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Head-to-head comparison of ^{11}C-PiB and ^{18}F-FC119S for Aβ imaging in healthy subjects, mild cognitive impairment patients, and Alzheimer's disease patients

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Abstract

As a new beta amyloid (Aβ) positron emission tomography (PET) tracer, ^{18}F-FC119S has shown higher cortical uptake in patients with Alzheimer's disease (AD) than that in healthy control subjects without adverse effects in a previous preliminary study. The aim of this study was to compare ^{18}F-FC119S PET and ^{11}C-PiB PET in healthy control (HC) subjects, mild cognitive impairment (MCI) patients, and AD patients.

A total of 48 subjects, including 28 HC subjects, 10 MCI patients, and 10 AD patients, underwent static ^{18}F-FC119S PET (30 minutes after intravenous [i.v.] injection) and ^{11}C-PiB PET (40 minutes after i.v. injection) on the same day. Both PET images were visually and quantitatively assessed. Standardized uptake value ratios (SUVRs) were calculated for each brain region using the cerebellar cortex as a reference region.

None (0%) of the 28 HC subjects and 4 (40%) of 10 MCI patients had positive scans on both PET images. Of the 10 AD patients, 7 (70%) had positive scans on ^{11}C-PiB PET while 6 (60%) had positive scans on ^{18}F-FC119S PET. Overall, 47 (98%) of 48 participants showed identical results based on visual analysis. Cortical SUVR of ^{18}F-FC119S was higher in AD patients (1.38 ± 0.16), followed by that in MCI patients (1.24 ± 0.10) and in HC subjects (1.14 ± 0.05). Compared with ^{11}C-PiB PET, ^{18}F-FC119S PET yielded a higher effect size ($d = 2.02$ vs. 1.67) in AD patients and a slightly lower effect size ($d = 1.26$ vs. 1.38) in MCI patients. In HC subjects, the nonspecific binding of ^{18}F-FC119S to white matter (with the frontal cortex-to-white matter SUV ratio of 0.76) was slightly lower than that of ^{11}C-PiB (ratio of 0.73). There was a significant linear correlation (slope = 0.41, $r = 0.78$, $P < 0.001$) between ^{11}C-PiB and ^{18}F-FC119S cortical SUVR.

We could safely obtain images similar to ^{11}C-PiB PET imaging Aβ in the brain using ^{18}F-FC119S PET. Therefore, ^{18}F-FC119S might be suitable for imaging Aβ deposition.

Abbreviations: Aβ = beta amyloid, AD = Alzheimer's disease, HC = healthy control, MCI = mild cognitive impairment, SUVR = standardized uptake value ratio.

Keywords: Alzheimer's disease, beta amyloid (Aβ), PET

1. Introduction

As population ages, the number of dementia patients worldwide is expected to increase steadily. It is estimated to reach 63 million by 2030 and 114 million by 2050.[1] Alzheimer's disease (AD) accounts for 60% to 70% of all dementia. Brain beta amyloid (Aβ) plaques and neurofibrillary tangle have been used as neuropathological hallmarks of AD.[2] ^{11}C-Pittsburgh compound B (PiB) is the first studied positron emission tomography (PET)

tracer for Aβ imaging. It has been reported that the accumulation of Aβ in the brain evaluated by ^{11}C-PiB PET is in good agreement with postmortem biopsy result of AD patients.[3,4] However, due to radioactive half-life of ^{11}C which is only 20 minutes, ^{11}C-PiB PET has limitations. It is only available in places where there are on-site cyclotron and radiochemistry experts.[5]

To overcome these limitations, ^{18}F labeled Aβ PET tracers with longer radioactive half-lives (110 minutes) were developed and approved by the US Food and Drug Administration (FDA) as Aβ PET tracers in 2012 (^{18}F-florbetapir),[6] 2013 (^{18}F-flutemetamol),[7,8] and 2014 (^{18}F-florbetaben).[9,10] However, these ^{18}F labeled AB PET tracers have been reported to have somewhat lower cortical uptake compared with ^{11}C-PiB PET.[11–13] Higher non-specific white matter uptake compared with ^{11}C-PiB PET has also been reported in some studies.[14–16] Furthermore, some of these ^{18}F labeled AB PET tracers are reported to be inconvenient for clinical use because of the long waiting time (90[15] and 45–130 minutes,[16] respectively) after i.v. administration of tracer to start PET imaging.

