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Development of radioligands using *in vivo* microSPECT

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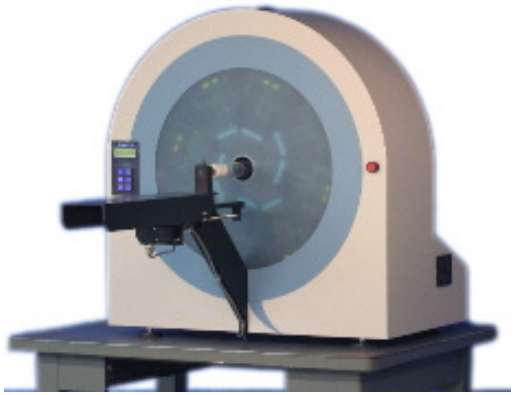
Improving Efficiency in Drug Development

Number of Compounds → **Relative Cost**

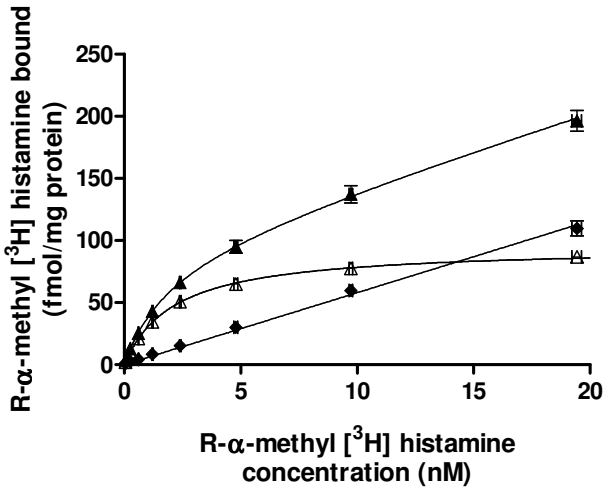
Bridging Preclinical and Clinical Research

Preclinical — *microSPECT* *microPET* — **Imaging Biomarkers** — *SPECT* *PET* — **Clinical**

