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Intrascanner Reproducibility of an SPM-based Head MR-based Attenuation Correction Method

David Izquierdo-Garcia,

Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital / Harvard Medical School, Bld. 149, 13th St. Room 1106, Charlestown, MA 02129

Mark C. Eldaief,

Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital / Harvard Medical School, Bld. 149, 13th St. Room 1106, Charlestown, MA 02129

Mark G. Vangel,

Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital / Harvard Medical School, Bld. 149, 13th St. Room 1106, Charlestown, MA 02129

Ciprian Catana

Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital / Harvard Medical School, Bld. 149, 13th St. Room 1106, Charlestown, MA 02129

Abstract

Recently, an exhaustive examination of 11 state of the art MR-based attenuation correction (AC) concluded that there are currently a few methods showing similar results compared to the gold-standard, CT-based AC. While the study presented a thorough portfolio of metrics to quantify accuracy (bias) and quality, it lacked one of the most important metrics to quantify robustness that is critical for its clinical applicability: intrascanner reproducibility (repeatability). In this work, we provide for the first time a study of the repeatability of one of the outperforming brain MR-based AC methods: the SPM-based pseudo-CT approach. 22 subjects undergoing 3 ¹⁸F-FDG PET/MRI visits within 2 months were retrospectively analyzed in this study. Pseudo-CT mu-maps were obtained from the coregistered MR images for all 3 visits and the PET data from visit 1 was reconstructed using all three mu-maps. Relative changes (RC), Intraclass correlation coefficient (ICC), Reproducibility coefficient (RDC_{95%}) and Bland-Altman Limits of Agreement (LoA) were used to measure repeatability. Voxel-based and ROI-based results showed that absolute RC for the reconstructed PET images are within ~2%. The brain cortex and the cerebellum were the regions with the largest variability (~3%). The differences across visits were not statistically significant (p=0.90). In conclusion this study shows for the first time the repeatability of the SPM-based pseudo-CT approach for brain MR-AC. These results, in addition to the ease of implementation and the quality and robustness previously demonstrated, confer this SPM-based method an ideal candidate for routine brain PET/MRI research and clinical studies.

Keywords

attenuation correction; PET; MRI; PET/MRI; pseudo-CT; repeatability

I. Introduction

ATTENUATION correction (AC) is one of the main challenges for accurate PET data quantification in integrated PET/MRI scanners. MR-based AC (MR-AC) approaches aim to convert the information from the MR images related to proton density and relaxation times into an attenuation map reflecting the electron density of the scanned subject.

MR-AC approaches can be divided into four different categories: segmentation- atlas-, regression- and emission-based [1] and a new additional deep-learning based strategy [2-4]. In brief, segmentation-based approaches use the MRI information to separate (segment) tissue classes and assign them pre-estimated linear attenuation coefficients (LACs) [5-8]. Regression-based methods rely on probabilistic (Bayesian) estimation [9] and/or regression analysis such as a Gaussian mixture regression [10-12] or a support vector regression [13]. The emission-based approaches use the information from the PET images to estimate the LACs, generally in an iterative joint estimation scheme [14-16] or using an external transmission (Tx) source [17-19]. Finally, atlas-based approaches use a template pair of MR and CT or Tx images [20-23]. There are also approaches that follow a joint strategy combining an atlas approach with other local information (such as segmentation or patch-based techniques) [24, 25].

We recently introduced a simple and robust head attenuation map estimation method based on the widely available Statistical Parametric Mapping 8 (SPM; Wellcome Trust Centre for Neuroimaging, University College London, UK) software that combines the flexibility and adaptability of the segmentation approaches using local information through tissue probability maps and the robustness conferred by the atlas approaches [26]. We demonstrated the robustness of the method by creating an atlas from 15 glioblastoma subjects and confirming its accuracy in a different set of 16 subjects scanned on an integrated PET/MR scanner (Biograph mMR, Siemens Healthineers, Erlangen, Germany). The method, freely available, is currently been routinely used in different centers around the world, is user friendly (one mouse click to select the MR input image) and does not require any prior knowledge of dedicated software (e.g. SPM or Matlab) operation. More recently, eleven of the latest state-of-the-art MR-AC methods, including the SPM-based approach, were compared in an international multi-center study [27]. The methods were compared in a systematic fashion using a large set of data acquired from Alzheimer's disease patients who underwent sequential CT and PET/MR examinations. The study not only was able to reproduce independently our original results in terms of quality and robustness of the method, but also concluded that four of the MR-AC methods, the SPM-based approach as well as two atlas-based approach and another mix-based approach, outperformed the rest.

