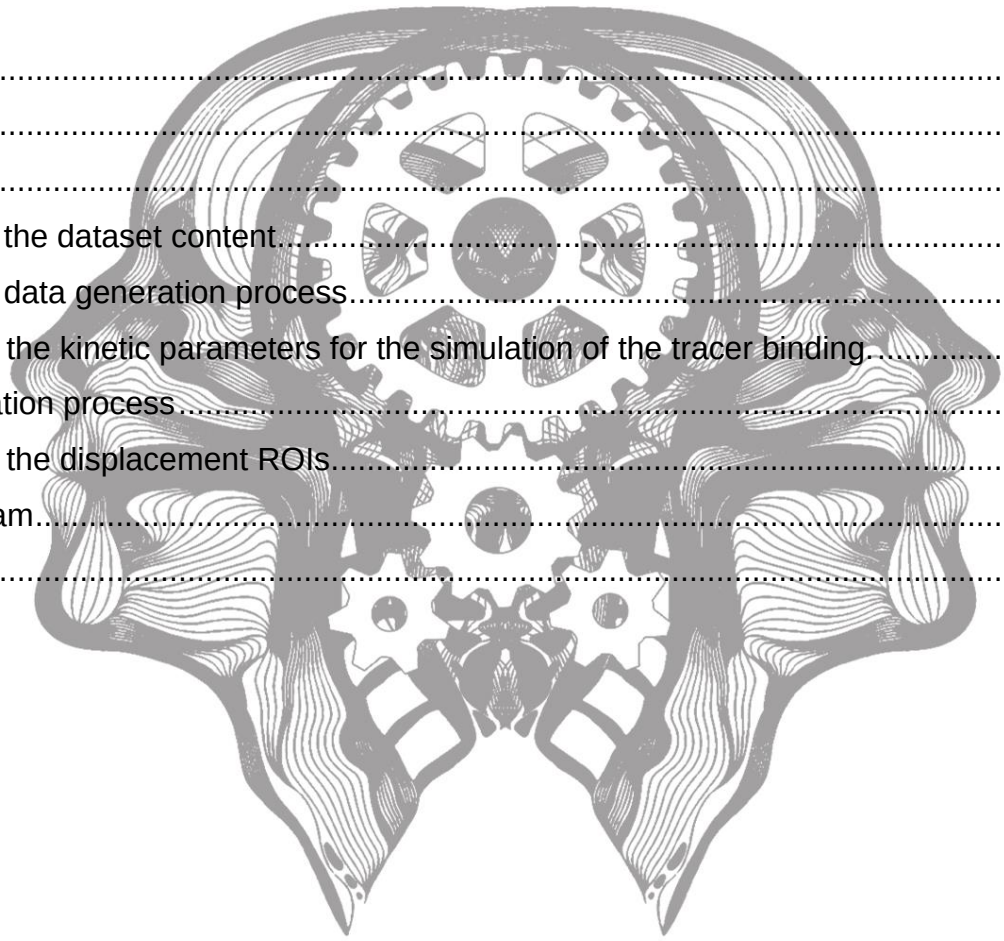
NRM2018 – PET Grand Challenge Dataset

An event part of London 2018 Neuroreceptor Mapping meeting (www.nrm2018.org)

Contents



Supported by

Invicro

King's College London & Guy's and St Thomas' PET Centre

Introduction

Rationale

For many years PET centres around the world have developed and optimised their own analysis pipelines, including a mixture of in-house and independent software, and have implemented different modelling choices for PET image processing and data quantification. As a result, many different methods and tools are available for PET image analysis.

This dataset aims to provide a normative tool to assess the performance and consistency of PET modelling approaches on the same data for which the ground truth is known.

Aims

This dataset was created and released for the NRM2018 PET grand challenge. The challenge aimed at evaluating the performances of different PET analysis tools to identify areas and magnitude of receptor binding changes in a PET radioligand neurotransmission study.

Description of the dataset content

The PET dataset refers to 5 simulated human subjects scanned twice. For each subject the first PET scan (*PET1 – baseline*) represents baseline conditions; the second scan (*PET2 – displaced*) represents the scan after a competitive pharmacological challenge in which the tracer binding has been displaced in certain regions of interest. A total of 10 dynamic PET scans are provided.

