CCSVI- Chronic Cerebrospinal Venous Insufficiency

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MULTIPLE SCLEROSIS

In Canada: 

- 55,000-75,000 MS patients
- most common neurological disease affecting young adults
- ~1,000 new cases of MS diagnosed each year
- Economic impact > **$1 billion** annually

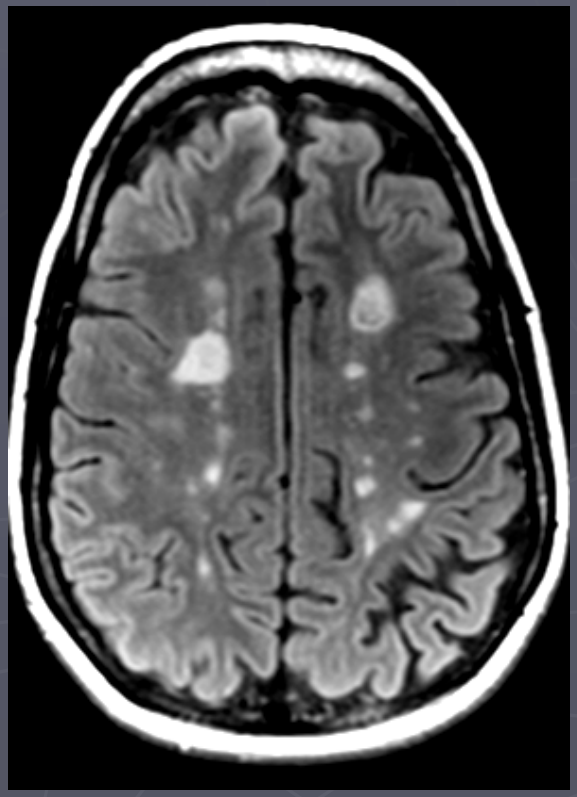
- **In the USA multiply by roughly 8!**

- **Throughout the world 2.5 million people may be affected by MS**

MULTIPLE SCLEROSIS

Facts about MS:

- Cause unknown…there is no cure
- 2 to 3 times more women than men
- The symptoms - mild to debilitating :
  - vision problems;
  - loss of balance and/or coordination,
  - extreme fatigue,
  - speech or memory failure;
  - muscle stiffness and paralysis.



CCSVI

Chronic cerebro-spinal venous insufficiency

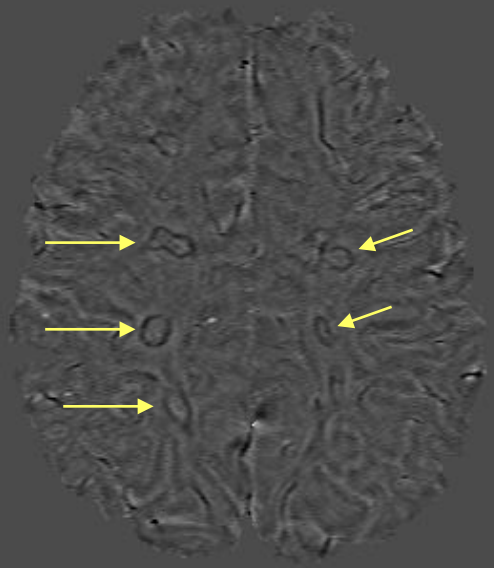
Zamboni noted narrowing of the veins at the neck or spine was restricting blood flow and potentially high levels of iron were accumulating in the brain (65 case studies)

Paolo Zamboni demonstrated that there were major venous abnormalities in MS patients

