

**Brain imaging of sequential acquisition using a flexible PET scanner and 3-T MRI:
quantitative and qualitative assessment**

Satoshi Nakajima, MD, PhD¹, Yasutaka Fushimi, MD, PhD^{1*}, Takuya Hinoda, MD,
PhD¹, Akihiko Sakata, MD, PhD¹, Sachi Okuchi, MD, PhD¹, Yoshiki Arakawa, MD,
PhD², Takayoshi Ishimori, MD, PhD¹, Yuji Nakamoto, MD, PhD¹

¹Department of Diagnostic Imaging and Nuclear Medicine and ²Department of
Neurosurgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

***Corresponding author:** Yasutaka Fushimi, MD, PhD

Department of Diagnostic Imaging and Nuclear Medicine,

Graduate School of Medicine, Kyoto University,

54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto, 606-8507, Japan

Phone: +81-75-751-3760, FAX: +81-75-771-9709

E-mail: yfushimi@kuhp.kyoto-u.ac.jp

Article type: Original article

Funding: This work was supported by JSPS KAKENHI Grant No. 22K07746,

21K15826, 21K20834, and 21K15623.

Abstract

Objective: A mobile PET scanner termed flexible PET (fxPET) has been designed to fit existing MRI systems. The purpose of this study was to assess brain imaging with fxPET combined with 3-T MRI in comparison with conventional PET (cPET)/CT.

Methods: In this prospective study, 29 subjects with no visible lesions except for mild leukoaraiosis on whole brain imaging underwent 2-deoxy-2-[^{18}F]fluoro-D-glucose ([^{18}F]FDG) cPET/CT followed by fxPET and MRI. The registration differences between fxPET and MRI and between cPET and CT were compared by measuring spatial coordinates. Three-dimensional magnetization-prepared rapid acquisition gradient-echo T1-weighted imaging (T1WI) was acquired. We applied two methods of attenuation correction to the fxPET images: MR-based attenuation correction, which yielded fxPET_{MRAC}; and CT-based attenuation correction, which yielded fxPET_{CTAC}. The three PET datasets were co-registered to the T1WI. Following subcortical segmentation and cortical parcellation, volumes of interest were placed in each PET image to assess physiological accumulation in the brain. SUV_{mean} was obtained and compared between the three datasets. We also visually evaluated image distortion and clarity of fxPET_{MRAC}.

Results: Mean misregistration of fxPET/MRI was <3 mm for each margin. Mean registration differences were significantly larger for fxPET/MRI than for cPET/CT except for the superior margin. There were high correlations between the three PET datasets regarding SUV_{mean} . On visual evaluation of image quality, the grade of distortion was comparable between fxPET_{MRAC} and cPET, and the grade of clarity was acceptable but inferior for fxPET_{MRAC} compared with cPET.

Conclusions: fxPET could successfully determine physiological [^{18}F]FDG uptake; however, improved image clarity is desirable. In this study, fxPET/MRI at 3-T was feasible for brain imaging.

Keywords: Flexible PET, 3-T MRI, Brain PET/MRI, MR-based attenuation correction, CT-based attenuation correction

Manuscript text**Introduction**

PET/CT has become widely used in clinical practice because it successfully combines the superior metabolic information obtained by PET with anatomical information from CT [1, 2]. PET/MRI has been introduced into the clinical setting and shows several important advantages over PET/CT [3-5]. The simultaneous acquisition of high-quality PET and MRI data with the superior soft-tissue contrast of MRI are advantageous for lesion diagnosis [6]. MRI can provide additional functional information such as perfusion, diffusion, and metabolism simultaneously with PET [7-9]. Co-registration with motion correction for PET and MRI also becomes possible [10]. Using MRI instead of CT for attenuation correction can reduce radiation exposure, especially for patients undergoing repeat PET examinations [11, 12]. However, not all institutes can afford PET/MRI scanners.

As an alternative modality to integrated PET/MRI, mobile PET scanners have been developed to overcome the prohibitive cost of PET/MRI equipment [13]. Flexible PET (fxPET) is a prototype MRI-compatible mobile PET system, as an external-type scanner that fits into existing MRI systems [14-16]. The fxPET system has two arc-shaped detector heads consisting of a silicon photomultiplier-based detector, which

Flexible PET and 3-T MRI for brain

enables fused PET and MR images to be obtained by sequential PET and MR scanning [17, 18]. The central angle of each detector head is 135 degrees. The time-of-flight (TOF) detector effectively compensates for the count loss caused by incomplete detector coverage. An MR-insertable PET has been reported as suitable for simultaneous PET and MR imaging of the human brain [19]; however, PET of the body is compromised owing to the limited field of view (FOV). The next step in this process is to develop a clinically applicable PET system that could be used for both brain PET and body PET.

A previous imaging study of the brain showed the feasibility of fxPET combined with 1.5-T MRI in terms of image quality, registration accuracy, and accuracy of regional 2-deoxy-2- ^{18}F fluoro-D-glucose (^{18}F FDG) uptake [15]. With regard to ^{18}F FDG uptake, the above study reported that the mean standardized uptake value (SUV_{mean}) was significantly higher in fxPET than in conventional PET (cPET) for normal structures, possibly because of the attenuation correction method used for fxPET. Therefore, in the present study we reconstructed the original fxPET data using a μ -map derived from CT acquired as part of cPET/CT to perform CT-based attenuation correction (CTAC), using an MRI-derived μ -map to perform MR-based attenuation correction (MRAC). It has been reported that the degradation in image quality associated with incomplete coincident data acquisition due to the open ring geometry

can be reduced by moving the detector heads closer to the subject [20]. In terms of registration accuracy and metrics of image quality such as distortion and clarity, it is necessary to determine whether changing the FOV would affect brain PET imaging. In addition, as integrated PET/3-T MRI has already been introduced into clinical practice, a mobile PET scanner with 3-T MRI would be desirable for brain imaging.

This prospective study aimed to perform quantitative and qualitative assessment of brain imaging conducted by fxPET/MRI at 3-T using MRAC and CTAC with a closer layout of the two detector heads, in comparison with cPET/CT.

Materials and methods

Subjects

This prospective study was approved by Kyoto University Certified Review Board and was registered with the Japan Registry of Clinical Trials (No. jRCTs052190034).

Informed consent was obtained from each subject. The study was conducted between October 2019 and August 2020, and included 29 subjects (17 men and 12 women; mean age, 69 years; age range, 42–84 years) who had no visible lesions on whole brain imaging except for mild leukoaraiosis.

Imaging Protocol

All subjects underwent a single-injection, dual-imaging protocol consisting of cPET/CT and subsequent fxPET/MRI on the same day. They fasted for at least 4 h prior to the intravenous administration of 3.5 MBq/kg of [^{18}F]FDG, and rested for 30 min before scanning. None of the subjects had a blood glucose level >200 mg/dl. After cPET/CT was performed, each subject was moved to the fxPET/MRI unit where fxPET was performed, followed by MRI.

cPET/CT

cPET/CT scans were performed using Discovery IQ (GE Healthcare, Waukesha, WI, United States). Low-dose CT parameters were as follows: 120 kVp; transaxial FOV, 500 $\times$ 500 mm; matrix size, 512 $\times$ 512; slice thickness, 3.75 mm. Attenuation correction was performed using the CT data. cPET images were reconstructed with a 3D ordered subsets expectation–maximization algorithm (VUE Point HD) and point spread function using the following parameters: iterations, 10; subsets, 12; transaxial FOV, 250 $\times$ 250 mm; matrix size, 192 $\times$ 192; axial FOV, 250 mm; voxel size, 1.3 $\times$ 1.3 $\times$ 3.3 mm; post-filtering at 2 mm full-width at half-maximum. The sensitivity of cPET was 22.80 cps/kBq [21] TOF reconstruction was not available for cPET. An emission scan of the

Flexible PET and 3-T MRI for brain

brain was conducted for 15 min, according to our routine clinical protocol. CT images were registered to the corresponding cPET images based on the routine clinical protocol.

fxPET/MRI

fxPET has two arc-shaped detector heads with a ring diameter of 778 mm and an axial extent of 150 mm. Each of the detector heads comprises 18 detector modules in the transaxial direction and three rings in the axial direction. The detector module consists of four-layer depth-of-interaction crystal blocks of 16×16 arrays of lutetium gadolinium oxyorthosilicate crystal ($2.9 \times 2.9 \times 20$ mm), a light guide, and a 64-channel MRI-compatible silicon photomultiplier array. The coincidence timing resolution was approximately 500 ps. Scatter correction was performed using TOF-single scatter simulation. Table 1 shows the scanner characteristics of fxPET and cPET. Silicon photomultipliers have been reported to have superior sensitivity and spatial resolution compared to photomultiplier tubes [22].

fxPET scans were performed with the detector heads arranged in a top–bottom configuration. The inner diameter of the detector was set to 628 mm, which brought the two detector heads closer than described in previous studies [14, 15]. The estimated

Flexible PET and 3-T MRI for brain

sensitivity of fxPET using the manufacturer's PET simulation software was 4.08 cps/kBq for the detector with inner diameter of 628 mm. All fxPET data were acquired in listmode. The reconstruction algorithm was a non-local means regularized version of 3D dynamic row-action maximum-likelihood algorithm with point spread function [23], using the following parameters: iteration, 1; subsets, 32; matrix size, $480 \times 480 \times 100$; voxel size, $1.5 \times 1.5 \times 1.5$ mm; regularization parameter, $\alpha = 0.016$; relaxation control parameter, $\beta = 30$; no post-filtering. The acquisition time was 10 min.

