High Monthly T2 Lesion Burden Associated with Improved EDSS upon Starting Treatment in Multiple Sclerosis

Yu, Charles C.[1, 3]; Lancias, Samantha[1]; Tutlam, Nhial[1]; Xu, Junqian[2];
Cook, Stuart[4], Cadavid, Diego[5], Naismith, Robert T.[1]

[1]Neurology, Washington University School of Medicine, St. Louis, MO. [2]Radiology, Mount Sinai School of Medicine, New York, NY.
[3]Case Western Reserve University School of Medicine, Cleveland, OH. [4]UMDNJ, Newark, NJ. [5]Biogen Idec, Cambridge, MA

THE CONSORTIUM OF MULTIPLE SCLEROSIS CENTERS

Washington University in St. Louis SCHOOL OF MEDICINE

CASE WESTERN RESERVE UNIVERSITY SCHOOL OF MEDICINE

Background

- Multiple sclerosis is characterized by inflammation, demyelination, and axonal loss.
- Contrast enhancing lesions (CELs) represent regions of active inflammation and blood-brain barrier breakdown. T2 hyperintensities represent demyelinated plaques.
- CELs can be disseminated in time and space, and may lead to adverse clinical outcomes.

Objectives

- To determine the relationship between acute Gadolinium (Gd) enhancing or non-enhancing T2/FLAIR (fluid-attenuated inversion recovery) lesion volumes and clinical outcome measurements.
- To stratify the correlation with respect to treatment, age, gender, and ethnicity.

Method

- Monthly MRIs were collected from 75 treated relapsing MS subjects over 2 years.
- Amira v5.4 (Visage Imaging) was used for manual segmentation of T2/FLAIR lesions, which were cross-referenced against proton-density-weighted (PDW) images.
- Volume quantification was obtained via a MATLAB script within Amira.
- Lesion volumes over time were evaluated by EDSS (better, stable, or worse), treatment (interferon vs. glatiramer acetate), age (<36 vs. 36+), gender, and ethnicity (Caucasian vs. African American vs. Hispanic).

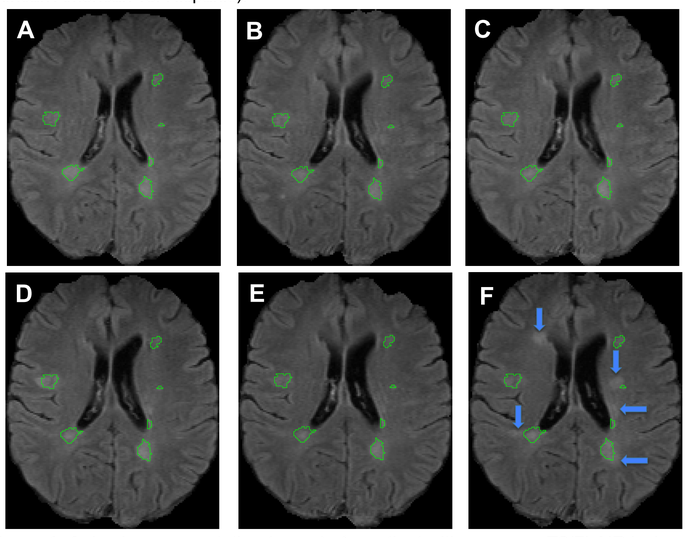


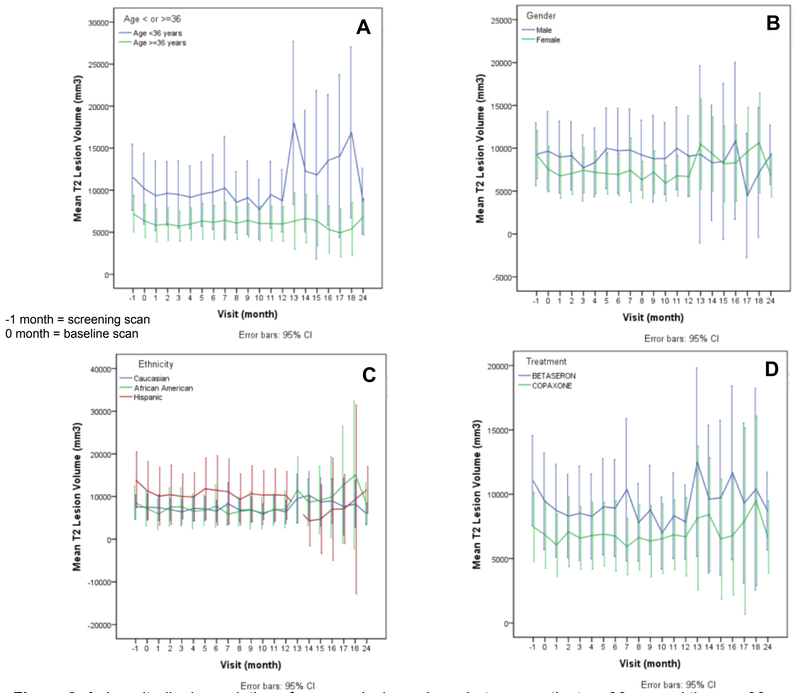
Figure 1. A. Lesion segmentation (green) of a patient with numerousT2/FLAIR lesions at 1 month. **B-F.** Lesion progression with superimposed baseline segmentation markers of T2/FLAIR scans at months 3, 6, 9, 12, and 15, respectively. Blue arrows represent newly developed lesions.

