

Supplemental Materials

Supplemental Table 1. V_T data from baseline/ post-rotenone monkey and baseline human ^{18}F -BCPP-EF scans

ROI	MONKEY (n=4)		HUMAN (n=30)
	Baseline	Post-block	-
Centrum semiovale	N/A	N/A	10.9 ± 1.9
Cerebral white matter	13.4 ± 3.0	10.6 ± 2	15.5 ± 3.0
Cerebellum	26.2 ± 3.0	16.2 ± 1.4	28.1 ± 4.9
Frontal cortex	26.0 ± 1.0	17.0 ± 0.9	23.6 ± 4.2
Temporal cortex	26.7 ± 1.9	17.1 ± 0.9	23.4 ± 3.8
Occipital cortex	34.4 ± 4.8	20.6 ± 2.7	26.2 ± 4.6
Striatum	30.6 ± 1.9	19.3 ± 3.3	27.4 ± 5.2
Hippocampus	23.4 ± 1.0	15.0 ± 1.2	20.4 ± 3.5
Parietal cortex	28.5 ± 1.7	17.4 ± 0.8	24.4 ± 4.7
Cingulate	27.7 ± 1.8	18.3 ± 0.09	25.4 ± 4.5

Data are mean $\pm$ SD

Supplemental Table 2. Summary of injection parameters

Group	Injected Activity (MBq)	Injected Mass (μg)
All Subjects (n = 30)	89 ± 4	0.07 ± 0.04
Test (n = 5)	92 ± 3	0.08 ± 0.03
Retest (n = 5)	91 ± 3	0.08 ± 0.02

Data are mean $\pm$ SD. Days between scans: 25 ± 4

Supplemental Table 3. Test-retest demographic information, radioligand injection parameters and plasma analysis results

Group	Demographics			Injection Parameters		Plasma Analysis		
	Subject	Age	Sex	Injected Activity (MBq)	Injected Mass (μg)	f_p	Plasma clearance rate ($\text{L} \cdot \text{h}^{-1}$)	$Ppf^{90\text{min}}$
Test	001	26	M	91	0.04	0.068	96.9	19%
	002	29	F	98	0.05	0.085	84.0	18%
	003	54	F	90	0.12	0.057	84.0	19%
	004	25	F	93	0.08	0.083	68.7	24%
	005	49	M	90	0.10	0.066	72.7	24%
Retest	001	26	M	92	0.11	0.067	125.7	13%
	002	29	F	95	0.08	0.071	90.7	18%
	003	54	F	88	0.05	0.050	86.8	17%
	004	25	M	89	0.09	0.075	109.5	17%
	005	49	M	89	0.09	0.062	106.0	15%

$Ppf^{90\text{min}}$ = Fraction of parent ^{18}F -BCPP-EF in plasma at 90 minute time-point.

Supplemental Table 4. Outcome parameters derived from ¹⁸F-BCPP-EF test and retest scans

