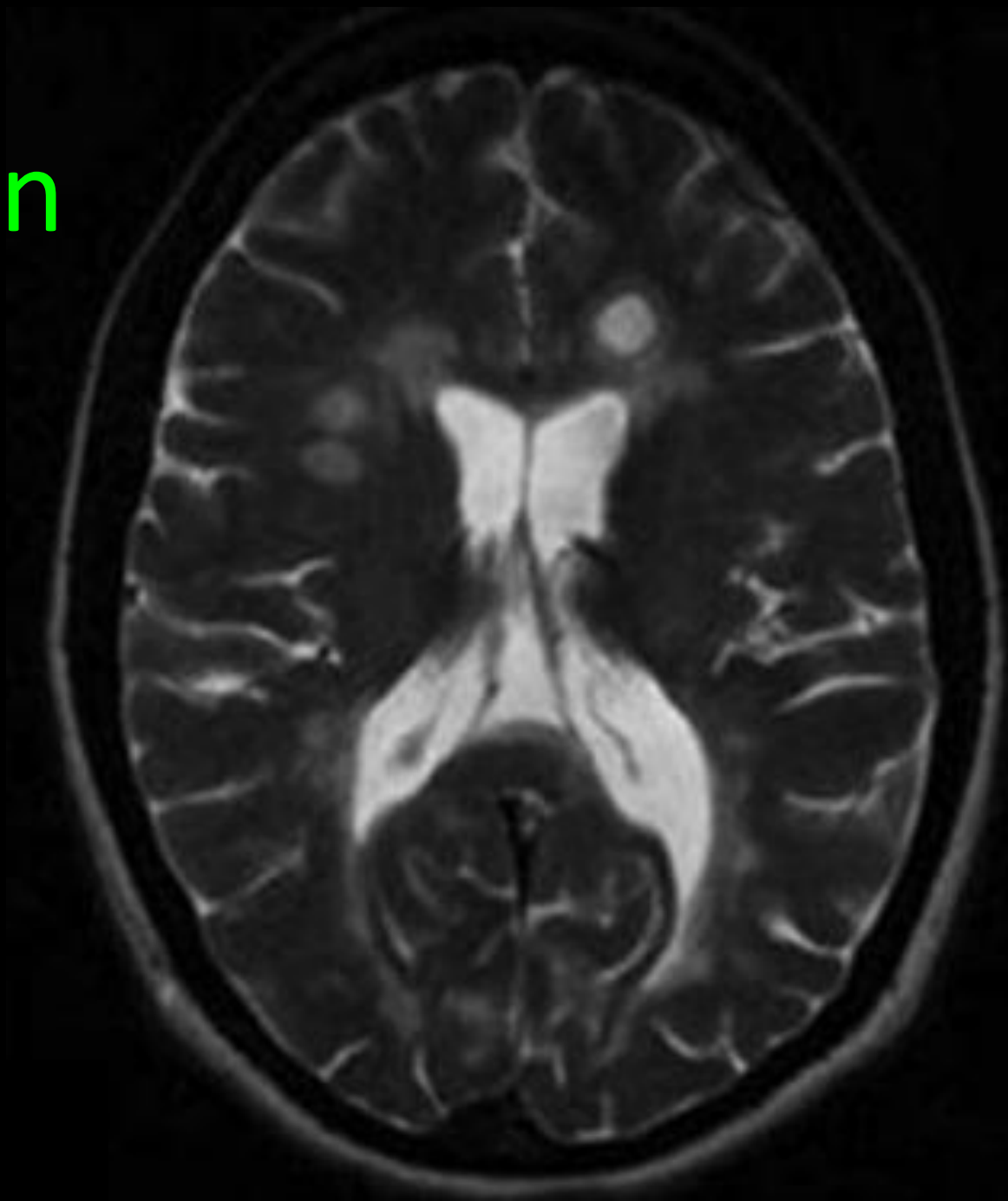
Quantitative MRI in Benign Multiple Sclerosis



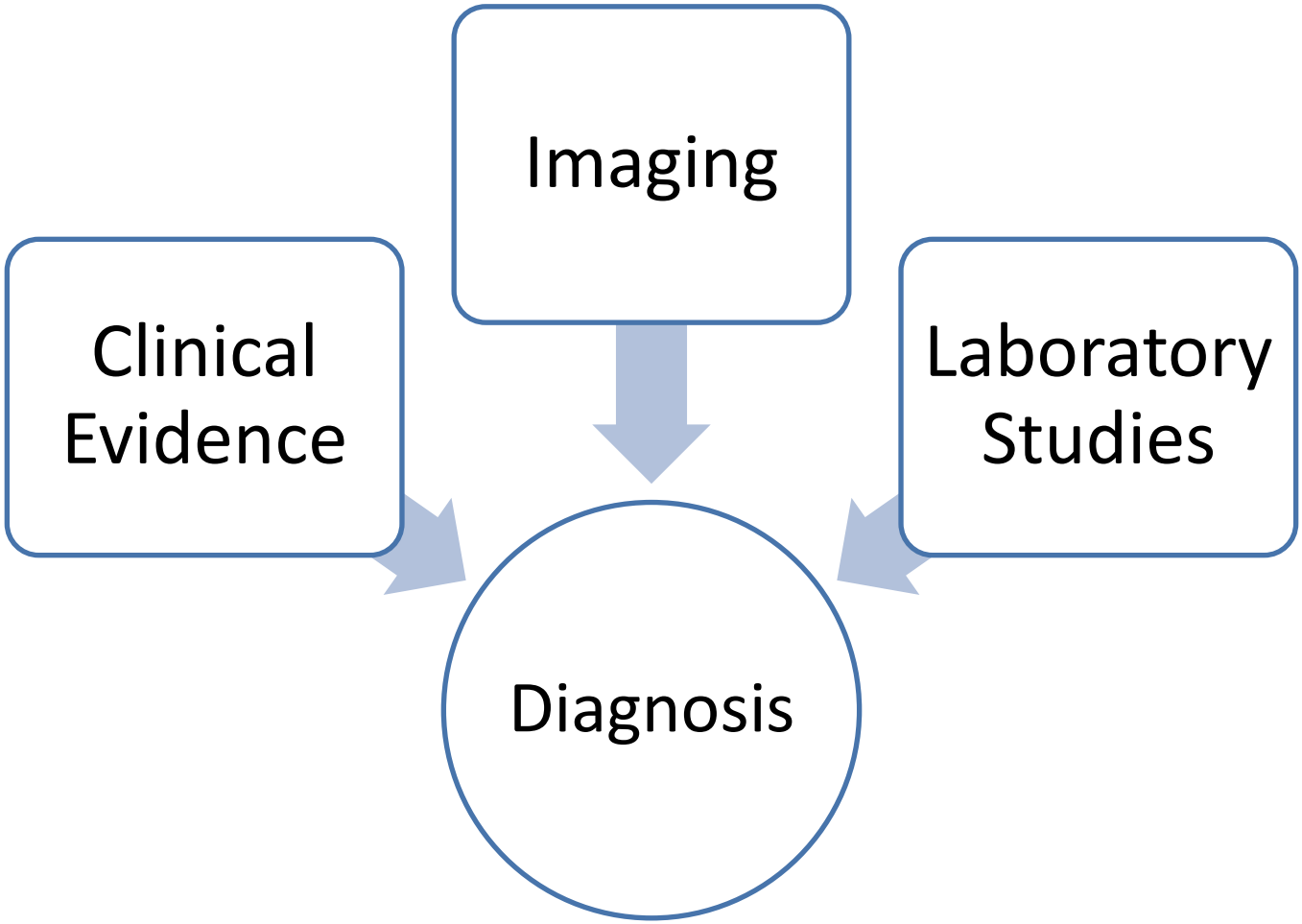
Jonathon Schwartz
February 1st, 2013

Advisors:
Dr. Anat Achiron
Dr. Shmuel Miron
Yael Nissan
Dr. Chen Hoffmann

Overview

- MS Diagnosis & Clinical Subtypes
- Quantitative MRI
- Experiment Set-up
- Results to date
- On the Horizon

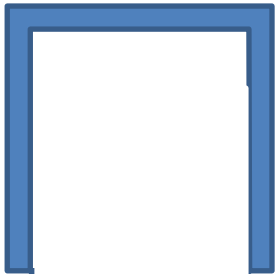
Diagnosing Multiple Sclerosis


Imaging
Clinical Evidence
Laboratory Studies
Diagnosis

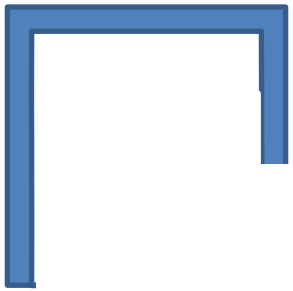
Clinical Presentation	Additional Data Needed for MS Diagnosis
Two or more attacks; objective clinical evidence of 2 or more lesions	None[a]
Two or more attacks; objective clinical evidence of 1 lesion	Dissemination in space, demonstrated by MRI[b] *or* Two or more MRI-detected lesions consistent with MS plus positive CSF[c] *or* Await further clinical attack implicating a different site
One attack; objective clinical evidence of 2 or more lesions	Dissemination in time, demonstrated by MRI[d] *or* Second clinical attack
One attack; objective clinical evidence of 1 lesion (monosymptomatic presentation; clinically isolated syndrome)	Dissemination in space, demonstrated by MRI[b] *or* Two or more MRI-detected lesions consistent with MS plus positive CSF[c] *and* Dissemination in time, demonstrated by MRI[d] *or* Second clinical attack
Insidious neurological progression suggestive of MS	Positive CSF[c] *and* Dissemination in space, demonstrated by 1) Nine or more T2 lesions in brain *or* 2) 2 or more lesions in spinal cord, *or* 3) 4–8 brain plus 1 spinal cord lesion *or* abnormal VEP[e] associated with 4–8 brain lesions, or with fewer than 4 brain lesions plus 1 spinal cord lesion demonstrated by MRI *and* Dissemination in time, demonstrated by MRI[d] *or* Continued progression for 1 year

