THE ROLE OF SWI IN NEURODEGENERATIVE DISEASES: 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

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

Fetal brain injury due to Hypoxic-Ischemic (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.

**Venous Anatomy with SWI**

- Thalamostriate vein
- Anterior septal vein
- Basal vein of Rosenthal
- Superior sagittal sinus
- Thalamostriate vein
- Internal cerebral veins

GA – 37 1/7

**Development of the Venous System as a Function of Gestational Age**

- GA – 34 4/7
- GA – 31 4/7
- GA – 28 2/7
- GA – 24 5/7

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. Da Yongming
MR Collaboration NE Asia, Siemens Healthcare China

**MRA – 3D - Time of Flight Angiography**

- Carotids
- Vertebral arteries
- Sagittal Sinus

Maximum Intensity Projection Image
Resolution – 0.8 x 0.8 x 1.6 mm³

Animation of the original time of flight MRA data

**SWI - Venography in Pediatric Population**

- T2
- SWI

2-day old infant
Neonatal encephalopathy
**Venous Thrombosis:** before treatment and after thrombolysis

Guangbin Wang M.D.
Shandong Medical Imaging Research Institute

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**Sturge Weber Syndrome**

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

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**Motorcycle trauma:** medullary vein involvement

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**Major venous and medullary vein involvement**

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**SWI reveals MVD**

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**Stroke case for a young woman in her mid 30s**

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Acute Basal Ganglia Infarct

DWI reveals the infarct but no surrounding effects. SWI shows the entire left central circulation affected. 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 patient. 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 patient 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 in 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.
High resolution MR angiography

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


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 1mm³ objects

50µ objects can manifest as 1mm³ objects

time to go sailing

Black dots count

- 1 - 4/29/03
- 2 - 5/27/04
- 3 - 6/9/05
- 4 - 3/2/06

Scan no

No of counts
SWI is not quantitative in nature, it is basically a pretty diagnostic image.


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 SWI

Ability to quantify susceptibility can provide critical physiological/pathophysiological 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.

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The phase of venous vessels and subcortical structures is dependent on their orientation with the main magnetic field $B_0$.

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.

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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 vessel 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.

Streaking artifact reduction:

Using a=0.1

Difference Image

Maximum Intensity Projection (MIP) over 8mm

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

Pre and Post Caffeine Administration

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

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

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

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


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.


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.


Left: Stenosis at the stump of the LUV with collateral input from the vertebral system

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

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

2D TOF MRV MIPed images showing the Inferior Petrosal Sinus draining into the Left IJV
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 $159 \pm 60$ ppb and the contralateral measured only $131 \pm 43$ ppb.

Headache can be associated with bad venous vasculature. 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.

A,B show iron build up in the basal ganglia for a patient with Parkinson’s.

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

Category 1: Parkinson’s disease
- 1) missing one or both transverse sinuses
- 2) missing one or both sigmoid sinuses
- 5) 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) $F_{sd}/tA < 14.1\%$

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_s at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
- 5) F_d/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 ($\chi^2=16.1, p<0.01$).

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

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.