Edinburgh 2012

Special Focus Session on Multiple Sclerosis

"MRI diagnostic criteria in MS"

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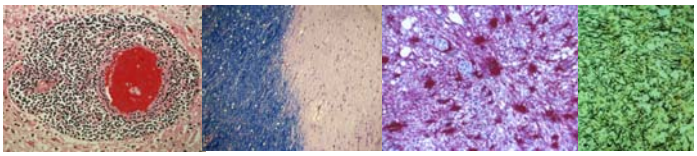
MAGNIMS

IDI Institut de Diagnòstic per la Imatge

Multiple Sclerosis

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



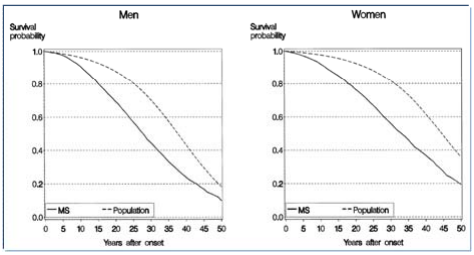
Inflammation Demyelination Gliosis Axonal loss

- Most common disabling neurological disease of young adults
- Women affected more than men (2:1)
- Symptoms onset between 20 and 40 years of age
- 1.3 to 2.5 million estimated cases of MS worldwide; 350,000 in Western Europe

Multiple Sclerosis

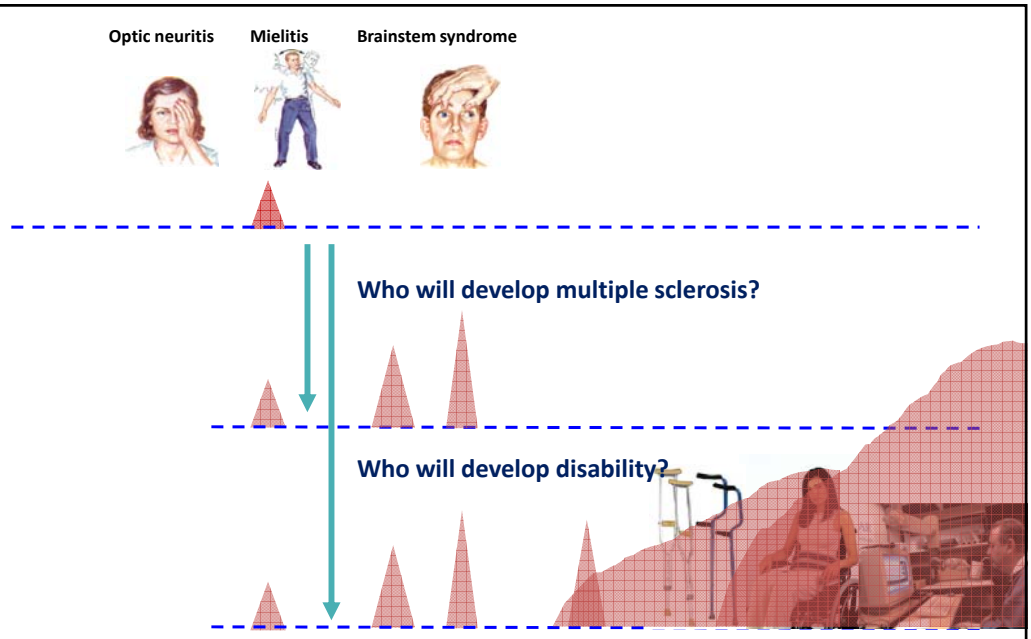
Most people with MS have a normal or near-normal life expectancy (median survival time from onset is ~10 years shorter)

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

•No curative treatment, although different disease modifying treatments (DMT) significantly decrease the frequency and severity of relapses and delay permanent disability



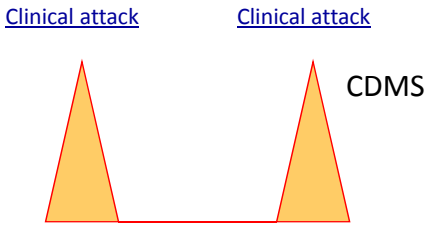
No single clinical feature or diagnostic test is sufficient for the diagnosis of this disease

Diagnostic criteria
Clinical

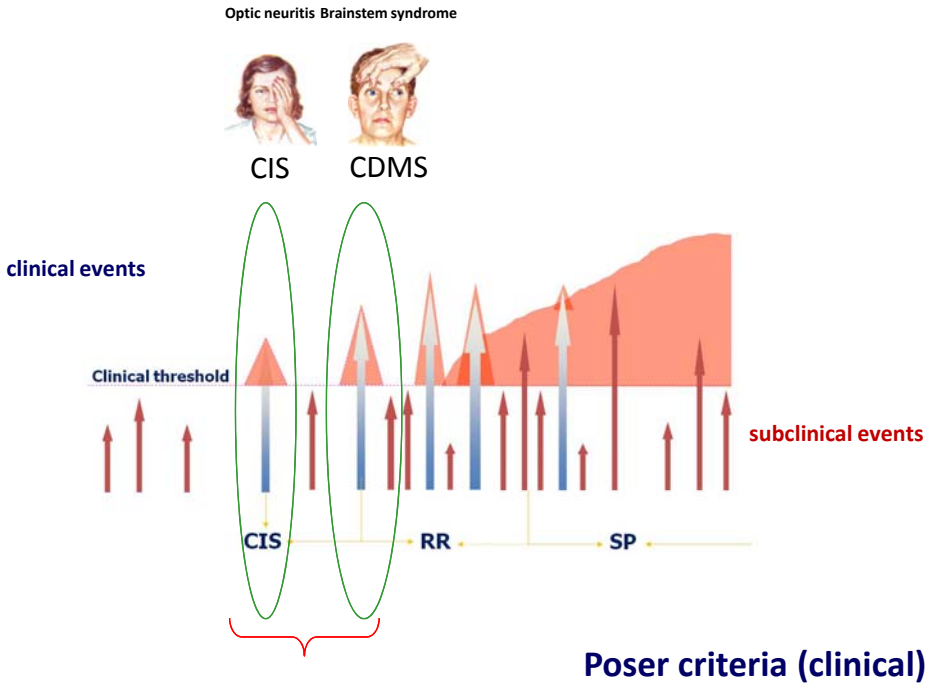
Diagnostic Criteria:

- Allison y Millar (1954)
- McAlpine (1965)
- Schumacher (1965)
- Rose (1976)
- **Poser et al.** *(Ann Neurol. 1983)*

Dissemination in space and time
Exclusion of other diagnosis

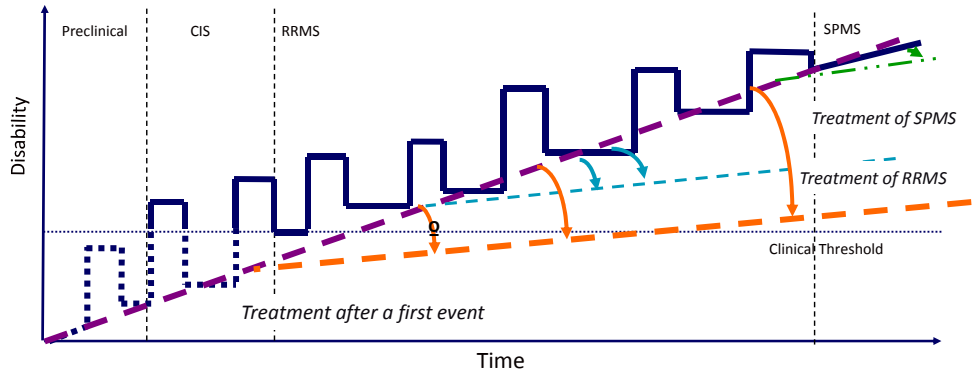


Different CNS topographies



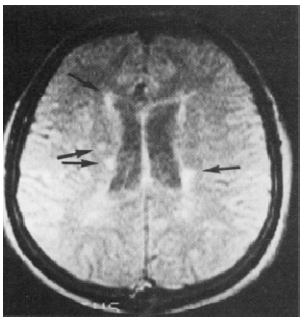
Poser criteria (clinical)

Treatment initiated at different stages of MS can affect outcomes

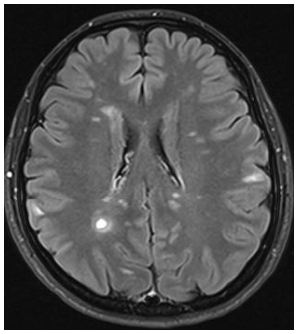


MRI revolution in clinical practice

1981



MORE THAN 30 YEARS OF PROGRESS



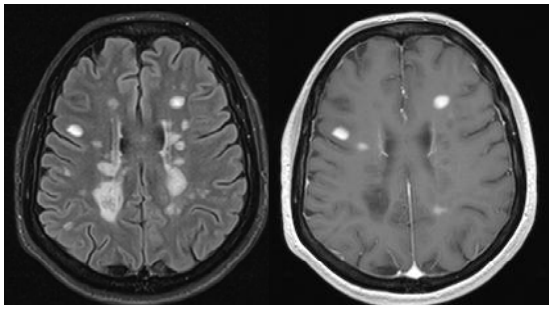
2012

Ten patients with multiple sclerosis (MS) were scanned by means of cranial X-ray computed tomography (CT) with and without intravenous contrast enhancement, and by nuclear magnetic resonance (NMR) using an inversion-recovery sequence. NMR demonstrates abnormalities in MS on a scale not previously seen except at necropsy.

Nuclear magnetic resonance imaging of the brain in multiple sclerosis.
Young et al. Lancet 1981

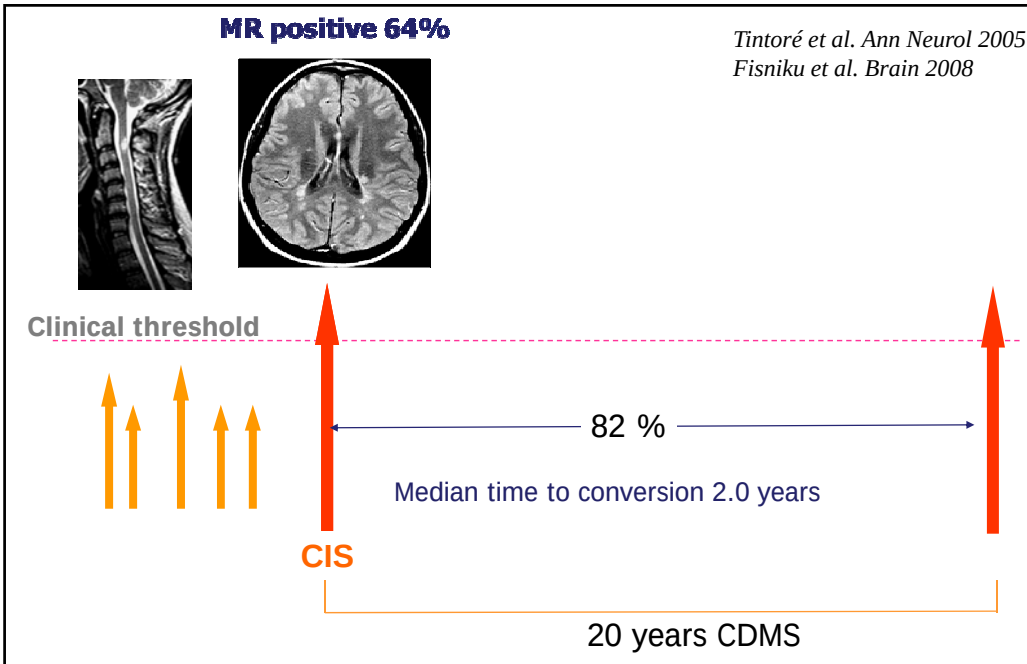
Multiple Sclerosis
Conventional MR imaging