Clinical Course of MS: The Building Blocks

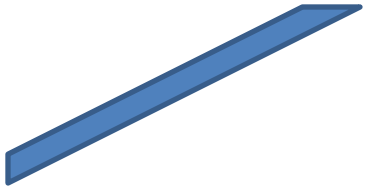
Relapse & full recovery



Relapse without full recovery

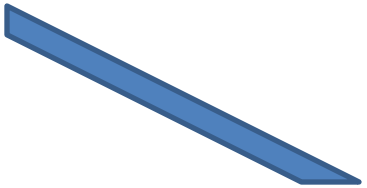


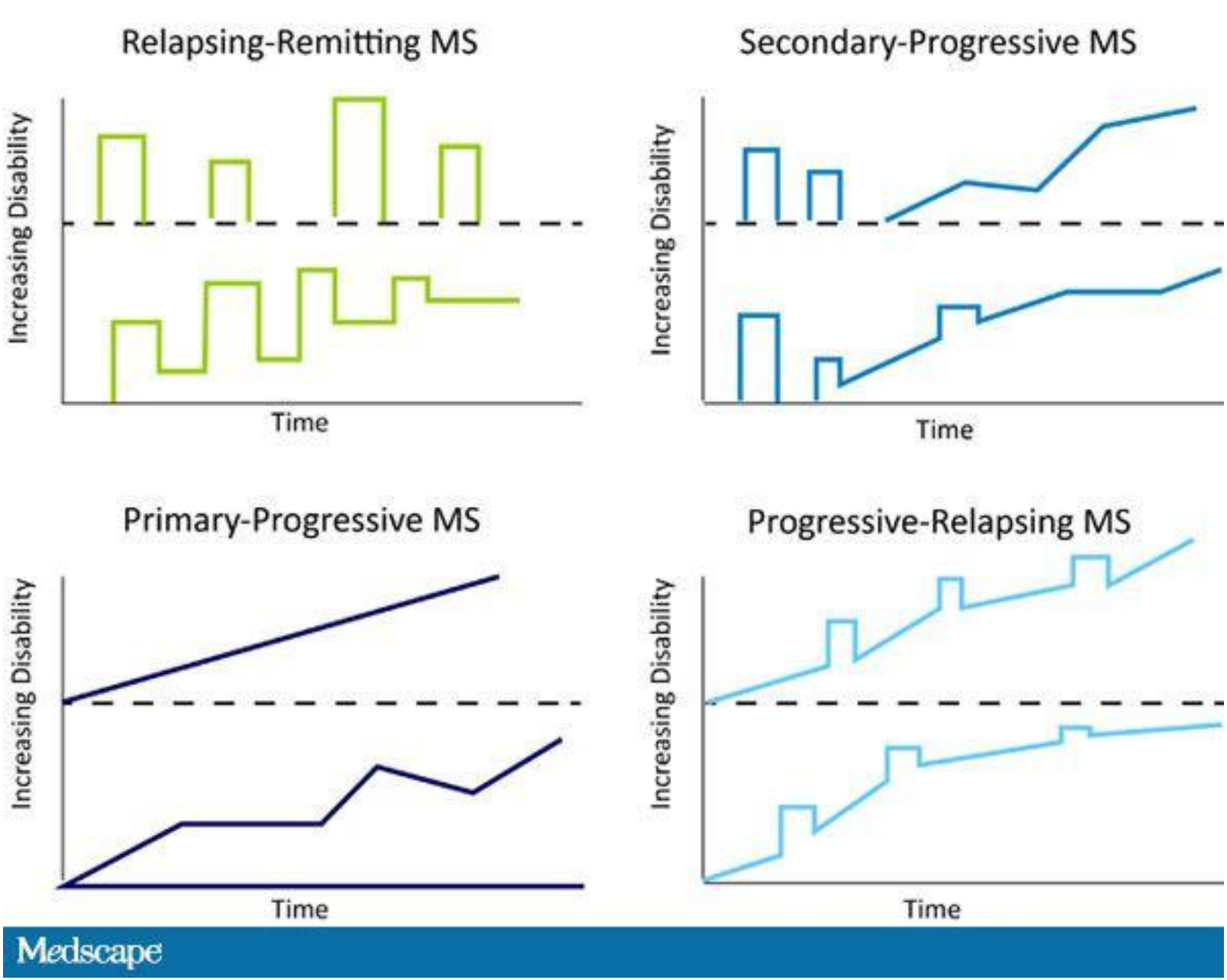
Progression



Plateau

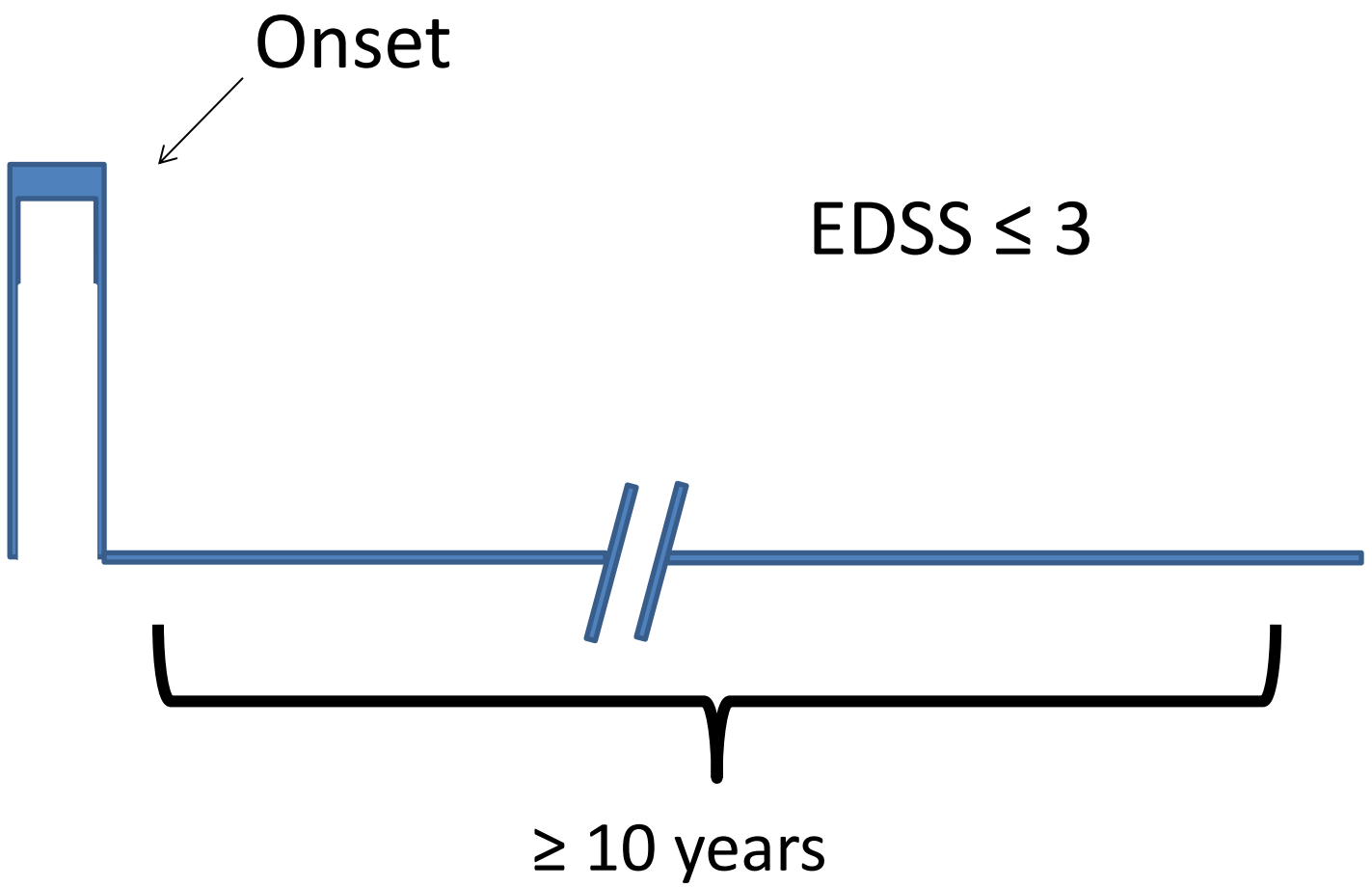
Minor Remissions

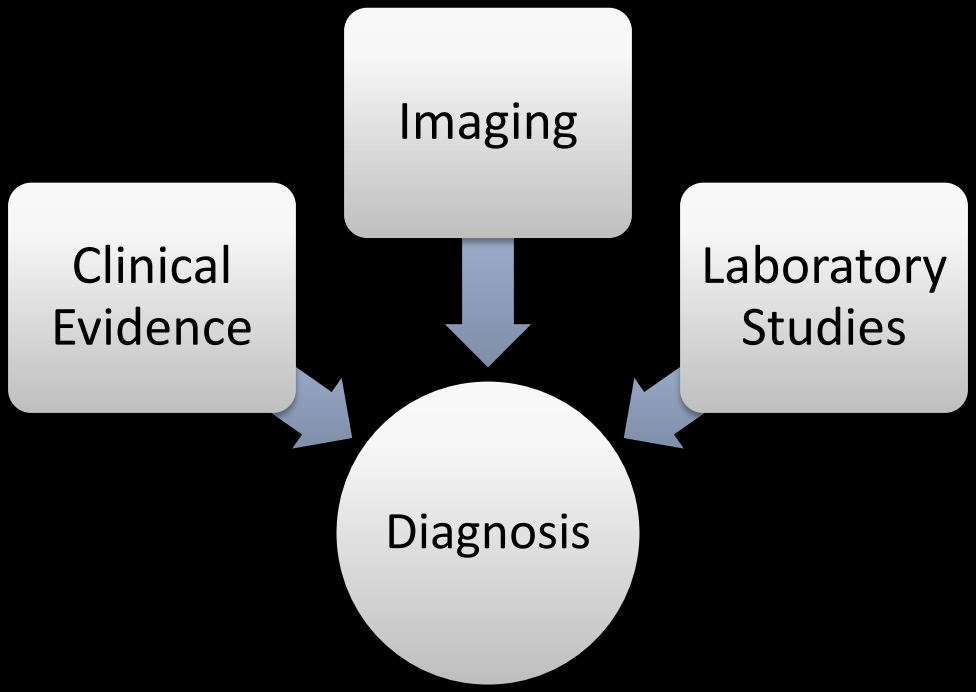




http://www.medscape.org/viewarticle/739432

Benign Multiple Sclerosis




Imaging
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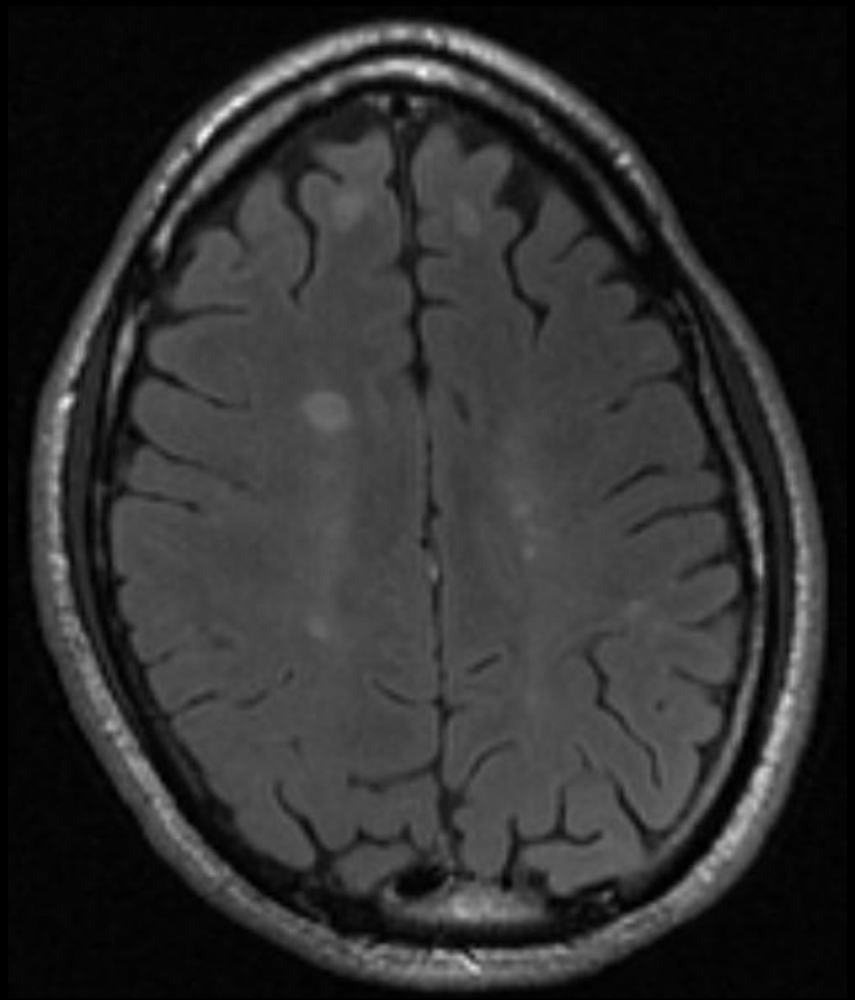
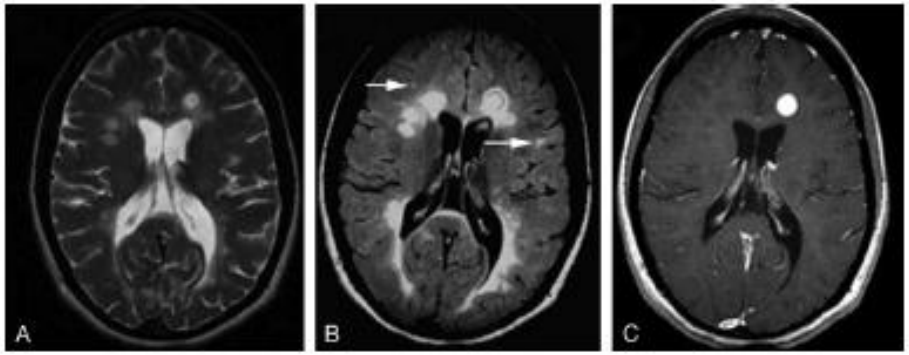


