Supplementary Materials

Brief summary for partial volume correction (PVC) methods

Geometric transfer matrix (GTM)

The GTM method [17] is a region-based MR-PVC algorithm using VOIs extracted with MR segmentation algorithm. In the GTM method, spillover between target and its surrounding regions are computed with VOIs and point spread function (PSF). This matrix is called with 'geometric transfer matrix (GTM)'. Then, true activities on VOIs are estimated from the GTM and measured activities averaged on each VOI as follows:

$$T = G^{-1} \cdot r$$

where T and r indicate the n × 1 vectors containing true and measured activities on VOIs, respectively; G indicates the GTM, n × n matrix containing g_{ij}, which indicates the fractional contribution of activity from region *j* to region *i*; and n indicates number of VOIs. Note that the GTM method assumes homogeneous activity on each VOI.

For voxelwise PVC with region-based voxelwise (RBV) algorithm and iterative registration processes in the PoR method, the synthetic PET image ($s(x)$) is calculated as follows:

$$s(x) = \sum_{i=1,\ldots,n} [T_i \cdot p_i(x)]$$

where *x* indicates position of each voxel; T_i indicates the true activity on region *i*, estimated with the GTM method; and $p_i(x)$ is 1 if *x* is inside region *i*, otherwise 0.

Region-based voxelwise (RBV)

The RBV algorithm [19] is an extension method for the GTM method to perform voxelwise PVC. In the RBV algorithm, voxelwise PV-corrected map ($f_c(x)$) is computed with the measured and synthetic PET images as follows:

$$f_c(x) = f(x) \cdot \left[\frac{s(x)}{s(x) \otimes h(x)}\right]$$

where $f(x)$ indicates measured PET image, and $h(x)$ indicates PSF.

Figures and Tables

Table S1. **List of image and voxel sizes for the downloaded original PET images in the present study.**

Manufacturer	PET model	No. of subjects	Image size			Voxel size [mm]		
			X	Y	Z	X	Y	Z
Siemens	ECAT Exact HR+	30	128	128	63	2.06	2.06	2.06
		5	128	128	63	2.25	2.25	2.25
		6	128	128	63	2.57	2.57	2.57
	HRRT	23	256	256	256	1.22	1.22	1.22
GE	Advance	21	128	128	35	2.00	2.00	4.25
	Discovery RX	7	128	128	47	2.00	2.00	3.27

Table S2. **Sizes of Gaussian kernel applied to the downloaded original PET images in the present study.**

Manufacturer	PET model	No. of subjects	X	Y	Z
Siemens	ECAT Exact HR+	41	5.0	5.0	5.0
	HRRT	23	6.0	6.0	6.0
GE	Advance	21	5.0	5.0	2.0
	Discovery RX	7	5.0	5.0	3.5

Unit for X, Y and Z: mm at full width half-maximum (FWHM)

Table S3. **List of FreeSurfer parcellation regions merged into each VOI in the present study.**

VOI	FreeSurfer parcellation
Frontal cortex	ctx-lh(rh)-caudalmiddlefrontal
	ctx-lh(rh)-lateralorbitofrontal
	ctx-lh(rh)-medialorbitofrontal
	ctx-lh(rh)-parsopercularis
	ctx-lh(rh)-parsorbitalis
	ctx-lh(rh)-parstriangularis
	ctx-lh(rh)-rostralmiddlefrontal
	ctx-lh(rh)-superiorfrontal
	ctx-lh(rh)-frontalpole
Parietal cortex	ctx-lh(rh)-inferiorparietal

	ctx-lh(rh)-superiorparietal
	ctx-lh(rh)-supramarginal
Precuneus	ctx-lh(rh)-precuneus
Occipital cortex	ctx-lh(rh)-cuneus
	ctx-lh(rh)-lateraloccipital
	ctx-lh(rh)-lingual
	ctx-lh(rh)-pericalcarine
Lateral temporal cortex	ctx-lh(rh)-bankssts
	ctx-lh(rh)-inferiortemporal
	ctx-lh(rh)-middletemporal
	ctx-lh(rh)-superiortemporal
	ctx-lh(rh)-temporalpole
	ctx-lh(rh)-transversetemporal
Medial temporal cortex	ctx-lh(rh)-enthorhinal
	ctx-lh(rh)-fusiform
	ctx-lh(rh)-parahippocampal
Anterior cingulate cortex	ctx-lh(rh)-caudalanteriorcingulate
	ctx-lh(rh)-rostralanteriorcingulate
Posterior cingulate cortex	ctx-lh(rh)-isthmuscingulate
	ctx-lh(rh)-posteriorcingulate
Sensory motor cortex	ctx-lh(rh)-paracentral
	ctx-lh(rh)-postcentral
	ctx-lh(rh)-precentral
Insula	ctx-lh(rh)-insula
Caudate	Caudate
Putamen	Putamen
Thalamus	Thalamus-Proper
	Thalamus
	VentralDC
Accumbens area	Accumbens area
Pallidum	Pallidum
Brainstem	Brainstem

