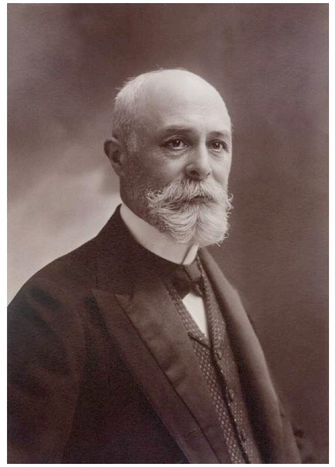
Nuclear Medicine - From Physics to Diagnostic and Therapeutic Principles

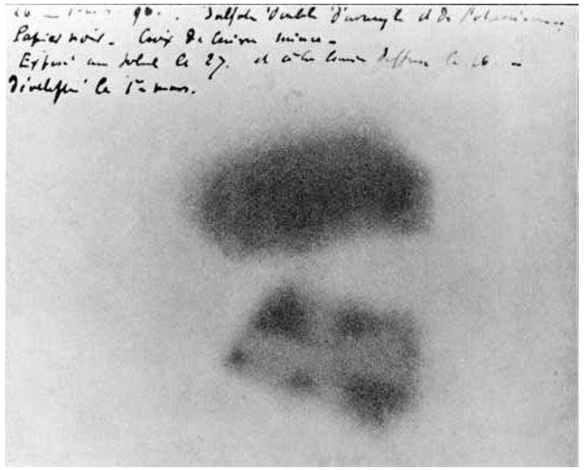
Dr. Alexander Haseloer
Group Meeting
MacMillan Group
October 3rd, 2023

Discovery of the Unknown - 1890's

Wilhelm Konrad Röntgen



Antoine Henri Becquerel



The Nuclear Craze - 92 Nobel Laureates

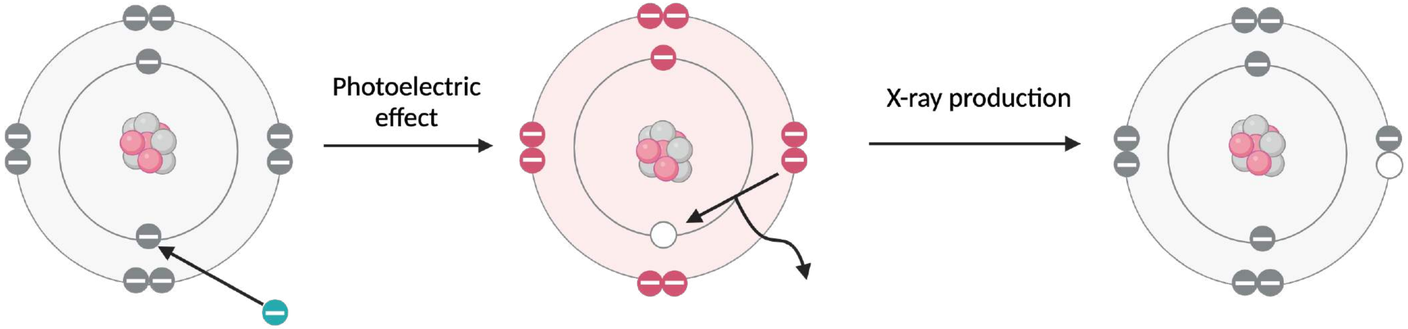
W. Röntgen (1901), H. Becquerel, M. Curie , P. Curie (1903), P. Lennard (1905), E. Rutherford (1908, C), M. Curie (1911, C), T.W. Williams (1914), C.E. Guillaume (1920), A. Einstein (1920), F. Soddy (1920, C), N. Bohr (1921), A. Compton, C.T.R. Wilson (1927), L. De Borglie (1929), W. Heisenberg (1932), E. Schrödinger, P. Dirac (1933), H. Urey (1934, C), F. Joliot-Curie, I. Joliot-Curie (1935,C), J. Chadwick (1935), V.F. Hess, C.D. Anderson (1936), E. Fermi (1938), E. Lawrence (1939), O. Stern (1943), G. De Hevesy (1943, C), O. Hahn (1944, C), I.I. Rabi (1944), E.V. Appleton (1947), P. Blackett (1948), H. Yukawa (1949), C. F. Powell (1950), J. Cockroft, E.T.S. Walton (1951), E. M. McMillan, G. T. Seaborg (1951, C), M. Born, W. Bothe (1954), C.-N. Yang, T.-D. Lee (1957), P. Cherenkov, I. Frank, I. Tamm (1958), E.G. Segrè, O. Chamberlain (1959), W. F. Libby(1960, C), D. A. Glaser (1960), R. Hofstadter, R. Mößbauer (1961), E. Wigner, M. Goeppert-Mayer, A. Prokhorov (1964), S.-I. Tomonagava, J. Schwinger, R. Feynman (1965), A. Kastler (1966), H. Bethe (1967), L. W. Alvarez (1968), M. Gell-Mann (1969), A. N. Bohr, B. R. Mottelson, J. Rainwater (1975), B. Richter, S.C.C. Ting (1976), S.L. Glashow, M.A. Salam, S. Weinberg (1979), J. Cronin, V. L. Fitch (1980), K.G. Wilson (1982), W.A. Fowler, S. Chandrasekhar (1983), C. Rubia, S. Can der Meer (1984), L.M. Lederman, M. Schwartz, J. Steinberger (1988), J.I. Friedman, H.W. Kendall, R.E. Taylor (1990), G. Charpak (1992), M.L. Perl, F. Reines (1995), G. 't Hooft, M.J.G. Veltman (1999), Y. Nambu, M. Kobayashi, T. Maskawa (2008), F. Englert P. Higgs (2013), T. Kajita, A. B. McDonald (2015), P. Agostini, F. Krausz, A. L'Huillier (2023)

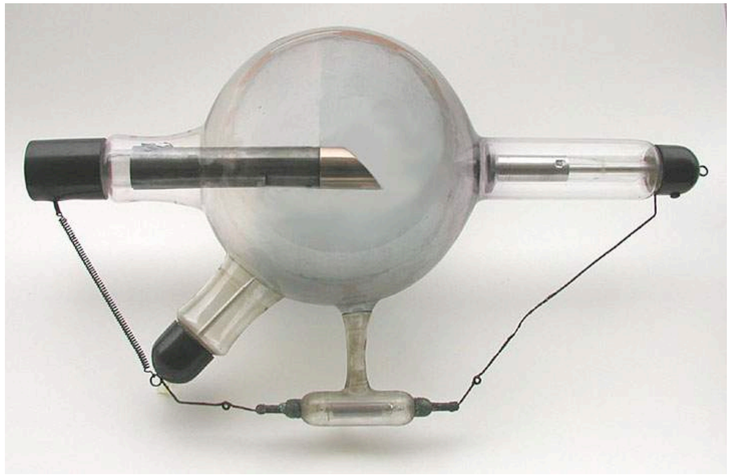
>3 times as many as for all of Org Chem

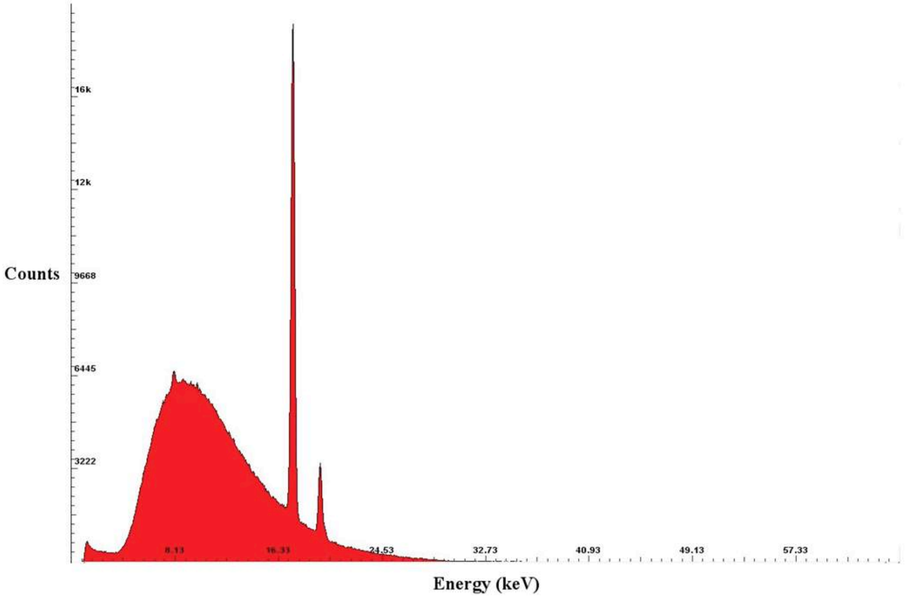
Plus additional 'spin-off' Nobel Prizes

The origin of the 'X-rays'

Wilhelm Konrad Röntgen

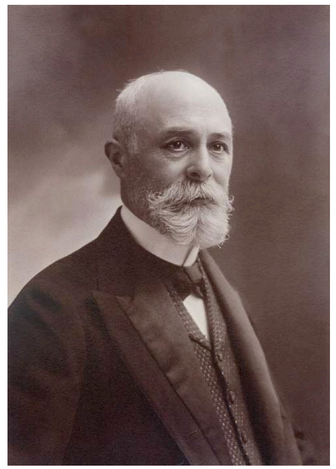




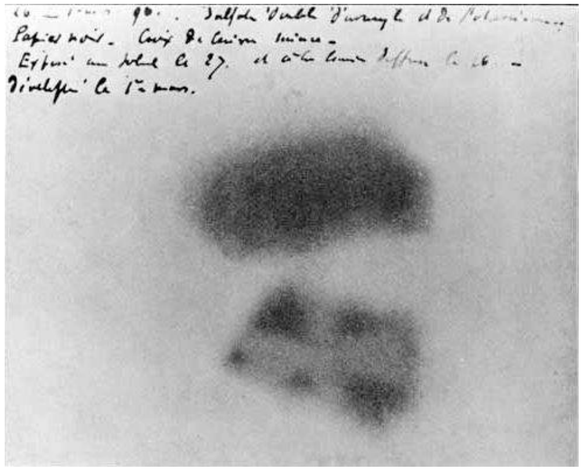


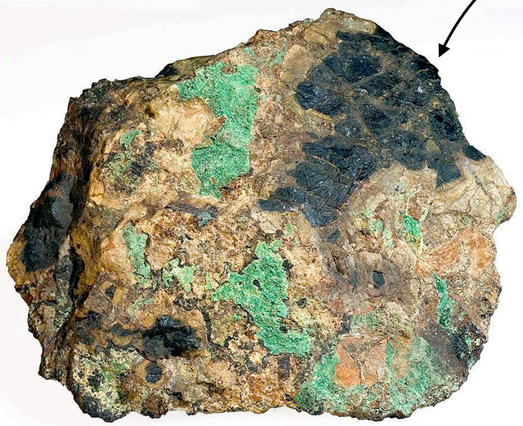
Molybdenum X-Ray Tube (Oxford Instruments)

What did Becquerel do to get his Image?

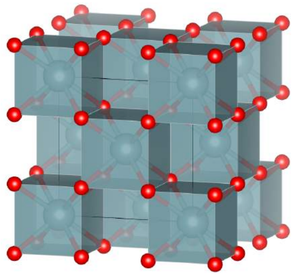


Antoine Henri Becquerel

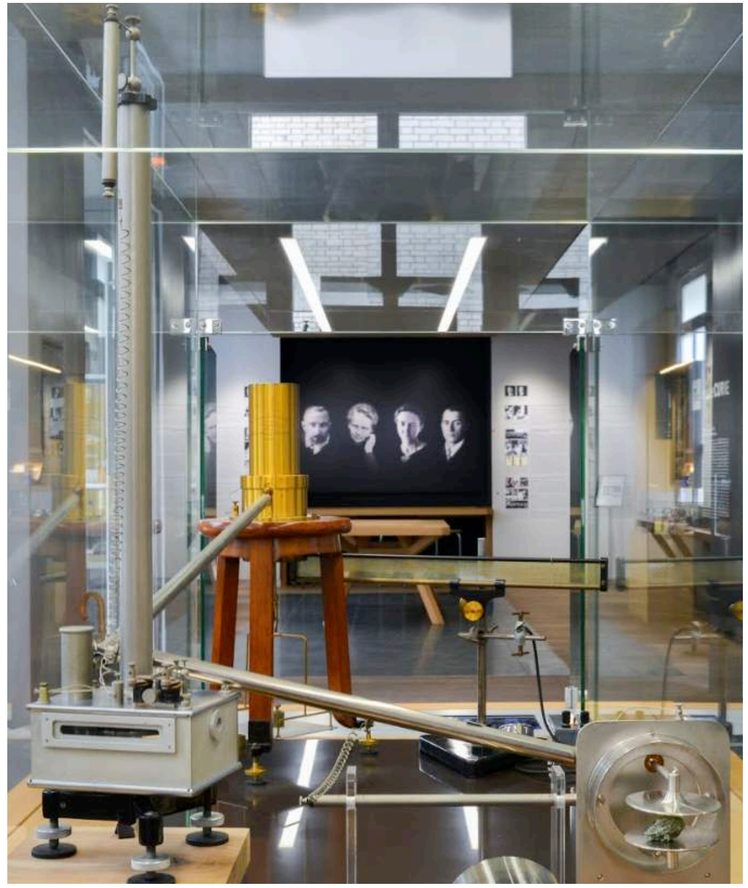




Humbolt Museum, Berlin. Uraninit sample used to isolate Uranium for the first time in 1789.

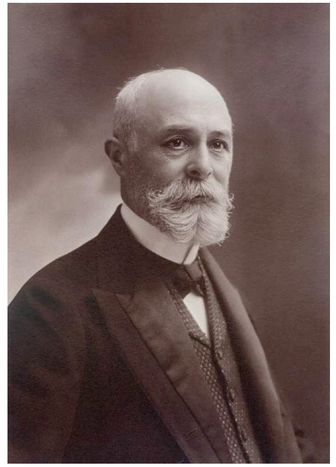


UO_2 Crystal Structure

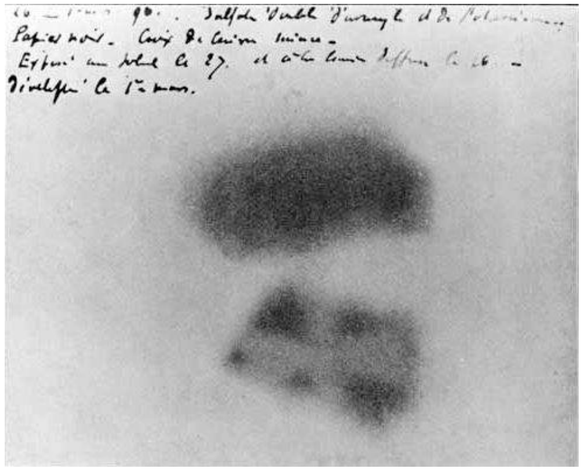


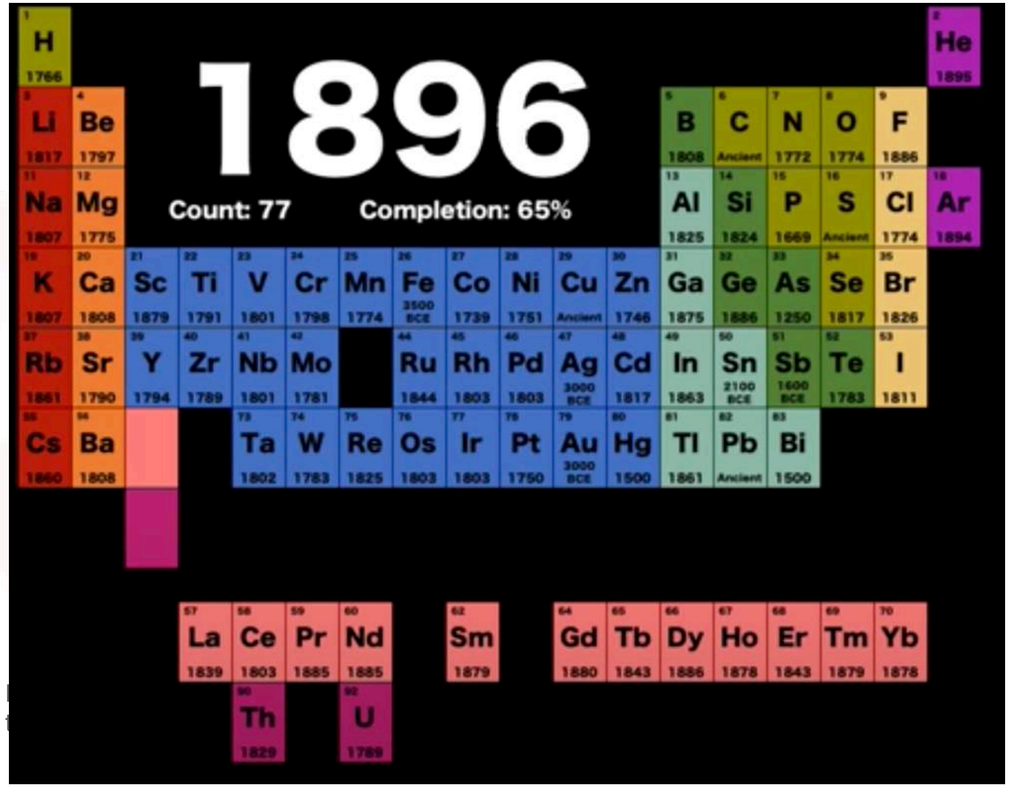
Curie Method for detection of ionized air

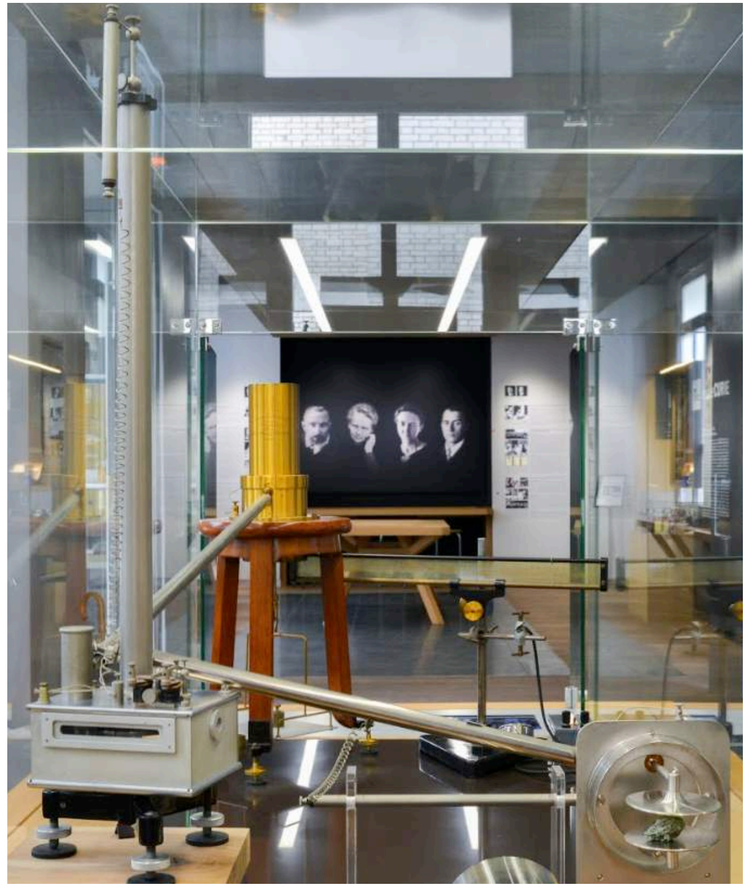
What did Becquerel do to get his Image?



Antoine Henri Becquerel







Curie Method for detection of ionized air

Atomic Substructure to be resolved!

Alpha Decay
Beta Decay
Electron
Radioactivity
1904
1896
Plum-Pudding Model

Periodic Table Reordered
Isotopes
Proton
1911
1913
1917
Planetary Model

Atom Split for first time
Deuteron
Positron
Neutron
1926
Quantum Mechanical Model

Muon
1932
1937
Pauli hypothesis on Neutrino

Pile-1
1942

Trinity
1945

Kaon
Pion
1947

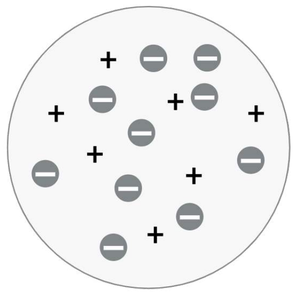
Lambda Baryon
1950

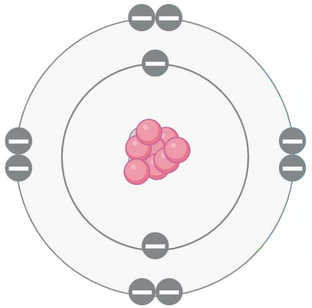
Antiproton
1955

Well… What about Quarks?

Or QED/QCD?
1960's

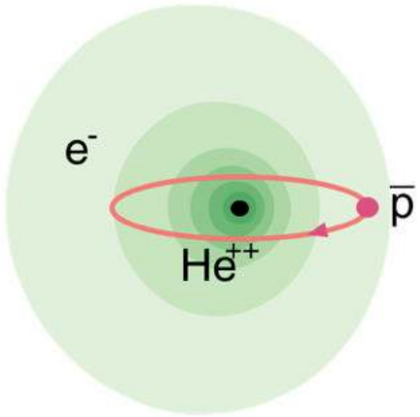
Alex Talking about Nuclear Medicine

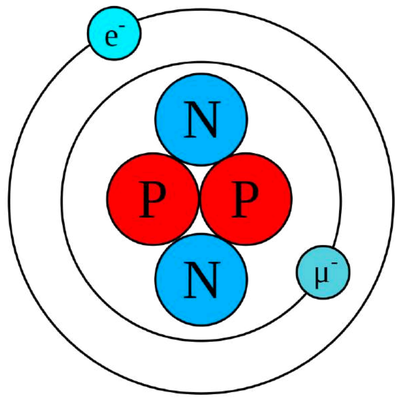




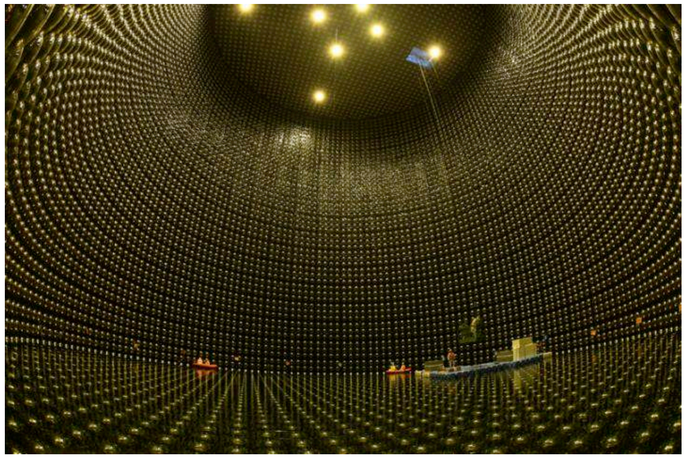
Current Quirky things in Nuclear Physics

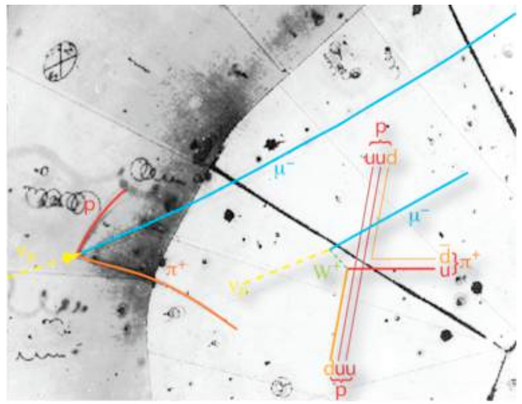
Exotic Atoms



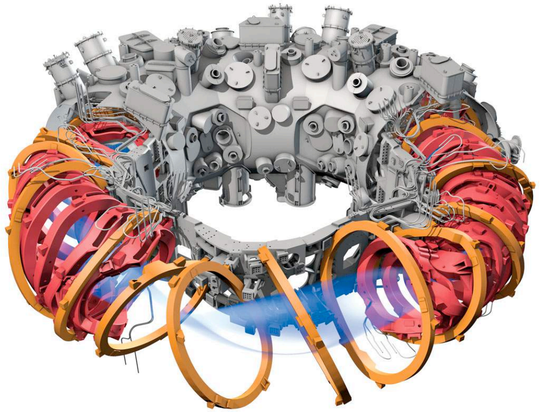


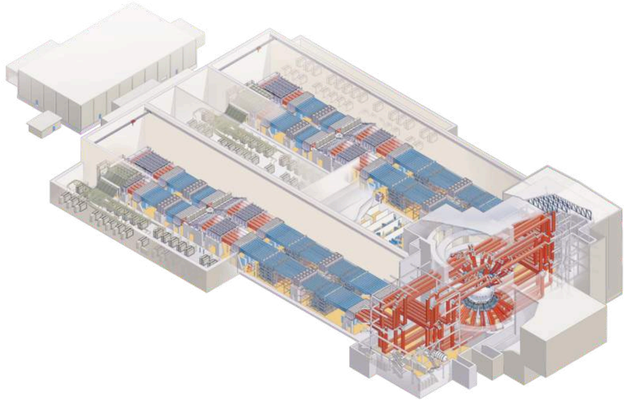
Super-kamiokande and Neutrinos



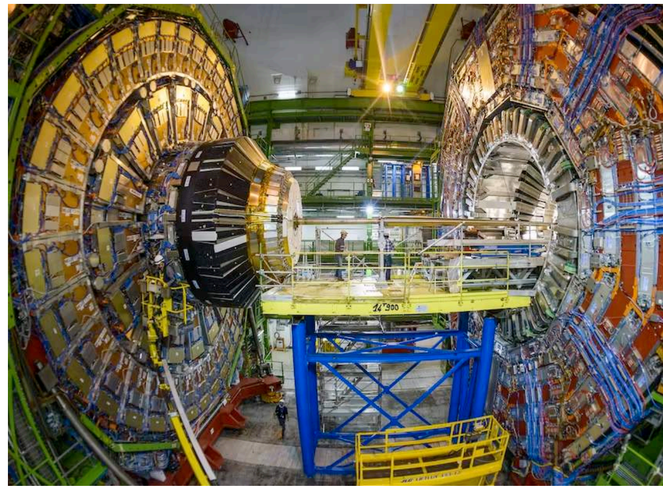


Wendelstein 7-X NIF And Fusion

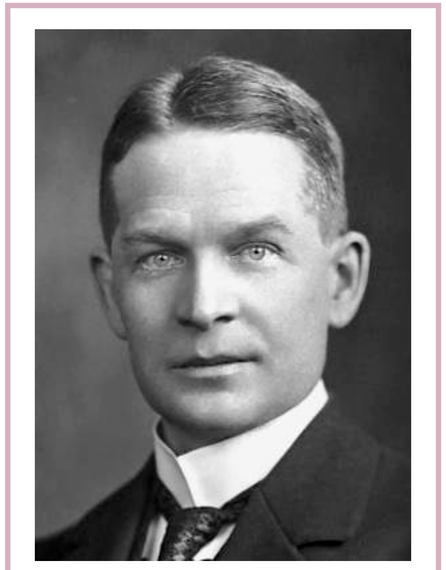




CERN Subatomics and Supersymmetry



The Isotope model



Frederick Soddy

Mass Number Charge

$$ {}^{A}_{Z}X^{C}_{N} $$

Proton Number Neutron Number

$$ {}^{1}_{1}H_{0} \qquad {}^{2}_{1}H_{1} \qquad {}^{3}_{1}H_{2} $$

Stable Stable 12.32 a

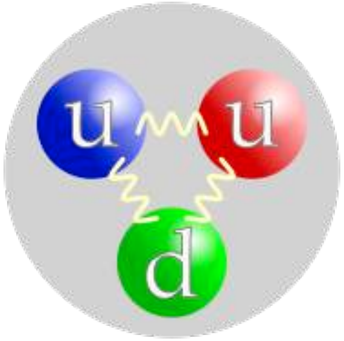
$$ {}^{99}_{43}Tc_{56} \qquad {}^{99m}_{43}Tc_{56} $$