- Surprise!
  - BMS ≠ ↓Lesion Load
  - BMS ≠ ↓Lesion Count
- Location assoc. with differences
- Rate, Repair, Location

Table Summary findings from MRI-based studies of BMS

MRI features	Main findings in patients with BMS	Possible interpretations
Focal lesions	Similar, if not higher, brain T2 lesion load compared with RRMS	Wider interindividual variability in BMS than in other MS phenotypes
	Similar or lower brain T2 lesion load compared with SPMS	Low rate of lesion load accrual in BMS
	Smaller infratentorial lesion burden than in SPMS	Importance of lesion location
	Less intracortical lesions than in RRMS	
	Mild inflammatory activity	
Tissue loss	Similar whole brain atrophy compared with SPMS	Importance of tissue preservation in clinically eloquent CNS regions
	Less severe cerebellar, spinal, and GM atrophy than in SPMS	
Microscopic tissue damage	No clear-cut differences vs RRMS	Importance of tissue preservation in clinically eloquent CNS regions
	Less severe tissue damage within lesions and in the GM than in SPMS	More effective compensatory/reparative mechanisms in BMS
	More pronounced abnormalities in patients with BMS with cognitive deficits	Need for a new clinical definition of BMS including cognitive features


A
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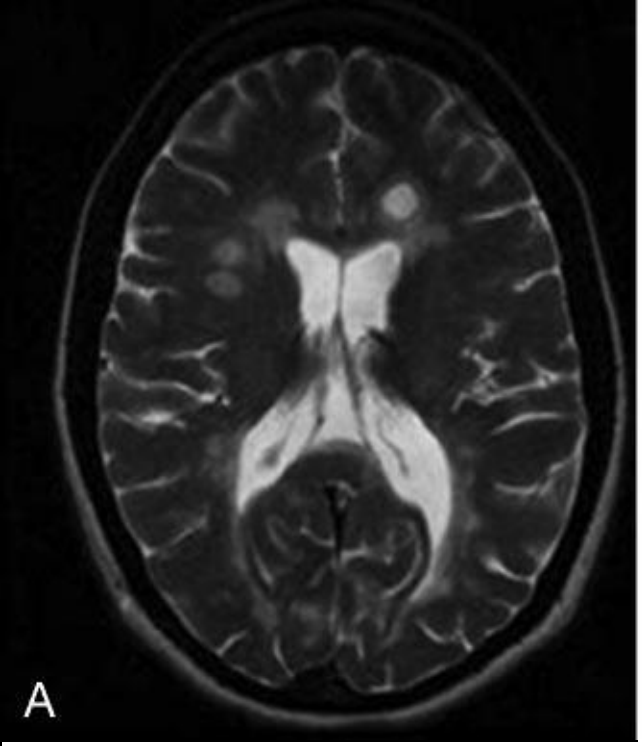
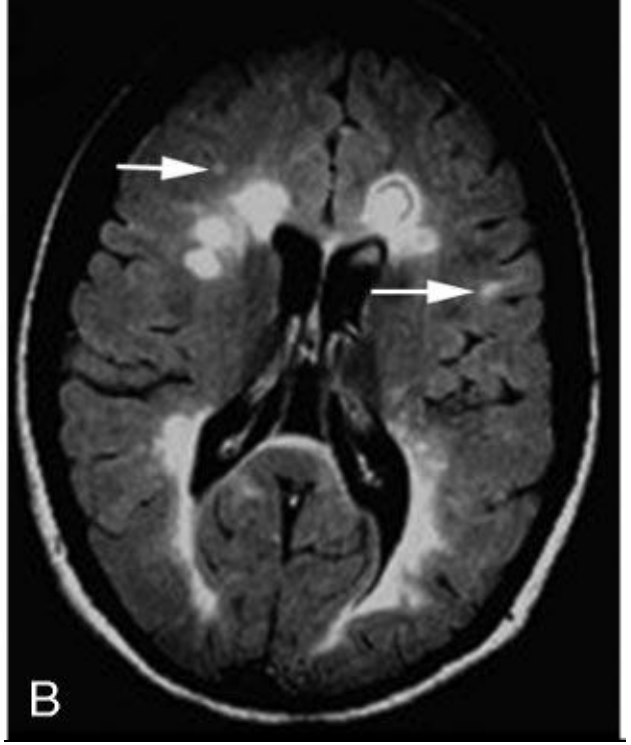


