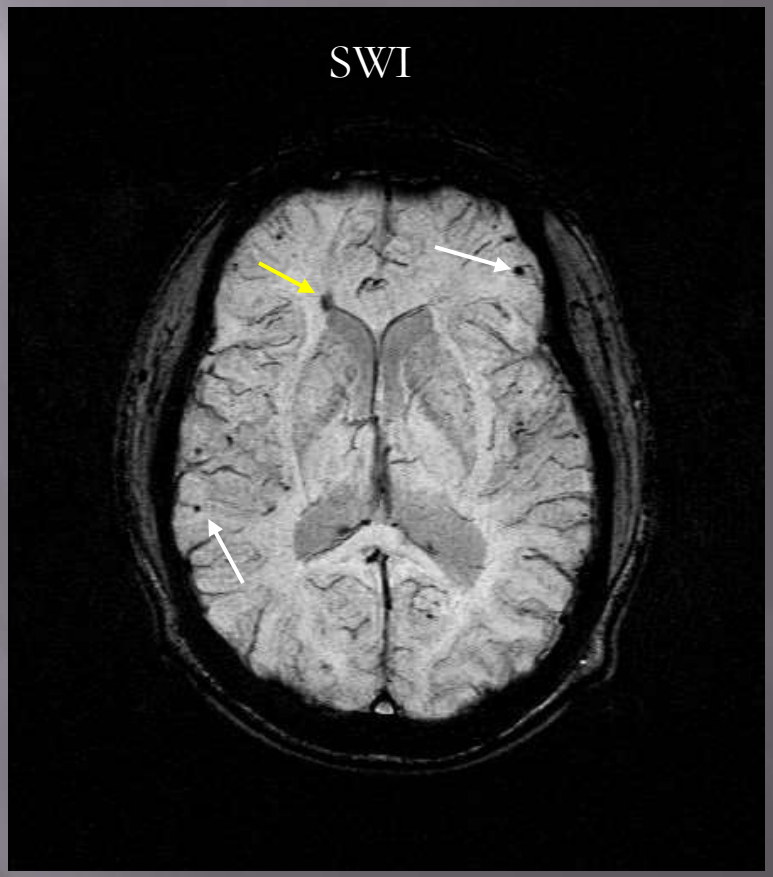


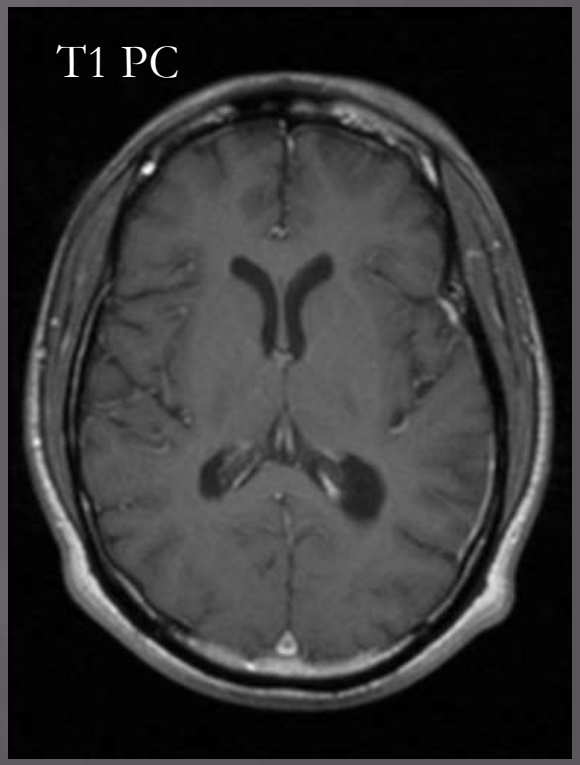
3D-T1 Post Gd 3D T1 SWI (no contrast agent)

Czabo Juhasz, Yang Xuan and Dr. E. Haacke, Wayne State University

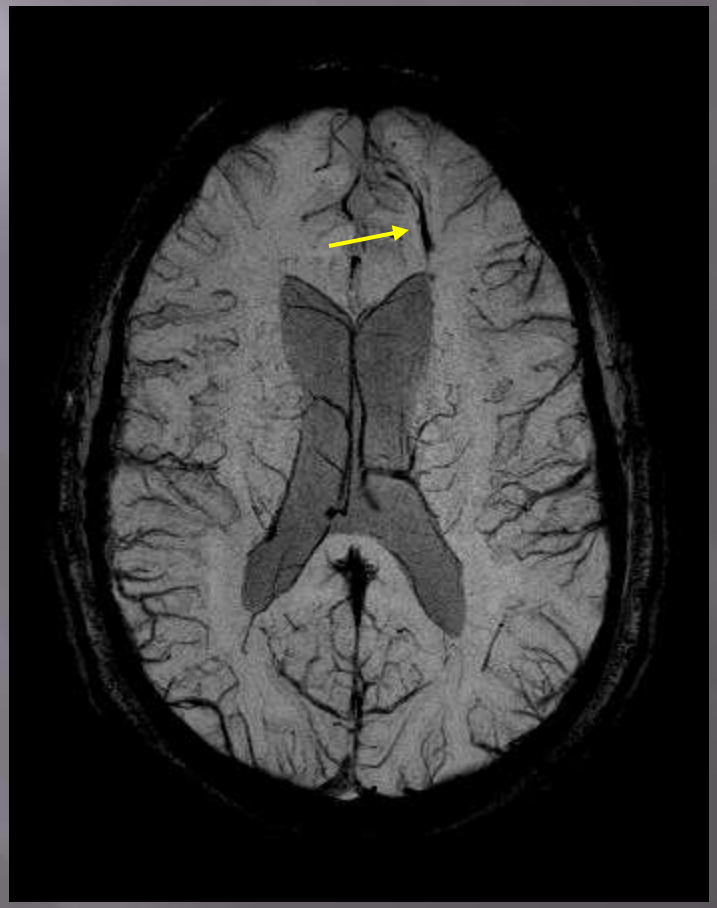
Motorcycle trauma: medullary vein involvement





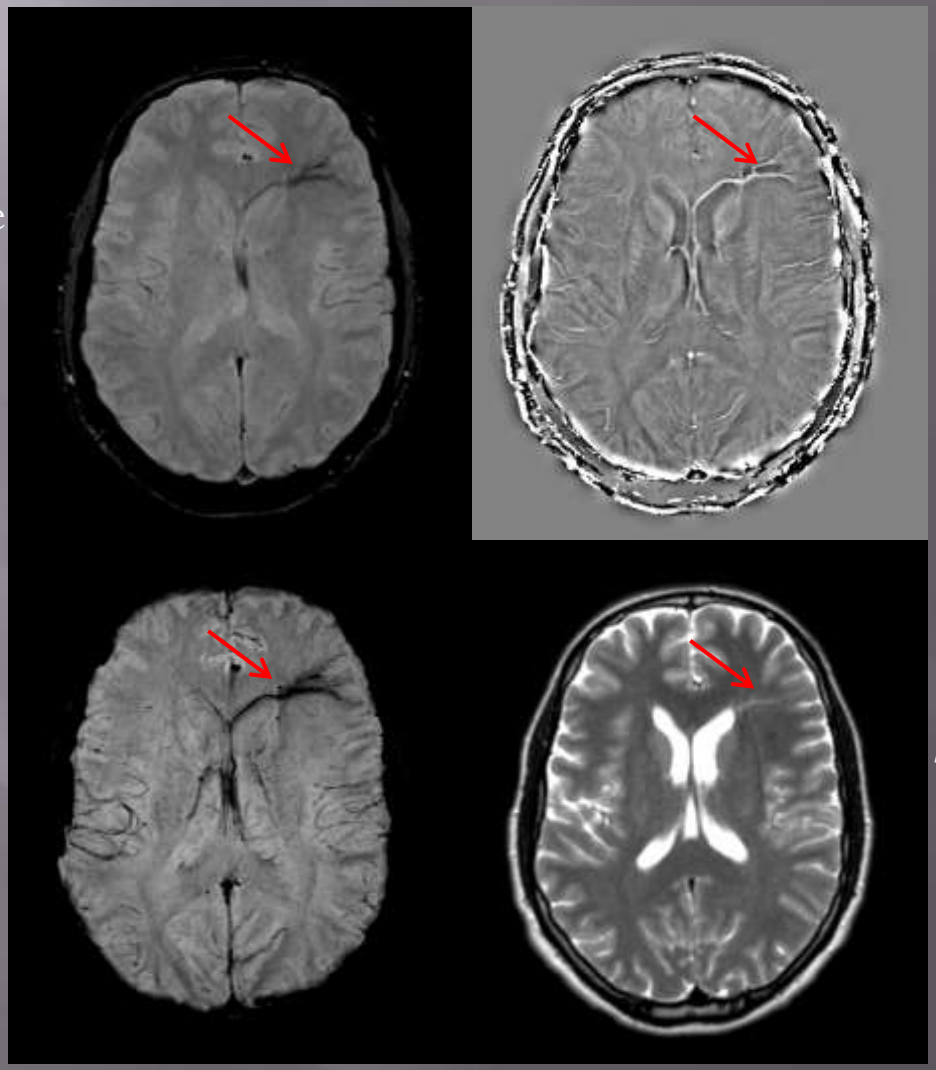


Major venous and medullary vein involvement



SWI reveals MVD

SWI-Magnitude

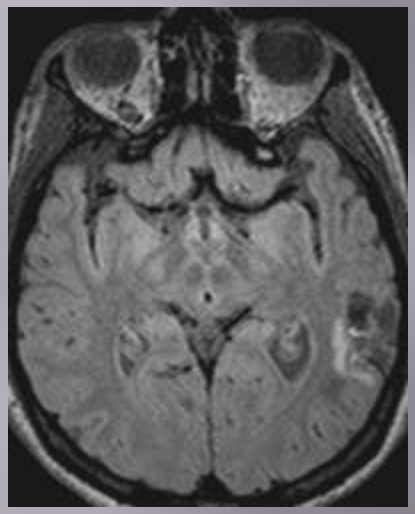


SWI-Phase

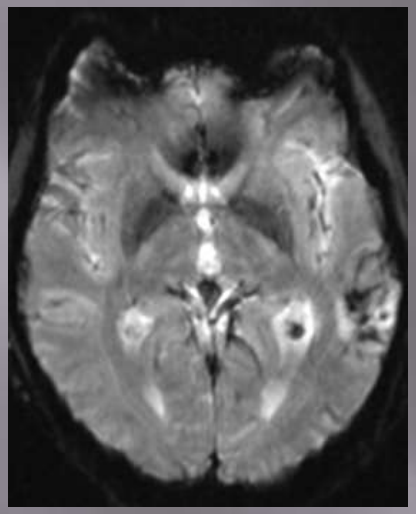
SWI-mIP

T2

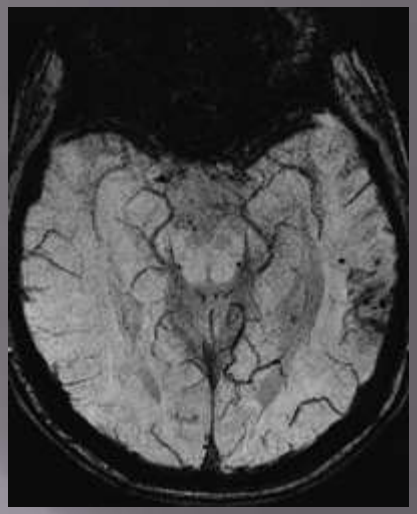
Stroke case for a young woman in her mid 30s



FLAIR

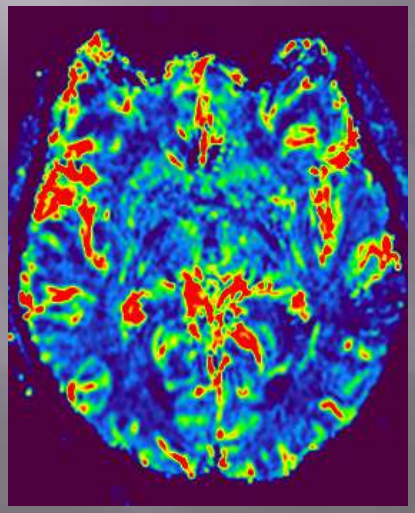


PWI (1st)

