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

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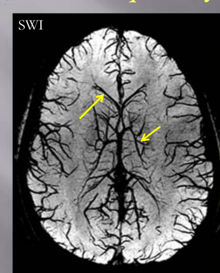
Outline

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

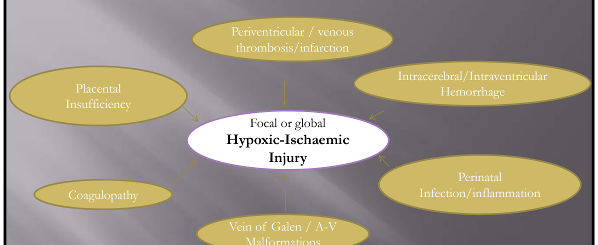
- The role of abnormal venous flow in neurodegenerative diseases: MS as an example
- See www.ms-mri.com

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

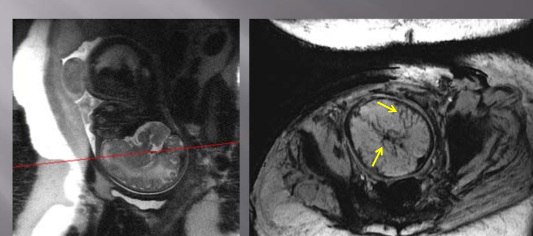
Haacke EM et al. Susceptibility weighted imaging. Magnetic Resonance in Medicine, 52: 612; 2004.



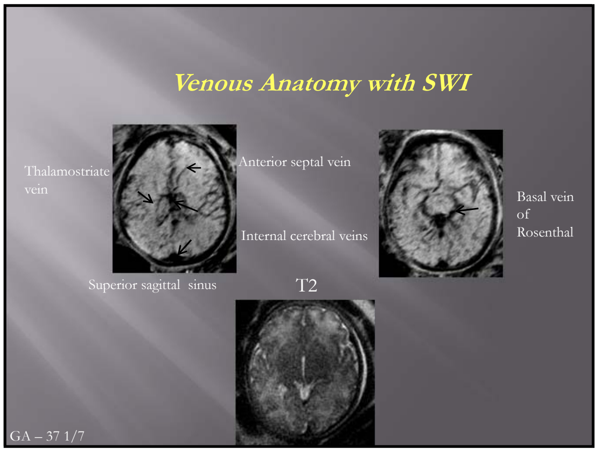
Fetal brain injury, due to Hypoxic-Ischaemic (HII) or hemorrhagic events, may be associated with debilitating neurological sequelae post partum. Early detection and possible quantification of HII in-utero may help predict outcome

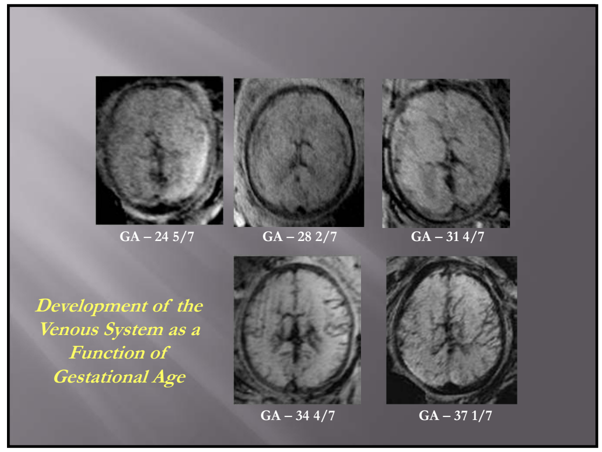
Volpe, J.J., 2009. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. Lancet Neurol. 8, 110–124.

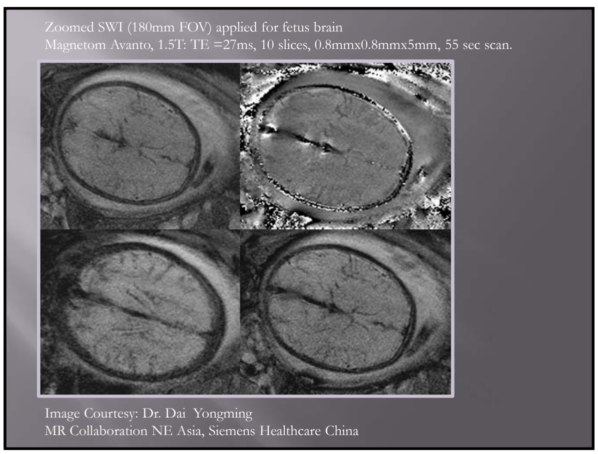
PRESENTING THE FIRST VISUALIZATION OF THE FETAL VENOUS ANATOMY OF THE BRAIN USING SWI

