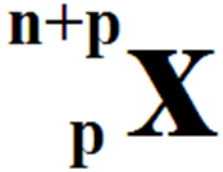
Radiopharmacy in Nuclear Medicine

By Dr. Fakhari, Radiopharmacist , phD

What is ……?

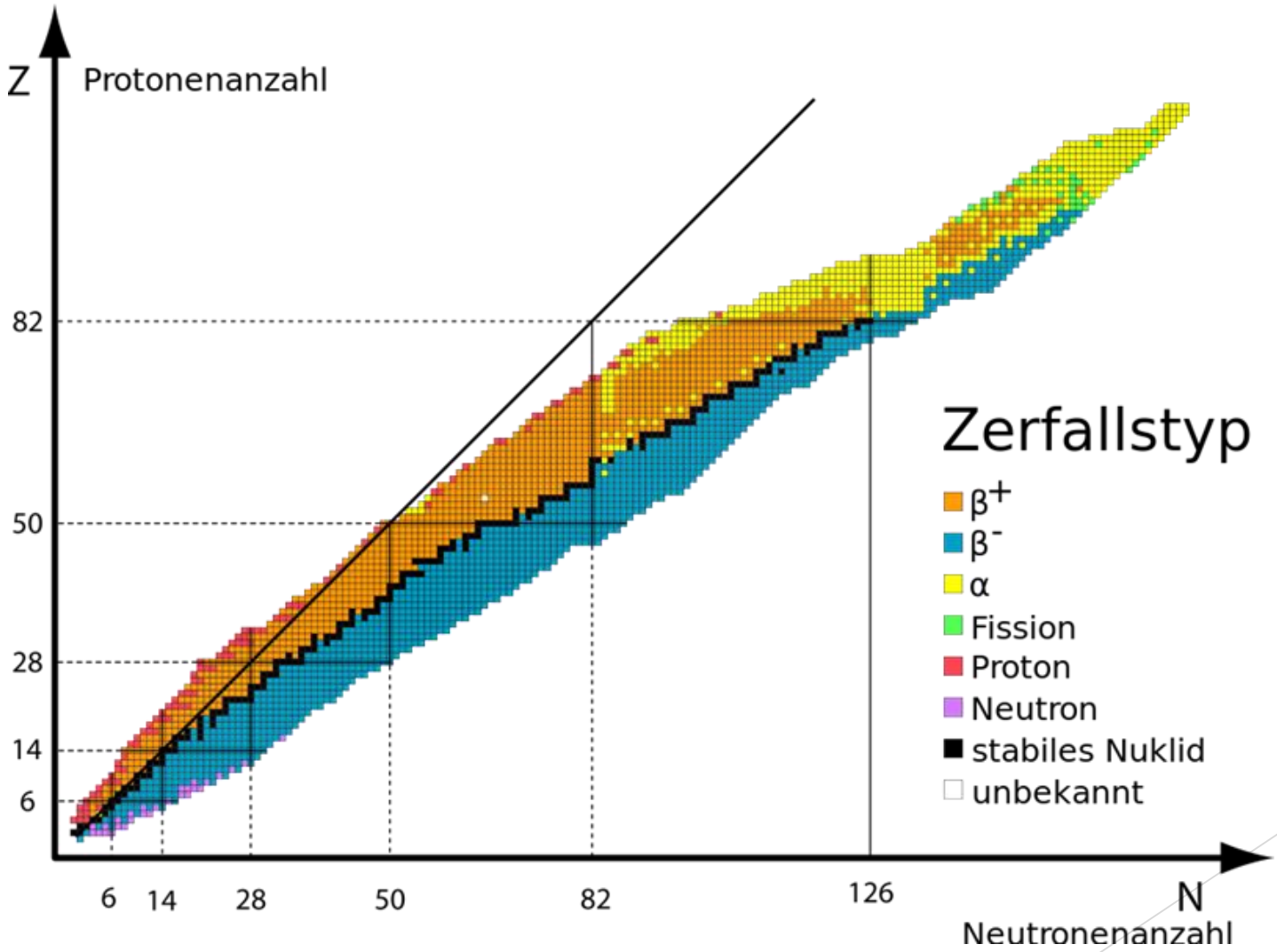
- Radioisotope



- Radiotracer
- Radiopharmaceutical
- Half time
- Effective half time

$$T\,(eff) = \frac{T(b) * T\,(p)}{T(b) + T(p)}$$

segre diagram



Units of radioactivity

- becquerel (Bq) ⟶ equal to one reciprocal second
- curie (symbol Ci) ⟶ $1\ \text{Ci} = 3.7 \times 10^{10}\ \text{Bq} = 37\ \text{GBq}$

- **Radioisotope production ways:**

- Reactor
- Cyclotron
- generator

Radioisotope decay:

- Alpha
- Beta
- Gamma ray
- positron

kinds of radiopharmaceutical :

- **Diagnostic (gamma)**
- **Therapy (alpha , beta, auger)**

Therapeutic radiopharmaceuticals:

- **Electron auge:**

125I

- **Alpha emitters:**

212Bi ， 212At ， 223Ra

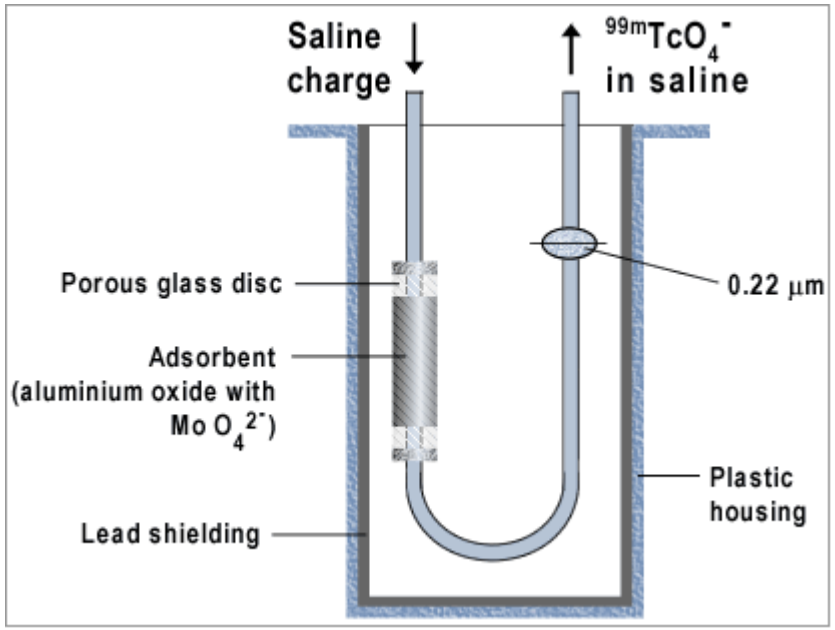
Beta emitters:

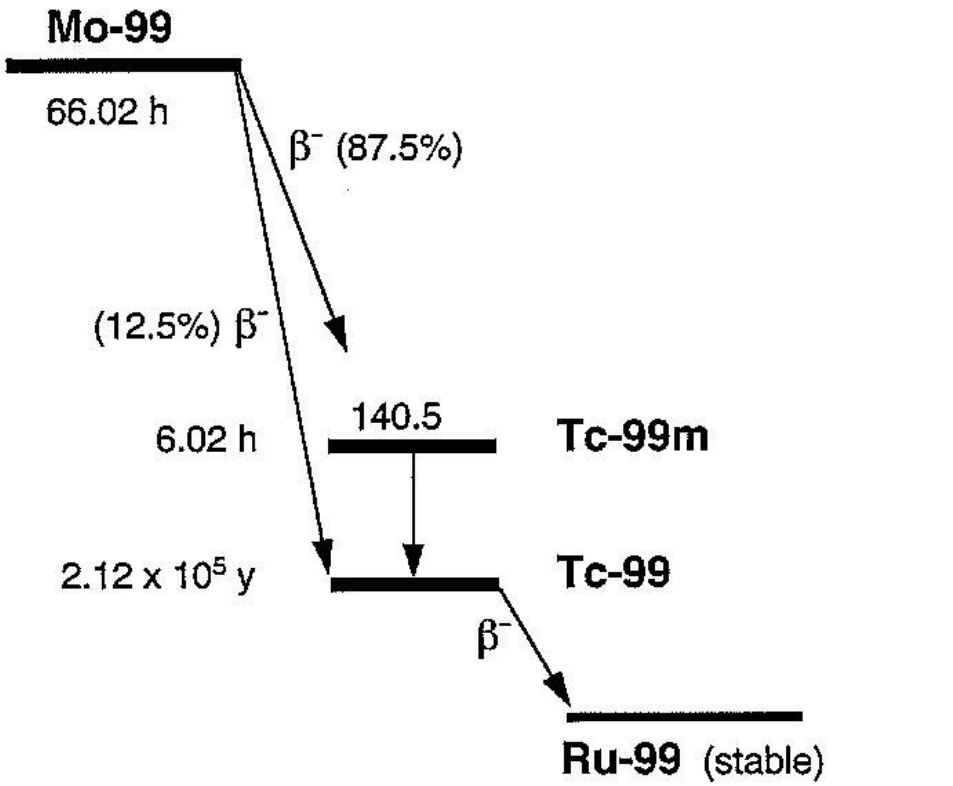
- 131I , 131I-MIBG (iodine-131-meta-iodobenzylguanidine)
- 32P
- 90Y
- 90Sr
- 198Au
- 89Sr
- 186/188Re
- 177Lu
- 153Sm

