

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Interrater and Intrarater Reliability of Cortical Lesion Identification

Lin's Concordance Coefficient for:	Total Lesions	Leukocortical	Intracortical	Subpial
Interrater Reliability	0.54	0.75	0.34	0.13
Intrarater Reliability	0.96	0.86	0.46	0.86

Lesion counts from 10 sample scans performed by two independent raters were analyzed for inter-rater reliability for total lesion count and the individual lesion sub-types. Intra-rater reliability was assessed by having each rater rate the same scan twice. Lin's concordance correlation coefficient (range from -1 to 1) was calculated to statistically assess reliability.

eTable 2. Prediction of Clinical Outcomes by MRI Outcome

	EDSS ≥ 5.0		Progressive Phenotype		Cognitive Impairment	
	Odds Ratio	P	Odds Ratio	P	Odds ratio	P
Age + Gender	1.15* (1.01 – 1.33)	0.034	1.07 (0.95 – 1.20)	0.269	1.09* (1.01 – 1.18)	0.031
Total Cortical Lesion Count	1.04 (0.98 - 1.10)	0.190	1.04 (0.99 - 1.10)	0.130	1.02 (0.97 - 1.06)	0.441
Log [Total Cortical Lesion Volume]	2.19 (0.65 - 7.43)	0.207	1.77 (0.55 - 5.69)	0.339	3.36* (1.07 - 10.59)	0.038
Leukocortical Lesion Count	1.06 (0.94 - 1.183)	0.353	1.09 (0.98 - 1.22)	0.119	1.09 (1.00 - 1.19)	0.054
Log [Leukocortical Lesion Volume]	1.73 (0.72 - 4.16)	0.218	1.63 (0.67 - 3.99)	0.282	9.65* (1.70 - 54.59)	0.010
Intracortical Lesion Count	1.06 (0.92 - 1.21)	0.415	1.10 (0.95 - 1.26)	0.193	1.00 (0.89 - 1.11)	0.965
Log [Intracortical Lesion Volume]	1.40 (0.62 - 3.17)	0.422	1.44 (0.59 - 3.5)	0.423	0.46 (0.17 - 1.25)	0.129
Subpial Lesion Count	1.11 (0.96 - 1.29)	0.147	1.06 (0.94 - 1.19)	0.344	0.96 (0.87 - 1.07)	0.494
Log [Subpial Lesion Volume]	1.57 (0.51 - 4.82)	0.430	1.01 (0.35 - 2.86)	0.990	0.87 (0.37 - 2.07)	0.757
BPF %	0.87 (0.71 - 1.08)	0.213	0.95 (0.77 - 1.17)	0.611	0.93 (0.77 - 1.11)	0.414
Cerebral White Matter Volume %	0.88 (0.71 - 1.10)	0.274	0.94 (0.76 - 1.15)	0.531	0.76 (0.57 - 1.00)	0.053
Cortical Gray Matter Volume %	1.07 (0.77 - 1.47)	0.703	1.06 (0.76 - 1.47)	0.735	1.23 (0.89 - 1.70)	0.207
Log [White Matter Lesion Volume]	2.02 (0.30 - 13.71)	0.470	0.39 (0.08 - 1.90)	0.244	1.07 (0.35 - 3.33)	0.901
Cortical Lesion Subtype Ratio – Count	0.99 (0.73 - 1.36)	0.966	1.20 (0.87 - 1.66)	0.262	1.30 (0.97 - 1.75)	0.084
Cortical Lesion Subtype Ratio – Volume	0.95 (0.79 - 1.14)	0.582	0.96 (0.81 - 1.12)	0.579	1.50* (1.00 - 2.25)	0.048
Cortical Lesion to White Matter Lesion Burden Ratio %	0.34 (0.84 – 1.17)	0.900	1.20 (0.92 – 1.55)	0.175	1.05 (0.87 – 1.28)	0.609