MRI scans were performed using 3-T MRI (Magnetom Skyra; Siemens Healthineers, Erlangen, Germany) with a 32-channel head coil. The acquisition parameters of three-dimensional magnetization-prepared rapid acquisition gradient-echo T1-weighted imaging (T1WI) were as follows: TR, 1900 ms; TE, 2.58 ms; inversion time, 900 ms; FOV, 230×230 mm; matrix size, 256×256 ; slice thickness, 0.9 mm. MR images were registered to the fxPET images using location information obtained by an optical camera (Polaris; Northern Digital Inc., Waterloo, Canada). Figure 1 shows the MRI scanner with the fxPET attached.

We reconstructed the original fxPET data with a μ -map derived from T1WI to produce MRAC, as well as with another μ -map derived from CT acquired as part of cPET/CT to produce CTAC. The MRAC method considered signal attenuation from

Flexible PET and 3-T MRI for brain

bone [24] and MR devices. The attenuation map was estimated by a hybrid segmentation-atlas method, which is based on segmentation of the MR image into three regions (bone–air, soft tissue, and water) using Otsu’s thresholding method [25] and the non-rigid spatial transformation of a template attenuation map to assign the template bone and air attenuation values to subject-specific bone and air regions (i.e., low MR signal regions), respectively. The attenuation map for the MRI table and head coil was obtained by means of a transmission scan using the background activity from lutetium gadolinium oxyorthosilicate scintillators as a transmission source. The attenuation map in CTAC was created in three steps. We first converted CT values to μ -values, as described previously [26]. The converted images were then registered to the attenuation map in MRAC by voxel-based similarity maximization with reference to a previous study [27]. We then added the patient bed component to the registered image.

Registration Accuracy

For evaluation of misregistration, we measured the spatial coordinates using Freeview implemented on FreeSurfer (ver. 7.1.1; <https://surfer.nmr.mgh.harvard.edu>). We determined six margins (right, left, anterior, posterior, upper and lower) of physiological [^{18}F]FDG uptake in the brain on fxFET_{MRAC} and cPET, and measured the spatial

Flexible PET and 3-T MRI for brain

coordinates of the margins. We also determined six margins of the brain on T1WI and CT, and measured the spatial coordinates of each. The coordinate differences between $\text{fxPET}_{\text{MRAC}}$ and T1WI and between cPET and CT were then calculated for each margin. The above evaluation was performed by two radiologists (S.N. and T.H., with 16 and 13 years of experience, respectively, in neuroradiology) and we averaged the coordinate differences. Figures 2 and 3 show representative images of fxPET/MRI and cPET/CT of the same subject (72-years-old male).

Regional [^{18}F]FDG Uptake

Three datasets of PET imaging ($\text{fxPET}_{\text{MRAC}}$, $\text{fxPET}_{\text{CTAC}}$, and cPET) were co-registered to the T1WI volume using the rigid body registration function of SPM12 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm12>) implemented in Matlab (R2018a; MathWorks, Natick, MA, United States). T1WI volumes were segmented by the recon-all function of FreeSurfer. A volume of interest (VOI) for physiological [^{18}F]FDG accumulation was placed in each segmented region of the bilateral Cerebral-Cortex, Cerebellum-Cortex, Thalamus-Proper, Caudate, Putamen, Pallidum and Cerebral-White-Matter, and the SUV_{mean} was obtained on $\text{fxPET}_{\text{MRAC}}$, $\text{fxPET}_{\text{CTAC}}$, and cPET using 3D Slicer (<https://www.slicer.org>). In addition, parcellation (aparc+aseg) was

Flexible PET and 3-T MRI for brain

performed for the cerebral cortex, and the SUV_{mean} was obtained in each parcellated region on $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET. Figure 4 shows representative PET images overlaid with VOIs.

Statistical Analysis

A paired t test was used to compare coordinate differences between paired images ($fxPET/MRI$ and $cPET/CT$) and SUV_{mean} of the difference between $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET. Pearson's correlation coefficients (r) were calculated to compare SUV_{mean} of $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET. In addition, the degree of consistency of SUV_{mean} among $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET was assessed by calculating the intraclass correlation coefficients (ICCs). ICCs and the 95% confidence intervals were calculated using a two-way random model with single measurement. Furthermore, we calculated the differences of SUV_{mean} between Cerebral-Cortex and Cerebral-White-Matter on $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET, and performed a paired t test to compare them. A P value < 0.05 was considered to indicate statistical significance. A commercially available statistical software package (MedCalc, ver. 19.8; MedCalc Software, Ostend, Belgium) was used for statistical analysis.

Voxel-by-voxel Analyses of Regional [^{18}F]FDG Distribution

To evaluate the differences in regional [^{18}F]FDG distribution between fxPET (fxPET_{MRAC} and fxPET_{CTAC}) and cPET, voxel-by-voxel analyses were performed using SPM12. T1WI were spatially normalized to Montreal Neurological Institute space. The same spatial transformation was applied to co-registered PET images. Normalized images were smoothed with an 8 mm isotropic Gaussian kernel. A paired t test was used to compare the regional uptake differences between fxPET and cPET. Correction for multiple comparisons was conducted at the voxel level using a familywise error corrected peak threshold of $P < 0.05$.

In addition, we compared μ -maps of MRAC and CTAC for one subject shown in Figures 2 and 3.

Image Quality of fxPET_{MRAC}

We visually evaluated image distortion and clarity of fxPET_{MRAC} in horizontal section using a four-point grading scale, based on the consensus decision of two radiologists (S.N. and A.S., with 16 and 14 years of experience, respectively, in neuroradiology), using ImageJ (ver. 1.52a; <http://imagej.nih.gov/ij/index.html>). The following grading system was used: 0 = unacceptable; 1 = acceptable but inferior to cPET; 2 = comparable

Flexible PET and 3-T MRI for brain

to cPET; 3 = superior to cPET. We also evaluated the fxPET_{MRAC} images for the presence of artifacts.

Results

All subjects underwent cPET/CT and subsequent fxPET/MRI without any problems. No subject was excluded from the study. Time from [¹⁸F]FDG injection to the start of fxPET scan was 100 ± 16 min (range, 75–129 min).

Registration Accuracy

Mean misregistration of fxPET/MRI and cPET/CT in the six margins is shown in Table 2. Registration accuracy of fxPET/MRI was <3 mm. Mean registration differences of fxPET/MRI were significantly larger than those of cPET/CT except for the superior margin.

Regional [¹⁸F]FDG Uptake

SUV_{mean} of fxPET_{MRAC} was significantly higher than that of cPET ($P < 0.001$). SUV_{mean} of fxPET_{CTAC} was significantly higher than that of cPET ($P < 0.001$). SUV_{mean} of fxPET_{MRAC} was significantly higher than that of fxPET_{CTAC} ($P < 0.001$). Table 3 shows

Flexible PET and 3-T MRI for brain

SUV_{mean} in bilateral Cerebral-Cortex, Cerebellum-Cortex, Thalamus-Proper, Caudate, Putamen, Pallidum and Cerebral-White-Matter on $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET.

Supplementary Table S1 shows P values for SUV_{mean} of the difference between

$fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET. Supplementary Table S2 shows SUV_{mean} in each parcellated region of the cerebral cortex.

We found high correlations for SUV_{mean} between $fxPET_{MRAC}$ and cPET ($r = 0.92$, $P < 0.001$), between $fxPET_{CTAC}$ and cPET ($r = 0.93$, $P < 0.001$), and between $fxPET_{MRAC}$ and $fxPET_{CTAC}$ ($r = 0.99$, $P < 0.001$) (Fig. 5). High correlations were also found in each segmented region of bilateral Cerebral-Cortex, Cerebellum-Cortex, Thalamus-Proper, Caudate, Putamen, Pallidum and Cerebral-White-Matter (Table 4); and in each parcellated region of the cerebral cortex (Supplementary Table S3). We found high consistency for SUV_{mean} in each region among $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET (Table 5 and Supplementary Table S4).

Regarding the differences of SUV_{mean} between Cerebral-Cortex and Cerebral-White-Matter, cPET was significantly higher than $fxPET_{MRAC}$, cPET was significantly higher than $fxPET_{CTAC}$, and $fxPET_{CTAC}$ was significantly higher than $fxPET_{MRAC}$ (Supplementary Tables S5 and S6).

Voxel-by-voxel Analyses of Regional [^{18}F]FDG Distribution

The [^{18}F]FDG uptake was higher mainly in the deep cerebral region for fxPET than for cPET (Supplementary Figures 1 and 2). On the other hand, the [^{18}F]FDG uptake was higher mainly in the cortex for cPET, especially in the frontal lobe, compared with fxPET.

Compared with CTAC, the attenuation coefficients in MRAC were slightly higher in the brain region and lower in the skull region (Supplementary Figure 3).

Image Quality of fxPET_{MRAC}

On visual evaluation of image quality of fxPET_{MRAC}, the grade of distortion was 2 (comparable to cPET) and the grade of clarity was 1 (acceptable but inferior to cPET) for all subjects. No artifacts were observed on fxPET_{MRAC} images.

Discussion

We assessed sequential brain fxPET/MRI at 3-T using a setup in which the two detector heads were located closer together, in comparison with cPET/CT. Mean misregistration of fxPET/MRI was <3 mm for each margin. The VOI analysis using segmented regions on T1WI obtained for fxPET/MRI showed that SUV_{mean} of fxPET_{MRAC} and fxPET_{CTAC}

Flexible PET and 3-T MRI for brain

demonstrated high correlations with that of cPET. The grade of distortion was comparable to cPET and the grade of clarity was acceptable, but inferior to cPET. No artifacts were observed on fxPET_{MRAC} images.

