Radiopharmaceuticals in Neurological and Psychiatric Disorders

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Everything that healthcare providers do has a real, meaningful impact on human life.

Nuclear medicine is the only imaging modality that depends on the injected radiopharmaceutical.

Every radiopharmaceutical that is administrated holds far more than just a radionuclide.

Radiopharmaceuticals want it to deliver confidence, efficiency and a higher standard of excellence. And above all, renewed hope for each patient’s future.

Radiopharmaceuticals for planar imaging, (SPECT), (PET), PET-CT or SPECT-CT fusion imaging. PET-MRI is currently being developed for clinical application.
Understanding the utilization of radiopharmaceuticals for neurological and psychiatric disorders

First contact...Projects related to International Atomic Energy Agency - IAEA:
1. (technical cooperation) 1995-1997 Preparation and QC of Technetium 99m Radiopharmaceuticals

99mTc - HMPAO

<table>
<thead>
<tr>
<th>Agent</th>
<th>Solvent</th>
<th>ITLC-SG</th>
<th>GMCP-SA</th>
<th>Whatman#1</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMPAO</td>
<td>Saline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMPAO</td>
<td>MEK</td>
<td></td>
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</tr>
</tbody>
</table>

![Images of brain scans and graphs]
DIAGNOSTIC APPLICATION OF SPECT RADIOPHARMACEUTICALS IN NEUROLOGY AND PSYCHIATRY

The principal application areas for brain imaging include:

- evaluation of brain death - brain imaging to assess the absence of cerebral blood flow
- epilepsy
- cerebrovascular disease
- neuronal function
- cerebrospinal fluid (CSF) dynamics
- brain tumours

Primarily technetium agents, including

- **nondiffusible tracers** 99mTc-pertechnetate, 99mTc-pentetate (Tc- DTPA) and 99mTc-gluceptate (Tc-GH)
- **diffusible tracers** 99mTc-exametazime, hexamethylpropyleneamine oxime - (Tc-HMPAO) and 99mTc-bicisate, ethylcysteinate dimer (Tc-ECD)
**Evaluation of brain death - brain imaging to assess the absence of cerebral blood flow**

![Chemical structures](image)

**Properties of SPECT Blood Flow Markers for Brain Imaging**

<table>
<thead>
<tr>
<th>Property</th>
<th>Tc-HMPAO</th>
<th>Tc-ECD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Charge/Lipophilicity</td>
<td>Neutral/Lipophilic</td>
<td>Neutral/Lipophilic</td>
</tr>
<tr>
<td>Brain Extraction Efficiency</td>
<td><strong>72 – 80 %</strong></td>
<td>47 – 60 %</td>
</tr>
<tr>
<td>Maximum Brain Uptake Localization Mechanism</td>
<td>4.1% (20 min) Glutathione reduction</td>
<td>6.5% (5 min) Esterase hydrolysis</td>
</tr>
<tr>
<td>Brain Washout</td>
<td>15% over 2 min T(_{1/2}) = 72 hr (slow component)</td>
<td><strong>20% over 1 hr T(_{1/2}) = 42.3 hr (slow component)</strong></td>
</tr>
<tr>
<td>Blood Levels</td>
<td>12% ID (1 hr)</td>
<td>5% ID (1 hr)</td>
</tr>
<tr>
<td>Excretion</td>
<td>Urine (40% in 48 hr) Hepatobiliary (30% immediate)</td>
<td>Urine (72% in 24 hr) Hepatobiliary (12% in 48 hr)</td>
</tr>
<tr>
<td>Critical Organ</td>
<td>Lacrimal Glands 5.16 rad/20 mCi</td>
<td>Urinary Bladder Wall 5.6 rad/20 mCi</td>
</tr>
</tbody>
</table>
Cerebral delivery of radiotracer to the brain after i.v. administration

Major arteries that distribute blood in the brain

Major veins that drain blood from the brain

Normal posterior radionuclide cerebral angiogram (flow study). Images shown are acquired at 2 second intervals after IV injection of 20 mCi (740 MBq) of 99mTc-glucose

Images show venous drainage through the lateral (transverse) venous sinuses and the jugular veins, which return blood to the heart.
**Epilepsy** - neurologic disorder of the brain that causes recurring excessive neuronal discharge resulting in repeated episodes of seizure. Radiopharmaceutical administration has been an effective method for identifying partial seizure foci - SPECT during a seizure (ictally) following administration of Tc-HMPAO or Tc-ECD. Increased blood flow to the seizure focus during ictus and the rapid first-pass uptake of these tracers relative to rCBF.

