Chinese SPECT semi-quantitative analysis of striatum

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Abstract To study and analyze reconstruction parameters in ^{99m}Tc-Trodat-1 SPECT (Tomography Emission-Computed Single-Photon) brain semi-quantitative analysis, and the outlined methods of ROIs (regions of interests). The ^{99m}Tc-trodat-1 SPECT brain imaging was processed, and the ROIs were outlined four times from December 2009 to July 2011. The results for each method were analyzed and compared to improve our experience. There was no statistically significance between the outlined number of pixel in both sides of the cerebellum and the ratio of the radioactive counts. From LEHR and FAN beam collimator, the average ratio became better with increasing the outlining method, especially the fourth time. It could be estimated that striatum mean volume (±SD) was (39.51±9.54 ml, in the range of 19.97–51.98 mL) and mean weight (±SD) was (44.09±10.64 g in the range of 22.28–58.01 g). The details of image processing and data analysis should not be ignored to outline appropriate methods, and withstand the repetitive inspection. The total striatum was outlined and its volume and weight was analyzed.

Key words Tomography Emission-Computed Single-Photon, Image enhancement, ^{99m}Tc-trodat-1, Striatum

1 Introduction

Single Photo Emission Computed Tomography (SPECT) development has been restricted by two factors of instruments, which related to hard/software and drugs. As to the software, except that the program itself should be powerful, the software users should master skillfully the program essentials and the various parameters.

Due to the different software application, engineers should design and develop their novel features and functions, such as 3D, virtual endoscopy, and other techniques, to demonstrate the software functionality to the users. For the software users, the easy operation, reproducibility, and high accuracy are their primary consideration.

Trodat-1, a dopamine transporter (DAT), has been widely used in the ratings and follow-up of Parkinson's disease, children's attention deficit disorder, and drug addiction[1–3] because of its good sensitivity and specificity.

The numbers of SPECT brain perfusion imaging are required to analyze after injecting ^{99m}Tc-Trodat-1. The semi-quantitative analysis is used to conduct imaging quality in the striatum, in order to judge whether the imaging is clear, or good and bad. Also, the ^{99m}Tc-Trodat-1 is rarely absorbed by brain tissues except for the striatum, but it is difficult to match image with SPM of Matlab because of limits of software and hardware, thus not reconstructing and analyzing the images. Because there is a wide gap between developing and developed countries in medical hardware and software, it is necessary to find a convenient method of sketching region of interests (ROIs), which extensively spread to China undeveloped areas and take semi-quantitative analysis.

In order to ensure experimental reproducibility, each step detail of the operation and different information in their period will be recorded. The pros and cons were summarized to obtain the repeated operations and the reliable experimental results.

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2 Materials and Methods

2.1 SPECT and Acquisition Conditions

This study used Germany's Siemens E. CAM Gantry Dual Head Ex.Base SPECT. Image processing and analysis software was Siemens esoft version 2.1.6.5. In December 2009, thirty-one right-hander healthy subjects, which included the 16-male subjects (mean=29.19 years, SD=6.89) and15 female subjects (mean=34.27 years, SD=7.51), were collected and canned by ^{99m}Tc-Trodat-1 brain SPECT. BMI (Body Mass Index) of all subjects were between 19 and 22. The whole acquisition time by low-energy high-resolution (LEHR) collimator was about 3.5 h. Datum acquisition was in a 128×128 matrix and 1.0 ZOOM. Double detector was automatically close to acquire data within 360° at 5.6°/ frame and 45 s/per frame. Five subjects were randomly selected to add Fan-beam collimator imaging. The acquisition time was approximately 4 h, the acquisition condition was identical to LEHR collimator, and press the probe of 14-cm radius by hand (one case is first collected by FAN Beam collimator, then by LEHR collimator).

This study was approved by the Ethical Committee of the Huashan Hospital of Fudan University. All participants provided the written informed consent.

2.2 Data Analysis and Processing

(1) The first image processing. After the acquisition in December 2009, the data was immediately analyzed by Butterworth function of filtered back-projection (Butterworth was used to conduct reconstruction algorithm, cutoff = 0.55, order = 7, attenuation correction was obtained using Chang's AC automatically to outline regions of interest, attenuation coefficient was 0.15 cm^{-1}). The information should avoid any loss as far as possible when choosing layers to reconstruct, including all layers of the acquisition.