Diagnostic radiopharmaceuticals

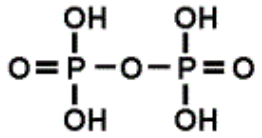
- 123I
- 67Ga
- 201Ti
- 99mTc
- Positron emitters(PET based radiotracers)

99mTc generator

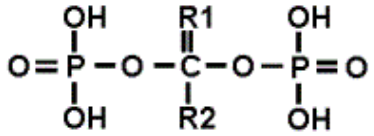




bone 99mTc-Radiopharmaceuticals

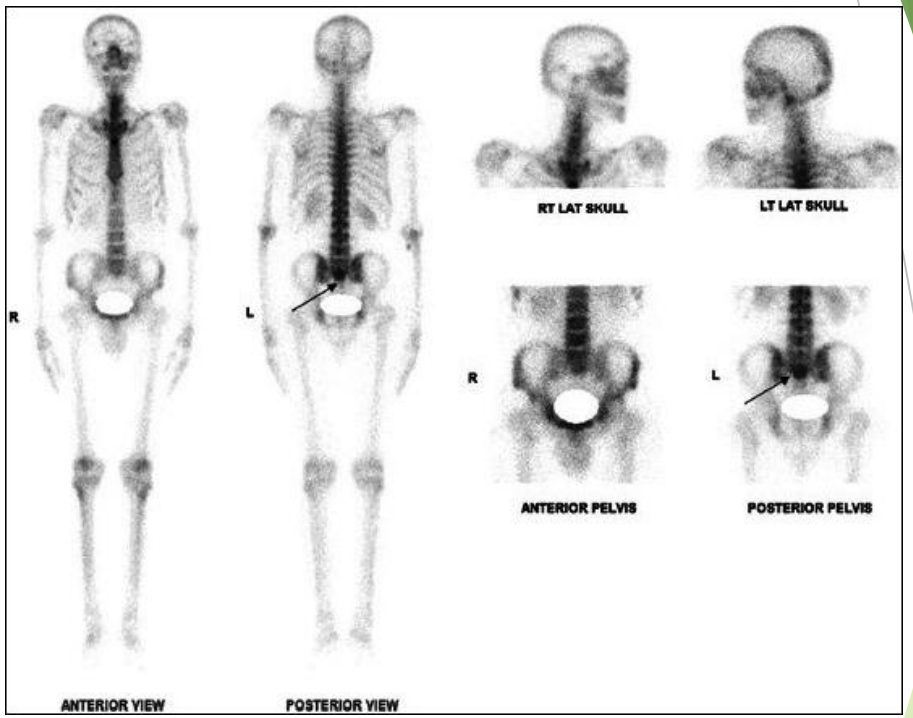


Pyrophosphate

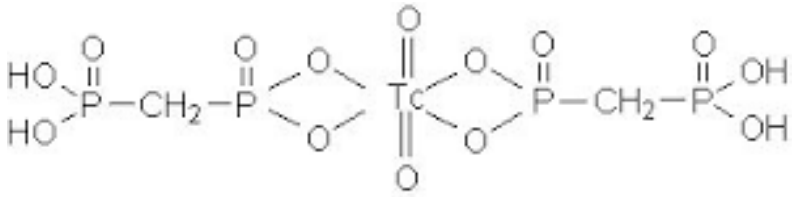


Diphosphonate

	R1	R2
HEDP	OH	CH_3
MDP	H	H
HMDP	OH	H



MDP + SnCl2 + 99mTcO4-

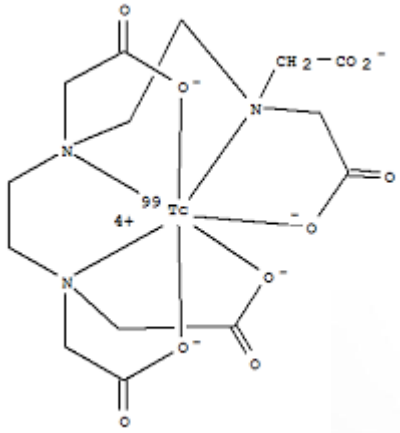


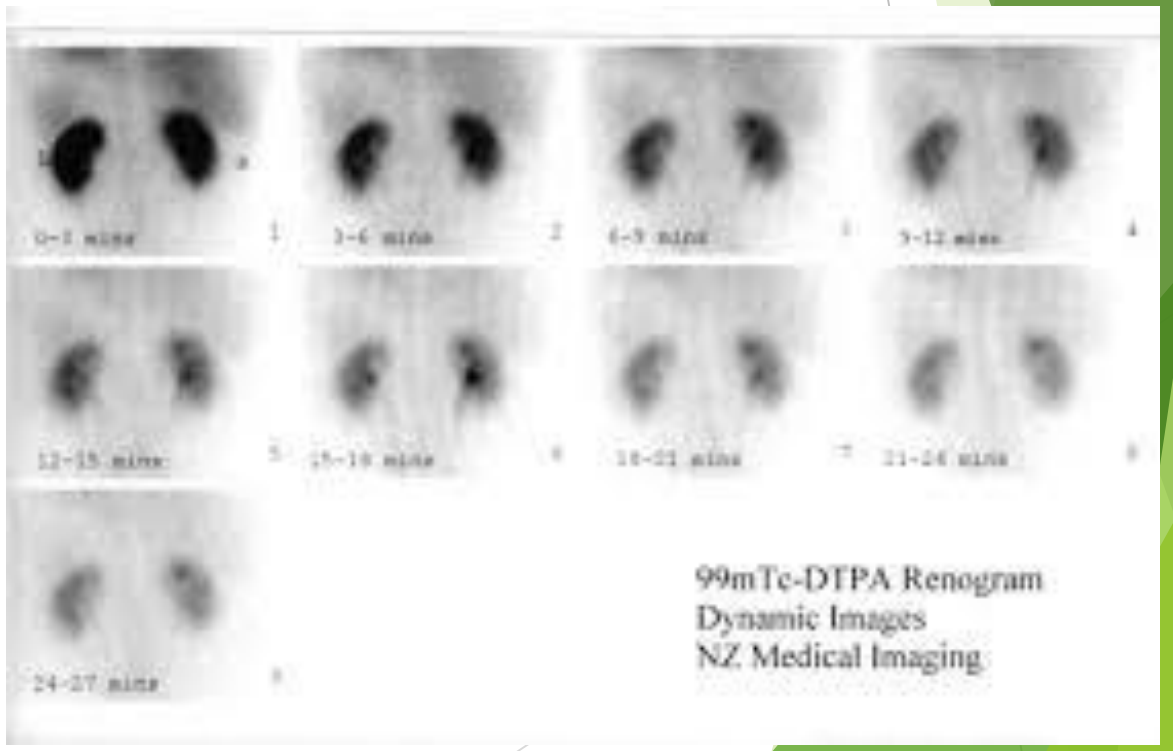
[^{99m}Tc] Medronate

Renal 99mTc-Radiopharmaceuticals

- **1: Glomerular filtration rate (GFR)**
- **99mTc-DTPA (diethylenetriaminepentaacetic acid)**