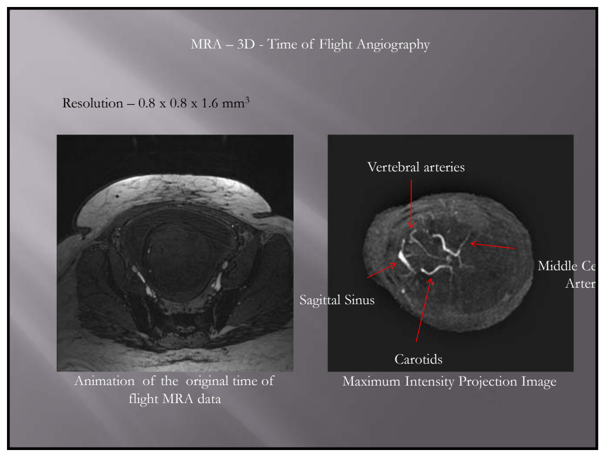


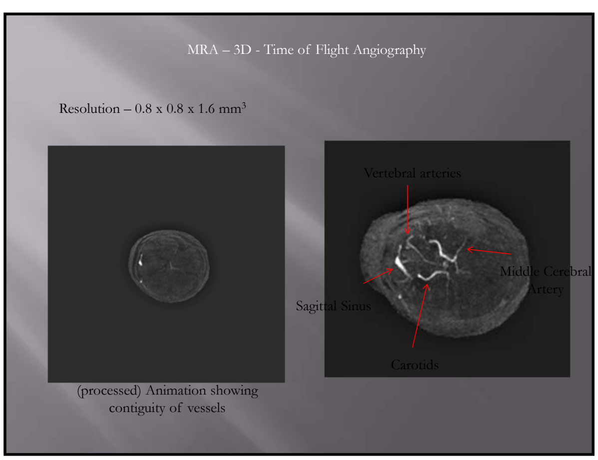
Pilot scan on the left, effective transverse SWI on the right: 37 weeks 1 day

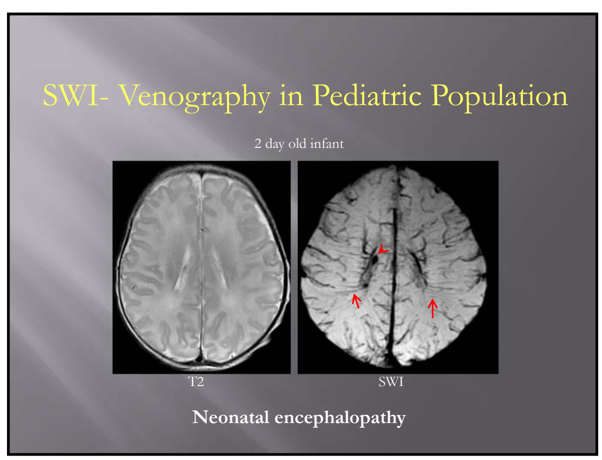

Venous Anatomy with SWI
Thalamostriate vein
Anterior septal vein
Internal cerebral veins
Basal vein of Rosenthal
Superior sagittal sinus
T2
GA – 37 1/7

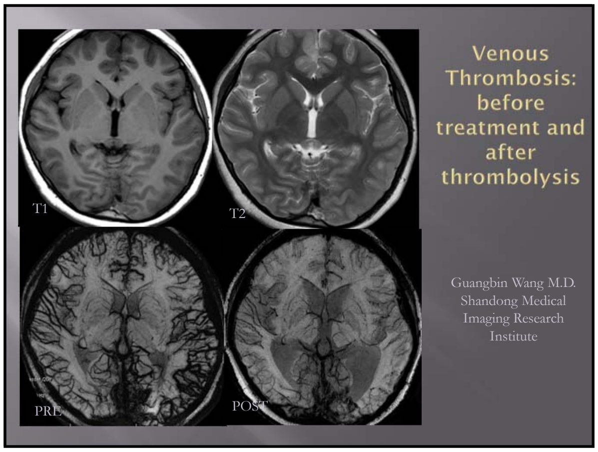

GA – 24 5/7
GA – 28 2/7
GA – 31 4/7
Development of the Venous System as a Function of Gestational Age
GA – 34 4/7
GA – 37 1/7

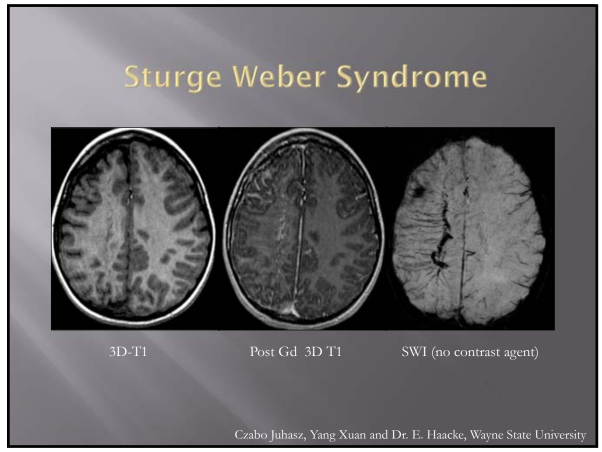

Zoomed SWI (180mm FOV) applied for fetus brain
Magnetom Avanto, 1.5T: TE =27ms, 10 slices, 0.8mmx0.8mmx5mm, 55 sec scan.
Image Courtesy: Dr. Dai Yongming
MR Collaboration NE Asia, Siemens Healthcare China

