Tracer-specific PET and SPECT templates for automatic co-registration of functional rat brain images

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Tracer-specific PET and SPECT templates for automatic co-registration of functional rat brain images

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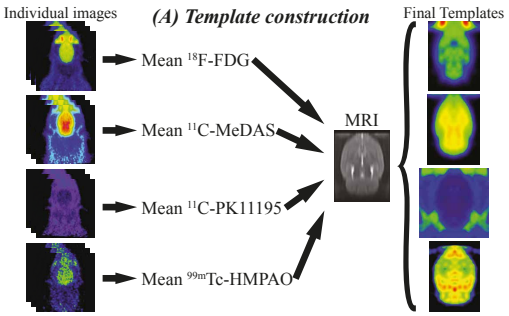
Objective
Construction of tracer-specific PET and SPECT rat brain templates for automatic co-registration, spatially aligned with Paxinos space.

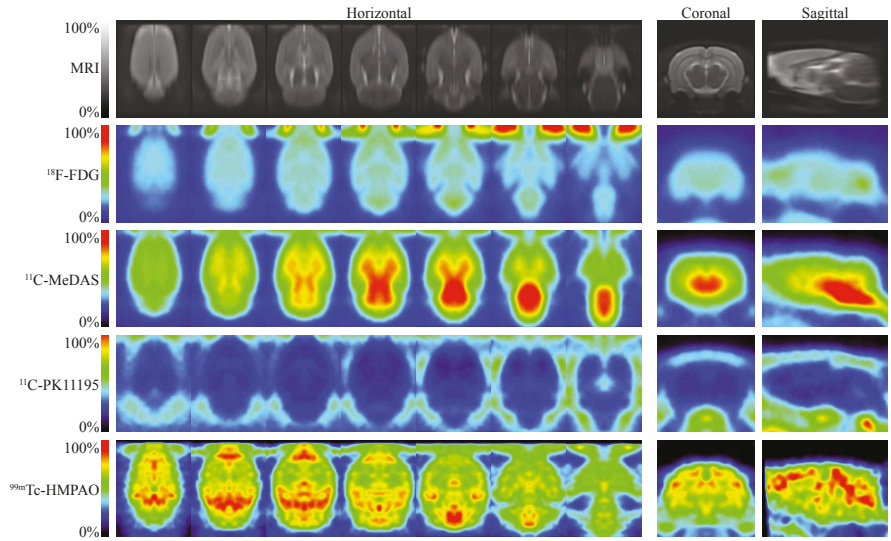
Introduction
Template based spatial co-registration of PET and SPECT data is an important first step in its semi-automatic processing, facilitating VOI- and voxel-based analysis. Although this procedure is standard in human, using corresponding MRI images, these systems are often not accessible for preclinical research. Alternatively, manual co-registration of images to a MRI template is frequently performed. However, this is operator dependent and can introduce bias. Therefore, we constructed several tracer-specific PET and SPECT rat brain templates for automatic co-registration, which were evaluated in a rat model of multiple sclerosis.

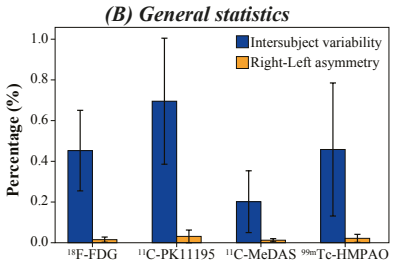


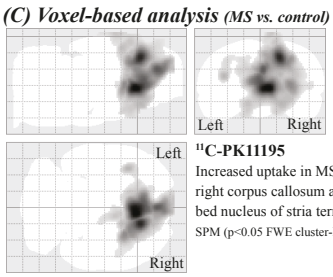
Materials and Methods

PET imaging	Animals: Male Sprague-Dawley rats (8-10 weeks; 267-337 g) Scanner: microPET Focus 220 (Siemens, Inc.) Static scan: ^{18}F-FDG (20-30 MBq) i.p.; ^{11}C-PK11195 (50-60 MBq) i.v. Dynamic scan: ^{11}C-MeDAS (50-60 MBq) i.v. Reconstruction: OSEM2D, 4 iterations, 16 subsets
SPECT imaging	Animals: Healthy male Wistar rats (8-10 weeks; 255-280 g) Scanner: U-SPECT-II (MILabs, The Netherlands) Static scan: ^{99m}Tc-HMPAO (45-60 MBq) Reconstruction: POSEM, 6 iterations, 16 subsets
Template construction (A)	Symmetrical left-right templates by averaging the scans PET: ^{18}F-FDG (n=9), ^{11}C-PK11195 (n=10), and ^{11}C-MeDAS (n=8) SPECT: ^{99m}Tc-HMPAO (n=7)
Cost function within modality	Minimizing the sum of squared differences (affine transformation)
Cost function template-to-MRI	Normalized mutual information maximization
Validation	Rat model of multiple sclerosis (MS) 1% lysolecithin (or control saline) in the right corpus callosum and striatum ^{18}F-FDG and ^{11}C-PK11195: 3 days after injection ^{11}C-MeDAS: 7 days after injection
General statistics (B)	Inter-subject variability, and right-to-left asymmetry
Registration accuracy	Random misalignments (translation, rotation, stretching, and combination)
Voxel-based analysis (C)	Statistical Parametric Mapping (SPM)

Results
The obtained mean registration errors were 0.097–1.277mm for PET, and 0.059–0.477mm for SPECT. These values are below spatial resolution of the cameras (1.4mm and 0.8mm, respectively) and in agreement with human literature [3]. Results from voxel-based analyses correspond with those previously reported using VOI-based analysis [4], and correlate with the regions where lesion was induced.







