

MAGIA PIPELINE: AUTOMATED PROCESSING AND KINETIC MODELLING FOR BRAIN PET IMAGES

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CONTENTS


- PET-processing & Magia toolbox overview
- How to install and use Magia toolbox
- Magia toolbox outputs and quality control results
- Example data & matlab code in the course web page

PET-DATA PROCESSING DEPENDS ON SEVERAL FACTORS

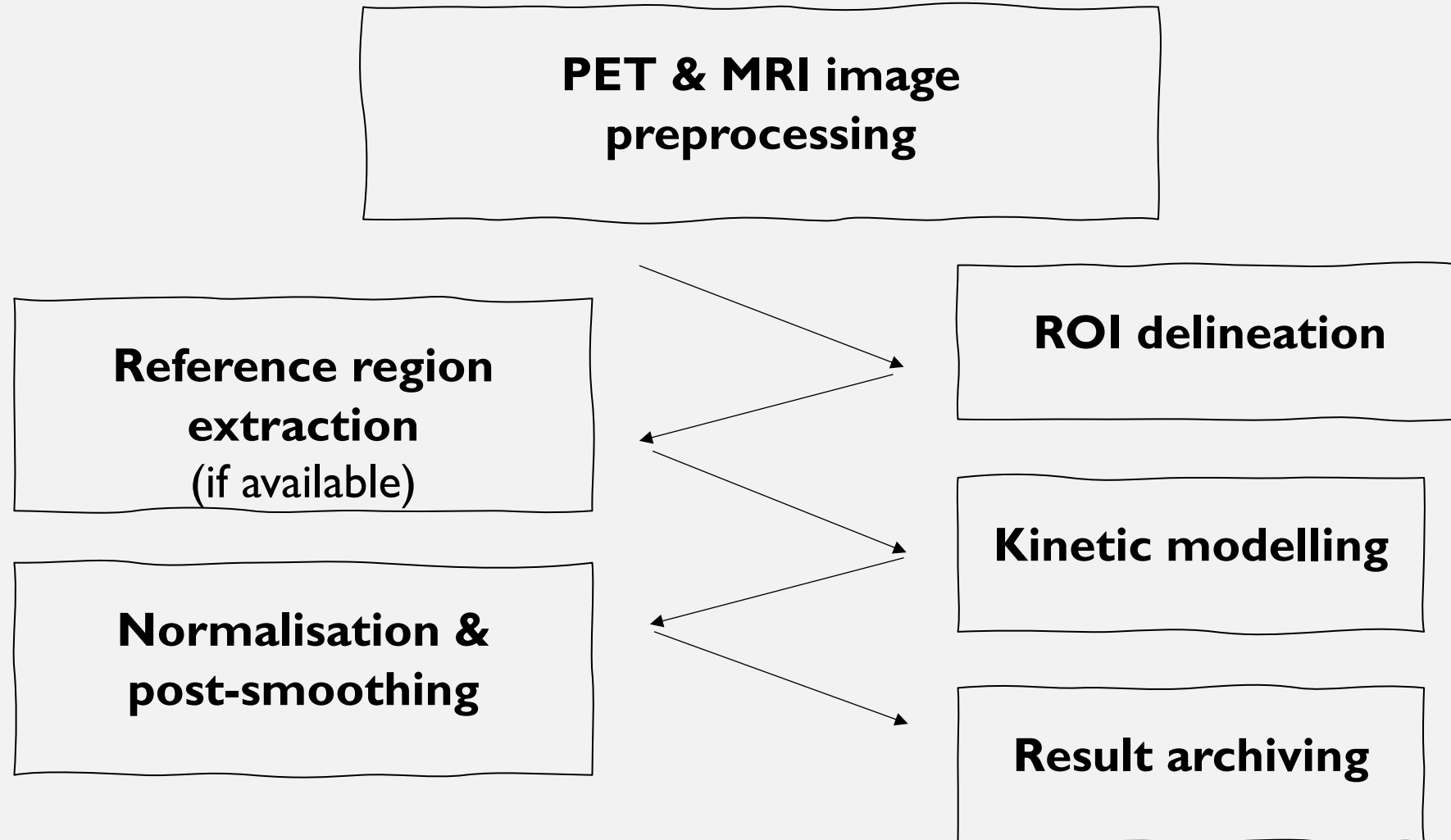
- Radioligand
 - Dynamic 4D data; consists subsequent time intervals (frames)
 - Static study data
- Pharmacokinetic model
- Input function for modelling
 - arterial input
 - reference region

MAGIA PIPELINE

Enables easy interface & automated data processing

- Usable for wide range of different PET radioligands
- Currently limited to human brain data
- Reduced manual (re)work
 - Scripts / batch processing offer increased reproducibility and reliability
 - version control with GitHub
- Integration with Turku PET centre  AIVO database
 - Contains data from over 10 000 brain PET-images acquired in Turku

MAGIA PROCESSING FLOWCHART



I. PET & MRI IMAGE PREPROCESSING (SPM)

- PET (& MRI) dicom or nifti raw data structure:

- PETdatafolder / *ID* / PET / nii / pet_*ID*.nii

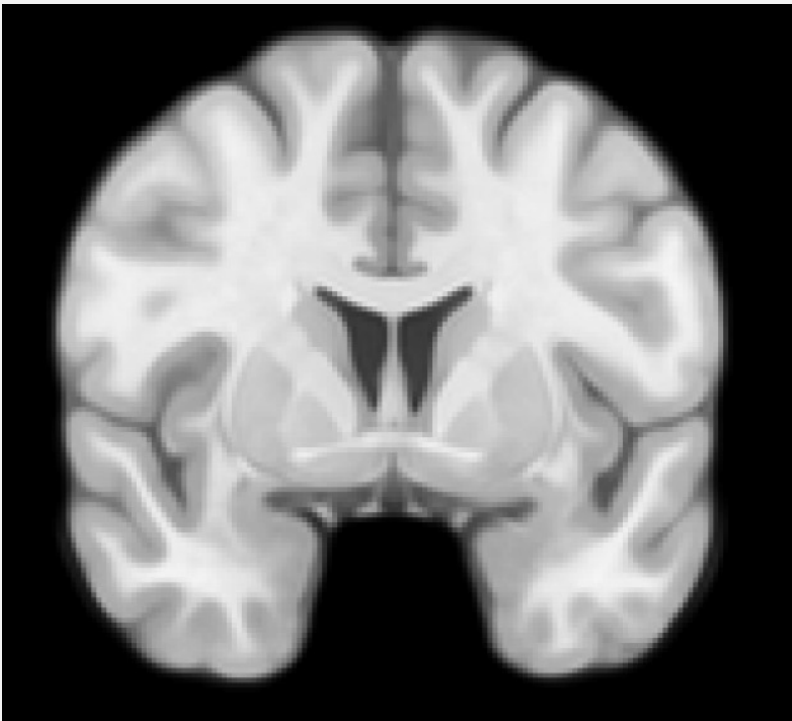
- MRIdatafolder / *ID* / T1 / *ID*.nii

Format is similar to PET BIDS
(brain imaging data structure)
> allows raw-data sharing easily

- 4D PET framewise realignment (motion correction)
- PET ↔ T1 MR image co-registration
- T1 MRI tissue segmentation / normalisation parameter calculation

2. ROI DELINEATION (MRI/FREESURFER)

Input:
T1w MRI (gradient corrected)



