

WAYNE STATE UNIVERSITY



Measurement of Flow in MS Patients using MRI

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Conflict of Interest Statement

I am affiliated with:
Wayne State University
McMaster University
The MRI Institute for Biomedical Research
and have an interest in
MR Innovations, Inc
and have support from
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Why perform MR imaging before and after treatment?

We need to:

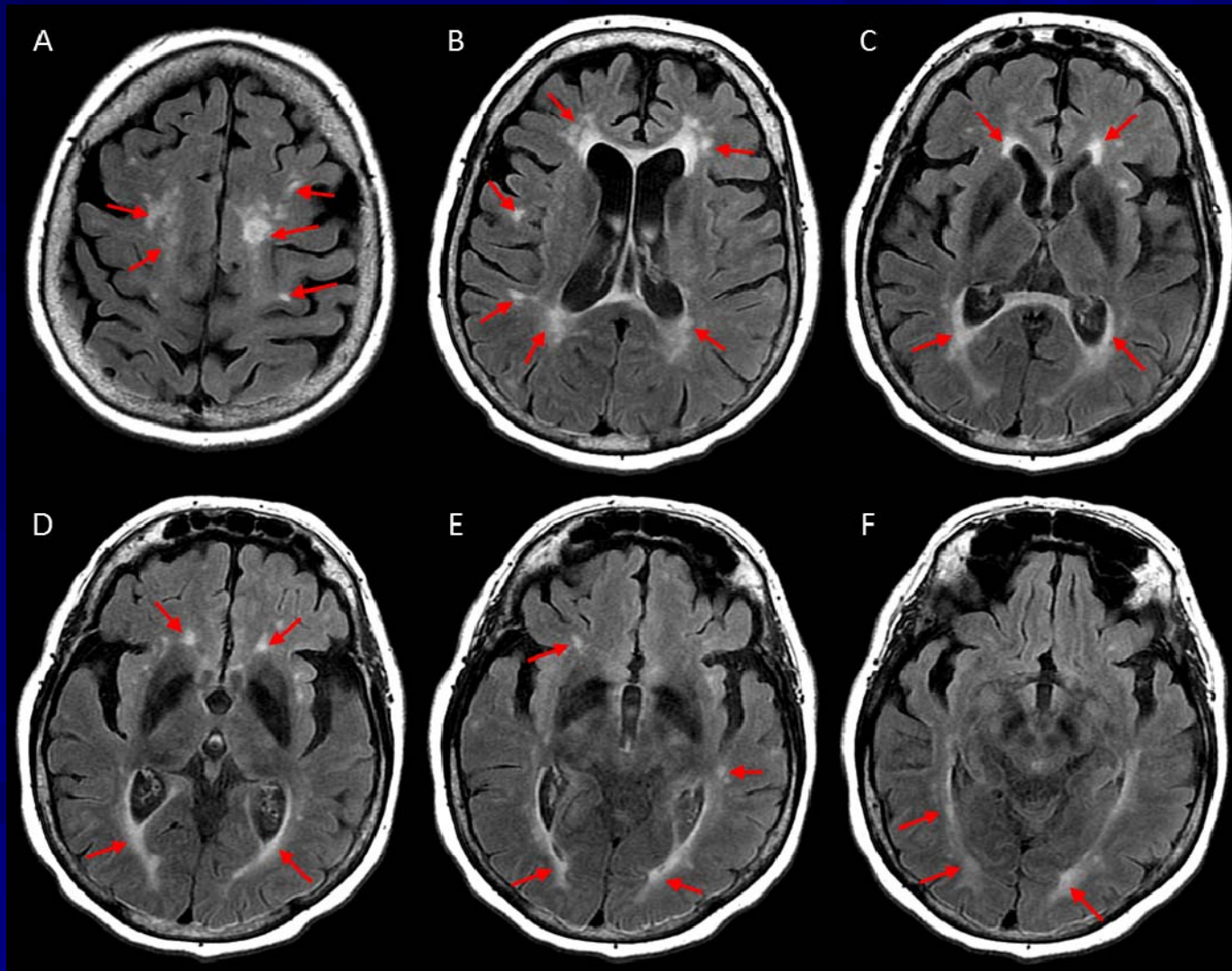
- monitor lesions and iron content quantitatively
- monitor arterial, venous and CSF flow changes
- use the 3D vascular data to plan the intervention, (and if appropriate avoid the intervention)
- categorize different types of MS populations
- serve as a baseline pre-treatment
- make meaningful correlations between post treatment clinical status and current vascular hemodynamics
- track anatomic changes, assess effects of other treatments, and assess the need for reintervention in a noninvasive manner.

Conventional MS MRI Protocol

Conventional Neuro MS: Tier I

Sequence	Time (approx.)
Axial T2 Head	4:30
Saggital FLAIR Head	5:22
Axial T1 Head (prefer 3D)	4:30
Saggital T2/PD Cspine	3:40
Saggital T1 Cspine	3:30
Select Axial T2 Cspine through lesions	4:00 est
Inject Gadolinium	5:00
Axial T1 Head post Gad	4:30
Cspine T1 FS post Gad	3:40
Total Time	38:42

NEURO-ANATOMICAL INFORMATION:
Multiple white matter lesions from high resolution 3D
FLAIR including diffuse WM hyper-intensities.



CCSVI MS MRI Protocol: Tier II(a)

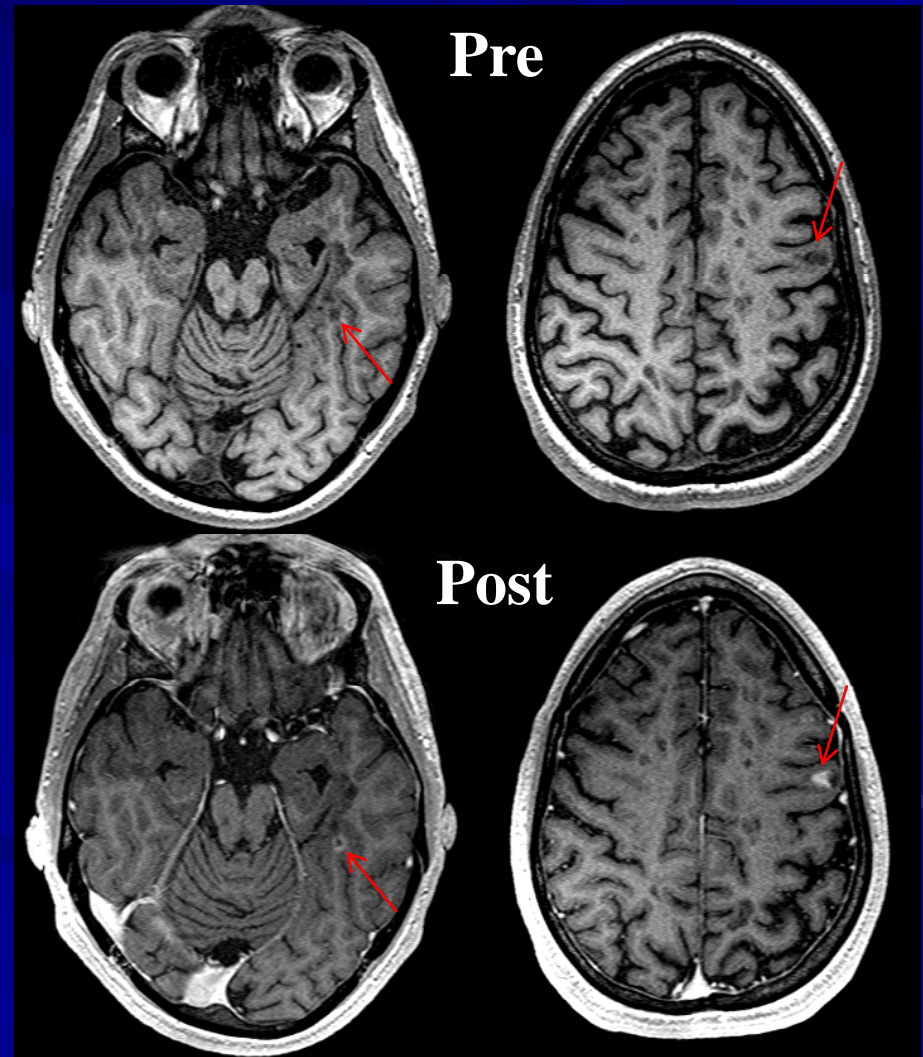
Head and Neck without Contrast

Sequence	Time (approx.)
Axial T2 Head	4:30
Sagittal FLAIR Head	5:30
Axial T1 Head (prefer 3D)	4:30
Sagittal T2/PD Cspine	3:40
Sagittal T1 Cspine	3:30
Select Axial T2 Cspine through lesions	4:00*
2D TOF MRV Neck	7:00
Flow Quantification at C2/C3 and C6/C7 with Venc = 50cm/s	6:00
Total Time	34:40 *(38:40)

Blood Brain Barrier Breakdown: T1 WI Post-Contrast Enhancement of Lesions

Data from a secondary progressive MS patient.

Pre-contrast T1 weighted images show hypo-intense lesions which enhance post contrast injection presumably representing acute lesions associated with a breakdown of the blood brain barrier.

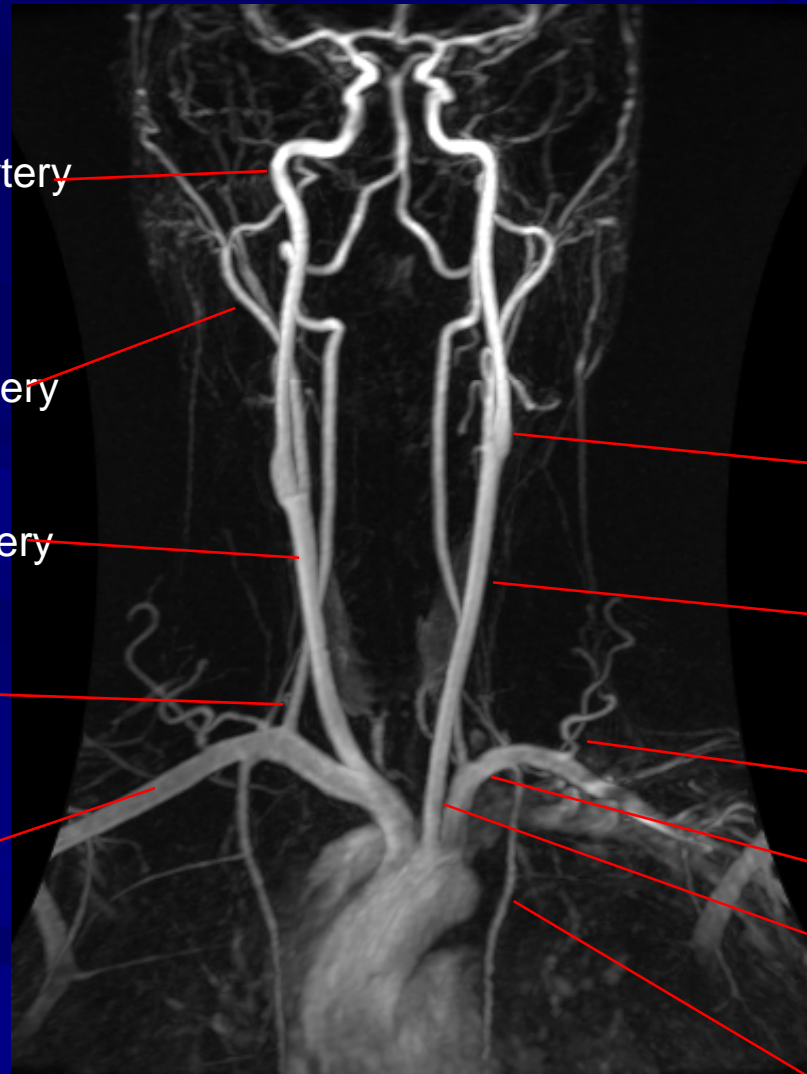
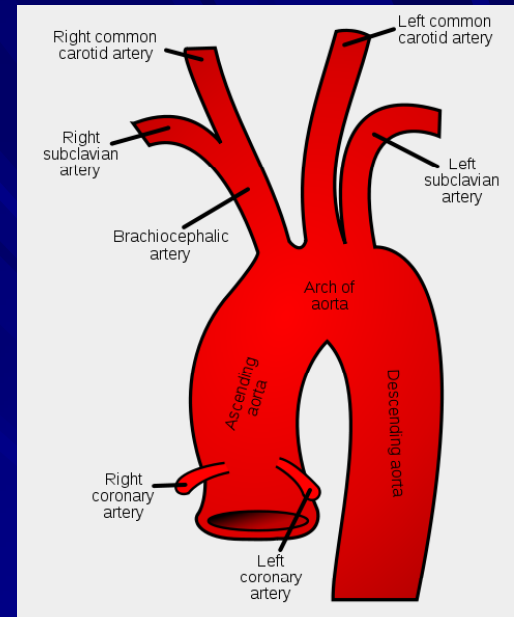