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

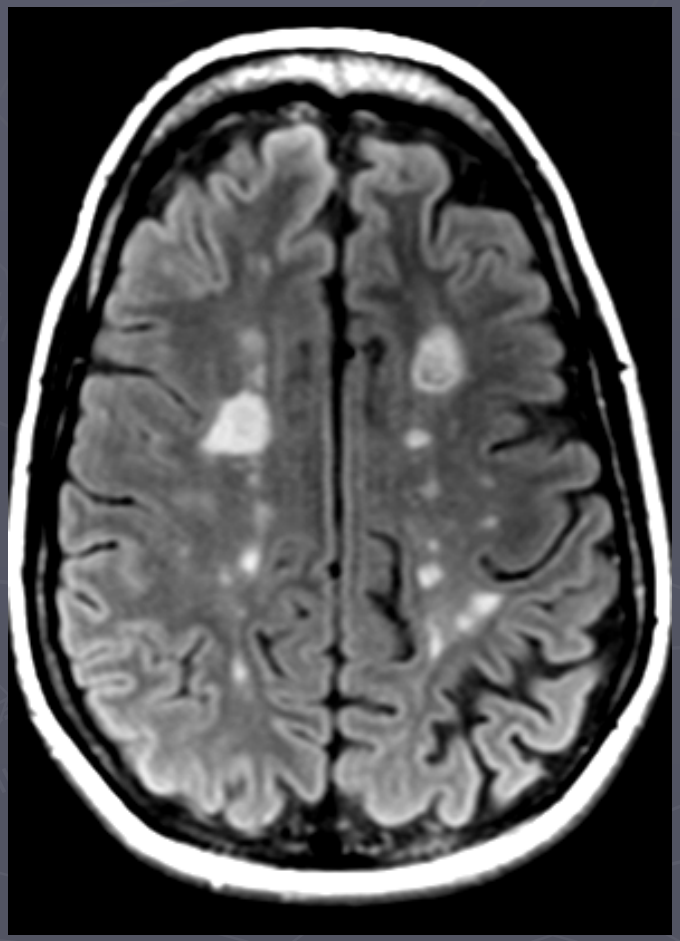
IRON IN MULTIPLE SCLEROSIS LESIONS:
(data courtesy of Liu Jiangtao, Beijing, China)

Phase from SWI data showing ring structures around MS lesions likely representing macrophage activity and a leakage of iron at the edge of the lesion.

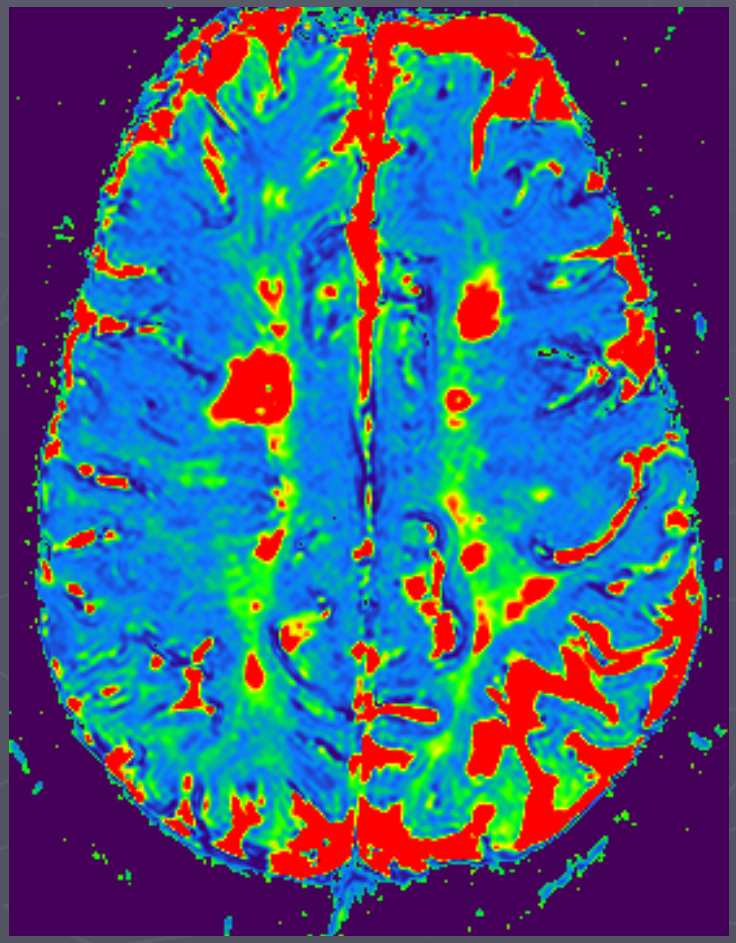


Using perfusion weighted imaging (PWI), it can be shown that most MS lesions show the same vascular abnormalities:

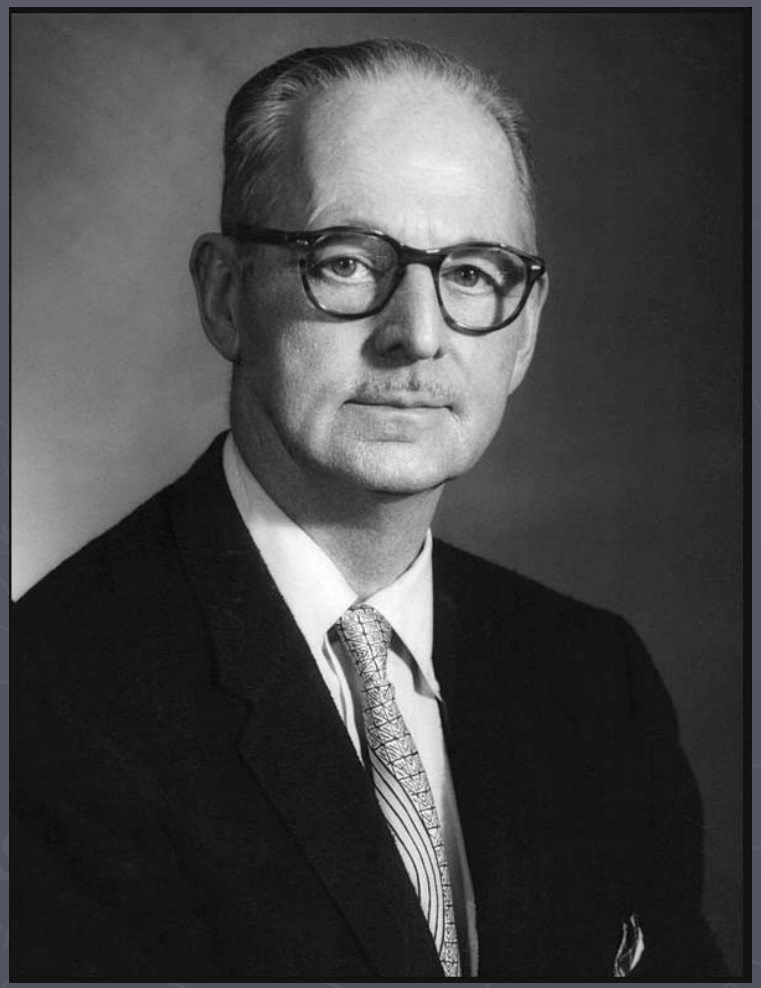
Anatomic evidence of lesions from FLAIR imaging



PWI shows all MS lesions have the same vascular characteristics



Recall 1935 work on venous obstruction



Tracey Putnam, Boston City Hospital, 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.

Venous Interventions: Dr. Monte Harvill

- Dialysis access venous interventions (angioplasty and stents)
- Venous thrombolysis
- Vena cava filters
- Venous access devices
- Pelvic congestion syndrome
- Varicose vein therapy

Interventional radiologists perform these procedures every day in Canada.

Complications of PTA

Ludyga T et al. Endovascular treatment for chronic cerebrospinal venous insufficiency: is the procedure safe? Phlebology. 2010; 25: 286-95.

- Access site complications
- Thrombosis
- Vessel rupture
- Distal embolization
- Flow-limiting dissection

Venous PTA: Dr. Monte Harvill

Why use percutaneous transluminal angoplasty?