While being a remarkable international collaborative effort that allowed a comprehensive assessment of the pros and cons, and characterization of the bias of all the methods, the study lacked a required measure to demonstrate clinical feasibility – attenuation map

estimation intrascanner reproducibility (also called repeatability, variability or precision). High accuracy (i.e. small bias) does not necessarily imply or translate into high precision/repeatability (i.e. small variability). Bias and variability are both highly desired but independent properties that need to be evaluated in order to fully validate novel methods. In the case of MR-based pseudo-CT methods, there are several factors that could reduce repeatability, such as the variability in the acquired MR data ranging from changes in subject anatomy or hydration status to intrinsic scanner variability to methodological aspects related to the data postprocessing (e.g. coregistration accuracy). Additionally, the use of probability-based priors and Bayesian techniques for pseudo-CT image generation, as is the case for the SPM-based approach, could potentially lead to additional variability. The objective of this study is therefore to fill this gap by assessing for the first time the repeatability of the SPM-based MR-AC approach. To achieve this goal, we analyzed the attenuation maps and corresponding reconstructed PET images from subjects who underwent repeated PET/MR examinations.

II. Material and Methods

A. Image Acquisition

The data collected from twenty-two subjects enrolled in a different study (healthy subjects: N=13; subjects with depression: N=9) were retrospectively analyzed. The subjects underwent three PET/MRI sessions within two months (visit 2 to visit 1 delay: 30 ± 22 days; visit 3 to visit 1 delay: 59 ± 57 days). Three of the subjects could only complete two of imaging sessions. All subjects gave written informed consent, and the local Institutional Review Board approved the study. The BrainPET prototype (Siemens Healthineers, Erlangen, Germany) was used for these studies. All the visits followed the same protocol: emission data were collected for 1 hour in listmode format after the injection of ~ 185 MBq of ^{18}F -FDG approximately 30 minutes prior to imaging. Simultaneously to the PET acquisition, a T1-weighted 3D magnetization-prepared rapid gradient echo (MPRAGE) image was acquired with the following parameters: TE = 1.64ms, TR = 2,530ms, TI = 1,200ms, reconstruction matrix size = $256 \times 256 \times 256$ voxels, voxel size = $1 \times 1 \times 1$ mm, 4 averages, total acquisition time = 6:02 min:sec. The acquisition of the MPRAGE image of visit 1 of one subject resulted in minor aliasing in both directions (nose-to-back and ear-to-ear) that required manual anti-aliasing intervention to avoid aliasing biasing the interpretation of the final results.

B. Image Coregistration

The first session of each subject was designated as the reference. The MPRAGE images from the second and third visits were rigidly coregistered to the MPRAGE from the reference visit using the SPM automatic coregistration tool with normalized mutual information (NMI) as similarity metric. Visual inspection of the coregistered images and the joint probability distributions (before and after registration) was used to ensure that the images were indeed coregistered (joint probability distribution becomes closer to a diagonal matrix as expected for two perfectly coregistered identical images). We denote the resulting volumes as MR_1 , MR_2 and MR_3 .

C. Attenuation Correction

Pseudo-CT attenuation maps were then generated from all three MPRAGE volumes using the SPM-based method described in detail in [26]. Briefly, after intensity normalization using FreeSurfer [28], the MPRAGE image was segmented into 6 tissue probability maps (gray matter, white matter, cerebrospinal fluid, bone, soft tissue and air) using the SPM New Segment tool. The six tissue probability maps were simultaneously non-rigidly coregistered using the SPM diffeomorphic image registration tool (Dartel). The attenuation maps were obtained by converting the resulting pseudo-CT images to LACs using the bi-linear transformation [29], applying smoothing using a Gaussian filter (3 mm FWHM isotropic) and a radial motion-blurring filter ($m=12$) to match the BrainPET scanner spatial resolution [30] and reslicing the volume into the PET space. We denote μ_i ($i = 1, 2$ and 3) the final attenuation maps from the three sessions.