CCSVI MS MRI Protocol: Tier II(b)

Head and Neck with Contrast and without 2D TOF MRV

Sequence	Time (approx.)
Axial T2 Head	4:30
Sagittal FLAIR Head	5:30
Axial T1 Head (prefer 3D)	4:30
Sagittal T2/PD Cspine	3:40
Sagittal T1 Cspine	3:30
Select Axial T2 Cspine through lesions	4:00*
3D CE MRAV Neck	2:30
Flow Quantification at C2/C3 and C6/C7 with Venc = 50cm/s	6:00
Axial T1 Head post Gad	4:30
Cspine T1 FS post Gad	3:40
Total Time	38:20 *(42:20)

Major Arteries of the Neck



Right internal carotid artery

Right external carotid artery

Right common carotid artery

Right vertebral artery

Right subclavian artery

carotid bulb (bifurcation)

Left common carotid artery

Thyrocervical artery

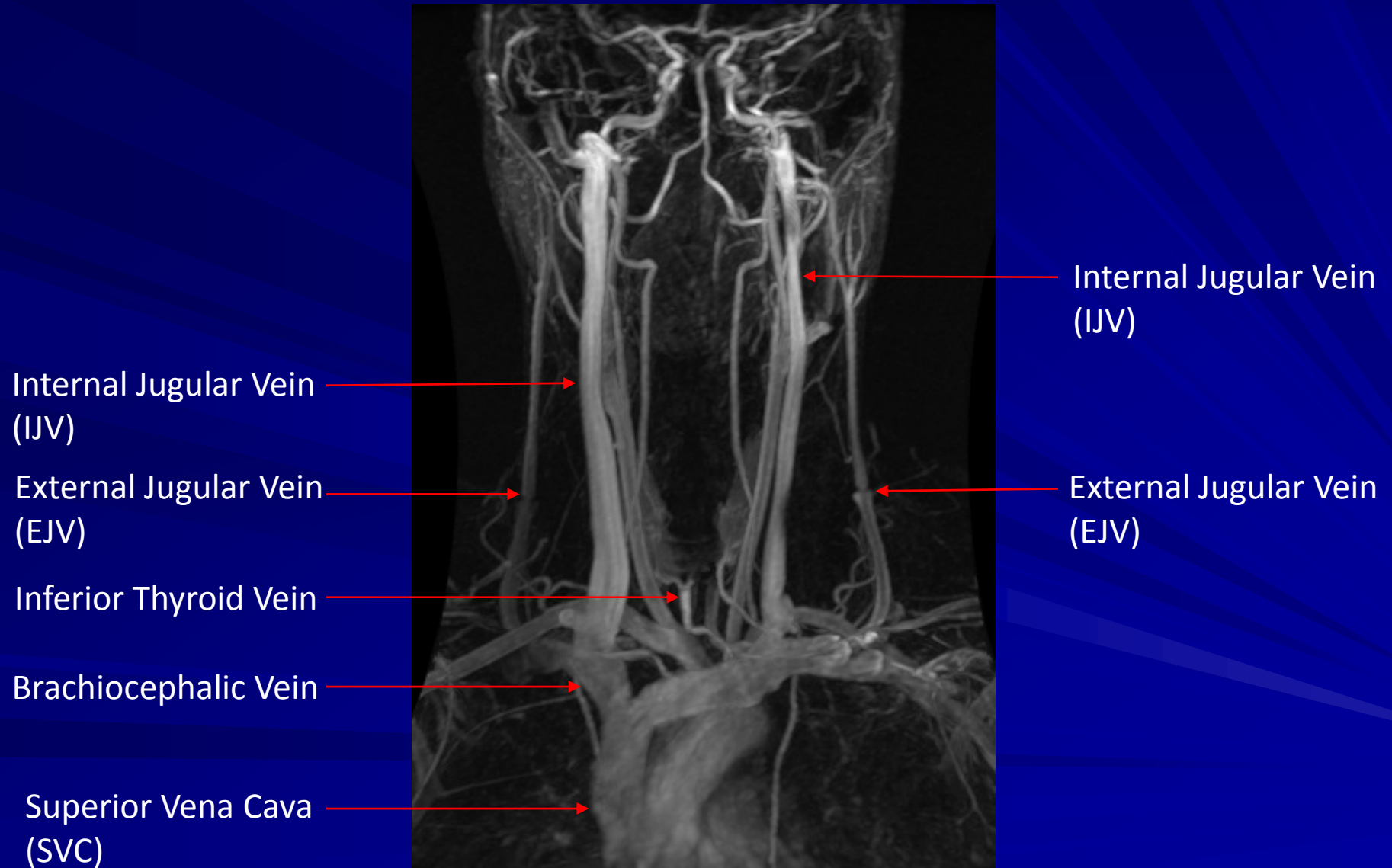
Left subclavian artery

Innominate artery
(brachiocephalic truck)

Internal thoracic artery

Coronal MIP: Time resolved 3D CE MRA of arterial phase

Major Extracranial Veins of the Neck: Critical to also gain experience in visualizing collaterals



Coronal MIP: Time resolved 3D MRAV of the early venous phase (0.6x0.6x2.0mm³)

Dural Sinus by 3D High Resolution

Superior Sagittal Sinus



Straight Sinus

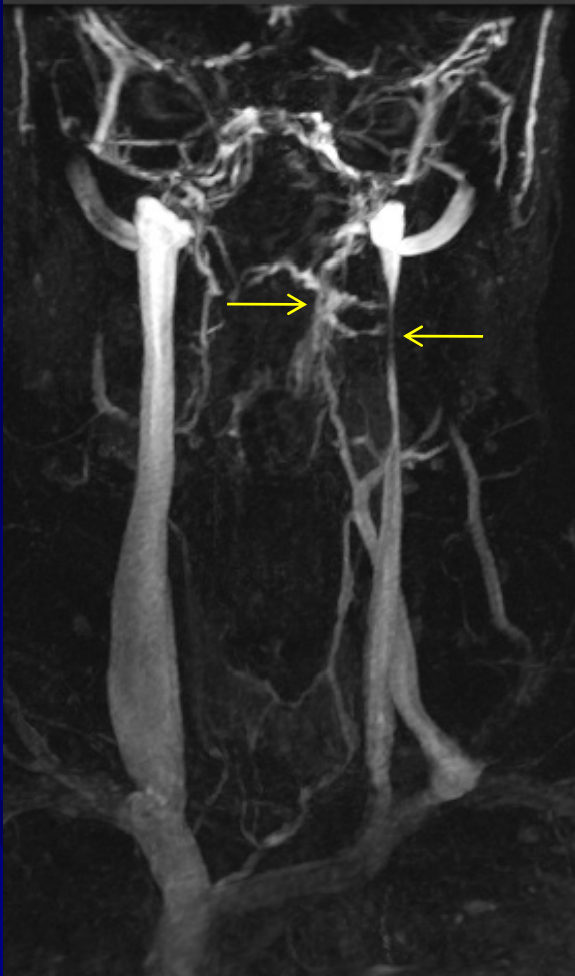
Sigmoid sinus



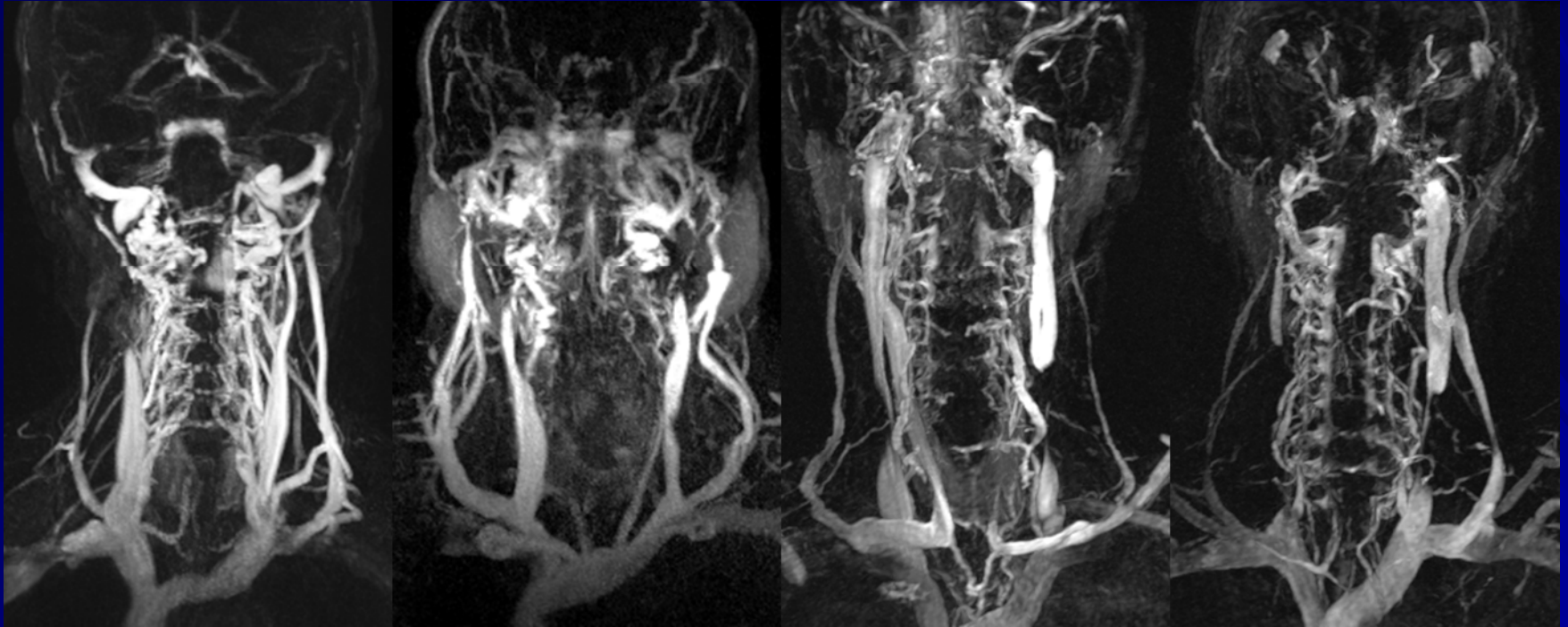
Transverse Sinus

(Right: Blue, Left: Red)
Sagittal MIP: CE 3D VIBE, Axial MIP: CE T1WI with Fat Signals Saturated

ABNORMAL VENOUS STRUCTURE:
Upper level stenosis and string stenosis.
Notice the presence of collaterals.