ROI	V_T (mL/cm ³)		V_T/f_p (mL/cm ³)		DVR-1		SUVR-1	
	Test	Retest	Test	Retest	Test	Retest	Test	Retest
CS	9.0 ± 1.4	10.3 ± 1.5	130 ± 31	160 ± 41	-	-	-	-
BS	13.7 ± 2.1	15.0 ± 2.8	197 ± 50	235 ± 70	0.51 ± 0.06	0.45 ± 0.11	0.5 ± 0.1	0.5 ± 0.1
SN	16.6 ± 2.5	18.2 ± 3.6	240 ± 57	286 ± 86	0.84 ± 0.06	0.77 ± 0.14	0.8 ± 0.1	0.8 ± 0.2
THA	18.7 ± 3.7	20.3 ± 4.2	272 ± 83	318 ± 99	1.06 ± 0.24	0.97 ± 0.22	1.1 ± 0.3	1.0 ± 0.3
STR	23.9 ± 5.0	25.8 ± 5.5	347 ± 107	405 ± 127	1.63 ± 0.32	1.50 ± 0.31	1.6 ± 0.4	1.4 ± 0.4
GP	22.5 ± 3.6	24.9 ± 4.3	328 ± 95	393 ± 127	1.50 ± 0.27	1.42 ± 0.24	1.4 ± 0.3	1.3 ± 0.3
VSTR	25.8 ± 4.5	29.1 ± 5.6	373 ± 103	455 ± 135	1.84 ± 0.18	1.82 ± 0.31	1.8 ± 0.3	1.7 ± 0.3
CAU	18.5 ± 5.6	19.5 ± 6.1	269 ± 102	308 ± 119	1.01 ± 0.46	0.88 ± 0.41	1.0 ± 0.6	0.8 ± 0.5
PUT	26.7 ± 4.8	29.0 ± 5.3	388 ± 113	455 ± 135	1.95 ± 0.32	1.82 ± 0.26	1.9 ± 0.4	1.8 ± 0.4
PC	22.2 ± 4.7	24.7 ± 4.9	320 ± 90	387 ± 112	1.43 ± 0.18	1.39 ± 0.19	1.5 ± 0.3	1.5 ± 0.3
AC	21.0 ± 4.2	22.8 ± 4.5	303 ± 83	357 ± 104	1.30 ± 0.13	1.21 ± 0.23	1.4 ± 0.2	1.3 ± 0.3
FTCX	19.5 ± 3.8	21.2 ± 3.9	282 ± 79	331 ± 94	1.15 ± 0.19	1.06 ± 0.20	1.2 ± 0.3	1.1 ± 0.3
INS	21.6 ± 3.6	23.5 ± 4.2	313 ± 83	368 ± 104	1.39 ± 0.12	1.29 ± 0.20	1.4 ± 0.2	1.3 ± 0.2
HIP	17.4 ± 3.1	18.5 ± 3.3	252 ± 73	290 ± 84	0.92 ± 0.20	0.80 ± 0.20	0.9 ± 0.3	0.8 ± 0.2
AMY	18.6 ± 3.3	19.9 ± 3.3	268 ± 72	311 ± 82	1.05 ± 0.11	0.94 ± 0.17	1.0 ± 0.2	0.9 ± 0.2
TL	19.8 ± 2.9	21.6 ± 3.6	286 ± 71	337 ± 91	1.19 ± 0.09	1.10 ± 0.16	1.2 ± 0.2	1.1 ± 0.2
PL	20.0 ± 4.1	22.0 ± 4.2	290 ± 87	345 ± 103	1.20 ± 0.24	1.14 ± 0.16	1.3 ± 0.3	1.2 ± 0.2
CER	22.3 ± 3.2	24.2 ± 4.5	323 ± 84	380 ± 112	1.47 ± 0.17	1.35 ± 0.17	1.5 ± 0.2	1.4 ± 0.2

CS: centrum semiovale, BS: brainstem, SN: substantia nigra, THA: thalamus, STR: Striatum, GP: globus pallidus, VSTR: ventral striatum, CAU: caudate, PUT: putamen, PC: posterior cingulate cortex, AC: anterior cingulate cortex, FTCX: frontal cortex, INS: insular cortex, HIP: hippocampus, AMY: amygdala, TL: temporal lobe, PL: parietal lobe, CER: cerebellum. Kinetic outcome measures derived using MA1. Data are mean ± SD. N=5

Supplemental Table 5. Test-retest reproducibility of 2TC derived ¹⁸F-BCPP-EF outcome measures

