



presenta:

Slide di presentazione del dr. Zivadinov (University of Buffalo) dal workshop di Hamilton del 7 febbraio 2010 sulla CCSVI.

N.B. Abbiamo ritenuto non opportuna la traduzione di alcune slide, visto l'alto contenuto tecnico.

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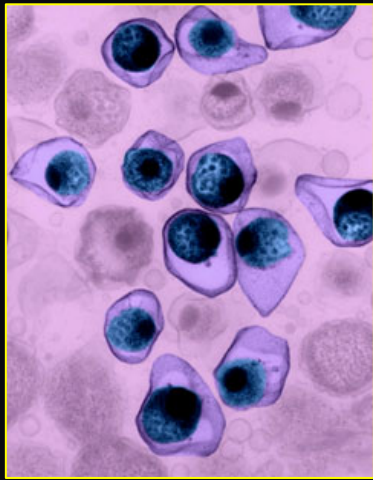
CCSVI e Risultati RM nella SM

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Director, Buffalo Neuroimaging Analysis Center
Associate Professor of Neurology
University at Buffalo, State University of New York



Potenziali Cause Scatenanti della S.M.



Predisposizione genetica

Agenti Infettivi



Fattori ambientali

Risposta immunologica anormale



SM

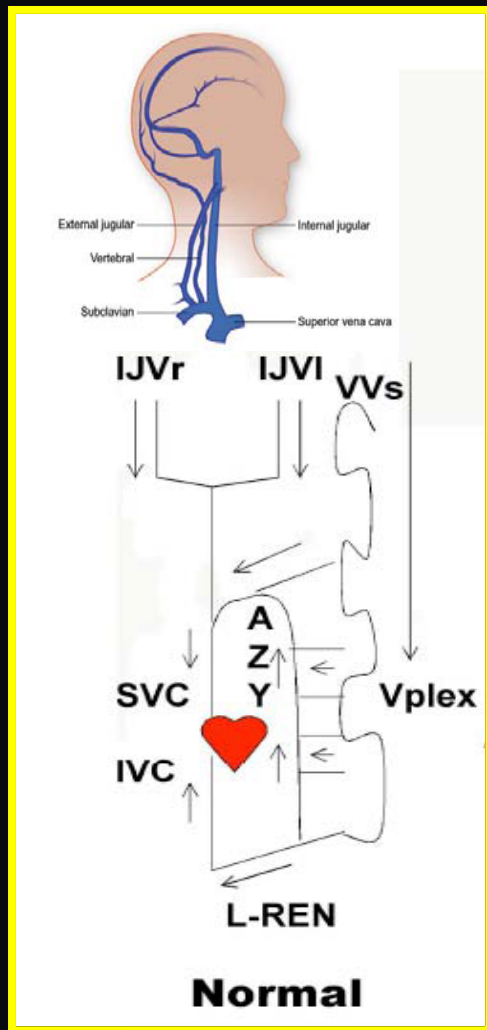
SM = Sclerosi Multipla

Gilden DH *Lancet Neurol* 2005;4:195-202, Noseworthy et al. *N Engl J Med* 2000;343:938

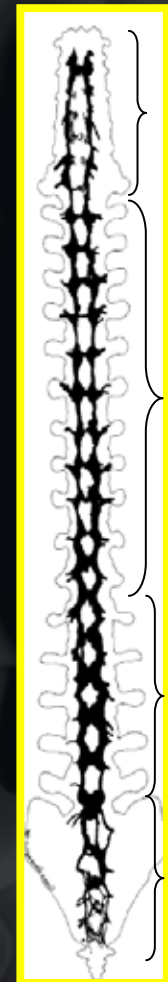
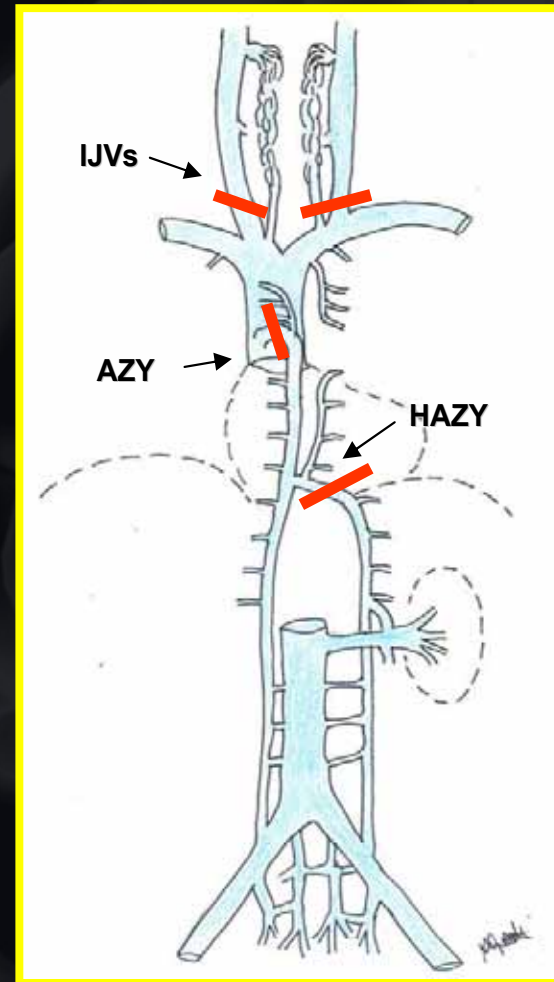
la SM è una malattia vascolare?

- Una patogenesi vascolare della SM fu suggerita molto tempo fa.
- L'estensione delle anomalie vascolari e la relazione con le lesioni è stata difficile da valutare sino ai più recenti progressi della MRI (Risonanza Magnetica)
- La RM a “campo ultra alto” è divenuto uno strumento per la valutazione del coinvolgimento vascolare nelle lesioni tipiche della SM
- Recenti studi mostrano un'associazione perivenosa delle lesioni nei pazienti con SM attraverso la Risonanza del tipo: “high-contrast 7T susceptibility-sensitive”

Insufficienza Venosa Cronica Cerebrospinale (CCSVI) e Sclerosi Multipla



CCSVI



C

T

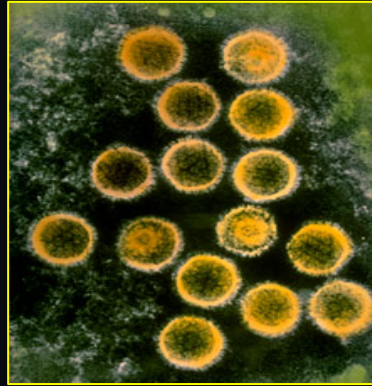
L

S

Ipotesi di patogenesi della CCSVI ed SM



Potenziati cause scatenanti nella Sclerosi Multipla



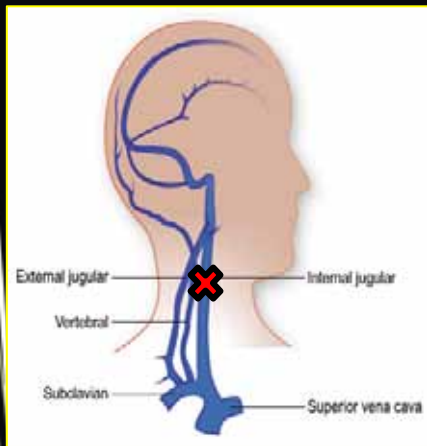
Agenti
infettivi



Predisposizione
genetica



Fattori
ambientali



CCSVI

accumulo di ferro

Risposta immunologica anormale
e neurodegenerazione

SM

MS = multiple sclerosis

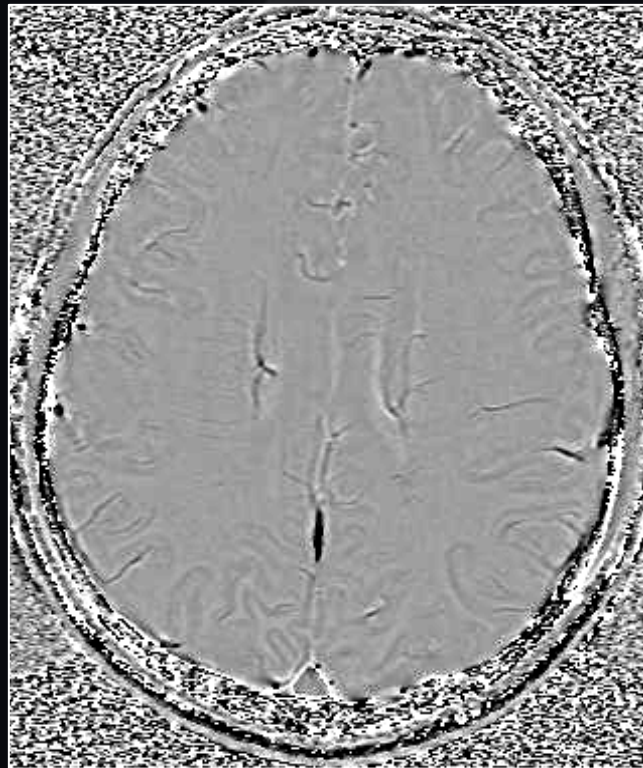
Adapted from Gilen DH *Lancet Neurol* 2005;4:195-202, Noseworthy et al. *N Engl J Med* 2000;343:938