T2-weighted



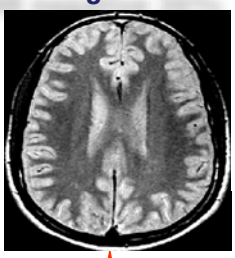
Post-contrast T1-weighted

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



Tintoré et al. Ann Neurol 2005
Fisniku et al. Brain 2008

MR negative 36 %



Tintoré et al. Ann Neurol 2005
Fisniku et al. Brain 2008

38% MRI evidence of MS

Clinical threshold

21 %

Median time to conversion 6.0 years

CIS

20 years CDMS

Brain and spinal cord MRI

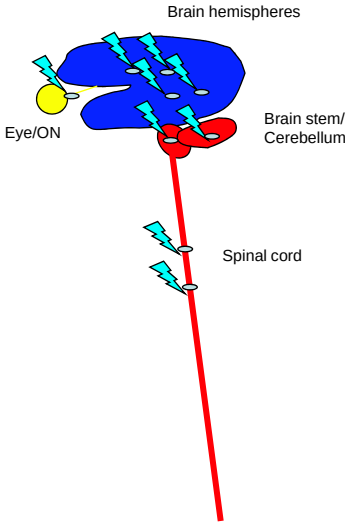
Role in the initial diagnosis

SPECIAL REPORT

Recommended Diagnostic Criteria for Multiple Sclerosis: Guidelines from the International Panel on the Diagnosis of Multiple Sclerosis

- International Panel
- AIMS:
  - ✓ Re-assess existing criteria
  - ✓ Retain useful features of prior criteria
  - ✓ **Integrate imaging in diagnostic criteria**
  - ✓ Clarify definitions; simplify categories
  - ✓ Create a scheme useful for practitioners

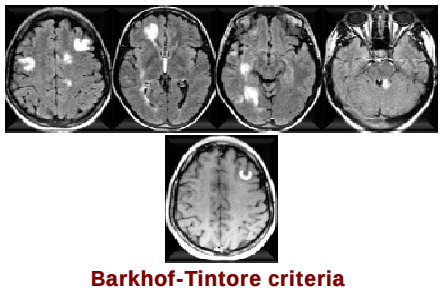
McDonald criteria



Dissemination in time and space
Exclusion of other diagnosis

- Clinical evidence:
  - Historical symptoms
  - Objective signs
- Paraclinical investigations:
  - MRI
  - CSF
  - VEP (PPMS)

MRI criteria for dissemination in space (DIS) for MS

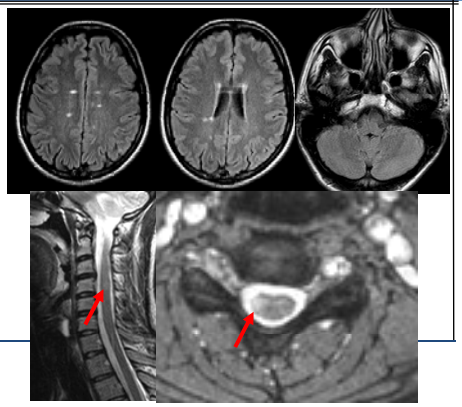
McDonald 2001 (McDonald et al. Ann Neurol 2001)		
DIS	3 or more of: • 9 T2 lesions or 1 Gd-enhancing lesion • 3 or more PV lesions • 1 or more JC lesions • 1 or more PF lesions 1 cord lesion can replace 1 brain lesion	

Barkhof-Tintore criteria

Gd = gadolinium enhancing lesion; **PV** = periventricular; **JC** = juxtacortical; **PF** = posterior fossa; **BS** = brainstem; **SC** = spinal cord

MRI criteria for dissemination in space (DIS) for MS

	McDonald 2001 (McDonald et al. Ann Neurol 2001)	McDonald 2005 (Polman et al. Ann Neurol 2005)
DIS	3 or more of: • 9 T2 lesions or **1 Gd-enhancing lesion** • 3 or more PV lesions • 1 or more JC lesions • 1 or more PF lesions 1 cord lesion can replace 1 brain lesion	3 or more of: • 9 T2 lesions or **1 Gd-enhancing lesion** • 3 or more PV lesions • 1 or more JC lesions • 1 or more PF lesions •A SC lesion can replace an infratentorial lesion •An enhancing SC lesion is equivalent to an enhancing brain lesion •Any number of SC lesions can be included in total lesion count

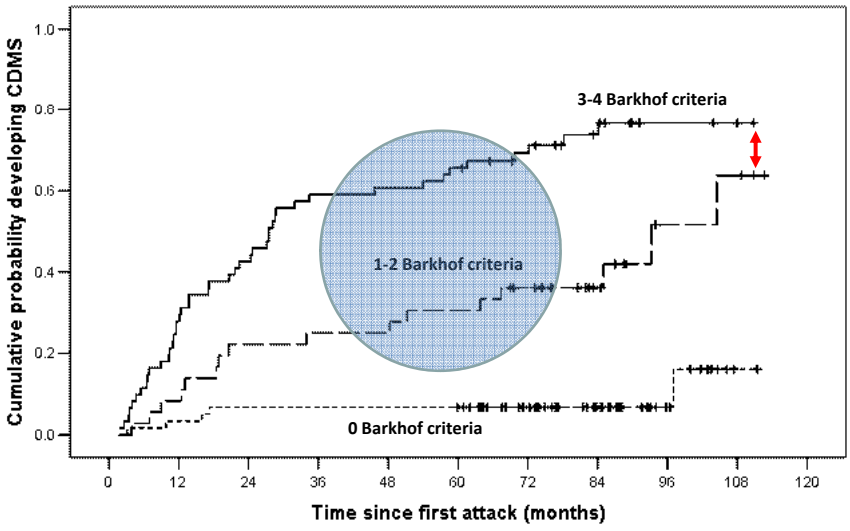


Barkhof-Tintore criteria + SC

Gd = gadolinium enhancing lesion; **PV** = periventricular; **JC** = juxtacortical; **PF** = posterior fossa; **BS** = brainstem; **SC** = spinal cord