A new Aβ PET tracer, ^{18}F-FC119S, has shown a high binding affinity (Kd, 0.16 nM) for synthetic $A\beta_{1-42}$ protein aggregate showing excellent clearance from the frontal cortex in a preclinical study.[17] In preliminary clinical trial with ^{18}F-FC119S PET conducted on 11 control subjects and 8 patients with AD, brain cortical uptake has been reported to be significantly higher in AD patients than that in control subjects without significant adverse effects.[18]

The aim of the present study was to perform head-to-head comparison for Aβ deposition assessed by ^{18}F-FC119S and ^{11}C-PiB PET in healthy control subjects (HC), patients with mild cognitive impairment (MCI), and patients with AD.

2. Materials

2.1. Participants

A total of 48 subjects were enrolled in the study from November 2014 to July 2015, including 28 HC subjects, 10 patients with MCI, and 10 patients with AD. The inclusion criteria for normal HC subjects were: aged 19 years or older, had no abnormal findings on neurological examination, had Mini-Mental State Examination (MMSE) score[19] of 28 or more, and had Clinical Dementia Rating (CDR) scale[20] of 0. The inclusion criteria for MCI patients were: aged 55 years or older who were abnormal or demented, had objective cognitive impairment, and had no disability in their daily lives.[21] The inclusion criteria for AD patients were: those who aged 55 years or older with definite AD or probable AD based on the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association Alzheimer's criteria.[22] Those with severe medical conditions or with physical imaging findings of other neurological disorders other than dementia were excluded from this study.

Subjects were recruited from 3 institutions located in the city of Seoul. All neurological examinations and imaging tests were conducted at the Korea Institute of Radiological and Medical Sciences (KIRAMS). The trial was approved by the Korea Food and Drug Administration (KFDA) and the Institutional Review Board of KIRAMS (IRB No.: K-1405-001-003). Written informed consent was obtained from all subjects or the subject's close family members.

2.2. Tracer synthesis

An efficiency automated method for radiosynthesis of ^{18}F-labeled FC119S using sCUBE auto-synthesis module made by Futurechem (Seoul, Republic of Korea)[17] has been optimized in our PET center. The total synthesis time was 53 minutes and the non-decay corrected radiochemical yield was $27 \pm 5\%$ (n = 48). Specific activity of ^{18}F-FC119S was >1200 Ci/mmol and the average radiochemical purity was 99%. The ^{11}C-PIB was synthesized automatically using the Tracer LAB FXC-PRO synthesizer. Since ^{11}C radionuclide generated by a cyclotron was transferred to the synthesizer, total synthesis time including high performance liquid chromatography purification was approximately 35 minutes. The non-decay corrected radiochemical yield base on the starting ^{11}C was $15 \pm 5\%$ (n = 48). The average specific activity of final products was >950 Ci/mmol and the average radiochemical purity was 98%.

2.3. PET and MR imaging

All subjects underwent ^{18}F-FC119S PET/computed tomography (CT), ^{11}C-PiB PET/CT, and magnetic resonance imaging (MRI) within 3 months after cognitive function test. Both PET/CT scans were performed on the same day using a Siemens Biograph 6 TruePoint TrueV scanner (Siemens, Malvern, PA) with axial field of view of 216 mm and the slice thickness of 3 mm. ^{11}C-PiB PET images were obtained from 40 to 70 minutes after i.v. injection of 970 ± 139 MBq of ^{11}C-PiB. ^{18}F-FC119S PET was intravenously injected at least 120 minutes after the i.v. injection of ^{11}C-PiB. In a previous study, the ratio of cerebral cortical SUV and cerebellar cortical SUV for ^{18}F-FC119S PET reached a peak after 30 minutes after i.v. injection of ^{18}F-FC119S and held the shape of plateau.[18] Therefore, ^{18}F-FC119S PET images were obtained from 30 to 60 minutes after the i.v. injection of 416 ± 59 MBq of ^{18}F-FC119S. Imaging parameters used for CT scanning were as follows: 130 kVp, 30 mA, 0.6-s/CT rotation, and a pitch of 6. CT data were used for attenuation correction. Images were reconstructed using a conventional iterative algorithm (ordered—subsets expectation—maximization, 4 iterations and 8 subsets) and the post Gaussian filter with the full width at half maximum of 4 mm was applied on the reconstructed image. Partial volume correction was not applied to avoid overestimation of cerebral cortical uptake due to the proximity of white matter. In addition, this study was designed for the comparison of ratio of target and reference regions between both images from a subject. Therefore, benefit of partial volume correction on images analysis would be canceled out. A volumetric T1-weighted MRI (3T, MAGNETOM Trio A Tim; Siemens, Germany) was used for screening and subsequent coregistration for PET images.