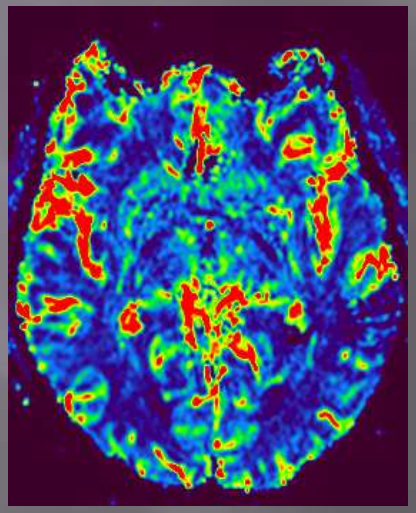


SWI mIP

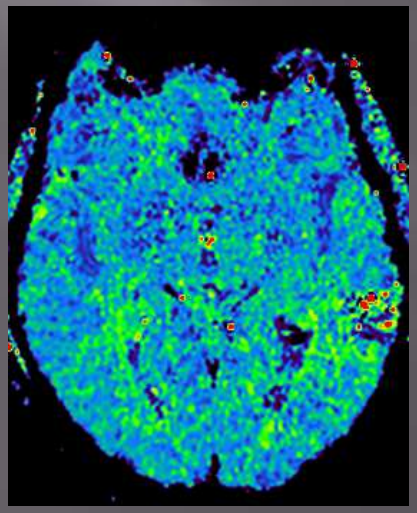
MRA



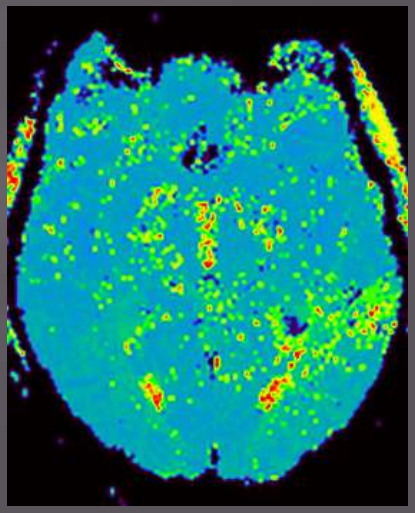
CBV



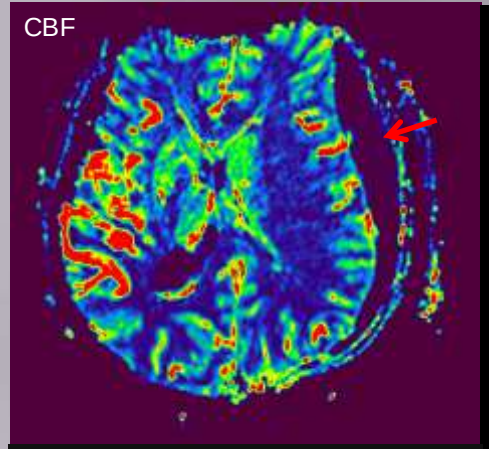
CBF

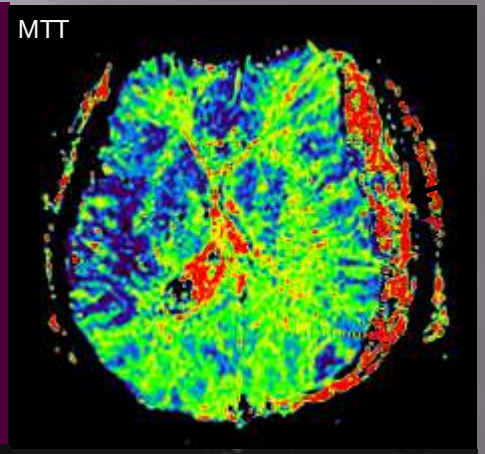


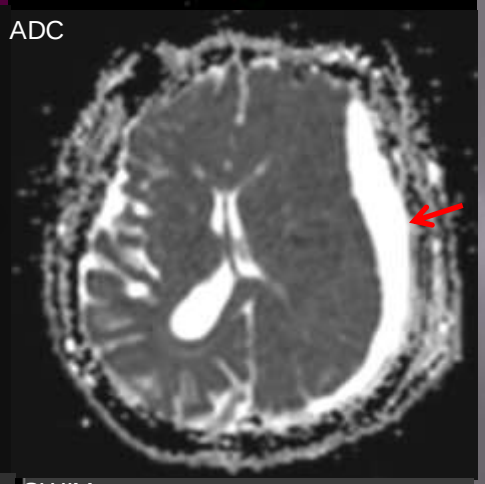
MTT

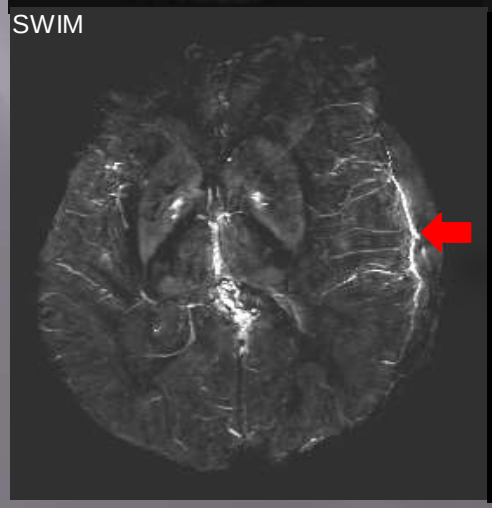


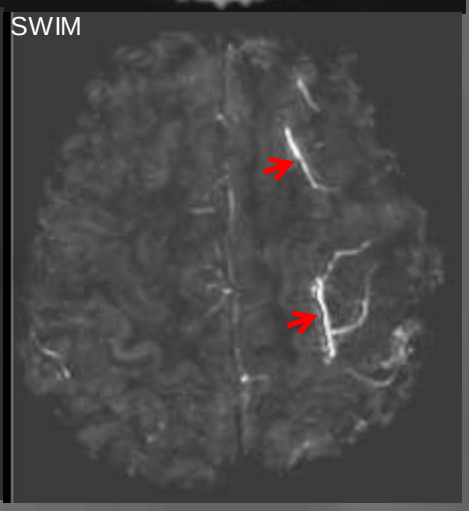
TTP









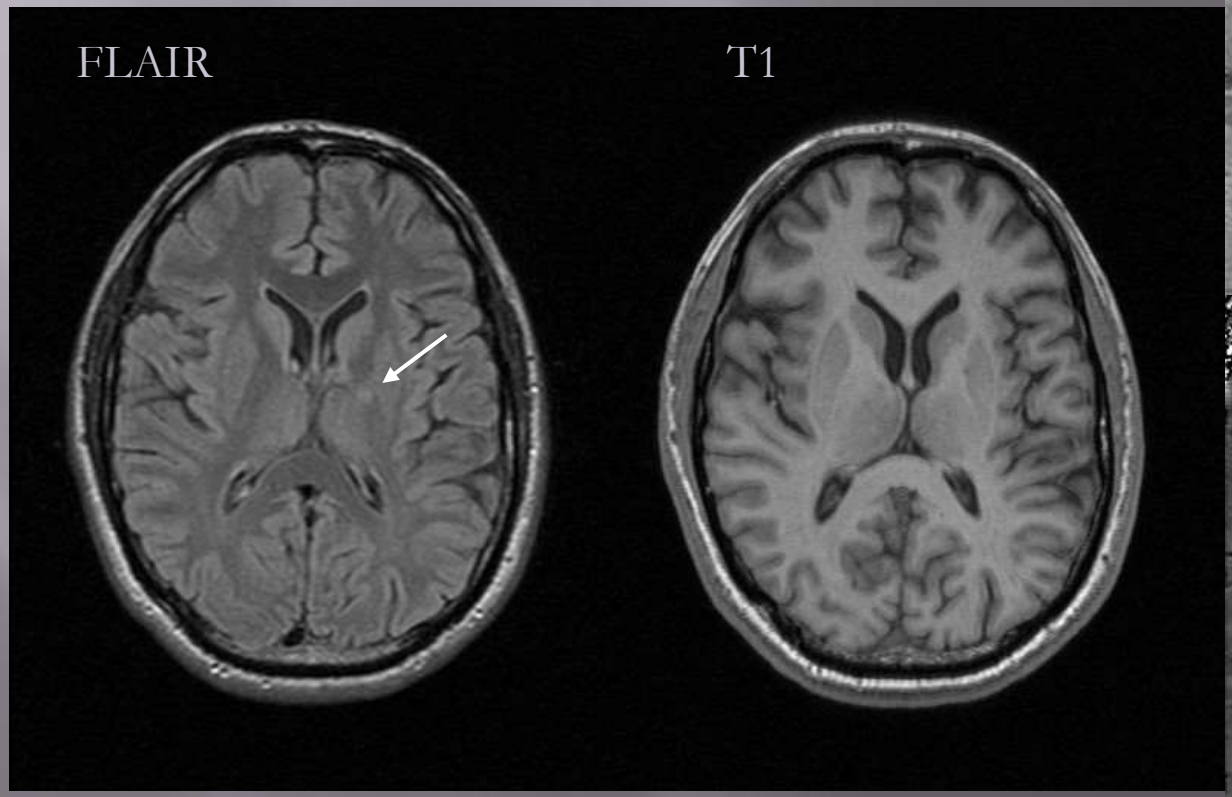


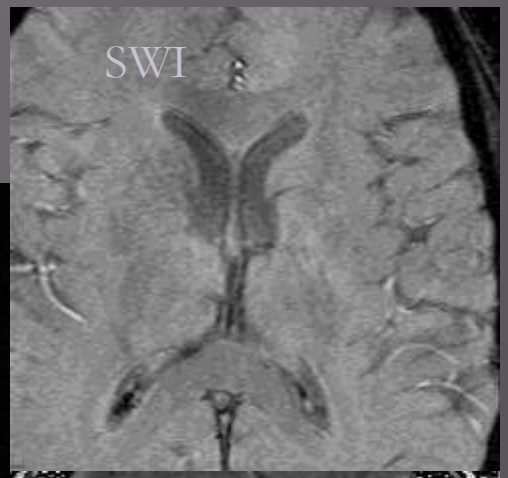
TBI

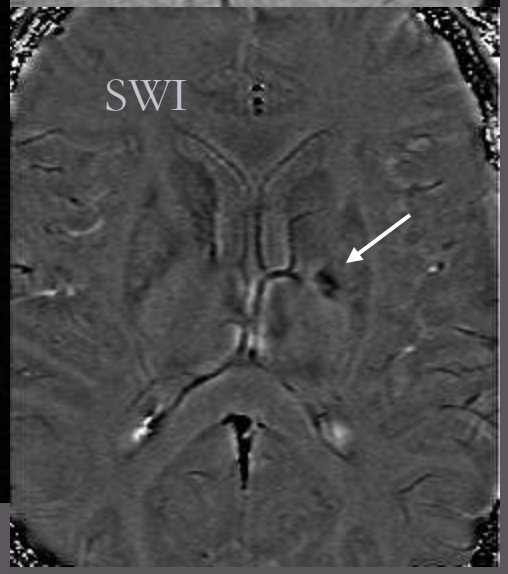
A 64 year old male suffered severe TBI after motor vehicle accident.

An MRI scan was performed 36 days after injury.

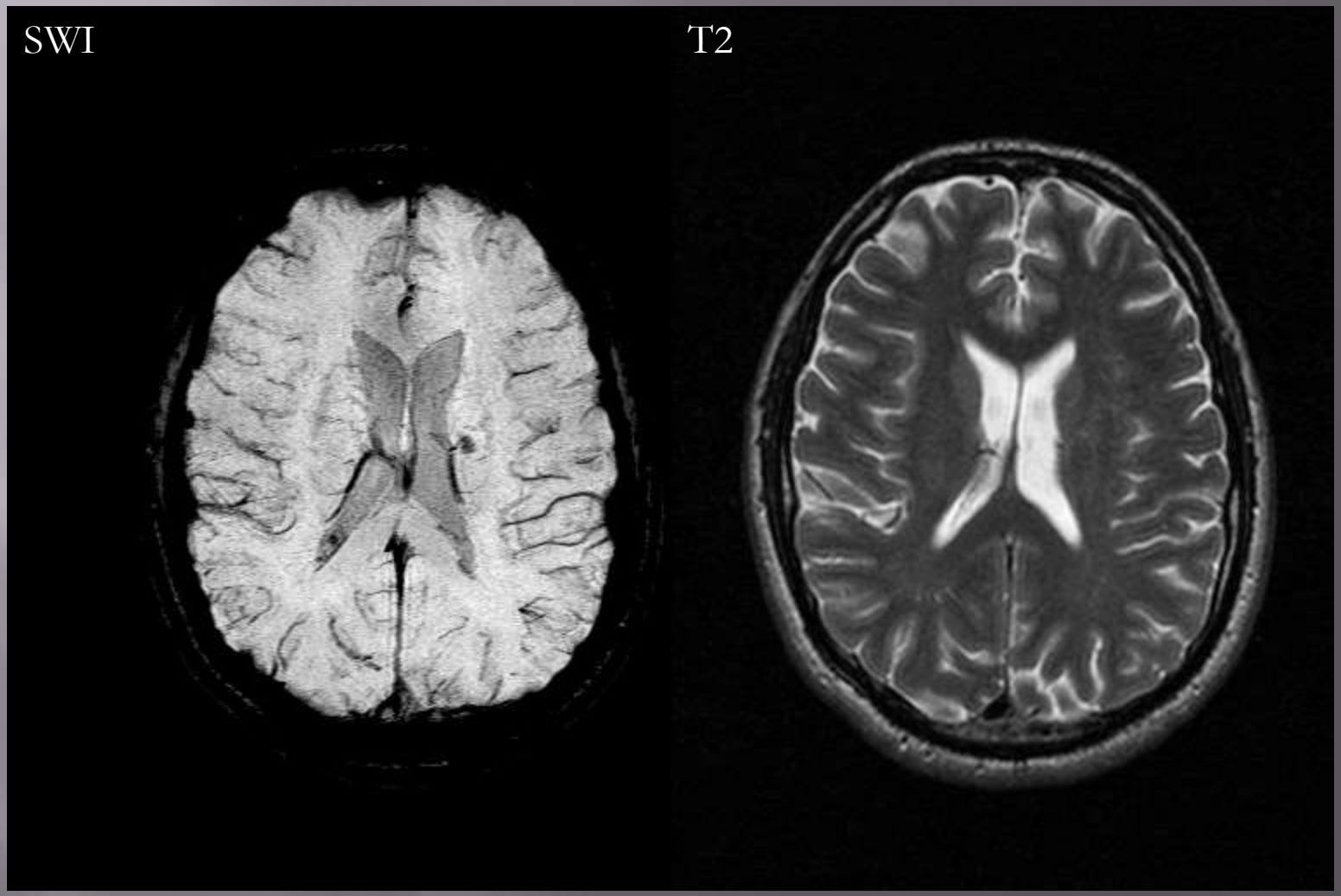
Low concentration iron is still seen on 7 slices with SWI and barely discernable on FLAIR!