Output:
FreeSurfer parcellation
in native subject space



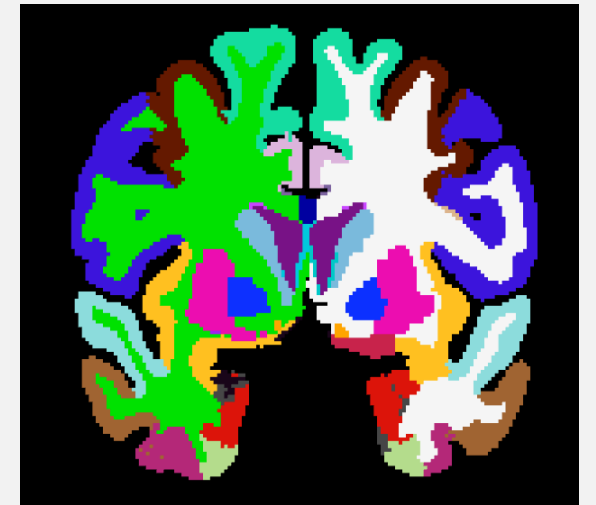
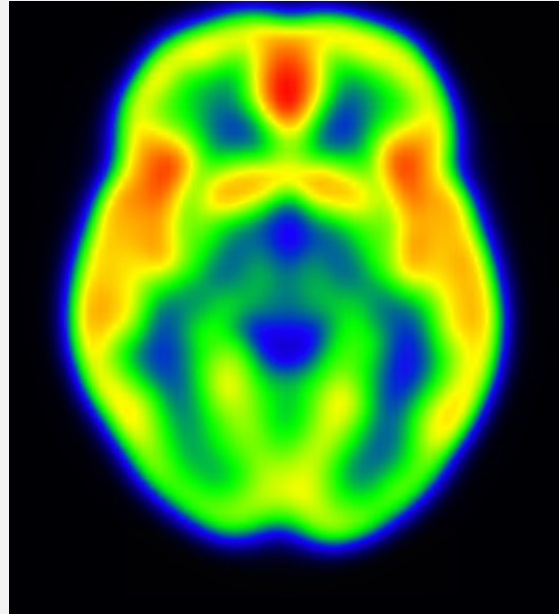
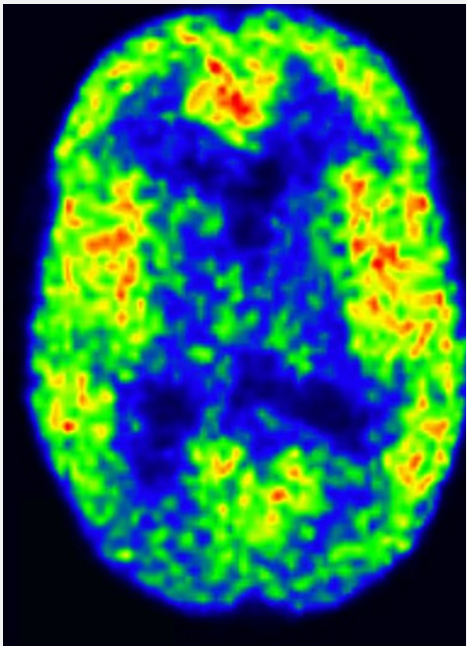
2. ROI DELINEATION (PET-TEMPLATE)

Inputs:

- PET mean image (motion corrected)
- Radioligand template image in MNI space
- ROI mask images in MNI space

Output:

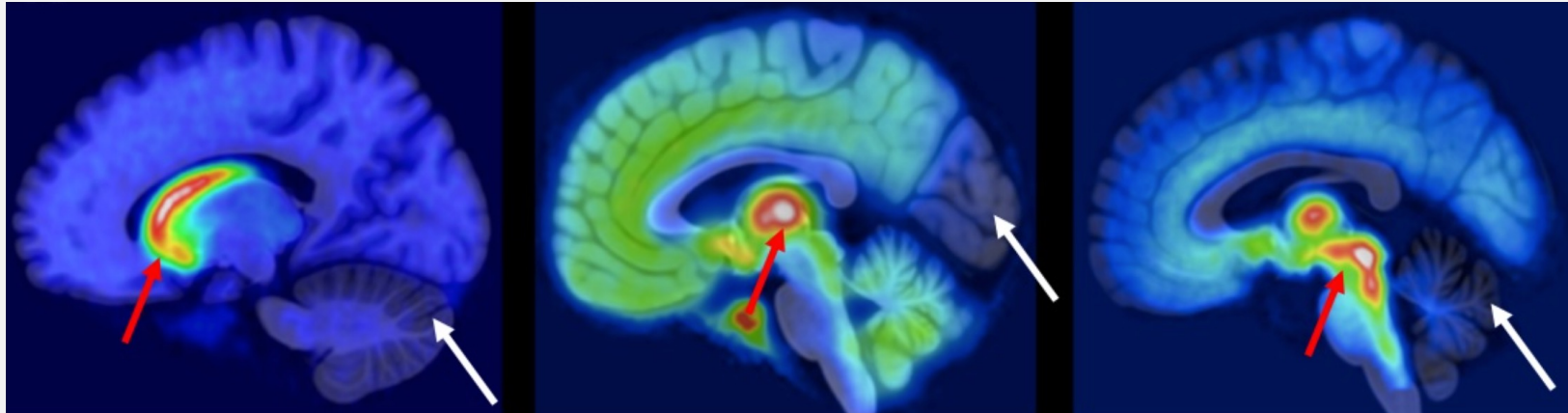
- Spatially normalised PET image
- ROI masks in MNI standard space