Vital signs and clinical symptoms were evaluated before and after PET imaging. Adverse events and side effects were evaluated within 48 hours after the completion of imaging.

2.4. Image analysis

For visual analysis of ^{18}F-FC119S PET and ^{11}C-PiB PET, a "positive scan" was defined when there was an increased tracer uptake in any cortical region. A "negative scan" was defined when there was no increased tracer uptake in any cortical region.[12] Three nuclear medicine physicians independently assessed PET images without clinical information. Before reading PET images, these readers were trained with typical positive scans and typical negative scans of ^{18}F-FC119S PET and ^{11}C-PiB PET which were obtained from our previous study.[18] If these reviewers found a discrepancy, images were reviewed simultaneously and decisions were made by consensus.

Quantitative PET image analysis was performed without clinical information. First, 3D segmental T1-weighted MR images were automatically segmented to remove areas with high signal (such as

white matter) and low signal (such as CSF). By doing so, images of the gray area were obtained for each subject. Second, PET images were fused with each segmented MR image and spatially normalized. Third, an automated anatomical labeling template[23] was applied to this image to obtain the standardized uptake value (SUV) for each region of the brain. SUV ratios (SUVRs) were calculated using the cerebellar cortex as a reference region. Global SUVR was defined as the arithmetic mean of frontal cortex, lateral temporal cortex, parietal cortex, anterior cingulate and posterior cingulate cortex, and occipital cortex SUVR.[15] Finally, we calculated the frontal cortex-to-white matter SUV ratios to assess the degree of nonspecific binding to white matter.[24] SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK) was used for segmentation of MRI. PMOD (PMOD Technologies, Zurich, Switzerland) was used for other quantitative analysis.

2.5. Statistical analysis

Normal distributions for all continuous variables were evaluated using Shapiro-Wilk test. Comparisons of age, cognitive function scores, and SUVR between HC subjects and MCI or AD patients were made using independent sample t test for normally distributed variables (SUVR of frontal cortex, temporal cortex, parietal cortex, occipital cortex, and global SUVR) or Mann–-Whitney U test for non-normally distributed variables (age, cognitive function scores, SUVR of anterior cingulate, posterior cingulate, and cerebral white matter). The proportion of subjects with positive findings in visual analysis was calculated for each group and the percentage of cases in which visual analysis was consistent in ^{18}F-FC119S PET and ^{11}C-PiB PET images were calculated. SUVRs and the frontal cortex-to-white matter SUV ratios for ^{18}F-FC119S PET and ^{11}C-PiB PET were compared using the Wilcoxon test. Pearson correlation analysis was performed to test correlations between the regional and global SUVRs for ^{18}F-FC119S PET and ^{11}C-PiB PET. Effect size for the SUVR differences between HC subjects and MCI or AD patients was calculated with Cohen d. Statistical tests were performed using Medcalc (version 16.8; Medcalc software bvba, Ostend, Belgium). All P values were 2-sided. Statistical significance was considered when P value was less than 0.05.

3. Results

3.1. Cognitive function

Demographic characteristics of the 3 populations are summarized in Table 1. MCI (n=10) and AD patients (n=10) were significantly older than HC subjects (n=28). All 3 populations had higher (about twice) proportions of women than men. AD patients had significantly lower mean MMSE score (17.1±7.5) and significantly higher CDR score (1.2±0.9) than HC subjects or MCI patients. MCI patients had significantly lower mean MMSE score (26.8±1.7) and significantly higher CDR score (0.5±0) than HC subjects.

3.2. Safety analysis

No adverse reaction was observed during or after the i.v. administration of ^{18}F-FC119S or ^{11}C-PiB. There was no adverse event during the follow-up period either.

3.3. Visual analysis

The typical negative images in a control subject and positive images in an AD patient are shown in Fig. 1. After adjusting the window

Table 1

Demographics of the 3 populations used in this study.