Immagini pesate in suscettività *

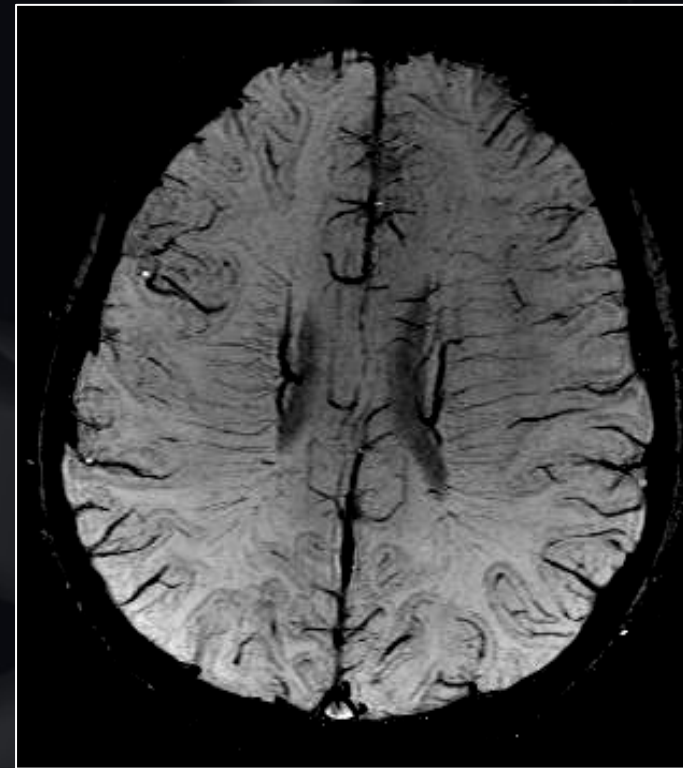
- Eco di gradiente 3D con magnitude and phase image
- Alta risoluzione per ridurre il convenzionale “spin dephasing”
- Flusso compensato appieno in 3 dimensioni
- Modificando il contrasto magnitude image using phase mask
- mIPping the images to create an angiographic effect (venography)