3. REFERENCE REGION EXTRACTION

Red = high specific binding

White = low specific binding

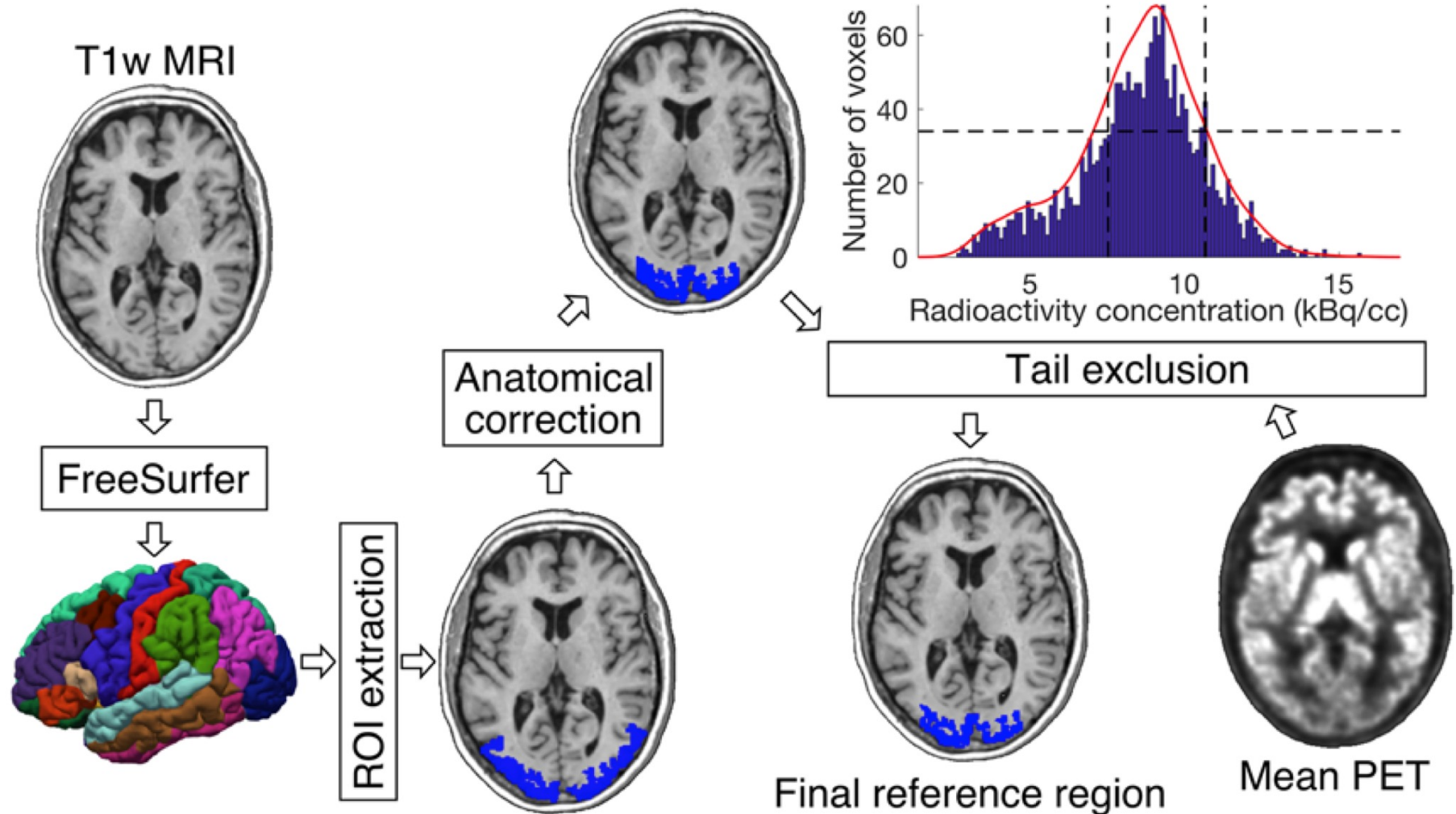


[¹¹C]raclopride /
dopamine D2-receptors

[¹¹C]carfentanil /
 μ -opioid receptors

[¹¹C]madam /
serotonin transporter

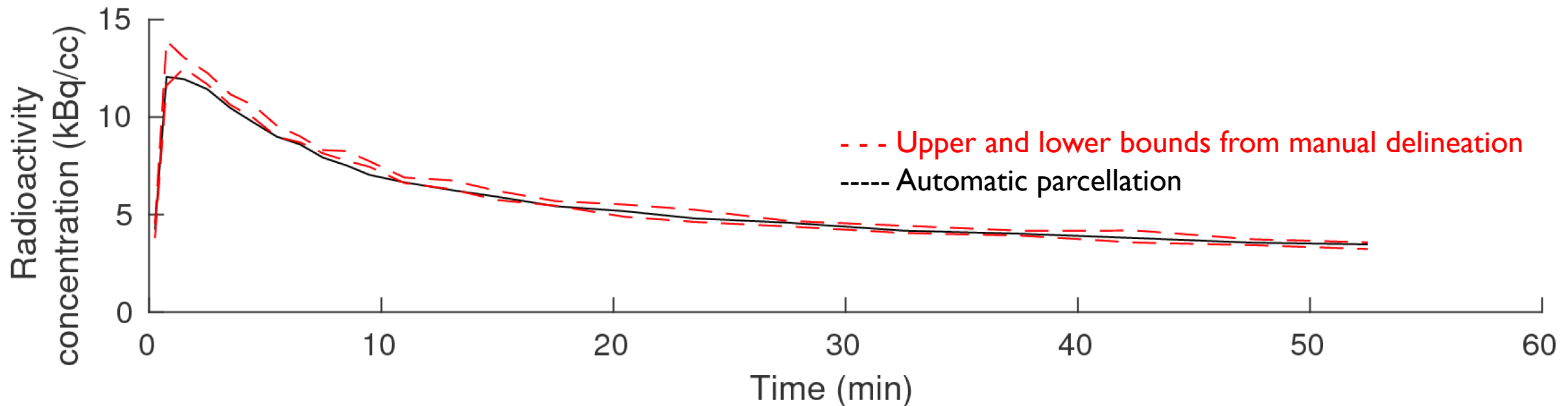
3. AUTOMATIC REFERENCE REGION EXTRACTION



3. AUTOMATIC REFERENCE REGION EXTRACTION

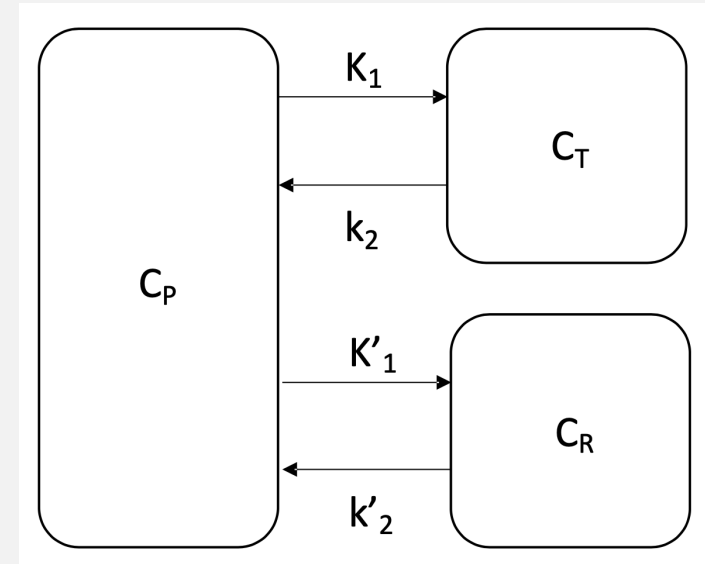
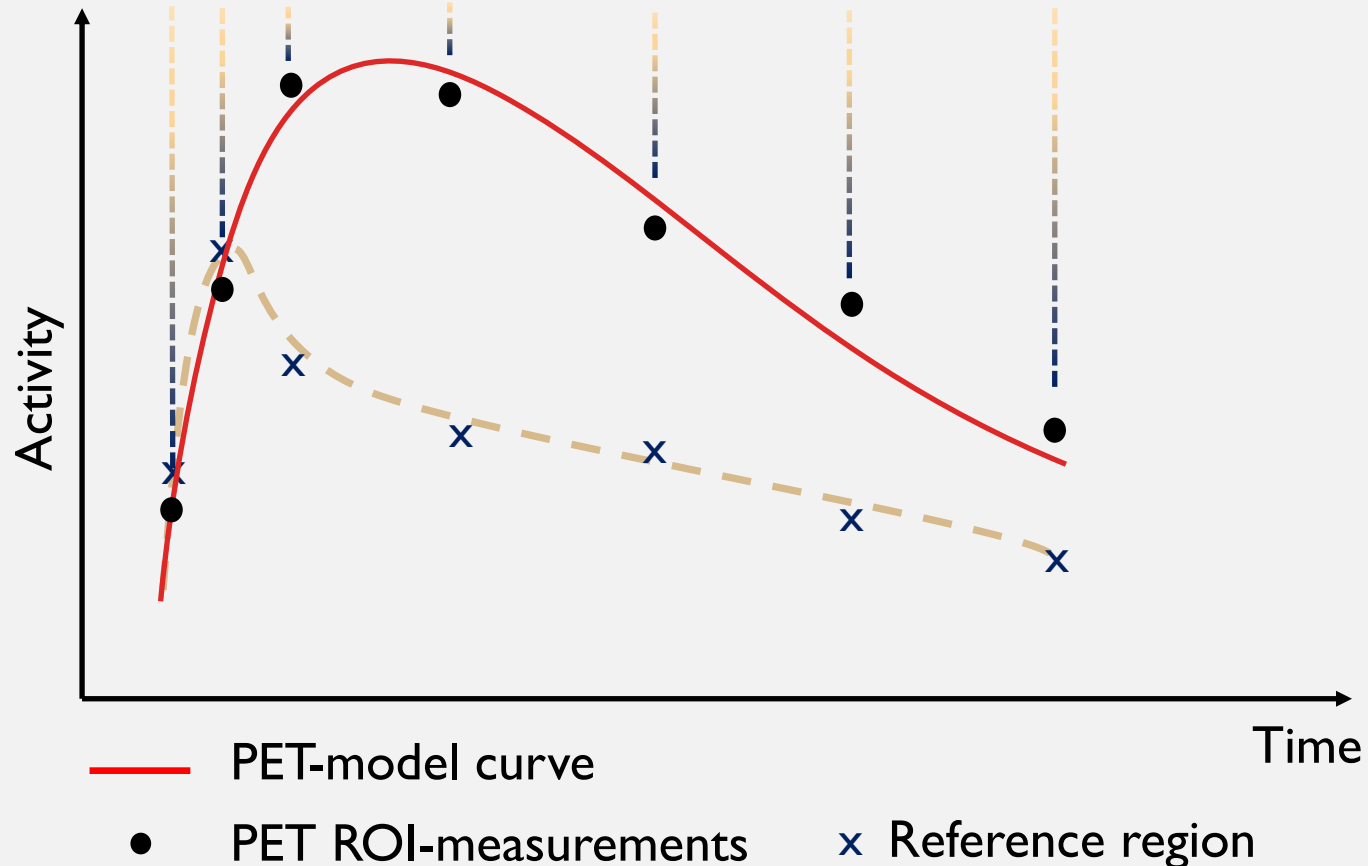
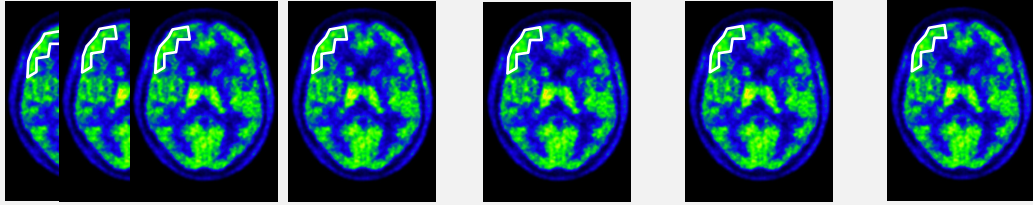
- Magia ROIs compare well with the manually drawn ROIs (Karjalainen et al. 2020)

