Evaluation of scatter correction in neurotransmission SPECT

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Abstract: As a result of photon interaction with matter, a SPECT image is affected by attenuation, scatter and statistical noise. In clinical practice, scatter correction is still a problem to be solved. In the present report, Monte Carlo techniques are used to obtain a database of SPECT simulated studies in order to evaluate the importance of scatter correction in Parkinson's Disease diagnosis. Even though scatter correction allows for obtaining better results, in some cases, when standardization is performed, it does not introduce a big improvement.

I. INTRODUCTION

Parkinson's Disease (PD) [1, 2] is a neurodegenerative disease characterized by motor disorders such as tremor, rigidity, slowness of movement, reduced and even loss of movement and impaired balance and coordination. PD is due to the death of dopaminergic neurons in the Substantia Nigra pars compacta (SNpc) of the midbrain, which is the source of a clinically important dopaminergic pathway to the striatum (caudate and putamen). Movement disorders arise from that dopamine deficiency. Presynaptic dopamine transporter (DAT) is a protein that controls dopamine levels located in the plasma membrane of the presynaptic neuron. It decreases when the number of dopaminergic neurons decrease.

Single Photon Emission Computed Tomography (SPECT) is a nuclear medical technique useful to obtain images from patient tissues activity by detecting gamma rays emitted after the injection of a radiotracer. [¹²³I]FP-CIT is the most common radiotracer for DAT SPECT imaging, as its rapid absorption permits SPECT acquisition a few hours after radiotracer administration. Besides, it is highly affine and has specific binding to DAT. Thus, [¹²³I]FP-CIT neurotransmission SPECT is helpful to diagnose PD when clinical evidence is inconclusive.

In a SPECT study several 2D projections are acquired from multiple angles around the patient. Thereupon tomographic reconstruction must be performed to obtain 3D images from acquired 2D projections. The mostcommonly used method is the Filtered Back Projection (FBP), although it only works well for images without degradation. An acceptable SPECT reconstruction can be obtained after applying diverse corrections even though acquired images are not ideal due to the interaction of gamma rays with the patient and with the collimator-detector. That interaction leads to attenuation, scattering and statistical noise. The problem with scattered photons is that they are diverted from their original direction. This phenomenon transmits scanty information of their emission spot. Therefore, they affect image contrast and resolution.

Furthermore, quantification must be accomplished for obtaining objective values, specially in cases that it is difficult to visually distinguish whether striatal uptake is normal or diminished. Quantification is also important to evaluate new therapies, as it is necessary to detect striatal uptake changes that occur after treatment. As quantification is dependent on the equipment and protocol used, there is a need to accomplish standardization. Moreover, it is important to determine whether scatter correction is needed when standardization is performed.

The aim of this work was to study whether scatter correction is necessary for SPECT neuroimaging in PD. In order to perform the study, Monte Carlo (MC) simulation was used to obtain a database of $[^{123}I]$ FP-CIT SPECT simulated studies.

II. MATERIAL AND METHODS

A. Simulation

MC techniques allow us to simulate realistic SPECT studies. In this project, a modified version of the Simulation System for Emission Tomography (SimSET) MC code [3] was used. It is a computational procedure that mimicks the physical processes that occur in nuclear medicine such as scattering or attenuation. Moreover, different collimators and detector designs can be selected. MC simulation provides realistic projections as it models diverse photon histories (both non-scattered and scattered photons) to exemplify all relevant aspects of the physical phenomena [4]. The SimSET MC code was used to simulate the SPECT projections from 23 healty patients. $[^{123}I]$ photons with 159 keV (low-energy) and gamma-rays with 529 keV (high-energy) were simulated independently and finally added up together to obtain the total projections. In order to perform the simulation, SimSET needs two inputs: activity maps and attenuation maps. The activity maps represent the radiotracer distribution, and to generate them, magnetic ressonance (MR) images were segmented into grey matter, white matter and cerebrospinal fluid. Non-specific uptake was considered to be the same for grey and white matter, whereas the activity in the cerebrospinal fluid was presupposed to be zero. The FIRST segmentation tool from FSL [5] was used to obtain caudate and putamen regions for each patient. Attenuation maps determine the photon-matter

interactions in patient and they were obtained by setting the corresponding attenuation coefficients for brain tissue and bone depending on the energy of the simulated photons. Brain tissue and bone were derived from the MRI of each subject and from a generic phantom, respectively [6]. FIG. 1 shows a MR of a patient which is used to determine caudate and putamen regions, and both activity and attenuation maps.



FIG. 1: Axial views of a randomly selected subject, corresponding to: (a) original MR image, (b) activity distribution map and (c) attenuation map.