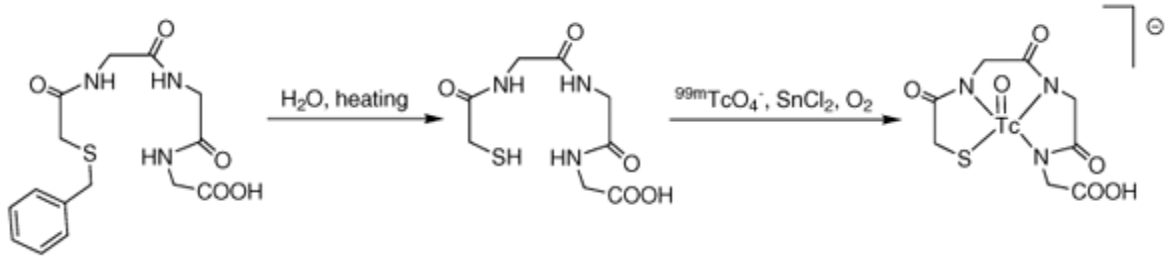
DTPA + SnCl2 + 99mTcO4-

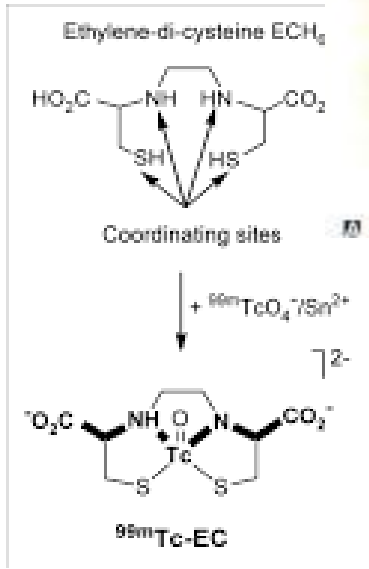


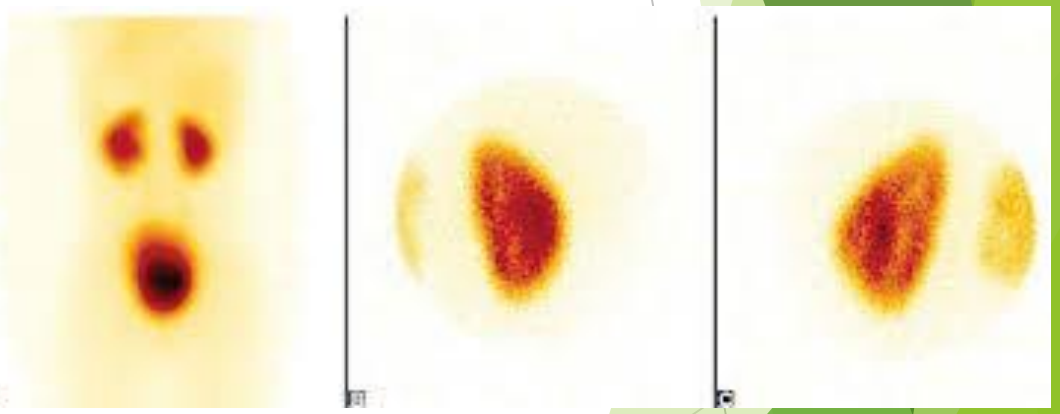


- **2: Effective Renal Plasma Flow (ERPF)**

- **99mTc-MAG3 (mercaptoacetyltriglycine) , 131I-OIH**



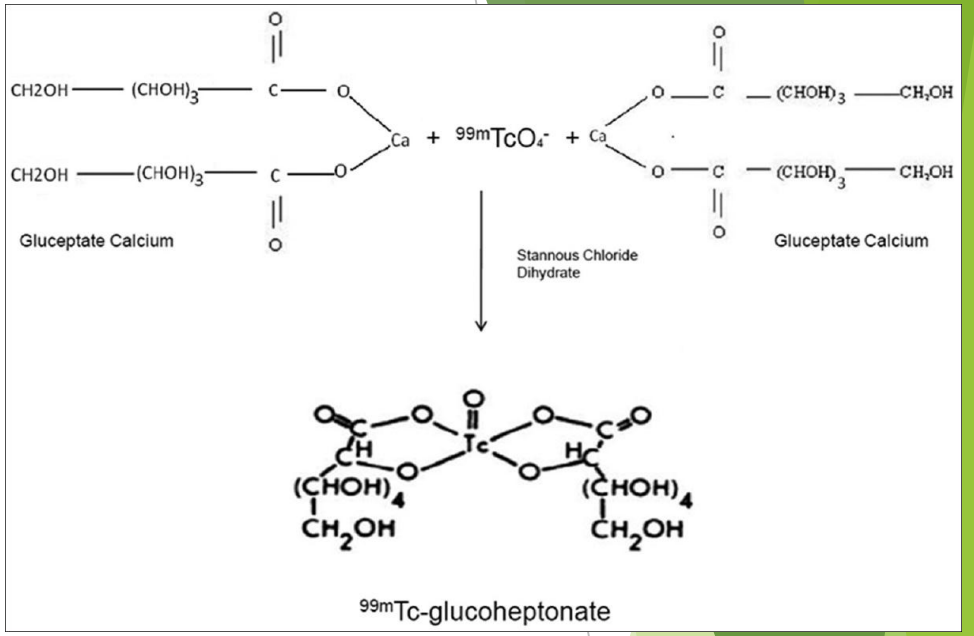




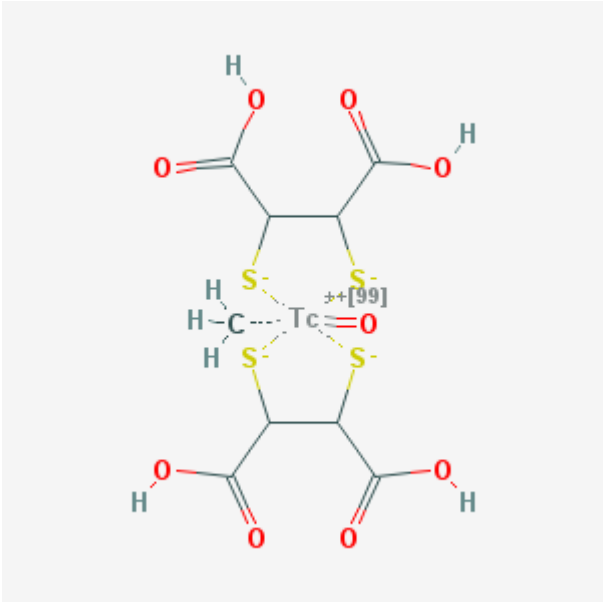
- **99mTc-EC (Ethylenedicysteine)**

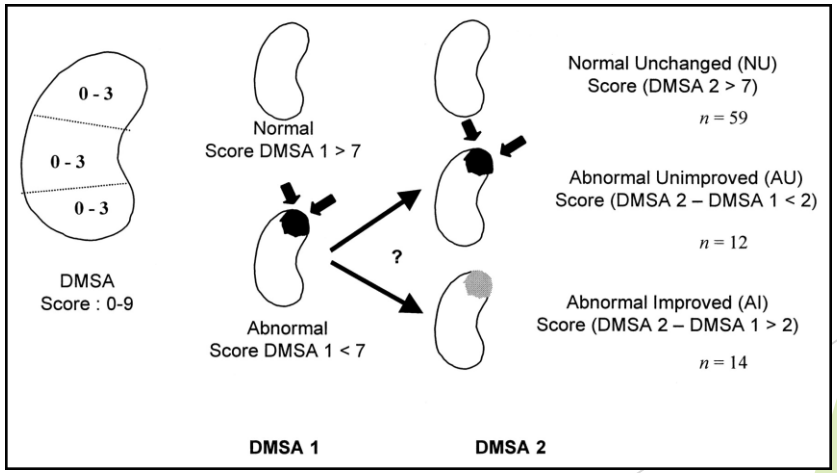
3: morphology

- 1: 99mTc-Glucoheptonate (GFR / morphology)