ROI	V_T (mL/cm ³)			V_T/f_p (mL/cm ³)			DVR-1		
	TRV (%)	aTRV (%)	ICC	TRV (%)	aTRV (%)	ICC	TRV (%)	aTRV (%)	ICC
CS	11 ± 15	17 ± 5	0.43	20 ± 21	25	0.51	-	-	-
BS	9 ± 13	13 ± 7	0.62	17 ± 16	21	0.62	-9 ± 27	16	0.17
SN	11 ± 15	15 ± 8	0.56	19 ± 18	24	0.55	-2 ± 21	14	0.10
THA	9 ± 11	13 ± 4	0.75	17 ± 17	22	0.71	-6 ± 8	8	0.92
STR	9 ± 13	14 ± 5	0.75	17 ± 18	22	0.70	-5 ± 8	7	0.92
GP	10 ± 13	14 ± 6	0.59	18 ± 18	22	0.65	-2 ± 13	10	0.79
VSTR	12 ± 16	17 ± 8	0.47	21 ± 19	26	0.54	2 ± 8	7	0.84
CAU	6 ± 13	12 ± 6	0.90	14 ± 18	20	0.83	-12 ± 8	12	0.96
PUT	9 ± 13	14 ± 5	0.66	17 ± 18	23	0.65	-3 ± 10	8	0.81
PC	12 ± 15	17 ± 6	0.64	20 ± 20	25	0.56	0.3 ± 4	3	0.97
AC	9 ± 13	13 ± 7	0.70	17 ± 18	21	0.62	-5 ± 11	9	0.81
FTCX	9 ± 14	14 ± 7	0.67	17 ± 20	22	0.61	-6 ± 8	8	0.89
INS	8 ± 11	12 ± 6	0.71	16 ± 15	20	0.66	-6 ± 12	10	0.62
HIP	8 ± 9	10 ± 5	0.79	16 ± 14	19	0.73	-9 ± 17	15	0.72
AMY	7 ± 11	10 ± 6	0.73	15 ± 15	19	0.68	-11 ± 16	14	0.59
TL	9 ± 11	12 ± 6	0.65	17 ± 15	20	0.63	-6 ± 15	11	0.38
PL	10 ± 15	16 ± 5	0.65	18 ± 21	25	0.62	-2 ± 6	4	0.92
CER	8 ± 11	12 ± 6	0.70	16 ± 15	20	0.68	-6 ± 14	10	0.34
mean	9	14	0.65	17	22	0.64	-5	10	0.69
SD	2	2	0.10	2	2	0.08	4	4	0.28

TRV: Test-retest variability, aTRV: absolute test-retest variability, ICC: intra-class correlation. Data are mean ± SD. CS: centrum semiovale, BS: brainstem, SN: substantia nigra, THA: thalamus, STR: Striatum, GP: globus pallidus, VSTR: ventral striatum, CAU: caudate, PUT: putamen, PC: posterior cingulate cortex, AC: anterior cingulate cortex, FTCX: frontal cortex, INS: insular cortex, HIP: hippocampus, AMY; amygdala, TL: temporal lobe, PL: parietal lobe, CER: cerebellum. N = 5

Supplemental Table 6. Test-retest reproducibility of ¹⁸F-BCPP-EF DVR and SUVR

ROI	DVR			SUVR		
	TRV (%)	aTRV (%)	ICC	TRV (%)	aTRV (%)	ICC
CS	-	-	-	-	-	-
BS	-4 ± 7	6	0.31	-4 ± 4	4	0.83
SN	-4 ± 8	7	0.15	-3 ± 4	4	0.86
THA	-5 ± 5	5	0.84	-4 ± 3	4	0.94
STR	-5 ± 5	5	0.87	-6 ± 3	6	0.91
GP	-3 ± 6	5	0.83	-5 ± 4	5	0.89
VSTR	-1 ± 6	5	0.81	-4 ± 4	5	0.89
CAU	-7 ± 4	7	0.94	-7 ± 5	7	0.94
PUT	-5 ± 6	6	0.75	-6 ± 3	6	0.89
PC	-1 ± 1	2	0.97	-1 ± 2	2	0.98
AC	-4 ± 5	5	0.78	-4 ± 2	4	0.94
FTCX	-4 ± 3	5	0.86	-4 ± 1	4	0.94
INS	-5 ± 7	6	0.51	-5 ± 3	5	0.86
HIP	-7 ± 8	9	0.63	-5 ± 4	5	0.89
AMY	-6 ± 6	6	0.57	-5 ± 4	5	0.79
TL	-5 ± 8	7	0.16	-4 ± 4	4	0.81
PL	-3 ± 4	3	0.88	-2 ± 4	4	0.94
CER	-5 ± 8	7	0.31	-5 ± 4	5	0.82
Mean	-4	6	0.66	-4	5	0.89
SD	2	2	0.27	1	1	0.05

