Vall d'Hebron Hospital

Institut Català de la Salut

Generalitat de Catalunya
Departament de Salut

IDI
INSTITUT DE DIAGNÒSTIC PER LA IMATGE

38th ESNR Annual Meeting & Advanced Course
Naples, 16-20 September 2015

"Update on MR Imaging features in multiple sclerosis"

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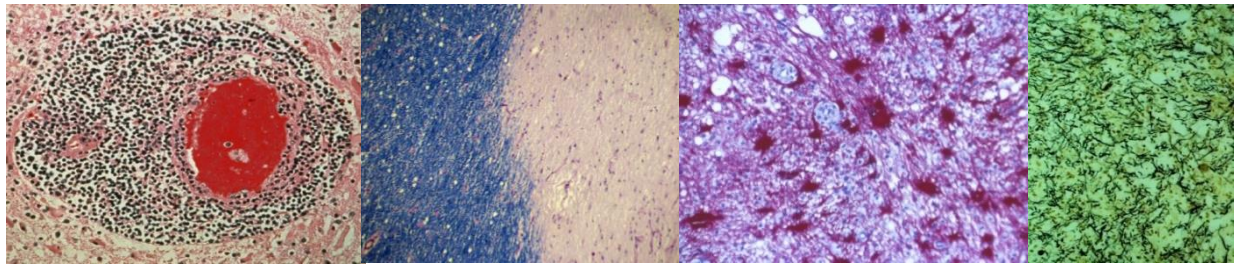
Magnims
Magnetic Resonance Imaging in Multiple Sclerosis

www.magnims.eu

Multiple Sclerosis

- Chronic and persistent inflammatory-demyelinating disease of the CNS, characterized pathologically:



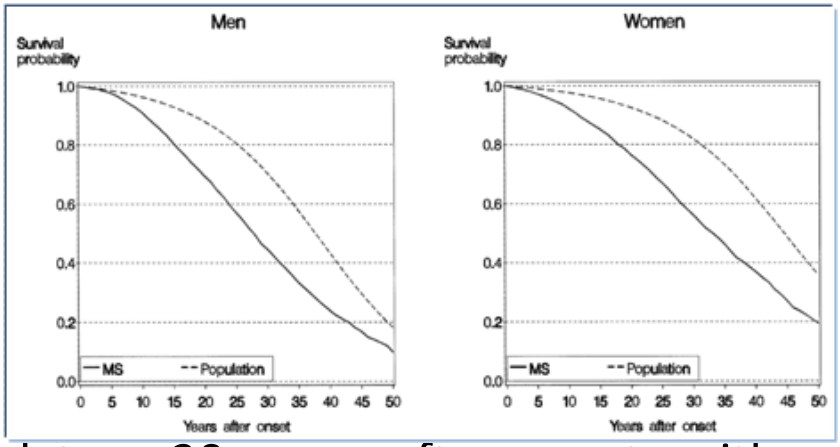
Inflammation Demyelination Gliosis Axonal loss

- Most common disabling neurological disease of young adults
- Women affected more than men (2:1)
- Symptoms onset between 20 and 40 years of age
- 2.5 million estimated cases of MS worldwide

Multiple Sclerosis

Most people with MS have a near-normal life expectancy (median survival time from onset is ~7-14 years shorter)

Scalfari et al. Neurology 2013
Brùnnum-Hansen et al. Brain 2004



- Up to 60% are no longer fully ambulatory 20 years after onset, with major implications for their quality of life and the financial cost to society

- Cognitive Dysfunction: prevalence 43%-65%

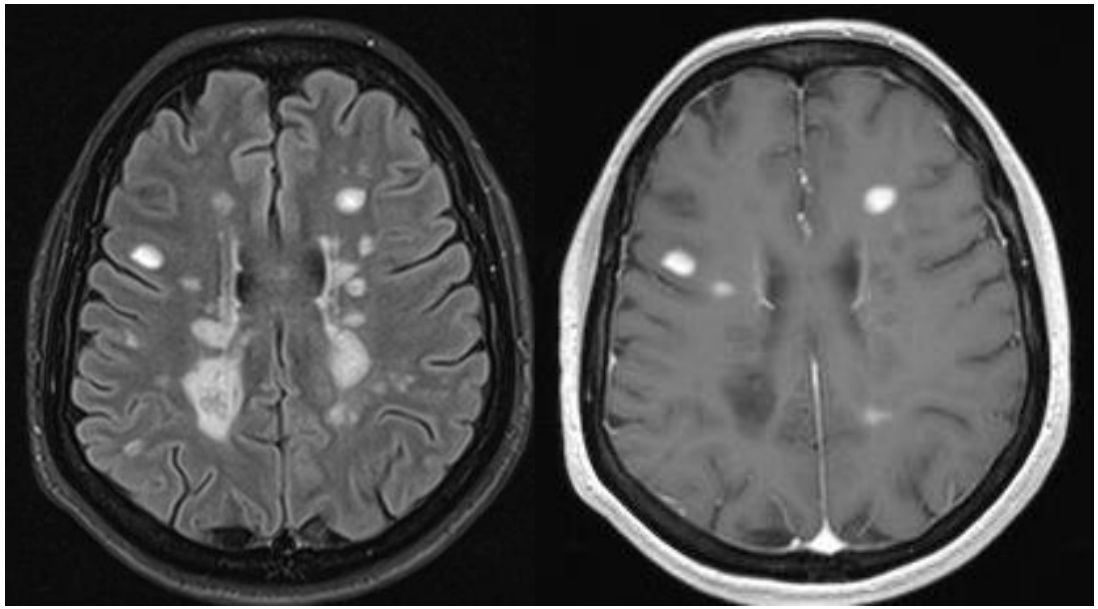
- No curative treatment, although different DMTs significantly decrease the frequency and severity of relapses and delay permanent disability

- Prompt and accurate diagnosis of MS is required

Conventional MRI measures

T2 and CE T1-WI

T2-weighted (FLAIR)



Post-contrast T1-weighted

- Highly sensitive for detecting MS plaques
- Provide quantitative assessment of inflammatory activity and lesion load
- Most important paraclinical tool for diagnosing and monitoring MS

Multifocal WM signal abnormalities: “white spots” (young patients)

Incidental finding
- Virchow-Robin spaces
- normal population (5-10%)
- migraine (x4)

Hipoxic-ischemic vasculopathies
- small-vessel disease
- hyperhomocysthenimia
- CADASIL
- Susac’s syndrome

Primary demyelinating diseases
- multiple sclerosis and variants
- ADEM
- neuromyelitis optica

Vasculitis
- primary
- sys… *…inçet, APLAS*

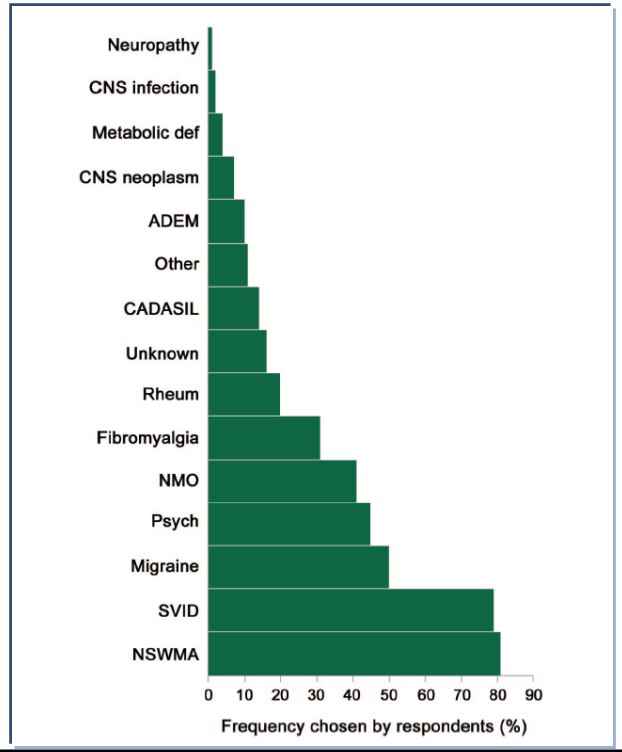
Miscellaneous
- neurosarcoidosis
- Lyme disease
- PML
- metabolic: Fabry, Leber, xantomatosis, adult forms of leukodystrophy
- effects of radiation therapy or drugs
- lymphoma
- metastasic disease

Brain MRI changes are not disease specific

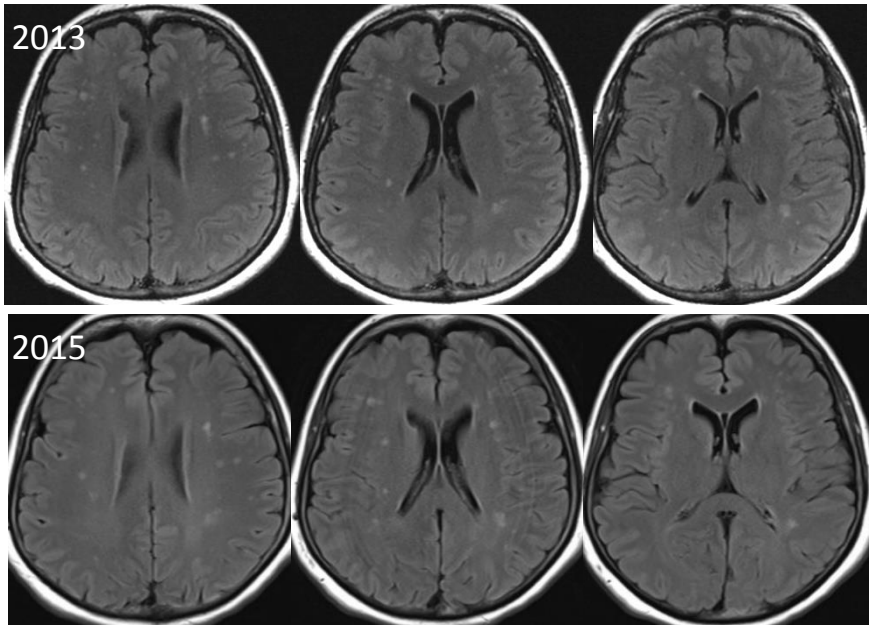
Misdiagnosis of Multiple Sclerosis

- Common (academic institutions)
- Mainly due to overuse and improper interpretation of MRI (non specific findings)
- >25% under treatment (difficult to take away)

Increase specificity of MRI findings is highly required



Solomon et al. Neurology 2012

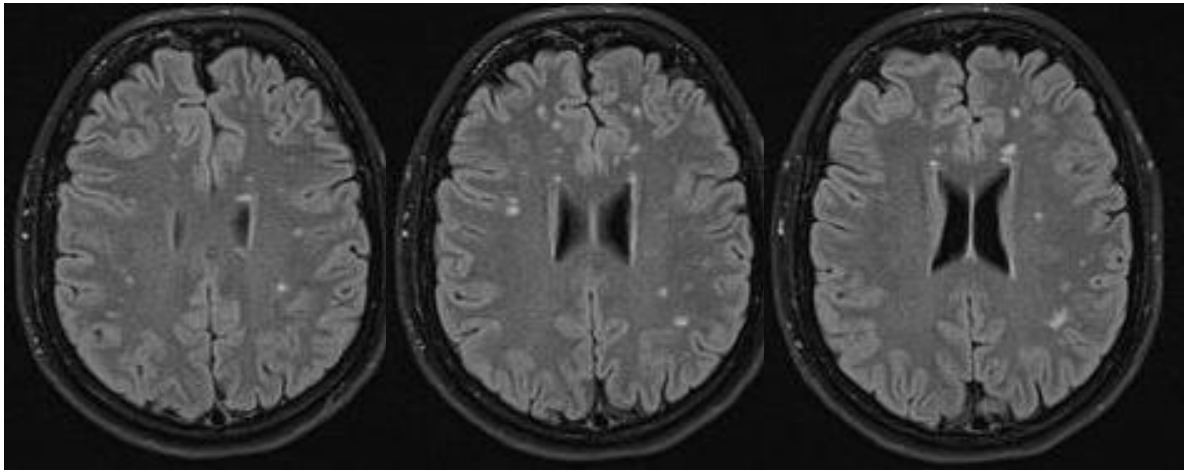


55 year old female with a diagnosis of multiple sclerosis.