(A) Sagittal, coronal and axial interictal SPECT of a patient with complex partial seizures in the right temporal lobe. SPECT image shows a decrease in perfusion in the right anteromesial temporal region.  
(B) Sagittal, coronal and axial brain SPECT images SPECT image shows an increase in perfusion in the right temporal lobe, exactly where the EZ is located.  
(C) Images showing fusion of the ictal-interictal SPECT subtraction coregistered to the MRI of the same patient. An increase in perfusion in the anterior pole of the right temporal lobe with mesial region predominance is observed.
cerebrovascular disease – Stroke (ischemic and hemorrhagic)

Ischemic stroke results from sudden occlusion of arterial blood flow due to thromboembolism.

Hemorrhagic stroke is the result of blood vessel rupture, such as from an aneurysm.

A patient with an old infarct (CT image on left) showed a corresponding small area of right parietal hypoperfusion (arrow) on routine 99mTc-HMPAO SPECT scan (center).

The acetazolamide stress study (right) revealed a much larger area of reduced vascular reserve in the right middle cerebral artery territory, reflecting the area at risk for further vascular compromise that is not apparent on the baseline SPECT or CT study.
Cerebrospinal fluid (CSF) dynamics Studies - formed by active secretion of ependymal cells of the choroid plexuses of the lateral, third, and fourth ventricles.

The brain and CSF space showing the site of CSF production (choroid plexus) in the lateral, third, and fourth ventricles. CSF flow proceeds out of the ventricles in a caudal direction around the spinal cord and cephalad over the cerebral hemispheres and is absorbed at the arachnoid villi into the superior sagittal sinus. The cord cross-section demonstrates the meninges and subarachnoid space.
Normal CSF cisternogram. $^{111}$In-DTPA study showing normal radiotracer accumulation in the basal cisterns, interhemispheric and sylvian fissures on the 4 hour images (trident appearance). Images at 24 hours demonstrate normal ascent of the radiotracer over the convexities to the superior sagittal sinus. Normal-pressure hydrocephalus. The 6 hour images demonstrate $^{111}$In-DTPA activity in the spinal subarachnoid space, basal cisterns, and lateral ventricles. At 24 hours the activity persists in the lateral ventricles and in this patient there is very slow progression over the hemispheres. This pattern is essentially the same at 48 hours and indicates extraventricular obstruction and normal-pressure hydrocephalus.
neuronal function – to investigate with radiopharmaceuticals dopamine system, serotonin system, cholinergic system, γ-aminobutyric acid (GABA) system, and opioid receptors.

Presynaptic neuron with neurotransmitter (dopamine) in storage vesicles. Signal transmission releases neurotransmitter into the synaptic cleft where it activates receptor sites on the postsynaptic neuron. Excess neurotransmitter is returned to the presynaptic neuronal cytoplasm via the dopamine transporter (DAT) and taken back up into storage vesicles via the vesicular monoamine transporter (VMAT).
<table>
<thead>
<tr>
<th>Radiopharmaceuticals</th>
<th>Site of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>18F-FDG, or 18F-6-fluorodopa</td>
<td>Dopamine synthesis</td>
</tr>
<tr>
<td>123I-βCIT, or 123I-2β-carbomethyl-3β-(4-iodophenyl)tropane</td>
<td>Dopamine transporter</td>
</tr>
<tr>
<td>123I-FP-CIT, or 123I-ioflupane, or 123I-N-ω-fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl)nortropane</td>
<td>Dopamine transporter</td>
</tr>
<tr>
<td>11C-DTBZ, or 11C-dihydrotetрабеназин</td>
<td>Vesicular monoamine transporter 2</td>
</tr>
<tr>
<td>11C-DTBZ, or 11C-dihydrotetрабеназин 18F-FP-DTBZ, or 9-[18F]-fluoropropyl-9-Odesmethyldihydrotetрабеназин</td>
<td>Vesicular monoamine transporter 2</td>
</tr>
<tr>
<td>18F-AV-133, or 18F-(+)-fluoropropyl-dihydrotetрабеназин</td>
<td>Vesicular monoamine transporter 2</td>
</tr>
<tr>
<td>99mTc-TRODAT-1, or 99mTc-[2-[[2-<a href="2-mercaptopethyl">[3-(4-chlorophenyl)-8-methyl-8-azabicylo [3.2.1]oct-2-yl]methyl</a>amino]ethyl]amino] ethanethiolato(3-)-N2,N2′S2,S2′]oxo-[1R-(exo-exo)]</td>
<td>Dopamine transporter</td>
</tr>
<tr>
<td>123I-altropane, or 123I-2β-carbomethoxy-3β-(4-fluorophenyl)-N-(1-iodoprop-1-en-3-yl)nortropane</td>
<td>Dopamine transporter</td>
</tr>
</tbody>
</table>
BASIC REQUIREMENTS FOR A CNS RECEPTOR RADIOPHARMACEUTICALS