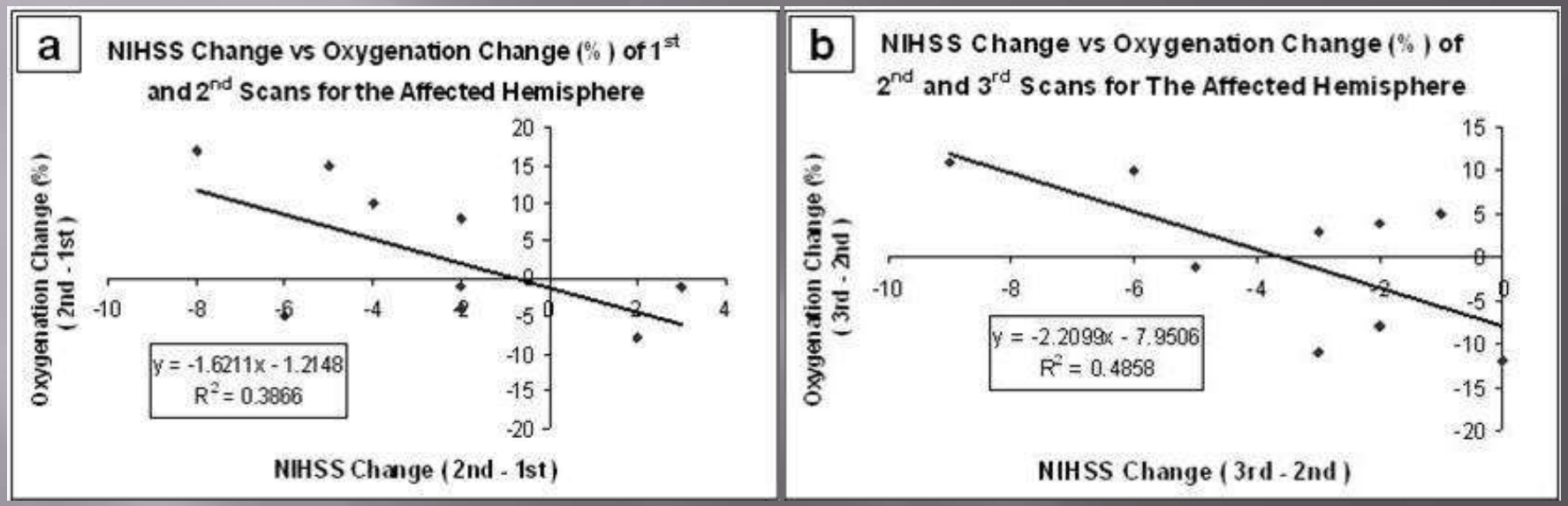
Stroke with almost imperceptible bleeding



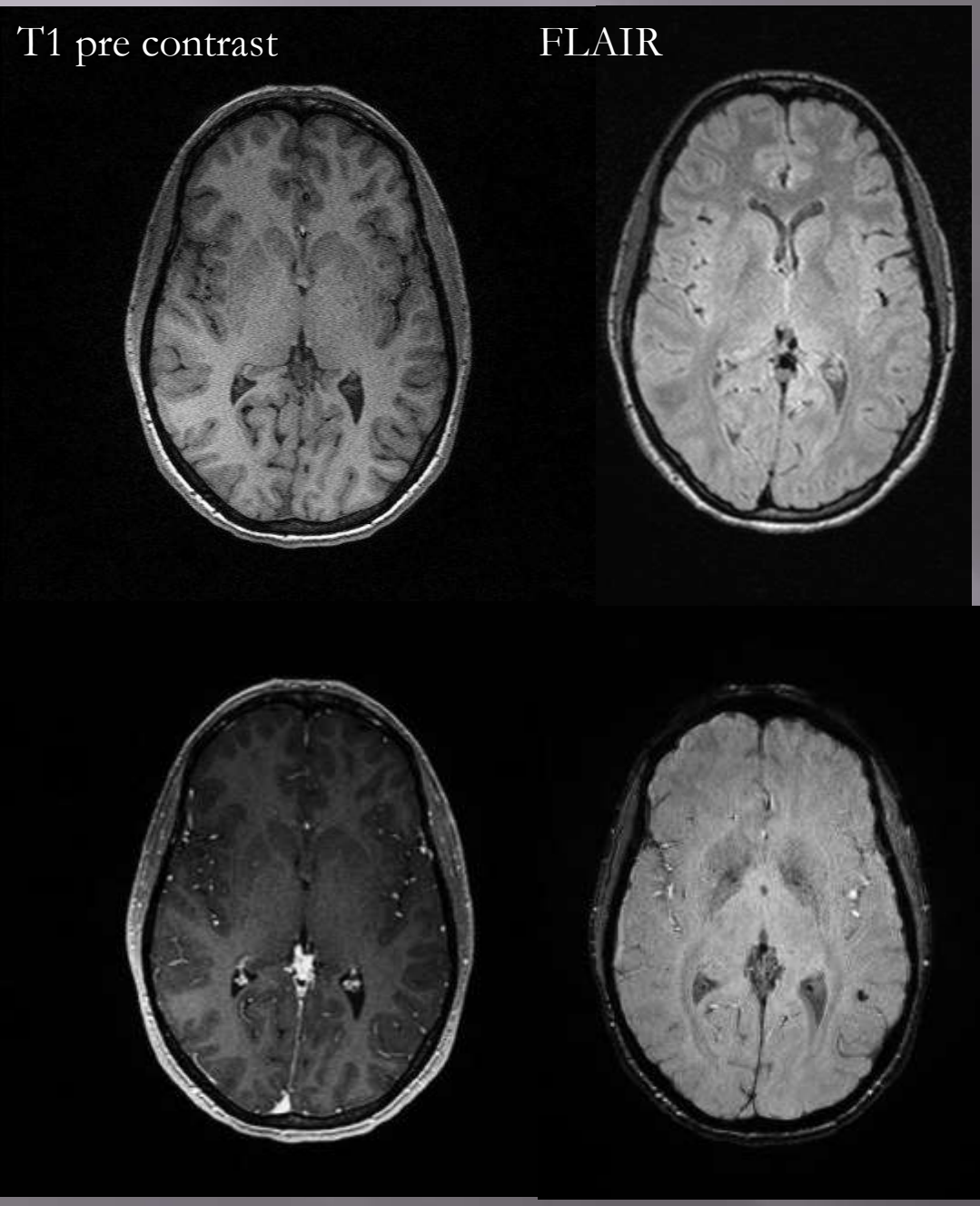
SWI shows the bleed

short TE GRE T1

Oxygen saturation as a biomarker in stroke recovery

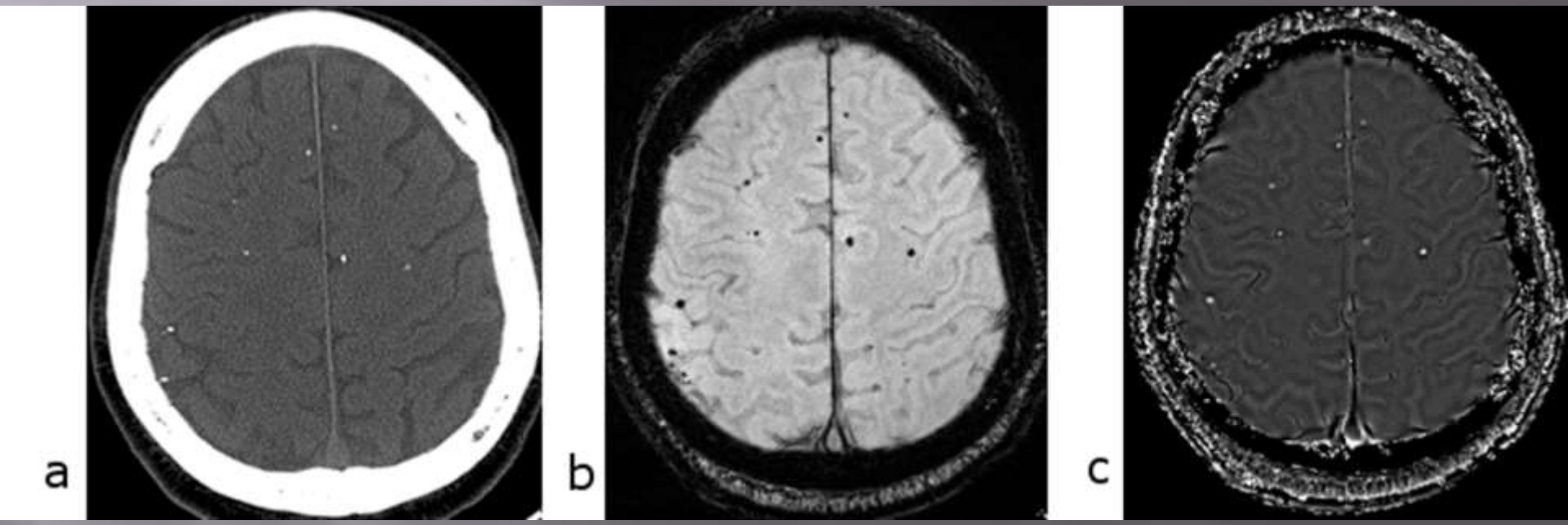


a) Correlation between the NIH stroke scale and change in oxygen saturation from the first day to week two. Increases in oxygen saturation bode well for the patients. b) Correlation between the NIH stroke scale and change in oxygen saturation from week two to week six. Increases in oxygen saturation still bode well for the patients but not as dramatically as in the first two time points.

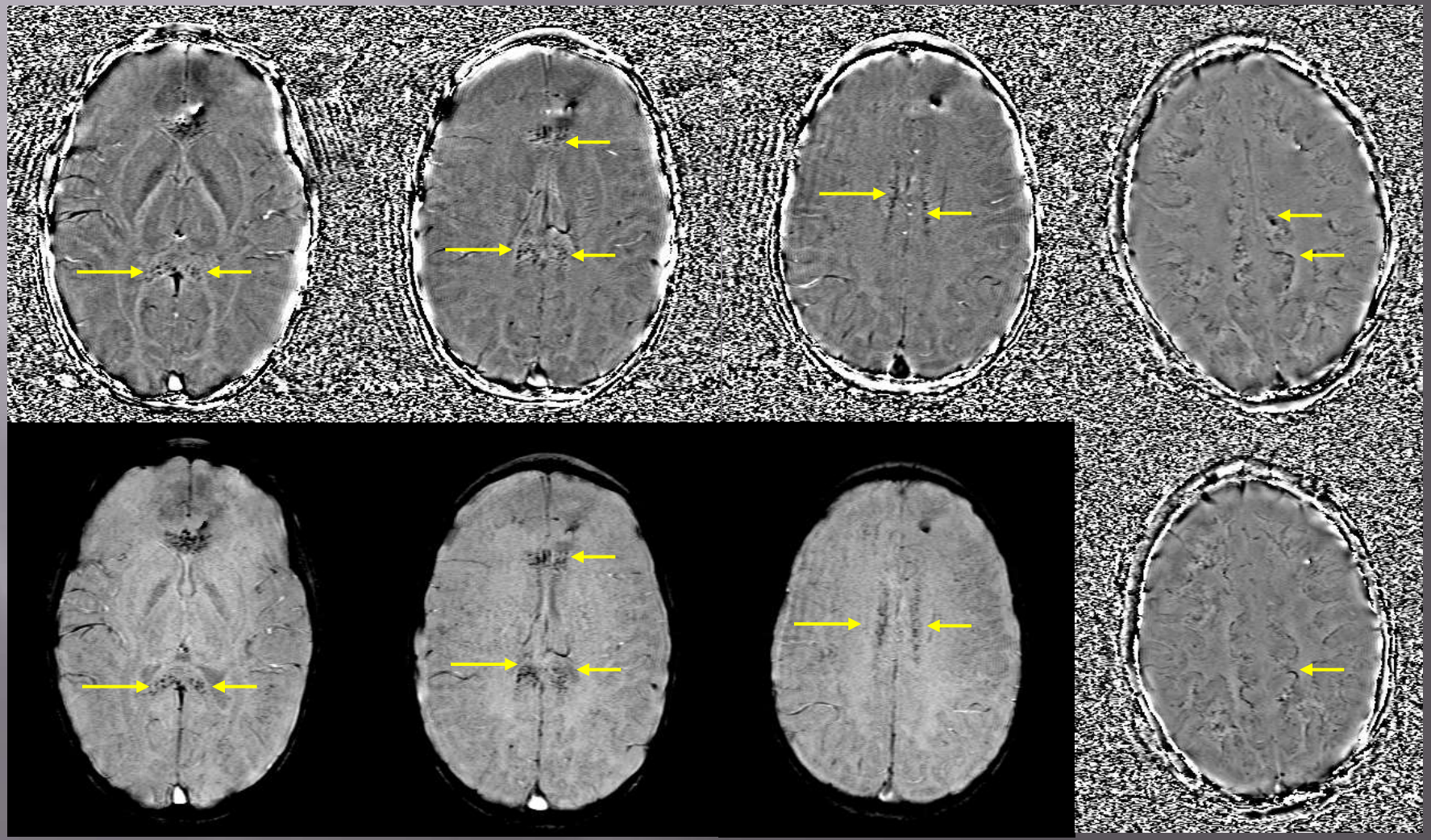


SEIZURE CASE

Cysticircosis



DN001 – 6yr old M left and 8 yr old F right
Note the iron deposition throughout the corpus callosum on the left 3 panels and the iron deposition throughout the GM near the WM boundaries.



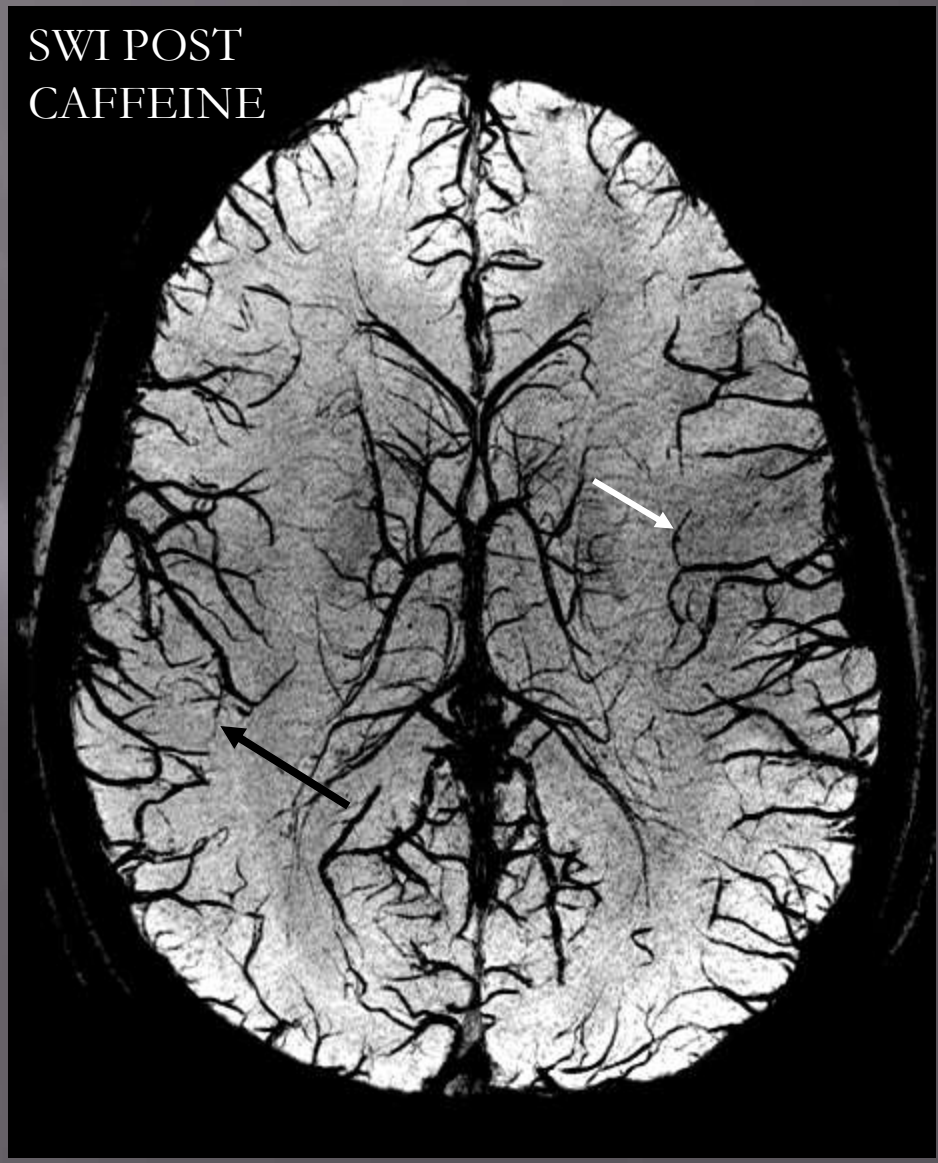
Using caffeine decreases blood flow to the brain

