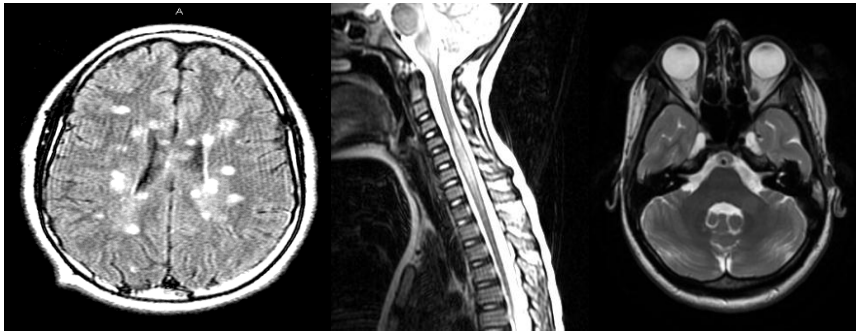
MRI parameters for prediction of conversion of clinically isolated syndromes to Multiple Sclerosis in children



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Supervisors:

Dr. Shay Menascu

Dr. Shmuel Miron

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- MS is a chronic inflammatory demyelinating disease. Its cause is still unknown.
- Pathophysiology is immune mediated damage to the CNS, in particular the axons of nerves, caused by disruption of the BBB and inflammation which leads to focal demyelination.
- Childhood MS or pediatric MS, is apperance before the age of 18, 19, or 21. There is still no consensus.
  - It is accepted to divide MS into 3 age groups:

    Childhood MS <12

    Juvenile MS 12-18

    Adult MS >18
- Until a decade ago it was a largely unknown disease. Awareness is growing nowadays.
- There have been cases reported as young as 4 y.o.

- 2.7-5% have an onset in the pediatric age range, with onset generally being in the teenage years. **Under age 10** represent about **0.2% to 0.9%** of the total number of cases.

- The incidence in Israel is 0.1/100,000.

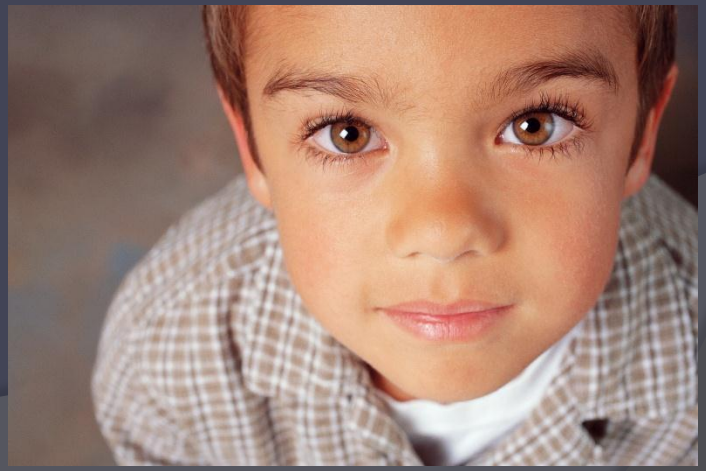
- Similar to adults with MS, girls are disproportionately represented, though ratios vary with age. Female-to-male ratios:

<6	-	0.8:1.
6-10	-	1.6:1.
>10	-	2:1.

- Children, in contrast to adults, almost exclusively present with relapsing-remitting disease.

Is the disease less or more aggressive in children?

- Progress to significant disability is much slower in children in the same follow up time.
- There is a more active inflammatory process. Second attack at a shorter time interval and higher relapse rate during first years.
- Recovery from relapse is also more rapid.
- Brain plasticity in children allows better recovery from damage.



MRI parameters for prediction of conversion of clinically isolated syndromes to MS in children

We don’t know who will progress and how soon

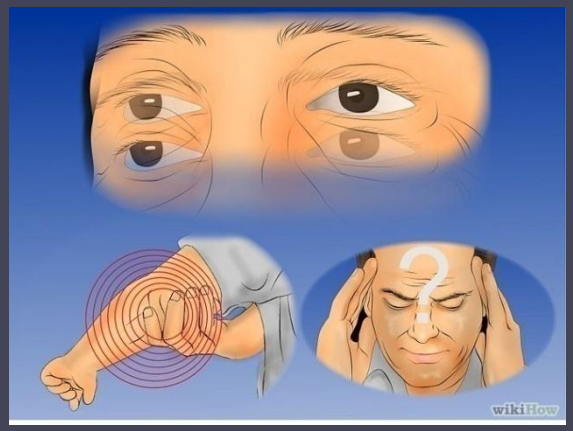
First neurological event

?

Second neurological event

CIS

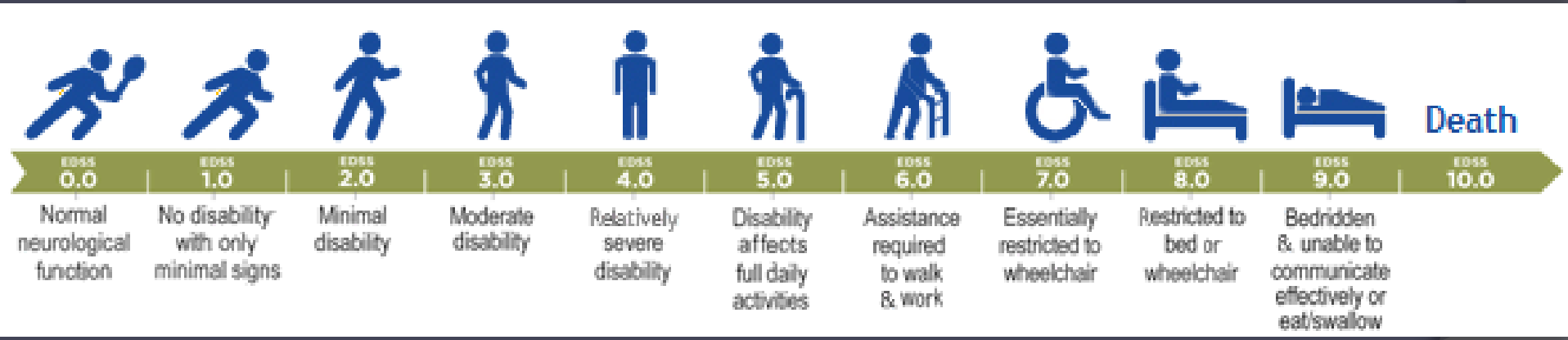
MS



Why do we want to know who will progress and who won't?

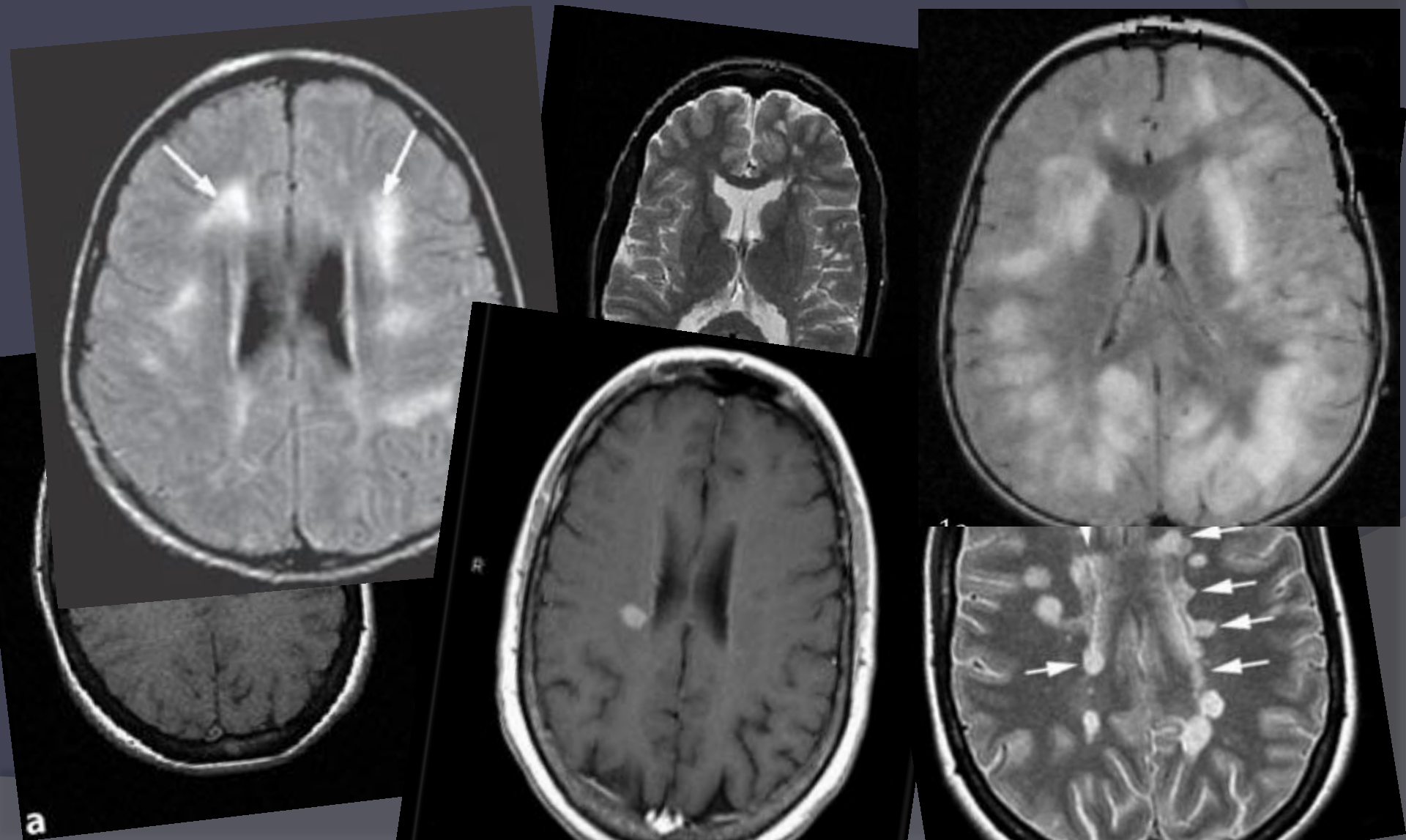
Diagnose & treat early

- Children progress slowly, but they become disabled at a younger age. Starting sooner makes them gain disability in their 20´s-40´s.



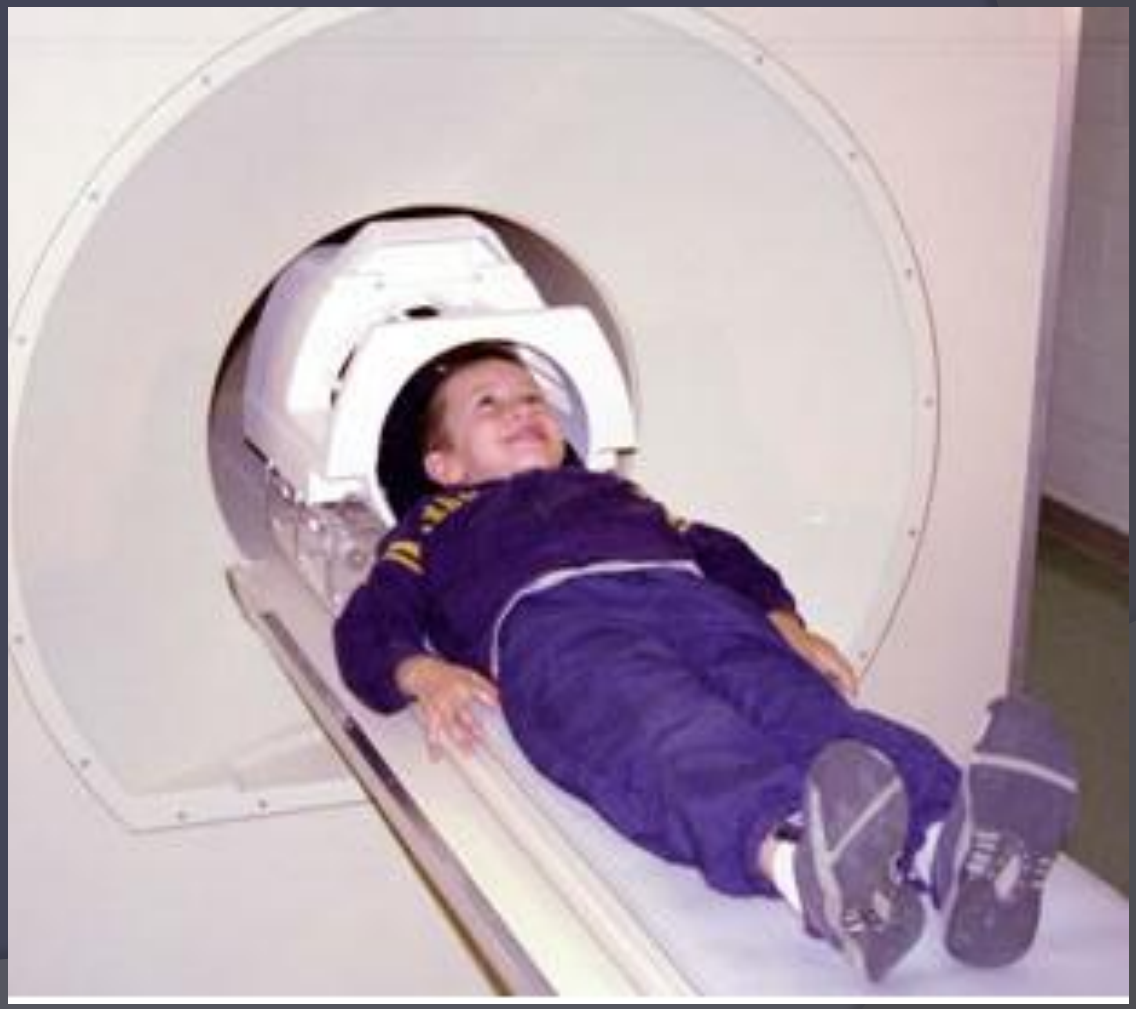
Currently, for the child who presents with a first inflammatory demyelinating event, we are unable to predict if he will subsequently remain asymptomatic or develop the lifelong disease of MS.

Our study is looking for parameters in MRI that can answer these questions

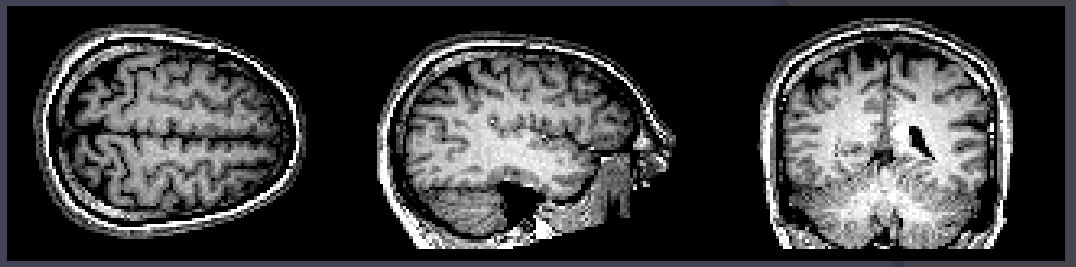


The study

MRI – why?