Registration accuracy of fxPET/MRI was <3 mm, which is comparable with the result of a previous phantom study [14]. Brendle et al. reported that misalignment was significantly larger for sequentially acquired PET/MRI than for PET/CT or simultaneously acquired PET/MRI [28]. Mean registration differences of fxPET/MRI were significantly larger than those of cPET/CT except for the superior margin, probably because the head fixation method of cPET/CT was more secure than that of fxPET/MRI. It might be possible to adopt retrospective registration correction to improve registration accuracy.

The SUV_{mean} of fxPET (fxPET_{MRAC} and fxPET_{CTAC}) and cPET showed a strong positive correlation regardless of region, which indicates that fxPET could successfully determine physiological [¹⁸F]FDG uptake. The correlation of SUV_{mean} between fxPET and cPET was higher in the cerebral cortex and much higher in the cerebellar cortex than that reported in a previous study [15], which we attribute to the improved uptake accuracy in fxPET due to the layout with the two detector heads closer together [20]. The SUV_{mean} of fxPET_{MRAC} and fxPET_{CTAC} showed a very strong positive correlation,

which is consistent with a previous report that compared MRAC and CTAC using the same PET data [29]. Although the difference in SUV_{mean} between $fxPET_{CTAC}$ and $cPET$ was smaller than the difference in SUV_{mean} between $fxPET_{MRAC}$ and $cPET$, SUV_{mean} values tended to be larger for $fxPET_{CTAC}$ than for $cPET$. There are several possible reasons for this difference, which include the smaller cross-sectional size of its scintillator crystal and higher spatial resolution as hardware considerations (Table 1); the TOF effect with fast convergence [30]; the four-layer depth-of-interaction system, which mitigated parallax error [31]; and the lack of a need for post-filtering of the non-local means algorithm, which had a positive quantitative effect on SUV in terms of partial volume effect [23, 32]. Regarding the results of voxel-by-voxel analyses, the higher uptake for $cPET$ (early scan) than for $fxPET$ (late scan) in the cerebellum was consistent with the literature [33], which might reflect changes in regional $[^{18}F]FDG$ distribution due to the difference in time from intravenous administration to the start of scanning. However, regarding the cerebrum, the regional $[^{18}F]FDG$ uptake differences between $fxPET$ and $cPET$ could be attributed to causes on the equipment or software, which is assumed that errors in the scatter correction had the largest effect, and other causes included errors in the attenuation correction and a high degree of smoothing by non-local means regularization. The same could be considered for the results of the

differences of SUV_{mean} between Cerebral-Cortex and Cerebral-White-Matter.

Furthermore, the SUV_{mean} of $fxPET_{MRAC}$ tended to be larger than that of $fxPET_{CTAC}$.

When the MR table and head coil are enclosed within the $fxPET$ gantry, as in this study,

it is theoretically possible to estimate and correct their attenuation by the

aforementioned transmission-based method. However, the attenuation correction for the

MRI table and head coil might have been inaccurate due to the low-quality attenuation

map for the MRI table and head coil reconstructed from the limited-count transmission

scan data. Compared with CTAC, the hybrid segmentation–atlas method for MRAC in

$fxPET$ could have a tendency to overestimate attenuation coefficient in the brain region,

resulting in excessive SUV.

Image quality of $fxPET_{MRAC}$ was lower than that of $cPET$ in terms of clarity;

however, the $fxPET_{MRAC}$ images were acceptable and no artifacts were demonstrated

after installing the $fxPET$ device near the existing MR system at 3-T. The possible

factors for $fxPET$ image quality include misregistration and incomplete data acquisition.

Misregistration between $fxPET$ and MRI would interfere with the application of

attenuation maps, resulting in inaccurate MRAC and CTAC. In this study,

misregistration of $fxPET/MRI$ were significantly larger than those of $cPET/CT$ except

for the superior margin. Incomplete data acquisition due to the open ring geometry

would lead to image degradation. Although the two detector heads were closer, remaining data acquisition loss would lead to image degradation. In order to improve image quality, the scatter correction algorithm would need to be improved and the regularization parameters adjusted. In addition, it might be a good idea to use anatomical high-resolution MR information in image reconstruction to compensate for the incomplete geometric coverage of fxPET. Acquisition time was 15 min for cPET and 10 min for fxPET, and this difference might have contributed to image quality. Also, the difference in time from [^{18}F]FDG injection to the start of scanning could have affected the image quality of fxPET and cPET because regional [^{18}F]FDG distribution changes depending on scanning starting time after intravenous administration [33, 34]. Advantages of fxPET are its low cost and that the system requires little additional space. In this study, we demonstrated the consistency of fxPET with MRI-compatibility at 3-T.

This study has several limitations. First, a relatively small number of subjects were studied. Second, patients with brain tumors and other conditions were not included. Third, all subjects received a single injection of [^{18}F]FDG, and the imaging sequence was cPET/CT first, followed by fxPET/MRI on the same day. Therefore, the elapsed time between [^{18}F]FDG injection and scanning differed between cPET and fxPET.

In conclusion, fxPET/MRI exhibited registration accuracy less than 3 mm for each margin and [^{18}F]FDG uptake highly correlated with cPET/CT. Although improved image clarity is desirable, the results of this study suggest the feasibility of fxPET/MRI at 3-T for brain imaging.

Acknowledgments

We are grateful to Tetsuya Kobayashi, Junichi Ohi, and Keishi Kitamura from Shimadzu Corporation for their technical advice. We also thank Taisuke Nagao, Masaaki Kajisako, and Shigeto Kawase for their technical support.

Declarations**Conflict of Interest**

Yuji Nakamoto obtained financial support from Shimadzu Corporation, Kyoto, Japan.

This prototype mobile PET scanner was developed by the company and was provided free of charge for use in this study. The other authors have no conflicts of interest directly relevant to the content of this article.

References

1. Bar-Shalom R, Yefremov N, Guralnik L, Gaitini D, Frenkel A, Kuten A, et al. Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. *J Nucl Med*. 2003;44:1200-9.
2. Antoch G, Saoudi N, Kuehl H, Dahmen G, Mueller SP, Beyer T, et al. Accuracy of whole-body dual-modality fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) for tumor staging in solid tumors: comparison with CT and PET. *J Clin Oncol*. 2004;22:4357-68.
3. Bailey DL, Pichler BJ, Gückel B, Antoch G, Barthel H, Bhujwalla ZM, et al. Combined PET/MRI: Global Warming-Summary Report of the 6th International Workshop on PET/MRI, March 27-29, 2017, Tübingen, Germany. *Mol Imaging Biol*. 2018;20:4-20.
4. Broski SM, Goenka AH, Kemp BJ, Johnson GB. Clinical PET/MRI: 2018 Update. *AJR Am J Roentgenol*. 2018;211:295-313.
5. Hope TA, Fayad ZA, Fowler KJ, Holley D, Iagaru A, McMillan AB, et al. Summary of the First ISMRM-SNMMI Workshop on PET/MRI: Applications and Limitations. *J Nucl Med*. 2019;60:1340-6.
6. Drzezga A, Souvatzoglou M, Eiber M, Beer AJ, Fürst S, Martinez-Möller A, et

Flexible PET and 3-T MRI for brain

al. First clinical experience with integrated whole-body PET/MR: comparison to PET/CT in patients with oncologic diagnoses. *J Nucl Med.* 2012;53:845-55.

7. Catana C, Drzezga A, Heiss WD, Rosen BR. PET/MRI for neurologic applications. *J Nucl Med.* 2012;53:1916-25.

8. Kishi S, Maeda M, Kogue R, Umino M, Matsubara T, Sakuma H. Hemangioblastoma of the Cerebellopontine Angle Evaluated with Pseudocontinuous Arterial Spin Labeling. *Magn Reson Med Sci.* 2021;20:18-9.

9. Imaizumi A, Obata T, Kershaw J, Tachibana Y, Inubushi M, Koizumi M, et al. Imaging of Hypoxic Tumor: Correlation between Diffusion-weighted MR Imaging and (18)F-fluoroazomycin Arabinoside Positron Emission Tomography in Head and Neck Carcinoma. *Magn Reson Med Sci.* 2020;19:276-81.

10. Chen KT, Salcedo S, Chonde DB, Izquierdo-Garcia D, Levine MA, Price JC, et al. MR-assisted PET motion correction in simultaneous PET/MRI studies of dementia subjects. *J Magn Reson Imaging.* 2018;48:1288-96.

11. Chawla SC, Federman N, Zhang D, Nagata K, Nuthakki S, McNitt-Gray M, et al. Estimated cumulative radiation dose from PET/CT in children with malignancies: a 5-year retrospective review. *Pediatr Radiol.* 2010;40:681-6.

12. Varoquaux A, Rager O, Poncet A, Delattre BM, Ratib O, Becker CD, et al.

Flexible PET and 3-T MRI for brain

Detection and quantification of focal uptake in head and neck tumours: (18)F-FDG PET/MR versus PET/CT. *Eur J Nucl Med Mol Imaging*. 2014;41:462-75.

13. Zeng T, Zheng J, Xia X, Chen X, Wang B, Zhang S, et al. Design and system evaluation of a dual-panel portable PET (DP-PET). *EJNMMI Phys*. 2021;8:47.

14. Nakamoto R, Nakamoto Y, Ishimori T, Fushimi Y, Kido A, Togashi K. Comparison of PET/CT with Sequential PET/MRI Using an MR-Compatible Mobile PET System. *J Nucl Med*. 2018;59:846-51.