Results

	IFNβ 1b (n=36)	GA (n=39)
Age, y, mean (range)	36 (18-49)	36 (22-55)
Women, n (%)	27 (75)	25 (64)
Ethnicity, n (%)		
White	15 (42)	24 (62)
Black	10 (28)	11 (28)
Hispanic	10 (28)	4 (10)
Indian-Asian	1 (3)	0
Subtype of MS, n (%)		
Relapsing-remitting	31 (86)	30 (77)
Clinically isolated syndrome	5 (14)	9 (23)
Time since onset of MS		
Median yrs (range)	0.9 (0.1-24)	1.2 (0.2-34)
EDSS, median (range)	2.0 (0-5)	2.0 (0-5.5)

Table 1. Baseline characteristics of the 75 patients randomized in the BECOME study (Cadavid et al. Neurology 2009.). Nearly half of the patients were not white.

IFNβ 1b = interferon beta 1b (Betaseron); GA = glatiramer acetate (Copaxone);
EDSS = Expanded Disability Status Scale



-1 month = screening scan
0 month = baseline scan

Figure 2. A. Longitudinal correlation of average lesion volume between patients < 36 yrs and those ≥ 36 yrs (NS). The younger group had more lesions and MRI activity, but there was overlap between the groups. **B.** Correlation between male and female patients (NS). No difference between men and women in terms of MRI lesions and activity. **C.** Correlation among Caucasian, African American, and Hispanic patients (NS). Hispanics qualitatively had higher lesion loads at baseline and through the first year of the study, but the groups were not statistically different. **D.** Correlation between patients with Betaseron treatment and those with Copaxone (NS). Those randomized to Betaseron at baseline had more T2 lesions, but there was no difference between treatments when medication was started (month 0).

Results - continued

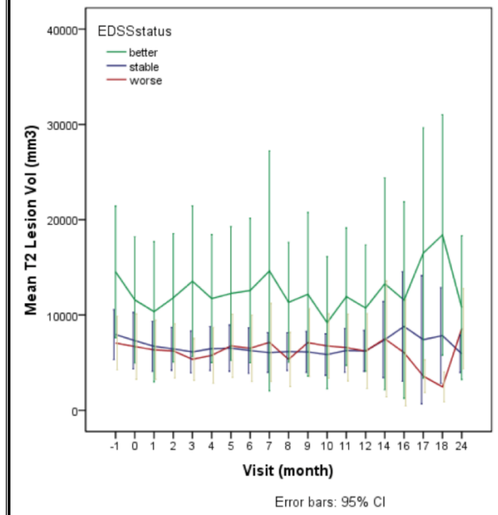


Figure 3. Over 2 years, patients with improved EDSS status by the end of the trial trended towards higher baseline EDSS score (ANOVA, p=0.06) and had higher monthly T2 lesion burdens (ANOVA, p<0.001).

EDSS categorization:
better = negative ΔEDSS score of ≥ 1.0;
stable = ± ΔEDSS score < 1.0;
worse = positive ΔEDSS score of ≥ 1.0

Conclusions

- Preliminary analyses suggests that patients with higher baseline EDSS scores and higher MRI lesion burdens benefited the most from disease-modifying therapy over 2 years.
- Medications are anti-Inflammatory. Perhaps those with the most inflammation have higher baseline EDSS and better response to treatment over the short term.
- In this cohort with early MS and CIS, no differences were seen in T2 lesion burden by treatment or baseline demographic features.
- Perhaps with longer follow-up, MS lesion volume and progression can provide insight for predicting clinical outcomes.
- A 7-year clinical and MRI follow-up of the BECOME subjects is underway. Results may shed light on the early MRI findings and long-term effect of lesions and clinical outcomes.

Correspondence & Acknowledgement

Charles Cong Yu
Case Western Reserve University School of Medicine
cxy177@case.edu

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