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

SWI as a high resolution BOLD imaging method



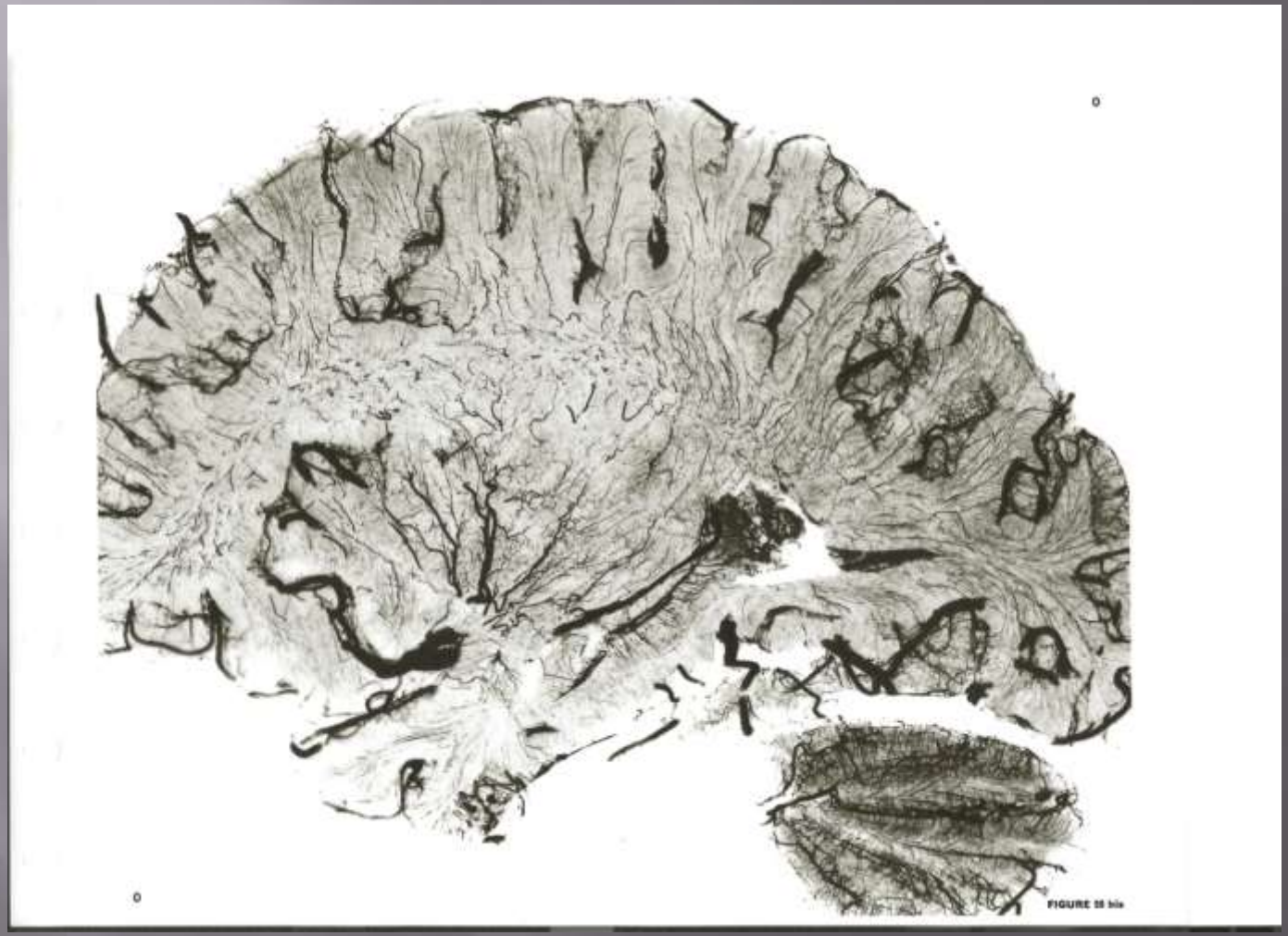
MinIP of caffeine/Gd over 28 slices with 4 phase multiplications

High resolution MR angiography

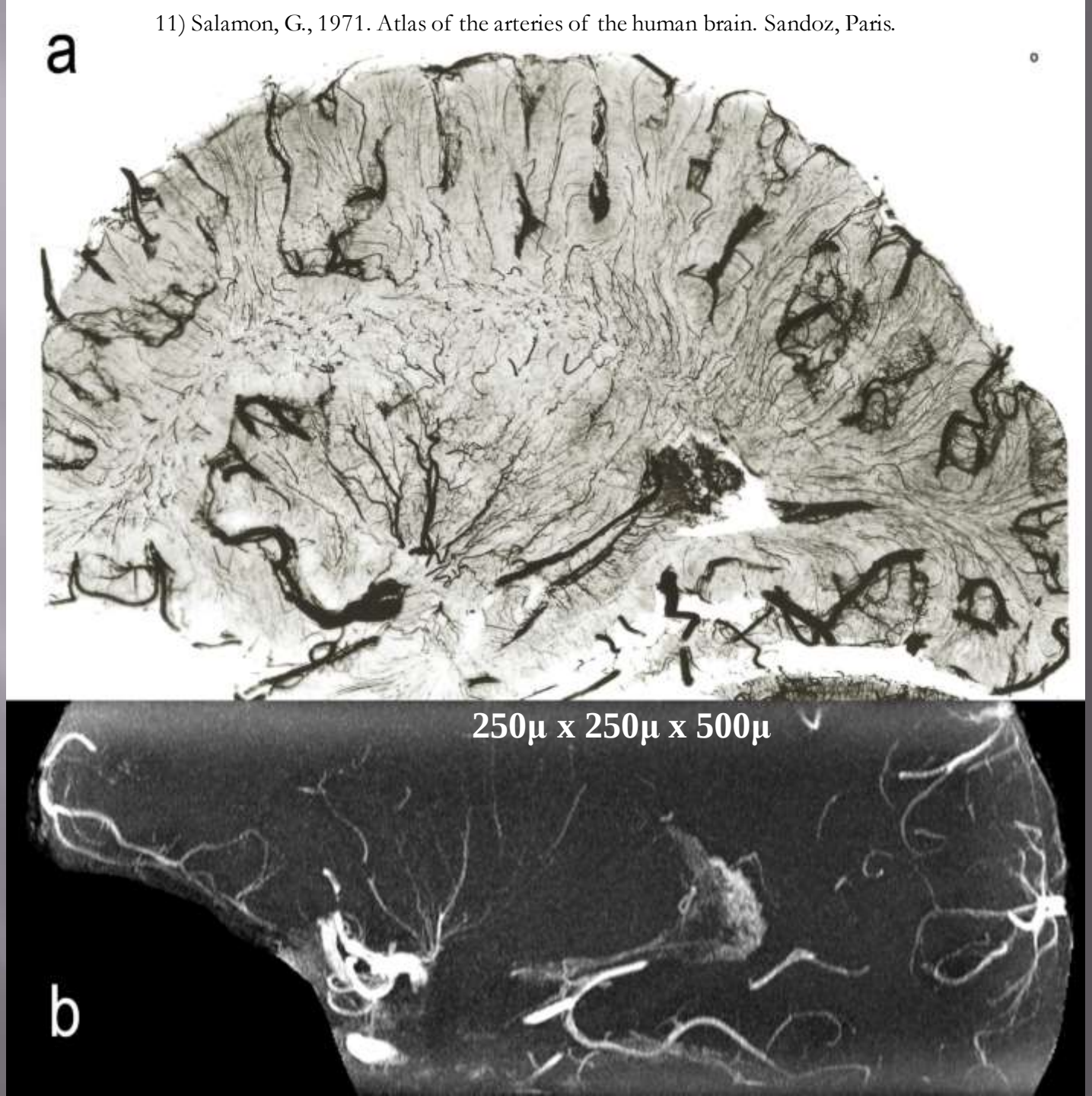
Small arteries around 250 microns are beginning to become visible even without a contrast agent (0.5mm isotropic resolution).

Cadaver brain imaging of arteries using an injection technique

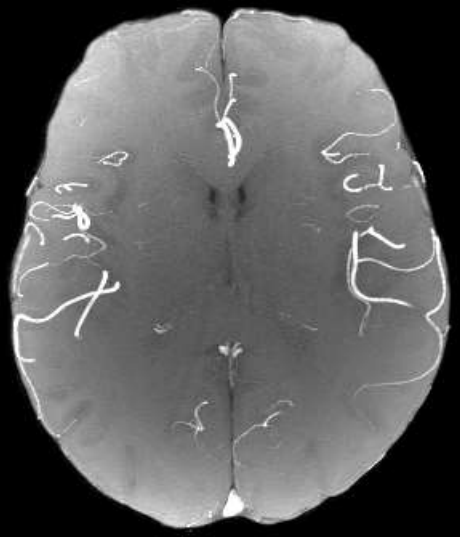
Salamon, G., 1971. Atlas of the arteries of the human brain.



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



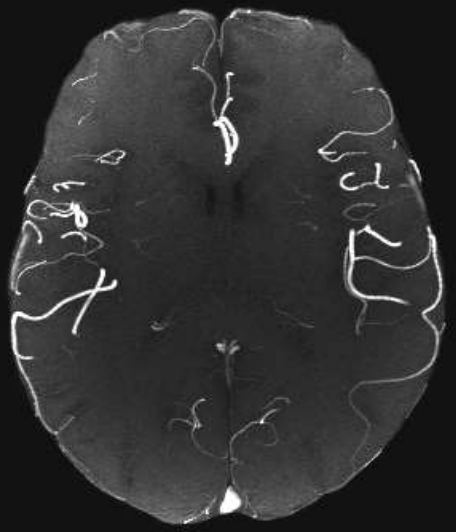
MRA short echo SWI



RP-DP MRA

SWI only veins

NLS MRA no veins

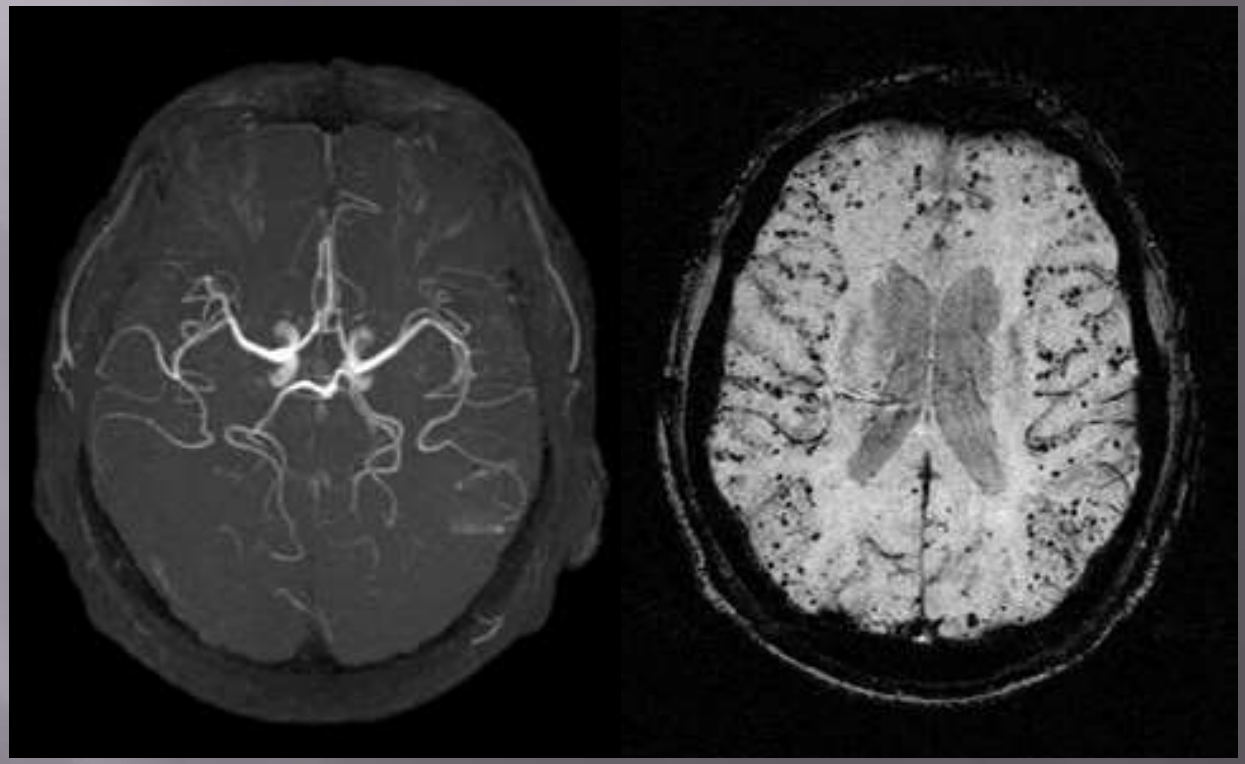


Simultaneous MRV and MRI using a double echo interleaved SWI rephased/dephased sequence