Example [¹¹C]raclopride cerebellum TAC



4. ROI-LEVEL PHARMACOKINETIC MODELLING

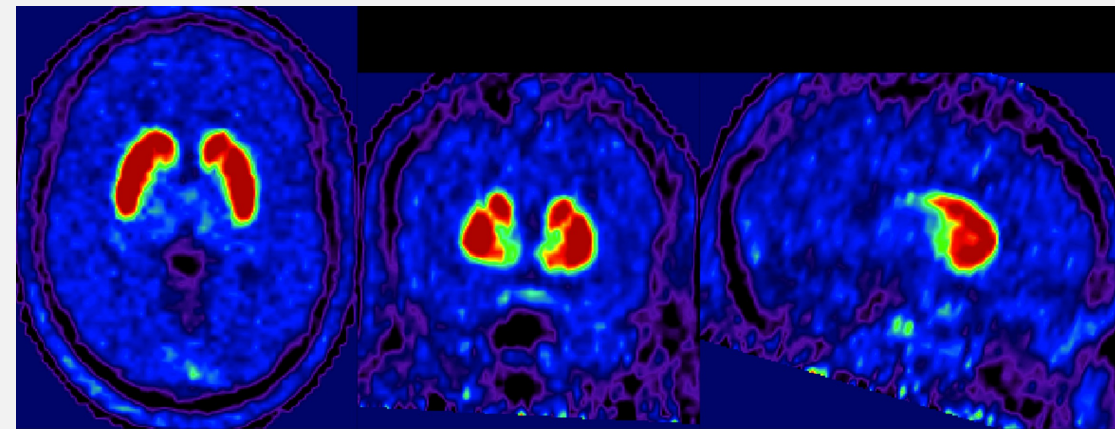
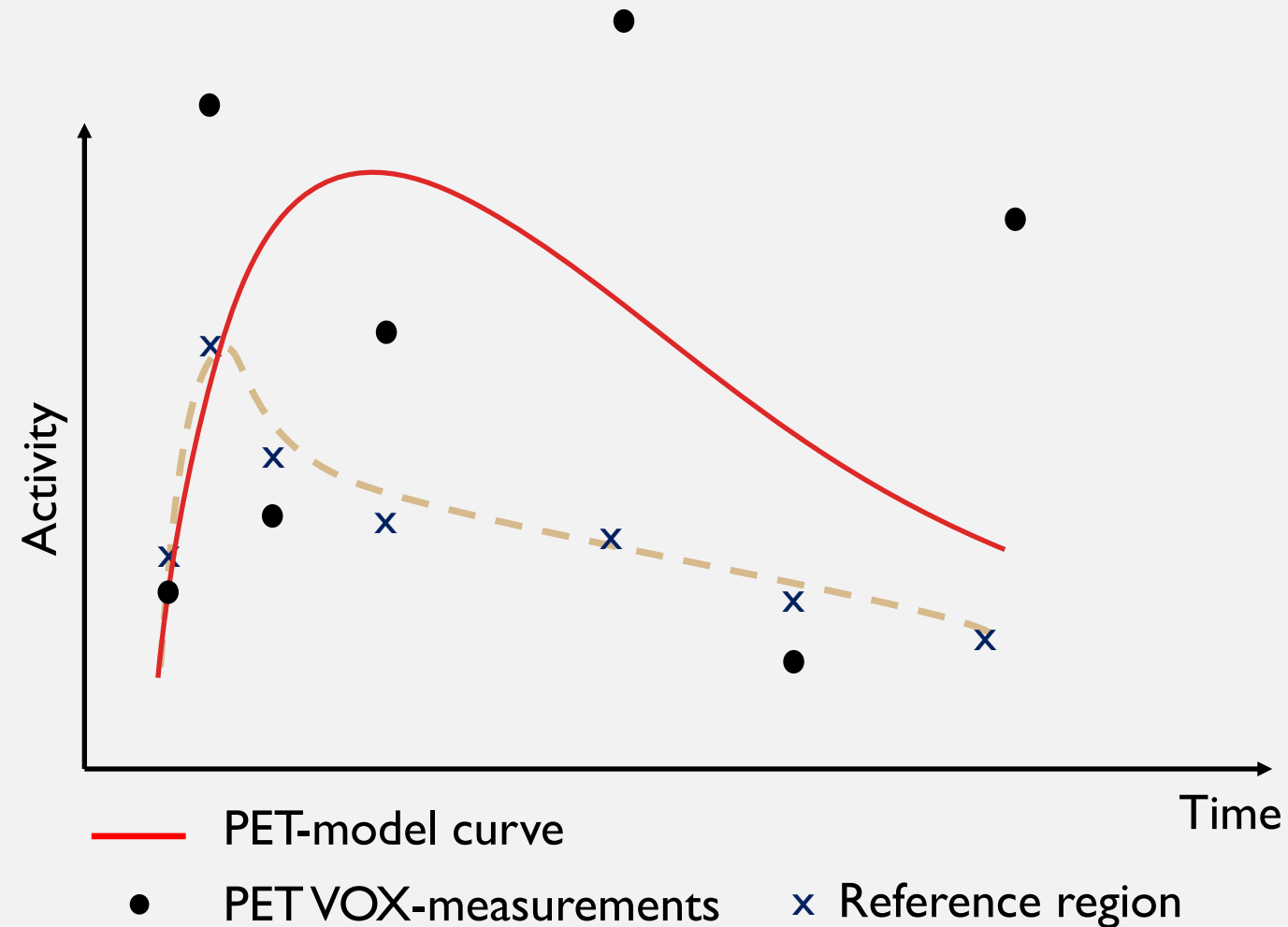
3D PET images corresponding to each time point



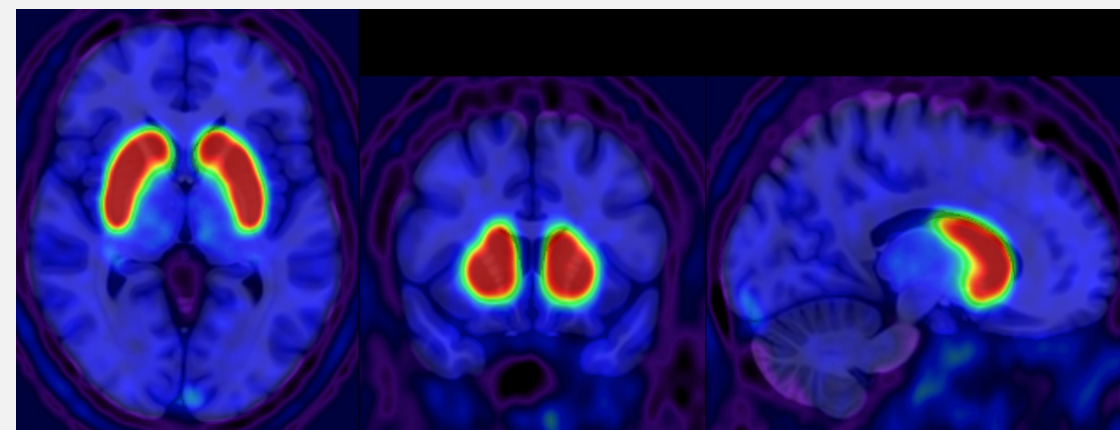
Simplified reference tissue model (SRTM)