Group	n	Age (y)	M: F	MMSE
HC	28	49±13	9: 19	29±1
MCI	10	72±8*	3: 7	27±2*
AD	10	74±9*	3: 7	17±7*

Data are presented as mean ± standard deviation.
AD = Alzheimer's disease, HC = healthy control, MCI = mild cognitive impairment, MMSE = mini-mental state examination score.
* Significantly different from controls (P < 0.05).

level of ^{18}F-FC119S PET and ^{11}C-PiB PET with reference to the cerebellar cortex, both images showed similarly higher white matter uptake than gray matter uptake in negative cases (Fig. 1, left images). In positive cases, however, slightly lower gray matter uptake was observed in ^{18}F-FC119S PET images than that in ^{11}C-PiB PET images (Fig. 1, right images). The typical positive ^{18}F-FC119S PET images showed highly increased uptakes in the frontal, temporal, parietal, and occipital cortical regions as well as cingulate gyrus as observed in typical positive ^{11}C-PiB PET images.

All 28 HC subjects had negative scans. Of the 10 MCI patients, 4 (40.0%) had positive scans on both ^{11}C-PiB PET and ^{18}F-FC119S PET. Of the 10 AD patients, 7 (70.0%) had positive scans on ^{11}C-PiB PET. One of these 7 patients had a negative scan on ^{18}F-FC119S PET. Therefore, 6 (60.0%) of 10 AD patients had positive scans on ^{18}F-FC119S PET. Overall, 47 of 48 participants (98%) showed identical results based on visual analysis of both PET images.

3.4. Quantitative analysis

The mean values of SUVR and effect sizes by brain regions for the 3 populations are summarized in Table 2. SUVRs for ^{11}C-PiB PET and ^{18}F-FC119S PET were significantly higher in most cortical regions as well as global cortex in MCI or AD patients than those of HC subjects. Interestingly, SUVRs for ^{18}F-FC119S PET in frontal, parietal cortex, anterior cingulate, and global cortex in AD patients were significantly higher than those in MCI patients. These findings were not observed in ^{11}C-PiB PET. In HC subjects, the mean value of SUVR in cerebral white matter was about 1.5 in both tracers, which was lower than that in MCI or AD patients. ^{18}F-FC119S PET yielded a higher effect size than ^{11}C-PiB PET in AD patients (d=2.02 and 1.67 for ^{18}F-FC119S and ^{11}C-PiB, respectively). On the contrary, ^{18}F-FC119S PET yielded a slightly lower effect size than ^{11}C-PiB PET in MCI patients (d=1.26 and 1.38 for ^{18}F-FC119S and ^{11}C-PiB, respectively).

Comparisons of SUVRs for ^{11}C-PiB PET and ^{18}F-FC119S PET in each population are illustrated in Fig. 2. In HC subjects, the global SUVR for ^{18}F-FC119S PET was significantly higher than that for ^{11}C-PiB PET. However, there was no significant difference between SUVR of ^{18}F-FC119S PET and that of ^{11}C-PiB PET in MCI or AD patients.

The frontal cortex-to-white matter SUV ratios in HC subjects, MCI and AD patients were 0.73±0.04, 0.78±0.14, and 0.86± 0.13, respectively, for ^{11}C-PiB PET and 0.76±0.06, 0.76±0.12, and 0.79±0.03, respectively, for ^{18}F-FC119S PET. In HC subjects, the frontal cortex-to-white matter SUV ratios for ^{18}F-FC119S PET were significantly higher than those for ^{11}C-PiB PET (P=0.025). However, there were no significant differences in the frontal cortex-to-white matter SUV ratios in MCI or AD patients.

