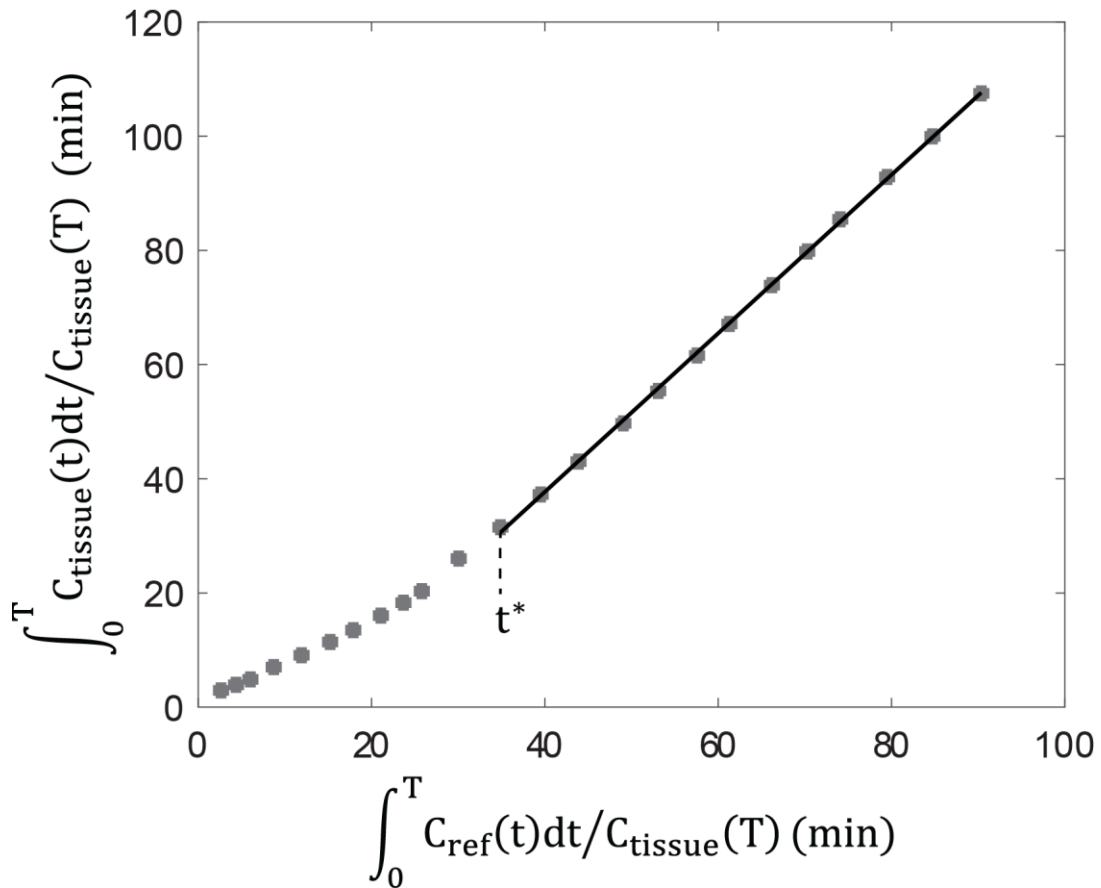


### Supplemental Figure 1



Logan plot with reference region in the normal appearing white matter of a representative patient with multiple sclerosis. The DVR is estimated from the following equation:  $\int_0^T C_{tissue}(t)dt / C_{tissue}(T) = DVR \cdot \int_0^T C_{ref}(t)dt / C_{tissue}(T) + const$ , where  $C_{tissue}(t)$  is the activity concentration in the voxel under analysis and  $C_{ref}(t)$  is the activity concentration in the reference region extracted using a supervised clustering algorithm. The linear fit (black line) was obtained after an equilibration time of  $t^* = 27.5$  min.

## Supplemental Table 1

Difference in mean <sup>18</sup>F-DPA-714 DVR values and percentages of DPA+ voxels between ROIs (NAWM, perilesional area, T2 lesions, and T1-se lesions).