15. Suzuki M, Fushimi Y, Okada T, Hinoda T, Nakamoto R, Arakawa Y, et al. Quantitative and qualitative evaluation of sequential PET/MRI using a newly developed mobile PET system for brain imaging. *Jpn J Radiol*. 2021;39:669-80.

16. Watanabe M, Kawai-Miyake K, Fushimi Y, Ishimori T, Nakajima A, Yoshimura M, et al. Application of a Flexible PET Scanner Combined with 3 T MRI Using Non-local Means Reconstruction: Qualitative and Quantitative Comparison with Whole-Body PET/CT. *Mol Imaging Biol*. 2022;24:167-76.

17. Yamakawa Y, Kobayashi T, Furuta M, Sato M, Ohi J, Tonami H, et al. Development of a dual-head mobile DOI-TOF PET system having multi-modality compatibility. 2014 IEEE Nucl Sci Symp Med Imag Conf. Seattle, WA, USA: IEEE; 2014. p. 1-3. doi:10.1109/NSSMIC.2014.7430879.

18. Furumiya T, Tsuda T, Tonami H, Satoh M, Nakazawa M, Ohi J, et al. Development of a SiPM based MR-compatible DOI-TOF-PET detector. 2014 IEEE Nucl Sci Symp Med Imag Conf. Seattle, WA, USA: IEEE; 2014. p. 1-3. doi:10.1109/NSSMIC.2014.7430888.
19. Hong KJ, Choi Y, Jung JH, Kang J, Hu W, Lim HK, et al. A prototype MR insertable brain PET using tileable GAPD arrays. *Med Phys*. 2013;40:042503.
20. Watanabe M, Nakamoto Y, Nakamoto R, Ishimori T, Saga T, Togashi K. Performance Evaluation of a Newly Developed MR-Compatible Mobile PET Scanner with Two Detector Layouts. *Mol Imaging Biol*. 2020;22:407-15.
21. Reynés-Llompart G, Gámez-Cenzano C, Romero-Zayas I, Rodríguez-Bel L, Vercher-Conejero JL, Martí-Climent JM. Performance Characteristics of the Whole-Body Discovery IQ PET/CT System. *J Nucl Med*. 2017;58:1155-61.
22. Wagatsuma K, Miwa K, Sakata M, Oda K, Ono H, Kameyama M, et al. Comparison between new-generation SiPM-based and conventional PMT-based TOF-PET/CT. *Phys Med*. 2017;42:203-10.
23. Watanabe M, Nakamoto Y, Nakamoto R, Ishimori T, Saga T, Togashi K. Qualitative and Quantitative Assessment of Nonlocal Means Reconstruction Algorithm in a Flexible PET Scanner. *AJR Am J Roentgenol*. 2021;216:486-93.

24. Tanigawa A, Yamaya T, Kawaguchi H, Hirano Y, Shiraishi T, Tanimoto K, et al. Hybrid segmentation-atlas method for PET-MRI attenuation correction. 2012 IEEE Nucl Sci Symp Med Imag Conf. Anaheim, CA, USA; 2012. p. 2727-9. doi:10.1109/NSSMIC.2012.6551620.
25. Otsu N. A Threshold Selection Method from Gray-Level Histograms. IEEE Trans Syst Man Cybern Syst. 1979;9:62-6.
26. Burger C, Goerres G, Schoenes S, Buck A, Lonn AH, Von Schulthess GK. PET attenuation coefficients from CT images: experimental evaluation of the transformation of CT into PET 511-keV attenuation coefficients. Eur J Nucl Med Mol Imaging. 2002;29:922-7.
27. Maes F, Collignon A, Vandermeulen D, Marchal G, Suetens P. Multimodality image registration by maximization of mutual information. IEEE Trans Med Imaging. 1997;16:187-98.
28. Brendle CB, Schmidt H, Fleischer S, Braeuning UH, Pfannenberger CA, Schwenzer NF. Simultaneously acquired MR/PET images compared with sequential MR/PET and PET/CT: alignment quality. Radiology. 2013;268:190-9.
29. Eiber M, Martinez-Möller A, Souvatzoglou M, Holzapfel K, Pickhard A, Löffelbein D, et al. Value of a Dixon-based MR/PET attenuation correction sequence for

Flexible PET and 3-T MRI for brain

the localization and evaluation of PET-positive lesions. *Eur J Nucl Med Mol Imaging*. 2011;38:1691-701.

30. Conti M. Focus on time-of-flight PET: the benefits of improved time resolution. *Eur J Nucl Med Mol Imaging*. 2011;38:1147-57.

31. Nakazawa M, Ohi J, Tonami H, Yamada Y, Furumiya T, Furuta M, et al. Development of a prototype DOI-TOF-PET scanner. 2010 IEEE Nucl Sci Symp Med Imag Conf. Knoxville, TN, USA; 2010. p. 2077-80. doi:10.1109/NSSMIC.2010.5874142.

32. Soret M, Bacharach SL, Buvat I. Partial-volume effect in PET tumor imaging. *J Nucl Med*. 2007;48:932-45.

33. Ishii K, Sakamoto S, Hosaka K, Mori T, Sasaki M. Variation in FDG uptakes in different regions in normal human brain as a function of the time (30 and 60 minutes) after injection of FDG. *Ann Nucl Med*. 2002;16:299-301.

34. Ishii K, Higashi Y, Tabata M, Miyaishi M, Mizutani T, Sasaki M. Necessity of a uniform start for scanning after FDG injection in brain PET study. *Ann Nucl Med*. 2006;20:329-31.

Figure Legends

Fig. 1 Flexible PET (fxPET) with two arc-shaped detector heads arranged in a top–bottom configuration, in combination with an existing MRI system. The fxPET scanner is seen in the middle and the MRI scanner is seen on the right

Fig. 2 Representative images of flexible PET (fxPET) using MR-based attenuation correction (MRAC) combined with 3-T MRI. **a** and **d**, T1-weighted imaging; **b** and **e**, fxPET_{MRAC}; **c**, fused image of **a** and **b**; **f**, fused image of **d** and **e**

Fig. 3 Representative images of conventional PET (cPET)/CT. **a** and **d**, CT; **b** and **e**, cPET; **c**, fused image of **a** and **b**; **f**, fused image of **d** and **e**

Fig. 4 Representative PET images (**a** fxPET_{MRAC}, **b** fxPET_{CTAC} and **c** cPET) overlaid with volumes of interest created by the recon-all function of FreeSurfer (aparc+aseg).

See Supplementary Table 2 for details of the anatomical sites.

cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET;

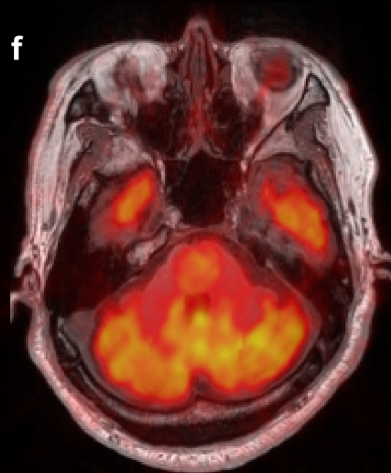
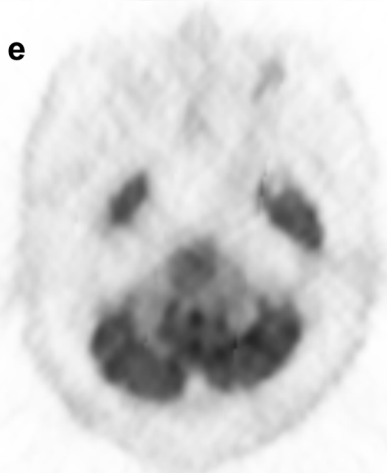
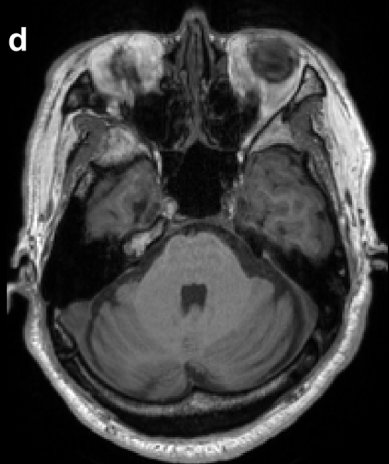
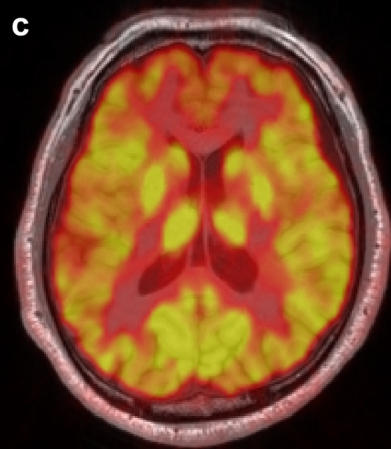
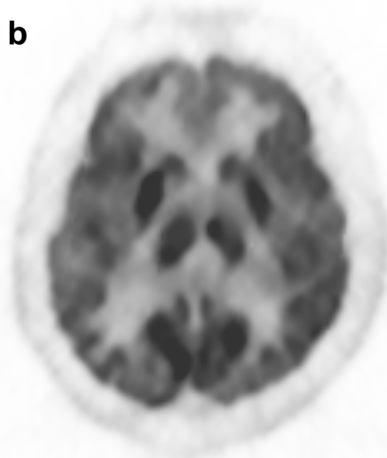
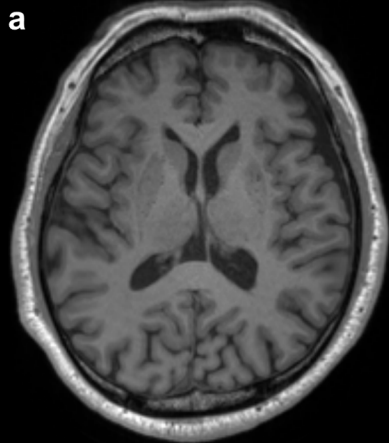
MRAC, MR-based attenuation correction