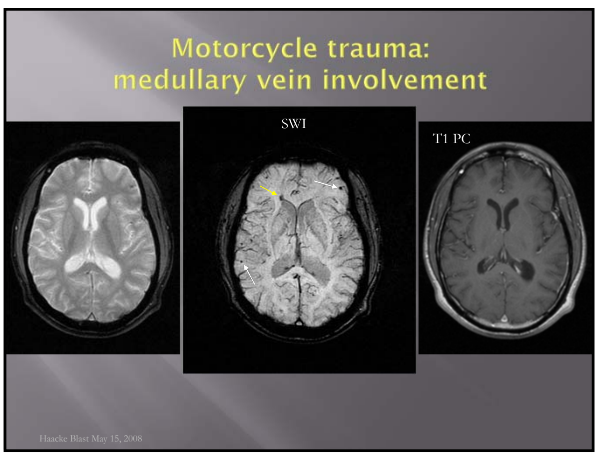

MRA – 3D - Time of Flight Angiography
Resolution – 0.8 x 0.8 x 1.6 mm3
Vertebral arteries
Middle Ce
Arter
Sagittal Sinus
Carotids
Animation of the original time of flight MRA data
Maximum Intensity Projection Image

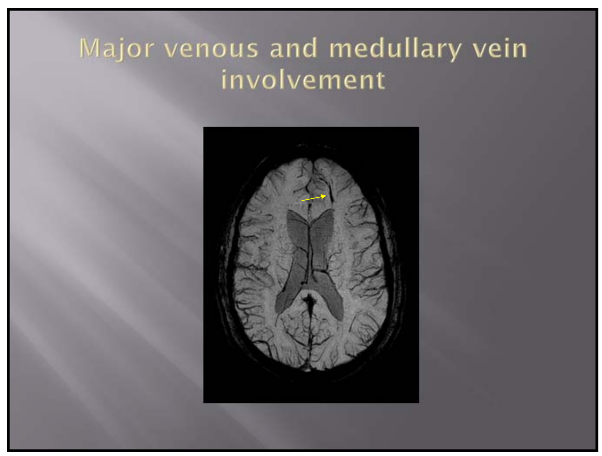

MRA – 3D - Time of Flight Angiography
Resolution – 0.8 x 0.8 x 1.6 mm3
Vertebral arteries
Middle Cerebral Artery
Sagittal Sinus
Carotids
(processed) Animation showing contiguity of vessels

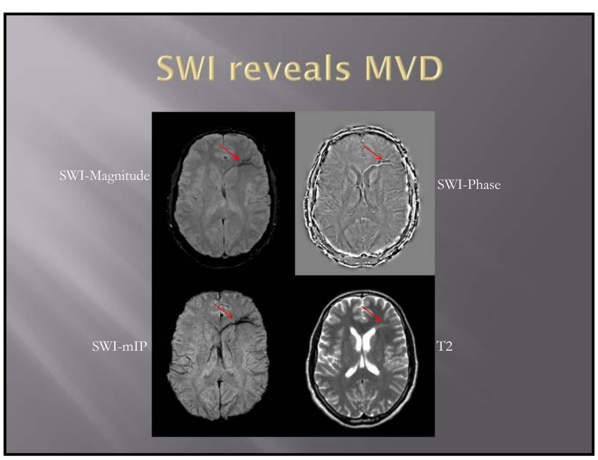

SWI- Venography in Pediatric Population
2 day old infant
T2
SWI
Neonatal encephalopathy

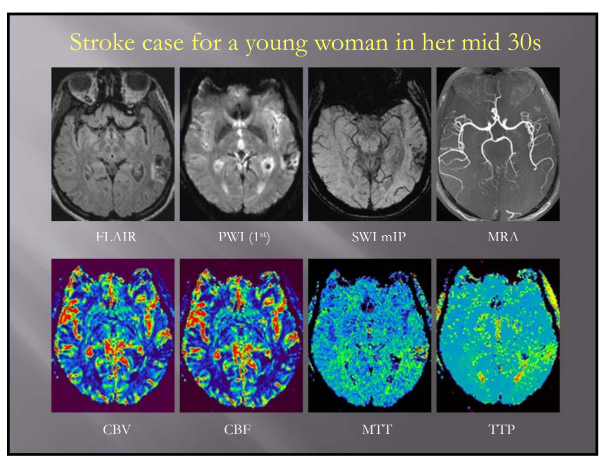

Venous Thrombosis: before treatment and after thrombolysis
T1
T2
PRE
POST
Guangbin Wang M.D.
Shandong Medical Imaging Research Institute