VASCULAR ANATOMIC ABNORMALITIES



Venous abnormalities, including stenosis and atresia, observed in dynamic contrast-enhanced 3D MR venography.

Coronal MIP: Time resolved 3D MRV of the early venous phase

Phase Contrast Flow Quantification at 2 Levels in the Neck

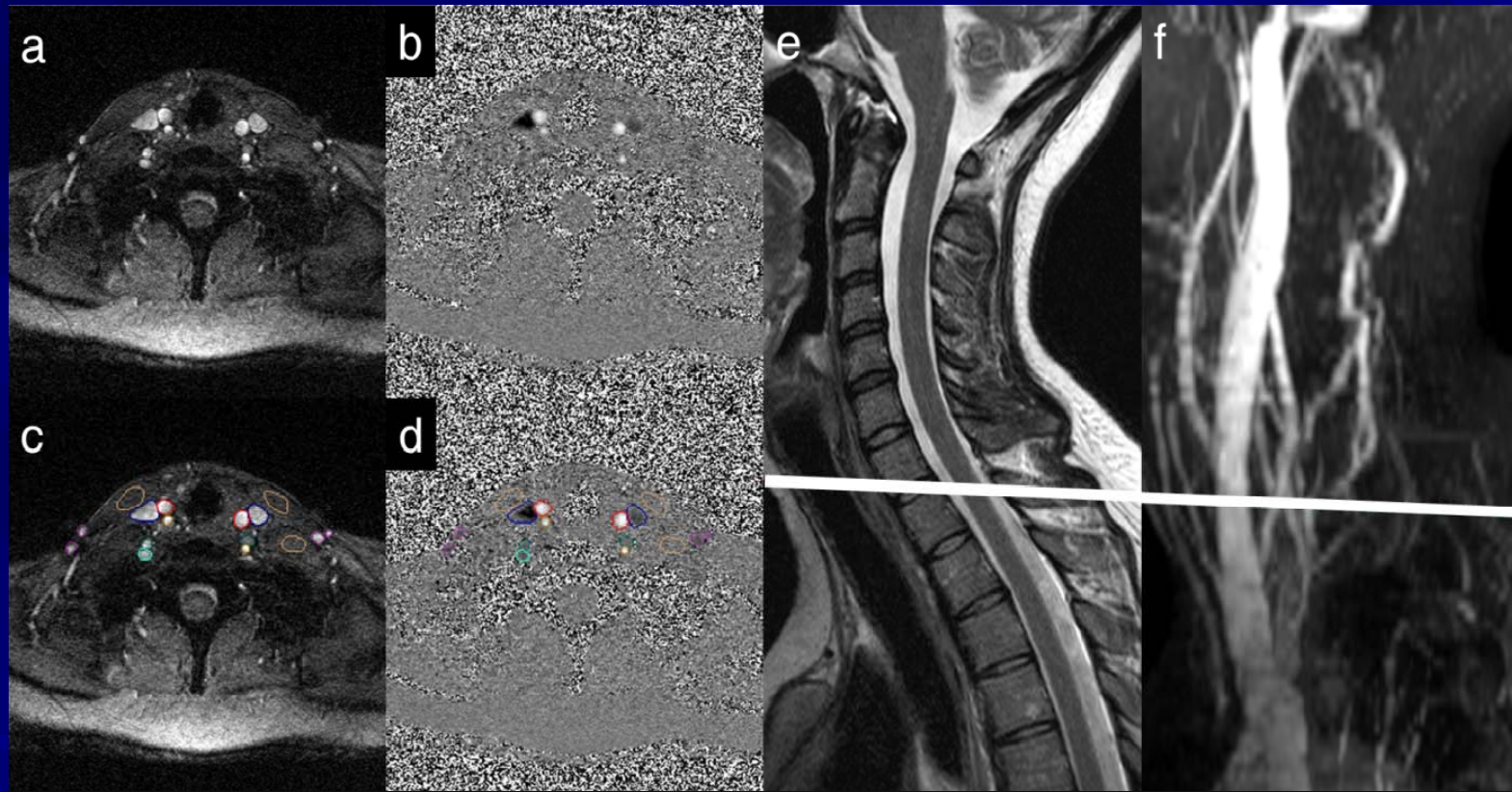


C2/C3 CORE



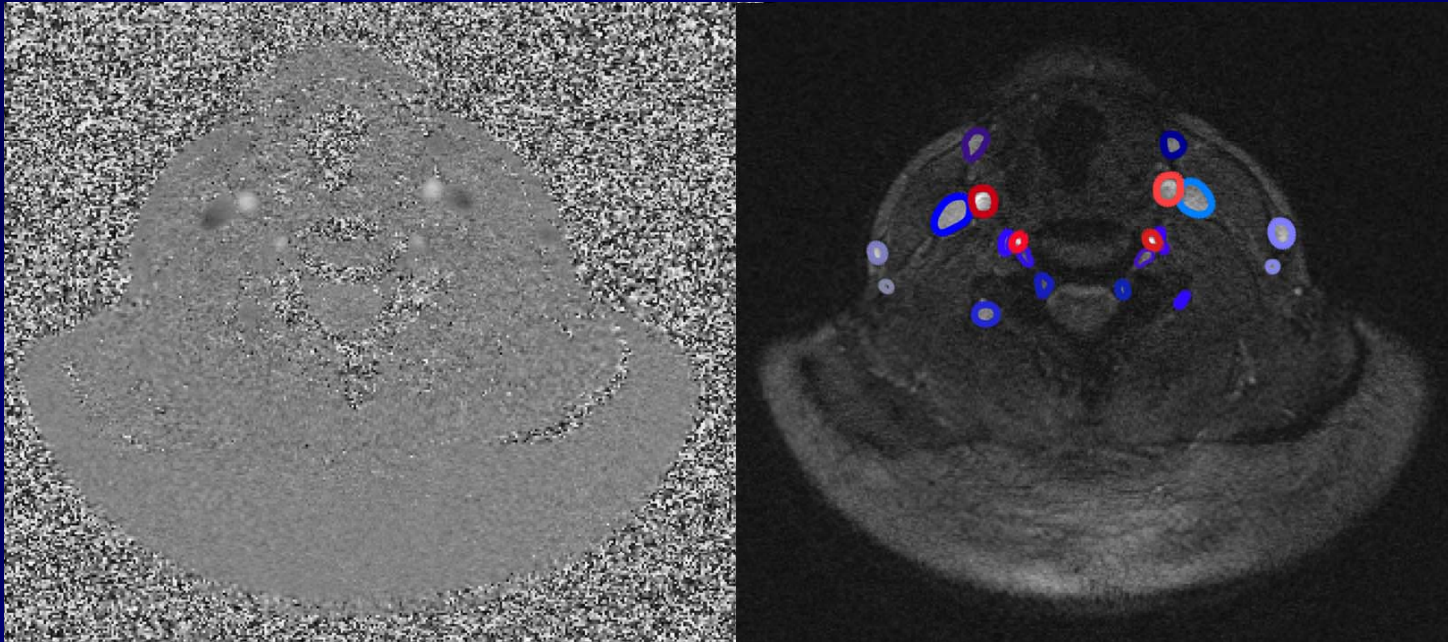
C5/C6/C7 CORE

Flow at the cross sectional cut at C6/C7



High in-plane resolution of 0.5mm x 0.5mm is used.

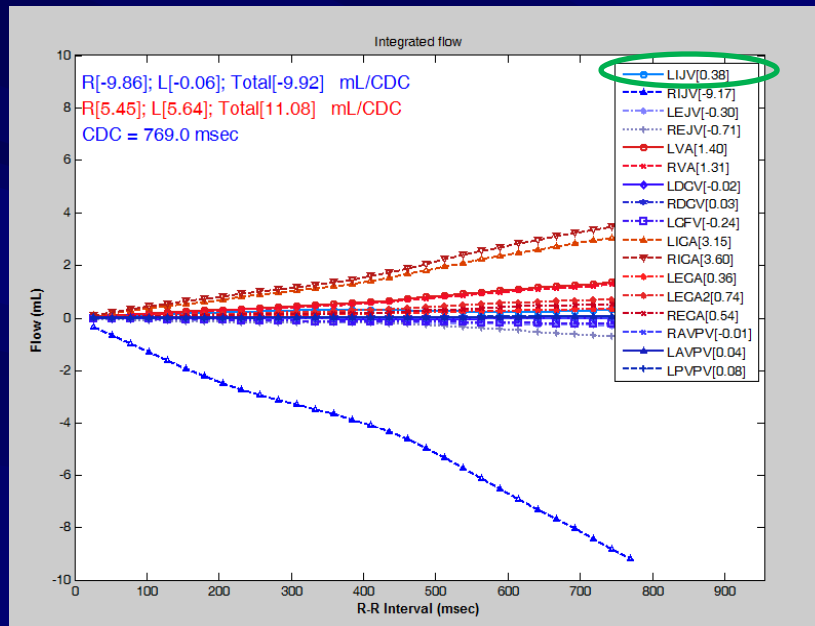
Flow quantification with PC-MRI



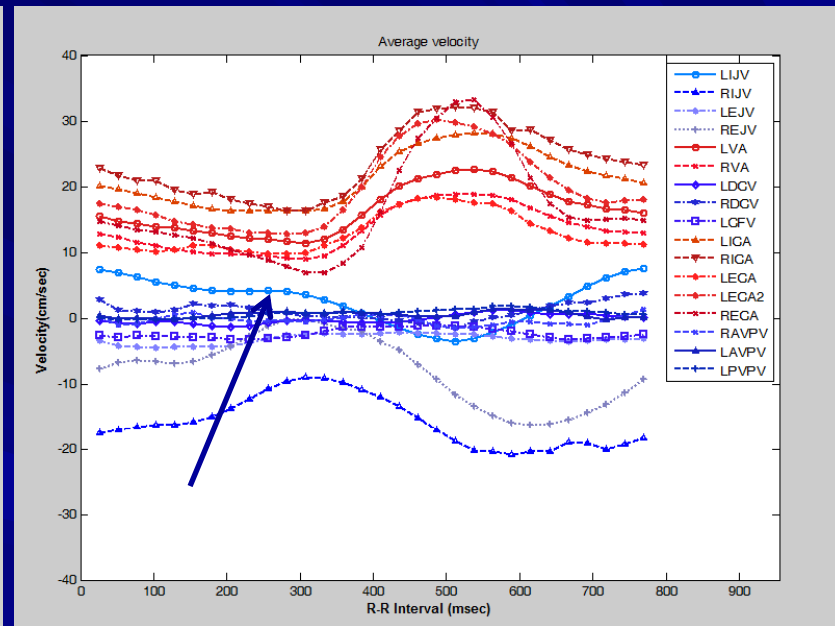
- ❖ Vessel contours (red-arteries, blue-veins) were drawn on both magnitude and phase images
- ❖ Only phase image was used for flow quantification

Flow analysis at C2-C3 Level

Integrated Flow Plot



Average Velocity Plot



The LIJV has a reflux in its flow pattern which likely extends back to the inferior petrosal sinus.

The goal of early MR imaging flow studies

To examine the extracranial flow characteristics using MR imaging methods (especially IJV flow) in order to identify risk factors or potential biomarkers associated with venous flow in the MS population.

Study design

Subjects:

300 MS Patients
recruited at Applied fMRI in San Diego
22 were excluded due to degraded
image quality,

The data from the remaining 278 MS patients
will be reported here.