D. PET Image Reconstruction

To avoid the physiological variability in brain glucose consumption to bias the repeatability study, we used the PET raw data from the first session for comparisons of the PET images reconstructed using the attenuation maps (μ_i) from all 3 sessions. The images were reconstructed using an ordered-subsets expectation maximization (oSEM) algorithm using 6 iterations and 16 subsets and correcting for random coincidences, dead time, isotope decay, detector sensitivity, photon attenuation and scatter. The final PET volume consists of a $256 \times 256 \times 153$ matrix of 1.25 mm isotropic voxels. We denote PET_i ($i = 1, 2$ and 3) the PET images reconstructed using the attenuation maps μ_i .

E. Image Analysis

Voxel- and region-based analyses were performed to assess the repeatability of the attenuation maps and the reconstructed PET images as previously described [26]. Briefly, relative changes (RC) were calculated, taking the first session as the reference, as follows:

$$RC_{I_x}(\%) = 100 \cdot \frac{I_x - I_1}{I_1} \quad (1)$$

where X corresponds to the imaging session (i.e. $X=2$ or 3), I_x corresponds to either the attenuation map (μ_2 or μ_3) or the reconstructed PET image (PET_2 or PET_3) and I_1 corresponds to the image chosen as reference (μ_1 or PET_1). Both absolute and non-absolute relative changes (aRC and naRC, respectively) were calculated.

For the region-based analysis, 12 regions of interest (ROIs) were defined in the Montreal Neurological Institute (MNI) standard space: 10 from the Automatic Anatomical Labeling (AAL) template (Frontal, Insula, Cingulate, Limbic, Occipital, Parietal, Basal ganglia, Thalamus, Temporal and Cerebellum), one from white matter (WM) and one from cerebrospinal fluid (CSF). The ROIs were mapped into the original subject space (MR_1) using the diffeomorphic non-rigid coregistration (DARTEL) tool from SPM [31, 32]. A brain mask obtained from the subject specific GM, WM and CSF tissue probability maps and a brain cortex mask defined as the 5 outermost voxels of the brain mask were used for the voxel-based analysis [26].

F. Statistical Analysis

Repeated measures Analysis of Covariance (ANCOVA) was performed on the log-transformed values to evaluate statistical significance using a multilevel analysis to accommodate the nested structure of the data (longitudinal correlated data) and using fixed effects for ROIs, visits, group, weight and sex and random effects for visits and subjects. Statistical significance was considered for $p < 0.05$. Bonferroni method was used for correction of multiple comparisons. Mean and SD in % (Mean $\pm$ SD) of the aRCs and naRCs were computed across subjects for the voxel- and ROI-based analysis. Additionally, for ROI analysis, minimum and maximum percentage values (Mean $\pm$ SD% [min max %]) of the average RCs across subjects were also calculated as well as box and whiskers plot to better visualize outliers within each region. Intraclass correlation coefficient (ICC), Reproducibility coefficient (RDC_{95%}) (also called repeatability coefficient) and Bland-Altman Limits of Agreement (LoA) [33-37] were also reported as measures of repeatability for the ROI-based analysis using the ROI averages. Bland-Altman plots were used for the voxel-based results. Statistical analysis was performed using the software R v.3.5.0. [38].