Hippocampus	Hippocampus
Amygdala	Amygdala
Cerebellar gray matter	Cerebellum–Cortex
Subcortical white matter	Cerebral white matter
	WM hypointensities
	CC_Posterior
	CC_Mid_Posterior
	CC_Central
	CC_Mid_Anterior
	CC_Anterior
Cerebellar white matter	Cerebellum–white matter
Cerebrospinal fluid	Lateral ventricle
	Inf–Lat–Vent
	3rd ventricle
	4th ventricle
	CSF
	vessel
	choroid plexus
	5th ventricle

The 113 regions parcellated using FreeSurfer (aparc + aseg) were merged into 22 regions for region-based PVC and VOI analysis in this study. MR image and VOI map for a representative case are shown in Figure S1.

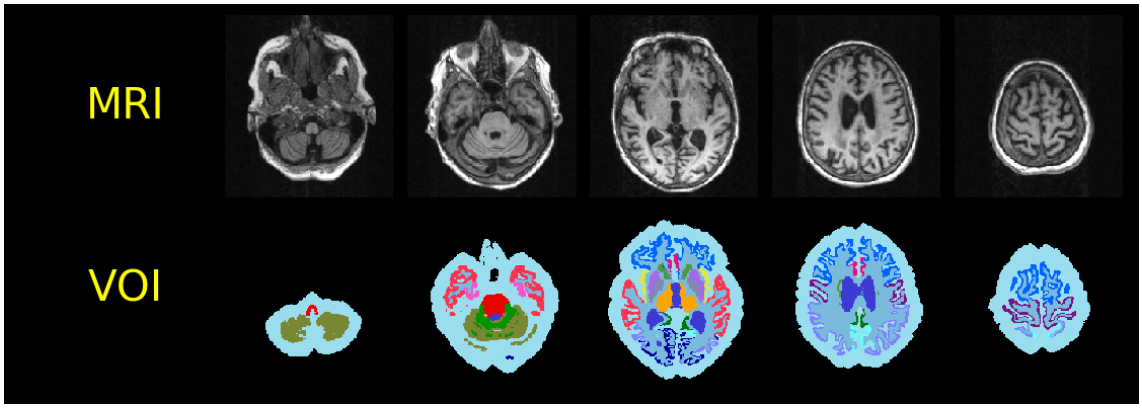


Figure S1　MR image and VOI map for a representative case.

Figure S2　VOI and SUV maps zoomed to the sensory motor cortex in the same case shown in Figure 4. Note that the colormaps for the SUV maps differ from those in Figure 4 because different software was used to show maps to view VOI contours.

