Evaluating intensity concentrations during the spatial normalization of functional images for Parkinson's Disease

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Abstract. The aim of this study is to assess the changes in imaging of dopamine transporters using [123]I-FP-CIT SPECT when applying a deformation of the striatum using a linear and/or a non-linear registration to a reference template. For that, the deformation has been indirectly measured studying the changes in the intensity values in two different scenarios when, during the interpolation stage, the amount or the concentrations of intensity values are preserved. As showed by our results, the degree of deformation is greater in images from patients with Parkinson's Disease than in healthy control subjects.

Keywords: Spatial normalization · FP-CIT SPECT · Neuroimaging · Parkinson's Disease

1 Introduction

[123]I-FP-CIT SPECT (DaTSCAN) is a complementary tool in the differential diagnosis of patients with Parkinsonism (PKS). This functional imaging modality allows the evaluation of synaptic parts of the dopaminergic system in the striatum region [14,9].

When a Computer-Aided-Diagnosis (CAD) system is being developed, generally, the image acquisition is followed by a preprocessing step that consists in the spatial normalization of the input brain scans. This registration allows us to perform a direct voxel-by-voxel comparison between brain scans from different patients and/or different acquisitions from the same subject.

When we evaluate [123]I-FP-CIT SPECT scans from patients with PKS, we can observe an accentuated loss of dopaminergic neurons in the nigrostriatal pathway, with a certain degree of asymmetry and a rounded shape [7]. On the contrary, images from healthy control subjects (NOR) are, in general, symmetric and with a well defined c-shape highly illuminated in the striatum [5]. As shown in Figure 1, these patterns help us to discriminate between NOR and PKS [10,8].

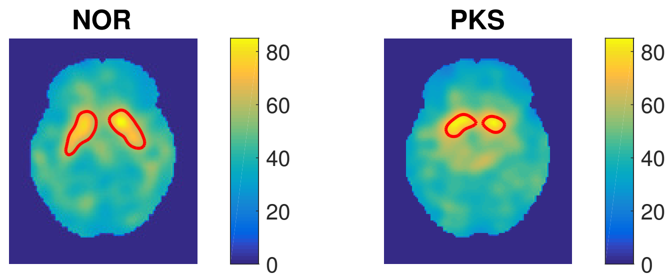


Fig. 1: Examples of [123]I-FP-CIT SPECT scans from NOR and PKS subjects in HUVN database.

Nevertheless, when the registration process is applied, usually by using a reference template built from a control subjects database, scans from PKS patients exhibit greater changes in their shape after the warping process in comparison with scans from control (NOR) subjects. This also applies to intensity preservation before/after the spatial normalization and it might alter artificially the interclass separation between the classes, which leads classification models based on Machine Learning to false optimistic results [4]. In this work we propose a comparison between intensity preservation of the concentration and intensity preservation of the amount during the spatial registration of [123]I-FP-CIT SPECT scans and determined their potential use when differentiating PKS and NOR subjects.

2 Materials & Methods

2.1 HUVN dataset

Dataset used for this work was supplied by the Service of Nuclear Medicine from Hospital Universitario Virgen de las Nieves de Granada (https://www.huvn.es/). It comprises a total of 118 [123]I-FP-CIT SPECT scans from NOR and PKS patients recruited between 2007 and 2012 whose demographics have been summarized in Table 1.

Table 1: Demographics (age given in terms of mean ± standard deviation) from HUVN dataset.

		Male	Female
HC	#	25	20
	Age	69.24 ± 10.80	73.20 ± 9.24
PD	#	45	28
	Age	69.34 ± 9.38	69.57 ± 8.81

All functional scans were obtained after the injection of 185 MBq of I123-Ioflupane radiotracer on previously thyroid-blocked participants.

Diagnostic labels were established by three experienced specialists from the Service of Nuclear Medicine of HUVN. All the informed consents are available through the institutional review boards from HUVN and approved by their local ethics committee local ethics committee.

2.2 Image preprocessing: Spatial registration

For this work we have compared a balanced subset of 20 NOR and 20 PKS scans randomly selected from patients included in HUVN database. During the preprocessing step, all the input scans have been spatially registered to a reference template generated ad-hoc following the procedure explained in [13]. For that, we have made use of the Statistical Parametric Mapping package available at https://www.fil.ion.ucl.ac.uk/spm/.

