## SPECT Image Reconstruction

Mean radius of rotation was 15.7 cm. (range 14.9-16.4 cm). Scanning was performed in continuous mode and projection data was acquired with 40 angular steps of 3° for each camera head. Squared 2.33 mm pixels were acquired in a 128×128 matrix. Three separate energy windows were acquired simultaneously. The main window containing the primary photons of 159 keV from I-123 was centered at 159 keV with a width of 20%. A down scatter window was centered at 200 keV with a width of 16% and a scatter window was centered at 127 keV, with a width of 25%.

Reconstruction was performed in Matlab 7.14 (Mathworks) with the rampfiltered backprojection method. Three dimensional low-pass postfiltering was performed by applying a fourth order (*n*) Butterworth filter with frequency (*f*) response of  $(1+F^{2n})^{-1}$  with  $F=f/f_c$  and a cutoff frequency  $f_c$  of 0.12 Nyquist for the first ten frames and 0.175 Nyquist for the consecutive frames. Before reconstruction the scatter windows were subtracted with appropriate weights. Correction for Compton scattered primary photons was performed by using the Dual Energy Window (DEW) method (*1*) with a weight of 0.5. Down scatter (DS) correction for septal penetration and down scatter of high energy photons (mainly 529 keV photons with a yield of 1.4% which backscatter into the crystal with an energy peak centered at 172 keV) was performed by subtraction of the DS window with an experimental determined weight of 1.36 (2). For simultaneous DEW and DS the weight for the DS window was adjusted to 0.82 in order to compensate for the down scattered photons in the scatter window (3). Attenuation correction was done according to Chang's method based on head segmentation of the sinogram of the summed scatter and primary window (2). For scatter corrected images a narrow beam linear attenuation coefficient of 0.15 cm<sup>-1</sup> was used, where a value of 0.10 cm<sup>-1</sup> was used for the non scatter corrected images (4).

A 6.6 L acrylic cylindrical phantom filled with a homogeneous activity solution in water was used for determining the conversion factor between count rate and activity. Activity concentration was determined both by measuring four 0.5 mL samples from this solution in a gamma counter (Cobra II Auto Gamma, Perkin-Elmer Packard, Waltham, Massachusetts, USA) with an energy window of 15-240 keV and measurement of the added amount of activity with a dose calibrator (Capintec CRC®-15R). Count rate was calculated from the counts in a 2.7 L volume of interest inside the phantom and the one hour measuring time. At the time of measurement the activity concentration was 14.5 kBq/mL and the conversion factors were 4.2, 5.2, 4.0 and 5.0 kBq/cps for the reconstructions with no scatter corrections, DS, DEW and DEW+DS, respectively.

## **TSPO** Genotyping

Notably, we used 200  $\mu$ l buffy coat/saliva per QIAamp Mini Spin Column and genomic DNA was eluted in 100  $\mu$ l AE buffer. The exact DNA quality and concentration were measured by use of UV-Vis spectrophotometer (NanoDrop2000, Thermo Scientific) to enable calculation of target DNA concentration of approximate 10-50 ng/ $\mu$ l.

The TSPO-Ala147Thr (rs6971) genotyping was performed using TaqMan<sup>®</sup> SNP Genotyping Assay (Applied Biosystems, Assay-on-Demand<sup>TM</sup> SNP Genotyping product: C\_2512465\_20). Allelic discrimination PCR amplification was carried out on LightCycler® 480 Real-Time PCR System (Roche Applied Science) using standard thermal cycling (Initiation step at 94°C for 10 minutes, 40 cycles of denaturation 94°C for 30 seconds, annealing 60°C for 45 seconds and extension at 72°C for 1.30 minute, a cooling at 36°C for 5 minutes) and TaqMan® 2x PCR Master Mix (TaqMan Universal RCR Master Mix, Applied Biosystems).

References

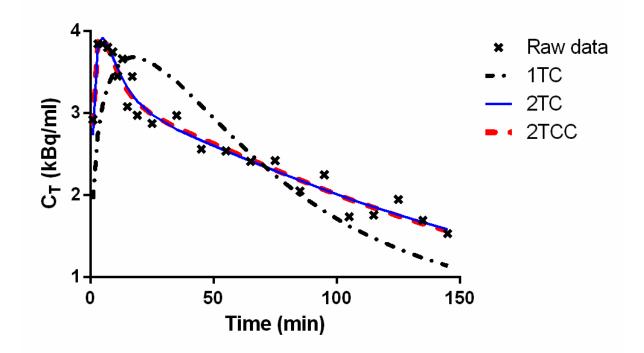
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**2.** de Nijs R, Holm S, Thomsen G, Ziebell M, Svarer C. Experimental determination of the weighting factor for the energy window subtraction-based downscatter correction for I-123 in brain SPECT studies. *J Med Phys.* 2010;35:215-222.

**3.** Lagerburg V, de Nijs R, Holm S, Svarer C. A comparison of different energy window subtraction methods to correct for scatter and downscatter in I-123 SPECT imaging. *Nucl Med Commun.* 2012;33:708-718.

**4.** Zaidi H, Montandon ML. Which attenuation coefficient to use in combined attenuation and scatter corrections for quantitative brain SPET? *Eur J Nucl Med Mol Imaging*. 2002;29:967-969; author reply 969-970.

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**SUPPLEMENTAL FIGURE 1** Raw and modelled time-activity curves of the peri-infarct zone of patient 6

Raw data are shown with stars. TC: tissue compartment model; TCC: tissue compartment model with constraints.  $C_T$  is the tracer concentration in the peri-infarct zone.

**SUPPLEMENTAL TABLE 1** Rate constant from the plasma to tissue  $K_1$  and the distribution volume  $V_T$ 

	Gd lightup		Total CB	
G	$K_1$	<b>T</b> 7	$K_1$	17
Scan ID	(mL cm <sup>-3</sup> min <sup>-1</sup> )	$V_T$ (mL cm <sup>-3</sup> )	(mL cm <sup>-3</sup> min <sup>-1</sup> )	$V_T$ (mL cm <sup>-3</sup> )
C003	0.128	1.78	0.187	1.04
C012	0.091	1.88	0.164	1.18
C005	0.306	4.87	0.179	1.91
C006	0.186	12.1	0.126	4.08
C013	0.242	39.1	0.232	6.81
C008	0.197	10.6	0.327	4.02

This table provides  $K_I$  and  $V_T$  of two-tissue compartment modelling for the regions indicated in T1 Gd images and the reference region (total cerebellum (CB)).