Sturge Weber Syndrome
3D-T1
Post Gd 3D T1
SWI (no contrast agent)
Czabo Juhasz, Yang Xuan and Dr. E. Haacke, Wayne State University

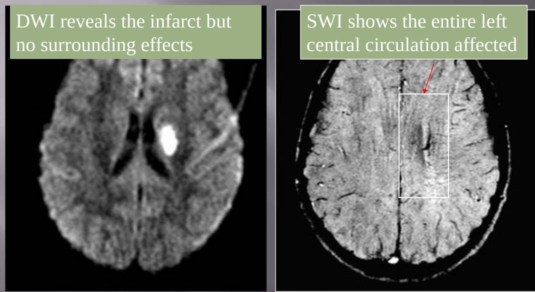

Motorcycle trauma: medullary vein involvement
SWI
T1 PC
Haacke Blast May 15, 2008


Major venous and medullary vein involvement

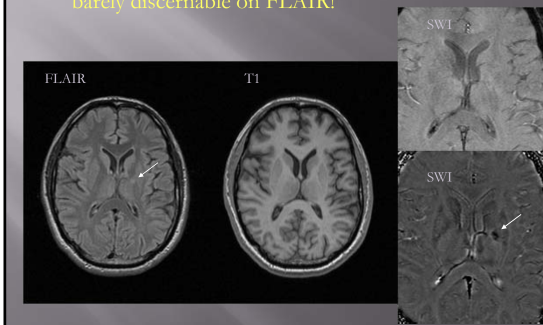

SWI reveals MVD
SWI-Magnitude
SWI-Phase
SWI-mIP
T2


Stroke case for a young woman in her mid 30s
FLAIR
PWI (1st)
SWI mIP
MRA
CBV
CBF
MTT
TTP

Acute Basal Ganglia Infarct



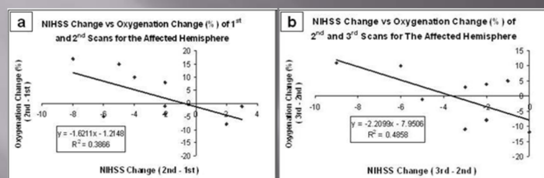
Low concentration iron is still seen on 7 slices with SWI and barely discernable on FLAIR!



Stroke with almost imperceptible bleeding

SWI shows the bleed short TE GRE T1

Oxygen saturation as a biomarker in stroke recovery



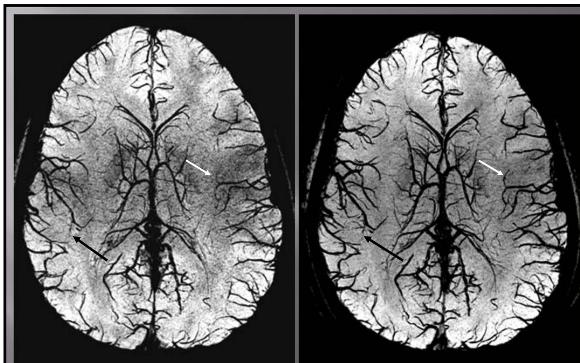
a) Correlation between the NIH stroke scale and change in oxygen saturation from the first day to week two. Increases in oxygen saturation bode well for the patients. b) Correlation between the NIH stroke scale and change in oxygen saturation from week two to week six. Increases in oxygen saturation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

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

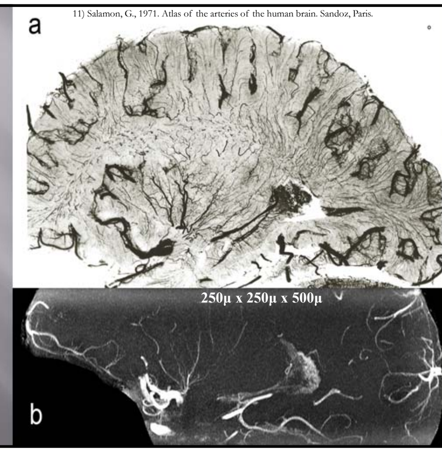


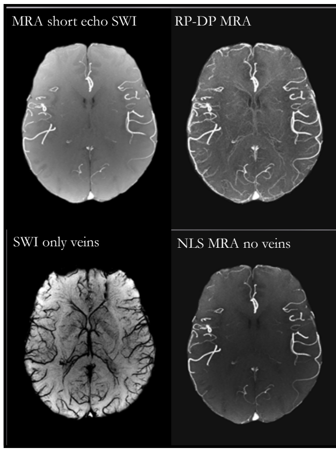
PRE POST

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

High resolution MR angiography

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



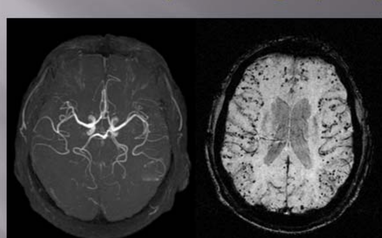


Simultaneous MRV and MRI using a double echo interleaved SWI rephased/dephased sequence