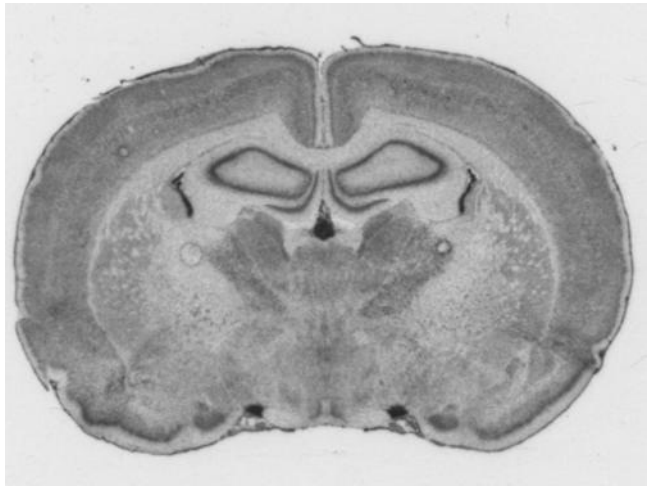


Critical Criteria in Tracer Development

(*In vitro*) Binding Assays

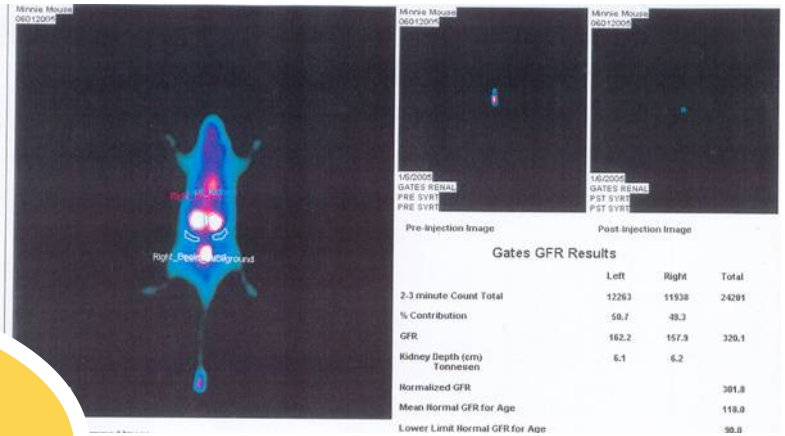


(*In vitro/Ex vivo*) Regional Distribution