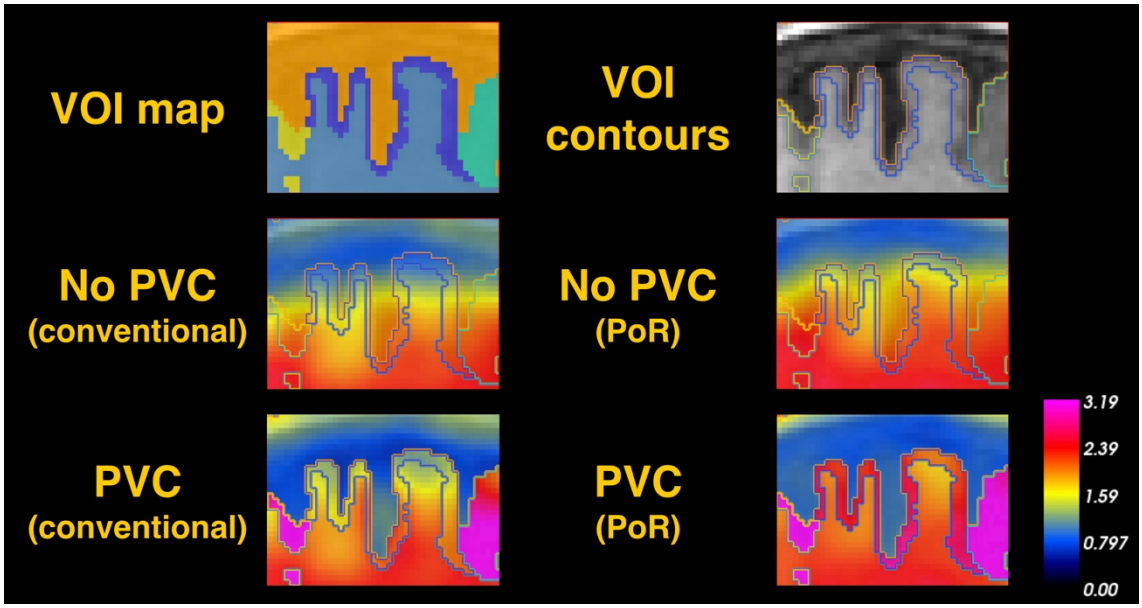
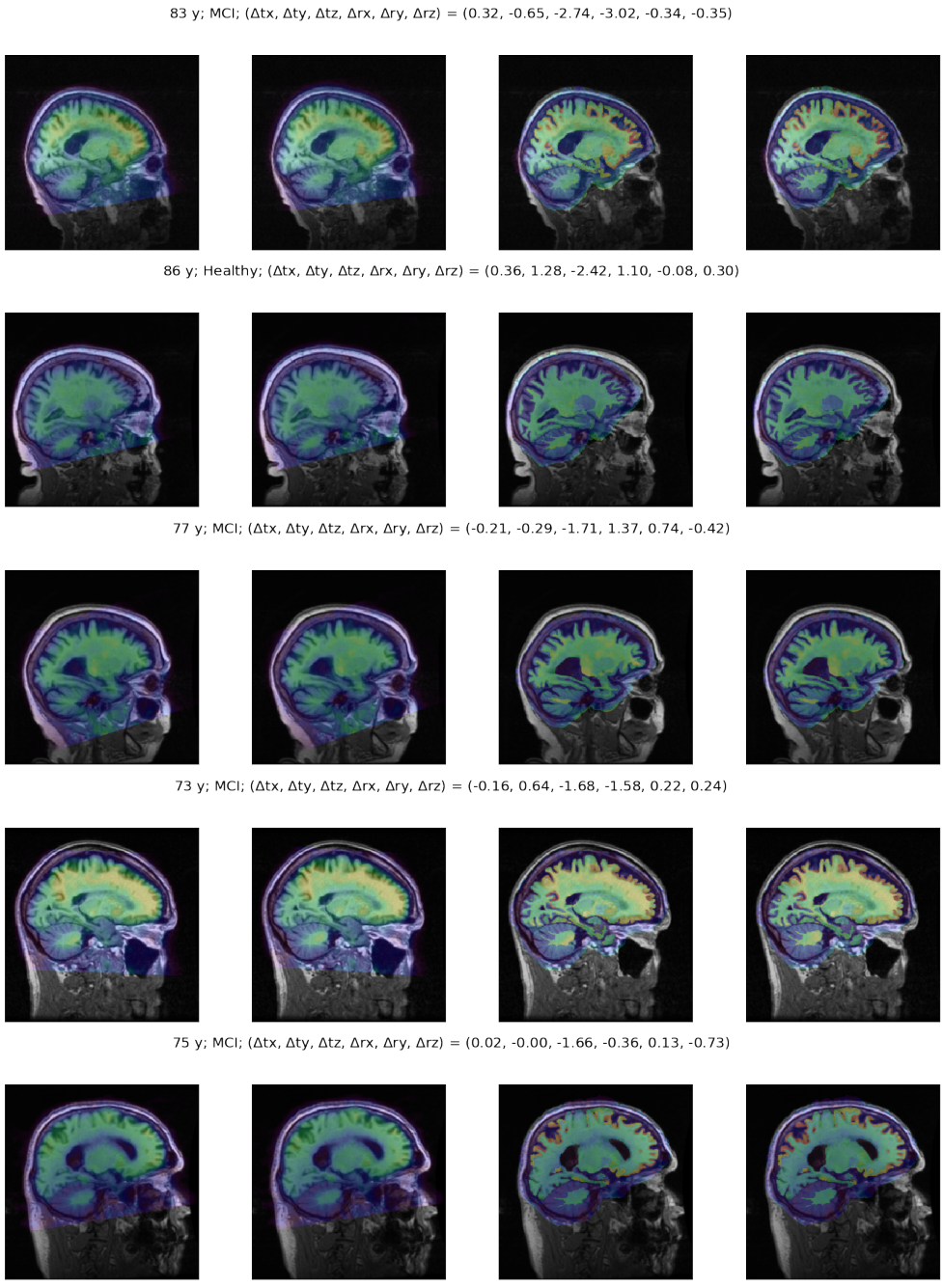


Figure S3.**Comparison of SUV images between conventional registration and PoR methods**



SUV images without PVC (1st and 2nd columns) and with PVC (3rd and 4th columns) for the five cases with the largest differences in translation in the z-axis between conventional registration (1st and 3rd columns) and PoR (2nd and 4th columns). Each row indicates images for a single participant. PVC, partial volume correction; SUV, standardized uptake value

