PET imaging of adenosine A2A receptors
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After one and a half years of painstaking experiments on my first project — PET imaging of alpha-synuclein, I was sitting in Rudi’s office, feeling sad about the termination of my first project, and worried about the plan B — imaging of adenosine A2A receptors. I had no clue about the A2A project, so I asked a good deal of questions based on the limited literature that I had read, hoping to get some support and comfort from Rudi and my daily supervisors — Philip and Erik. But rather disappointingly, Rudi seemed unsatisfied at my reaction to my new project, he responded that I should not only post questions but find the way to solve them. ‘What! I am just a beginner. It’s already a great encouragement to ask these questions’, I went out of the office, unhappy. Rudi is right. Finally, I truly understood his attitude one year after the appointment. Now I am at the end of my PhD career and I know how a responsible researcher should be: asking interesting questions and dealing with them to the best of your ability. Thanks Rudi, your criticism pushes me moving forward in science.

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Xiaoyun Zhou
26 November 2016

‘In a thousand different forms you may hide yourself, but all the same, my best-beloved, I will recognize you’

— Johann Wolfgang von Goethe
List of Abbreviations

Aβ  Amyloid-β peptide
A_nR  Adenosine A_n receptor
AC  Adenylyl cyclase
AD  Alzheimer’s disease
AIC  Akaike information criterion
AIM  Abnormal involuntary movement
ANOVA  Analysis of variance
ARG  Autoradiography
ATP  Adenosine triphosphate
AUC  Area under the curve
BBB  Blood brain-barrier
BD  Biodistribution
B_{max}  Total density of target molecules
BOLD  Blood oxygenation-level dependent
B_{ND}  Non-displaceable binding potential
Bq  Becquerel
BRET  Bioluminescence resonance energy transfer
cm  Centimeter
CBV  Cerebral blood volume
Ci  Curie
CNS  Central nervous system
COV  Coefficient of variation
C_P  Radioactivity concentration in plasma
C_R  Radioactivity concentration in a reference region
C_T  Radioactivity concentration in tissue
CT  Computed tomography
Da  Atomic mass unit dalton
D_{nR}  Dopamine D_n receptor
DMAA  N,N-Dimethylacetamide
DMSO  Dimethyl sulfoxide
2D-OSEM  2-Dimensional ordered-subset expectation maximization algorithm
DVR  Distribution volume ratio
ED  Effective dose
$ED_{50}$  Drug dose corresponds to 50% occupancy
ERK  Extracellular signal–regulated kinase
ESI-HRMS  Electro-spray ionization high-resolution mass spectrometry
fmol  Femtomole
fMRI  Functional magnetic resonance imaging
FDG  Fluo-2-rodeoxy-D-glucose
FOV  Field of view
g  Gram
GBq  Gigabecquerel
GCF  Global correction factor
GDNF  Glial cell line-derived neurotrophic factor
GPe  Globus pallidus pars externa
GPi  Globus pallidus pars interna
HCl  Hydrogen chloride
HD  Huntington’s disease
HIV  Human immunodeficiency virus
HPLC  High performance liquid chromatography
Hz  Herz
ICC  Intra-class correlation coefficient
ICRP  International Commission on Radiological Protection
keV  Kiloelectronvolt
$K_{1-k_n}$  Rate constant ‘n’
kBq  Kilobecquerel
kDa  Kilodalton
$K_d$  Dissociation constant
kg  Kilo gram
$K_i$  Inhibition constant
$K_m$  Metabolic rate constant
L-DOPA  Levodopa
LGA  Logan graphical analysis
LID  Levodopa-induced dyskinesia
LogD$_{7.4}$  Octanol water partition coefficient at pH7.4
mg  Minigram
min  Minute
mL  Minilitre
mm  Minimitre
### List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>mmol</td>
<td>Minimole</td>
</tr>
<tr>
<td>mM</td>
<td>Minimolar</td>
</tr>
<tr>
<td>M</td>
<td>Molar concentration (1 M = 1 mole/litre)</td>
</tr>
<tr>
<td>MBq</td>
<td>Mega becquerel</td>
</tr>
<tr>
<td>MHz</td>
<td>Megahertz</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRTM</td>