Logistic regression model for prediction of clinical outcome. Initial model shown for prediction by age and gender, followed by prediction by MRI outcome, adjusted for age and gender. Odds ratio (%95 CI) reported. Odds ratio for lesion counts represent the increase in odds for assignment to clinical category for each increase in lesion count. Normalized volumes were log transformed before regression, and thus reported odds ratios for normalized lesion volumes represent the increase in odds for each log increase in normalized volume ($e^{\sim 2.718 \times \text{normalized volume value}}$). BPF, WM volume, GM volume, and CL/WML Burden Ratio were converted to % prior to regression, and thus odds ratios represent the increase in odds for each 1% increase in these quantities. * = $p < 0.05$.

eTable 3. Odds of Cognitive Impairment by Cortical Lesions and Conventional MRI Measures, Combined

Base model			Base model + Cerebral WM Volume %		Base model + Cortical GM Volume %		Base model + log [WM Lesion Volume]		Base model + Cerebral WM Volume % + Cortical GM Volume % + log [WM Lesion Volume]	
	Odds ratio	P	Odds ratio	P	Odds ratio	P	Odds ratio	P	Odds ratio	P
Total Cortical Lesion Count	1.02 (0.97 - 1.06)	0.441	1.00 (0.94 - 1.05)	0.888	1.03 (0.98 - 1.09)	0.221	1.02 (0.97 - 1.07)	0.399	1.01 (0.94 - 1.07)	0.862
Log [Total Cortical Lesion Volume]	3.36* (1.07 - 10.59)	0.038	3.75 (0.93 - 15.07)	0.063	17.25* (1.18 - 252.52)	0.038	1.07 (0.35 - 3.33)	0.901	14.26* (1.06 - 192.37)	0.045
Leukocortical Lesion Count	1.09 (1.00 - 1.19)	0.054	1.07 (0.97 - 1.19)	0.191	1.11* (1.01 - 1.23)	0.033	1.13* (1.01 - 1.26)	0.039	1.11 (0.98 - 1.25)	0.088
Log [Leukocortical Lesion Volume]	9.65* (1.70 - 54.59)	0.010	37.23 (0.77 - 1796.93)	0.067	42.87* (1.43 - 1288.34)	0.030	17.36* (1.26 - 238.59)	0.033	40.96* (1.23 - 1369.23)	0.038
Intracortical Lesion Count	1.00 (0.89 - 1.11)	0.965	0.91 (0.78 - 1.05)	0.204	1.00 (0.89 - 1.13)	0.939	1.00 (0.89 - 1.12)	0.956	0.91 (0.78 - 1.06)	0.222
Log [Intracortical Lesion Volume]	0.46 (0.17 - 1.25)	0.129	0.08* (0.01 - 0.97)	0.047	0.37 (0.10 - 1.32)	0.124	0.17 (0.02 - 1.20)	0.075	0.01 (<0.01 - 1.94)	0.085
Subpial Lesion Count	0.96 (0.87 - 1.07)	0.494	0.91 (0.78 - 1.05)	0.194	1.00 (0.88 - 1.13)	0.961	0.97 (0.87 - 1.08)	0.563	0.89 (0.74 - 1.06)	0.197
Log [Subpial Lesion Volume]	0.87 (0.37 - 2.07)	0.757	0.94 (0.40 - 2.18)	0.880	0.94 (0.40 - 2.24)	0.894	1.08 (0.45 - 2.57)	0.869	1.05 (0.42 - 2.66)	0.913

Logistic regression model for prediction of cognitive impairment. Base model shown for prediction by cortical lesion count or volume, adjusted for age and gender. Subsequent models for prediction of cognitive impairment by base model plus cerebral WM volume, cortical GM volume, WM lesion volume, or all 3 combined. Odds ratio (%95 CI) reported. * = p < 0.05.

eTable 4. Correlation of Cortical Lesions With Conventional MRI Measures

	BPF	WM Volume	Cortical GM Volume	WM Lesion Volume
Total Cortical Lesion Volume	-0.50*	-0.22	-0.42*	0.34
Leukocortical Lesion Volume	-0.53*	-0.30	-0.33	0.50*
Intracortical Lesion Volume	-0.43*	-0.35*	-0.13	0.19
Subpial Lesion Volume	-0.21	<0.01	-0.36*	-0.04

Spearman correlation was performed between variables. Rho values shown. * = $p < 0.05$.