

Analysis of Brain PET and MR Images

Precise knowledge of the functional brain areas in the individual subject is crucial for the accurate quantitative analysis of brain PET images and their meaningful interpretation. Often however, functional regions are manually outlined in a casual manner, with subjective results as the outcome. This fundamental flaw can be overcome with PMOD's PNEURO tool, which offers both objective region outlining as well as pattern analysis methods via straightforward step-by-step procedures. These methods are provided as three individual tool sets.

PNEURO offers automated processing for research brain PET/MR, including parametric mapping.

Automatic Brain Regions by T1-MRI Parcellation

It is desirable that every brain PET study be complemented with a T1-weighted brain MRI that precisely represents the subject's anatomy. PMOD's PNEURO tool includes a sophisticated component to take advantage of this complementary information. Applying knowledge-base technology, it accurately segments the cortex and the basal ganglia from human T1-MRIs. These segments are then projected onto the PET images, and the regional signals are calculated, after which quantitative analysis can be performed.

Automatic Brain Regions by Atlas Normalization

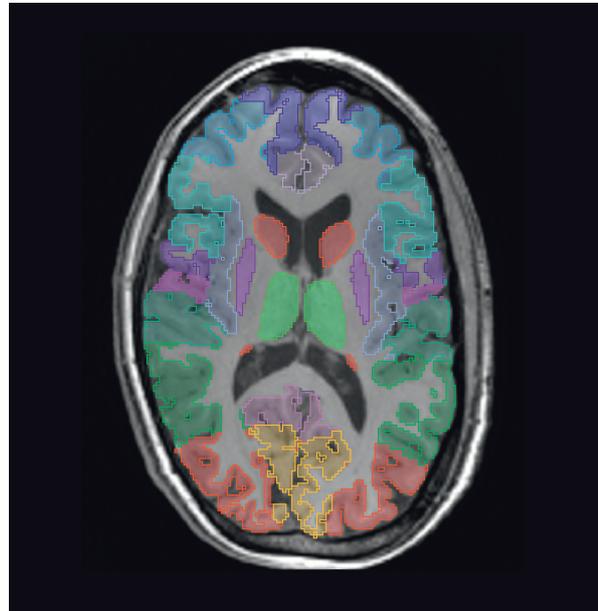
An alternative way of obtaining brain volumes of interest (VOIs) automatically is by leveraging the localization of brain areas as encoded in an atlas. The corresponding PNEURO component allows the user to adjust the atlas to the individual brain anatomy using a spatial normalization procedure, preferably obtained from the T1-MR image, or directly from the PET image. This solution has the advantage that it is also applicable for PET-only studies. The tool provides the probabilistic Hammers atlas but can also leverage alternative atlases, even from non-human species.

PNEURO offers easy-to-use methods for objective region outlining and for pattern analysis.

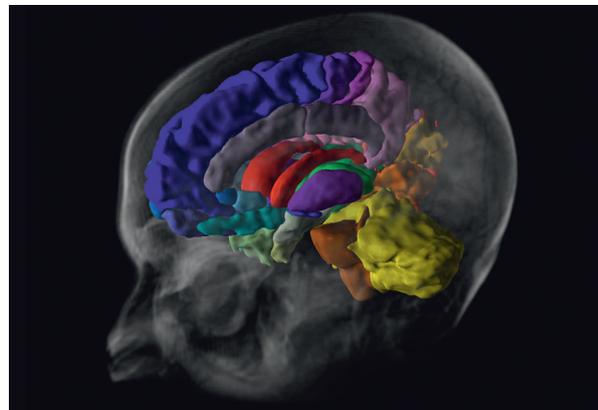
Normal Brain PET Databases

Often a static image of the PET tracer concentration is acquired after an appropriate equilibration time. In this situation, the analysis is based on the fact that, with consistent study protocols, the normal brain uptake exhibits a characteristic pattern. The database component in PMOD's PNEURO tool enables pooling of tracer uptake across a set of normal volunteers, thus establishing the normal pattern and its variability.

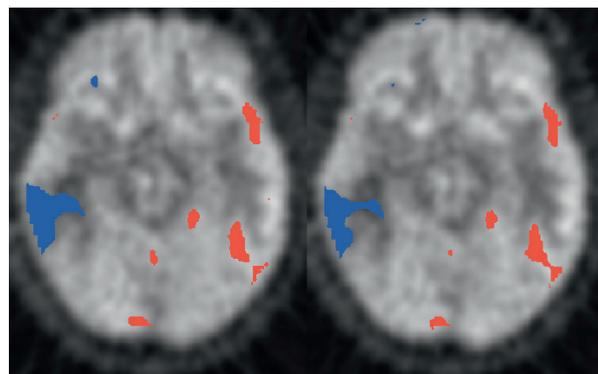
Once such a normal database has been created, the anomalies of the tracer uptake in a test subject brain can be easily localized without any prior assumptions or operator variability.