Figure S4. **Scatter plots between uncorrected SUVR on the cerebral cortex and differences in the registration results between the conventional registration and PoR based on five iterations. The red line indicates a regression line in case that correlation was significant ($p < 0.05$).**

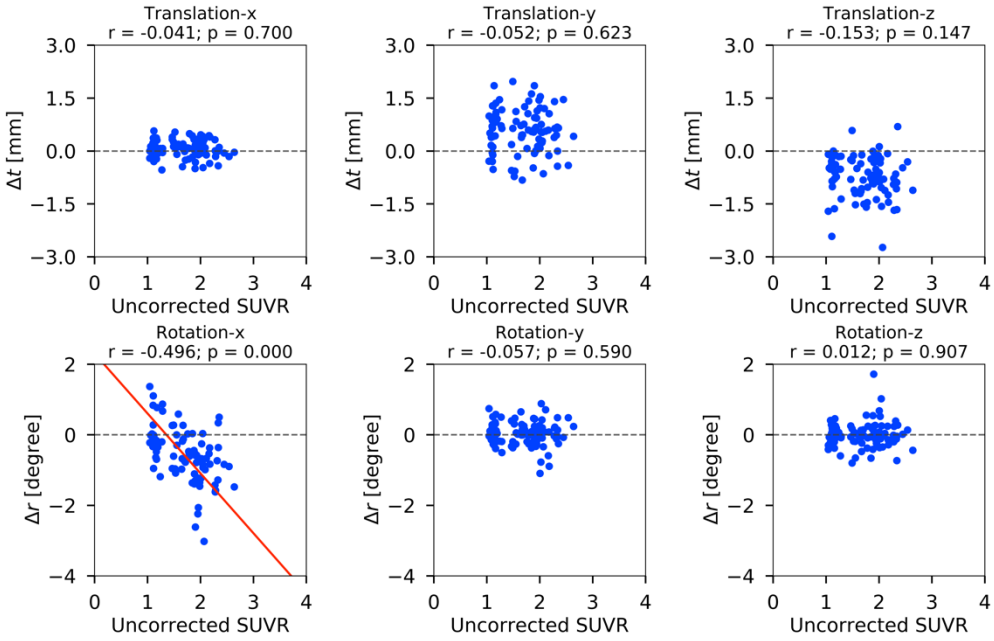
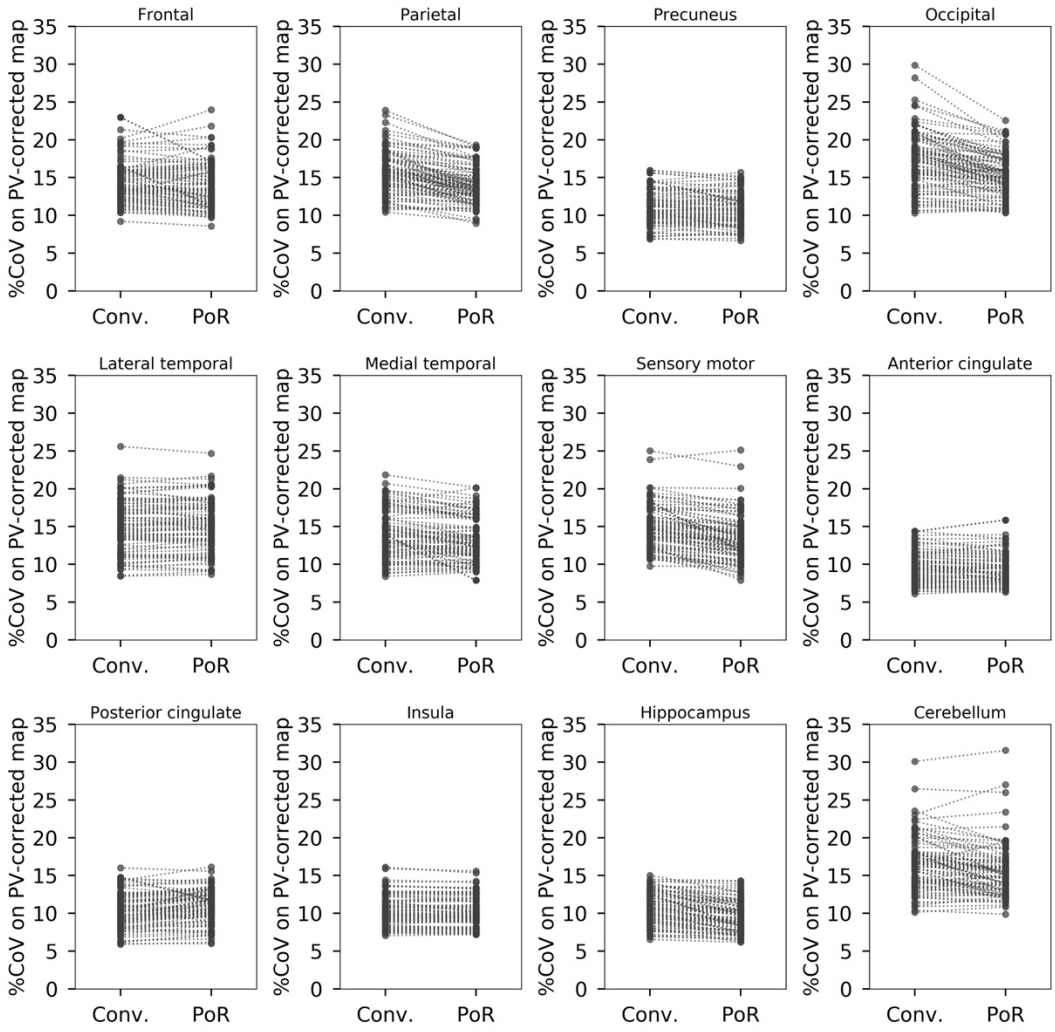
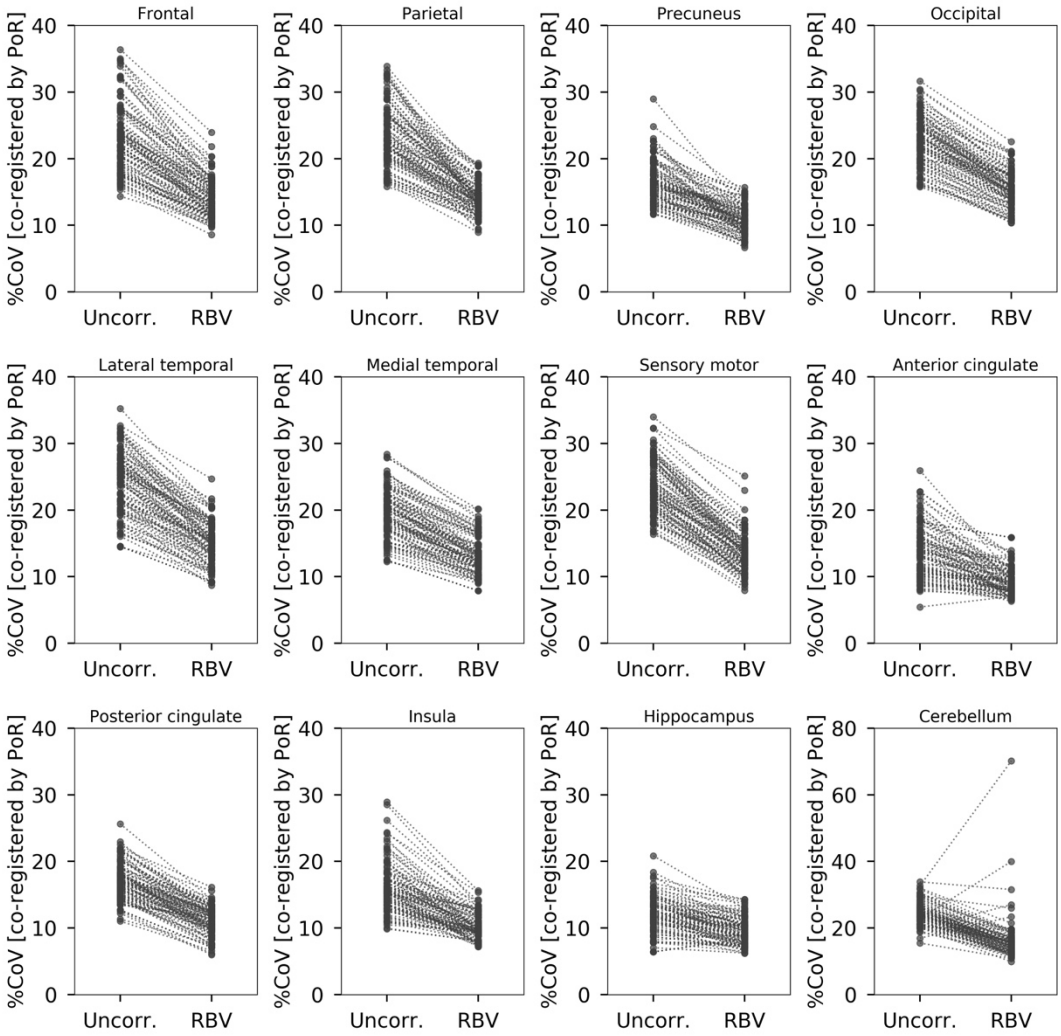


Figure S5. **Changes in CoV on PV-corrected SUV maps between conventional registration and PoR for all VOIs.**