211,100 a 6.01 h

^{177}Lu Lu-177 Lutetium-177

[^{18}F] Fluorodesoxyglucose

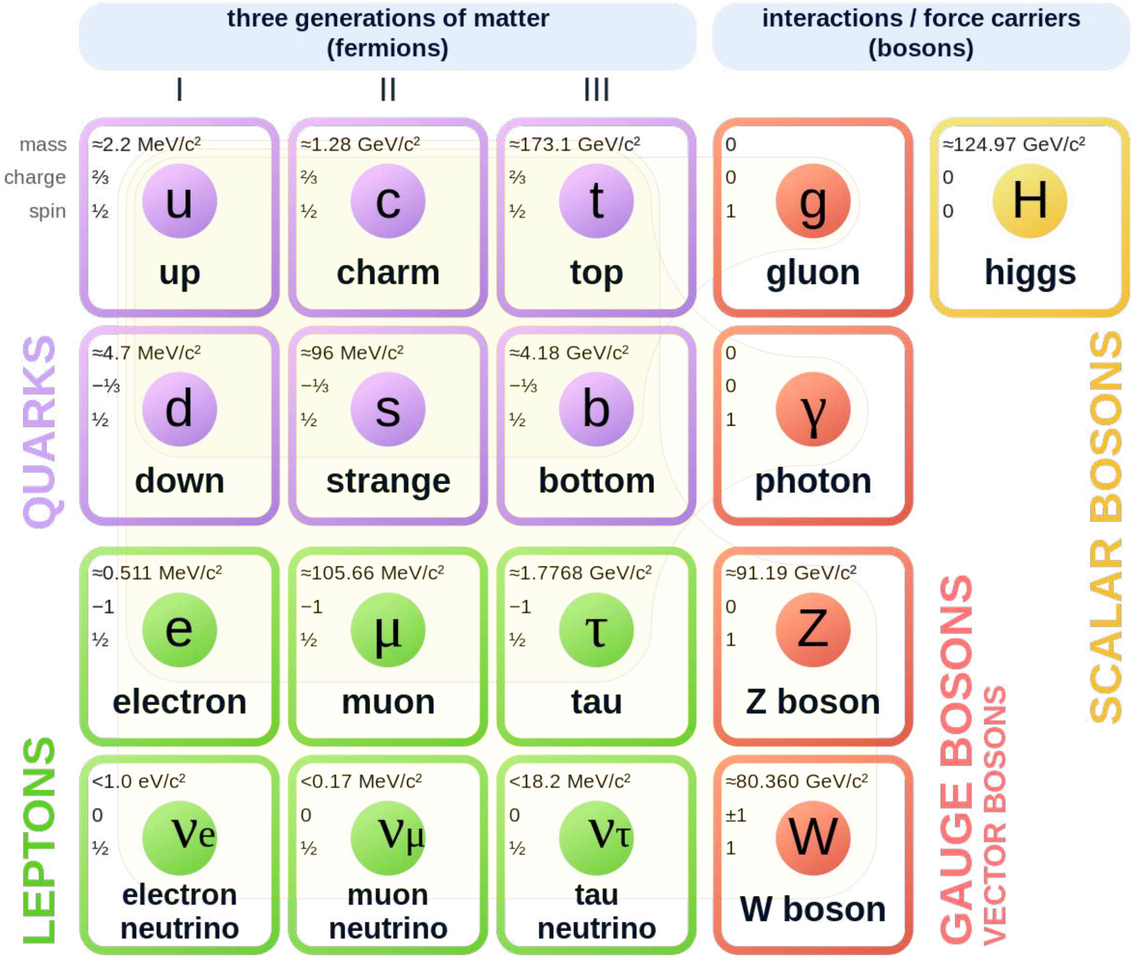
'12.3'

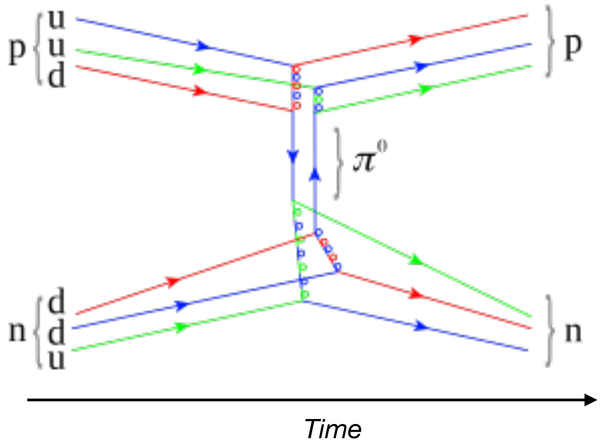


$m_p = 1.672\ 10^{-27}\ kg$

$E = mc^2$

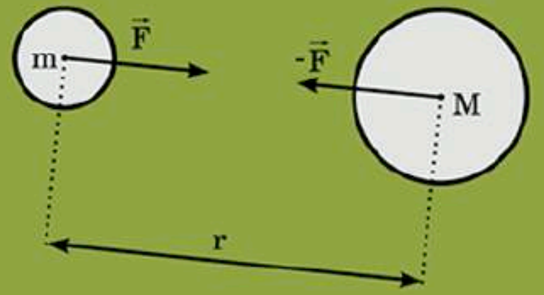
$m_p = 938.272\ MeV/c^2$





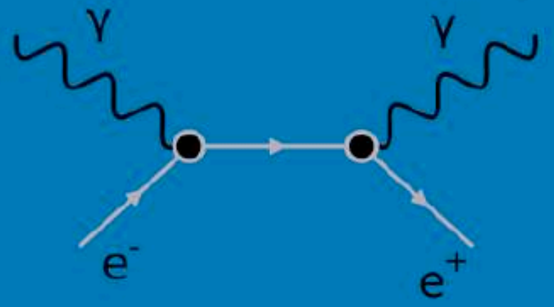
Quarkmodel - Stability and Decay

$$G_{\mu\nu} - \frac{1}{2}g_{\mu\nu}R + g_{\mu\nu}\Lambda = \frac{8\pi G}{c^4}T_{\mu\nu}$$



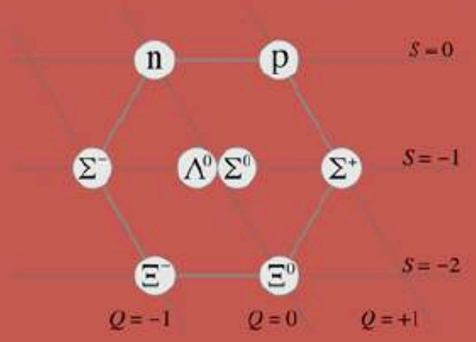
Gravity

$$\mathcal{L} = \bar{\psi}\left(i\gamma^\mu D_\mu - m\right)\psi - \frac{1}{4}F_{\mu\nu}F^{\mu\nu}$$



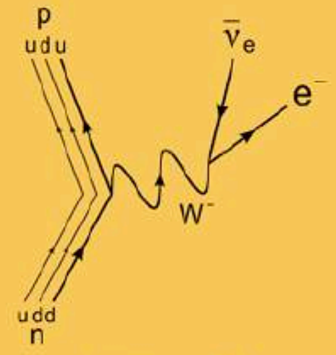
Electromagnetism

$$\mathcal{L} = \bar{\psi}_i\left(i\gamma^\mu\left(D_\mu\right)_{ij} - m\delta_{ij}\right)\psi_j - \frac{1}{4}G^a_{\mu\nu}G^{\mu\nu}_a$$



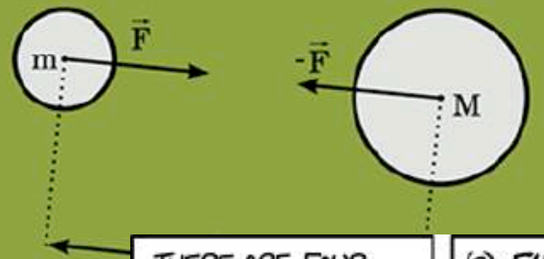
Strong

$$\mathcal{L} = g\left(\bar{\nu}_{eL}, \bar{e}\right)\gamma^\mu\left\{\begin{pmatrix} -\sqrt{1+\xi^2}Z_\mu & 0 \\ 0 & \frac{\xi A_\mu}{\sqrt{1+\xi^2}} - \frac{\xi^2}{\sqrt{1+\xi^2}}Z_\mu \end{pmatrix} + \frac{1-\gamma^5}{4}\begin{pmatrix} -\sqrt{1+\xi^2}Z_\mu & -\sqrt{2}W^+_\mu \\ -\sqrt{2}W_\mu & \sqrt{1+\xi^2}Z_\mu \end{pmatrix}\right\}\begin{pmatrix}\nu_{eL} \\ e\end{pmatrix}$$

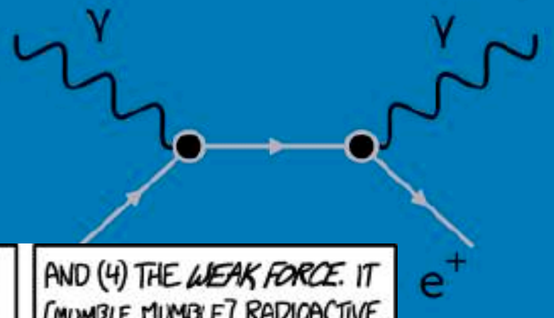


Weak

$$G_{\mu\nu} - \frac{1}{2}g_{\mu\nu}R + g_{\mu\nu}\Lambda = \frac{8\pi G}{c^4}T_{\mu\nu}$$



$$\mathcal{L} = \bar{\psi}\left(i\gamma^\mu D_\mu - m\right)\psi - \frac{1}{4}F_{\mu\nu}F^{\mu\nu}$$

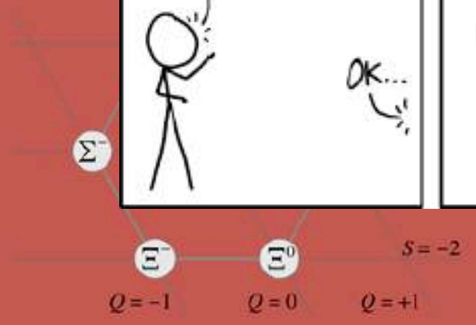


Gravity

Electromagnetism

$\mathcal{L} = \bar{\psi}_i \left(i\gamma^\mu (D$

$\left(\begin{matrix} -\sqrt{1+\xi^2}Z_\mu & -\sqrt{2}W_\mu^+ \\ -\sqrt{2}W_\mu & \sqrt{1+\xi^2}Z_\mu \end{matrix}\right)\right\}\left(\begin{matrix}\nu_{eL} \\ e\end{matrix}\right)$

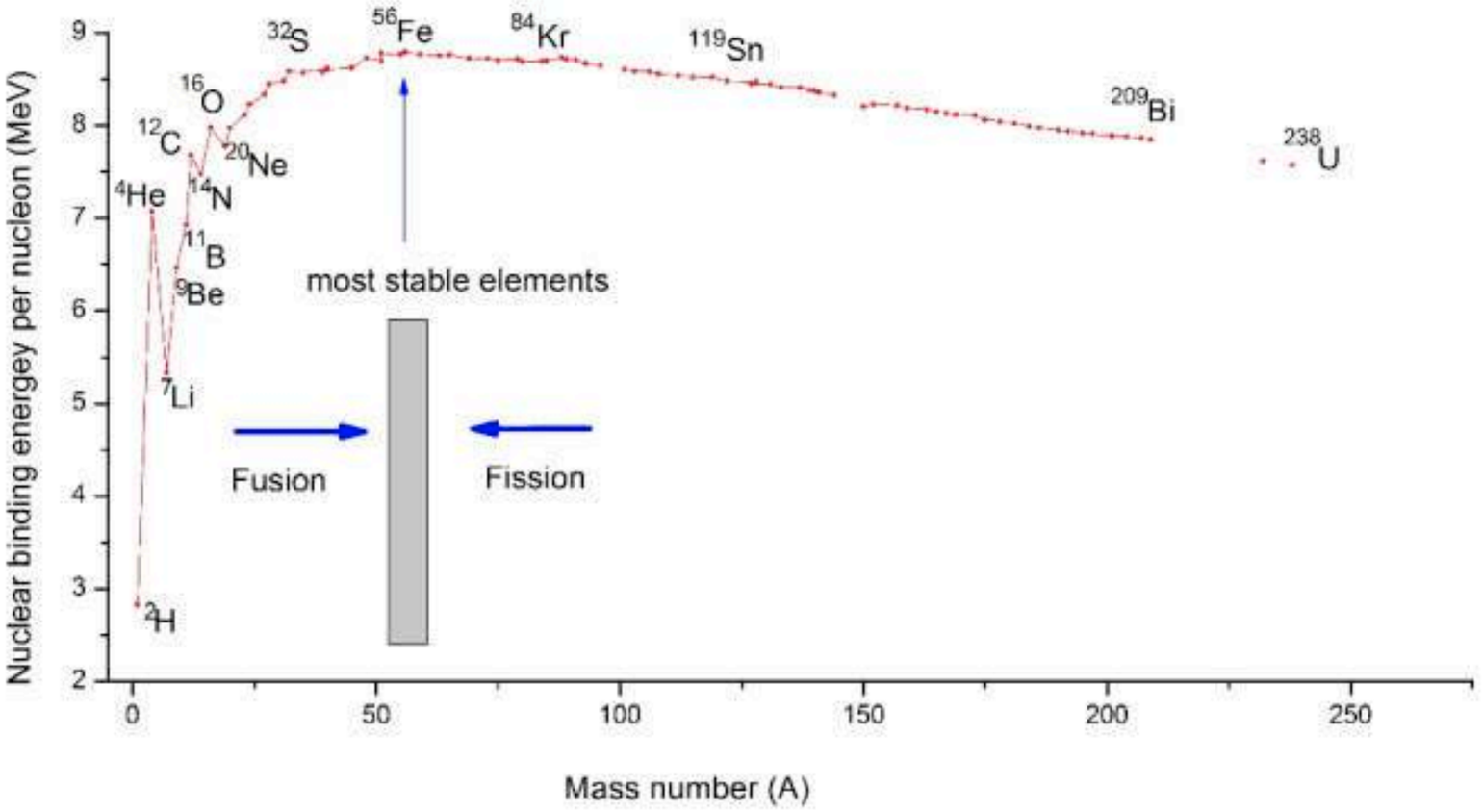


e^-

Strong

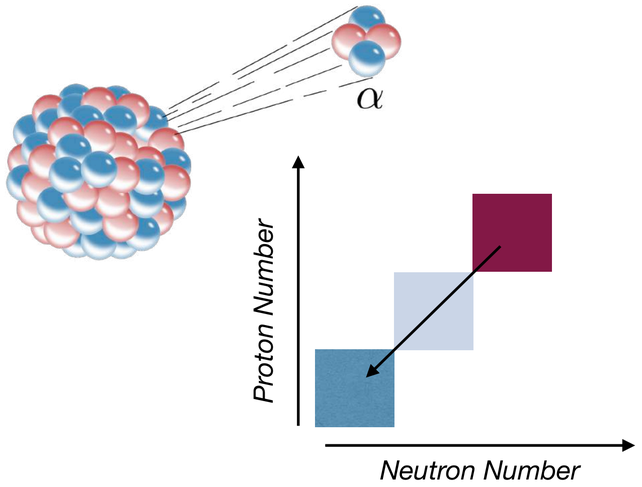
Weak

Binding Energy per Nucleon

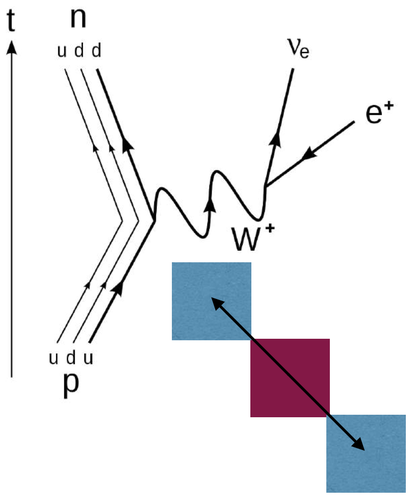


Decay Types

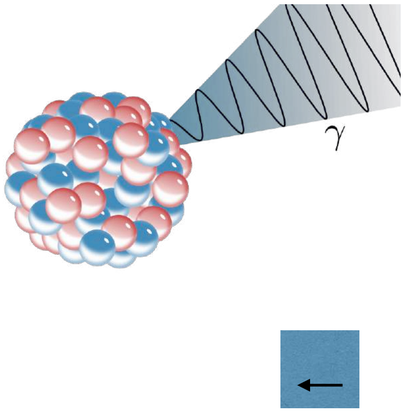
Alpha Decay



Beta Decay

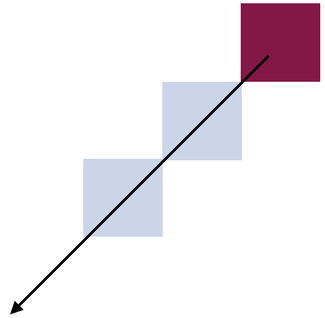


‘Gamma Decay’

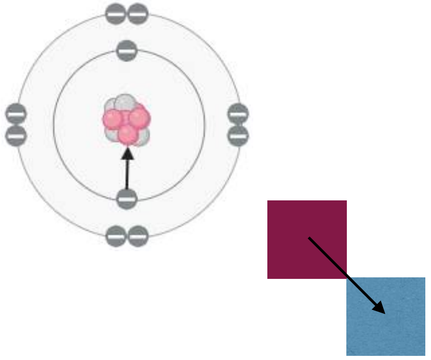


Cluster

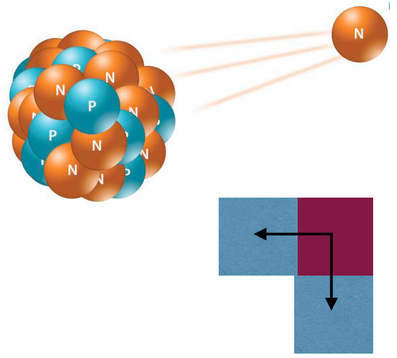
$^{242}Cm \rightarrow {}^{208}Pb + {}^{34}S$



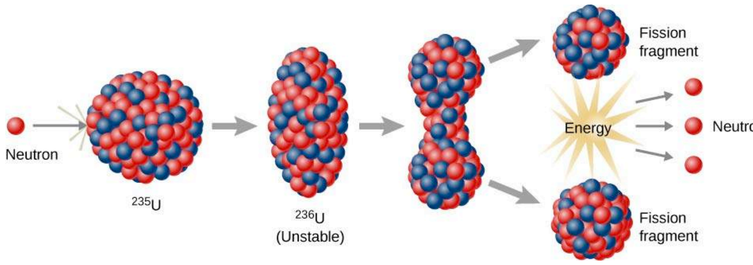
Electron Capture



Particle Emission



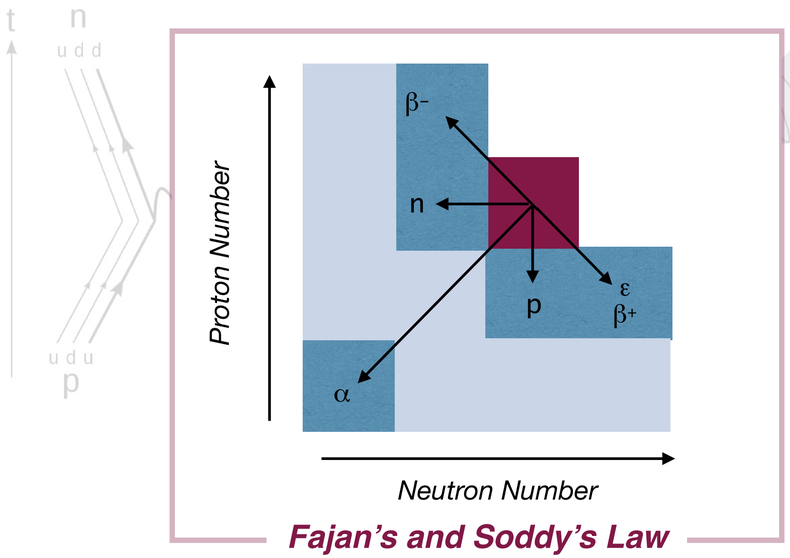
Fission



Decay Types

Alpha Decay

Beta Decay



Fajan's and Soddy's Law

'Gamma Decay'

Cluster

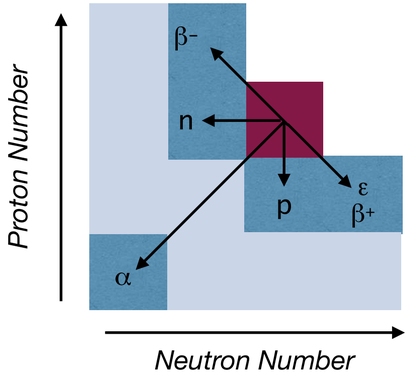
$^{242}Cm \rightarrow {}^{208}Pb + {}^{34}S$