Brain parcellation result overlaid on T₁-MRI.



3D rendering of the VOIs from a brain parcellation combined with the volume rendered T₁-M.



Pixels deviating by more than two standard deviations from normal database values highlighted in red ($>$ normal) and blue ($<$ normal).

Automatic Brain Regions by T1-MRI Parcellation

This module implements a methodology licensed from CEA, Orsay, France. It uses a knowledge base of 26 normal human brains which were carefully segmented by a neurologist. The procedure can be optimized with several options:

- MR denoising strength
- Gray/white matter separation weight
- Number of used subjects from the knowledge base used
- PET averaging range for matching with the MRI
- Space for the regional statistics: MR or PET
- PET scanner resolution for partial-volume correction

Results:

- Segments or outline VOIs in the MR space
- Structures with separate left/right parts: gray matter, caudate, putamen, thalamus, globus pallidus
- Structures without laterality: cerebellum, liquor
- Statistics on MR-matched or original PET images
- Cortical area subdivision of gray matter
- Optional partial-volume correction of statistics

Automatic Brain Regions by Atlas Normalization

This module includes the following functionality:

- Adjustment of the VOI atlas to subject images by spatial normalization
- Normalization based on PET or MR images
- Intersection of VOIs with a gray and white matter probability mask
- Transfer of VOIs between spaces
- VOI statistics on template-matched, MR-matched or original PET images
- Optional partial-volume correction of statistics

The module bundles the Hammers Maximum Probability VOI Atlas (N30R83), which is licensed from Imperial College, London¹⁻². However, the methodology is applicable for other human atlases and those for other species. Atlases are included for the pig, cynomolgus and rhesus monkeys.

Parametric Mapping (Option)

If the pixel-wise modeling tool PXMOD has been licensed, PNEURO supports PET and MR parametric mapping as part of the workflow. At the end of the workflow, the parametric maps can readily be evaluated within the outlined VOIs.

Normal Brain PET Databases

This module supports the creation of normal PET databases from a consistent set of normal volunteer images. The following options are available:

- Normalization template: Standard MNI or user-defined templates
- Value scaling: relative to average, maximum,

average of % highest values, average in percentile range; within a mask or VOI

- z-score calculation: using the individual standard deviation in each pixel or a regional average (variance pooling)
- Result mask for background removal
- Smoothing filters

The comparison of a PET image against a database results in a z-score map of the deviation from the normal pattern. It can be explored visually and analyzed numerically:

- Fusion of z-score map with PET or template image
- Saving of z-score maps for pooled SPM analysis
- VOI statistics

PNEURO for Amyloid PET

In a recent study, Brendel et al. [3] studied the effects of reference region selection and partial-volume correction on the analysis of amyloid PET. They fully automatically processed the data of 962 subjects using PNEURO. Their conclusion was that detection of longitudinal amyloid increases is optimized when using partial-volume correction and white matter as reference tissue. Another study by Tuszynski et al. [4] compares software tools, including PNEURO, for the automatic contouring of brain structures. It clearly documents the value and reliability of PNEURO in the analysis of amyloid PET images, making it a useful alternative to tedious standard manual outlining.

Performance

Brain parcellation involves heavy number crunching and therefore requires an appropriate computer system. A 64-bit operating system with ≥ 32 GB RAM and at least 8 cores is required. Batch procedures are available to run a job queue during off-peak hours.

References

- ¹ Hammers A, et al.: Implementation and application of a brain template for multiple volumes of interest. *Hum Brain Mapp* 2002, 15(3): 165–174.
- ² Hammers A, et al.: Three-dimensional maximum probability atlas of the human brain, with particular reference to the temporal lobe. *Hum Brain Mapp* 2003, 19(4): 224–247.
- ³ Brendel M, et al.: Improved longitudinal (18F)-AV45 amyloid PET by white matter reference and VOI-based partial volume effect correction. *NeuroImage* 2015, 108(0): 450–459.
- ⁴ Tuszynski T, et al: Evaluation of software tools for automated identification of neuroanatomical structures in quantitative beta-amyloid PET imaging to diagnose Alzheimer's disease. *Eur J Nucl Med Mol Imaging* 2016.