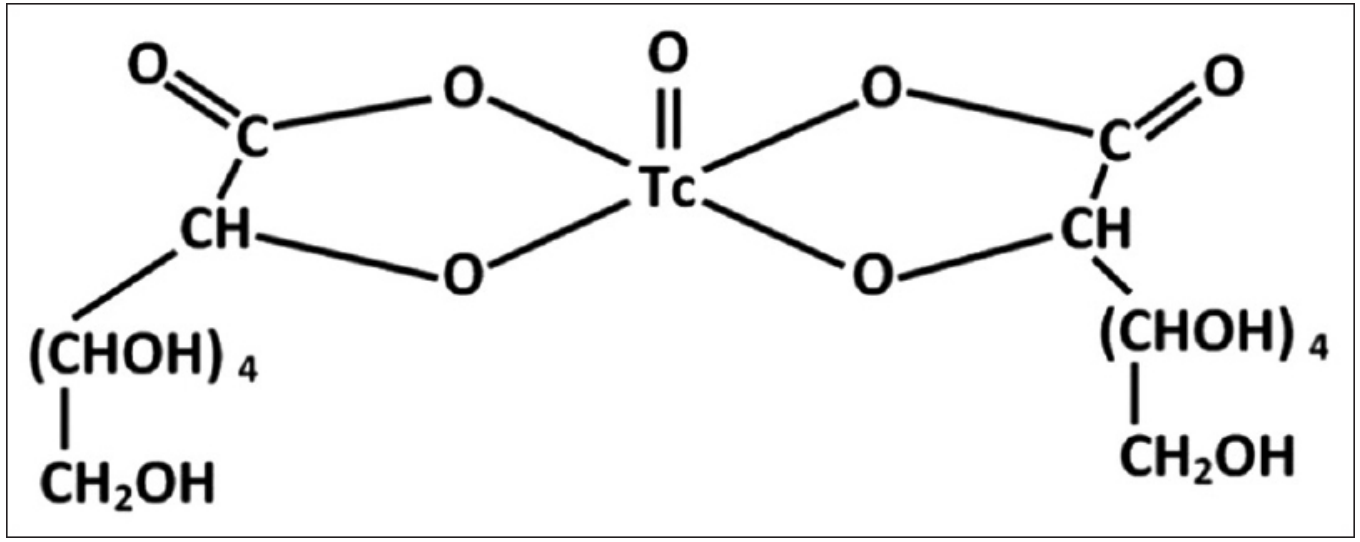


- 2: 99mTc-DMSA (Dimercaptosuccinic acid)

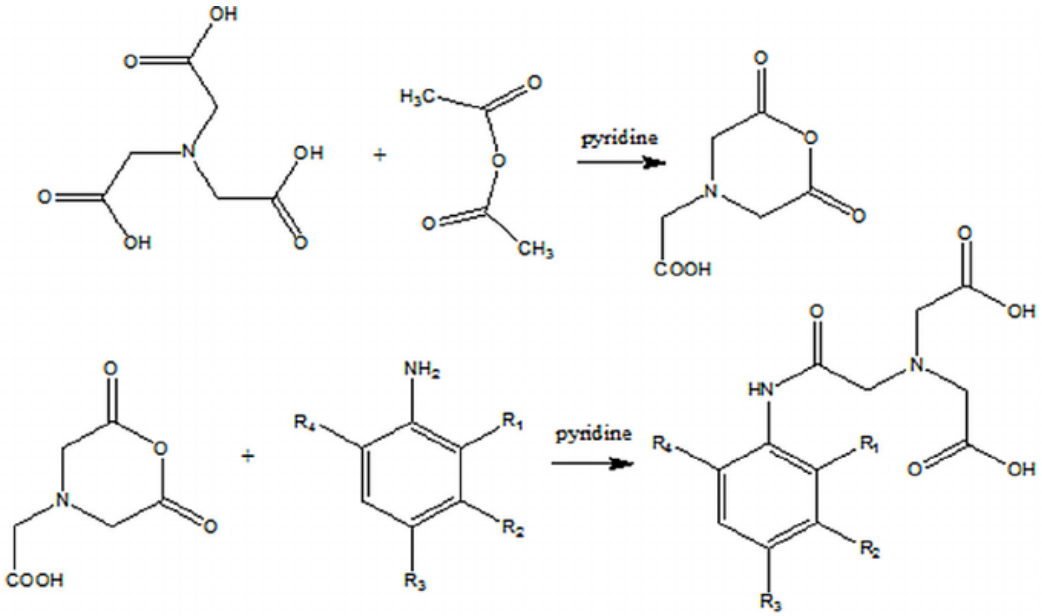




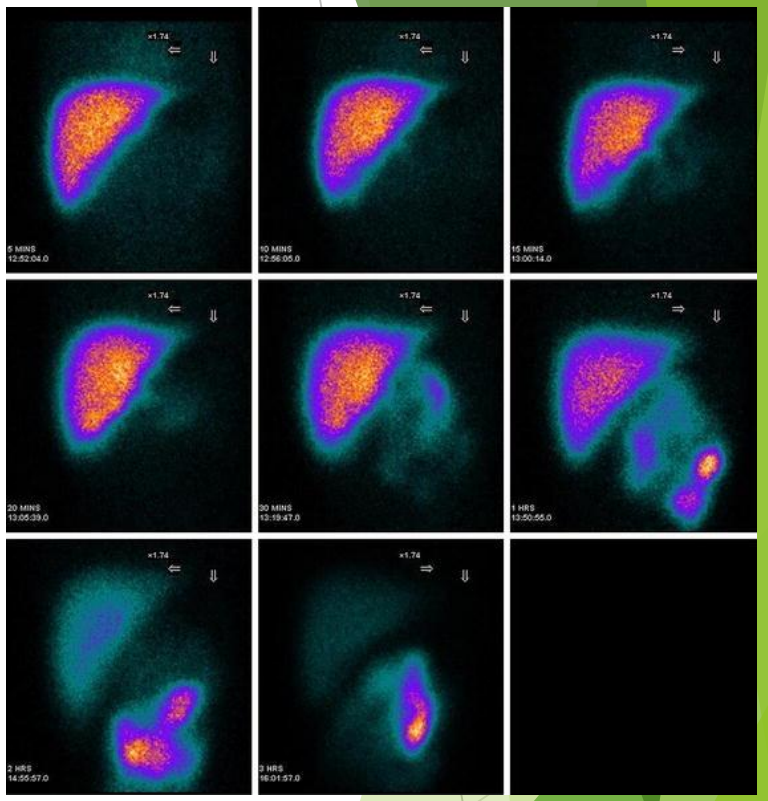
٩٩mTc-GHA

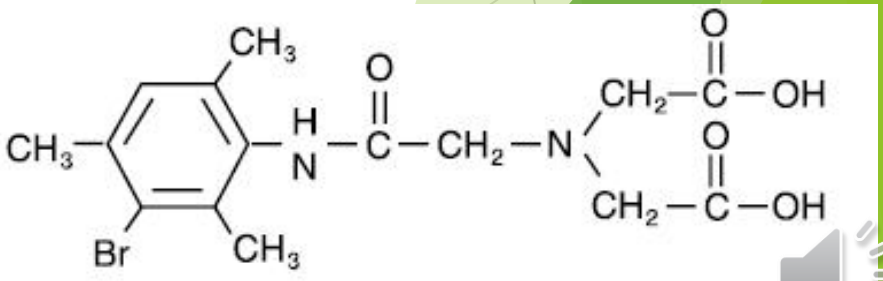


Liver 99mTc-Radiopharmaceuticals



Synthesized compound	R_1	R_2	R_3	R_4
N-(4-methylacetanilide)iminodiacetic acid (Met-IDA)	H	H	CH_3	H
N-(2,4-dimethylacetanilide)iminodiacetic acid (DMet-IDA)	CH_3	H	CH_3	H
N-(2,4,6-trimethylacetanilide)iminodiacetic acid (TMet-IDA)	CH_3	H	CH_3	CH_3
N-(3-bromo-2,4,6-trimethylacetanilide)-iminodiacetic acid – mebrofenin (MBR)	CH_3	Br	CH_3	CH_3

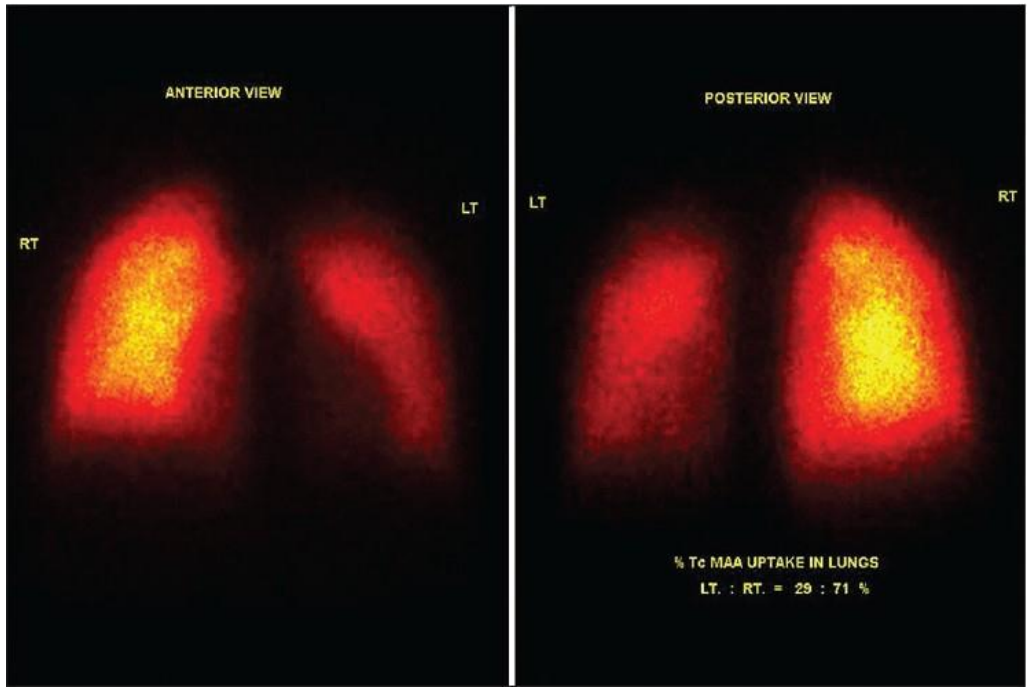




Lung 99mTc-Radiopharmaceuticals

perfusion

- Particle including size 20-40 micron
- 99mTc-Macroaggregated Albumin (10-45)



