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Accuracy of partial volume effect correction in clinical molecular imaging of dopamine transporter using SPECT

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Abstract

Objectives: Partial volume effect (PVE) is a major source of bias in brain SPECT imaging of dopamine transporter. Various PVE corrections (PVC) making use of anatomical data have been developed and yield encouraging results. However, their accuracy in clinical data is difficult to demonstrate because the gold standard (GS) is usually unknown. The objective of this study was to assess the accuracy of PVC.

Method: Twenty-three patients underwent MRI and 123I-FP-CIT SPECT. The binding potential (BP) values were measured in the striata segmented on the MR images after coregistration to SPECT images. These values were calculated without and with an original PVC. In addition, for each patient, a Monte Carlo simulation of the SPECT scan was performed. For these simulations where true simulated BP values were known, percent biases in BP estimates were calculated. For the real data, an evaluation method that simultaneously estimates the GS and a quadratic relationship between the observed and the GS values was used. It yields a surrogate mean square error (sMSE) between the estimated values and the estimated GS values.

Results: The averaged percent difference between BP measured for real and for simulated patients was $0.7 \pm 9.7\%$ without PVC and was $-8.5 \pm 14.5\%$ with PVC, suggesting that the simulated data reproduced the real data well enough. For the simulated patients, BP was underestimated by $66.6 \pm 9.3\%$ on average without PVC and overestimated by $11.3 \pm 9.5\%$ with PVC, demonstrating the greatest accuracy of BP estimates with PVC. For the simulated data, sMSE were 27.3 without PVC and 0.90 with PVC, confirming that our sMSE index properly captured the greatest accuracy of BP estimates with PVC. For the real patient data, sMSE was 50.8 without PVC and 3.5 with PVC. These results were consistent with those obtained on the simulated data, suggesting that for clinical data, and despite probable segmentation and registration errors, BP were more accurately estimated with PVC than without.

Conclusion: PVC was very efficient to greatly reduce the error in BP estimates in clinical imaging of dopamine transporter.

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Keywords: Partial volume effect correction; Evaluation method; Brain; SPECT

1. Introduction

In SPECT imaging of the dopaminergic system, semi-quantification is highly recommended using, for instance, a measure of the specific binding potential (BP) of striatal sub-regions. The value of attenuation and scatter corrections for improving the accuracy of quantitative measurements has already been demonstrated. Even with these corrections, BP values remain underestimated by about 50% when measured within anatomical volumes of interest, because of partial volume effect (PVE) [1–3]. Simulations and phantom studies suggest that anatomically guided partial volume correction (PVC) combined with attenuation and scatter corrections reduce the biases in BP estimates to about 10% [1,2]. However, the accuracy of BP estimates in clinical data is difficult to demonstrate, first because the accurate value (gold standard—GS) of the BP to be estimated is usually unknown, and second because PVC is greatly affected by the accuracy of segmentation of

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anatomical data and of co-registration of SPECT with anatomical images, which are hard to control in clinical data. The objective of this study was to assess the accuracy of a PVC on clinical dopamine transporter SPECT studies.

2. Materials and methods

2.1. Patients

Twenty-three patients suffering from Dementia with Lewy Bodies (10 patients) and Alzheimer's disease (13 patients) were studied. All patients gave informed and written consent. They were intravenous injected with 185 MBq of 123I-FP-CIT 4 h before the SPECT scan.

2.2. SPECT and MRI acquisitions

SPECT were acquired on a three-headed camera PRISM 3000 XP (Philips) using high-resolution low energy fan-beam collimators. The camera was equipped with a line transmission source filled with Tc-99m. For all tomographic acquisitions in emission and transmission, 120 projections were acquired over 360°. Total examination duration was 50 min per patient.

Each patient underwent an MRI acquisition on a GEMS system (1.5 T) 1 week before the SPECT acquisition. A 3-D echo-gradient sequence was used (TR = 5000 ms, TE = 105 ms). The MRI slices were 2 mm thick with a pixel size of 3.6 mm. Five compartments (left and right caudate nuclei, left and right putamen, rest of the brain) were manually segmented on the MRI images.