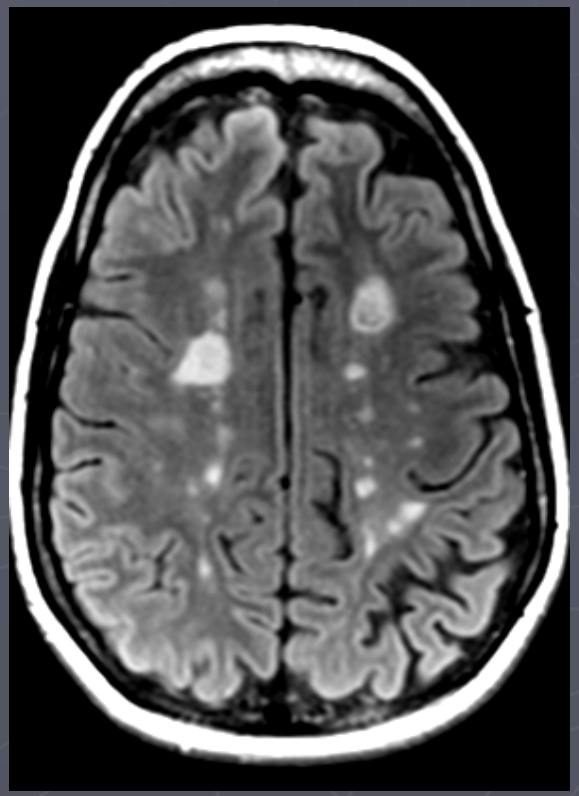
- Always the first choice for hemodynamically significant venous stenosis
- Valves (stuck, stiff, extra-competent)
- Membranous lesions
- Ostial lesions

The role of magnetic resonance imaging (MRI) in diagnosing and monitoring patients with multiple sclerosis (MS)

Part of the McDonald criteria is based on the number of non-enhancing and enhancing lesions seen in MR scans.

But there is much more possible today:

- Monitoring iron content
- Visualizing arteries and veins
- Measuring blood flow in each major vessel
- Quantifying perfusion to brain tissue



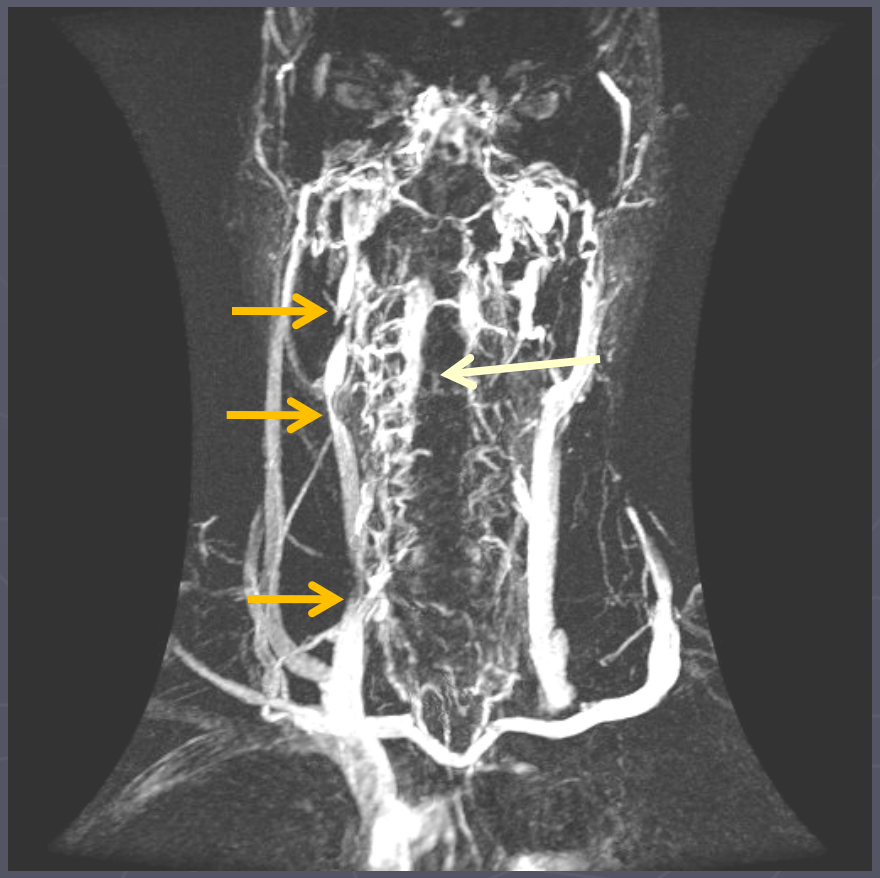
Why perform MR imaging before and after treatment?