III. Results

Fig. 1 shows the coregistered MPRAGE images as well as the fused images for visits 2 and 3 with respect to visit 1 from the three sessions for a representative subject, demonstrating similar image quality across the visits and accurate coregistration of visits 2 and 3 to visit 1. Fig. 2 shows the attenuation maps generated for the three visits for the same representative subject (left columns), as well as the differences between visits 2 and 3 with respect to visit 1 (right columns). The largest RC values occur outside the brain in the nasal cavity and around the sinuses, while the brain and skull show only minor changes. Fig. 3A and 3B show the average differences with respect to visit 1 between visits 2 and 3 (Fig. 3A and 3B respectively) across all subjects, in MNI space, confirming the results shown in Fig. 2 across all subjects. Fig. 3C and 3D show the box and whisker plots of the absolute relative changes (aRC) for the voxel- and ROI-based analysis across all subjects for visits 2 (Fig. 3C) and 3 (Fig. 3D) with respect to visit 1. Table 1 presents a detailed summary of the results achieved for the attenuation maps across all subjects. Briefly, the whole brain showed a small variability: $0.35\pm0.19\%$ and $0.41\pm0.39\%$ for visits 2 and 3 respectively compared to visit 1. The differences across visits were not statistically significant ($\chi^2=0.03$, $p=0.98$). As expected, the largest differences were found in the cortex: $1.26\pm0.69\%$ and 1.45 ± 1.37 for visits 2 and 3 respectively, since it is the area where GM, CSF, sinuses and skull are in contact with each other; while the smallest differences were found in the WM: $0.01\pm0.01\%$ and $0.01\pm0.02\%$ for visits 2 and 3 respectively.

The reconstructed PET images for the representative subject are shown in Fig. 4 for all three visits (left side from top to bottom). Fig. 4 (right side) also shows the RC(%) for visits 2 and 3, respectively. These results show that differences are around $\pm 3\%$ across the whole brain. Fig. 5A and 5B show the average differences across visits 2 and 3 in comparison with visit 1 across all subjects in the MNI space. Fig. 5C and 5D (box and whiskers) and Table 2 summarize the voxel- and ROI-based results for the repeatability results on the PET images across all subjects. Briefly, the whole brain also showed a small variability $1.65\pm0.54\%$ and

1.96±0.87% for visits 2 and 3 respectively compared to visit 1. Similarly to the attenuation maps comparisons, the differences across visits were not statistically significant ($\chi^2=0.20$, $p=0.90$).

Table 3 compiles the results of ICC, RDC and LoA per individual ROIs. These results confirm the great repeatability of the method, with all ICC values around 0.99 and differences (RDC and LoA) expected to be in 95% of the cases within 3%. Only CSF and Cerebellum show slightly higher RDC above 3% (3.50 and 3.35% respectively) and LoA for visit 3 around 4%. Fig. 6 shows the Bland-Altman plots for the reconstructed PET images (voxel by voxel) across all subjects for visits 2 (Fig. 6A) and 3 (Fig. 6B), demonstrating very similar profiles for the differences across all voxels for the two visits and showing that 95% of all brain voxels are within 5%.

IV. DISCUSSION

We previously proposed a user-friendly method to generate a subject-specific attenuation map from a single MPRAGE volume and demonstrated its accuracy even in extremely challenging cases such as high-grade glioblastoma subjects with large anatomical deformations [26]. The software relies on dedicated software (SPM and Matlab). To minimize this impact, we provide a freely available package that allows the generation of a pseudo-CT independently. In a recent multicenter evaluation of 11 state-of-the-art MR-AC approaches [27], the SPM-based method consistently ranked in top 4 across all the different figures of merit (e.g. bias, regional average errors) together with another mix-based approach and two pure atlas-based approaches. Among the main conclusions of the study the study highlighted the fact that the quantification bias of the best performing methods (i.e. ~2-3% across the brain compared to the gold-standard CT-AC) was sufficient to perform brain PET/MRI studies with the required level of confidence for clinical applications [27]. Although the accuracy (bias) of the various MR-AC methods was very thoroughly assessed, the analysis did not focus on intrascanner reproducibility (also called repeatability or variability), an important aspect that also needs to be considered to demonstrate the potential clinical utility of the approaches investigated. To the best of our knowledge, none of the 11 state-of-the-art MR-AC methods investigated in [27] has been demonstrated to be repeatable.