18F-DPA-714 DVR						
test	Coef.	SE	t	p	95% CI	
NAWM in MS vs WM in HC	0.07	0.02	3.35	0.002	0.03	0.11
test	Coef.	SE	z	p (bonf)	95% CI	
PERI in MS vs NAWM in MS	0.09	0.03	3.60	<b>0.002</b>	0.03	0.16
LES in MS vs NAWM in MS	0.07	0.03	2.63	0.052	-0.00	0.14
BH in MS vs NAWM in MS	0.11	0.03	4.19	<b>0.000</b>	0.04	0.19
LES in MS vs PERI in MS	-0.03	0.03	-0.97	1.000	-0.10	0.04
BH in MS vs PERI in MS	0.02	0.03	0.71	1.000	-0.05	0.09
BH in MS vs LES in MS	0.05	0.03	1.65	0.595	-0.03	0.12
Percentage of DPA+ voxel						
test	Coef.	SE	t	p	95% CI	
NAWM in MS vs WM in HC	9.96	2.47	4.03	<b>0.000</b>	5.00	14.92
test	Coef.	SE	z	p (bonf)	95% CI	
PERI in MS vs NAWM in MS	13.24	2.64	5.02	<b>0.000</b>	6.28	20.20
LES in MS vs NAWM in MS	20.08	2.64	7.61	<b>0.000</b>	13.12	27.04
BH in MS vs NAWM in MS	26.90	2.69	10.02	<b>0.000</b>	19.82	33.99
LES in MS vs PERI in MS	6.84	2.64	2.59	0.057	-0.12	13.80
BH in MS vs PERI in MS	13.67	2.69	5.09	<b>0.000</b>	6.58	20.75
BH in MS vs LES in MS	6.83	2.69	2.54	0.066	-0.26	13.91

## Supplemental Table 2

Difference in the number of DPA-active/inactive lesions between MS subgroups.

	Predictors	test	Coef.	SE	z	p (bonf)	95% CI	
T2 active	MS subgroups	RR vs PP	3.43	2.16	1.59	0.345	-1.81	8.67
		SP vs PP	4.13	1.76	2.35	0.061	-0.13	8.39
		SP vs RR	0.70	1.77	0.40	1.000	-3.58	4.98
T2 inactive	MS subgroups	RR vs PP	-1.72	1.40	-1.23	0.664	-5.10	1.67
		SP vs PP	0.80	1.13	0.71	1.000	-1.95	3.55
		SP vs RR	2.52	1.14	2.21	0.087	-0.25	5.28

### Supplemental Table 3

Associations between parameters of interest and EDSS step change over the 2 years preceding study entry or EDSS at study entry.

	Predictors	Coef.	SE	z	P (bonf)	95% CI	
EDSS step change	T2 lesion load	0.00	0.00	1.20	1.00	0.00	0.00
	T1-se lesion load	0.00	0.00	0.81	1.00	-0.00	0.00
	number of T2 lesions	0.04	0.02	1.91	0.513	-0.00	0.08
	percentage of DPA+ voxels in NAWM	0.15	0.04	3.47	<b>0.009</b>	0.06	0.23
	percentage of DPA+ voxels in perilesional area	0.07	0.03	2.64	0.072	0.02	0.13
	percentage of DPA+ voxels in T2 lesions	0.05	0.02	2.15	0.279	0.00	0.09
	percentage of DPA+ voxels in T1-se lesions	0.06	0.02	2.89	<b>0.036</b>	0.02	0.09
	number of DPA-active lesions	0.12	0.03	3.41	<b>0.009</b>	0.05	0.19
	number of DPA-inactive lesions	-0.22	0.09	-2.59	0.081	-0.39	-0.05
EDSS	T2 lesion load	7.53e-7	2.65e-5	0.03	0.977	-5.11e-5	5.26e-5
	T1-se lesion load	-1.71e-5	8.54e-5	-0.20	0.842	-1.85e-4	1.50e-4
	number of T2 lesions	-0.01	0.02	-0.80	0.424	-0.05	0.02
	percentage of DPA+ voxels in NAWM	-0.03	0.03	-0.78	0.433	-0.09	0.04
	percentage of DPA+ voxels in perilesional area	-0.01	0.02	-0.35	0.726	-0.06	0.04
	percentage of DPA+ voxels in T2 lesions	-0.01	0.02	-0.43	0.664	-0.05	0.03
	percentage of DPA+ voxels in T1-se lesions	0.00	0.01	0.15	0.879	0-.03	0.03
	number of DPA-active lesions	-0.02	0.03	-0.65	0.513	-0.07	0.03
	number of DPA-inactive lesions	-0.03	0.06	-0.56	0.576	-0.15	0.08