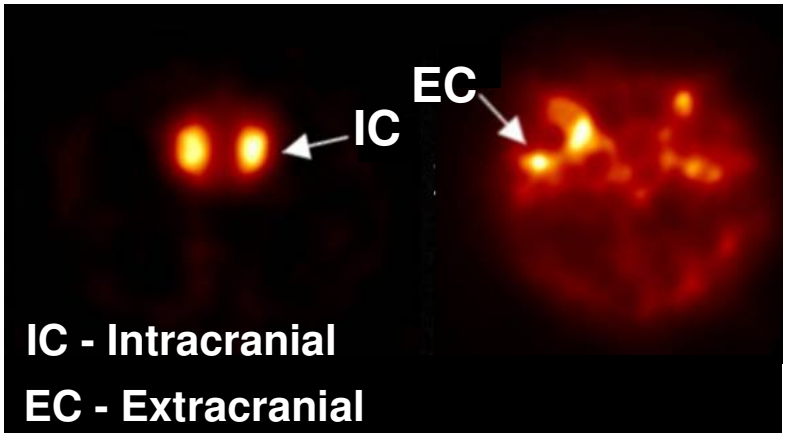


Tracer Development

(*In vivo/Ex vivo*) Whole Body Distribution



(*In vivo*) Signal to Noise



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NeuroPhysics CORPORATION