We need to:

- monitor lesions and iron content
- monitor arterial, venous and CSF flow changes
- use the 3D data to help plan the intervention
- serve as a baseline to study the anatomy and flow after treatment if complications develop and generally monitor lesions, flow and iron over time

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

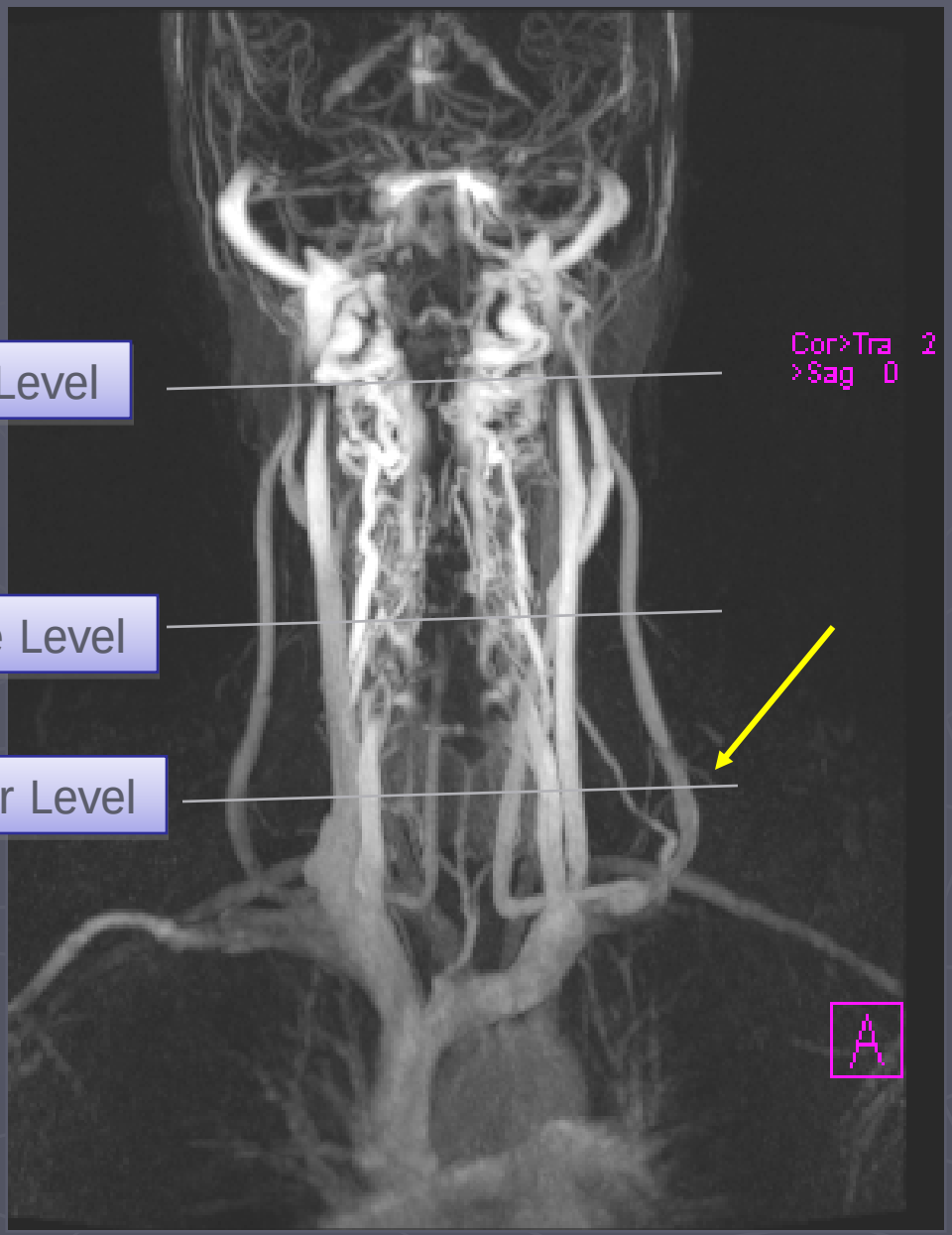
Collateral development on the same side as the stenosis



