Ecole Joliot Curie 20224

Innovative radioisotopes

PRISMA

Physics of Radiation InteractionS with Matter and Applications

Subatech
Unité Mixte de Recherche 6457
Laboratoire de physique subatomique et des technologies associées

IMT Atlantique
Bretagne-Pays de la Loire
École Mines-Télécom

cnrs

Nantes Université

Ecole Joliot Curie 20224

Innovative radioisotopes for health

PRISMA

Physics of Radiation InteractionS with Matter and Applications

Subatech
Unité Mixte de Recherche 6457
Laboratoire de physique subatomique et des technologies associées

IMT Atlantique
Bretagne-Pays de la Loire
École Mines-Télécom

cnrs

Nantes Université

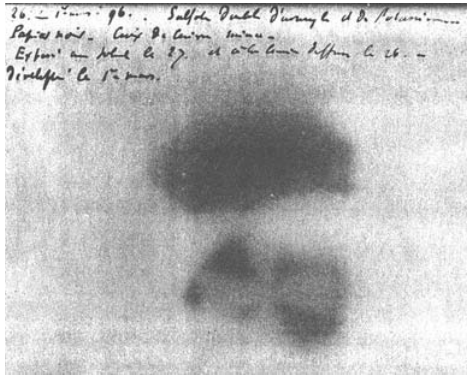
Plan

- **A little history**
- **Conventional imaging and therapy, Nuclear medicine**
- **Isotopes, Facilities**
- **Molecular Imaging and RadioligandTherapy, Radiotheranostics**
- **SPECT, PET, Therapy isotopes and Generators**
- **Focus on alpha particle emitters**
- **Irradiation conditions and production yields**
- **Focus on cross section measurements**
- **Quantitative and qualitative productions**

Plan

- **A little history**
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- Focus on cross section measurements
- Quantitative and qualitative productions

History



The Becquerel Maltese cross

1895 Wilhelm Conrad Röntgen: discovery of **X-rays**

1896 Henri Becquerel: discovery of **natural radioactivity**

1897 Joseph John Thomson: discovery of **electrons**

1898 Ernest Rutherford: **alpha** and **beta** radiations

X-ray of Bertha Röntgen's hand

M. And P. Curie in the "discovery hangar" at the Paris School of Industrial Physics and Chemistry

1898 Marie and Pierre Curie: discovery of Polonium and **Radium**

1899 J. J. Thomson: **β-** consisting of electrons

1900 Paul Villard: discovery of **gamma rays**

1903 M. and P. Curie, H. Becquerel: Nobel prize in physics

1911 M. Curie: Nobel prize in chemestry

History

Early 1900: necklace of radium

1916: Marie Curie at the wheel of an X-ray car and her daughter, Irène Curie, getting out of an X-ray car.

1934 Irène Curie and Frédéric Joliot: discovery of **artificial radioactivity**

1935 I. Curie and F. Joliot: Nobel prize in chemestry

1939 **Iodine-131** for the treatment of thyroid-related diseases

1946 **Iodine-131** to locate brain tumours in 12 patients during surgery

1949 **Phosphorus-32** to diagnostic a brain tumour

Irène Curie et Frédéric Joliot

Plan

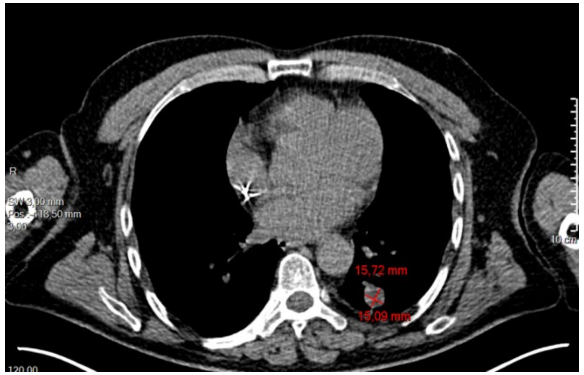
- A little history
- **Conventional imaging and therapy, Nuclear medicine**
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- Focus on cross section measurements
- Quantitative and qualitative productions

Conventional imaging in oncology

Visualize and localize tumors, measure them and evaluate the response to treatments

Centre François Baclesse

Radiography



Centre René Gauducheau

Computed Tomography Scanner

Institut Roi Albert II

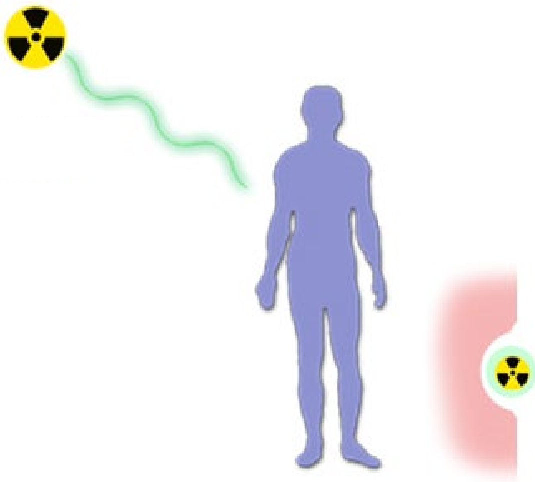
Magnetic Resonance Imaging

These techniques allow to get accurate information on the morphology but give limited information on the metabolism

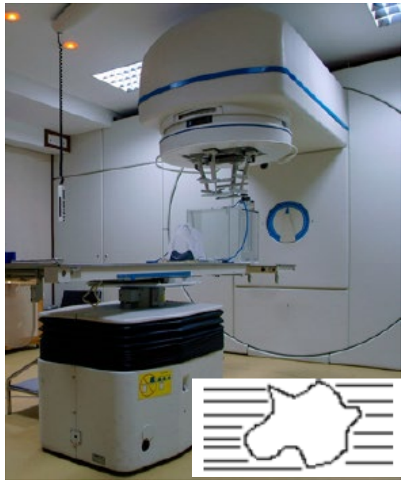
A gain can be obtain by coupling them with nuclear medicine technique (SPECT or PET) which gives these information

Conventional therapy

External beam radiotherapy:
- X rays, gamma, electrons
- Hadrontherapy



Brachytherapy
“Curietherapy” 



Institut de cancérologie de l’Ouest

ProteusOne, IBA

Institut de cancérologie de l’Ouest

These techniques are very efficient to treat a localized disease but does not target disseminated disease or residual disease

This can be address by nuclear medicine techniques

Nuclear medicine

Medical specialty which deals with **radionuclide** use **as open sources.**

Must not be confused with other medical specialties:

- **Radiology** which uses **X-rays** for imaging or closed radioactive sources for therapy
- **External radiotherapy** which uses external beam of ionizing radiation

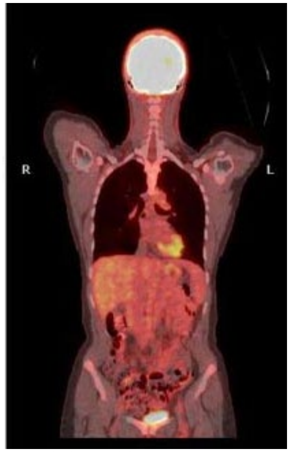
Nuclear medicine:

- One tools to fight cancer
- in complement **to surgery**, **chemotherapy**, **radiotherapy**

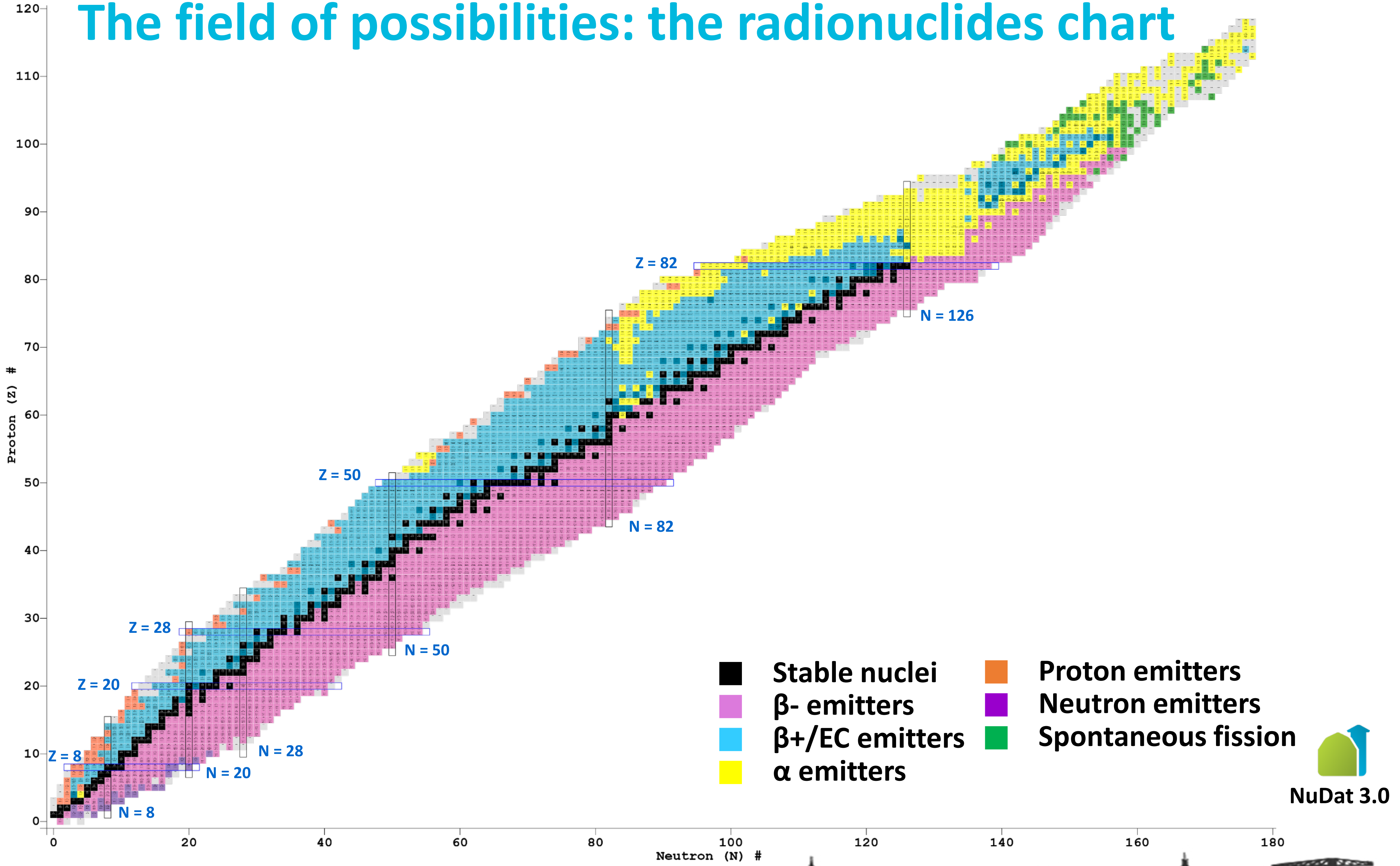
50 million of nuclear medicine procedures performed worldwide each year and **demand for radioisotopes is increasing**. **World Nuclear Association, 2024**

In France:

- 328 centers of nuclear medicine
- Most often used radionuclides: Tc-99m, F-18, I-131

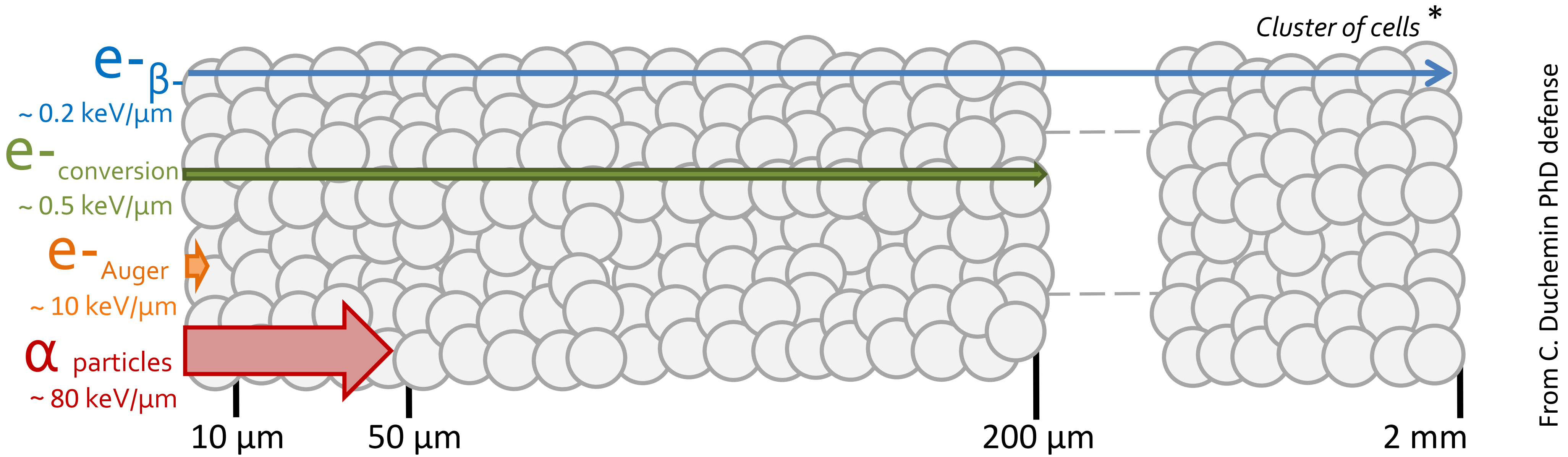


The field of possibilities: the radionuclides chart



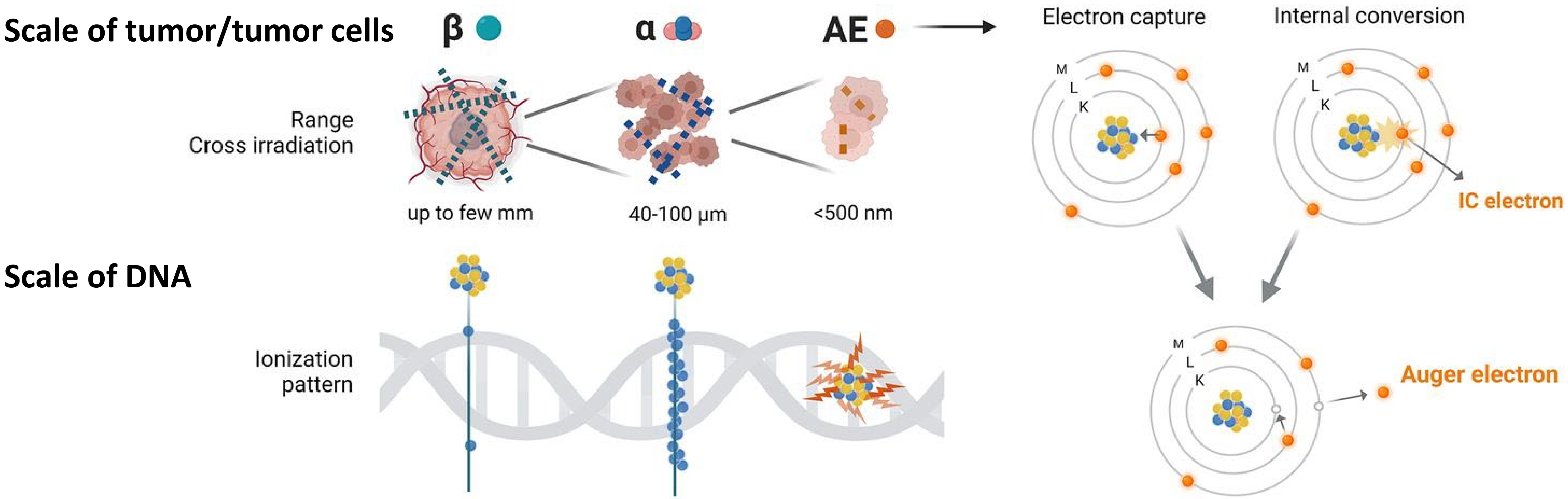
LET and medical applications

Low LET	⇨ Highly penetrating radiation	⇨ **Diagnosis**	**(X, γ, β+)**
High LET	⇨ Weakly penetrating radiation	⇨ **Therapy**	**(α, β-,e-, Auger e-)**



* These are not eggs

Range, cross irradiation, ionization patterns



Marshalling the Potential of Auger Electron Radiopharmaceutical Therapy, Julie Bolcaen et al. J Nucl Med 2023;64:1344-1351

Plan

- A little history
- Conventional imaging and therapy, Nuclear medicine
- **Isotopes, Facilities**
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- Focus on cross section measurements
- Quantitative and qualitative productions

Where medical isotopes are coming from?

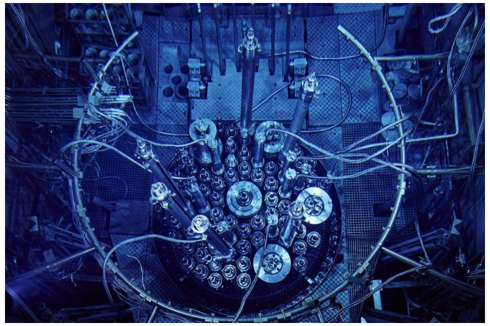
Few directly available in nature, belonging to radioactive chain of heavy nuclei

- ^{223}**Ra**: belongs to the radioactive chain of ^{235}U
  Xofigo ($RaCl_2$) available for bone metastases
- ^{212}**Pb/**^{212}**B**i: belongs to thee radioactive chain of ^{232}Th
  2 clinical trials ongoing for NeuroEndocrineTumors (clinical.org)
- ^{225}**Ac** : belongs to the radioactive chain of ^{233}U

Most of them are produced artifically

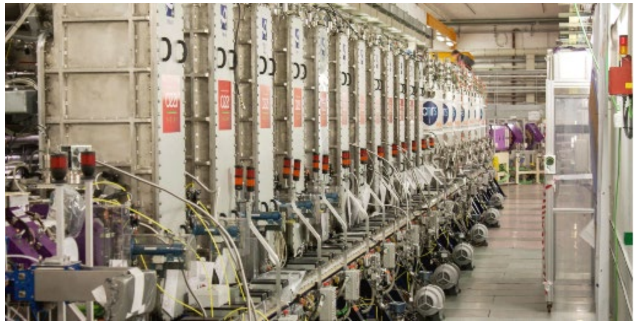
Many of them using neutron induced reactions in **nuclear reactors**

Quick progress and achievements using charged particle induced reactions in **accelerators** like **cyclotrons** and **linacs**



BR2 reactor @ SCK•CEN

C70XP @ ARRONAX



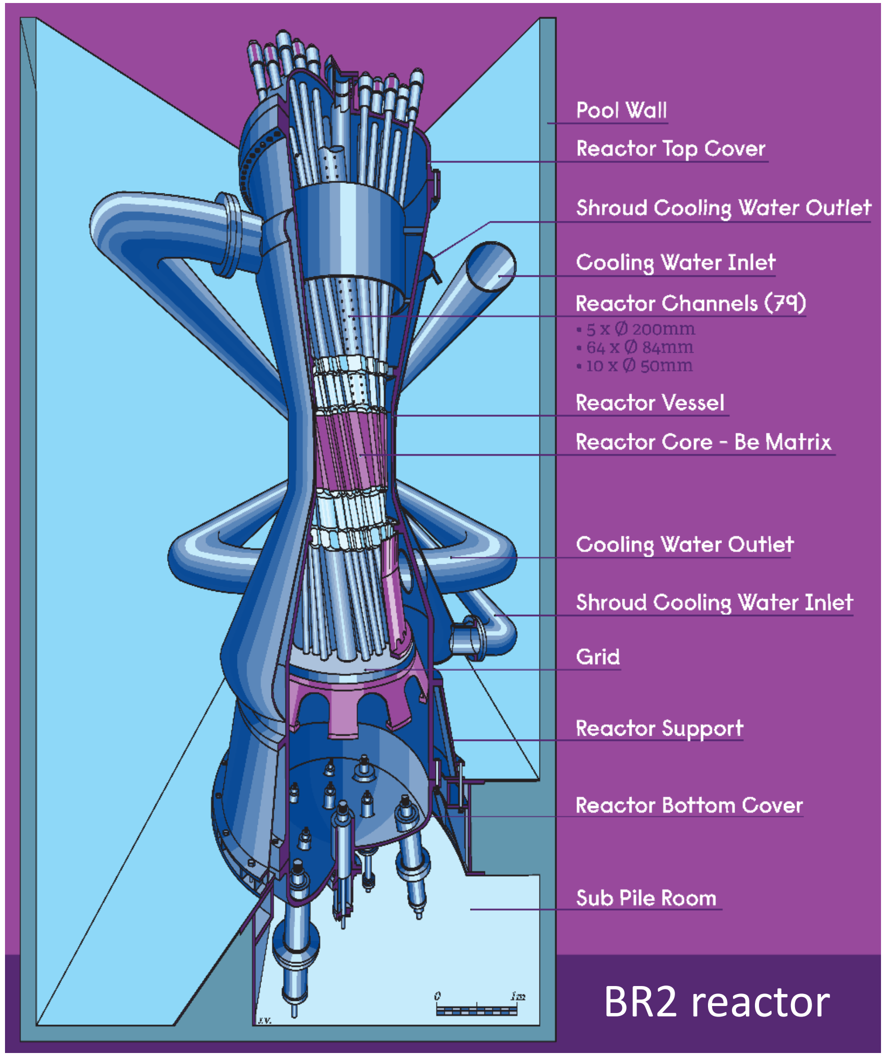
SPIRAL 2 @ GANIL

Facilities

Reactors: variable energy [0 up to ~ 100 MeV], flux [0 up to 10^{15} n/cm^2.s]

- ✓ BR2 — SCK•CEN, Belgium
- ✓ ILL — Grenoble, France

- Single neutron capture (n,γ):
  most common route, ^{177}Lu, ^{186}Re, ^{166}Ho …
- Double neutron capture (2n,2γ):
  ^{188}W/^{188}Re
- Inelastic reactions (n,n'γ):
  ^{117m}Sn
- Exchange reaction (n,p):
  ^{67}Cu
- Fission reaction (n,f):
  ^{99}Mo/^{99m}Tc, ^{131}I, ^{133}Xe …



Facilities

Cyclotrons:

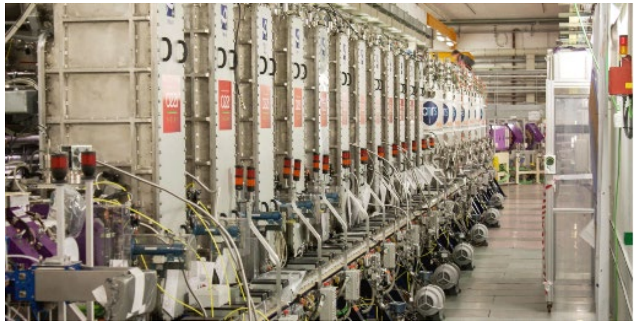
- Fixed energy [0 up to ~ 100 MeV]
- Low intensity [0 up to ~ 50 µA]
- ✓ Cyclone 30XP IBA
  Polatom - CERAD, Poland – FZ Jülich, Germany
- ✓ Cyclone 70XP IBA
  GIP ARRONAX, France

C70XP @ GIP ARRONAX

Extracted	Energy (MeV)	Max. current (µA)
H^+	30 – 70	2 x 375
D^+	15 – 35	2 x 50
He^{2+}	68	70
HH^+	17	50

LINACS:

- Variable energy [0 up to ~ 20 MeV/A]
- High intensity [0 up to ~ mA*]
- ✓ ATLAS
  Argonne National Laboratory, USA
- ✓ SPIRAL 2
  GIE GANIL, France



SPIRAL 2 @ GIE GANIL

Beam	P+	D+	Ions	Ions
A/Q	1	2	< 3	< 6 or 7
Imax (mA)	5	5	1	1
Emin (MeV/A)	2	2	2	2
Emax (MeV/A)	33	20	14.5	8
Max. power (kW)	165	200	44	48

*High LET and "thin targets" [~ tens of µm up to ~ hundreds of µm], ! thermal load

There is not one fit all accelerator

^{11}C, ^{13}N, ^{15}O,
^{18}F, ^{64}Cu

11 MeV

^{67}Ga, ^{111}In, ^{123}I,
^{201}Tl, ^{68}Ge

30 MeV

^{82}Sr, ^{117m}Sn ...