MollyQ 50™ microSPECT

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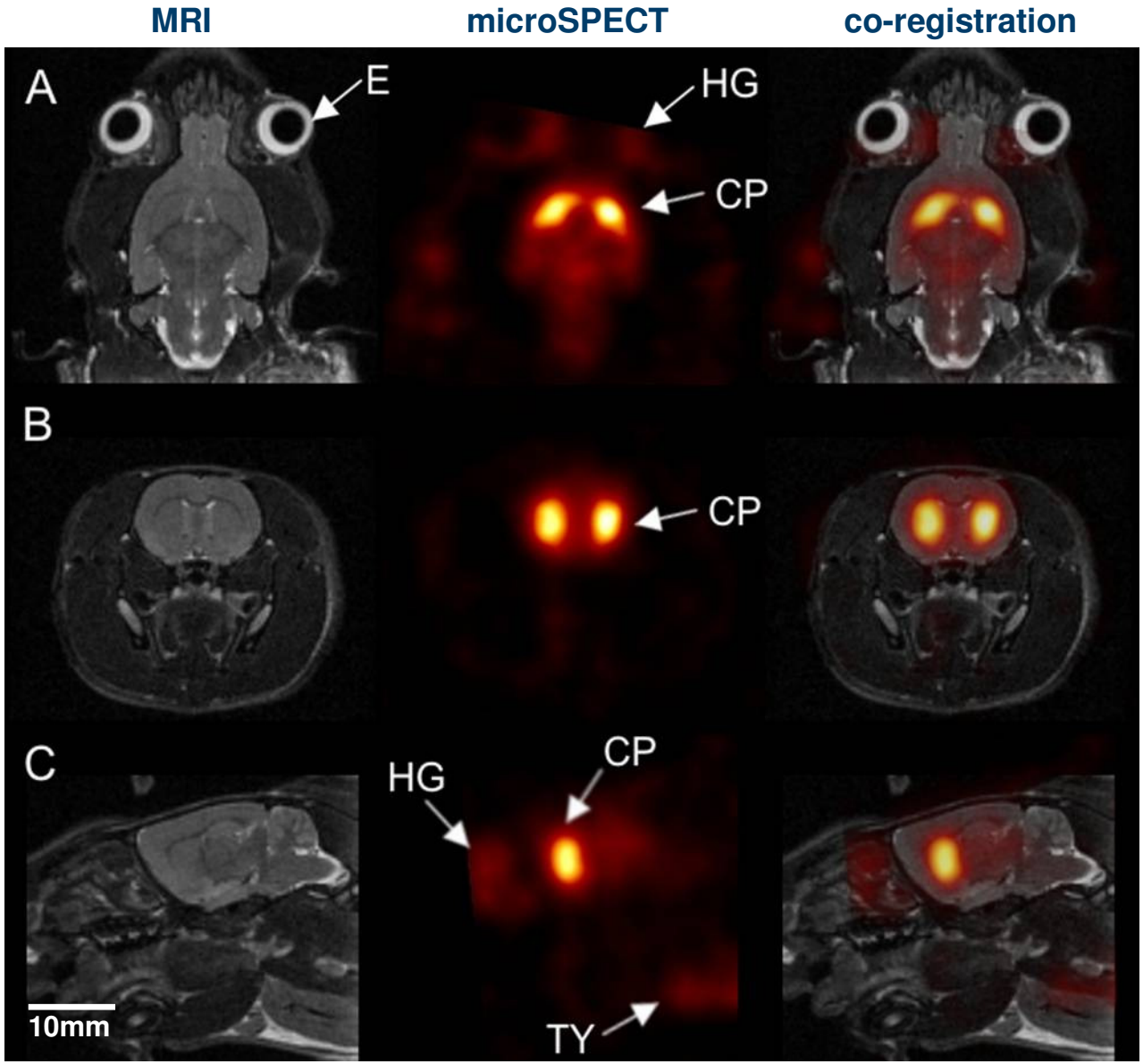
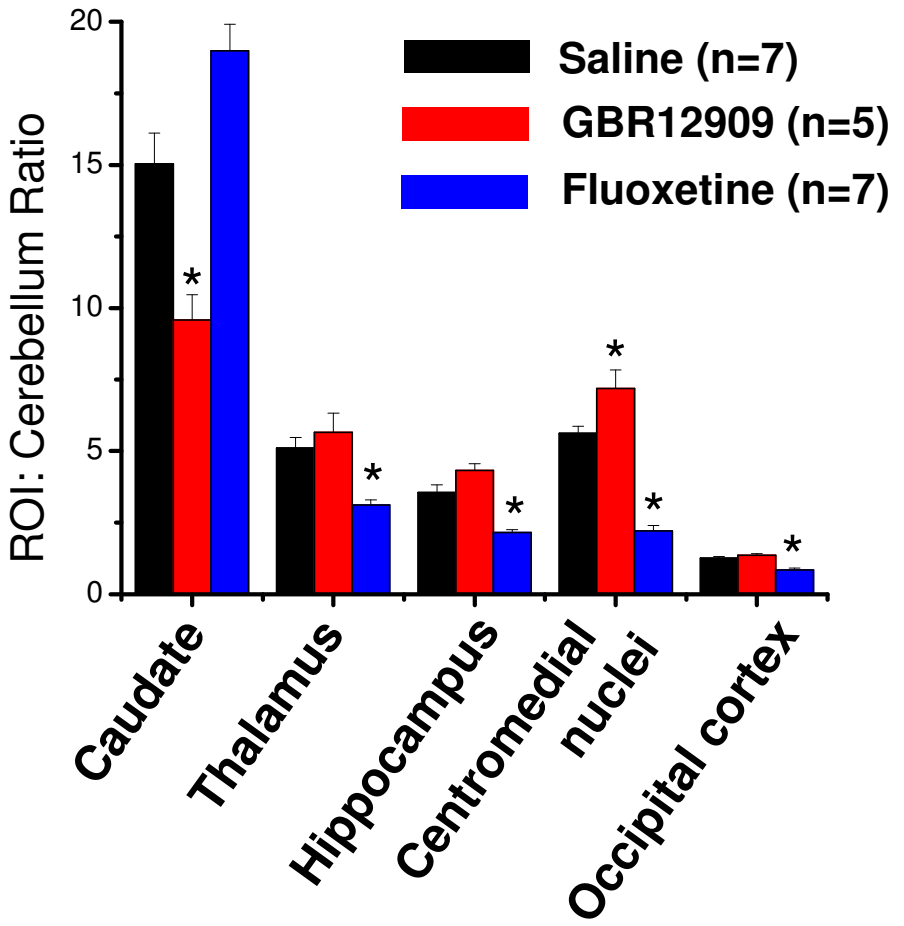
MicroSPECT: [^{125}I]βCIT binding in rat brain