Conversion to CDMS

Baseline MRI



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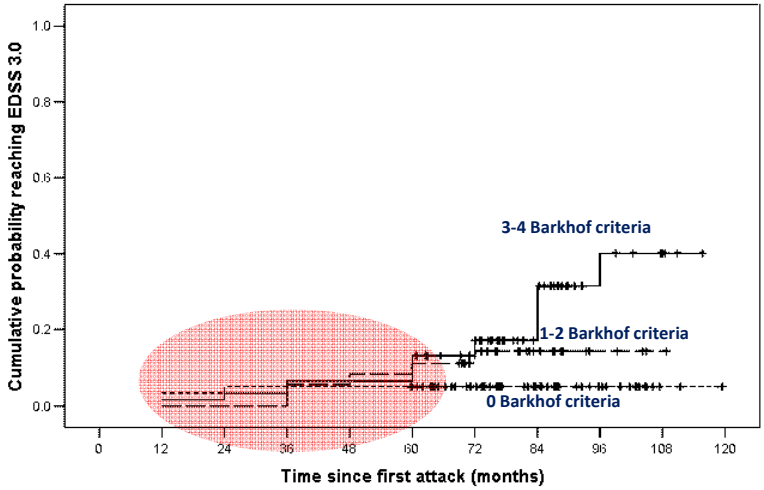
Tintore et al. Neurology 2006

Time to reach EDSS 3.0

Baseline MRI

EDSS at 5 years correlates with number of Barkhof criteria at baseline (r=0.46, p<0.0001)

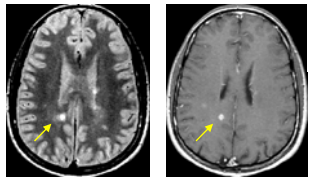


Vall d'Hebron

Tintore et al. *Neurology 2006*

MRI criteria for dissemination in time (DIT) for MS

McDonald 2001 (McDonald et al. Ann Neurol 2001)	McDonald 2005 (Polman et al. Ann Neurol 2005)



> 3 months

0 — 1 m — 3 m — 1 y

CIS

Timing of Scanning

DIT

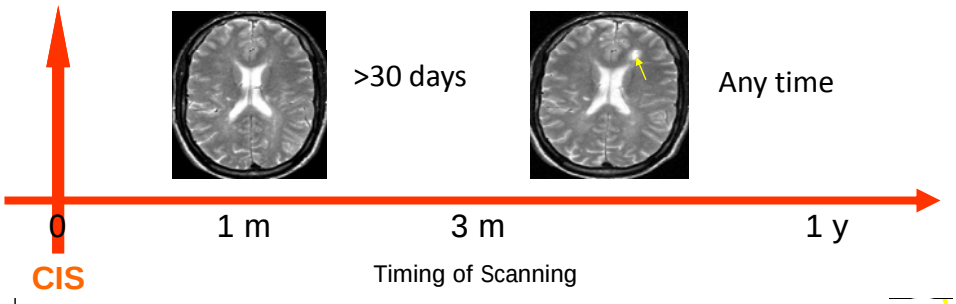
(i) A Gd-enhancing lesion at least 3 months after CIS onset

(ii) A new T2 lesion with reference to a baseline scan obtained at least 30 days after CIS onset

Gd = gadolinium enhancing lesion; **PV** = periventricular; **JC** = juxtacortical; **PF** = posterior fossa; **BS** = brainstem; **SC** = spinal cord

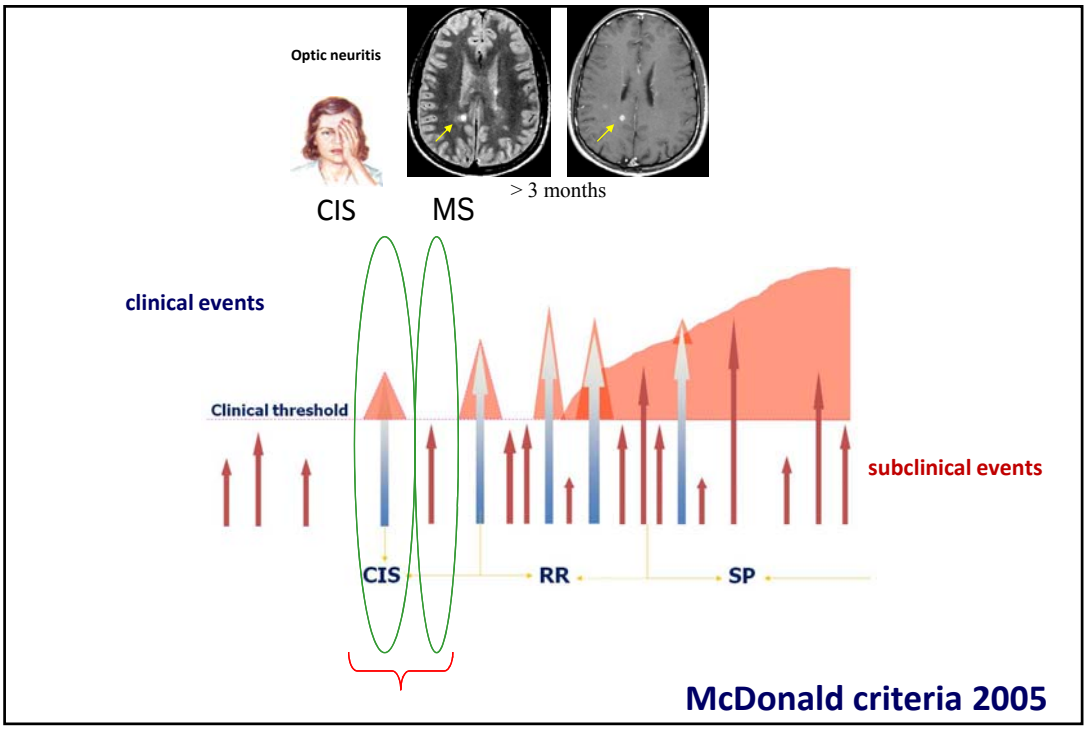
MRI criteria for dissemination in time (DIT) for MS