The four SUM layer pictures on the axial images were selected, the cascading images with largest and full basal ganglia were found, and the ROIs of the left and right striatum at all levels were sketched. The SUM of two cerebellum axial layers in the stacked images was selected to find the clearest images, and the cerebellum ROIs at all levels were drew. After solving above stacked images, there were three lapses of ROIs in each transverse. The counts, number of pixels, maximum and minimum were took, when drawing both sides of the cerebellum ROIs. The four layers of the striatum were selected from the four levels, and the four data were used to sketch ROIs. The sum of left and right striatum of each layer counts was divided by the number of pixels. When the ratio of four consecutive layers data was greater than the other two, the 4-layer data were took, this guaranteed that left and right striatum data were at the same level. In January 2010, six LEHR objects were randomly selected, the cerebellum ROIs were re-painted in the original reconstruction image, and the ROIs data of cerebellum were compared with the previous in order to estimate human errors.

(2) The second image processing. In March -April 2010, Metz function (cutoff=0.55, order=15) of the filtered back-projection was used to reconstruct the image, and the occipital ROIs was painted. Two SUM axial images in the transverse layers of the striatum were selected, two central layers of the most clear cascading images were found, the occipital ROIs at all levels were drew, then the counts and number of pixels were got as the first image processing.

(3) The third image processing. In August 2010, the Metz function was used to re-sketch the occipital and cerebellum ROIs. A close level of the cerebellum to the base of the skull was adopted, and the outlined occipital areas were reduced. Only part of occipital cortex was selected to take counts and number of pixels. The ROIs was selected and sketched from occipital lobe to the occipital cortex.

(4) The fourth image processing. In about June -July 2011, Metz function of the filtered back-projection was used for image processing again by Fluorine-18 labeled 2β-carbomethoxy-3β-(4-chloro phenyl)-8-(2-fluoroethyl) nortropane (^{18}F-FECNT) imaging[4–7]. Generally, 30 layers of the basal ganglia excluding nasopharynx and skull roof were selected to reconstruct. ROIs were outlined by manual, the ZOOM was 1.2, Chang's attenuation coefficient was 0.12 cm^{-1}. The ROIs were outlined layer by layer, and their size each layer was different. Finally, the total striatum was outlined, and the area and the volume of total ROIs were calculated. The outlined parts of

cerebellum was about 5−7 layers, the left and the right occipital were about 4–6 layers, the left and the right caudate nucleus were about 8−10 layers, and the left and the right putamen nucleus were about 7−9 layers, as shown in Fig.1.

Fig.1 The forth image processing striatum ROIs.

To outline ROIs, the anatomical factors, counts, number of pixels and maximum were taken into account, such as the unclear boundary of the caudate nucleus and putamen nucleus, structures near the base of the skull. The ratio of each counts and number of pixels was calculated separately when selecting data. The minimum sum of two consecutive layers ratio of cerebellum, and the left and right occipital were selected. Also, the maximum sum of four consecutive layers of both sides of caudate nucleus and putamen nucleus were selected. Because the selecting ROIs were different from above three methods, it was not guaranteed that both sides of symmetrical ROIs were at the same layers as well as the caudate nucleus and putamen nucleus were successful at the same lever. As the third image processing, the ROIs of the cerebellum and occipital were outlined.

The results above four image processing were compared, and the statistical analysis was conducted by the IBM SPSS19.0 to analyze the changes of parameters in outlined ROIs.

3 Results

In the fourth image processing, the mean ratios of the radioactive counts at per pixel per injection dose were analyzed. The four times outlined ROIs data and the statistical results of the fourth were shown in Table 1 and Table 2. The average ratio became better and better with the outlining method increase, and mean ratio of the fourth time was the best by LEHR and FAN beam collimators (Table1). Table 2 shows that mean ratio of caudate nucleus was better than that of putamen nucleus.

Table 1 Four times ROIs ratio of the radioactive counts per pixel per injection dose.

