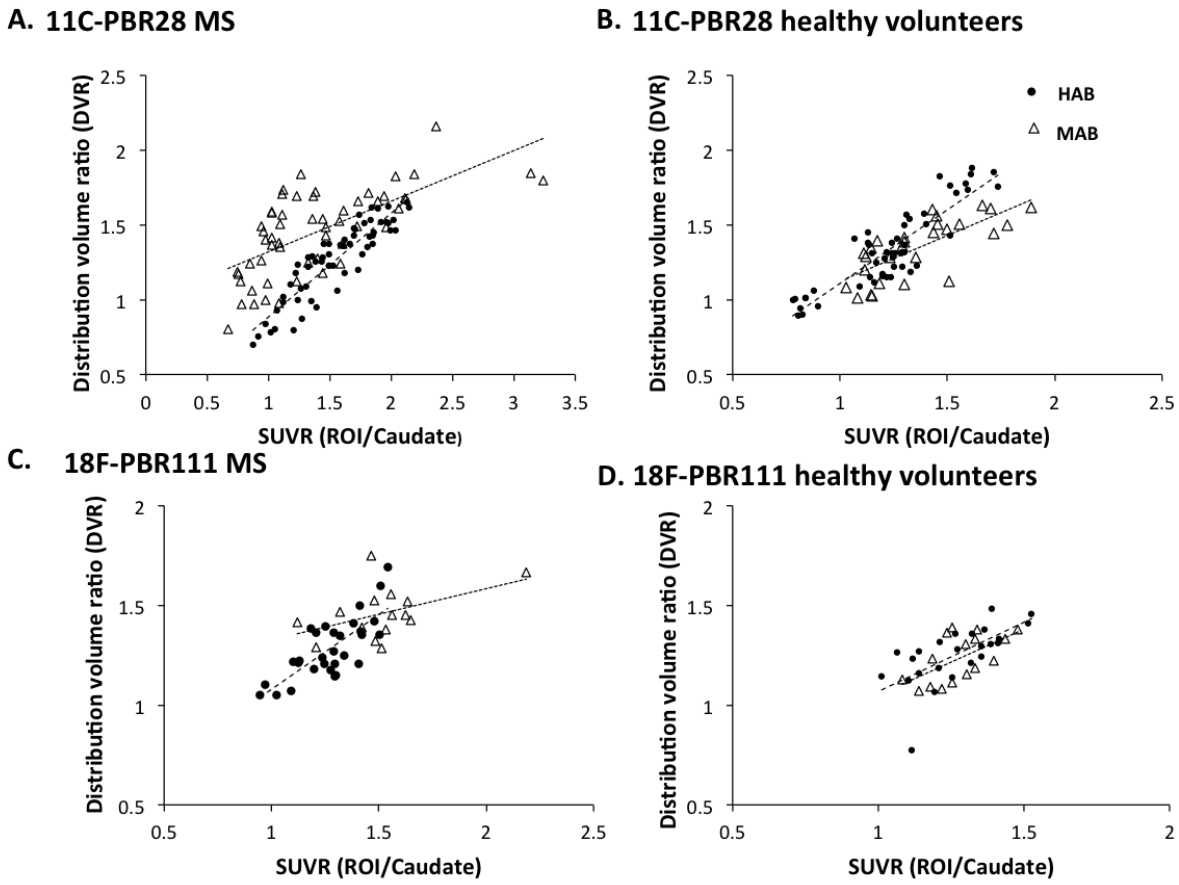
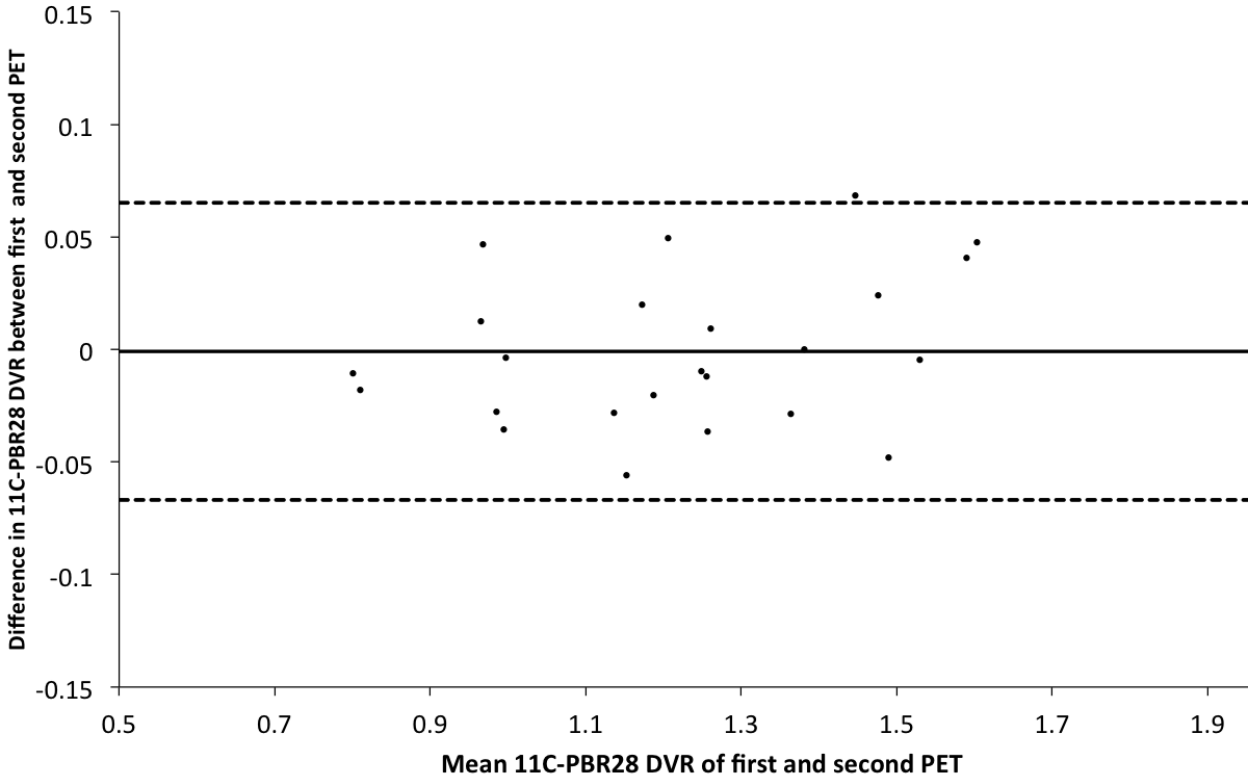