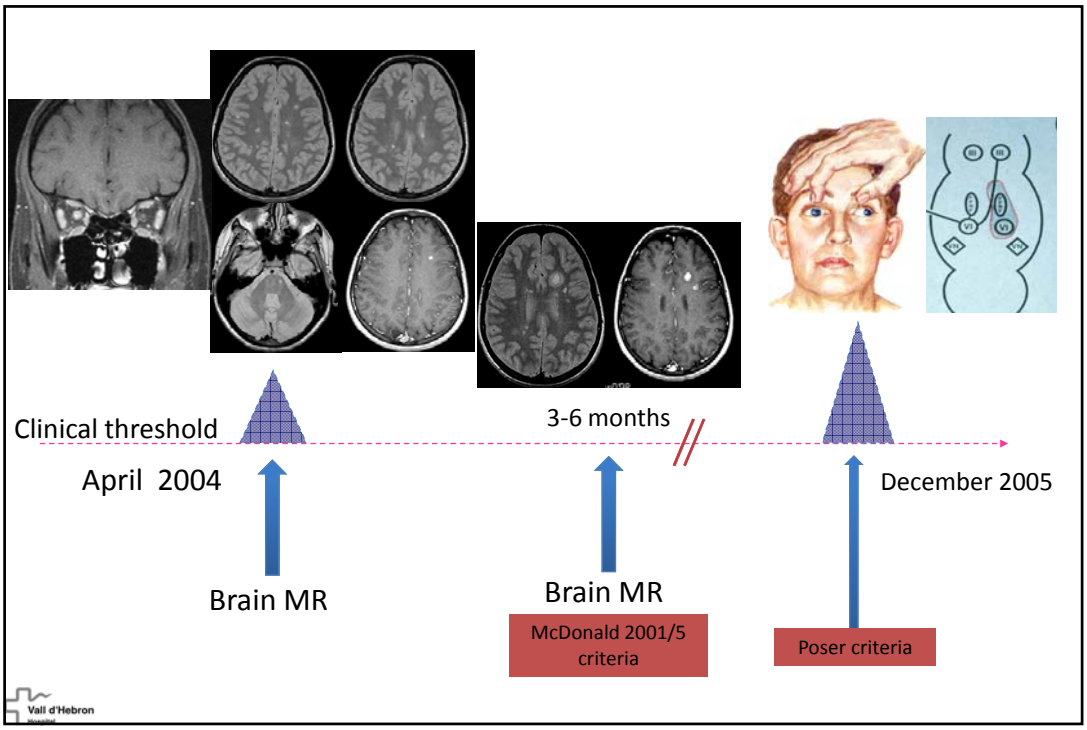
McDonald 2001 (McDonald et al. Ann Neurol 2001)	McDonald 2005 (Polman et al. Ann Neurol 2005)

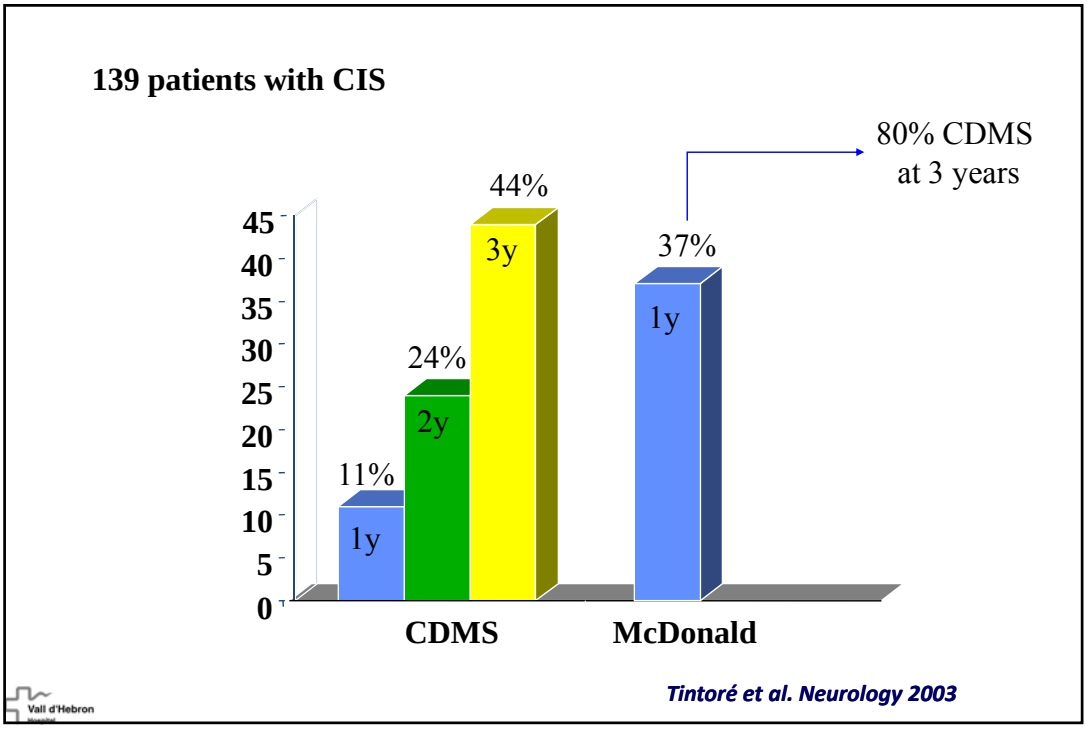


DIT	
	(i) A Gd-enhancing lesion at least 3 months after CIS onset **(ii) A new T2 lesion with reference to a baseline scan obtained at least 30 days after CIS onset**

Gd = gadolinium enhancing lesion; **PV** = periventricular; **JC** = juxtacortical; **PF** = posterior fossa; **BS** = brainstem; **SC** = spinal cord




Clinical threshold
April 2004
Brain MR
3-6 months
Brain MR
McDonald 2001/5 criteria
December 2005
Poser criteria


139 patients with CIS
80% CDMS at 3 years
45
40
35
30
25
20
15
10
5
0
11%
1y
24%
2y
44%
3y
37%
1y
CDMS
McDonald
Tintoré et al. Neurology 2003

Criticism to McDonald 2005 criteria

- **Too complicated for demonstration DIS and DIT**
- **Difficult to remember**
- **Too restrictive: DIS/DIT**
- **Require two MRI examinations in most cases**