70 MeV

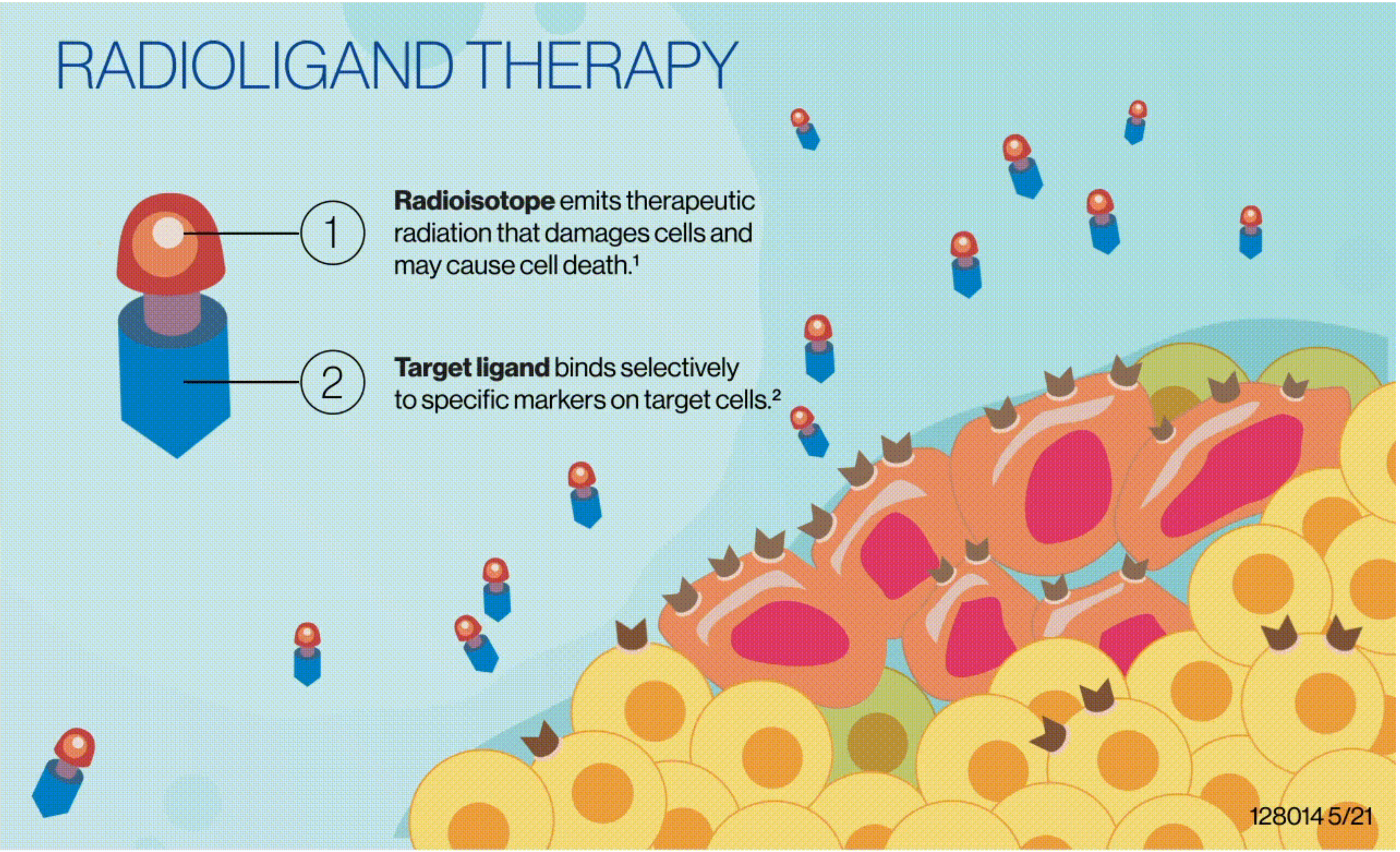
Linear Accelerator
160 MeV

^{82}Sr, ^{117m}Sn, ^{225}Ac...

Plan

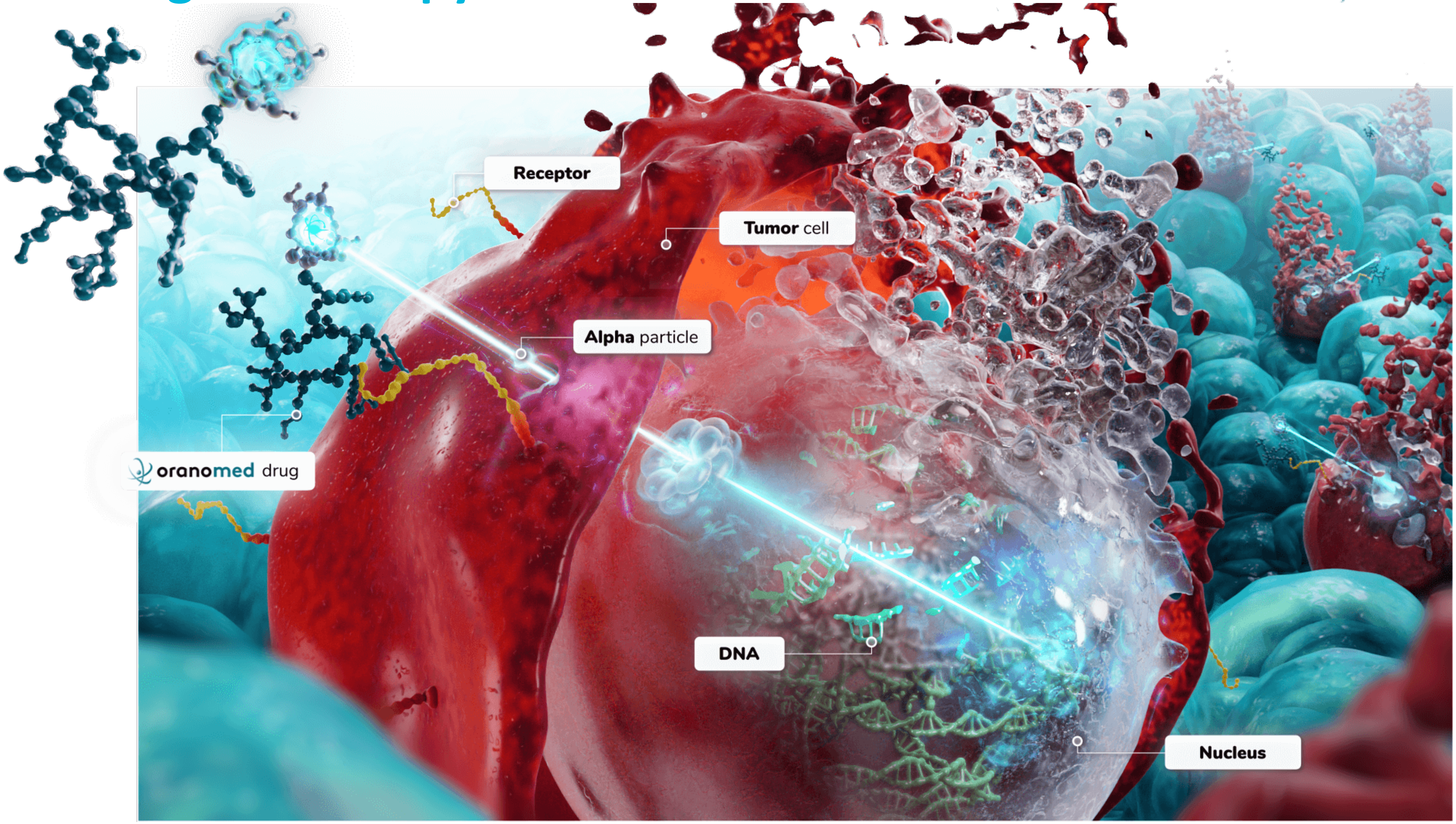
- A little history
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- **Molecular Imaging and RadioligandTherapy, Radiotheranostics**
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- Focus on cross section measurements
- Quantitative and qualitative productions

Radioligand therapy

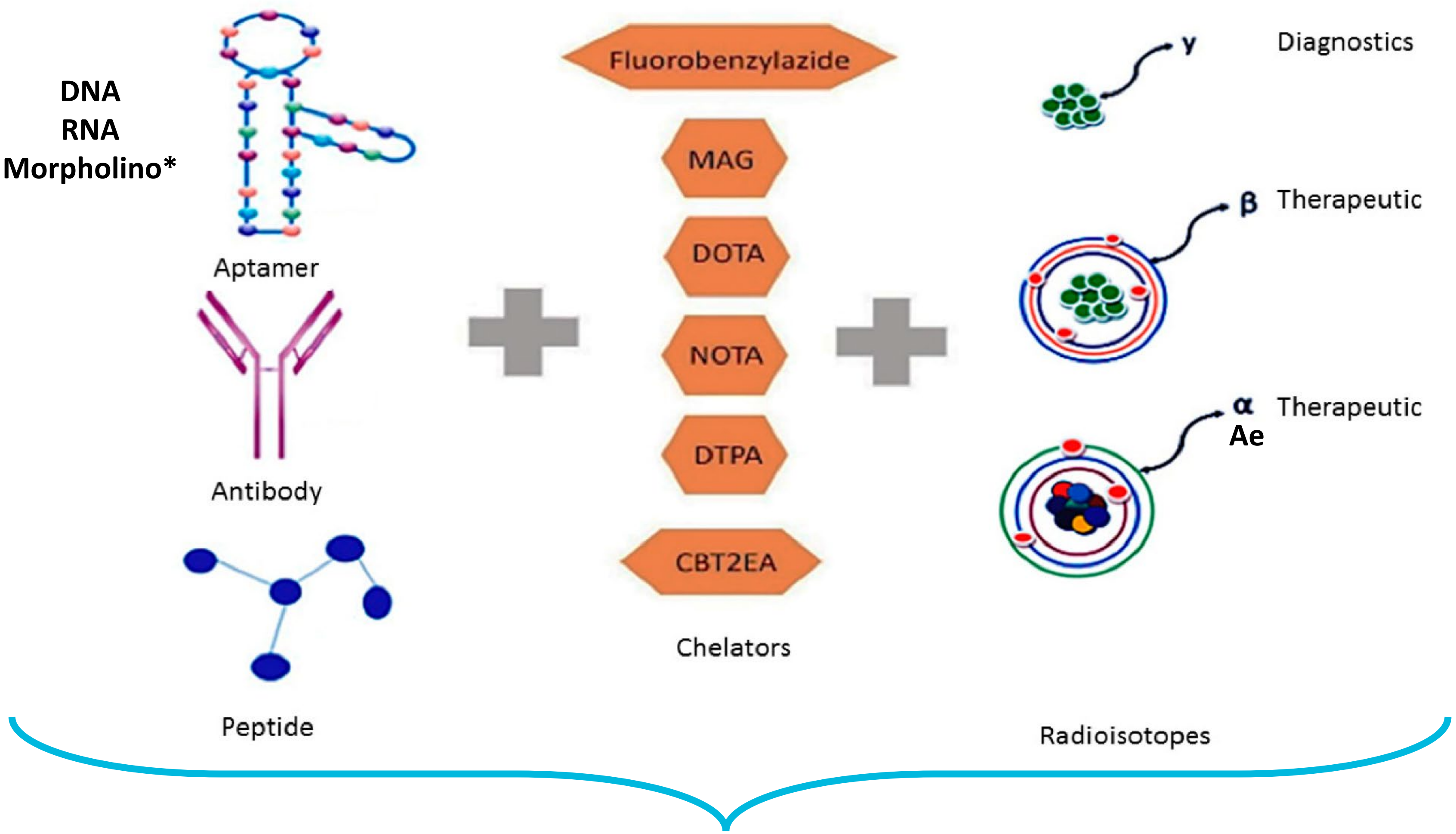


References: 1. Jadvar H. Targeted radionuclide therapy: an evolution toward precision cancer treatment. *AJR Am J Roentgenol*. 2017;209(2):277-288. **2.** Jurcic JG, Wong JYC, Knox SJ, et al. Targeted radionuclide therapy. In: Tepper JE, Foote RE, Michalski JM, eds. *Gunderson & Tepper's Clinical Radiation Oncology*. 5th ed. Elsevier, Inc; 2021;71(3):209-249.

Radioligand therapy



Radioligand imaging and therapy



RadioPharmaceutical

Khalid, U.; Vi, C.; Henri, J.; Macdonald, J.; Eu, P.; Mandarano, G.; Shigdar, S. Radiolabelled Aptamers for Theranostic Treatment of Cancer. Pharmaceuticals 2019, 12, 2. https://doi.org/10.3390/ph12010002

*In molecular biology, a morpholino is a type of molecule used to modify gene expression.

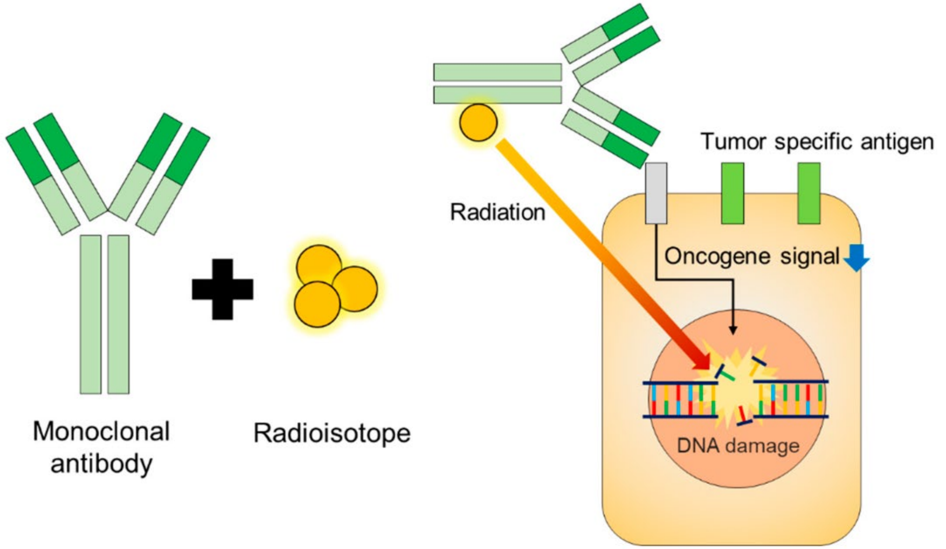
Radioimmunotherapy, RIT

Treatment designed to stimulate the body's immune defences against cancer cells.

In cancer therapy, an antibody with specificity
for a tumor-associated antigen is used
to deliver a lethal dose of radiation to the tumor

Routine treatment :

- Zevalin® : mAb anti-CD20 + chelator + Yttrium-90, 2002-…
- Bexxar® : mAb anti-CD20 + chelator + Iodine-131, 2003-2014
- Betalutin® : mAb anti-CD37 + chelator + Lutetium-177, 2020-…



Alpha emitters in clinical development :

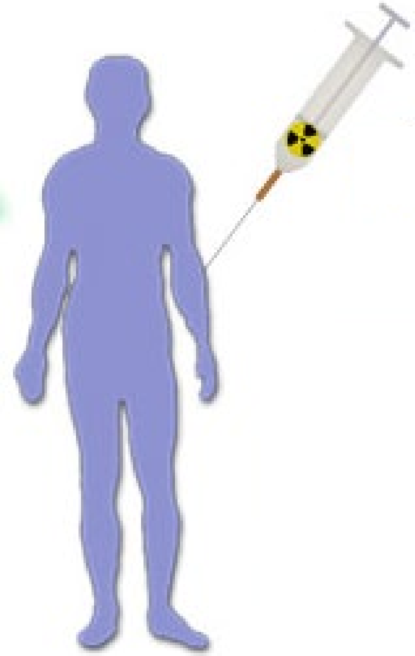
- Bismuth-213
- Actinium-225
- Astatine-211

"Combination Radioimmunotherapy Strategies for Solid Tumors" Zaheer, Javeria; Kim, Hyeongi; Lee, Yong-Jin; Kim, Jin Su; Lim, Sang Moo. International Journal of Molecular Sciences 20 (22): 5579. DOI:10.3390/ijms20225579

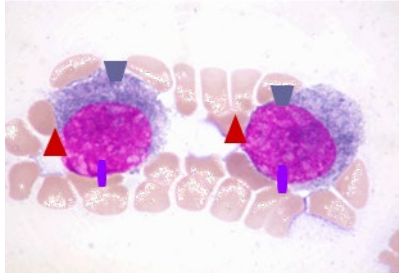
Radioimmunotherapy of human tumours, Steven M. Larson, M.D., Jorge A. Carrasquillo, M.D., Nai-Kong V. Cheung, M.D., PhD, and Oliver Press, M.D., Ph.D. Nat Rev Cancer. 2015 Jun; 15(6): 347–360. doi: 10.1038/nrc3925

Molecular Imaging and RadioPharmaceutical Therapies

Inject a tracer

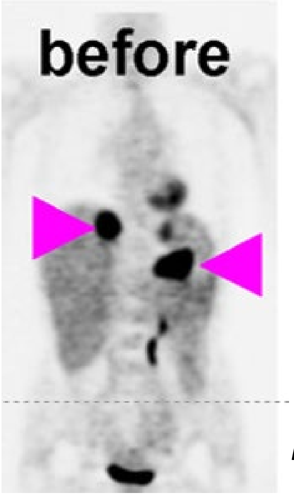


Target a tumor marker



γ, β+ ➡

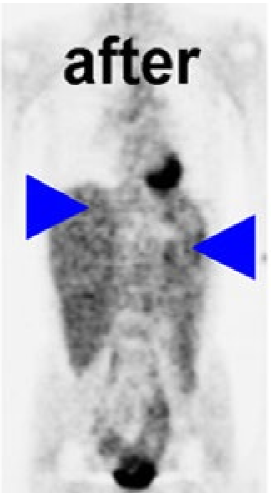
Detect the disease



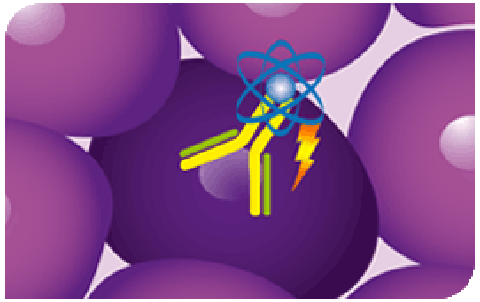
NIRS, Shiba, MIC

γ, β+ ➡

Follow-up



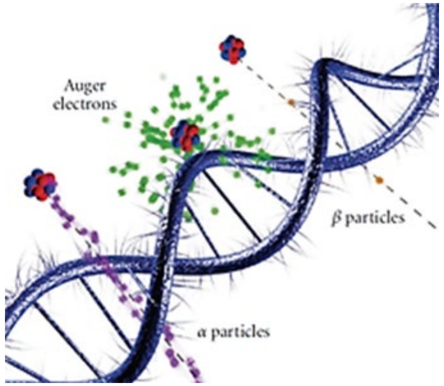
NIRS, Shiba, MIC



ORANO Med

β-, α, e_{Auger} ➡

Treat the disease



B.Q. LEE et al.