	First			Second	Third	Fourth	
	Minimum	Average	Maximum	Average	Average	Average	Maximum
LEHR (n = 31)							
Right striatum	1.60 ± 0.59	2.74 ± 0.82	3.95 ± 1.18	8.06 ± 2.56		9.04 ±2.39	11.90 ± 3.46
Left striatum	1.48 ± 0.52	2.69 ± 0.80	3.94 ± 1.19	7.96 ± 2.51		8.99 ±2.38	11.83 ± 3.45
Striatum	1.21 ± 0.46	2.71 ± 0.81	4.05 ± 1.20	8.01 ± 2.53		9.02 ±2.38	12.11 ± 3.39
Cerebellum	0.93 ± 0.37	1.57 ± 0.40	2.25 ± 0.53	2.62 ±0.72	3.44 ±0.91	3.13 ±0.78	5.74 ± 1.40
Occipital*	/	/	/	3.47 ±0.92	3.91 ±1.17	3.07 ±0.74	4.48 ± 0.97
FAN (n = 5)							
Right striatum	12.76 ±6.64	22.64 ±11.56	34.28 ±17.53	7.77 ± 5.66		7.70 ±0.54	9.83 ± 1.36
Left striatum	13.35 ±7.09	23.58 ±12.12	35.21 ±17.96	7.89 ± 5.92		7.73 ±0.65	9.92 ± 1.40
Striatum	8.39 ± 6.56	23.09 ±11.74	35.92 ±18.17	7.83 ± 5.79		7.71 ±0.59	10.19 ± 1.47
Cerebellum	4.54 ± 2.27	7.76 ± 3.70	12.54 ± 6.17	2.07 ±0.55	3.25 ±2.18	2.83 ±0.17	4.31 ± 0.27
Occipital*	/	/	/	2.48 ±0.88	3.57 ±2.63	2.36 ±0.33	± 0.43

Note: Counts / pixel / mci.

*In the third and fourth, occipital cortex data was analyzed.

Table 3 shows the ratios of the radioactive counts and the number of pixel for thirty-one healthy subjects, and the fourth time ratio was greater than the others. In first image processing, the wilcoxon matched-pairs signed-ranks test was used to analyze re-painting and original pixel data and ratios of six objects (pixel data: $z = -1.26$, $P = 0.207$; and $z= -3.14$, $P = 0.753$). There is no statistically significance for the outlined number of pixel between both sides of the cerebellum and the ratio of the radioactive counts and pixel.

Thirty-one healthy subjects in the fourth image processing could estimate the imaging pixel, volume and weight of caudate nucleus, putamen and striatum (the image pixel was 0.4 mm×0.4 mm, the image thickness was about 0.39 mm, the striatum density was 1.116 g/ml[8]). The results were showed in Table 4.

LEHR collimator wilcoxon matched-pairs signed-ranks test results of right striatum and right occipital ratio of second/third, second/fourth, and third/ fourth are $z = 4.252$, $P < 0.001$; and $z = -4.723$, $P < 0.001$; and $z = -4.860$, $P < 0.001$.

LEHR collimator wilcoxon matched-pairs signed-ranks test results of left striatum and left occipital ratio of second/third, second/fourth, third/ fourth are $z = 1.764$, $P = 0.078$; and $z = -4.801$ $P < 0.001$; and $z = -4.782$, $P < 0.001$.

LEHR collimator wilcoxon matched-pairs signed-ranks test results of striatum and occipital ratio of second/third, second/fourth, third/fourth are $z = 3.684$ $P<0.001$; and $z = -4.840$, $P < 0.001$; and $z = -4.860$, $P < 0.001$.

Table 2 Ratios of radioactive counts per pixel per injection dose of the fourth with two collimators.

	LEHR		Fan-beam	
	right	left	right	left
Caudate nucleus	9.23±2.45	9.15±2.43	7.88±0.58	7.90±0.58
Putamen nucleus	8.85±2.43	8.83±2.33	7.51±0.52	7.56±0.72
Occipital cortex	3.08±0.79	3.07±0.74	2.25±0.38	2.46±0.36

Note: Counts / pixel / mci.

Table 3 Healthy subjects ratio of the radioactive counts and pixel.

	First	Second	Third	Fourth
LEHR (*n* = 31)				
Right striatum / right occipital	/	2.32 ±0.32	2.00 ±0.29	2.96 ±0.47
Left striatum / left occipital	/	2.28 ±0.30	2.15 ±0.27	2.95 ±0.55
Striatum / occipital	/	2.30 ±0.30	2.06 ±0.22	2.95 ±0.46
Striatum / cerebellum	1.71 ±0.16	3.07 ±0.51	2.31 ±0.30	2.90 ±0.36
FAN (*n* = 5)				
Right striatum / right occipital	/	2.91 ±1.26	2.09 ±0.39	3.48 ±0.46
Left striatum / left occipital	/	2.94 ±1.18	2.27 ±0.33	3.18 ±0.39
Striatum / occipital	/	2.93 ±1.22	2.16 ±0.33	3.31 ±0.35
Striatum / cerebellum	2.82 ±0.71	3.64 ±2.28	2.33 ±0.38	2.73 ±0.24

Note: LEHR collimator wilcoxon matched-pairs signed-ranks test results of striatum and cerebellum ratio of first/second, first/third, first/ fourth, second/third, second/fourth; third/fourth are $z =-4.860$, $P < 0.001$; and $z = -4.801$, $P < 0.001$; and $z = -4.860$ P <0.001; and $z = 4.860$, $P < 0.001$; and $z = 1.803$, $P = 0.071$; and $-z = 4.801$, $P < 0.001$.