Correlations between SUVRs for ^{11}C-PiB PET and those for ^{18}F-FC119S PET in brain regions and global cortex are shown in Table 3 and Fig. 3. A strong positive linear relationship was
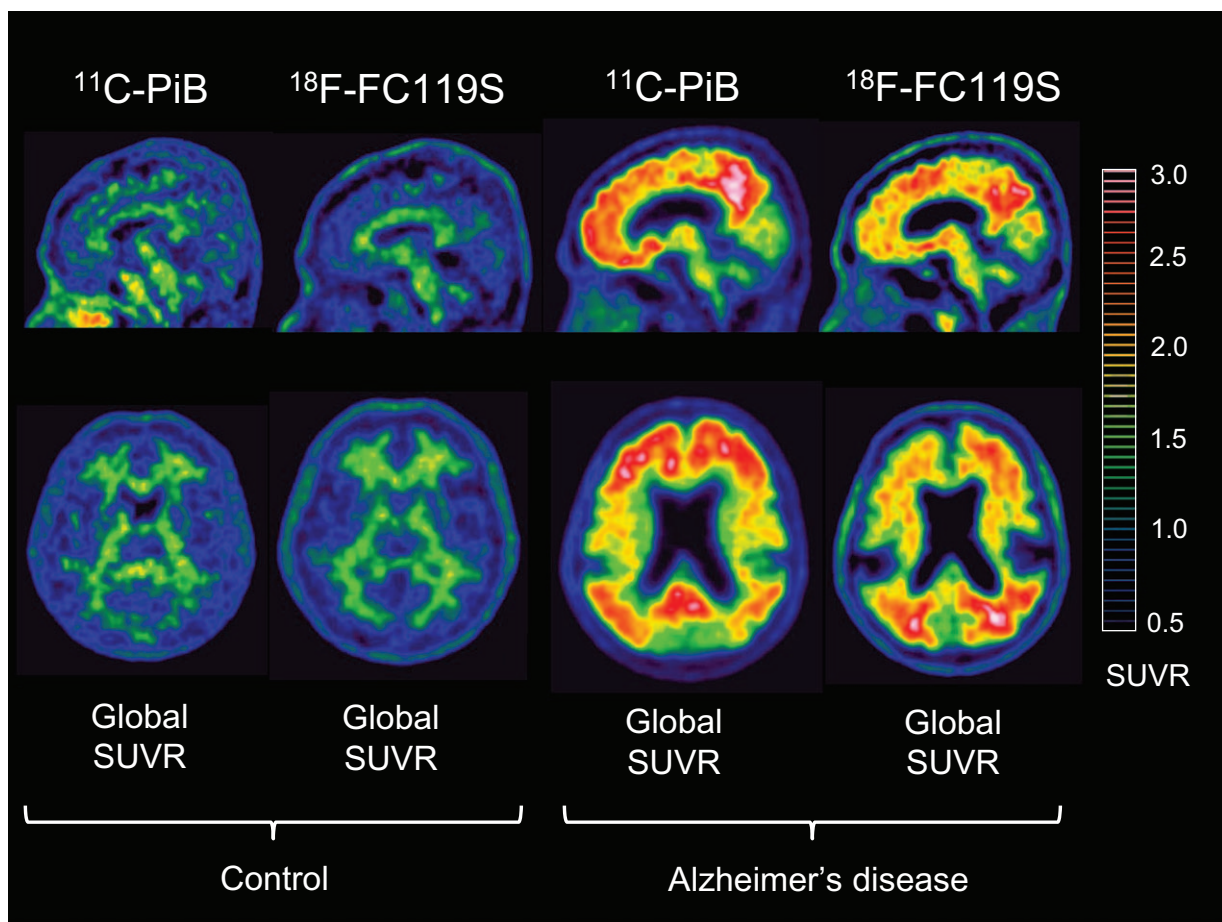
Figure 1. Sagittal (upper row) and transaxial (lower row) ^{11}C-PiB PET and ^{18}F-FC119S PET images of the same control and the same Alzheimer's disease patient. Images scaled to the same SUVR are shown. SUVR = standardized uptake value ratio.

observed between ^{11}C-PiB and ^{18}F-FC119S global SUVR ($r = 0.78$, $P < 0.001$) as described by the following equation: ^{18}F-FC119S global SUVR = (^{11}C-PiB × 0.41) + 0.72. Also, for each cortical region, caudate nucleus, and putamen, SUVRs for ^{18}F-FC119S PET significantly correlated with SUVRs for ^{11}C-PiB PET. There was no significant relationship between SUVRs for ^{11}C-PiB PET and those for ^{18}F-FC119S PET in cerebral white matter.

4. Discussion

We demonstrated that the cortical uptake of ^{18}F-FC119S was higher in AD patients, followed by that in MCI patients and HC subjects. Cortical uptakes of ^{18}F-FC119S PET were significantly correlated with those of ^{11}C-PiB PET images. The degree of nonspecific white matter binding of ^{18}F-FC119S was slightly

Table 2

Comparison of SUVRs for ^{11}C-PiB and ^{18}F-FC119S and effect sized (d) in HC, MCI, and AD subjects.