Treated with DMDs since 2009

Misdiagnosis of Multiple Sclerosis

- Incidental multifocal WM brain lesions on MRI
  - normal population aged 18-50 (5-10%)
  - migraine (x4)



Misdiagnosis has significant consequences:

- Patient care
- Health care system cost (overtreatment)

Rudick and Miller. Neurology 2013
Kim et al. Mult Scler J 2013

Diagnostic strategy in subjects with incidental multifocal brain T2 lesions of unknown origin

Comprehensive checklist for evaluation of WM spots

Systematic reading

- **Lesion distribution / involvement**
  - ✓subcortical/periventricular
  - ✓U-fibers
  - ✓cortical grey matter
  - ✓deep grey matter
  - ✓corpus callosum
  - ✓brainstem
  - ✓spinal cord
- **Lesion shape**
- **Signal characteristics on various sequences (SWI)**
- **Enhancement pattern**
- **Ancillary findings**
  - ✓microbleeds
  - ✓vascular abnormalities

→

Brief and precise diagnostic impression that must consider:

- ✓Demographics
- ✓Family history
- ✓Vascular risk factors
- ✓Clinical information and question
- ✓Lab findings

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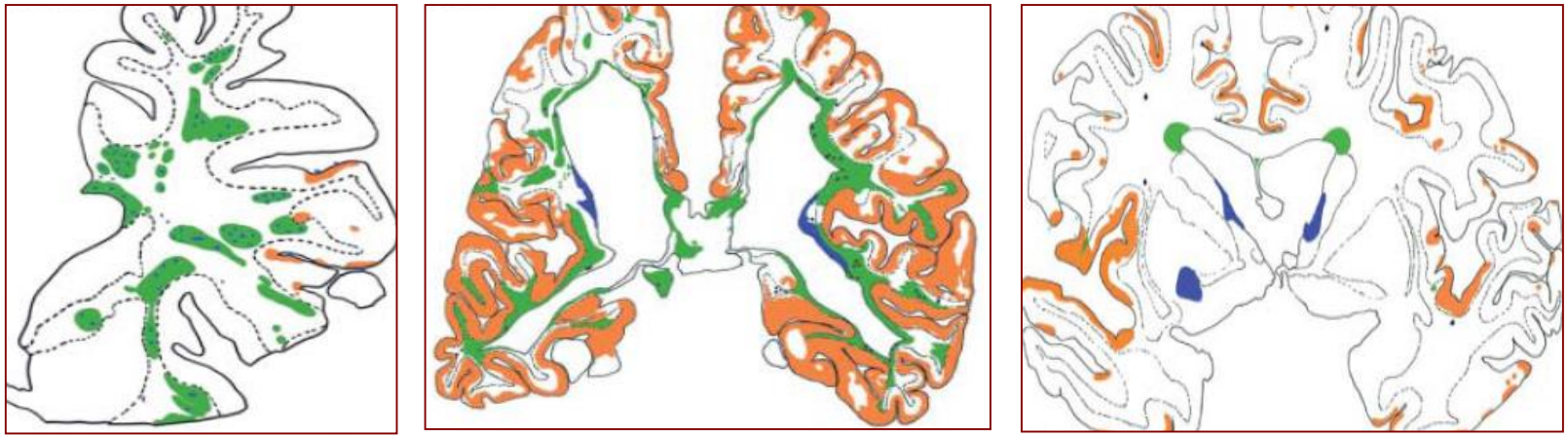
Cortical gray matter involvement in MS

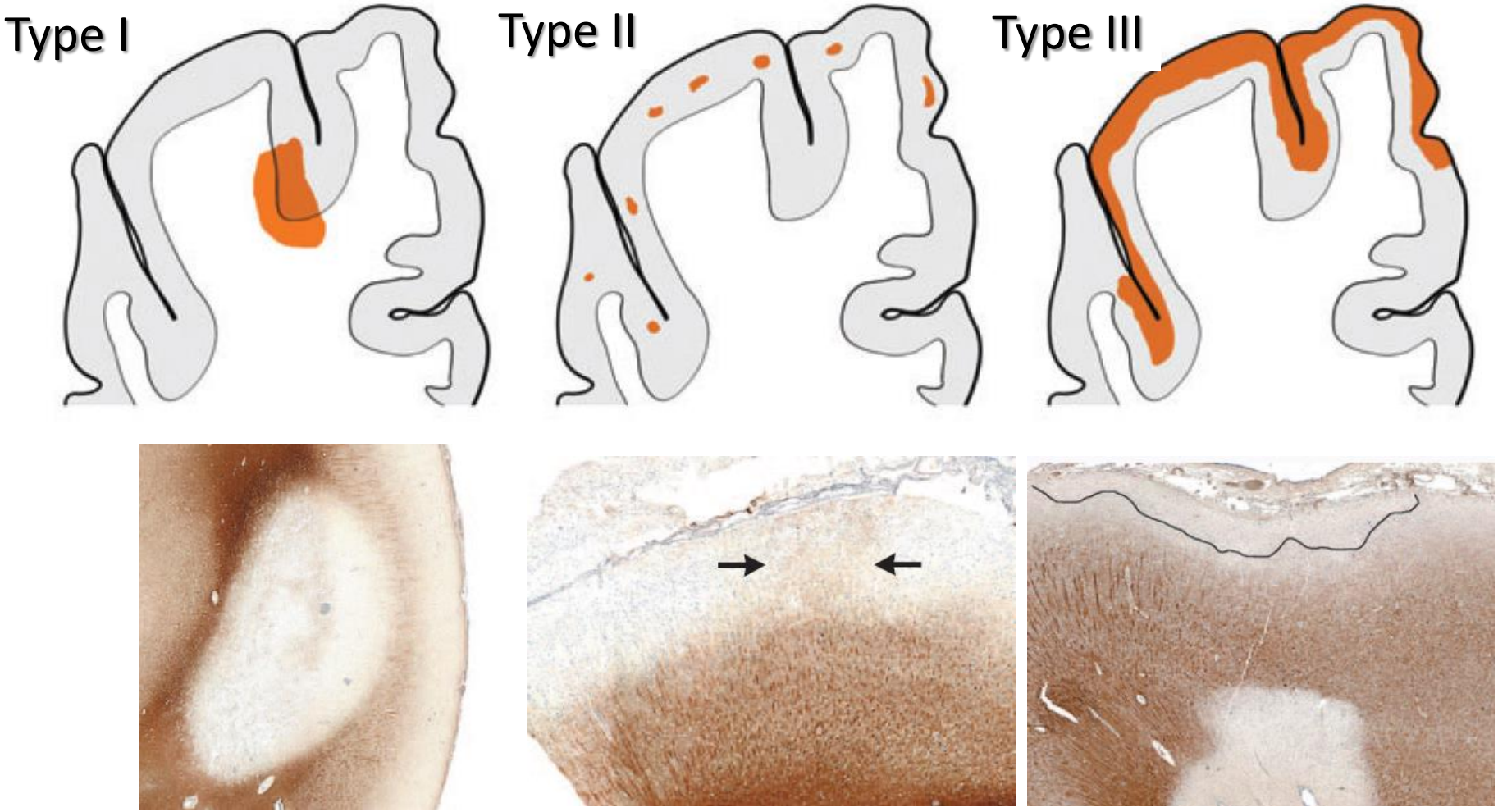
RRMS **SPMS** **PPMS**



- focal demyelinated plaques in the white matter
- cortical demyelination
- demyelinated lesions in the deep grey matter

Kutzelnigg et al. Brain 2005

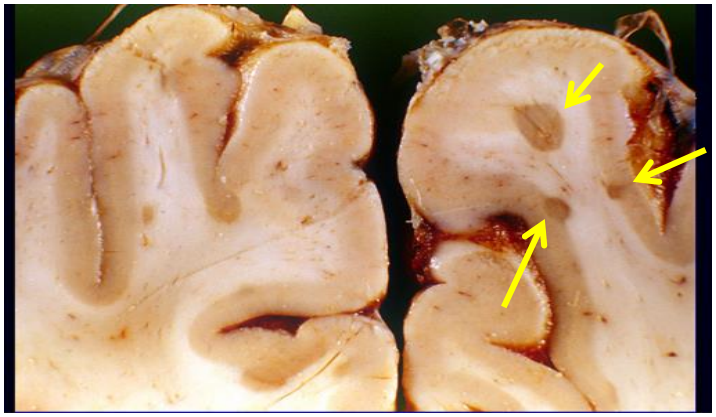
Cortical gray matter involvement in MS

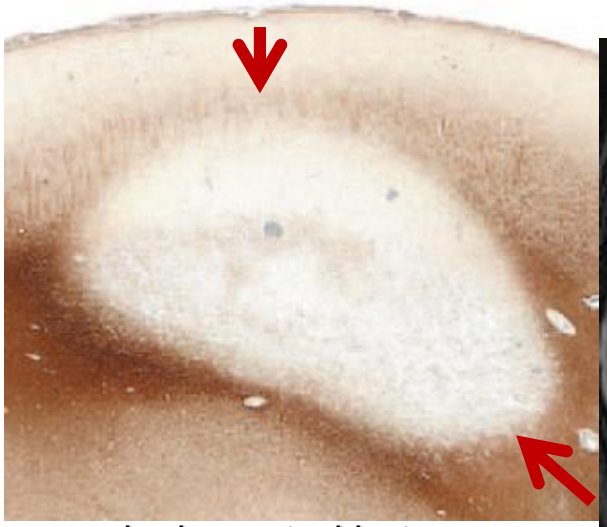


Trapp and Nave. Ann Rev Neurosci 2008
Lucchinetti et al. NEJM 2012

Juxtacortical lesions (type I)