11C-PK11195
Increased uptake in MS rats in the right corpus callosum and right bed nucleus of stria terminalis
SPM (p<0.05 FWE cluster-level)

Conclusion
The constructed tracer-specific templates allow accurate registration of functional rat brain data, using automatic normalization algorithms available in standard packages (e.g., SPM, FSL), supporting either VOI- or voxel-based analysis. The templates will be made freely available for the research community.

References
[1] A J Schwarz, et al. *Neuroimage*, 2006, 32:538 [2] C Casteels, et al. *J. Nucl. Med.*, 2006, 47:1858 [3] C P Karger, et al. *Phys. Med. Biol.*, 2003, 48:211 [4] D de Paula Faria, et al. *Mult. Scler.*, 2014, (ahead of print)

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Objectives: Template based spatial co-registration of PET and SPECT data is an important first step in its semi-automatic processing, facilitating VOI- and voxel-based analysis. Although this procedure is standard in human, using corresponding MRI images, these systems are often not accessible for preclinical research. Alternatively, manual co-registration of images to a MRI template is often performed. However, this is operator dependent and can introduce bias.
Therefore, we constructed several tracer-specific PET and SPECT rat brain templates for automatic co-registration, spatially aligned with a widely used MRI-based template in Paxinos stereotactic space [1].
Methods: PET (^{18}F-FDG, ^{11}C-PK11195, and ^{11}C-MeDAS) and SPECT (^{99m}Tc-HMPAO) brain scans were acquired from healthy male Sprague-Dawley and Wistar rats. Symmetrical left-right templates were constructed by averaging the scans. Within-modality registration was performed by minimizing the sum of squared difference and template to MRI registration by normalized mutual information maximization algorithm.
For validation purposes, PET scans were acquired from a rat model of multiple sclerosis (MS) where focal demyelination was induced by injection of lysolecithin (or control saline) in right corpus callosum and striatum. Parametric SUV images were created for automatic co-registration.
The validity of the templates was assessed by estimation of registration accuracy errors, inter-subject variability, right-to-left asymmetry indices, and voxel-based analysis of the MS model [2].
Results: The obtained mean registration errors were 0.097-1.277mm for PET, and 0.059-0.477mm for SPECT. These values are below spatial resolution of the cameras (1.4mm and 0.8mm, respectively) and in agreement with human literature [3]. Results from voxel-based analyses (Figure 1) correspond with those previously reported using VOI-based analysis [4], and correlate with the regions where lesion was induced.
Conclusion: The constructed tracer-specific templates allow accurate registration of functional rat brain data, using automatic normalization algorithms available in standard packages (e.g., SPM, FSL), supporting either VOI- or voxel-based analysis. The templates will be made freely available for the research community.
References: [1] A J Schwarz, et al. *Neuroimage*, 2006, 32:538. [2] C Casteels, et al. *J. Nucl. Med.*, 2006, 47:1858 [3] C P Karger, et al. *Phys. Med. Biol.*, 2003, 48:211. [4] D de Paula Faria, et al. (submitted).

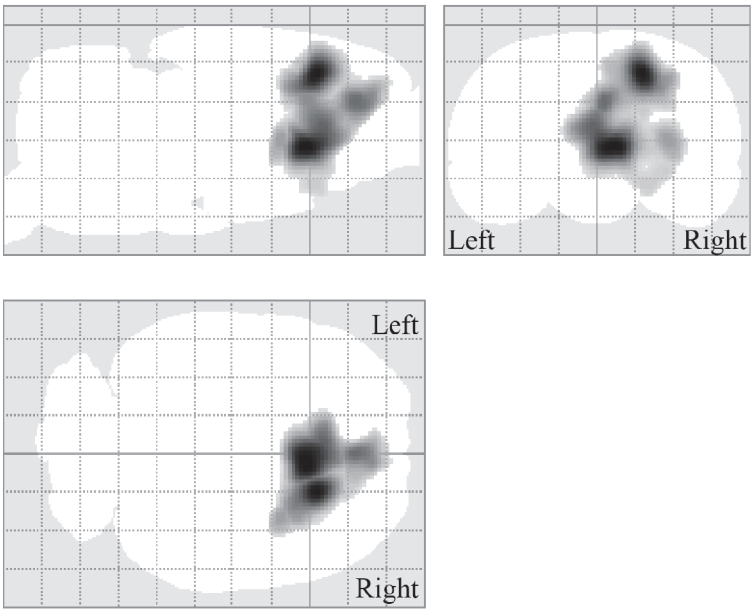

Figure 1. Voxel-based analysis performed in SPM8:
A statistically significant ($p < 0.001$ unc.; $T = 4.14$) increased uptake of ^{11}C-PK11195 was found in the group with the focal demyelinating lesion, compared with control animals. These regions correspond with the right corpus callosum and the right stria terminallis.