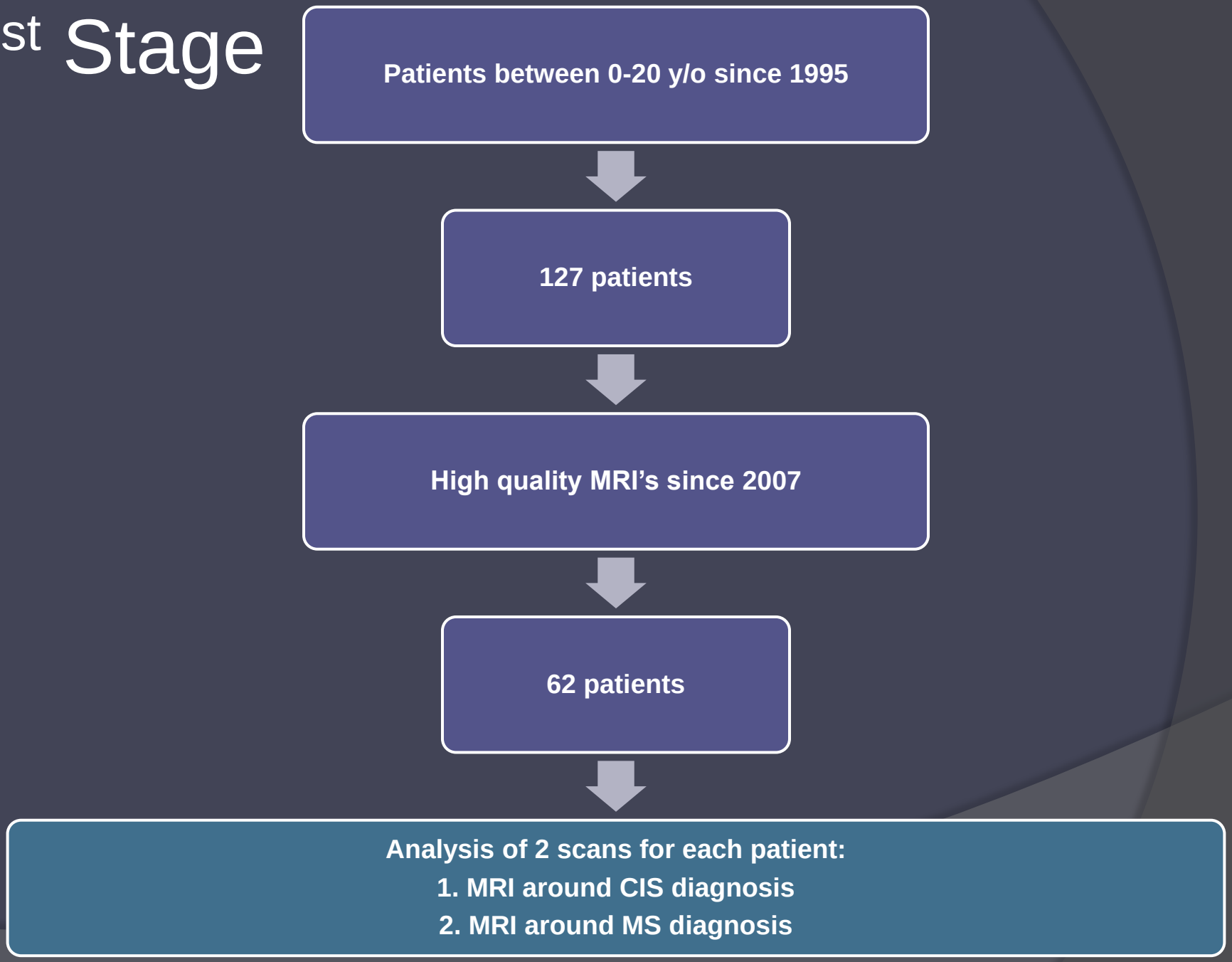
The study



- MRI is a **sensitive, non-invasive, no radiation** means of tracking MS pathology. Pediatric patients are scanned periodically, what makes these characteristics to be of such value.

- The questions we want to answer:
  1. What are the differences in the MRI of children that developed RRMS to those who did not?
  2. What can the first MRI of a patient tell us about his future?

1st Stage


Patients between 0-20 y/o since 1995
127 patients
High quality MRI's since 2007
62 patients
Analysis of 2 scans for each patient:
1. MRI around CIS diagnosis
2. MRI around MS diagnosis

2nd Stage


Add Modality
Zoom
Smooth
modality
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contrast preset
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transparency
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save seg.
save excel
Case management
New Case
Segmentation
segment
auto
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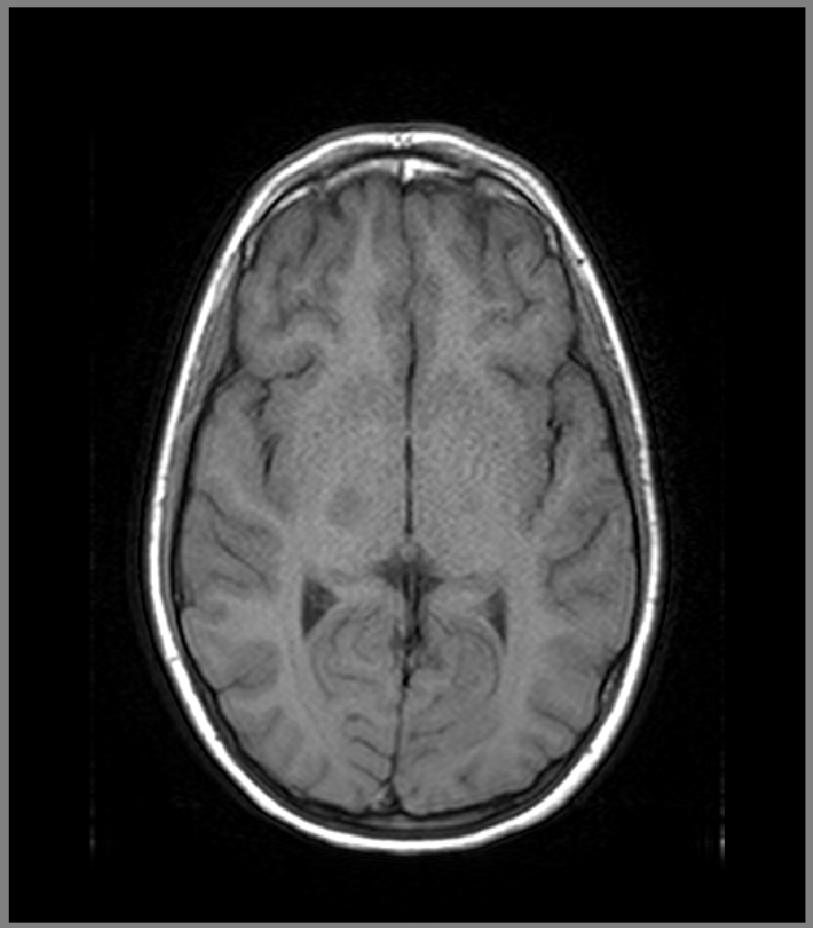
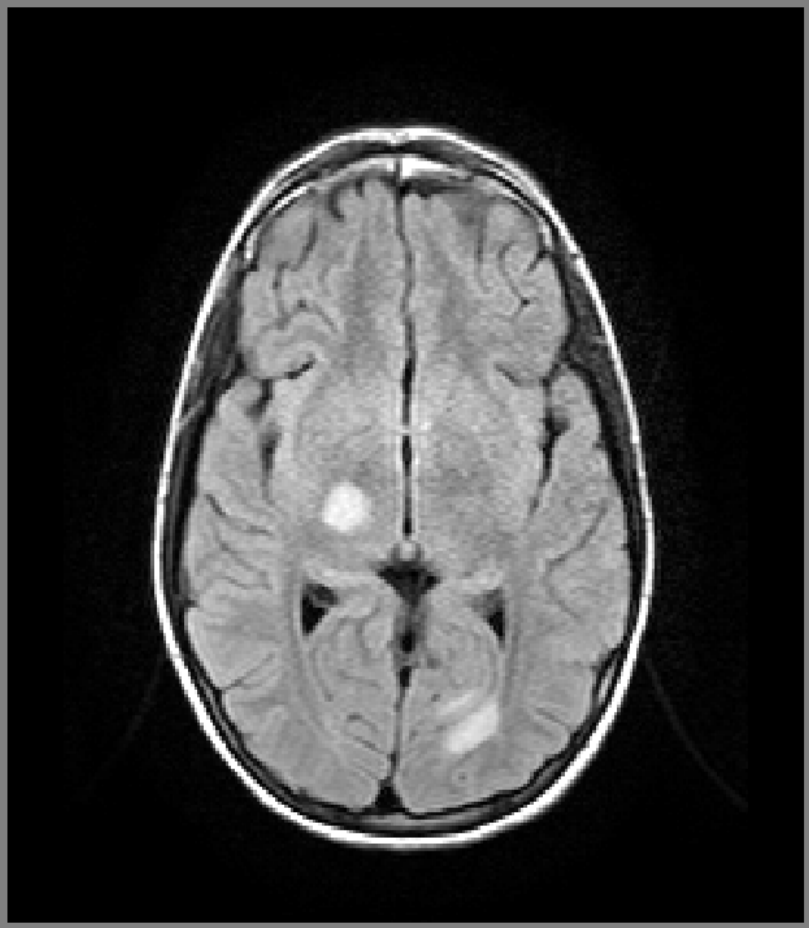
area/vol:
UNDO/ REDO
Synchronization
synch
show 2
seg. 2





13/26

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Case management
New Case

Segmentation
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Synchronization
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MSET v1.9 - C:\Users\Carolina\Desktop\MS\analyzed\LACHKAR_AYELET_ALY\Study20100421_224255
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UNDO/ REDO
Synchronization
synch
show 2
seg. 2


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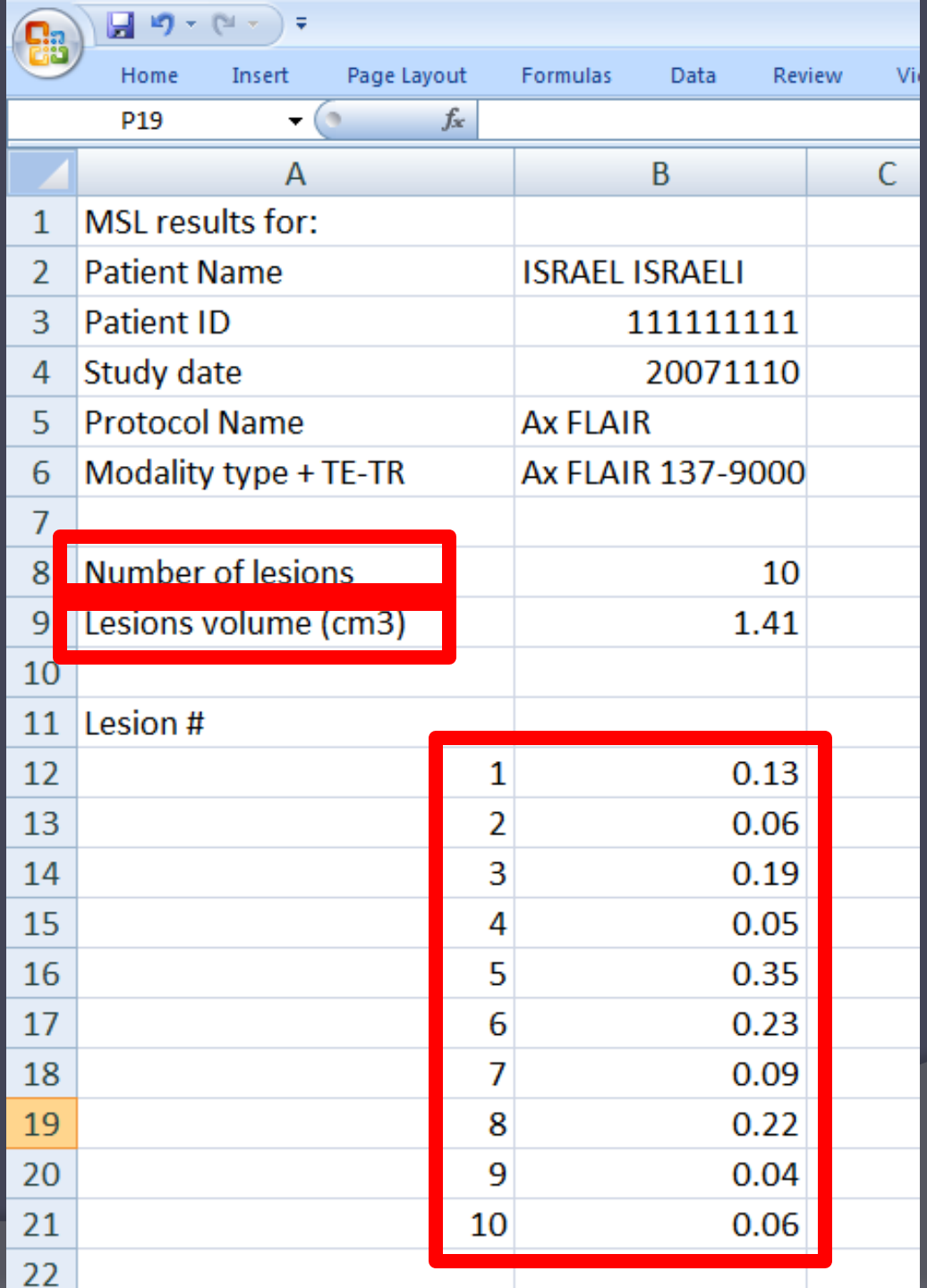