Magnitude



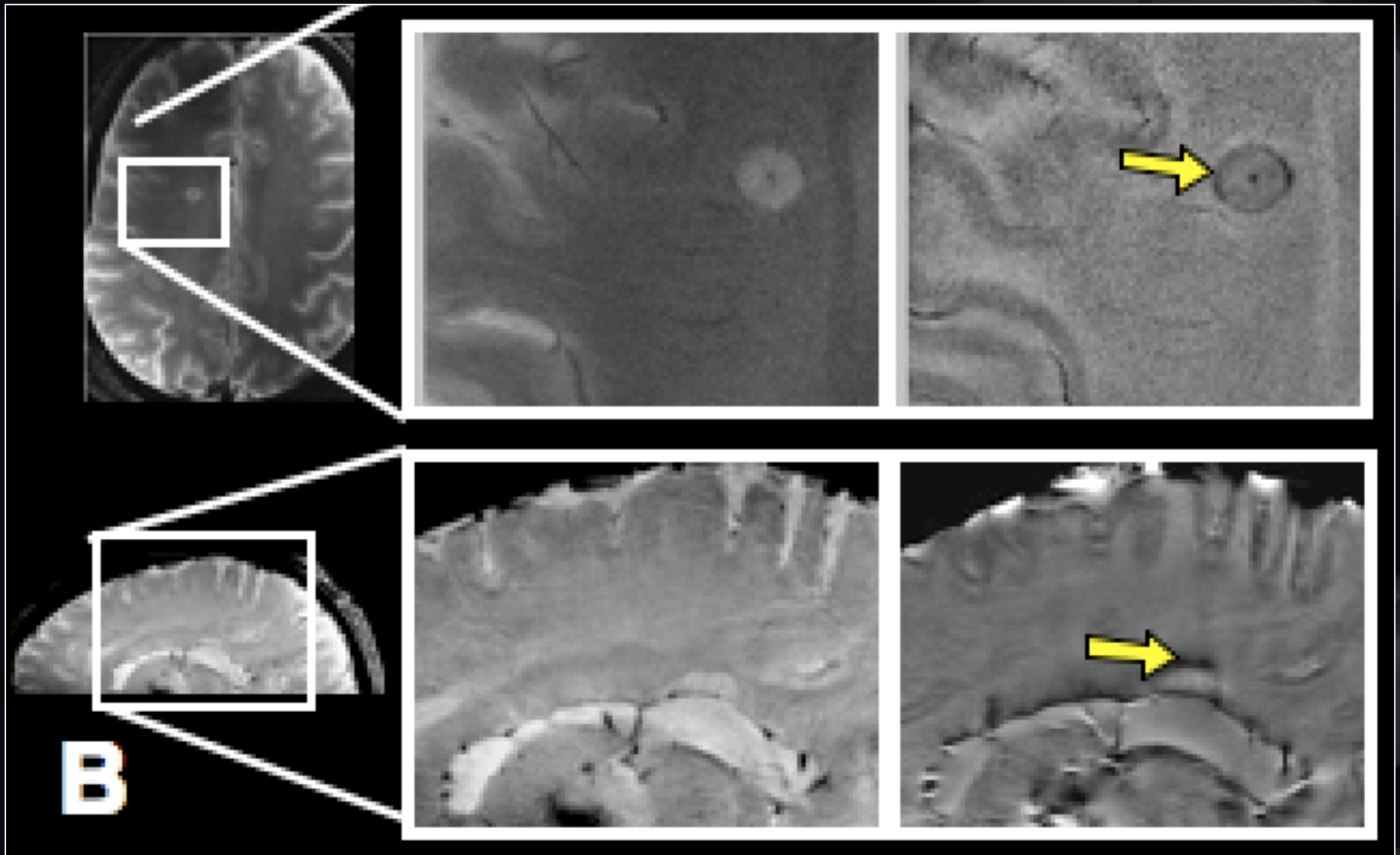
Phase



mIP

* Haacke EM 2004, MRM

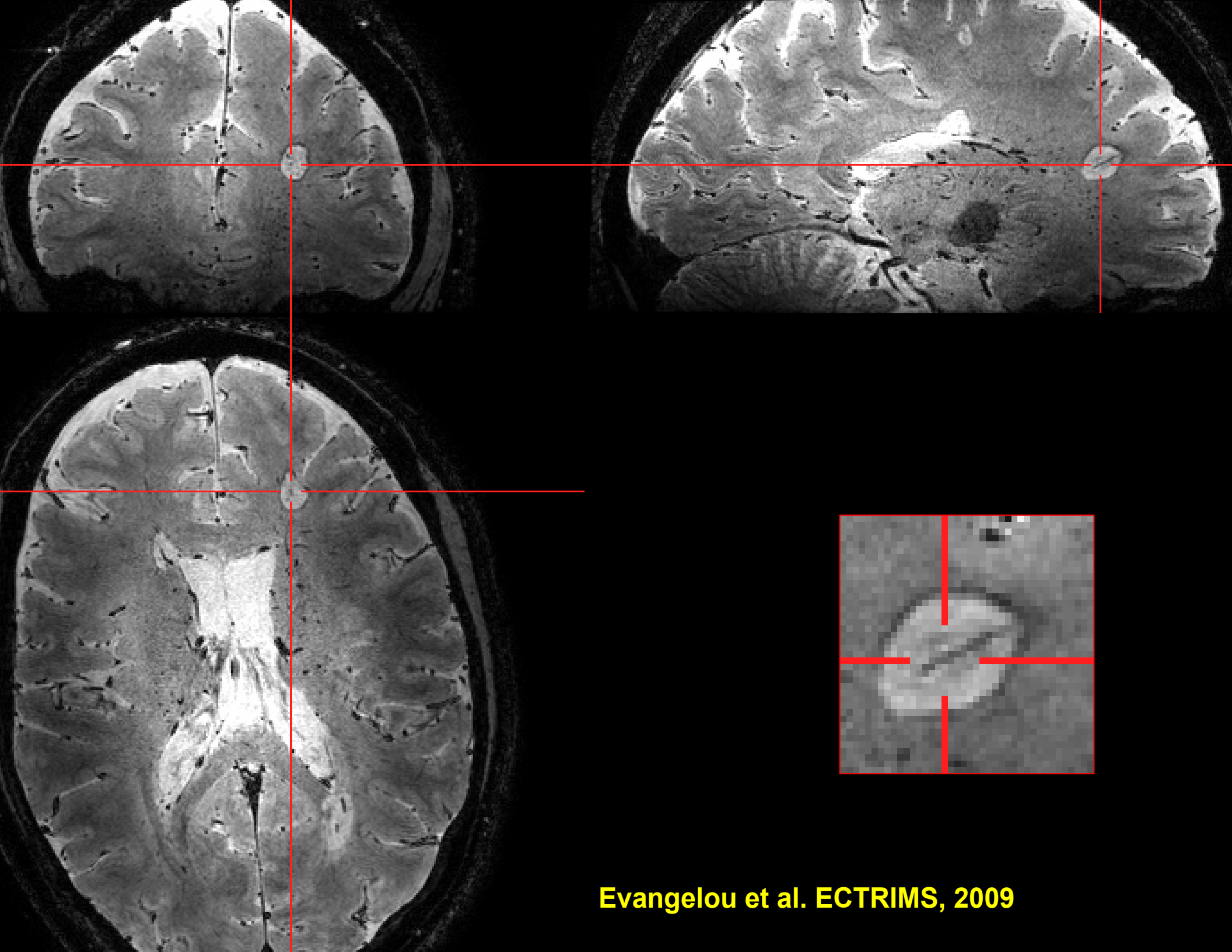
Phase Imaging of MS at 7T



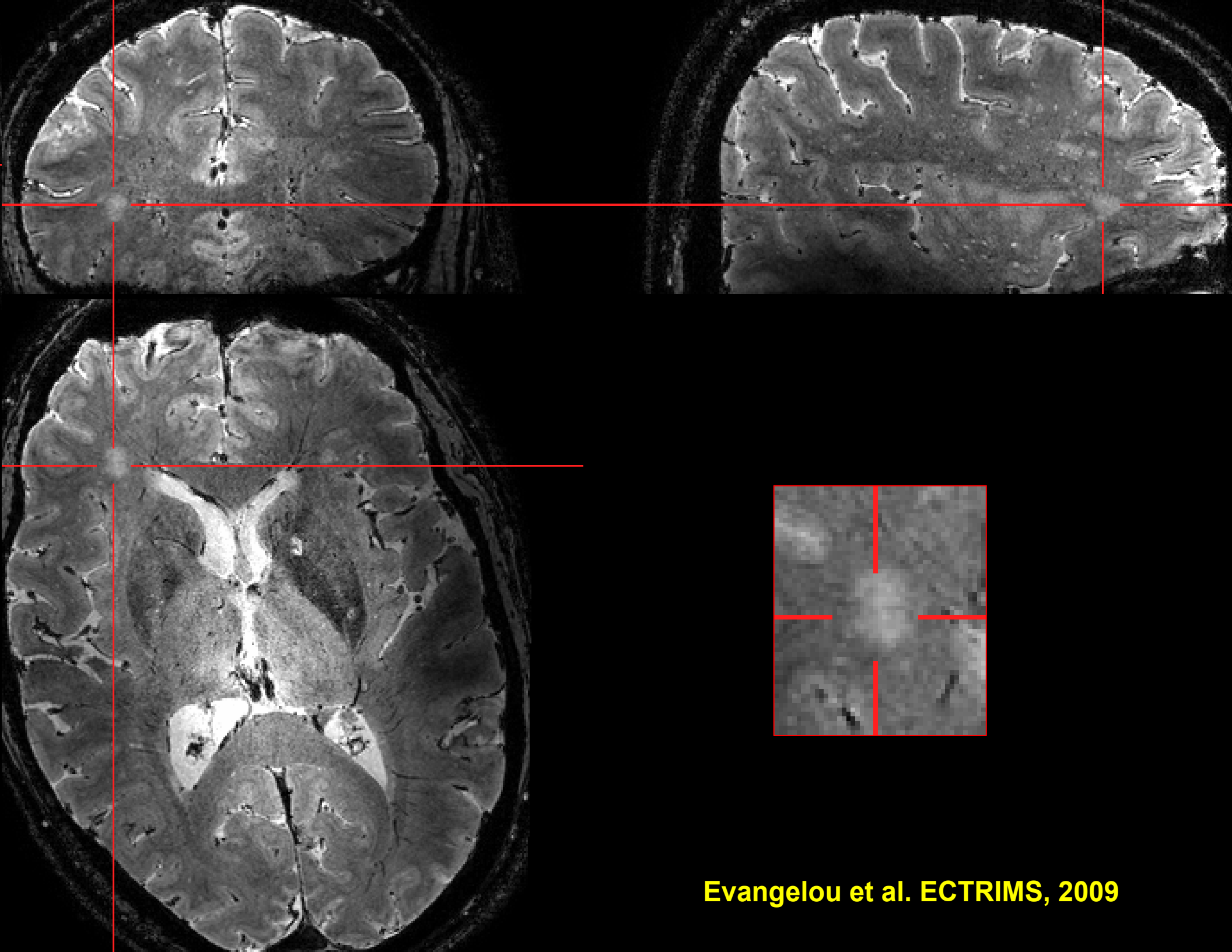
Magnitude images

Phase images

Hammond et al. Ann Neurol, 2008



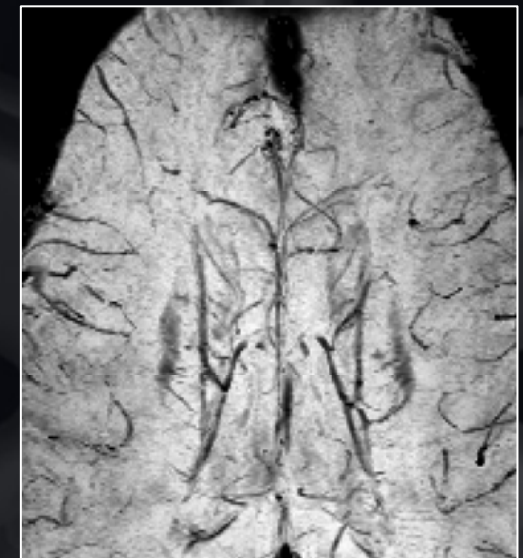
Evangelou et al. ECTRIMS, 2009



Evangelou et al. ECTRIMS, 2009

SWI nella Sclerosi Multipla e Controlli Sani.

- ↓ utilizzazione di ossigeno causato dalla distruzione dei tessuti → meno deossiemoglobina nel sangue venoso?
- Occlusione dei vasi ?