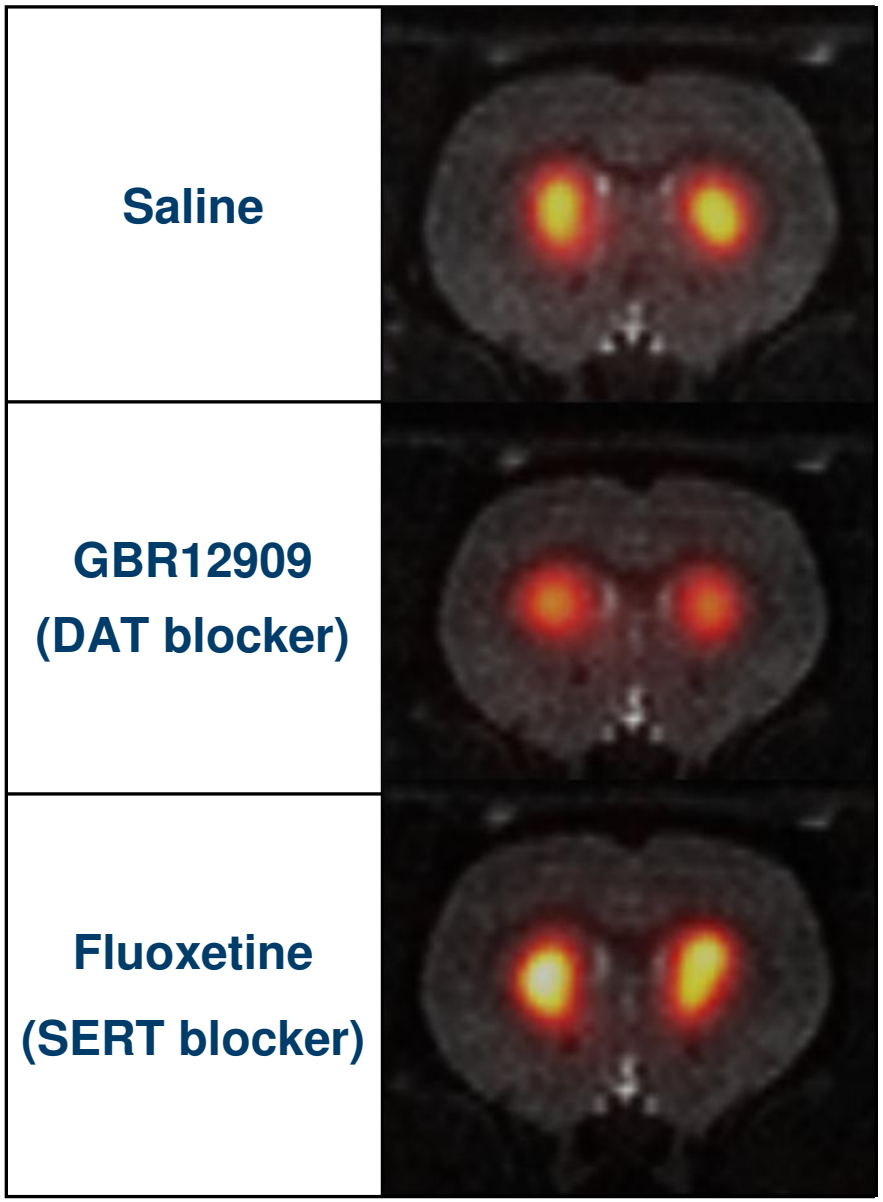


HG – Harderian Glands CP – Caudate Putamen TY – Thyroid

Pharmacological Displacement of [^{125}I]βCIT



Cain *et al.*, 2009; *Epilepsia*



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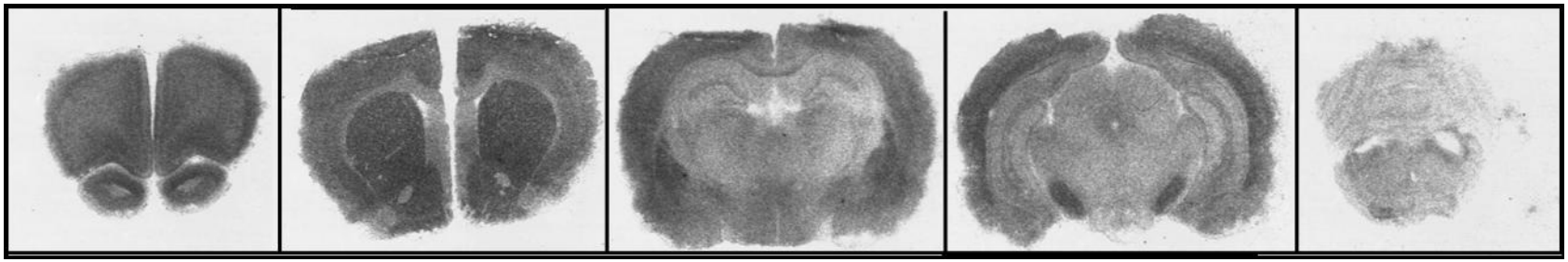
H3 SPECT Tracer Development: *In vitro* characterisation

Radioligand Binding

Radioligand	K_d (nM)	B_{max} (fmol/mg protein)	*n* number
[^{125}I]Compound 1	6.9 ± 1.3	508.6 ± 34.9	9

Receptor Autoradiography



Lipophilicity

- [^{125}I] Compound 1 Log P = 1.59 ± 0.28 (n = 3)
- [^{125}I] Compound 1 Log D 7.4 = 1.64 ± 0.27 (n = 3)

