

## Analysis of Rodent Brain Images

The detailed analysis of rodent brain images poses inherent difficulties: the resolution is often limited, the contrast in the images suffers from artefacts, and often there is high uptake of radiotracer in nearby soft tissue. In this situation, manual analyses of the regional characteristics are prone to operator bias and poor reproducibility.

The PNROD tool overcomes the challenge of automatic and accurate structure delineation by leveraging the well-defined functional areas defined in rodent brain atlases. Convenient workflows guide the user, so that brain regions adjusted to the subject anatomy are reproducibly obtained and can be applied for statistical analyses. Depending on the image content, data from a whole cohort can automatically be processed in a batch.

*PNROD offers easy-to-use methods for objective brain region outlining.*

## PET/MR and PET/CT Workflows

Multi-modal acquisitions have become routine, often using hybrid scanners which directly reconstruct matched anatomical and functional images. PNROD supports a dual-modality workflow whereby the anatomical images serve for adjusting the atlas to the subject brain, overcoming the problem of lacking anatomy in the functional images which are the target of the analysis. If the images originate from individual acquisitions on separate scanners, a rigid matching step is included in the workflow.

*Batch processing is included in PNROD for the effective analysis of cohort data.*

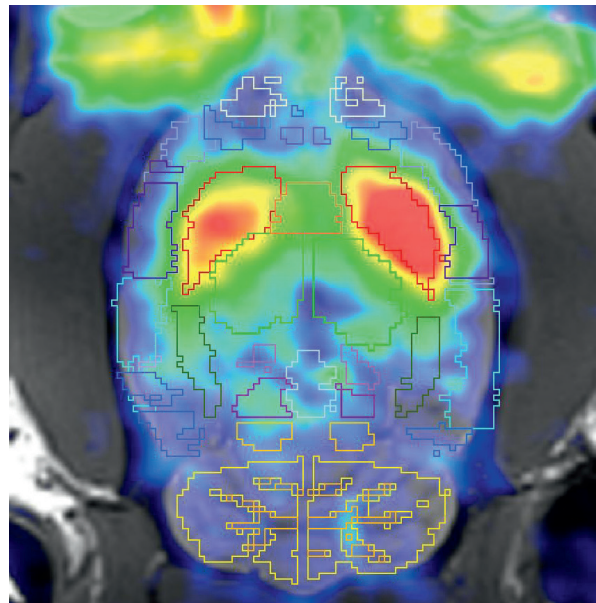
## Single-modality Workflows

If images from only one modality are available, direct atlas matching becomes necessary. Hereby it is essential that appropriate normalization templates are available for the atlases. Users can easily add their own templates, if they start working with a new PET tracer, to arrive at a standardized data analysis methodology.

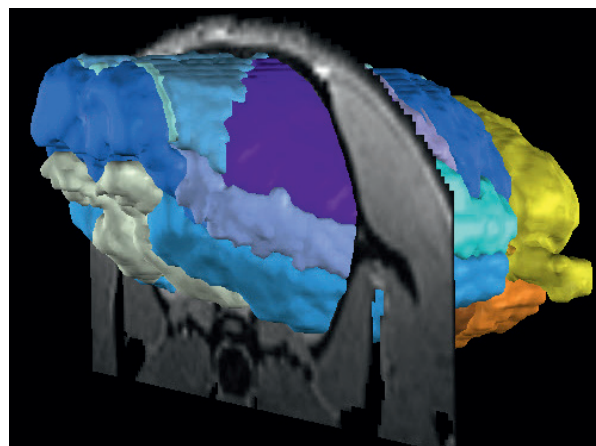
*With the integration of parametric mapping, PNROD represents a comprehensive solution for quantitative PET studies in rodents.*