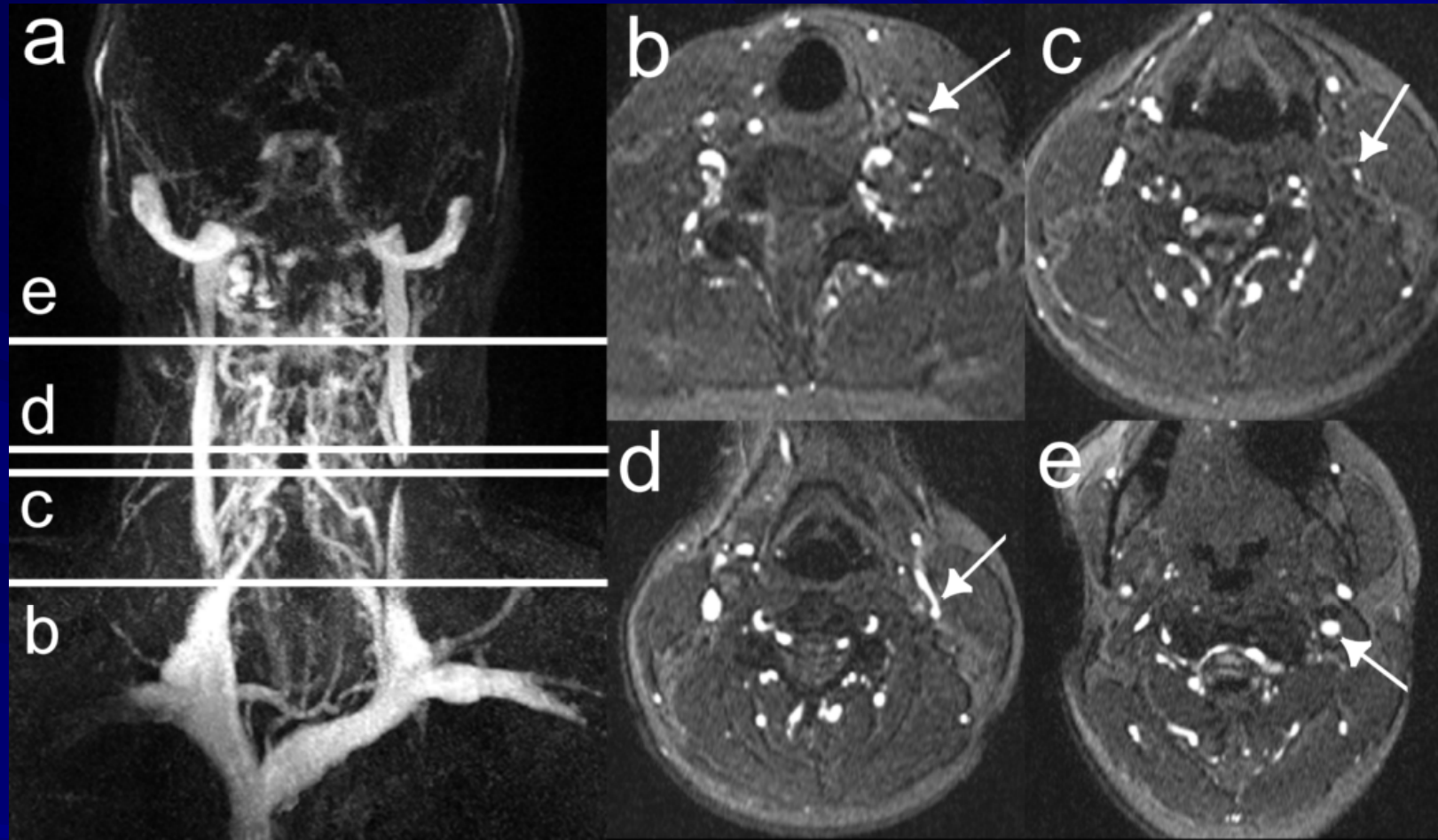
MR imaging protocol (CCSVI protocol): Data collected on a 3T Siemens TRIO

Sequence	CE-MRA	TOF-MRV*	PC-MRI**
Orientation	Coronal	Transverse	\perp IJV@C6
TR (ms)	3.06	21	14.4
TE (ms)	1.25	4.78	4.41
Flip Angle	19°	60°	25°
Field-of-View (mm x mm)	340 x 255	320 x 255	256 x 256
Resolution (mm x mm x mm)	0.9 x 0.9	0.63 x 0.63	0.57 x 0.57
Bandwidth (Hz/pixel)	590	215	530

* arterial saturation band = 40mm, separation from slice = 10mm

** *VENC = 50cm/sec; retrospective gating; 25 phases/R-R interval*

Stenoses identification with CE-MRA and TOF-MRV



Stenosis threshold = 25 mm^2 (C6) / 12.5 mm^2 (C2).

1/3 of a normal IJV cross-sectional area with a diameter of 1cm^(1,2) at C6.

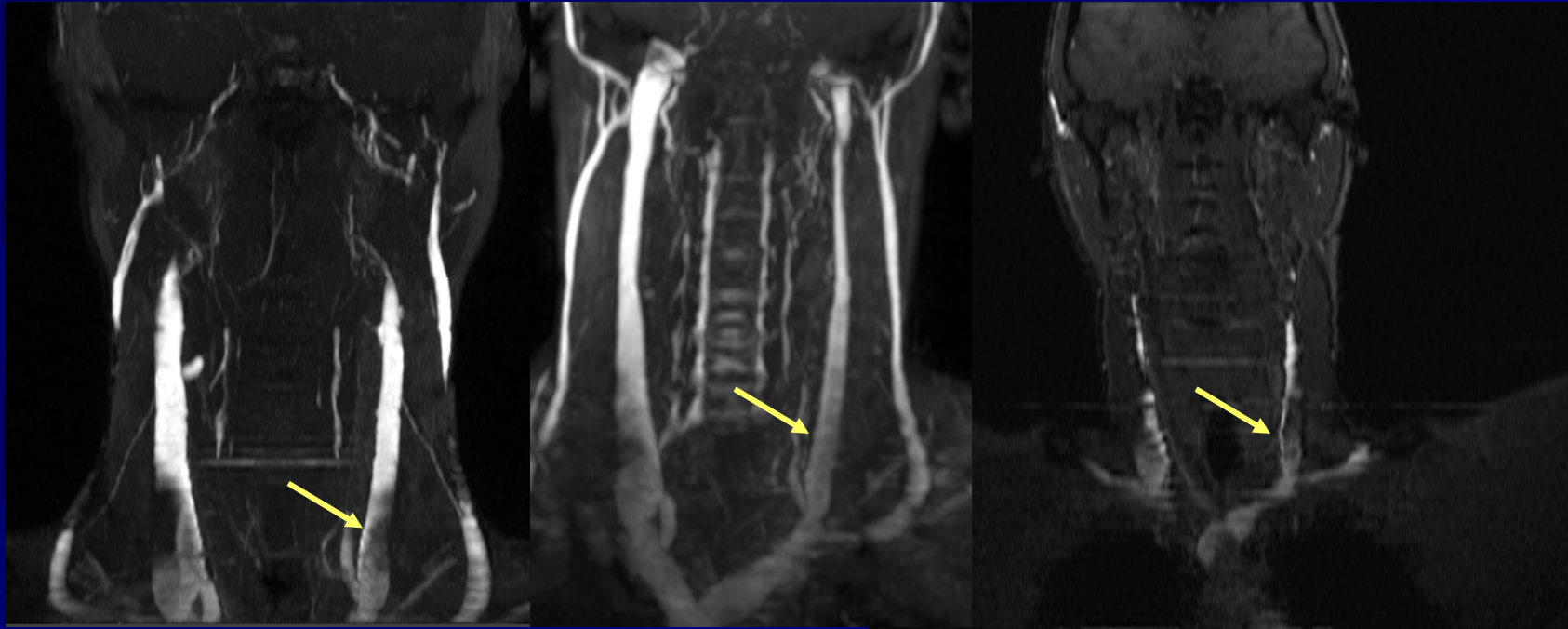
A threshold of 30 cm^2 was used by Mayer³ (US, supine position).

1. Tartiere et al., Crit Care, 2009; 2. Furukawa et al., Romanian J Legal Med, 2010
3. Mayer et al. J Neurol Neurosurg Psychiatry, 2011

Results – Anatomical assessment with CE-MRA + TOF-MRV

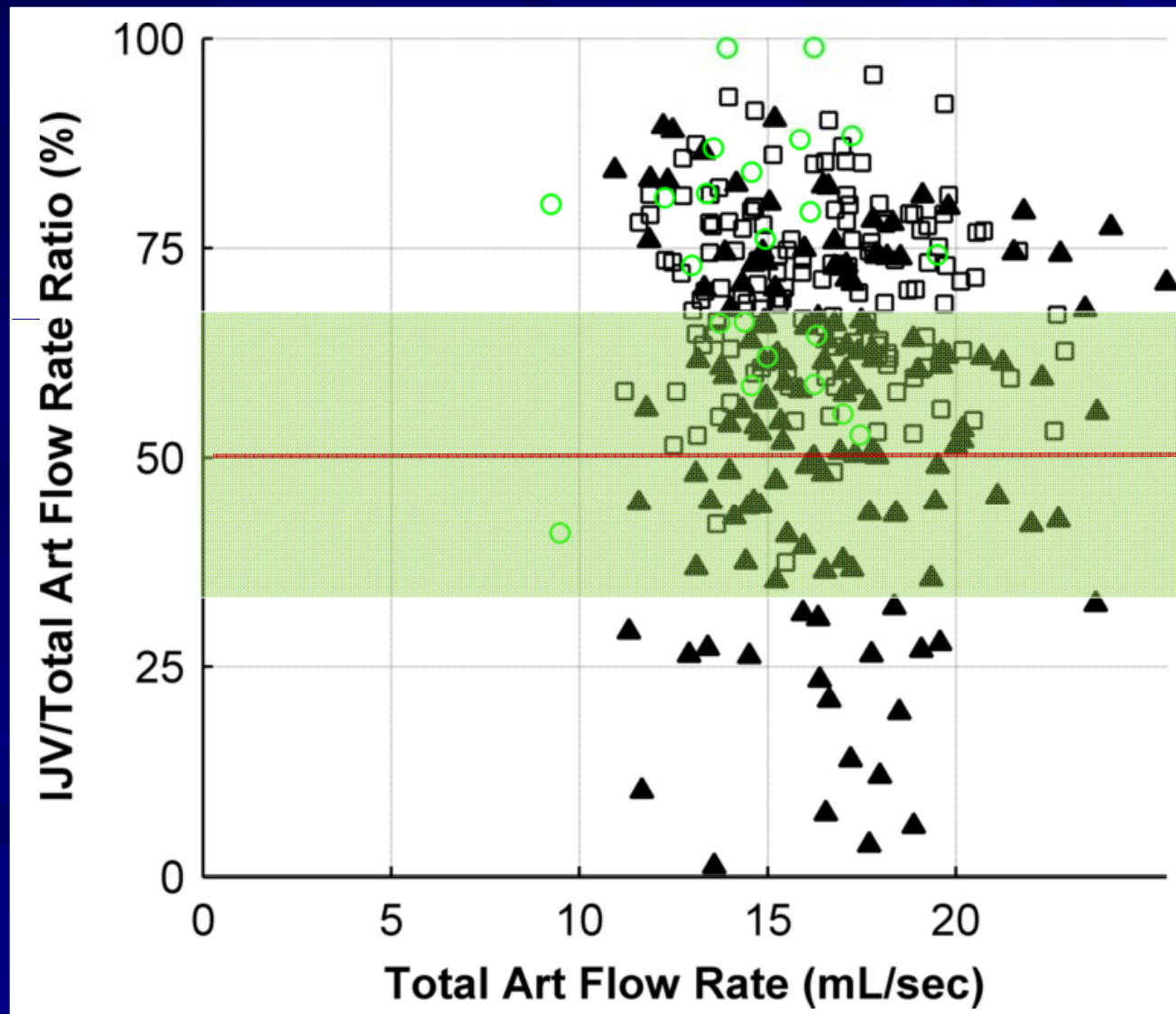
Stenotic	Unilateral C6 stenosis	51 (36%)
	Unilateral C2 stenosis	50 (35%)
	Bilateral C6 stenosis	27 (19%)
	Bilateral C2 stenosis	15 (10%)
	Diffuse stenosis	16 (11%)
	Atresia	26 (18%)
	Aplasia	0 (0%)
	Total	143
Non-Stenotic		135