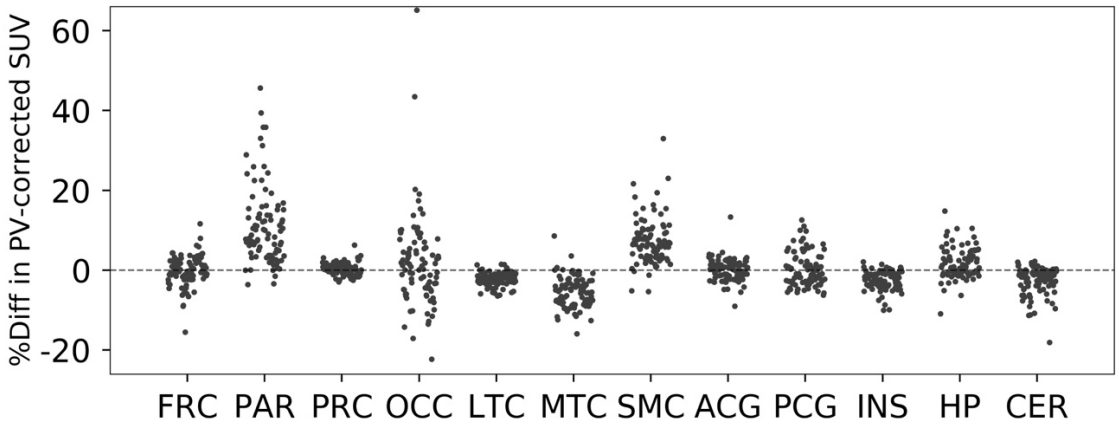
CoV, coefficient of variation; PoR, PVC-optimized registration; PV, partial volume; SUV, standardized uptake value; VOI, volume of interest.

Figure S6. **Changes in CoV between PV-uncorrected and PV-corrected SUV maps coregistered by PoR for all VOIs.**



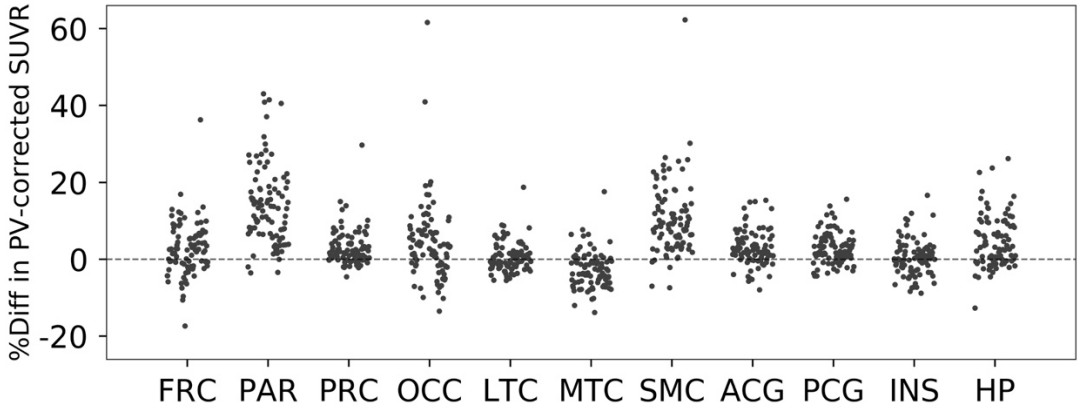
CoV, coefficient of variation; PoR, PVC-optimized registration; PV, partial volume; RBV, region-based voxelwise; SUV, standardized uptake value; VOI, volume of interest.

Figure S7. **% Differences in PV-corrected SUV between conventional registration and PoR for all VOIs.**



ACG, anterior cingulate cortex; CER, cerebellum; FRC, frontal cortex; HP, hippocampus; INS, insula; LTC, lateral temporal cortex; MTC, medial temporal cortex; OCC, occipital cortex; PAR, parietal cortex; PCG, posterior cingulate cortex; PoR, PVC-optimized registration; PRC, precuneus; PV, partial volume; RBV, region-based voxelwise method; SMC, sensory motor cortex; SUV, standardized uptake value; VOI, volume of interest.

Figure S8. **% Differences in PV-corrected SUVR between conventional registration and PoR for all VOIs.**



ACG, anterior cingulate cortex; CER, cerebellum; FRC, frontal cortex; HP, hippocampus; INS, insula; LTC, lateral temporal cortex; MTC, medial temporal cortex; OCC, occipital cortex; PAR, parietal cortex; PCG, posterior cingulate cortex; PoR, PVC-optimized registration; PRC, precuneus; PV, partial volume; RBV, region-based voxelwise method; SMC, sensory motor cortex; SUVR, standardized uptake value ratio; VOI, volume of interest.