Table 4 Fourth image processing ROIs pixels, volume, and weight.

	ROIs pixels		Volume / mL		Weight / g	
	Mean (±*SD*)	Range	Mean (±*SD*)	Range	Mean (±*SD*)	Range
Right caudate nucleus	156.55±37.89	70−236	9.77±2.36	4.37−14.73	10.90±2.64	4.87−16.43
Left caudate nucleus	155.65±40.01	72−207	9.71±2.50	4.49−12.92	10.84±2.79	5.01−14.42
Right putamen	169.32±42.20	89−235	10.57±2.63	5.55−14.66	11.79±2.94	6.20−16.37
Left putamen	151.61±44.27	68−206	9.46±2.76	4.24−12.85	10.56±3.08	4.74−14.35
Striatum	633.13±152.81	320−833	39.51±9.54	19.97−51.98	44.09±10.64	22.28−58.01

4 Discussion and Conclusions

The first image processing was fully in accordance with foreign reports[9−12], and the system analysis of parameters was conducted by some foreign references, and the result was very large after adjusting some parameters, especially Chang's AC and key points in selecting layers. Because of complex painting, the cerebellum ROIs were repainted a month later in order to check the repeatability of our method. Redrawn by a same doctor, there was no obvious difference between the two paintings. If not by the same person, it will lead to the considerable errors, especially choosing the ROI levels.

Other tests demonstrated that the image contrast for image reconstruction was larger in Metz function than in Butterworth function. Affected by foreign studies on ^{99m}Tc-trodat-1, the Metz function was used to reprocess the image in order to obtain a larger ratio of striatum and occipital[13]. Through the Metz function, the edge of the basal ganglia was smoother, and the boundary of ROIs was painted easily. Some researchers suggested that dopamine transporter was mainly concentrated in the occipital cortex. So the third image processing was taken.

The ROIs were repainted, and the putamen and caudate nucleus were sketched separately in two parts. Exchanging with the Siemens engineers, it was still unable to obtain the thickness of transverse-sectional images and know whether there were gaps or overlaps between the layers. Other image programs analysis of thickness might not be correct. The outlined ROIs were significantly associated with the ratio. If the ROIs reduced, the radioactive counts per pixel increased. According to the actual height of the striatum in MRI, the basal ganglia drawing the 10 layers can complete the correlation between the outlined ROIs, and the radioactive counts per pixel canbe evaluated.

The ROIs radioactive counts per pixel rose with the thickness thinner of the same 4-layer painting. Therefore, the image reconstruction took a bigger ZOOM in order to establish a better healthy subjects' database, this brought convenience for the future epidemic investigation.

Because the adjustment of the color bar (0, 100) would bring the organ volume amplification of the visual interest, it was always used to conduct imaging analysis and outline of ROIs. In first image processing, the reconstruction chose all layers; and in fourth image processing, the 30 layers of the basal ganglia excluding the nasopharynx and skull roof were selected to reconstruct. The image contrast of the final striatum including the nasopharynx and parietal was less than excluding that. In this artificial drawing, the larger the radioactive concentration was, the greater the frame was.

Many references have used the SPM software to conduct semi-quantitative analysis. Our study also tried to establish SPM model, but the brain image registration results were particularly poor when only the striatum images were matched, especially choosing a different angle on the *z* axis images, the SPM registration was not accurate. So we gave up the semi-quantitative analysis of SPM. There were also other limits of our research, no SPECT/ CT in the hospital and MRI data from different machines brought a great deal of inconvenience to the image registration (Old version was made in Siemens software and some programs did not authorized).

Though the ratio of striatum and cerebellum has been demonstrated, our study has shown that the fourth image processing got better, and was a suitable own way. This method can be recommended to the underdeveloped areas without advanced medical equipments. The outlined ROIs demanded proficiency in anatomical structures, and the details should not be ignored in the image processing and datum analysis. It should withstand the repetitive inspection. In this process, the total striatum should be outlined, and the volume and weight of the striatum should be analyzed.

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