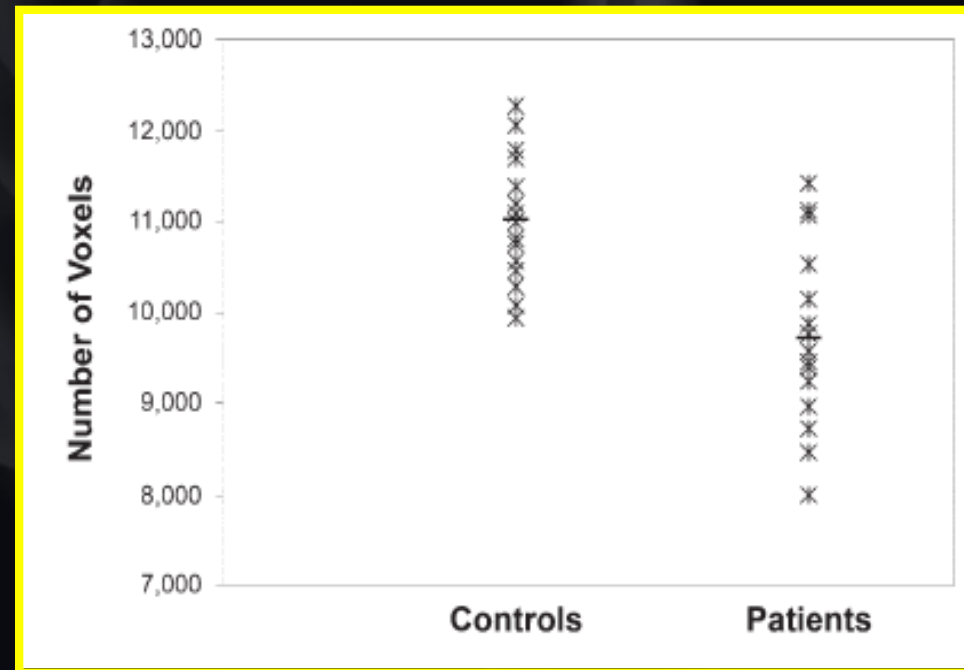
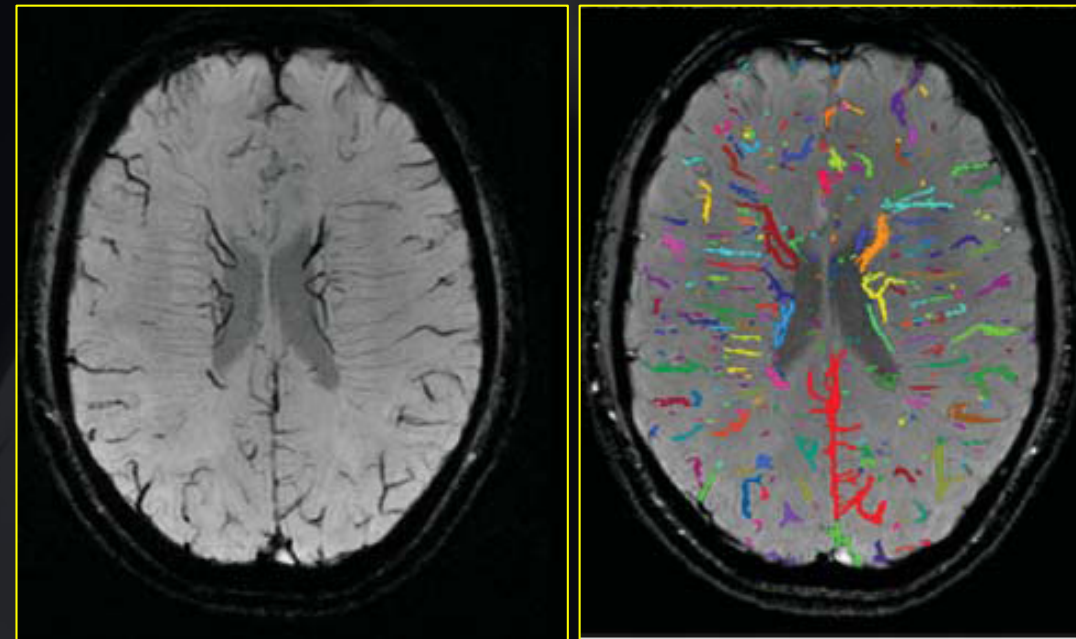
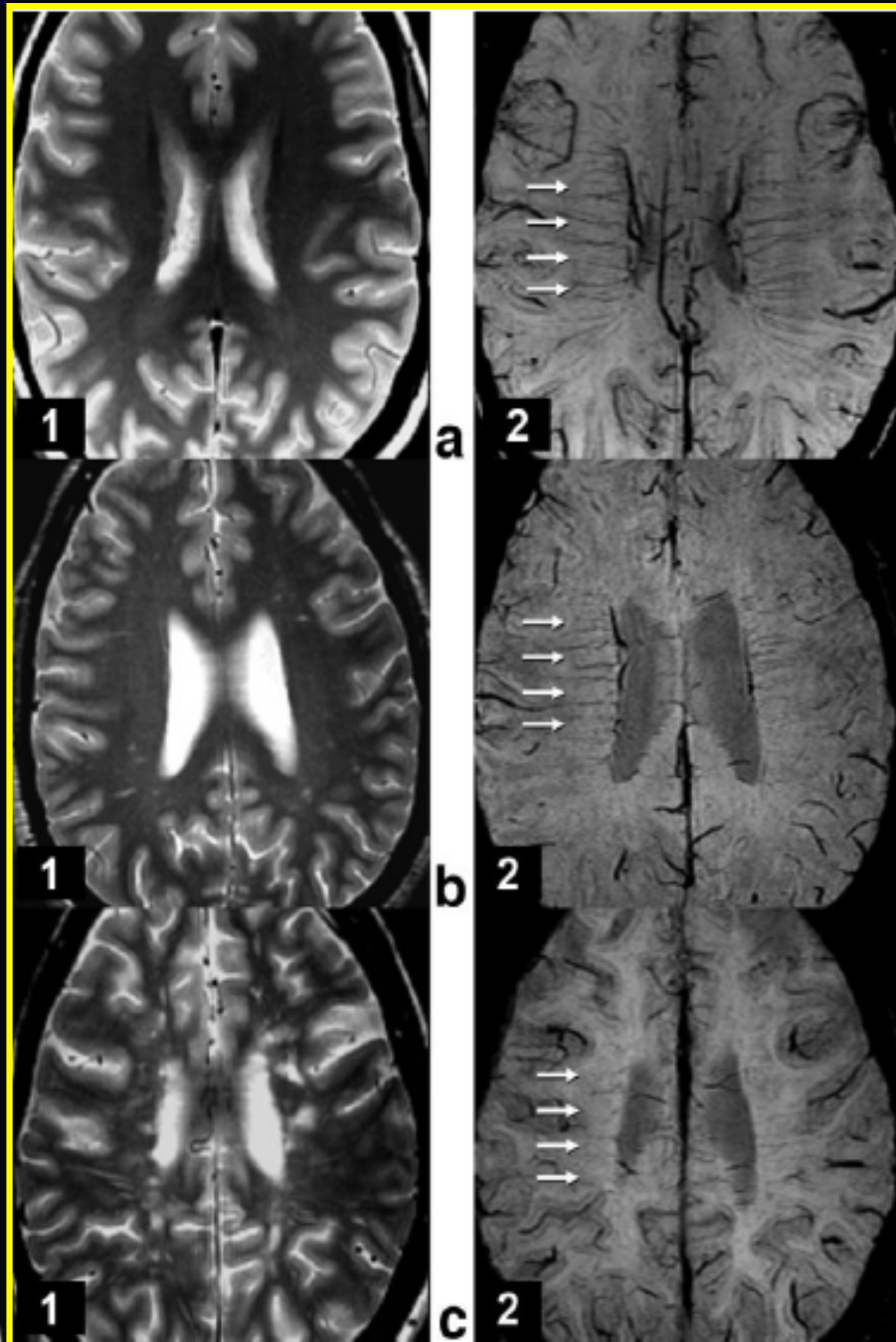
HC

RRMS (EDSS 2.0)

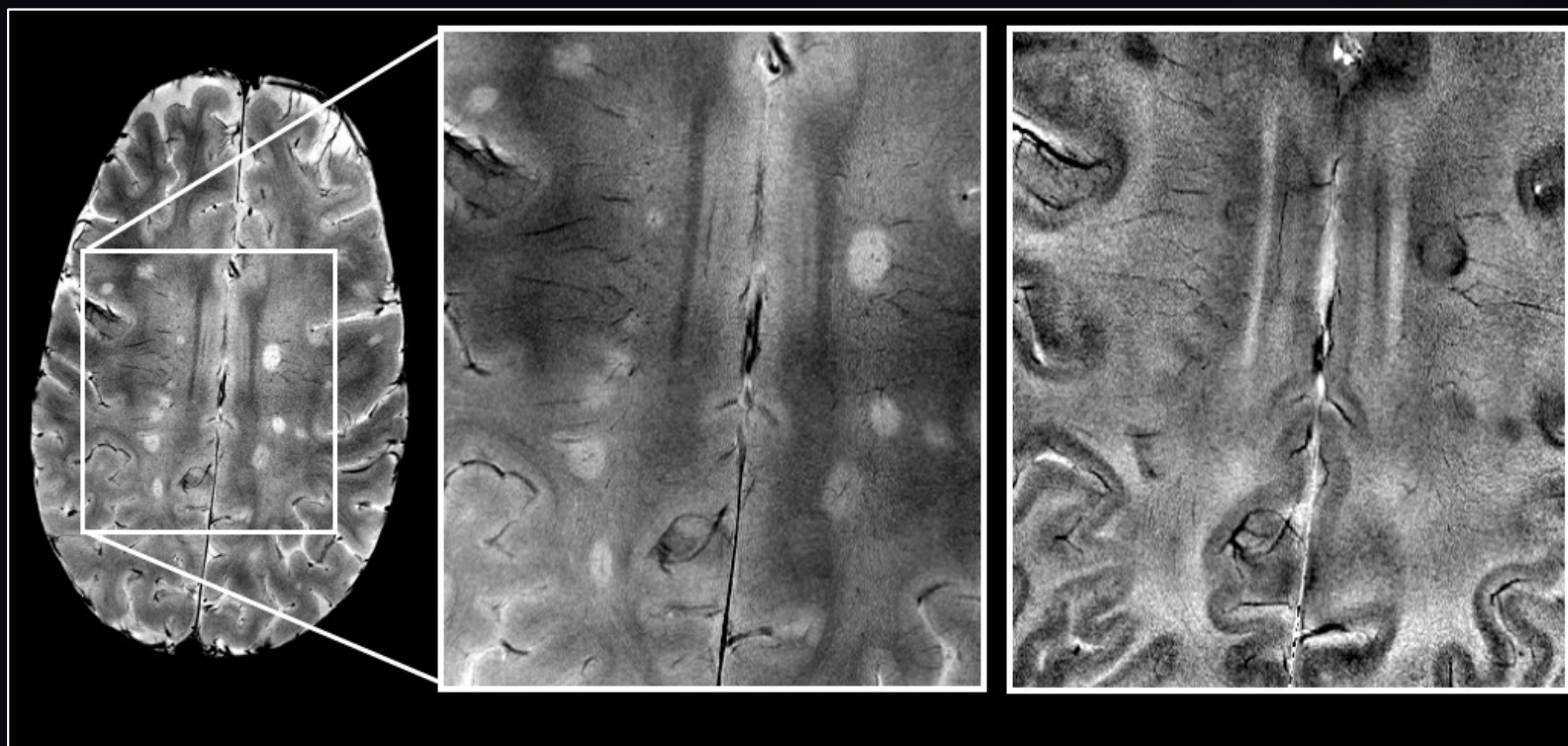
RRMS (EDSS 4.0)