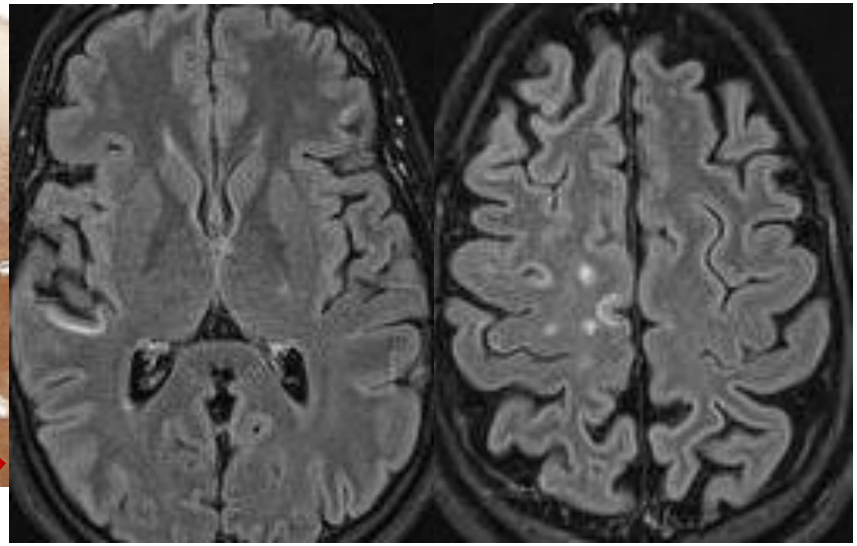
Courtesy of Dr. García-Merino





leukocortical lesion

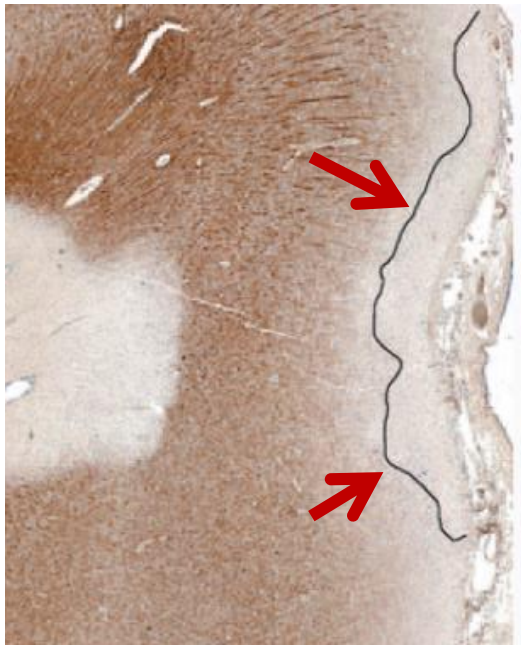
T2-FLAIR



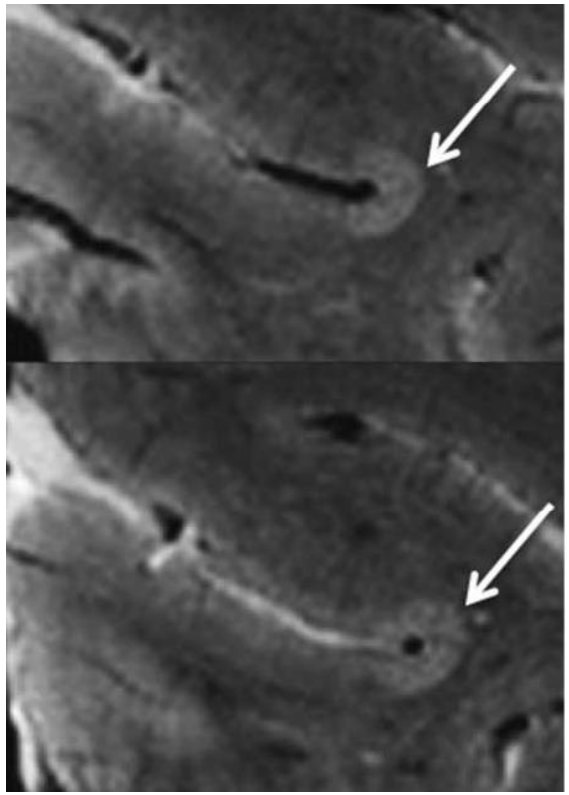
Lucchinetti et al. NEJM 2011

Intracortical lesions (type II and III)

- cMRI detects <10% of intracortical lesions
- Subpial lesion (III): a highly specific pathological marker of MS
- Cortical lesion detection: Impact on early and accurate diagnosis?

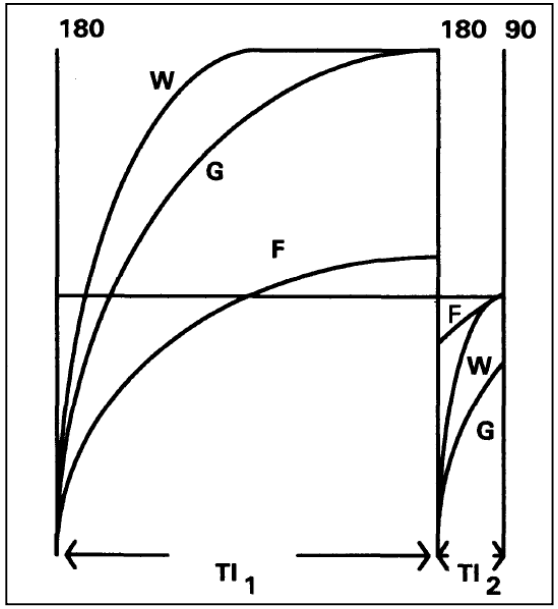


Lucchinetti et al. NEJM 2011



Nielsen et al. Neurology. 2013

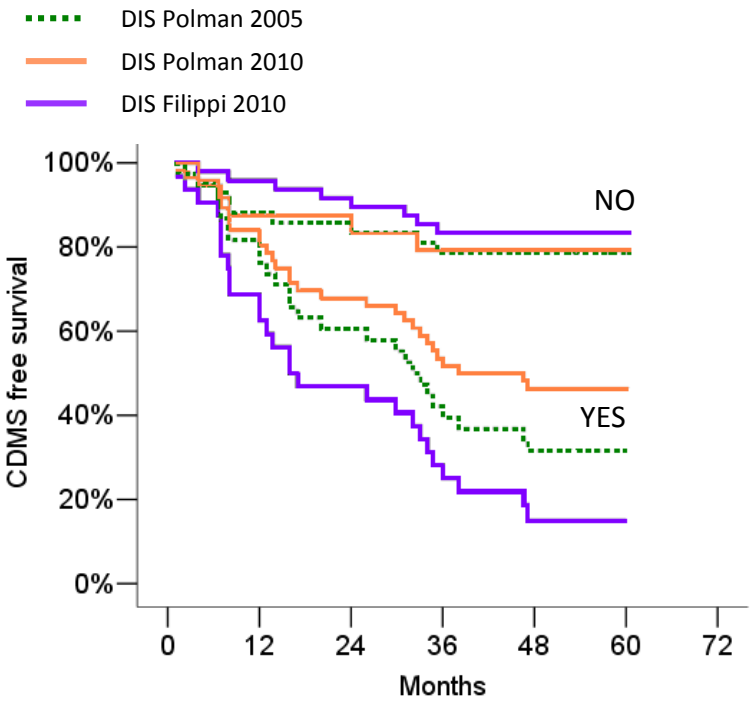
DIR (Double Inversion Recovery)

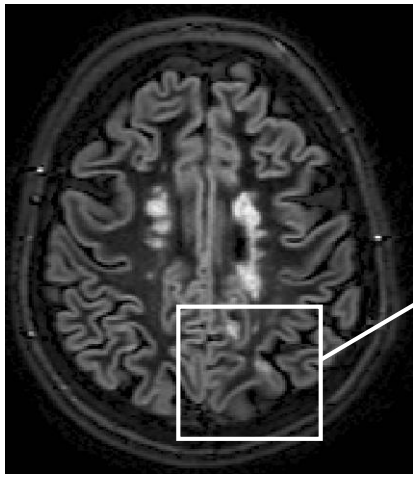


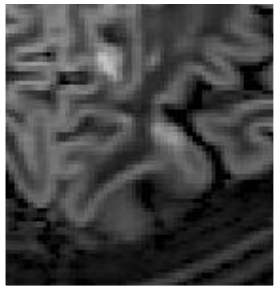
- ✓ Selective saturation of CSF and white matter (two inversion pulses)
- ✓ Improve the visualization of cortical-juxtacortical and infratentorial lesions
- ✓ Low signal/noise
- ✓ Regional variations in GM signal intensities (differences in T2 relaxation times and in cortical thickness)
- ✓ Low inter-observer concordance of this sequence, particularly for detecting pure intracortical lesions
- ✓ Not to be used as a stand-alone sequence

Redpath and Smith BJR 1994; 67:1258-63; Geurts et al. Radiology Radiology. 2005;236:254-60; Roosendaal et al. Mult Scler. 2009;15:708-14

Double-inversion recovery sequence
Diagnostic value of cortical lesion detection







At least 2 of the following:

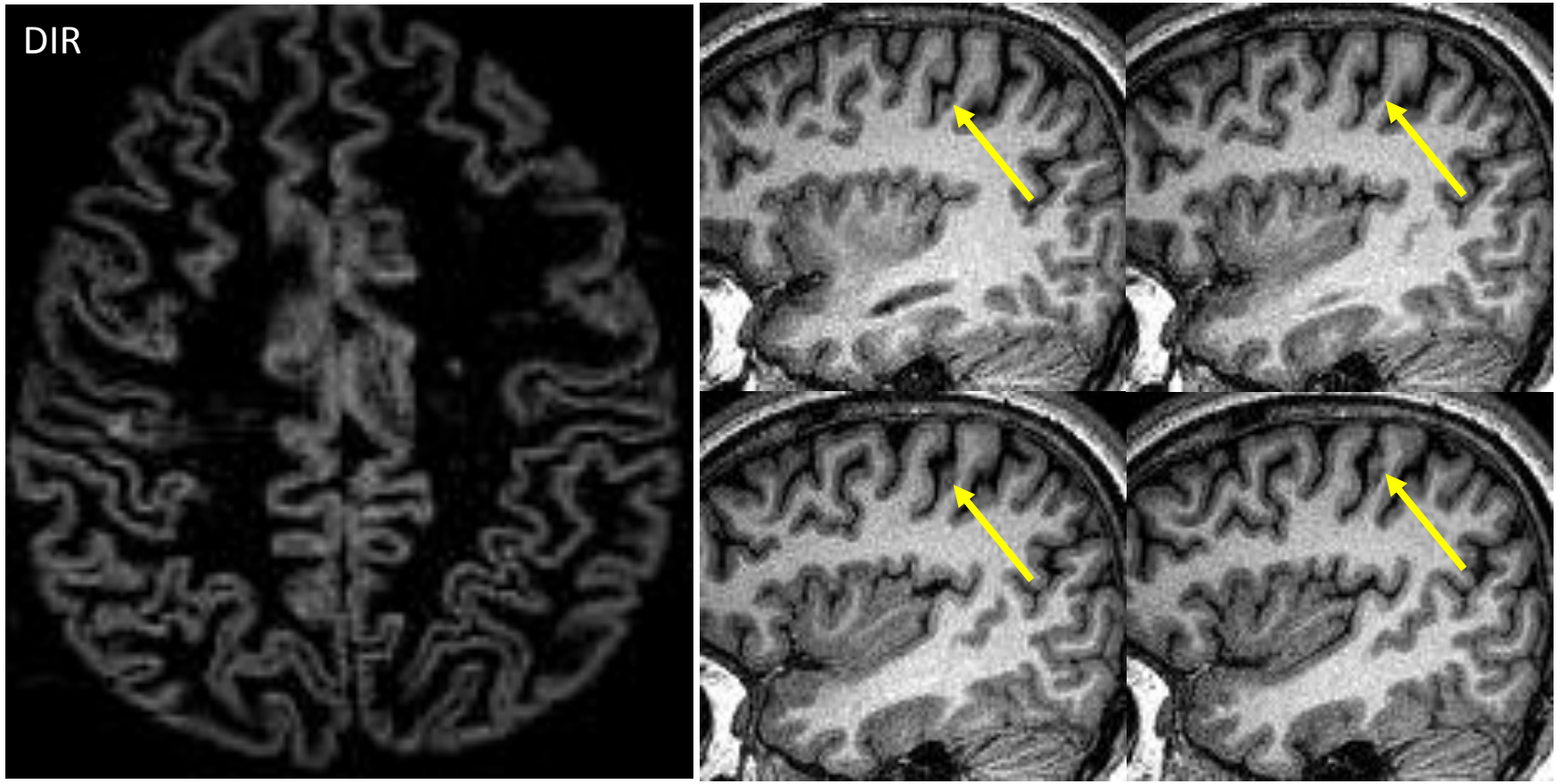
- *1 enhancing or 1 spinal cord lesion*
- *1 infratentorial lesion*
- *1 cortical lesion*

	Sensitivity	Specificity	Accuracy	OR
DIS Polman 2005	74 %	73%	74%	7.9
DIS Polman 2010	86%	42%	61%	4.3
DIS Filippi 2010	**77%**	**93%**	**86%**	**47.3**