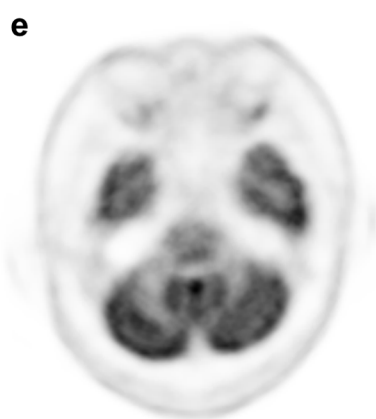
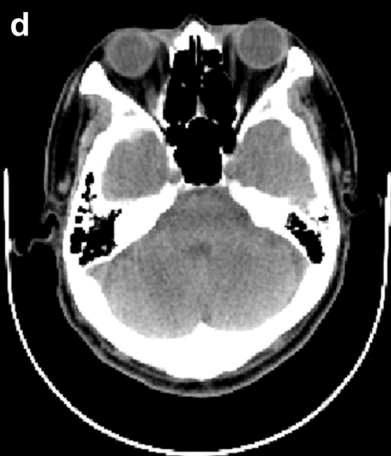
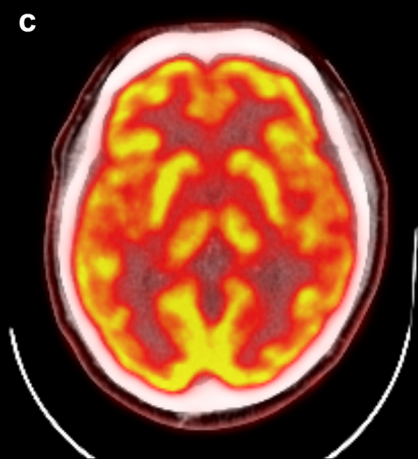
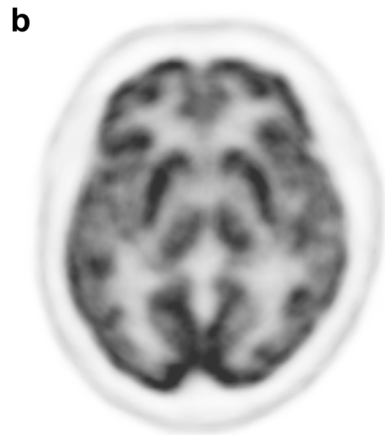
Fig. 5 Correlations for SUV_{mean} **a** between $fxPET_{MRAC}$ and cPET, **b** between $fxPET_{CTAC}$ and cPET, and **c** between $fxPET_{MRAC}$ and $fxPET_{CTAC}$.

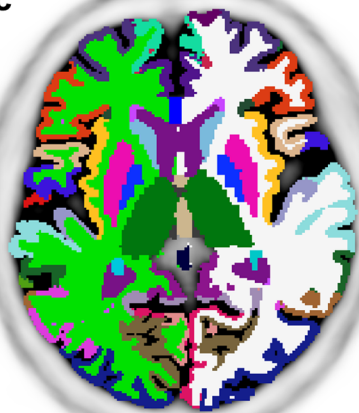
cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET;

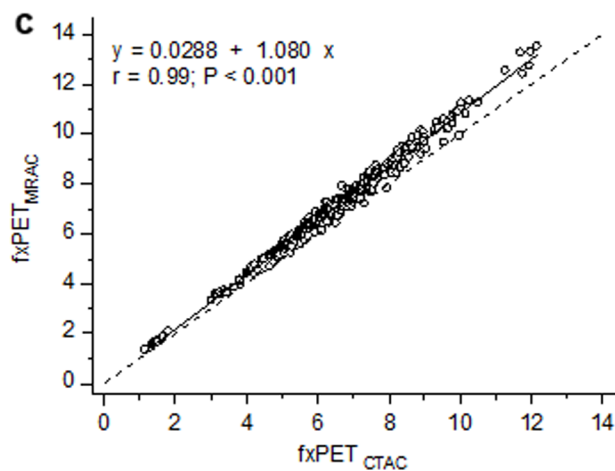
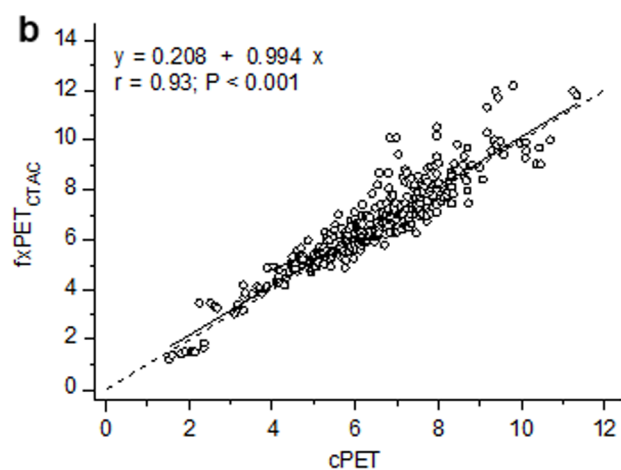
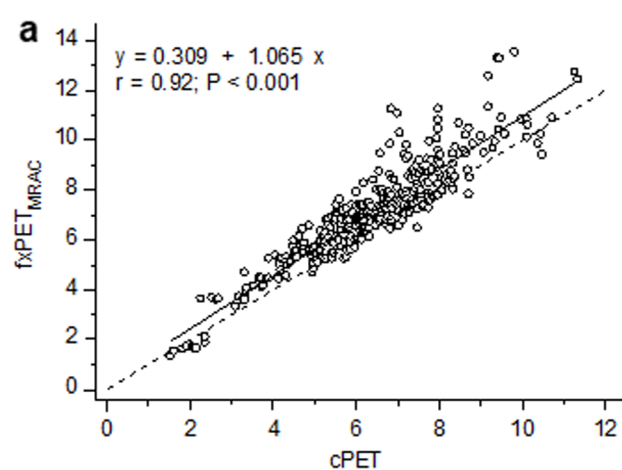
MRAC, MR-based attenuation correction; SUV, standardized uptake value







a**b****c**



Electronic Supplementary Material

**Brain imaging of sequential acquisition using a flexible PET scanner and 3-T MRI:
quantitative and qualitative assessment**

Journal: Annals of Nuclear Medicine

Satoshi Nakajima, MD, PhD¹, Yasutaka Fushimi, MD, PhD^{1*}, Takuya Hinoda, MD, PhD¹,
Akihiko Sakata, MD, PhD¹, Sachi Okuchi, MD, PhD¹, Yoshiki Arakawa, MD, PhD²,
Takayoshi Ishimori, MD, PhD¹, Yuji Nakamoto, MD, PhD¹

¹Department of Diagnostic Imaging and Nuclear Medicine and ²Department of Neurosurgery,
Graduate School of Medicine, Kyoto University, Kyoto, Japan

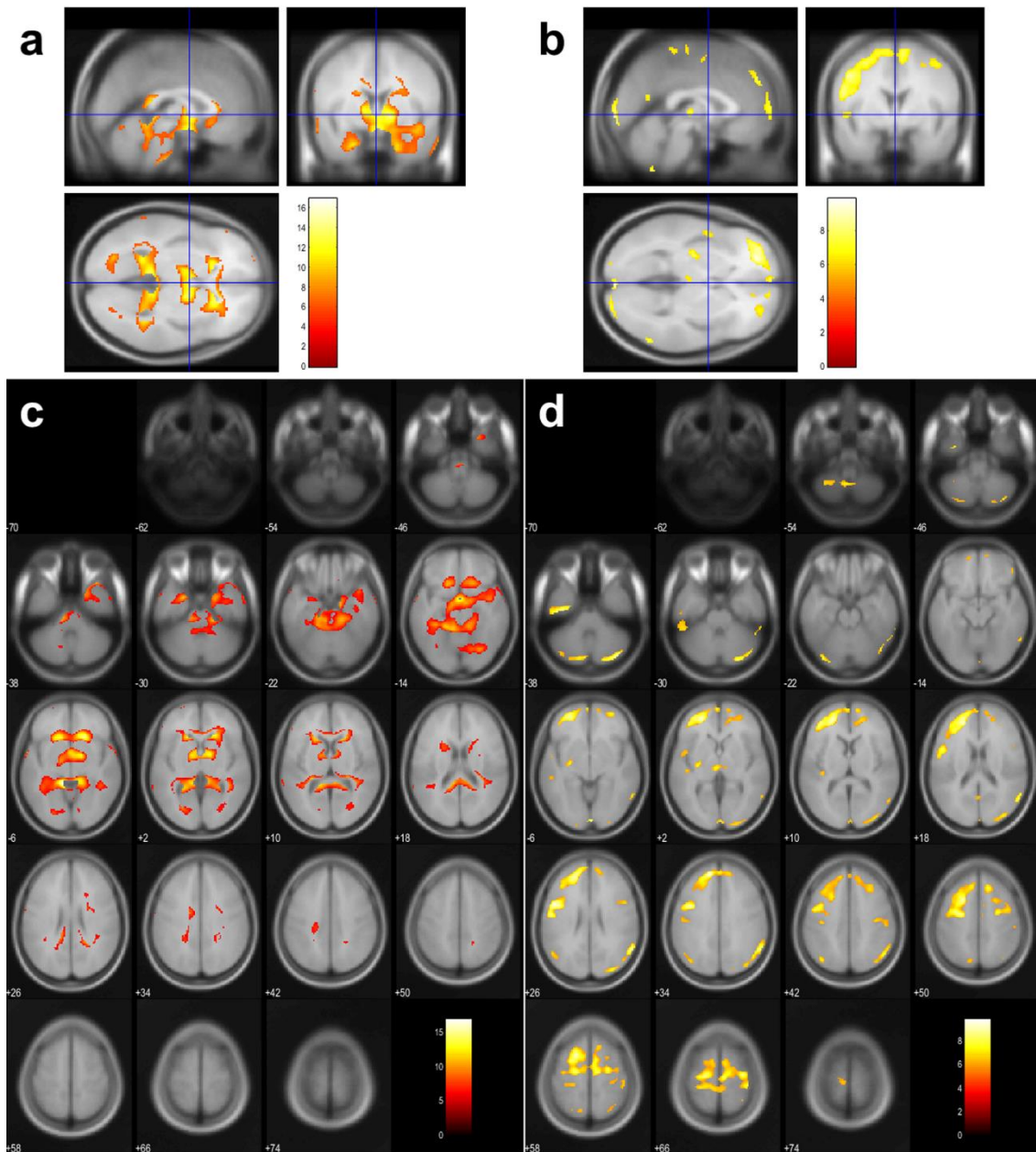
***Corresponding author:** Yasutaka Fushimi, MD, PhD