Home Insert Page Layout Formulas Data Review

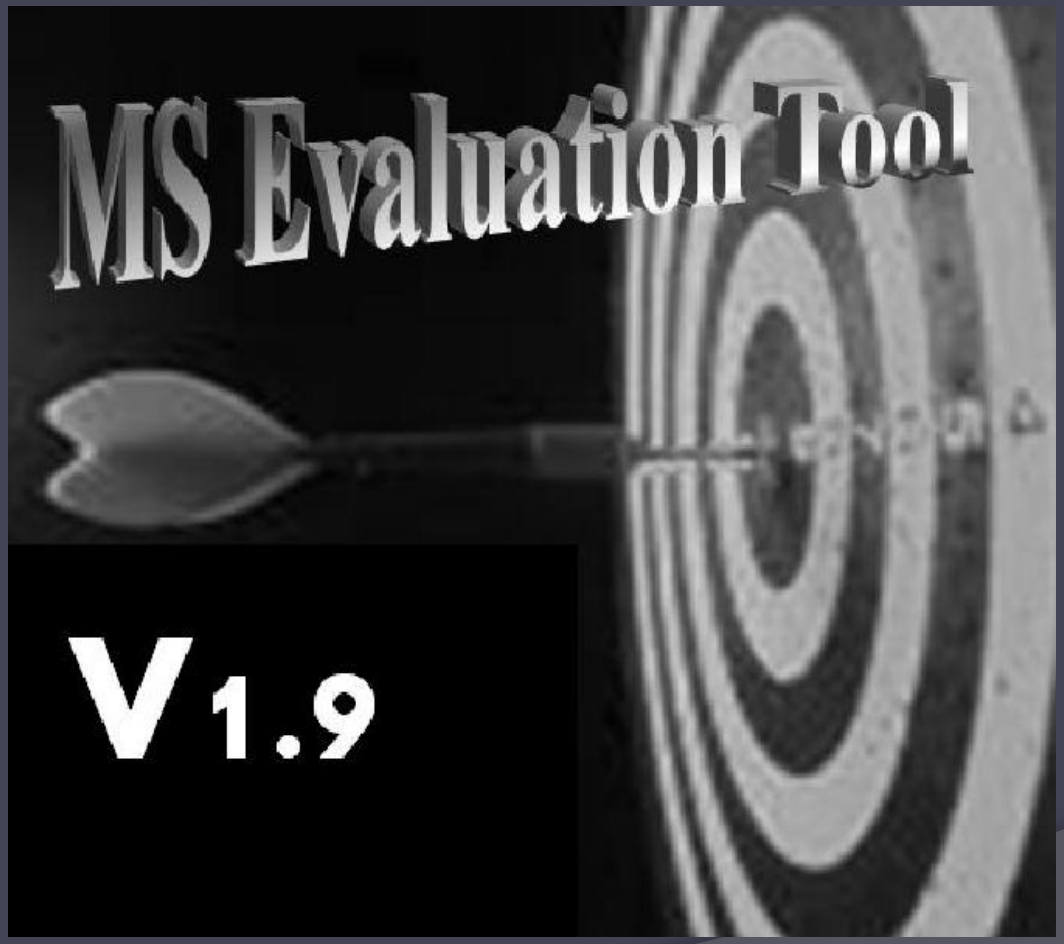
P19

	A	B	C
1	MSL results for:		
2	Patient Name	ISRAEL ISRAELI	
3	Patient ID	111111111	
4	Study date	20071110	
5	Protocol Name	Ax FLAIR	
6	Modality type + TE-TR	Ax FLAIR 137-9000	
7			
8	Number of lesions	10	
9	Lesions volume (cm3)	1.41	
10			
11	Lesion #		
12	1	0.13	
13	2	0.06	
14	3	0.19	
15	4	0.05	
16	5	0.35	
17	6	0.23	
18	7	0.09	
19	8	0.22	
20	9	0.04	
21	10	0.06	
22			

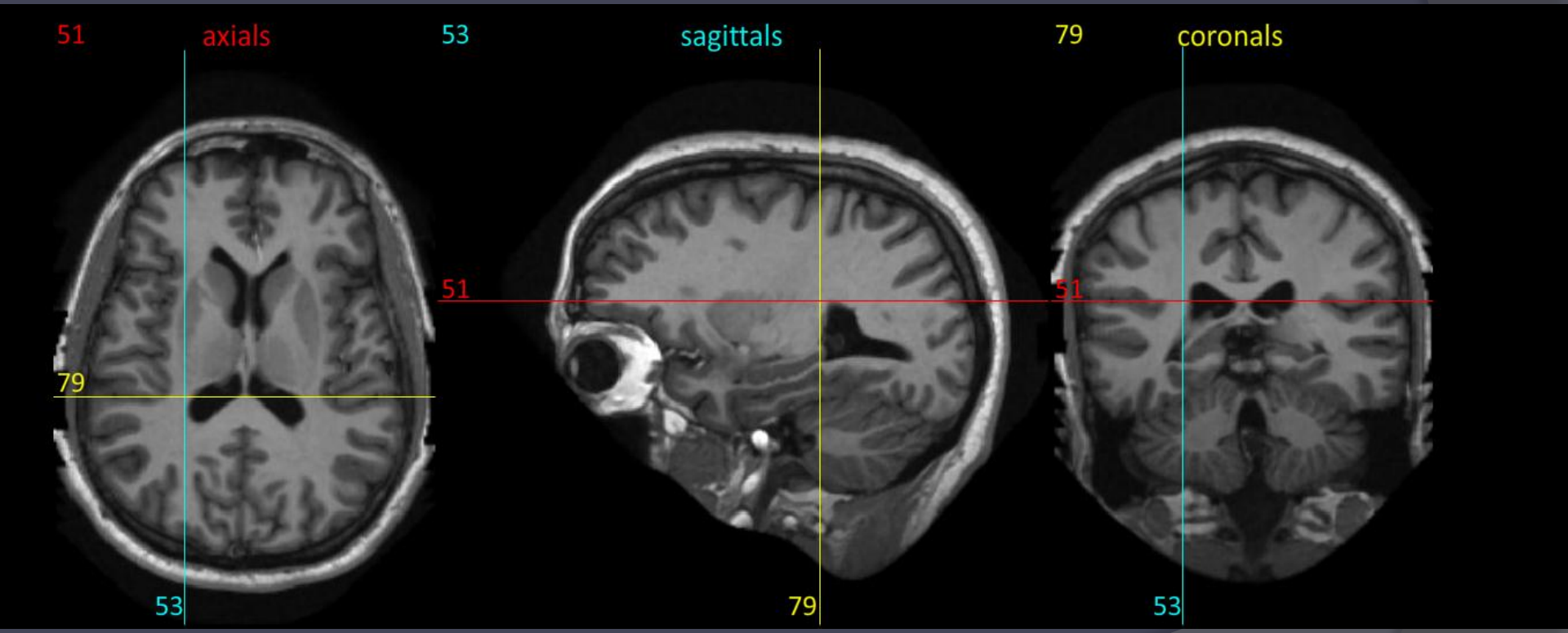
Lesion count - manual

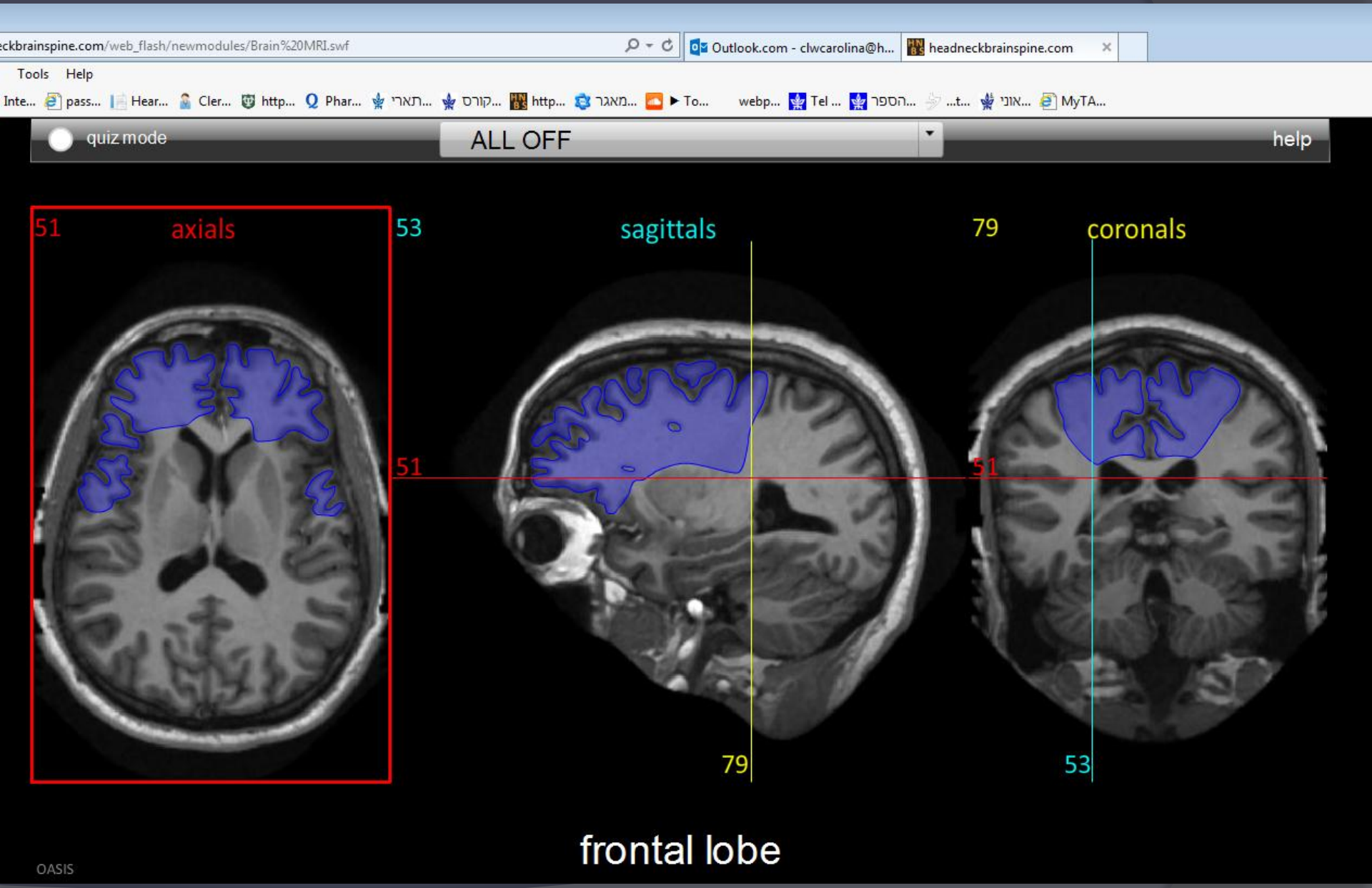
	T2							Flair						
	Front	Occip	Temp	Pariet	Intern	CC	Infrate	Front	Occip	Temp	Pariet	Intern	CC	Infrate
10/11/07	4	0	1	5	0	0	2	4	0	1	5	0	0	2
21/11/08	9	2	2	10	0	1	0	9	2	2	10	0	1	0

Lets try one…



How can we know the lesion location?