DIS, dissemination in space

Filippi. *Neurology* 2010

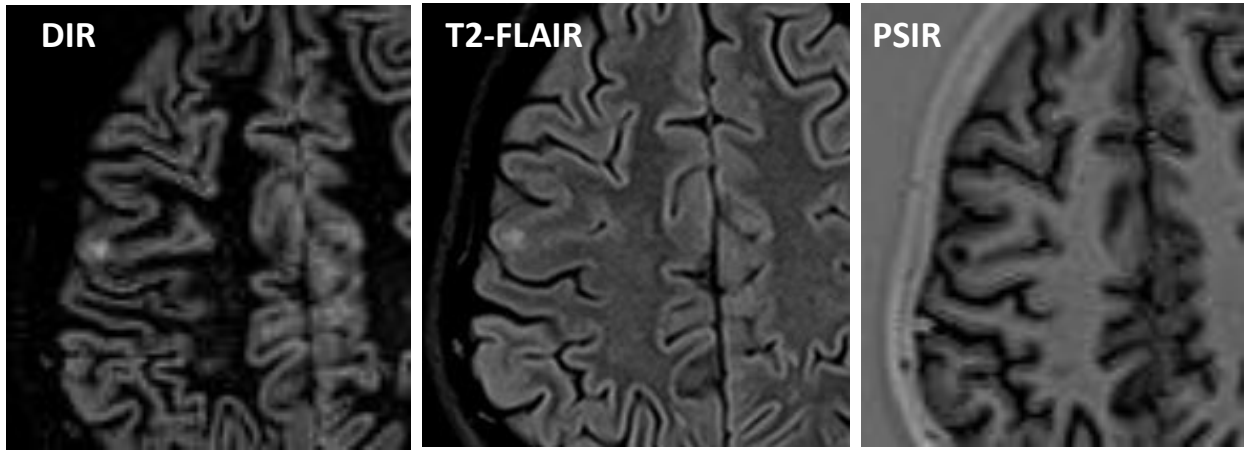
DIR: intracortical vs leukocortical lesions



A significant proportion of cortical lesions on DIR are leukocortical

(Nelson et al. Mult Scler 2008)

DIR / T2-FLAIR: intracortical vs leukocortical lesions



Sethi et al. JNNP 2012
Sethi et al. PLOS One 2014
Geurts et al. Neurology 2011

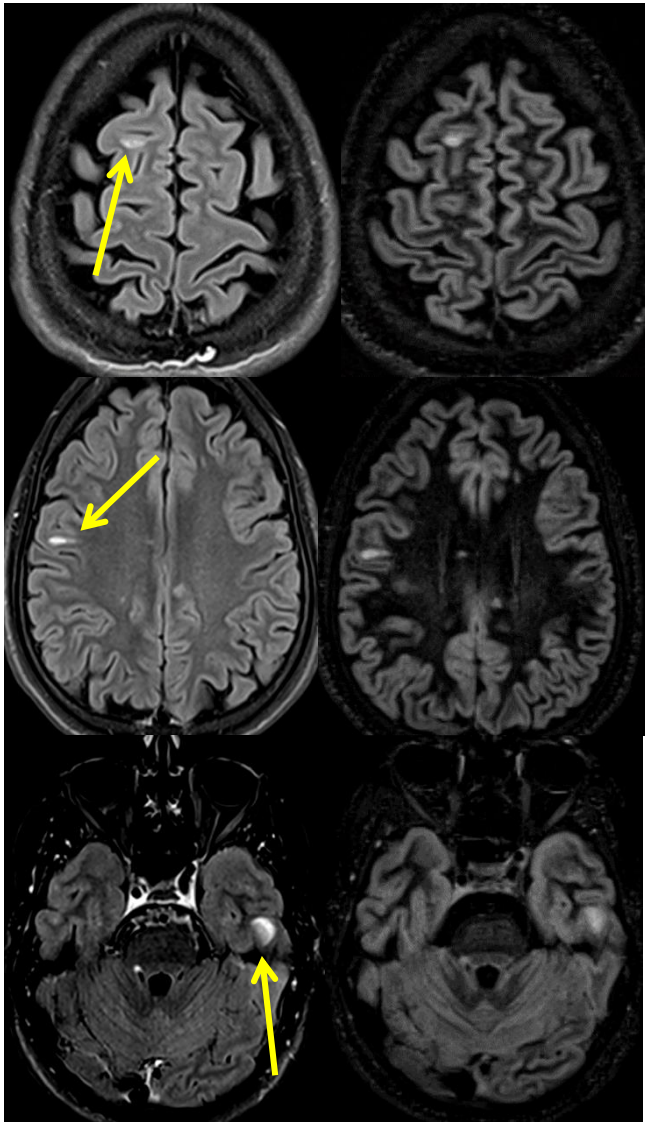
62 CIS patients (3.0 T) (Vall d'Hebron)

Concordance analysis (two observers)

- Corpus callosum lesions: 0.857
- Subependymal lesions: 0.821
- Type I-III lesions (FLAIR): 0.838
- Type II-III lesions (DIR): 0.477
- Type I lesions (DIR): 0.430

Mean of kappa for all coder-pairs
Agreement (Landis and Koch)
0.0-0.2 = slight
0.21-0.40 = fair
0.41-0.60 = moderate
0.61-0.80 = substantial
0.81-1.0 = almost perfect/perfect

Type I-III lesions

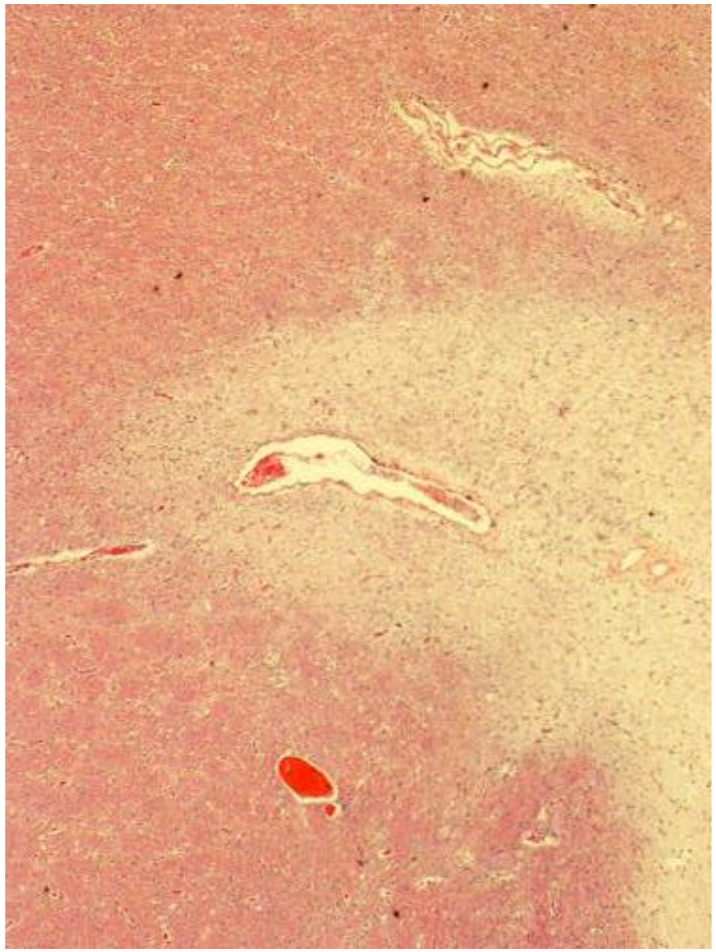


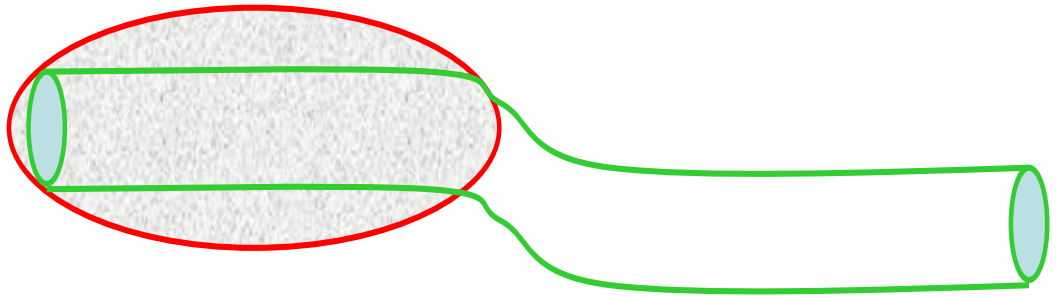
Present in **44% of CIS** and in **70% of MS** patients

Absent in NMO, migraine…

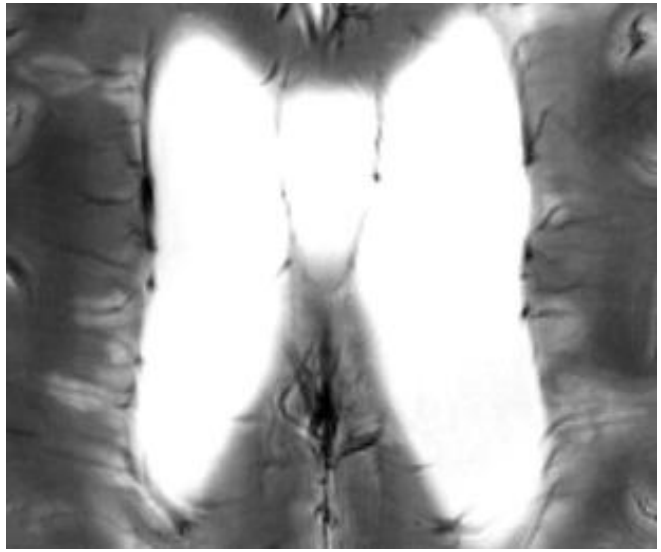
Calabrese et al. Neurology 2012; Absinta et al. J Neurol 2012; Pareto et al. Am J Neuroradiol in press

Perivenular topography of MS plaques
"Dawson's fingers"