2.3. Monte Carlo simulations

To get clinical-like data for which all characteristics and true BP values were known, a Monte Carlo simulation of the FP-CIT SPECT scan of each patient was performed using the SimSET code [4]. The anatomical data needed to describe the propagation media, which serve as an input of the simulations were derived from the segmented MRI of the patient. 123I activity concentrations equal to those found from the patient SPECT data after all corrections, were set in the five compartments.

2.4. SPECT data processing

The SPECT projections were corrected for scatter using the Triple Energy Window (TEW) method. Attenuation was compensated for by modelling attenuation in the Ordered Subset Expectation Maximization (OSEM) reconstruction algorithm [5]. The projections were then reconstructed using OSEM involving a fan-beam projector with 12 iterations and 12 subsets to ensure convergence. Reconstructed images were then convolved using a 3-D Gaussian filter, so that spatial resolution in the reconstructed images was 14 mm. The reconstructed pixel size was 2.1 mm, slice thickness was 3.6 mm.

For the patient data, the reconstructed SPECT images were registered with the MRI data using a rigid transformation maximizing mutual information. PVC was performed using a method adapted from a PVE correction proposed in PET imaging [1,2,6]. This method first estimates the contamination between the five functional compartments and then calculates the PVE corrected activity values in each compartment, given the contamination coefficients and the values measured in each compartment.

Putamen and caudate nucleus activities were measured in the left and right VOI's manually defined on MRI images. Mean background brain activity was measured in a cylindrical region in the occipital area. A BP value between striata and brain region was calculated as (striatal activity−background activity)/(background activity) for putamen and caudate nucleus, yielding four values per patient. For each dataset (real patient data or simulated patient data), BP were calculated on the reconstructed images without and with PVC.

2.5. Evaluation method

For Monte Carlo simulations, for which simulated BP values were known, percent biases in BP estimates were calculated as

$$\text{Percent bias} = 100 * |\text{estimated BP} - \text{true BP}|/\text{true BP}.$$

For the real data, an evaluation method that did not require the GS to be known was used. This method was an extension of a maximum-likelihood approach (EWAGS) [7] that has been proposed for comparing several estimation methods without a GS. The generalized method (GEWAGS) we propose [8] simultaneously estimates the GS and a quadratic relationship between the observed and the GS values using three hypotheses: (1) the statistical distribution of the unknown GS follows a beta law; (2) the relationship between estimated and (unknown) GS values is supposed to be quadratic; (3) the minimum and maximum values of the GS are approximately known. A surrogate mean square error (sMSE) between the estimated values and the estimated GS values is proposed as a figure of merit.

3. Results

3.1. Comparison between real and simulated patient data

Without PVC, in the putamen, BP was on average 2.0 ± 1.1 for real patients and was 1.9 ± 1.0 for the corresponding simulated patients. In the caudate nuclei, BP averaged over all real patients was 2.1 ± 0.8 and was 2.1 ± 0.8 for the simulated patients. With PVC, in the putamen, the average BP was 5.7 ± 3.6 for real patients and 5.9 ± 3.6 for simulated patients, respectively. In the caudate nuclei, the average BP was 7.9 ± 3.4 for real patients and 8.6 ± 3.4 for simulated patients. With or without PVC, BP

values measured on simulated data were almost identical to those measured on the corresponding patient data suggesting that the simulated data properly mimicked the real data.

3.2. Impact of PVC upon the BP estimates.

Combining scatter and attenuation corrections, the mean BP calculated over all patients was 2.1 ± 0.8 for the caudate nuclei and 2.0 ± 1.1 for the putamen. PVC introduced large changes in BP estimates. Combined with scatter and attenuation corrections, it increased BP to 7.9 ± 3.4 for the caudate nuclei and 5.7 ± 3.6 for the putamen.

Monte Carlo simulations of the 23 patient scans allowed us to objectively assess the quantitative accuracy in BP estimates. In the simulated patients without PVC, BP was underestimated by 71.3% on average in the caudate nuclei and by 55.1% in the putamen. Similar to what was observed on the patient data, PVC greatly affected BP values. When combined with scatter and attenuation corrections, it yielded a 13.4% overestimation of BP estimates in the caudate nuclei and a 16.1% overestimation in the putamen, hence largely decreasing the error magnitude compared to the absence of PVC.