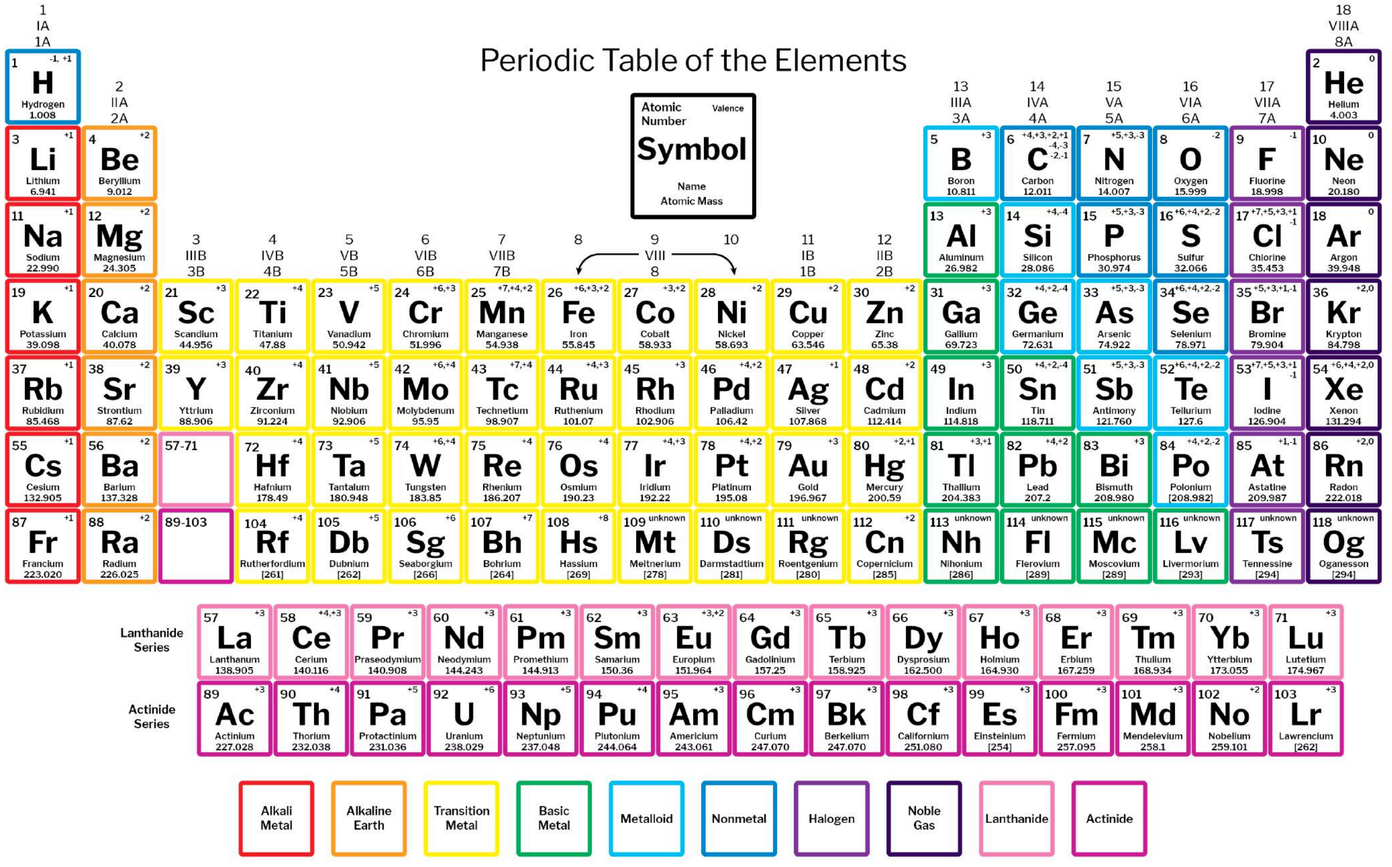
Electron Capture

Particle Emission

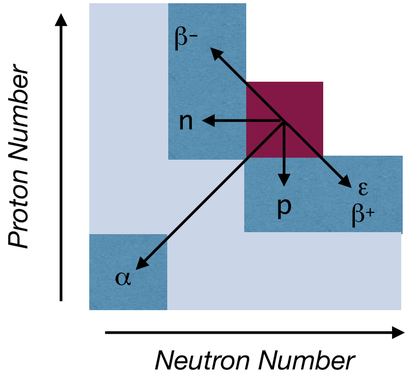
Fission

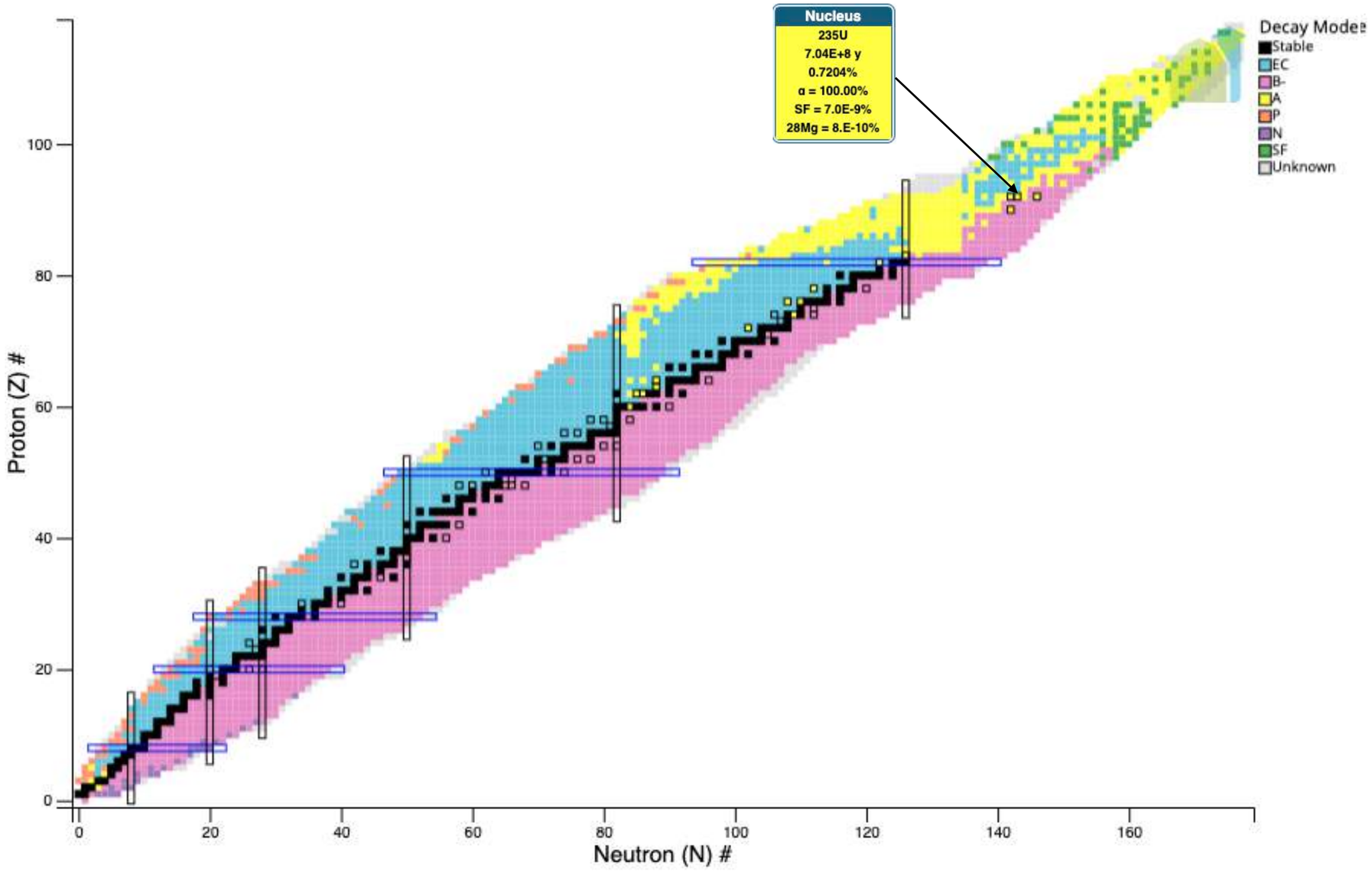
Karlsruher Nuclide Chart - NuDat3 & KNCO++





Karlsruher Nuclide Chart - NuDat3 & KNCO++





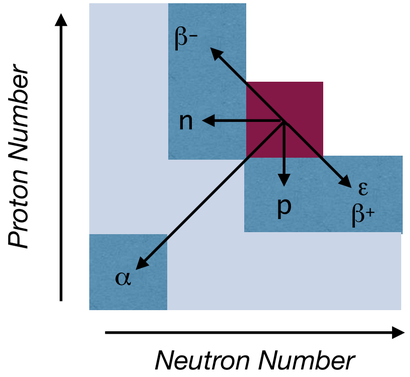
Mattusch Isobar Rule

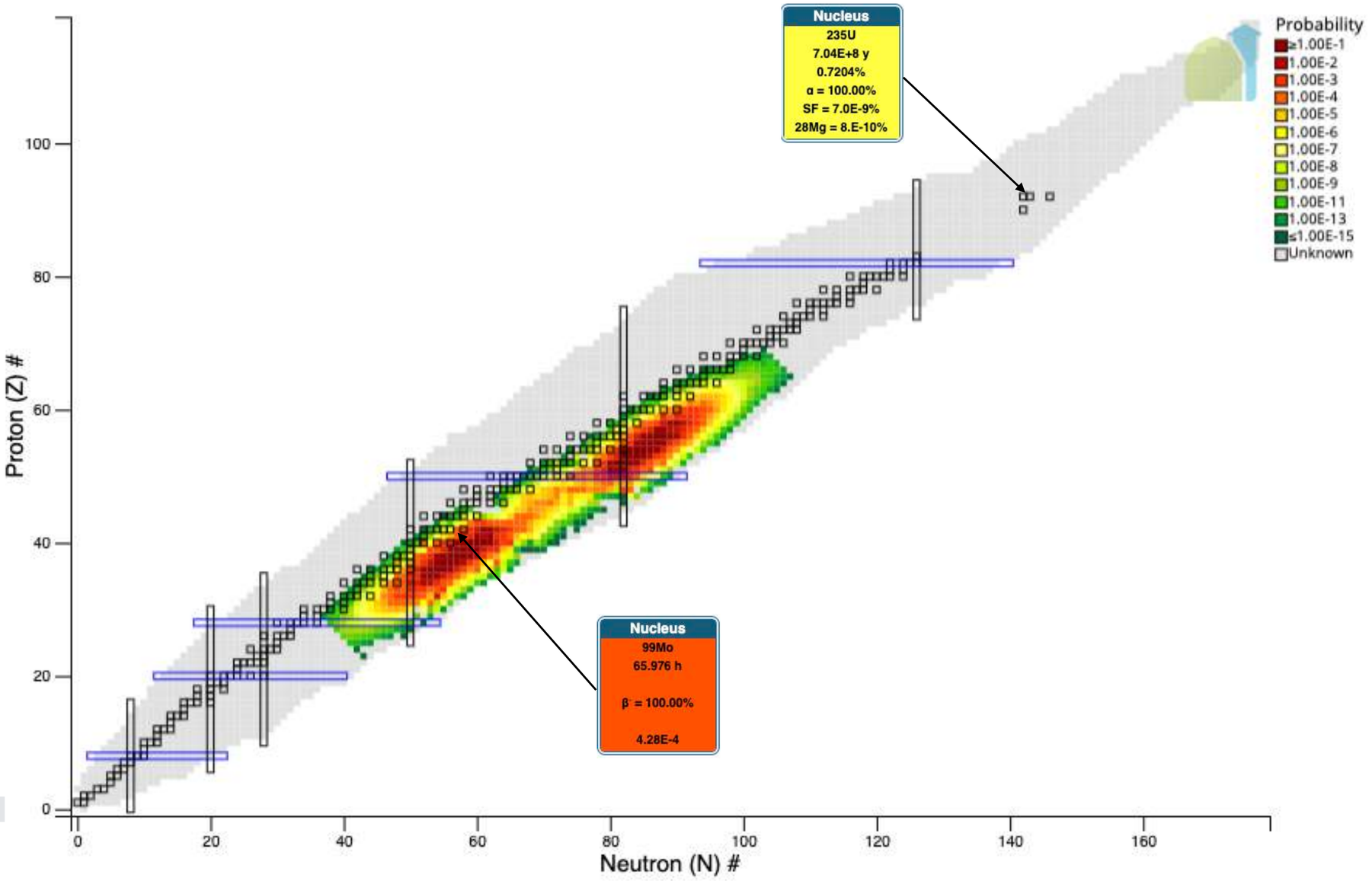
Even-Odd Rule

P,N	OO	OE	EO	EE
#	5	48	53	145

^{2}H, ^{6}Li, ^{10}B, ^{14}N, ^{180m}Ta

Karlsruher Nuclide Chart - NuDat3 & KNCO++





Mattusch Isobar Rule

Even-Odd Rule

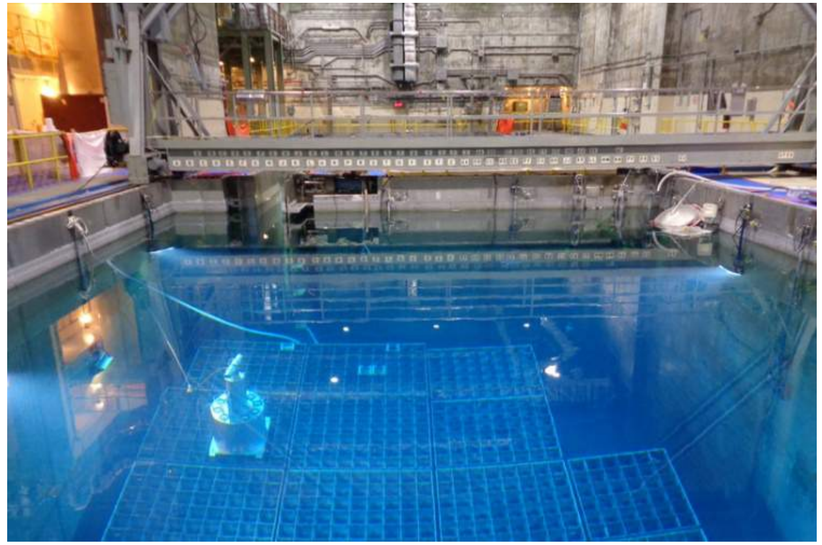
P,N	OO	OE	EO	EE
#	5	48	53	145

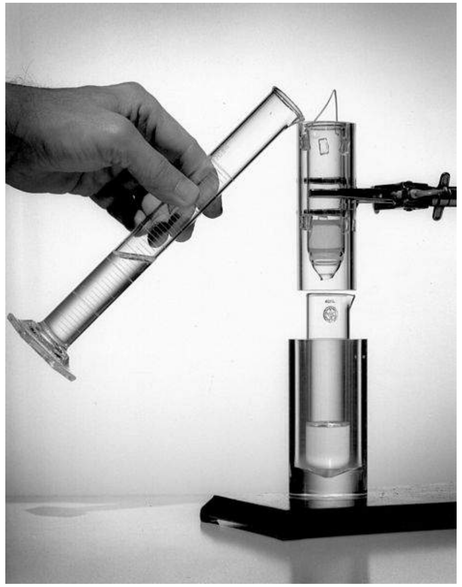
^{2}H, ^{6}Li, ^{10}B, ^{14}N, ^{180m}Ta

Where do you get these “isotopes” from?

Spent Fuel Rods

^{99m}Tc, ^{188}Re, ^{225}Ac





			$t_{1/2}$
^{99}Mo	→	^{99m}Tc	6.01 h
^{82}Sr	→	^{82}Rb	1.24 min
^{62}Zn	→	^{62}Cu	9.67 min
^{188}W	→	^{188}Re	17.01 h
^{229}Th	→	^{225}Ac	9.92 d

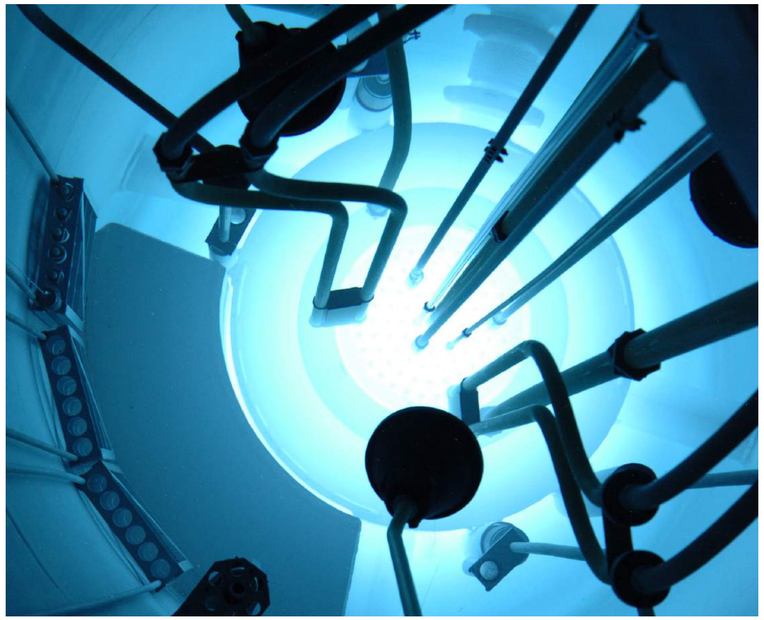
Where do you get these “isotopes” from?

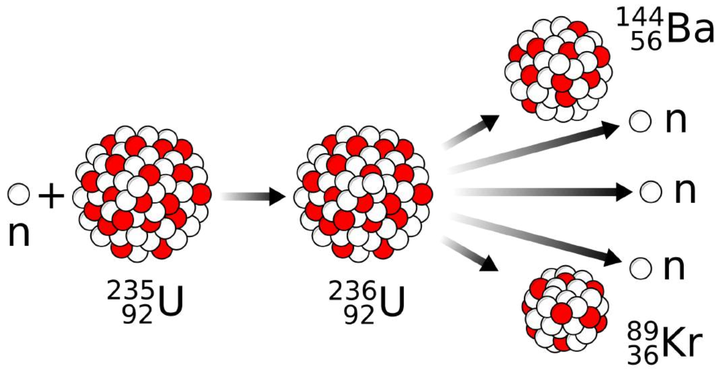
Spent Fuel Rods

^{99m}Tc, ^{188}Re, ^{225}Ac

Reactor Nuclei (n-rich)

^{60}Co, ^{177}Lu





$^{30}Si(n,\gamma)^{31}Si(\beta^-)^{31}P$
$^{59}Co(n,\gamma)^{60}Co$
$^{194}Pt(n,\gamma)^{195m}Pt$
$^{198}Pt(n,\gamma)^{199}Pt(\beta^-)^{199}Au$
$^{176}Yb(n,\gamma)^{177}Yb(\beta^-)^{177}Lu$

Where do you get these “isotopes” from?

Spent Fuel Rods

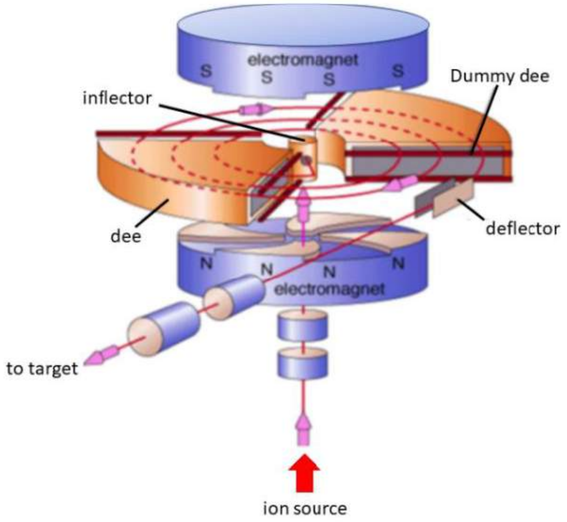
^{99m}Tc, ^{188}Re, ^{225}Ac

Reactor Nuclei (n-rich)

^{60}Co, ^{177}Lu

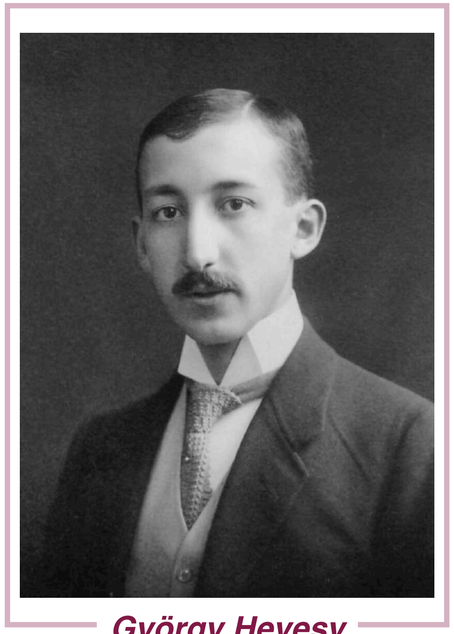
Cyclotron nuclei (p-rich)

^{11}C, ^{15}O, ^{18}F, ^{195m}Pt



$^{18}O(p,n)^{18}F$
$^{14}N(d,n)^{15}O$
$^{14}N(p,He)^{11}C$
$^{192}Os(He,ng)^{195m}Pt$
$^{249}Cf(^{48}Ca,3n)^{294}Og$

George de Hevesy and Tracer Principle



György Hevesy

Development of X-Ray Fluorescence Analysis

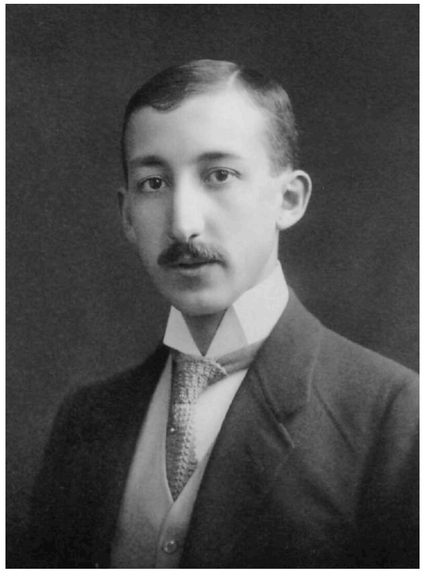
Discoverer of Hafnium with Dirk Coster (1922)

Development of Neutron Activation Analysis (1943)

Traced selective distribution of Isotopes in plants, Rabbits and Hungarian Chemists…

Nobel Prize 1943 - ‘Tracer principle’

George de Hevesy and Tracer Principle



György Hevesy

Development of X-Ray Fluorescence Analysis

Discoverer of Hafnium with Dirk Coster (1922)

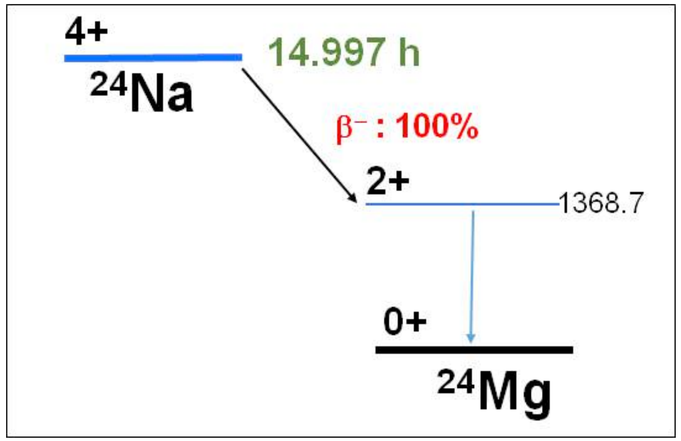
Development of Neutron Activation Analysis (1943)

Traced selective distribution of Isotopes in plants, Rabbits and Hungarian Chemists…

Nobel Prize 1943 - ‘Tracer principle’

Joseph Gilbert Hamilton and Robert Eugene Marshak drinking Radiosodium during Manhattan Project

Single Photon Emission Computed Tomography (SPECT)



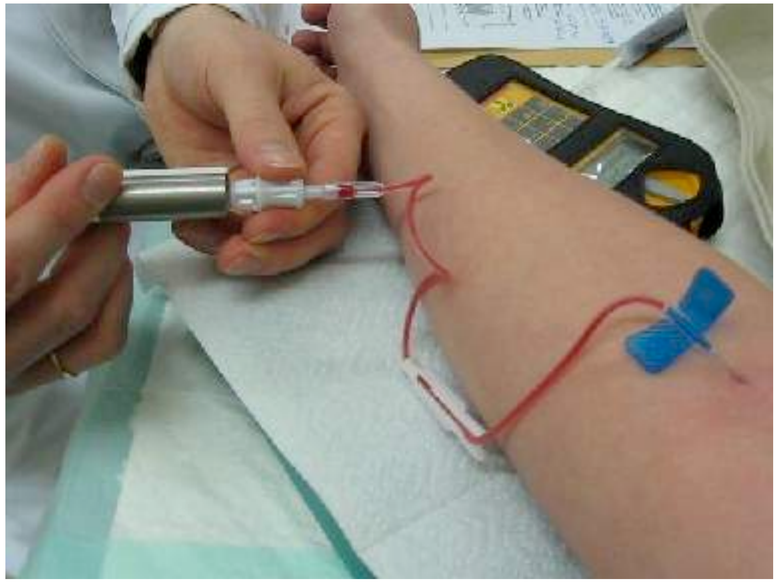
Suitable Isotope should not emit further particles

‘Short lived’ Nuclide

Chemically stable when bound

Target a biological problem

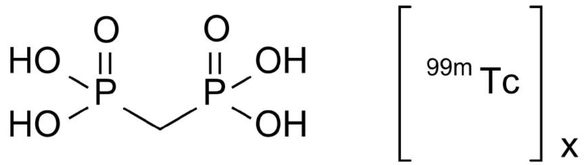
Enrich the nuclide in area



Case Study - Osteosarcoma

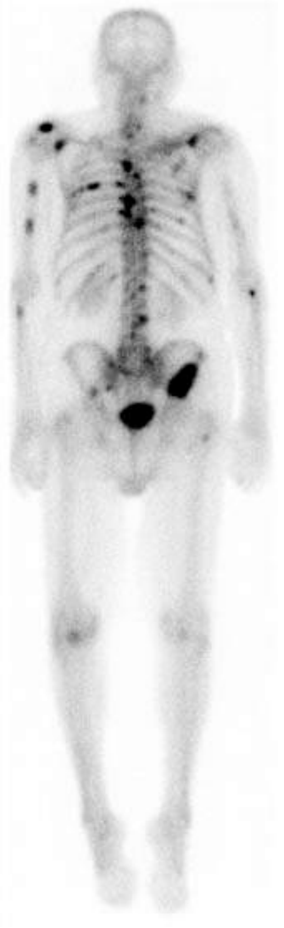
Target Evaluation
- Osteoblast, Mineralisation of Hydroxyapatite (e.g. bone growth)

Vector
- use of diphosphates (HDP, MDP, DPD etc.)