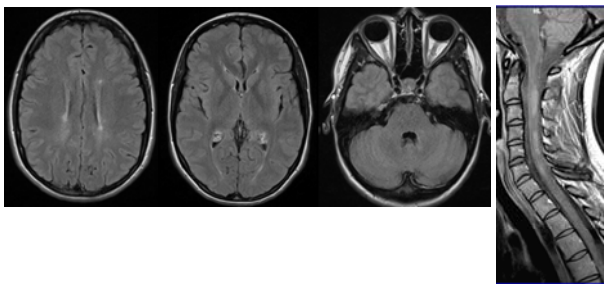
New version required

- ✓**Based in new evidences**
- ✓**Keep especificity, increase sensibility**
- ✓**Simplify current definitions**
- ✓**Create useful schemes for daily practice**

New proposal: Dissemination in space

≥ 1 lesion in each of ≥2 characteristic locations:

- Periventricular
- Juxtacortical
- Posterior fossa
- Spinal cord



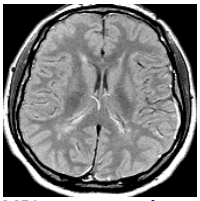
Symptomatic lesions excluded in BS and SC syndromes

Vall d'Hebron Hospital

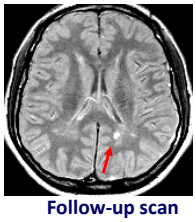
Swanton et al. JNNP 2006

New proposal: Dissemination in time

A new T2 lesion on follow up MRI irrespective of timing of baseline scan



MRI at presentation



Follow-up scan

No gadolinium required

Minimum of **two** scans needed

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Swanton et al. JNNP 2006

Multicenter validation of the new criteria for DIS (Swanton): conversion to CDMS 217 patients

DIS y DIT	Sensitivity (95% C.I)	Specificity (95% C.I)	Accuracy (95% C.I)	PPV (95% C.I)
McDonald 2001	47.1% (36-58%)	91.1% (85-95%)	73.1% (67-79%)	78.4% (65-89%)
McDonald 2005	60.0% (49-70%)	87.8% (81-93%)	76.4% (70-82%)	77.3% (65-87%)
Swanton 2006	71.8% (61-81%)	87.0% (80-92%)	80.8% (75-86%)	79.2% (68-88%)

MRI criteria for multiple sclerosis in patients presenting with clinically isolated syndromes: a multicentre retrospective study

Josephine K Swanton, Alex Rovira, Mar Tintoré, Daniel R Altmann, Frederik Barkhof, Massimo Filippi, Elena Huerga, Katherine A Miszkiel, Gordon T Plant, Chris Polman, Marco Rovaris, Alan J Thompson, Xavier Montalban, David H Miller

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Lancet Neurology 2007

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New proposal: Dissemination in time

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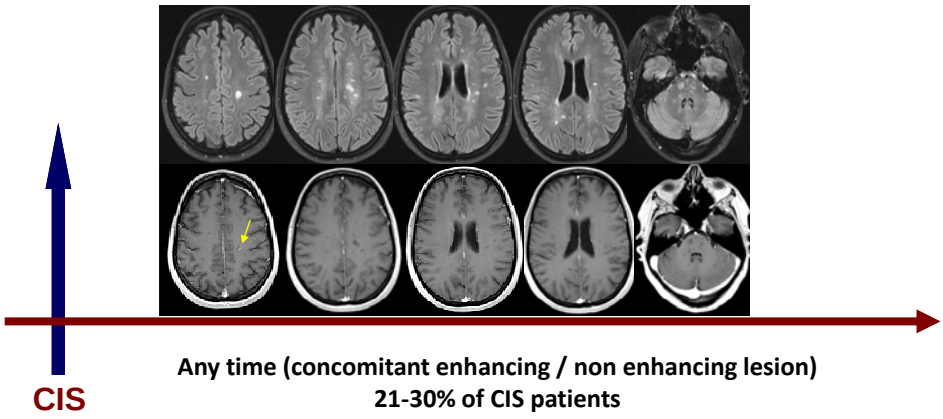
Multicenter European study on 250 CIS patients: conversion to CDMS



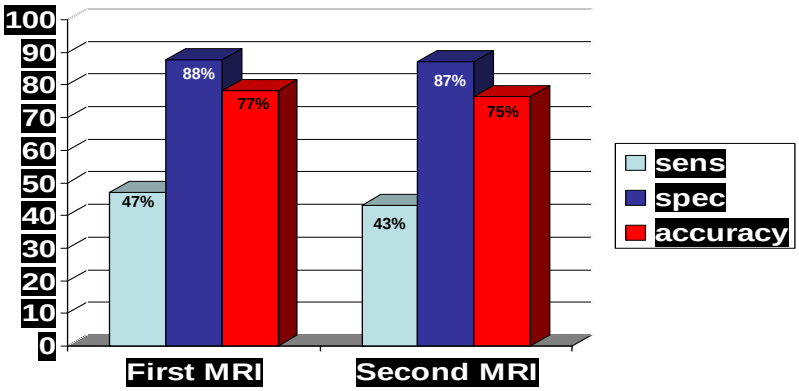
32 year-old woman with brainstem syndrome

Rovira et al. Arch Neurol 2009

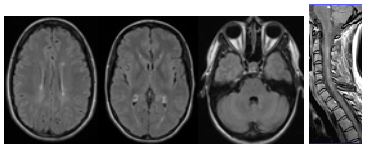
New proposal: Dissemination in time

MAGNIMS

Multicenter European study on 250 CIS patients: conversion to CDMS



Rovira et al. Arch Neurol 2009



MAGNIMS

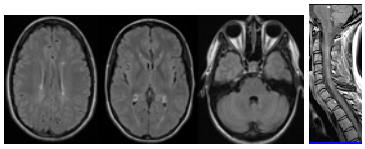
Brain MRI ± spinal cord
(any time)
DS + and DT +

Multiple Sclerosis

DS: Swanton criteria (Lancet Neurol 2007)
DT: Swanton, Rovira criteria (Lancet Neurol 2007; Arch Neurol 2009)