When using MRI, the spatial normalization procedure on SPM is based on segmentation [2]. On the contrary, [123]I-FP-CIT SPECT scans require having a reference MRI image at their same position. If this condition is not matched, an alternative method based on minimizing the mean squared difference between the template and a warped version of the image [11]. In any case, the finding of the deformation that better fits with the given data can be perform in two different ways:

1. Following an affine registration using a 12-parameter transformation that places each scan on the template applying translations, rotations, scaling and trimming. To optimize these parameters, one commonly used method is to minimize the mean squared differences between the image and the template [6].
2. Using a non-linear registration that also includes non-linear deformations to correct the residual differences between the input scan and the template by, for example, applying a linear combination of smooth cosine transform basis functions, as explained in [1].

During spatial normalization, the intensities of some brain regions are redistributed to compensate for the deformation applied by the spatial transformation. To this end, SPM proposes two models of intensity preservation [3]:

– **Intensity preservation of the concentration**. Where the spatially normalized images represent a weighted average of the signal under the smoothed kernel, roughly preserving the intensity of the original scans.
– **Intensity preservation of the amount**. In this case, the normalized scans preserve the total amount of signal for each region so intensities from expanded areas during warping are reduced.

Figure 2 includes an schema explaining how intensity preservation of the concentration and intensity preservation of the amount work.

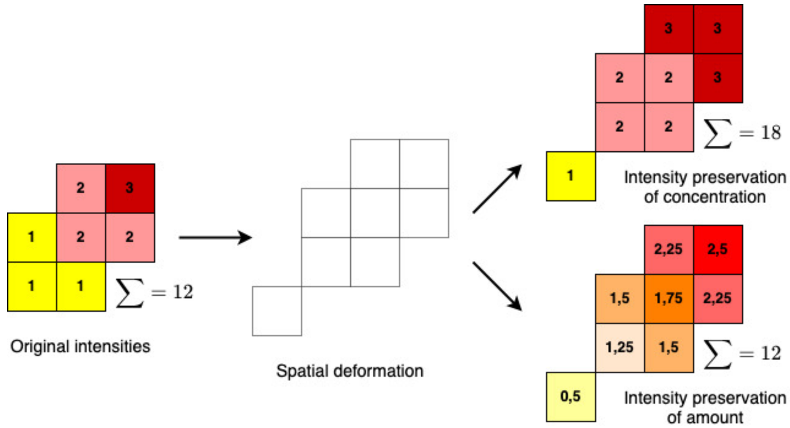


Fig. 2: Schema depicting the two models of intensity preservation included in `SPM12`.

2.3 Overview

For this work, we have normalized a total of 40 I[123]-FP-CIT SPECT scans (20 NOR and 20 PKS) to a reference space calculated following [13], for both affine and non-linear spatial registrations procedures and using both intensity preservation techniques (concentration or amount) in `SPM12`. Once the spatial registration was performed, we have selected a common reference Region Of Interest (ROI) given by the Automated Anatomical Labeling atlas [16], co-registered to our reference template, to focus our analysis on the striatum region [9]. Then, we have analyzed the distribution of intensity values within this region and compared all scenarios to determine the conditions where the interclass separation between NOR and PKS subjects is largest. Figure 3 shows a diagram with an overview of the procedure followed in this work.

3 Results

For this work, [123]I-FP-CIT SPECT scans from HUVN database have been spatially registered to the same reference space to evaluate differences between spatial registration preserving intensity concentration or preserving the amount of intensity for both affine and non-linear transformations. Figure 4 depicts the average of all the registered brain images and how intensities from NOR and PKS scans are altered as a function of the intensity preservation during the normalization when applying non-linear spatial deformations using `SPM12`.