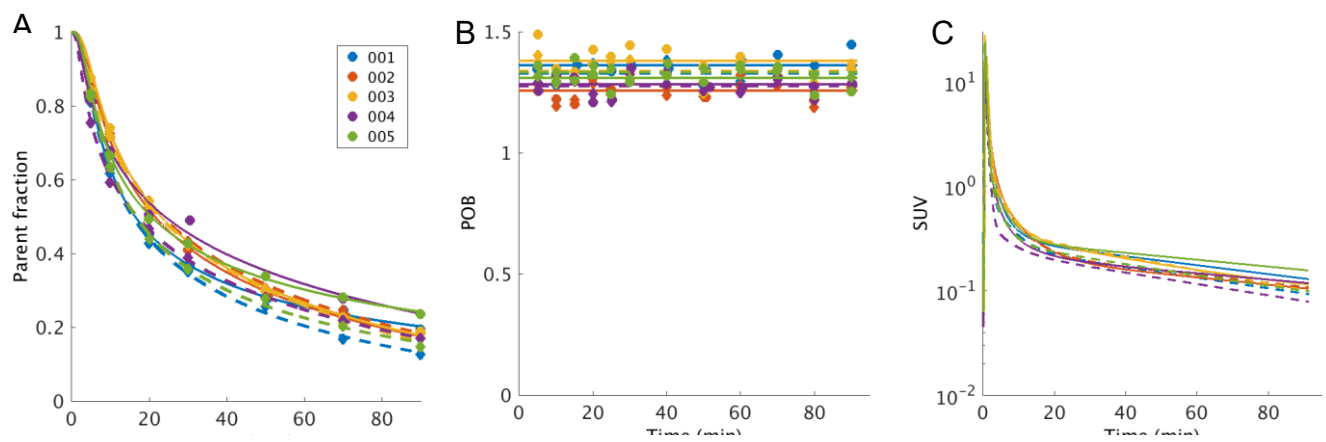
TRV: Test-retest variability, aTRV: absolute test-retest variability, ICC: intra-class correlation. Data are mean ± SD. CS: centrum semiovale, BS: brainstem, SN: substantia nigra, THA: thalamus, STR: Striatum, GP: globus pallidus, VSTR: ventral striatum, CAU: caudate, PUT: putamen, PC: posterior cingulate cortex, AC: anterior cingulate cortex, FTCX: frontal cortex, INS: insular cortex, HIP: hippocampus, AMY; amygdala, TL: temporal lobe, PL: parietal lobe, CER: cerebellum. N=5.

Supplemental Table 7. Test-retest reproducibility of ^{18}F -BCPP-EF K_1					
ROI	Test	Retest	TRV (%)	aTRV (%)	ICC
CS	0.16 ± 0.02	0.17 ± 0.03	8 ± 14	13	0.53
BS	0.29 ± 0.02	0.29 ± 0.05	1 ± 16	12	0.50
SN	0.32 ± 0.02	0.34 ± 0.06	6 ± 20	17	-0.03
THA	0.39 ± 0.05	0.40 ± 0.07	0 ± 16	13	0.61
GP	0.36 ± 0.04	0.36 ± 0.08	-1 ± 17	11	0.78
VSTR	0.42 ± 0.06	0.41 ± 0.10	-5 ± 15	12	0.75
CAU	0.30 ± 0.09	0.29 ± 0.09	-3 ± 15	12	0.89
PUT	0.46 ± 0.08	0.45 ± 0.11	-4 ± 15	12	0.83
PC	0.50 ± 0.08	0.49 ± 0.10	-2 ± 17	14	0.67
AC	0.45 ± 0.08	0.43 ± 0.10	-5 ± 15	12	0.79
FTCX	0.41 ± 0.07	0.41 ± 0.10	-2 ± 16	12	0.78
INS	0.45 ± 0.07	0.45 ± 0.10	-2 ± 14	11	0.80
HIP	0.34 ± 0.05	0.36 ± 0.07	2 ± 15	13	0.73
AMY	0.33 ± 0.05	0.34 ± 0.07	3 ± 15	13	0.70
TL	0.38 ± 0.04	0.38 ± 0.08	0 ± 15	10	0.68
PL	0.40 ± 0.06	0.41 ± 0.10	1 ± 15	11	0.78
CER	0.44 ± 0.05	0.44 ± 0.08	-1 ± 10	10	0.70
Mean	0.38	0.38	-0.1	12.3	0.68
SD	0.08	0.08	3.6	1.7	0.21
TRV: Test-retest variability, aTRV: absolute test-retest variability, ICC: intra-class correlation. Data are mean $\pm$ SD. CS: centrum semiovale, BS: brainstem, SN: substantia nigra, THA: thalamus, STR: Striatum, GP: globus pallidus, VSTR: ventral striatum, CAU: caudate, PUT: putamen, PC: posterior cingulate cortex, AC: anterior cingulate cortex, FTCTX: frontal cortex, INS: insular cortex, HIP: hippocampus, AMY: amygdala, TL: temporal lobe, PL: parietal lobe, CER: cerebellum. N=5.					