Post-mortem pathology studies show central vein in > 90% white matter lesions



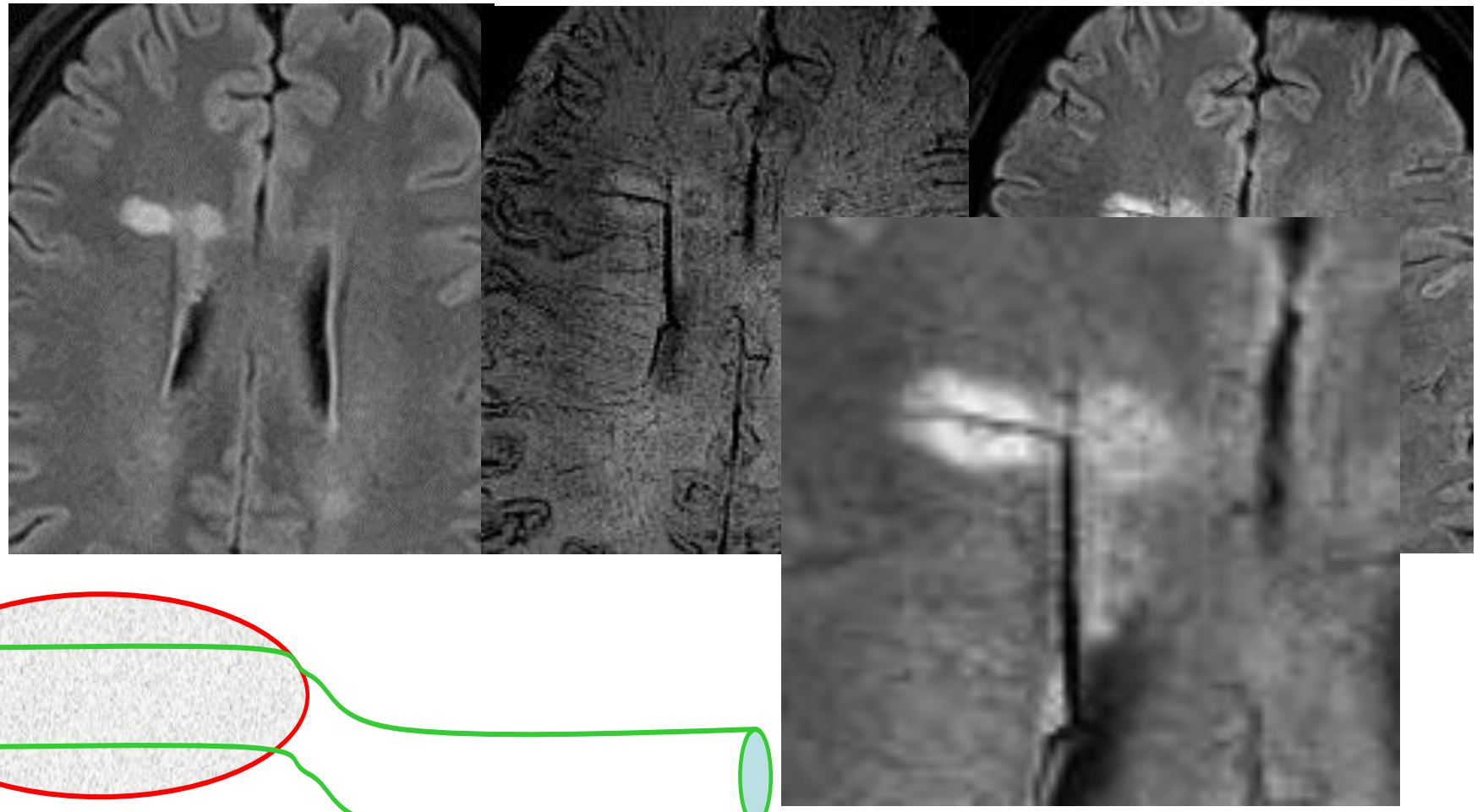
Jens Wuerfel
Berlin

FLAIR* sequence (SWI+ T2 FLAIR at 3T)
Central vein visibility

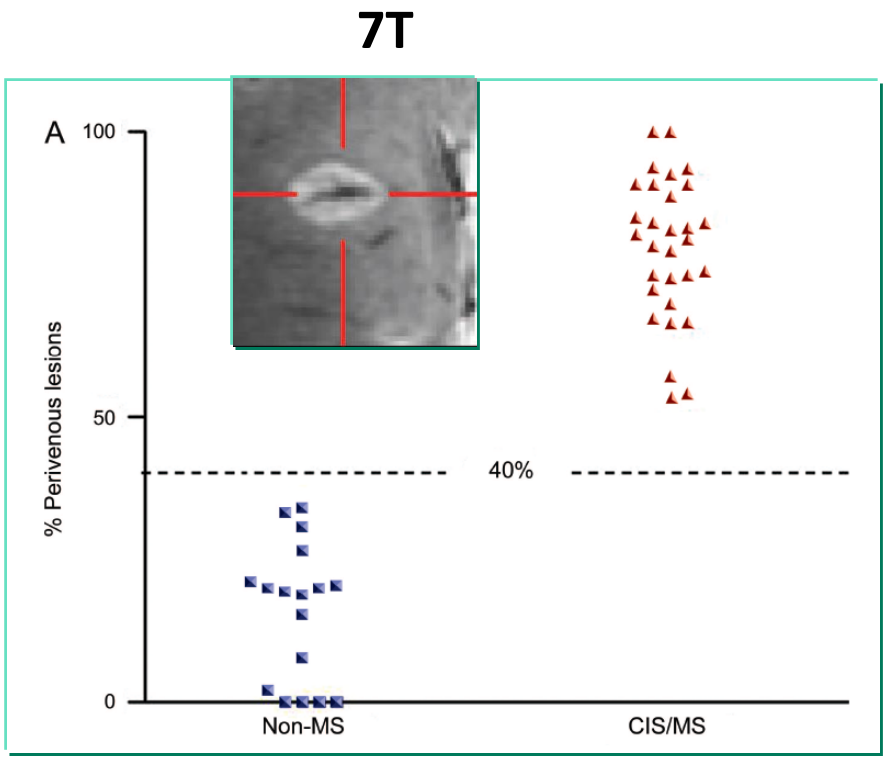
FLAIR

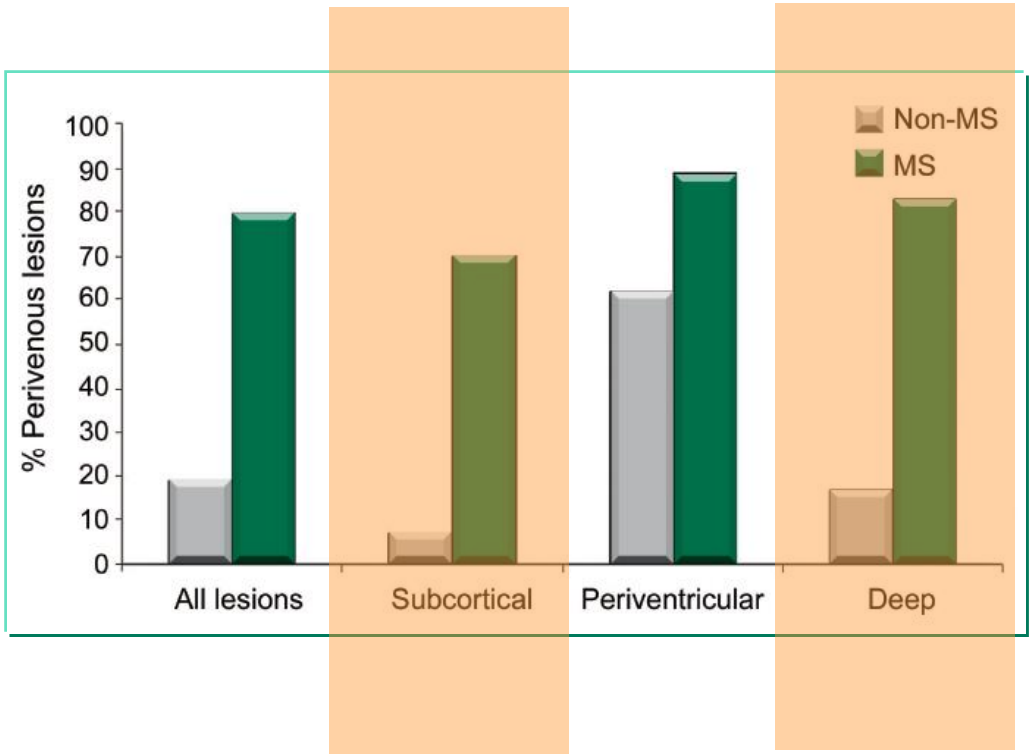
SWI

FLAIR*



FLAIR* sequence (3D GRE + 2D FLAIR at 3T)
Central vein visibility



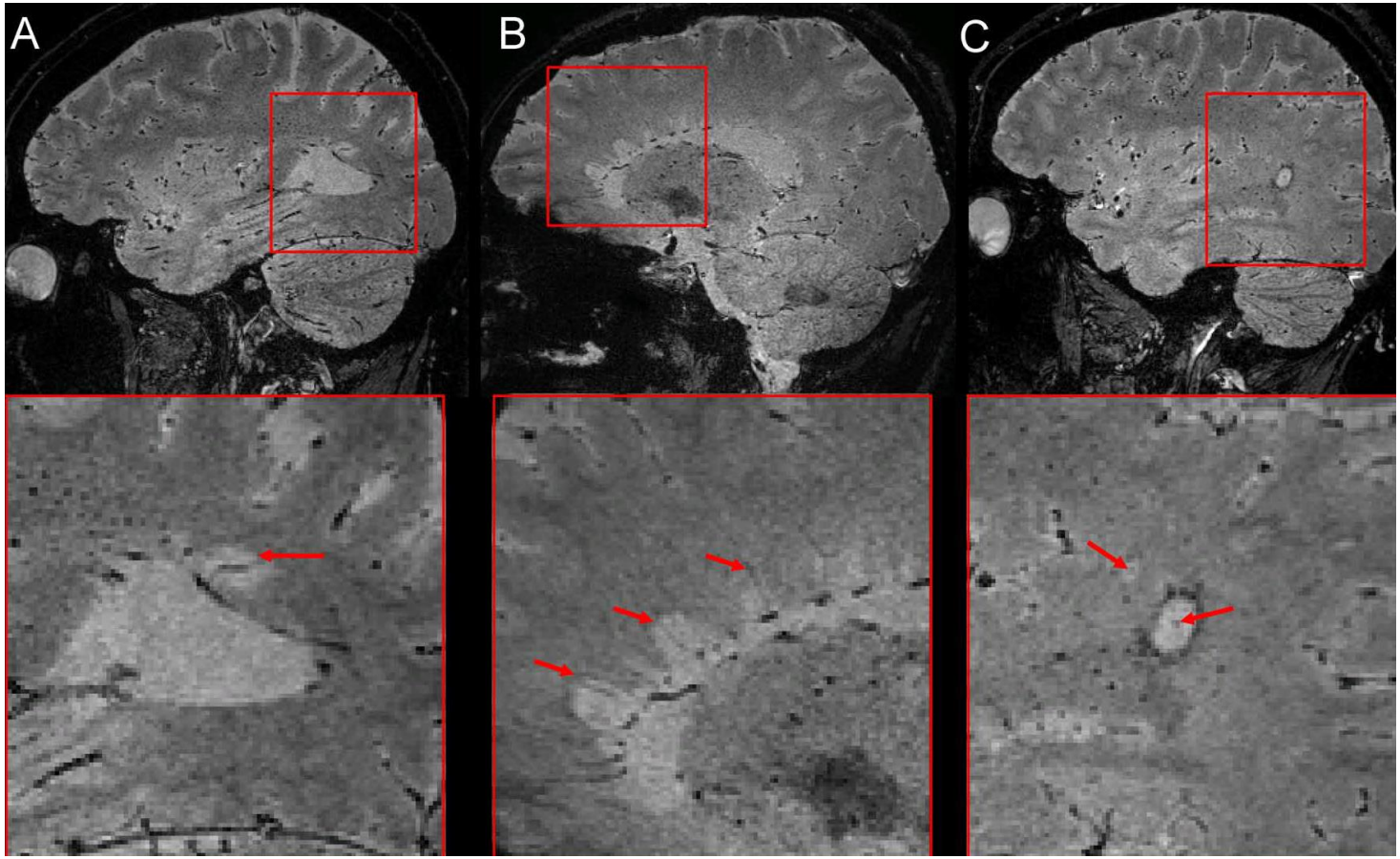


Presence of a central vein could be a marker to discriminate between MS and non-MS WM lesions

Tallantyre et al. Neurology 2011

3D-EPI sequence to rapidly acquire high-resolution T2*-weighted and phase contrast images of the whole brain (3T)

96% of the lesions (123 out of 128 lesions) detected in a MS cohort depicted a central vein (during contrast injection)

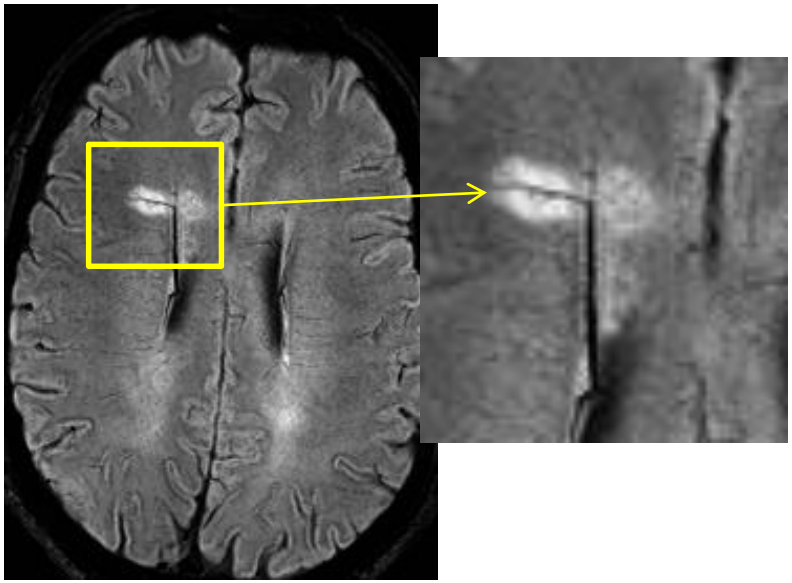


Sati et al. MSJ 2014

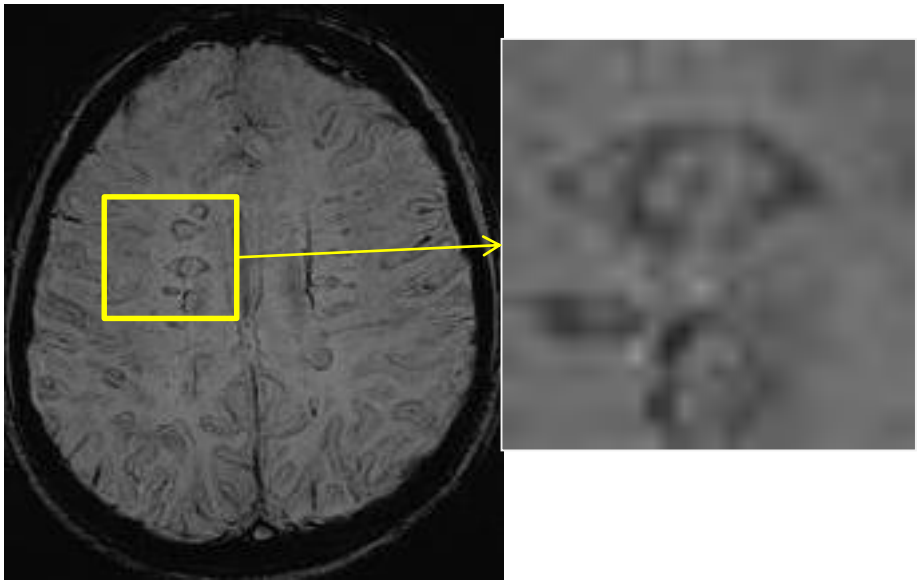
Susceptibility-weighted MR imaging

Diagnostic value in Multiple Sclerosis

Source of contrast: mostly deoxygenated blood (veins), non-heme tissue iron, proteins, lipids