The nature of the neuroreceptor tracer used for the simulation (hereafter referred to as [11C]LondonPride) wants to be as general as possible. Any similarity to real PET tracer uptake is purely coincidental.

Each simulated scan consists of a 90 minutes dynamic PET acquisition after bolus tracer injection as obtained with a Siemens Biograph mMR PET/MR scanner. The data were simulated including attenuation, randoms and scatters effects, the decay of the radiotracer and considering the geometry and resolution of the scanner. PET data can be considered motion-free as no motion or motion-related artifacts are included in the simulated dataset. The data were binned into 23 frames: 4×15 s, 4×60 s, 2×150 s, 10×300 s and 3×600 s. Each frame was reconstructed with the MLEM algorithm with 100 iterations. The reconstructed images available in the dataset are already decay corrected. Details on scan binning are reported in the ancillary file (.anc) associated with each dynamic PET image. No blood data is provided for any of the PET acquisitions.

All provided PET images are already normalised in standard MNI space (182x218x182 – 1mm). A structural co-registered and resliced MRI template is provided (MNI_T1_2PET.img/.hdr and MNI_T1_brain_2PET.img/.hdr).

Individual noise-free dynamic PET data have been simulated from individual set of kinetic parameters (K_1, k_2, k_3, k_4 and V_b). Kinetic parametric maps are provided for each subject to define the ground truth of the tracer binding to tissues. Further information on the data simulation is reported in the next section.

No region segmentation is provided but is known that the cerebellum is the ideal reference region (k_3=0) and that the data have been simulated to have K_1/k_2, $k_4$and $V_b$are fixed to the same values for all the brain voxels.

The regions of displacement (6 in total) are the same for all subjects as reported by the DisplacementROIs.img/.hdr map. The map is already co-registered and resliced to the PET scans and to the MRI template.

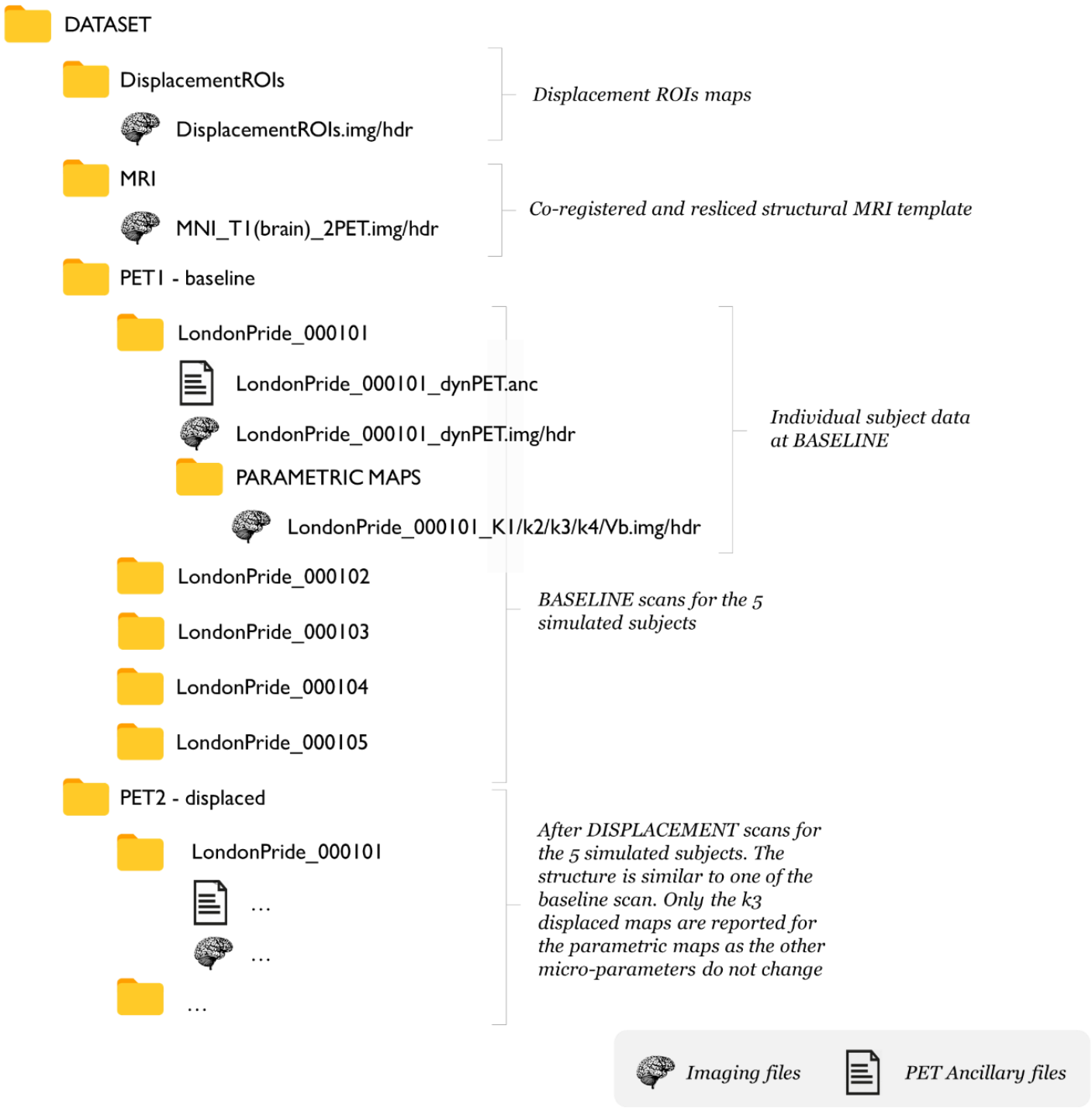
The tracer binding displacement has been simulated by manipulating the individual $k_3$maps only. Specifically, displaced k_3 maps have been obtained from the baseline k_3 maps by applying the following percental reduction to each of the following displacement ROIs:

- ROI 1 – Displacement Map value = 1 – Displacement 27%
- ROI 2 – Displacement Map value = 2 – Displacement 27%
- ROI 3 – Displacement Map value = 3 – Displacement 21%
- ROI 4 – Displacement Map value = 4 – Displacement 18%
- ROI 5 – Displacement Map value = 5 – Displacement 18%
- ROI 6 – Displacement Map value = 6 – Displacement 18%

All the other kinetic parameters have been maintained identical between PET1 and PET2.

A summary of the dataset folder hierarchy is reported in Figure 1.

Figure 1 – Overview of the dataset folder hierarchy



Description of data generation process

Definition of the kinetic parameters for the simulation of the tracer binding.

We used a dataset of 8 brain [11C]Ro154513 PET scans to generate the reference data. The best 5 subjects (in term of quality of the parametric maps) were used as starting point to generate the data. We preferred to start from real measured PET data rather than arbitrary generated parametric maps in order to biologically account for the spatial covariance of the brain tissues.

An unconstrained 2TCM was used for the quantification of the data applied at voxel. The variational Bayesian method (Castellaro, Rizzo et al. 2017) was used to reach a satisfying level of homogeneity on the final parametric maps and a limited outlier percentage (*first level analysis*).

A constrained 2TCM was hence used for the re-quantification of the data. The following constraints were imposed to fulfil FRTM (Cunningham, Hume et al. 1991) requirements (*second level analysis*):

Cerebellum was artificially constrained to be reference region (by setting k_3=0);

K_1/k_2,$k_4$and V_b were fixed as the whole-brain average values obtained in the first level analysis (after elimination of outliers);

Note that in cerebellum, white matter and brainstem only, quantification of PET data was performed with 1TCM_constrained (i.e. with K_1/k_2 and V_b fixed to the whole-brain average values obtained in the first level analysis).

As post-processing, the parametric maps were smoothed with a local 'median' filter, 4 mm and normalized in in MNI space (2 mm), then interpolated in 1 mm MNI space using the individual structural MRI.