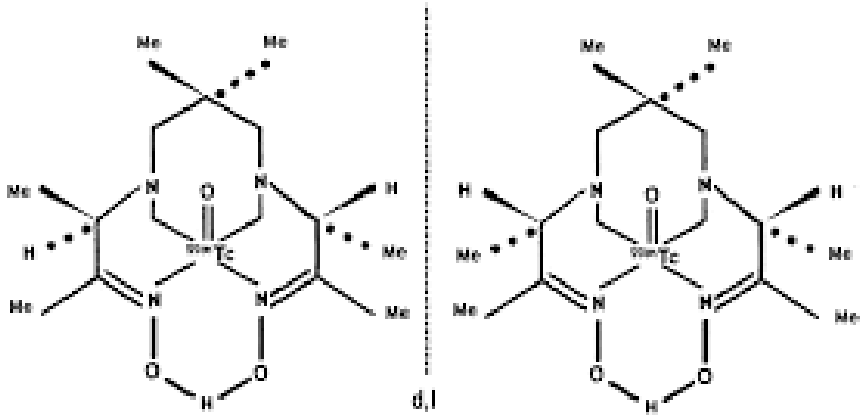
ventilation

133Xe
81mKr

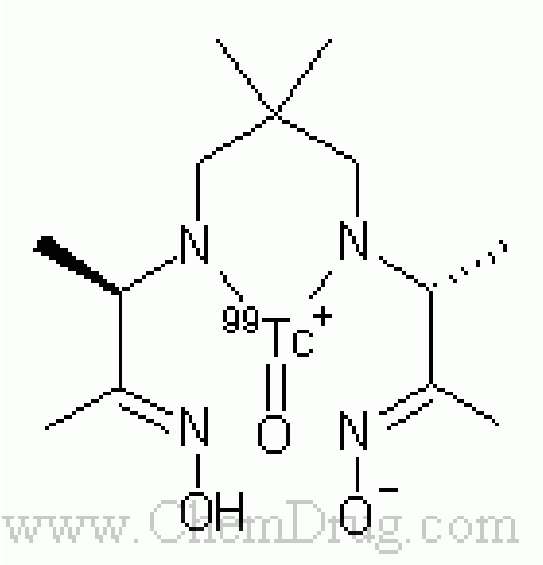
99mTc-DTPA-Aerosol

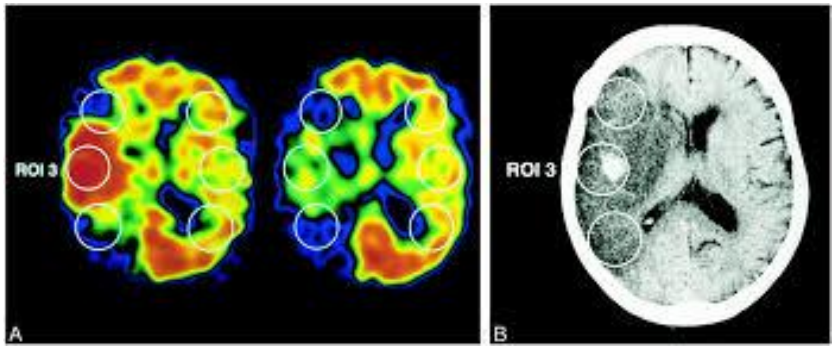
brain 99mTc-Radiopharmaceuticals

- **1: 99mTc-HMPAO (exametazime)**

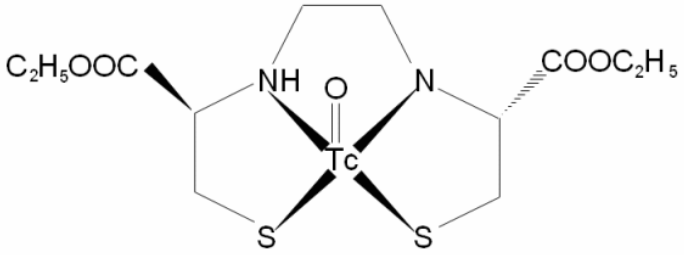


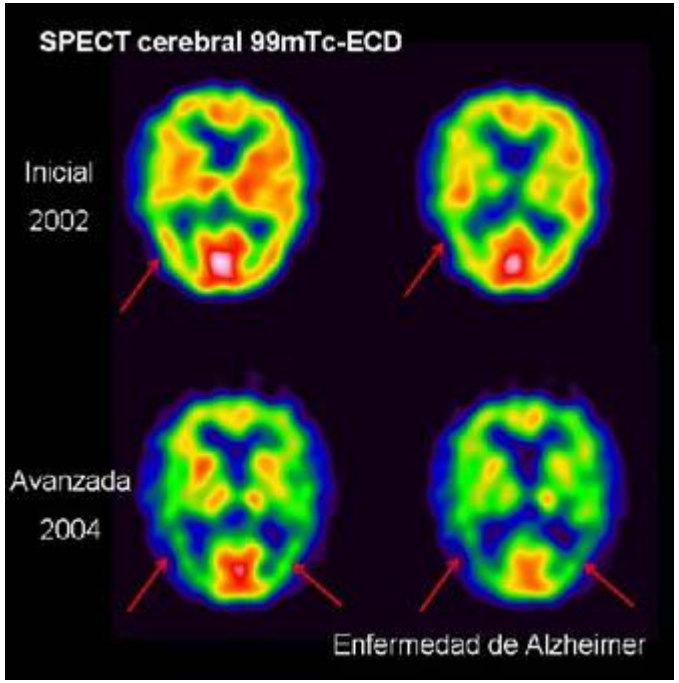
99mTc-labeled d,l Diastereoisomers of HMPAO





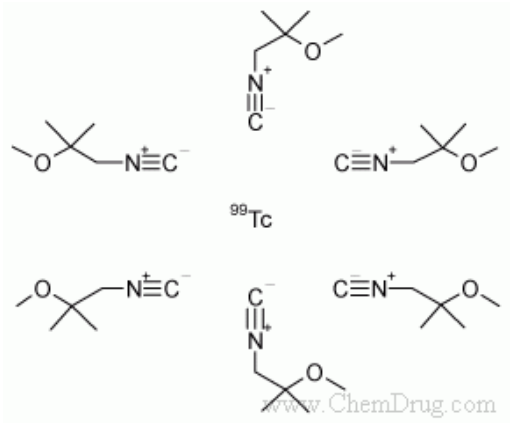
2:99mTc-ECD (ethyl cysteinate dimer)