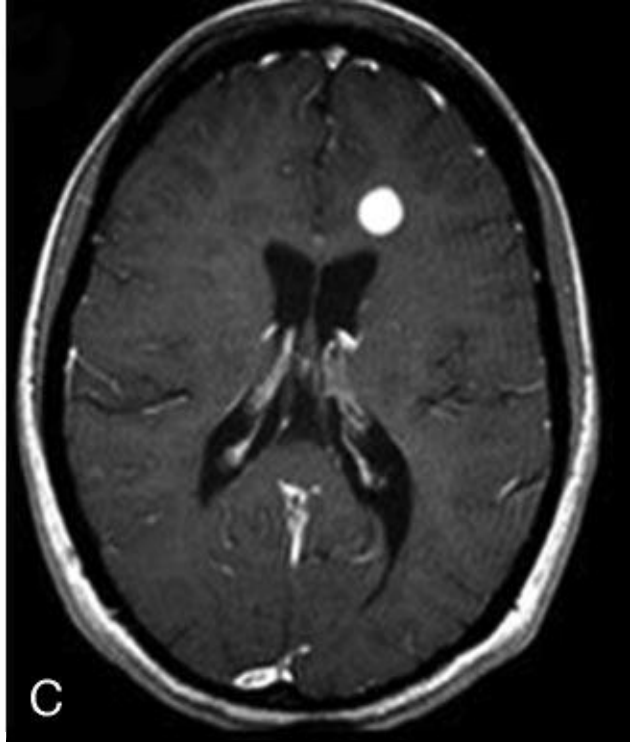
T2 - Weighted

- White matter inflammation
- Hyperintensities



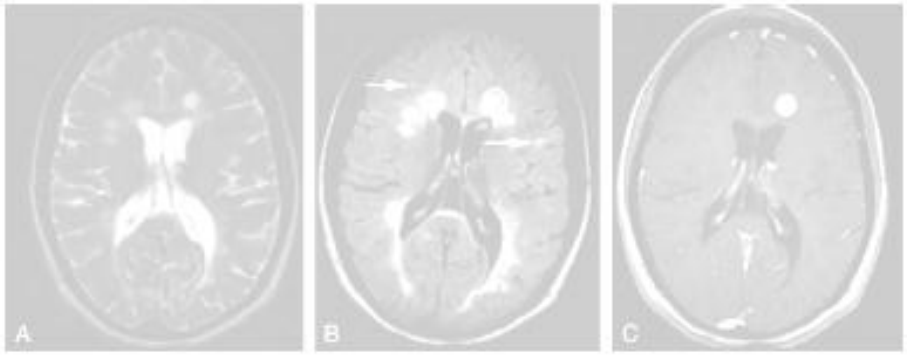
FLAIR

- Highly sensitive
- Supratentorial
- Periventricular



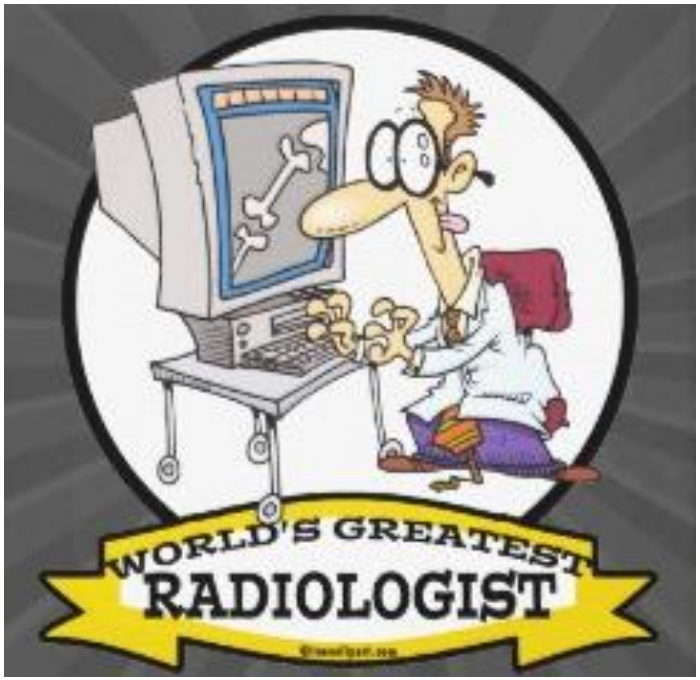
T1 - Weighted + Gd

- Active lesions enhancing
- Improves specificity

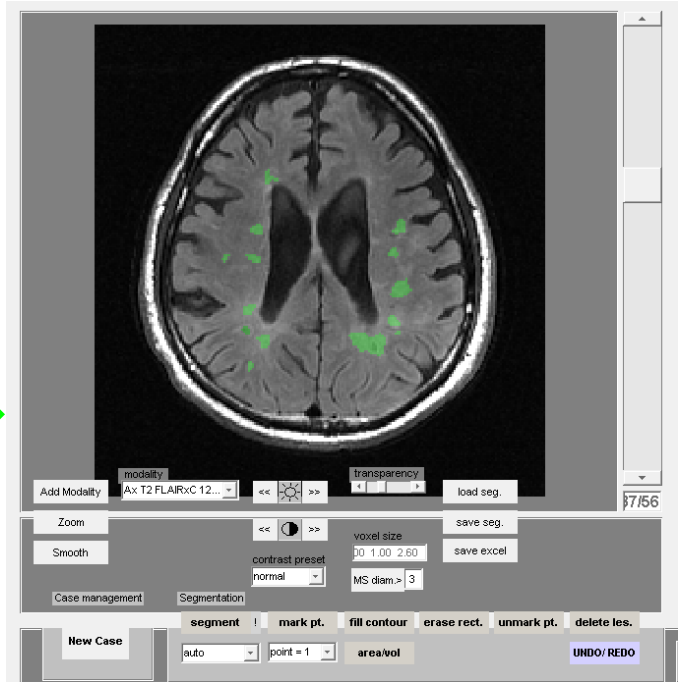


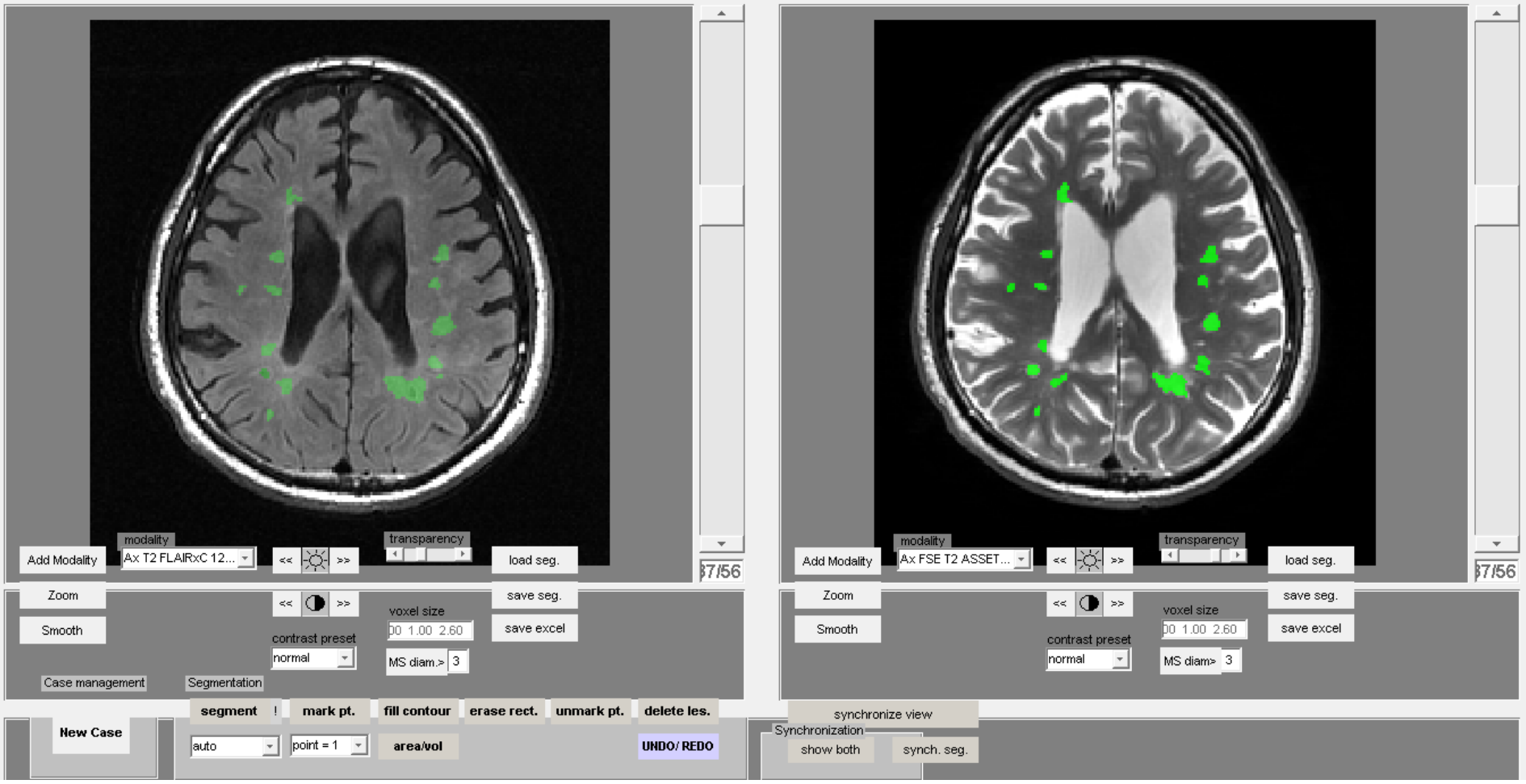
DICOM Files

MSET .img file



Lesion I.D.

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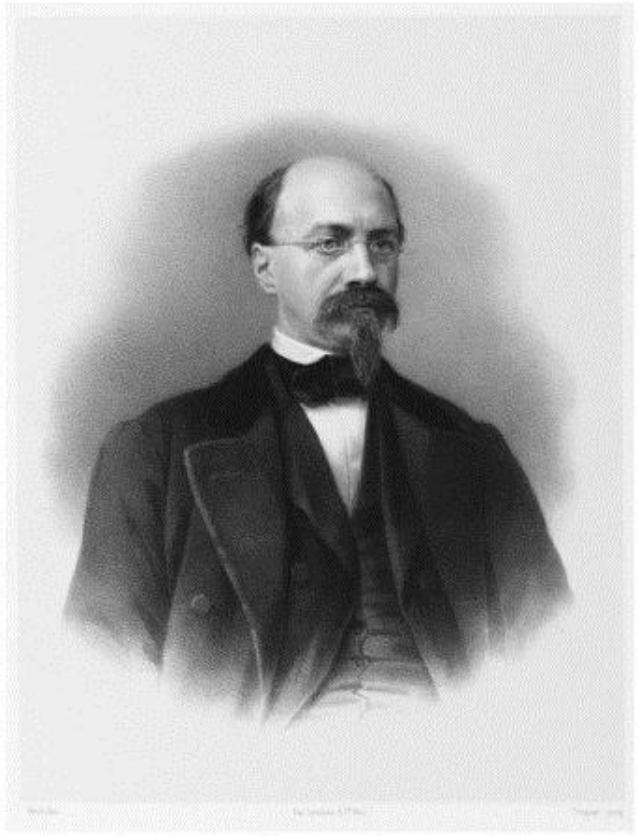
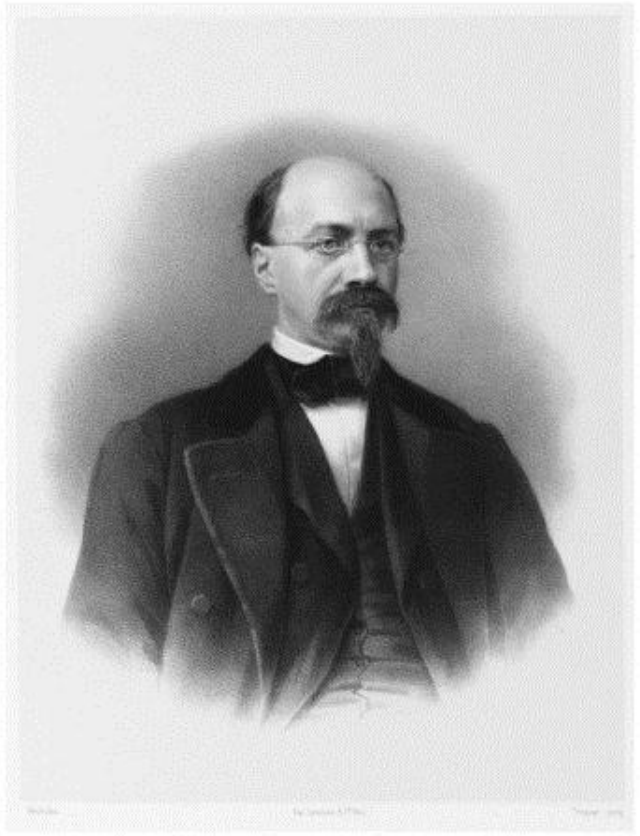
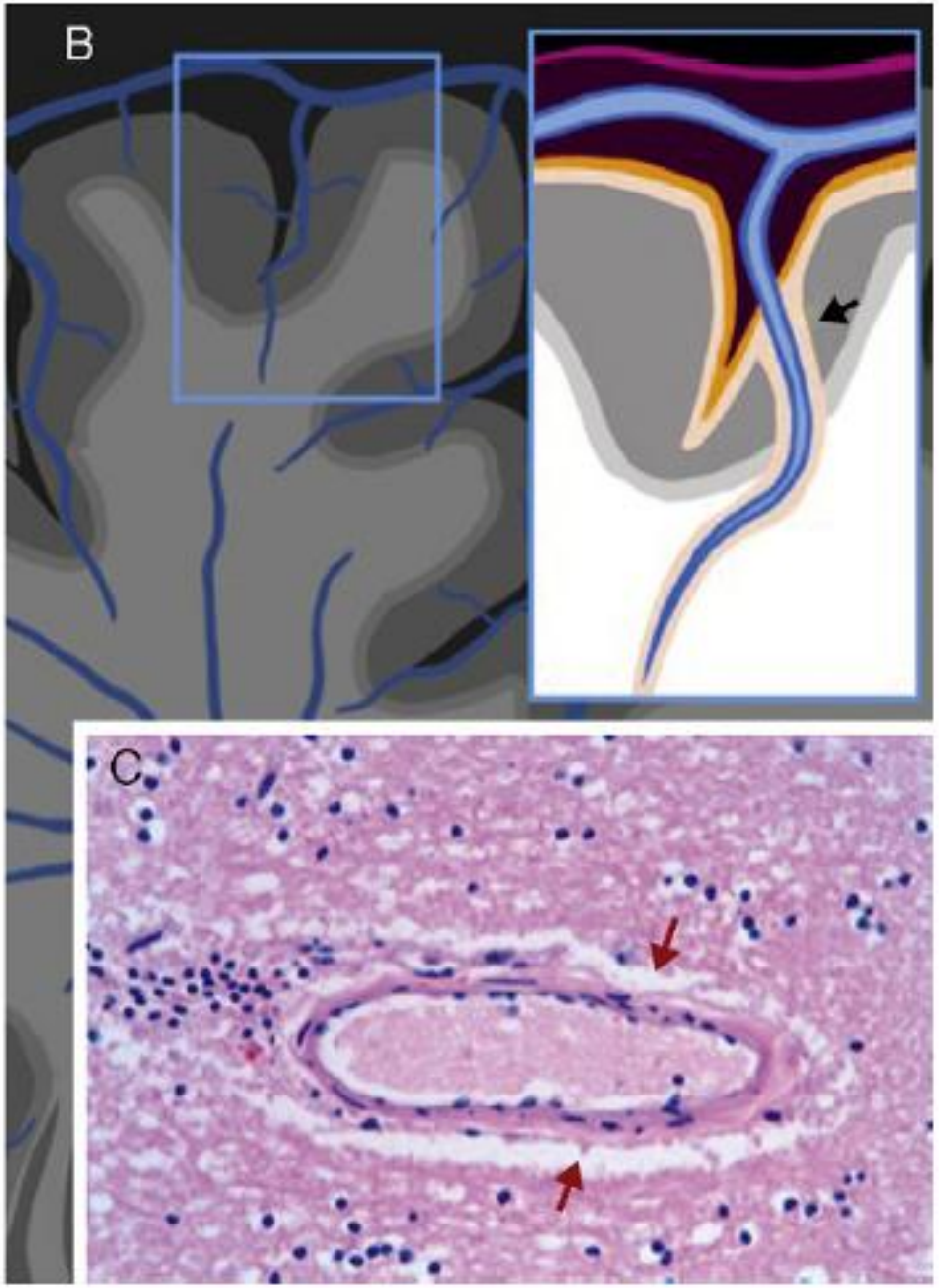


Rudolph Carl Virchow 13) October 1821 – 5 September 1902) was a German doctor ,anthropologist , pathologist