Our goal in this study was to assess the variability/repeatability of the SPM-based method. To achieve this aim we have retrospectively analyzed data from a cohort of 22 subjects undergoing 3 consecutive PET/MRI visits within 2 months. Both the voxel- and ROI-based analyses showed the method is highly repeatable, with variability of 2-3% across the three visits (Tables 1 and 2). The detailed statistical analysis, using repeated measures ANCOVA with a multi-level approach to accommodate the intrinsically correlated data of the longitudinal studies, has shown no statistical differences across the visits in any region of the brain. All figures of merit used to evaluate repeatability (Table 3) demonstrate a high degree of repeatability: ICC > 0.98 across all ROIs, and RDC_{95%}, that calculates the expected absolute differences among two measurements in 95% of the cases, as well as LoA, that defines the interval where to find the expected differences in 95% of the cases assuming normally distributed data, were both ~3%.

None of the differences observed in this study was statistically significant. Across the whole brain, the variability for the reconstructed PET images was $\sim 2 \pm 1\%$, $\text{ICC} = 0.999$. The regions with the largest variability for the reconstructed PET images are the brain cortex (aRC: $\sim 3 \pm 1\%$, $\text{ICC} = 0.999$) and the cerebellum (aRC: $\sim 2 \pm 2\%$, $\text{ICC} = 0.998$). Given the importance of the cortex for most neuroscience applications, we assessed the performance of our method in an artificial cortical region defined as the 5 outermost voxels of the brain mask in our original publication [26]. Regarding the accuracy of the pseudo-CT method in the cerebellum (a region often used as reference for kinetic analysis studies), it is worth noting that our method had the lowest bias in this region out of all 11 methods compared by Ladefoged et al. (see Supplementary Figure 16 in [27]). Despite both the cortex and cerebellum being the most challenging areas for pseudo-CT approaches in general, due to the challenge task of estimating skull attenuation accurately and to the normal physiological differences across visits on the frontal sinuses, our results show a variability $\sim 3\%$ across all brain regions (Figure 5 and Tables 1 to 3). Some of these differences could be due to small natural anatomical variations across the 2-month period between the visits, particularly in the frontal sinuses and nasal cavities where the largest RCs are seen in the attenuation maps. The voxels in these regions have very small attenuation values (close to zero) and therefore small differences across visits translate into large RC values (Figures 2 and 3). The use of rigid-body coregistration across visits may also explain some of this small anatomical variability across visits. The fact that visit 3 presents slightly larger differences than visit 2 compared to visit 1 suggests that larger separation in time (2 months for visit 3 vs. 1 month for visit 2 with respect to visit 1) slightly increases the differences. We purposely used rigid registration for two reasons: first the relatively short interval between visits and the lack of surgical procedures should minimize anatomical variations/deformation across visits; second and most importantly, the use of a non-rigid registration technique does not ensure a perfect alignment and could introduce more variability, complicating the interpretation of the results since the pseudo-CT generation technique already uses a non-rigid registration technique. The accuracy of the coregistration across visits was assessed by inspecting the joint probability distribution of the images before and after registration and ensuring the similarity metric NMI was increased, and by visually confirming the fused images were in agreement. Regardless of its source, the observed $\sim 2\%$ variability is also within the limits of the normal range variation for CT-based AC previously observed in PET/CT scanners [39]. The $\sim 2\%$ variability range is also comparable to other repeatability measurements obtained from CT on the brain [40] and certainly smaller than the variability for FDG-PET per se [41, 42].

This study has several limitations. First, the method was developed using BrainPET data as training but it has been successfully applied to data acquired on the Biograph mMR, both in our original validation study [26], the multi-center evaluation study [27] as well as on other MR scanners (data not shown). Also, all our subjects in this study had relatively normal brain anatomy. Repeatability of the method would still need to be evaluated in more challenging cases. The fact that our method was originally developed using data acquired from glioblastoma patients suggests it is robust to large anatomical variants as shown in the Supplementary Figures 3 to 5 of our original report describing the pseudo-CT method [26]. Encouragingly, very similar attenuation maps were generated from the data acquired one week apart in glioblastoma patients (data not shown). Finally, we have analyzed only voxels

corresponding to brain, where most of the research and clinical studies focus. Further analyses would be required to assess the reproducibility of the method in other regions (e.g. skull, head and neck, etc.).