Personalized nuclear medicine

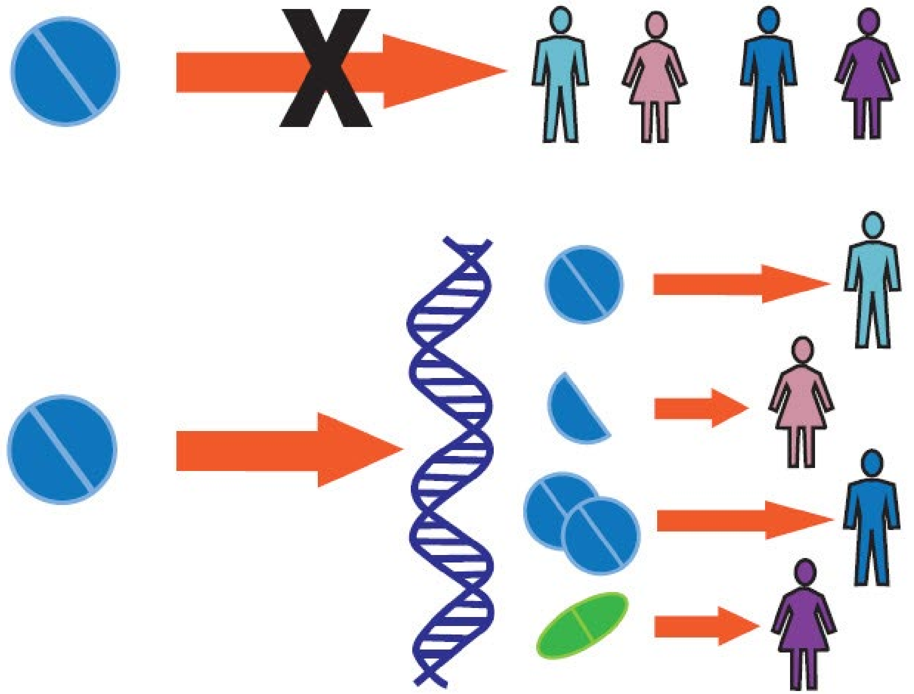
Imaging and diagnosis

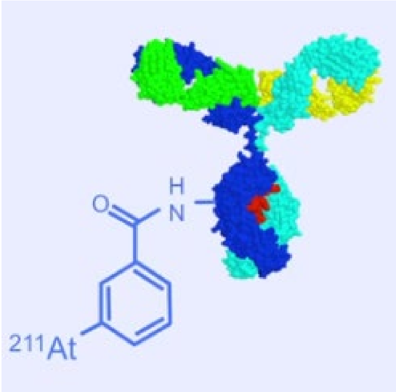
Choose the best treatment

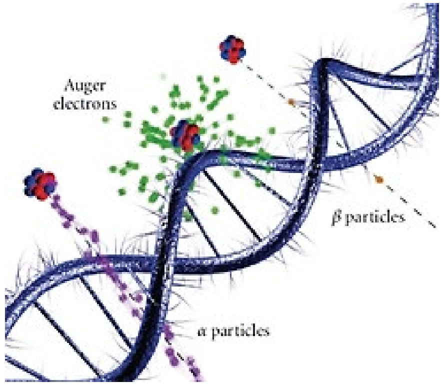
Evaluate its efficacy

Therapy

Destroy tumor cells





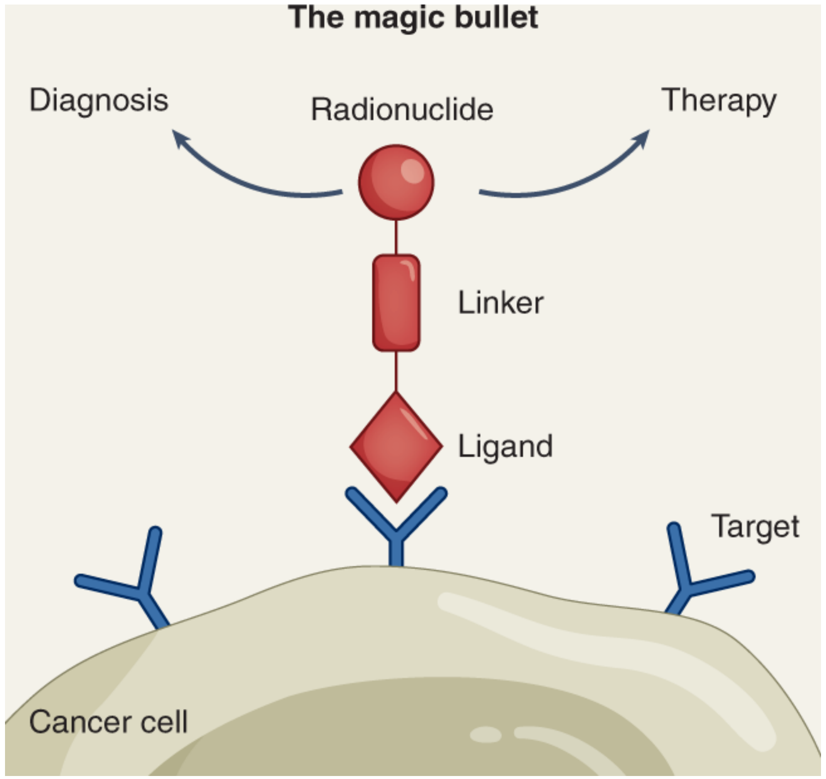


The Right Drug To The Right Patient For The Right Disease
At The Right Time With The Right Dosage

Radiotheranostics : what you see is what you treat

Combination of
Molecular Imaging, mainly PET and SPECT,
with RadioPharmaceutical Therapies:

- a RadioNuclide emitting a diagnostic radiation, such as γ or β+ particles
  - ⇨ to assess the tumour localization and extension
  - ⇨ to verify the targeting capability of the radiopharmaceutical
- a compound radiolabelled with a β- or α particles emitter
  - ⇨ the therapeutic counterpart

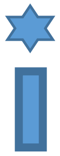


Arnold, C. Theranostics could be big business in precision oncology. *Nat Med* **28**, 606–608 (2022). https://doi.org/10.1038/s41591-022-01759-6

Radiotheranostics : what you see is what you treat

1 molecule, 1 radioisotope

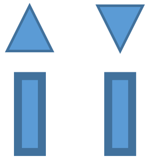
1 RP radiolabelled with a radioisotope emitting
- both a diagnostic
- and a therapeutic radiation



⇨ ^{177}Lu, ^{47}Sc

1 molecule, 2 radioisotopes

1 RP radiolabelled with 2 different radioisotopes of the same element (“real” theranostic pair):
- 1 RI with a diagnostic emission
- 1 RI with a therapeutic emission

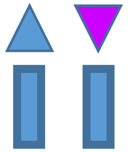


⇨ ^{123}I/^{131}I, first radiotheranostics approach in 1930’s

⇨ ^{44}Sc/^{47}Sc, ^{64}Cu/^{67}Cu, ^{155}Tb/^{161}Tb

1 molecule, 2 radionuclides

1 RP radiolabelled with 2 different radionuclides from 2 different elements (theranostic pair):
- 1 RN with a radioactive emission for diagnosis
- 1 RN for therapy

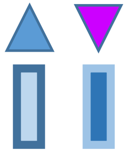


⇨ ^{68}Ga/^{177}Lu

2 molecules, 2 radionuclides

2 different RPs are used in combination to perform both diagnosis and treatment.
- 2 vector molecules quite similar

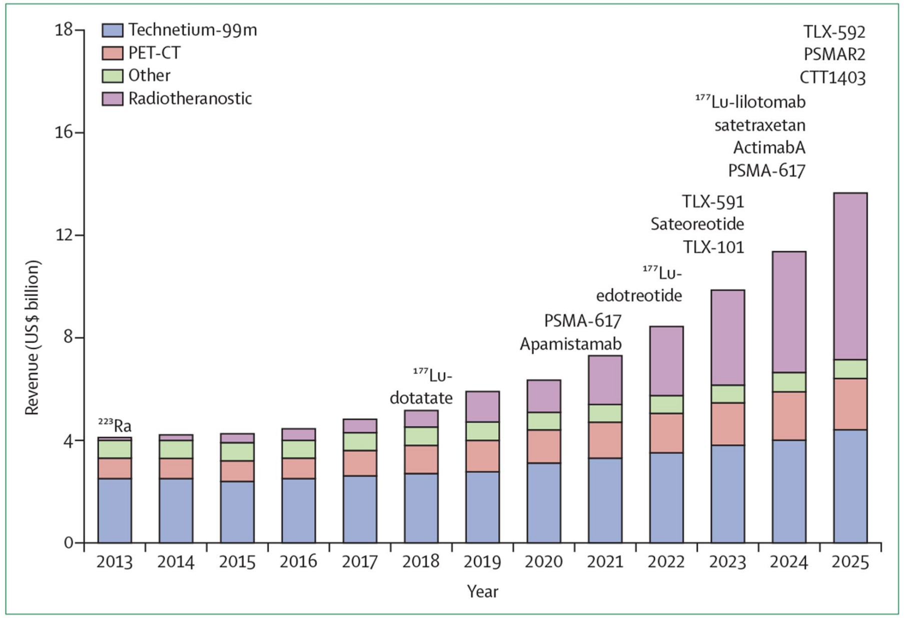
biodistribution$_{\text{diagnostic imaging}}$ = biodistribution$_{\text{during treatment}}$



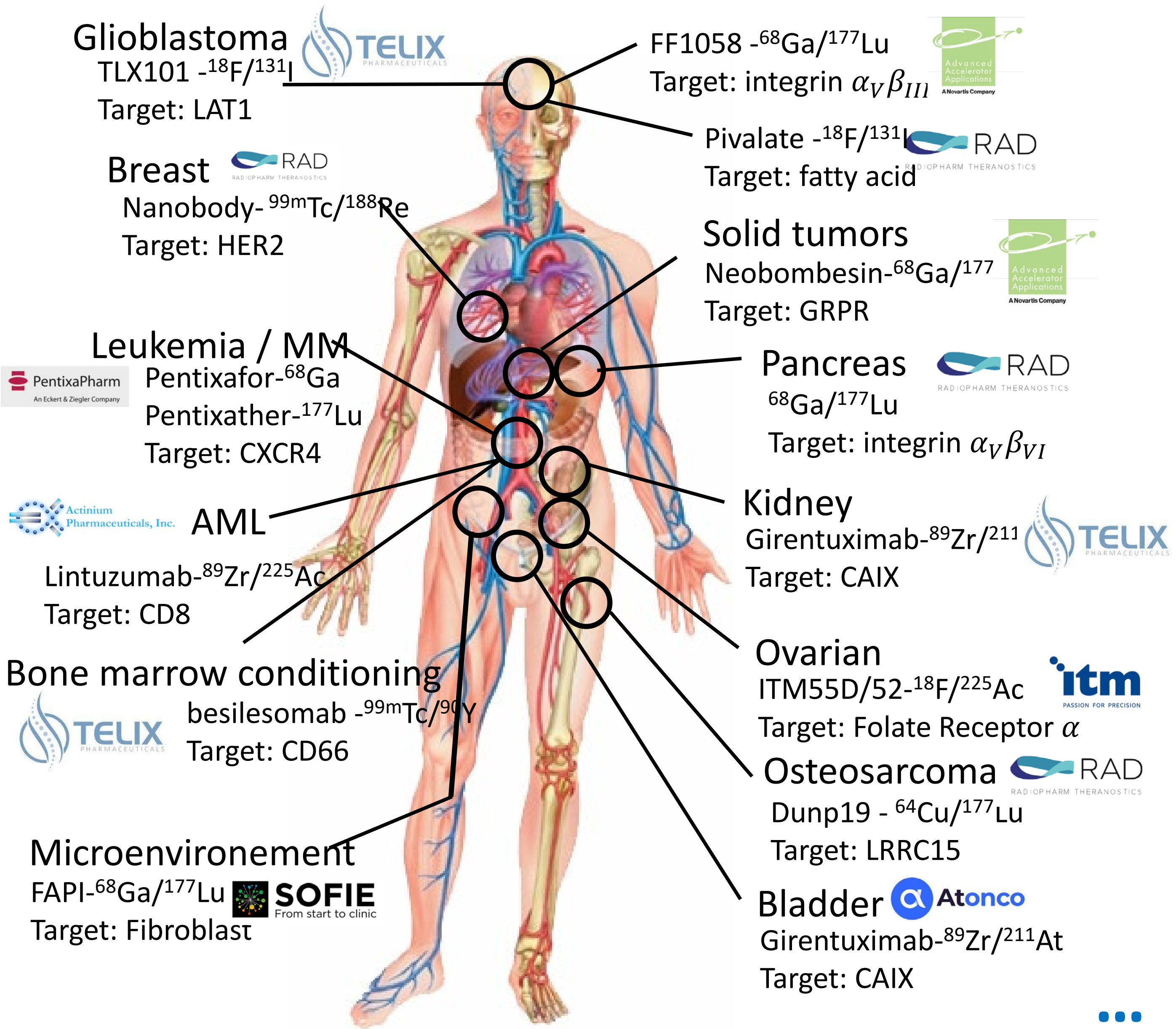
⇨ ^{68}Ga/^{177}Lu

From L. de Dominicis PhD thesis

Radiotheranostics applications:

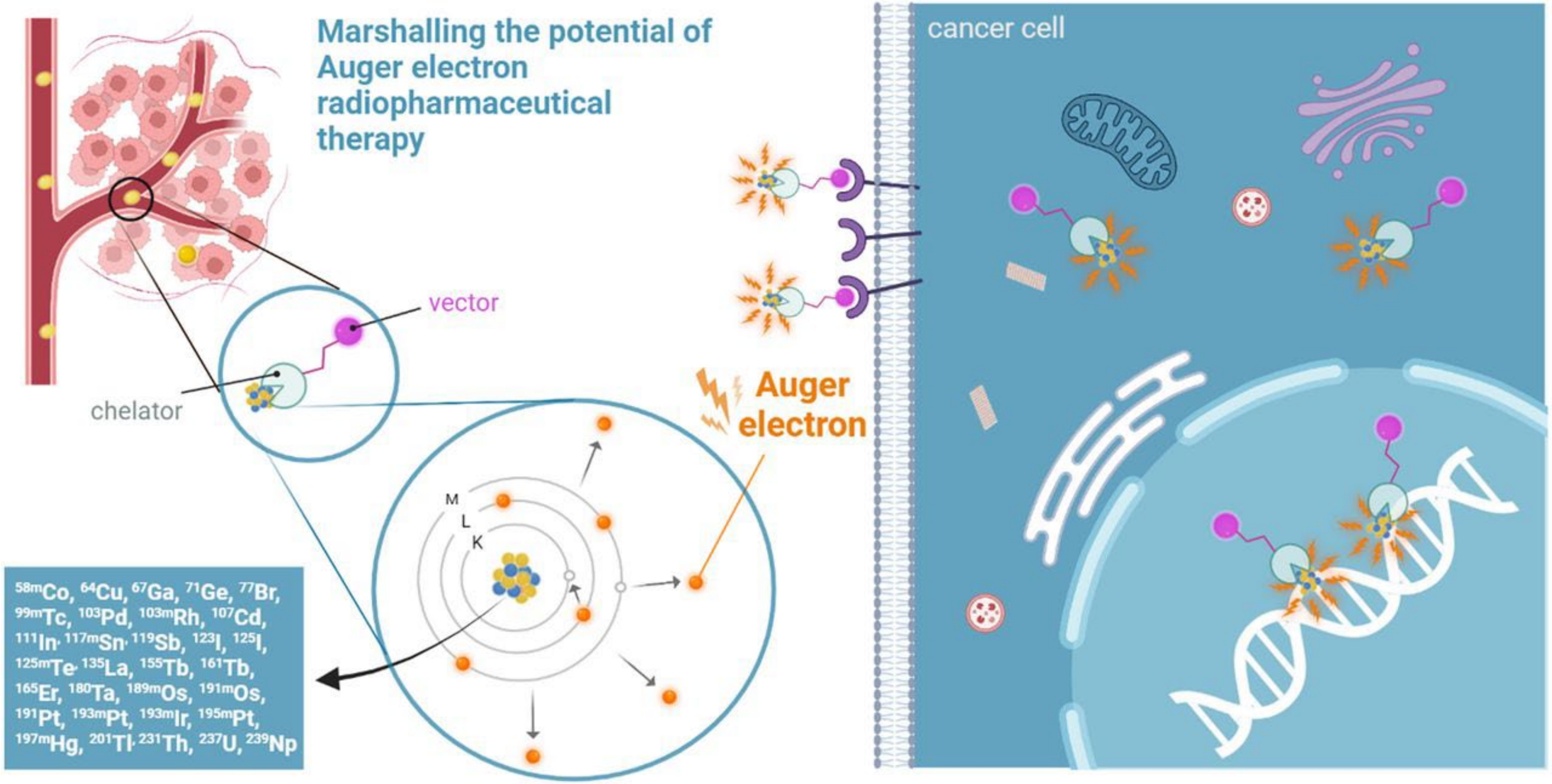


Radiotheranostics: a roadmap for future development, Hermann et al. Lancet Oncol 2020



Courtesy of Prof. Michaël Bourgeois

Auger electron therapy



This is not an egg

Nucleus and DNA are typically the primary cellular targets of radiation damage. Internalization into cancer cells and delivery to cell nucleus is not required for cell killing with Ae-emitting radionuclides ⇨ Bystander effect

Julie Bolcaen et al. J Nucl Med 2023;64:1344-1351

Plan

- A little history
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- **SPECT, PET, Therapy isotopes and Generators**
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- Focus on cross section measurements
- Quantitative and qualitative productions

SPECT radionuclides*:

ISOTOPE	DECAY MODE	$T_{1/2}$	E_γ[keV] (%)
^{99m}Tc	IT	6.01 h	140.5 (87.7)
^{123}I	EC	13.2 h	159.0 (83.3)
^{131}I	β-	8.02 d	364.5 (81.2)
^{67}Ga	EC	78.3 h	93.3 (37) 184.6 (20.4) 300.2 (16.6)
^{111}In	EC	67.4 h	245.4 (94) 171.3 (90.3)

* Non exhaustive list

SPECT radionuclides*:

ISOTOPE	DECAY MODE	$T_{1/2}$	E_γ[keV] (%)
^{99m}Tc	IT	6.01 h	140.5 (87.7)
^{123}I	EC	13.2 h	159.0 (83.3)
^{131}I	β-	8.02 d	364.5 (81.2)
^{67}Ga	EC	78.3 h	93.3 (37) 184.6 (20.4) 300.2 (16.6)
^{111}In	EC	67.4 h	245.4 (94) 171.3 (90.3)

PET radionuclides*:

ISOTOPE	$T_{½}$[min]	$E_{\beta+max}$[MeV]	Maximum range in water [mm]
^{11}C	20.38	1.0	4.1
^{13}N	9.96	1.2	5.4
^{15}O	2.03	1.7	8.2
^{18}F	109.7	0.6	2.4
^{64}Cu	762.0	0.7	2.5
^{68}Ga	67.6	1.9	10.0
^{82}Rb	1.27	3.3	20

* Non exhaustive list

Therapy radionuclides*:

Radionuclide	Type	Half-life	E_{max}(MeV)	Mean range (mm)	Imageable
^{90}Y	β	2.7 d	2.3	2.76	No
^{131}I	β, γ	8.0 d	0.81	0.40	Yes
^{177}Lu	β, γ	6.7 d	0.50	0.28	Yes
^{153}Sm	β, γ	2.0 d	0.80	0.53	Yes
^{186}Re	β, γ	3.8 d	1.1	0.92	Yes
^{188}Re	β, γ	17.0 h	2.1	2.43	Yes
^{67}Cu	β, γ	2.6 d	0.57	0.6	Yes

* Non exhaustive list

Therapy radionuclides*:

Radionuclide	Type	Half-life	E_{max}(MeV)	Mean range (mm)	Imageable
^{90}Y	β	2.7 d	2.3	2.76	No
^{131}I	β, γ	8.0 d	0.81	0.40	Yes
^{177}Lu	β, γ	6.7 d	0.50	0.28	Yes
^{153}Sm	β, γ	2.0 d	0.80	0.53	Yes
^{186}Re	β, γ	3.8 d	1.1	0.92	Yes
^{188}Re	β, γ	17.0 h	2.1	2.43	Yes
^{67}Cu	β, γ	2.6 d	0.57	0.6	Yes
^{225}Ac	α, β	10 d	5.83	0.04 – 0.1	Yes
^{213}Bi	α	45.7 min	5.87	0.04 – 0.1	Yes
^{212}Bi	α	1.0 h	6.09	0.04 – 0.1	Yes
^{211}At	α	7.2 h	5.87	0.04 – 0.1	Yes
^{212}Pb	β	10.6 h	0.57	0.6	Yes
^{125}I	Auger	60.1 d	0.35	0.001 – 0.02	Yes
^{123}I	Auger	13.2 h	0.16	0.001 – 0.02	No
^{67}Ga	Auger	3.3 d	0.18	0.001 – 0.02	Yes
^{196m}Pt	Auger	4.0 d	0.13	0.001 – 0.02	No

* Non exhaustive list

Generator systems*:

Generator System	PARENT ISOTOPE T$_{1/2}$	Main Production Route	Main Decay	DAUGHTER ISOTOPE T$_{1/2}$	Main Emission	Application
^{99}Mo - ^{99m}Tc	66 h	Reactor	β-	6.006 h	γ	SPECT
^{82}Sr - ^{82}Rb	25.3 d	Accelerator	EC	1.27 m	β+	PET
^{68}Ge - ^{68}Ga	270.8 d	Accelerator	EC	1.135 h	β+	PET
^{62}Zn - ^{62}Cu	9.26 h	Accelerator	EC	9.74 m	β+	PET
^{44}Ti - ^{44}Sc	47.3 y	Accelerator	EC	3.927 h	β+	PET
^{90}Sr - ^{90}Y	28.5 y	Reactor	β-	2.671 d	β-	RT
^{225}Ac - ^{213}Bi	10.0 d	Decay chain, Accelerator	α	45.6 m	α, β-	RT
^{229}Th - ^{225}Ac	7880 y	Decay chain	α	10 d	α, β-	RT
^{188}W - ^{188}Re	69.4 d	Reactor	β-	16.98 h	β-	RT
^{134}Ce - ^{134}La	3.16 d	Accelerator	EC	6.4 m	β+	PET
^{140}Nd - ^{140}Pr	3.37 d	Accelerator	EC	3.39 m	β+, Ae	PET
^{166}Dy - ^{166}Ho	3.40 d	Reactor	β-	26.80 h	β-	RT
^{212}Pb - ^{212}Bi	10.64 h	Decay chain	β-	60.6 m	β-, α,	RT

* Non exhaustive list

Plan

- A little history
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- **Focus on alpha particle emitters**
- Irradiation conditions and production yields
- Focus on cross section measurements
- Quantitative and qualitative productions

Alpha particle emitters, why?