Charles-Philippe Robin 4) June 1821–5 October 1885) was a French anatomist , biologist ,and histologist born in Jasseron ,département Ain.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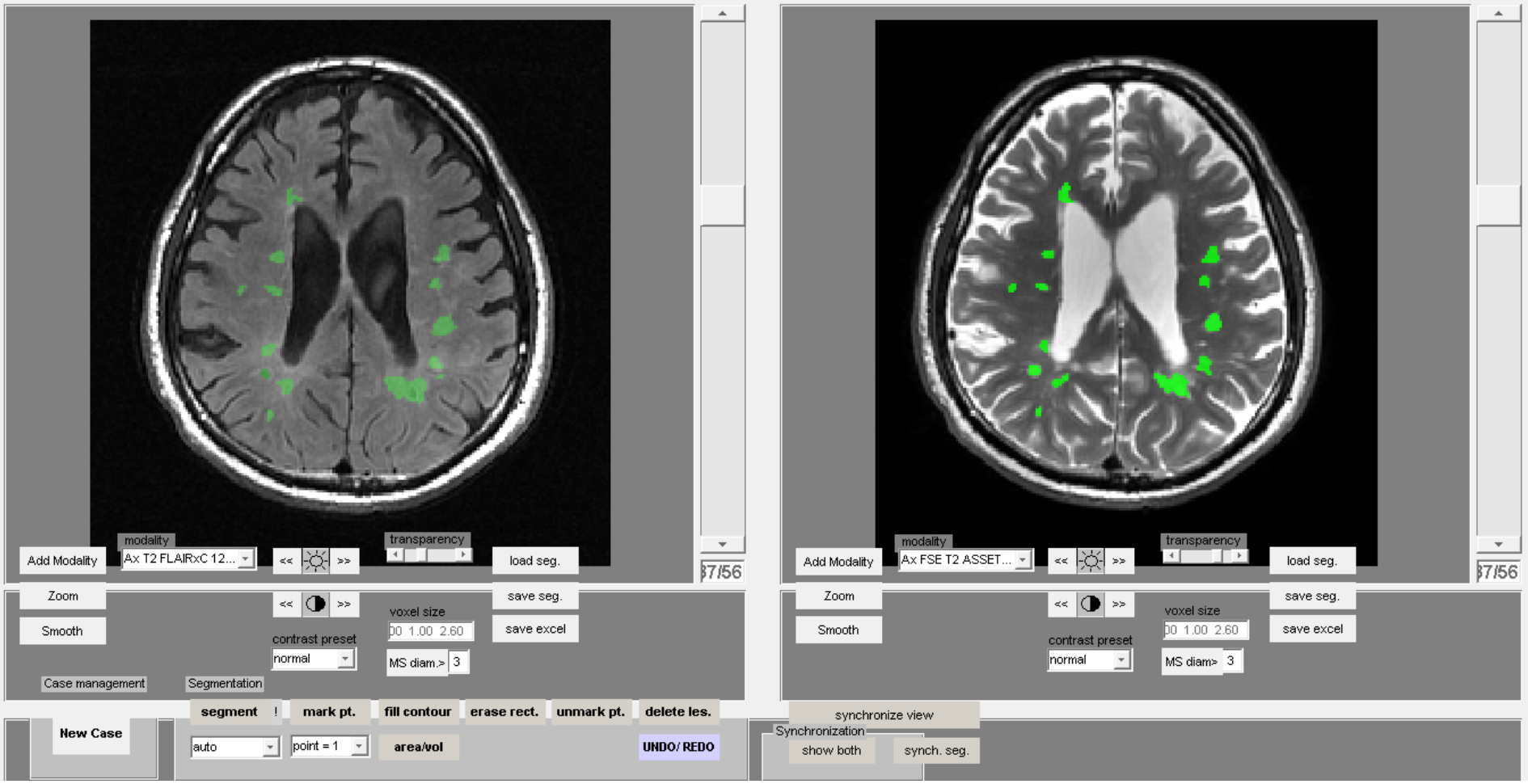
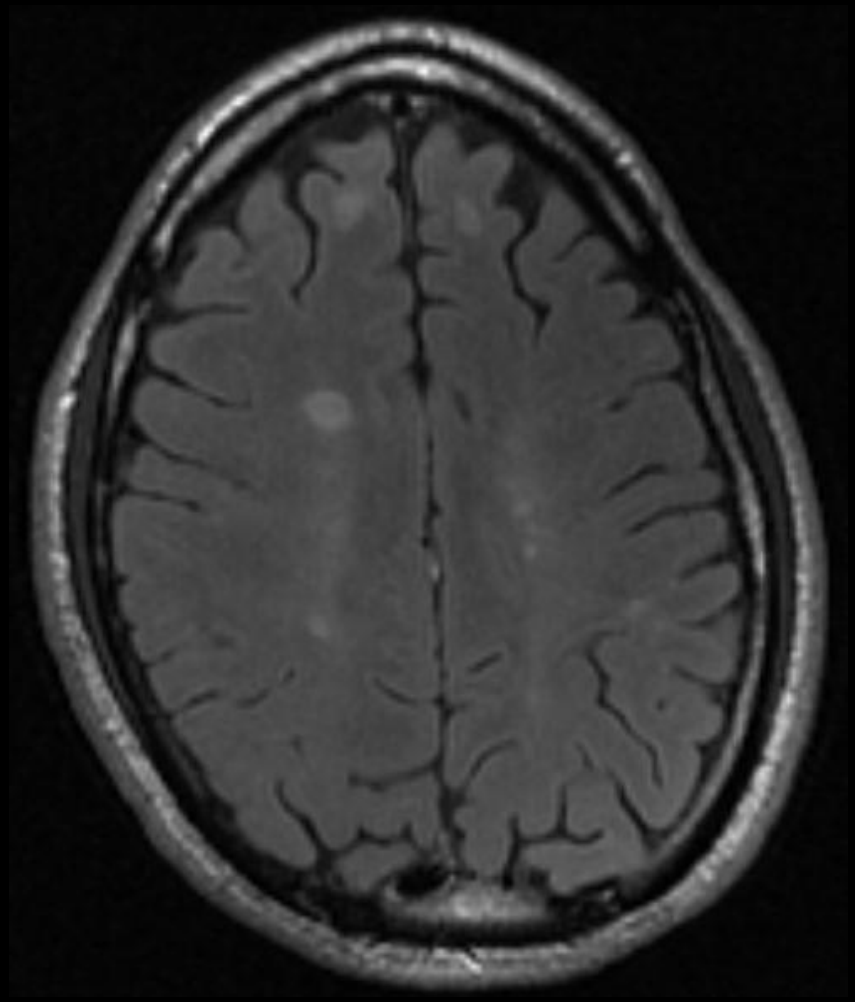
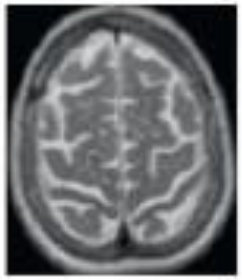


Type I: Slice 23-4, Type II: Slice 36-7

Classical Imaging Features



- Multiple lesions
- Ovoid shape
- Dilated perivascular space
- Optic nerve, U fiber, & Callosum involved
- Generalized atrophy at relatively younger age
- Enhancing lesions (ring, rim, or solid)
- Gradually ↑ # of lesions

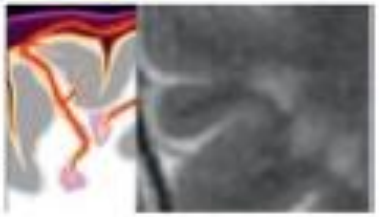


HPIWM

Normal

Virchow-Robin, aging (ARWMC I, ARWMC II >75 years)

VP

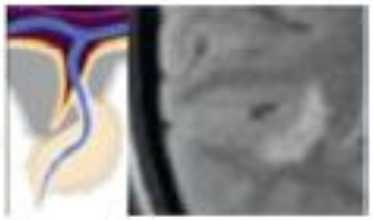


- Not juxtacortical
- U-subcortical
- Deep bordering
- Periventricular irregular
- Supra- > infratentorial
- Supratentorial FP
- Basal ganglia
- No enhancement (if not acute) or mild enhancement

With typical CVRFs: AH, DLP, DM, etc.

With no typical CVRFs:
atypical CVRFs (hyperhomocysteinemia, pro-thrombotic states); migraine; amyloid angiopathy; vasculitis; CADASIL, etc.

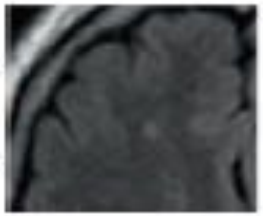
PvP



- Periventricular ovoid
- Juxtacortical
- Fusiform or ovoid (Dawson)
- Supra- and infratentorial
- Large lesions

Typical MS: ovoid (Dawson); enhancement (typical incomplete ring); supra- / infra-; corpus callosum; infra-peripheral

NsP



- Profundo no limitrofe
- Amorphous, punctate, round

With CVRFs

Vasculitis, other demyelinating diseases, toxic-metabolic diseases, etc.

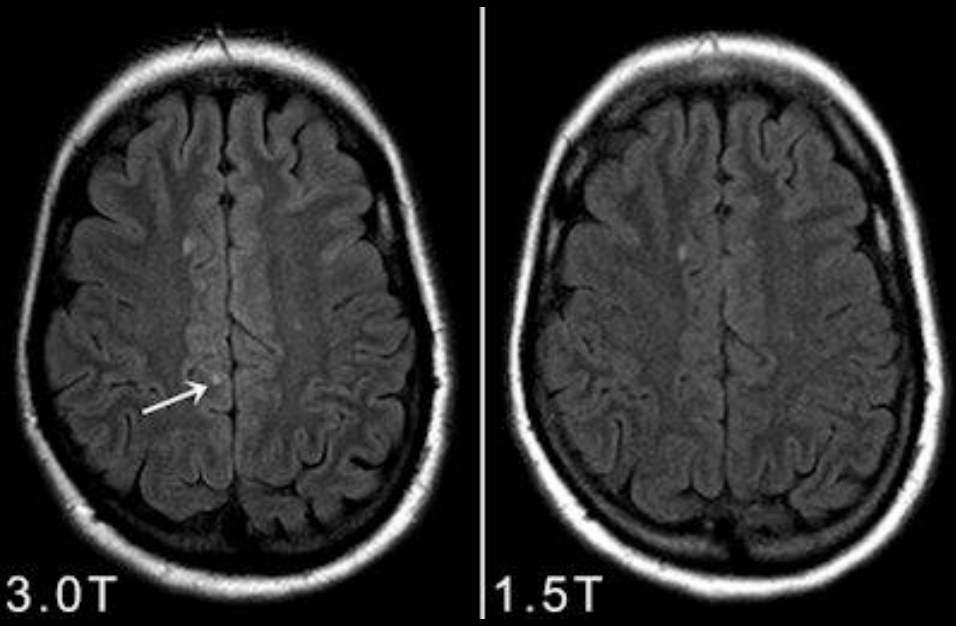
Autoimmune disease:
atypical multiple sclerosis; ADEM; other diseases (SLE, Sjögren's syndrome, etc.)

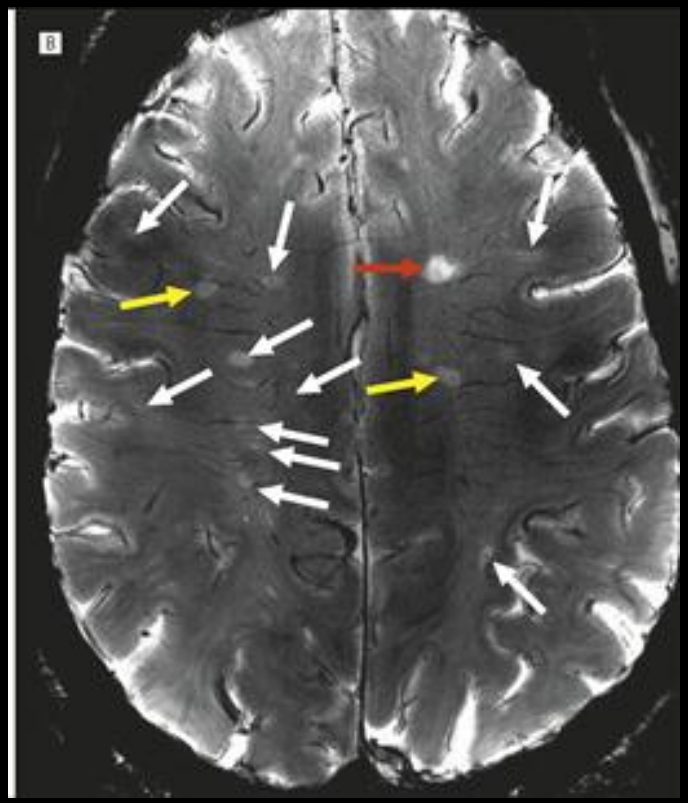
Sarcoidosis

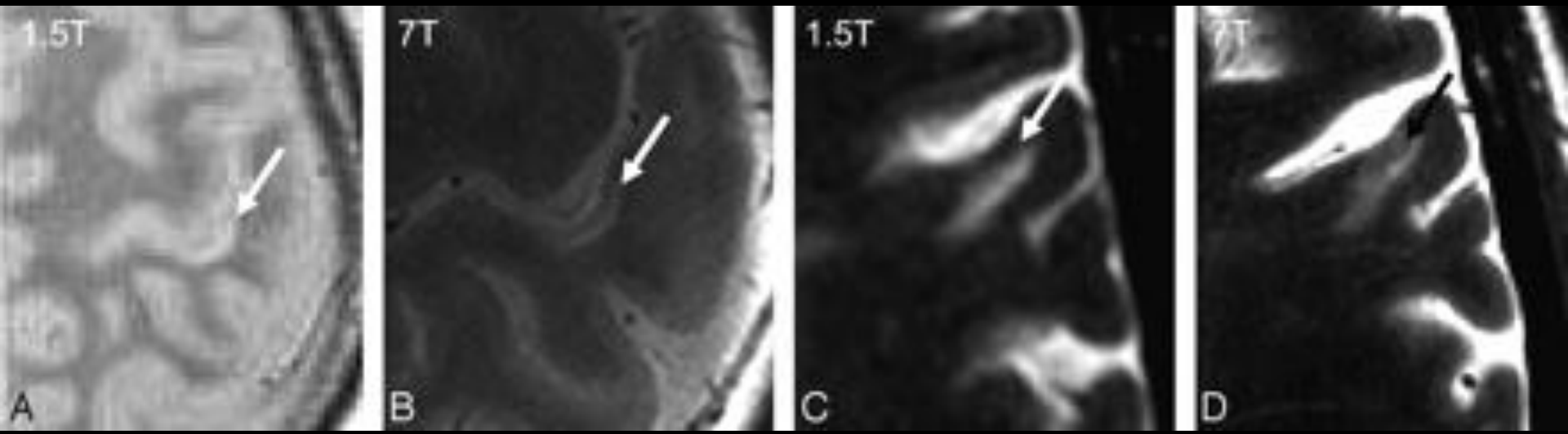
Infections: Lyme, cryptococcosis, etc.