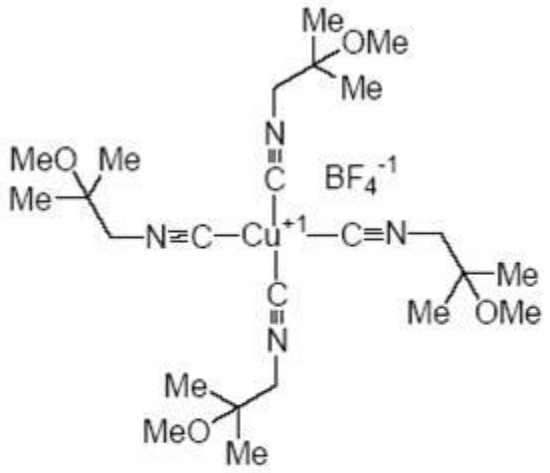




Heart 99mTc-Radiopharmaceuticals

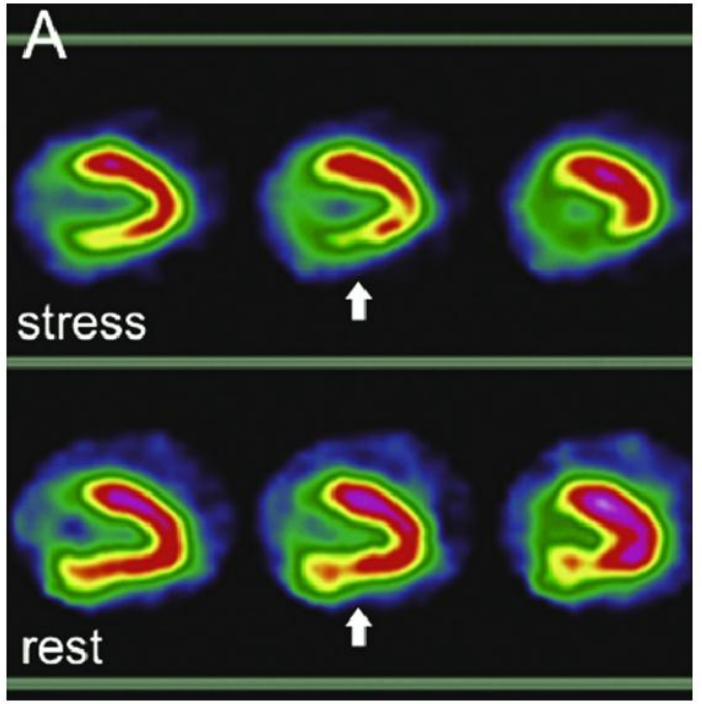
- **99mTc-MIBI (methoxyisobutyl isonitrile)**





Molecular Formula
$C_{24}H_{44}N_4O_4BF_4Cu$

Molecular Weight
602.98



RBC radiolabeling methods

- **1: in vitro**

Blood ⇨ centrifuge ⇨ RBC ⇨ SnCl2

⇨ 30min ⇨ 15-12mCi (99mTcO4-) ⇨ RBC*

- **2: in vivo**

pyrophosphate + SnCl2

or

pyrophosphate + DTPA + SnCl2

⇨ 1: mixing in saline

2: administering to patient

⇨ RBC + SnCl2 (30min) ⇨ 15-12mCi (99mTcO4-) ⇨ RBC*

RBC labeling with 99mTc

- 1: ejection fraction $\%\ EF = \frac{AED - AE}{AED} * 100$
- 2: Vascular malformations and internal bleeding
- 3: Spleen scan
- $TcO_4^- + (Sn^{+2}, RBC) = RBC^*$

3: invivitro:

5 micro/Kg (SnCl2) ⇨ adminestre 30min

⇨Blood ⇨ 99mTcO4- ⇨ RBC*

4: New invitro:

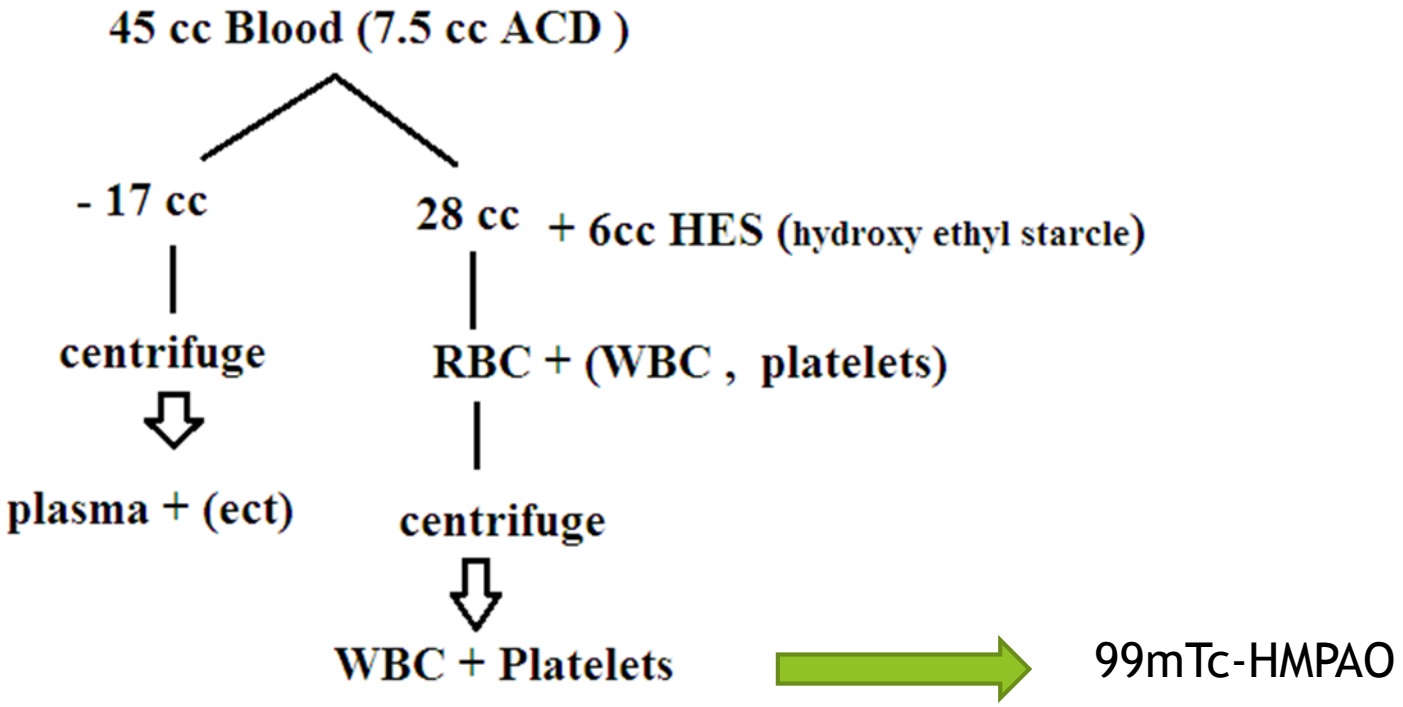
Blood ⇨ citrate + SnCl2 ⇨ACD (acid citrate dectroz)