3.3. Evaluation method

Fig. 1 shows GEWAGS results without and with PVC for the simulated patients. Although the BP GS were known for these patients, we assumed they were not when applying GEWAGS. The quadratic regression curve estimated by GEWAGS was closer to the identity line (corresponding to estimated BP = GS BP) when PVC was applied than without PVC. The quadratic regression curves were almost superimposed with the optimal regression curves that would be obtained if the GS was known (these curves could be calculated here as we were dealing with simulated data) proving the efficiency of GEWAGS. The

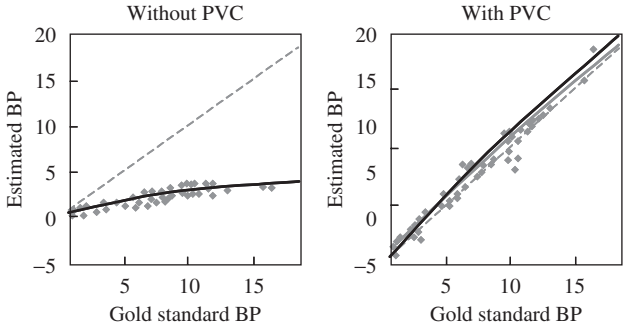

Fig. 1. GEWAGS results for the simulations of the real patients. The dashed grey lines correspond to the identity line (estimated BP = gold standard BP). The black curves are the quadratic regression curves estimated by GEWAGS. The grey curves correspond to the optimal quadratic regression curves that could be calculated as the GS was known. Estimated BP against gold standard BP are shown as grey diamonds.

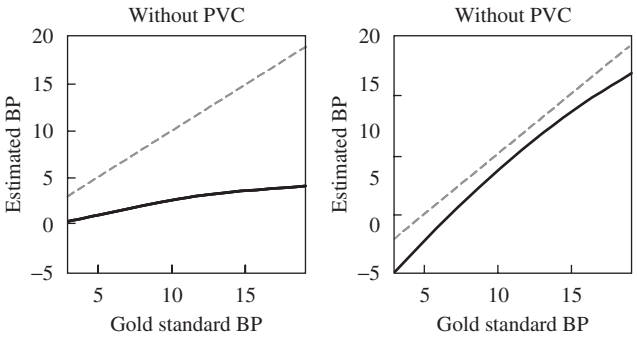

Fig. 2. Examples of GEWAGS results for the real patients. The dashed grey lines correspond to the identity line (estimated BP = gold standard BP). The black curves are the quadratic regression curves estimated by GEWAGS.

sMSE characterizing the accuracy of BP estimate were 27.3 without PVC and 0.90 with PVC, confirming that our sMSE index properly captured the greatest accuracy of BP estimates with PVC when the GS was not supposed to be known.

Fig. 2 shows GEWAGS results for real patient data. For these patients, BP bias could not be calculated as the GS was unknown.

Similar to what was observed for the simulated data, the quadratic regression curve estimated by GEWAGS was closer to the identity line when PVC was applied than without PVC. sMSE in BP estimates were 50.8 without PVC and 3.5 with PVC. These results were very consistent with those obtained using the simulated data, suggesting that for clinical data, and despite probable segmentation and registration errors, BP were more accurately estimated with PVC than without.

4. Conclusion

Using simulations and phantom experiments, we previously demonstrated that when combined with attenuation and scatter corrections, PVC was effective at reducing the biases in BP estimates, with errors of about 10% in dopaminergic neurotransmission 123I SPECT imaging. Considering 23 patients, we found that BP measured with PVC were much higher than BP measured without PVC. By simulating the SPECT data corresponding to these 23 patients and using an evaluation method appropriate for assessing the accuracy of estimation methods when the GS is unknown, we gathered evidences that the PVC considered in this study was very efficient to greatly reduce the errors in BP estimates in real patients undergoing dopamine transporter SPECT scans.

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