Table S4. **Values in CoV on PV-uncorrected and PV-corrected SUV maps coregistered by conventional registration and PoR**

VOI	PV-uncorrected		PV-corrected	
	Conventional [median (Q1, Q3)]	PoR [median (Q1, Q3)]	Conventional [median (Q1, Q3)]	PoR [median (Q1, Q3)]
Frontal cortex	23.1 (20.2, 25.8)	22.9 (19.1, 27.0)	13.6 (12.5, 15.8)	13.5 (11.7, 16.1)
Parietal cortex	25.7 (22.5, 29.8)	22.9 (20.5, 26.7)	15.7 (13.9, 17.4)	13.6 (12.4, 15.3)
Precuneus	16.0 (14.5, 18.6)	16.0 (14.3, 18.1)	10.6 (9.6, 11.9)	10.6 (9.2, 12.2)
Occipital cortex	23.8 (21.1, 27.2)	22.9 (20.0, 25.2)	17.3 (14.8, 19.4)	15.1 (13.6, 17.2)
Lateral temporal cortex	24.2 (20.5, 26.7)	24.7 (20.9, 27.7)	14.8 (13.1, 17.3)	15.0 (12.9, 17.5)
Medial temporal cortex	19.4 (16.7, 21.9)	19.8 (17.2, 22.0)	13.2 (11.4, 16.1)	12.9 (11.2, 15.2)
Sensory motor cortex	24.6 (22.4, 27.8)	23.1 (20.4, 27.0)	14.4 (12.5, 16.2)	13.2 (11.4, 14.9)
Anterior cingulate cortex	13.1 (10.6, 16.4)	13.2 (10.5, 16.0)	9.1 (7.7, 10.6)	8.9 (7.8, 10.4)
Posterior cingulate cortex	16.1 (14.7, 18.2)	17.0 (15.2, 18.7)	10.4 (9.0, 11.8)	11.2 (9.7, 12.5)
Insula	15.4 (13.1, 17.7)	15.4 (13.4, 18.2)	9.9 (8.9, 11.5)	9.6 (8.9, 11.5)
Hippocampus	12.3 (10.6, 14.3)	11.8 (10.3, 13.6)	10.5 (8.9, 12.3)	9.4 (8.1, 10.7)
Cerebellum	24.3 (22.6, 26.2)	24.0 (22.2, 26.1)	16.5 (14.1, 18.0)	15.0 (13.1, 16.9)

Q1 and Q3 refer to the 1st and 3rd quantiles of %difference, respectively. CoV, coefficient of variation; PoR, PVC-optimized registration; PV, partial volume; PVC, partial volume correction; SUV, standardized uptake value; VOI, volume of interest.

Table S5. **Values and their differences in intra-region CoV between PV-uncorrected and PV-corrected SUV maps, coregistered with PoR**

VOI	PV-uncorrected [median (Q1, Q3)]	PV-corrected [median (Q1, Q3)]	ΔCoV [median (Q1, Q3)]	*p* value	Effect size
Frontal cortex	22.9 (19.1, 27.0)	13.5 (11.7, 16.1)	−8.4 (−12.0, −6.8)	< 0.001	−2.73
Parietal cortex	22.9 (20.5, 26.7)	13.6 (12.4, 15.3)	−8.5 (−12.7, −6.7)	< 0.001	−2.32
Precuneus	16.0 (14.3, 18.1)	10.6 (9.2, 12.2)	−5.1 (−7.2, −3.8)	< 0.001	−1.87
Occipital cortex	22.9 (20.0, 25.2)	15.1 (13.6, 17.2)	−7.2 (−9.0, −5.9)	< 0.001	−3.41
Lateral temporal cortex	24.7 (20.9, 27.7)	15.0 (12.9, 17.5)	−8.6 (−11.4, −7.1)	< 0.001	−2.87
Medial temporal cortex	19.8 (17.2, 22.0)	12.9 (11.2, 15.2)	−6.1 (−8.1, −4.8)	< 0.001	−2.78
Sensory motor cortex	23.1 (20.4, 27.0)	13.2 (11.4, 14.9)	−10.2 (−12.2, −8.3)	< 0.001	−3.78
Anterior cingulate cortex	13.2 (10.5, 16.0)	8.9 (7.8, 10.4)	−3.2 (−6.8, −1.8)	< 0.001	−1.25
Posterior cingulate cortex	17.0 (15.2, 18.7)	11.2 (9.7, 12.5)	−5.7 (−7.3, −4.5)	< 0.001	−2.73
Insula	15.4 (13.4, 18.2)	9.6 (8.9, 11.5)	−5.2 (−8.1, −3.4)	< 0.001	−1.79
Hippocampus	11.8 (10.3, 13.6)	9.4 (8.1, 10.7)	−2.3 (−3.5, −1.2)	< 0.001	−1.25
Cerebellum	24.0 (22.2, 26.1)	15.0 (13.1, 16.9)	−9.6 (−11.1, −7.2)	< 0.001	−1.24

Q1 and Q3 refer to the 1st and 3rd quantiles of % difference, respectively. CoV, coefficient of variation; PoR, PVC-optimized registration; PV, partial volume; PVC, partial volume correction; SUV, standardized uptake value; VOI, volume of interest.