⇨ NaOCl ⇨ 10-20 mCi (99mTcO4-) 20min ⇨ centrifuge

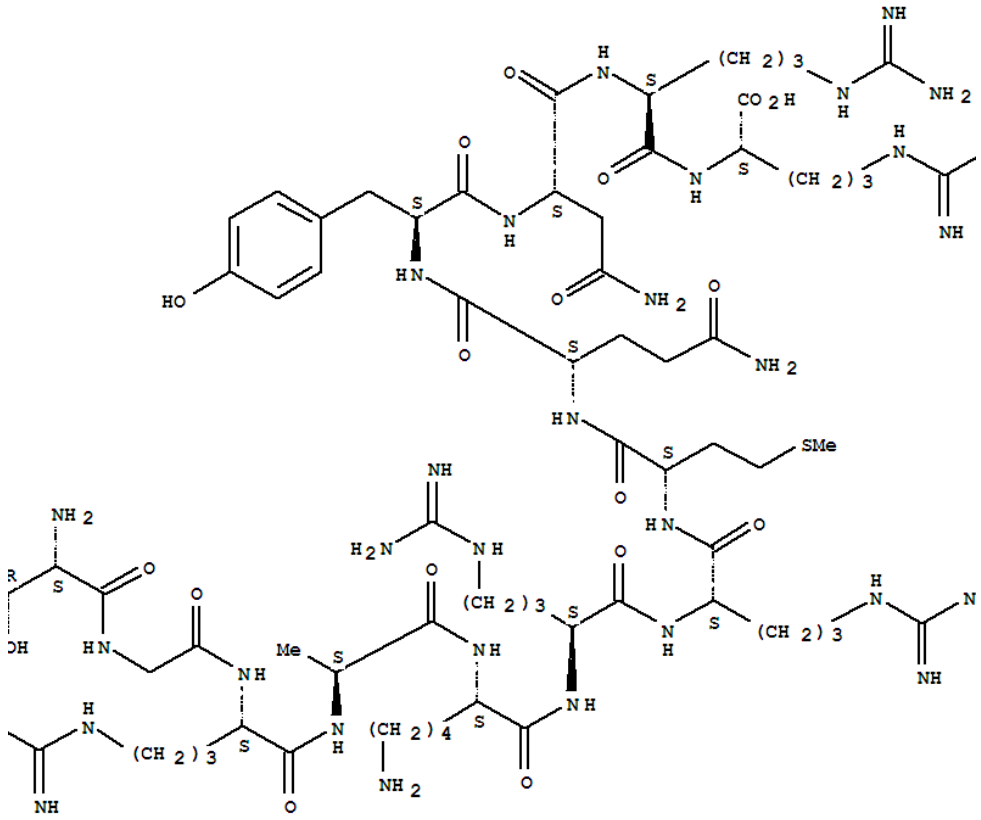
⇨ RBC*

Radiolabeling of WBC

1: infection



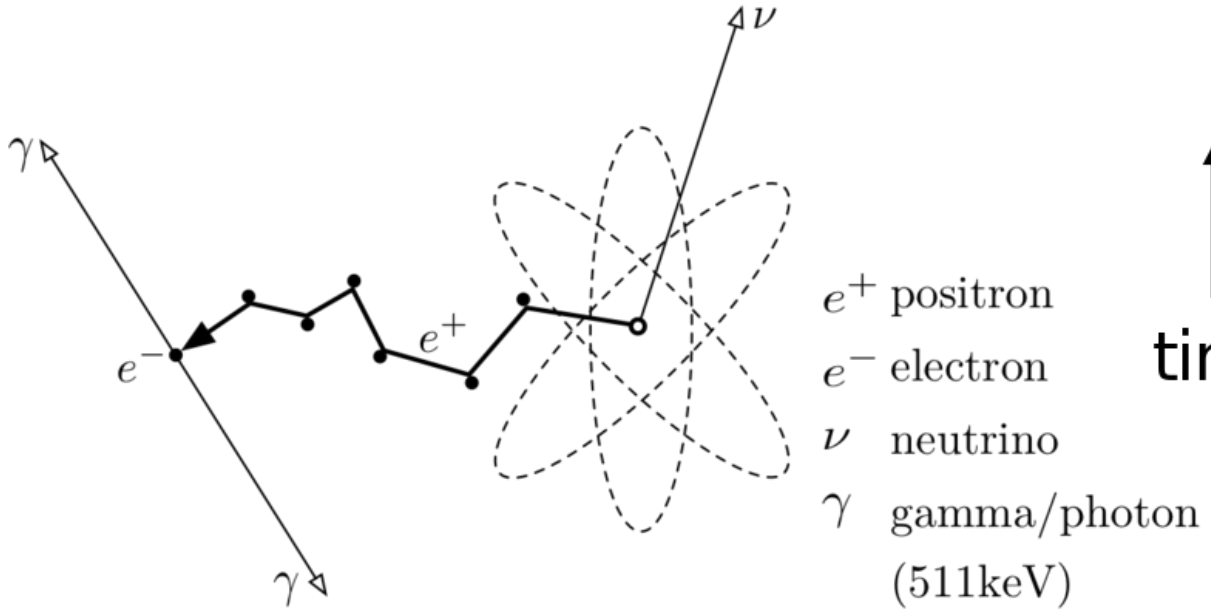
99mTc-ubiquicidin

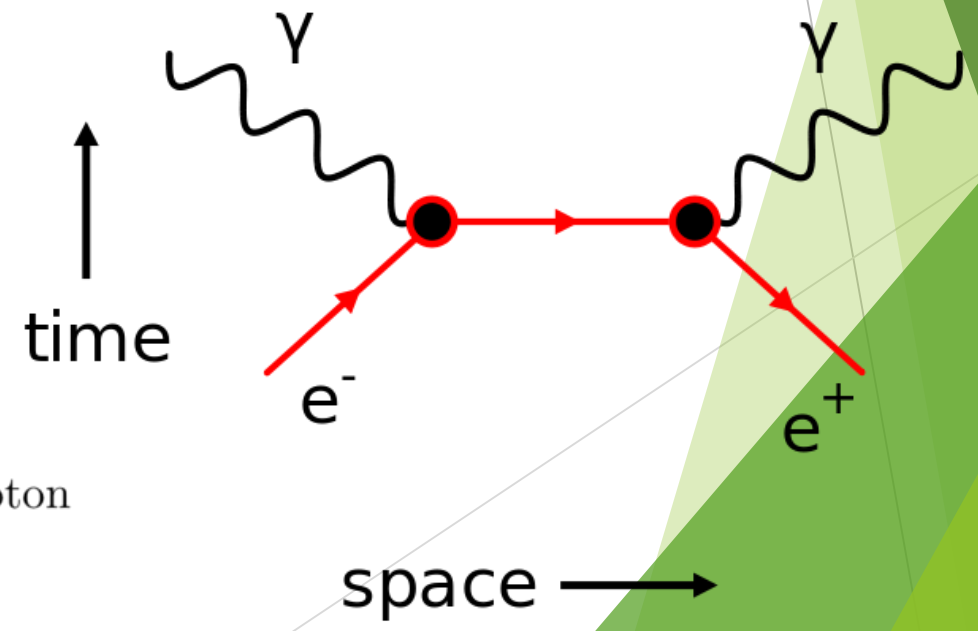


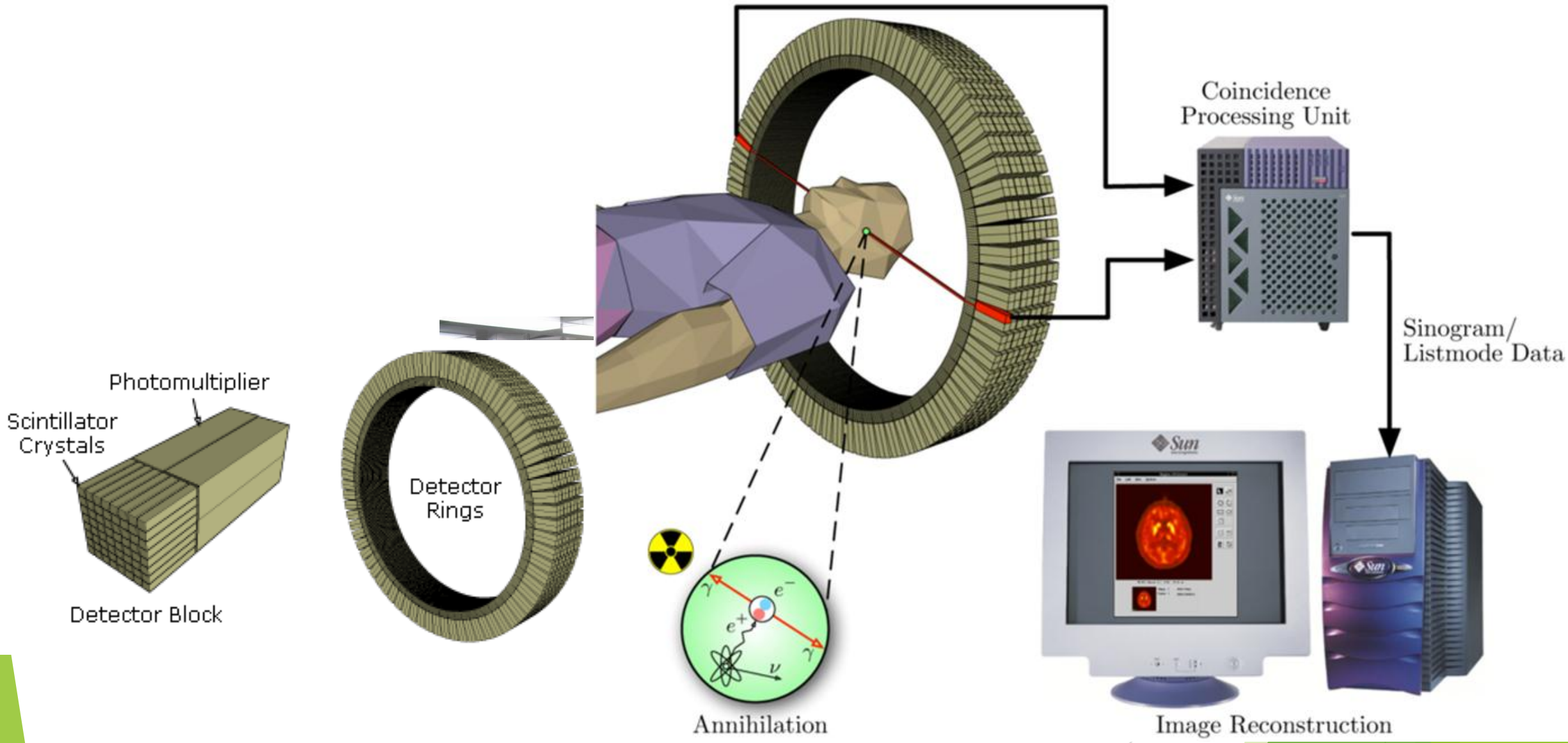
PET radiopharmaceuticals

Electron–positron annihilation

- **Electron–positron annihilation occurs when an electron (e−) and a positron (e+, the electron's antiparticle) collide. The result of the collision is the annihilation of the electron and positron, and the creation of gamma ray photons or, at higher energies, other particles:**