Imaging Aging

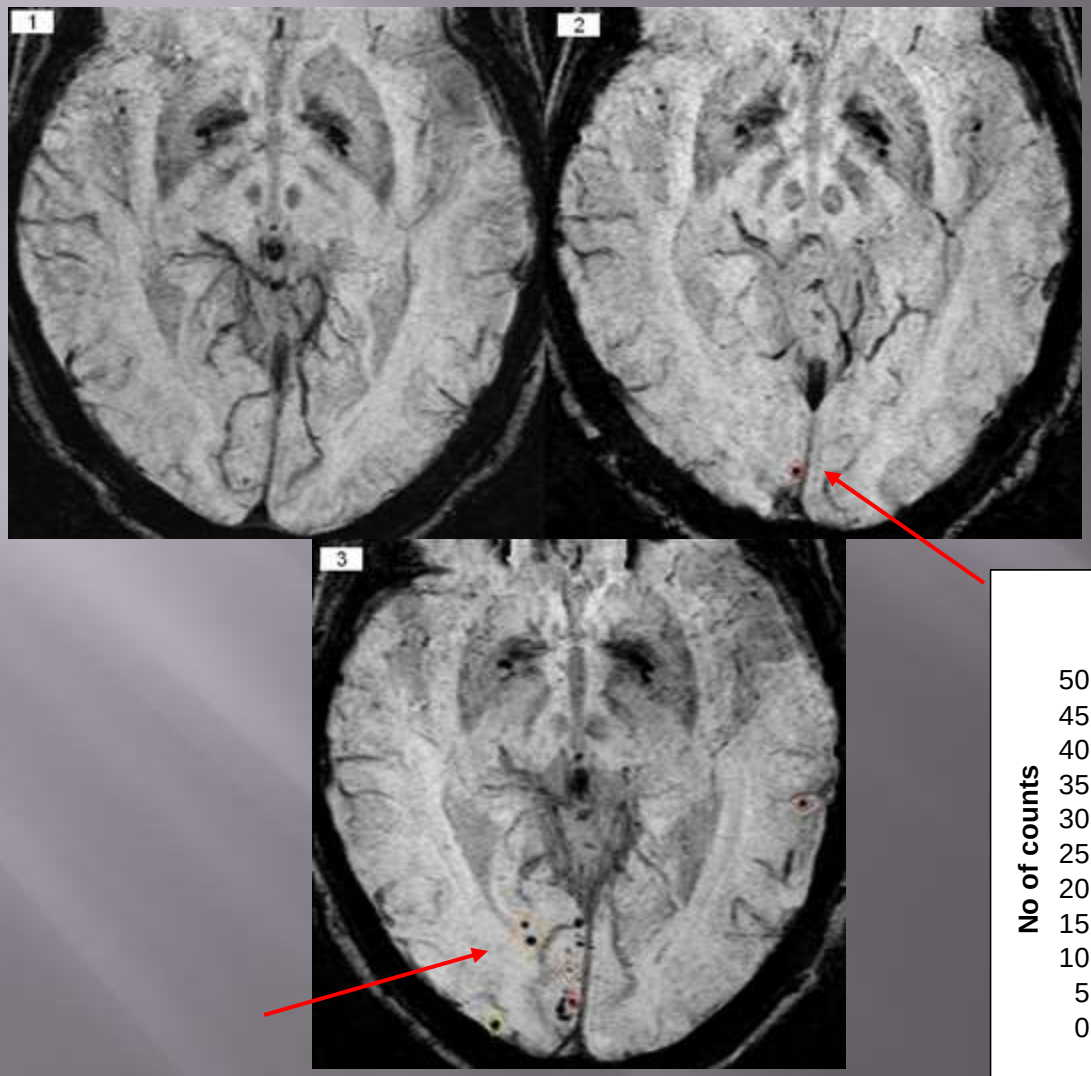
- It is now believed that up to 35% of dementia cases may be caused by vascular dementia.
- We see microhemorrhages as a means to predict who will get Alzheimer's disease.
- These may lead to "cognitive strokes".
- Hopefully this work will lead to collaborations with the pharmaceutical industry to come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

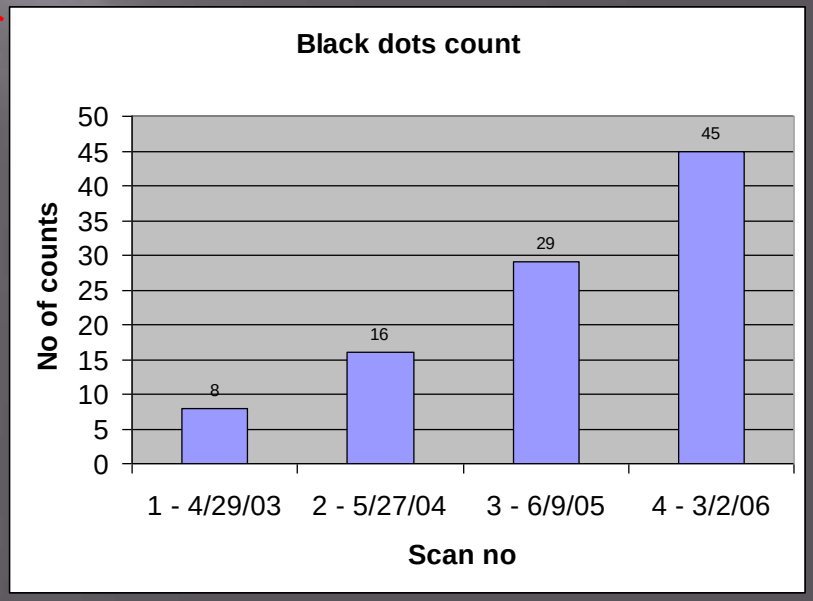
Cerebral amyloid angiopathy



50μ objects can manifest as 1mm^3 objects

time to go sailing

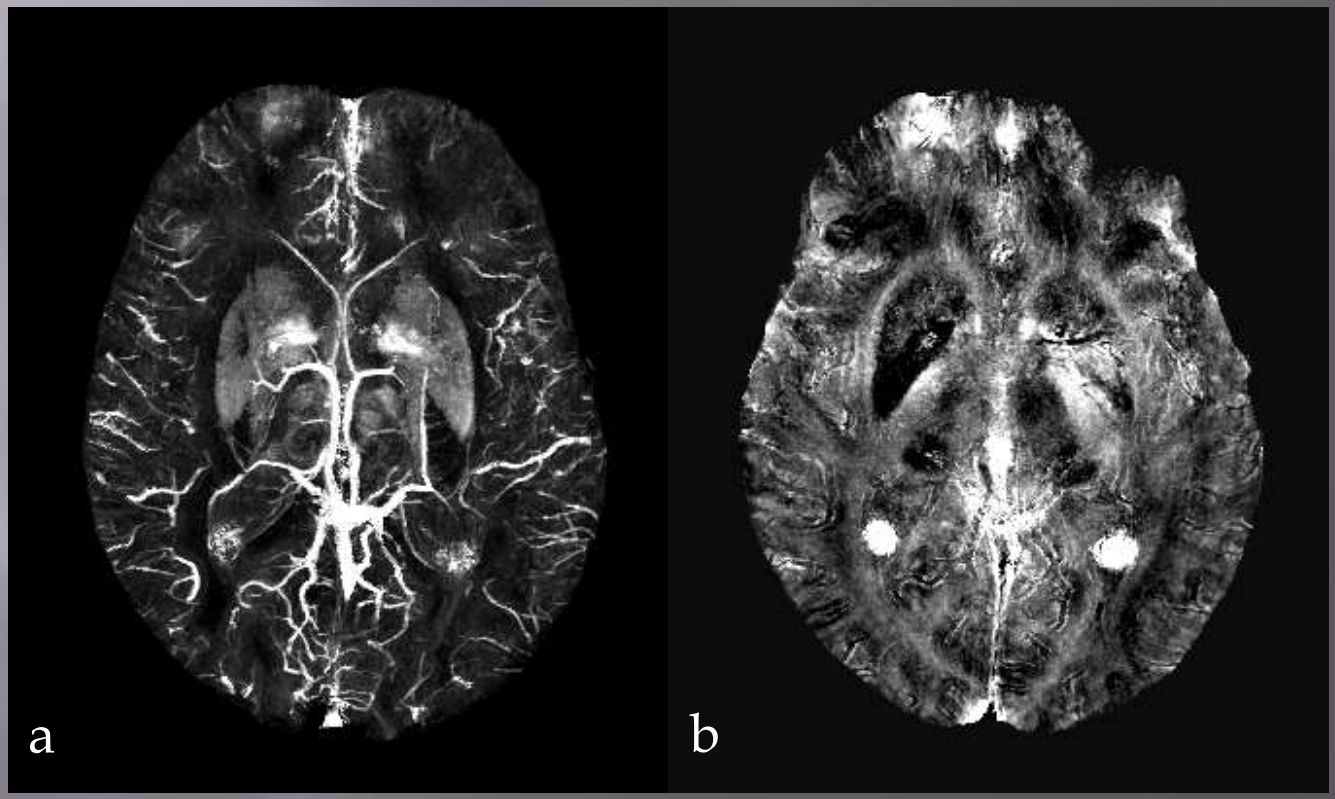




SWIM versus Iterative SWIM

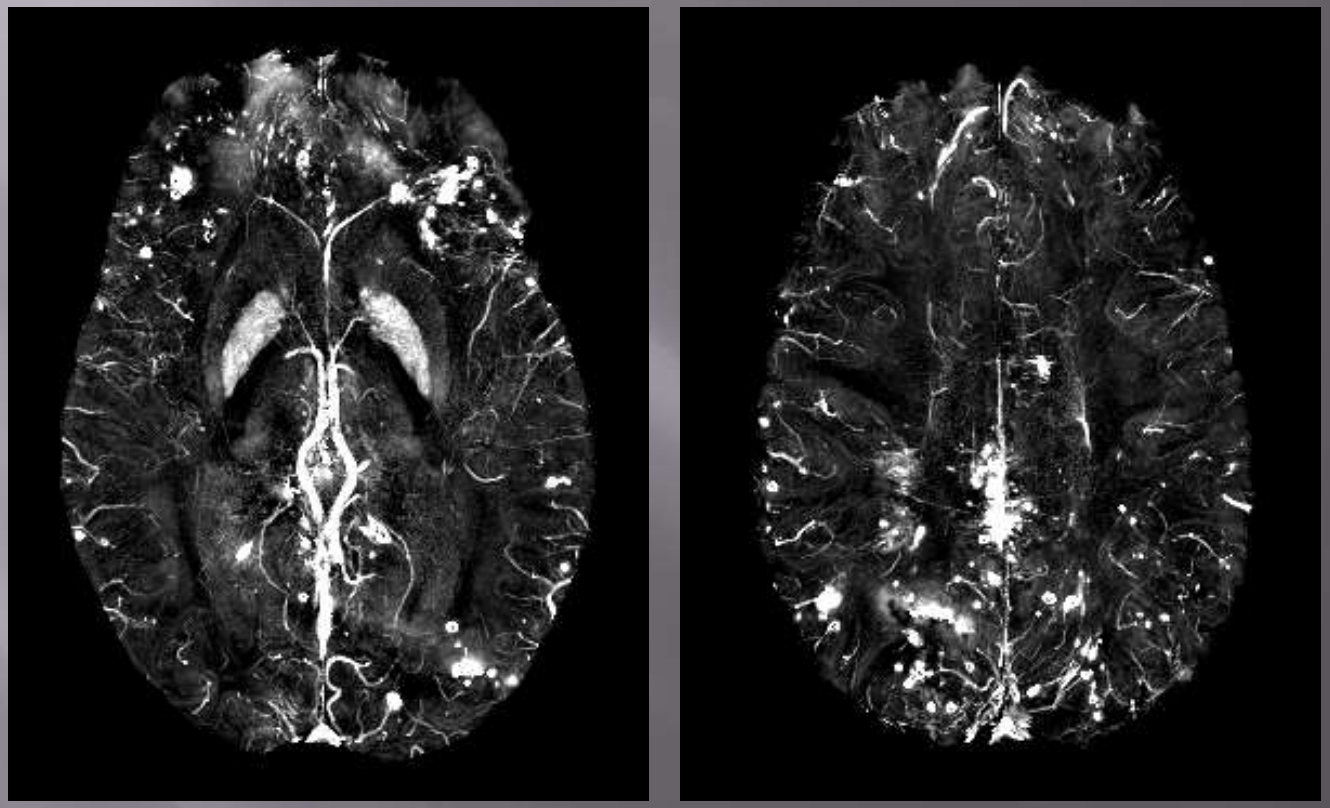
SWIM data MIPped over 32mm (64 slices)
a) SWIM and b) iterative SWIM with a threshold value of 0.1

SWIM: Positive shows paramagnetic structures such as iron while negative shows diamagnetic such as calcifications

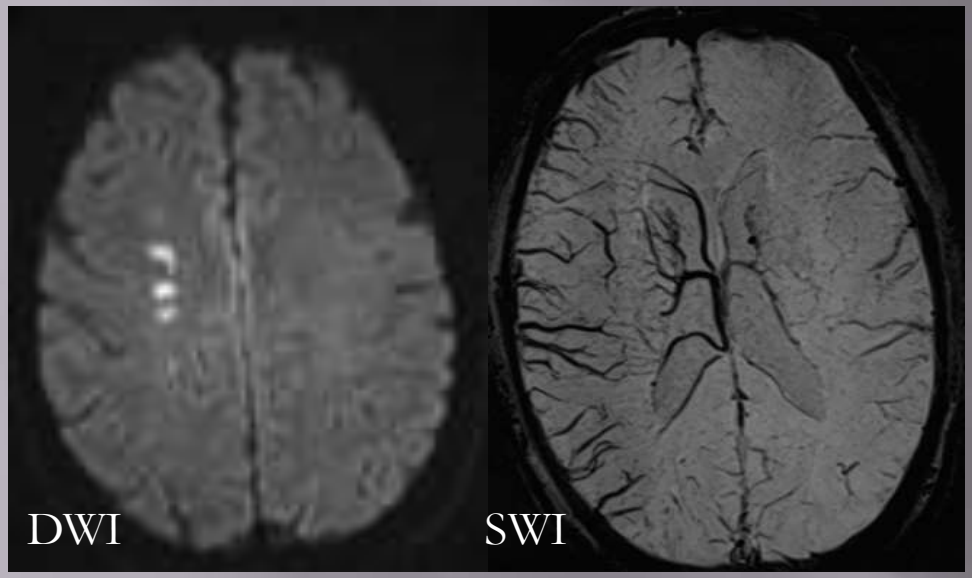


(a)Maximal intensity projection over 32mm, and (b) minimal intensity projection over 8mm