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sagittals
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coronals
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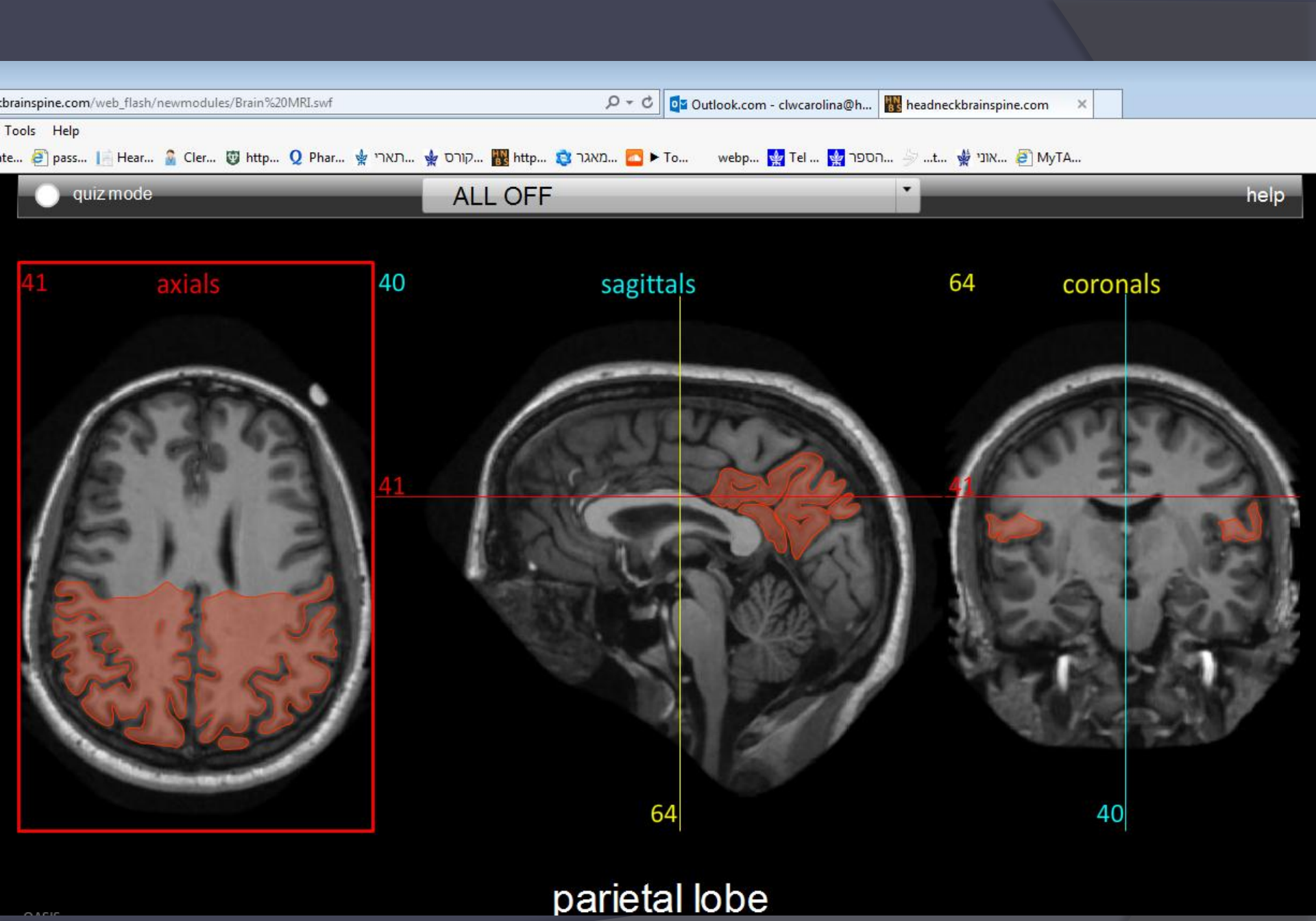
frontal lobe
OASIS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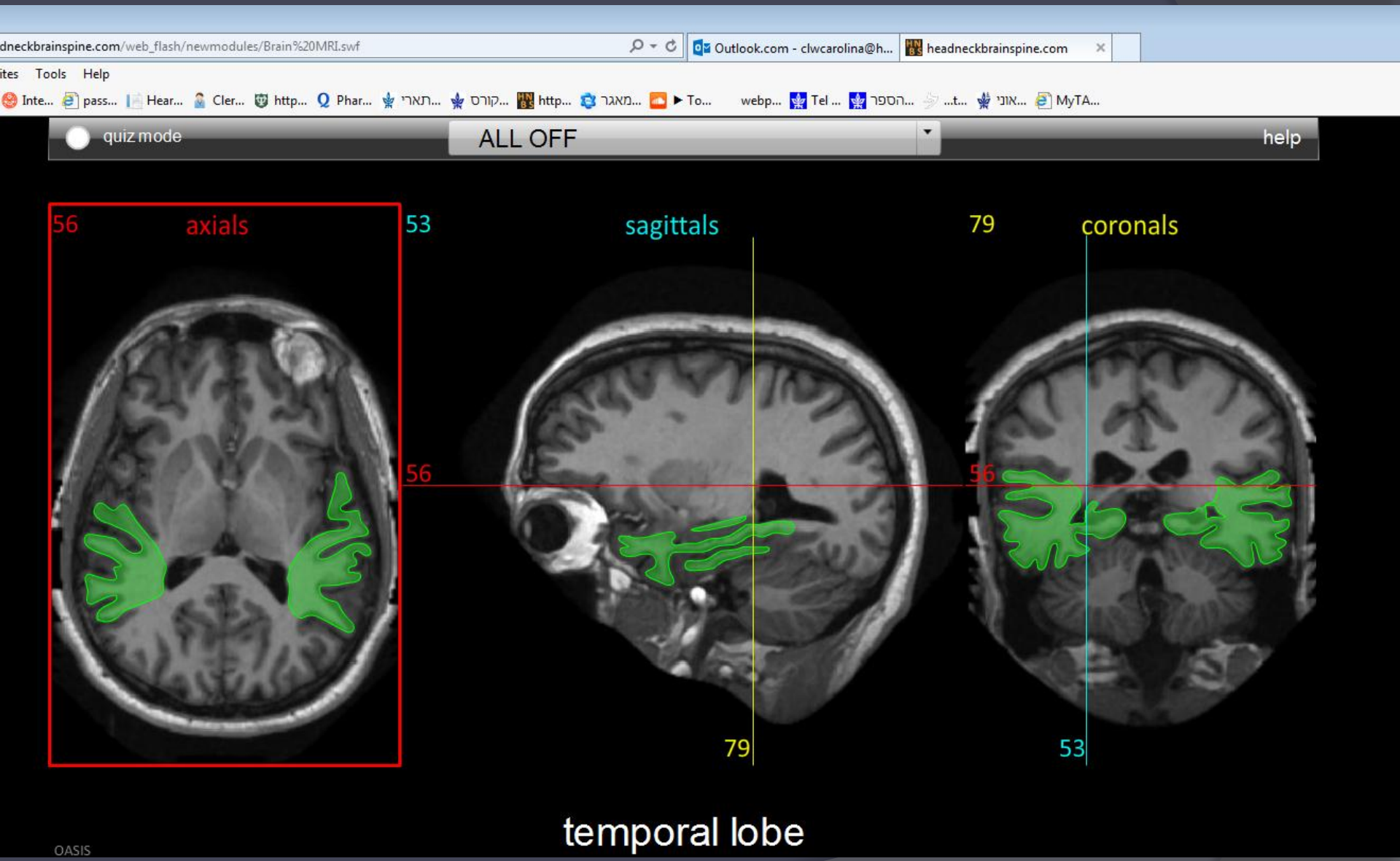
parietal lobe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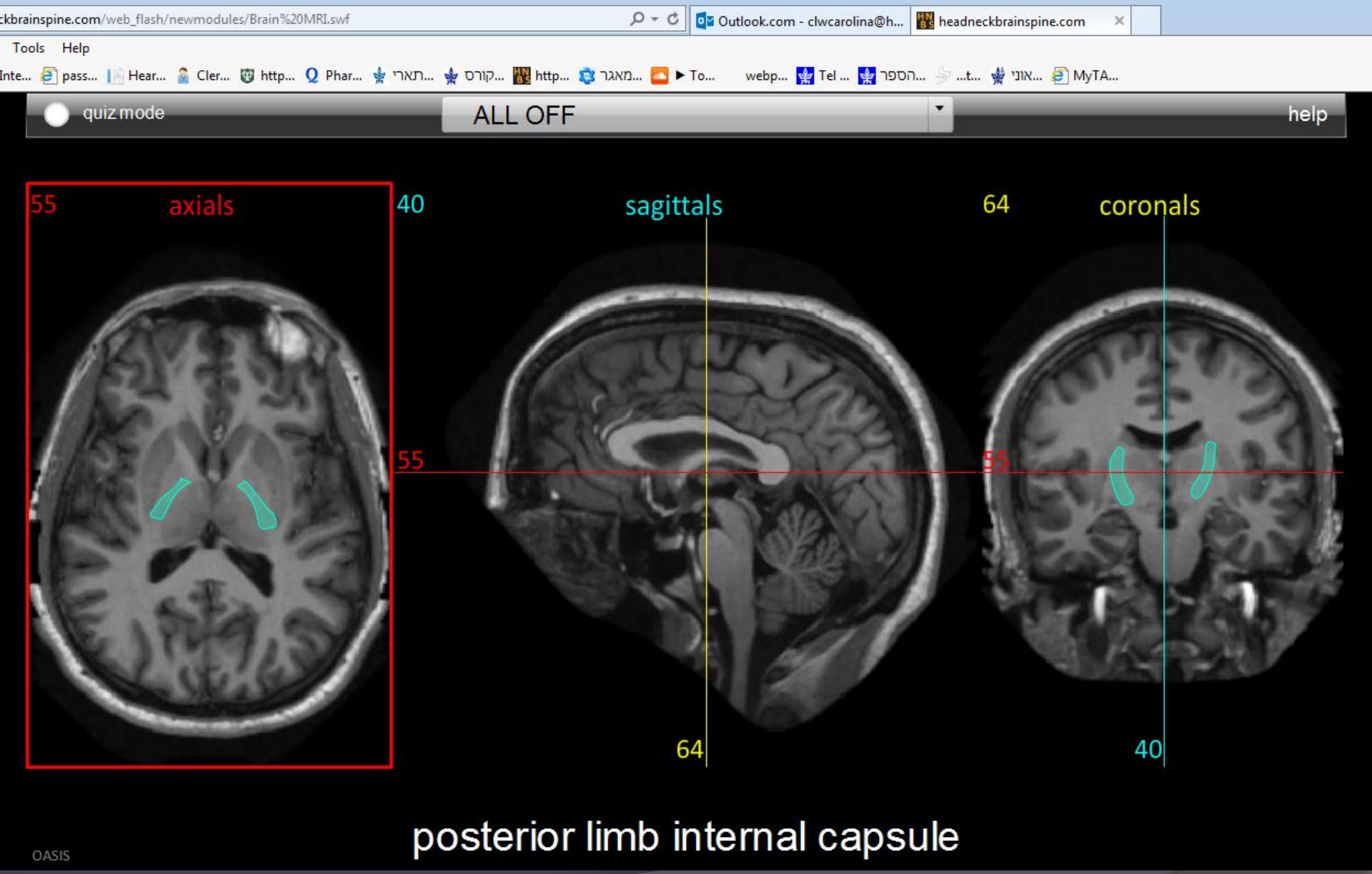
OASIS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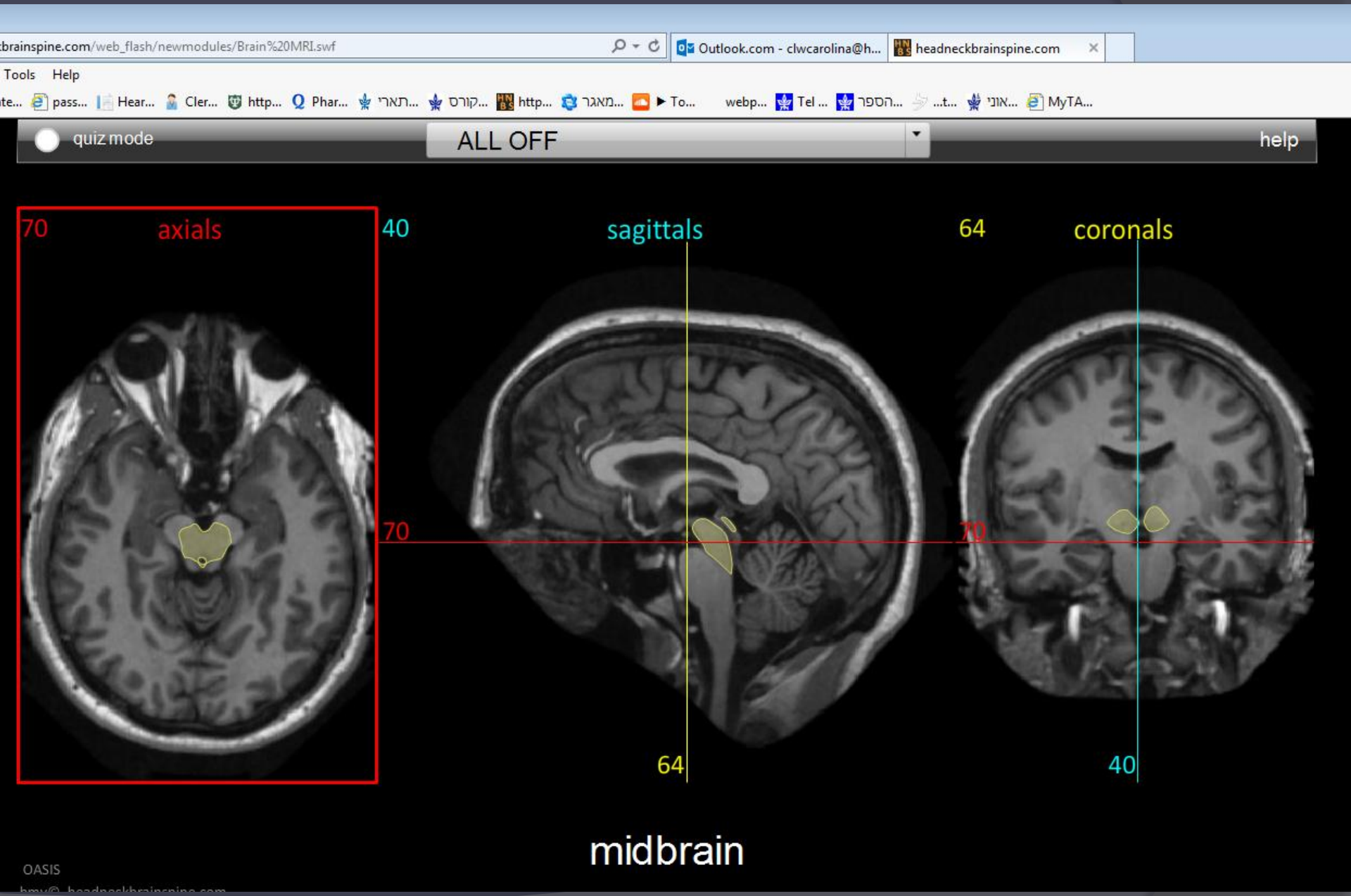
posterior limb internal capsule
OASIS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sagittals
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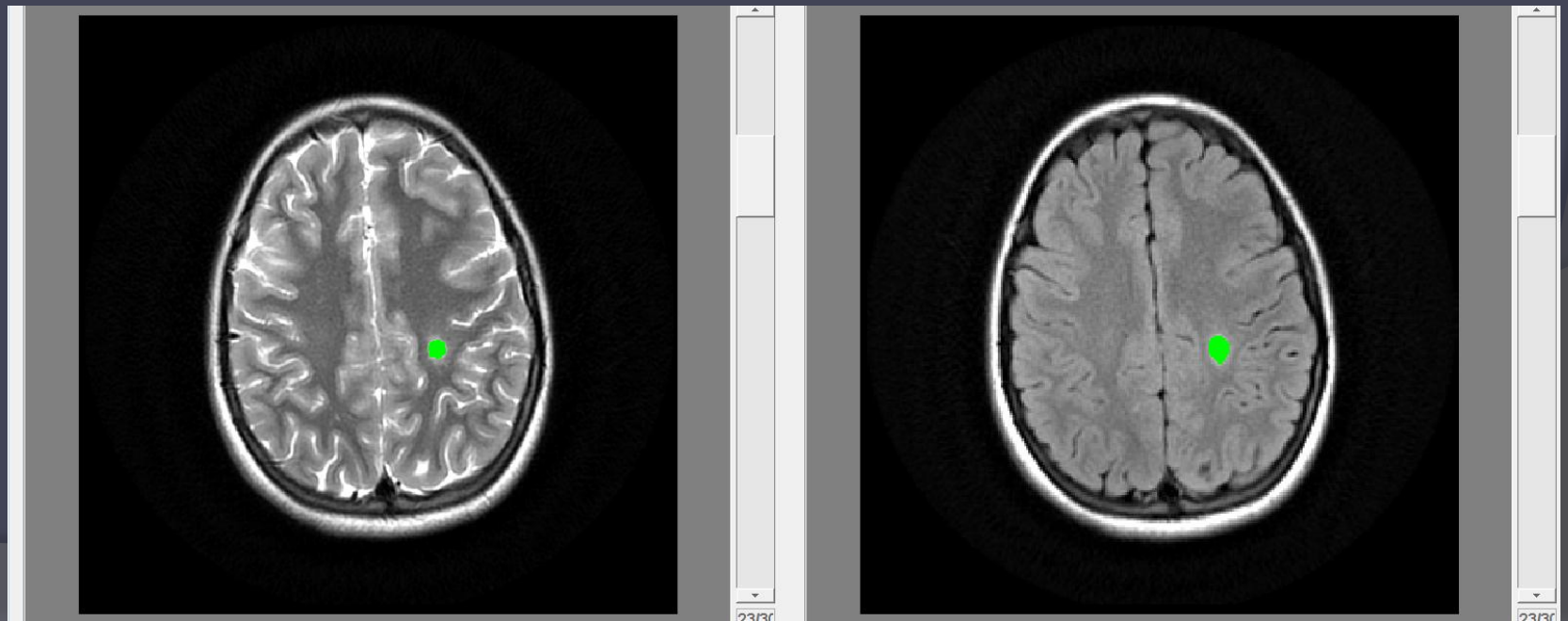
midbrain
OASIS

Assesing the degree of accuracy

1. Comparison to MSET count.
2. Comparison to the radiologists analysis.
3. Review of a random sample of patients.
4. Comparison to the count of the technician at the MS Center.

What data do we have?