Imaging Aging

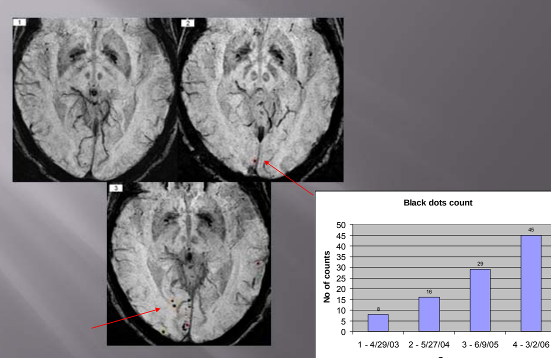
- It is now believed that up to 35% of dementia cases may be caused by vascular dementia.
- We see microhemorrhages as a means to predict who will get Alzheimer's disease.
- These may lead to "cognitive strokes".
- Hopefully this work will lead to collaborations with the pharmaceutical industry to come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

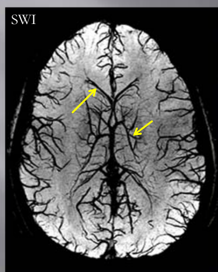
Cerebral amyloid angiopathy



50µ objects can manifest as 1mm^3 objects

time to go sailing

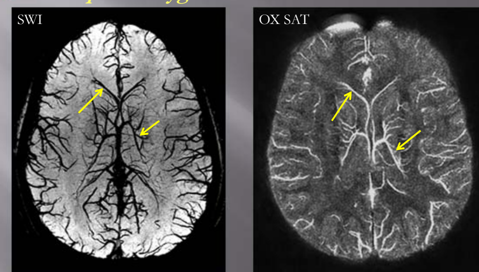




➢ SWI it is not quantitative in nature, it is basically a pretty diagnostic image.

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

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.

Motivation for SWIM

Ability to quantify susceptibility can provide critical physiological/patho-physiological information, for example:

A) Measuring oxygen saturation in a vessel,

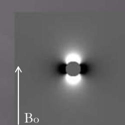
B) Measuring the iron concentration in a tissue, which is important in conditions like anemia and sickle cell disease, hemachromatosis, Parkinson's and Alzheimer's disease, etc.

Dipole Field Equations

Sphere

$$\Delta B_{in} = 0$$

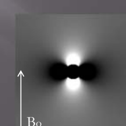
$$\Delta B_{out} = \frac{\Delta x}{3}\frac{a^3}{r^3}(3cos^2\theta - 1)B_o$$



Cylinder (perpendicular to the main field)

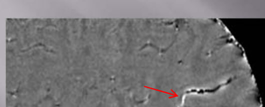
$$\Delta B_{in} = \frac{\Delta x}{6}(3cos^2\theta - 1)B_o$$

$$\Delta B_{out} = \frac{\Delta x}{2}\frac{a^2}{\rho^2} sin^2\theta cos2\emptyset B_o$$

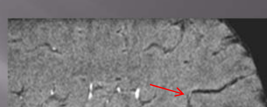


Motivation

The phase of venous vessels and sub-cortical structures is dependent on their orientation with the main magnetic field B_0.



Phase image



Processed SWI magnitude

As the vessel changes its orientation with respect to the external field B_0, the phase value inside the vessel shifts from being negative to positive (arrow).

This causes variability in the appearance of venous vessels in the processed SWI magnitude on the right.

Inverse Process

$$\varphi(r) = \gamma \Delta B(r) TE$$

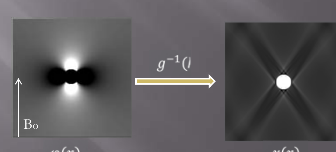
$$x(r) = FT^{-1}\left[g^{-1}(k)\cdot\frac{FT[\varphi(r)]}{\gamma B_o TE}\right]$$

where

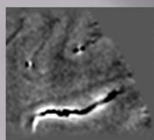
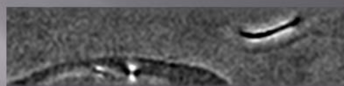
$$g(k) = \frac{1}{3} - \frac{k_z{}^2}{k_x{}^2 + k_y{}^2 + k_z{}^2}$$

$$g^{-1}(k) = \frac{3(k_x{}^2 + k_y{}^2 + k_z{}^2)}{k_x{}^2 + k_y{}^2 - 2k_z{}^2}$$

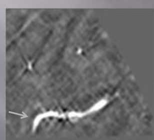
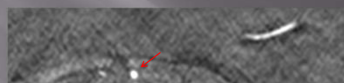
Challenge: The filter g(k) goes to 0 at k_{zo} where $2k_z^2 = k_x^2 + k_y^2$, making $g^{-1}(\mathbf{k})$ undefined causing singularities.