Veins mapping



Signal loss in focal lesions

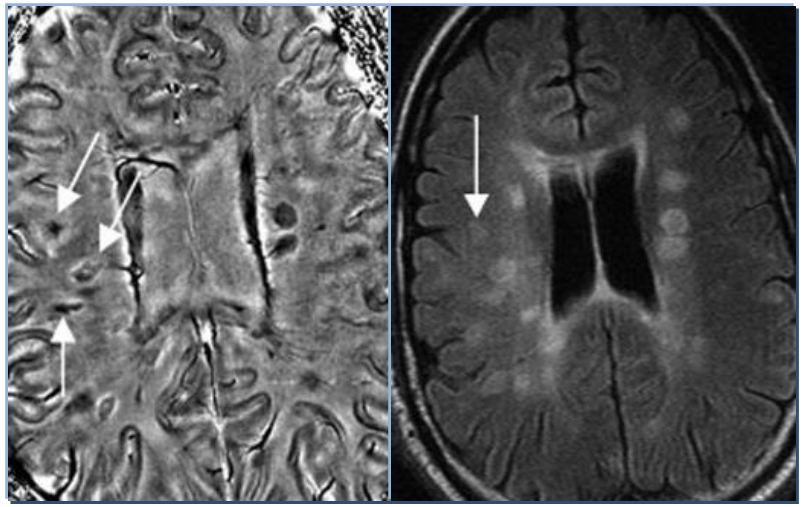
SWI in MS lesions

1.5T / 3T / 4T

Category	Description	1.5 T	3 T	4 T
A	Uniform darkening of lesions in phase	101 (63 m)	46 (38 m)	72 (33 m)
B	Magnitude lesions not seen with phase	7	32	31
C	Lesions associated with veins	6	3	4
D	Lesions surrounded by a rim of hypointense signal	7	1	3
E	Lesions with central darkening of signal	4	1	1
F	Gray matter lesions (including the basal ganglia)	16	6 (1 m)	5
Total		141	90	116

m = magnitude.

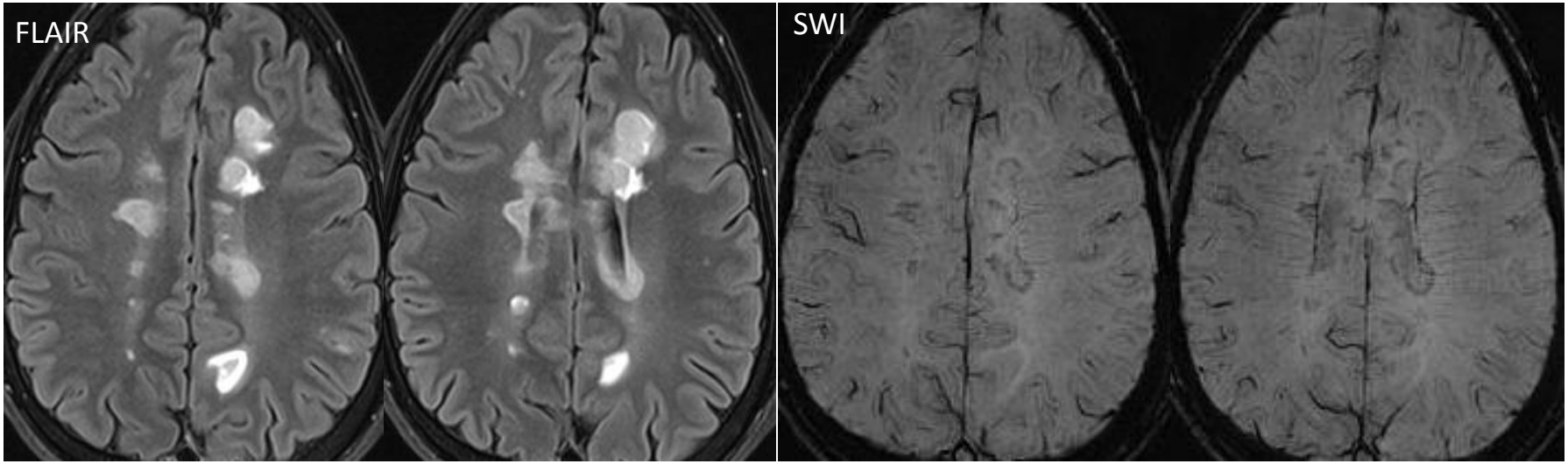
- Signal loss (increase iron content) inside and outside MS lesions



Haacke et al. JMRI 2009

Susceptibility-weighted MR imaging

Intralesional susceptibility signal (ISS) in MS (3T)



Intralesional susceptibility signal (ISS)

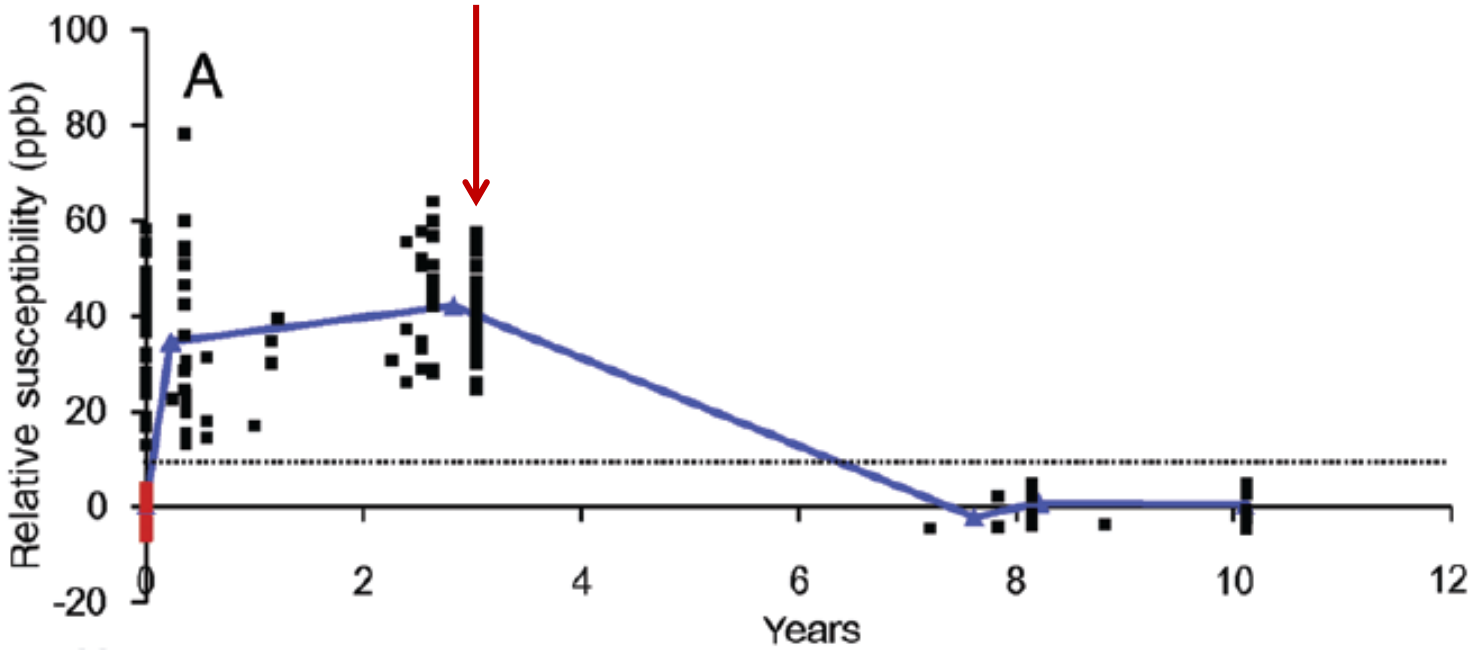
48% of non-enhancing MS lesions
58% of enhancing MS lesions

Rovira et al. ECTRIMS 2013

Likely represents iron-rich macrophages / microglia
Myelin loss also contributes

Susceptibility-weighted MR imaging in focal MS lesions

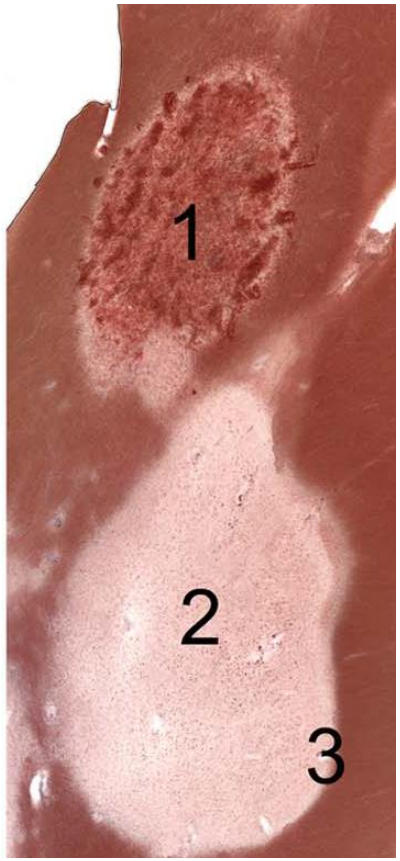
Serial analysis with QS mapping at 3T



- Magnetic susceptibility increases rapidly as it changes from enhanced to non-enhanced
- High susceptibility values during the first 2-4 years
- Then gradually decreases (susceptibility similar to NAWM)