Data Simulation process

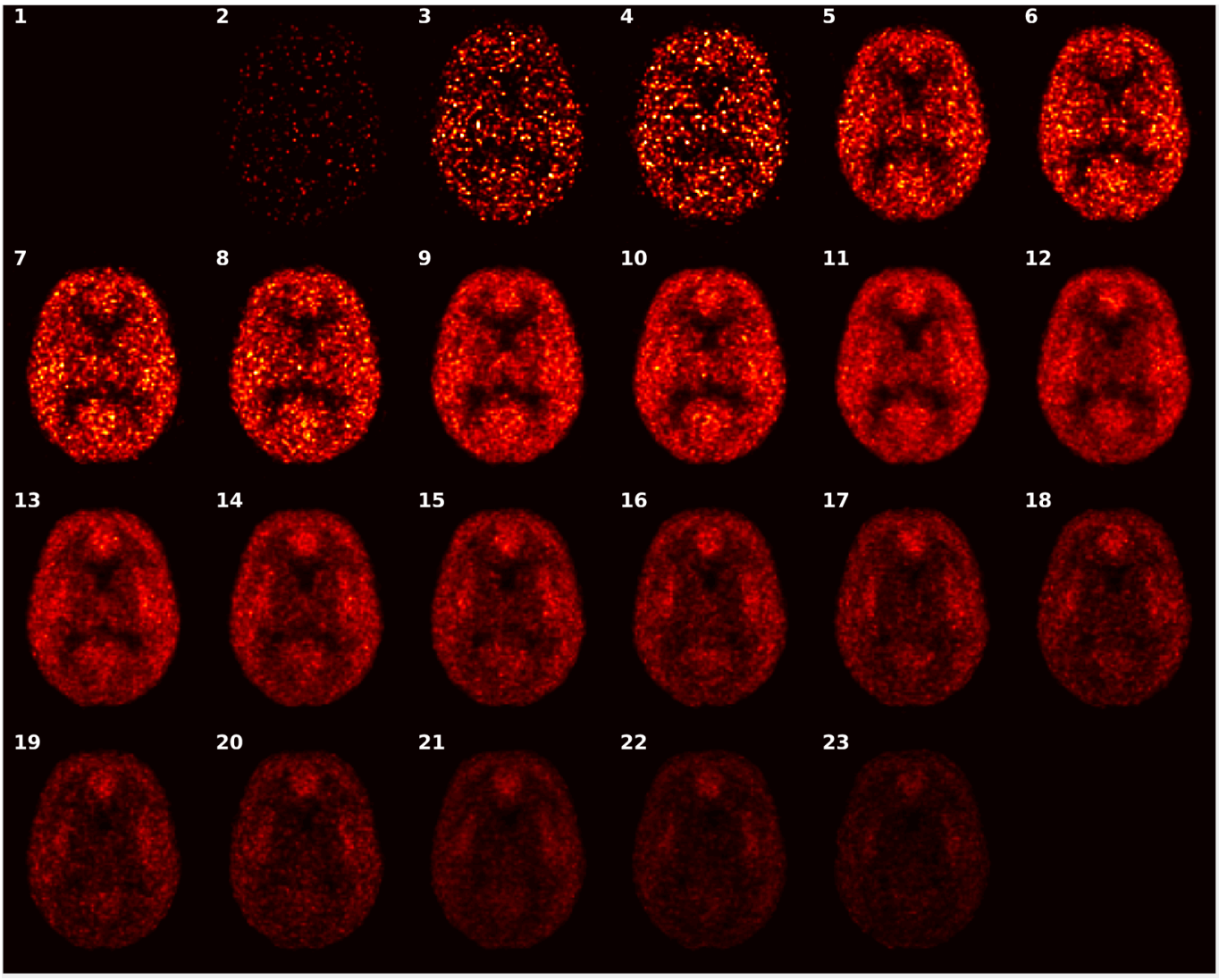
For the simulation of each of the 10 scans (5 patients, 2 scans each), time activity curves (TACs) for each voxel of the phantom were generated from the kinetic parameters using the 2TCM equations. The TACs had a resolution of 1 sec and included the effect of the radiotracer decay, which was simulated with a half-life of 20.34 min (^{11}C half-life). Each voxel TAC was binned with the following framing: 4×15 s, 4×60 s, 2×150 s, 10×300 s and 3×600 s by using the mean activity value for each time frame. After this process, the dynamic phantom for each scan is ready to be used in the simulation of each scan. The phantoms had the same resolution as the parametric maps (1×1×1 mm^3).