Results from in vivo MR Data

Phase image of a normal volunteer showing dipolar phase around the venous vessels (TE 19.2msec at 4T)

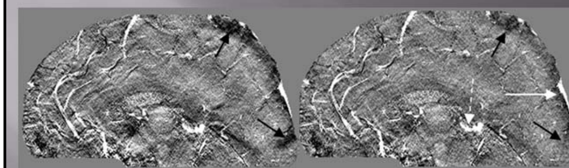



Corresponding susceptibility map showing the vessels. Note that the dipolar phase of the veins is almost completely deconvolved (red arrow) and the vein has uniform signal.

Note the slight negative dip seen in the immediate neighborhood of the vessels. This is an artifact resulting from the inverse filter, as observed in the simulation plots.

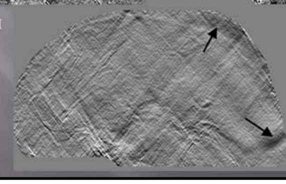
Reducing streaking artifacts

Streaking artifact reduction:



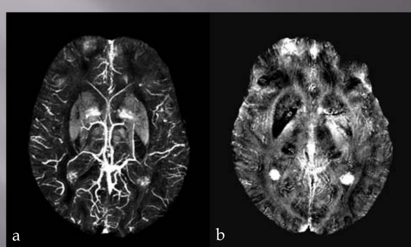
Before Iterative SWIM

After Iterative SWIM Using a=0.1



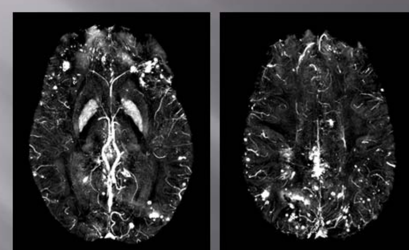
Difference Image

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



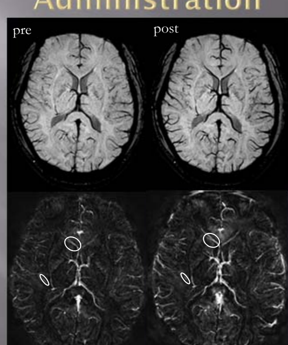
(a)Maximal intensity projection over 32mm, and (b) minimal intensity projection over 8mm

SWIM of cerebral microbleeds in TBI



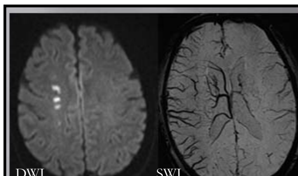
Maximum Intensity Projection (MIP) over 8mm

Pre and Post Caffeine Administration

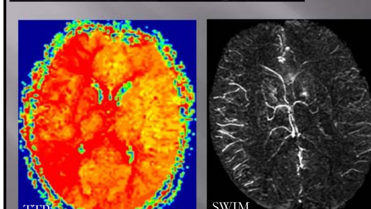


Minimum intensity projections (mIP) of SWI images(slice thickness: 8mm)

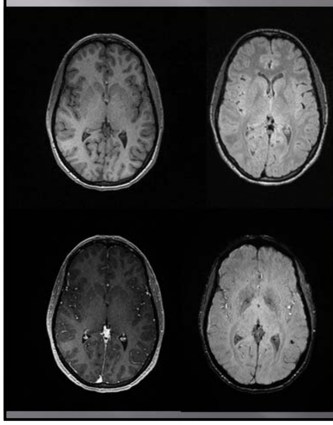
Maximum intensity projections of susceptibility maps (slice thickness: 4mm)



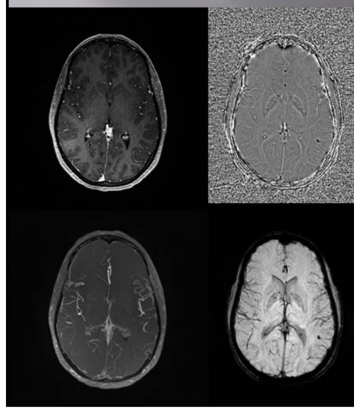
A 57 year old male patient with left limb weakness was scanned 144 hours after onset.