Vasculitis (Behçet)

Mucopolysaccharidosis


3.0T
1.5T


B


1.5T
7T
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A
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C
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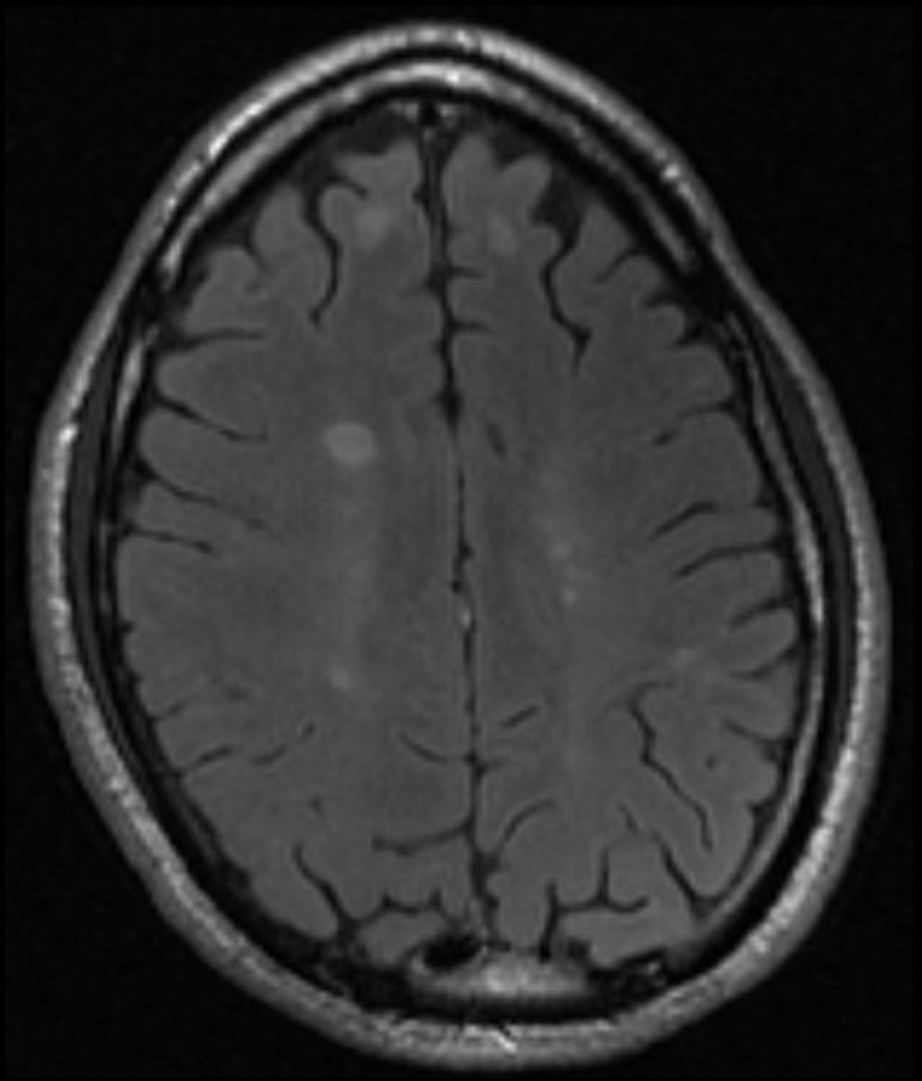
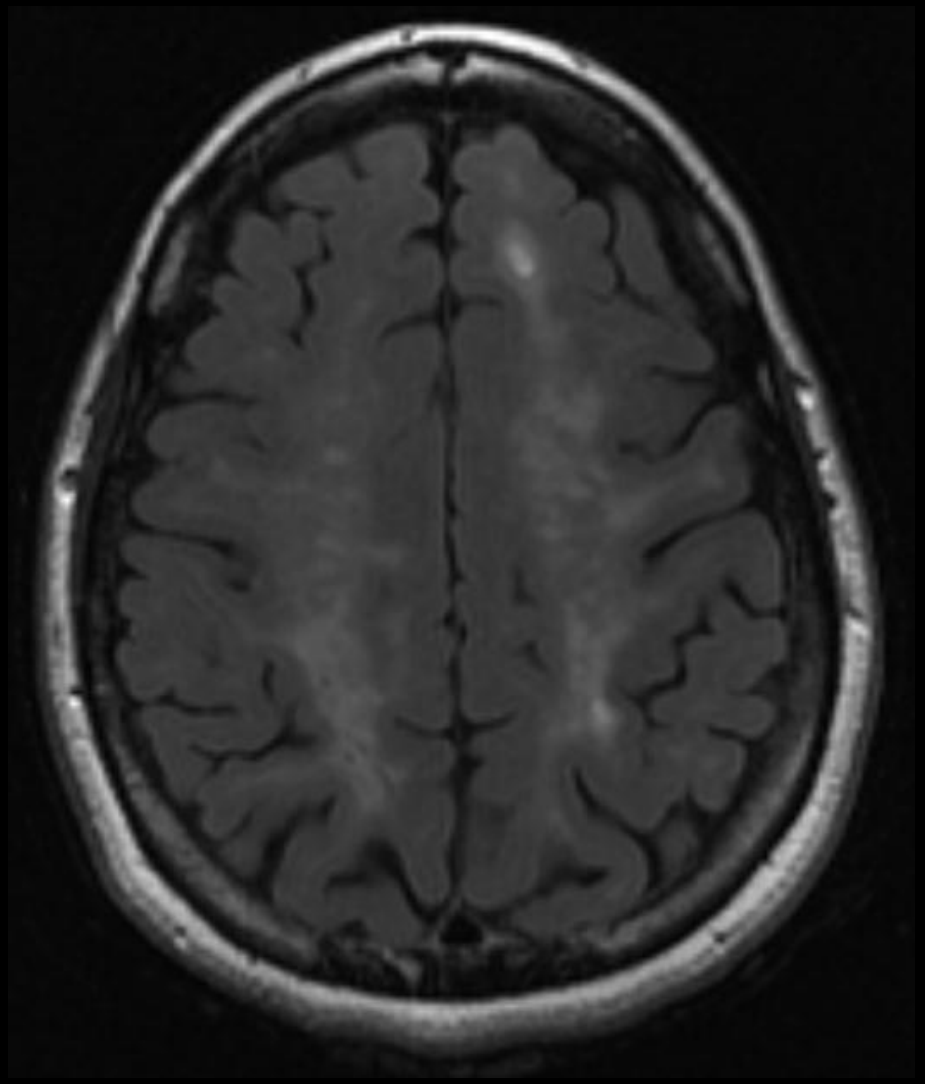
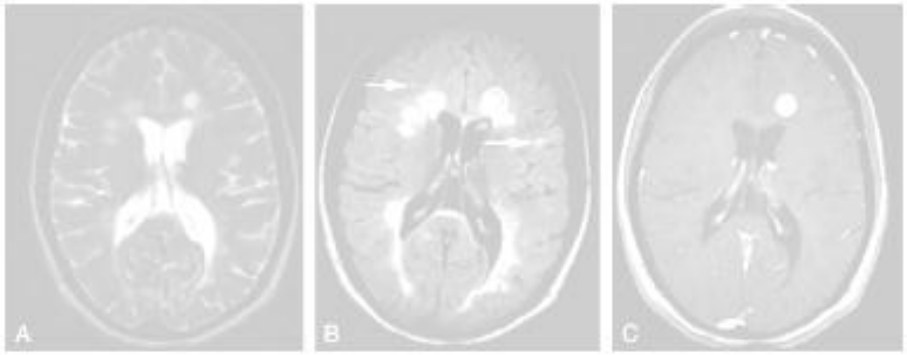
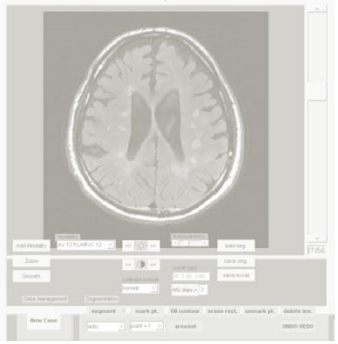






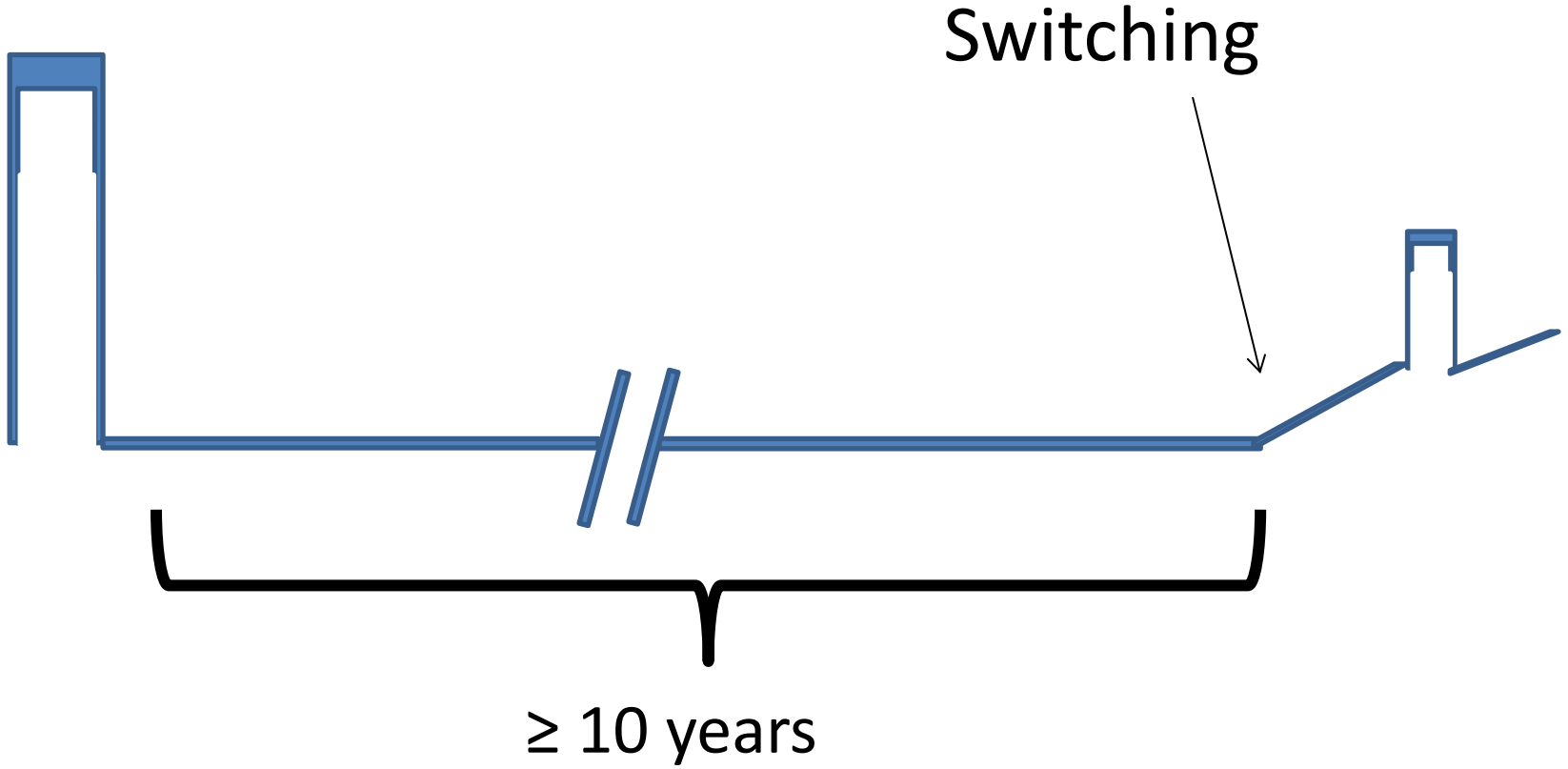


	A	B	C	D
4	Study date	20100614		
5	Protocol Name	8CH NEW MS PROTO/6		
6	Modality type + TE-TR	Ax T2 FLAIRxC 123x156-9502		
7				
8	Number of lesions	33		
9	Lesions volume (cm3)	16.46		
10				
11	Lesion #			
12	1	0.03		
13	2	1.86		
14	3	1.52		
15	4	6.3		
16	5	0.05		
17	6	3.78		
18	7	0.06		
19	8	0.03		
20	9	0.32		
21	10	0.17		
22	11	0.07		
23	12	0.1		
24	13	0.18		
25	14	0.05		
26	15	0.07		
27	16	0.1		
28	17	0.08		