Each scan was simulated with a total of 3×10^8 counts and by modelling the different physical effects of a PET acquisition. For each frame of a scan, the phantom was smoothed with a 2.5 mm FWHM kernel (lower than the spatial resolution of the mMR scanner since the phantom was already low resolution) and projected into a span 11 sinogram using the mMR scanner geometry. Then the resulting sinograms were multiplied by the attenuation factors, obtained from an attenuation map generated from the CT image of the patient, and by the normalization factors of the mMR scanner. Next, Poisson noise was introduced by simulating a random process for every sinogram bin,

obtaining the sinogram with true events. A uniform sinogram multiplied by the normalization factors was used for the randoms and a smoothed version of the emission sinogram for the scatters, which were scaled in order to have 20% of randoms and 25% of scatters of the total counts. Poisson noise was introduced to randoms and scatters and added to the trues sinogram.

Finally, each frame was individually reconstructed using the MLEM algorithm with 100 iterations, a 2.5 mm PSF and the standard mMR voxel size (2.09x2.09x2.03 mm^3). The reconstructed images were corrected for the activity decay and resampled into the original MNI space. For the simulation and reconstruction, an in-house reconstruction framework was used (Belzunce and Reader 2017).

Figure 2 – Reconstructed and calibrated images for each frame



Definition of the displacement ROIs

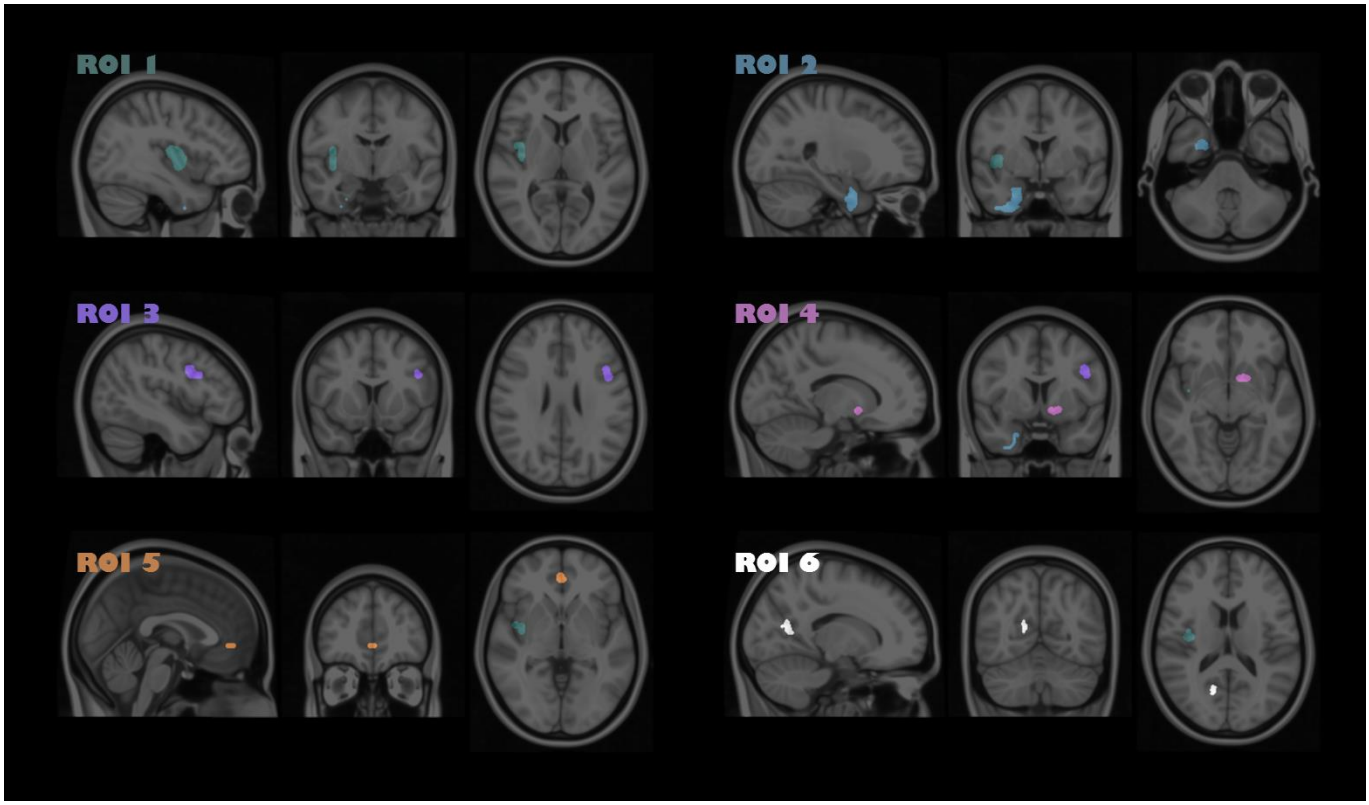
Six regions of displacement have been manually generated (using ITKSnap) and applied consistently to all the subjects to generate displaced k_3 parametric maps. Based on the neuroreceptor theory (Innis, Cunningham et al. 2007), any change in k_3 would produce an equivalent change in BP_{nd}.