Region	^{11}C-PiB			^{18}F-FC119S		
	HC	MCI (effect size[§])	AD (effect size[‖])	HC	MCI (effect size[§])	AD (effect size[‖])
Frontal cortex	1.09 ± 0.04	1.30 ± 0.23[*] (1.27)	1.55 ± 0.39[*] (1.65)	1.16 ± 0.05	1.22 ± 0.09[*] (0.82)	1.35 ± 0.13[*,†] (1.92)
Temporal cortex	1.09 ± 0.02	1.22 ± 0.15[*] (1.21)	1.32 ± 0.30[*] (1.08)	1.21 ± 0.04	1.36 ± 0.12[*] (1.67)	1.49 ± 0.15[*] (2.55)
Parietal cortex	1.10 ± 0.05	1.33 ± 0.25[*] (1.27)	1.61 ± 0.42[*] (1.70)	1.12 ± 0.07	1.18 ± 0.12 (0.61)	1.36 ± 0.21[*,†] (1.53)
Occipital cortex	1.10 ± 0.03	1.26 ± 0.15[*] (1.47)	1.38 ± 0.26[*] (1.51)	1.11 ± 0.05	1.25 ± 0.14[*] (1.25)	1.39 ± 0.22[*] (1.75)
Anterior cingulate	1.11 ± 0.04	1.43 ± 0.29[*] (1.54)	1.84 ± 0.58[*] (1.77)	1.25 ± 0.04	1.40 ± 0.12[*] (1.67)	1.56 ± 0.13[*,†] (3.22)
Posterior cingulate	1.26 ± 0.09	1.60 ± 0.37[*] (1.26)	1.77 ± 0.42[*] (1.67)	1.26 ± 0.10	1.43 ± 0.18[*] (1.16)	1.63 ± 0.24[*] (2.01)
Cerebral white matter	1.49 ± 0.11	1.65 ± 0.10[*] (1.52)	1.77 ± 0.23[*] (1.55)	1.54 ± 0.14	1.67 ± 0.47 (0.37)	1.70 ± 0.11[*] (1.27)
Global[‡]	1.09 ± 0.04	1.30 ± 0.21[*] (1.38)	1.52 ± 0.36[*] (1.67)	1.14 ± 0.05	1.24 ± 0.10[*] (1.26)	1.38 ± 0.16[*,†] (2.02)

Data are presented as means ± standard deviation.

AD = Alzheimer's disease, HC = healthy control, MCI = mild cognitive impairment, SUVR = standardized uptake value ratio.

[*] Significantly different from HC ($P < 0.05$).

[†] Significantly different from MCI ($P < 0.05$).

[‡] Arithmetic mean of frontal cortex, lateral temporal cortex, parietal cortex, anterior cingulate and posterior cingulate cortex, and occipital cortex SUVR.

[§] Effect size (Cohen d) for the SUVR differences between HC subjects and MCI patients.

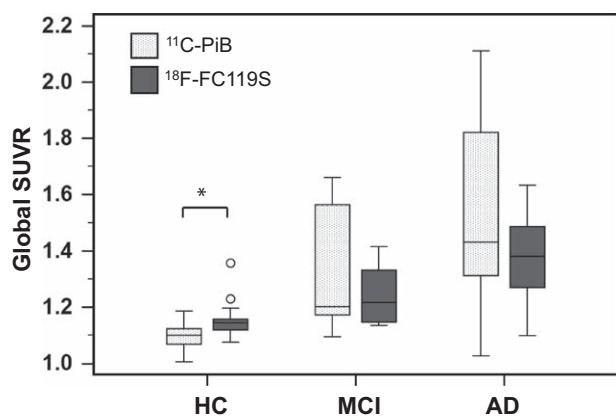[‖] Effect size (Cohen d) for the SUVR differences between HC subjects and AD patients.

Figure 2. Box plots comparing global SUVR assessed with ^{11}C-PiB PET and that with ^{18}F-FC119S PET in HC, MCI, and AD participants. An asterisk represents significant difference between the global SUVR of ^{11}C-PiB PET and that of ^{18}F-FC119S PET ($P < 0.001$). AD = Alzheimer's disease, HC = healthy control, MCI = mild cognitive impairment, SUVR = standardized uptake value ratio.