Department of Diagnostic Imaging and Nuclear Medicine,
Graduate School of Medicine, Kyoto University

54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto, 606-8507, Japan

Phone: +81-75-751-3760, FAX: +81-75-771-9709

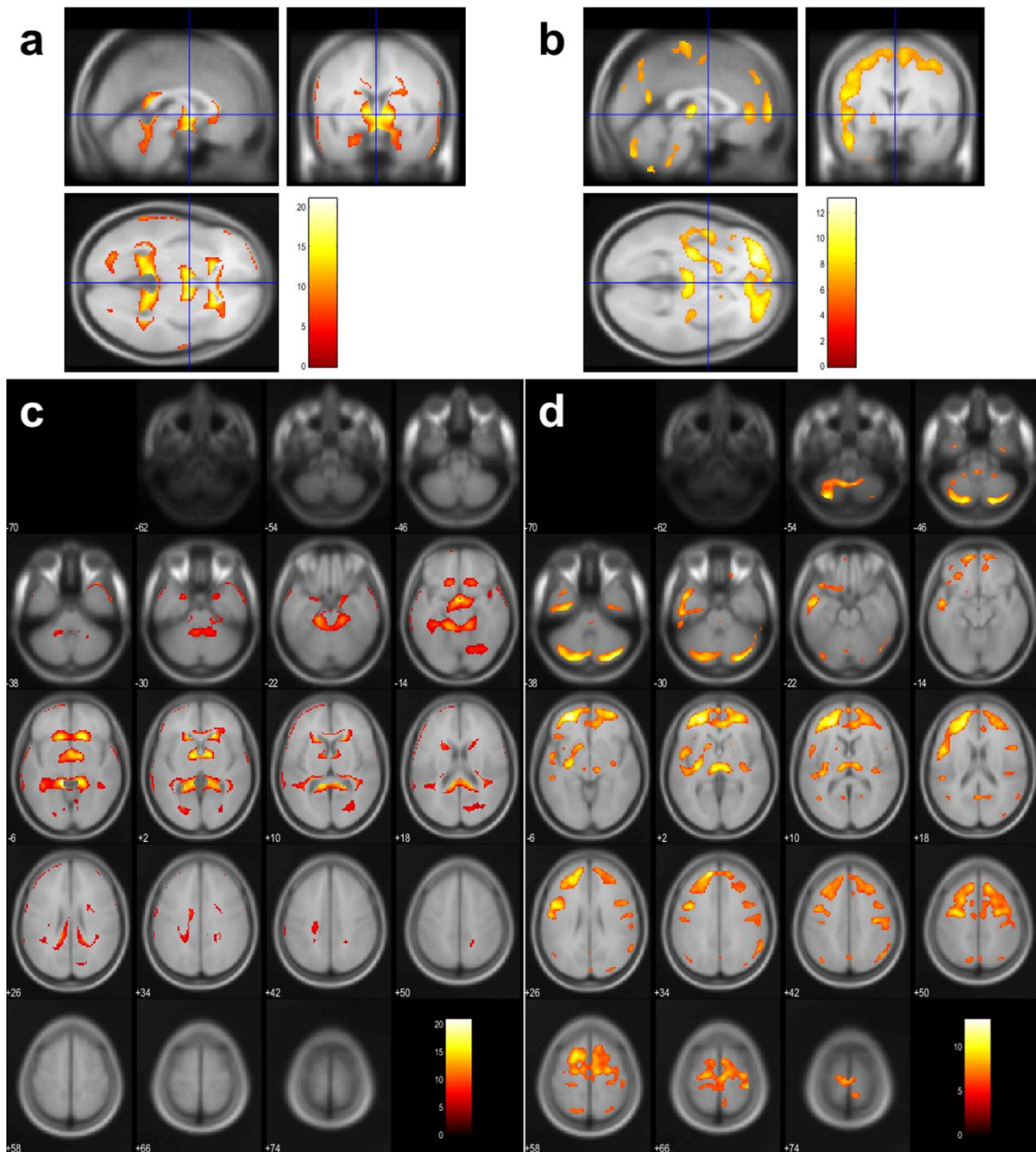
E-mail: yfushimi@kuhp.kyoto-u.ac.jp



Supplementary Fig. 1

Results of comparison between fxPET_{MRAC} and cPET (**a** and **c**, fxPET_{MRAC} > cPET; **b** and **d**, fxPET_{MRAC} < cPET). The [¹⁸F]FDG uptake is higher mainly in the deep cerebral region for fxPET_{MRAC} than for cPET (**a** and **c**). The [¹⁸F]FDG uptake is higher mainly in the cortex for cPET, especially in the frontal lobe, compared with fxPET_{MRAC} (**b** and **d**).

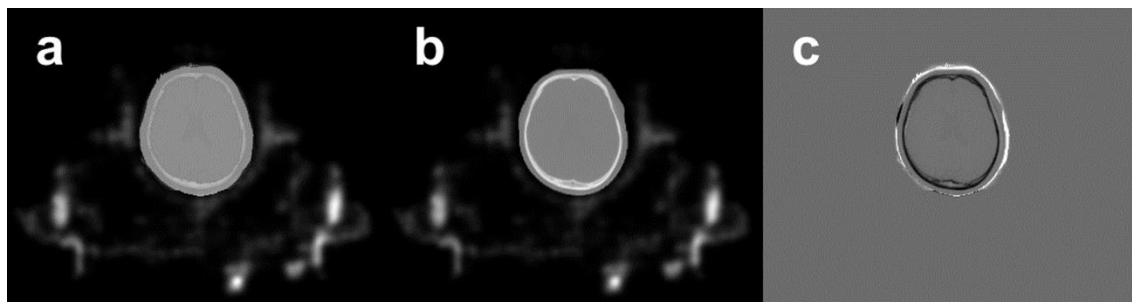
cPET, conventional PET; fxPET, flexible PET; MRAC, MR-based attenuation correction



Supplementary Fig. 2

Results of comparison between fxPET_{CTAC} and cPET (**a** and **c**, fxPET_{CTAC} > cPET; **b** and **d**, fxPET_{CTAC} < cPET). The [¹⁸F]FDG uptake is higher mainly in the deep cerebral region for fxPET_{CTAC} than for cPET (**a** and **c**). The [¹⁸F]FDG uptake is higher mainly in the cortex for cPET, especially in the frontal lobe, compared with fxPET_{CTAC} (**b** and **d**).

cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET



Supplementary Fig. 3

Representative images of μ -maps in **a** MRAC and **b** CTAC, and **c** MRAC minus CTAC.

Compared with CTAC, the attenuation coefficients in MRAC are slightly higher in the brain region and lower in the skull region.