1. Ability to cross the BBB (neutral, MW < 700, log P 1.0–3.0)
2. In vivo stability
3. High and selective binding affinity for the target receptor (IC50 < 10 nM)
4. High uptake in brain
5. Localized in target sites
6. Formation (if any) of non-binding radiometabolites

Schematic representation of a receptor specific radiopharmaceutical
TECHNETIUM-99m COMPLEXES FOR THE DOPAMINE TRANSPORTER

99mTc labelled tropane analogues that display selective DAT binding

99mTc-TRODAT/SPECT images of a control (a) and a patient with Parkinson’s disease (b). The uptake decreased on both sides of the striatal region in the patient with Parkinson’s disease.
TECHNETIUM-99m COMPLEXES FOR THE 5-HT\textsubscript{1A} RECEPTOR – the concentration or function of these receptors are implicated in neurological and psychological disorders such as anxiety, depression, schizophrenia and Alzheimer’s disease.

Design features of technetium based 5-HT\textsubscript{1A} ligands employing structural elements of the selective antagonist WAY 100635.
Normal and abnormal DaTscan SPECT Images.

(A) Normal DaTscan SPECT image: characterized by uptake of the tracer in both right and left putamen and caudate nuclei. Abnormal DaTscan images fall into at least one of the following three categories (all are considered abnormal).

(B) Abnormal DaTscan SPECT image type 1: included asymmetrical uptake with almost normal or reduced putamen activity in one hemisphere and a more marked change on the other side, likely on the side opposite the patient's first clinically affected side, and characterized by a significantly lower or no uptake in the putamen. The uptake was limited to a roughly circular area.

(C) Abnormal DaTscan SPECT image type 2: included significantly reduced putamen uptake on both sides. Activity was confined to the caudate nuclei and formed two roughly circular areas.

(D) Abnormal DaTscan SPECT image type 3: had virtually no uptake from both the putamen and caudate nuclei on both sides of the brain, resulting in a significant reduction in contrast and the visualization of background activity throughout the rest of the image.
PET can be used for the assessment of many neurophysiological and neuropathophysiological processes in vivo:

- parameters of regional cerebral energy supply including blood flow ($^{15}$O-water or $^{15}$O-butanol), glucose ($^{18}$F-deoxyglucose or FDG),
- oxygen metabolism to evaluate neural cell degeneration ($^{15}$O$_2$, $^{18}$F-misonidazole or FMISO).

- brain protein synthesis and turnover for local measurement with labeled amino acids ($^{11}$C-Methionine, $^{11}$C-Leucine, $^{18}$F-Tyrosine, alpha$^{11}$C-Methyl-Tryptophan or AMT) or nucleoside ($^{18}$F-Thymidine or FLT), allowing the assessment and follow-up of brain cell division.

- For research purposes, investigation of brain neurotransmission systems - regional distribution, kinetic parameters and metabolism of neurotransmitters and membrane receptors quantified for the dopaminergic ($^{11}$C-Raclopride, $^{18}$F-DOPA), serotonergic ($^{18}$F-Altanserin, $^{18}$F-CWAY), cholinergic, gabaergic-A central ($^{11}$C-Flumazenil, FMZ), peripheral benzodiazepine ($^{11}$C-PK1185), and opioid ($^{11}$C-Carfentany) systems, to name the most important of them.
Diagnostic application of PET radiopharmaceuticals in neurology and psychiatry – for the assessment of many neurophysiological and neuropathophysiological processes in vivo