Schirda et al. AAN, 2009

Visibilità diminuita della Vascolatura Cerebrale nella SM con SWI da 3.0Tesla

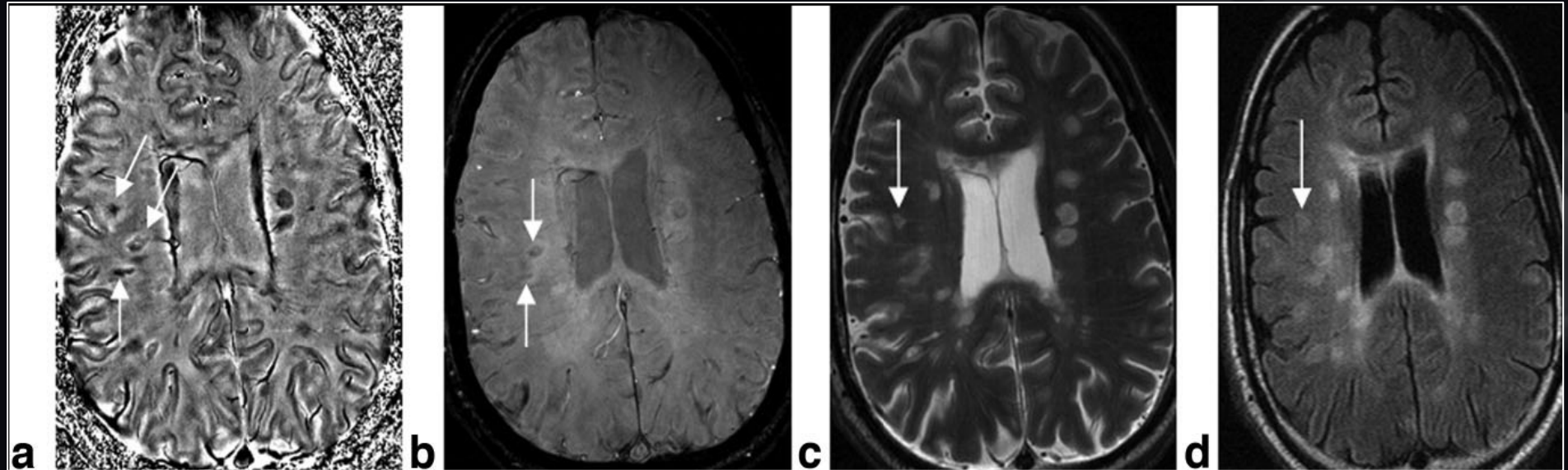


Phase Imaging of MS at 7T



- Phase images of demyelinating lesions highlighted:
- periphery of lesions, the site of iron-rich macrophages*
- penetrating vessels in 70% of lesions
- 30% more lesions than seen in magnitude
- *Phase provides a novel MR contrast for studying neurodegeneration, one sensitive to the presence of iron.*

Accumuli di ferro focali nella SM e SWI



Lesion Counts for 14 Patients at 1.5 T

	T2	T2-FLAIR	FLAIR	SWI Only	Total
Seen on SWI	30	30	3	78	141
Not seen on SWI	18	27	3		48
Total	48	57	6	78	189

Table 6
Lesion Counts for Seven Patients at 3 T

	T2	SWI Only	Total
Seen on SWI	38 p + 32 m	20	90
Not seen on SWI	21		21
Total	91	20	111

m = magnitude, p = phase.

Table 7
Lesion Counts for Six Patients at 4 T

	T2	FLAIR	SWI Only	Total
Seen on SWI	33 p + 18 m	20	45	116
Not seen on SWI		6		6
Total	51	26	45	122

m = magnitude, p = phase.



Haacke et al. JMRI, 2009

Phase Imaging della SM a 7T

Il ganglio basale nei pazienti con SM era più paramagnetico ($P < 0.05$) rispetto ai controlli, suggerendo una maggiore deposizione di ferro

Region	Patients Mean \pm SD (<i>N</i> =)	Controls Mean \pm SD (<i>N</i> =)	P
Putamen	4.29 \pm 1.13 (<i>N</i> = 14)	2.82 \pm 0.52 (<i>N</i> = 14)	<0.01
Globus pallidus	6.35 \pm 1.67 (<i>N</i> = 12)	4.71 \pm 1.24 (<i>N</i> = 14)	<0.01
Thalamus	3.03 \pm 0.98 (<i>N</i> = 13)	2.49 \pm 0.64 (<i>N</i> = 14)	<0.05
Head of caudate	5.85 \pm 1.40 (<i>N</i> = 14)	4.84 \pm 1.09 (<i>N</i> = 15)	<0.05
Splenium of corpus callosum	0.66 \pm 0.15 (<i>N</i> = 14)	1.02 \pm 0.43 (<i>N</i> = 15)	0.77

[Left] Quantitative color-coded B0 field (phase) maps

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Hammond et al. Ann Neurol, 2008

Misure regionali dell'Atrofia Cerebrale nella SM

Controllo normale, 26 anni donna

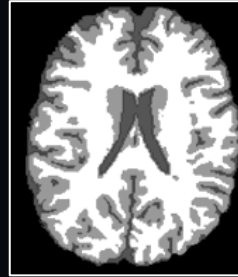
Sindrome clinicamente isolata, 27 anni donna; DD=1 year; EDSS=1.0

Sm a cadute e remissioni, 27 anni donna; DD=7 years; EDSS=3.0

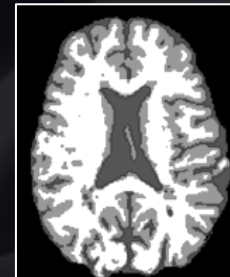
Sm secondariamente prog., 34 anni donna; DD=15 years; EDSS=5.5



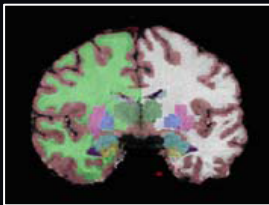
NBV diff -2.9%
NGMV diff -6.3%
NWMV diff -1.3%



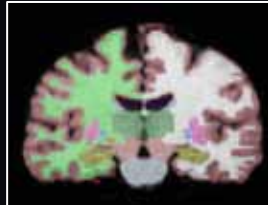
NBV diff -8.9%
NGMV diff -13.9%
NWMV diff -3.6%



NBV diff -14.7%
NGMV diff -18.9%
NWMV diff -7.4%



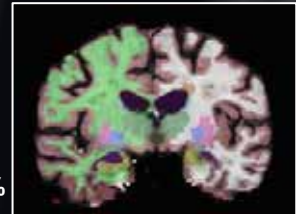
Thalamus diff -20.1%
Caudate diff -3.1%
Putamen diff -18.3%
Hippocampus diff -8.8%



Thalamus diff -32.9%
Caudate diff -20.8%
Putamen diff -31.2%
Hippocampus diff -20.4%



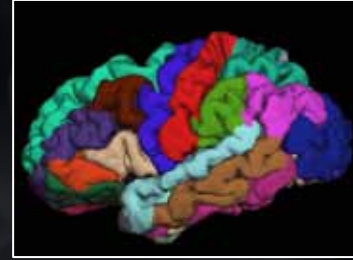
Thalamus diff -43.4%
Caudate diff -29.2%
Putamen diff -43.3%
Hippocampus diff -29.7%



Postc diff -7.1%
Prec diff -8.7%
CC diff -15%
EN diff -2.1%



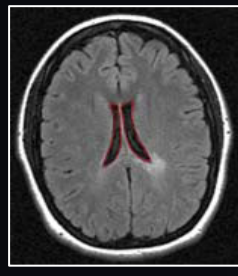
Postc diff -12.2%
Prec diff -11%
CC diff -25%
EN diff -5.9



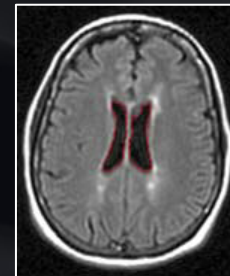
Postc diff -13.8%
Prec diff -14.8%
CC diff -27%
EN diff -13.7%