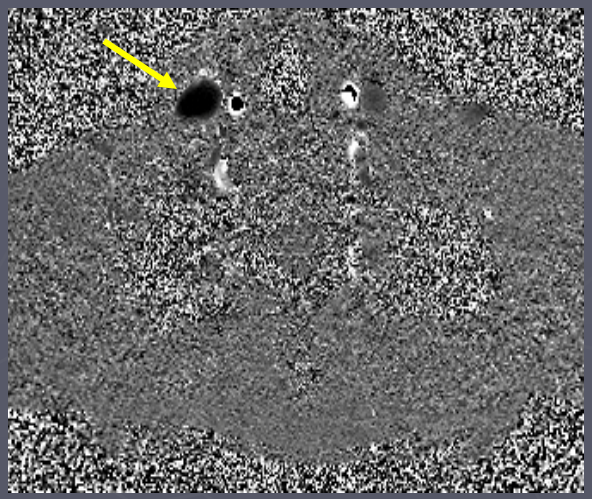
MR examples of CCSVI in MS patients where pre-treatment planning would reveal significant data that could affect how the veins are accessed.

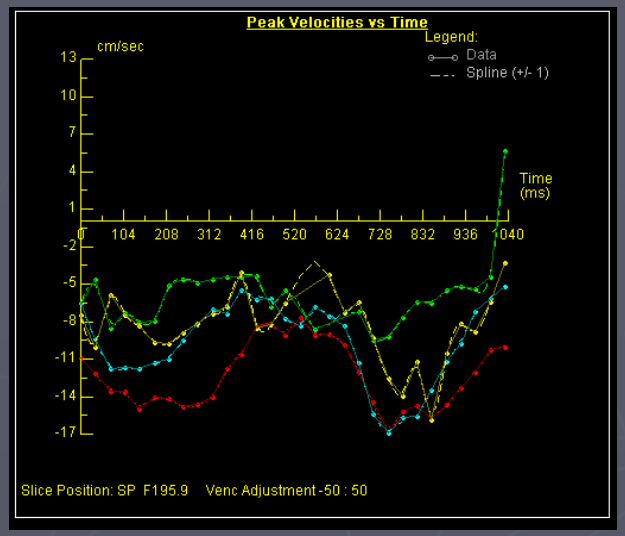
Stenosed RIJV

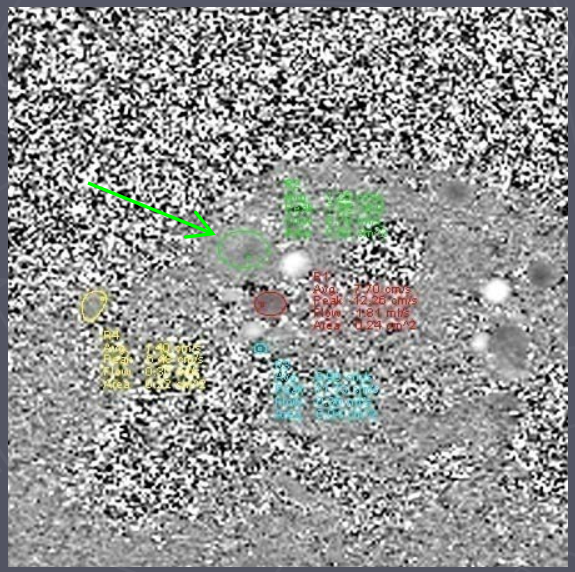
Choosing transverse planes for flow quantification