Photomultiplier
Scintillator Crystals
Detector Block
Detector Rings
Coincidence Processing Unit
Sinogram/ Listmode Data
Annihilation
Image Reconstruction

Isotope	Halflife	fraction Max.	Energy range(mm)	production
C-11	20.4 mins	0.99 0.96 MeV	0.4 mm	cyclotron
N-13	9.96 mins	1.00 1.20 MeV	0.7 mm	cyclotron
O-15	123 secs	1.00 1.74 MeV	1.1 mm	cyclotron
F-18	110 mins	0.97 0.63 MeV	0.3 mm	cyclotron
Cu-62	9.74 mins	0.98 2.93 MeV	2.7 mm	generator
Cu-64	12.7 hours	0.19 0.65 MeV	0.3 mm	cyclotron
Ga-68	68.3 mins	0.88 1.83 MeV	1.2 mm	generator
Br-76	16.1 hours	1.00 1.90 MeV	1.2 mm	cyclotron
Rb-82	78 secs	0.96 3.15 MeV	2.8 mm	generator
I-124	4.18 days	0.22 1.50 MeV	0.9 mm	cyclotron

18F is the most important

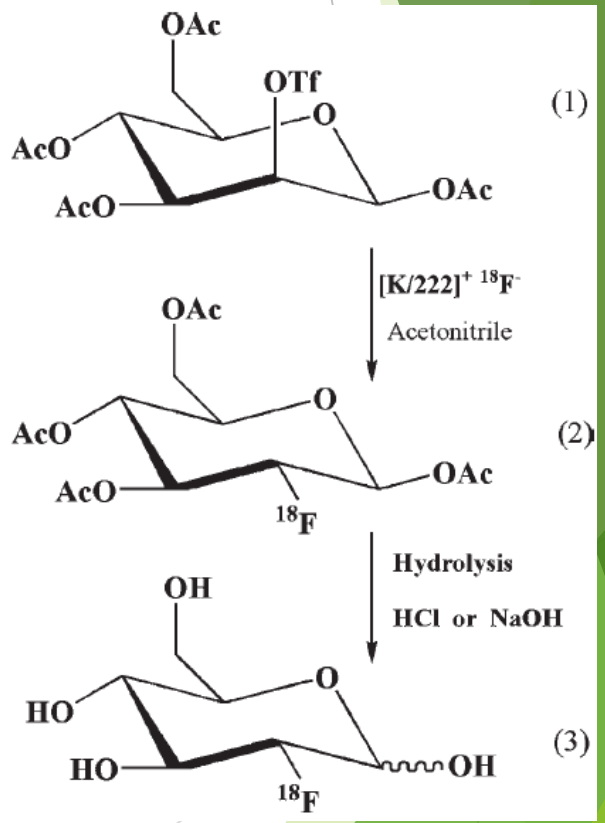
- 1: Low positron energy (0.64 MeV) with a short range in tissue (Max. 2.4 mm)
- 2: Can be produced in high specific activity
- 3: Fluorine is the most electronegative of all elementsand can react with many organic and inorganic chemicals.
- 4: It can react as an electrophile or a neucleophile chemical specie.
- 5:Relatively high labeling yields (20–70%) in the synthesis of 18F-PET tracers
- 7: Acceptable radiation dosimetry for multiple studies in a patient
- 8:The physical T½ (110 min) allows for the transport from the production site to the PET centers

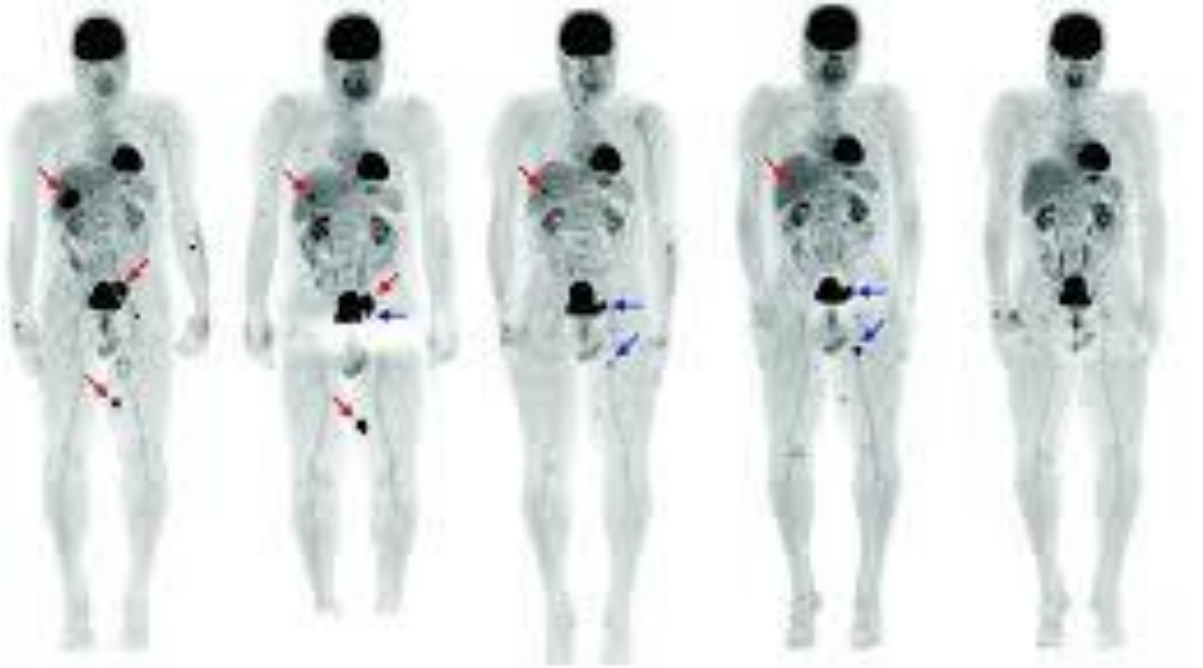
Biochemical process	Radiotracer	Mechanism of uptake or localization
Glucose metabolism	[^{18}F]FDG	Substrate for *hexokinase* in glucose metabolism
Bone metabolism	^{18}F-fluoride	Incorporation in the hydroxyapatite crystals in bone
Membrane synthesis	[^{18}F]Fluorocholine	Substrates for *choline kinase* in choline mtabolism
Lipid synthesis	[^{18}F]Fluoroacetate	Substrate for *acetyl-CoA synthetase*
DNA synthesis	[^{18}F]Fluorothymidine (FLT)	Substrates for *thymidine kinase* in DNA synthesis
	[^{18}F]FMAU	
Hypoxia	[^{18}F]FMISO	Intracellular reduction and binding
	[^{18}F]FAZA	
Receptor Binding	[^{18}F]FES	Specific binding to estrogen receptors
Somatostatin Receptors	[^{18}F]Gluco-TOC	Specific binding to somatostatin receptor (SSTR-II)
Dopamine receptors	[^{18}F]Fallypride	Specific binding to D2/D3 receptors
Dopamine transporters	[^{18}F]FP-CIT	Binding to presynaptic dopamine transporters
Benzodizzepine receptors	[^{18}F]Flumazenil	Specific binding to central benzodiazepine receptors to assess neuronal integrity
Amino Acid transport and protein synthesis	[^{18}F]FDOPA	Precursor for the synthesis of dopamine
	[^{18}F]Fluoroethyltyrosine	
	[^{18}F]Fluoro-α-methyltyrosine	Brain amino acid transport
	[^{18}F]FCCA	
Apoptosis	^{18}F-Annexin V,	Specific binding to Phosphatidylserine (PS)
Angiogenesis	^{18}F-FB-E[c(RGDyK)]2	Integrin receptors ($\alpha_v\beta_3$) on endothelial cells
Gene expression	[^{18}F]Oligonucleotide	In vivo hybridization with mRNA
	[^{18}F]FHBG	Substrate to herpes virus *thymidine kinase*

Synthesis of [18F]FDG

Following production of 18F in the cyclotron, the target water ([18O]H2O), containing several curies of [18F]fl uoride ion, is trapped on a small column of anion exchange resin

The [18F]fluoride ion is eluted into a reaction vial using a solution of aqueous base, potassium carbonate (K2CO3), and Kryptofix 222 in acetonitrile. Some procedures substitute Kryptofix with either tetramethyl ammonium carbonate or tetrabutyl ammonium bicarbonate or hydroxide.





Baseline	12 weeks	24 weeks	43 weeks (before retreatment)	56 weeks (after retreatment)
20/08/2010	17/11/2010	15/02/2011	28/06/2011	27/09/2011