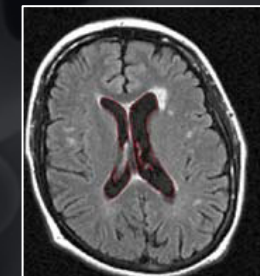
LVV diff +57%



LVV diff +208.5%



LVV diff +533%

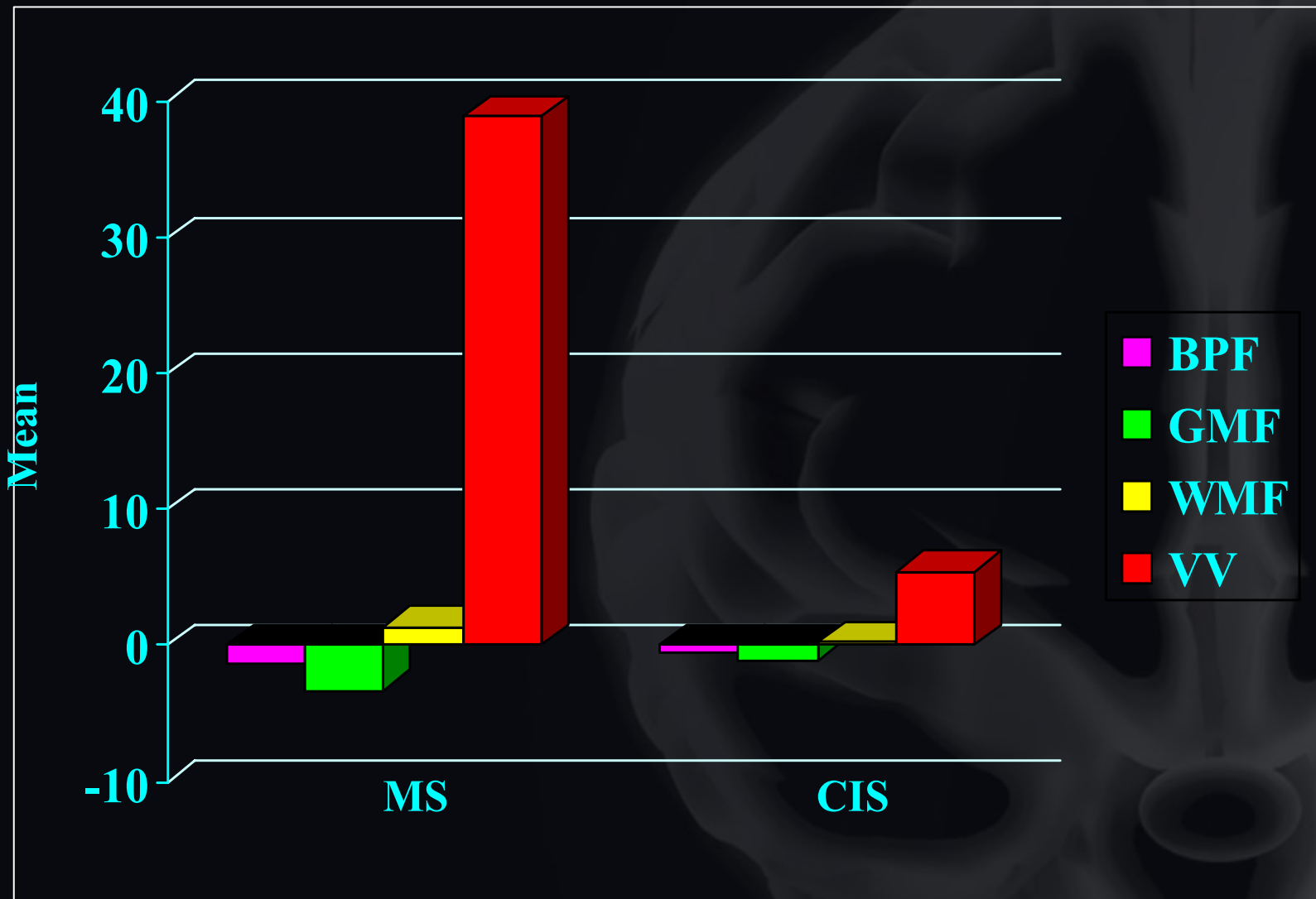


Benedict et al. JNMP, 2009

Ramasamy et al. J Neurol Sci 2009

-SIENAX, -LVV, 3VW, Feesurfer subcortical segmentation, Feesurfer cortical segmentation; Postc- Postcentral; Prec- Precentral; CC- Corpuscallosum; EN- Entorhinal; Colors: Light turquoise-Superior frontal, Violet-Rostral middle frontal, Dark brown-Caudal middle frontal, Dark green-Lateral orbitofrontal, Orange-Parstriangularis, Skin tone-Parsopercularis, Blue-Precentral, Crimson Red-Postcentral, Parrot green-suupramarginal, Dark turquoise-SuperiorParietal, Light blue-SuperiorTemporal, Light Pink-InferiorParietal, Light brown-Middle temporal, Dark Blue-Lateral Occipital, Dark pink-Inferior Temporal

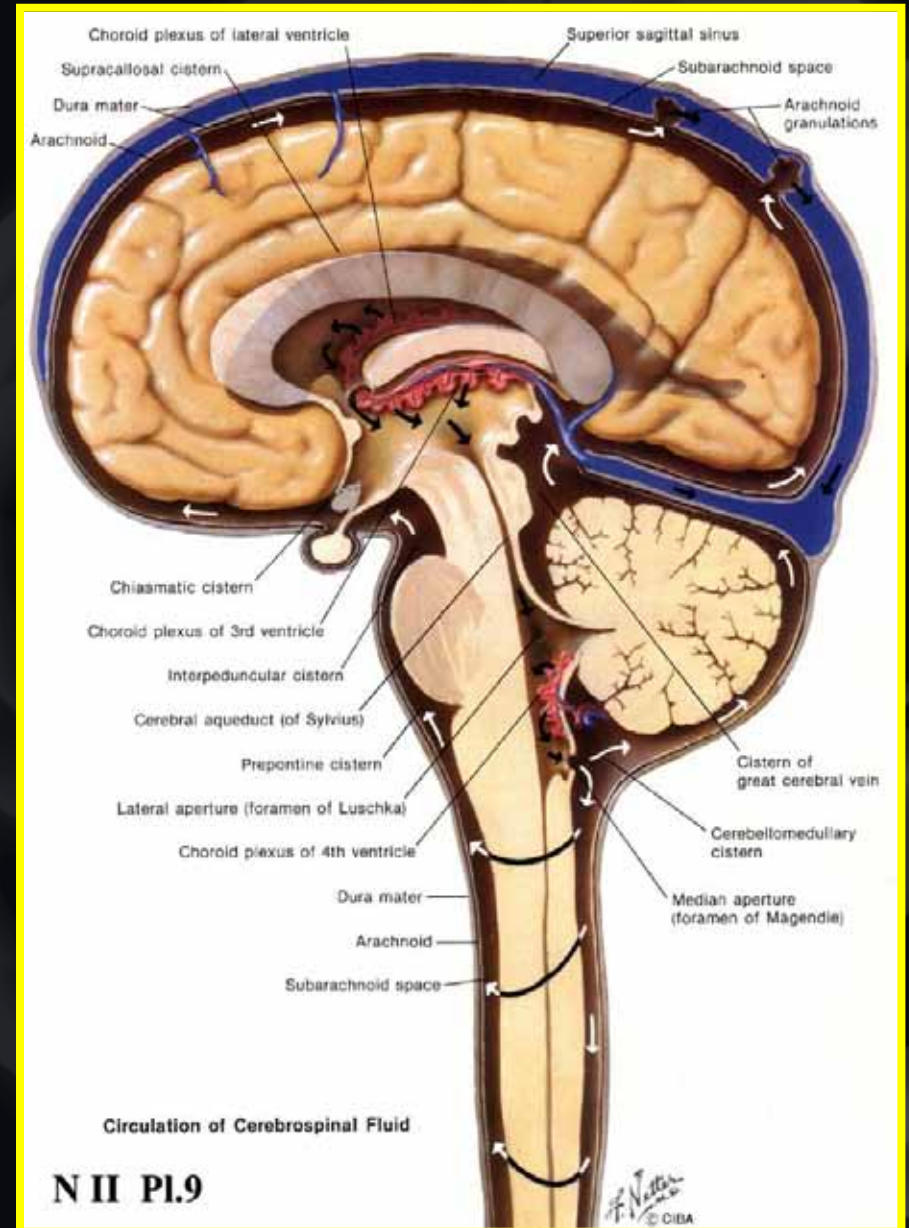
Cambi dell'Atrofia Cerebrale in 3 Anni



Dalton et al. Brain, 2004

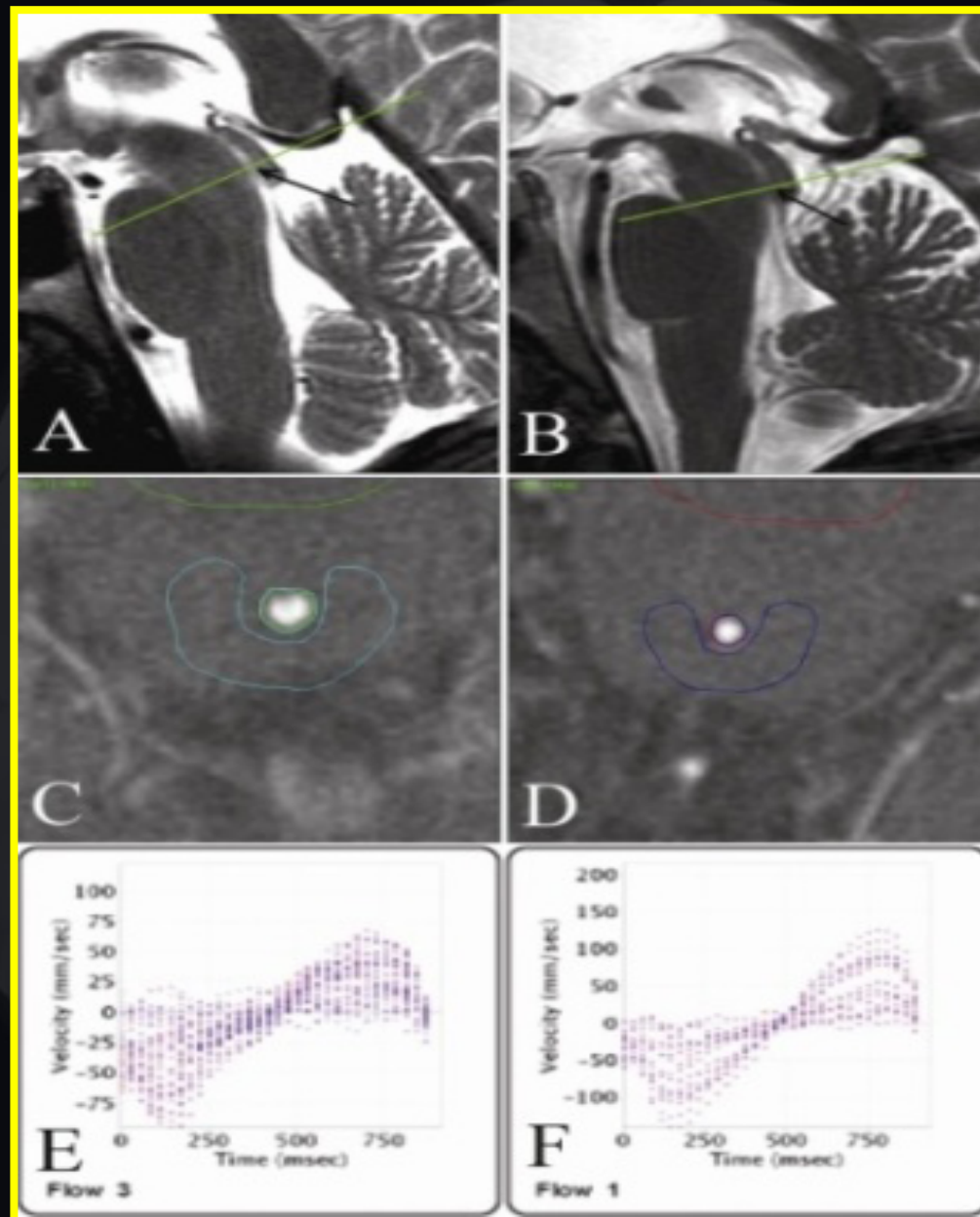
Drenaggio Venoso & Dinamica CSF

- la dinamica CSF è dipendente dal drenaggio venoso
- Si tratta di un equilibrio:
 - tra l'ultra-filtrazione CFS dalle vene del ventricolo laterale
 - ed il riassorbimento CSF nel sistema venoso al livello dei seni durali