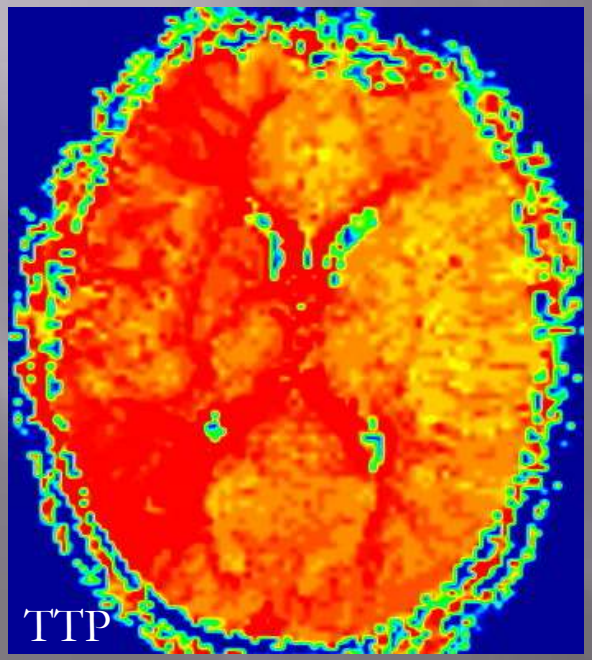
SWIM of cerebral microbleeds in TBI

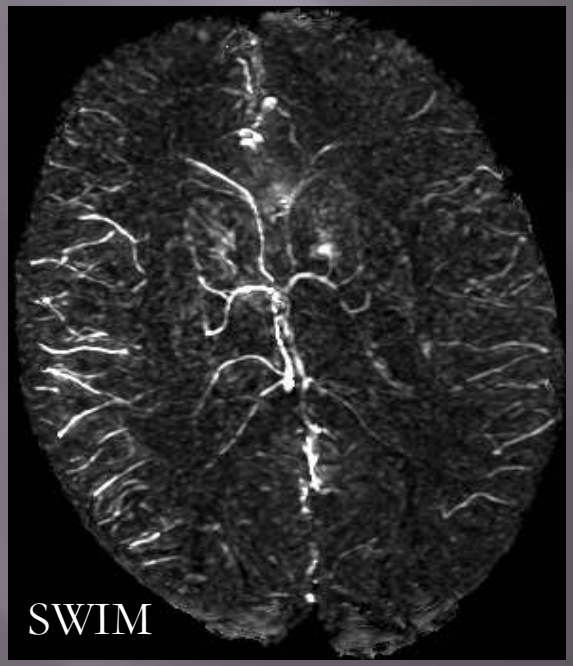


Maximum Intensity Projection (MIP) over 8mm



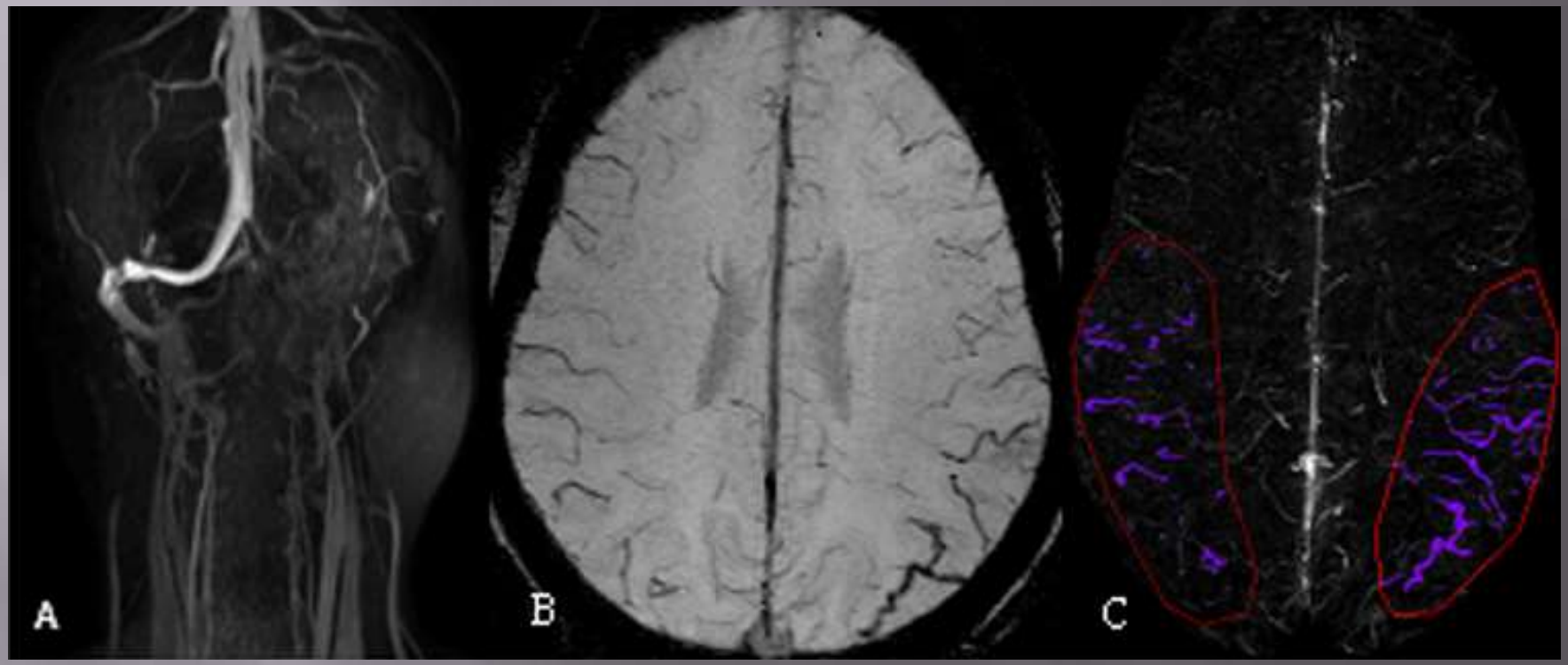
A 57 year old male patient with left limb weakness was scanned 144 hours after onset.





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

Headache can be associated with bad venous vasculature



A 32-year-old female with headache and intracranial hypertension. Occlusion of the left transverse sinus (CE MRAV, A) and APCVs on the mIPped-SWI images (B). The susceptibility value of the ipsilateral pial veins measured 159±60 ppb and the contralateral measured only (131±43) ppb.

Putnam's 1935 work on venous obstruction in a dog model

Tracey Putnam developed an experimental dog model of venous obstruction to study MS. His work supports the recent rediscovery of this concept by Dr. Paolo Zamboni of Italy.

He stated:

"The similarity between such lesions and many of those seen in cases of multiple sclerosis in man is so striking that the conclusion appears almost inevitable that venular obstruction is the essential immediate antecedent to the formation of typical sclerotic plaques."

Putnam (1935). Studies in multiple sclerosis: encephalitis and sclerotic plaques produced by venular obstruction. Archives of Neurology and Psychiatry. 33: 929-940.

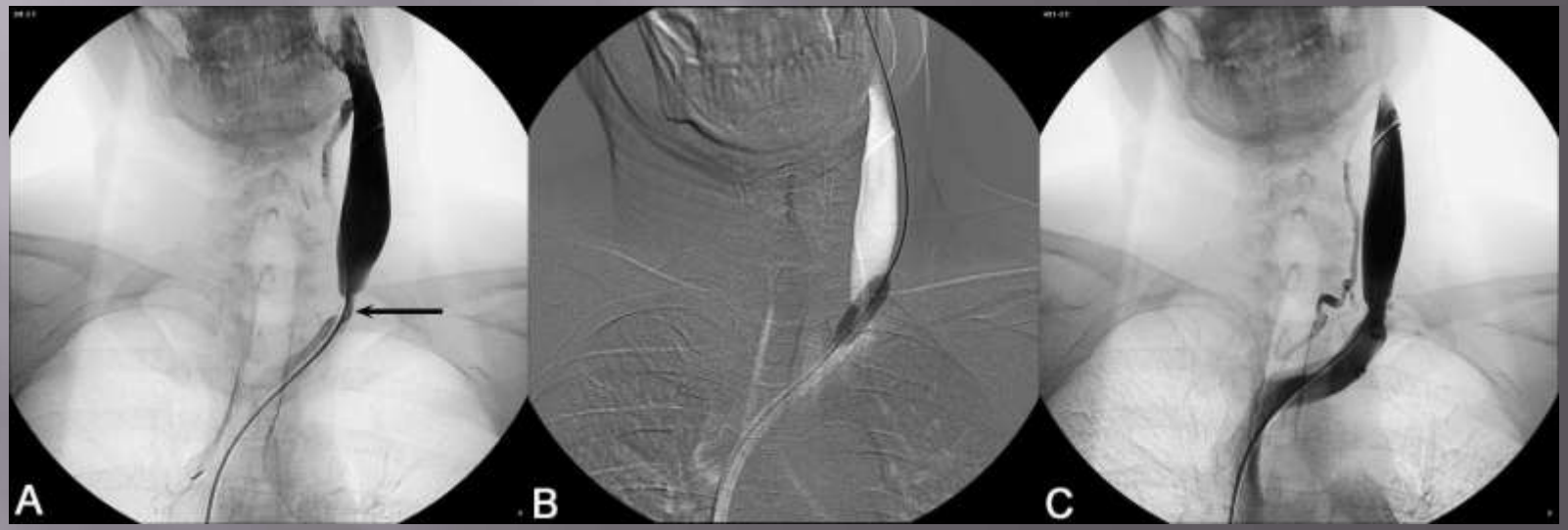
The role of the caval system in chronic venous hypertension

- Aboulker et al studied 176 patients with myelopathies

- They found stenosis of the left iliac; obstruction of the left renal vein; anomalies of the azygous vein; compression of the brachiocephalic vein; atresia of the internal jugular veins; compression of the vena cava.

Aboulker J et al. Myelopathies par hypertension veneuse intra-rachidienne. Ste De Neurochirurgie de la langue francaise. 1971.

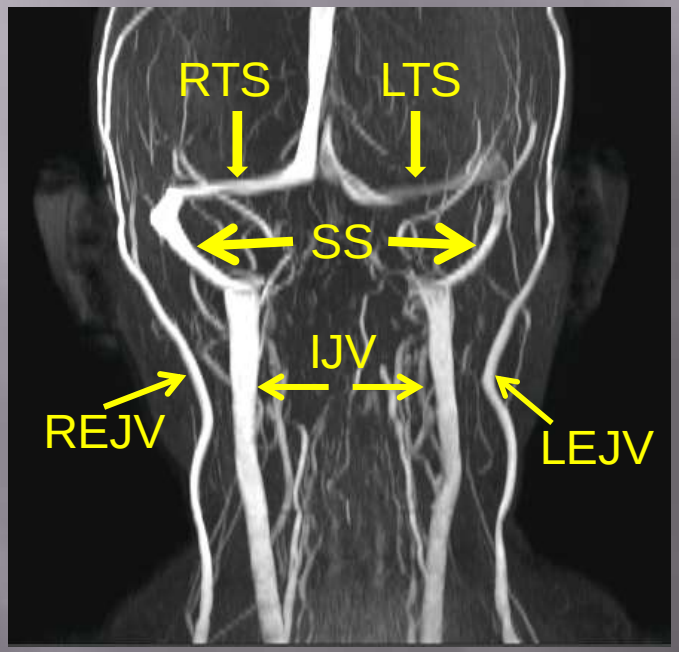
Paolo Zamboni demonstrated that there were venous abnormalities in MS patients both anatomically and functionally using angiograms as the gold standard. He called it **chronic cerebrospinal venous insufficiency** or CCSVI. He also defined a set of flow ultrasound criteria that have since been hard to replicate.

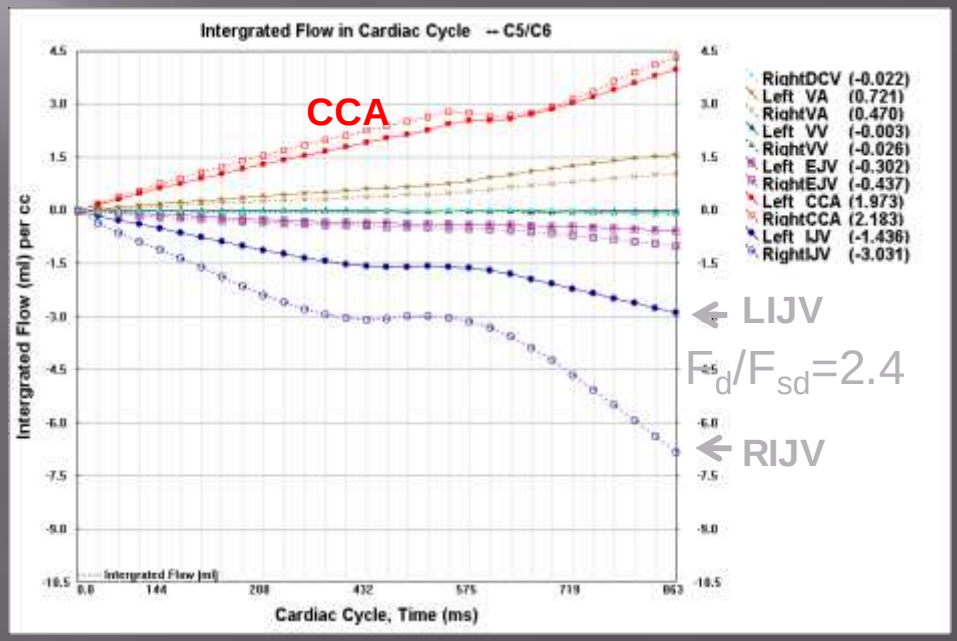


Zamboni P et al. Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2009;80:392-399.

Category 4: Normal venous structures and normal flow

- 1) the transverse/sigmoid sinuses are visible in 2D TOF
- 2) neither IJV is stenotic
- 3) F_d/F_{sd} (IJV) at C6/C7 is less than 3.4





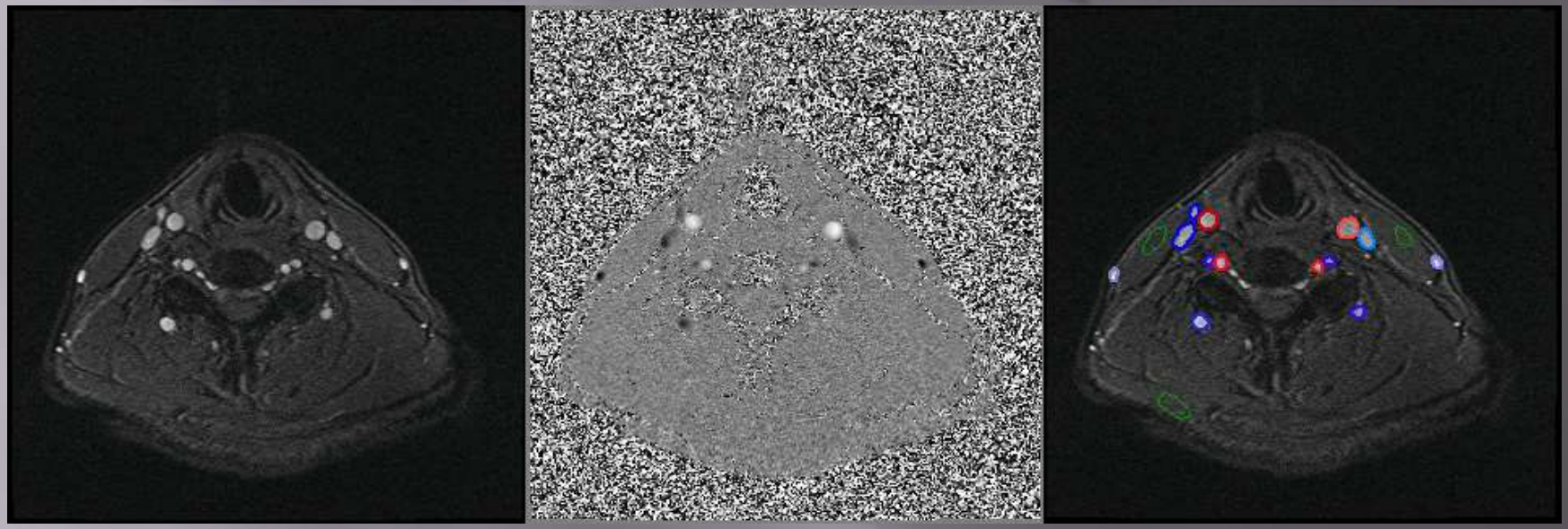
RTS: right transverse sinus; LTS: left transverse sinus;
SS: sigmoid sinus; IJV: internal jugular vein;
REJV: right external jugular vein; LEJV: left external jugular vein