A **limited number** of candidates

Radionuclide	Half-life	# of α / decay	Eγ (keV)
Tb-149	4,1 h	0,17 (β and ε)	165
At-211	7,2 h	1	79
Bi-212	1 h	1 (β)	727
Bi-213	45 m	1 (2β)	440
Ra-223	11,4 d	4 (2β)	269
Ac-225	10 d	4 (2β)	100
Th-226	31 m	4	111
Th-227	18,7 d	5 (2β)	256

Alpha particle emitters, why?

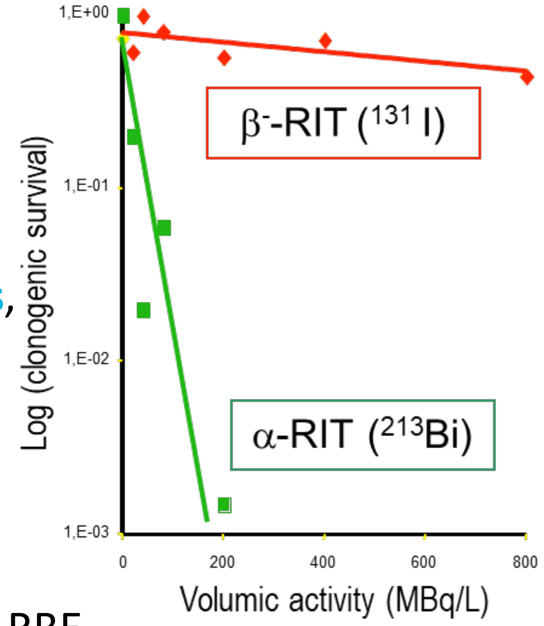
A **limited number** of candidates

Radionuclide	Half-life	# of α / decay	Eγ (keV)
Tb-149	4,1 h	0,17 (β and ε)	165
At-211	7,2 h	1	79
Bi-212	1 h	1 (β)	727
Bi-213	45 m	1 (2β)	440
Ra-223	11,4 d	4 (2β)	269
Ac-225	10 d	4 (2β)	100
Th-226	31 m	4	111
Th-227	18,7 d	5 (2β)	256

But,

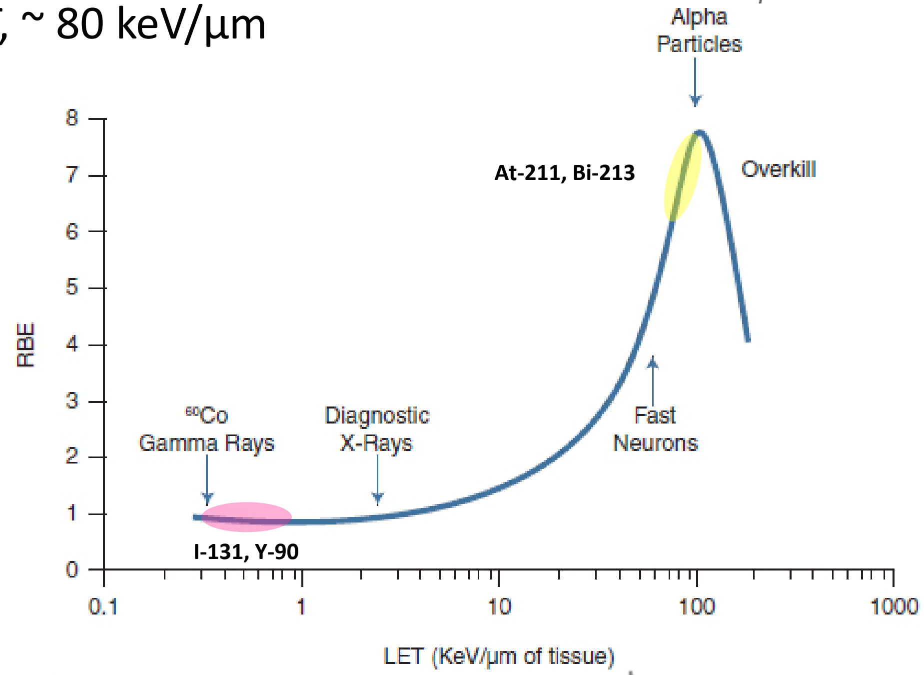
Highly cytotoxic, Eα [5 - 9] MeV potentially more than β radiation

Better **preservation of healthy tissues**, range 40 to 100 µm in water, few cell lengths



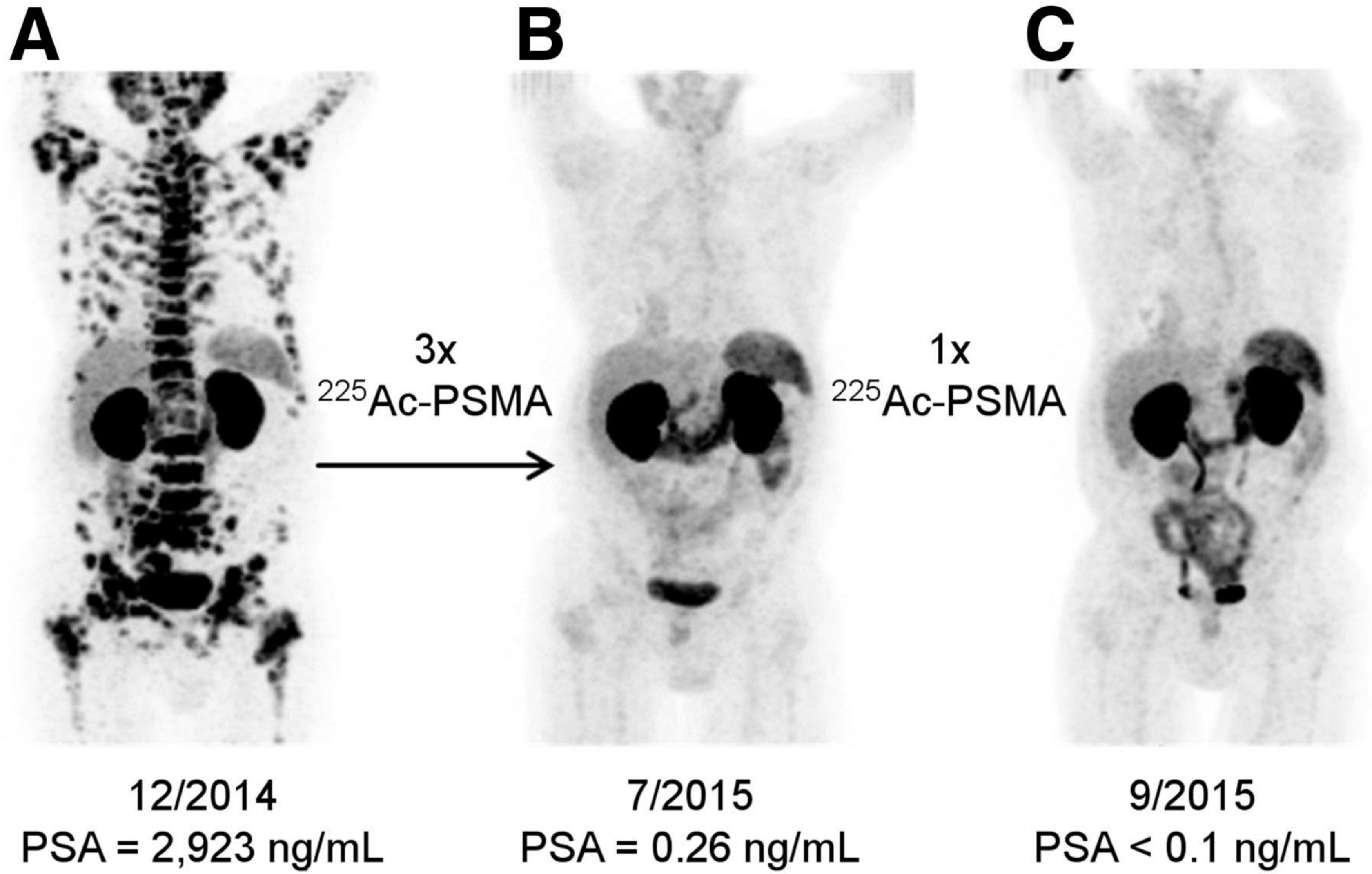
Supiot S. et al. Cancer 2002. 94: 1202-9

High relative biological effectiveness, RBE, high LET, ~ 80 keV/µm



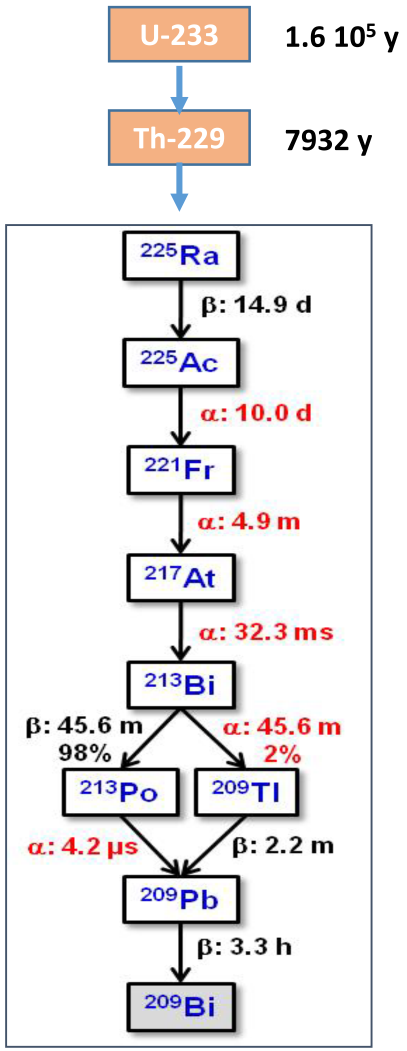
The essential Physics of Medical Imaging, Book, Bushberg et al., 2002

Alpha particle emitters, why?



68Ga-PSMA-11 PET/CT scans of patient A. Pretherapeutic tumor spread (A), restaging 2 mo after third cycle of **225Ac-PSMA-617** (B), and restaging 2 mo after one additional consolidation therapy (C). Clemens Kratochwil et al. J Nucl Med 2016;57:1941-1944

Actinium-225, the most popular

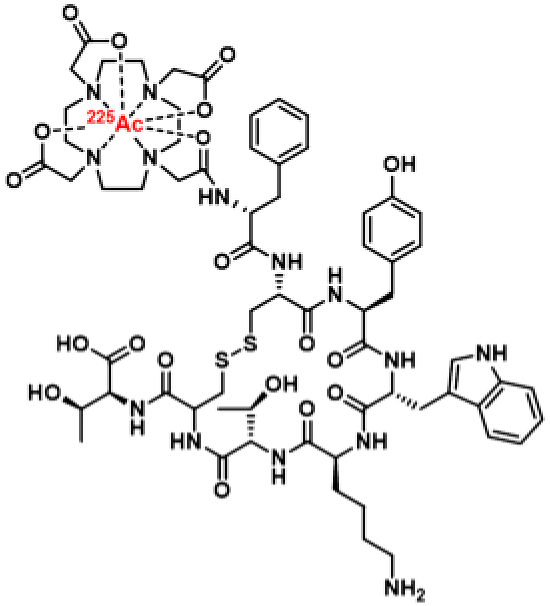


Emitted radiations:

- 4 α + 2 β-

Main interests:

- Half-life
  - Centralised production possible
- Chemical properties
  - Radiolabelling with DOTA possible
  - Therefore reuse of Lu-177-based compounds possible



[^{225}Ac]Ac-DOTA-TATE

Clinical trials:

- 23 clinicaltrials.gov

Production methods, a lot are investigated:

- **Decay of Th-229** Th-229 coming from U-233 bred from Th-232
- **p + Ra-226** ⇨ « strategic » isotope, nuclear proliferation
- n + Ra-226 Ra-226 recovered from legacy medical devices
- **p + Th-232** ⇨ limited stocks
- **γ + Ra-226** ⇨ radioprotection issues (Rn-222 …)
- Isol technic using uranium carbide target at MEDICIS in the PRISMAP project

Actinium-225 from Thorium-229 decay

Production method:

- Th-229 is obtained from U-233, produced in USA and Russia during the 50s and 60s for various reactor studies
  - ⇨ Risk of nuclear proliferation
- **Reference method for Ac-225 used in preclinical and clinical trials**

Producers:	ORNL (USA)	ITU (Germany)	IPPE (Obninsk, Russia)
Production capacity:	33 GBq/year	13 GBq/year	22 GBq/year → 68 GBq/year

Contaminants:

- No radioactive contaminants
- Presence of stable metallic contaminants in certain sources

Limited availability but:

- ONRL has signed an agreement with TerraPower: thorium extraction from the site's historical waste.
  - ⇨ production capacity of 500,000 doses compared with the current 4,000 doses.
- Russian capacity to increase production? Impact of the war?
- ORNL also interested in Ra-226(3n,ɣ)Ra-229 ⇨Ac-229 ⇨ Th-229

Actinium-225 production using high energy protons

Production method:

p + Th-232 ⇨ Ac-225 + X

Producers:

- BLIP @ BNL and IPF @ LANL (USA)
  - 1 production/month, 50 mCi (1.85 GBq) end of process
  - New treatment capacity at BNL (2023)
  - Tri-Lab effort to increase Ac-225 supply : BNL, LANL and ORNL
- Linac @ INR RAS (Troitsk , Russie)
- Cyclotron @ TRIUMF (Canada)

BNL, long-exposure image

To keep in mind:

- Radionuclidic purity not better than ≥98% (~ 0.12% Ac-227 EOB, $T_{1/2}$ = 21,773 ans)
  - Impact on patients?
    Biodistribution/dosimetry/toxicity studies have been carried out with this product, showing no differences from the product derived from the Th229 generator. *(Z. Jiang et al)*
  - Impact on waste management in hospitals?

Brookhaven Linac Isotope Producer: 66-202 MeV at 165 mA
Institute for Nuclear Research: 160 MeV at 140 µA (500 µA)
Isotope Production Facility: 100 MeV up to 275 mA
TRIUMF: 500 MeV at 120 µA

Alternative Ac-225 production methods under development

Production route: **Ra-226 + p ⇨ Ac-225 + 2n**

Advantages:

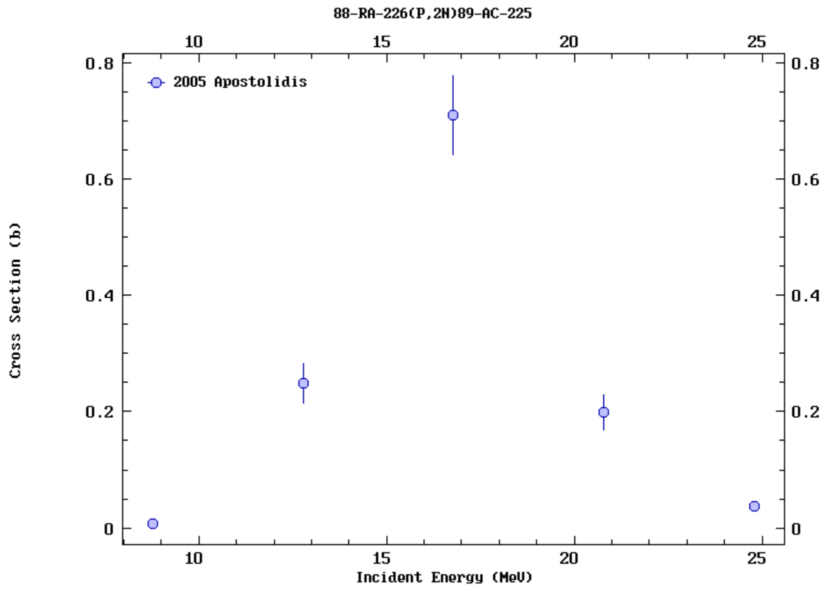
- Use of commercial cyclotrons (18 MeV, 24 MeV or 30 MeV)
  - ⇨ Easy to deploy
- Product available without Ac-227

Disadvantage:

- Need to use Ra-226, highly radiotoxic and in short supply

Method under development:

- e.g. by Eckert and Ziegler, SpectronRx



Production route: **Ra-226 + γ ⇨ n + Ra-225 ⇨ Ac-225**

Advantages:

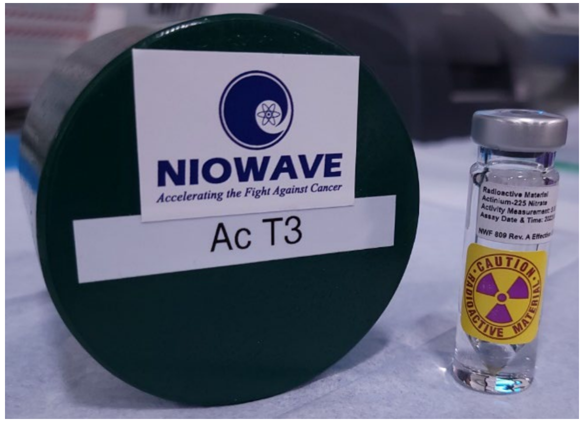
- Use of commercial electron accelerators (Niowave, IBA, …)
- Product available without Ac-227

Disadvantages:

- Need to use Ra-226, highly radiotoxic and in short supply
- High-intensity irradiation required (mA)

Method under development:

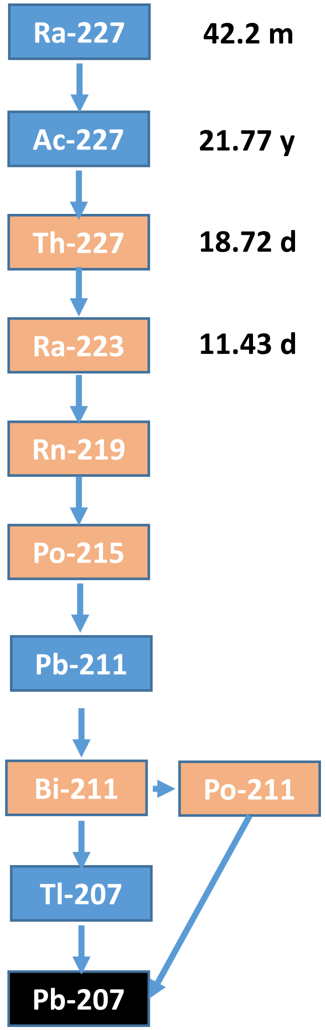
- PanTera (Belgium – 2027/2028), Niowave and Northstar (USA)



18.5 TBq/year using a 20 MeV, 210 kW beam

Ac-225 production: PanTera facility coming soon

Radium-223, the first α emitter approved by the FDA



Emitted radiations:

- 4 α + 2 β-

Application:

- (Ra-223)Cl2 is used for bone metastases in prostate cancer since 2013
- Xofigo®, Bayer

Production method:

- High Flux Isotope Reactor at Oak Ridge National Laboratory

  n + Ra-226 (from legacy medical devices) ⇨ γ + Ra-227 ⇨ Ac-227 ⇨ Th-227 ⇨ Ra-223

Production capacity:

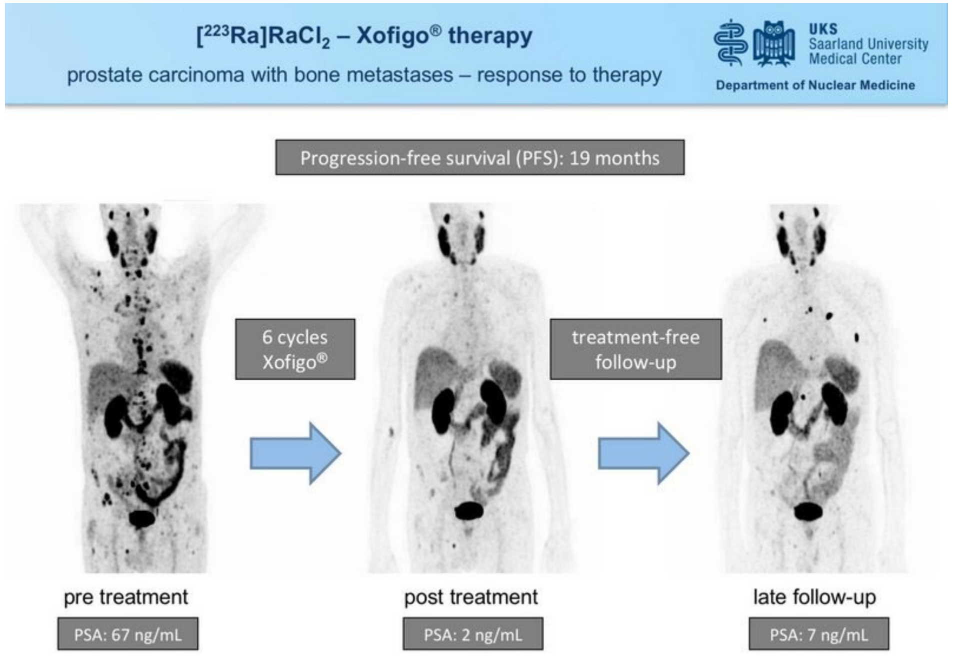
- Bayer Consumer Care AG has a supply contract of Ac-227 with DOE (ORNL) over the 2018-2028 period

Clinical trials:

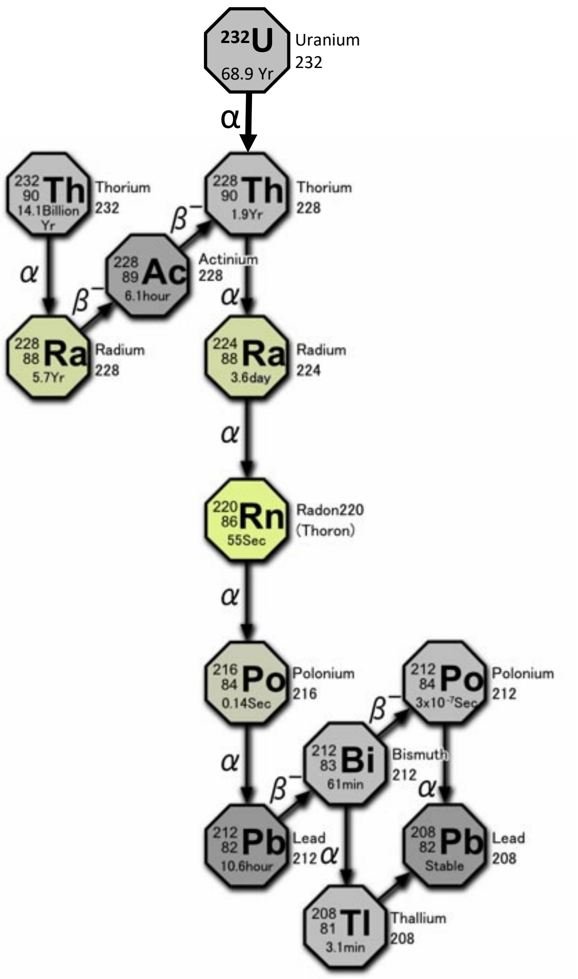
- 23 clinicaltrials.gov

Potential limitation:

- Radium does not link easily to vectors
  - Research ongoing on encapsulation
  - Use of the in-vivo generator Th-227/Ra-223



Pb-212/Bi-212 in vivo generator



Emitted radiations:

- 2 α + 2 β-

Production methods:

- From Th-232, thorium nitrate, monazite, Madagascar (France - ORANO Med)
- From U-232 (USA – DOE, ORNL)

Producers:

ORANO Med (France) DOE (USA) NRG (Netherlands)

Limites production capacity but:

- Planned increase in production capacity
- GMP production planned for 2024

Clinical trials:

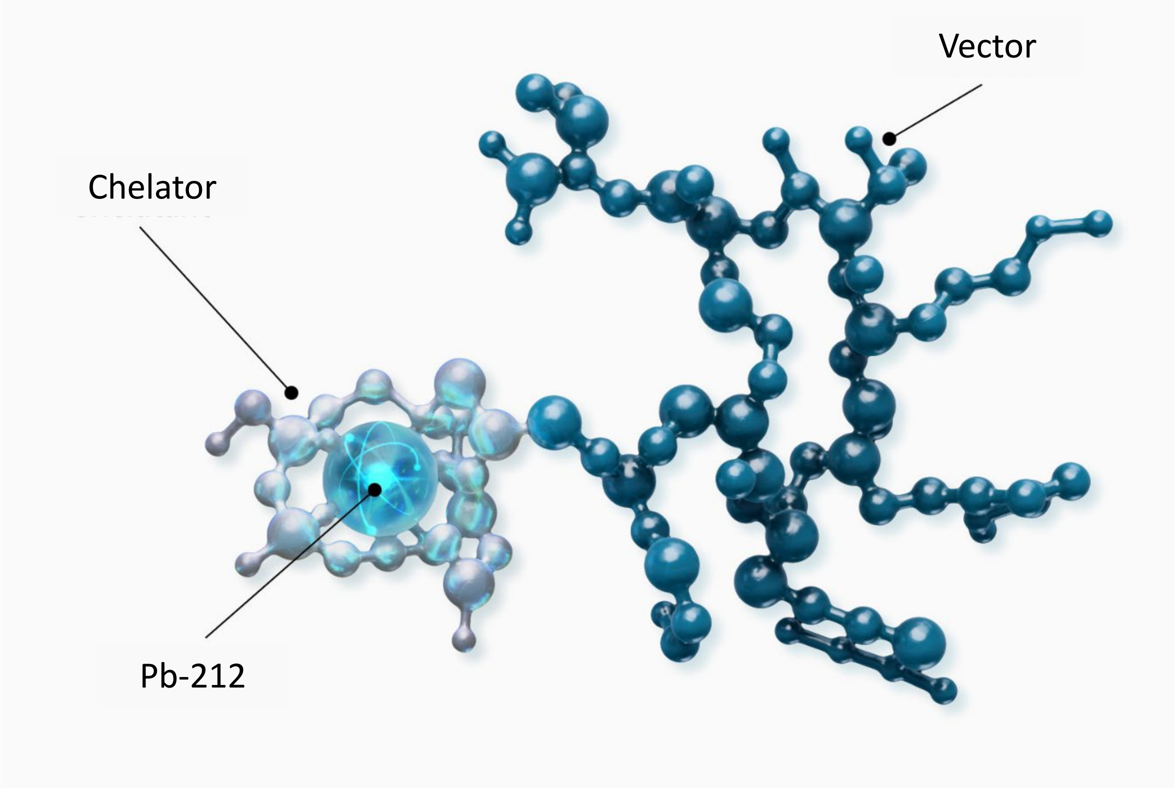
- 5 clinicaltrials.gov
  ORANO-MED
  - 2023 : phase 1 on various cancer types with a peptide anti-GRPR*
  - 2023 : phase 2 on Neuro Endocrine Tumors with AlphaMedix

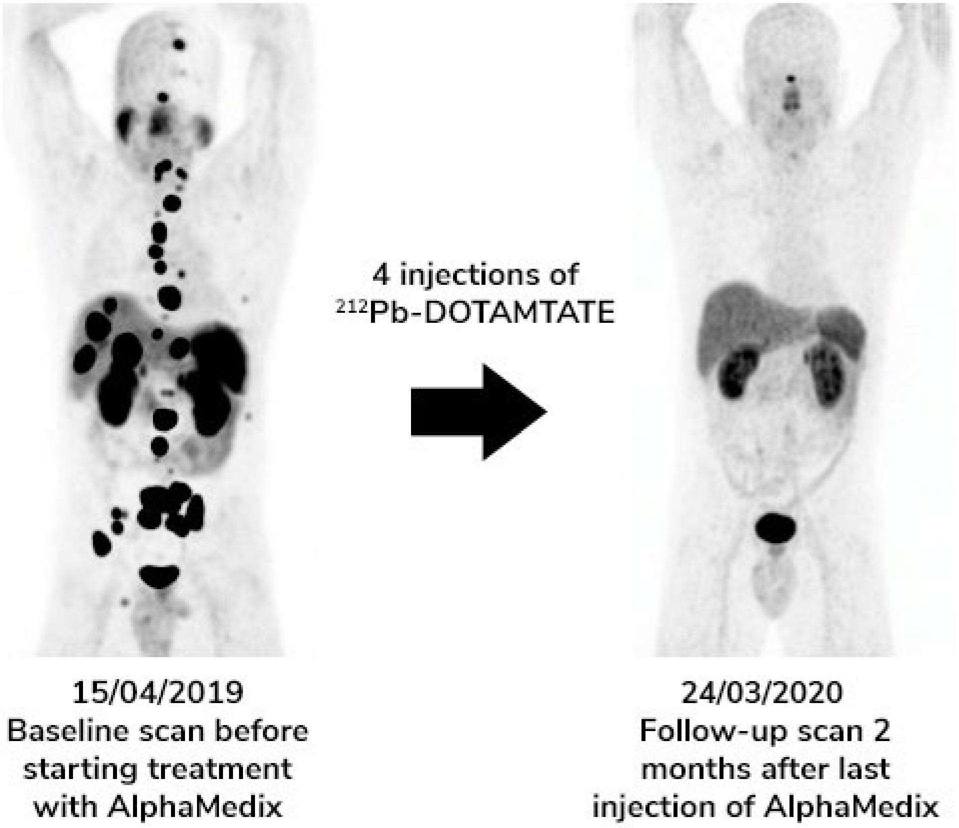
* Gastrin-Releasing Peptide Receptor

Pb-212/Bi-212 in vivo-generator: ORANO-MED

Pb-212-DOTAMTATE

^{212}Pb-DOTAMTATE





an SSTR-targeting peptide complete radiolabeled with Pb-212
SSTR, SomatoSTatin Receptor

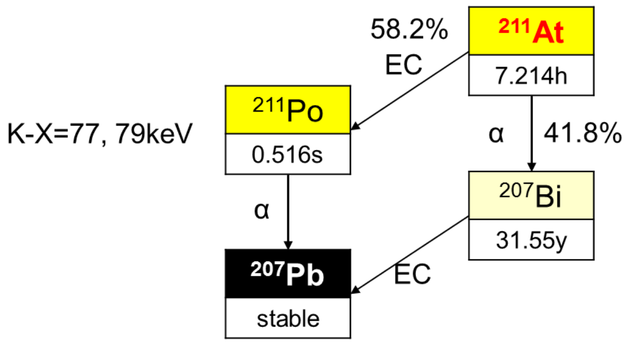
Patient with metastatic neuroendocrine tumors included in the phase 1 clinical trial of AlphaMedix (^{212}Pb-DOTAMTATE), a drug currently being developed by Orano Med and RadioMedix.

Astatine-211

Main interests:

- Half-life: not too short, not too long
  - ⇨ Adapted to Internal Vectorised Radiotherapie
- One alpha particle per decay
  - ⇨ Better control of the deposited dose
- Accelerator production
  - ⇨ IBA: C30 XP, multiparticles
  - ⇨ ACSI: TR-ALPHA, 30 MeV « alpha only »

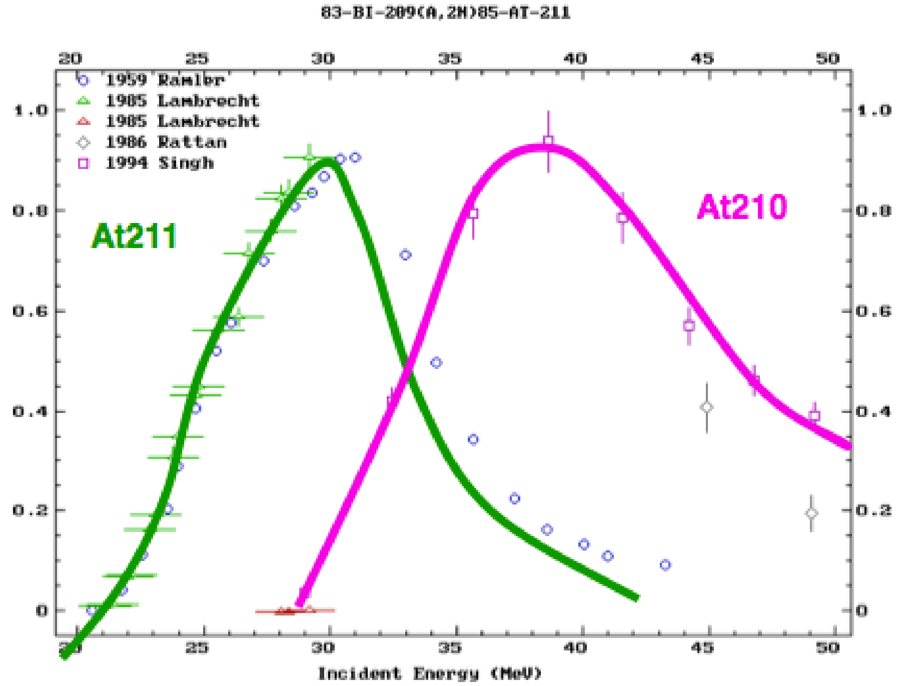
    All necessary equipments available ⇨ simple scale-up



Production route: $^{209}Bi + \alpha \rightarrow {}^{211}At + 2n$

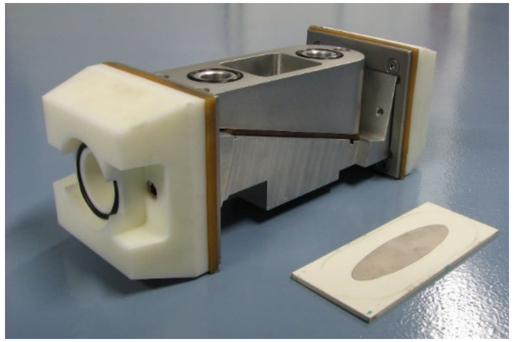
To keep in mind:

- Precise tuning of the beam energy to avoid At-210 production
  - ⇨ At-210 impurities starts to be produced above 28.613 MeV



Astatine-211 production: C70 XP @ ARRONAX

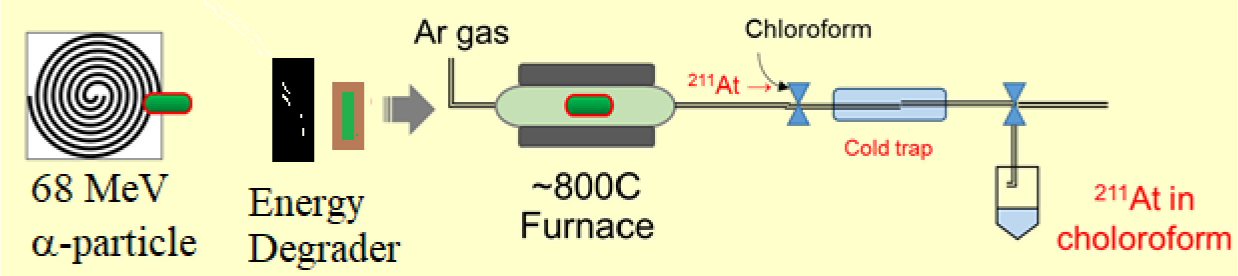
Production route: $^{209}Bi + \alpha \rightarrow {}^{211}At + 2n$



The IBA rabbit system (left) and
a target for astatine production (right)

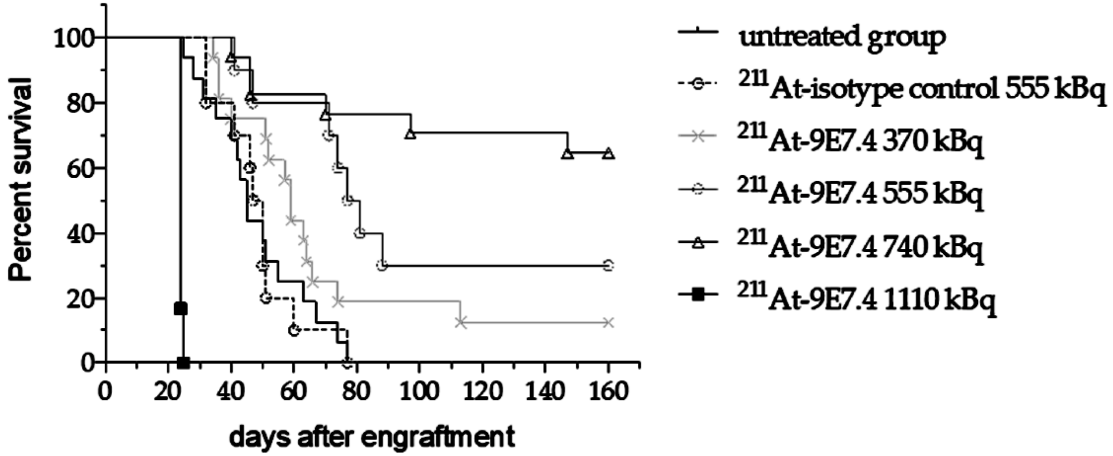
Production scheme:

- 68 MeV alpha particle beam
- Energy degrader in Al or graphite to reach 28 MeV
- Target material evaporated under vacuum
- Irradiated in an IBA rabbit system
- At-211 extraction using dry chemistry
- At-211 recovered in chloroform



In vivo application:

- At-211-labelled anti-mCD138 in mouse syngeneic multiple myeloma



Gouard S et al. Cancers (Basel). 2020 Sep 22;12(9):2721

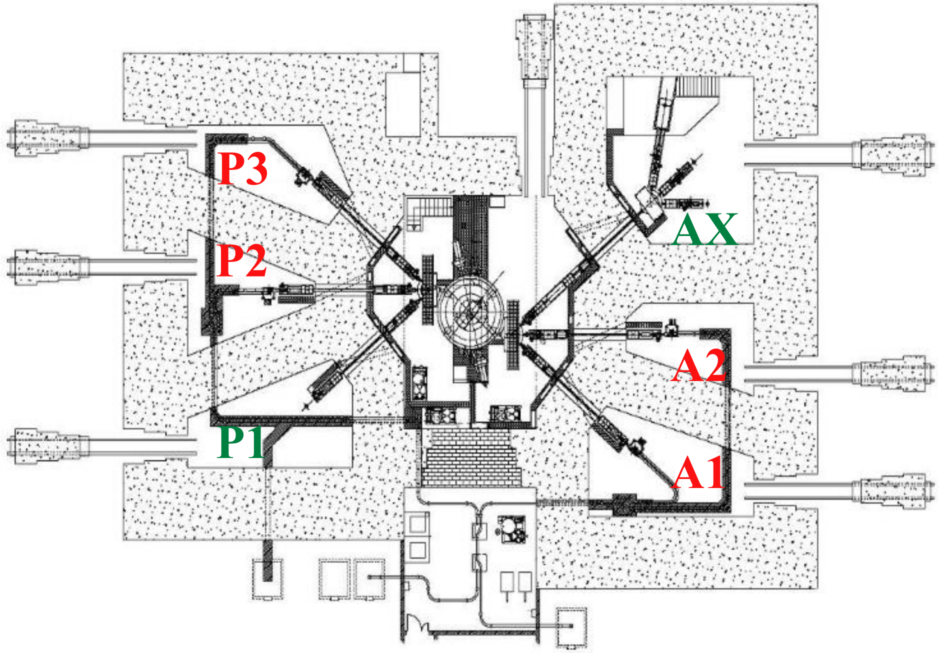
Production capacity:

- 3-4 batches/month
- Between 0.9 and 1.2 GBq EOB

C70XP @ GIP ARRONAX

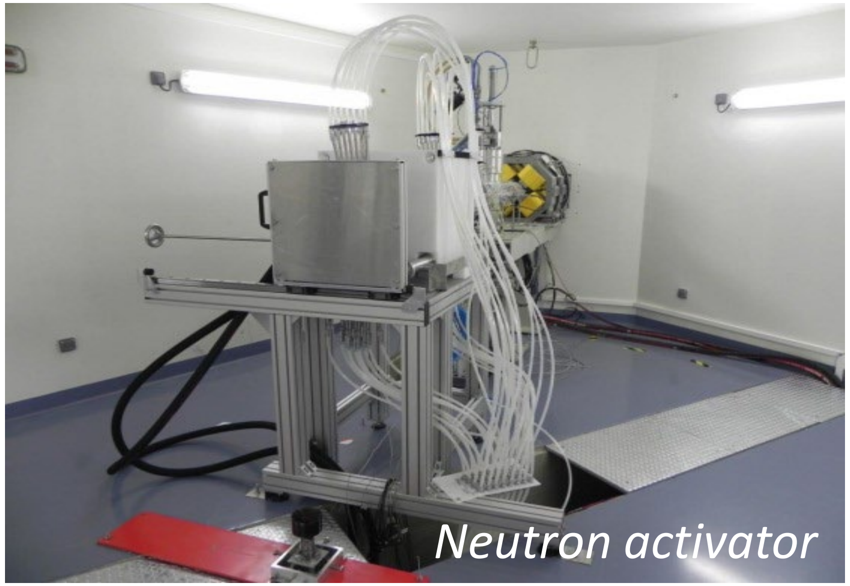
Main features: multi-particles, high energy, high intensity

Beam	Accelerated ions	Energy (MeV)	Intensity (eµA)	Dual beam
Proton	H-	30-**70**	<**375**	**Yes**
	HH+	17	<50	No
Deuteron	D-	15-35	<50	Yes
Alpha	He++	**68**	<70	No



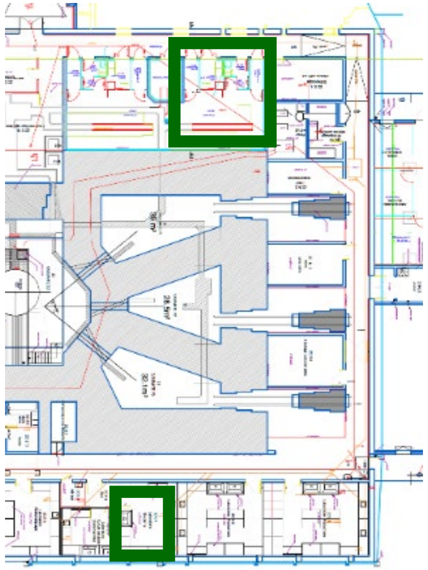
A range of laboratories: radiochemistry, biochemistry, radiolabelling, cell culture, chemical analysis, nuclear metrology, quality control, etc.

High technology environment @ GIP ARRONAX



The radiopharmacy - NU hospital / GIP ARRONAX

Purpose: production of radiopharmaceuticals for clinical trials in Europe



GMP S2

In use since May 2018

GMP S3

COMECER

QI/QO

Final qualification 2023

Several clinical trials performed using Lu-177 and Cu-64 (ARRONAX production)

Several clinical trials under preparation using Lu-177, Ac-225, At-211 (ARRONAX production) and Cu-64 (ARRONAX production)

Plan

- A little history
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- **Irradiation conditions and production yields**
- Focus on cross section measurements
- Quantitative and qualitative productions

How to choose the best irradiation conditions ?