The regions volumes of the regions ranged from 343mm^3 to 2275mm^3 and were selected to be in regions of higher tracer uptake at baseline. None of the displacement ROIs has a purely geometrical (e.g. cube or sphere) or anatomical shape. The regions have been created to represent different sizes and different levels of tracer displacement according to the following values:

ROI	Volume (mm^3)	Displacement (%)
ROI 1	2555	27
ROI 2	2275	27
ROI 3	1152	21
ROI 4	493	18
ROI 5	343	18
ROI 6	418	18

Their spatial distribution is not symmetrically distributed across the brain. An overview of the displacement ROIs is reported in Figure 3.

Figure 3 – Overview of the displacement ROIs



Acknowledging the resource

Using the dataset is free for research and educational purposes. Please make sure you credit the resource when using it.

Note that the dataset contains only simulated data and none of the PET exams included here refer to a real human participant. Hence its use is not limited by any data protection act.

Organising team

The following people have been involved in the generation and release of the dataset:

- Mattia Veronese – King's College London
- Gaia Rizzo – Invicro London/Imperial College London
- Martin Belzunce – King's College London
- Julia Schubert – King's College London
- Barbara Santangelo – King's College London
- Ayla Mansur – Invicro London/Imperial College London
- Alex Whittington – Invicro London/Imperial College London
- Joel Dunn – King's College London
- Graham Searle – Invicro London/Imperial College London
- Andrew Reader – King's College London
- Roger Gunn – Invicro London/Imperial College London

For any information please contact Mattia Veronese at mattia.veronese@kcl.ac.uk

References

Belzunce, M. A. and A. J. Reader (2017). "Assessment of the impact of modeling axial compression on PET image reconstruction." Medical physics **44**(10): 5172-5186.

Castellaro, M., G. Rizzo, M. Tonietto, M. Veronese, F. E. Turkheimer, M. A. Chappell and A. Bertoldo (2017). "A Variational Bayesian inference method for parametric imaging of PET data." Neuroimage **150**: 136-149.

Cunningham, V. J., S. P. Hume, G. R. Price, R. G. Ahier, J. E. Cremer and A. K. Jones (1991). "Compartmental analysis of diprenorphine binding to opiate receptors in the rat in vivo and its comparison with equilibrium data in vitro." J Cereb Blood Flow Metab **11**(1): 1-9.

Innis, R. B., V. J. Cunningham, J. Delforge, M. Fujita, A. Gjedde, R. N. Gunn, J. Holden, S. Houle, S. C. Huang, M. Ichise, H. Iida, H. Ito, Y. Kimura, R. A. Koeppe, G. M. Knudsen, J. Knuuti, A. A. Lammertsma, M. Laruelle, J. Logan, R. P. Maguire, M. A. Mintun, E. D. Morris, R. Parsey, J. C. Price, M. Slifstein, V. Sossi, T. Suhara, J. R. Votaw, D. F. Wong and R. E. Carson (2007). "Consensus nomenclature for in vivo imaging of reversibly binding radioligands." J Cereb Blood Flow Metab **27**(9): 1533-1539.