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Anatomically guided voxel-based partial volume effect correction in brain PET: Impact of MRI segmentation

Daniel Gutierrez[a], Marie-Louise Montandon[a], Frédéric Assal[b], Mohamed Allaoua[a], Osman Ratib[a], Karl-Olof Lövblad[c], Habib Zaidi[a,d,e,*]

[a] Division of Nuclear Medicine and Molecular Imaging, Geneva University Hospital, CH-1211 Geneva, Switzerland
[b] Neurology Clinic, Geneva University Hospital, CH-1211 Geneva, Switzerland
[c] Division of Neuroradiology, Geneva University Hospital, CH-1211 Geneva, Switzerland
[d] Geneva Neuroscience Center, Geneva University, CH-1205 Geneva, Switzerland
[e] Department of Nuclear Medicine and Molecular Imaging, University of Groningen, University Medical Center Groningen, 9700 RB Groningen, Netherlands

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ABSTRACT

Partial volume effect is still considered one of the main limitations in brain PET imaging given the limited spatial resolution of current generation PET scanners. The accuracy of anatomically guided partial volume effect correction (PVC) algorithms in brain PET is largely dependent on the performance of MRI segmentation algorithms partitioning the brain into its main classes, namely gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). A comparative evaluation of four brain MRI segmentation algorithms bundled in the successive releases of Statistical Parametric Mapping (SPM) package (*SPM99*, *SPM2*, *SPM5*, *SPM8*) using clinical neurological examinations was performed. Subsequently, their impact on PVC in ^{18}F-FDG brain PET imaging was assessed. The principle of the different variants of the image segmentation algorithm is to spatially normalize the subject's MR images to a corresponding template. PET images were corrected for partial volume effect using GM volume segmented from coregistered MR images. The PVC approach aims to compensate for signal dilution in non-active tissues such as CSF, which becomes an important issue in the case of tissue atrophy to prevent a misinterpretation of decrease of metabolism owing to PVE. The study population consisted of 19 patients suffering from neurodegenerative dementia. Image segmentation performed using *SPM5* was used as reference. The comparison showed that previous releases of SPM (*SPM99* and *SPM2*) result in larger gray matter regions (~20%) and smaller white matter regions (between −17% and −6%), thus introducing non-negligible bias in PVC PET activity estimates (between 30% and 90%). In contrary, the more recent release (*SPM8*) results in similar results (<1%). It was concluded that the choice of the segmentation algorithm for MRI-guided PVC in PET plays a crucial role for the accurate estimation of PET activity concentration. The segmentation algorithm embedded within the latest release of SPM satisfies the requirement of robust and accurate segmentation for MRI-guided PVC in brain PET imaging.

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1. Introduction

Molecular brain imaging using positron emission tomography (PET) has emerged as one of the most promising modalities that steadily gained importance in the clinical and research arenas [1]. Considerable progress has been made to optimize the design of dedicated high resolution PET scanners and to integrate multimodality images to correlate functional findings to anatomy through the use of CT and MRI and to improve the quality and quantitative accuracy of brain PET images, however, emerging clinical and research applications of functional brain imaging promise even greater levels of accuracy and precision and therefore impose more constraints with respect to the information provided to clinicians and research scientists [2]. Since MRI is more suitable than CT for brain imaging owing to its high soft tissue contrast and better spatial resolution, combined PET-MRI systems dedicated for brain imaging have emerged as alternatives to PET-CT [3]. One of the first steps to obtain the best of the various imaging modalities is to coregister functional and anatomical images, and to a pre-segmented atlas if available. Wu et al. [4] has shown that this task can be optimized using non-rigid registration procedures compared to rigid or semi-rigid procedures such as those implemented in the Automated Image

* Corresponding author at: Division of Nuclear Medicine and Molecular Imaging, Geneva University Hospital, CH-1211 Geneva, Switzerland. Tel.: +41 22 3727258; fax: +41 22 3727169.
E-mail address: habib.zaidi@hcuge.ch (H. Zaidi).

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Registration (AIR) and the Statistical Parametric Mapping (SPM) packages. These techniques are, however, especially useful when dealing with inter-subject image registration.

Unfortunately PET imaging suffers from many physical degrading effects, partial volume effect (PVE), which is common to all medical imaging techniques owing to the discrete sampling of the image formation process, being one of them. In brain PET imaging, this effect is not negligible owing to the large voxel size, which produces images where high activity regions spillover into low activity regions, potentially leading to erroneous results in the qualification of functional brain imaging [5,6]. Since neurological PET imaging was developed very early, the first attempts to reduce the impact of the PVE and restore the image content focused on brain imaging [7]. This has been addressed through the calculation of recovery coefficients [8], thus limiting the methods to the use of only PET data, since in these early years multimodality imaging was still not readily available as it is nowadays. The advent of modern multimodality imaging, and particularly brain PET/MR, stimulated the development of new partial volume correction (PVC) techniques which exploit a priori information gathered from anatomical information through partitioning MR images into different compartments, typically gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) [9]. More recently, a novel class of PVC algorithms that do not require segmentation of anatomical images was introduced [10]. This includes very promising approaches such as the wavelet decomposition technique [11] and the Bayesian approach [12]. In both cases, the algorithm is able to find the high frequency information lacking in low resolution PET images at a voxel-level without increasing the noise.

