Role of MRI in 2013 MS Phenotype

John A. Lincoln, MD, PhD
University of Texas HSC, Houston
Assistant Professor, Dept. of Neurology
Residency Program Director

UTHealth
The University of Texas
Health Science Center at Houston

Disclosures

I am currently a paid speaker for Acorda, Biogen, Genzyme-Sanofi, Novartis and Teva and was previously a paid speaker for EMD-Serono. Additionally I have been on advisory boards for Bayer, Biogen, Genzyme-Sanofi, Novartis and Questcor.

Outline

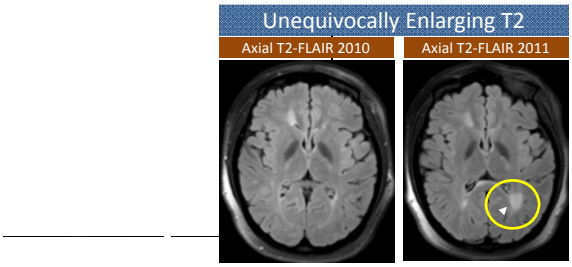
- Overview of imaging modifiers of 2013 MS phenotypes
- Practical Case: Imaging modifiers in relapsing MS phenotypes
- Practical Cases: Imaging modifiers in progressive MS phenotypes

Outline

- Overview of imaging modifiers of 2013 MS phenotypes
- Practical Case: Imaging modifiers in relapsing MS phenotypes
- Practical Cases: Imaging modifiers in progressive MS phenotypes

Activity on Imaging

- Evidence of MRI activity supplements clinical evaluations in relapsing and progressive disease
- Occurrence of contrast-enhancing T1 (Gd+) hyperintense or new or unequivocally enlarging T2 hyperintense lesions



Outline

- Overview of imaging modifiers of 2013 MS phenotypes
- Practical Case: Imaging modifiers in relapsing MS phenotypes
- Practical Cases: Imaging modifiers in progressive MS phenotypes

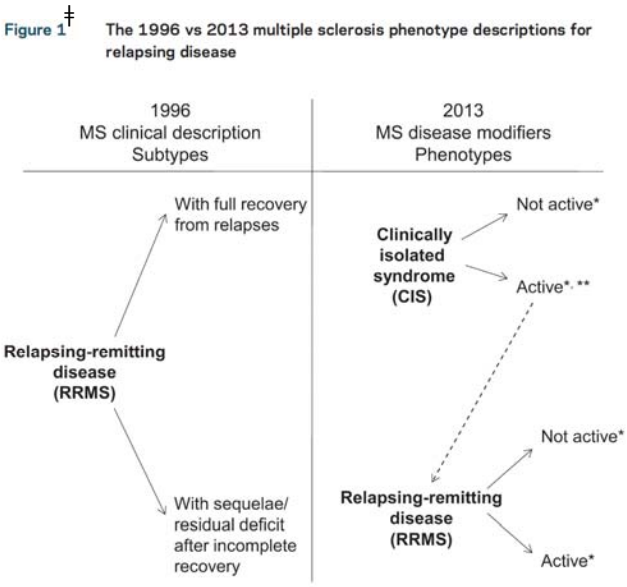


Figure 1‡ The 1996 vs 2013 multiple sclerosis phenotype descriptions for relapsing disease

*Activity determined by clinical relapses and/or MRI activity (contrast-enhancing lesions; new or unequivocally enlarging T2 lesions assessed at least annually); if assessments are not available, activity is "indeterminate." **CIS, if subsequently clinically active and fulfilling current multiple sclerosis (MS) diagnostic criteria, becomes relapsing-remitting MS (RRMS).

‡ Lublin et al, Neurology, 2014;83:278-86

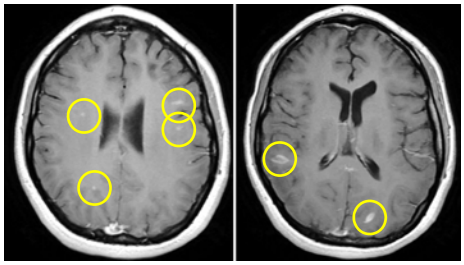
Relapsing Disease – Case

- 36 y/o right-handed African-American female diagnosed with RRMS three years ago and currently treated with injectable DMT
  - Exam last year
    - Lower extremity monoparesis – MRC* scale 4/5 right hip flexor but normal in remainder of muscle groups tested
    - T25FW 8.5 seconds without assistance
    - MRI brain last year showed no Gd+ enhancing or unequivocal new or enlarged T2 lesions when compared with her baseline scan
- At routine follow-up visit, she denies any new clinical symptoms or worsening decline in function and remains independent in all ADLs
  - Current exam
    - Lower extremity monoparesis - MRC scale 4/5 right hip flexor but normal in remainder of muscle groups tested
    - T25FW 8.1 seconds without assistance