Pre-post treatment of a young Canadian with severe MS



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

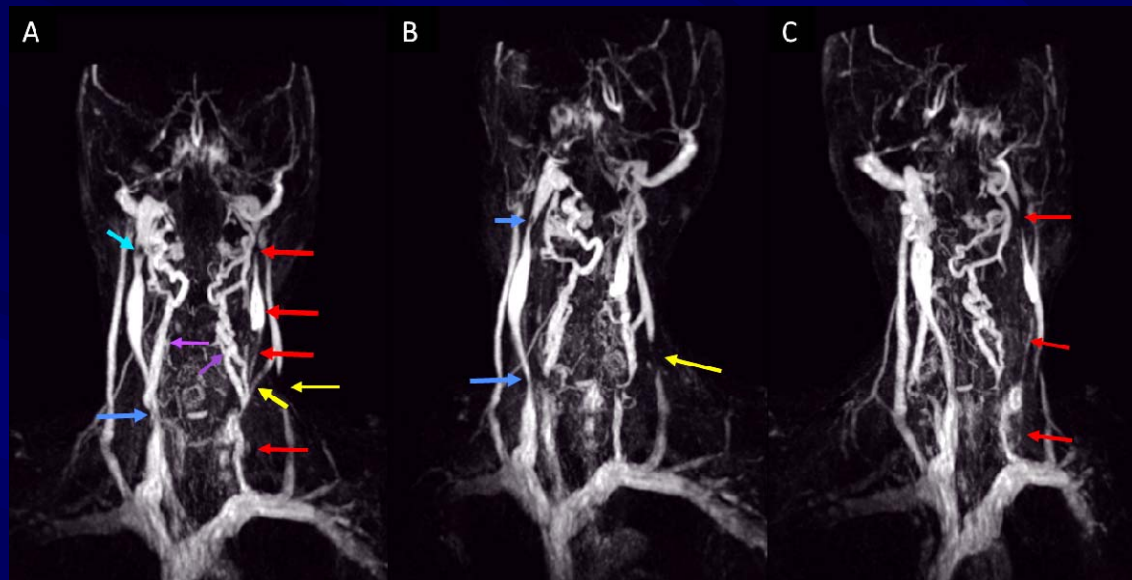
Total internal jugular flow as a biomarker for a sub-population of MS patients



Type 1

Type 2

Type 3

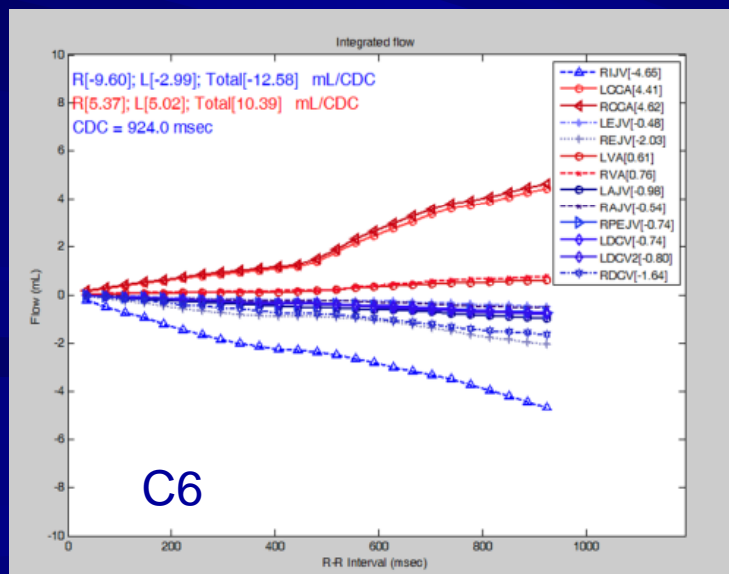


LIJV is stenosed at UL
and truncated at LL

RIJV is stenosed at LL

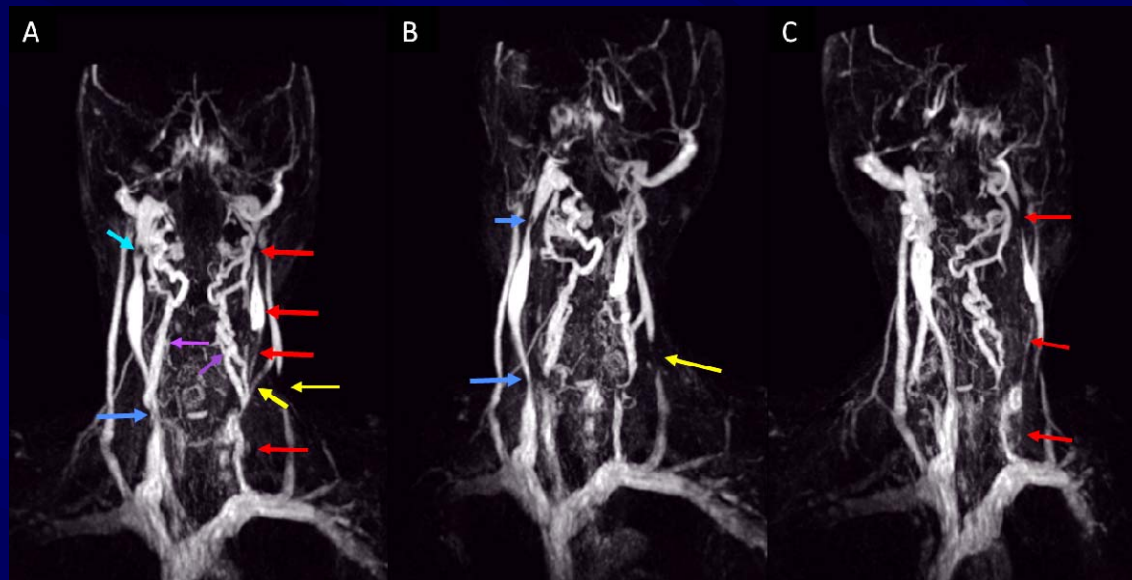
LEJV is stenosed at LL

Note the flow is carried
mostly by only one
internal jugular vein.



Flows for all major veins
can be determined and
for all major arteries to
study the cardiovascular
input/output to the brain.
This will complement
the PWI data nicely.

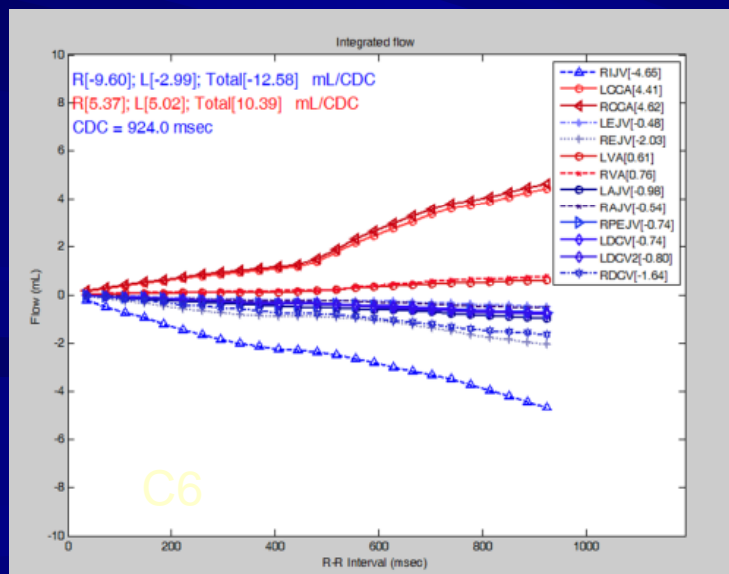
Parkinson's study: CCSVI look alike



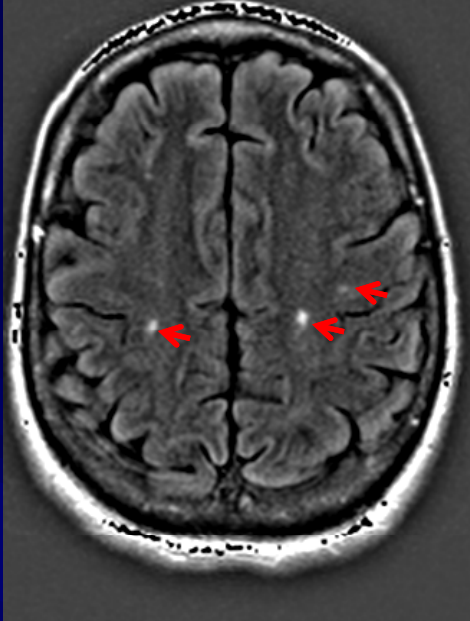
LIJV is stenosed at UL
and truncated at LL

RIJV is stenosed at LL

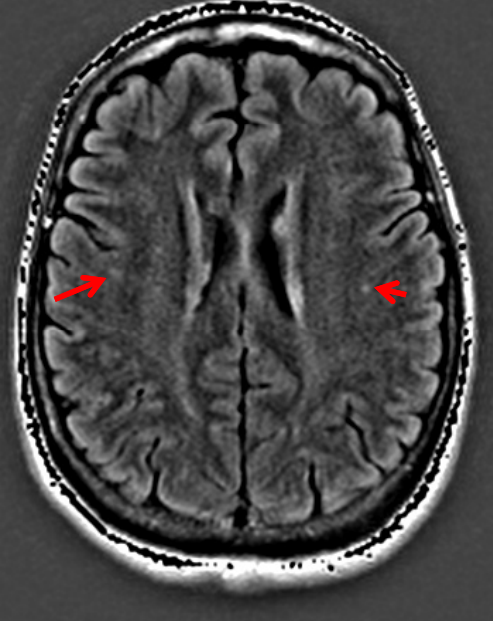
LEJV is stenosed at LL



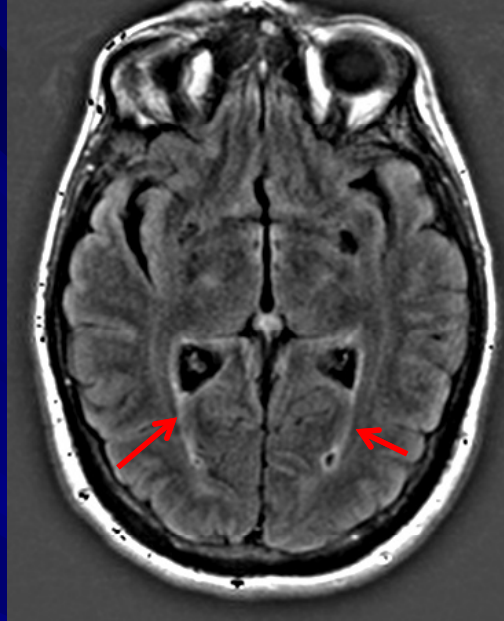
2005 scan



2005 scan

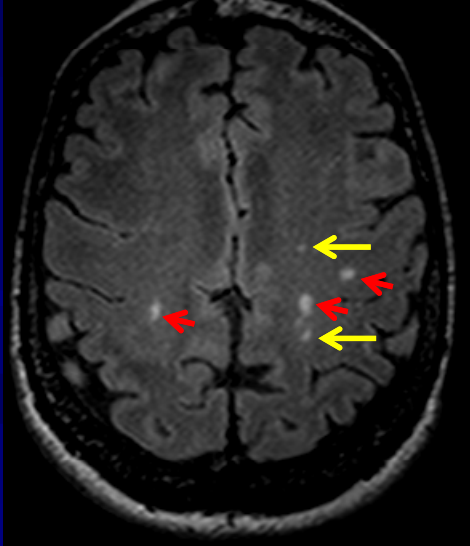


2005 scan

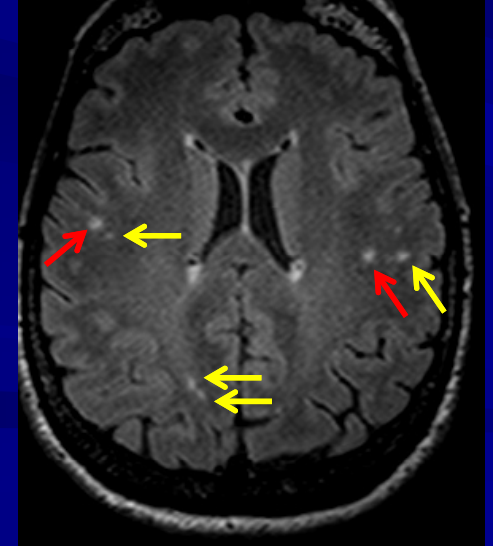


Lesions are seen in 2005 scans-red arrows; the lesions are at the same level as seen in the 2010 scans