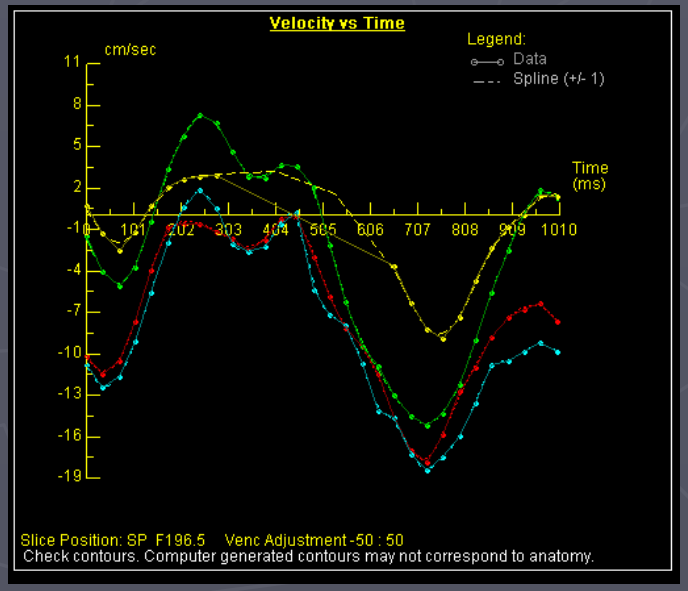


Flow Quantification







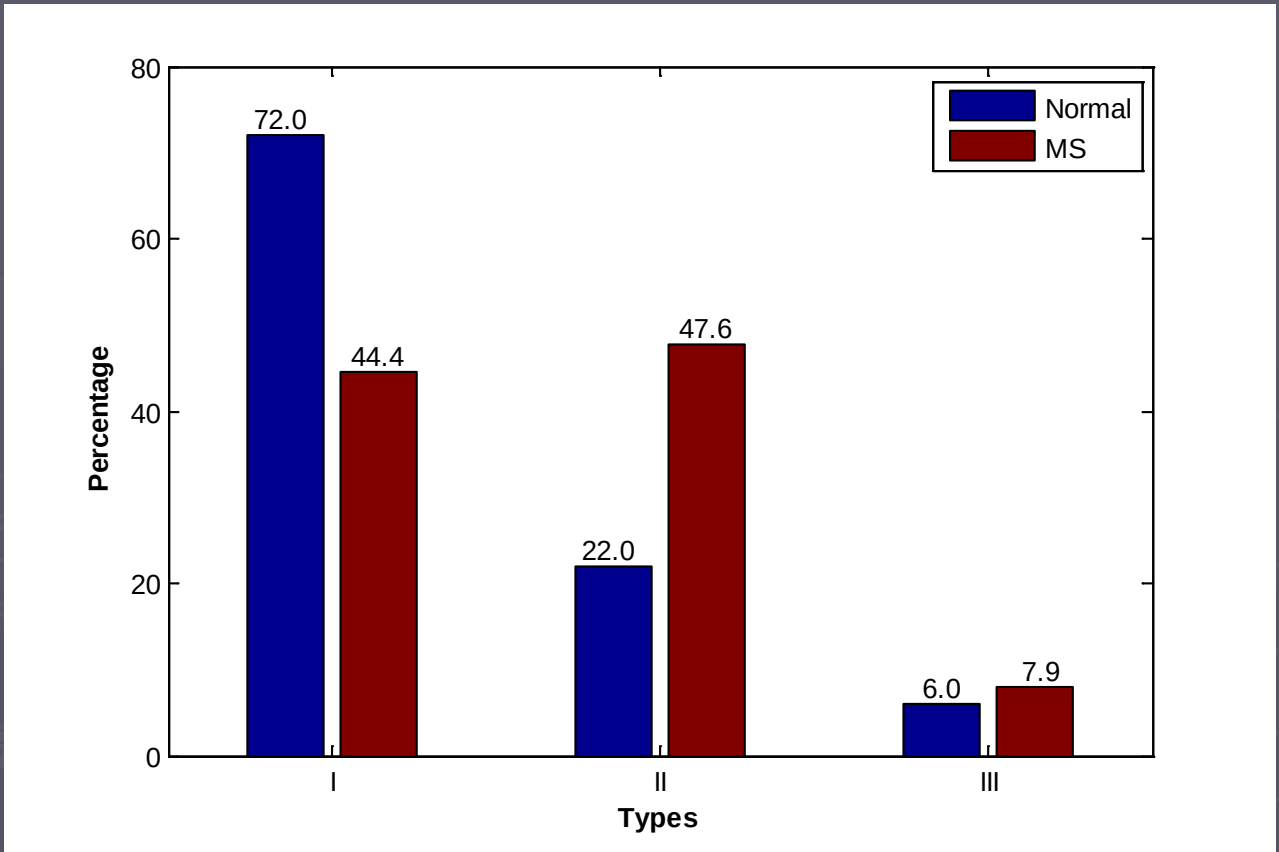


Categorization of 126 AFI MS patients vs. Normals w.r.t. R = total IJV/total arterial flow:

Type I: 0.67 < R < 1

Type II: 0.33 < R < 0.67

Type III: 0 < R < 0.33



Doepp F et al. “How does the blood leave the brain? A systematic ultrasound analysis of cerebral venous drainage patterns,” *Neurorad.*, 46: 565-570; 2004.