Figure 3. Scatter plot of the relationship between global SUVR for ^{11}C-PiB and that for ^{18}F-FC119S. Global SUVR for ^{18}F-FC119S is significantly correlated with that for ^{11}C-PiB. SUVR = standardized uptake value ratio.

lower than ^{11}C-PiB in HC subjects and ^{18}F-FC119S PET yielded a higher effect size than ^{11}C-PiB PET in AD patients. These results suggest that ^{18}F-FC119S PET can be effectively and safely used for brain Aβ imaging while overcoming the short radioactive half-life of ^{11}C-PiB.

In visual analysis, cortical uptake of ^{18}F-FC119S was slightly lower than that of ^{11}C-PiB in positive scans. Although quantitative analysis showed that ^{18}F-FC119S global SUVR and ^{11}C-PiB global SUVR were not significantly different from each other in AD and MCI patients, ^{18}F-FC119S global SUVR tended to be lower than ^{11}C-PiB global SUVR in 10 patients with visually positive scans both on ^{18}F-FC119S PET and ^{11}C-PiB PET images (median, 1.41 vs. 1.58, $P = 0.084$, data not shown). These results are in agreement with previous studies showing that cortical SUVR of ^{18}F-labeled amyloid PET in AD patients is lower than that of ^{11}C-PiB PET.[11–13] However, since visual analysis of ^{18}F-FC119S PET and ^{11}C-PiB PET showed the same results for 98% of the total subjects, the difference in cortical uptake might only have slight effect on the diagnostic ability of ^{18}F-FC119S PET.

In HC subjects, cortical uptake of ^{18}F-FC119S was significantly higher than that of ^{11}C-PiB. High white matter uptake might affect the quantification of cortical intake. For example, if white

Table 3

Regional relationships for ^{11}C-PiB and ^{18}F-FC119S SUVRs.

Region	r (correlation coefficient)	P
Frontal cortex	0.80	<0.001
Temporal cortex	0.69	<0.001
Parietal cortex	0.71	<0.001
Occipital cortex	0.68	<0.001
Anterior cingulate	0.84	<0.001
Posterior cingulate	0.74	<0.001
Caudate nucleus	0.73	<0.001
Putamen	0.55	<0.001
Cerebral white matter	0.21	0.142
Global[*]	0.78	<0.001

SUVR = standardized uptake value ratio.
[*] Arithmetic mean of frontal cortex, lateral temporal cortex, parietal cortex, anterior cingulate and posterior cingulate cortex, and occipital cortex SUVR.
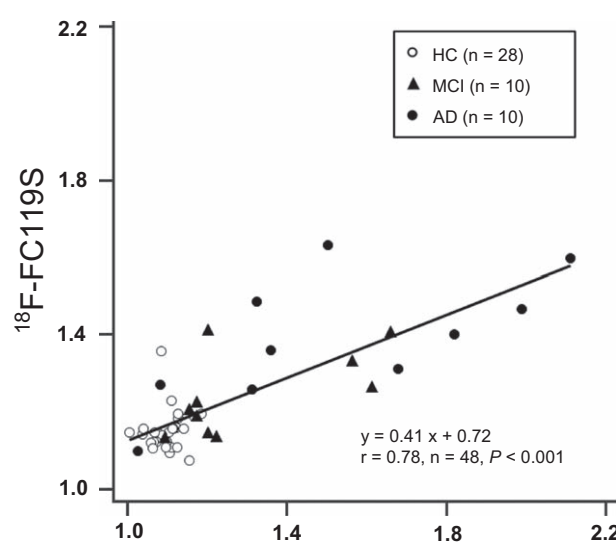
matter is set as the reference region to quantify cortical uptake, high cortical uptake may reduce SUVR.[13] In addition, the spill-over effect of white matter might results in higher measurement of cortical uptake than its actual value. However, when measuring SUVR in amyloid PET, the reference area is set to cerebellum in most studies,[11,12,15,24–26] which is known to have very little accumulation of Aβ.[27] Furthermore, the difference between ^{18}F-FC119S SUVR and ^{11}C-PiB SUVR was very small (SUVR, 1.14 vs. 1.09), suggesting that such spill-over effect on the measurement of cortical uptake might be very small.