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



WSU SWI-JOT



WSU SWI-JOT

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

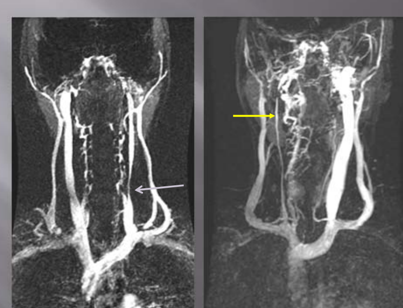
- Aboulker et al studied 176 patients with myelopathies
- They found stenosis of the left iliac; obstruction of the left renal vein; anomalies of the azygous vein; compression of the brachiocephalic vein; atresia of the internal jugular veins; compression of the vena cava.

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.

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



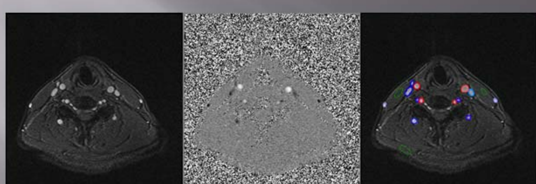
MR examples of CCSVI in MS patients where pre-treatment planning would reveal significant data that could affect how the veins are accessed.

Stenosed RIJV

Pre-post treatment of a young Canadian with severe MS

Using MRI and angiography, it is clear that MS patients HAVE venous abnormalities

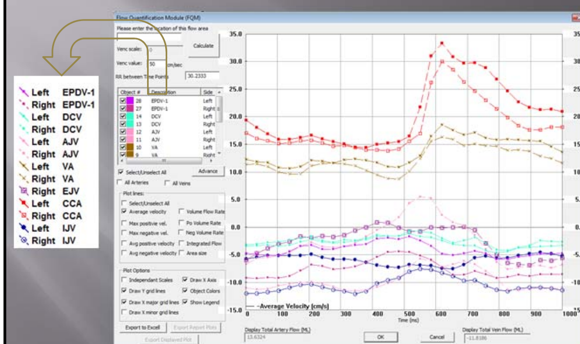
VASCULAR FUNCTION: Flow Quantification



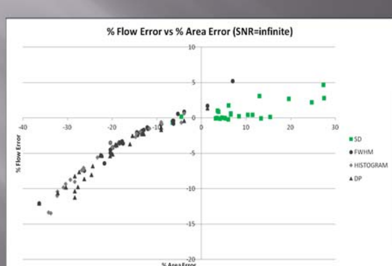
Integrated Flow Plot

Average Velocity Plot

Flow as a function of the cardiac cycle



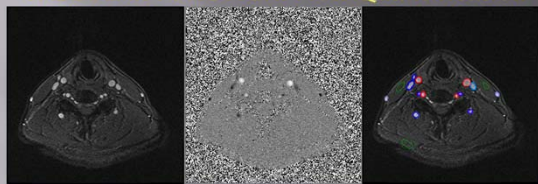
It is better to overestimate the cross sectional area in MRFQ



MIPed Coronal Image

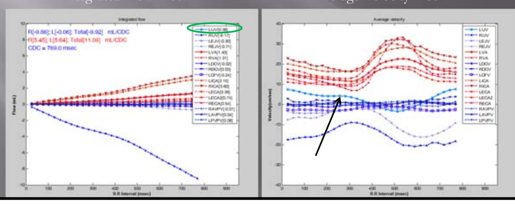
2D TOF MRV MIPed images showing the Inferior Petrosal Sinus draining into the Left IJV

VASCULAR FUNCTION: Flow Quantification

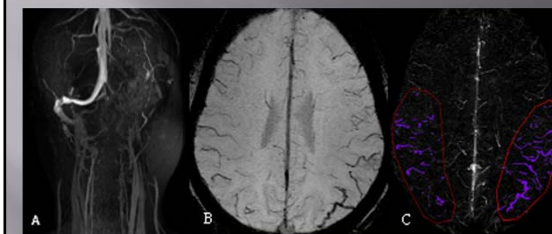


Integrated Flow Plot

Average Velocity Plot

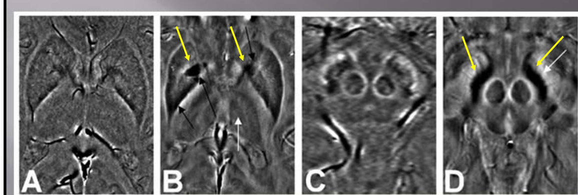


Headache can be associated with bad venous vasculature



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.

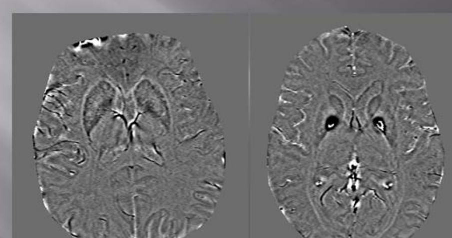
Iron build-up in the basal ganglia



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.