1. # of Lesions
2. Total Volume

List of lesions

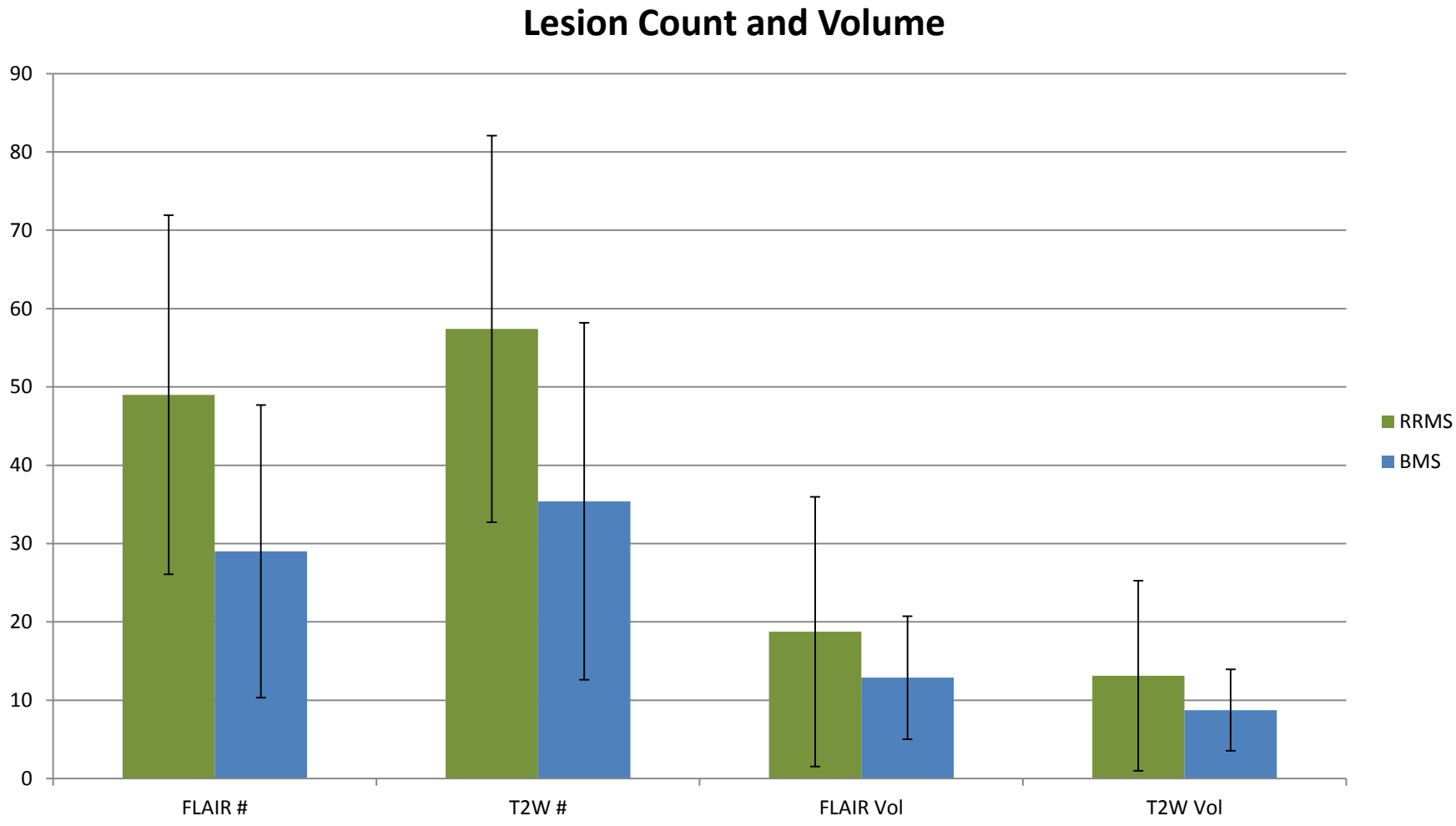
Benign Multiple Sclerosis



Study Population

- Pilot Study
  - 14 total patients
    - 6 RRMS
    - 8 BMS
  - 10 total patients with both T2W and FLAIR
    - 5 RRMS
    - 5 BMS
- New Group
  - 27 Patients with BMS
    - Switchers & Non-switchers
    - Randomized
  - T2W, FLAIR, T1W+Gd, some have T1W sets
- Slice numbers: 56 & 112 most common

Preliminary results



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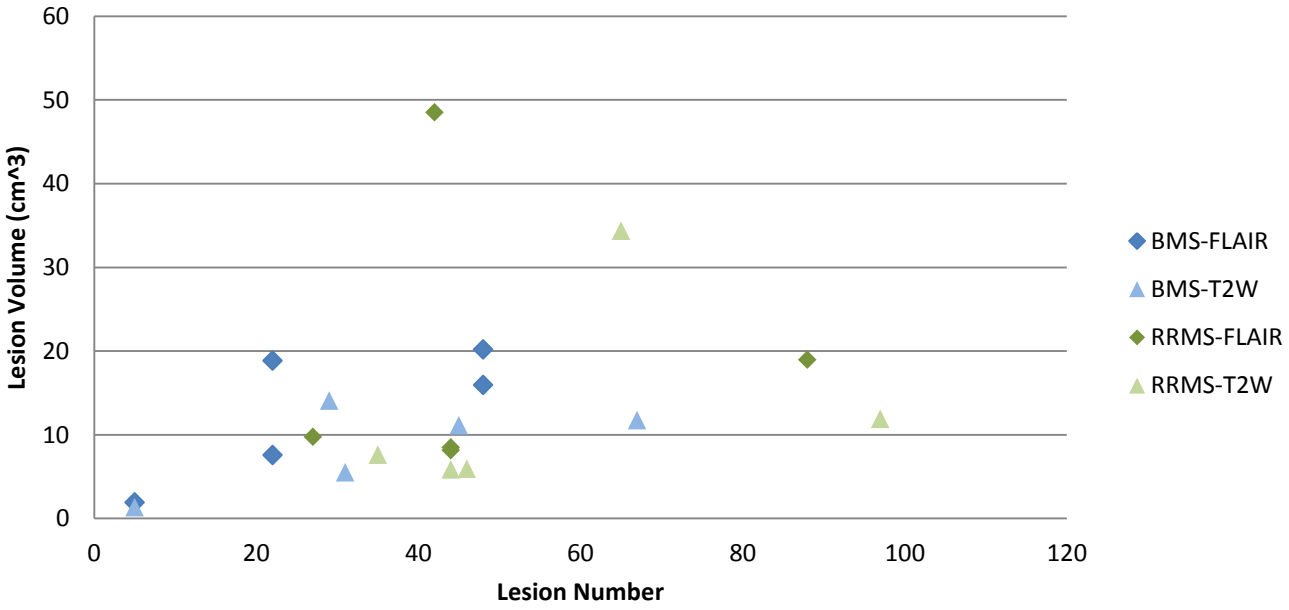
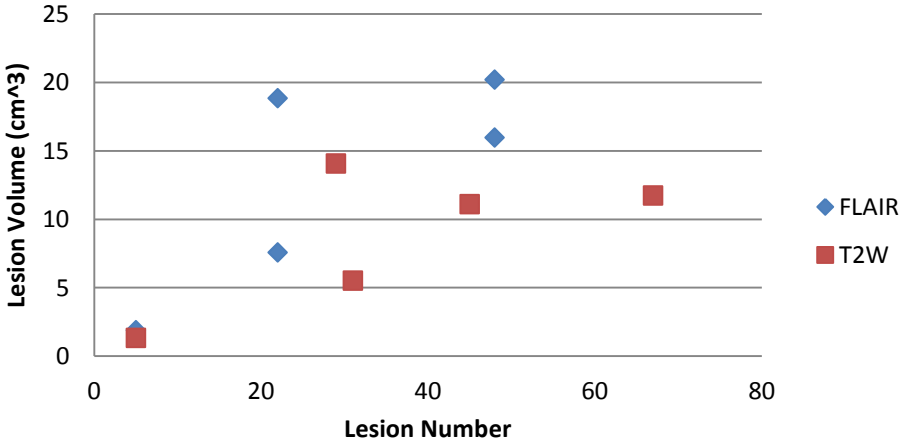
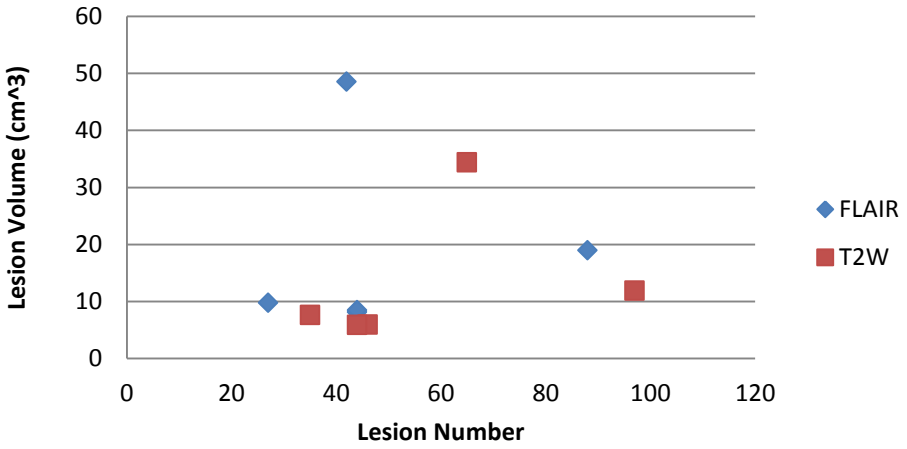
Volume vs. Count