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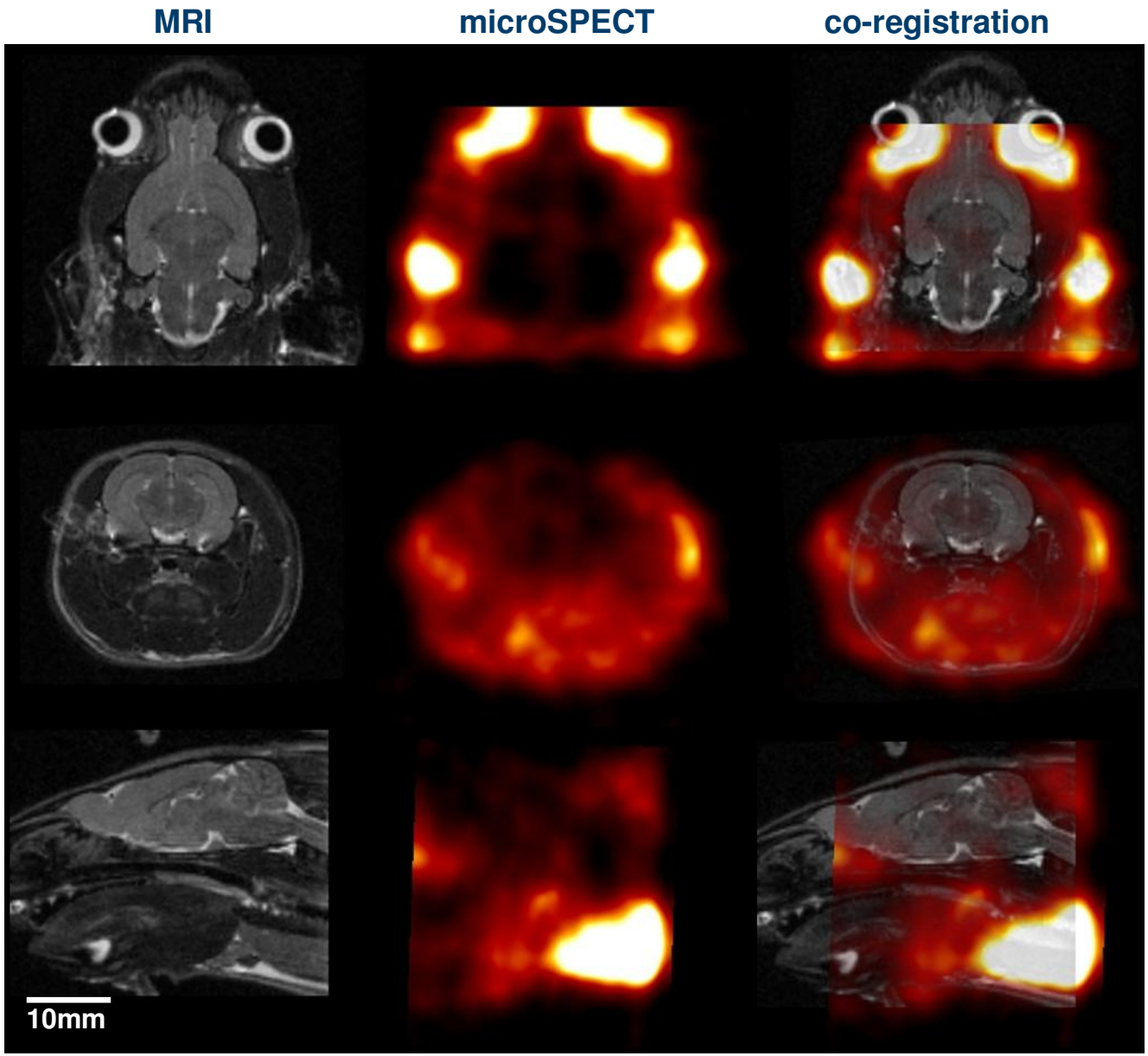
H3 SPECT Tracer Development: MicroSPECT imaging of [^{125}I] Compound 1