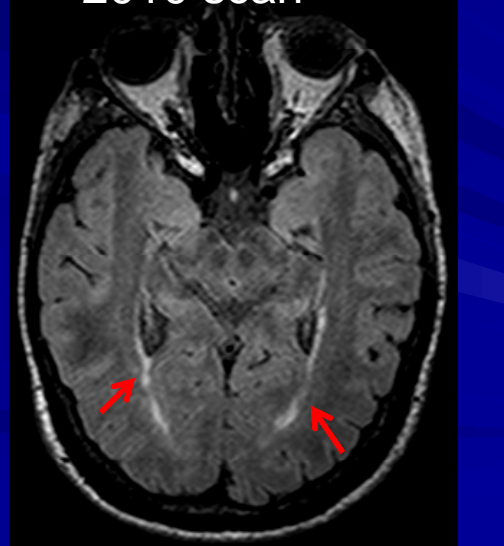
2010 scan



2010 scan



2010 scan

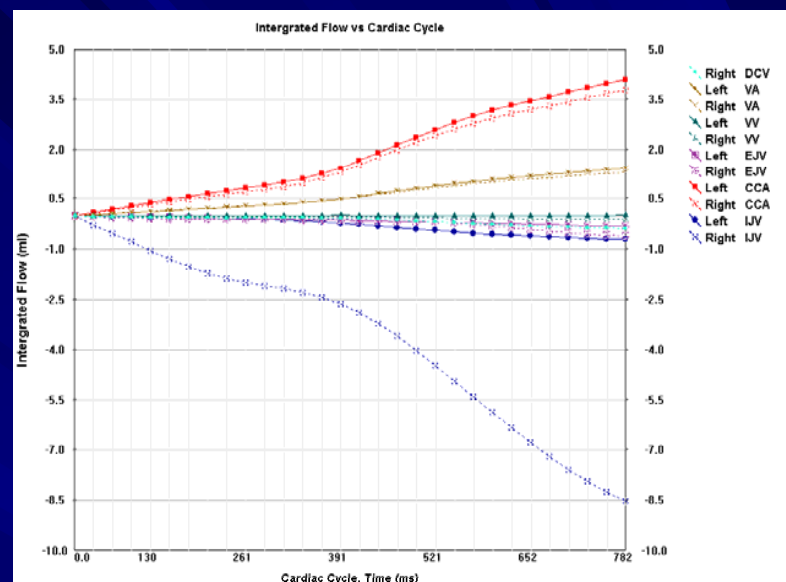
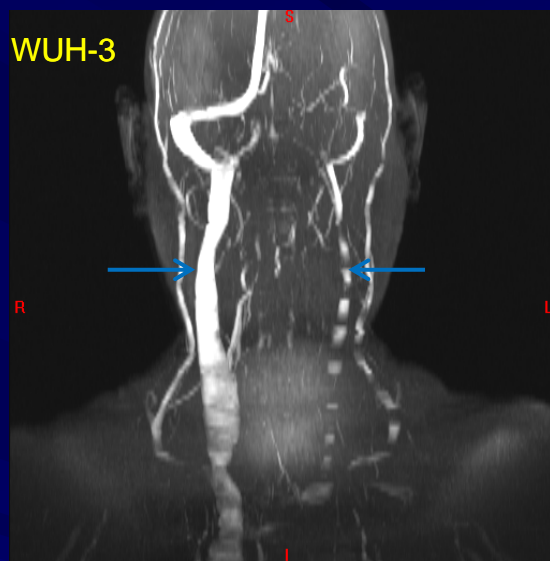


The 2010 scans shows multiple new lesions: yellow arrows

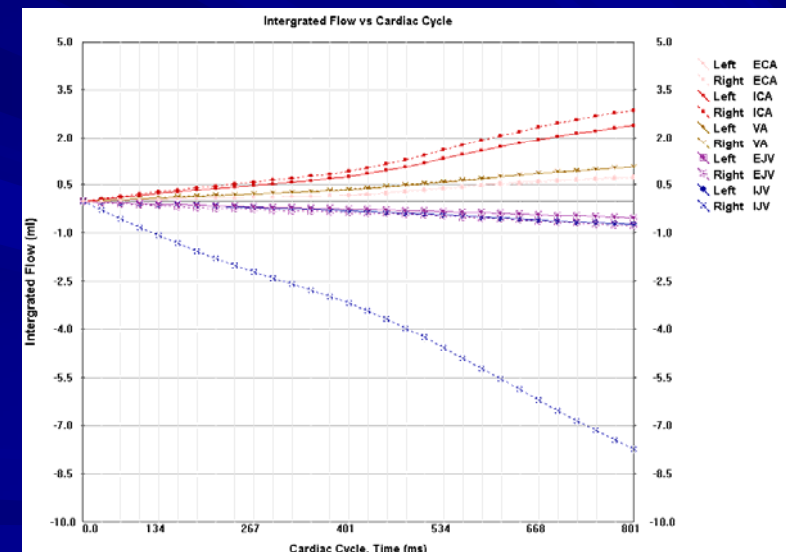
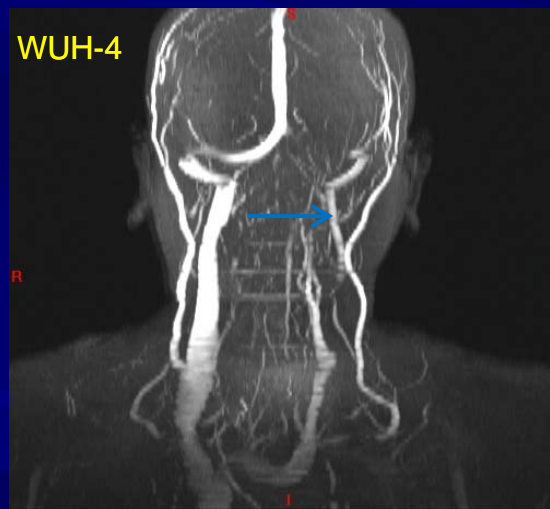
Data collected at Wuhan Hospital under the auspices of Haibo Xu

- ❖ Total: 29 cases processed
- ❖ Age range 36 – 76 years
age mean: 61.3 years
age SD : 9.5 years
- ❖ 16 males and 13 females processed
- ❖ Symptoms included: hand shaking, leg shaking, bilateral pain in legs, swelling of limbs, weakness of limbs, etc.
- ❖ UPDRS scores ranged from 8 to 56
- ❖ 24 have FLAIR data of which 12 have white matter lesions

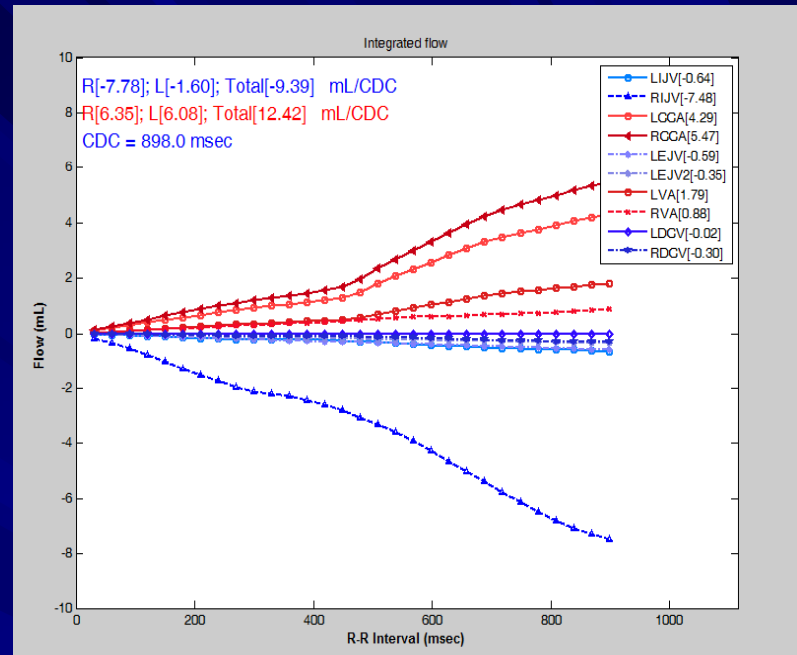
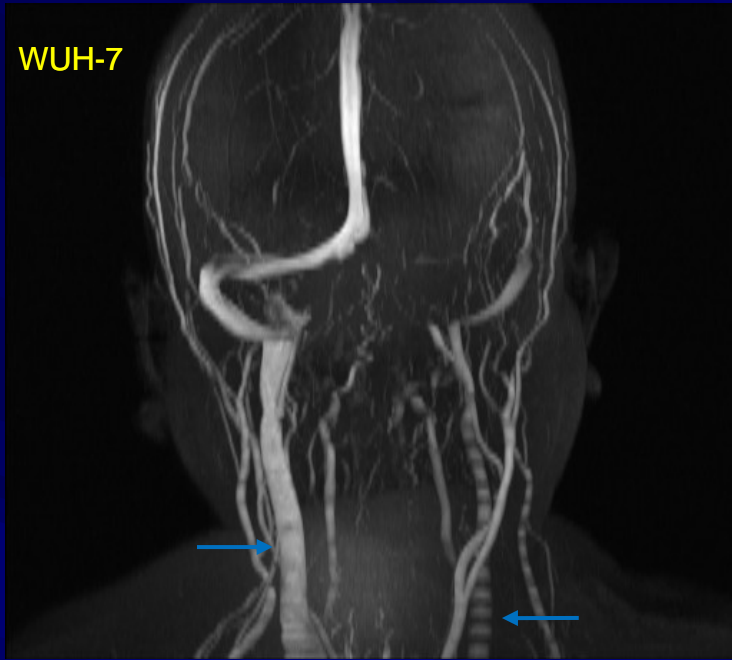
WUH-3