Identify all possible production route:

- different projectile/energy/target combinations

Select the most promising one based on:

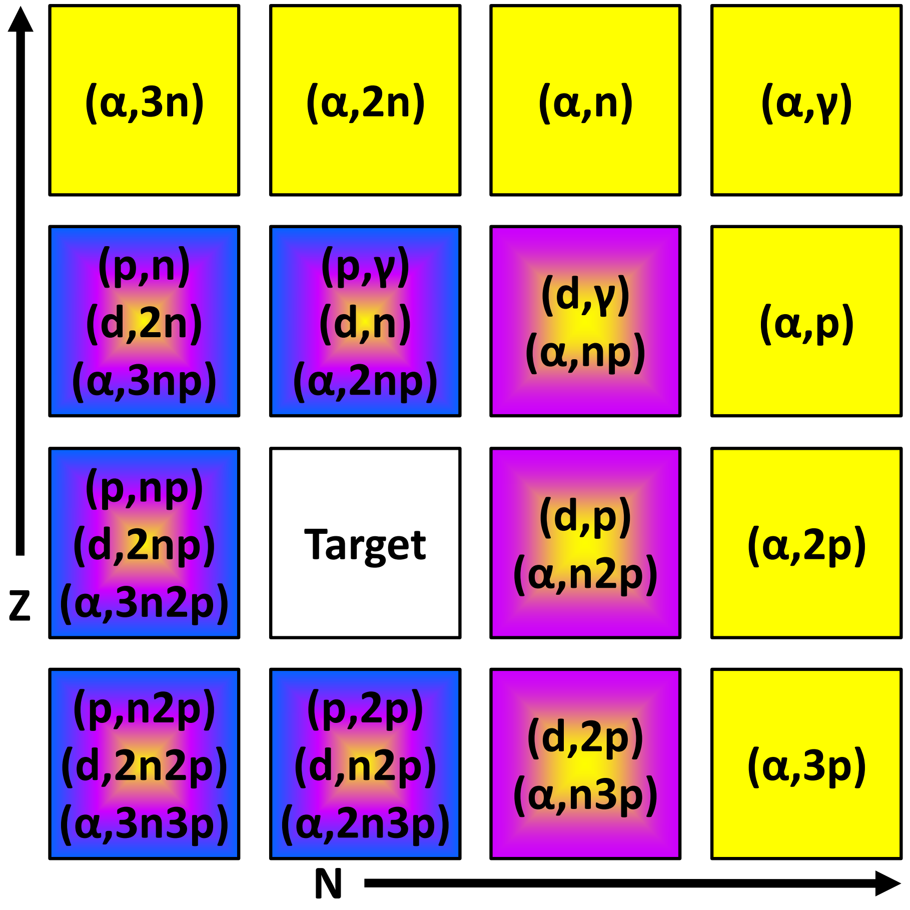
- production yield, contaminants, costs …

Fulfil physics laws is mandatory:

- Charge conservation and mass conservation
- Energy conservation: an energy threshold exists in most cases

Enlarge the choice of radionuclide that can be produced by:

- Changing the incident energy of the projectile,
- Using a given couple of
  - **Target** material, often stable or very long lived isotopes
  - **Projectile**, proton, deuteron, alpha particle …



Production yield

$$Act = \Phi \cdot \chi \cdot \frac{Na \cdot \rho}{A} \cdot (1 - \exp(-\lambda . t_{irr})) \cdot \int_{E_{fin.}}^{E_{in.}} \frac{\sigma(E)}{\frac{dE}{dx}} \cdot dE$$

Radionuclide of interest

- Activity Bq
- Radioactive constant s^{-1}
- Production cross section cm^2

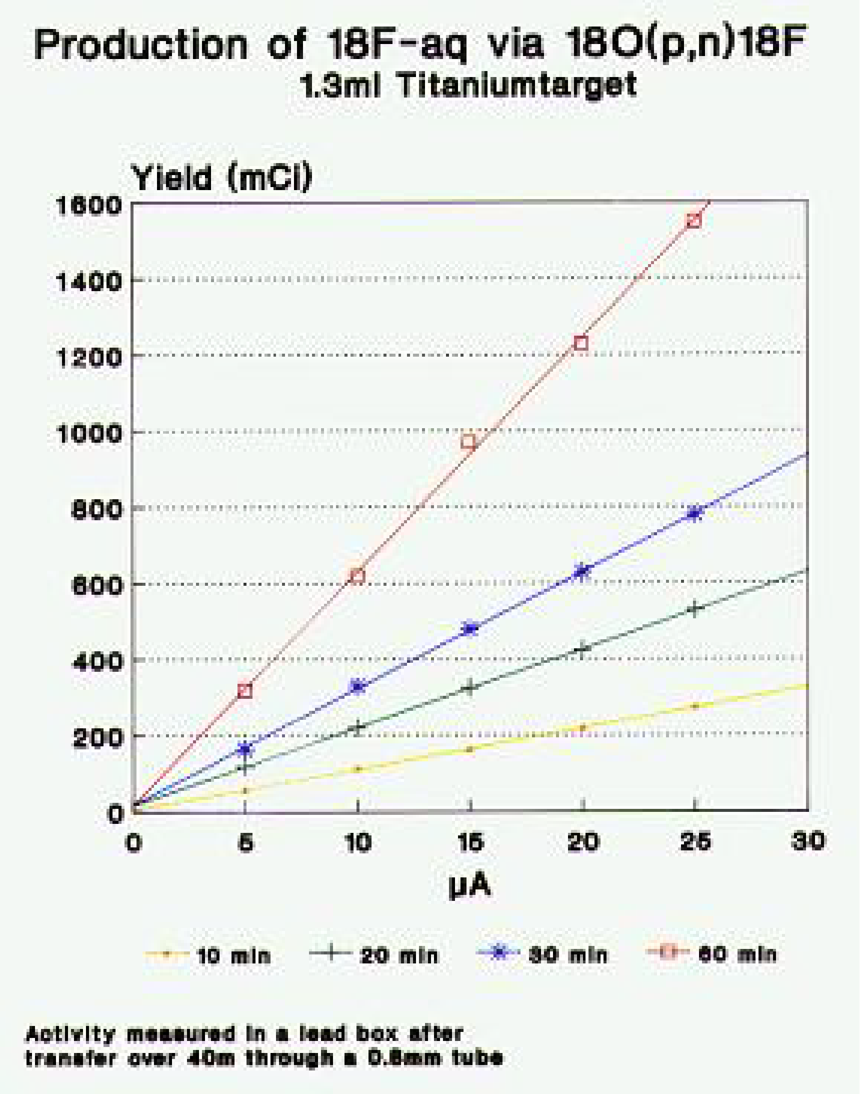
Target material

- Isotopic purity
- Density $g.cm^{-3}$
- Mass number $g.mol^{-1}$
- Target thickness cm

Irradiation conditions

- Projectile flux $projectile.s^{-1}$
- Irradiation time s
- Projectile energy MeV

What parameters impact the production yield ?

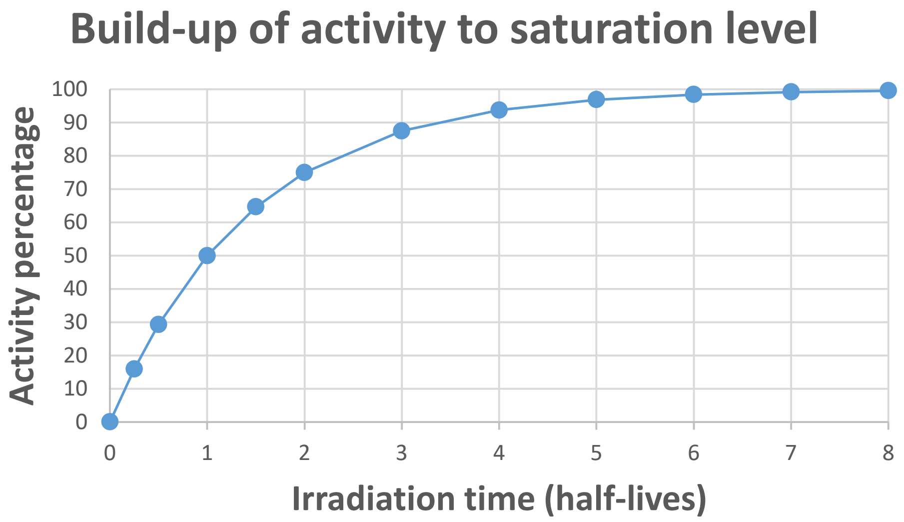


⇨ **Projectile flux**

- linear effect

⇨ **Irradiation time**

- linear effect for few half-lives
- then saturation, $f = 1 - (1/2)^n$



What parameters impact the production yield ?

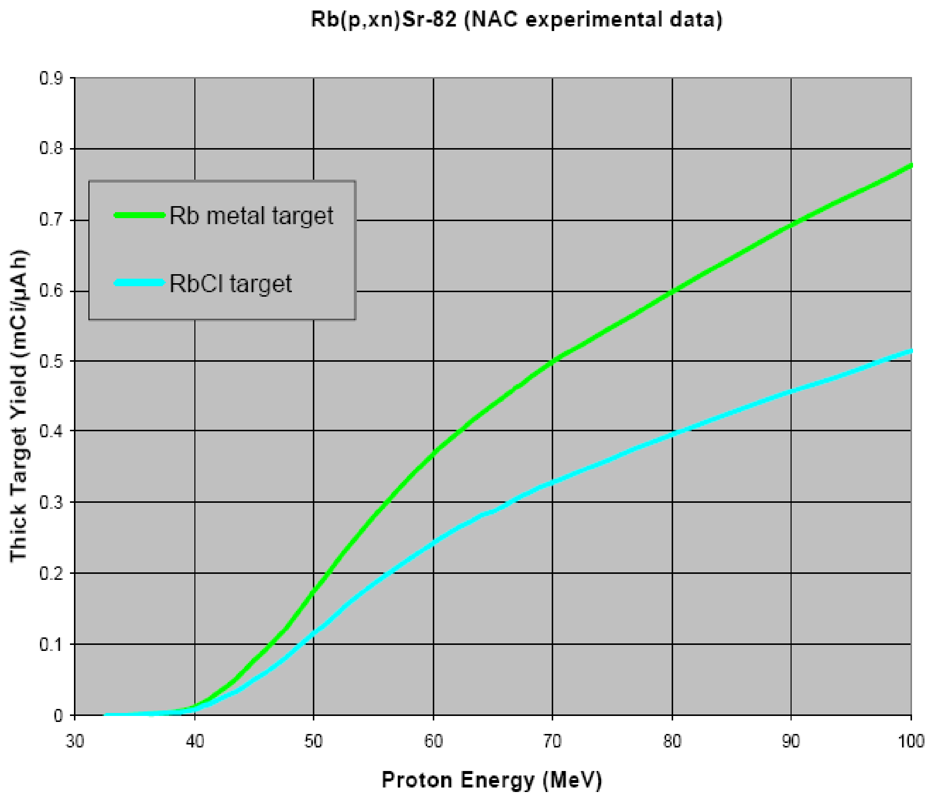
⇨ **Number of target nucleus**

↳ Target thickness

- effect depending of the excitation function

↳ Enriched material

- linear effect on production
- but not on price



Courtesy of Pr. Férid HADDAD

⇨ **Chemical form of the target material**

- Example, Sr-82/Rb-82 generator

RbCl vs Rb metal

7.6 W/(m.K) | 58.2 W/(m.K)

⇨ Higher current on target

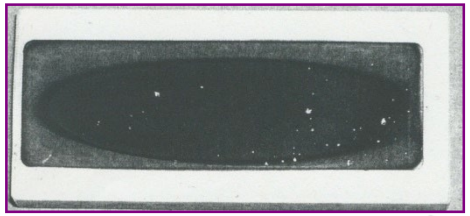
No hazard | Danger

⇨ Releases flammable gases in contact with water, which may ignite spontaneously

⇨ Causes severe skin burns and serious eye damage

⇨ **Physical form of the target material**

Ni-64 electroplating on Au
⇨ **Cu-64**



Bi deposition under vacuum on Al
⇨ **At-211**

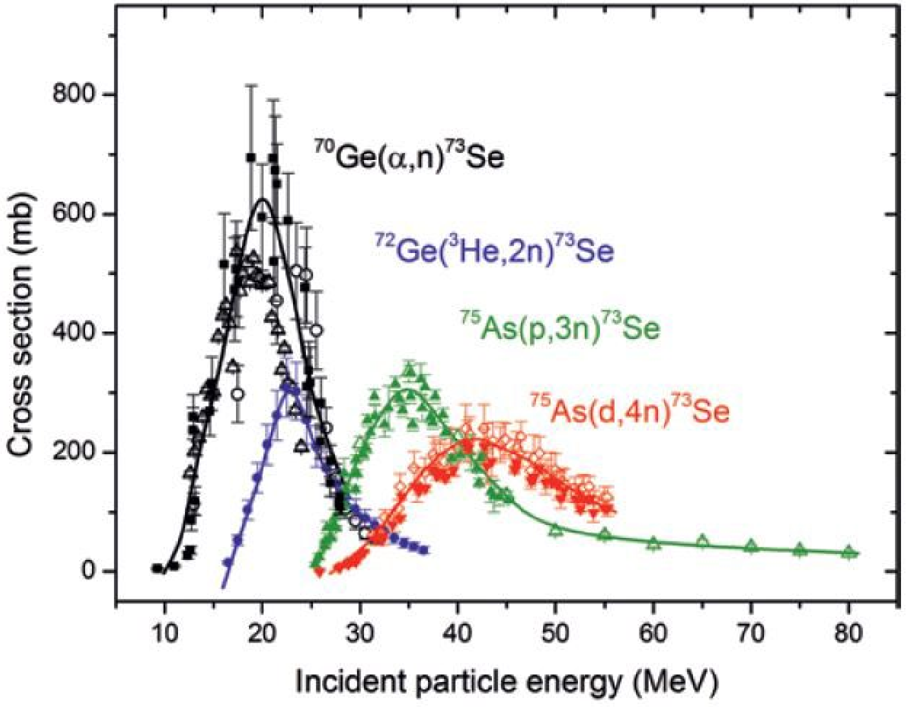
$CaCO_3$ pellet
⇨ **Sc-47**

What parameters impact the production yield ?

⇨ **Production cross section shape**

- Incident projectile energy
- Target material thickness
    - Maximize radionuclide of interest production
    - Minimize contaminants production

- Se-73, positon emitter, as an example



Nuclear reaction	Energy range [MeV]	Yield of ^{73}Se [MBq/µAh]	$^{72,75}Se$ Impurity [%]
$^{75}As(p,3n)$	40 → 30	1406	0.1
$^{75}As(d,4n)$	40 → 33	700	0.2
$^{72}Ge(^{3}He,2n)$	35 → 15	130	1.8
$^{70}Ge(\alpha,n)$	26 → 13	300	0.5

$^{75}As(p,3n)^{73}Se$ reaction is the method of choice

Qaim et al, RCA 104, 601 (2016)

Cross section shape: production of ^{82}Sr @ GIP ARRONAX

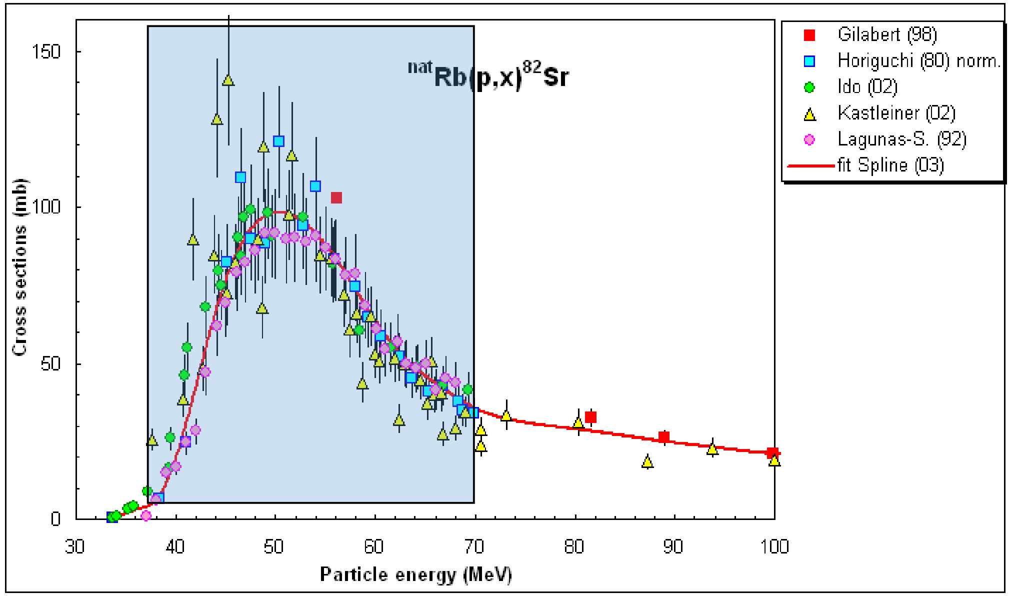
Main characteristics:

+ Decay to ^{82}Rb used for PET imaging in cardiology
+ $T_{1/2}$ = 25.34 days

Main Production route:

$^{nat}Rb + p \rightarrow {}^{82}Sr + x\ n$

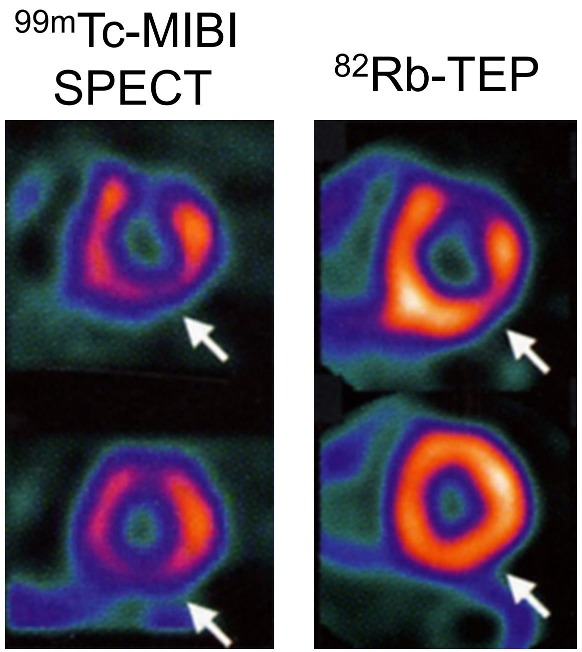
Beam characteristics:



Low cross section
~ 100 mb

Energy range of interest
40 MeV-70 MeV

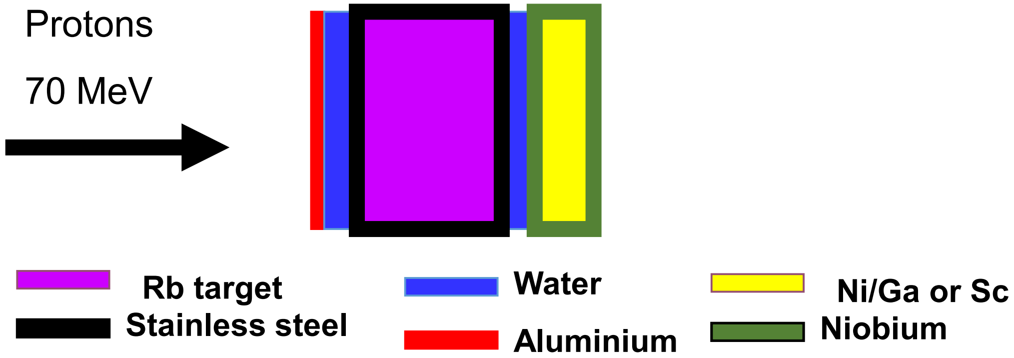
⇨ **Routine production of ^{82}Sr**
More than 500 000 patients