Estimates: $R_1 = K_1/K'_1$, k_2 , BP_{ND}

4. VOXEL-LEVEL PHARMACOKINETIC MODELLING



SRTM BPnd image in subject native space



SRTM BPnd image in MNI152 space

MAGIA ROI/VOXEL-LEVEL KINETIC MODELS

Simplified techniques:

- SUV (Standardised Uptake Value) & ROI-reference ratio analysis
- FUR (Fractional Uptake Ratio)

Reference tissue input models:

- Simplified Reference Tissue Model (SRTM) (Lammertsma et al. 1996)
- Logan plot with reference tissue input (Logan et al. 1996)
- Patlak plot with reference tissue input (Patlak & Blasberg 1985)

Arterial input models (requires manual processing):


- Logan plot (Logan et al. 1990)
- Patlak plot (Patlak et al. 1983)
- Ichise's multilinear analysis I (Ichise et al. 2003)
- Two-tissue compartment model (2TCM)

6. ARCHIVING

- Archived result data structure :

- PETarchivefolder / *ID* / method / PET /
- PETarchivefolder / *ID* / method / MRI /
- PETarchivefolder / *ID* / method / results /
 - method = model_normalisation-type_ROI-type

Format is similar to PET BIDS
(brain imaging data structure)
> allows result sharing easily



MAGIA REQUIREMENTS

- MATLAB (version 2016b or newer)
- SPM (Statistical Parametric Mapping, version 12)
- FreeSurfer (version 6.0)
- Supported operating systems: Linux & Mac

INSTALLATION: (<https://github.com/tkkarjal/magia>)

tkkarjal / magia

Notifications Star 15 Fork 5

<> Code Issues 8 Pull requests 5 Actions Projects Wiki Security Insights

7. Installation

Tomi Karjalainen edited this page on 22 Oct 2019 · 4 revisions

Preparation

Please start by downloading Magia (<https://github.com/tkkarjal/magia>), SPM (<https://www.fil.ion.ucl.ac.uk/spm/>) and FreeSurfer (<http://www.freesurfer.net>). Install SPM and FreeSurfer according to the instructions given by the developers.

Create the necessary folders for your data using the specifications outlined in <https://github.com/tkkarjal/magia/wiki/4.-Preparing-your-data-for-MAGIA>.

Installing Magia

Please first add the magia-directory to your MATLAB's path: `addpath('/installation/directory/magia')`

Magia requires the following environmental variables in MATLAB:

- DATA_DIR: The directory where the PET data are stored under, and where Magia will operate before archiving the results
- MRI_DIR: The directory where the MRI data are stored under
- SPM_DIR: The directory where SPM is installed in
- FREESURFER_HOME: The directory where FreeSurfer has been installed in

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Find a Page...

- Home
- 1. MAGIA pipeline for automated neuroimage analysis
- 10. How to add Magia specs to Aivo (Turku only)
- 2. List of the MAGIA functions
- 3. Overview of the pipeline
- 4. Preparing your data for MAGIA
- 5. Filling in the metadata to AIVO (Turku only)
- 6. Common problems
- 7. Installation
- 8. Usage

HOW TO USE IT?

Output = function_name(input)

Inputs:

- Study ID
- Study specifications
- Modelling specifications
- Magia preprocessing specifications
- PET (& MRI) dicom or nifti data stored in a predefined structure:
 - PETdatafolder / *ID* / PET / nii / pet_*ID*.nii
 - MRIDatafolder / *ID* / T1 / *ID*.nii

STUDY SPECIFICATIONS

```
%study specs
specs.study.dose = 500; %MBq
specs.study.mri_code = 'nrm2018mri';
specs.study.scanner = 'siemens biograph mmr pet-mri';
specs.study.tracer = '[11c]ro15-4513';
specs.study.weight = 70; %Kg
|
specs.study.frames = [ 0 0.25;0.25 0.5;0.5 0.75;0.75 1;1 2;2 3;3 4;4 5; ...
    5 7.5;7.5 10;10 15;15 20;20 25;25 30;30 35;35 40;40 45;45 50; ...
    50 55;55 60;60 70;70 80;80 90];
```

MAGIA PREPROCESSING SPECIFICATIONS

```
%magia specs
```

```
specs.magia.mc_excluded_frames = '1,2';  
specs.magia.mc_fwhm = 7;  
specs.magia.mc_ref_frame = 10;  
specs.magia.mc_rtm = 1;
```

} Motion correction options

```
specs.magia.norm_method = 'mri';  
specs.magia.rc = 0;  
specs.magia.roi_set = 'rs2';  
specs.magia.roi_type = 'freesurfer';
```

```
specs.magia.dc = 1;  
specs.magia.fwhm_pre = 2;  
specs.magia.fwhm_post = 8;  
specs.magia.fwhm_roi = 0;
```

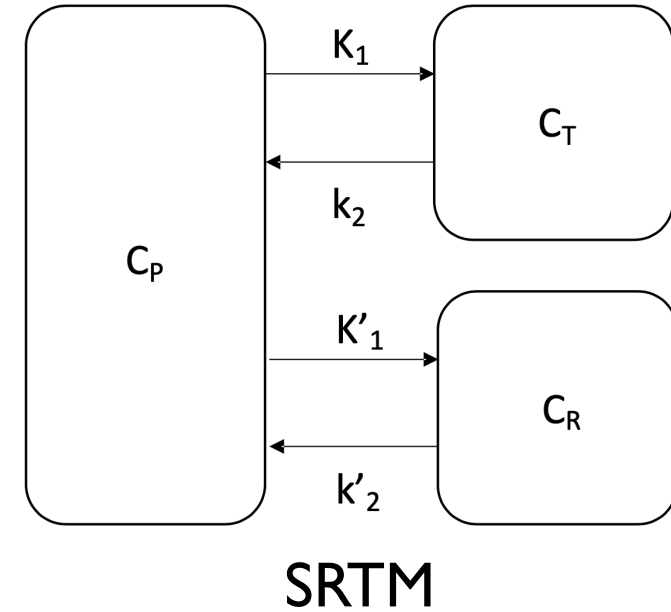
MODELLING SPECS AND OPTIONS

```
%modelling options // SRTM
specs.magia.cpi = 1;
specs.magia.input_type = 'ref';
specs.magia.model = 'srtm';

modeling_options.lb = [0 0 0];
modeling_options.ub = [3 1 8];
modeling_options.theta3_lb = 0.06;
modeling_options.theta3_ub = 0.8;
modeling_options.nbases = 200;
```

```
%[R1 k2 BPnd]
%[R1 k2 BPnd]
```

Voxel level modelling
options; different defaults
for each tracer



RUNNING MAGIA

```
%run magia  
ID = 'nrm2018baseline1';  
run_magia(ID,specs,modeling_options)
```

ALTERNATIVE WAY:



AIVO DATABASE

- Excel data sheet for importing metadata to database

patient_id	ID	ac_number	study_date	project	group_name	description	scanner	tracer	frames
26031988-1000	nrm2018baseline1	nrm2018baseline1	2018-03-26	NRM2018_	baseline	baseline	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1001	nrm2018baseline2	nrm2018baseline2	2018-03-26	NRM2018_	baseline	baseline	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1002	nrm2018baseline3	nrm2018baseline3	2018-03-26	NRM2018_	baseline	baseline	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1003	nrm2018baseline4	nrm2018baseline4	2018-03-26	NRM2018_	baseline	baseline	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1004	nrm2018baseline5	nrm2018baseline5	2018-03-26	NRM2018_	baseline	baseline	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1005	nrm2018displaced1	nrm2018displaced1	2018-03-26	NRM2018_	displaced	displaced	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1006	nrm2018displaced2	nrm2018displaced2	2018-03-26	NRM2018_	displaced	displaced	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1007	nrm2018displaced3	nrm2018displaced3	2018-03-26	NRM2018_	displaced	displaced	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1008	nrm2018displaced4	nrm2018displaced4	2018-03-26	NRM2018_	displaced	displaced	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1
26031988-1009	nrm2018displaced5	nrm2018displaced5	2018-03-26	NRM2018_	displaced	displaced	Siemens mMR PET-MRI	[11c]Ro15-4513	0 0.25; 0.25; 0.5 ; 0.5 0.75; 0.75 1; 1 2; 2 3; 3 4; 4 5; 5 7.5; 7.5 10; 1