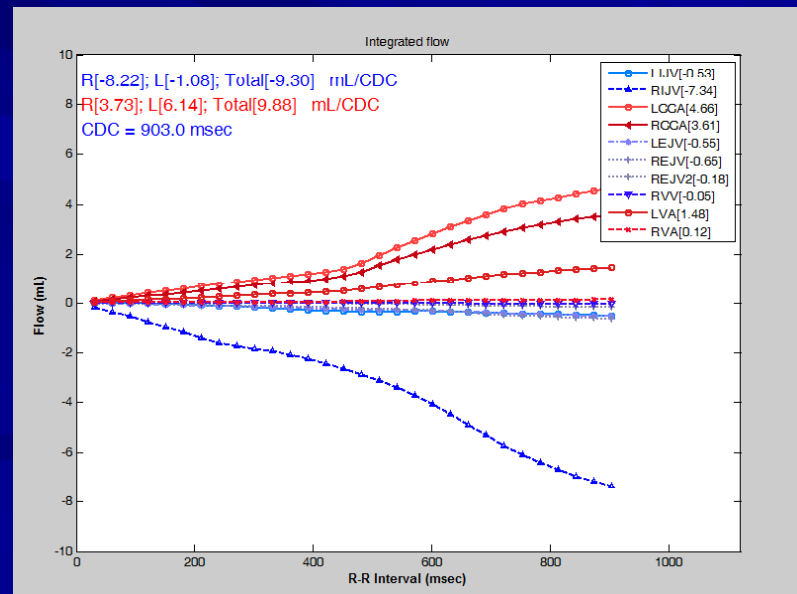
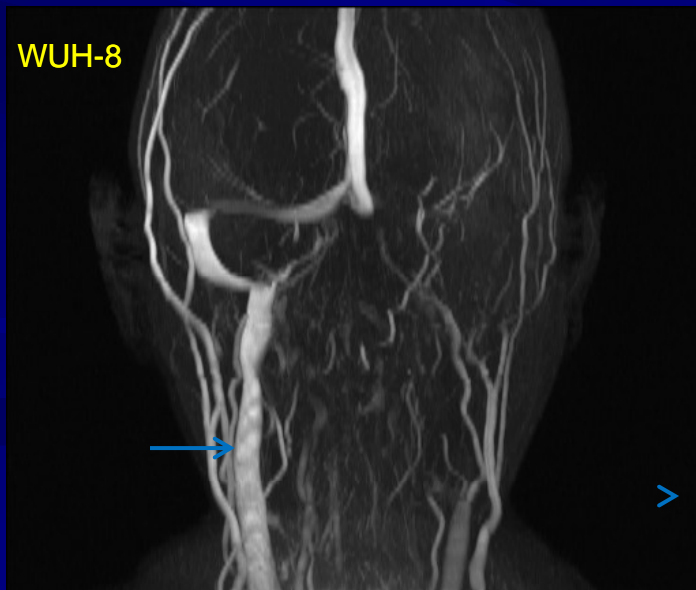
WUH-4



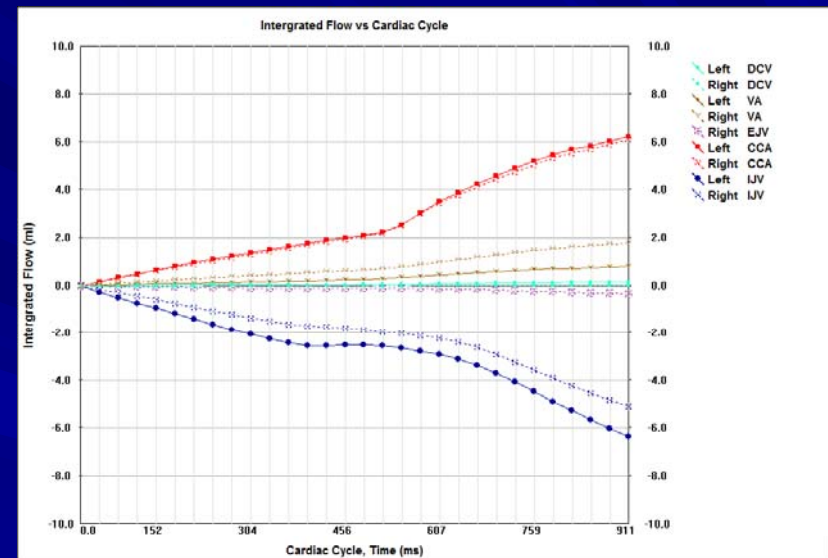
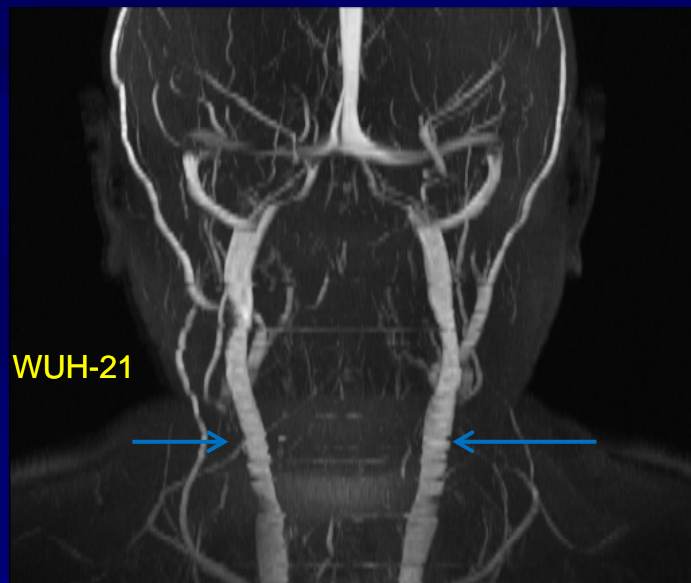
WUH-7



WUH-8

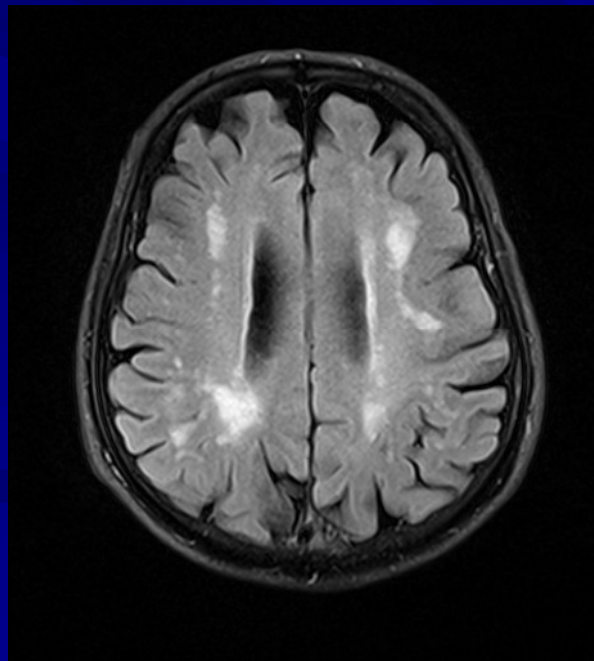
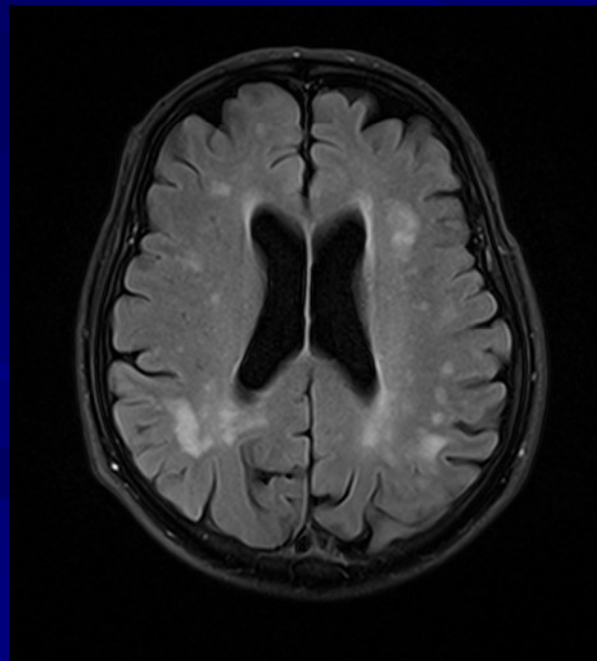
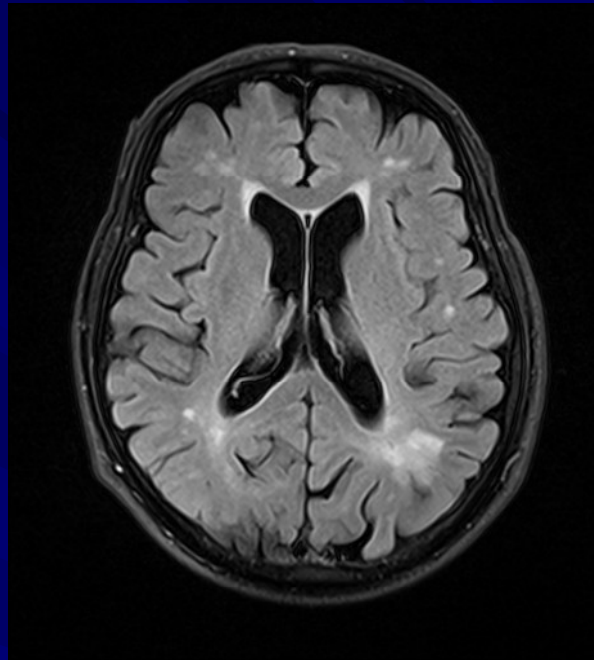
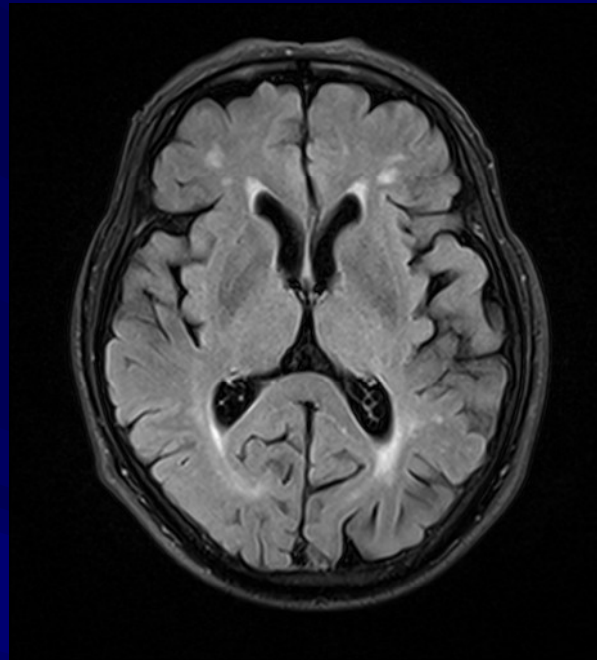