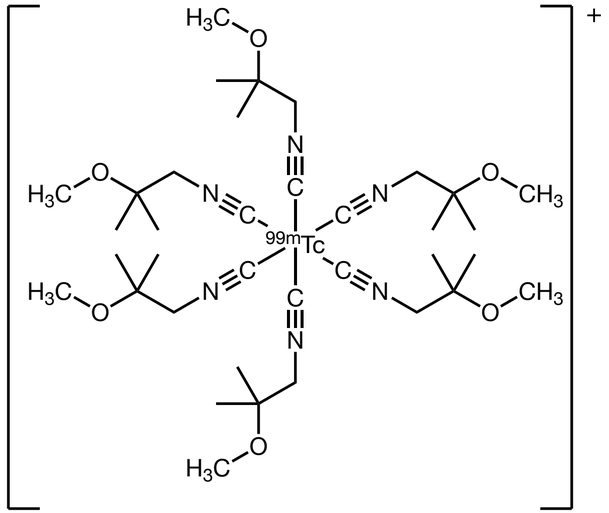


Nuclide
- Technetium binds phosphates

Dose
- *740 MBq Tc-99m, equivalent to 6.3 mSv Dose (less than Chest CT scan 7 mSv)*
- *38 pmol (0.000000038 mmol, 0.0001 mg)*

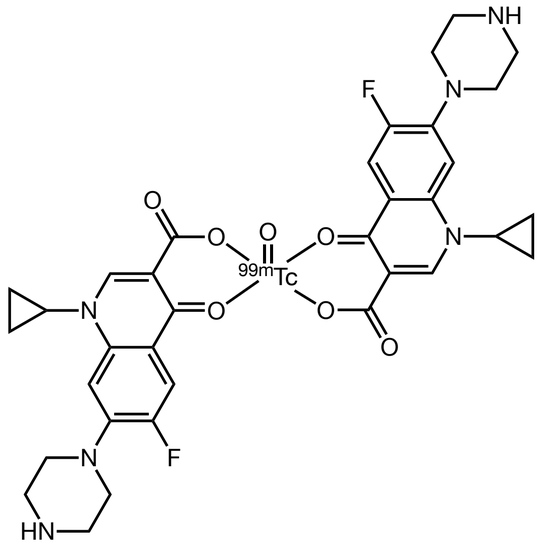


Technetium Small Molecule Tracers



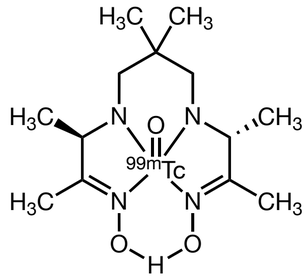
^{99m}Tc Sestamibi

Myocardial Perfusion
Parathyroid scintigraphy
Breast Cancer Detection



^{99m}Tc Ciprofloxacin

Tracing Bacterial Infection
Pulmonary Tuberculosis

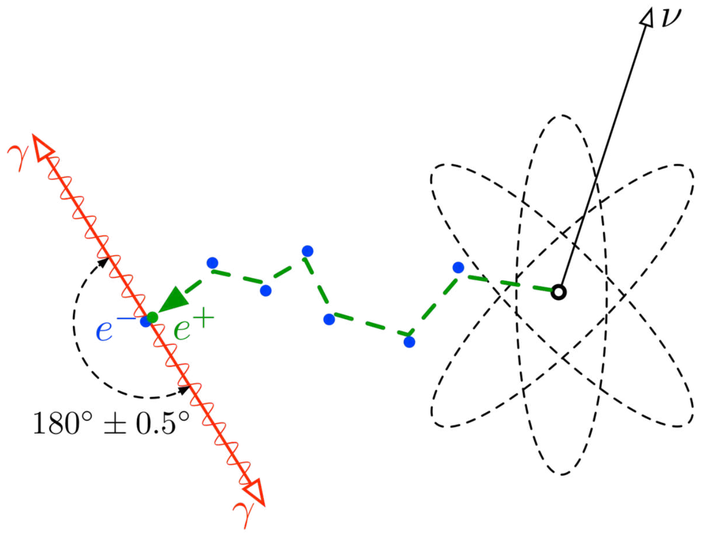


^{99m}Tc Exametazime

Cerebral Perfusion after Stroke

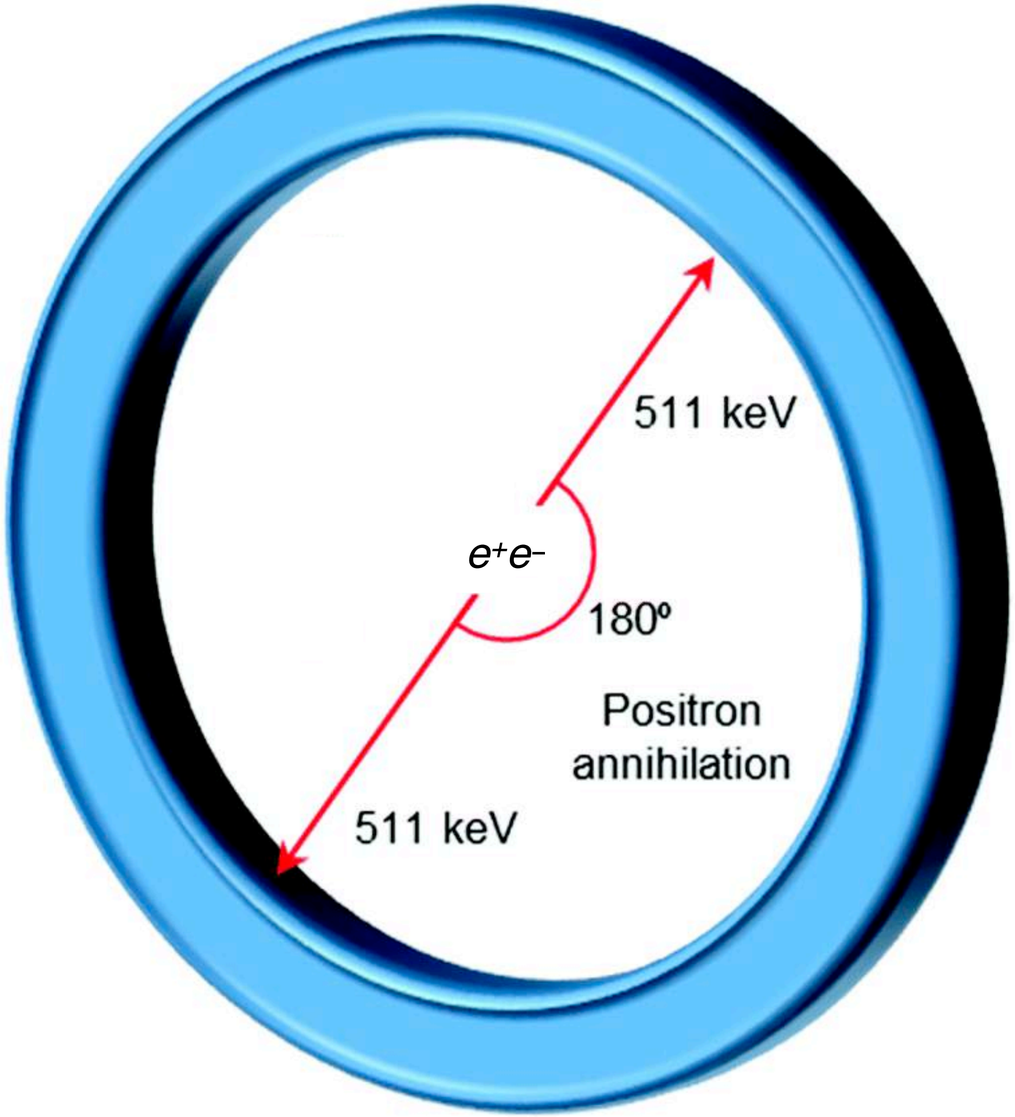
Miller, D.D.; Donohue, T.J.; Younis, L.T.; Bach, R.G.; Aguirre, F.V.; Wittry, M.D.; Goodgold, H.M.; Chaitman, B.R.; Kern, M.J, *Circulation*, **1994**, *899*, 2150.
Britton, K.E.; Wareham, D.W.; Das, S.S.; Solanki, K.K.; Amaral, H.; Bhatnagar, A.. Katamihardja, A.H.S.; Malamitsi, J.; Moustafa, H.M.; Soroa, V.E.; Sundram, F.X.; Padhy, A.K., *J. Clin. Pathol.* **2002**, *55*, 817.
Gartshore, G.; Bannan, P.; Patterson, J.; Higley, B.; McCulloch, *J. Eur. J. Nuc. Med.,* **1994**, *21*, 913.

Positron in tissue

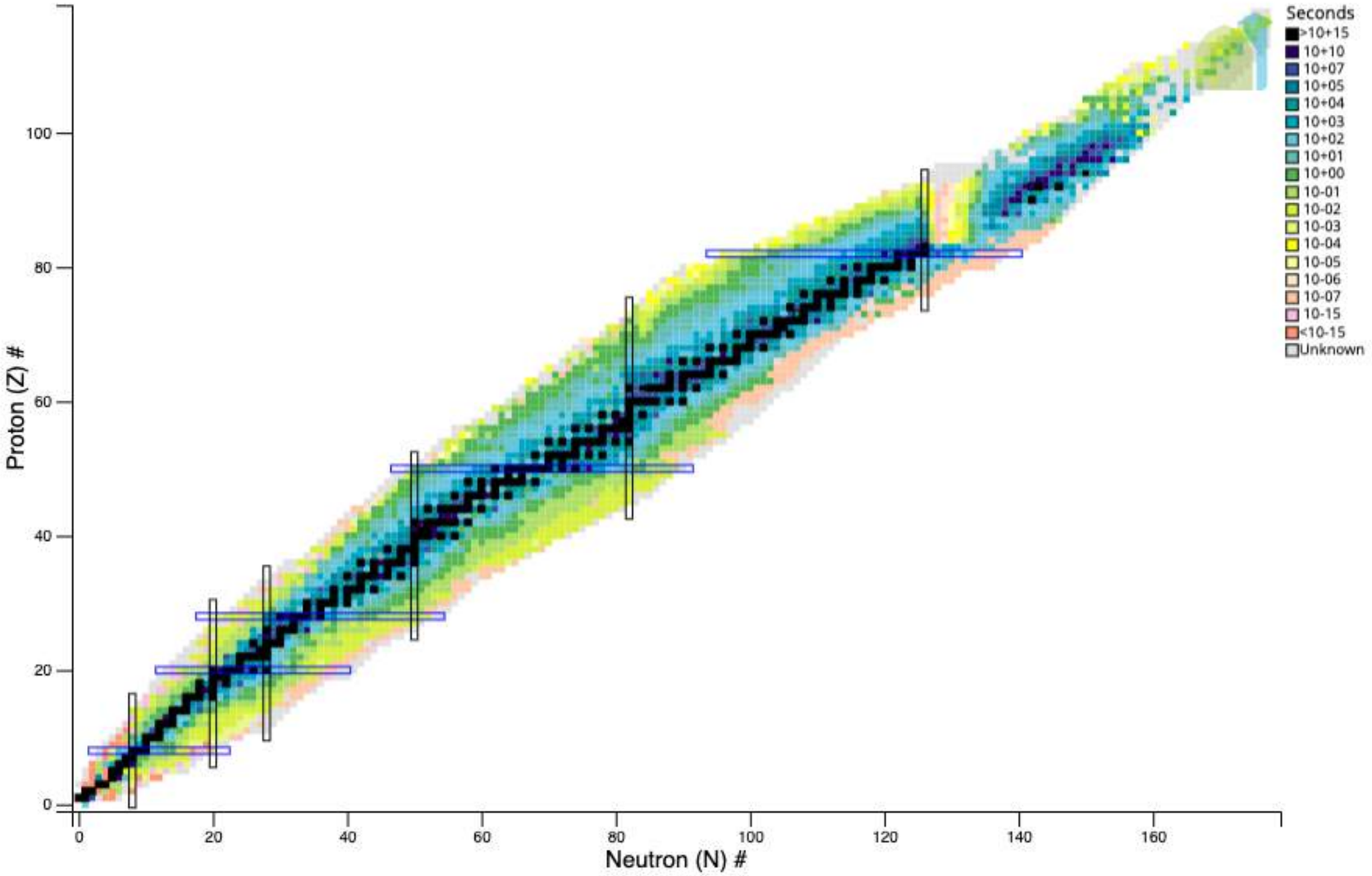


e^+ positron
e^- electron
ν neutrino
γ quantum/photon (511 keV)

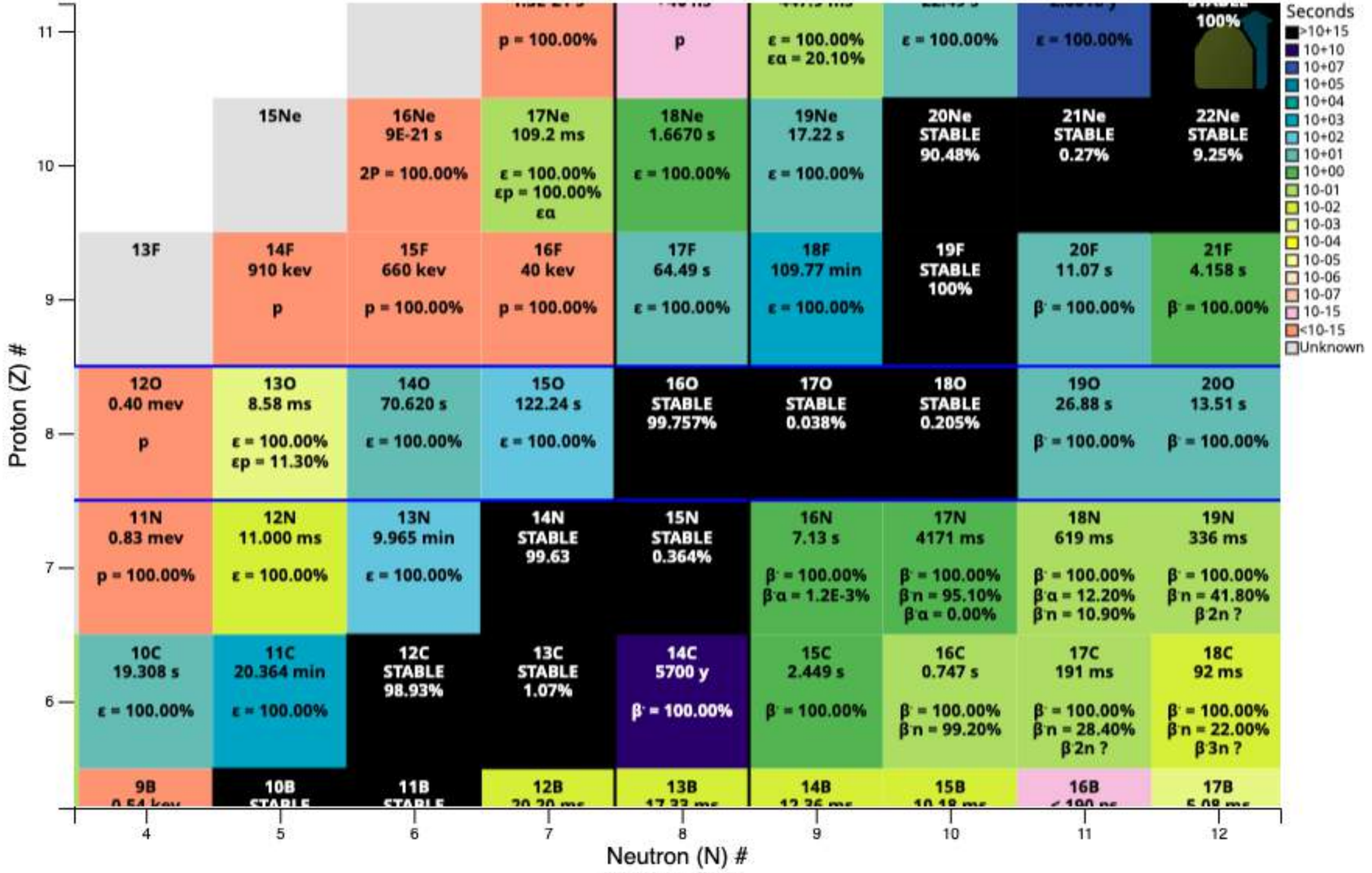
Detector ring



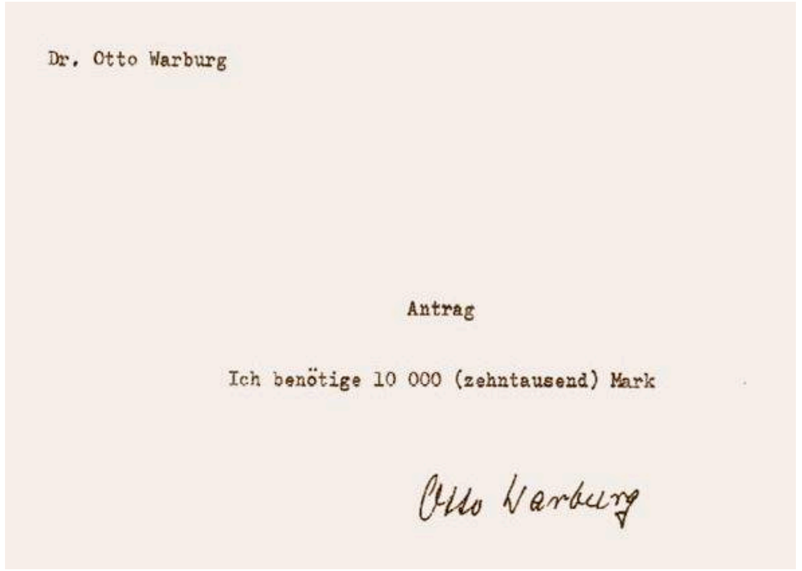
Search for Isotopes



Search for Isotopes



Warburg Effect

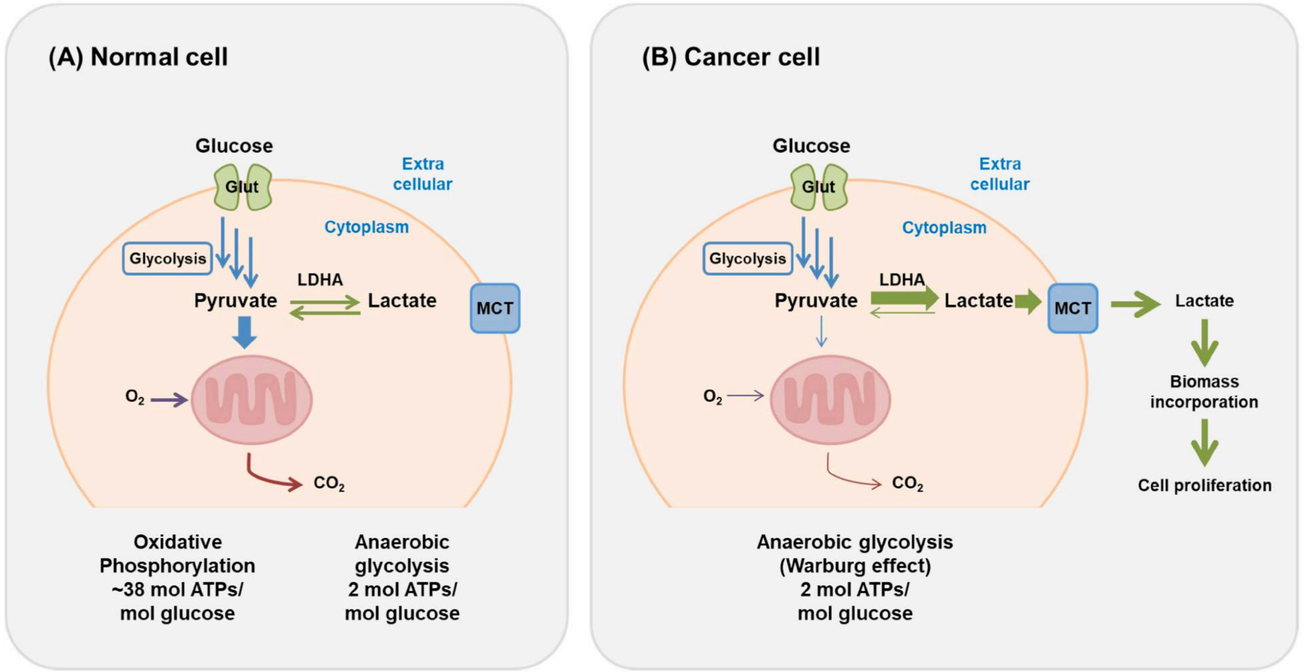


Dr. Otto Warburg

Antrag

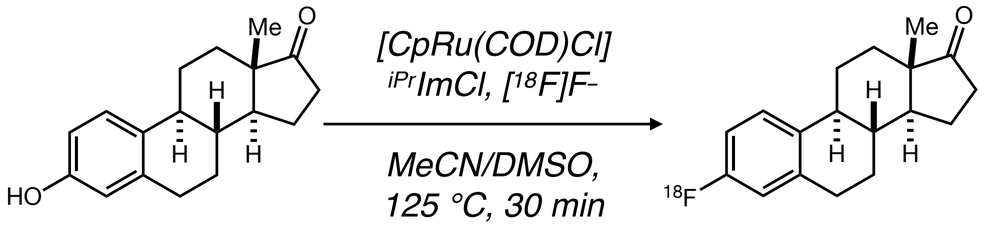
Ich benötige 10 000 (zehntausend) Mark

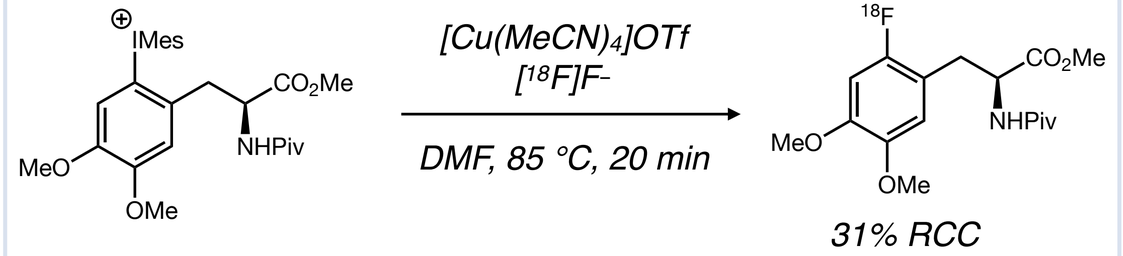
Otto Warburg

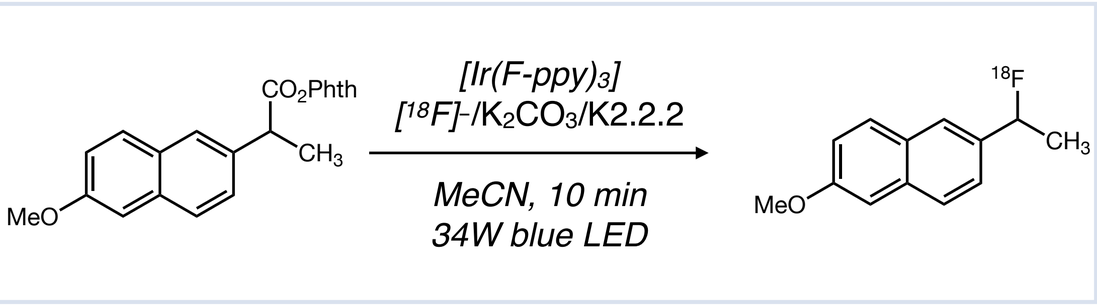


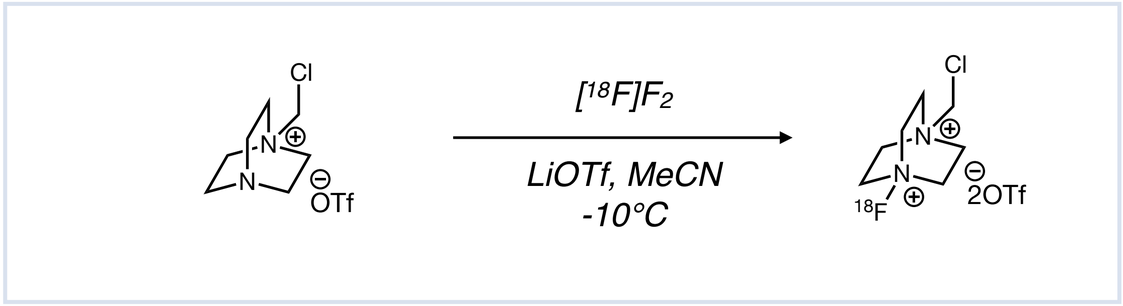
Warburg, O.; Wind, F.; Negelein, E., *J. Gen. Phys.*, **1927**, *8*, 519.
Kim, S.-H.,; Baek, K.-H., *Molecules* **2021**, *22*, 6173.

Radiofluorination Strategies



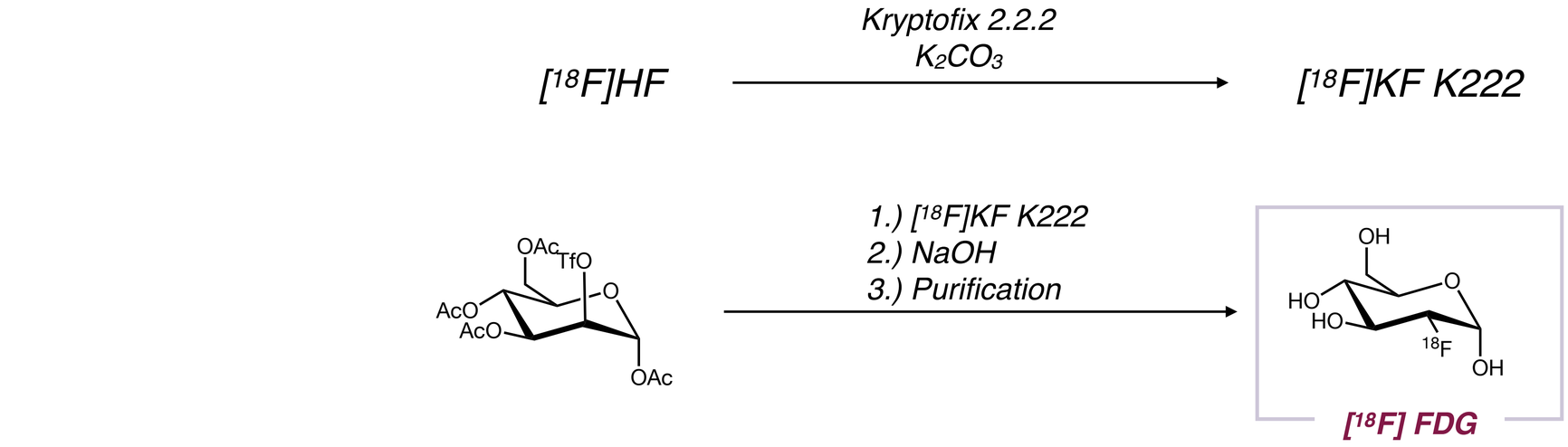






Webb, E.W.; Park, J.B.; Cole, E.L.; Donelly, D.J.; Bonacorsi, S.J.; Ewing, E.R.; Doyle, A.G., *J. Am. Chem. Soc*., **2020**, *20*, 9493.
Teare, H.; Robins, R.G.; Kirjavainen, A.; Forsback, S.; Sandford, G.; Solin, O.; Luthra, S.K.; Gouverneur, V., *Angew. Chem. Int. Ed.*, **2010**, *49*, 6821.
Beyzavi, H.; Mandal, D.; Strebl, M.G.; Neumann, C.N.; D'Amato, E.M.; Chen, J.; Hooker, J.C.; Ritter, T., *ACS Cent. Sci.*, **2017**, *3*, 944.,
Ichiishi, N.; Brooks, A.F.; Topczewski, J.J.; Rodnick, M.E.; Sanford, M.S.; Scott, P.J.H., *Org. Lett*, **2014**, *16*, 3224.