CTAC, CT-based attenuation correction; MRAC, MR-based attenuation correction

Supplementary Table S1 *P* values for SUV_{mean} of the difference between $fxPET_{MRAC}$, $fxPET_{CTAC}$, and $cPET$

Volume of Interest	$fxPET_{MRAC}$ - $cPET$	$fxPET_{CTAC}$ - $cPET$	$fxPET_{MRAC}$ - $fxPET_{CTAC}$
Left-Cerebral-Cortex	0.012	0.486	< 0.001
Left-Cerebellum-Cortex	0.019	0.105	< 0.001
Left-Thalamus-Proper	< 0.001	0.953	< 0.001
Left-Caudate	< 0.001	< 0.001	< 0.001
Left-Putamen	0.003	0.454	< 0.001
Left-Pallidum	0.003	0.305	< 0.001
Right-Cerebral-Cortex	0.003	0.388	< 0.001
Right-Cerebellum-Cortex	0.002	0.584	< 0.001
Right-Thalamus-Proper	< 0.001	0.698	< 0.001
Right-Caudate	< 0.001	< 0.001	< 0.001
Right-Putamen	< 0.001	0.042	< 0.001
Right-Pallidum	< 0.001	< 0.001	< 0.001
Left-Cerebral-White-Matter	< 0.001	0.022	< 0.001
Right-Cerebral-White-Matter	< 0.001	0.009	< 0.001

$cPET$, conventional PET; CTAC, CT-based attenuation correction; $fxPET$, flexible PET; MRAC, MR-based attenuation correction; SUV, standardized uptake value

Supplementary Table S2 SUV_{mean} in each parcellated region of the cerebral cortex on $fxPET_{MRAC}$, $fxPET_{CTAC}$, and $cPET$

Volume of Interest	$fxPET_{MRAC}$	$fxPET_{CTAC}$	$cPET$
ctx-lh-caudalanteriorcingulate	6.39 ± 1.69	6.02 ± 1.64	5.98 ± 1.60
ctx-lh-caudalmiddlefrontal	7.22 ± 2.01	7.15 ± 2.06	7.46 ± 1.97
ctx-lh-cuneus	8.29 ± 2.37	8.00 ± 2.30	7.67 ± 2.14
ctx-lh-entorhinal	5.05 ± 1.30	4.55 ± 1.18	4.62 ± 1.05
ctx-lh-fusiform	7.07 ± 1.90	6.65 ± 1.81	6.28 ± 1.51
ctx-lh-inferiorparietal	7.23 ± 2.02	6.99 ± 1.96	6.93 ± 1.83
ctx-lh-inferiortemporal	6.69 ± 1.79	6.32 ± 1.72	6.33 ± 1.57
ctx-lh-isthmuscingulate	8.43 ± 2.26	8.03 ± 2.19	7.17 ± 1.81
ctx-lh-lateraloccipital	7.31 ± 2.03	7.33 ± 2.01	7.01 ± 1.79
ctx-lh-lateralorbitofrontal	7.08 ± 1.77	6.51 ± 1.67	6.73 ± 1.72
ctx-lh-lingual	8.15 ± 2.20	7.77 ± 2.12	7.11 ± 1.77
ctx-lh-medialorbitofrontal	6.91 ± 1.86	6.28 ± 1.72	6.25 ± 1.59
ctx-lh-middletemporal	6.91 ± 1.88	6.65 ± 1.85	6.26 ± 1.54
ctx-lh-parahippocampal	6.14 ± 1.50	5.71 ± 1.40	5.01 ± 1.15
ctx-lh-paracentral	6.84 ± 1.78	6.59 ± 1.74	6.67 ± 1.72
ctx-lh-parsopercularis	7.46 ± 2.02	7.12 ± 1.98	7.18 ± 1.87
ctx-lh-parsorbitalis	6.78 ± 1.79	6.42 ± 1.72	6.66 ± 1.75
ctx-lh-parstriangularis	7.48 ± 2.00	7.12 ± 1.93	7.00 ± 1.79
ctx-lh-pericalcarine	9.13 ± 2.62	8.65 ± 2.46	8.26 ± 2.26
ctx-lh-postcentral	6.69 ± 1.78	6.54 ± 1.78	6.43 ± 1.56
ctx-lh-posteriorcingulate	7.96 ± 2.19	7.54 ± 2.14	7.27 ± 2.01
ctx-lh-precentral	6.66 ± 1.73	6.53 ± 1.73	6.82 ± 1.68
ctx-lh-precuneus	8.36 ± 2.32	7.96 ± 2.23	7.76 ± 2.12
ctx-lh-rostralanteriorcingulate	6.52 ± 1.72	5.97 ± 1.61	6.05 ± 1.55
ctx-lh-rostralmiddlefrontal	7.09 ± 1.87	6.94 ± 1.91	7.21 ± 1.86
ctx-lh-superiorfrontal	6.55 ± 1.73	6.43 ± 1.74	6.64 ± 1.71
ctx-lh-superiorparietal	6.89 ± 1.85	6.70 ± 1.83	6.58 ± 1.76
ctx-lh-superiortemporal	6.26 ± 1.63	5.95 ± 1.58	5.68 ± 1.35
ctx-lh-supramarginal	7.18 ± 1.94	6.94 ± 1.91	6.60 ± 1.65
ctx-lh-frontalpole	5.89 ± 1.58	5.80 ± 1.54	5.86 ± 1.52
ctx-lh-temporalpole	5.10 ± 1.27	4.65 ± 1.20	4.40 ± 0.98
ctx-lh-transversetemporal	8.22 ± 2.23	7.76 ± 2.11	7.79 ± 1.94
ctx-lh-insula	6.22 ± 1.61	5.72 ± 1.51	5.70 ± 1.42

ctx-rh-caudalanteriorcingulate	6.38 ± 1.62	5.99 ± 1.58	6.08 ± 1.57
ctx-rh-caudalmiddlefrontal	7.31 ± 1.98	7.12 ± 1.97	7.38 ± 1.92
ctx-rh-cuneus	7.98 ± 2.34	7.76 ± 2.30	7.50 ± 2.13
ctx-rh-entorhinal	5.83 ± 1.52	5.00 ± 1.28	4.79 ± 1.11
ctx-rh-fusiform	7.31 ± 1.88	6.77 ± 1.75	6.29 ± 1.50
ctx-rh-inferiorparietal	7.10 ± 1.96	6.85 ± 1.91	6.90 ± 1.82
ctx-rh-inferiortemporal	7.10 ± 1.91	6.58 ± 1.76	6.34 ± 1.57
ctx-rh-isthmuscingulate	8.80 ± 2.40	8.34 ± 2.31	7.39 ± 1.91
ctx-rh-lateraloccipital	7.34 ± 2.02	7.28 ± 1.99	6.90 ± 1.76
ctx-rh-lateralorbitofrontal	7.46 ± 1.90	6.85 ± 1.79	6.67 ± 1.71
ctx-rh-lingual	8.18 ± 2.18	7.76 ± 2.09	7.00 ± 1.79
ctx-rh-medialorbitofrontal	7.07 ± 1.84	6.42 ± 1.71	6.38 ± 1.63
ctx-rh-middletemporal	7.21 ± 1.93	6.79 ± 1.86	6.38 ± 1.62
ctx-rh-parahippocampal	6.45 ± 1.60	5.84 ± 1.46	5.04 ± 1.16
ctx-rh-paracentral	6.72 ± 1.81	6.48 ± 1.78	6.68 ± 1.75
ctx-rh-parsopercularis	7.80 ± 2.12	7.31 ± 2.00	7.32 ± 1.99
ctx-rh-parsorbitalis	7.20 ± 1.91	6.91 ± 1.88	6.92 ± 1.88
ctx-rh-parstriangularis	7.70 ± 2.05	7.32 ± 1.98	7.10 ± 1.85
ctx-rh-pericalcarine	9.25 ± 2.73	8.83 ± 2.56	8.42 ± 2.39
ctx-rh-postcentral	6.53 ± 1.62	6.29 ± 1.60	6.42 ± 1.55
ctx-rh-posteriorcingulate	7.93 ± 2.11	7.50 ± 2.05	7.36 ± 1.98
ctx-rh-precentral	6.72 ± 1.69	6.48 ± 1.66	6.81 ± 1.68
ctx-rh-precuneus	8.32 ± 2.30	7.93 ± 2.21	7.74 ± 2.10
ctx-rh-rostralanteriorcingulate	6.47 ± 1.69	5.93 ± 1.59	6.22 ± 1.58
ctx-rh-rostralmiddlefrontal	7.43 ± 1.94	7.17 ± 1.94	7.28 ± 1.90
ctx-rh-superiorfrontal	6.64 ± 1.75	6.47 ± 1.76	6.65 ± 1.68
ctx-rh-superiorparietal	6.71 ± 1.82	6.48 ± 1.77	6.48 ± 1.76
ctx-rh-superiortemporal	6.64 ± 1.68	6.16 ± 1.58	5.77 ± 1.38
ctx-rh-supramarginal	6.77 ± 1.75	6.46 ± 1.70	6.54 ± 1.70
ctx-rh-frontalpole	6.19 ± 1.62	6.02 ± 1.60	6.09 ± 1.58
ctx-rh-temporalpole	5.74 ± 1.45	5.05 ± 1.31	4.52 ± 1.07
ctx-rh-transversetemporal	8.34 ± 2.04	7.68 ± 1.90	7.73 ± 1.90
ctx-rh-insula	6.58 ± 1.70	5.96 ± 1.55	5.79 ± 1.44

SUVs are shown as mean ± standard deviation. cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET; MRAC, MR-based attenuation correction; SUV, standardized uptake value

Supplementary Table S3 Pearson's correlation coefficient (r) for SUV_{mean} in each parcellated region of the cerebral cortex between $fxPET_{MRAC}$, $fxPET_{CTAC}$, and $cPET$