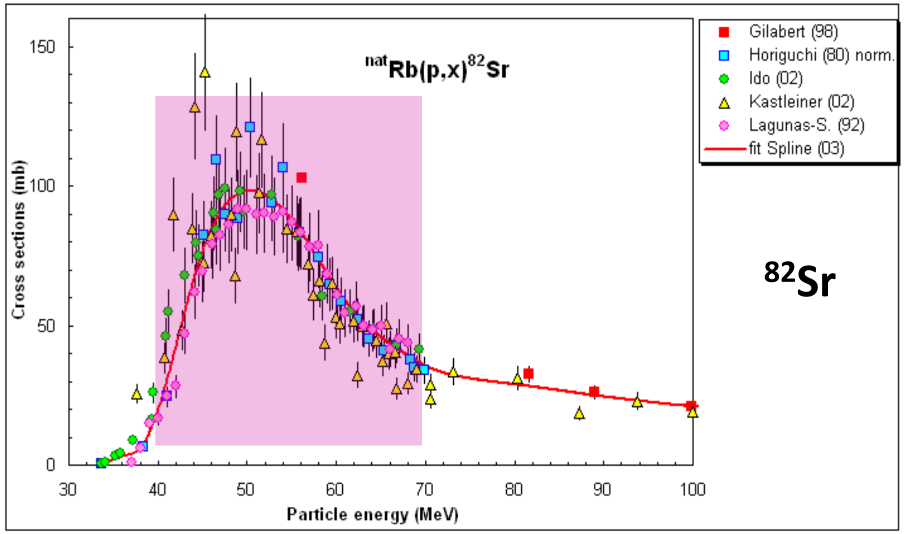


D. Le Guludec et al, Eur J Nucl Med Mol Imaging 2008; 35: 1709-24

Tandem target concept: ^{68}Ge and ^{44}Ti

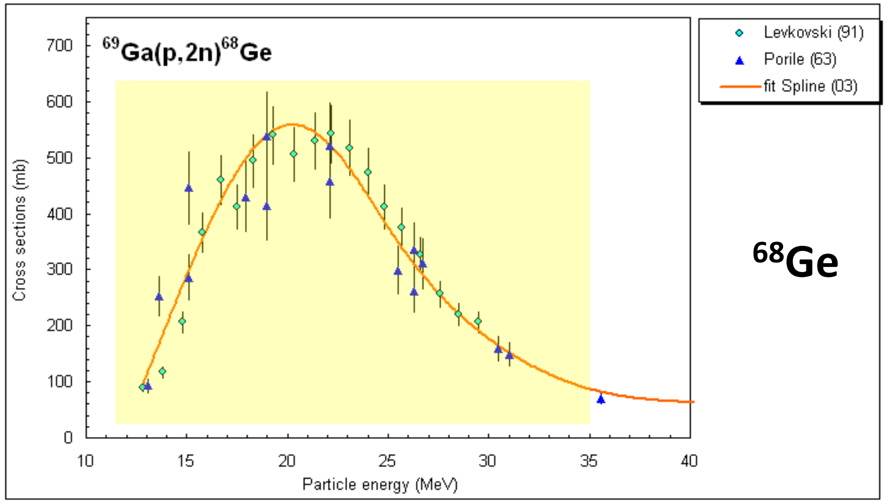
Tandem target scheme under review

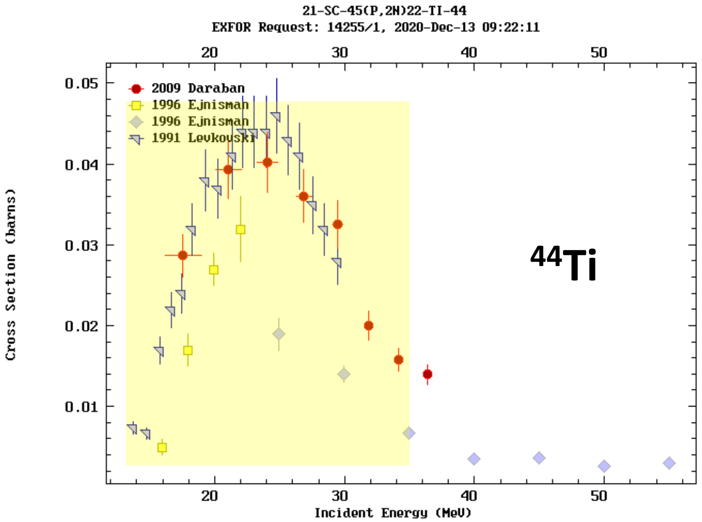




^{82}Sr

Taking advantage of production cross sections

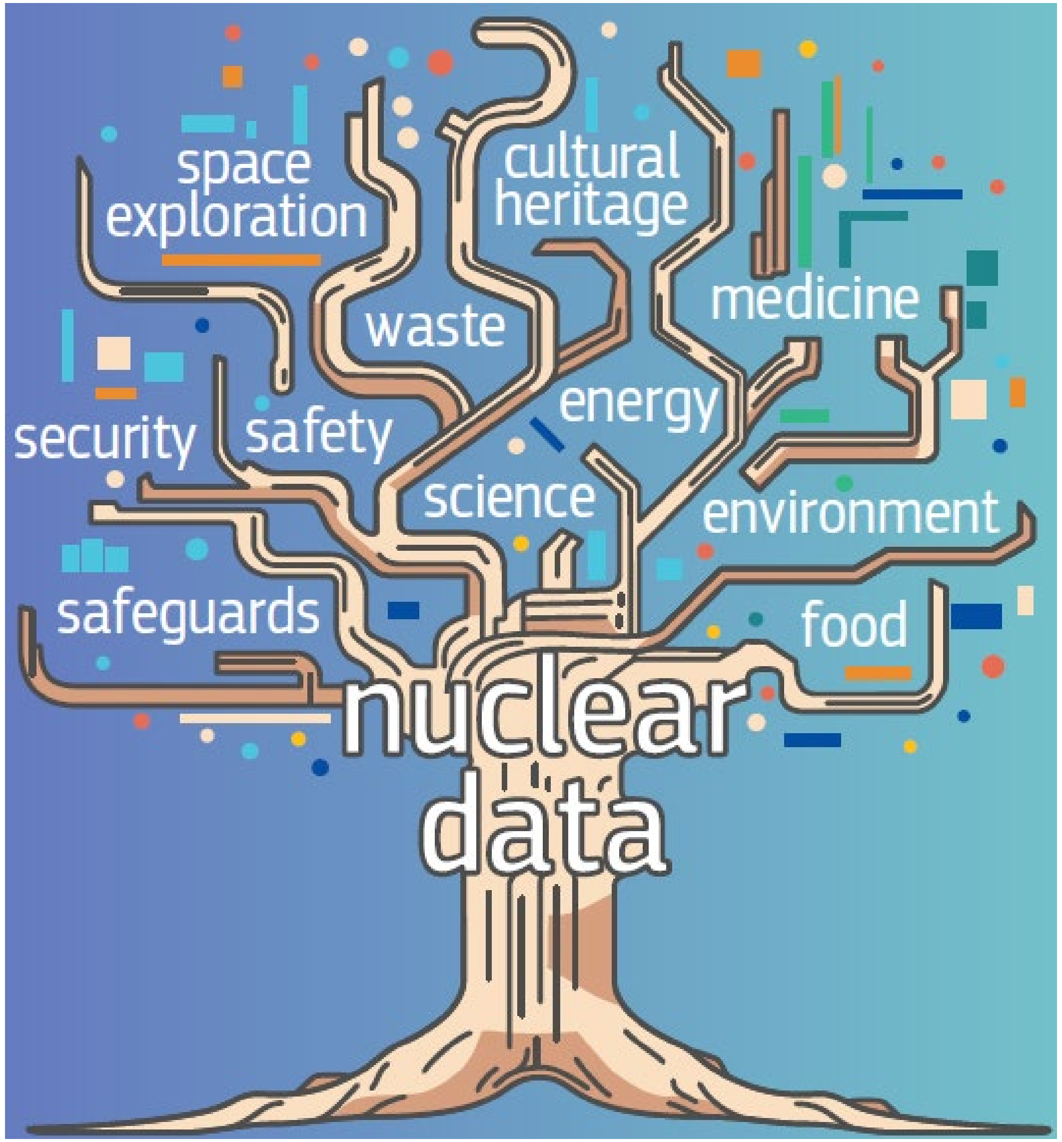




Plan

- A little history
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- **Focus on cross section measurements**
- Quantitative and qualitative productions

Nuclear data needs: focus on cross section measurements



Nuclear data needs addressed by successive:

- Experimental physicist generations
- IAEA Coordinated Research Projects initiated in the 90's, European FPs, national programs

- **Accurate and reliable** sets of data
- Well defined **production routes and decay properties**

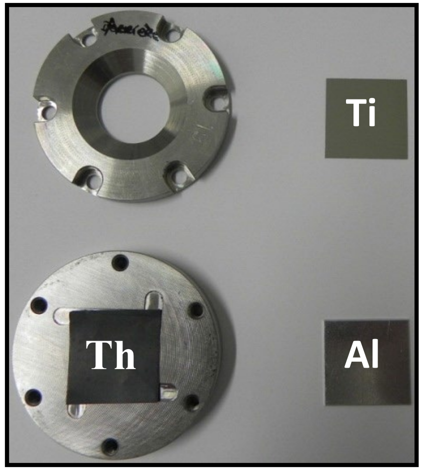
- **Optimum production** of specific radionuclides, minimization / elimination of **impurities**, **realistic dose calculations**

- Provide **a large set of nuclear data** in terms of targets, projectiles and energy range **to constrain and develop** predictive simulation tools of nuclear reactions

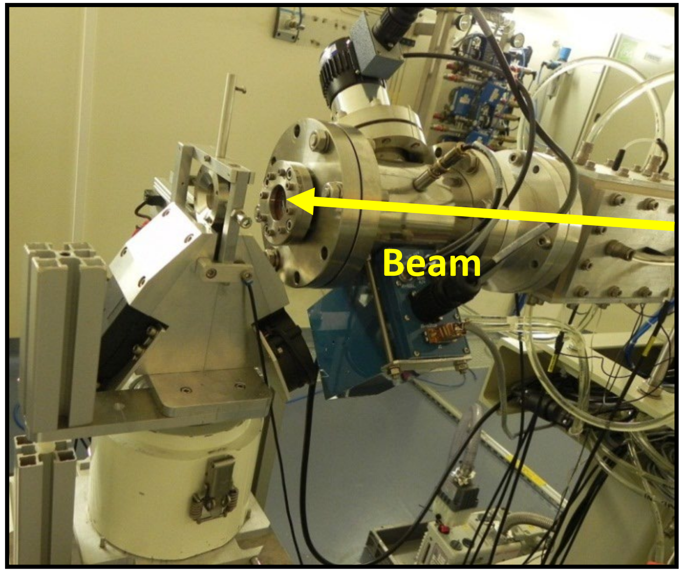
Stacked-foils technique in air

Stacked-foil technique:

- Target/monitor/degrader **pattern**
- **Thin** foils:
  E loss small and constant
- One cross section value per foil



Capsule and foils



Irradiation station and beam line

Activity and cross section:

$$\sigma = \frac{Act \,.\, A}{\chi . \Phi \,.\, \mathcal{N}_A \,.\, \rho \,.\, e \,.\, (1 - e^{-\lambda . t})}$$

Use of a Faraday cup:

- Beam dump placed at the end of the stack to control the intensity during the irradiation

Use of a monitor foil:

$$\sigma = \sigma' . \frac{\chi' . Act \,.\, A \,.\, \rho' \,.\, e' \,.\, (1 - e^{-\lambda' . t})}{\chi . Act' \,.\, A' \,.\, \rho \,.\, e \,.\, (1 - e^{-\lambda . t})}$$

- error on e, e': ≤ 1%
- error on t: negligible

IAEA recommended cross sections:

- 11 reactions available for protons
  ^{27}Al (2), ^{nat}Ni, ^{nat}Ti (2), ^{nat}Cu (5), ^{nat}Mo
- 11 reactions available for deuterons
  ^{27}Al (2), ^{nat}Fe, ^{nat}Ni(3), ^{nat}Cu (3), ^{nat}Ti(2)
- 6 reactions available for alpha-particles
  ^{27}Al (2), ^{nat}Ti and ^{nat}Cu (3)

https://www-nds.iaea.org/medical/monitor_reactions.html

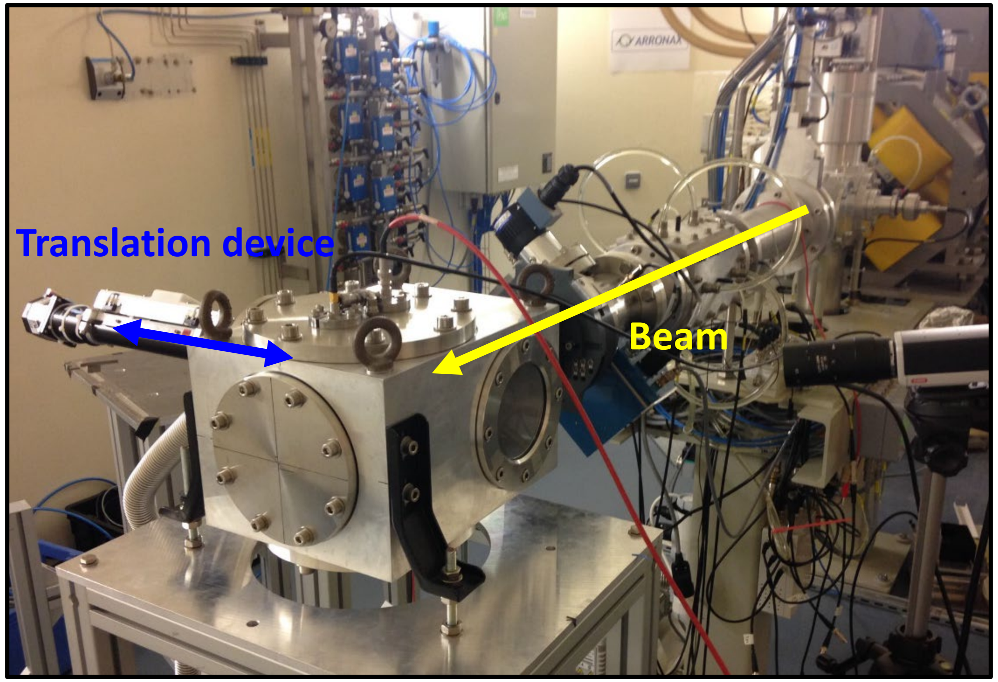
Stacked-foils technique under vacuum

Activity and cross section:

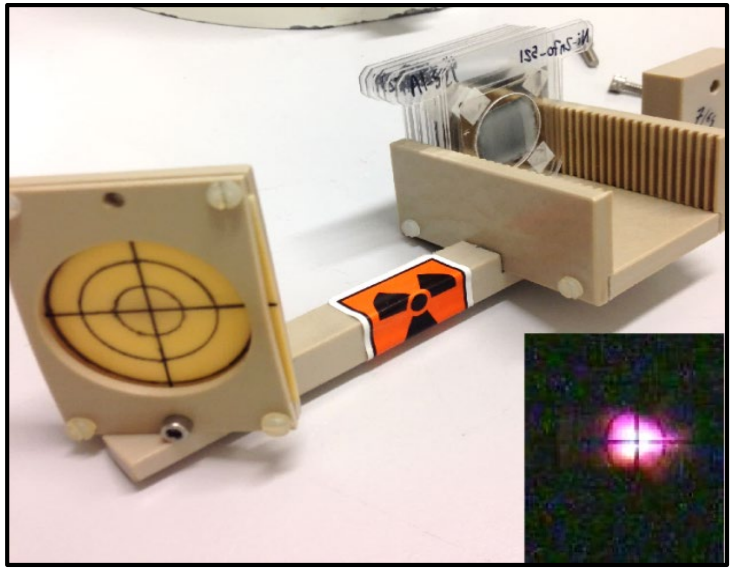
$$\sigma = \frac{Act\,.\,A}{\chi.\,\Phi\,.\,\mathcal{N}_A\,.\,\rho\,.\,e\,.\,(1\ -\ e^{-\lambda.t})}$$

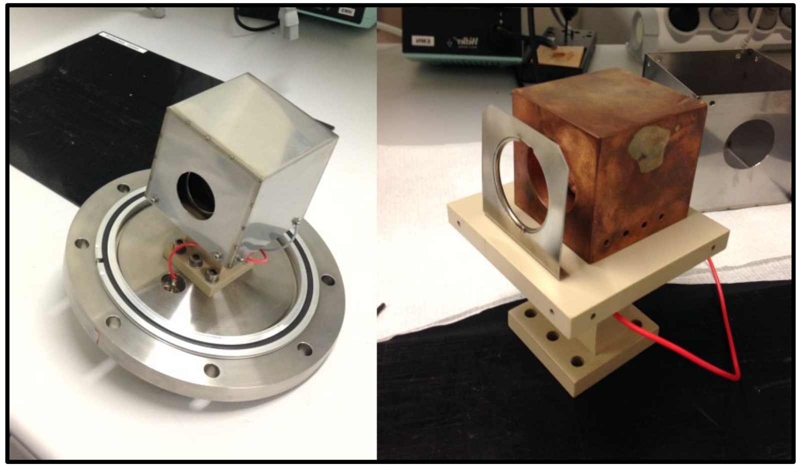
Use of a Faraday cup:

- Placed at the end of the stack to measure the intensity during the irradiation



Irradiation station and beam line

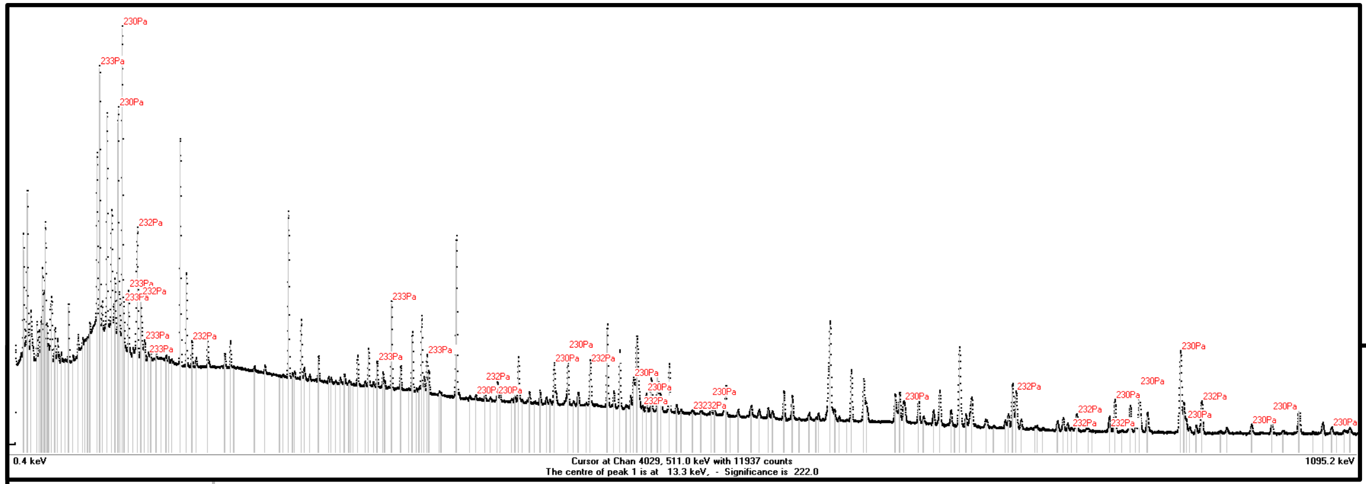

Translation device : stack, empty, Al_2O_3


Faraday Cup

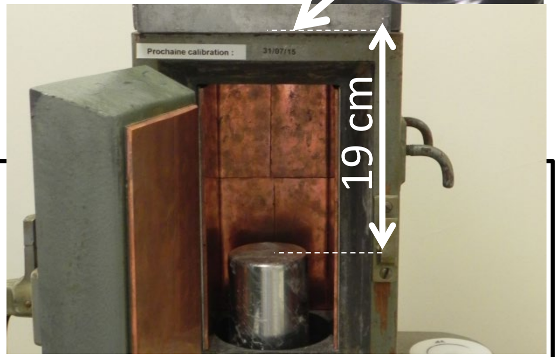
Off line gamma spectroscopy

- **HPGe** coaxial detector
- Dead time: < 10% (sum peak)
- Activity values: FitzPeaks
- $T_{1/2}$, E_γ, I_γ: Lund/LBNL, NNDC

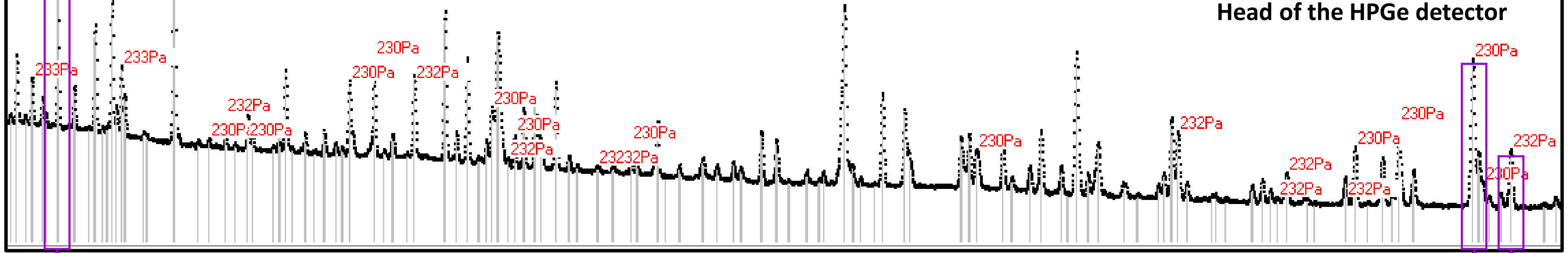
- γ spectra recorded on **8192 channels**
  - FWHM: 1.04 keV at 122 keV (^{57}Co)
    1.97 keV at 1332 keV (^{60}Co)
  - Energy and efficiency calibrations: Co and Eu



Target and monitor:
✓ counted twice
✓ during > 24 hrs
✓ 2 week delay



Head of the HPGe detector



γ rays used to extract production cross section of $^{230,232,233}Pa$

Collected data sets: proton induced reactions

Ac-225 from Th-232(p,x)	C. Duchemin et al, Phys Med Biol **60** (2015) **931-946**
Ra-223 from Th-232(p,x)	C. Duchemin et al, Phys Med Biol **60** (2015) **931-946**
Fission fragment distribution from Th-232(p,x)	V. Métivier et al, EPJ Web of Conf. **146** (2017) **08008**
Cu-67 from Zn-68(p,2p)	G. Pupillo et al., Nucl Instr Meth Phys Res B **415** (2018) **41-47**
Ga-67 from (p,2n), Ga-66 from (p,3n)	
Cu-67 and Cu-64 from Zn-70(p,x)	G. Pupillo et al., Radiochimica Acta **108** (2020) **593-602**
Ga-67, Ga-66, Zn-65 and Zn-69m	
Tb-149 from Gd-nat(p,x)	R. Formento Cavaier, PhD thesis (2019)
Tb-150,151,152,153,154,154m2,155,156	Nucl Instr Meth Phys Rev B **478** (2020) **174-181**
Tb-155 new data set for $^{h.e.155}$Gd(p,x)	M. Bouteculet et al, Appl Radiat Isot **213** (2024) **111485**
Monitor reactions on Ti, Ni and Cu	E. Garrido et al., Nucl Instr Meth Phys Res B **383** (2016) **191-212**
Sc-43 from V(p,x)	G. Pupillo et al., Nucl Instr Meth Phys Res B **464** (2020) **32-35**
Sc-47,Sc-44m,Sc-44 from V-nat(p,x)	G. Pupillo et al., Il Nuovo Cimnto **42 C** (2019) **139**
Sc-48,46,43, K-43,42 ,V-48, Cr-51,49,48	G. Pupillo et al., J Radioanal Nucl Chem **322** (2019) **1711**
Sc-47,Sc-44m,Sc-44 from Ti-48(p,x)	F. Barbaro et al., Phys. Rev. C **104** (2021) **044619**

Collected data sets: deuteron induced reactions

Sc-44 New data set for Ca-44(d,x)	C. Duchemin et al, Phys Med Biol **60** (2015) **6847-6864**
Tb-155 New data set for Gd-nat(d,x)	C. Duchemin et al, Appl Radiat Isot **118** (2016) **281-289**
Tb-155,156,160,161 from Dy-nat(d,x)	M. Colucci et al., Eur Phys Jour Plus **137** (2022) **1180**
Tb-155 from Gd-155(d,2n)	Y. Wang et al. Appl Radiat Isot **201** (2023) **110996**
Re-186g New data set for W-186(d,x)	C. Duchemin et al, Appl Radiat Isot **97** (2015) **52-58**
Pa-230 for U-230/Th-226 New data set for Th-232(d,x)	C. Duchemin et al., Nucl Med Biol **41** (2013) **19-22**
Fission fragment distribution from Th-232(d,x)	V. Métivier et al, EPJ Web of Conf. **146** (2017) **08008**
Monitor reactions on Ti, Ni	C. Duchemin et al, Appl Radiat Isot **103** (2015)**160-165** E. Nigron
Rh-105 New data set for Ru-104(d,x)	M. Sitarz, PhD thesis 2019
Hg-197m New data set for Au-197(d,x)	E. Nigron, PhD thesis 2019
Mn-52g from Cr-nat(d,x)	F. Bianchi et al., Appl Radiat Isot **166** (2020) **109329**
Cu-67 New data set for Zn-70(d,x)	E. Nigron, PhD thesis 2019 and Front. Med. **8** (2021) **674617**
Tb-161 from Gd-160(d,n)	E. Nigron et al., Appl Radiat Iso **200** (2023) **110927**
Pb-203 from Tl-205(d,4n)	T. Sounalet et al., EPJ Web of Conferences **285** (2023) **09001**

Collected data sets: alpha induced reactions

Mo-99 New data set from Zr-96(α,n) — G. Pupillo et al., J. Radioanal. Nucl. Chem. **302** (2014), 2, **911-917**

Sn-117m New data set from Cd-116(α,x) — C. Duchemin et al, Appl Radiat Isot **115** (2016) **113-124**

Monitor reactions on Cu, Ti, Ni

Ru-97 New data set from Mo-nat(α,x) — M. Sitarz et al, Instruments **3** (2019) **7**

A PhD work started in October 2023 — L. Puren

“What role can alpha particle beams play in the production of radionuclides of medical interest?”