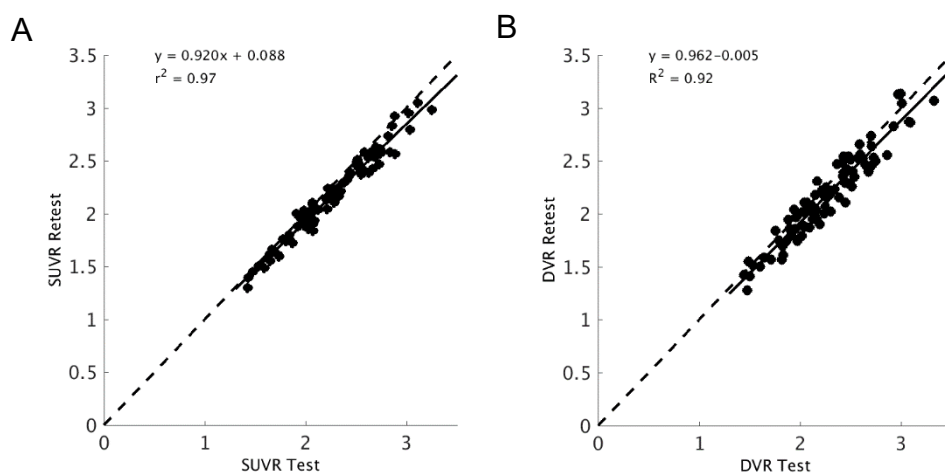
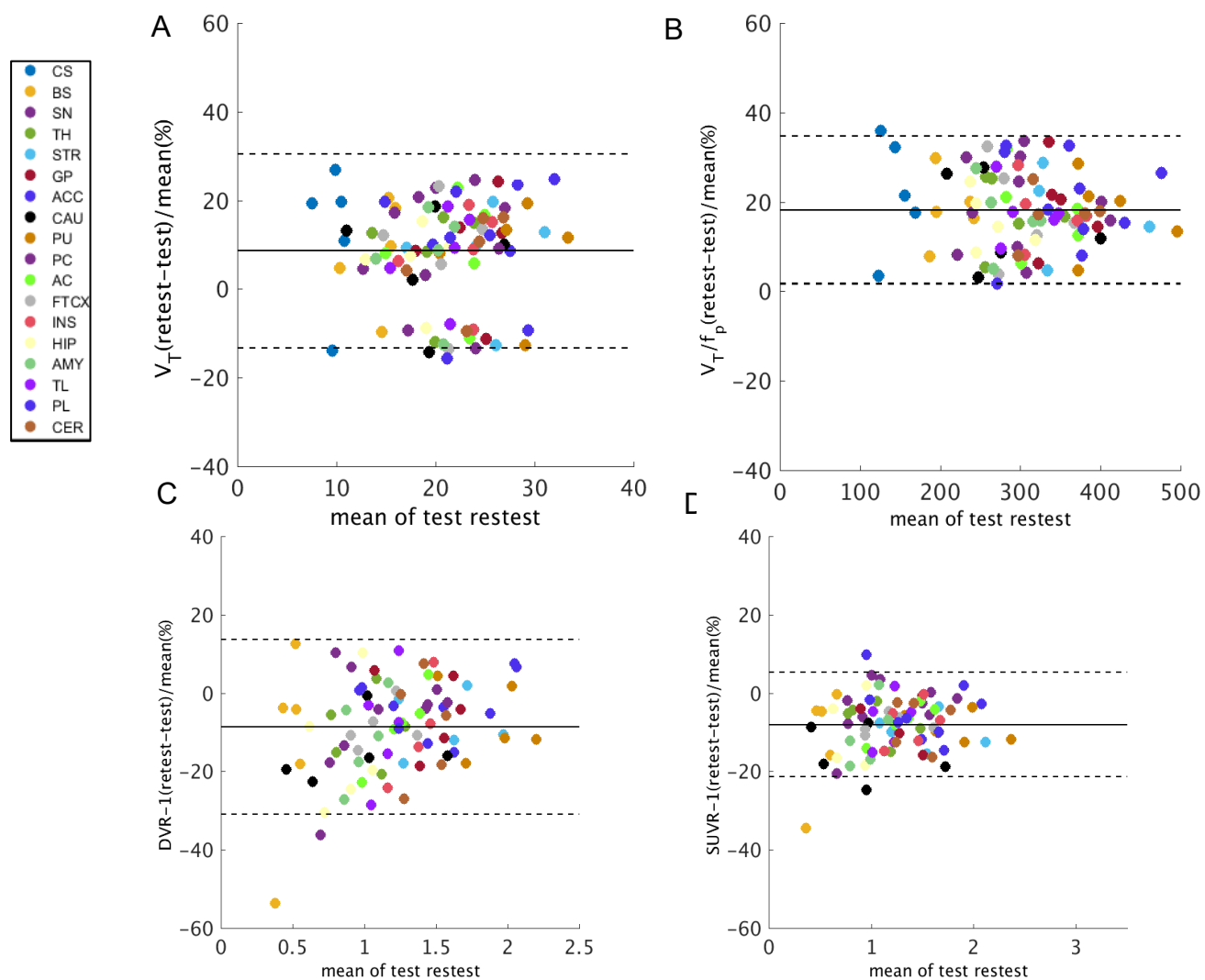
Application of Simultaneous Estimation (SIME) Method