Specific Uptake Ratio (SUR) is a parameter that quantifies the specific radioligand uptake in the striatal volume. SUR is defined as:

$$SUR = \frac{S-B}{B}$$

where S is the concentration activity in the striatum (caudate and putamen regions) and B is the concentration activity in a reference region of non-specific uptake placed in the occipital area. For each patient, six sinograms were created with SUR values from 0.5 to 10 randomly taken for both caudate and putamen. Simulated studies included normal uptake, pathological cases with uniform global striatal uptake reduction and a variety of unilateral and bilateral uptake asymmetries between caudate and putamen, thus covering a wide range of possible clinical situations. Finally, for each SUR value, a very high signal-to-noise ratio (SNR) trial was generated, and from it, ten noise trials were produced [7], understanding noise trials as normal SNR (3.10^6 counts) . FIG. 2 shows the theoretical SUR values for caudate and putamen for each study.

As MC simulation allows to obtain separately projections with non scattered and scattered photons, two different scenarios were taken into account:

- Primary photons. Projections formed by photons corresponding to 159 keV that enter the collimator. It is the ideal situation (without scattered photons, thereby simulating an ideal scatter correction).
- Total photons, including both primary and scatter photons, the last corresponding to low and high energy. It is the real situation.



FIG. 2: Theoretical SUR values for caudate and putamen for each of the 138 simulated studies (hollow blue circle for right hemisphere and red cross for left hemisphere).

B. Reconstruction

Reconstruction was performed by the FBP. Reconstructed images consisted of $128 \times 128 \times 45$ voxels, with a voxel size of $3.90 \times 3.90 \times 3.90 \text{ mm}^3$. Firstly, MC projections were filtered with a 2D Butterworth filter (order 5; cut-off frequency of 0.64 cm^{-1}). Then, reconstruction was performed by using a ramp filter. Attenuation was corrected with Chang's method [8] using the corresponding attenuation maps and attenuation coefficients:

- Primary photons. Chang factors are obtained from the attenuation coefficients, which are 0.149 cm^{-1} for brain and 0.307 cm^{-1} for bone.
- Total photons. Chang factors are obtained from an effective attenuation coefficient, and its value is $0.10 \ cm^{-1}$. It is called effective coefficient because aside from attenuation, this coefficient also takes into consideration scattered photons.

C. Quantification

In order to calculate SUR values, the mean activity values in regions of interest (ROIs) were needed. These regions were both left and right caudate and putamen. Striatal cavities segmented from the original MR images were resized to fit the reconstructed images. The reference value was extracted from an occipital ROI (FIG. 3). Quantification was directly performed over reconstructed SPECT images.

D. Standardization

As SUR values depend on the operator, the gamma camera used and the acquisition protocol, a standardization procedure was performed in order to obtain values that were independent from the acquisition variables. In



FIG. 3: Central slice of a reconstructed study showing the striatal ROIs (a) and original MR image showing the reference region (occipital): axial (b), sagittal (c) and coronal (d) views.

other studies carried out with a phantom [3], a simple linear model relating calculated to theoretical SUR has been used. However, this model does not take into account the partial volume effect (PVE), which is due to the low resolution of the image and consists on the spill out from the considered region to other regions and the spill in from adjacent regions into caudate and putamen. In order to consider the influence of adjacent regions, a new multiple linear model [9] for individually calculated SURs in caudate and putamen (SUR_c^{cal} and SUR_p^{cal}) can be defined [6]:

$$\begin{pmatrix} SUR_c^{cal} \\ SUR_p^{cal} \end{pmatrix} = \begin{pmatrix} \alpha_c & k_p^c \\ k_c^p & \alpha_p \end{pmatrix} \cdot \begin{pmatrix} SUR_c \\ SUR_p \end{pmatrix} + \begin{pmatrix} B_c \\ B_p \end{pmatrix}$$

where α coefficients represent the fraction of true SUR recovered in the corresponding structure, k coefficients express the fraction of true SUR from adjacent regions that contributes to the calculated SUR and B terms are constants which depend on the reconstruction method. These values were obtained by reversing the matrix system, once the system parameters had been obtained from linear regression of the whole data set relating calculated and theoretical SUR values.

Finally, to evaluate differences between standardized and theoretical values for each simulation, chi-square value (χ^2) and Root Mean Square Deviation (RMSD) were calculated for both caudate and putamen, using the formulas below:

$$\chi^2 = \sum_{i=1}^N \frac{(\theta_i - \hat{\theta}_i)^2}{(\hat{\theta}_i)} \qquad RMSD = \sqrt{\frac{\sum_{i=1}^N (\theta_i - \hat{\theta}_i)^2}{N}}$$

where θ_i and $\hat{\theta}_i$ are, respectively, the standardized and theoretical SUR and N is the number of studies.

III. RESULTS

FIG. 4 shows an example of a MC simulated study reconstructed using FBP. It can be seen that FIG. 4b is brighter because of a higher number of photons.

Errors for both caudate and putamen are gathered in TABLE I. Results for very high SNR are represented by H-SNR, whereas images with a normal SNR can be identified by N-SNR.



FIG. 4: Reconstructed images using FBP for primary photons (a) and total photons (b).