Volume of Interest	$fxPET_{MRAC}$ - $cPET$	$fxPET_{CTAC}$ - $cPET$	$fxPET_{MRAC}$ - $fxPET_{CTAC}$
ctx-lh-caudalanteriorcingulate	0.91	0.92	0.989
ctx-lh-caudalmiddlefrontal	0.92	0.92	0.992
ctx-lh-cuneus	0.95	0.96	0.997
ctx-lh-entorhinal	0.86	0.89	0.970
ctx-lh-fusiform	0.92	0.94	0.992
ctx-lh-inferiorparietal	0.93	0.94	0.994
ctx-lh-inferiortemporal	0.92	0.94	0.987
ctx-lh-isthmuscingulate	0.90	0.91	0.997
ctx-lh-lateraloccipital	0.92	0.93	0.985
ctx-lh-lateralorbitofrontal	0.90	0.91	0.992
ctx-lh-lingual	0.93	0.94	0.994
ctx-lh-medialorbitofrontal	0.90	0.91	0.995
ctx-lh-middletemporal	0.93	0.94	0.993
ctx-lh-parahippocampal	0.91	0.93	0.990
ctx-lh-paracentral	0.90	0.92	0.992
ctx-lh-parsopercularis	0.90	0.91	0.993
ctx-lh-parsorbitalis	0.92	0.91	0.982
ctx-lh-parstriangularis	0.90	0.91	0.992
ctx-lh-pericalcarine	0.93	0.94	0.996
ctx-lh-postcentral	0.92	0.93	0.992
ctx-lh-posteriorcingulate	0.93	0.94	0.994
ctx-lh-precentral	0.91	0.93	0.990
ctx-lh-precuneus	0.93	0.94	0.996
ctx-lh-rostralanteriorcingulate	0.92	0.93	0.997
ctx-lh-rostralmiddlefrontal	0.90	0.92	0.985
ctx-lh-superiorfrontal	0.89	0.91	0.991
ctx-lh-superiorparietal	0.92	0.94	0.993
ctx-lh-superiortemporal	0.94	0.95	0.994
ctx-lh-supramarginal	0.94	0.95	0.994
ctx-lh-frontalpole	0.86	0.88	0.973
ctx-lh-temporalpole	0.88	0.91	0.982
ctx-lh-transversetemporal	0.93	0.94	0.995

ctx-lh-insula	0.92	0.93	0.996
ctx-rh-caudalanteriorcingulate	0.90	0.92	0.987
ctx-rh-caudalmiddlefrontal	0.89	0.91	0.990
ctx-rh-cuneus	0.94	0.95	0.996
ctx-rh-entorhinal	0.90	0.92	0.973
ctx-rh-fusiform	0.92	0.93	0.991
ctx-rh-inferiorparietal	0.92	0.93	0.996
ctx-rh-inferiortemporal	0.92	0.93	0.989
ctx-rh-isthmuscingulate	0.90	0.91	0.997
ctx-rh-lateraloccipital	0.91	0.93	0.990
ctx-rh-lateralorbitofrontal	0.92	0.93	0.991
ctx-rh-lingual	0.94	0.94	0.996
ctx-rh-medialorbitofrontal	0.90	0.91	0.993
ctx-rh-middletemporal	0.90	0.91	0.995
ctx-rh-parahippocampal	0.92	0.93	0.990
ctx-rh-paracentral	0.92	0.93	0.992
ctx-rh-parsopercularis	0.91	0.92	0.995
ctx-rh-parsorbitalis	0.91	0.91	0.983
ctx-rh-parstriangularis	0.90	0.91	0.992
ctx-rh-pericalcarine	0.92	0.93	0.996
ctx-rh-postcentral	0.88	0.89	0.992
ctx-rh-posteriorcingulate	0.92	0.93	0.994
ctx-rh-precentral	0.89	0.90	0.989
ctx-rh-precuneus	0.93	0.94	0.996
ctx-rh-rostralanteriorcingulate	0.88	0.90	0.995
ctx-rh-rostralmiddlefrontal	0.90	0.91	0.991
ctx-rh-superiorfrontal	0.88	0.91	0.987
ctx-rh-superiorparietal	0.91	0.93	0.992
ctx-rh-superiortemporal	0.90	0.91	0.996
ctx-rh-supramarginal	0.91	0.92	0.995
ctx-rh-frontalpole	0.86	0.89	0.977
ctx-rh-temporalpole	0.92	0.93	0.986
ctx-rh-transversetemporal	0.90	0.92	0.996
ctx-rh-insula	0.92	0.93	0.997

cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET; MRAC, MR-based attenuation correction; SUV, standardized uptake value

Supplementary Table S4 Degree of consistency of SUV_{mean} in each parcellated region of the cerebral cortex among $fxPET_{MRAC}$, $fxPET_{CTAC}$, and $cPET$

Volume of Interest	ICC	95% CI
ctx-lh-caudalanteriorcingulate	0.94	0.89–0.97
ctx-lh-caudalmiddlefrontal	0.94	0.90–0.97
ctx-lh-cuneus	0.96	0.94–0.98
ctx-lh-entorhinal	0.90	0.83–0.95
ctx-lh-fusiform	0.94	0.89–0.97
ctx-lh-inferiorparietal	0.95	0.92–0.98
ctx-lh-inferiortemporal	0.95	0.91–0.97
ctx-lh-isthmuscingulate	0.93	0.87–0.96
ctx-lh-lateraloccipital	0.94	0.89–0.97
ctx-lh-lateralorbitofrontal	0.93	0.88–0.97
ctx-lh-lingual	0.95	0.90–0.97
ctx-lh-medialorbitofrontal	0.93	0.88–0.96
ctx-lh-middletemporal	0.95	0.91–0.97
ctx-lh-parahippocampal	0.93	0.88–0.96
ctx-lh-paracentral	0.94	0.89–0.97
ctx-lh-parsopercularis	0.93	0.88–0.97
ctx-lh-parsorbitalis	0.94	0.89–0.97
ctx-lh-parstriangularis	0.93	0.88–0.97
ctx-lh-pericalcarine	0.95	0.91–0.98
ctx-lh-postcentral	0.95	0.90–0.97
ctx-lh-posteriorcingulate	0.95	0.91–0.98
ctx-lh-precentral	0.94	0.90–0.97
ctx-lh-precuneus	0.95	0.92–0.98
ctx-lh-rostralanteriorcingulate	0.95	0.91–0.97
ctx-lh-rostralmiddlefrontal	0.94	0.89–0.97
ctx-lh-superiorfrontal	0.93	0.87–0.96
ctx-lh-superiorparietal	0.95	0.91–0.97
ctx-lh-superiortemporal	0.95	0.92–0.98
ctx-lh-supramarginal	0.96	0.92–0.98
ctx-lh-frontalpole	0.91	0.84–0.95
ctx-lh-temporalpole	0.91	0.84–0.95
ctx-lh-transversetemporal	0.95	0.92–0.98
ctx-lh-insula	0.95	0.90–0.97
ctx-rh-caudalanteriorcingulate	0.93	0.88–0.97
ctx-rh-caudalmiddlefrontal	0.93	0.88–0.96

ctx-rh-cuneus	0.96	0.93–0.98
ctx-rh-entorhinal	0.91	0.84–0.95
ctx-rh-fusiform	0.94	0.89–0.97
ctx-rh-inferiorparietal	0.95	0.90–0.97
ctx-rh-inferiortemporal	0.94	0.89–0.97
ctx-rh-isthmuscingulate	0.93	0.87–0.96
ctx-rh-lateraloccipital	0.94	0.89–0.97
ctx-rh-lateralorbitofrontal	0.94	0.90–0.97
ctx-rh-lingual	0.95	0.91–0.97
ctx-rh-medialorbitofrontal	0.93	0.88–0.97
ctx-rh-midletemporal	0.93	0.88–0.96
ctx-rh-parahippocampal	0.93	0.87–0.96
ctx-rh-paracentral	0.95	0.90–0.97
ctx-rh-parsopercularis	0.94	0.90–0.97
ctx-rh-parsorbitalis	0.93	0.88–0.97
ctx-rh-parstriangularis	0.93	0.88–0.97
ctx-rh-pericalcarine	0.95	0.91–0.97
ctx-rh-postcentral	0.92	0.86–0.96
ctx-rh-posteriorcingulate	0.95	0.91–0.97
ctx-rh-precentral	0.93	0.87–0.96
ctx-rh-precuneus	0.95	0.91–0.98
ctx-rh-rostralanteriorcingulate	0.93	0.87–0.96
ctx-rh-rostralmiddlefrontal	0.93	0.88–0.97
ctx-rh-superiorfrontal	0.93	0.87–0.96
ctx-rh-superiorparietal	0.94	0.90–0.97
ctx-rh-superiortemporal	0.93	0.88–0.96
ctx-rh-supramarginal	0.94	0.89–0.97
ctx-rh-frontalpole	0.91	0.84–0.95
ctx-rh-temporalpole	0.93	0.87–0.96
ctx-rh-transversetemporal	0.94	0.89–0.97
ctx-rh-insula	0.94	0.90–0.97

CI, confidence interval; cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET; ICC, intraclass correlation coefficient; MRAC, MR-based attenuation correction; SUV, standardized uptake value

Supplementary Table S5 The difference of SUV_{mean} between Cerebral-Cortex and Cerebral-White-Matter on $fxPET_{MRAC}$, $fxPET_{CTAC}$, and cPET

Cerebral Hemisphere	$fxPET_{MRAC}$	$fxPET_{CTAC}$	cPET
Left	1.12 ± 0.38	1.16 ± 0.41	1.31 ± 0.46
Right	1.07 ± 0.36	1.10 ± 0.38	1.29 ± 0.45

SUVs are shown as mean $\pm$ standard deviation. cPET, conventional PET; CTAC, CT-based attenuation correction; $fxPET$, flexible PET; MRAC, MR-based attenuation correction; SUV, standardized uptake value

Supplementary Table S6 *P* values for the difference of SUV_{mean} between Cerebral-Cortex and Cerebral-White-Matter

Cerebral Hemisphere	fxPET _{MRAC} - cPET	fxPET _{CTAC} - cPET	fxPET _{MRAC} - fxPET _{CTAC}
Left	< 0.001	< 0.001	0.018
Right	< 0.001	< 0.001	0.047

cPET, conventional PET; CTAC, CT-based attenuation correction; fxPET, flexible PET; MRAC, MR-based attenuation correction; SUV, standardized uptake value