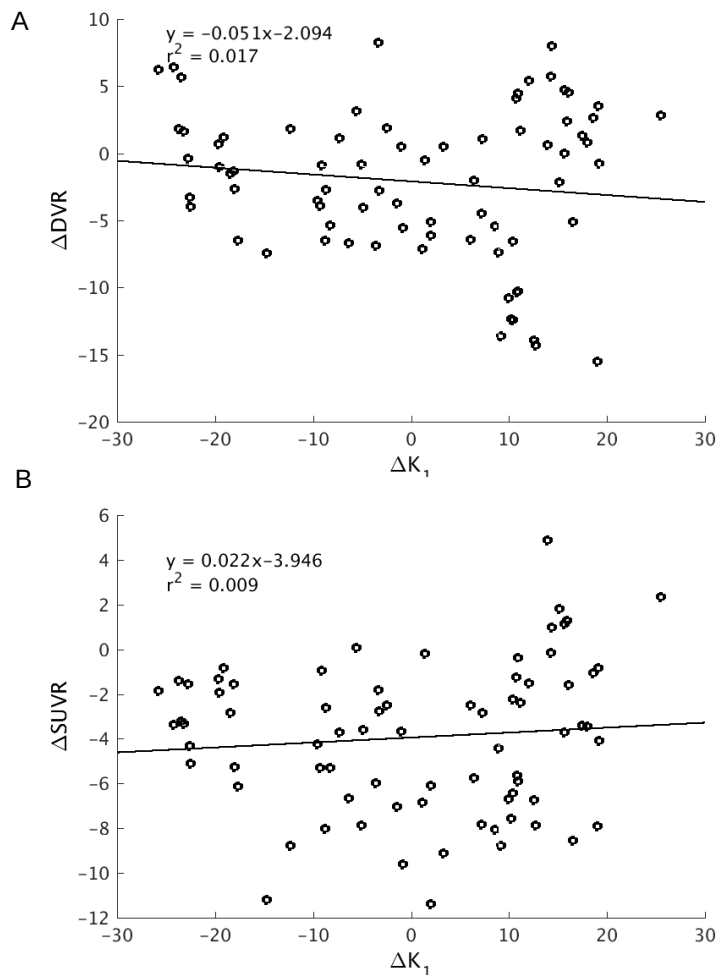
In our implementation of SIME, we evaluated 100 possible V_{ND} values (0 to 10, step size = 0.01). We fitted 18 regions simultaneously with a constrained two tissue compartment model where V_{ND} (K_1/k_2) was constrained to be equal to the V_{ND} being evaluated. For each V_{ND} value, the residual sum of squares (RSS) from the constrained 2TC fit was calculated. The V_{ND} value which produced the minimal RSS was chosen as the optimal V_{ND} value for that subject. The process was repeated for all 30 ^{18}F -BCPP-EF scans to derive a mean, a standard deviation and a range of V_{ND} estimates.