Key PET tracers in neurological research and diagnostic

<table>
<thead>
<tr>
<th>Pathophysiological process</th>
<th>Key biological parameters</th>
<th>PET radiopharmaceuticals</th>
<th>Diagnostic use</th>
<th>Research use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>Oligemia Ischemia</td>
<td>Blood flow Oxygenmetabolism</td>
<td>15O H2O 15O2</td>
<td></td>
</tr>
<tr>
<td>Alzheimer</td>
<td>Neurodegeneration Protein aggregates</td>
<td>Glucose metabolism A-beta plaque density</td>
<td>18F FDG 18F florbetapir</td>
<td>✓</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Hyperexcitabilty</td>
<td>Glucose metabolism GABA receptor density</td>
<td>18F FDG 11C flumazenil</td>
<td>✓ ✓</td>
</tr>
<tr>
<td>Parkinson</td>
<td>Loss of DA neurons</td>
<td>DA synthesis Monoamine transport</td>
<td>18F DOPA 18F DBZT</td>
<td>✓</td>
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EMA approved PET radiopharmaceuticals for clinical use in neurology and psychiatry

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Biological target</th>
<th>Indication</th>
</tr>
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<tr>
<td>18F-FDG</td>
<td>Glucose metabolism</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>18F-FDG</td>
<td>Glucose metabolism</td>
<td>Alzheimer disease</td>
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FDA approved PET radiopharmaceuticals for clinical use in neurology and psychiatry

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<td>Glucose metabolism</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>18F-FDG</td>
<td>Glucose metabolism</td>
<td>Alzheimer disease</td>
</tr>
<tr>
<td>18F-florbetapir</td>
<td>Amyloid accumulation</td>
<td>Alzheimer disease</td>
</tr>
</tbody>
</table>
Dementia - Causes of Dementia

- Alzheimer Disease (50-70%)
- Vascular dementia (15%)
- Frontotemporal dementia (5-10%)
- Lewy Body disease (25%)
- Normal Pressure Hydrocephalus (NPH)
- Depression
- Intracranial Mass

SPECT in Dementia

Vascular dementia shows multiple patchy perfusion defects

PET in Dementia

Brain atrophy dementia
Alzheimer’s Disease (AD)
Progressive neurodegenerative disorder
Deterioration in cognition, function, and behavior
Most common cause dementia in elderly

SPECT imaging - 89% sensitivity and 80% specificity for AD
PET imaging - FDG and blood flow

Deficits in temporoparietal metabolism seen in patients with AD

Sensitivity 87-96%, 73% specificity
Amyloid PET imaging
Carbon-11 (C-11)-labeled Pittsburgh compound B (PiB), Ab or amyloid PET [F-18]florbetapir

$^{11}$C-PiB
$^{11}$C-BF227
$^{11}$C-AZD2184
$^{18}$F-FDDNP
$^{18}$F-PiB
$^{18}$F-AV45
$^{18}$F-BAY94–9172
$^{18}$F-AZD4694

$[^{11}]$C-2-4-(methylaminophenyl)-6-hydroxybenzothiazole$^{62}$
$[^{11}]$C-2-[2-(2-Dimethylaminothiazol-5-yl)ethenyl]-6-[2-(fluorooxy)ethoxy]benzoxazole$^{28}$
N-$[^{11}]$C-methyl]-2-(6-methylamino-pyridine-3-yl)-benzo[d]thiazole-6-ol$^{66}$
2-(1-{6-[2-[^{18}F]fluoroethyl]methylamino}-2-naphthylethylidene)malononitrile$^{67}$
2-[3-{^{18}F}fluoro-4-(methylamino)phenyl]-3-benzothiazole-6-ol$^{68}$
(E)-4-(2-[(2-(2-[(^{18}F)fluoroethoxy]ethoxy)ethoxy]pyridin-3-yl)vinyl]-N-methyl benzenamine$^{30}$
4-(N-methylamino)-4'-(2-[(2-[(^{18}F)fluoroethoxy]ethoxy)ethoxy)-stilbene$^{69}$
2-(2-[^{18}F]fluoro-6-(methylamino)pyridin-3-yl)benzofuran-5-ol$^{30}$

Note: $^{18}$F-AV45 indicates florbetapir; $^{18}$F-BAY94–9172, florbetaben; $^{18}$F-PiB, flutemetamol.
PET- Autism - Increase in diffuse cortical metabolism noted
Brain tumor is the second most common childhood malignancy, and it is a common cause of cancer-related deaths in middle-aged adults. Glioma is the most common primary brain tumor (50-60%), followed by meningioma (20%) in adults. Diagnosis of brain tumors is based on the clinical features, neurological examination, and neuroimaging.