1. Number of lesions
2. Location of lesions
3. Volume of each lesion and total volume of lesions



The Database

Current diagnosis	Birth date	CIS	Age at CIS	MS diagnosis	Age at MS diagnosis	Days from Cis to MRI 1	Time from MRI 1 to MRI 2	Time between MS diagnosis and MRI 2	תאריך ביקור אחרון	זמן מCIS לביקור אחרון במרפאה		T2 Frontal	T2 Occipital	T2 Temporal	T2 Parietal	T2 Internal C	T2 CC	T2 Infratento	Flair Frontal	Flair Occip
Relapsing	11/10/90	20/10/07	17	15/10/08	18	21.00	377.00	37.00	18/6/14	6.66	10/11/07	4	0	1	5	0	0	2	4	
											21/11/08	9	2	2	10	0	1	0	9	
Relapsing	12/8/86	19/1/04	17	10/5/07	20	849.00	434.00	76.00	25/2/14	10.10	17/5/06	1	0	0	0	0	0	0	1	
											25/7/07	1	0	1	0	0	1	0	1	
Relapsing	1/5/88	25/10/07	19	2/3/08	19	10.00	120.00	1.00	23/6/14	6.66	4/11/07	5	0	0	3	0	1	1	6	
											3/3/08	3	0	1	3	0	1	1	6	
Relapsing	17/12/88	15/7/08	19	13/8/08	19	29.00	124.00	124.00	17/8/09	1.09	13/8/08	13	1	2	8	1	1	1	13	
											15/12/08	9	1	1	7	1	0	1	9	
Relapsing	10/11/91	15/9/06	14	1/6/07	15	5.00	462.00	208.00	9/6/14	7.73	20/9/06	5	2	1	2	1	1	2	8	
											26/12/07	22	1	1	10	1	5	5	22	
Relapsing	31/3/93	1/2/13	19	8/5/13	20	0.00	365.00	269.00	29/6/14	1.40	1/2/13	23	2	5	13	4	1	4	19	
											1/2/14	13	3	3	7	2	3	2	14	
Relapsing	19/7/92	25/7/10	18	16/9/10	18	12.00	461.00	420.00	9/6/14	3.87	6/8/10	15	2	4	9	0	1	0	14	
											10/11/11	10	2	1	1	0	0	0	9	
Relapsing	30/5/92	1/5/05	12	1/7/08	16	1163.00	168.00	174.00	29/5/12	7.08	7/7/08	7	0	4	1	1	1	1	8	
											22/12/08	9	1	6	2	0	4	1	8	
Relapsing	4/1/93	2/5/08	15	1/1/10	16	51.00	712.00	-376.00	27/3/14	5.90	22/6/08	9	2	0	0	0	0	1	12	
											1/1/10	14	3	2	6	0	1	0	16	
Relapsing	6/5/93	1/2/12	18	25/4/12	18	-16.00			3/		1/	0	0	0	1	0	0	0	0	
												0	0	0	0	0	0	0	0	
Relapsing	9/6/92	8/12/10	18	12/8/12	20	35.00	542.00	-36.00	16/1/14	3.11	12/1/11	0	0	0	0	0	0	0	0	
											7/7/12	0	0	0	0	0	0	0	0	
Relapsing	27/10/94	3/1/09	14	13/3/12	17	4.00	1155.00	-6.00	12/5/14	5.35	7/1/09	3	0	0	1	0	0	1	3	
											7/3/12	2	0	2	1	0	0	0	2	
Relapsing	17/11/94	14/6/09	14	3/11/09	14	5.00			13/2/14	4.67	19/6/09	6	1	2	5	1	0	3	6	
												0	0	0	0	0	0	0	0	
Relapsing	17/9/94	1/6/11	16	17/4/12	17	-11.00	332.00	0.00	8/5/12	0.94	21/5/11	6	0	0	3	0	0	2	6	
											17/4/12	8	0	0	2	0	0	1	8	
Relapsing	4/7/97	10/7/11	14	19/4/12	14	0.00	47.00	-237.00	19/4/12	0.78	10/7/11	0	0	1	2	0	0	0	0	
											26/8/11	4	0	2	0	0	0	1	4	
Relapsing	5/1/97	9/4/10	13	1/6/10	13	12.00	42.00	1.00	28/4/14	4.05	21/4/10	1	1	0	2	1	0	2	1	
											2/6/10	2	1	1	3	1	0	1	2	
Relapsing	12/7/98	12/2/07	8	6/2/08	9	2.00	474.00	117.00	1/5/14	7.21	14/2/07	4	1	1	1	1	0	0	5	
											2/6/08	14	2	1	0	1	0	0	14	
Relapsing	26/5/01	21/6/12	11	15/10/12	11	0.00	110.00	-6.00	23/6/14	2.00	21/6/12	1	0	0	1	0	0	0	1	
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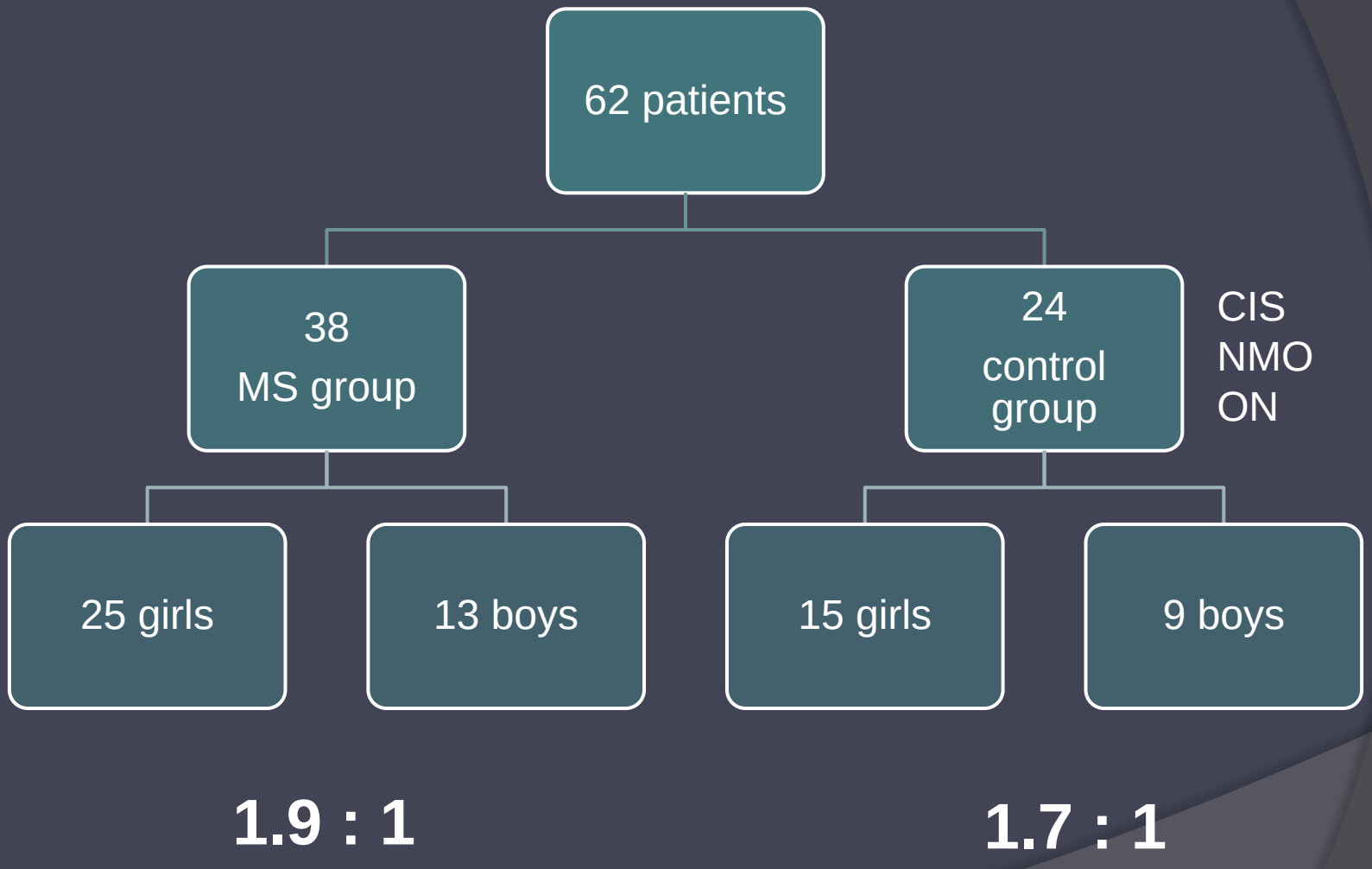
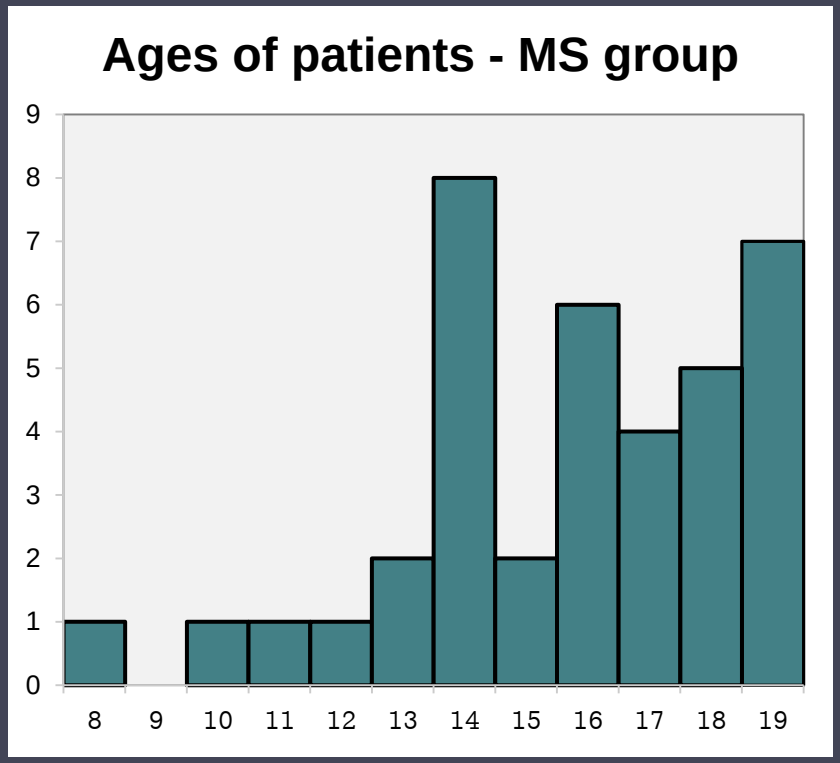
Relapsing	17/7/87	1/1/07	19	25/5/09	21	38.00	180.00	-657.00	16/3/14	7.20	8/2/07	9	1	1	11	0	1	1	8	
											7/8/07	9	1	5	0	1	0	0	9	
Relapsing	27/9/88	28/9/07	19	15/5/08	19	1.00			8/5/14	6.61	29/9/07	0	0	0	0	0	0	0	0	
												0	0	0	0	0	0	0	0	
Relapsing	21/6/89	1/2/07	17	9/7/08	19	55.00	259.00	-210.00	23/7/08	1.47	28/3/07	1	0	0	0	1	1	0	1	
											12/12/07	1	0	0	1	1	0	0	5	
Relapsing	30/4/90	1/6/09	19	1/2/10	19	28.00	185.00	-32.00	5/5/14	4.93	29/6/09	1	0	0	0	0	0	0	1	
											31/12/09	1	0	0	0	0	0	0	1	
Relapsing	18/12/90	19/4/07	16	1/6/07	16	1.00	93.00	51.00	27/2/14	6.86	20/4/07	6	0	2	4	1	0	0	6	
											22/7/07	6	2	2	5	1	1	3	6	
Relapsing	18/1/91	1/1/08	16	18/11/09	18	36.00	618.00	-33.00	6/1/10	2.02	6/2/08	0	0	0	2	0	0	0	0	
											16/10/09	0	1	0	2	0	0	0	0	
Relapsing	2/6/91	12/1/07	15	28/2/10	18	12.00	127.00	-1004.00	1/5/14	7.30	24/1/07	1	0	0	0	2	1	1	1	

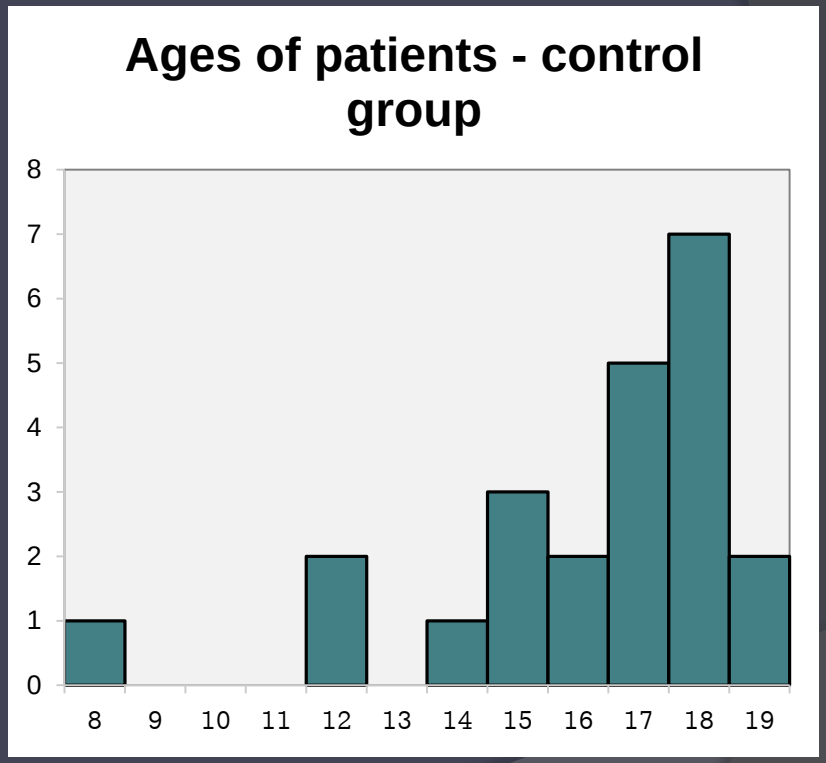

62 patients
38
MS group
24
control
group
CIS
NMO
ON
25 girls
13 boys
15 girls
9 boys
1.9 : 1
1.7 : 1

How do we know if our groups are comparable?

How to normalize data?