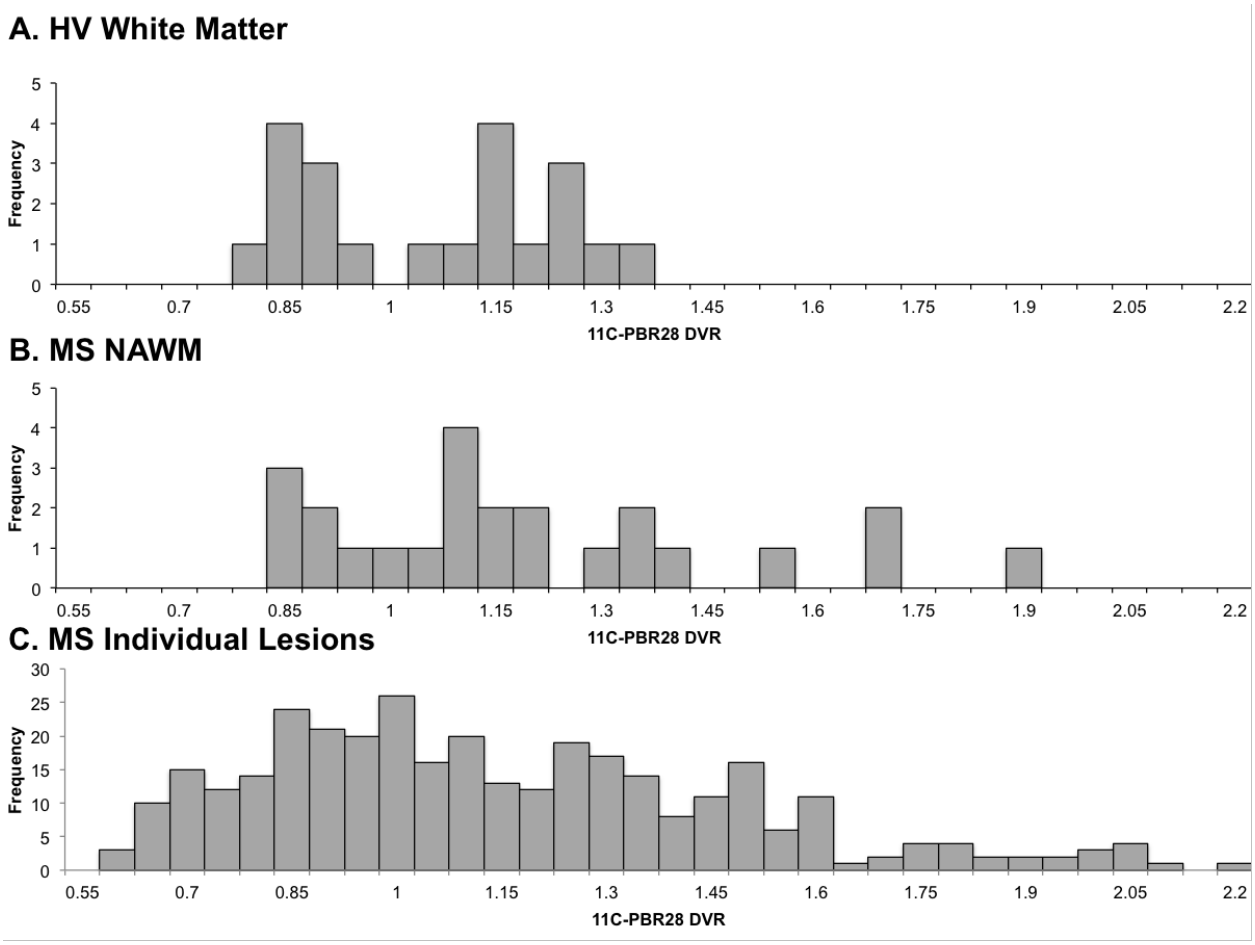