<table>
<thead>
<tr>
<th>Application</th>
<th>Radionuclide</th>
<th>Half-Life</th>
<th>Type of Radiation Emitted</th>
<th>Imaging Technique Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging</td>
<td>Carbon-11</td>
<td>20.33 min</td>
<td>Positron</td>
<td>PET</td>
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<tr>
<td>&quot;</td>
<td>Nitrogen-13</td>
<td>9.97 min</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>&quot;</td>
<td>Oxygen-15</td>
<td>2.04 min</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>&quot;</td>
<td>Fluorine-18</td>
<td>109.75 min</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>&quot;</td>
<td>Technetium-99m</td>
<td>6.02 hours</td>
<td>gamma</td>
<td>SPECT</td>
</tr>
<tr>
<td>&quot;</td>
<td>Indium-111</td>
<td>2.8 days</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>&quot;</td>
<td>Iodine-123</td>
<td>13 hours</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>&quot;</td>
<td>Thallium-201</td>
<td>73 hours</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
<tr>
<td>Therapy</td>
<td>Iodine-131</td>
<td>8 days</td>
<td>beta</td>
<td>&quot;</td>
</tr>
<tr>
<td>&quot;</td>
<td>Yttrium-90</td>
<td>2.7 days</td>
<td>&quot;</td>
<td>&quot;</td>
</tr>
</tbody>
</table>

Commonly used radionuclides for imaging and therapy.

Theranostic ???
**Brain cancer** is a tumour or tumours within the brain which consist of a group of strange and not normal cells. This tumour can be either malignant or benign.

Brain imaging

18 F – FDG is injected where it is then absorbed more in a tumour of the brain than elsewhere which allows us to see the growth.
Single photon emission computed tomography (SPECT) – more widely available and cheaper. 99m-technetium (99mTc)-glucoheptonate (GHA), excellent brain-scanning radiopharmaceutical in detection of residual tumor after initial surgery/radiotherapy or detecting recurrence after complete resection.
$^{18}$ F-fluorodeoxyglucose ($^{18}$ F-FDG) - PET metabolic activity of a suspicious lesion
The main limitation of $^{18}$ F-FDG PET - high false negative rate due to low lesion to background contrast, as glucose is also a normal substrate for the brain.
<table>
<thead>
<tr>
<th>PET Tracer</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| **MET**    | Convenient synthesis  
Most widely tested in multiple centers  
Better than FDG for low-grade tumors | $^{11}$C labeled: only 20 min half-life  
Multiple metabolic pathways (protein/nonprotein)  
Studies mostly rely on SUVs, no kinetic analysis  
Glioma recurrence vs radiation injury differentiation suboptimal ($< 80\%$) | |
| **FET**    | $^{18}$F labeled: 110 min half-life  
Low uptake in inflammatory cells  
Measures system L AA transport: conducive to kinetic analysis, which helps grading  
Lack of metabolism  
Glioma recurrence vs radiation injury differentiation excellent ($\geq 90\%$) | Available in limited centers only  
Limited information on intratumoral AA metabolism  
Limited specificity for gliomas | |
| **FDOPA** | $^{18}$F-labeled: 110 min half-life  
Measures system L AA transport  
Better than FDG for differentiation of glioma recurrence vs radiation injury | Few studies from limited centers  
Most studies rely on SUVs, limited kinetic analysis | |
| **AMT**    | Not incorporated in proteins but measures metabolism via the immunosuppressive kynurenine pathway  
Studies tested SUV, kinetic parameters  
Can differentiate low-grade glioma types | $^{11}$C labeled: only 20 min half-life  
All brain tumor studies from a single center | |

AA = amino acid; AMT = $^{11}$C-alpha-methyl-L-tryptophan; FDG = 2-deoxy-2-$^{18}$F-fluoro-D-glucose; FET = $^{18}$F-fluoroethyl-tyrosine; FDOPA = $^{18}$F-fluoro-L-dihydroxy-phenylalanine; MET = L-[methyl-$^{11}$C]methionine; PET = positron emission tomography; SUV = standardized uptake value.

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New PET radiopharmaceuticals beyond FDG for brain tumor imaging

- labelled nucleoside and amino acid analogues,
- tracers of oxidative metabolism,
- fatty acid metabolism and hypoxia,
- receptor ligands of various kinds

\[ ^{11}C \text{-alpha-methyl-L-tryptophan} - \text{AMT} \]
Glioma – level II

\[ ^{18}F \text{-fluoroethyl-L-tyrosine (FET)} \]
glioblastoma

\[ ^{18}F \text{-fluorothymidine (FLT)}, \]
\[ ^{18}F \text{-fluoro-\(\alpha\)-methyltyrosine (FMT)}, \]
\[ ^{18}F \text{-fluoromisonidazole (F-MISO)}, \]
\[ ^{11}C \text{-choline (CHO)} \text{ and } ^{18}F \text{-choline} \]

\[ ^{6} \text{-}[^{18}F] \text{-fluoro-dihydroxy-L-phenylalanine (F-DOPA)} \text{-high grade glioma} \]

\[ ^{11}C \text{-alpha-methyl-L-tryptophan} \text{ - AMT} \]
Glioma – level II
Radiopharmaceuticals for brain tumor treatment

Or for planning brain tumor treatment ??

