

symptoms in their left or right side, and the authors attempt to find associations between the SAI and these symptoms.

It is conventional in the art to compare the patient image with age-matched controls, since it is known that the striatal uptake of a dopamine transporter radiopharmaceutical declines with age. Such comparison requires the use of normal image databases. Such databases are, however, only really meaningful for a coherent set of data, which may well mean the same camera, same software, same imaging protocol etc.

There is therefore still a need for dopamine transporter imaging methodology which is robust enough to give comparable results across a range of camera types, and avoids the large spread of data seen in multi-site studies, which is statistically sound, and is suitable for any age of patient.

The Present Disclosure.

In dopamine transporter radiopharmaceutical imaging, when uptake of the radiopharmaceutical in the brain is quantified, the values obtained vary significantly depending on the camera configuration and set-up, image acquisition parameters, and many other factors. It has therefore so far proved impossible to establish a meaningful normal database that is built on data from more than one camera type, without considerable effort to apply 'correction factors'.

In the current GE Healthcare product 'DaTQUANTTM', normal data from non-GE cameras is removed from the data set before calculating. In the Hermes BRASS product, correction factors are applied but this significantly compromises the utility and applicability of the 'normal' average values reported.

In an aspect, there is provided a method of imaging useful in the diagnosis of neurological disease, which comprises:

- (i) provision of a subject previously administered with a dopamine transporter binding radiopharmaceutical suitable for imaging dopamine function and obtaining, via tomographic imaging, a dopamine transporter radiopharmaceutical image;
- (ii) assessing, by visual assessment of said dopamine transporter radiopharmaceutical image, the uptake of said radiopharmaceutical in an equivalent region of:

(A) the left; and

(B) the right;

of the striatum of the brain of said subject;

(iii) calculating the ratio of the uptake in the equivalent left and right striatum region from step (ii);

5 (iv) comparing the ratio for said subject from step (iii) with a normal range of such ratios for normal subjects,
with the proviso that said method excludes further analysis to carry out comparison with age-matched and gender-matched patients/controls.

10 In a further aspect, there is provided a method of selecting or excluding a subject for a particular therapy of a neurological disease, which comprises the method of imaging as defined above.

In another aspect, there is provided a method of monitoring the efficacy of a course of
15 therapy of a neurological disease of a subject, which comprises the method of imaging as defined above.

In another aspect, there is provided a software tool suitable for carrying out:

- 20 (a) steps (ii) to (iv) of the method of imaging as defined above; or
(b) the method of selection as defined above; or
(c) the method of monitoring as defined above; or
(d) combinations of one or more of (a) to (d).

In another aspect, there is provided the use of the radiopharmaceutical suitable for
25 imaging dopamine function as defined above in one or more of:

- (i) the method of imaging as defined above;

- (ii) the method of selection as defined above; or
- (iii) the method of monitoring as defined above.

5 In another aspect, there is provided the use of the software tool as defined above in one or more of:

- (i) the method of imaging as defined above;
- (ii) the method of selection as defined above;
- (iii) the method of monitoring as defined above.

10 In another aspect, there is provided the use of a tomographic imaging device in one or more of:

- (i) the method of imaging as defined above;
- (ii) the method of selection as defined above; or
- (iii) the method of monitoring as defined above.

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The present disclosure is based on the observation that left : right symmetry of striatum uptake in the normal patient population is maintained independent of the age and gender of the patient. This symmetrical left/right striatum uptake is shown to be independent of camera type and image acquisition parameters, and is proposed as a
20 more robust way to generate both a normal database and patient comparator data –

CLAIMS.

1. A method of imaging useful in the diagnosis of neurological disease, which comprises:

- 5 (i) provision of a subject previously administered with a dopamine transporter binding radiopharmaceutical suitable for imaging dopamine function and obtaining, via tomographic imaging, a dopamine transporter radiopharmaceutical image;
- (ii) assessing, by visual assessment of said dopamine transporter
10 radiopharmaceutical image, the uptake of said radiopharmaceutical in an equivalent region of:
- (A) the left; and
(B) the right;
of the striatum of the brain of said subject;
- 15 (iii) calculating the ratio of the uptake in the equivalent left and right striatum region from step (ii);
- (iv) comparing the ratio for said subject from step (iii) with a normal range of such ratios for normal subjects,
with the proviso that said method excludes further analysis to carry out
20 comparison with age-matched and gender-matched patients/controls.

2. The method of claim 1, where the radiopharmaceutical comprises a tropane, and is chosen from: ^{123}I -ioflupane, ^{18}F -ioflupane, ^{123}I -Altropane, ^{123}I -PE2I, ^{11}C -PE2I, ^{123}I -IPT, ^{123}I - β -CIT, ^{18}F - β -CFT, $^{99\text{m}}\text{Tc}$ - TRODAT or $^{99\text{m}}\text{Tc}$ -technepine.

3. The method of any one of claims 1 or 2 where the neurological disease is suspected to be Parkinson's disease, Parkinson's syndromes or Lewy Body Dementia.

4. The method of any one of claims 1 to 3, where the equivalent region of step

5 (ii) is chosen from:

- (a) the whole striatum;
- (b) the caudate;
- (c) the putamen; or
- (d) or combinations thereof.

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5. The method of any one of claims 1 to 4, which further comprises one or more of the following:

(I) calculating a caudate:putamen or putamen:caudate ratio for the left and right striatum separately;

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(II) calculating a striatal binding ratio (SBR; as defined above) for left and right hemisphere;

(III) calculating the ratio of counts in equivalent left and right regions of the brain;

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(IV) comparing left:right (or right:left) ratios obtained in (III) with normal values.

6. A method of selecting or excluding a subject for a particular therapy of a neurological disease, which comprises the method of imaging of any one of claims 1 to 5.

7. A method of monitoring the efficacy of a course of therapy of a neurological disease of a subject, which comprises the method of imaging of any one of claims 1 to 5.

8. A software tool suitable for carrying out:

(a) steps (ii) to (iv) of the method of imaging of any one of claims 1 to 5; or

(b) the method of selection of claim 6; or

(c) the method of monitoring of claim 7; or

(d) combinations of one or more of (a) to (c).

9. The software tool of claim 8, which runs on a personal computer, a gamma camera or a PET camera.

10. The software tool of claim 8 or 9, further comprising a database of ratios, wherein said database contains such ratios for normal subjects as defined in any one of claims 1 to 5.

11. The use of the radiopharmaceutical suitable for imaging dopamine function as defined in any one of claims 1 or 2 in one or more of:

(i) the method of imaging of any one of claims 1 to 5;

(ii) the method of selection of claim 6; or

(iii) the method of monitoring of claim 7.

12. The use of the software tool as defined in any one of claims 9 to 11 in one or more of:

(i) the method of imaging of any one of claims 1 to 5;

(ii) the method of selection of claim 6;

(iii) the method of monitoring of claim 7.

13. The use of a tomographic imaging device in one or more of:

(i) the method of imaging of any one of claims 1 to 5;

5 (ii) the method of selection of claim 6; or

(iii) the method of monitoring of claim 7.