

Supplemental information

Supplemental Methods

Supplemental Figure 1: Evaluation of relationships between MRI grading scales and clinical scores. MRI elements of (A) quantitative telencephalon score, (B) qualitative telencephalon score (C) infratentorial lesion load score, (D) infratentorial atrophy score, and (E) contrast-enhancing lesions score were evaluated for contribution to disability (EDSS, SNRS, and SDMT). Data (gray circles) are depicted with median (red bar) and interquartile range (black bars). EDSS = expanded disability status scale, SNRS = Scripps neurological rating scale, SDMT = symbol digit modality test

Supplemental Figure 2: Mathematical optimization of COMRIS Fifteen semi-quantitative MRI measures (a-o) and age were used as explanatory variables to determine the best linear model of correlation with clinical disability scores (EDSS, SNRS, and SDMT) used as response variables. (A) Redundant explanatory variables for each individual clinical measure were identified by calculating the cross-validation values for each clinical score; red dotted lines show number of explanatory variables contributing to the best fit of data to the model. (B) For each model of clinical disability, the explanatory variables were sorted in ascending order based on coefficients of variation of the difference between predicted and calculated values during the leave-one-out-cross-validation process. Selected explanatory variables for each tested model are highlighted with gray background. Abbreviations: EDSS = expanded disability status scale, SNRS = Scripps

neurological rating scale, SDMT = symbol digit modalities test, COMRIS = combinatorial age-adjusted MRI scale, CDO = cognitive disability-optimized, PDO = physical disability-optimized

Supplemental Table 1: Demographic data Demographic data for seven diagnostic categories represented by columns (a) – (g). All datasets (except for average age) underwent Box-Cox transformation prior to one-way ANOVA statistical analysis. Statistical significance ($p < 0.01$) was determined based on pair-wise multiple comparison with Tukey's correction method. Small letters below each number identify statistically significant diagnostic categories. HD = healthy donors, NIND = non-inflammatory neurological disorders, OIND = other inflammatory neurological disorder, CIS/RIS = clinically-/radiologically isolated syndrome, RRMS = relapsing-remitting multiple sclerosis, PPMS = primary progressive multiple sclerosis, SPMS = secondary progressive multiple sclerosis, EDSS = expanded disability status scale, SNRS = Scripps neurological rating scale, SDMT = symbol digit modality test, N = number of patients, NA = not available, SD = standard deviation, NS = non-significant

Supplemental Table 2: Template for calculation of various aspects of CAMRIS Green rectangle points to 11 variables that represent an input for successful calculation of all aspects of COMRIS, including the predicted clinical measures: EDSS, SNRS, and SDMT. MRI variables ([a]-[c], [h], [i]-[o]) offer a pre-defined selection of grades following standard operating procedure in Figure 1. The template is provided as downloadable Excel file. Abbreviations: EDSS = expanded disability status scale, SNRS = Scripps neurological rating scale, SDMT = symbol digit modality test, COMRIS-CTD-v1 = combinatorial MRI scale of CNS tissue destruction version 1, COMRIS-PDO-EDSS = combinatorial MRI scale – physical disability optimized by EDSS, COMRIS-PDO-SNRS = combinatorial MRI scale – physical disability optimized by SNRS, COMRIS-CDO-SDMT = combinatorial MRI scale – cognitive disability optimized by SDMT

Table 1: Semi-quantitative rating scores of MRIs and coefficients for linear equations determined by mathematical modeling