Drug development ...

Schematic Representation of a Drug for Imaging and Targeted Therapy

Target
- Antigens (CD20, HER2)
- GPCRs
- Transporters

Molecular Address
- Antibodies, their fragments and modifications
- Regulatory peptides and analogs thereof
- Amino Acids

Reporting Unit
- $^{99m}$Tc, $^{111}$In, $^{67}$Ga
- $^{64}$Cu, $^{68}$Ga
- $\text{Gd}^{3+}$
- Cytotoxic Unit
  - $^{90}$Y, $^{177}$Lu, $^{213}$Bi
  - $^{105}$Rh, $^{67}$Cu, $^{186,188}$Re

H.R. Maecke
DOTA-somatostatin analogue

DOTA-TATE

\[ \text{Zn}^{2+} \]

\[ \text{Fe}^{3+} \]

\[ \text{Ga}^{68} \]

\[ \text{Lu}^{177} \]

\[ \text{Y}^{90} \]
Copper in nuclear medicine

- Occurrence of many isotopes with the same chemical behavior, but different nuclear chemical properties
- Decay of the isotopes is useful for diagnostic imaging and therapy
- Exploitation of different properties for certain applications

### Advantages
- availability of generator systems
- $\beta^+$-emitter with high abundance
- high energy $\beta^-$-emitter

### Disadvantages

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-life</th>
<th>Decay (abundance)</th>
<th>$E_p$ (keV)</th>
<th>$E_{\text{ep}}$ (keV)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{60}\text{Cu}$</td>
<td>23.6 min</td>
<td>$\beta^+$ (93 %)</td>
<td>511</td>
<td>873</td>
<td>cyclotron</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC (7%)</td>
<td>1332</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{61}\text{Cu}$</td>
<td>3.3 h</td>
<td>$\beta^+$ (62 %)</td>
<td>511</td>
<td>527</td>
<td>cyclotron</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC (38%)</td>
<td>283</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{62}\text{Cu}$</td>
<td>9.76 min</td>
<td>$\beta^+$ (98 %)</td>
<td>511</td>
<td>1315</td>
<td>generator/cyclotron</td>
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<tr>
<td></td>
<td></td>
<td>EC (2%)</td>
<td>283</td>
<td></td>
<td></td>
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<tr>
<td>$^{64}\text{Cu}$</td>
<td>12.8 h</td>
<td>$\beta^+$ (19 %)</td>
<td>511</td>
<td>278</td>
<td>reactor/cyclotron</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC (41%)</td>
<td>1346</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{66}\text{Cu}$</td>
<td>5.4 min</td>
<td>$\beta^-$ (40%)</td>
<td>190</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{67}\text{Cu}$</td>
<td>62.0 h</td>
<td>$\beta^-$ (100%)</td>
<td>1109</td>
<td>121</td>
<td>reactor/cyclotron</td>
</tr>
</tbody>
</table>
Chelators

Chelator is used to tightly bind the a radiometal ion so that when injected into a patient, the targeting molecule can be delivered without any radiometal loss.

Syntheses of copper-radiopharmaceuticals

Targeting Molecule

Bifunctional chelate agent

Coordination of Cu(II)
in square planar manner

Or

\[ \text{copper (}^{64}\text{Cu)}\text{ chloride} \]
Applications in Nuclear Medicine

**Copper-labelled blood flow agents**
The most important clinical application of copper

- evaluate blood flow and metabolism in:
  - heart
  - brain
  - tumour
Copper-labeled hypoxia imaging agents

Detection of ischemia of the:
- brain
- heart
- hypoxic tumor

$^{62}\text{CuATSM}$

$^{64}\text{CuATSM}$
$^{64}$Cu - Outstanding Example of Excellent Potential
In conclusion

The development of new radiopharmaceuticals imaging in neurology and psychiatry and brain therapy will contribute to health care for a significant part of the population and will add to the knowledge of biological and biochemical processes taking place in the brain.
Thank you