Chen et al. Radiology 2014

MS: Lession categories



Myelin debris within macrophages detected with oil red-O

1. Early active

Large, myelin-laden macrophages without iron

2. Center, chronic-active

Small myelin-laden macrophages and occasional iron-containing macrophages

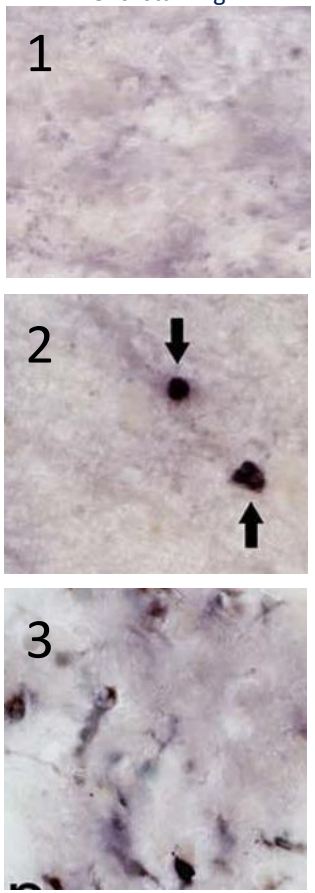
3. Rim, chronic-active

Macrophages with large amounts of iron, but without myelin

4. Chronic silent white matter lesions

No or only small amounts of iron

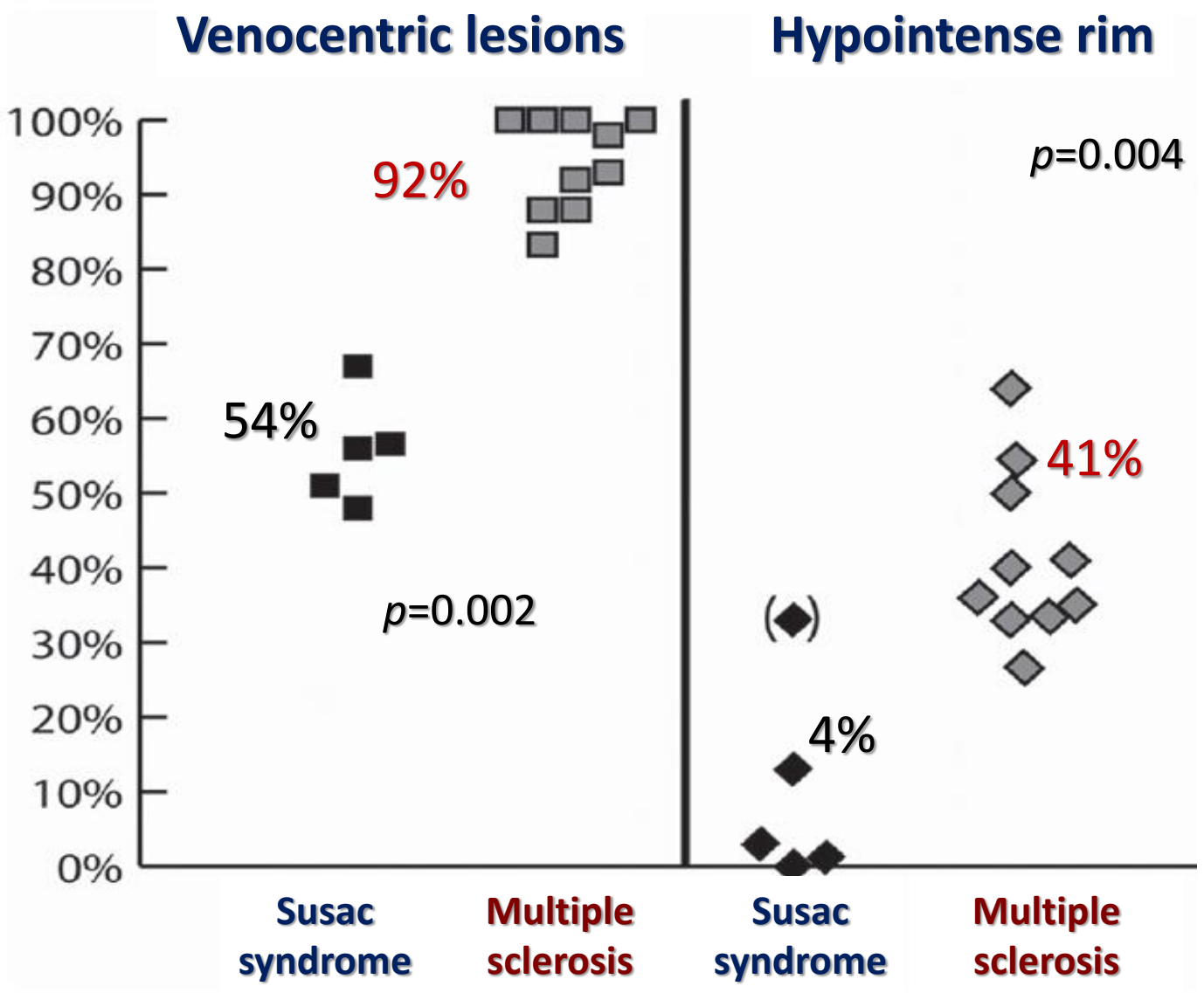
Perls' staining



Mehta et al. PLOS one 2013

SWI in T2 lesions (7T)