Plan

- A little history
- Conventional imaging and therapy, Nuclear medicine
- Isotopes, Facilities
- Molecular Imaging and RadioligandTherapy, Radiotheranostics
- SPECT, PET, Therapy isotopes and Generators
- Focus on alpha particle emitters
- Irradiation conditions and production yields
- Focus on cross section measurements
- **Quantitative and qualitative productions**

The field of possibilities

Quantitative production

- Irradiation time, number of projectiles, number of target nuclei
- Use of enriched materials, selection of nuclear reaction
- Selection of projectile energy

Qualitative production

- Action on physical parameters:
  energy, beam, decay time
- Use of chemical separation
- Use of mass separation
- And also laser ionization and mass separation

Why are we interested by mass separation ?

Main characteristics:

Multi-particles, High energy, High intensity

enlarge the scope of possible nuclear reactions for isotope production but …

Beam	Accelerated particles	Energy range (MeV)	Intensity (eμA)	Dual beam
Proton	H-	30-**70**	<**375**	**Yes**
	HH+	17	<50	No
Deuteron	D-	15-35	<50	Yes
Alpha	He++	**68**	<70	No

at the same time there is an increase of parasitic nuclear reactions

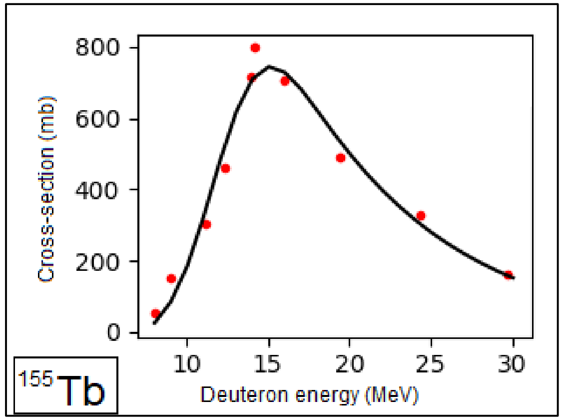
- Non isotopic contaminants could be eliminated by chemistry
- Production of isotopic contaminants could be controlled through a combination of:
  - The use of highly enriched target material (when possible)
  - Choosing the adequate projectile energy/target thickness
  - Choosing different nuclear reaction as (d,x), (α,x) … or even indirect reactions
  - Using decay if half lives are different

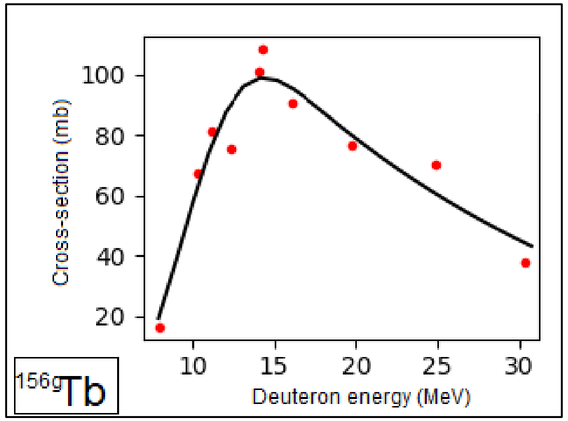
However, this is not always sufficient …

Contaminants are a limiting factor for production

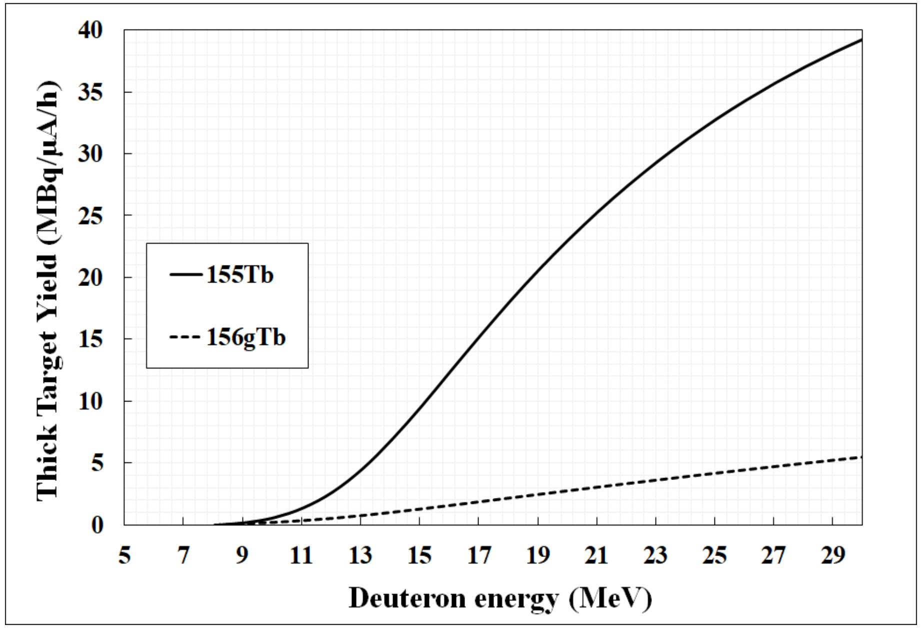
Terbium-155 production as an example

$^{155}Gd(d,x)$ – 93% enrichment
RYC calculation tool (Sitarz, 2019)





Thick target yield (TTY) of ^{155}Tb and ^{156g}Tb



Particles	H-	D-
Target thickness (µm)	300	390
Energy (MeV)	10.4	15.1
TTY (MBq/µA/h)	3.4	10.2
Purity (%)	93	88

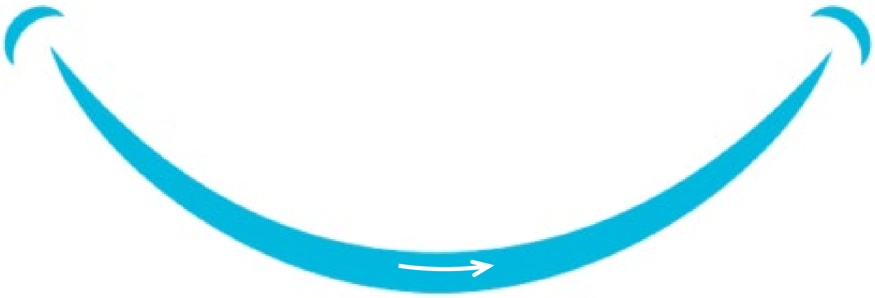
^{156}Tb always co-produced
$T_{1/2}$ similar to ^{155}Tb

- ^{64}Cu co-produced when using ^{68}Zn(p,x)^{67}Cu
- ^{46}Sc($T_{1/2}$=83.8d)co-produced when using ^{48}Ti(p,x)^{47}Sc
- Production of ^{210}At prevent us to benefit of the full cross section for ^{211}At
- And many more …

⇨ **Mass separation can be another way to gain in purity**

The SMILES project @ SUBATECH

Séparation en **M**asse
couplée à l'**I**onisation **L**aser
pour des applications
Environnementales
et en **S**anté

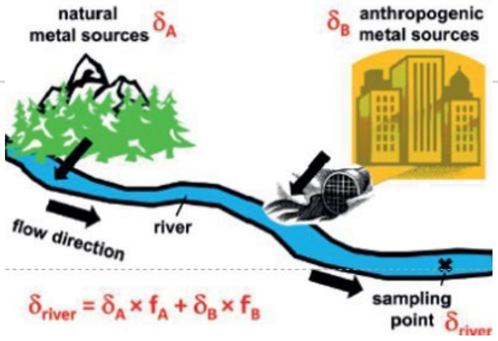


Laser ionization and mass separation for environmental and health applications

Main objectives

- Develop a mass separation device that includes resonant laser ionisation
- Be able to make analytical measurements on environmental sample (as for example from old U mines)
- Build expertise on these techniques and on simulation tools
- Prepare for off-line mass separator for radionuclide production

Environmental Applications



Health Applications

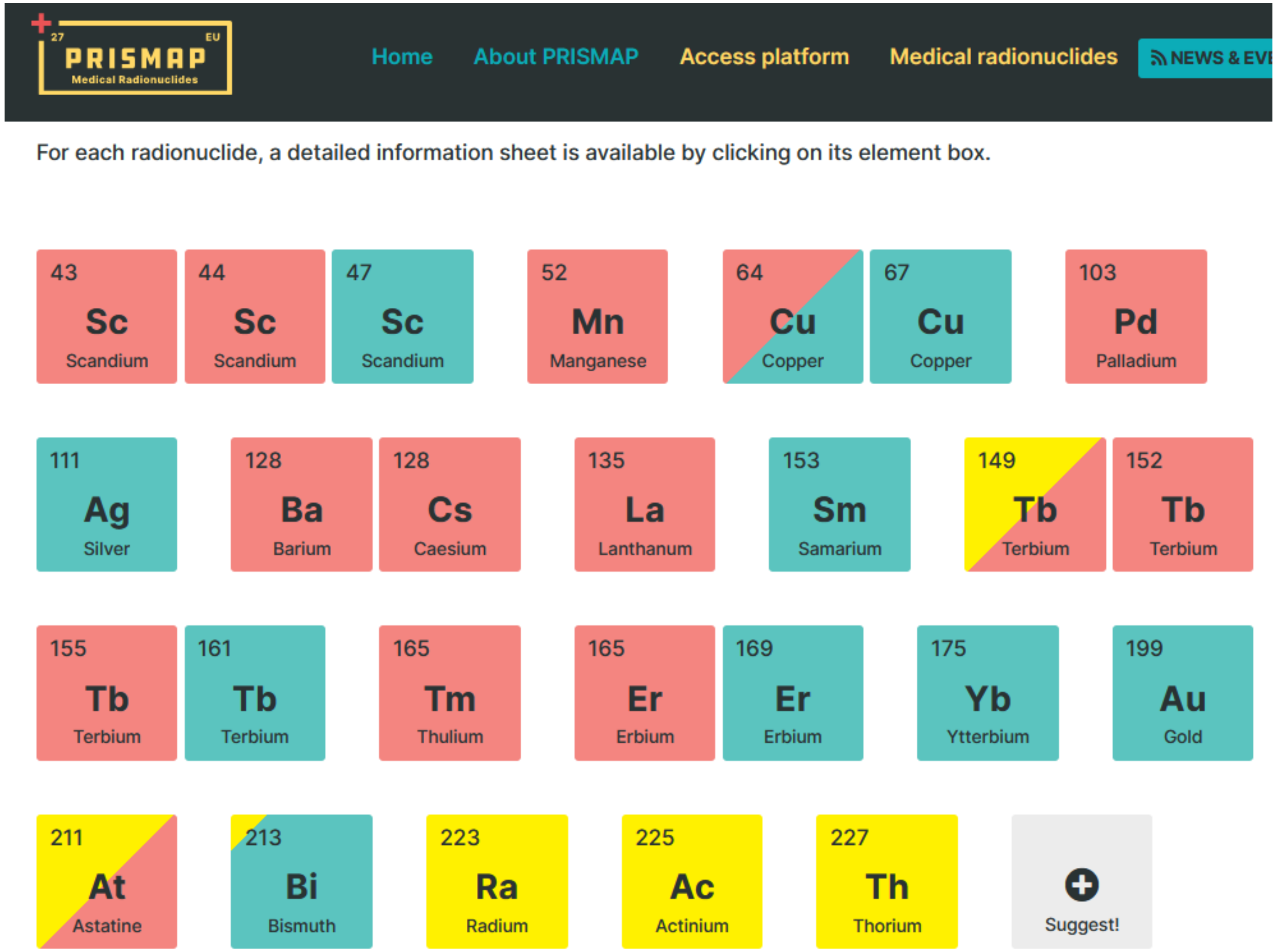
Stable element: Cu-65/Cu-63
Isotopic analysis: Pb , Am, Pu, Ra-226/Ra-228
Ultra trace analysis: Pb-210, Th-230,U-236

Stable element: Cu-65/Cu-63
Radioactive isotope: Er, Tb

EU INFRAIA PRISMAP Project

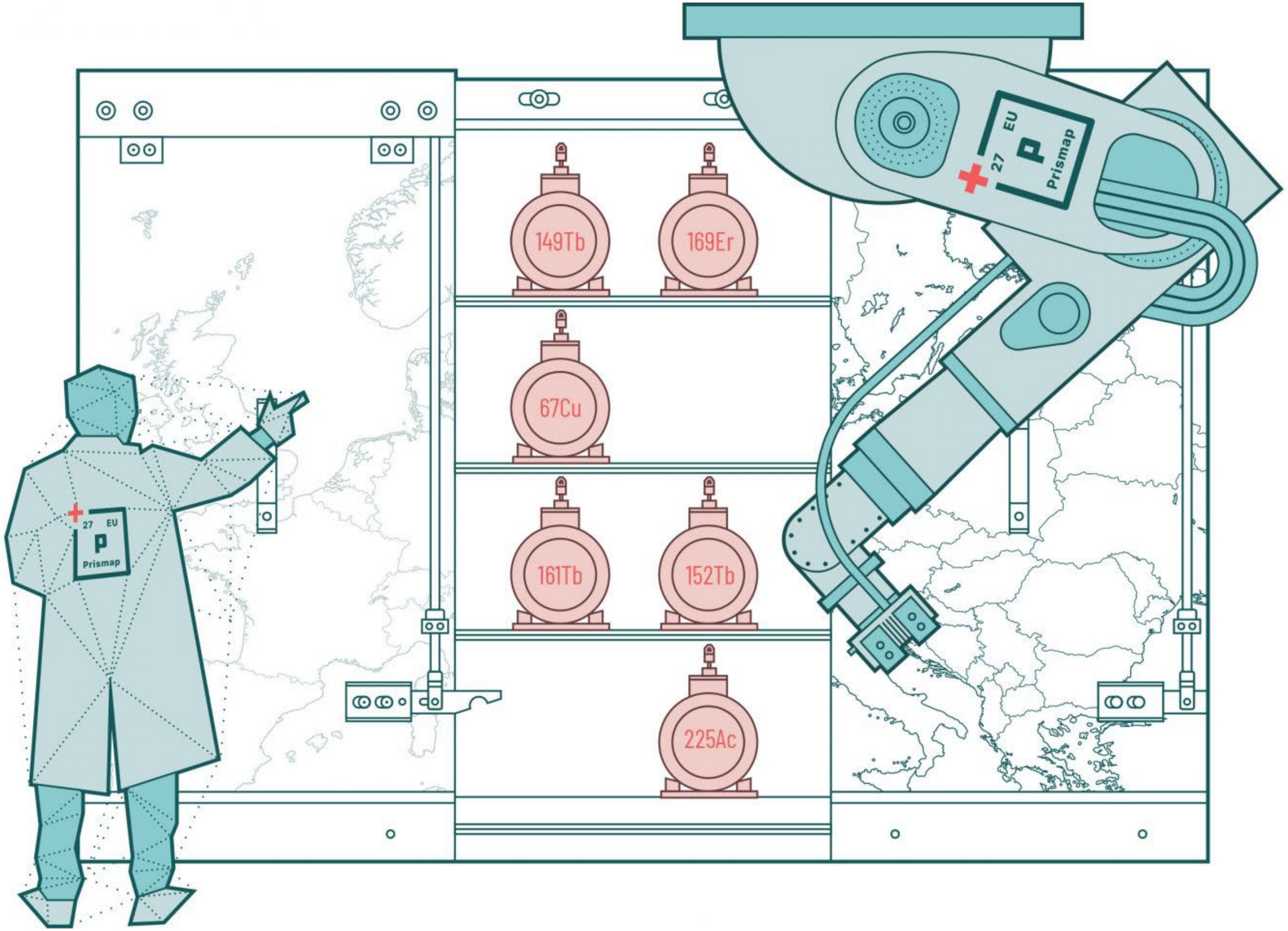
Objectives

- Provide **access to new radionuclides** and **new purity grades** for the medical research
- Create a common entry port and web interface to the **starting research community**
- Enhance clarity and regulatory procedures to **enhance research with radiopharmaceuticals**
- **Improve the delivered radionuclide data** and regulation, along with biomedical research capacity



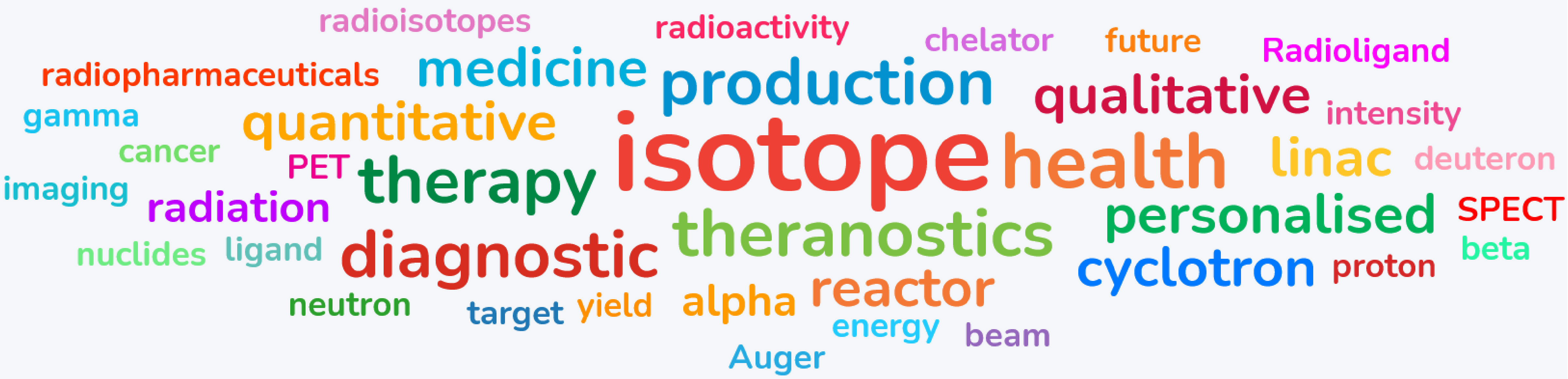
https://www.prismap.eu/

EU INFRAIA PRISMAP Project: collaboration across Europe



A conceptual image of collaboration across Europe for medical radioisotope production. (Image: PRISMAP/SCIPROM)

Summary

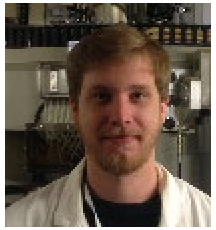

radioisotopes
radioactivity
chelator
future
Radioligand
radiopharmaceuticals
medicine
production
qualitative
gamma
quantitative
intensity
cancer
isotope
health
linac
deuteron
PET
therapy
imaging
radiation
personalised
SPECT
theranostics
nuclides
ligand
diagnostic
cyclotron
proton
beta
reactor
neutron
target
yield
alpha
energy
beam
Auger

Acknowledgments

Pr. F. Haddad, Nantes Université
GIP ARRONAX director
PRISMA Team member

Pr. V. Métivier, IMT Atlantique
Head of the PRISMA Team

Dr. E. Nigron, GIP ARRONAX
PRISMA Team member
Stacked-foils technique expert



Bibliography

Bibliography directly mentioned on slide

+

Radionuclides production with accelerators focus on solid target, ISINucMed, 2023, Pr. F. Haddad
Soigner en médecine nucléaire aspect production, 12ème Rendez-vous de la SOFRA, 2023, Pr. F. Haddad
From nuclear physics to nuclear medicine, EJC, 2015, Pr. F. Haddad

+

Study of the proton-induced production of the theranostic radionuclide ^{47}Sc, 2024, PhD thesis, L. De Dominicis
Développement d'une cible enrichie de gadolinium pour la mesure de la section efficace et la production future de terbium pour la médecine nucléaire, 2022, PhD thesis, Y. Wang
Isotopes radioactifs produits par voies non conventionnelles, 2019, PhD thesis, E. Nigron
Étude de voies alternatives pour la production de radionucléides innovants pour les applications médicales, 2015, PhD thesis, C. Duchemin

+

Le Musée Curie https://musee.curie.fr/
NuDat 3.0 https://www.nndc.bnl.gov/nudat3/guide/
Nuclear Data Services, Medical Radioisotopes Production https://www-nds.iaea.org/relnsd/vcharthtml/MEDVChart.html

Research areas

PRISMA
Physics of Radiation InteractionS with Matter and Applications

RAMI — **RAdionucléides Médicaux Innovants**
Health, nuclear medicine, radionuclides

HB — **HadronBiologie**
Health, dosimetry, hadrontherapy FLASH

IRMA — **Interactions Rayonnements Matière et Applications**
Elemental and isotopic analysis, Detectors

The PRISMA team

Permanents

Subatech

ARRONAX

Institut de Cancérologie de l'Ouest

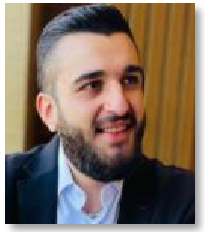
unicancer PAYS DE LA LOIRE

PRISMA

Physics of Radiation InteractionS with Matter and Applications

PhD students

Post- doc's



Thank you for your attention!

PRISMA
Physics of Radiation InteractionS with Matter and Applications

SF Team du 44