Supplemental Figures

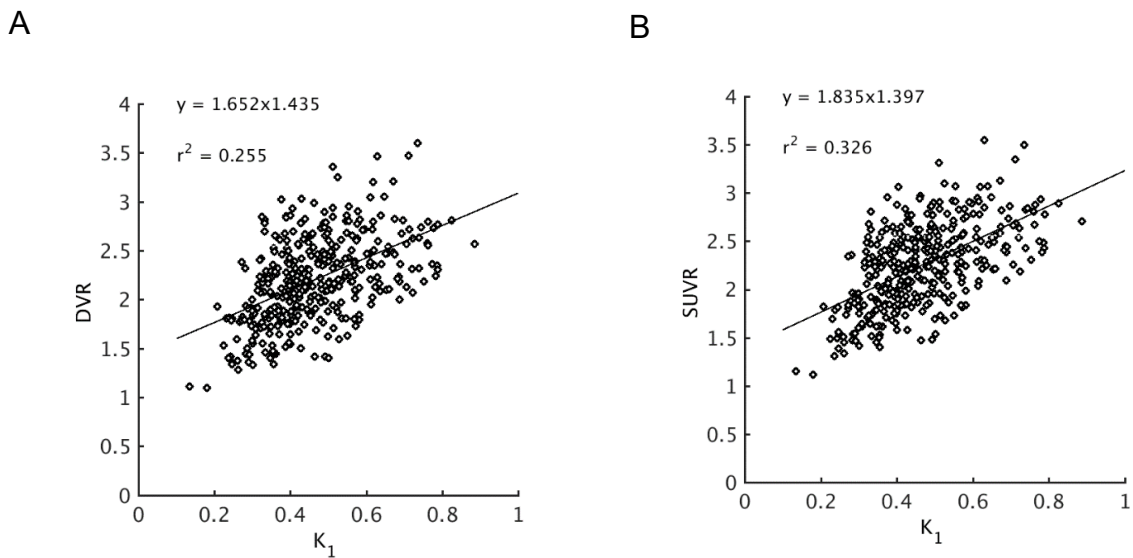


Supplemental Fig 1. Individual model fits to (A) parent fraction, (B) plasma/blood and (C) input function data





Supplemental Fig 4. Correlation between (A) relative difference in test and retest derived K_1 (ΔK_1) and relative difference in test and retest derived DVR (ΔDVR) and (B) and relative difference in test and retest derived SUVR ($\Delta SUVR$) (N=5)



Supplemental Fig 5. Correlation between (A) K_1 and DVR and (B) K_1 and SUVR (N=30)