Current PVC algorithms that require the segmentation of anatomical images correct functional PET images in the projection space, during the reconstruction process or after their reconstruction (post-reconstruction) at regional level using a region-of-interest (ROI)-based analysis or in a more general way at the voxel level (voxel-based) [13]. Among ROI-based post-reconstruction methods, the most popular techniques use recovery coefficients [7,8] or the geometric transfer matrix (GTM) method [14,15] used in our previous work [16]. The principle of ROI-based methods is to calculate the effective activity in different regions assuming that the tracer uptake in each particular region is homogeneous. Naturally, the complexity of the problem increases when the number of considered regions increases, rendering PVC of the whole brains a complex problem. Nevertheless, in a simple case using ROIs has shown promising results [15].

Conversely, voxel-based approaches are not limited to a particular ROI since they attempt to recover the actual activity concentration in the cortex on a voxel-by-voxel basis, though with a priori assumptions about the tracer distribution [10,17,18]. These techniques have the advantage of generating corrected image for qualitative assessment and visual interpretation. The principal drawback of voxel-based methods compared to ROI-based methods is that they are quantitatively less accurate and rely on many assumptions. Partition methods are one example of voxel-based methods, the simplest case being to define one unique partition corresponding to brain tissue classes (GM and WM) and to compensate the spillover on non-active regions (CSF) by converting PET intensities from activity per spatial volume to activity per tissue volume [19]. This is achieved by convolving the partition (brain mask) with the point spread function (PSF) of the PET imaging system. This approach was extended to two (GM and WM) [20] and three compartments assuming that the CSF activity is not only the result of spillover from contiguous regions [18].

MR image segmentation is the critical component of MRI-guided PVC in brain PET imaging [14,17,21]. In a previous work, we compared the impact of various MR image segmentation algorithms on the GTM algorithm for PVC of ^{18}F-FDG and ^{18}F-FDOPA brain PET data [16]. One of the conclusions of this work was that Statistical Parametric Mapping (*SPM2*) segmentation software is more suitable for clinical routine examinations owing to the robustness of its normalization algorithm for atypical brains.

In this work, we aim to assess the influence of 4 chronologically successive releases of SPM segmentation software on a voxel-based PVC method proposed by Matsuda et al. [9] in contrast to previous work referenced above.

2. Materials and methods

2.1. Brain MRI segmentation algorithms

SPM is among the well established packages used for statistical analysis of neuroimaging data including PET, SPECT and fMRI [22]. It is well-documented, freely available, technically supported by well established brain imaging centers [23] and widely used by the neuroimaging community. The brain MR image segmentation technique implemented in this package considers the three tissue classes of interest for PVC, namely gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF).

A comparative evaluation of the impact of brain MRI segmentation algorithms on PVC in ^{18}F-FDG PET imaging was performed using the implementations embedded in the last four successive releases of SPM, namely *SPM99*, *SPM2*, *SPM5* and *SPM8*. The main steps of the SPM segmentation algorithm are:

- Spatial normalization involving the transformation of the subject's images to corresponding template image;
- Segmentation of the images into a limited number of clusters (k). In this case the clusters correspond to GM, WM, CSF and background [24];
- Preprocessing of the segmentations through convolution with an isotropic Gaussian kernel to obtain the cluster concentration representing the probability distribution that the voxel belongs to a given region (GM, WM, or CSF).

A detailed description of the history of SPM and evolution of the segmentation toolbox is beyond the scope of this paper. Nevertheless, we give a brief description of the evolution of the MRI segmentation toolbox implemented in the SPM package for the above mentioned versions. One must note that *SPM99* [25], the earliest version used in this work, is already the 5th release of the SPM package [22]. This version has consolidated the image normalization procedure by introducing penalization factors on the non-linear deformation to obtain more robust invertible deformations. The *SPM2* release marked a turning point on the SPM software since this version introduced the Bayesian framework to replace the frequentist methods. *SPM5* release has consolidated the Bayesian formulation introduced in the previous version by its generalization in all the modules of the software. In the image registration and normalization this was made replacing the mean squared difference minimization between the subjects with Bayesian prior probabilities [26] allowing spatial normalization of different MRI sequences without the need to construct sequence-specific templates. The statistical analysis was also modified to include Bayesian formulation using spatial smoothness priors.

SPM8 version is the most recent release dating back to April 2009. The unified segmentation was rendered more stable by modeling, not only the brain, but the entire head using the Diffeomorphic Anatomical Registration Through Exponentiated Lie-algebra (DARTEL) [27]. These are deformations parameterized by a single flow field intended to obtain more accurate image registration between the brains of different subjects. This new version included routines for the construction of posterior probability maps