RUNNING MAGIA WITH AIVO-DATA I

Example: select all studies of a project named "Pleasure"

```
subjects =  
aivo_get_subjects('project', 'pleasure');  
  
for i = 1:length(subjects)  
    sub = subjects{i};  
    run_magia(sub);  
end
```


RUNNING MAGIA WITH SUB-FUNCTIONS

```
me_list = cell(length(subjects),1);
for k = 1:length(subjects)
    ID = subjects{k};
    specs = aivo_read_magia_specs(ID);
    modeling_options = aivo_read_modeling_options(ID)
    try
        specs = magia_clean_specs(specs);
        specs = magia_replace_empty_specs_with_defaults(specs);
        magia_check_specs(specs);
    } Check specifications

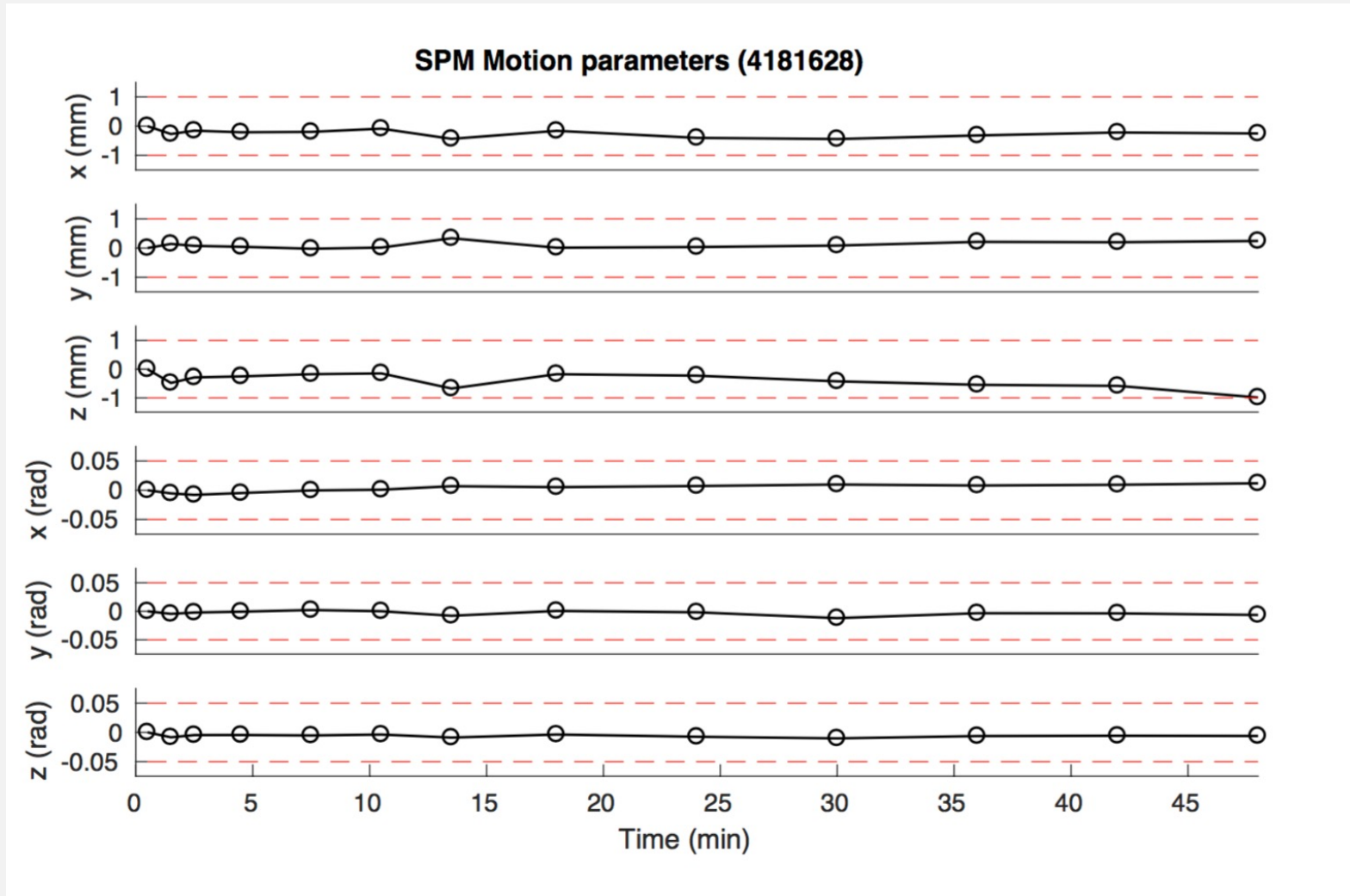
    magia_processor(ID,specs,modeling_options);
    magia_archive_results(ID,specs.magia);
    magia_clean_files(ID);
    aivo_store_magia_info(ID,specs);
} Magia processing
catch ME %error handling
    error_message = aivo_parse_me(ME);
    aivo_set_info(ID,'error',error_message);
    me_list{k} = ME;
end
end
```

HOW LONG DOES IT TAKE?

- `run_magia` may take 10-20 hours to complete
 - FreeSurfer step only needs to be executed once
 - Magia re-runs are ready in few minutes

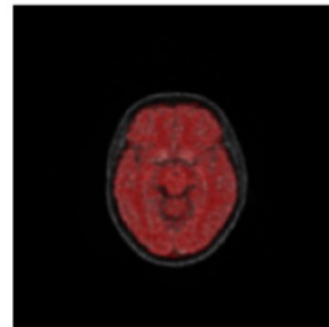
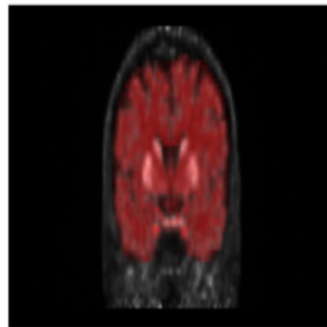
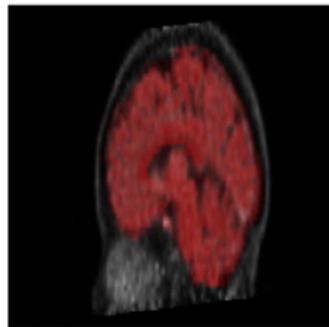
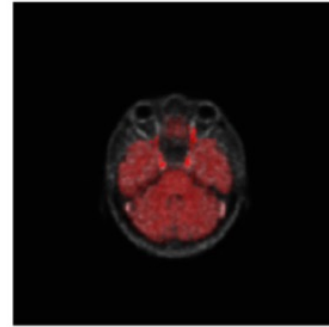
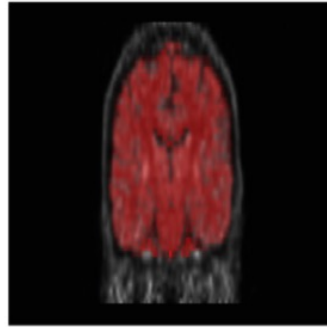
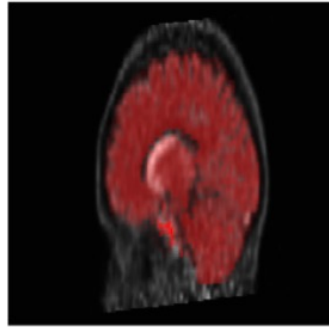
MAGIA OUTPUTS: MOTION CORRECTION QC