	Striatal Region	Noise	χ^2	RMSD
Primary	Caudate	H-SNR	5,20	0,35
photons		N-SNR	$65,\!28$	$0,\!54$
•	Putamen	H-SNR	5,00	0,29
		N-SNR	$63,\!66$	$0,\!45$
Total	Caudate	H-SNR	5,07	$0,\!34$
photons		N-SNR	$63,\!84$	$0,\!53$
-	Putamen	H-SNR	$7,\!18$	0,35
		N-SNR	89,10	0,53

TABLE I: χ^2 and RMSD errors between standardized and true values.

As it was expected, errors for both caudate and putamen are higher for cases with normal SNR than for cases with very high SNR. Moreover, as errors in caudate are similar for primary and for total photons, scatter correction when standardization is performed is not necessary to obtain better results. On the contrary, errors in putamen for total photons are higher, therefore scatter correction could be required in this case. Further experiments must be performed in order to determine its necessity.



FIG. 5: Standardized SUR against theoretical SUR for primary photons, for projections with very high SNR. The identity line is shown as a solid line and equations for both regression lines are displayed.

FIG. 5 to FIG. 8 show standardized SUR against theoretical SUR for each studied situation. In particular,

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FIG. 5 shows a practically linear relation between standardized SUR and theoretical SUR for primary photons in cases with very high SNR. Deviation is due to anatomical variability, as there are 23 different subjects. FIG. 6 shows a similar linear relation between either variables but with higher variance, as in this case variability coming from noise was added. Regression lines for both graphs are remarkably close to the identity line.



FIG. 6: Standardized SUR against theoretical SUR for primary photons, for projections with normal SNR. The identity line is shown as a solid line and equations for both regression lines are displayed.

For the study of total photons, the results are analogous to the outcome for primary photons. Both FIG. 7 and FIG. 8 show a linear behavior and regression lines for both graphs are also nearly close to the identity line.



FIG. 7: Standardized SUR against theoretical SUR for total photons, for projections very high SNR ratio. The identity line is shown as a solid line and equations for both regression lines are displayed.



FIG. 8: Standardized SUR against theoretical SUR for total photons, for projections with normal SNR. The identity line is shown as a solid line and equations for both regression lines are displayed.



FIG. 9: Standardized SUR for total photons against standardized SUR for primary photons, for projections very high SNR ratio. The identity line is shown as a solid line and equations for both regression lines are displayed.



FIG. 10: Standardized SUR for total photons against standardized SUR for primary photons, for projections with normal SNR. The identity line is shown as a solid line and equations for both regression lines are displayed.

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Finally it should be pointed out that the relationship between standardized SUR values obtained by using total photons or primary photons (FIG. 9 and FIG. 10) is essentially the identity line. Despite that almost perfect relation, mean relative errors going from 2.3% for caudate to 3.8% for putamen must be taken into account.

IV. CONCLUSIONS

Our findings show that when standardization procedures are performed, there is no need of further scatter correction for caudate, as in the end results obtained from total photons are practically the same obtained using primary photons. On the contrary, putamen needs additional scatter correction in order to obtain lower errors. For a first approximation, though, the scatter correction using an effective attenuation coefficient is acceptable. Further studies are necessary in order to evaluate whether scatter correction methods improve the results of working with total photons.

In our experiment, the parameters needed to calculate standardized SUR were obtained from the theoretical SUR of each patient. In clinical practice though, true values are not known. For that reason, it is necessary to use a generic phantom to obtain the parameters needed to perform the standardization procedure.

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- Schapira, A H V. Parkinson's disease. BMJ. 1999; 318(7179):311-4.
- [2] Kalia LV, Lang AE. Parkinson's disease. Lancet. 2015; 386(9996):896-912.
- [3] Crespo C, Gallego J, Cot A, Falcón C, Bullich S et al. Quantification of dopaminergic neurotransmission SPECT studies with 123I-labelled radioglands. A comparison between different imaging systems and data acquisition protocols using Monte Carlo simulation. Eur J Nucl Med Mol Imaging. 2008; 35(7):1334-42.
- [4] Manglos S, Floyd C, Jaszcak R, Greer K, Harris C and Coleman E. Experimentally measured scatter fractions and energy spectra as a test of Monte Carlo simulations. Phys Med Biol. 1987; 32(3):335-43.
- [5] Patenaude B, Smith SM, Kennedy DN, Jenkinson M. A Bayesian model of shape and appearance for subcortical brain segmentation. Neuroimage. 2011; 56(3):907-22

- [6] Gallego J, Niñerola-Baizán A, Cot A, Aguiar P, Crespo C, Falcón C, Lomeña F, Sempau J, Pavía J, Ros D. Validation of semi-quantitative methods for DAT SPECT: influence of anatomical variability and partial volume effect. Phys Med Biol. 2015; 60(15):5925-38.
- [7] Niñerola A. Quantification of striatal dopamine transporter SPECT in animal models and clinical research, PhD thesis. Universitat de Barcelona, unitat de Biofísica i Bioenginyeria, 2015.
- [8] Chang LT. Method for attenuation correction in radionuclide computed tomography. IEEE Transactions on Nuclear Science. 1978; 25(1):638-643.
- Rousset OG, Ma Y, Evans AC. Correction for partial volume effects in PET: principle and validation. J Nucl Med. 1998; 39(5):904-11.