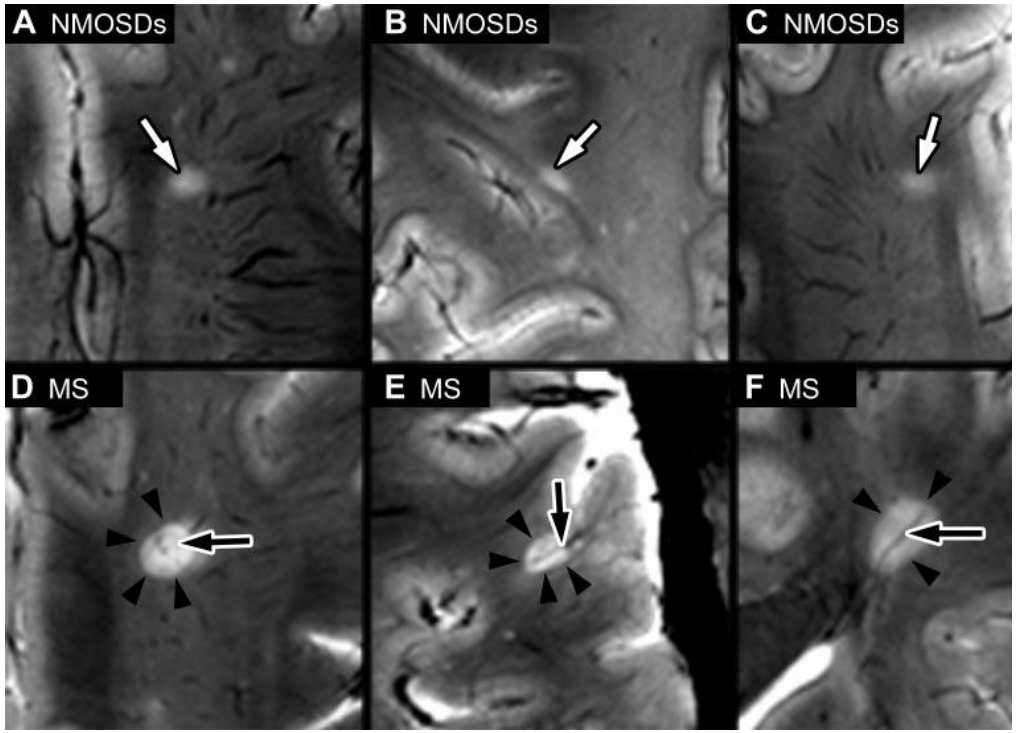
2D T2*- W FLASH

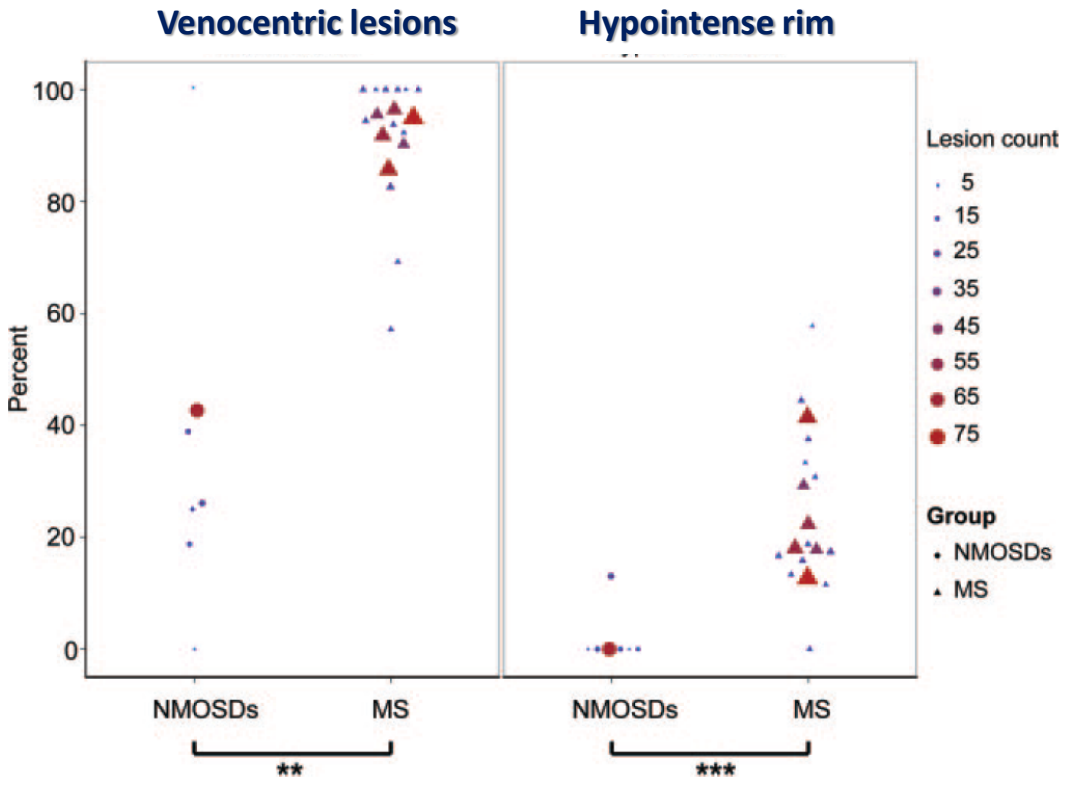


Wuerfel et al. MSJ 2012

SWI in T2 lesions (7T)
2D T2*- W FLASH

Neuromyelitis optica vs. multiple sclerosis



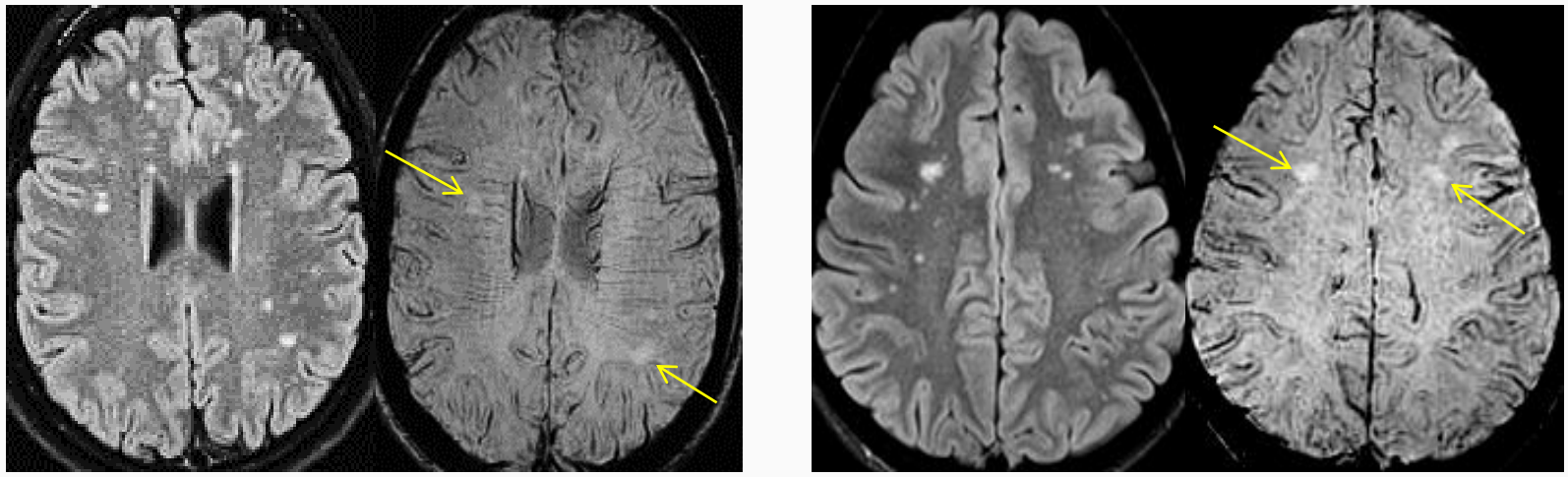


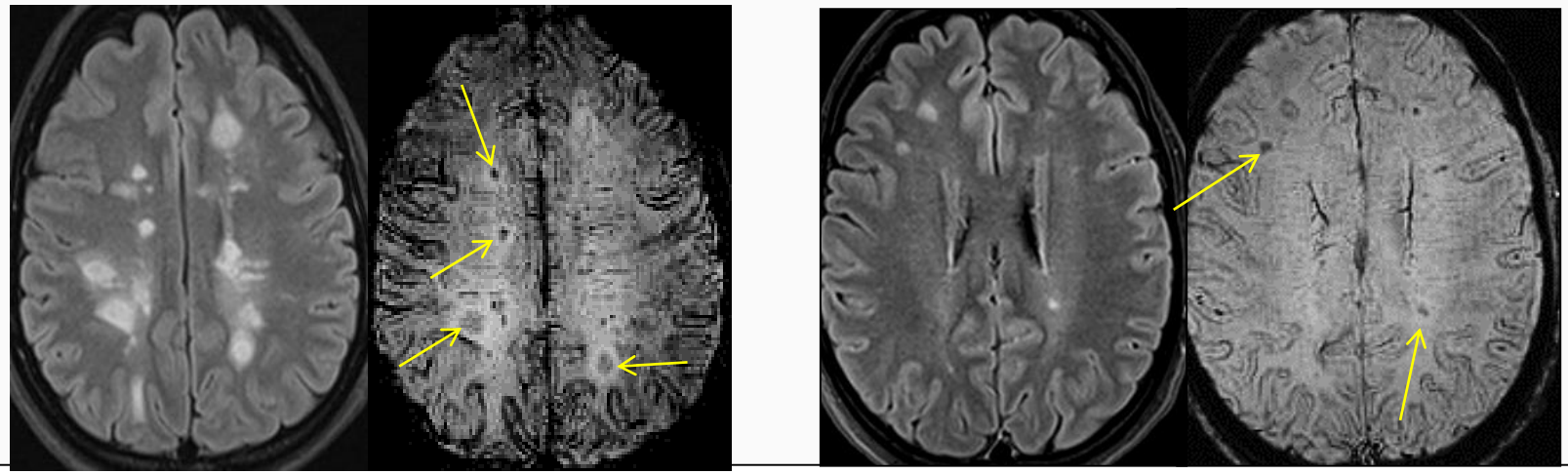
Sinneckeret al. Neurology 2012

SWI in T2 lesions (3T)

SWI

Migraine vs. multiple sclerosis

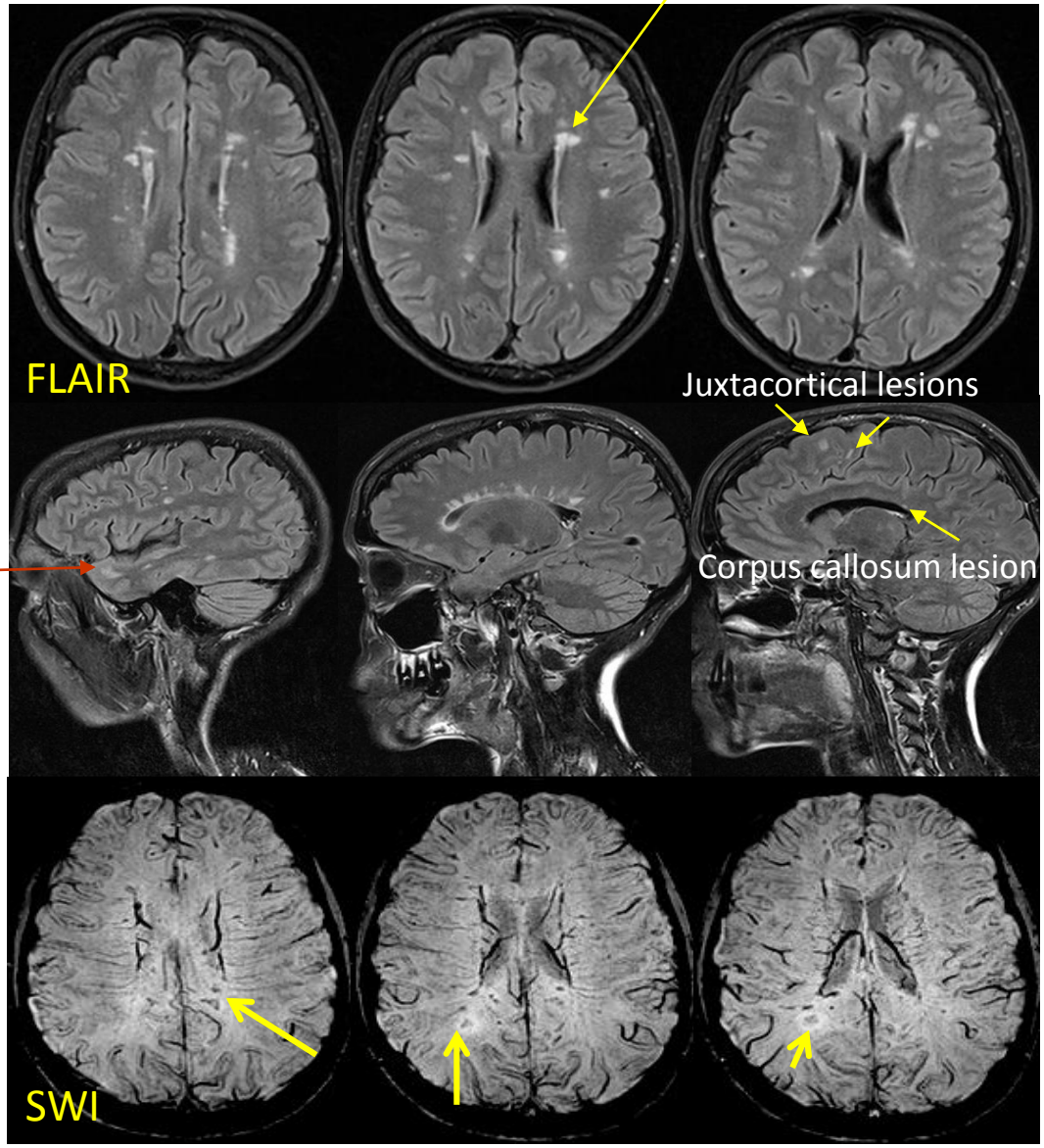




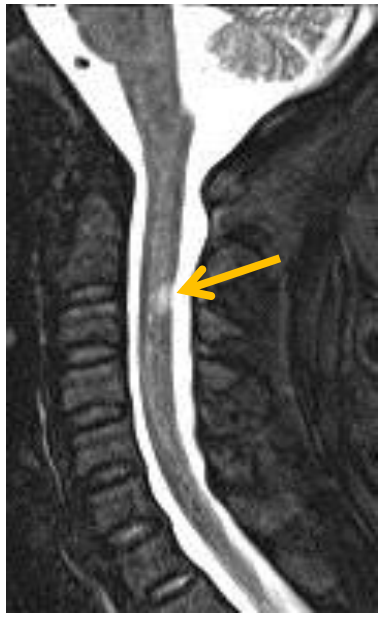
ISS on SWI increases diagnostic specificity and accuracy (McDonald criteria)

Rovira et al. ECTRIMS 2015

MS or incidental findings in a young asymptomatic subject?



ISS within lesions



Subclinical spinal cord lesions

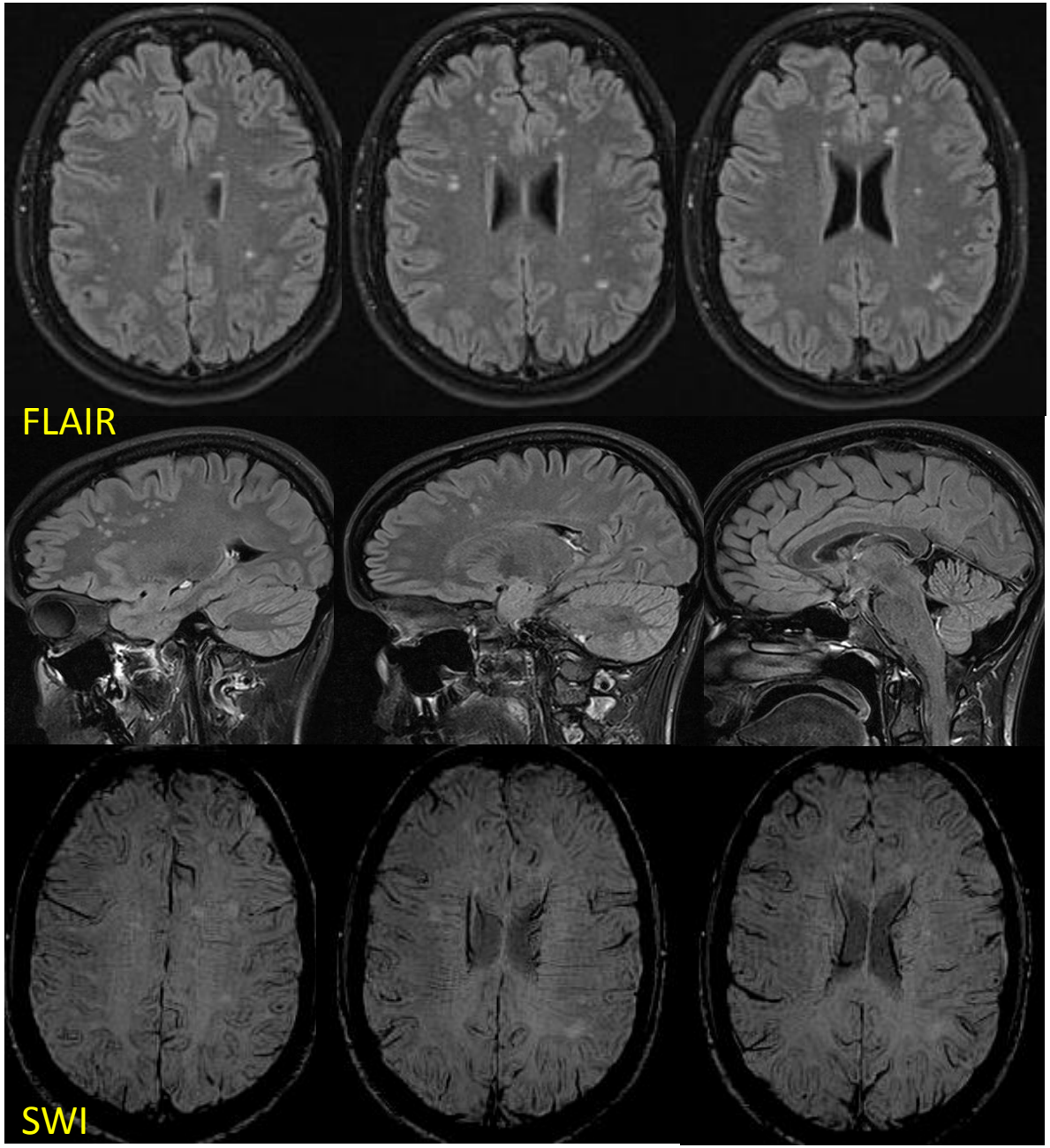
Preclinical multiple sclerosis or Radiologically isolated síndrome (RIS)

MS or incidental findings in a young asymptomatic subject?

Frontal subcortical lesions

No juxtacortical, corpus callosum lesions

No ISS



No subclinical spinal cord lesions

Incidental findings

Summary

- Wide variety of causes may present with multifocal WM lesions
- MRI is the preferred imaging technique for diagnostic workup
- Radiological interpretation with demographic, clinical history, and lab findings
- Standardized brain (spinal cord) MRI protocol
- Comprehensive checklist for evaluation of WM spots is crucial
- Detection of cortico-juxtacortical lesions, venocentric lesions and intralesional susceptibility signal may increase diagnostic specificity