Cine CSF Flow Imaging

- CSF flow measurement in the aqueduct of Sylvius for HC (left) and MS patient (right).
- A-B. Sagittal T2 scans showing positioning for the MRI Cine acquisition. Slice orientation is perpendicular on the aqueduct.
- C-D. Aqueduct and background ROIs drawn on the magnitude image.
- E-F. CSF velocity distribution within the aqueduct of Sylvius ROIs, for the 32 phases, calculated using the GE ReportCard software



Zamboni et al. *Funct Neurol*, 2009;

Schirda et al. *AAN* 2010; *ISMRM* 2010

numbers from Bellaria Hospital, Bologna, Italy

Insufficienza Venosa Cronica nella SM

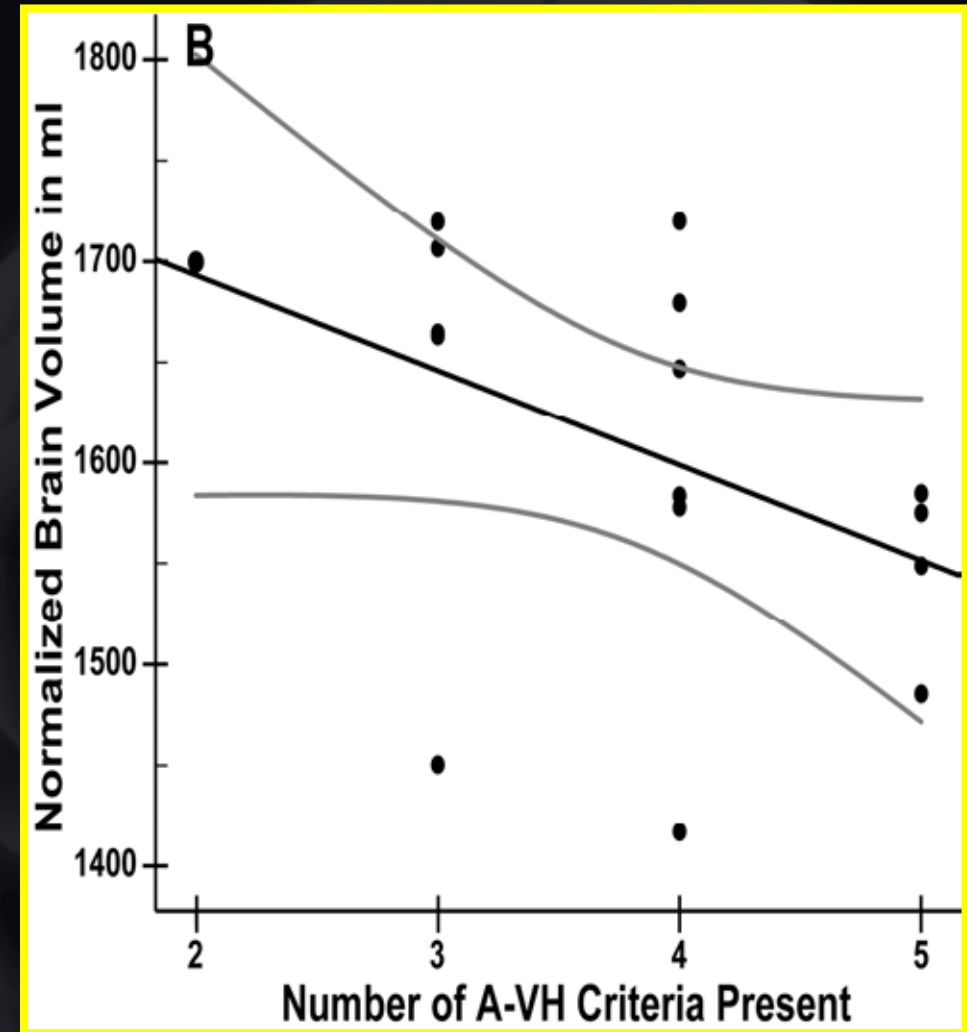
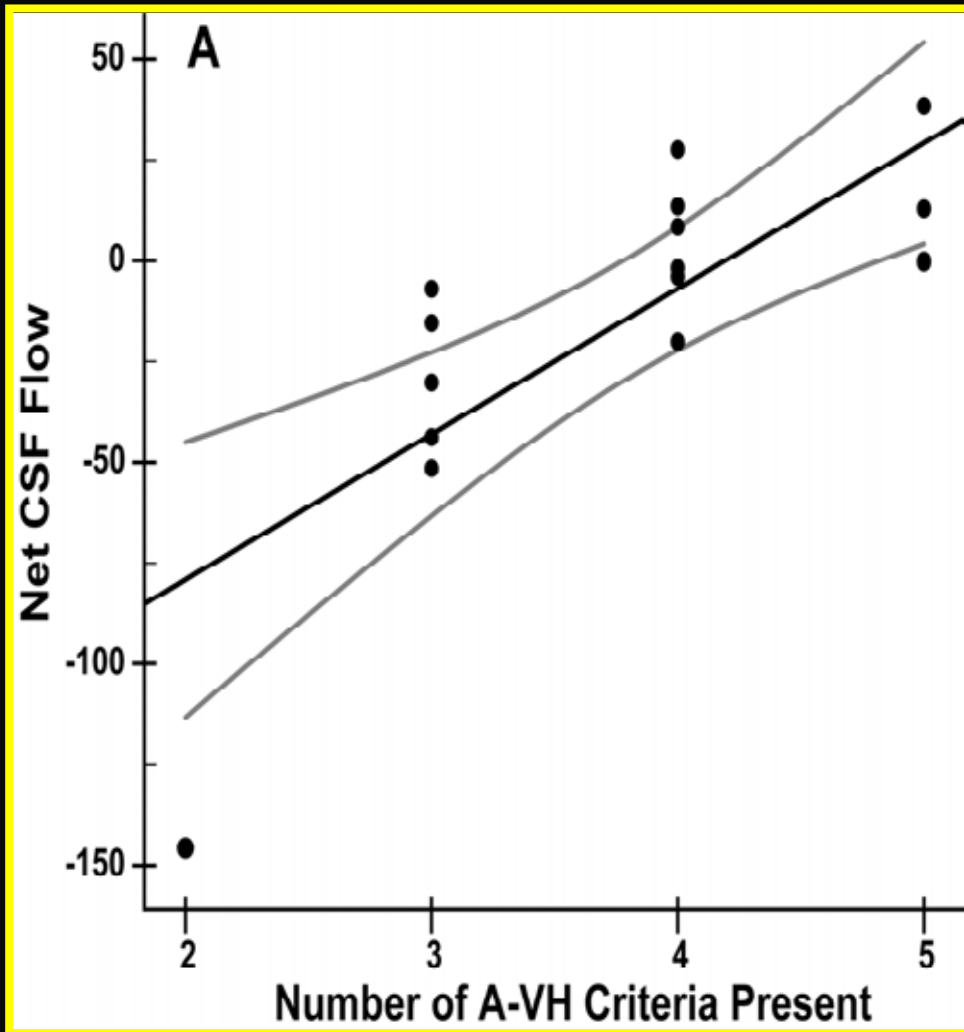
(Studio) CVIMS

- Studio trasversale
- 16 pazienti RRMS e gruppo di controllo abbinato
- Numeri uguali dall'Ospedale Bellaria, Bologna, Italia and dal Jacobs Neurological Institute, University at Buffalo, NY, USA
- Età media 36.1 ± 7.3 anni, durata media malattia 7.5 ± 1.9 anni e EDSS 2.5
- Tutti i pazienti con SM soddisfano la diagnosi di CCSVI (median VH=4, median VHISS=9) e nessuno del g.d.c.