Montalban et al. Neurology 2010

Vall d'Hebron



MAGNIMS

Brain MRI ± spinal cord
(any time)
DS + and DT +

Brain MRI ± spinal cord
(any time)
DS + and DT -

Repeat brain MRI ± spinal cord
(3-6 months)
DT +

Multiple Sclerosis

DS: Swanton criteria (Lancet Neurol 2007)
DT: Swanton, Rovira criteria (Lancet Neurol 2007; Arch Neurol 2009)

Montalban et al. Neurology 2010

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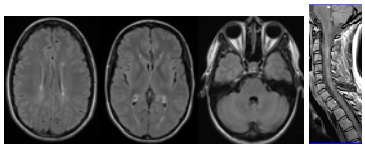


MAGNIMS

Brain MRI ± spinal cord
(any time)
DS + and DT +

Brain MRI ± spinal cord
(any time)
DS + and DT -

Brain MRI ± spinal cord
(any time)
DS - and DT -

Repeat brain MRI ± spinal cord
(3-6 months)
DT +

Repeat brain MRI ± spinal cord
(3-6 months)
DS + and DT +

Multiple Sclerosis

DS: Swanton criteria (Lancet Neurol 2007)
DT: Swanton, Rovira criteria (Lancet Neurol 2007; Arch Neurol 2009)

Montalban et al. Neurology 2010

Vall d'Hebron

Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the McDonald Criteria

Chris H. Polman, MD, PhD,[1] Stephen C. Reingold, PhD,[2] Brenda Banwell, MD,[3] Michel Clanet, MD,[4] Jeffrey A. Cohen, MD,[5] Massimo Filippi, MD,[6] Kazuo Fujihara, MD,[7] Eva Havrdova, MD, PhD,[8] Michael Hutchinson, MD,[9] Ludwig Kappos, MD,[10] Fred D. Lublin, MD,[11] Xavier Montalban, MD,[12] Paul O'Connor, MD,[13] Magnhild Sandberg-Wollheim, MD, PhD,[14] Alan J. Thompson, MD,[15] Emmanuelle Waubant, MD, PhD,[16] Brian Weinshenker, MD,[17] and Jerry S. Wolinsky, MD[18]

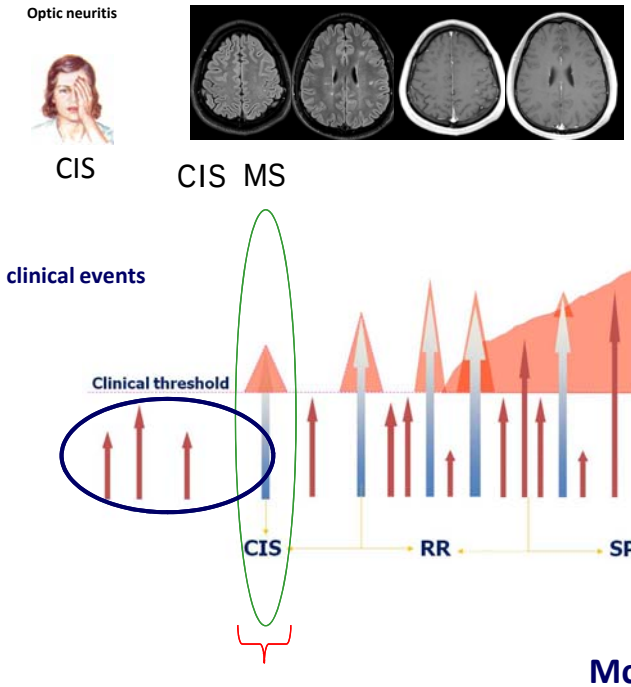
New evidence and consensus has led to further revision of the McDonald Criteria for diagnosis of multiple sclerosis. The use of imaging for demonstration of dissemination of central nervous system lesions in space and time has been simplified, and in some circumstances dissemination in space and time can be established by a single scan. These revisions simplify the Criteria, preserve their diagnostic sensitivity and specificity, address their applicability across populations, and may allow earlier diagnosis and more uniform and widespread use.

ANN NEUROL 2011;69:292–302

DIS Can Be Demonstrated by ≥1 T2 Lesion[a] in at Least 2 of 4 Areas of the CNS:
Periventricular
Juxtacortical
Infratentorial
Spinal cord[b]

Based on Swanton et al 2006, 2007.[22,27]
[a]Gadolinium enhancement of lesions is not required for DIS.
[b]If a subject has a brainstem or spinal cord syndrome, the symptomatic lesions are excluded from the Criteria and do not contribute to lesion count.

DIT Can Be Demonstrated by:
1. A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI
2. Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time



McDonald criteria 2010

2010 Diagnostic criteria: key points

Diagnostic Criteria for Multiple Sclerosis:
2010 Revisions to the McDonald Criteria

The use of imaging for demonstration of dissemination of central nervous system lesions in space and time has been simplified, and in some circumstances dissemination in space and time can be established by a single scan.

These revisions…

- …simplify the Criteria,
- …preserve their diagnostic sensitivity and specificity
- …address their applicability across populations (pediatric, Latino-America, Asian)
- …may allow earlier diagnosis
- …more uniform and widespread use

Polman et al., Ann Neurol 2011; 69:292-302

2010 Diagnostic criteria: key points

Diagnostic Criteria for Multiple Sclerosis:
2010 Revisions to the McDonald Criteria

"In applying the McDonald Criteria, it remains imperative that alternative diagnoses are considered and excluded."