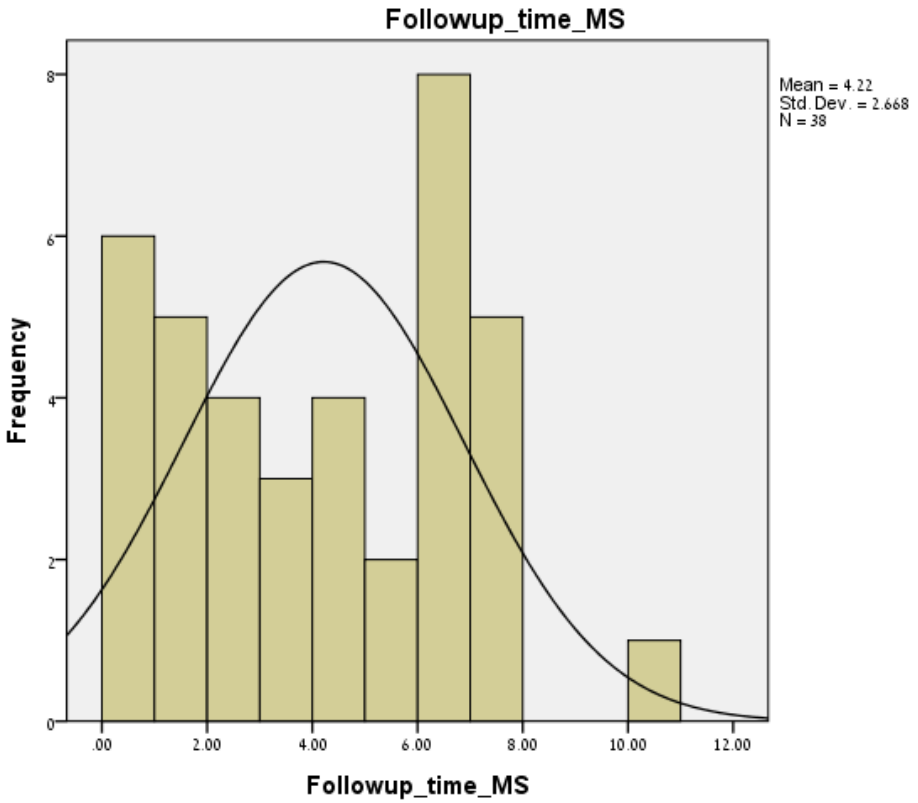
Age at CIS


Ages of patients - MS group
9
8
7
6
5
4
3
2
1
0
8 9 10 11 12 13 14 15 16 17 18 19

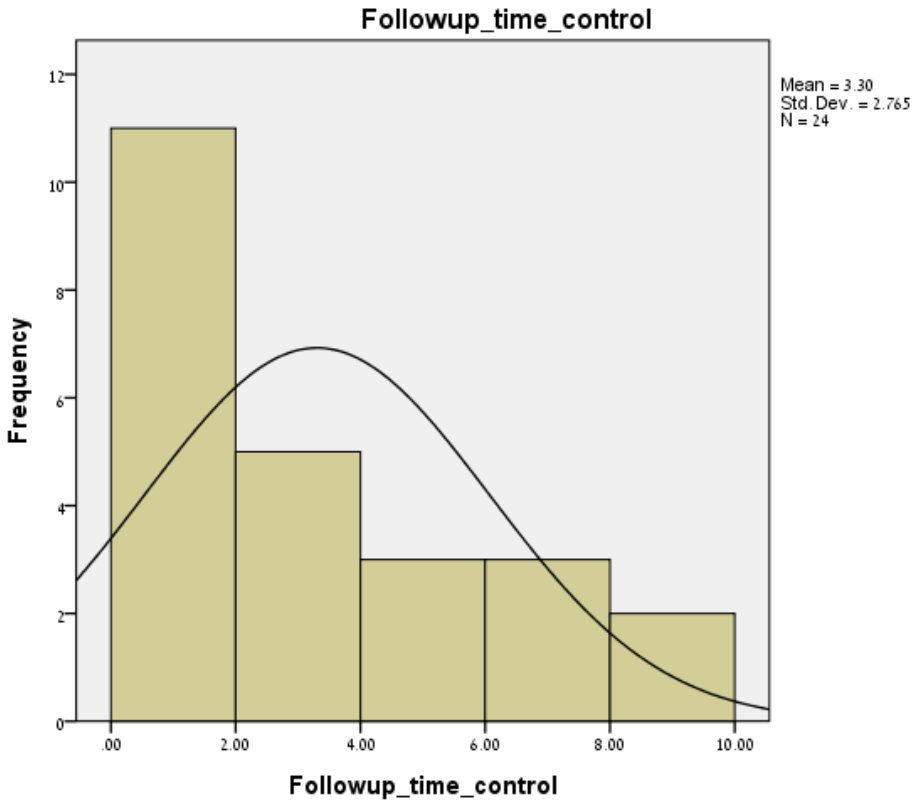

Ages of patients - control group
8
7
6
5
4
3
2
1
0
8 9 10 11 12 13 14 15 16 17 18 19

Follow up time

MS group



control group

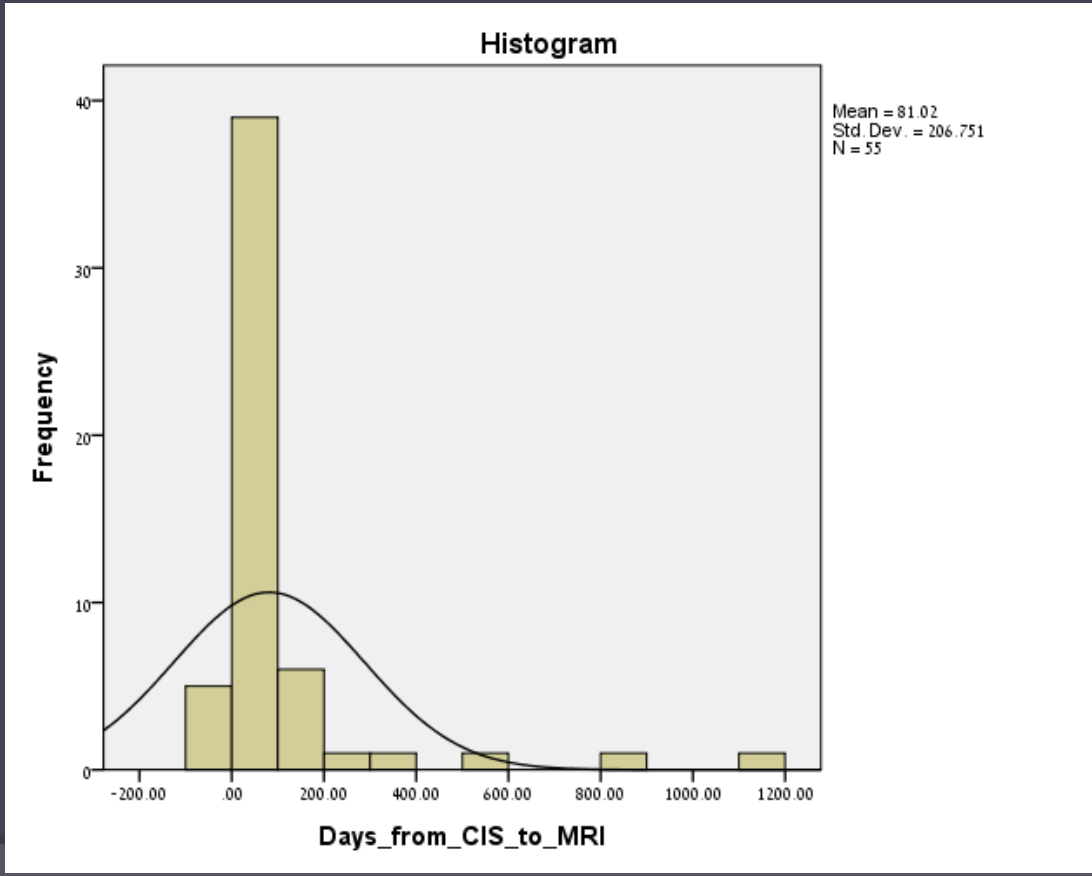


Time from CIS to 1st MRI

CIS **MS**

0 **6 months** **1 year**

Is the first MRI close enough to CIS?

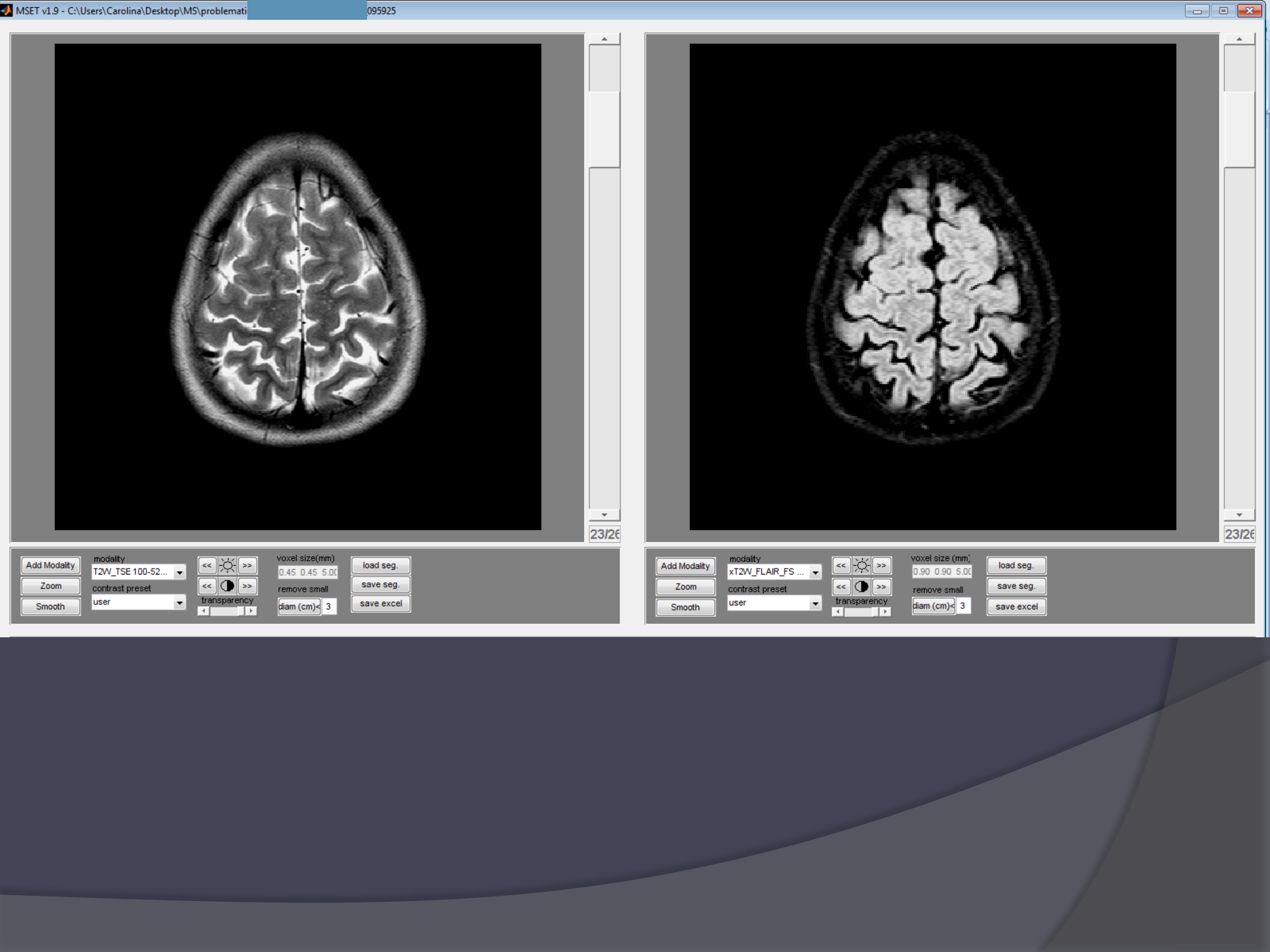


Normalizing – difficulties

Patient O.

12 y.o. girl presented with unspecific symptoms (vertigo) that resumed after fluid reconstitution and rest.

This is her MRI:


MSET v1.9 - C:\Users\Carolina\Desktop\MS\problemati
095925
23/26
Add Modality
Zoom
Smooth
modality
T2W_TSE 100-52...
contrast preset
user
<<
>>
transparency
voxel size(mm)
0.45 0.45 5.00
remove small
diam (cm)<
3
load seg.
save seg.
save excel
23/26
Add Modality
Zoom
Smooth
modality
xT2W_FLAIR_FS ...
contrast preset
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transparency
voxel size (mm)
0.90 0.90 5.00
remove small
diam (cm)<
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load seg.
save seg.
save excel


MSET v1.9 - C:\Users\Carolina\Desktop\MS\problemati
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xT2W_FLAIR_FS ...
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voxel size (mm)
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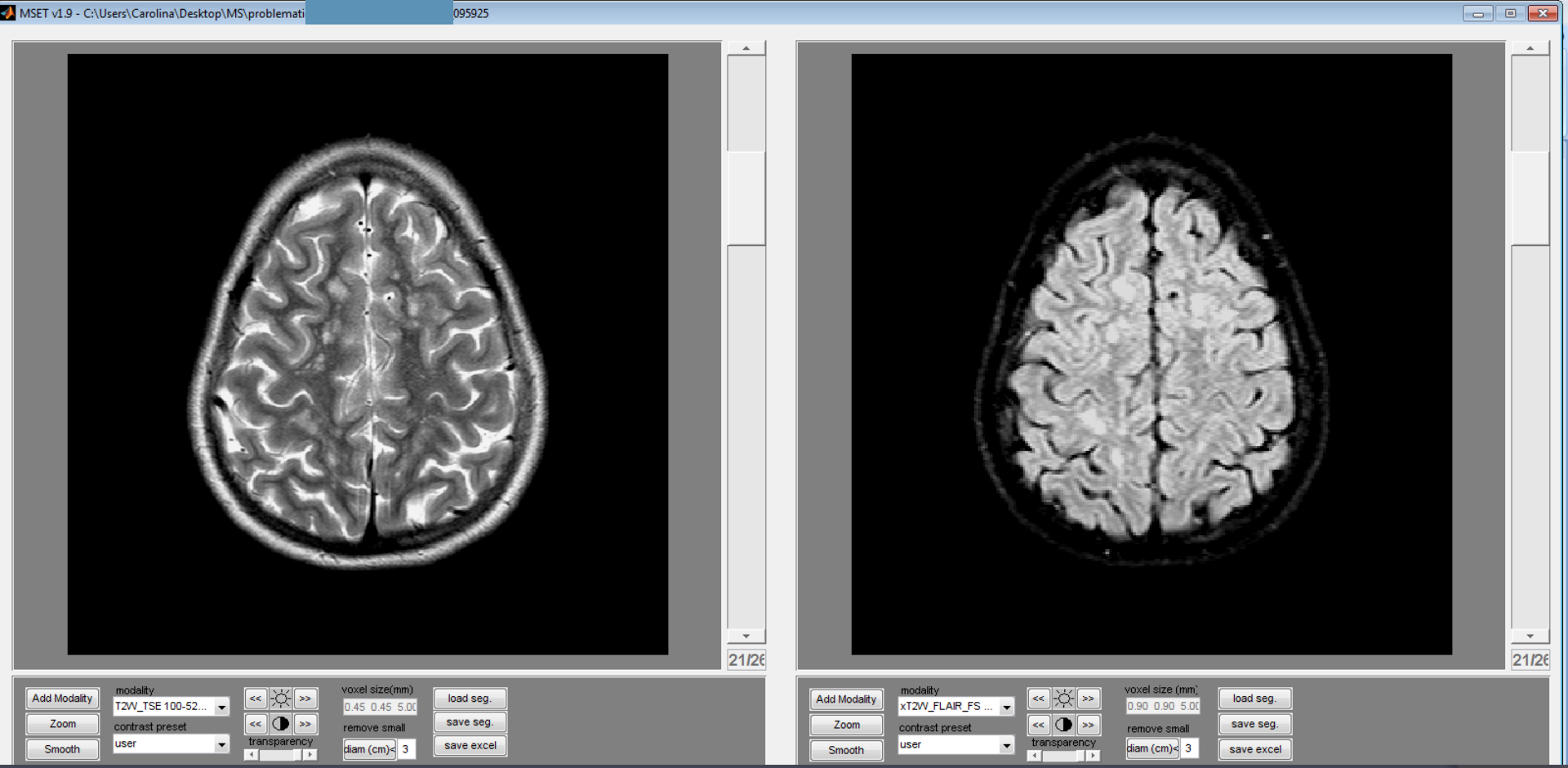
load seg.
save seg.
save excel