PETarchivefolder / ID / qc_ID.ps



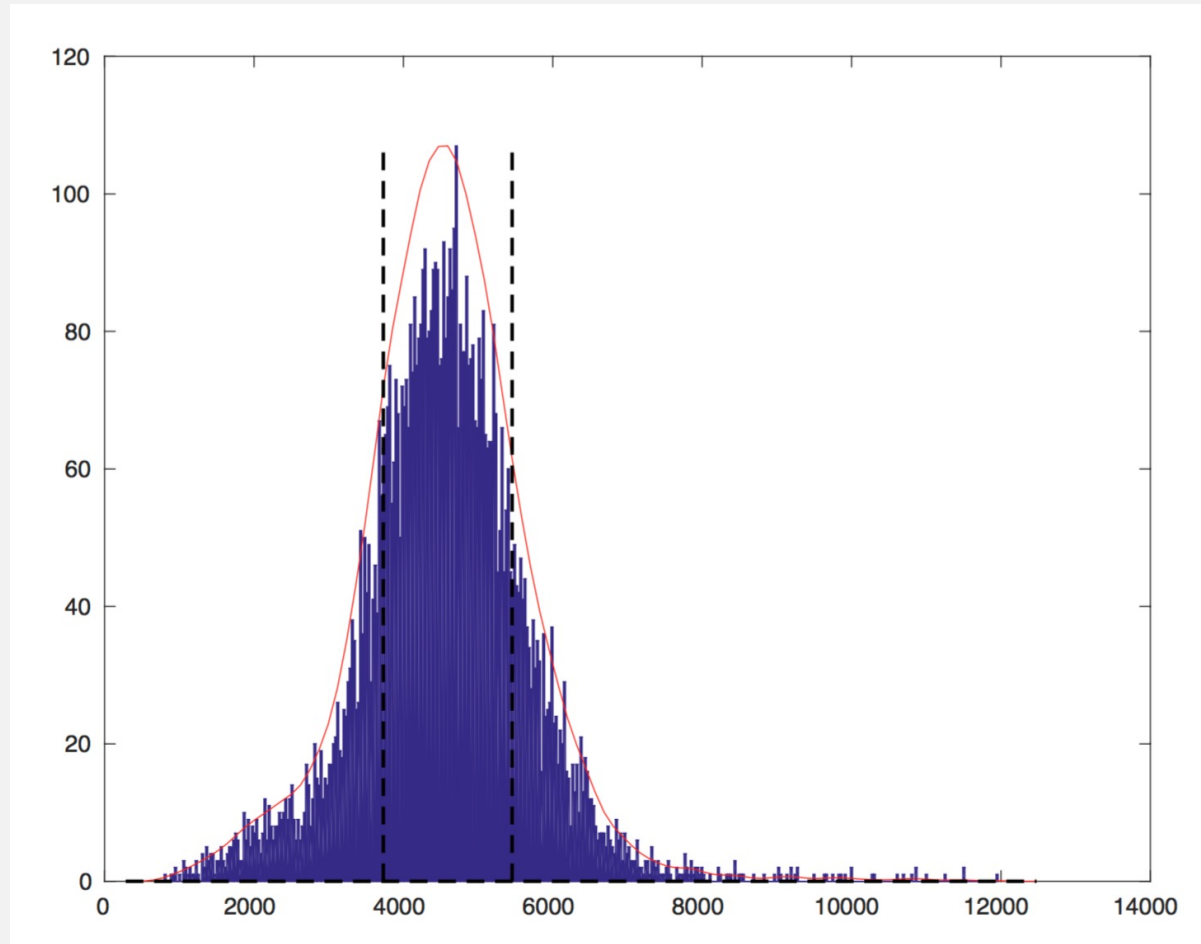
MAGIA OUTPUTS: COREGISTRATION QC

PETarchivefolder / ID / qc_ID.ps



MAGIA OUTPUTS: REFERENCE TISSUE DISTRIBUTION

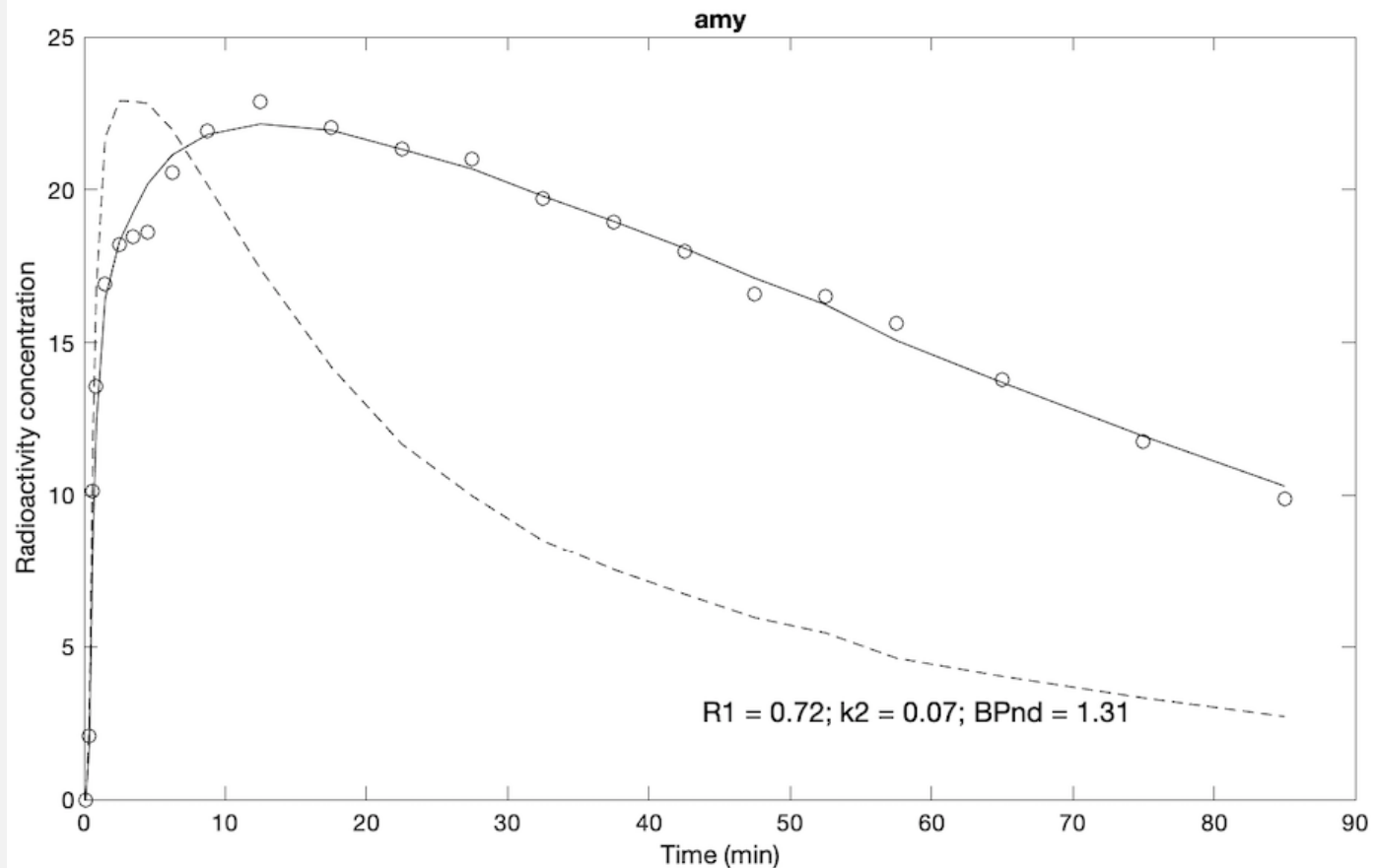
PETarchivefolder / ID / qc_ID.ps



MAGIA OUTPUTS: ROI LEVEL FIT & ESTIMATES

PETarchivefolder / ID / method / results / fits / ROI.png

PETarchivefolder / ID / results / roi_results.mat

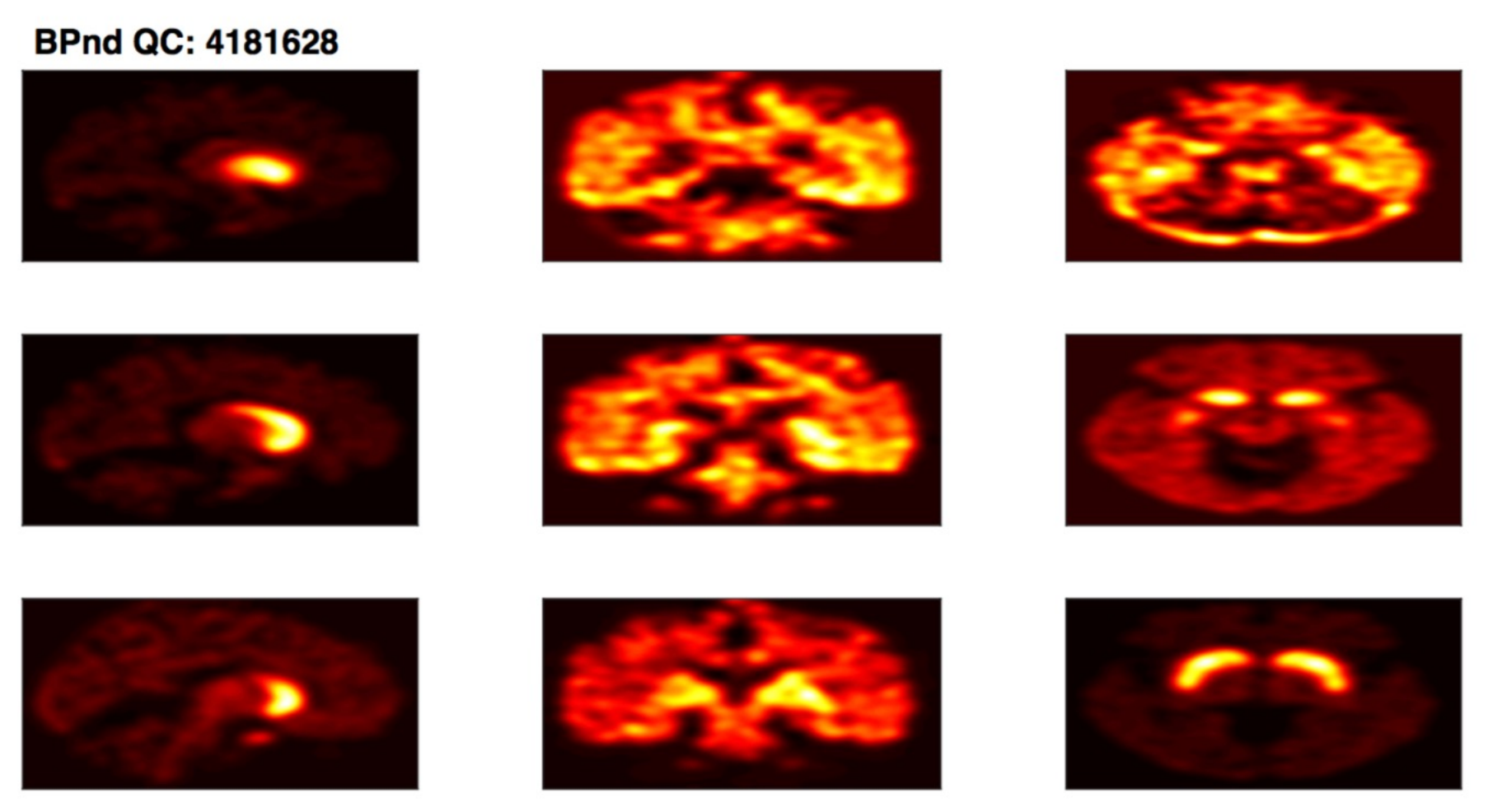


Row	R1	k2	BPnd	vol
amy	0.721	0.067	1.313	4181
cau	0.656	0.046	0.145	9316
amy	0.669	0.005	0.000	140267
dacc	0.880	0.081	1.044	5081
hip	0.672	0.062	1.037	10926
inftemp	0.888	0.080	0.774	27437
ins	1.048	0.088	1.342	16909
medul	0.346	0.007	0.005	5565
midbr	0.628	0.033	0.000	7915
midtemp	0.914	0.081	0.742	27802
nacc	0.849	0.079	1.518	1511
ofc	0.991	0.082	0.876	30532
parsop	1.082	0.083	0.691	11074
pcc	0.992	0.079	0.633	7530
pons	0.445	0.020	0.000	18316
put	0.957	0.062	0.537	12715
racc	1.061	0.104	1.679	5442
supfront	0.944	0.076	0.628	52053
suptemp	0.952	0.079	0.870	28373
tempol	0.670	0.067	1.090	5145
tha	0.808	0.052	0.028	21544

MAGIA OUTPUTS: PARAMETRIC IMAGES

PETarchivefolder / ID / srtm_mri_freesurfer / results / swrpet_a353_bfsrtm_BP.nii

{ s=smoothed
w=normalised
r=interpolated



MAGIA OUTPUTS: FILES

- PETarchivefolder / *ID* / method / PET / specs_ID.txt
- PETarchivefolder / *ID* / method / PET / modelling_options_ID.txt

MAGIA OUTPUTS: FILES

- PETarchivefolder / *ID* / method / PET /

- meanpet_ID.nii
- rpet_ID.nii

s = smoothed
w = normalised
r = interpolated

- PETarchivefolder / *ID* / method / MRI /

- mri_ID_full.nii
 - y_mri_ID_full.nii
 - iy_mri_ID_full.nii
- } Deformation fields
- c*mri_ID_full.nii (segmented mri)
 - cseg_ID.nii (freesurfer ROI labels)

MAGIA OUTPUTS: FILES

- PETarchivefolder / *ID* / method / masks /
 - ROI mask images

- PETarchivefolder / *ID* / method / results /
 - tacs.mat
 - roi_results.mat
 - rpet_modelling-method.nii

s = smoothed
w = normalised
r = interpolated

USING MAGIA MODELS

```
tacdata = load(tacs.mat)
roi_tac = tacdata.tacs(:,1);