* Medical Research Council

Relapsing Disease – Case

Axial T1-Post



Relapsing Disease – Case

Relapsing-Remitting Disease

1996

- Clinical Activity: Stable clinically

❖ Stable relapsing-remitting disease

2013

- Clinical Activity: Stable clinically
- Imaging Activity: Several asymptomatic Gd+ lesions

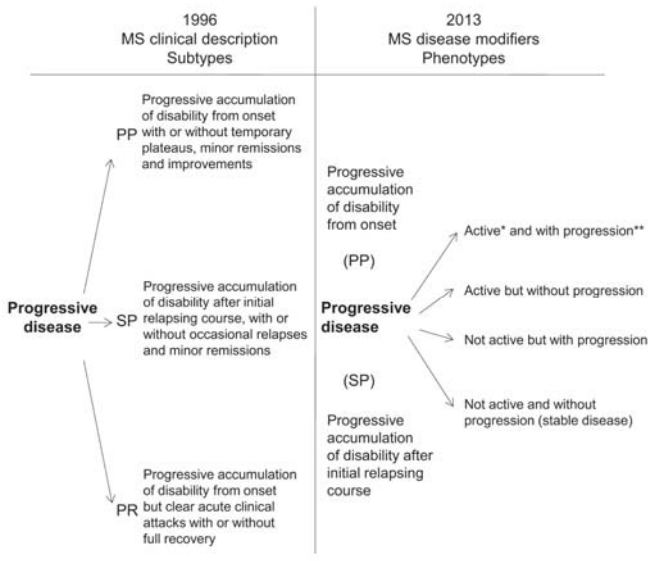
❖ Active (no clinical relapse but has radiologic activity)

❖ Possible use of steroids and consider change in DMT

Outline

- Overview of imaging modifiers of 2013 MS phenotypes
- Practical Case: Imaging modifiers in relapsing MS phenotypes
- Practical Cases: Imaging modifiers in progressive MS phenotypes

Figure 2 ‡ The 1996 vs 2013 multiple sclerosis phenotype descriptions for progressive disease



*Activity determined by clinical relapses assessed at least annually and/or MRI activity (contrast-enhancing lesions; new and unequivocally enlarging T2 lesions). **Progression measured by clinical evaluation, assessed at least annually. If assessments are not available, activity and progression are "indeterminate." MS = multiple sclerosis; PP = primary progressive; PR = progressive relapsing; SP = secondary progressive.

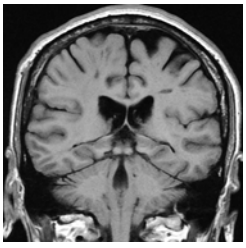
‡ Lublin et al, Neurology, 2014;83:278-86

Progressive Disease – Case #1

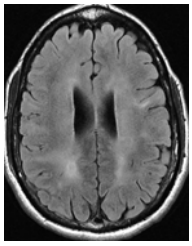
- 46 y/o right-handed Caucasian male who presents with two-year history of progressive difficulties with ambulation
  - Current exam
    - Bilateral lower extremity paraparesis - MRC scale 4-/5 left hip, knee flexor and ankle dorsiflexor; 3/5 right hip, knee flexor and 4/5 ankle dorsiflexor with 3/4 DTRs throughout
    - T25FW - 35 seconds with unilateral assistance
  - Denies any recent change

Progressive Disease – Case #1

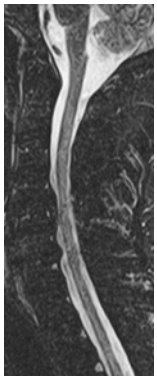
Coronal T1



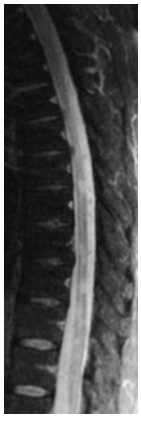
Axial T2-FLAIR



Sag T2 C-spine



Sag T2 T-spine



- No Gd+ lesions

Progressive Disease – Case #1

Primary Progressive Disease

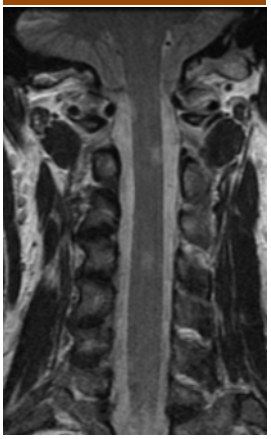
1996	2013
• Clinical Activity: Progressive lower extremity weakness and decreased ambulation	• Clinical Activity: Progressive lower extremity weakness and decreased ambulation • Imaging Activity: No active lesions
❖ Progression of disease	❖ Not active (no clinical relapse or radiologic activity) but with progression ❖ No DMT