<td>Ichise’s multilinear reference tissue model</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>nm</td>
<td>Namometre</td>
</tr>
<tr>
<td>nM</td>
<td>Nanomolar</td>
</tr>
<tr>
<td>NMDA</td>
<td>N-methyl-D-aspartate</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>( \text{Occ}_{\text{max}} )</td>
<td>Maximum occupancy</td>
</tr>
<tr>
<td>6-OHDA</td>
<td>6-Hydroxydopamine</td>
</tr>
<tr>
<td>OSEM3D/MAP</td>
<td>Ordered set expectation maximization-3-Dimension/maximum a posteriori</td>
</tr>
<tr>
<td>PBS</td>
<td>Phosphate-buffered saline</td>
</tr>
<tr>
<td>PD</td>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>PEG400</td>
<td>Polyethylene glycol 400</td>
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<tr>
<td>PET</td>
<td>Positron-emission tomography</td>
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<tr>
<td>PVE</td>
<td>Partial volume effect</td>
</tr>
<tr>
<td>QC</td>
<td>Quality control</td>
</tr>
<tr>
<td>RLogan</td>
<td>Reference tissue Logan plot</td>
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<tr>
<td>ROI</td>
<td>Regions of interest</td>
</tr>
<tr>
<td>RP</td>
<td>Reverse-phase</td>
</tr>
<tr>
<td>RT</td>
<td>Residence time</td>
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<tr>
<td>s</td>
<td>Second</td>
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<tr>
<td>SD</td>
<td>Standard deviation</td>
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<tr>
<td>SNc</td>
<td>Substantia nigra pars compacta</td>
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<tr>
<td>SNr</td>
<td>Substantia nigra pars reticulate</td>
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<tr>
<td>SPM</td>
<td>Statistical parametric mapping</td>
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<td>SPMS</td>
<td>Secondary progressive multiple sclerosis</td>
</tr>
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<td>SRTM</td>
<td>Simplified reference tissue model</td>
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<tr>
<td>STN</td>
<td>Subthalamic nucleus</td>
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<tr>
<td>SUV</td>
<td>Standardized uptake value</td>
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<tr>
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<td>Sv</td>
<td>Sievert</td>
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<td>-------------------------------------</td>
</tr>
<tr>
<td>t</td>
<td>Time</td>
</tr>
<tr>
<td>$t_{1/2}$</td>
<td>Half-life</td>
</tr>
<tr>
<td>T</td>
<td>Tesla</td>
</tr>
<tr>
<td>TAC</td>
<td>Time-activity curve</td>
</tr>
<tr>
<td>TAT</td>
<td>Trans-activator of transcription</td>
</tr>
<tr>
<td>nTCM</td>
<td>n-Tissue compartment model</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>Thin-layer chromatography</td>
</tr>
<tr>
<td>TM</td>
<td>Transmembrane</td>
</tr>
<tr>
<td>TRV</td>
<td>Test-retest variability</td>
</tr>
<tr>
<td>TSPO</td>
<td>Translocator protein 18 kDa</td>
</tr>
<tr>
<td>UPLC</td>
<td>Ultra-high performance liquid chromatography</td>
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<tr>
<td>v/v</td>
<td>Volume per volume</td>
</tr>
<tr>
<td>$V_B$</td>
<td>Fractional blood volume</td>
</tr>
<tr>
<td>$V_{ND}$</td>
<td>Non-displaceable volume of distribution</td>
</tr>
<tr>
<td>VOI</td>
<td>Volume of interest</td>
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<tr>
<td>$V_T$</td>
<td>Volume of distribution</td>
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<tr>
<td>YFP</td>
<td>Yellow fluorescent protein</td>
</tr>
<tr>
<td>$\mu g$</td>
<td>Microgram</td>
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<tr>
<td>$\mu L$</td>
<td>Microlitre</td>
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<tr>
<td>$\mu M$</td>
<td>Micromolar</td>
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<tr>
<td>$\mu m$</td>
<td>Micrometre</td>
</tr>
<tr>
<td>$\mu S$</td>
<td>Microsievert</td>
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