In Figure 5 we have included the histograms of the intensity values within the striatum region of each scan after the non-linear registration procedure using a preservation of the total amount of the signal in the brain images. As expected, areas that are expanded during the warping process are correspondingly reduced in intensity. For the sake of clarity, histograms have been ordered depending on

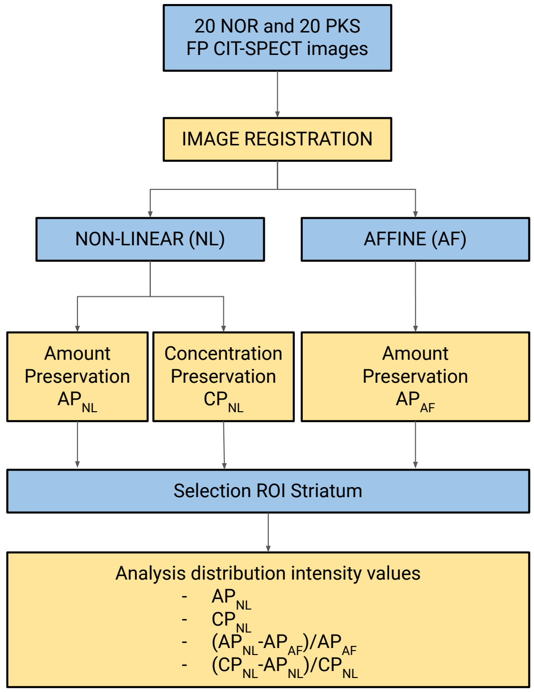


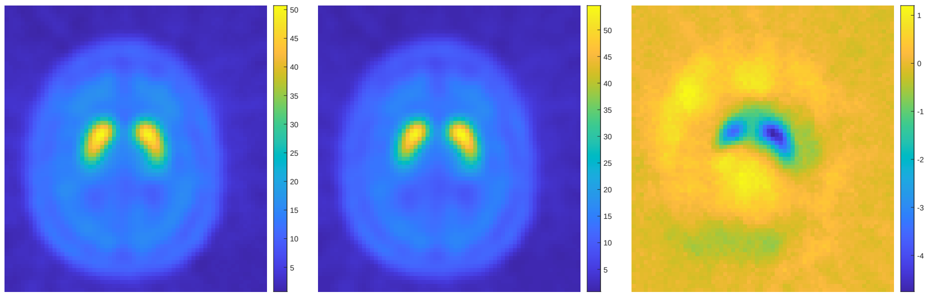
Fig. 3: General diagram.

the label of the images (NOR or PKS, having the first half of the figure filled with plots of NOR data).

Analogously, Figure 6 shows the distribution of intensity values in the striatum when the database is registered and the intensity concentrations of the original images are preserved. In that case, due to the fact that originally PKS images present a smaller striatum area according to the functional information provided by the [123]I-FP-CIT radiotracer, we obtain lower mean values.

To compare both methods, we have included in Figure 7 a representation of the distribution differences between the intensity values after preservation of the amount and concentration divided by the latter. This dimensionless factor provides a parsimonious way to measure the differences between NOR and PKS images [12].

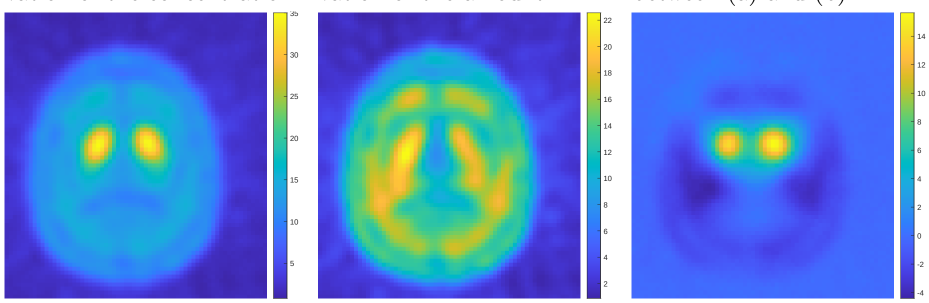
And finally, Figure 8 shows the histogram of the difference for the intensity values in the striatum between the registered database using both affine and nonlinear spatial registration referred to the preservation of the amount of intensity.



(a) Mean NOR with preservation of the concentration.

(b) Mean NOR with preservation of the amount.

(c) Map showing differences between (a) and (b).



(d) Mean PKS with preservation of the concentration.

(e) Mean PKS with preservation of the amount.

(f) Map showing differences between (d) and (e).

Fig. 4: Transaxial slices showing the average of HUVN dataset after the non-linear spatial registration. Note that affine registration scenario has not been included in order not to overload the figure.