Progressive Disease – Case #2

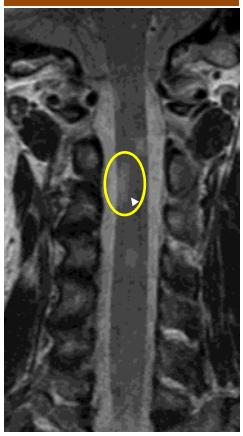
- 48 y/o right-handed Caucasian male who was recently diagnosed with PPMS
  - Exam at initial evaluation
    - Bilateral lower extremity paraparesis - MRC scale 4/5 hip and knee flexors and ankle dorsiflexors
    - T25FW - 15 seconds without assistance
    - Baseline MRI brain and spine showed no Gd+ enhancing lesions but showed several discrete T2 lesions adjacent to the lateral ventricle and lesions in the cervical cord
- Currently complains of four-month history of greater difficulty with ambulation and worsening right sided weakness
  - Current exam
    - Bilateral lower extremity paraparesis - MRC scale 4-/5 hip and knee flexors and ankle dorsiflexors
    - T25FW - 22 seconds with unilateral assistance

Progressive Disease – Case #2

Coronal T2 – 04/2008



Coronal T2 – 10/2008



Progressive Disease – Case #2

Primary Progressive Disease

1996

- Clinical Activity: Apparent "progression" of symptoms with decreased ambulation

❖ Progression of disease

2013

- Clinical Activity:
  a) Apparent worsening of symptoms with decreased ambulation
     - Related to new lesion
- Imaging Activity: Unequivocal new T2 lesion involving right lateral cord at C2-3

❖ Active (clinical/radiologic) but without progression

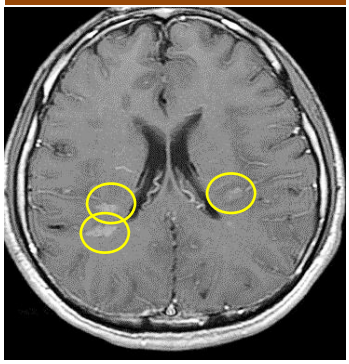
❖ Possible initiation of DMT

Progressive Disease – Case #3

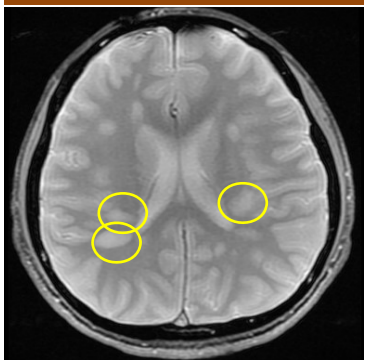
- 43 y/o right-handed Caucasian female who presents for follow-up of long-standing relapsing MS
  - Exam last year
    - Bilateral lower extremity paraparesis - MRC scale 4/5 hip and knee flexors and ankle dorsiflexors
    - T25FW - 15 seconds with unilateral assistance
    - MRI brain last year showed no Gd+ enhancing or unequivocal new or enlarged T2 lesions
- Currently complains of one month history of greater difficulty with ambulation and worsening left sided weakness. Additionally, over at least the past one year she has noted issues with dexterity of the right hand and deterioration of handwriting
  - Current exam
    - Bilateral lower extremity paraparesis - MRC scale 3-/5 bilateral hips, left knee flexors and ankle dorsiflexors; 4/5 right knee and ankle dorsiflexors
    - Slow rapid-rhythmic alternating movements both hands with MRC 4/5 finger abductors
    - T25FW - 25 seconds with unilateral assistance but needing rest after 10 feet

Progressive Disease – Case #3

T1-Post



PD



Progressive Disease – Case #3

Secondary Progressive Disease

1996

- Clinical Activity: Apparent "progression" of symptoms with decreased ambulation and hand weakness
  - Leg weakness might be due to activity
  - Progressive hand weakness