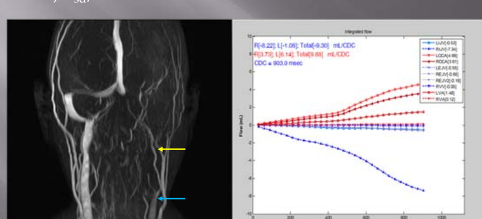
Iron build up in the globus pallidus for a patient with Parkinson's



Normal Control : 59 years old

PD patient: 63 years old

- 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) $F_{sd}/tA < 14.1\%$



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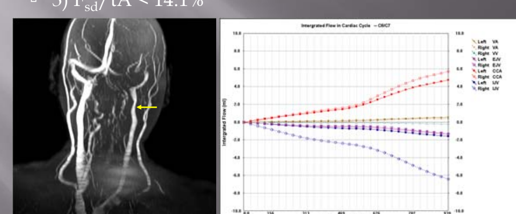
- Category 3:
  - 1) has sigmoid sinuses
  - 2) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
  - 3) $F_{sd}/tA < 14.1\%$



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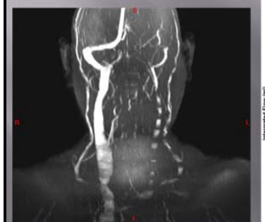
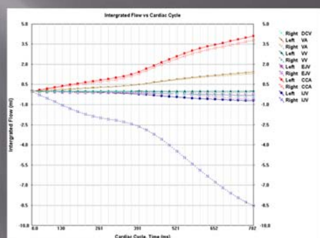
- Category 2:
- 1) missing one or both transverse sinuses
- 2) has sigmoid sinuses
- 3) presence of banding and/or stenosis along the IJVs
- 4) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
- 5) $F_{sd}/tA < 14.1\%$





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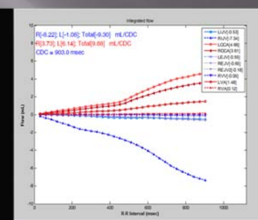
- Category 1:
  - 1) missing one or both transverse sinuses
  - 2) missing one or both sigmoid sinuses
  - 3) absence or local absence of IJVs on the TOF
  - 4) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
  - 5) $F_{sd}/tA < 14.1\%$



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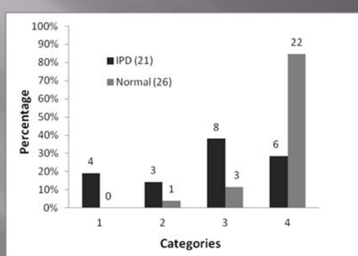
Distribution of IPD patients and normal controls according to the defined categories



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

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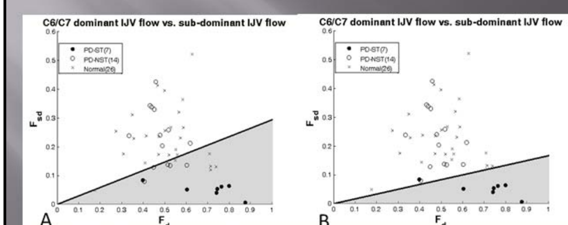
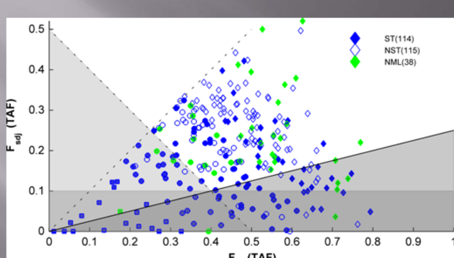
Scatter plot of dominant IJV flow vs. sub-dominant flow at C6/C7 level in IPD patients and normal controls

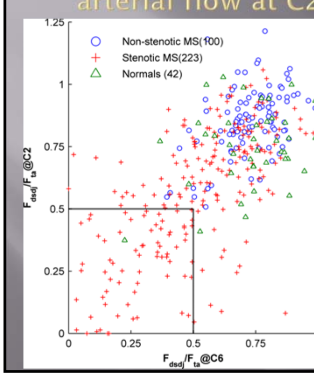


Results: Dominant vs. Sub-dominant Venous Flow Rates Normalized to the Total Arterial Flow



NST(115) open symbols
ST(114) closed symbols
NML(38) solid green symbols

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.

LIMITATIONS

- The small patient sample size
- The younger age range of the normal controls for the venous structural and flow analysis
- The lack of 3D time-resolved contrast-enhanced arteriovenography (3D CE MRAV) scans

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

CONCLUSION

- There are a variety of vascular abnormalities in patients with IPD.
- The structural and/or venous flow abnormalities in the transverse sinus, sigmoid sinus and IJVs may lead to an important imaging sub-classification of IPD that will enhance our understanding of the etiology of IPD and perhaps even lead to the development of new treatment regimens.
- Venous flow abnormalities and CCSVI may also play a role in intracranial hypertension and headache.

Conclusions

Venous flow abnormalities are an important aspect of neurodegenerative disease.

Both arterial and venous aspects are important in the study of neurodegenerative disease.

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