SUPPLEMENTAL FIGURE 1. Plots of distribution volume ratio (DVR) using the Logan method with a caudate pseudo-reference region against standardized uptake value ratio (SUV) as a ratio of the SUV in caudate (SUVR) for both 11C-PBR28 (SUV between 60 to 90 minutes) and 18F-PBR111 (SUV between 90 to 120 minutes) for high affinity binders (HAB) and medium affinity binders (MAB) for translocator protein (TSPO) across all brain regions of interest (ROI) analysed (thalamus, cerebellum, cortex, white matter, normal appearing white matter and white matter lesions). Regression lines are plotted separately for HAB (dashed line) and MAB (dotted line). Separate plots were made for (A) 11C-PBR28 multiple sclerosis (MS) patients (regression line gradient for HAB is 0.69, for MAB is 0.34), (B) 11C-PBR28 healthy volunteers (regression line gradient for HAB is 0.99, for MAB is 0.61), (C) 18F-PBR111 MS patients (regression line gradient for HAB is 0.75, for MAB is 0.26) and (D) 18F-PBR111 healthy

volunteers (regression line gradient for HAB is 0.70, for MAB is 0.66). Each data point represents a single brain region from an individual subject. These figures indicate that raw SUVR measures are correlated with DVR using a caudate pseudoreference region for all brain regions studied, both tracers and both MS and healthy volunteers, discussed in detail here in the Supplementary Methods.



SUPPLEMENTAL FIGURE 2. Bland-Altman plot for six MS patients who had two 11C-PBR28 PET scans within six weeks of each other with no clinical changes in that period for three brain regions (white matter lesions, normal appearing white matter, thalamus and cortex). Each data point represents a single brain region from one patient (n=24). The test-retest variability of DVR between the first PET scan ("test") and second scan ("retest") was calculated for each data point as ordinate value divided by abscissa value. The mean test-retest variability in DVR between the two PET scans was 2.26 % (standard deviation +/- 1.45 %). The DVR test-retest variability for all regions and patients was < 5 %. The unbroken line intersects the vertical axis at the mean test-retest difference in DVR; the upper and lower dotted lines intersect the vertical axis at the mean ± 1.96 standard deviations of the test-retest difference in DVR.



SUPPLEMENTAL FIGURE 3. Histograms showing the frequency distributions of 11C-PBR28 distribution volume ratio (DVR) in (A) white matter of healthy volunteers (HV), (B) normal appearing white matter (NAWM) of MS patients and (C) individual white matter lesions collated across all the MS patients in the 11C-PBR28 cohort.

