SPECT and PET

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Basics Nuclear Medicine

1. Radiopharmaceutical/radiotracer/radioligand: Pharmaceutical labeled with a radionuclide

2. Pharmaceutical: molecules with specific pharmacological/biochemical properties: determines its pharmacokinetics/dynamics (e.g., binds to dopaminergic cells or uptake via glucose transporter in cells)

3. Radionuclide: unstable atoms $\rightarrow \gamma$ -radiation (photons), which can be detected by a camera



[¹²³I]FP-CIT: DaTSCAN

¹²³I-FP-CIT

¹²³I-IDEX

123 I- β -CIT









muscarinic receptors serotonin transporter

SPECT tracers

Radionuclide	γ-ray	Half-lives
	energy (keV)	T _{1/2} (h)
^{99m} Tc	140	6
123 I	159	13.2

 $T_{1/2}$ = time until 50% of the radionuclides have been disintegrated

Basic principles SPECT tracers

Radionuclide - unstable atom

Atomic disintegration (radioactive decay)



γ-radiation

specific energy

(140 - 159 keV for ^{99m}Tc and ¹²³I, respectively)

principle of photon detection (SPECT/PET)

Visible light photon



scintillator:

-Crystals for SPECT: NaI (energies 100-350 keV) -Crystals for PET: BGO, LSO (energy 511 keV)

Why is a collimator needed for SPECT?





measured:(ph) photon peak(s) scatter(pnot measured:(a) absorption(at) attenuation

SPECT(/CT) scanners





PET



positron emission detection



Positron emission tomography: based on detection of both annihilation photons (511 keV; coincidence detection)



Line of response = line between the 2 detectors that detected 2 photons simultaneously

radionuclides	half-lives	
	T _{1/2} (min)	
¹⁵ O	2.1	
^{13}N	10	
11 C	20.4	
$^{18}\mathrm{F}$	110	

 $T_{1/2}$ = time until 50% of the radionuclides have been disintegrated

Pros SPECT: no on-site cyclotron is needed, images can be made hrs after injection

PET versus SPECT



Vastenhouw et al., *Molecular Psychiatry* 2007



Mouse brain: resolution < 0.5 mm

SPECT



- 1. SPECT: attenuation depends on position of activity within body
- 2. Attenuation cannot be measured exactly with external source; correction will be less accurate with SPECT

Clinical PET versus SPECT

- coincidence detection
- LOR
- efficiency = ++(0.5-3%)
- resolution = ++
 (4-7 mm FWHM)
- accurate quantification

- single photon detection
- collimator
- efficiency = +/-(0.04%)
- resolution = +/ (7-14 mm FWHM)
- quantification less accurate

Bringing two worlds together....VECTor system



Goorden et al., *JNM* 2013



Goorden et al., JNM 2013



¹²³I-FP-CIT (SPECT tracer)

¹⁸F-FDG (PET tracer) PET and SPECT tracers used in clinical practice and research



Wallert et al., J Nucl Med 2022







Fazio et al., JNM 2015

Dopaminergic degeneration not specific for PD

MSA

PSP





Joling et al., J Nucl Med 2017



O'Brien et al., Arch Neurol 2004

[¹²³I]FP-CIT
SPECT:
33 controls
34 AD
38 PD
23 DLB
36 PDD



Figure 2. Iodine 1123-radiolabeled 29-carbomethoxy-3p-(4-iodophenyl)-A-(3-fluoropropyl) nortropane with single-photon emission computed tomographic images. A, A healthy older control subject. B, Subjects with Alzheimer disease. C, Subjects with dementia with Lewy bodies. D, Subjects with Parkinson disease. F, Subjects with Parkinson disease with dementia.



Figure 3. Summary of specific-monspecific activity ratios for both hemispheres in the caudate nucleus (A), the anterior putamen (B), and the posterior putamen (C) in healthy older control subjects and subjects with Alzheimer disease (AD), dementia with Lewy bodies (DLB), Parkinson disease (PD), and PD with dementia (PDD). Means and 95% confidence intervals (CIs) are given.

DAT imaging in routine practice

Differentiate PD from drug-induced parkinsonism

Differentiate PD from essential tremor or dystonia

Differentiate DLB from AD



Wallert et al., J Nucl Med 2022

Eshuis et al., EJNMMI 2009



[¹⁸F]DOPA PET in a healthy control (a) and early-stage PD patient (b)



Wallert et al., *EJNMMI Res* 2022

22q11.2 deletion syndrome (22q11DS)

- genetic disorder caused by microdeletion on chromosome 22q11.2
- associated with an increased risk for developing psychosis
- catechol-O-methyltransferase (COMT) gene is located in the deleted region and involved in dopamine (DA) breakdown; particularly expressed frontal areas
- increased DA synthesis is associated with increased risk to develop psychosis

Dopamine $D_{2/3}$ receptor imaging



Wallert et al., J Nucl Med 2022



van Duin et al., *Psychol Med* 2020



Boot et al., Neurology 2018



Booij et al., Am J Med Genet A. 2010



Case 52 yrs old male > 10 years parkinsonism

FIG. 1. Transversal SPECT slices at the level of the striatum—left panel: 55-year-old male healthy control; right panel: 22q11DS case.

Muscarinic imaging in psychosis (or cognition)

Muscarinic receptor antagonist: induce cognitive deficits¹

Muscarinic M_1 receptor expressed in brain regions critical for cognition (e.g., hippocampus and DLPFC)²

M₁ agonist xanomeline: improved cognition in psychotic disorder³

¹Xiang et al., *J Pharmacol Exp Ther* 2012; ²Cortes et al., *Neuroscience* 1987; ³Shekhar et al., *Am J Psychiatry* 2008

Bakker et al., JNM 2015



¹²³I-IDEX binding in rats

Control

olanzapine pre-treated

Bakker et al., NeuroImage Clin 2018





New Eng J Med 2021

 $N = \sim 90/group$

Acute exacerbation Free of AP > 2 weeks



Naganawa et al., J Nucl Med 2021



¹¹C-LSN3172176:

Selective muscarinic M_1 tracer

Amyloid imaging

¹¹C-PIB

Klunk et al., Ann Neurol 2004

Amyloid PET

[¹⁸F]florbetaben

Villemagne et al., J Nucl Med 2011

Sevigny et al Nature 2016

aducanumab

Fisher and Wonnacott, Ch 13 – Acetylcholine in Basic Neurochemistry 2012 (8th edition)

Nejad-Davarani et al, Mol Psychiatry 2018

[¹⁸F]FEOBV PET (vesicular acetylcholine transporter)

Last, but not least...¹⁸F-FDG PET imaging

Booij et al., Clin Nucl Med 2022

47 yrs old female; acute cerebellar syndrome; normal MRI; PET/CT: cerebellar hypermetabolism and breast carcinoma; anti-Yo antibodies; case of paraneoplastic cerebellar syndrome

Moubtakir et al., Clin Nucl Med 2018

28 yrs old woman; subacute onset behavior disorder; suspicion of limbic encephalitis; PET: parietal and occ hypometabolism; ovarian teratoma; NMDA antibodies; A case of anti-NMDA encephalitis

Conclusions

Introduced the basic aspects of PET/SPECT

Several PET/SPECT tracers are clinically available and relevant for Neurology