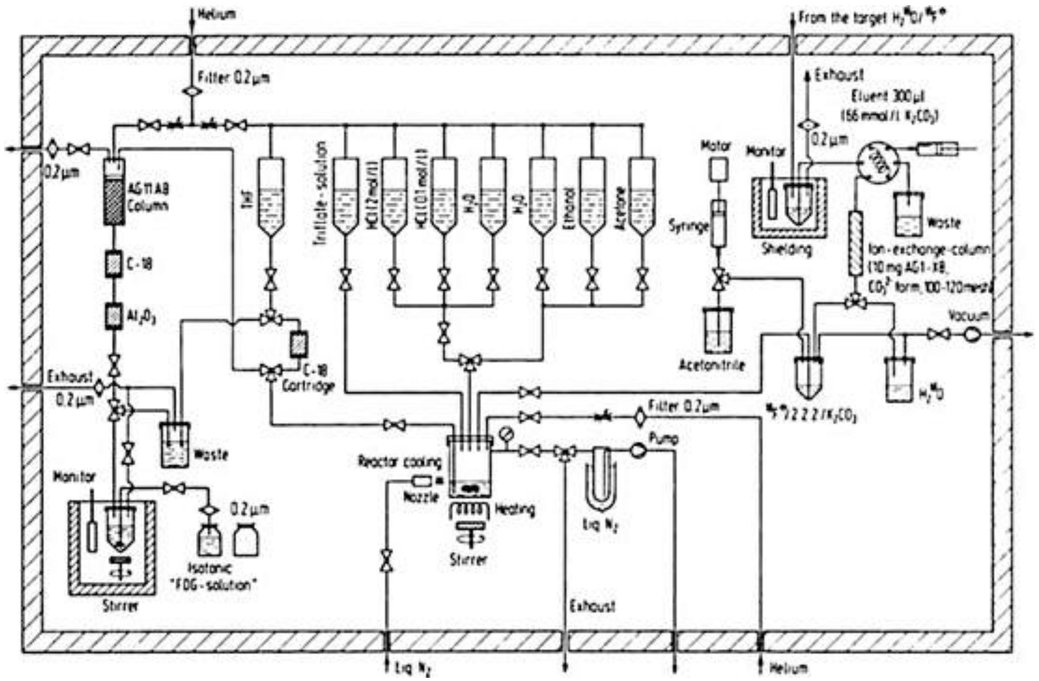
Radioactive Sugars and Automated Synthesis - Gerhard Stöcklin



RCY >60%

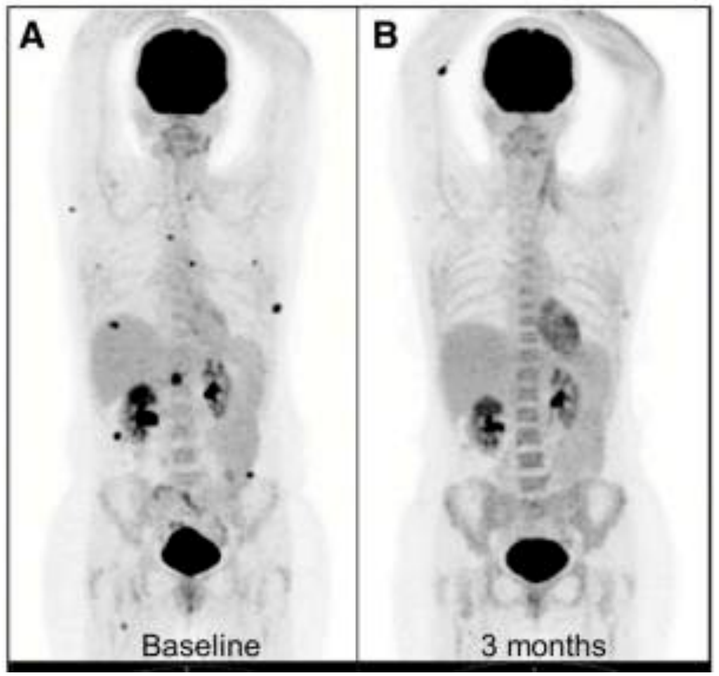
26 minutes

500 MBq ≈ 1.5 ng

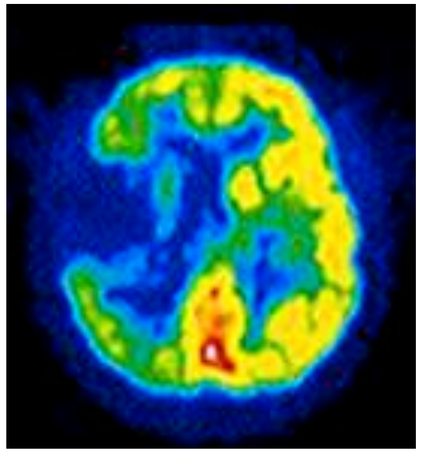


Cole, E.L.; Stewart, M.N.; Littich, R.; Hoareau, R.; Scott, P.J.H., *Curr. Top. Med. Chem.*, **2014**, *14*, 875.
Hamacher, K.; Coenen, H.H.; Stöcklin, G.; *J. Nuc. Med.*, **1986**, *27*, 235.

[^{18}F] FDG PET



Tracking Treatment Success

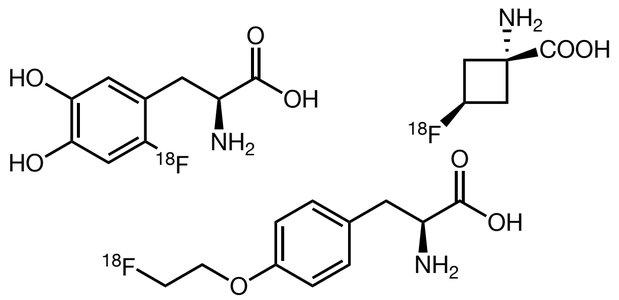


Decreased Glucose Metabolism in Crossed Cerebral Diaschisis (CCD)

Infective Coxitis

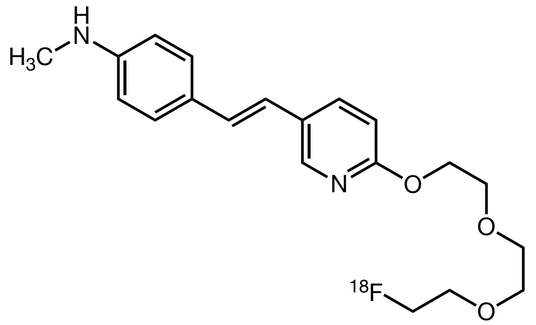
Irvani, A.; Hicks, R.J., *J. Nuc. Med.*, **2020**, *61*, 943.
Minoshima, S.; Cross, D.; Thientunzakit, T.; Foster, N.L.; Drezezga, A., *J. Nuc. Med.*, **2022**, *63*, 2S.
Weitzer, F.; Hooshmand, T.N.; Pernthaler, B.; Sorantin, E.; Aigner, R.M., *Sci. Rep.*, **2022**, *12*, 1883.

PET Tracers

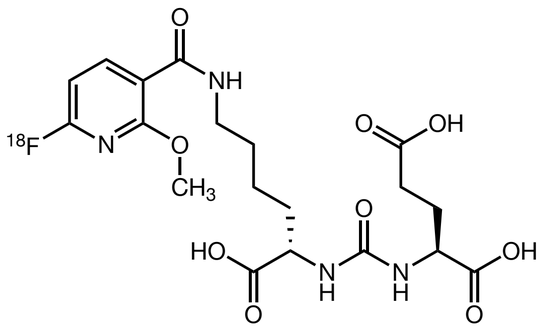


[18F] Amino Acid Derivatives

Mapping of Glioblastoma
Warburg Negative Cancer
Amyloid Plaques



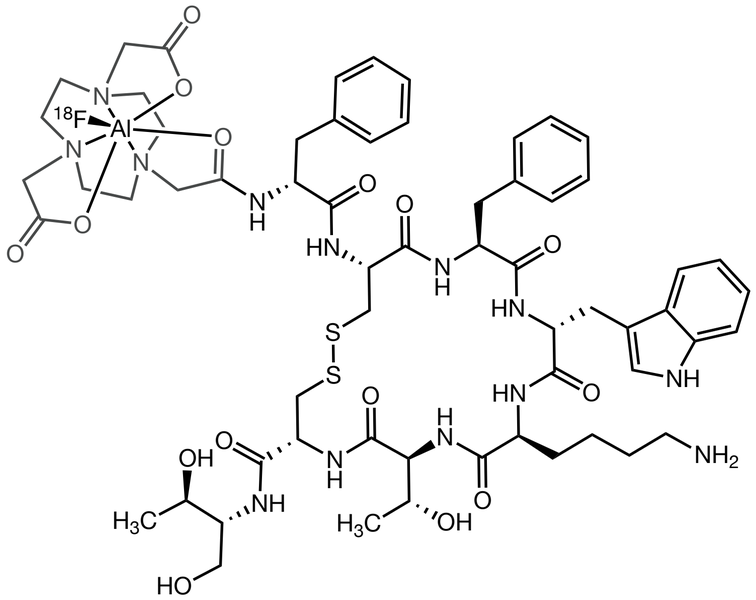
[18F] Florbetapir



[18F] JK-PSMA-7

Castration-resistant Prostate Cancer

Prostate Specific Membrane Antigen

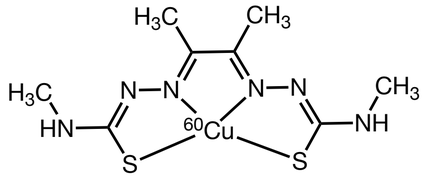


[18F] AlF-NOTA-Octreotide

SSTR2 Overexpressing Cancers

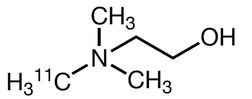
Zlatopolsky, B.D.; Endepols, H.; Krapf, P.; Guliyev, M.; Urusova, E.A.; Richarz, R.; Hohberg, M.; Dietlein, M.; Drzezga, A.; Neumaier, B., *J. Nuc. Med.*, **2019**, *60*, 817. (PSMA)
Rapp, M.; Heinzel, A.; Galldiks, N.; Stoffels, G.; Felsberg, J.; Ewelt, C.; Sabel, M.; Steiger, H.J.; Reifenberger, G.; Beez, T.; Coenen H.H.; Floeth, F.W.; Langen, K.-J., *J. Nuc. Med.* **2013**, *54*, 229. (FET)
Zaragori, T.; Ginet, M.; Marie, P.-Y.; Roch, V.; Grignon, R.; Gauchotte, G.; Rech, F.; Blonski, M.; Lamiral, Z.; Taillandier, L.; Imbert, L.; Verger, A., *EJNMMI Res.* **2020**, *10*, 56. (DOPA)
Archibald, S.J.; Allott, L., *EJNMMI Radiopharm. Chem,* **2021**, *6*, 30. (AlF-NOTA-Octreotide)
Wong, D.F.; Rosenberg, P.B.; Zhou, Y.; Kumar, A.; Raymont, V.; Ravert, H.T.; Dannals, R.F.; Nandi, A.; Brašić, J.R.; Ye, W.; Hilton, J.; Lyketsos, C.; Kung. H.F. Joshi, A.D.; Joshi, A.D.; Skovronsky, D.M.; Pontecorvo, M.J., *J. Nuc. Med.*, **2010**, *51*, 913. (Florbetapir)

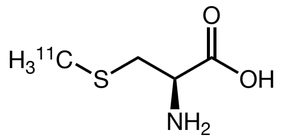
Other Elements as Positron Sources



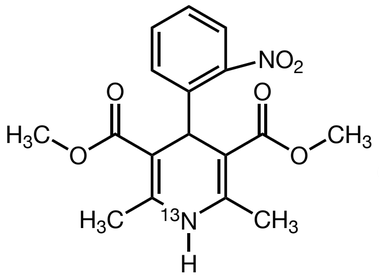
[^{60}Cu] Cu-ATSM

Hypoxic NSCLC





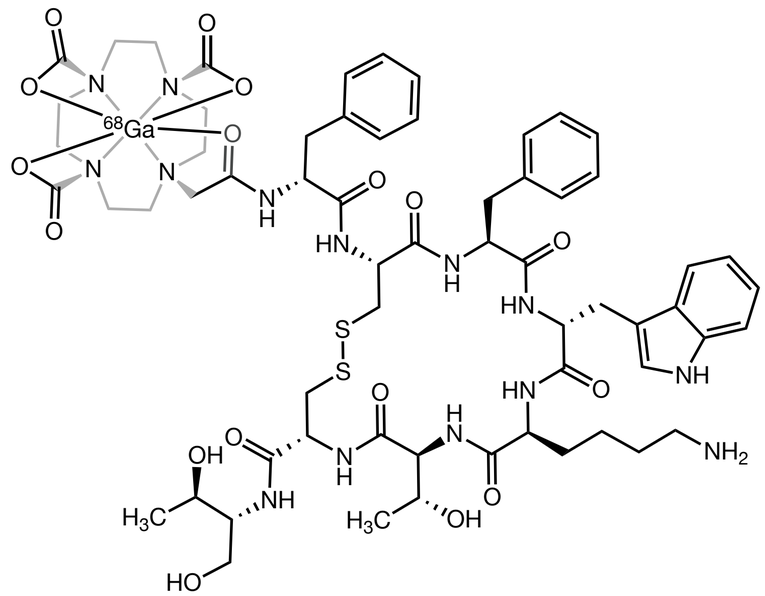
[^{11}C]-Choline & [^{11}C]-Methionine
e.g. Samnick, S. *Clin. Nuc. Med.* **2019**



[^{13}N]-Nifedipine
Gee, A. *Chem. Comm.* **2021**

[^{15}O]-O_2 [^{15}O]-H_2O
Wang, Y. *J. Cereb. Blood Flow Metab.* **2020**

Various Short Half Life Tracers

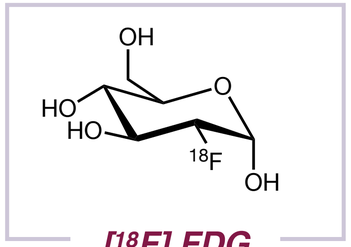


[^{68}Ga]-Ga-DOTATOC

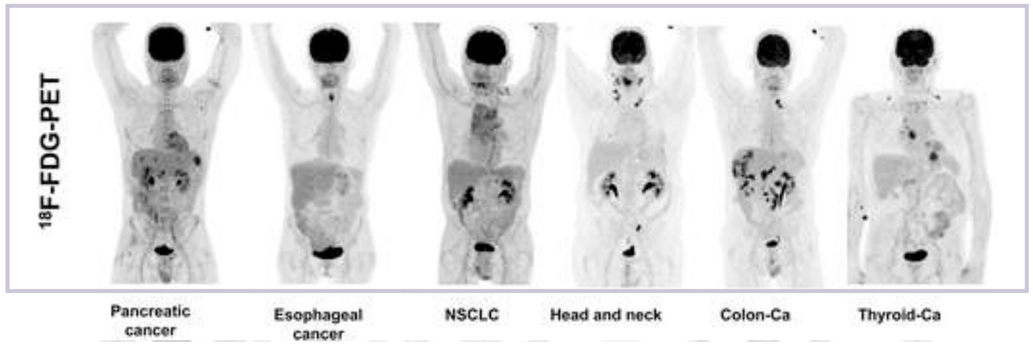
SSTR2 Overexpressing Cancers

Dehdashti, F.; Mintun, M.A.; Lewis, J.S.; Bradley, J.; Govindan, R.; Laforest, R.; Welch, M.J.; Siegel, B.A., *EJNMMI*, **2003**, *30*, 844. (Cu-ATSM)
Ullrich, M.; Richter, S.; Liers, J.; Drukewitz, S.; Friedemann, M.; Kotzerke, J.; Ziegler, C.G.; Nölting, S.; Kopka, K.; Pietzsch, J., *Theranostics,* **2023**, *13*, 278. (Ga-DOTATATE)

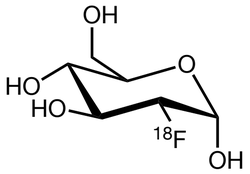
Current Trends in Nuclear Medical Diagnosis



[^{18}F] FDG



Mori, Y.; Dendl, K.; Cardinale, J.; Kratochwil, C.; Giesel, F.L.; Haberkorn, U., *Radiology*, **2023**, *306*, 2.



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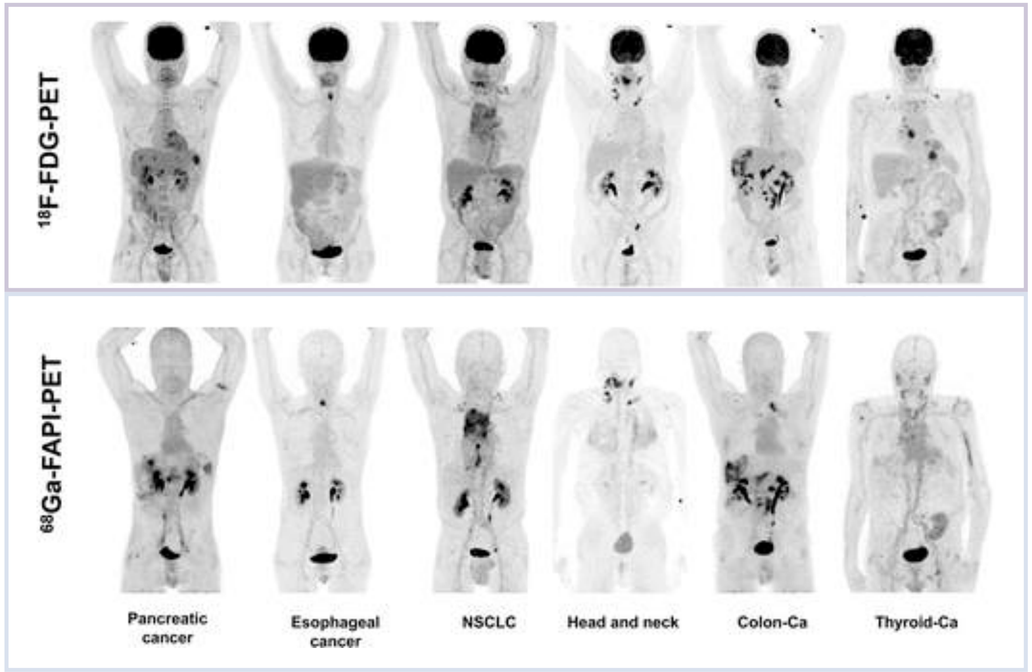
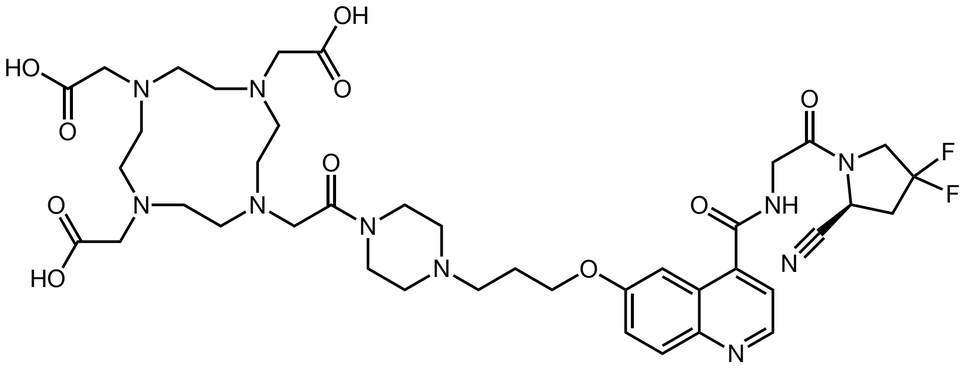
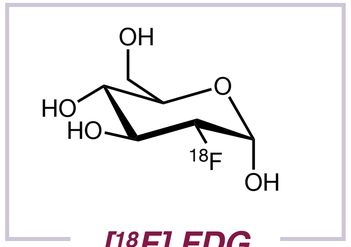




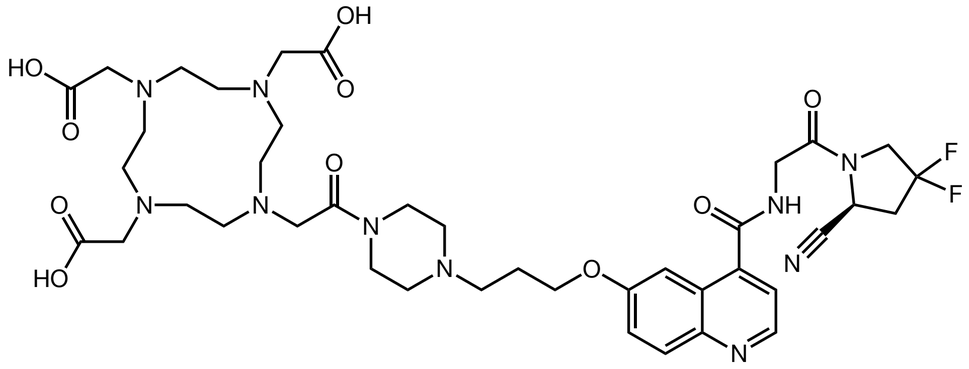
[^{68}Ga] Ga-DOTA-FAPI-4

Mori, Y.; Dendl, K.; Cardinale, J.; Kratochwil, C.; Giesel, F.L.; Haberkorn, U., *Radiology*, **2023**, *306*, 2.

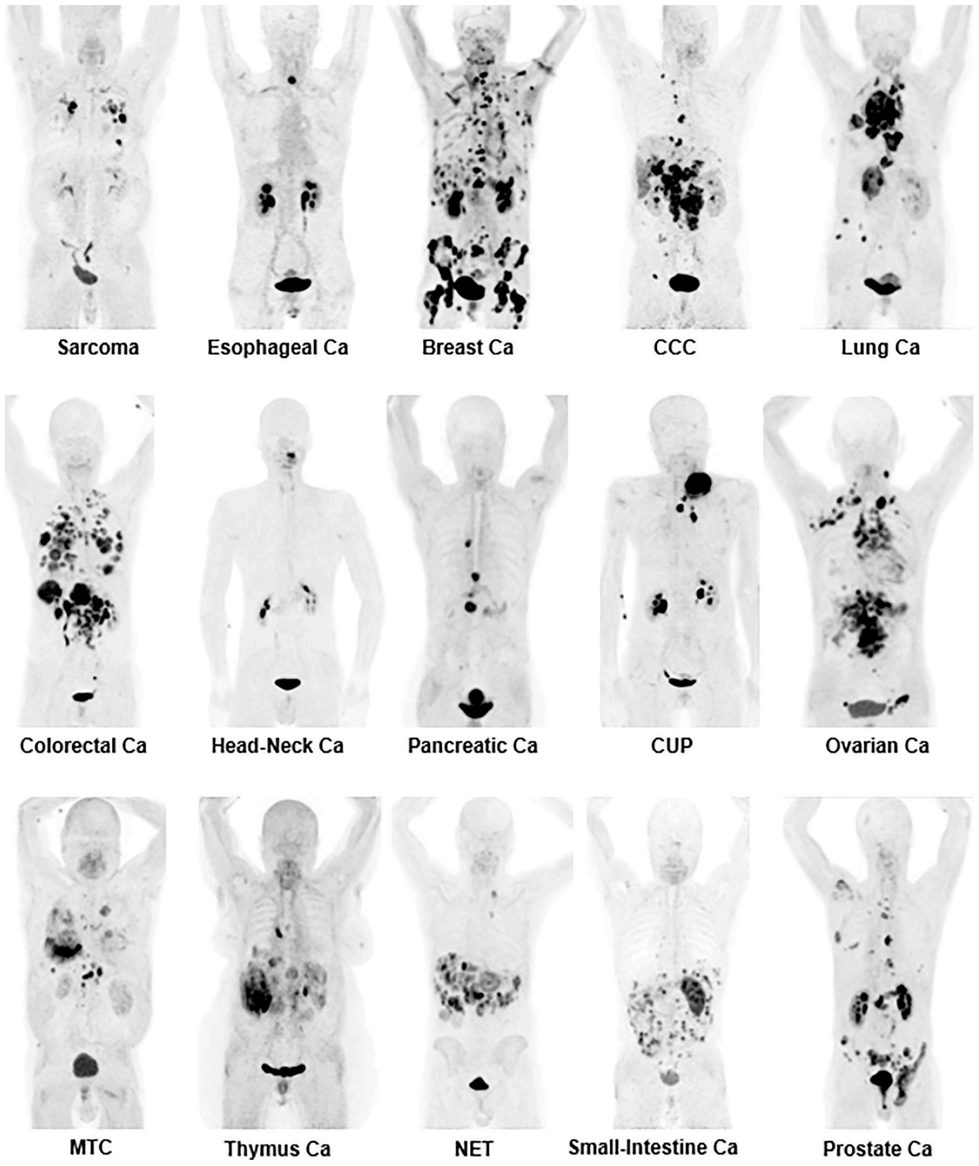
Current Trends in Nuclear Medical Diagnosis



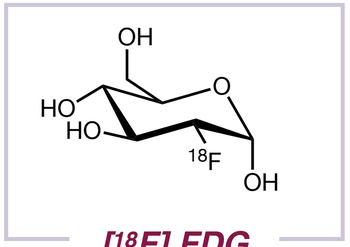
[^{18}F] FDG



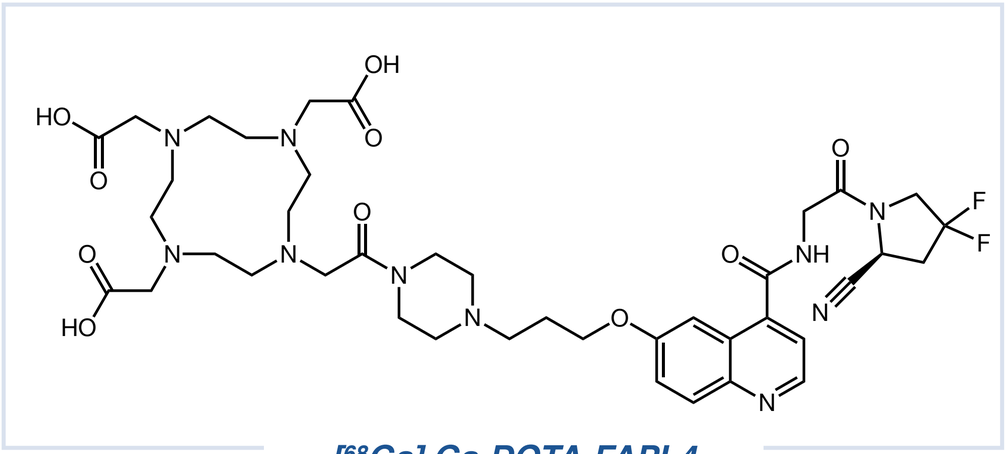
[^{68}Ga] Ga-DOTA-FAPI-4



Mori, Y.; Dendl, K.; Cardinale, J.; Kratochwil, C.; Giesel, F.L.; Haberkorn, U., *Radiology*, **2023**, *306*, 2.