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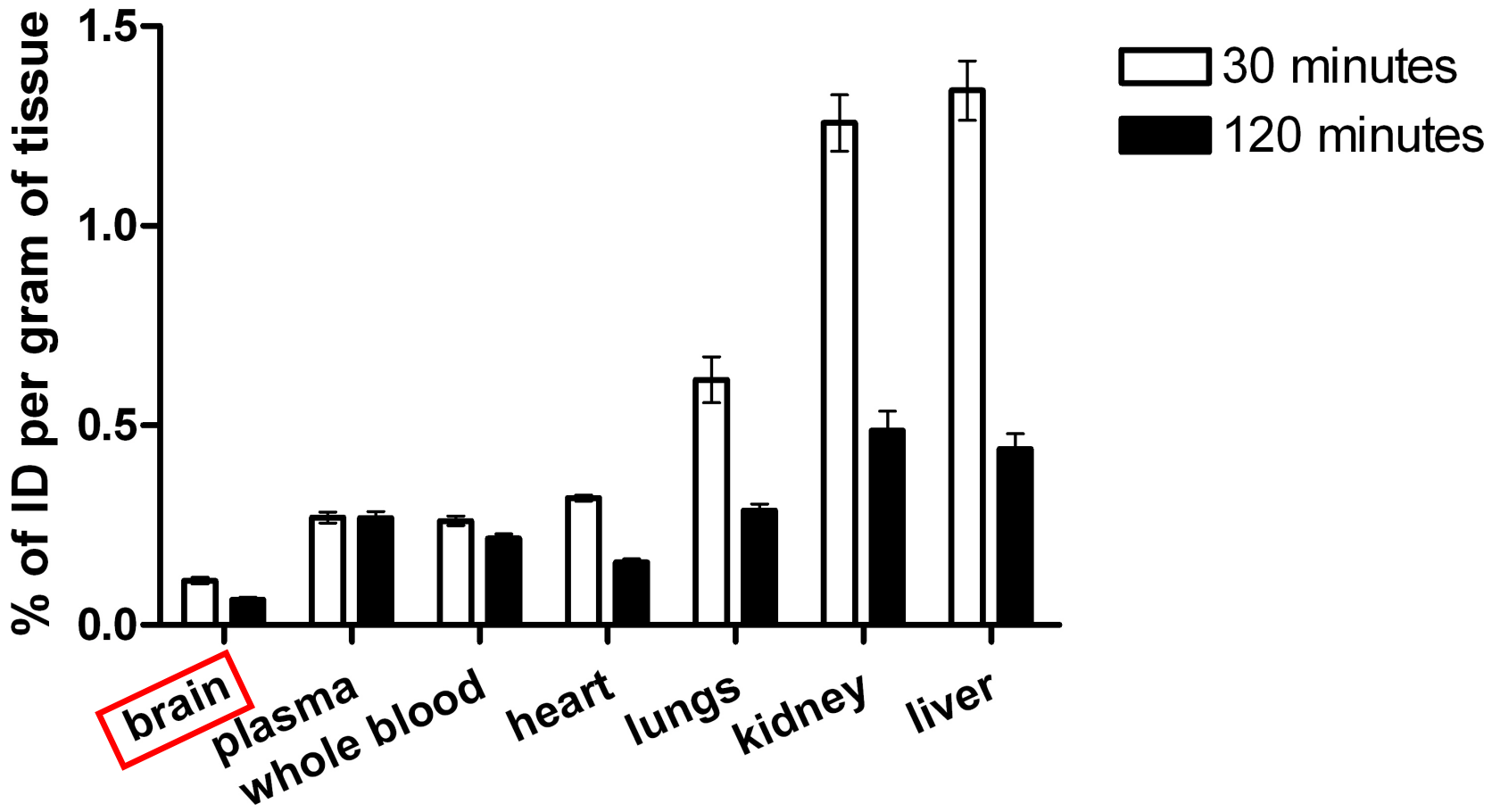
H3 SPECT Tracer Development: Whole body distribution of [^{125}I]Compound 1



***Measured *ex vivo* by dissection and gamma scintillation**

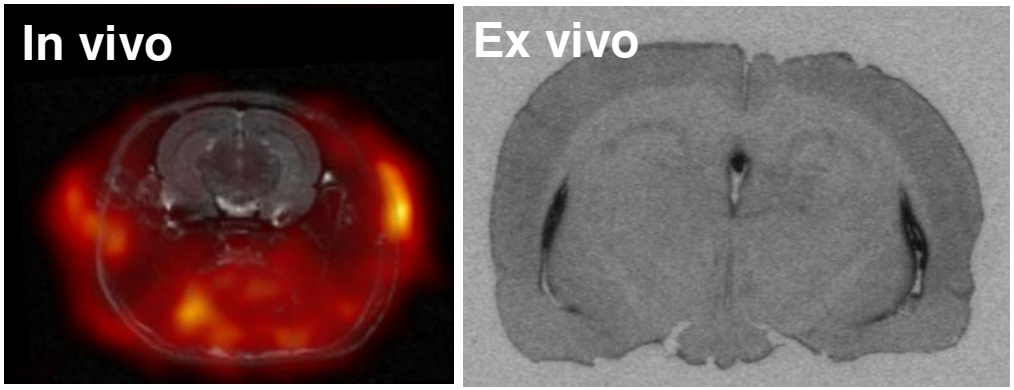
(n = 5 for brain, plasma and blood; n = 3 for all other organs)

Role of microSPECT imaging

[^{125}I]βCIT

Good imageability, microSPECT allows us to perform *in vivo* pharmacological displacement studies

[^{125}I]Compound 1



microSPECT enables decision making about the potential of tracers for clinical development

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Translational Medicine Research Collaboration

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SINAPSE
Scottish Imaging Network - A Platform for Scientific Excellence

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