Demographic/clinical characteristic	18F-PBR111 HV[1]	11C-PBR28 HV[2]	18F-PBR111 MS[1]	11C-PBR28 MS[3]
Number	10	20	10	24
Gender, Male : Female, n	3 : 7	14 : 6	2 : 8	10 : 14
Age, years, mean (SD)	42(11.1)	47 (14.8)	45 (8.8)	47 (11.4)
TSPO genotype, n				
High affinity binders	7	12	7	13
Medium affinity binders	3	8	3	11
MS subtype, RRMS: SPMS, n			10 : 0	17 : 7
Disease duration, years, mean (SD)			10 (5.8)	13.5 (6.5)
EDSS, median (range)			3.5 (1.5-6.5)	4.5 (1.0-7.0)
Treatments, n				
None			3	9
Interferons			5	1
Fingolimod			0	3
Dimethyl fumarate			2	1
Nataluzimab			0	6
Alemtuzimab			0	4
MRI metrics (normalised)				
Brain parenchymal volume(cm^3), mean (SD)	1534 (58)	1590(180)	1440 (126)	1380 (140)
Cortical volume(cm^3), mean (SD)	637 (33)	630 (55)	616 (61)	578 (66)
Mean T2 white matter lesion volume (cm^3) (SD)			9.7 (9.7)	17.9 (15.8)
Median T2 white matter lesion number (range)			31.5 (7-52)	38.5 (13-96)

Supplemental Table 1. Demographic characteristics of healthy volunteers (HV) and MS patients scanned with either 11C-PBR28 or 18F-PBR111

Abbreviations: MS=multiple sclerosis; RRMS=relapsing remitting MS; SPMS=secondary progressive MS; TSPO=translocator protein; EDSS=Expanded Disability Status Scale; SD=standard deviation

Data from subjects previously described in:
[1] Colasanti et al. 2014 (*1*)
[2] Owen et al. 2014; Guo et al. 2014; Vera et al. 2016 (*2-4*)
[3] Datta et al. 2016 (*5*)

Case	Age	Gender	EDSS	Disease duration	MSSS	MS Subtype	DMT
A1	22	F	3	16	2.6	RRMS	Fingolimod
A2	38	M	6	10	7.4	RRMS	Alemtuzimab
A3	42	F	1	13	0.6	RRMS	Nataluzimab
A4	50	F	2.5	9	3.5	RRMS	-
A5	59	M	6	23	5.2	SPMS	-
A6	36	M	1	6	1.1	RRMS	Dimethyl fumarate
A7	57	F	1	18	0.3	RRMS	Fingolimod
A8	48	M	7	12	8.6	RRMS	Nataluzimab
A9	53	M	5	14	5.2	RRMS	Nataluzimab
A10	43	M	5	13	5.3	SPMS	-
A11	29	F	1	1	2.4	RRMS	Interferon β
A12	51	F	6.5	8	8.7	RRMS	Nataluzimab
A13	62	F	6	24	5.0	SPMS	-
A14	56	M	7	17	7.8	SPMS	-
A15	52	F	2	6	3.5	RRMS	Alemtuzimab
A16	45	F	4	28	2.4	RRMS	Alemtuzimab
A17	66	F	6.5	17	6.9	RRMS	-
A18	53	F	3	16	2.6	RRMS	-
A19	30	F	4	6	6.8	RRMS	Nataluzimab
A20	36	M	7	10	8.9	SP	-
A21	47	M	7	11	8.8	SPMS	-
A22	39	M	4	10	5.3	RRMS	Alemtuzimab
A23	45	F	6.5	14	7.6	RRMS	Fingolimod
A24	64	F	2.5	22	1.3	RRMS	Nataluzimab
B1	42	F	6	2	9.6	RRMS	Interferon β
B2	40	F	4	11	4.9	RRMS	Natalizumab
B3	41	F	1.5	14	2.3	RRMS	-
B4	51	F	2	4	8.6	RRMS	Interferon β
B5	28	M	2	7	3.2	RRMS	-
B6	55	F	2	20	0.9	RRMS	Interferon β
B7	42	M	5.5	11	6.3	RRMS	-
B8	48	F	6.5	8	8.71	RRMS	Natalizumab
B9	59	F	3	16	2.6	RRMS	Interferon β
B10	41	F	5.5	4	9.1	RRMS	Interferon β

Supplemental Table 2. Demographic and clinical characteristics of individual MS patients. A1-24: 11C-PBR28 cohort (data from these patients was used in Datta et al. 2016(*5*)); B1-10:18F-PBR111 cohort (data from these patients was published with a different analysis in Colasanti et al.

2014(*1*))Abbreviations: MS=multiple sclerosis; M=male; F=female; EDSS=Expanded Disability Status Scale; RRMS=relapsing remitting multiple sclerosis; SPMS=secondary progressive multiple sclerosis

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