Table S6. **Differences in PV-corrected SUVs and the results of statistical analyses comparing conventional registration to PoR**

VOI	Conventional [median (Q1, Q3)]	PoR [median (Q1, Q3)]	%difference [median (Q1, Q3)]	Effect size
Frontal cortex	2.55 (1.16, 4.94)	2.55 (1.14, 5.03)	0.32 (−1.73, 2.40)	0.35
Parietal cortex	2.25 (0.94, 4.64)	2.48 (1.03, 4.95)	8.56 (3.73, 14.36)	0.83
Precuneus	3.07 (1.30, 6.37)	3.11 (1.33, 6.36)	0.17 (−0.60, 1.00)	0.15
Occipital cortex	1.39 (0.75, 2.80)	1.36 (0.74, 2.81)	0.77 (−4.85, 5.47)	−0.21
Lateral temporal cortex	2.13 (1.07, 4.00)	2.11 (1.05, 3.91)	−2.18 (−3.11, −1.17)	−0.78
Medial temporal cortex	2.30 (1.22, 3.61)	2.18 (1.22, 3.57)	−5.38 (−8.17, −2.64)	−0.90
Sensory motor cortex	1.87 (0.88, 3.74)	1.96 (0.93, 3.91)	6.46 (3.38, 9.37)	0.78
Anterior cingulate cortex	3.27 (1.50, 6.12)	3.31 (1.51, 6.00)	0.48 (−1.34, 1.38)	0.00
Posterior cingulate cortex	3.21 (1.41, 5.97)	3.16 (1.44, 5.92)	−1.00 (−2.81, 2.36)	−0.43
Insula	2.33 (1.31, 3.96)	2.32 (1.28, 3.92)	−1.87 (−3.63, −0.87)	−0.81
Hippocampus	1.90 (1.01, 2.79)	1.91 (1.01, 2.90)	0.90 (−0.59, 3.58)	0.51
Cerebellum	1.30 (0.75, 2.05)	1.25 (0.74, 2.02)	−1.50 (−3.94, −0.23)	−0.62

Q1 and Q3 refer to the 1st and 3rd quantiles of %difference, respectively. PVC, partial volume correction; SUV, standardized uptake value

Table S7. **Differences in PV-corrected SUVRs and the results of statistical analyses comparing conventional registration to PoR**

VOI	Conventional [median (Q1, Q3)]	PoR [median (Q1, Q3)]	%difference [median (Q1, Q3)]	Effect size
Frontal cortex	2.48 (0.98, 3.18)	2.57 (0.97, 3.32)	2.67 (−1.33, 6.63)	0.56
Parietal cortex	2.09 (0.79, 2.92)	2.24 (0.90, 3.42)	13.34 (6.60, 18.63)	1.14
Precuneus	3.14 (1.19, 4.23)	3.20 (1.18, 4.44)	2.08 (0.27, 4.77)	0.67
Occipital cortex	1.17 (0.68, 1.66)	1.18 (0.73, 1.70)	3.42 (−1.43, 7.52)	0.47
Lateral temporal cortex	1.74 (1.00, 2.62)	1.72 (0.98, 2.68)	−0.01 (−1.98, 1.88)	0.33
Medial temporal cortex	1.75 (1.23, 2.37)	1.64 (1.15, 2.36)	−3.55 (−6.01, −0.50)	−0.41
Sensory motor cortex	1.61 (0.85, 2.31)	1.73 (0.91, 2.57)	9.02 (4.08, 14.12)	0.91
Anterior cingulate cortex	2.86 (1.49, 3.52)	3.05 (1.49, 3.72)	2.44 (0.52, 5.35)	0.74
Posterior cingulate cortex	2.88 (1.49, 3.52)	2.93 (1.52, 3.54)	2.06 (0.45, 4.97)	0.57
Insula	1.86 (1.26, 2.44)	1.89 (1.23, 2.52)	0.10 (−2.28, 2.49)	0.30
Hippocampus	1.37 (1.30, 1.53)	1.42 (1.33, 1.61)	3.15 (−0.38, 9.32)	0.67

Q1 and Q3 refer to the 1st and 3rd quantiles of %difference, respectively. PVC, partial volume correction; SUVR, standardized uptake value ratio (reference region: cerebellum)