Pre-post treatment of a young Canadian with severe MS: What about the 1000s of Canadians who have been treated and need follow up? All MS patients get an MR anyway!

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

Possible characterization of venous abnormalities in CCSVI: 60 measures

Anatomical markers	***Possible Criteria Threshold***
Presence/Engorgement of Collaterals	*Present/Absent/Engorgement/Symmetry/Tortuous Shape*
External Jugular Vein	Absent/ Engorgement of CSA < 49mm²/ Symmetry/Tortuous shape
Anterior Jugular Vein	Absent/Engorgement of CSA < 25mm²/ Symmetry/Tortuous shape
Vertebral Vein	Absent/Engorgement of CSA < 25mm²/ Symmetry/Tortuous shape
Vertebral Plexus	Engorgement; Symmetry
Deep Cervical Vein	Absent/ Engorgement of CSA < 25mm²/ Symmetry/Tortuous shape
Stenosis in Neck	*Present/Absent*
IJV stenosis superior to C3 (UL)	CSA < 12.5mm²
IJV stenosis inferior to C3 (LL)	CSA < 25.0mm²
Truncular Venous Malformation	Present/Absent
Missing IJV (s)	One or Both IJVs missing including superior/inferior jugular bulbs
Missing Vertebral Veins	Present/Absent at the C6 level
Missing Deep Cervical Veins	Present/Absent
Stenosis in Thoracic Cavity	*Present/Absent*
Azygous stenosis	Stenosis of 75% of Azygous CSA
Azygous compression between heart and spine	Present/Absent
Missing Azygous	Present/Absent
Missing Hemi-azygous	Present/Absent
Missing both Azygous and Hemi-azygous	Present/Absent
Azygous engorgement	CSA>1cm²

Valves
Constrast Discontinuity at Confluence
Biphasic Flow
Jetting Effect
Developmental Anomalies
Narrowing at the Confluence
SWI Markers
Small veins
Visibility of veins
Iron content
Pulvinar Thalamus
Putamen
Globus Pallidus
Caudate Nucleus
Red Nucleus
Substantia Nigra
Dentate Nucleus
Micro-bleeds
Lesions

Quantitative Flow Markers	***Possible Criteria Threshold***
C6 level flow	*Present/Absent*
Dominant IJV: Sub-Dominant IJV	> 4:1
Dominant vein: Sub-Dominant vein	> 4:1
Total venous flow	< 8 ml/s
Total IJV flow	< 5 ml/s
Total percent of venous flow carried by IJV	< 32%
High velocity of flow through veins	> 25 cm/s
Low velocity of flow through veins	< 1 cm/s
C2 level flow	*Present/Absent*
Dominant IJV: Sub-Dominant IJV	> 5:1
Dominant vein: Sub-Dominant vein	> 5:1
Reflux	*Present/Absent*
Reflux of flow in IJV	> 10%
Percent of CDC that IJV demonstates low flow and reflux flow	> 30%
% of CDC Vertebral Vein shows reflux	> 30%
% of CDC Deep Cervical Vein shows reflux	> 30%
% of CDC External Jugular Vein shows reflux	> 30%

Qualitative Flow Markers	***Preferred MR Imaging Method***
Contrast Discontinuity through vessel	3D TRI
Loss of signal	2D TOF
Inhomogeneous signal at confluence	2D TOF

Conclusions

- Canada can be a leader in this direction but must have:
- 1) proper follow up for patients who have had treatment
- 2) a national registry to monitor patient outcomes
  - Minimal to no funding
- 3) a national trial of on the order of 1000 normals and 1000 patients marrying ultrasound, MRI and venous angiography
  - This requires dedicated funding just for this CCSVI study.
  - One avenue to fund this might be via a centers-of-excellence programme.
- If Canada takes action now, it can have answers in two years.