V. Conclusion

We have demonstrated the SPM-based MR-based pseudo-CT generation approach we previously introduced for brain PET/MRI is highly repeatable across the whole brain with ~2% variability across three visits over two months. These results complement those reported by Ladefoged et al., together demonstrating the pseudo-CT method is not only very accurate (low bias) and robust but also highly repeatable (low variability). These features, in addition to its ease of implementation using the widely used SPM software, make it an ideal candidate for routine use in brain PET/MRI research and clinical studies.

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Fig. 1.

Coregistered MRI images (MPRAGE) from a representative subject for all 3 visits (top to bottom, left side panel) and the fused images (right side panel) using visit 1 for comparison. All figures show the same axial (left), coronal (middle) and sagittal (right) slices across visits. Note the slight differences around the nasal cavities and sinuses and around the neck area due to natural non-rigid deformations and physiological changes of the tissues.

Fig. 2.

Attenuation maps (left side panel of the figure) of the same representative subject as in Fig. 1, showing the same slices in axial (left), coronal (middle) and sagittal (right) for all 3 visits (top to bottom). Relative changes, RC (%) of visits 2 and 3 with respect to visit 1 are shown to the right side of the images.

Fig. 3.

Average RC(%) of attenuation maps across all subjects in MNI space showing little bias throughout the brain across visit 2 (A) and visit 3 (B) with respect to visit 1. Subpanels C and D show the box and whiskers plots for the absolute RC (%) for visit 2 (aRC_{μ_2}) and visit 3 (aRC_{μ_3}) for the voxel- and ROI-based analysis.

Fig. 4.

Reconstructed PET images of the same representative subject as in Fig. 1 showing the same slices in axial (left), coronal (middle) and sagittal (right) using the attenuation maps for all 3 visits (top to bottom) on the same PET data from the first visit. The images show no observable difference to the naked eye. Relative changes, RC (%) of visit 2 and 3 with respect to visit 1 are shown to the right side of the images.

Fig. 5.

Average RC(%) of reconstructed PET images across all subjects in MNI space across visit 2 (A) and visit 3 (B) with respect to visit 1 showing little bias throughout the brain except the brain stem and areas of the brain cortex that show increased differences. Subpanels C and D show the box and whiskers plots for the absolute RC (%) for visit 2 (aRC_{PET2}) and visit 3 (aRC_{PET3}) for the voxel- and ROI-based analysis.

Fig. 6.

Bland-Altman plots of the reconstructed PET images across all subjects showing a voxel-by-voxel comparison of the visit 2 (A) and visit 3 (B) with respect to visit 1. RC (%) are used instead of the standard differences in the ordinate axis to produce more meaningful results. The red solid line indicates the average RC across all subjects and the two dashed red lines indicate the voxel-based LoA, 95% CI (mean $\pm$ 1.96 SD), of the RC.

TABLE I

Summary of the relative changes, RC(%) for the attenuation MAPS OF VISITS 2 AND 3 COMPARED TO VISIT 1.

		$RC\mu_2^*$	$RC\mu_3^*$
<i>Absolute aRC</i>	<i>All ROIs</i>	0.28±0.42%	0.34±0.64%
	<i>[min max]</i> [†]	[0.00 2.96]	[0.00 5.34]
	<i>Voxel-based</i>	0.35±0.19%	0.41±0.39%
<i>Non-Absolute naRC</i>	<i>All ROIs</i>	0.00±0.24%	-0.00±0.27%
	<i>[min max]</i> [†]	[-1.21 1.27]	[-1.91 2.14]
	<i>Voxel-based</i>	0.00±0.12%	0.00±0.08%

* Average across subjects of the mean absolute or non-absolute relative changes, aRC(%) and naRC(%) respectively: Mean±SD%;

[†] [min max] = minimum and maximum values (also in%) for ROI analysis.