Normal vessels and normal flow



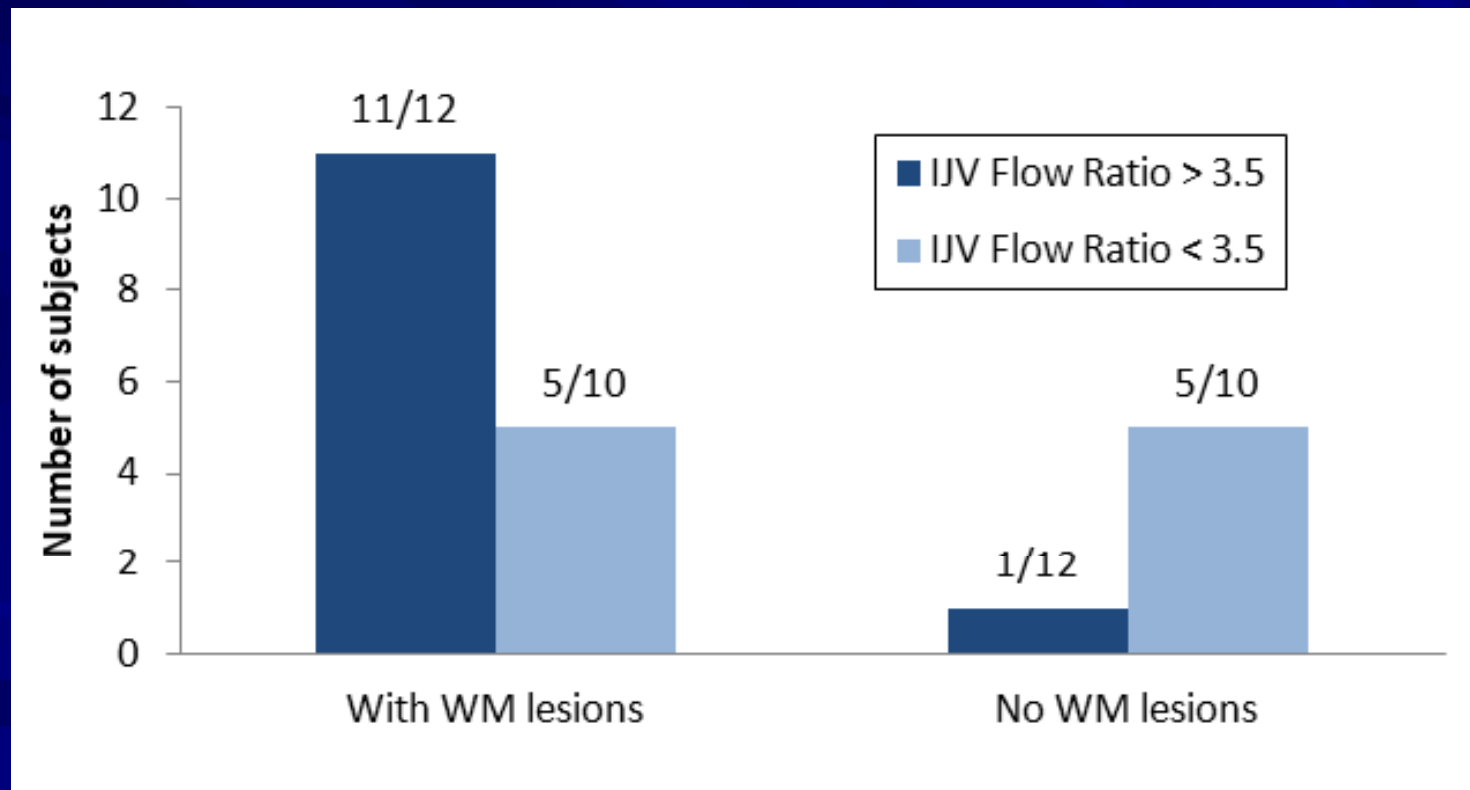
CCSVI and Parkinson's Disease

- Of 29 cases, 18 of them have potentially missing left transverse sinus or slow flow in the left transverse sinus.
- These 18 have abnormal flow in the left internal jugular vein.
- Of 50 normal controls, only 10 show this type of behavior.

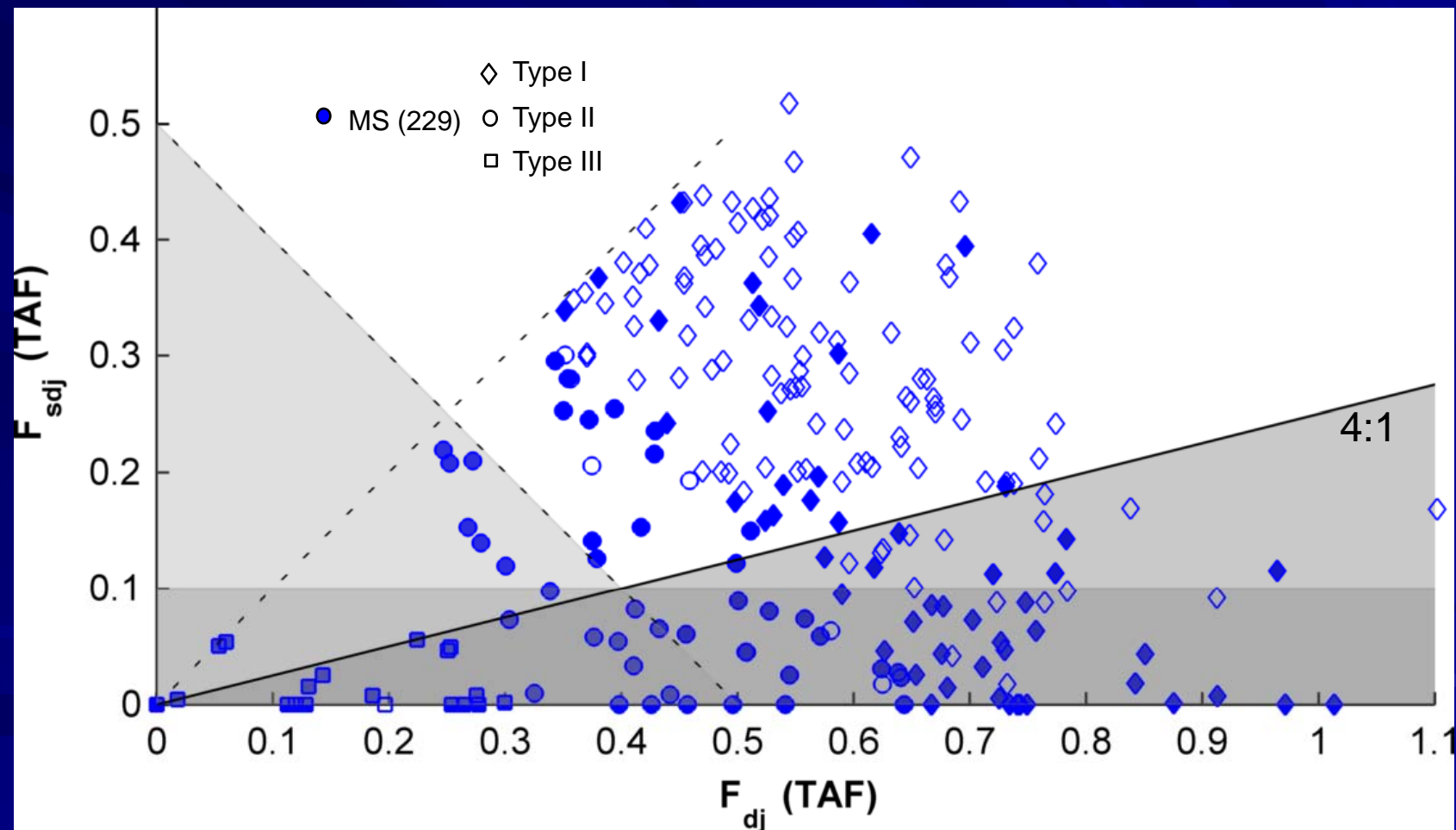


WM
hyper-
intensities
seen in
FLAIR

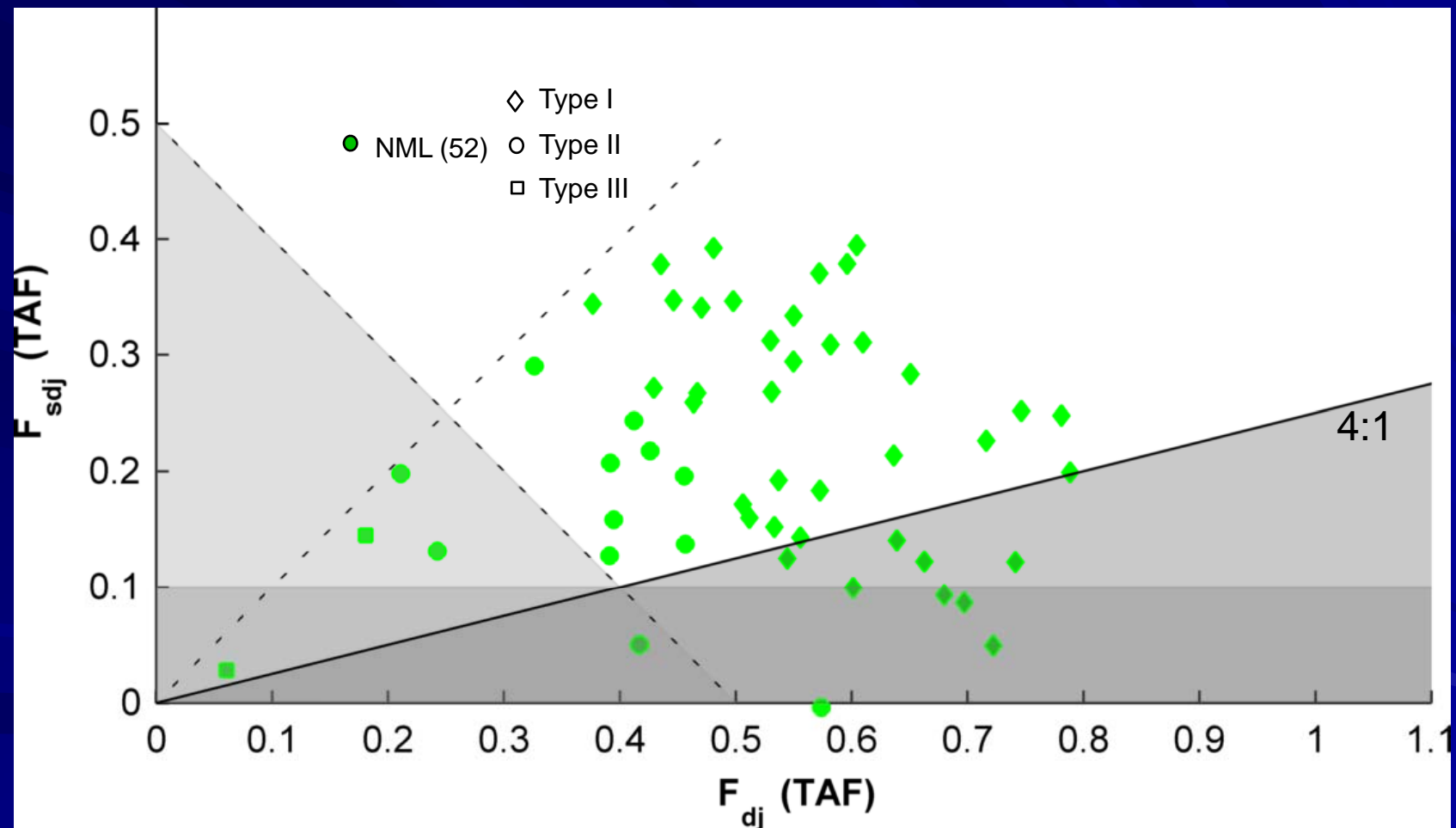
The distribution of PD patients with white matter lesions



$F(\text{sdj})$ vs $F(\text{dj})$: 229 MS patients at C2



$F(\text{sdj})$ vs $F(\text{dj})$: normal controls



Conclusions and future directions

- ❖ Quantitative flow imaging provides the potential to sub-characterize the MS population into:
 - ❖ low flow and high flow groups and
 - ❖ those dominated by one jugular
- ❖ Future work
 - ❖ Many more normal controls are needed to validate these biomarkers

Conclusions: CCSVI and Neurodegenerative Disease

CCSVI may be a very broad vascular problem associated with a number of different diseases:

Multiple sclerosis

Parkinson's

Optic neuritis

Exertional headache

Transient global amnesia