❖ Progression of disease

2013

- Clinical Activity:
  a) Apparent "progression" of symptoms with decreased ambulation
     - Related to new lesions
  b) Worsening of upper extremity weakness
- Imaging Activity: New Gd+ lesions in both centrum semiovale corresponding to areas of LE fibers

❖ Active (clinical/radiologic) and with progression

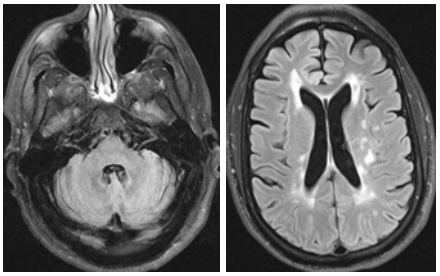
❖ Steroids for relapse and possible change in DMT

Progressive Disease – Case #4

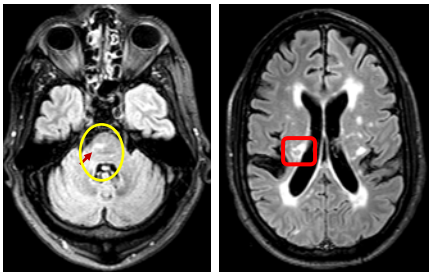
- 55 y/o right-handed Caucasian female who presents for follow-up for long-standing relapsing MS
  - Exam last year
    - Bilateral lower extremity paraparesis - MRC scale 4/5 hip and knee flexors and ankle dorsiflexors
    - T25FW 15 seconds with unilateral assistance
    - MRI brain last year showed no Gd+ enhancing or unequivocal new or enlarged T2 lesions
- Currently complains of three-month history of greater difficulty with ambulation and worsening left greater than right sided weakness
  - Current exam
    - Bilateral lower extremity paraparesis - MRC scale 3+/5 left hip and knee flexors and bilateral ankle dorsiflexors; 4/5 right hip and knee flexor
    - T25FW 25 seconds with unilateral assistance but needing rest after 10 feet

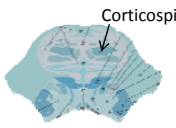
Progressive Disease – Case #4

T2-FLAIR 2012



T2-FLAIR 2013





Progressive Disease – Case #4

Secondary Progressive Disease

1996

- Clinical Activity: Apparent "progression" of symptoms with worsening ambulation
  - May be related to relapse

❖ Progression of disease

2013

- Clinical Activity: Apparent "progression" of symptoms with worsening ambulation
  - Related to new lesion
- Imaging Activity: Unequivocal new T2 lesion in right pons involving corticospinal fibers

❖ Active (clinical/radiologic) but without progression

❖ Steroids for relapse and possible change in DMT

Progressive Disease – Case #5

- 55 y/o right-handed Caucasian female who presents for follow-up for long-standing MS
  - Exam last year
    - Bilateral lower extremity paraparesis - MRC scale 4/5 hip and knee flexors and ankle dorsiflexors
    - T25FW 15 seconds with unilateral assistance
    - MRI brain last year showed no Gd+ enhancing or unequivocal new or enlarged T2 lesions
- Currently complains of six-month history of greater difficulty with ambulation and worsening right lower extremity weakness
  - Current exam
    - Bilateral lower extremity paraparesis - MRC scale 3/5 bilateral hip and knee flexors and bilateral ankle dorsiflexors
    - T25FW 25 seconds with bilateral assistance as well as need for rest after 10 feet
    - MRI of brain and spine show NO Gd+ or new or enlarging T2 lesions

Progressive Disease – Case #5

Secondary Progressive Disease

1996

- Clinical Activity: Apparent "progression" of symptoms with worsening paraparesis and decreased ambulation

❖ Progression of disease

2013

- Clinical Activity: No clinical activity
  - Gradually worsening paraparesis and decreased ambulation
- Imaging Activity: No new Gd+ or T2 lesion (BOD unchanged)

❖ Not active (clinical/radiologic) but with progression

Conclusions

- 2013 MS phenotypes incorporate important modifiers including disease activity and confirmed worsening disability
  - Assessment of disease activity is defined by either clinical evidence of relapse or lesion activity detected by CNS imaging
  - Lesion activity is defined as new Gd+, new or unequivocally enlarged T2
- PPMS is a part of the spectrum of progressive disease and differences from other forms are relative rather than absolute
  - Clinical and radiologic activity can be present in both PP and SPMS