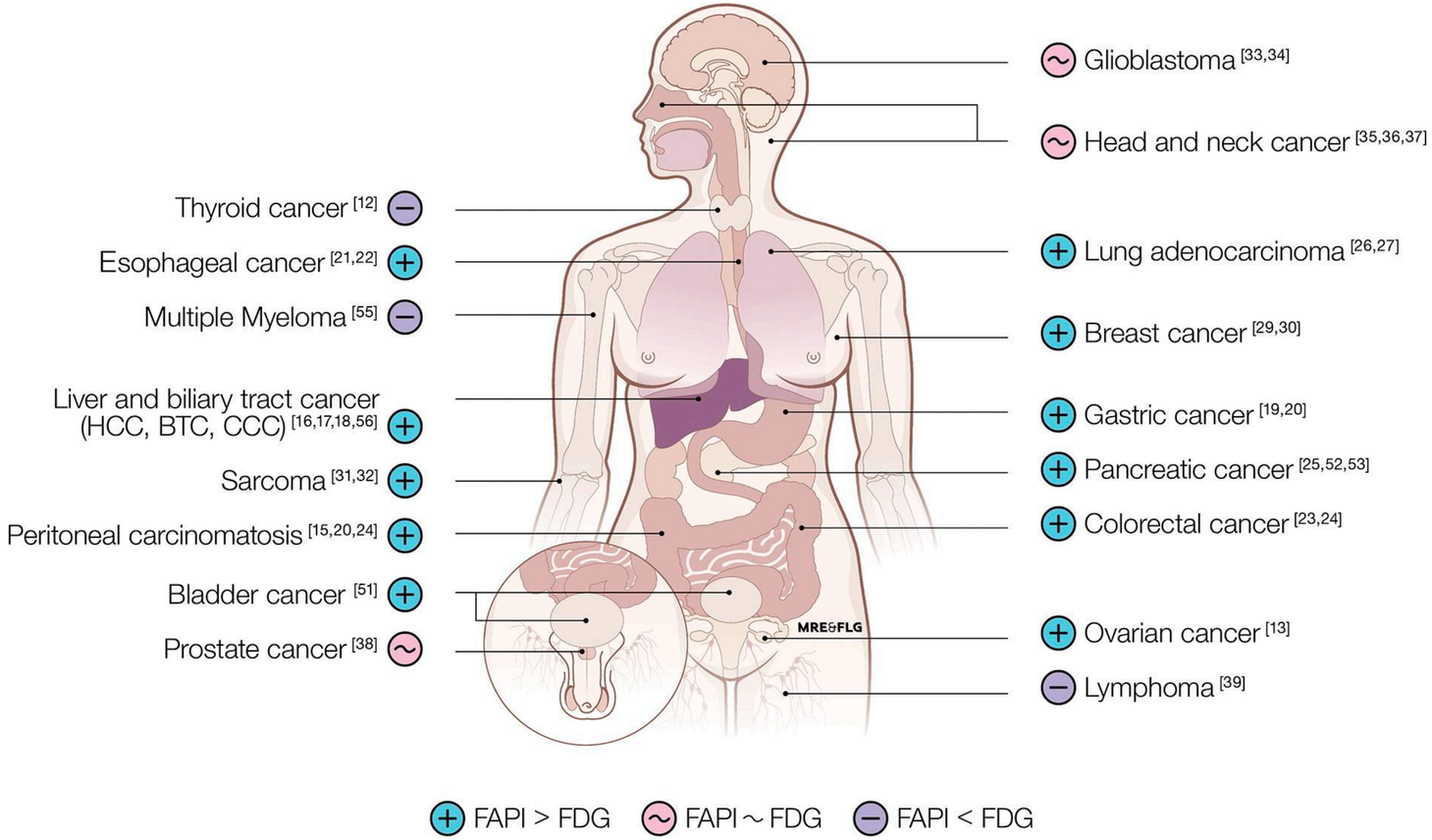


[^{18}F] FDG



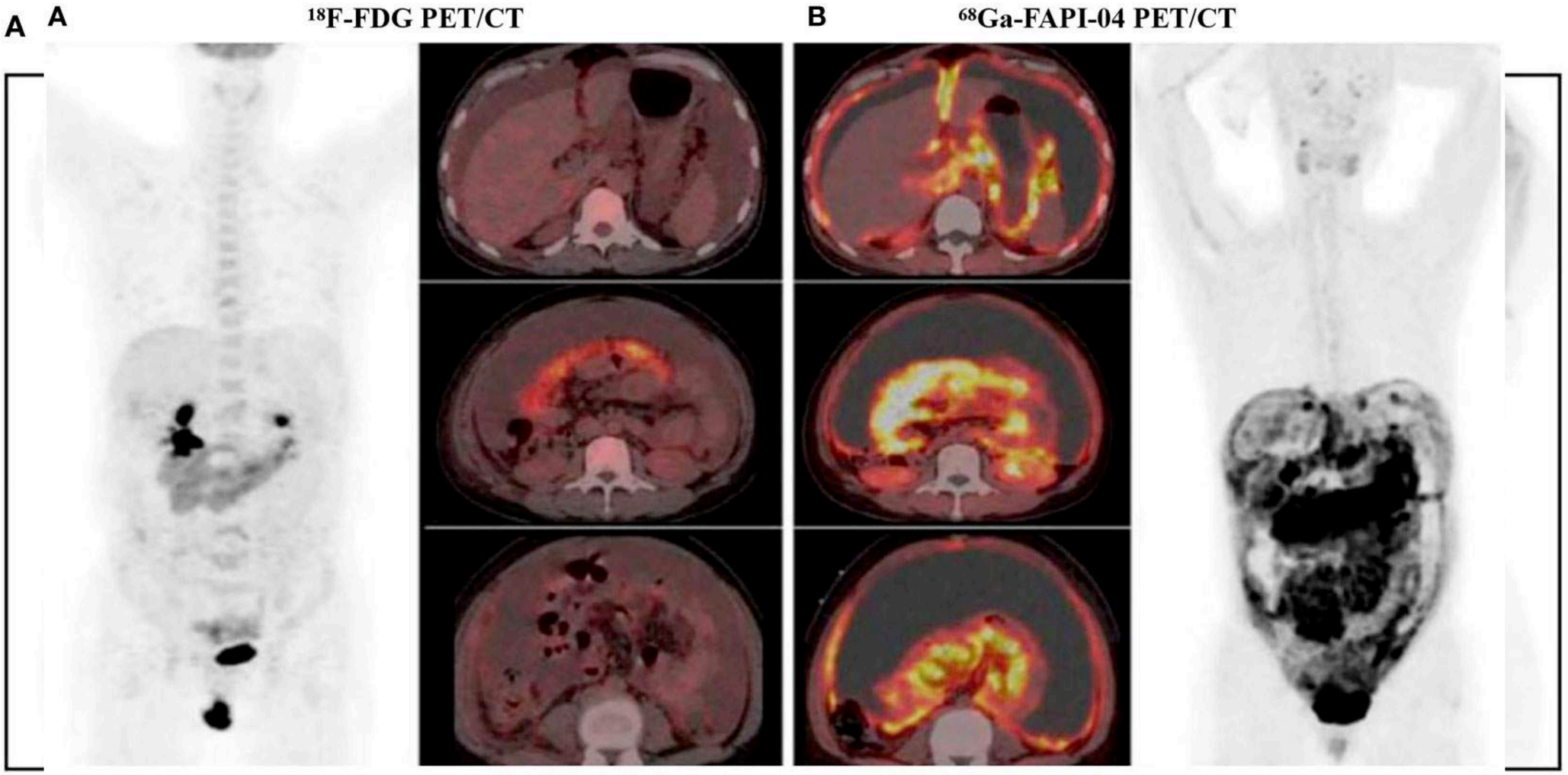
[^{68}Ga] Ga-DOTA-FAPI-4

Comparison of FAPI vs. FDG in oncological PET-imaging



Mori, Y.; Dendl, K.; Cardinale, J.; Kratochwil, C.; Giesel, F.L.; Haberkorn, U., *Radiology*, **2023**, *306*, 2.

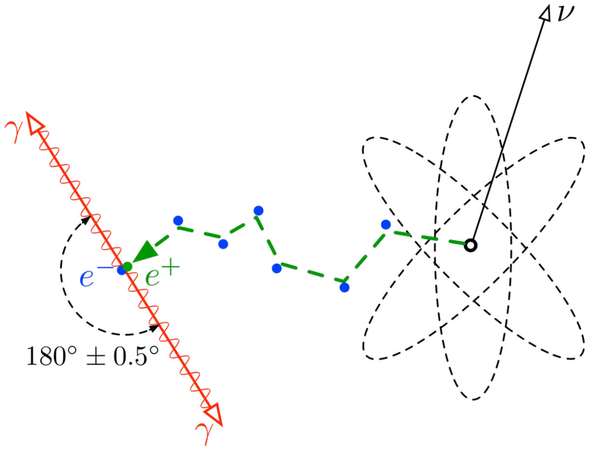
PET/CT



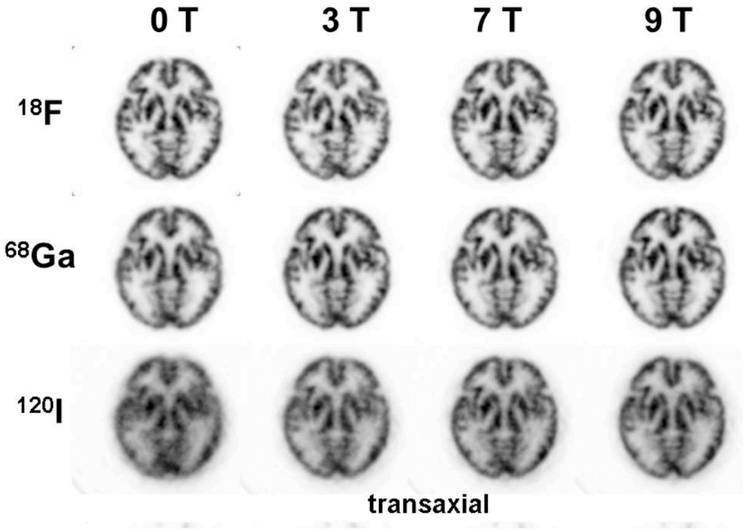
65-year old woman diagnosed with poorly differentiated gastric adenocarcinoma. 47-year old woman with pancreatic cancer.

Yang, T.; Ma, L.; Hou, H.; Gao, F.; Tao, W., *Front. Oncol.*, **2022**, *11*.

PET/MRI

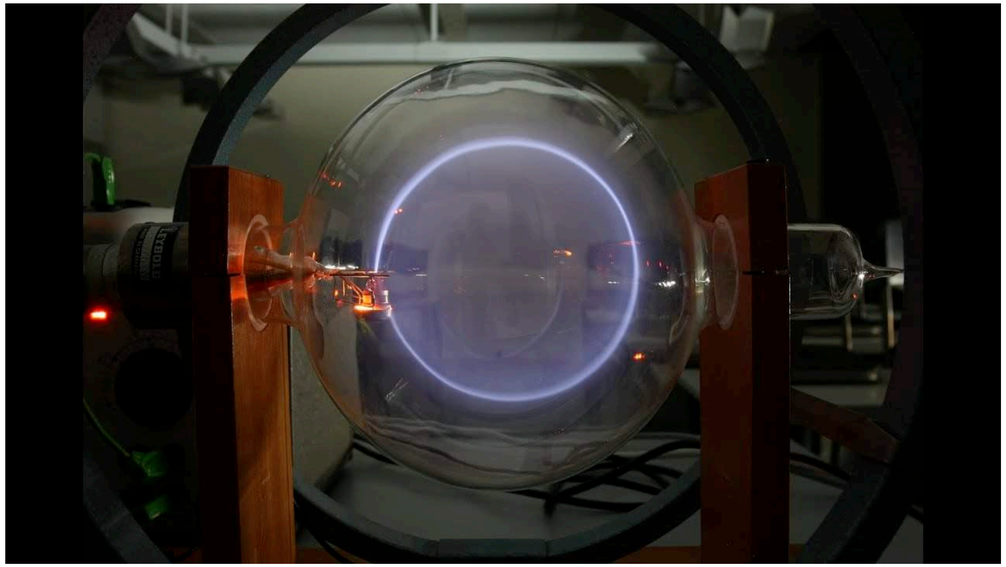


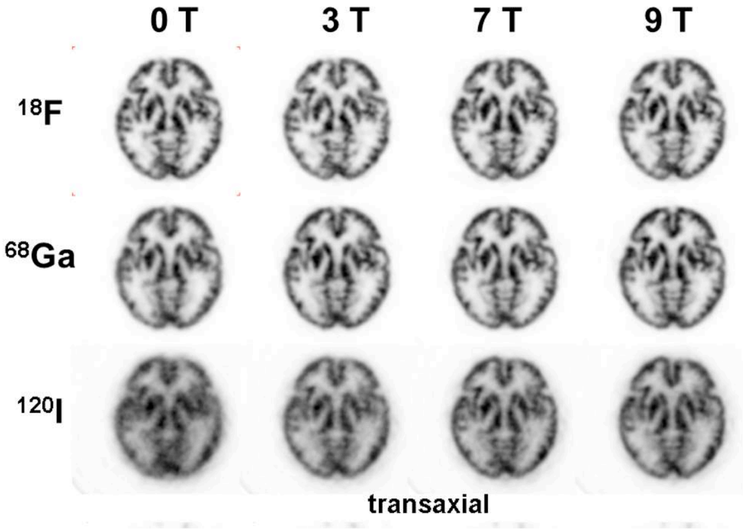
e^+ positron
e^- electron
ν neutrino
γ quantum/photon (511 keV)

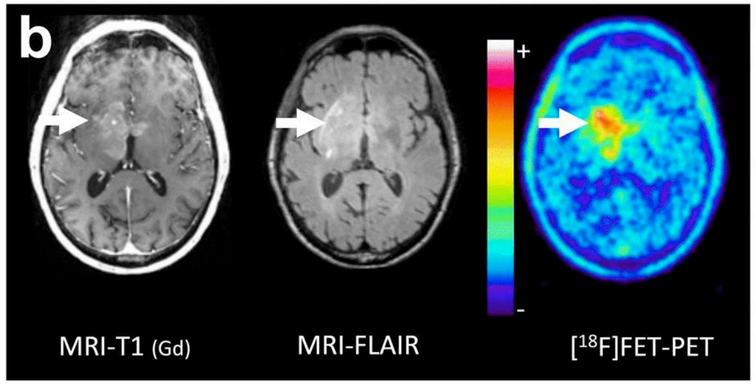


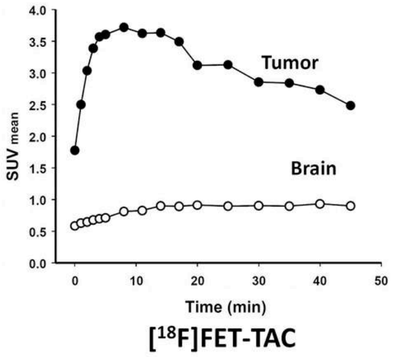
Shah, J.N.,; Herzog, H.; Weirich, C.; Tellmann, L.; Kaffanke, J.; Caldeira, L.; Rota Kops, E.; Qaim, S. M.; Coenen, H.H.; Iida, H., *PLOSOne*, **2014**, *11*.
Shymanskaya, A.; Worhoff, W.A.; Stoffels, G.; Lindemeyer, J.; Neumaier, B.; Lohmann, P.; Falldiks, N.; Langen, K.-J., Shah, N.J., *Mol. Imag. Biol.* **2020**, *22*, 198.

PET/MRI



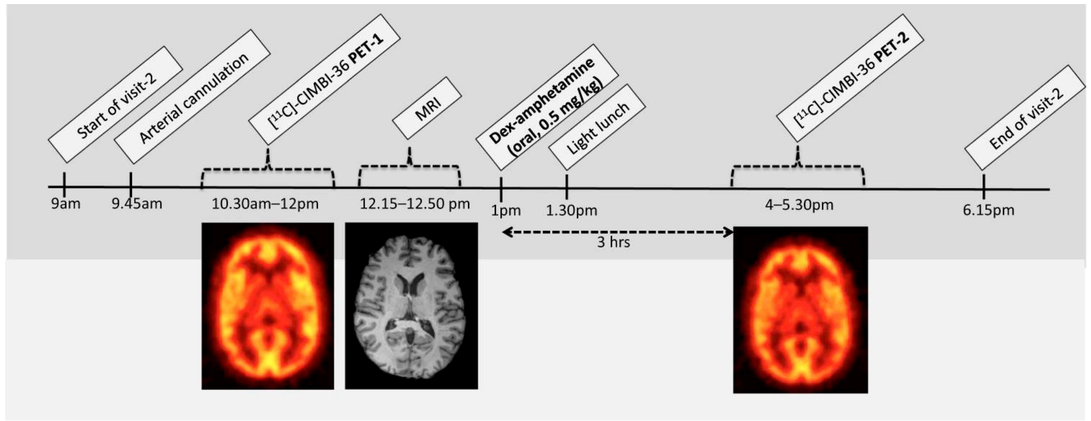




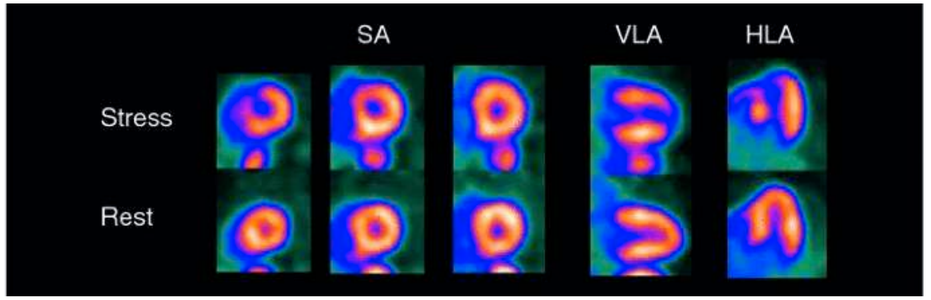


Shah, J.N.,; Herzog, H.; Weirich, C.; Tellmann, L.; Kaffanke, J.; Caldeira, L.; Rota Kops, E.; Qaim, S. M.; Coenen, H.H.; Iida, H., *PLOSOne*, **2014**, *11*.
Shymanskaya, A.; Worhoff, W.A.; Stoffels, G.; Lindemeyer, J.; Neumaier, B.; Lohmann, P.; Falldiks, N.; Langen, K.-J., Shah, N.J., *Mol. Imag. Biol.* **2020**, *22*, 198.

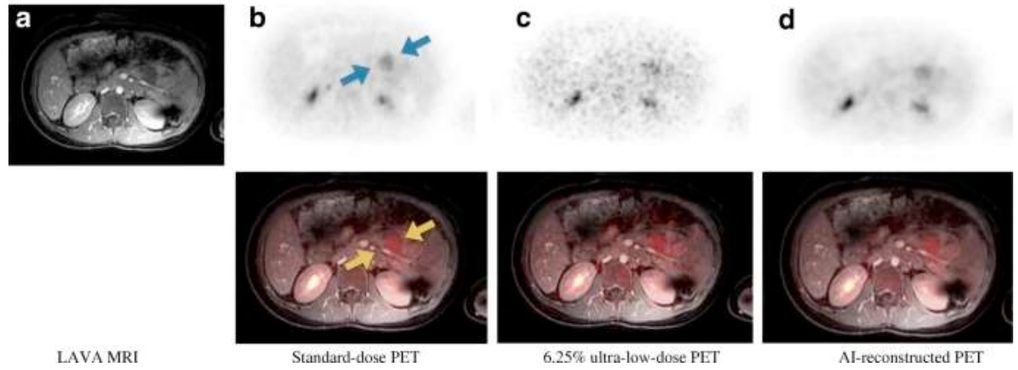
Beyond Traditional PET



Detection of Depression using [11C]2C-B and Amphetamine



Myocardial Perfusion Imaging using Rb-82



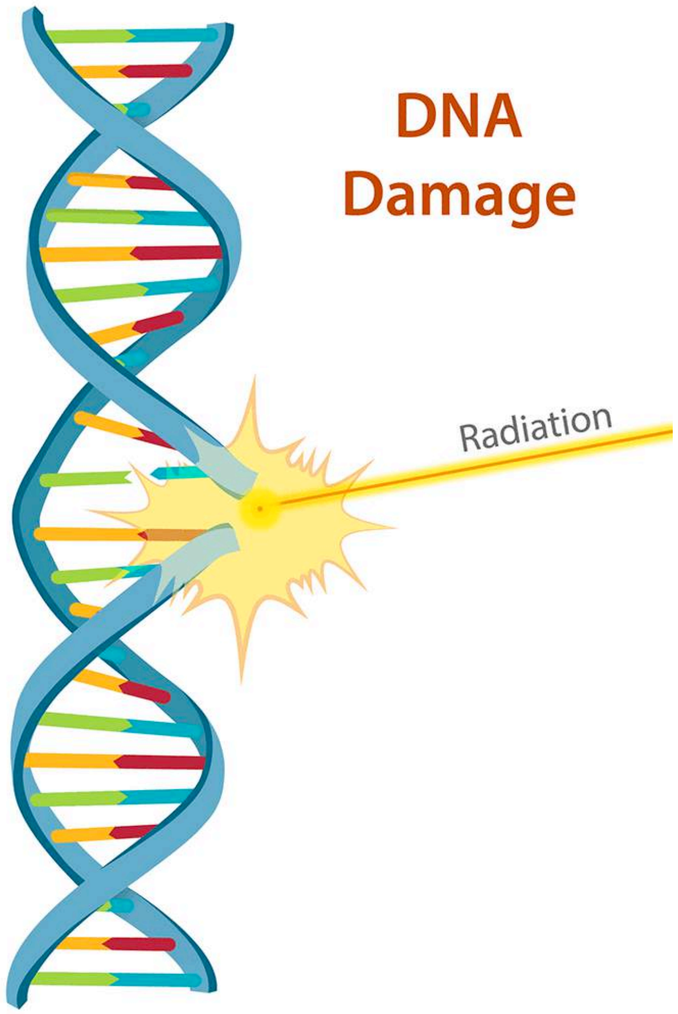
AI enhancement for Dose Reduction

Erritzoe, D.; Ashok, A.H.; Searle, G.E.; Colasanti, A.; Turton, S.; Lewis, Y.; Huiban, M.; Moz, S.; Passchier, J.; Saleem, A.; Beaver, J.; Lingford-Hughes, A.; Nutt, D.J.; Howes, O.D.; Gunn, R.N.; Knudsen G.M.; Rabiner, E.A., *Neuropsychophamacol.*, **2019**, *45,* 804. (Depression)

Wang, Y.-R.; Baratto, L.; Hawk, K.E.; Theruvath, A.J.; Pribnow, A.; Thakor, A.S.; Gatidis, S.; Lu, R.; Gummidipundi, S.E.; Garcia-Diaz, J.; Rubin, D.; Daldrup-Link, H.E., *EJNMMI*, **2021**, *48,* 2771. (AI)

Nakazato, R.; Berman, D.S.; Dez, D.; Le Meunier, L.; Hayes, S.W.; Fermin, J.S.; Cheng, V.Y.; Thomson, L.E.J.; Friedman, J.D.; Germano, G., Slomka, P.J., *J. Nuc. Cardiol.*, **2012**, *19*, 265.