TABLE II

Summary of the relative changes, RC(%) for the reconstructed PET images using the attenuation maps from visits 2 and 3 compared to visit 1.

		RC_{PET2}^*	RC_{PET3}^*
<i>Absolute aRC</i>	<i>All ROIs</i>	1.60±0.87%	1.88±1.20%
	<i>[min max]</i> [†]	[0.43 6.04]	[0.31 8.16]
	<i>Voxel-based</i>	1.65±0.54%	1.96±0.87%
<i>Non-Absolute naRC</i>	<i>All ROIs</i>	0.02±1.19%	0.14±1.70%
	<i>[min max]</i> [†]	[-3.30 5.40]	[-7.76 6.26]
	<i>Voxel-based</i>	0.00±0.96%	0.11±1.48%

* Average across subjects of the mean absolute or non-absolute relative changes, aRC(%) and naRC(%) respectively: Mean±SD%;

[†] [min max] = minimum and maximum values (also in%) for ROI analysis.

TABLE III

Summary of repeatability figures of merit per ROI of the reconstructed PET images: intraclass correlation coefficient (ICC) and reproducibility (or repeatability) coefficient (RDC) calculated across the 3 visits and the bland-altman limits of agreement (LoA) calculated for visits 2 and 3 compared to visit 1 (LoA₂ and LoA₃ respectively). In round brackets results in % of the mean across visits.

	ICC [95% CI]	RDC _{95%} (%)	LoA ₂ (%)	LoA ₃ (%)
Whole-Brain	0.999 [0.998 1]	0.13 (1.97%)	[-0.10 0.09] ([-1.57 1.55])	[-0.14 0.16] ([-2.25 2.59])
Brain cortex	0.999 [0.999 1]	0.15 (2.27%)	[-0.11 0.10] ([-1.71 1.64])	[-0.17 0.20] ([-2.68 3.05])
Frontal	0.999 [0.998 1]	0.15 (1.95%)	[-0.13 0.11] ([-1.79 1.55])	[-0.16 0.19] ([-1.96 2.35])
Insula	0.999 [0.998 1]	0.16 (2.10%)	[-0.12 0.13] ([-1.63 1.82])	[-0.16 0.18] ([-2.36 2.76])
Cingulate	0.999 [0.998 1]	0.13 (1.70%)	[-0.13 0.10] ([-1.72 1.37])	[-0.15 0.16] ([-1.96 2.09])
Limbic	0.998 [0.996 0.999]	0.14 (2.95%)	[-0.09 0.12] ([-2.16 2.77])	[-0.13 0.15] ([-3.05 3.45])
Occipital	0.999 [0.998 1]	0.17 (2.10%)	[-0.11 0.14] ([-1.62 1.99])	[-0.15 0.20] ([-2.08 2.70])
Parietal	0.999 [0.998 1]	0.15 (2.21%)	[-0.15 0.13] ([-2.21 1.95])	[-0.16 0.20] ([-2.44 2.94])
Basal ganglia	0.999 [0.999 1]	0.15 (1.98%)	[-0.12 0.13] ([-1.63 1.72])	[-0.15 0.17] ([-2.20 2.50])
Thalamus	0.999 [0.998 1]	0.18 (2.53%)	[-0.13 0.15] ([-2.04 2.23])	[-0.18 0.21] ([-2.83 3.29])
Temporal	0.999 [0.997 0.999]	0.17 (2.50%)	[-0.12 0.13] ([-1.76 1.92])	[-0.18 0.22] ([-2.86 3.50])
Cerebellum	0.998 [0.995 0.999]	0.20 (3.35%)	[-0.12 0.13] ([-2.21 2.42])	[-0.26 0.25] ([-4.41 4.34])
WM	0.998 [0.997 0.999]	0.08 (2.35%)	[-0.08 -0.07] ([-2.28 1.98])	[-0.09 0.09] ([-2.68 2.72])
CSF	0.998 [0.997 0.999]	0.09 (3.50%)	[-0.07 0.07] ([-3.17 3.04])	[-0.09 0.09] ([-4.05 4.07])