REVIEW *Multiple Sclerosis* 2008; **14**: 1157–1174

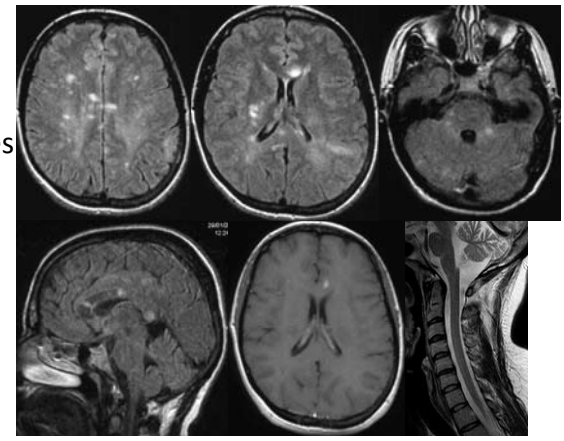
Differential diagnosis of suspected multiple sclerosis: a consensus approach

DH Miller[1], BG Weinshenker[2], M Filippi[3], BL Banwell[4], JA Cohen[5], MS Freedman[6], SL Galetta[7], M Hutchinson[8], RT Johnson[9], L Kappos[10], J Kira[11], FD Lublin[12], HF McFarland[13], X Montalban[14], H Panitch[15], JR Richert[16], SC Reingold[16,17] and CH Polman[18]

Polman et al., Ann Neurol 2011; 69:292-302

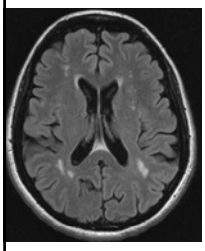
Diagnostic strategy in patients with multifocal brain T2 lesions of unknown origin

- ✓ Demographic data
- ✓ Family history
- ✓ Vascular risk factor profile
- ✓ Clinical information / CSF analysis
- ✓ Full range of imaging abnormalities
  - **Distribution and shape of lesions**
  - **Involvement:**
    - ***callososeptal interface***
    - ***U-fibers***
    - ***brainstem***
    - ***spinal cord***



Causes of MRI focal white matter lesions

Young patients (<50 years)



Incidental finding:
- normal population
- migraine

Hipoxic-ischemic vasculopathies
- small-vessel disease
- hyperhomocysthenimia
- CADASIL

Multiple sclerosis and variants

Vasculitis:
- primary
- systemic: *lupus, Behçet, APLAS*

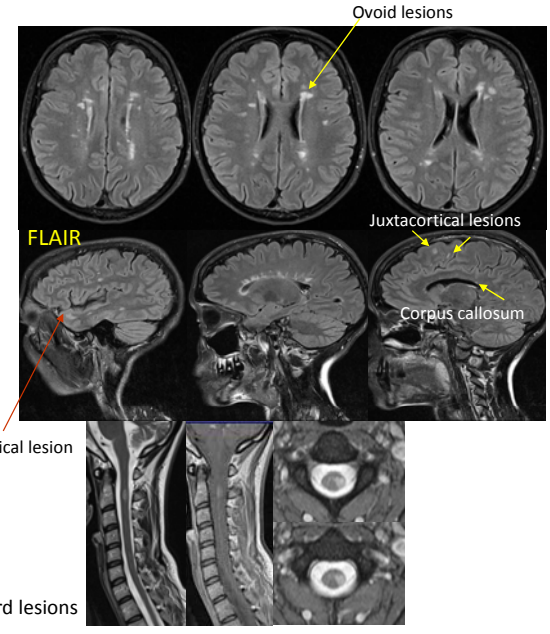
Metabolic:
- inherited: *Fabry, Leber, xantomatosis, adult forms of leukodystrophy*
- acquired: *B12 def, copper def*

Vall d'Hebron

Diagnostic strategy in patients with multifocal brain T2 lesions of unknown origin

- ✓ Demographic data
- ✓ Family history
- ✓ Vascular risk factor profile
- ✓ Clinical information / CSF analysis
- ✓ Full range of imaging abnormalities

  - **Distribution and shape of lesions**
  - **Involvement:**
    - ***callososeptal interface***
    - ***U-fibers***
    - ***brainstem***
    - ***spinal cord***



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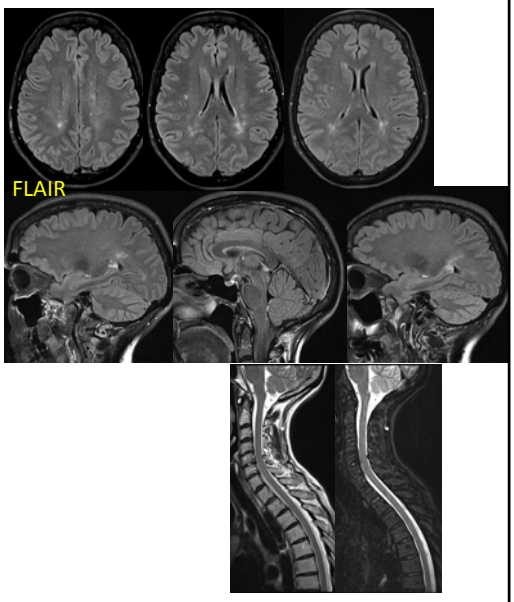

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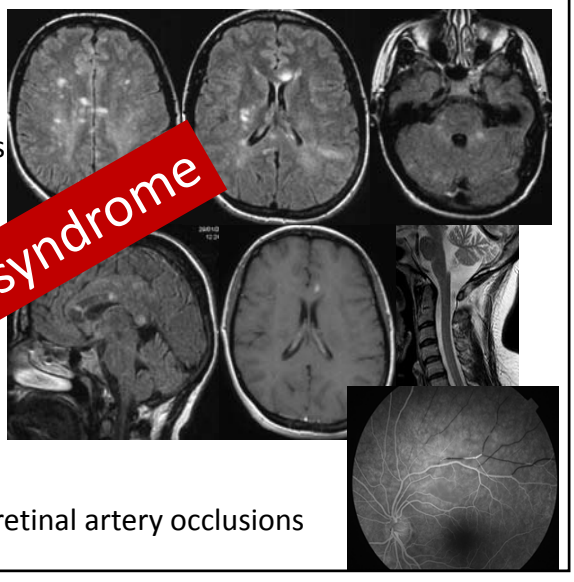

Sensorineural hearing loss, branch retinal artery occlusions

Multiple Sclerosis

MS diagnosis is a subjective and objective process

- **Subjective: best made by experts**
  - Clinical features, differential diagnosis
  - Interpretation of paraclinical test (MRI, CSF analysis, EP)
- **Objective: diagnostic criteria**
  - Based on demonstration of lesions disseminated in space and time
  - Minimize false positive/negative diagnosis
  - Facilitate a prompt and accurate diagnosis and early treatment with DMTs

ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

Barcelona 2015