Radiotherapy

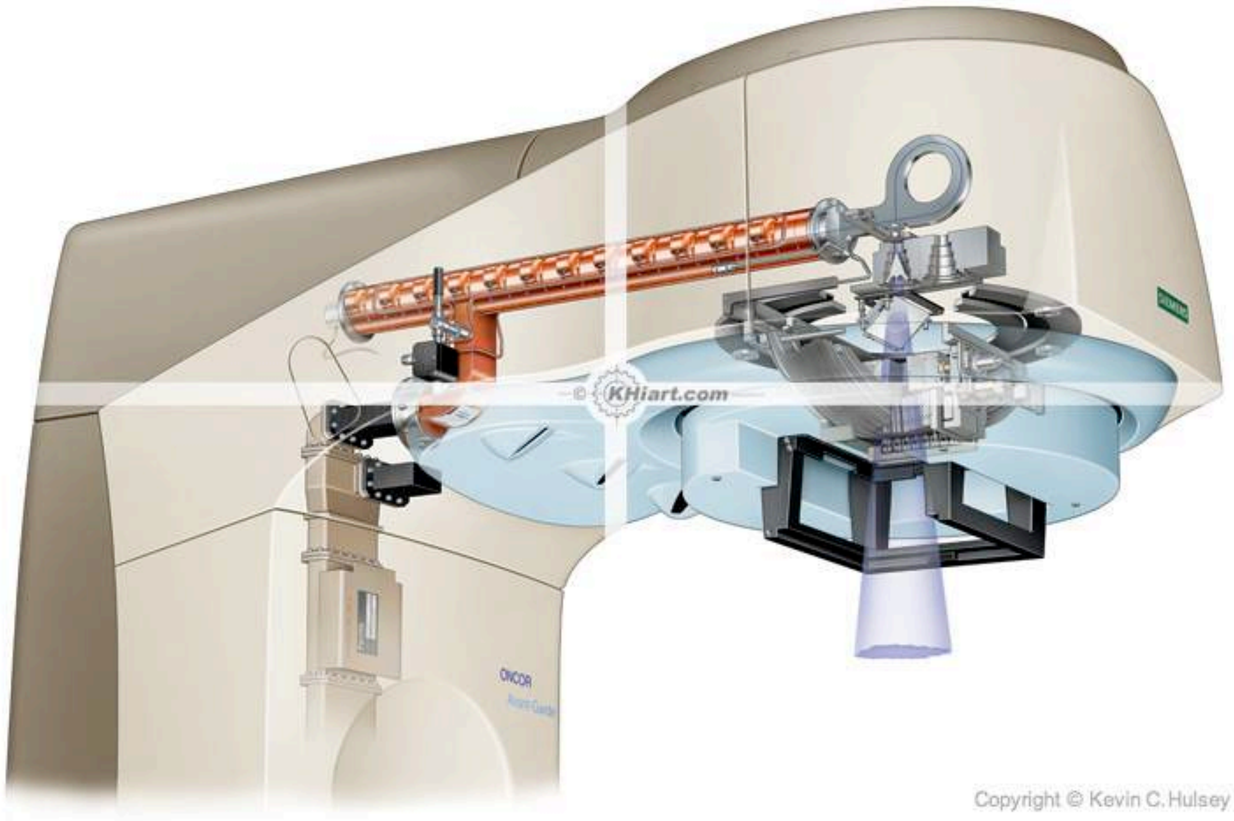


Use of Ionizing Radiation to Kill Cells

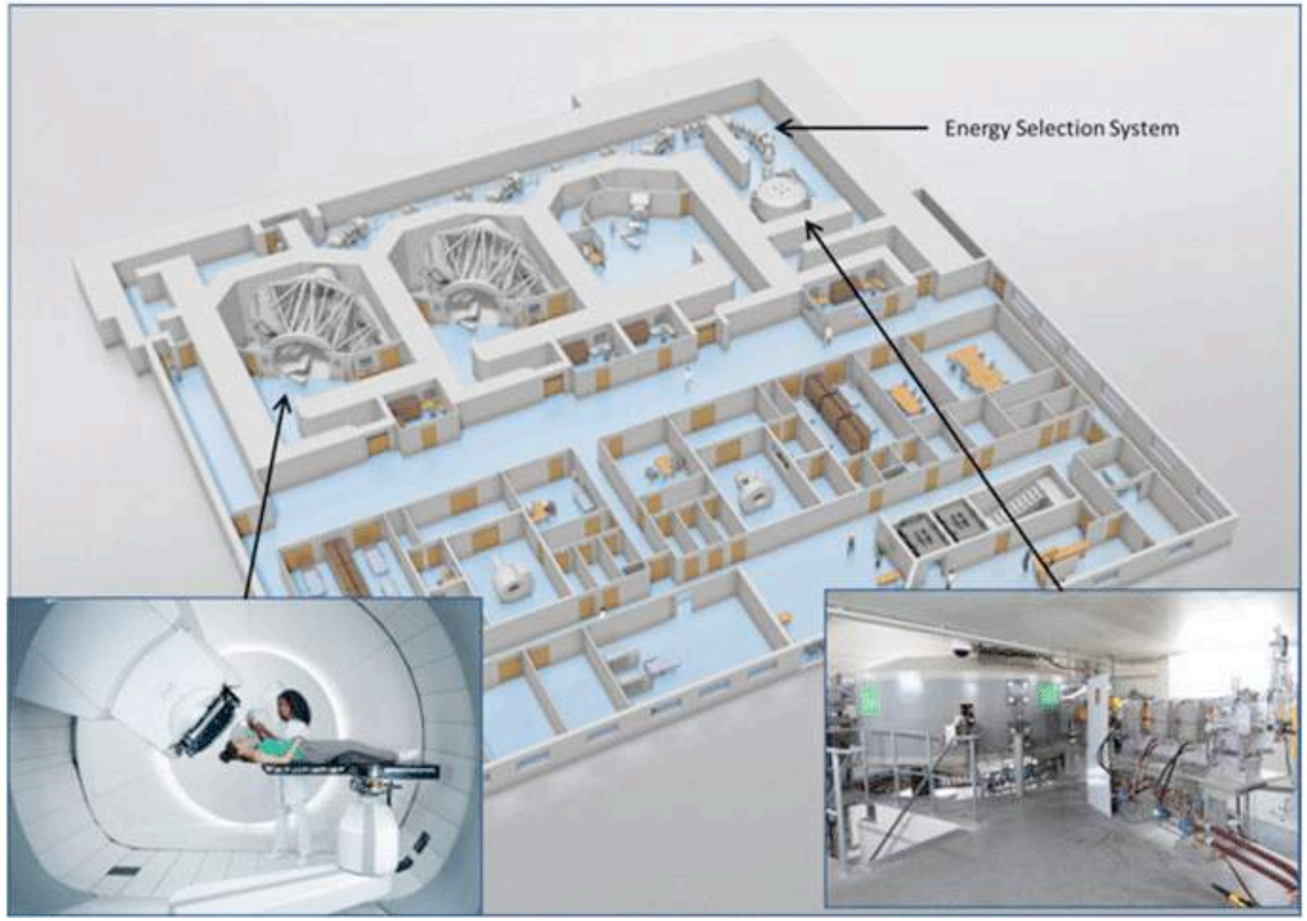
Internal and External Radiation

Not as 'Stand-alone' Technique

LINACs



Proton Therapy



The Nuclides

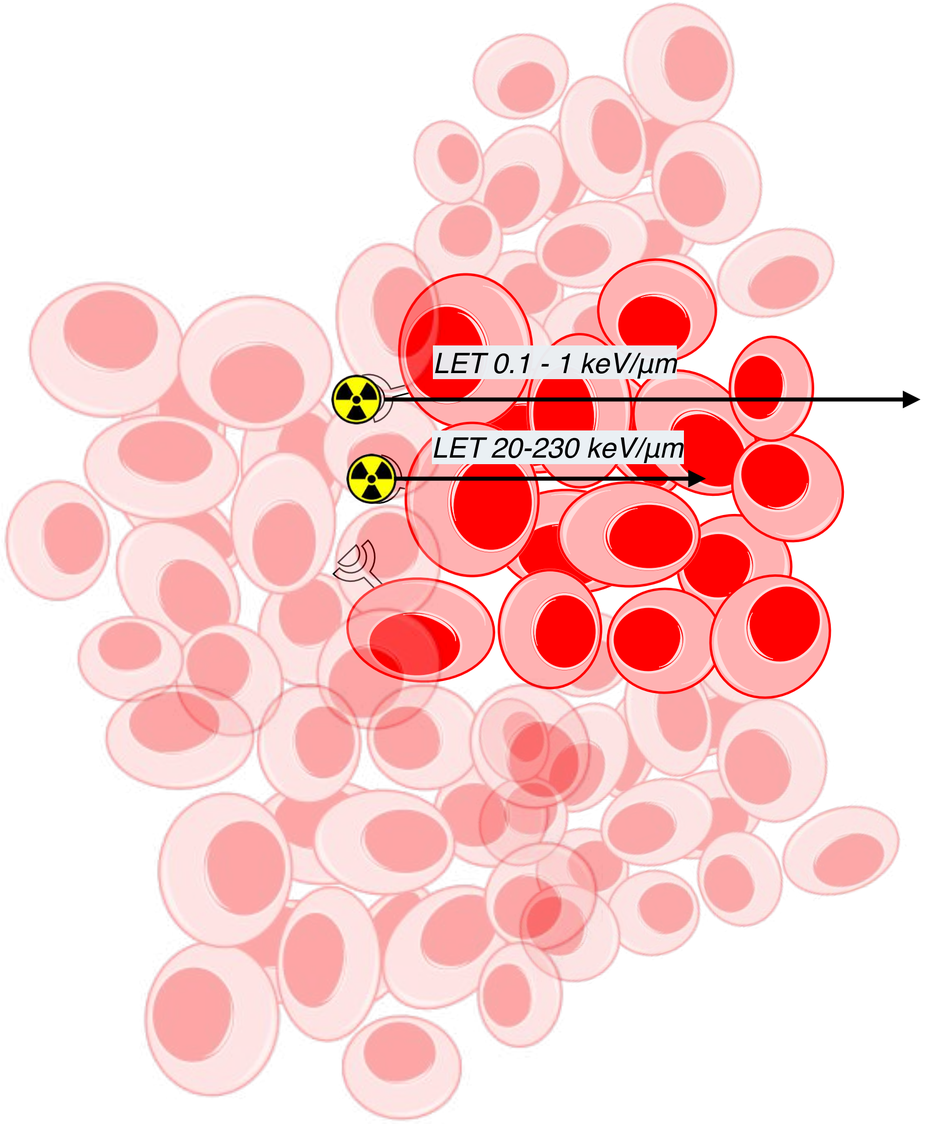
β^- decay

Nucleus	Nucleus	Nucleus	Nucleus
90Y	131I	177Lu	188Re
64.053 h	8.0252 d	6.647 d	17.003 h
β^- = 100.00%	β^- = 100.00%	β^- = 100.00%	β^- = 100.00%
E_{max} = 933 keV	E_{max} = 402 keV	E_{max} = 497 keV	E_{max} = 2120 keV

α decay

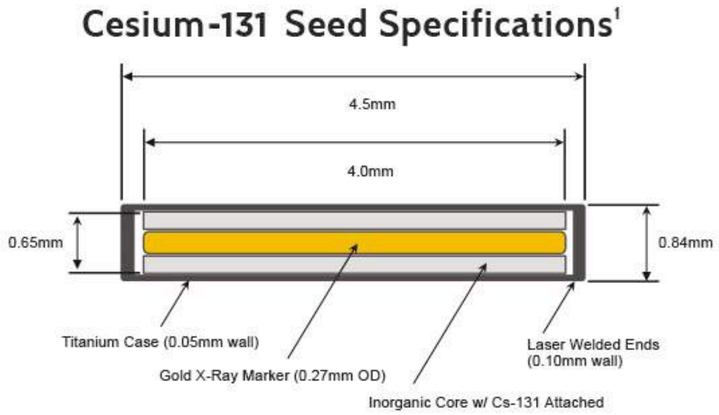
Nucleus	Nucleus	Nucleus	Nucleus
211At	223Ra	225Ac	227Th
7.214 h	11.43 d	9.920 d	18.697 d
ε = 58.20% α = 41.80%	α = 100.00% 14C = 8.9E-8%	α = 100.00% 14C = 4E-12%	α = 100.00%
E = 2.50 MeV	E = 5.78 MeV	E = 5.86 MeV	E = 6.01 MeV

Very specialized chemistry in development



Ku, A.; Facca, V.J.; Cai, Z.; Reilly, R.M., *EJNMMI Radiopharm. Chem.*, **2019**, *4, 27.*

Brachytherapy

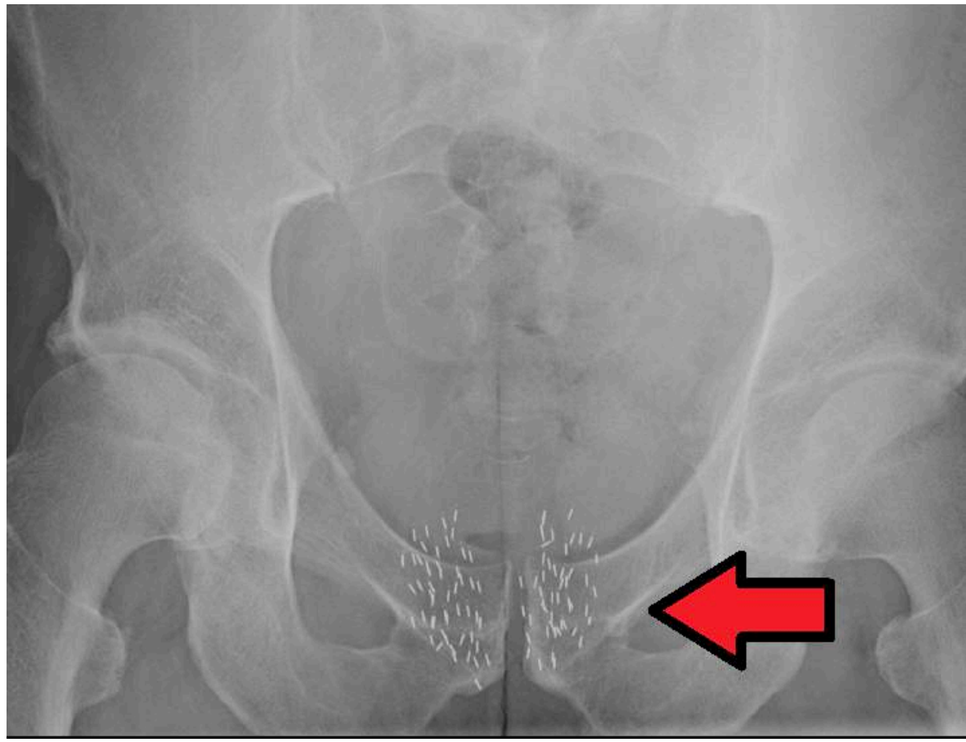


isoray™
BEYOND YOUR CANCER

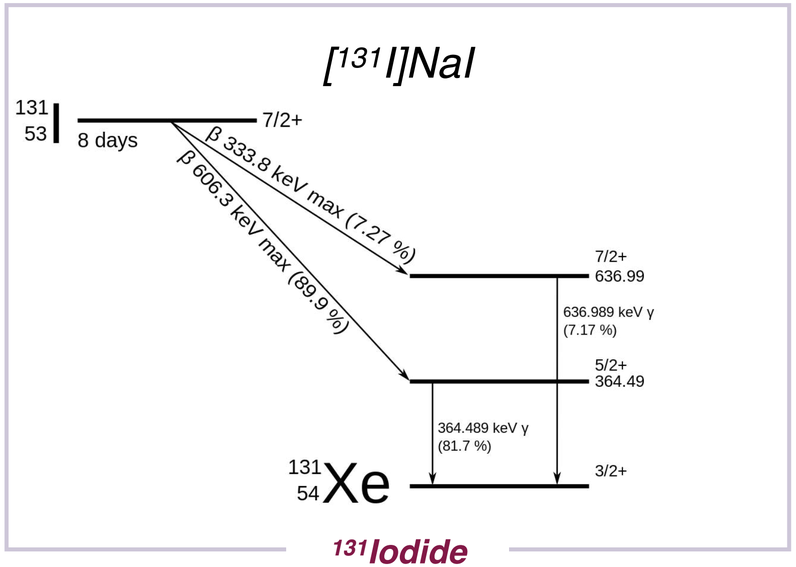
$^{131}Xe(p,n)^{131}Cs$

$t_{1/2} = 9.7\ d$

$E_{mean} = 30.4\ keV$



Radioiodine

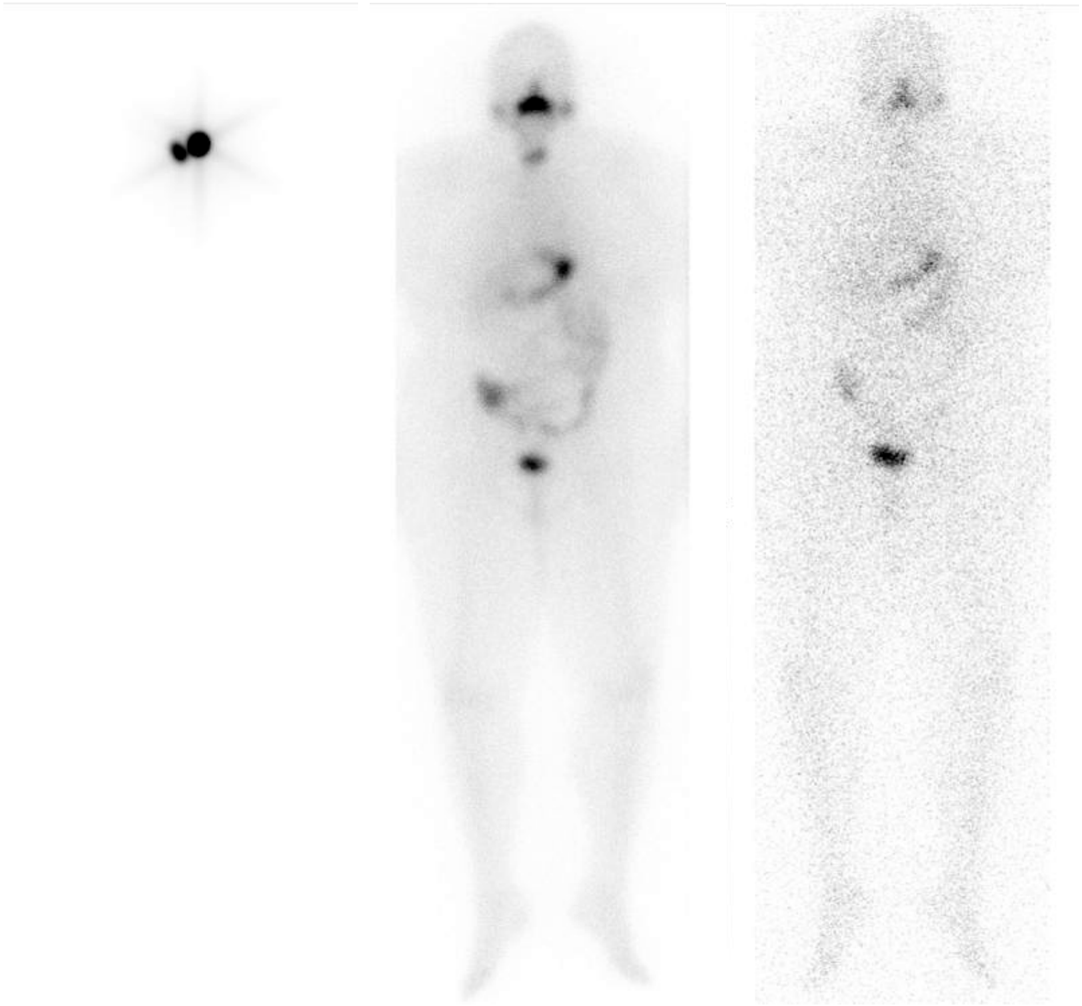


^{131}Iodide

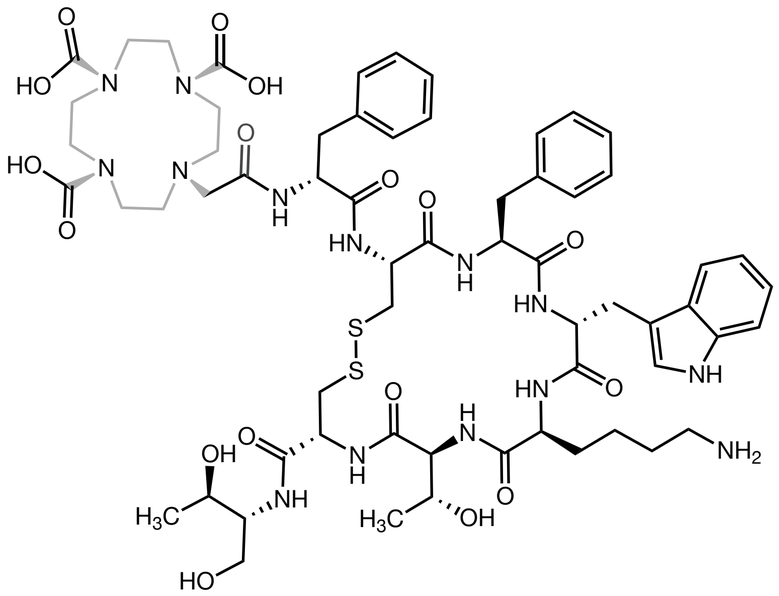
Grave's Disease, Thyroid Cancer and Goitre

Theranostic Isotope

Germany: 120 Facilities, 50,000 patients annually



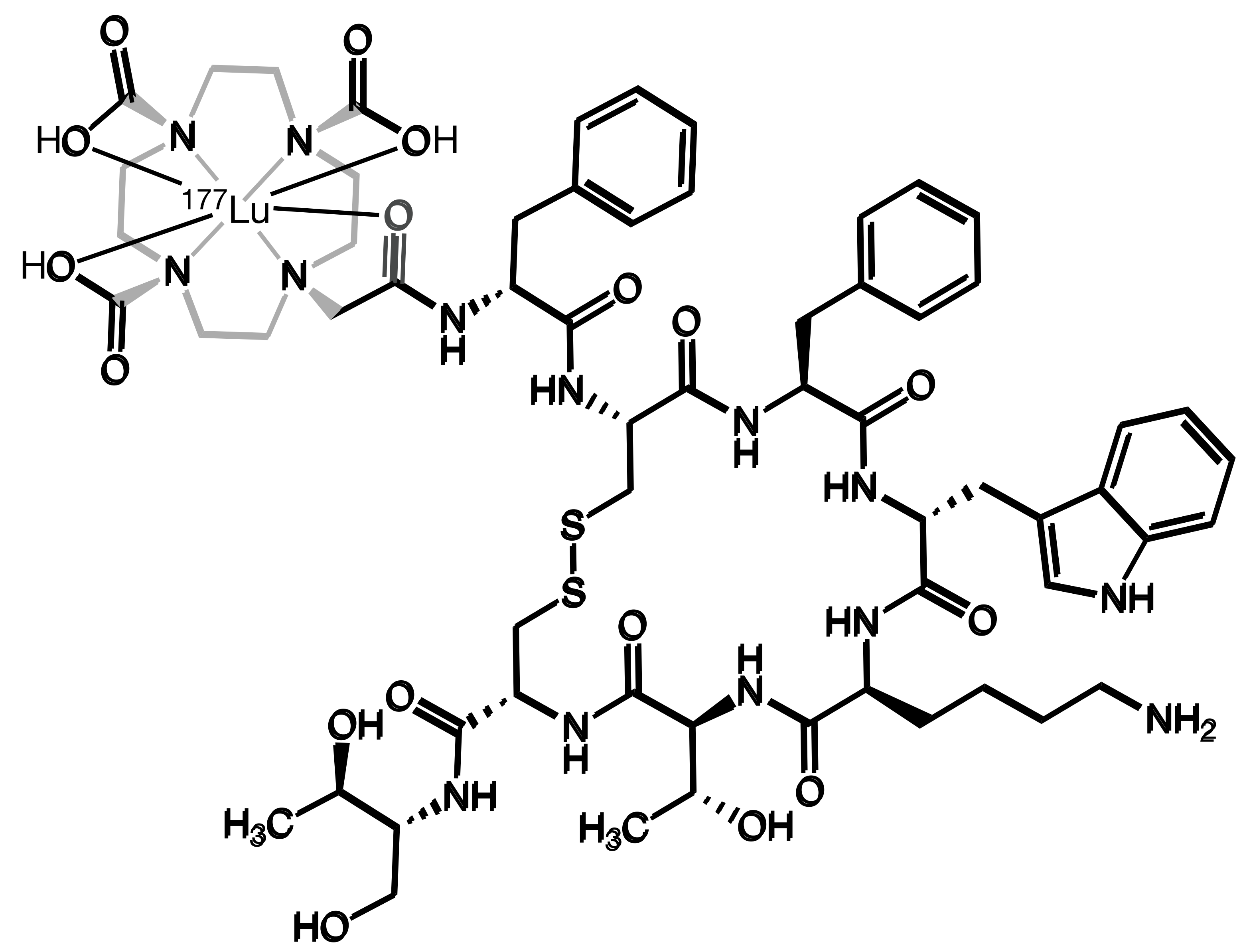
Fullbody scintigraphy of a patient with thyroid cancer.
First and Second treatments with 3.7 GBq ^{131}I, 370 MBq ^{131}I in last for Scintigraphy



Octreotide

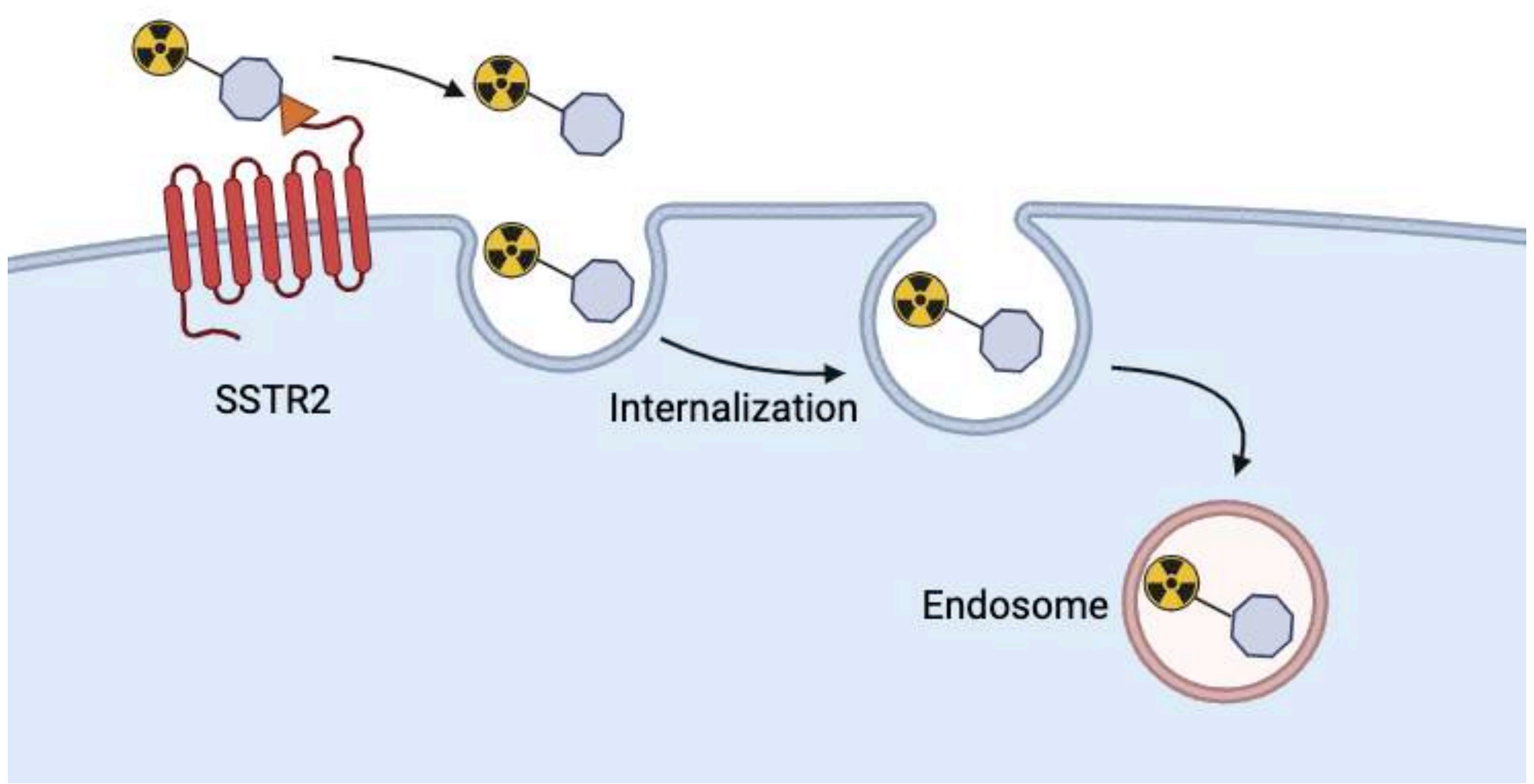
Henrich, U.; Kopka, K., *Pharmaceuticals*, **2019**, *12,* 114.