ref_tac = tacdata.cr;
times = tacdata.frames;
modeling_options = aivo_read_modeling_options(ID);
lb = modeling_options.lb;
ub = modeling_options.ub;
n_iterations = 50;

[modelfit,parameter_estimates,SSR] =
fit_srtm(roi_tac,ref_tac,times,lb,ub,n_iterations)
```

AIVO + MAGIA = EFFICIENT DATA ANALYSIS

- Together AIVO and Magia allow efficient preprocessing of PET data:
 1. The preprocessing only has to be run only once per study, after which the data is available to be used in the statistical analyses
 2. Metadata is easily retrieved from the centralized AIVO-database
 3. Allows analysis of massive ($N \gg 100$) datasets easily
 4. Results and quality control metrics are stored in AIVO

FURTHER DETAILS & MAGIA REFERENCE

Front. Neuroinform., 04 February 2020 | <https://doi.org/10.3389/fninf.2020.00003>

Magia: Robust Automated Image Processing and Kinetic Modeling Toolbox for PET Neuroinformatics

 [Tomi Karjalainen^{1*}](#),  [Jouni Tuisku¹](#),  [Severi Santavirta¹](#),  [Tatu Kantonen¹](#),  [Marco Bucci¹](#),  [Lauri Tuominen²](#),  [Jussi Hirvonen^{1,3}](#),  [Jarmo Hietala^{1,4}](#),  [Juha O. Rinne^{1,5}](#) and  [Lauri Nummenmaa^{1,6}](#)

OTHER EXAMPLES OF LARGE SCALE DATASET STUDIES

- Tuisku et al. 2019: Effects of age, BMI and sex on the glial cell marker TSPO - a multicentre [¹¹C]PBR28 HRRT PET study
- Nummenmaa et al. 2020: Lowered endogenous mu-opioid receptor availability in subclinical depression and anxiety
- Kantonen et al. 2021: Cerebral μ -opioid and CB₁ receptor systems have distinct roles in human feeding behavior
- Sun et al. 2021: Seasonal Variation in the Brain μ -Opioid Receptor Availability
- Malén et al. 2022: Atlas of type 2 dopamine receptors in the human brain: Age and sex dependent variability in a large PET cohort
- Nummenmaa et al. 2022: μ -opioid receptor availability is associated with sex drive in human males

<https://github.com/tkkarjal/magia>

[http://www.turkupetcentre.net/
petanalysis/modelling_intro.html](http://www.turkupetcentre.net/petanalysis/modelling_intro.html)