Contrary to cortical uptake, the nonspecific binding of ^{18}F-FC119S to white matter (with the frontal cortex-to-white matter SUV ratio of 0.76) was slightly lower than that of ^{11}C-PiB (ratio of 0.73) or other ^{18}F-labeled amyloid radiotracers (with reported ratios ranging from 0.66 to 0.72)[24,28,29] in HC subjects. As the visual analysis of amyloid PET is based on a comparison of cortical uptake and white matter uptake,[6,8,10] amyloid radiotracer with low white matter uptake may be advantageous for visual analysis.

^{18}F-FC119S global SUVR and ^{11}C-PiB global SUVR showed significant correlation with each other. The slope of the linear correlation was 0.41. This slope is similar to or somewhat lower than those of other ^{18}F labeled Aβ radiopharmaceuticals, such as ^{18}F-flutemetamol (slope of 0.81),[13] ^{18}F-florbetapir (slopes ranging from 0.33 to 0.64),[30,31] ^{18}F-florbetaben (slope of 0.71),[11] and ^{18}F-AZD4694.[24] Such discrepancy might be due to the similar or lower cortical uptake of ^{18}F-FC119S compared with that of other ^{18}F labeled Aβ radiopharmaceuticals.[11,13,30,31] However, future head-to-head comparison studies will be required to prove this.

In AD patients, ^{11}C-PiB SUVR was relatively higher in the frontal and parietal cortices compared with the temporal and occipital cortices but ^{18}F-FC119S SUVR was not. These findings are in line with the previous study comparing ^{11}C-PiB and ^{18}F-FACT, which has been considered to bind more preferentially to dense-cored amyloid plaque than ^{11}C-PiB.[32] Regional differences in cerebral cortical SUVR were not observed between ^{11}C-PiB and other ^{18}F labeled amyloid tracers.[24,28,29] Therefore,

the difference in regional distribution between diffuse and dense-cored amyloid plaque may be the cause of regional differences in cerebral cortical uptake between ^{11}C-PiB and ^{18}F-FC119S. However, further studies including histopathological evidence, such as postmortem brain analysis are necessary to support this hypothesis.

Compared with ^{18}F-flutemetamol (90 minutes after injection)[15] or ^{18}F-florbetaben (45–130 minutes after injection),[16]^{18}F-FC119S has the advantage of starting PET imaging in a relatively short time after i.v. injection (30 minutes after injection). For ^{18}F-florbetapir, PET images are obtained 30 to 50 minutes after i.v. injection.[6] On the other hand, image acquisition time of ^{18}F-FC119S PET is 30 minutes, which is somewhat longer than other ^{18}F labeled Aβ radiopharmaceuticals (10–20 minutes). Therefore, the total time spent for PET imaging after i.v. injection of ^{18}F-FC119S (60 minutes) is similar to or shorter than those of other ^{18}F labeled Aβ radiopharmaceuticals (40–150 minutes).[6,8,10]

The present study has several limitations. First, AD and MCI patients were diagnosed with clinical criteria only. No autopsy was performed. Second, the mean age of HC subjects (49 years) was significantly smaller than that of AD (74 years) or MCI patients (72 years). In visual analysis, none of the 28 HC subjects showed positive scan in this study. This was different from previous report showing that 18% and 10% of healthy controls showed positive scans on ^{11}C-PiB PET[33] and ^{18}F-florbetaben PET,[15] respectively. It has been also reported that 20% to 34% of healthy elderly aged over 75 years have Aβ neuropathology.[34] As all of our HC subjects were under the age of 62 years in the current study, future ^{18}F-FC119S PET studies with healthy elderly aged over 75 years might be needed. Finally, since this study was performed with a relatively small number of subjects in a single institution, a multi-institutional study involving a larger number of subjects is required to verify the results of this study.

In conclusion, we could safely obtain images similar to ^{11}C-PiB PET Aβ imaging for the brain using ^{18}F-FC119S PET. The cortical uptake of ^{18}F-FC119S was significantly correlated with the cortical uptake of ^{11}C-PiB. Visual analyses of the 2 PET images were also in good agreement. Compared with ^{11}C-PiB PET, ^{18}F-FC119S PET yielded a higher effect size in AD patients and showed the slightly lower binding to white matter in HC subjects. The total time spent for ^{18}F-FC119S PET imaging is similar or shorter than that for other ^{18}F labeled Aβ radiotracers. These results suggest that ^{18}F-FC119S might be suitable for imaging Aβ deposition.

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