MSET v1.9 - C:\Users\Carolina\Desktop\MS\problemati
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Add Modality
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modality
T2W_TSE 100-52...
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save seg.
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21/26
Add Modality
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diam (cm)<
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load seg.
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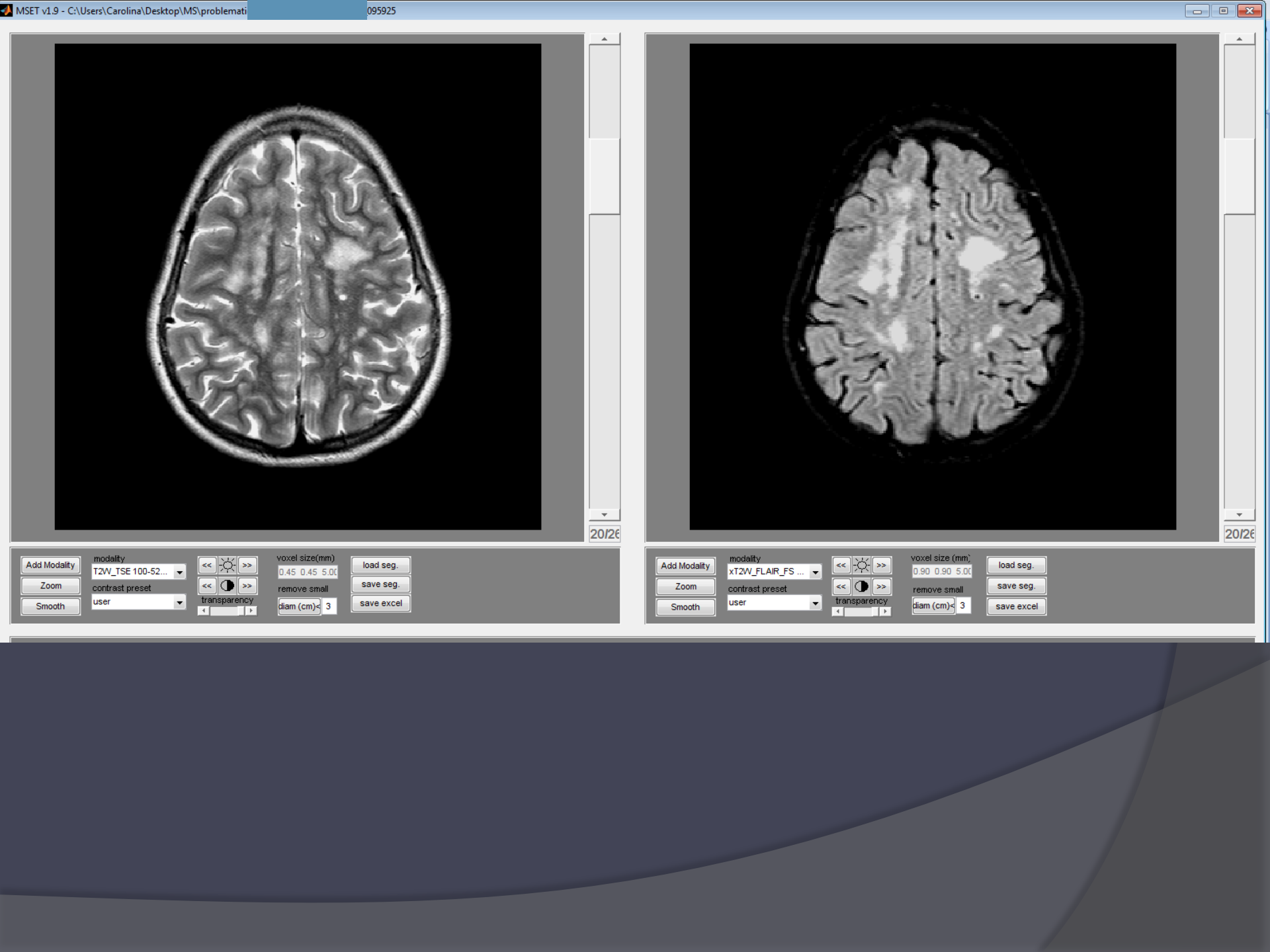
save excel


MSET v1.9 - C:\Users\Carolina\Desktop\MS\problemati
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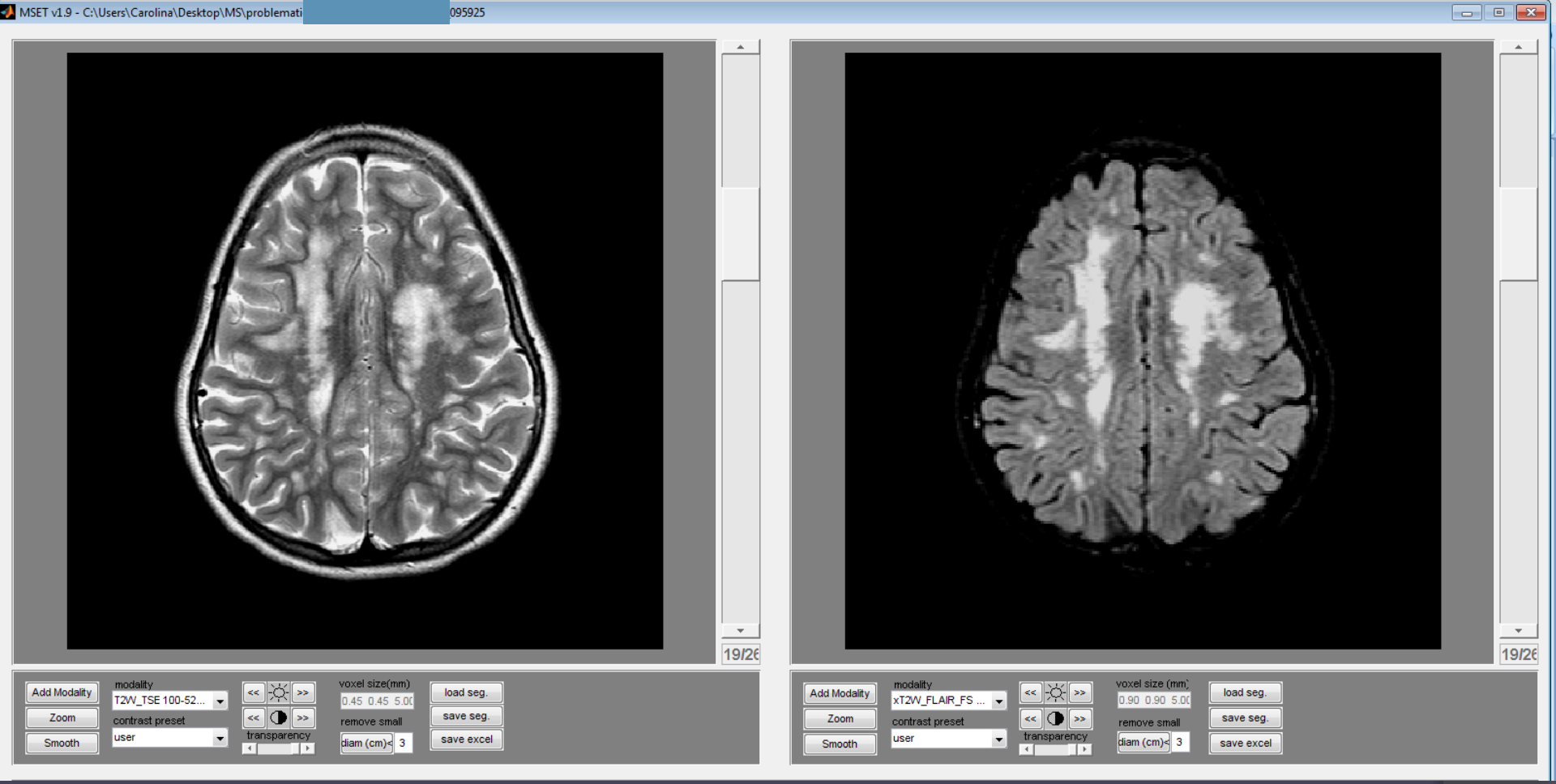
MSET v1.9 - C:\Users\Carolina\Desktop\MS\problemati
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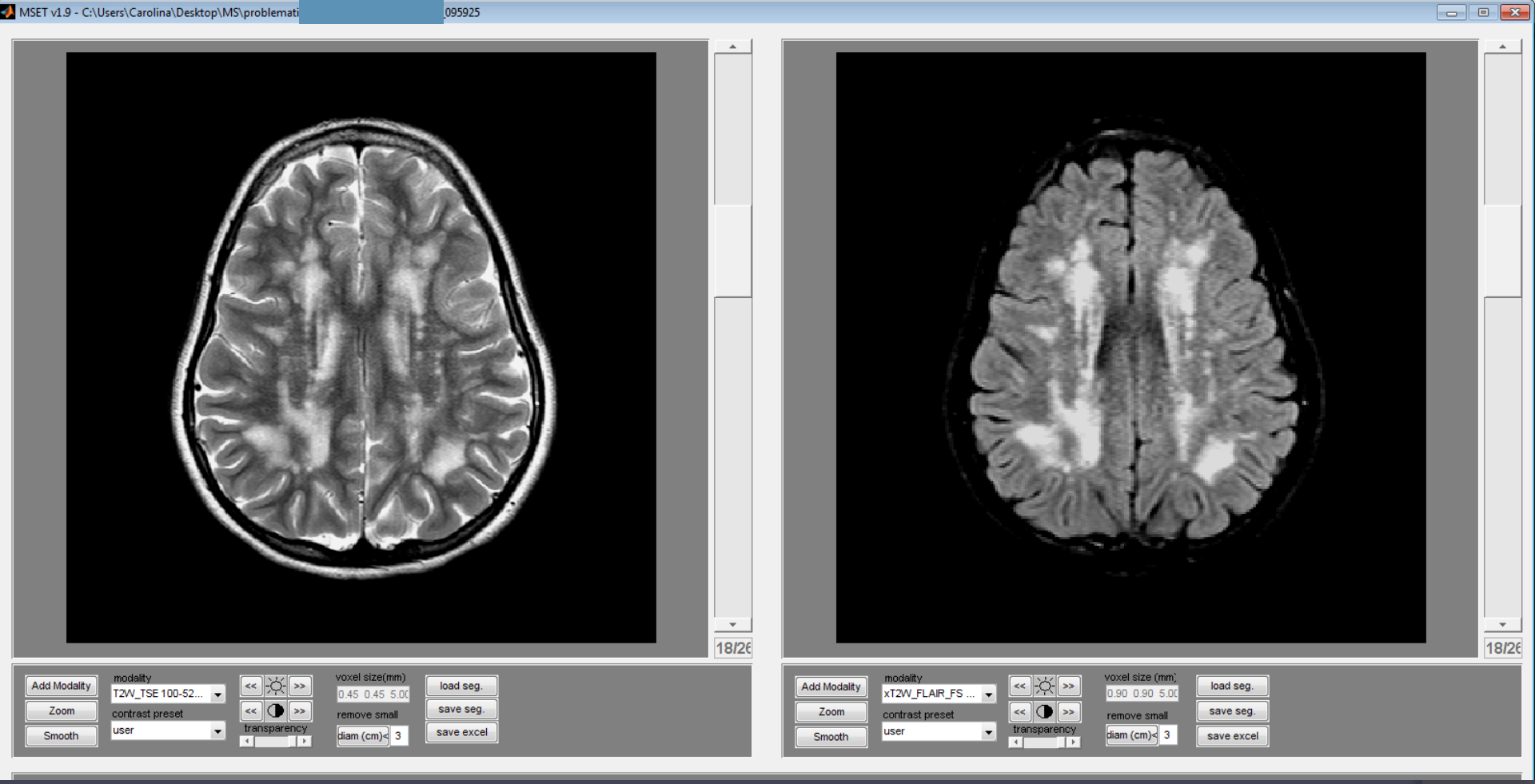
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modality
T2W_TSE 100-52...
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18/26
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xT2W_FLAIR_FS ...
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user
<<
>>
transparency
voxel size (mm)
0.90 0.90 5.0
remove small
diam (cm)<
3
load seg.
save seg.
save excel

Do these lesions look like MS?

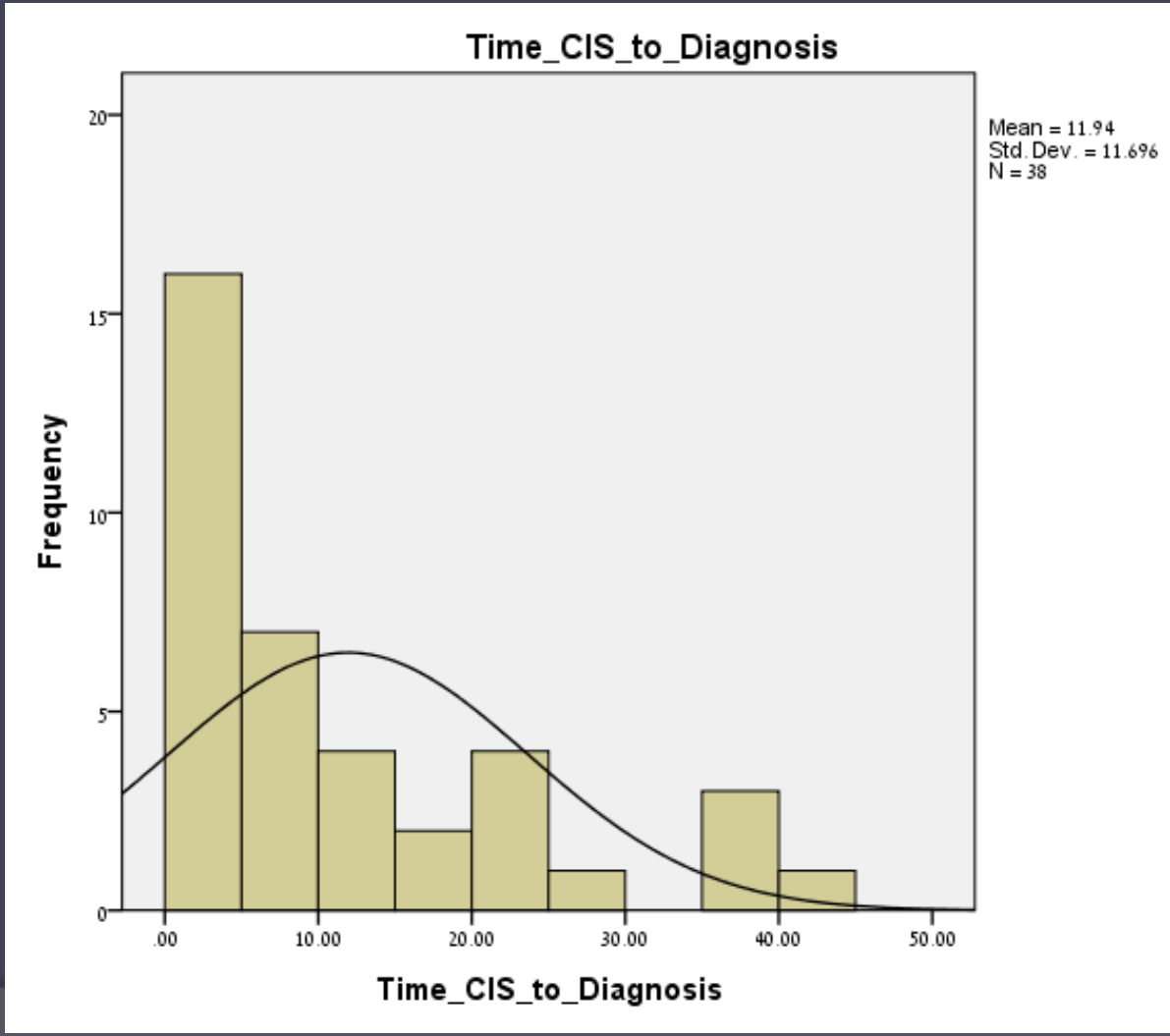
What does it look like?