Left: Stenosis at the stump of the LIJV with collateral input from the vertebral system Right: String like jugular in the RIJV

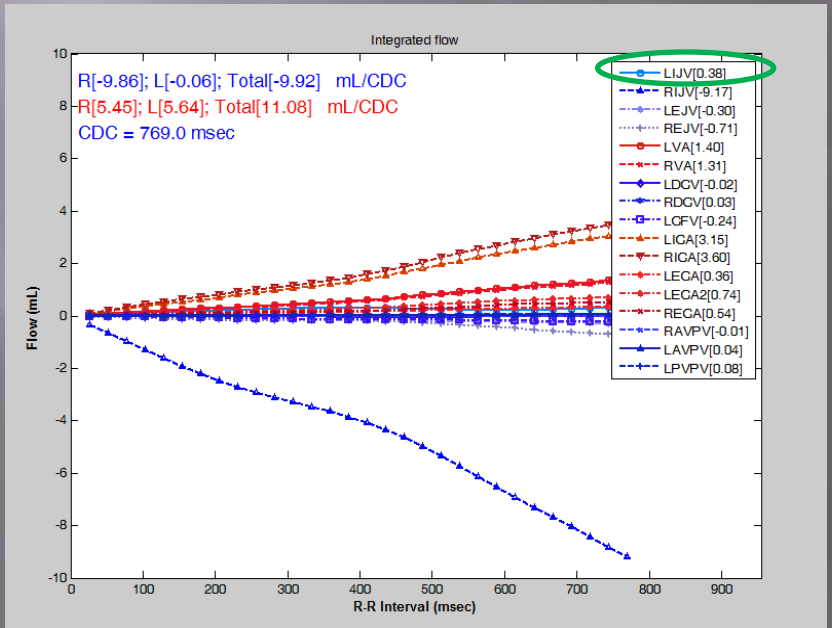
MIPed Coronal Image

2D TOF MRV MIPed images showing the Inferior Petrosal Sinus draining into the Left IJV

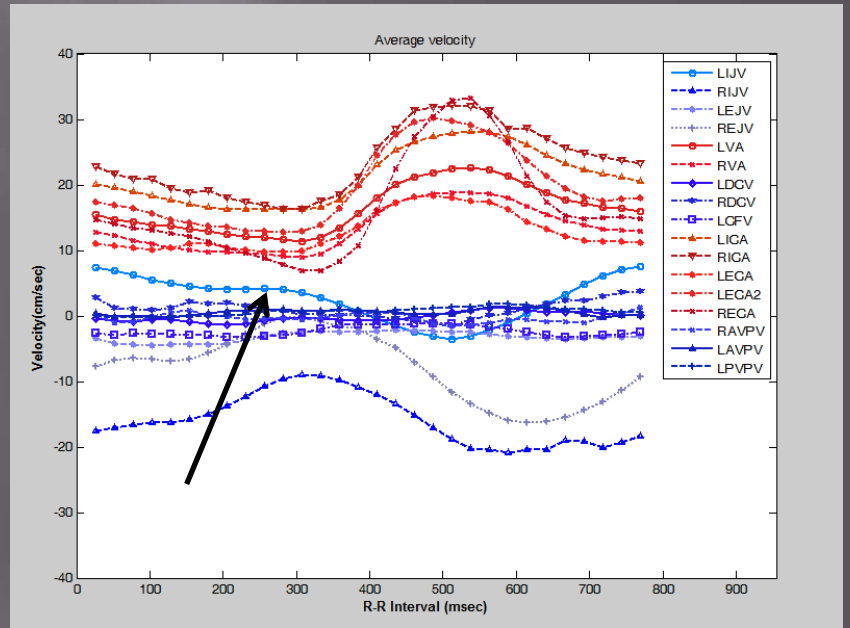
VASCULAR FUNCTION: Flow Quantification



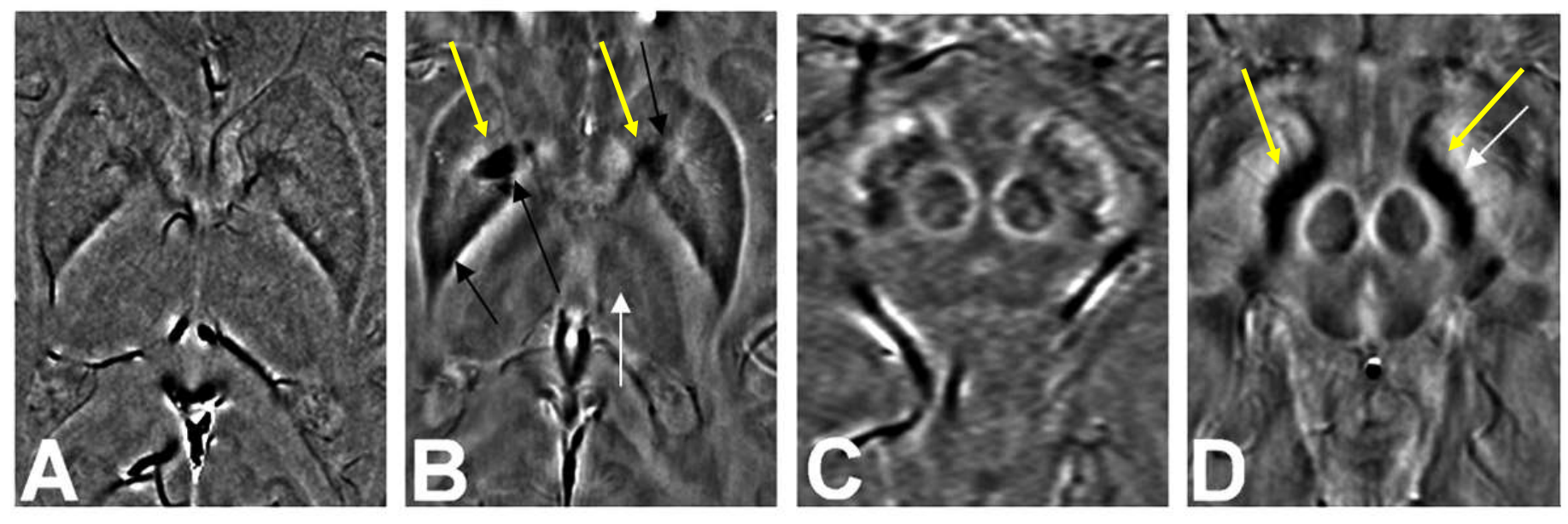
Integrated Flow Plot



Average Velocity Plot



Iron build-up in the basal ganglia



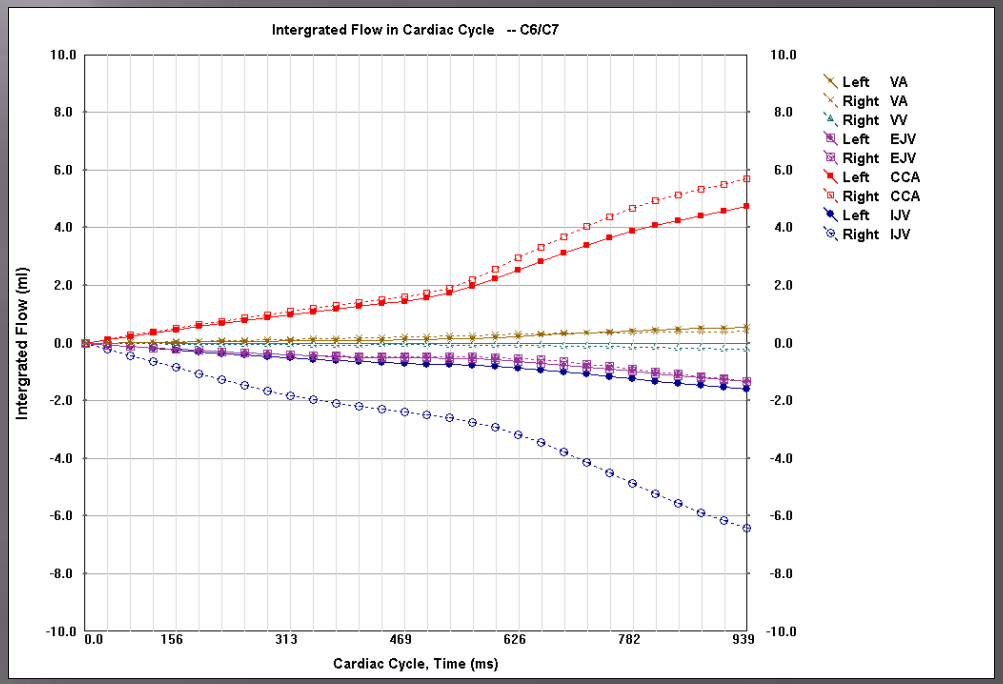
A,B show iron build up in the caudate and globus pallidus for an MS patient (B) compared with that from an age matched normal (A). C,D show iron build up in the substantia nigra for an MS patient (D) compared with that from an age matched normal (C).

Haacke EM et al. Iron stores and Cerebral Veins in MS Studied by Susceptibility Weighted Imaging (SWI); International Angiology 2010 Apr;29(2):149-57.

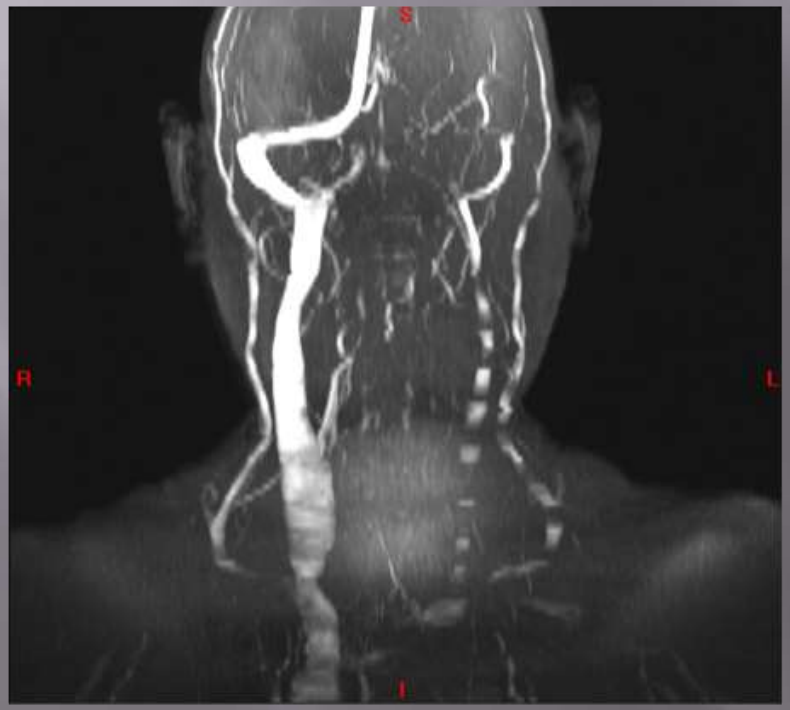
The integrating role of iron build up and venous abnormalities

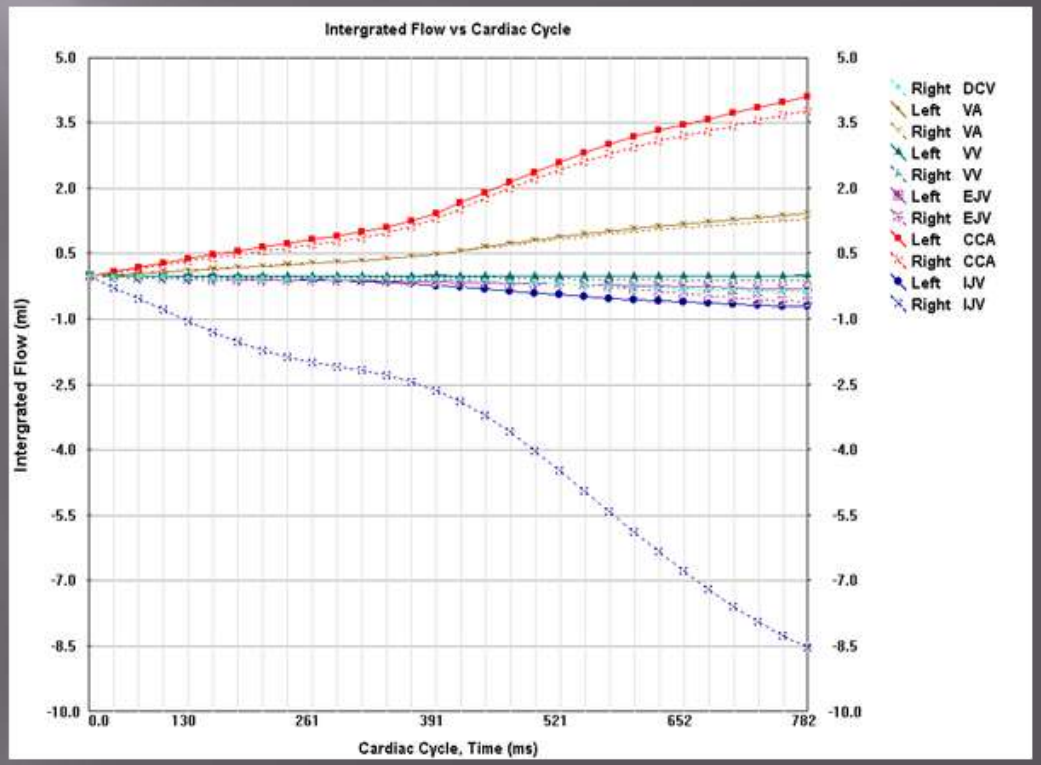
- Some elderly people show low iron
- Iron build up appears retrograde to the venous flow in many cases
- This has been shown in MS by our group
- The left transverse sinus drains the basal ganglia
- MS and PD cases show similar iron build up
- MS patients can also get PD
- If MS iron abnormalities are from CCSVI could it be that PD shows the same thing?