Zamboni et al. Funct Neurol, 2009;

Zamboni et al. Int Angiolog (in press)

Lower Net CSF Flow and Lower Brain Volume in MS Patients is Related to CCSVI



Net CSF flow vs. total number of pathologic VHISS

Brain Atrophy vs. total number of pathologic Venous Hemodynamic Criteria

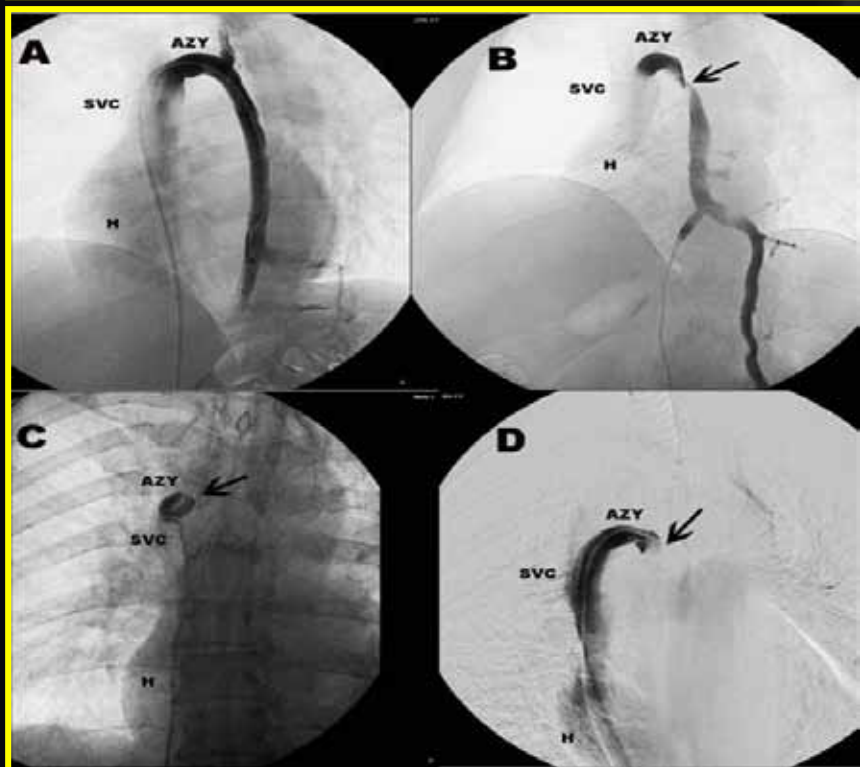
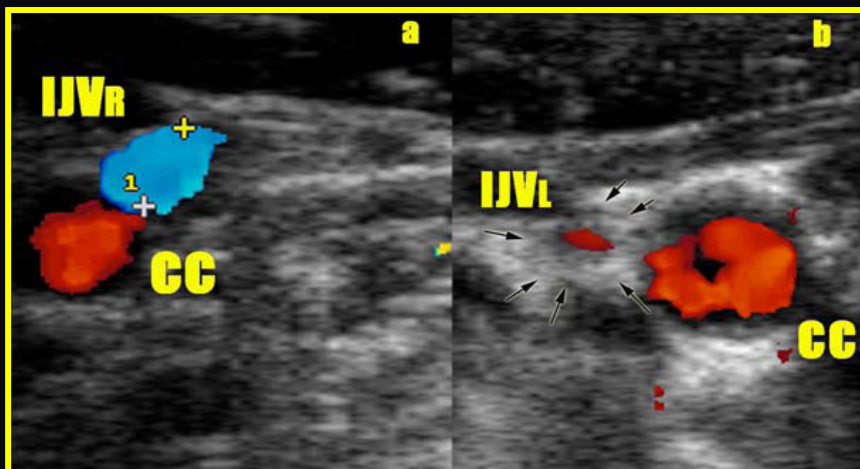
Zamboni et al. *Funct Neurol*, 2009

Zamboni et al. *Int Angiolog* (in press)

Diagnosi di CCSVI

“Situazione vascolare caratterizzata da stenosi combinate dei principali percorsi del drenaggio venoso extracranico ed extravertebrale”

Emodinamica Venosa (VH) Criteri per la CCSVI

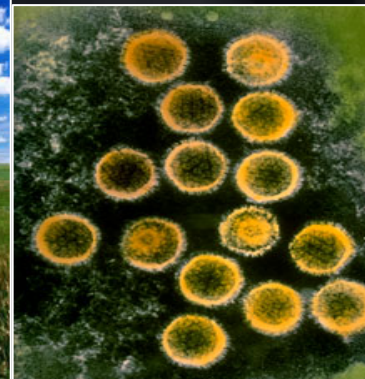
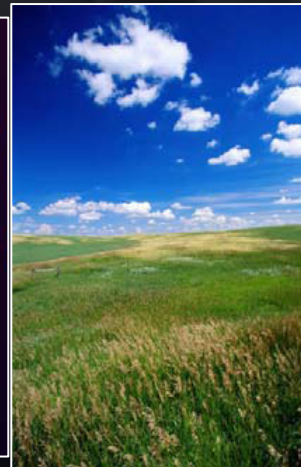
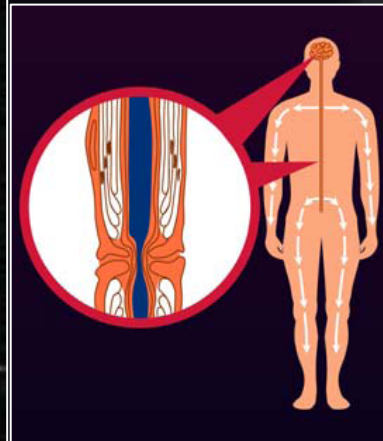
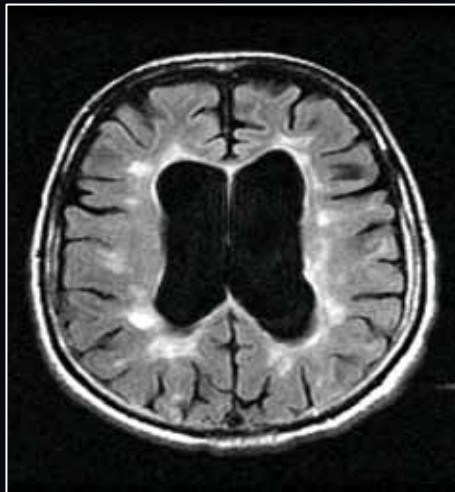
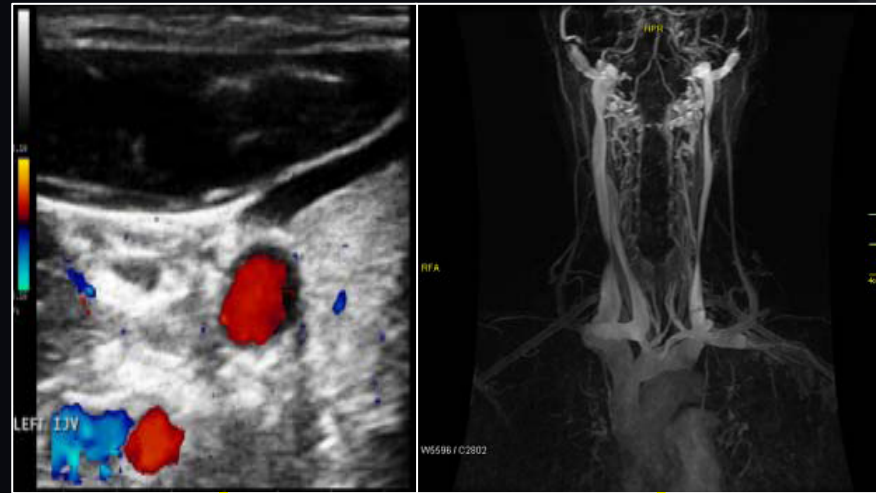


- **Criterio 1:** Reflusso nella IJV e/o nelle vene vertebrali (VVs) valutate nella posiz. seduta e supina
- **Criterio 2:** Reflusso nelle vene cerebrali profonde (DCVs)
- **Criterio 3:** Rilevamento B-mode delle stenosi delle IJVs nella forma di annulus septum, o valvole malformate
- **Criterio 4:** Assenza di segnale doppler nella IJV e/o nelle VVs
- **Criterio 5:** La presenza di una differenza negativa nella cross sectional area (CSA) della IJV
 - **VH (0-5; ≥ 2 è considerata patologica)**
- **VHISS** (Venous Hemodynamic Insufficiency Severity Score 0-16)

Zamboni et al. JNNP, 2009

Zamboni et al. Funct Neurol, 2009

Valutazione Transcranica ed Extracranica Combinata nella SM e nelle Patologie Collegate (CTEVD study)



Studio di Popolazione (1700 soggetti)

50 sm pediatriche

300 Controlli Adulti
Sani e Familiari

50 Sani pediatrici
e Controlli Familiari

900 CDMS Adulti

500 RRMS

300 SPMS

50 PPMS

50 NMO

150 CNS

Disordini Vascolari
Autoimmuni

SLE

PALP

Vascular

50 CIS

50 RIS

150 CNS

Disordini
Neurodegenerativi

AD

PD

Epilepsy

Valutazione Doppler Transcranico e Extracranico Combinata nella Sclerosi Multipla e Patologie Correlate

- Il cieco è pianificato in 3 diverse cornici di tempo
 - 500 soggetti - Gen 2010
 - 1000 soggetti – Autunno 2010
 - 1700 subjects – Primavera 2011
- Situazione corrente al 1 Febbraio 2010
 - 500 soggetti già esaminati
 - Reclutamento su base nazionale (>13,000 pazienti con SM in lista d'attesa)

Zivadinov et al. AAN 2010

Collaboratori

- **University of Buffalo**

- Bianca Weinstock-Guttman
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- Ilaria Bratolomei

- **University of Pavia**

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- **Wayne State University**

- Marck Haacke

- **University of Barcelona**

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