Benign MS: Volume vs. Count



RRMS: Volume vs. Count



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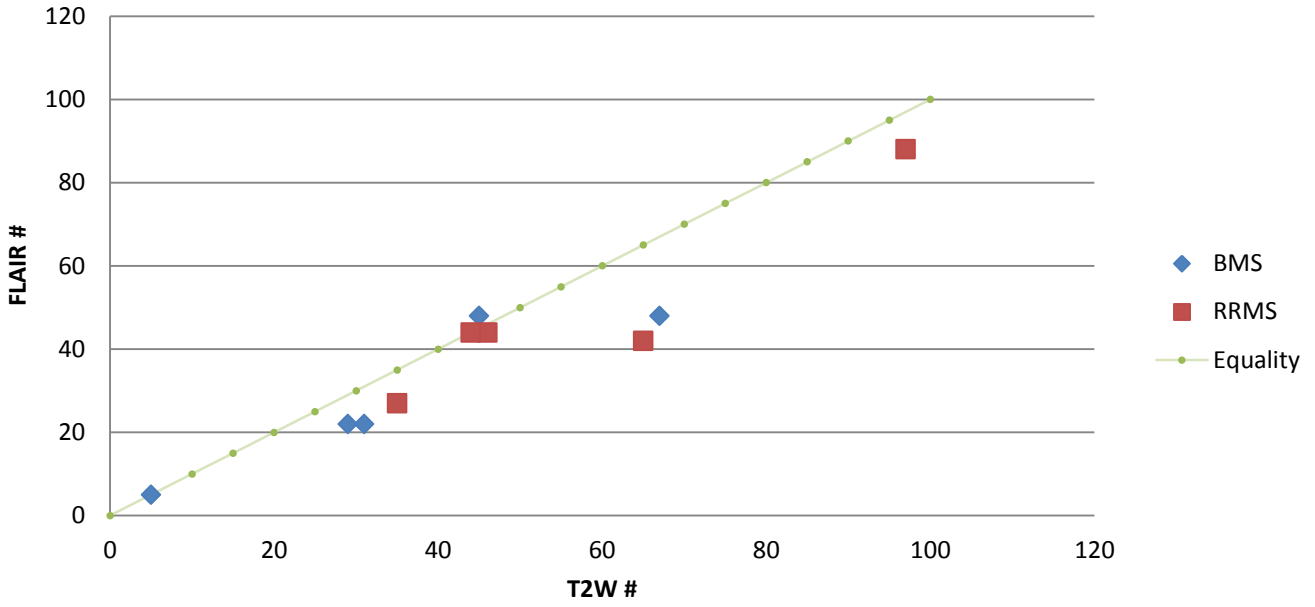
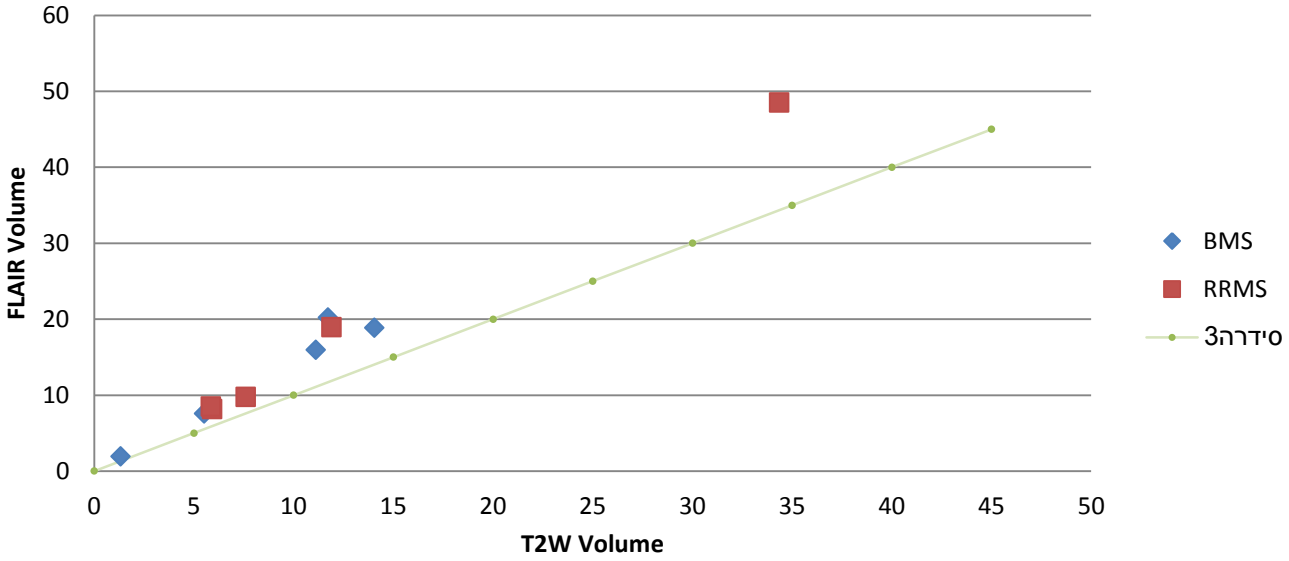
Lesion Counts



Lesion Volume



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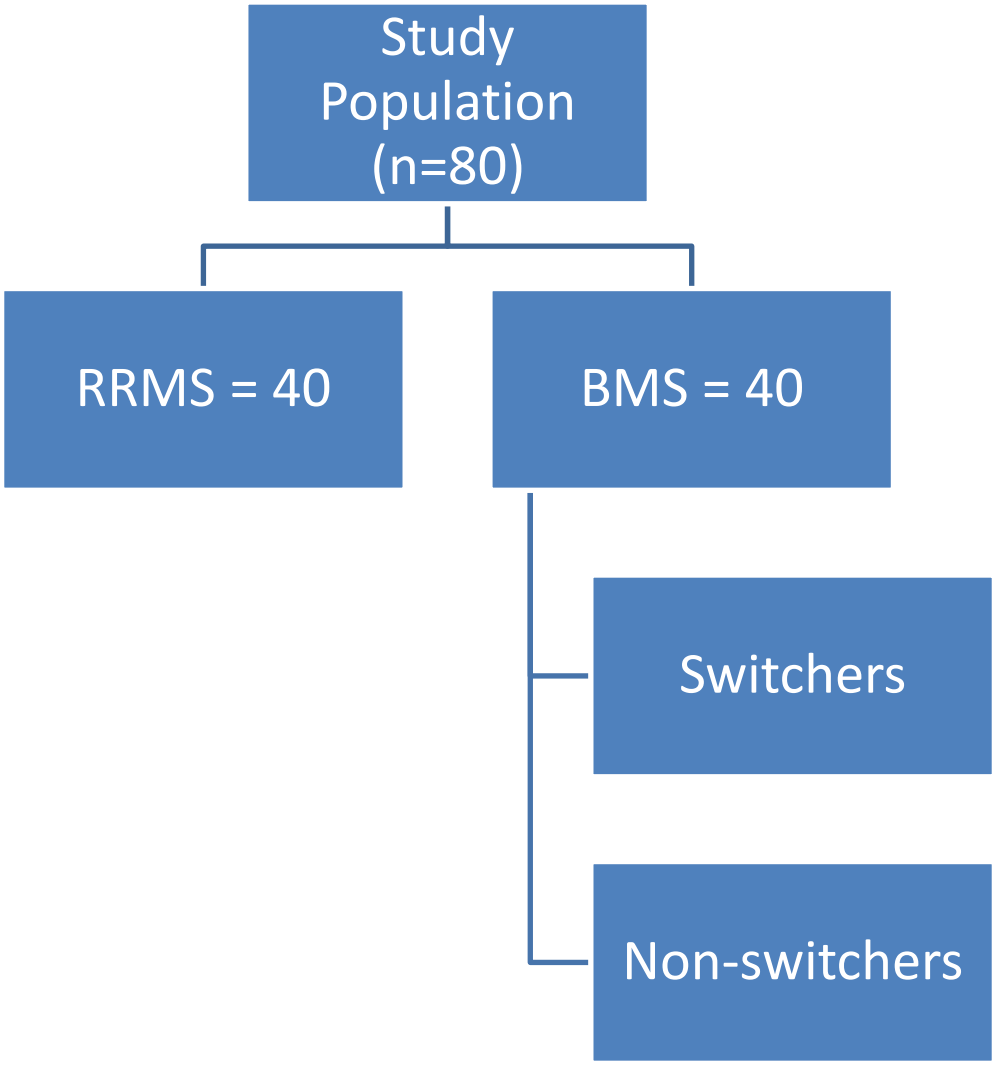
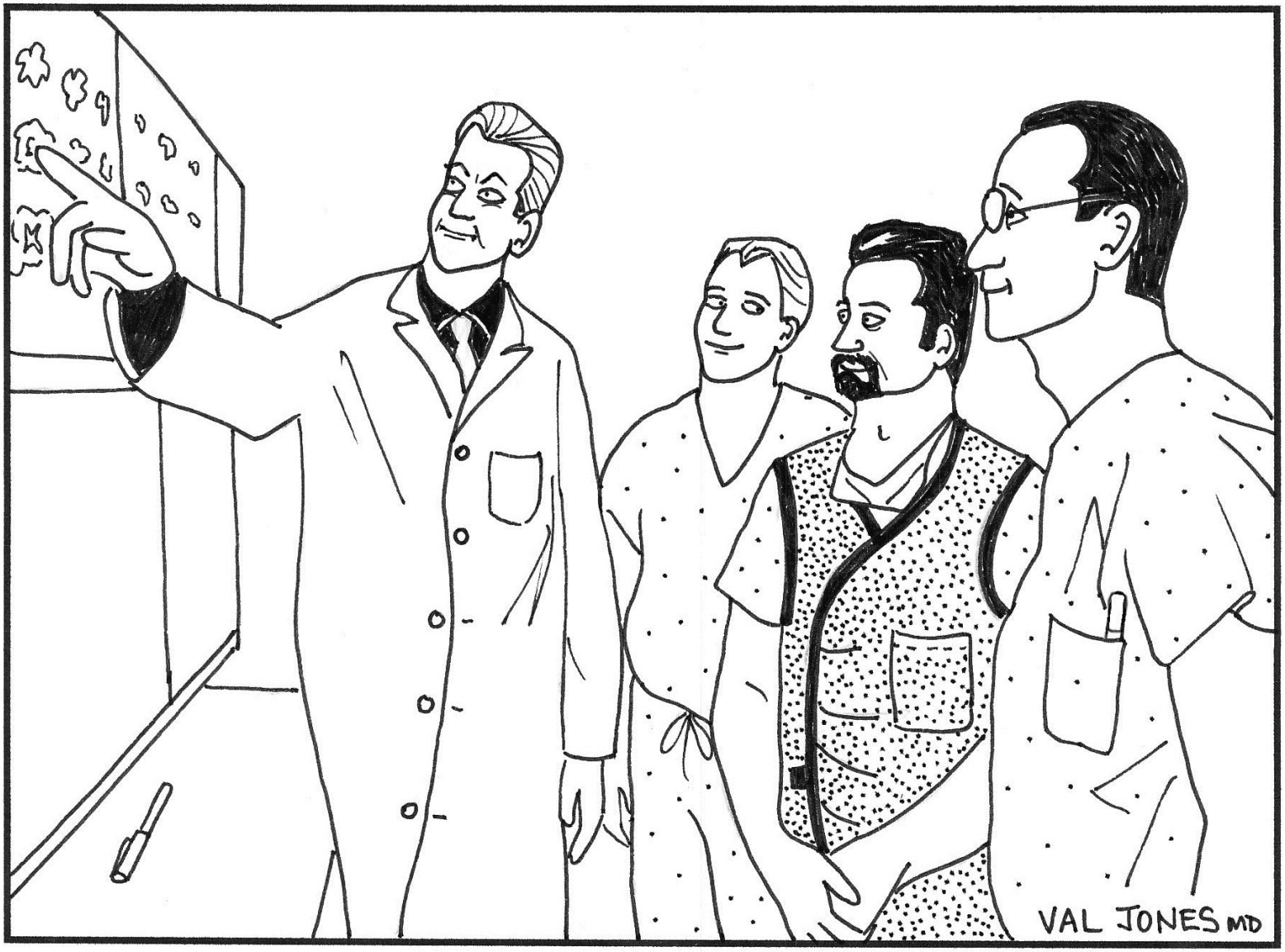
All Variables Considered

- Lesions:
  - Count
  - Total Volume
  - Volume Distribution
  - Location (?)
- EDSS score
- Demographics
- Date of MS onset
- Time to progression
- Time to second relapse

Future Steps: More Patients





"Dr. Richards had to scrape the resident's lunch drippings off the films in order to reveal the underlying pathology."