Radioligand and Radioimmuno Therapy



[^{177}Lu]Lutathera

Somastostatin Receptor (SSTR2) positive gastroenteropancreatic neuroendocrine tumors

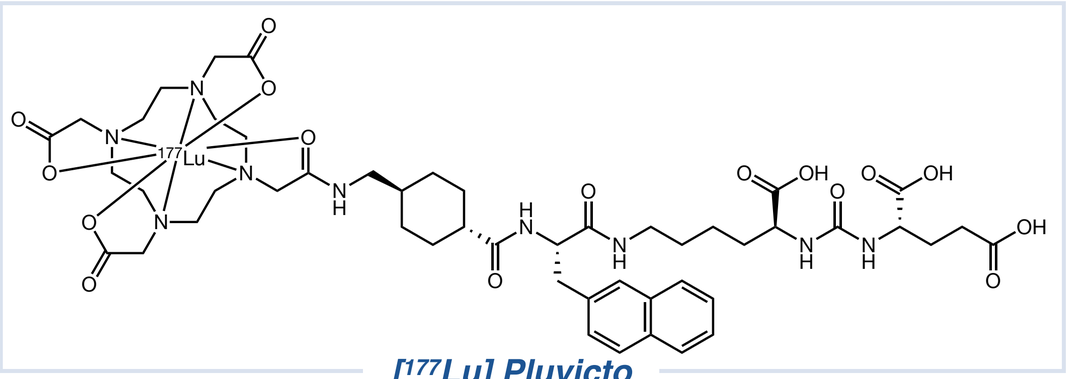


7.4 GBq ^{177}Lu per Treatment

No pharmacodynamical effects expected

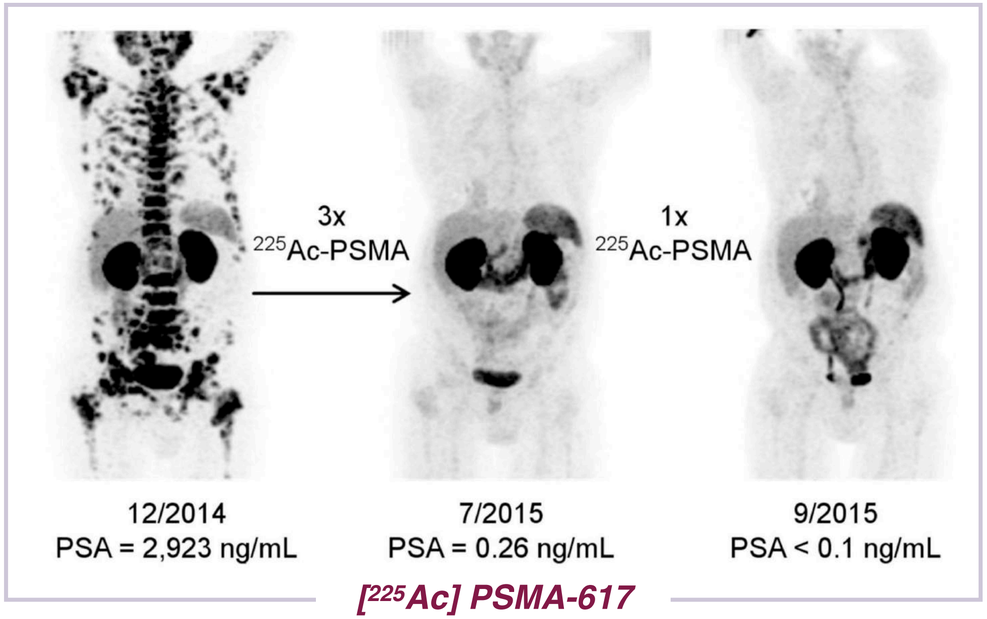
Henrich, U.; Kopka, K., *Pharmaceuticals*, **2019**, *12,* 114.

Current Trends in Industry

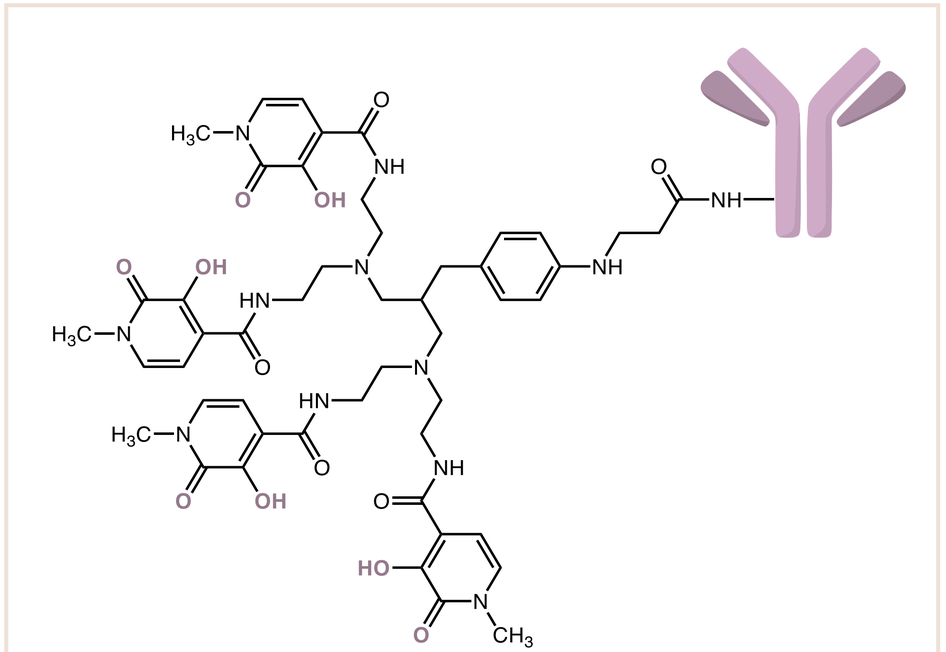


[177Lu] Pluvicto

mCRPC treatment
451 m$ H1, 2023

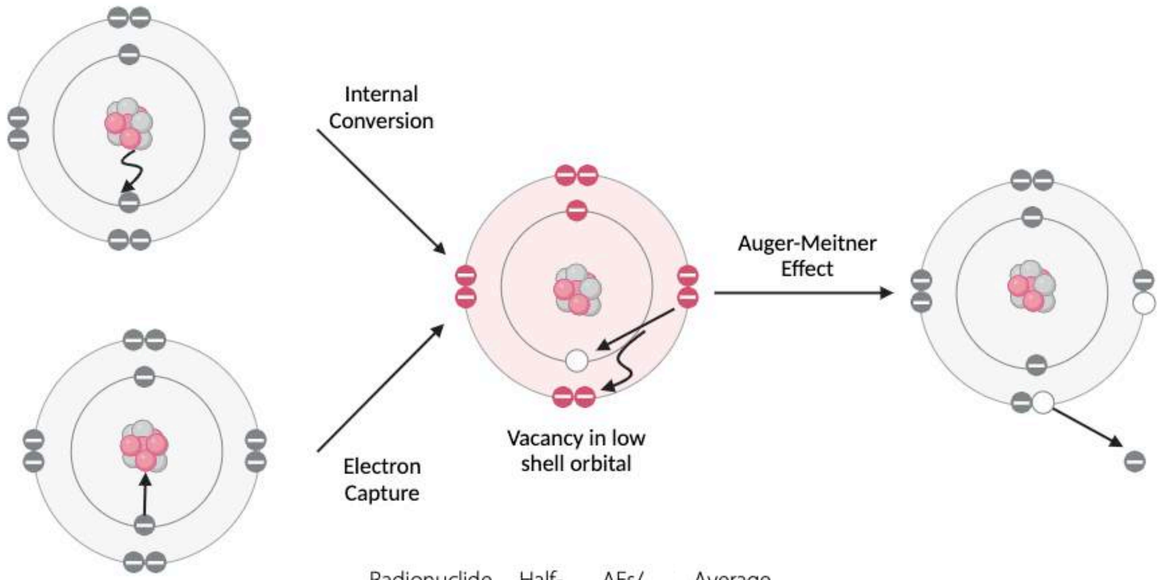


[225Ac] PSMA-617

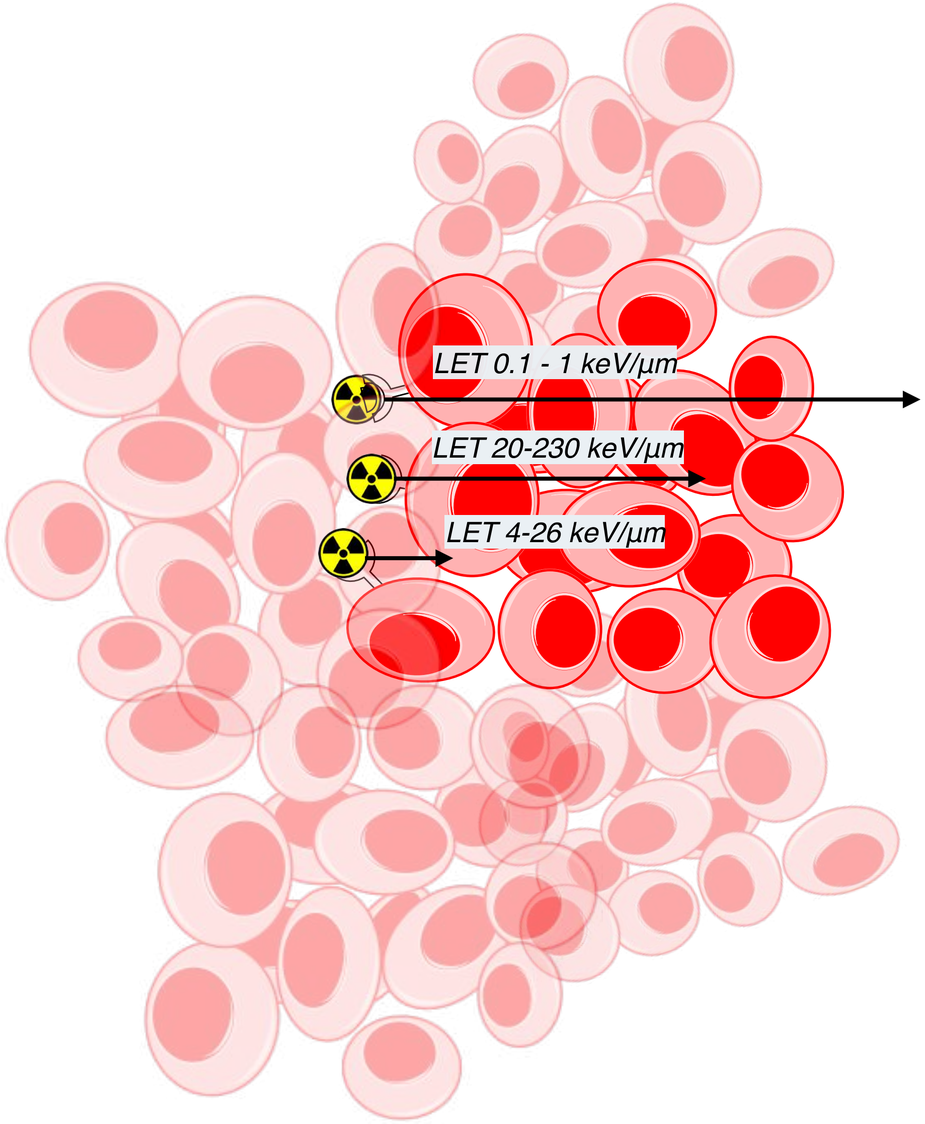


BAY2315497 - 227Th Conjugate

Upcoming Targets for future Early Career Scientists - AMER

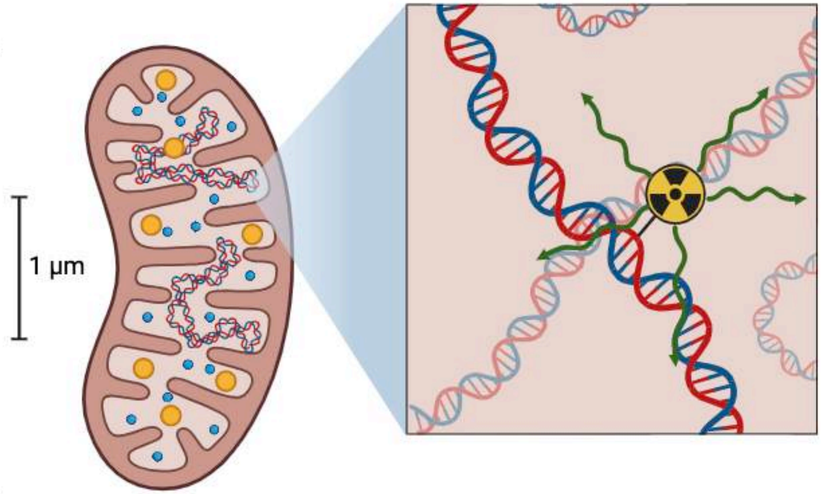


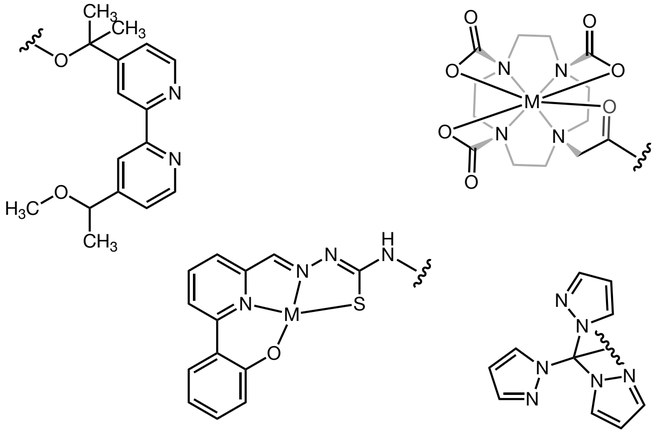
Radionuclide	Half-life	AEs/decay	Average energy per AE (keV)
^{125}I	57 d	23.0	0.5
^{123}I	13 h	13.7	0.5
^{67}Ga	78 h	5.0	1.3
^{99m}Tc	6 h	4.4	0.2
^{111}In	67 h	7.4	0.9
^{201}Tl	73 h	20.9	0.7
^{191}Pt	2.8 d	14	1.3
^{193m}Pt	4.3 d	27.4	0.4
^{195m}Pt	4.0 d	36.6	0.6
^{197}Hg	64.1 h	23.2	0.7
^{197m}Hg	23.8 h	19.4	0.7



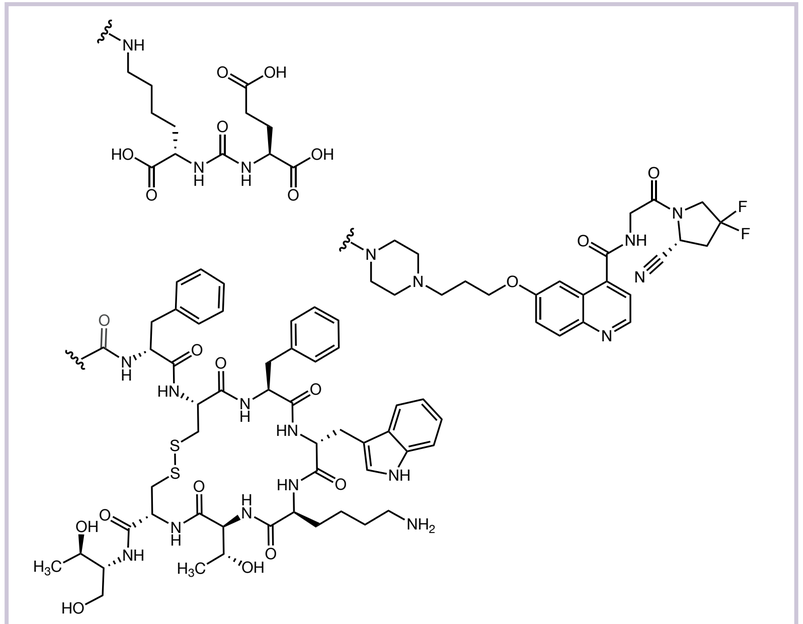
Ku, A.; Facca, V.J.; Cai, Z.; Reilly, R.M., *EJNMMI Radiopharm. Chem.*, **2019**, *4, 27.*

Upcoming Targets for future Early Career Scientists - AMER





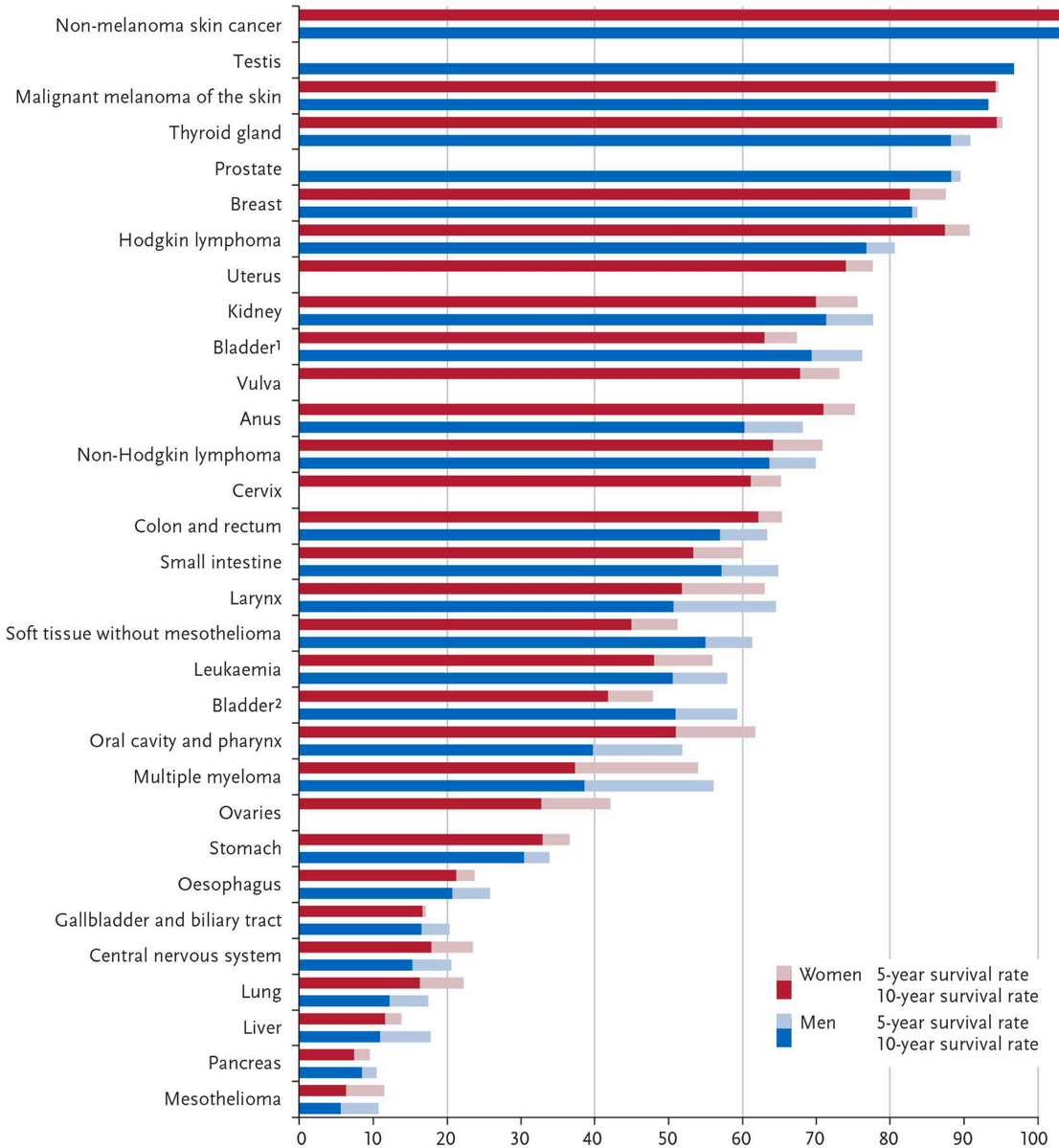
Ligands



Vectors

Upcoming Targets for future Early Career Scientists - Gender

Relative 5-/10-year survival rates, by tumour site and sex, Germany 2017–2018 (period analysis)



[1] including in situ tumours and neoplasms of uncertain or unknown behavior (D09.9, D41.4)
[2] malignant forms only (C67)

Upcoming Targets for future Early Career Scientists - Gender

Figure 3.12.7
International comparison of age-standardised incidence and mortality rates by sex, ICD-10 C33–C34, 2017–2018 or latest available year (details and sources, see appendix)
per 100,000 (old European Standard)

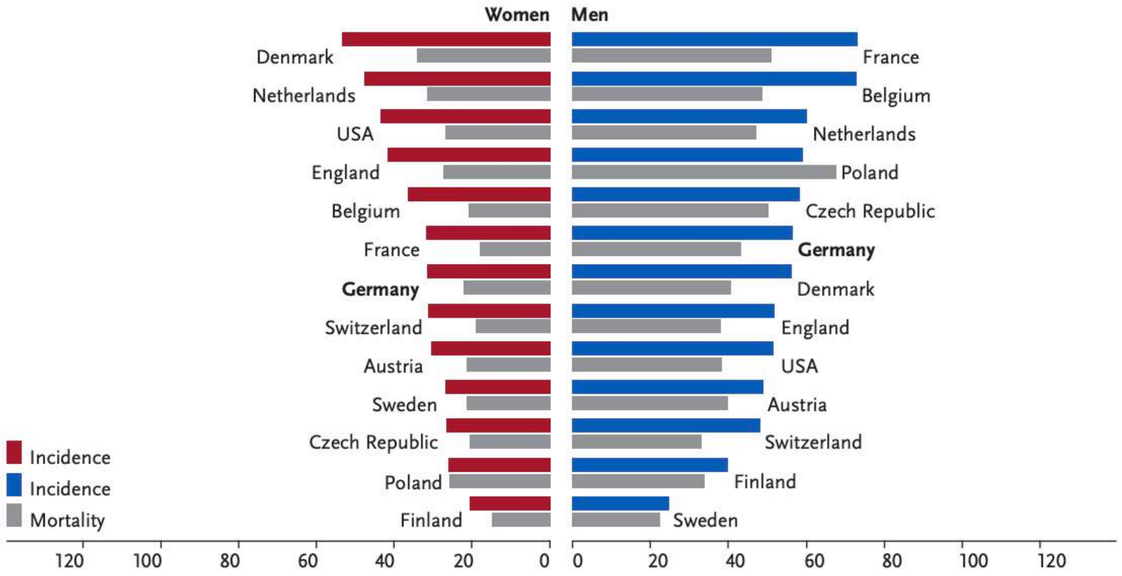
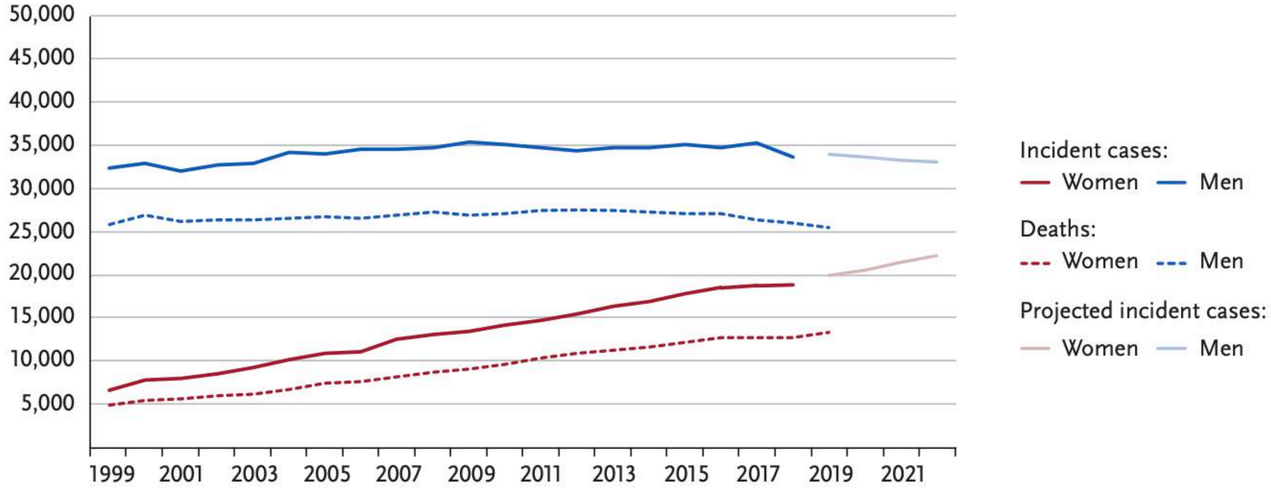


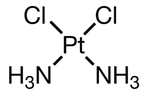
Figure 3.12.1b
Absolute numbers of incident cases and deaths by sex, ICD-10 C33–C34, Germany 1999–2018/2019, projection (incidence) through 2022



Kim, H.I.; Lim, H.; Moon, A., *Biomol. Ther.*, **2018**, *16,* 335.
German Cancer Registry of the Robert Koch Institute, Source: Krebsdaten.de

Upcoming Targets for future Early Career Scientists - Gender

cis-Platinum



Higher Toxicity for Females incl. more vomiting and nausea

Male Rats showed slower motor nerve conduction

IC_{50} in male cell lines lower than in female cell lines

Rituximab

Higher Clearance rate in Males

Better Treatment Response in Females

Male patients had a worse progression-free survival than females (diffuse Large B-Cell Lymphoma and follicular Lymphoma)

Kim, H.I.; Lim, H.; Moon, A., *Biomol. Ther.*, **2018**, *16,* 335.
German Cancer Registry of the Robert Koch Institute, Source: Krebsdaten.de

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Are there any Questions?

Mass Defect

Single Atom Chemistry

Heavy Atom Therapy

Neutron Therapy

Boron-Neutron-Capture Therapy

Magical numbers

Fission Fragmentation

Nuclear Reactors

Three Mile island (i mean its close)

Natural nuclear reactors (Oklo, Nuclear Explosions on Mars)

Helium 3 vs Helium 4

Laser Enrichment

Chemical/Physical Separation (PUREX)

Goiâna Incident (Cs source stolen)

Virtual Photons (Kasimir Effect)

Atomic Batteries

Ruthenium is in the air…

Radium Girls

Banana Equivalent Dose

Cloud Chamber