4 Discussion

As shown in Figure 4, the image registration process affects NOR and PKS images very differently with special emphasis on the striatum region. Whereas the NOR images remain approximately the same, when we focus on PKS scans, we observe that their striatum are highly illuminated when we choose concentration preservation in the registration process. This is due to the fact that, in the case of this type of images, the striatum region and its surrondings have been deformed (enlarged) in excess to fit with the size of the reference template built only using NOR images [13,4]. Conversely, striatum region in NOR images is similar regardless using concentration preservation or amount preservation. In any case, on average, the final image is slightly more compressed in the striatum, so that the amount preservation shows slightly higher intensity values.

When focusing on Figure 5, we can easily check that PKS images exhibit slightly lower intensity values in the striatum due to a decreased dopamine transport. This behaviour is also observed in Figure 6 but to a lesser extent due to the intensity preservation of amount. This can be explained as intensity inter-

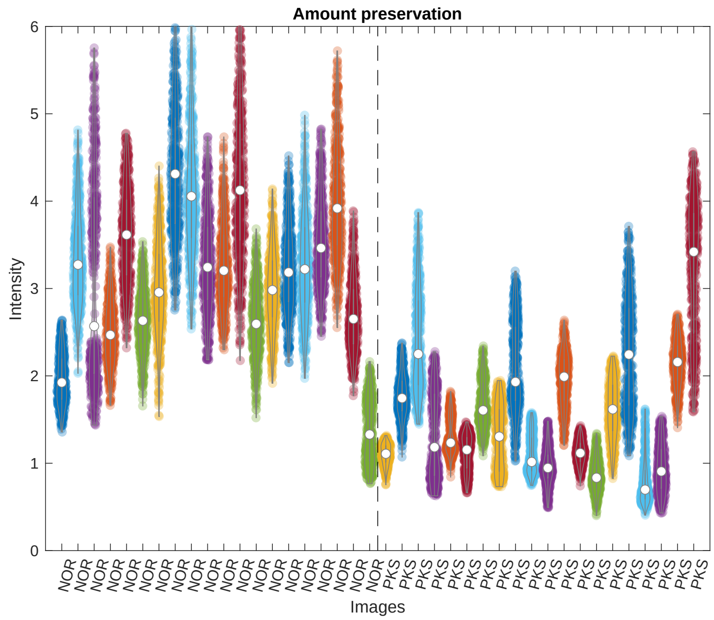


Fig. 5: Intensity distribution at striatum region for each image in HUVN dataset when referring to the amount preservation approach.

polations during the spatial normalization do not fill the space surronding the striatum with high intensity values from its borders. Note that as the PKS data is increased in the warped process to match the NOR template, the intensity values decrease.

Many CAD systems performing any morphological analysis of the brain, e.g. [15,5], may take advantage of a better delimitation of the striatum borders due to the intensity preservation of amount approach, which will probably lead to better classification rates. In any case, regardless being based on affine transformations or nonlinear transformations, these CAD models might also exploit the use of the dimensionless features computed when comparing the preservation of the amount and the preservation of the concentration in Figure 7 and Figure 8. As can be seen in both representations, there are large differences not only at the level of average intensity levels but also at the level of variability of the results when comparing NOR and PKS subjects.

5 Conclusions

Although intensity preservation of concentration is the default practice when normalizing brain scans to a reference template, its use for both affine and non-linear spatial registration should be taken with care. In this work we have shown

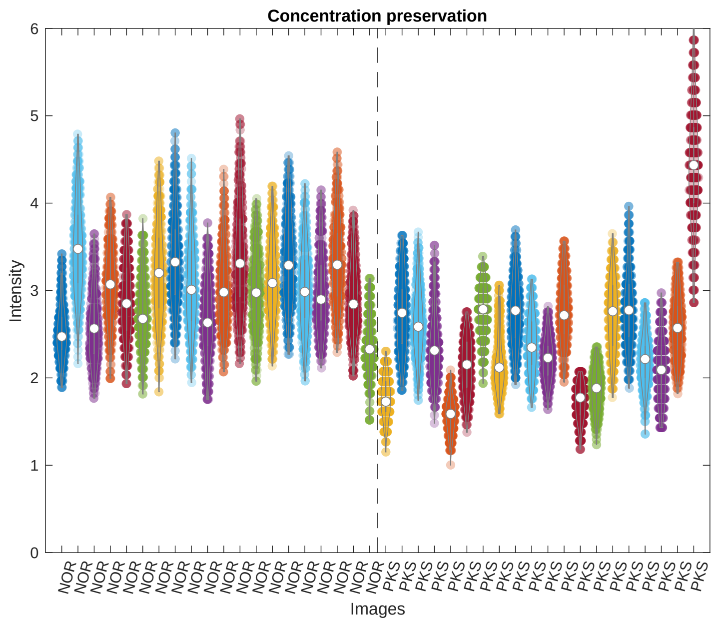


Fig. 6: Intensity distribution at striatum region for each image in HUVN dataset when referring to the concentration preservation approach.