Leukodystrophy?

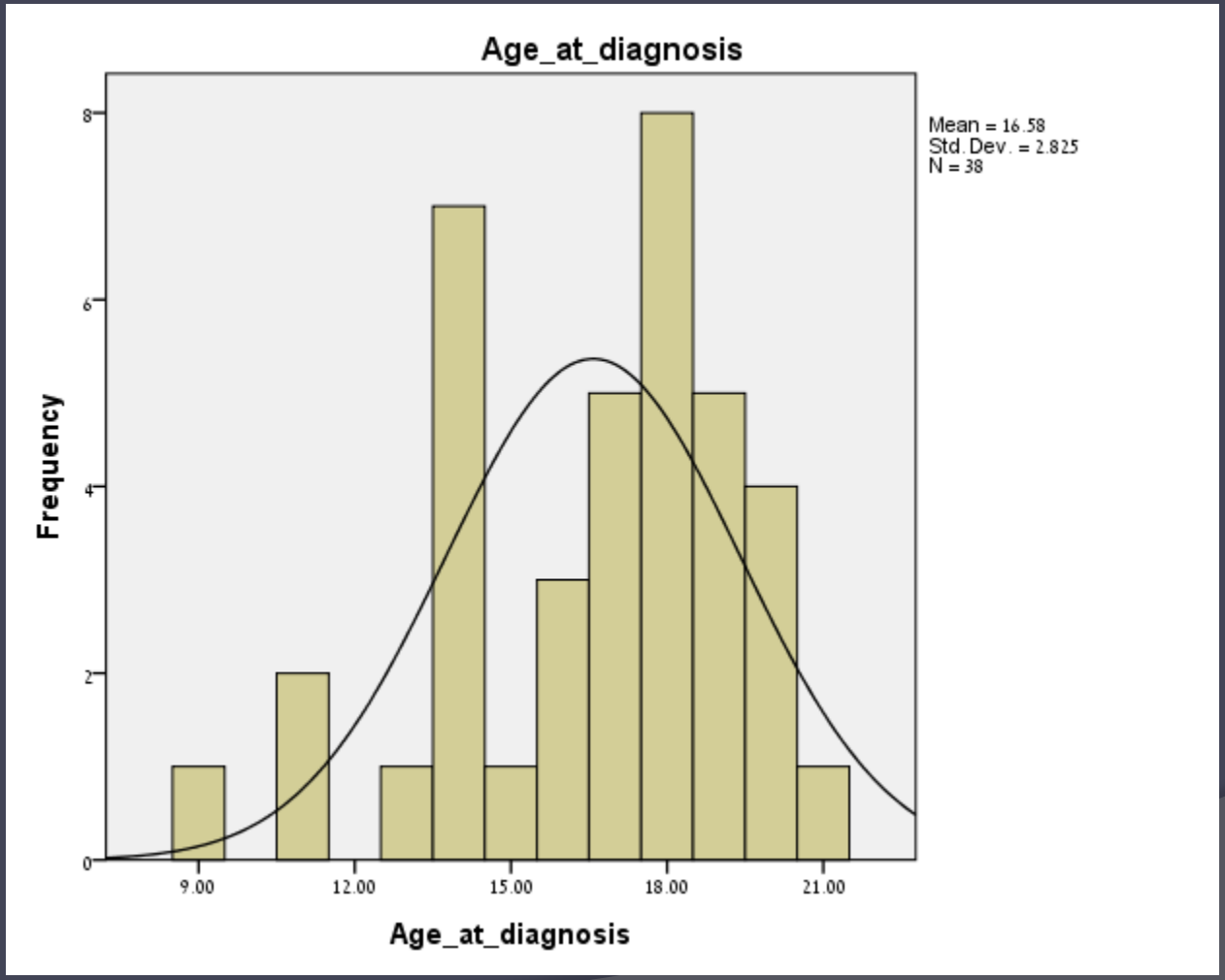
Metabolic disease?

Patient was taken out of study.

How quick is progression?



Age at MS diagnosis



Results

	T2							Flair							T1							Gadolinium						
	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infrate
ממוצע כל בדיקות החולים	5.8	0.7	1.3	2.8	0.6	0.6	0.8	6.1	0.7	1.2	3.0	0.6	0.6	0.7	1.0	0.1	0.1	0.3	0.2	0.1	0.3	1.0	0.2	0.2	0.6	0.1	0.1	0.1
ממוצע כל בדיקות הביקורת	2.0	0.2	0.3	0.9	0.2	0.1	0.2	2.0	0.2	0.4	0.9	0.2	0.1	0.2	0.5	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ממוצע בדיקה ראשונה בחולים	5	1	1	3	1	1	1	5	1	1	3	1	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה שנייה בביקורת	6	1	2	3	0	1	1	7	1	2	3	0	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה ראשונה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ממוצע בדיקה שנייה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

	T2 Total	T2flair Total	T1 Total	Gad Total
ממוצע כל בדיקות החולים	12.6	13.0	1.9	2.1
ממוצע כל בדיקות הביקורת	4.1	4.0	0.7	0.1
ממוצע בדיקה ראשונה בחולים	11	11	2	2
ממוצע בדיקה שנייה בביקורת	13	14	2	2
ממוצע בדיקה ראשונה בביקורת	5	5	1	0
ממוצע בדיקה שנייה בביקורת	3	3	1	0

Results

	T2							Flair							T1							Gadolinium						
	Fron	Occi	Tem	Parie	Inter	CC	Infr	Fron	Occi	Tem	Parie	Inter	CC	Infr	Fron	Occi	Tem	Parie	Inter	CC	Infr	Fron	Occi	Tem	Parie	Inter	CC	Infrate
ממוצע כל בדיקות החולים	5.8	0.7	1.3	2.8	0.6	0.6	0.	6.1	0.7	1.2	3.0	0.6	0.6	0.7	1.0	0.1	0.1	0.3	0.2	0.1	0.	1.0	0.2	0.2	0.6	0.1	0.1	0.1
ממוצע כל בדיקות הביקורת	2.0	0.2	0.3	0.9	0.2	0.1	0.	2.0	0.2	0.4	0.9	0.2	0.1	0.2	0.5	0.0	0.1	0.1	0.0	0.0	0.	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ממוצע בדיקה ראשונה בחולים	5	1	1	3	1	1	1	5	1	1	3	1	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה שנייה בביקורת	6	1	2	3	0	1	1	7	1	2	3	0	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה ראשונה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ממוצע בדיקה שנייה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

Results

	T2							Flair							T1							Gadolinium						
	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infrate
ממוצע כל בדיקות החולים	5.8	0.7	1.3	2.8	0.6	0.6	0.8	6.1	0.7	1.2	3.0	0.6	0.6	0.7	1.0	0.1	0.1	0.3	0.2	0.1	0.3	1.0	0.2	0.2	0.6	0.1	0.1	0.1
ממוצע כל בדיקות הביקורת	2.0	0.2	0.3	0.9	0.2	0.1	0.2	2.0	0.2	0.4	0.9	0.2	0.1	0.2	0.5	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ממוצע בדיקה ראשונה בחולים	5	1	1	3	1	1	1	5	1	1	3	1	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה שנייה בביקורת	6	1	2	3	0	1	1	7	1	2	3	0	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה ראשונה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ממוצע בדיקה שנייה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

	T2 Total	T2flair Total	T1 Total	Gad Total
ממוצע כל בדיקות החולים	12.6	13.0	1.9	2.1
ממוצע כל בדיקות הביקורת	4.1	4.0	0.7	0.1
ממוצע בדיקה ראשונה בחולים	11	11	2	2
ממוצע בדיקה שנייה בביקורת	13	14	2	2
ממוצע בדיקה ראשונה בביקורת	5	5	1	0
ממוצע בדיקה שנייה בביקורת	3	3	1	0

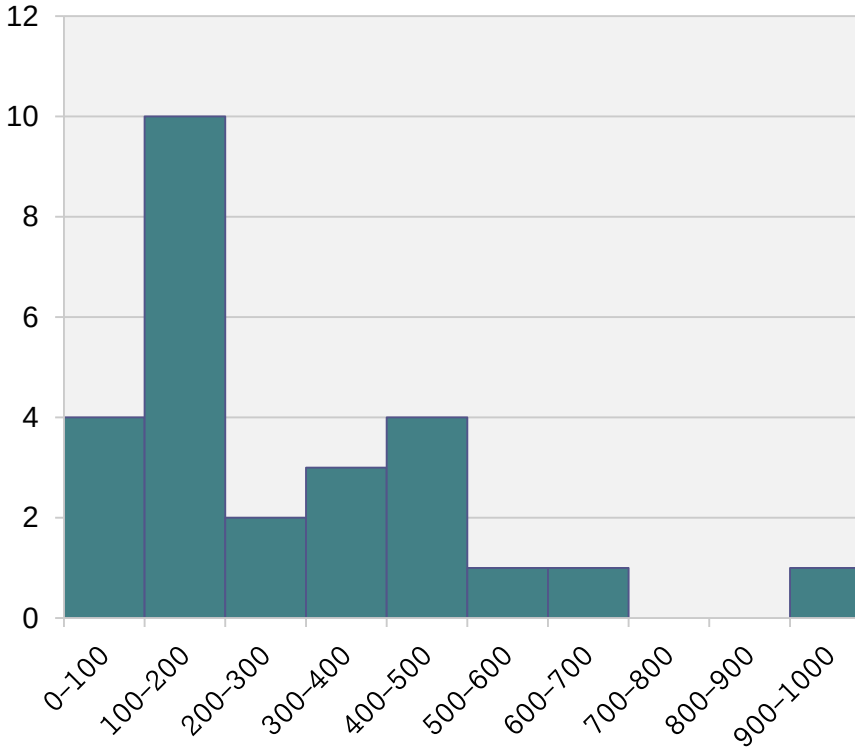
Results

	T2							Flair							T1							Gadolinium						
	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infra	Fron	Occi	Tem	Parie	Inter	CC	Infrate
ממוצע כל בדיקות החולים	5.8	0.7	1.3	2.8	0.6	0.6	0.8	6.1	0.7	1.2	3.0	0.6	0.6	0.7	1.0	0.1	0.1	0.3	0.2	0.1	0.3	1.0	0.2	0.2	0.6	0.1	0.1	0.1
ממוצע כל בדיקות הביקורת	2.0	0.2	0.3	0.9	0.2	0.1	0.2	2.0	0.2	0.4	0.9	0.2	0.1	0.2	0.5	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ממוצע בדיקה ראשונה בחולים	5	1	1	3	1	1	1	5	1	1	3	1	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה שנייה בביקורת	6	1	2	3	0	1	1	7	1	2	3	0	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0
ממוצע בדיקה ראשונה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ממוצע בדיקה שנייה בביקורת	2	0	0	1	0	0	0	2	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

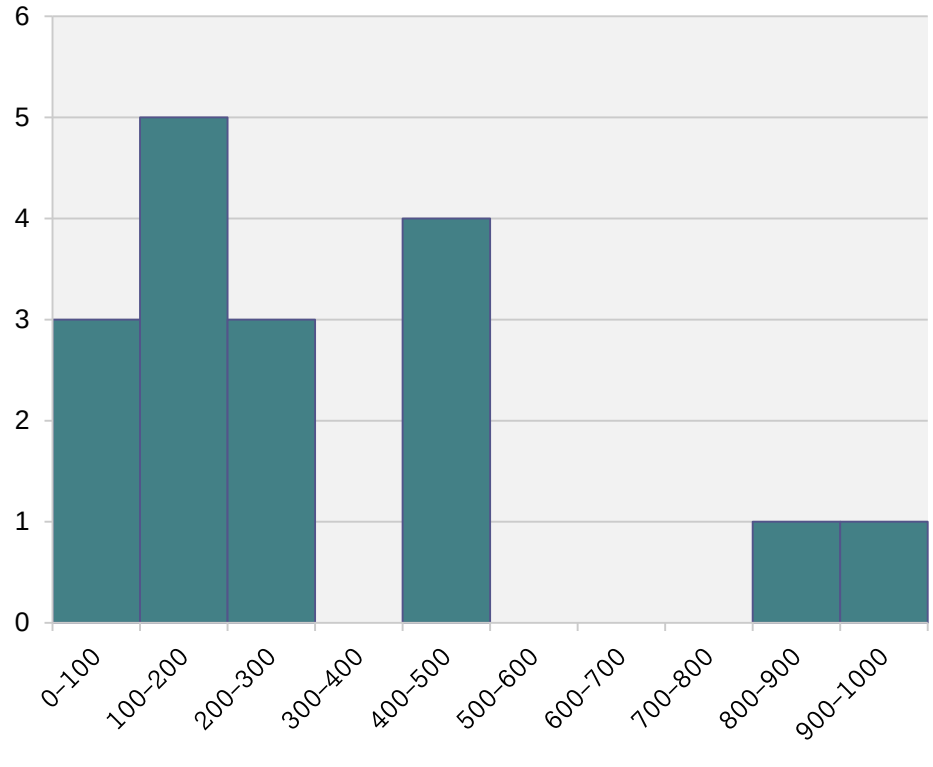
	T2 Total	T2flair Total	T1 Total	Gad Total
ממוצע כל בדיקות החולים	12.6	13.0	1.9	2.1
ממוצע כל בדיקות הביקורת	4.1	4.0	0.7	0.1
ממוצע בדיקה ראשונה בחולים	11	11	2	2
ממוצע בדיקה שנייה בביקורת	13	14	2	2
ממוצע בדיקה ראשונה בביקורת	5	5	1	0
ממוצע בדיקה שנייה בביקורת	3	3	1	0

Time from MRI #1 to MRI #2

MS group



control group



Something to think about…

Little is known about the ethiology of MS. Because children may be closer to the inciting events in MS, research pediatric MS may hold the key to understanding the cause of the disease itself.

Thank you for listening.