- Category 3:
  - 1) has sigmoid sinuses
  - 2) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
  - 3) $F_{sd}/tA < 14.1\%$

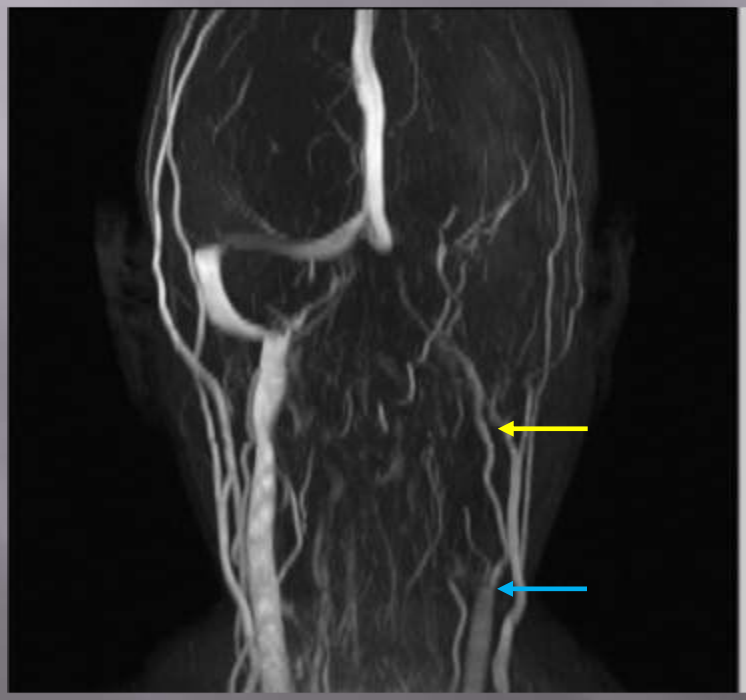


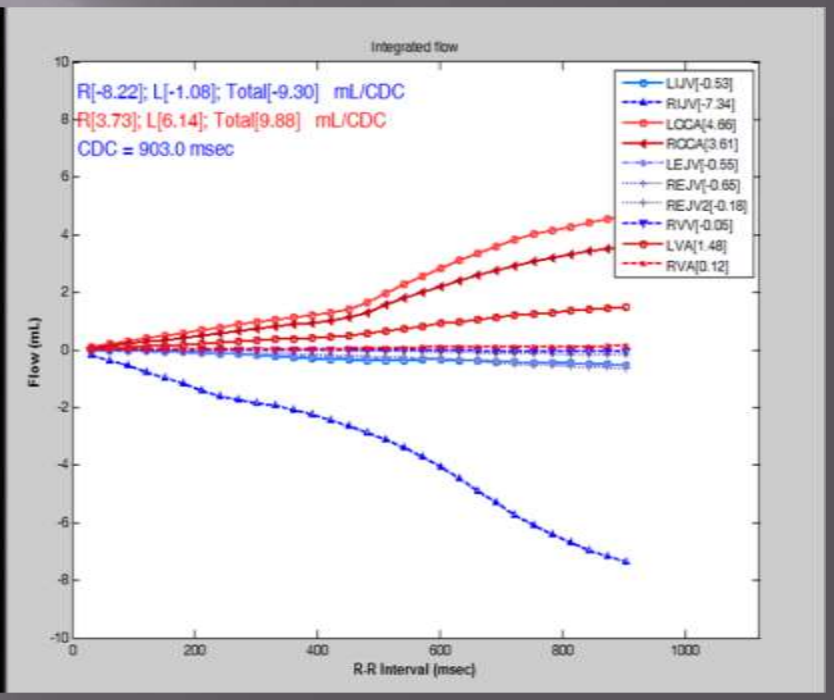
- Category 2:
- 1) missing one or both transverse sinuses
- 2) has sigmoid sinuses
- 3) presence of banding and/or stenosis along the IJVs
- 4) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
- 5) $F_{sd}/tA < 14.1\%$



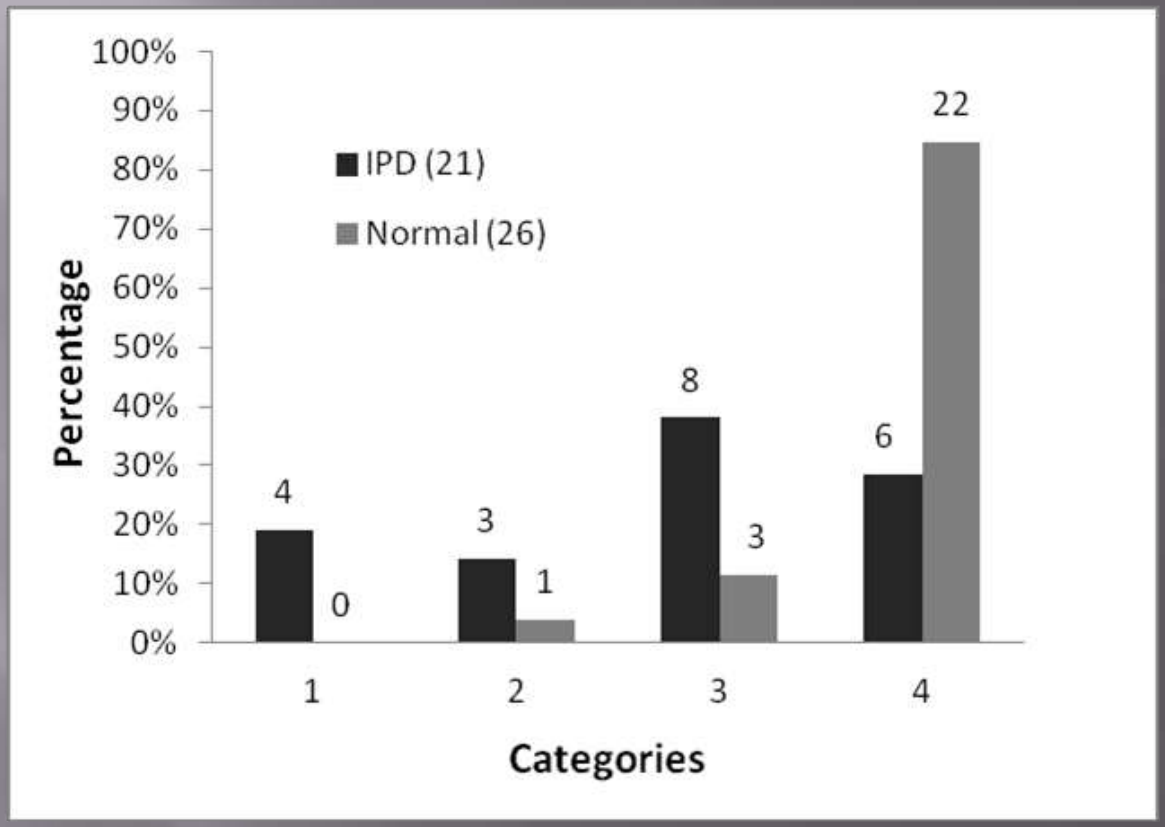


- Category 1: Parkinson's disease
  - 1) missing one or both transverse sinuses
  - 2) missing one or both sigmoid sinuses
  - 3) absence or local absence of IJVs on the TOF
  - 4) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
  - 5) $F_{sd}/tA < 14.1\%$



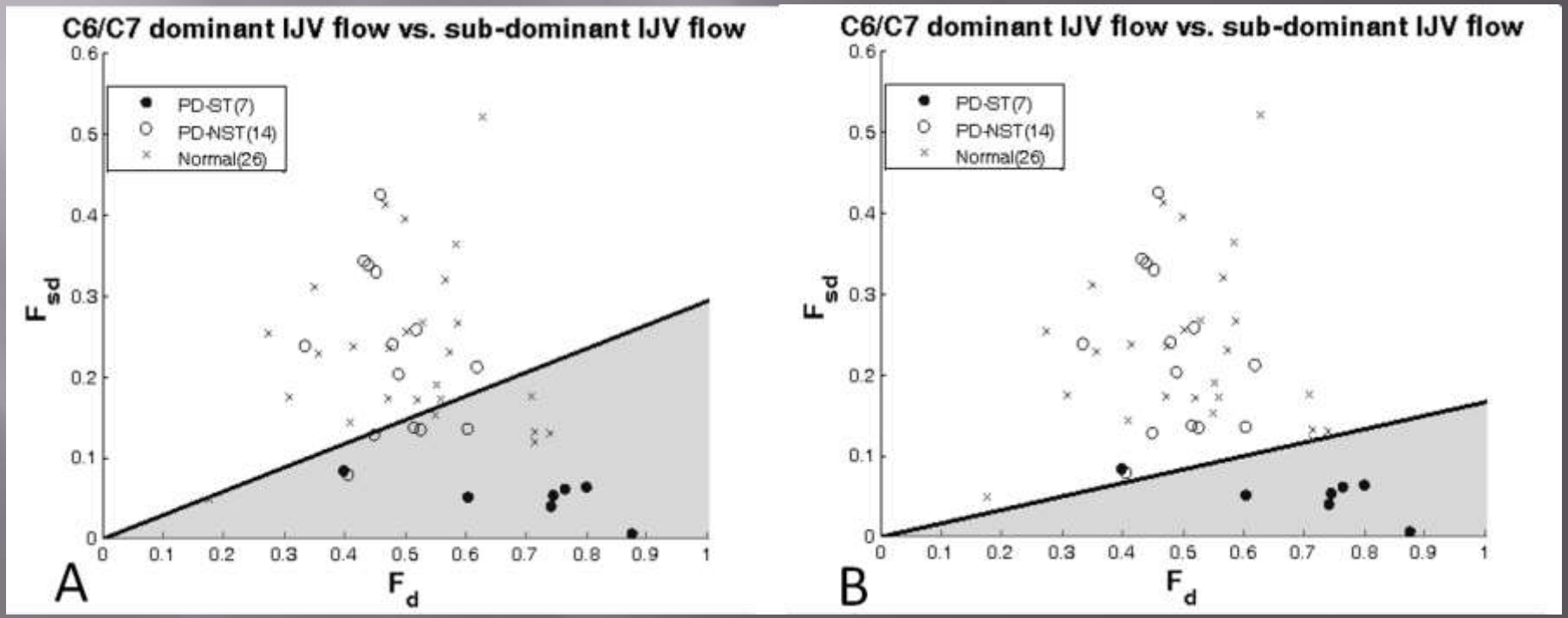


Distribution of IPD patients and normal controls according to the defined categories

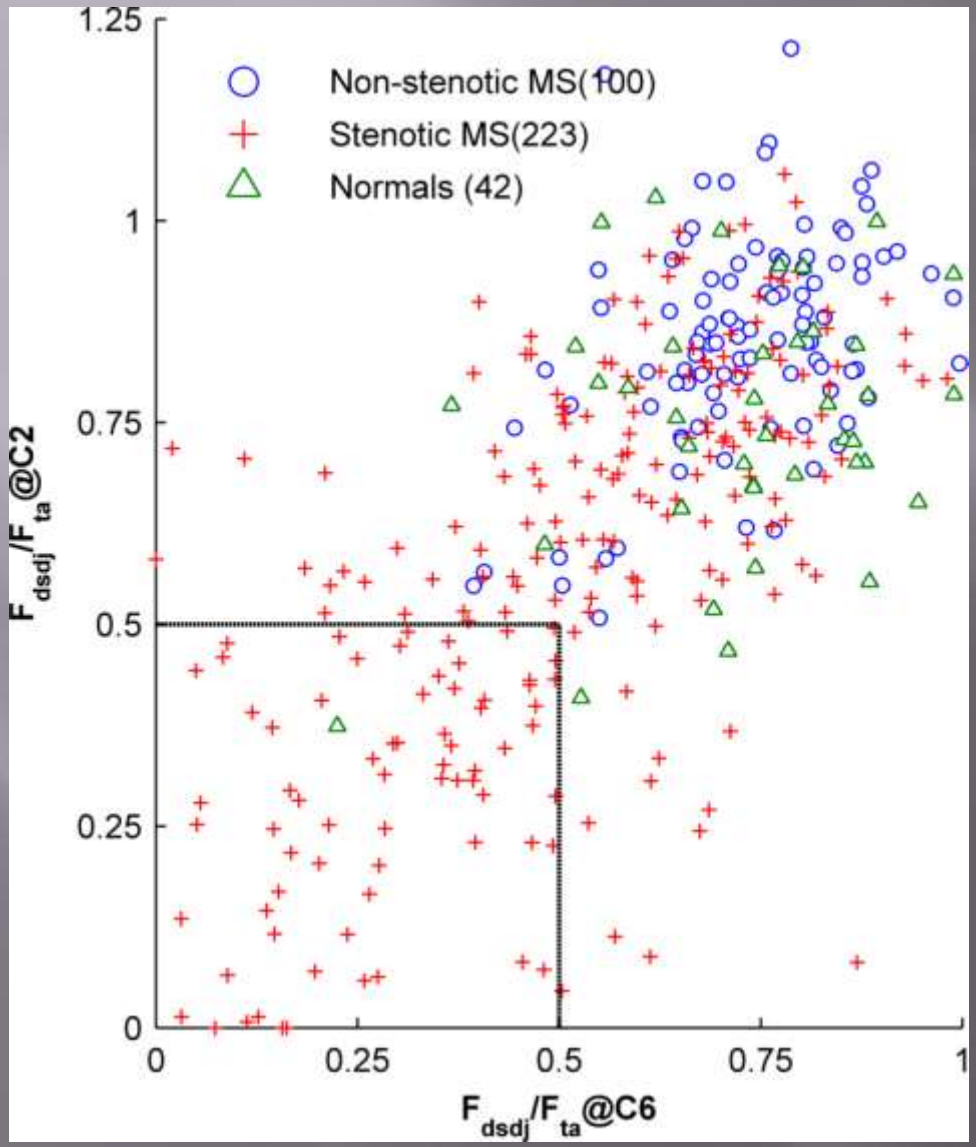


The distribution of the two populations had significant difference (χ^2=16.1, p<0.01).

Scatter plot of dominant IJV flow vs. sub-dominant flow at C6/C7 level in IPD patients and normal controls



Total IJV flow normalized to total arterial flow at C2/C3 and C5/C6



All MS patients with non-stenotic IJV show greater than 50% of total arterial input exiting through the IJV at both the C2/C3 and C5/C6 levels.

Conclusions

CCSVI is a condition that may lead to or exacerbate many diseases such as : headache, idiopathic intracranial hypertension, multiple sclerosis and Parkinson's disease

If your total IJV flow is less than 7-8ml/sec or the ratio normalized by the arterial flow is less than 0.5 or the sub-dominant flow is less than 0.1 you may be at risk for developing neurodegenerative disease.

MRI with perfusion, SWI, SWIM and flow offer a complete means by which to assess brain hemodynamics