that the preservation of the amount is more effective when comparing I[123]-FP-CIT SPECT scans for Parkinson's Disease due to the way it fills the space surrounding the striatum borders, specially in patients with Parkinsonism. This fact increases the interclass separation and help Computer-Aided-Diagnosis systems to differenciate between healthy controls and patients with Parkinson's. Apart from this, our proposal has identified a dimensionless imaging biomarker that increases this interclass separation when comparing both affine and non-linear spatial transformations referred to the intensity preservation of the amount.

Acknowledgments

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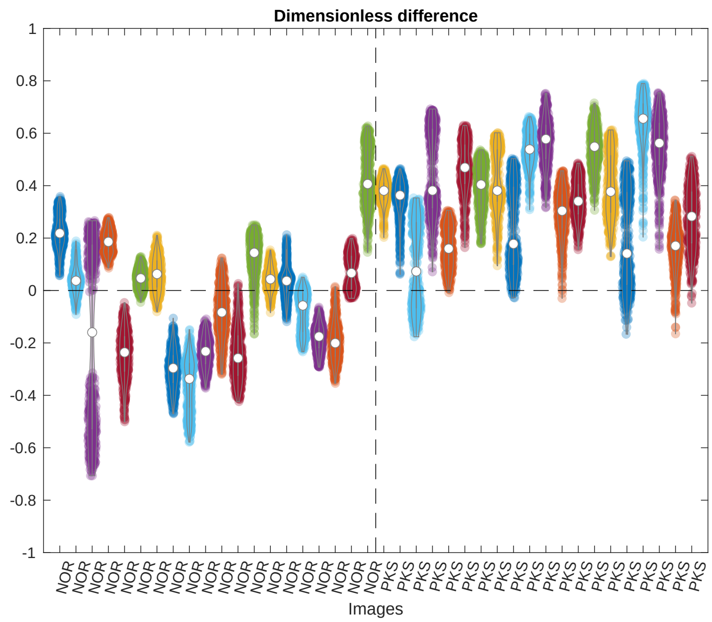

Fig. 7: Differences when using preservation of the amount and preservation of the concentration referred to the non-linear spatial registration scenario.

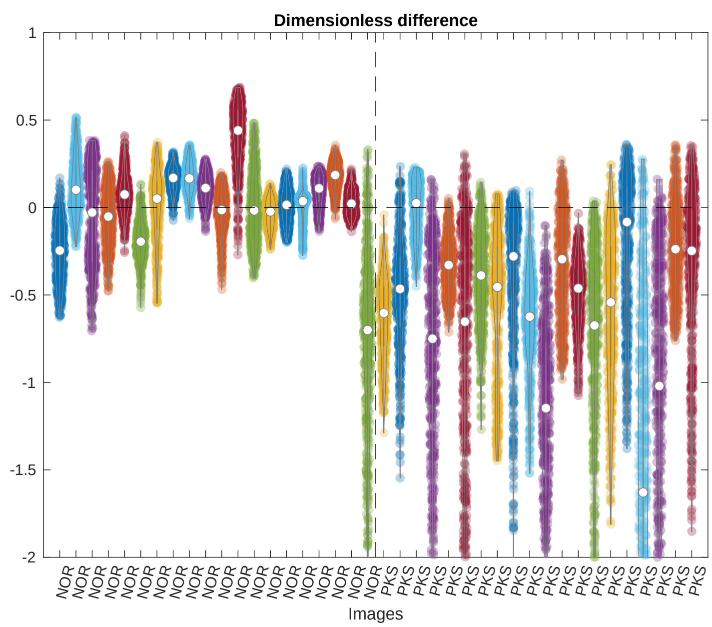

Fig. 8: Differences between affine and non-linear spatial registration referred the intensity preservation of the amount.

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