## Parametric Mapping (Option)

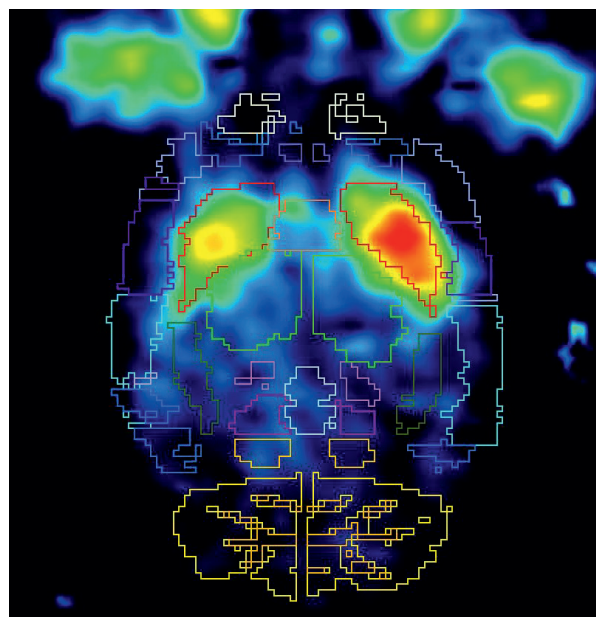
When processing dynamic PET series, the resulting VOIs can be applied for generating regional time-activity curves, with direct transfer to the kinetic modeling tool PKIN. Alternatively, the concentration change in each individual pixel can be analyzed, resulting in parametric maps which quantitatively portray tissue function.



Brain regions resulting from a PET/MR workflow overlaid on the fusion image.



3D rendering (option) of the brain VOIs combined with an MR slice.



Parametric map (option) derived from a dynamic Raclopride PET series

## Data Preparation

Consistent data is essential for the success of the automatic processing stages. PNROD includes a convenient cropping facility for extracting the part relevant for the brain analysis from whole-body data.

## Multi-Modality Image Registration

If an additional anatomical image of the same subject is available, PNROD tries to align the data. If the images originate from separate acquisitions, they are automatically matched. In difficult situations when automatic matching fails, the user can always resort to interactive matching.

## Atlas Normalization

The spatial normalization of an image to the selected atlas is based on a template image, and results in an estimate of the transformation that brings the subject image into alignment with the template. Three transformation types are supported:

- Elastic image warping based on the SPM5 normalization methodology
- Affine transformation which supports scaling and shearing
- Rigid transformation (applicable if the subject anatomy is sufficiently similar to the atlas anatomy)

There is an automatic image matching procedure for all transformations. If it fails, the user can resort to interactively aligning the subject image to the atlas to solve the situation.

## Atlases

PNROD includes 5 rat and 2 mouse brain atlases, each of them with their own set of normalization templates and brain region definitions.

Users can easily extend existing atlases by their own templates, modify the regions in the atlas to be better suited for their analysis, or create entirely new atlases using PMOD's VOI functionality.

## Parametric Mapping (Option)

If the pixel-wise modeling tool PXMED has been licensed, PNROD 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.

## VOI Statistics

The main result of a workflow is the set of brain VOIs adjusted to the subject. If the alignment is not fully satisfactory, the VOIs can be further trimmed using a comprehensive set of interactive VOI tools. For instance, individual VOIs or groups of them can be scaled, shifted, and rotated, or individual contours can be adjusted.

The final VOIs can then be applied to the data or the parametric maps for statistics calculation. In the case of dynamic images, the regional time activity curves are also generated which can directly be submitted to the PKIN tool for kinetic modeling.

## Partial Volume Correction (PVC)

PNROD includes two methods for correcting the spillover of signal between the VOIs, which occurs in PET or SPECT images due to the limited spatial resolution. The methods are based on the GTM method developed by Rousset et al. (J Nucl Med. 1998;39(5):90411).

If PVC is enabled for the statistics, both the uncorrected and the corrected regional values are listed. It is highly recommended to critically assess the PVC-corrected results, as the process depends on various assumptions and tends to increase noise.