“Production de radioisotopes pour l'imagerie nucléaire et le traitement”

Atelier « **Accélérateurs, Recherche et Société** »

25-27 Mars 2026, Grenoble

Ali OUADI
ali.ouadi@iphc.cnrs.fr

Many Thanks to Férid Haddad

Nuclear medicine at a glance

- **50 million** nuclear medicine procedures performed annually

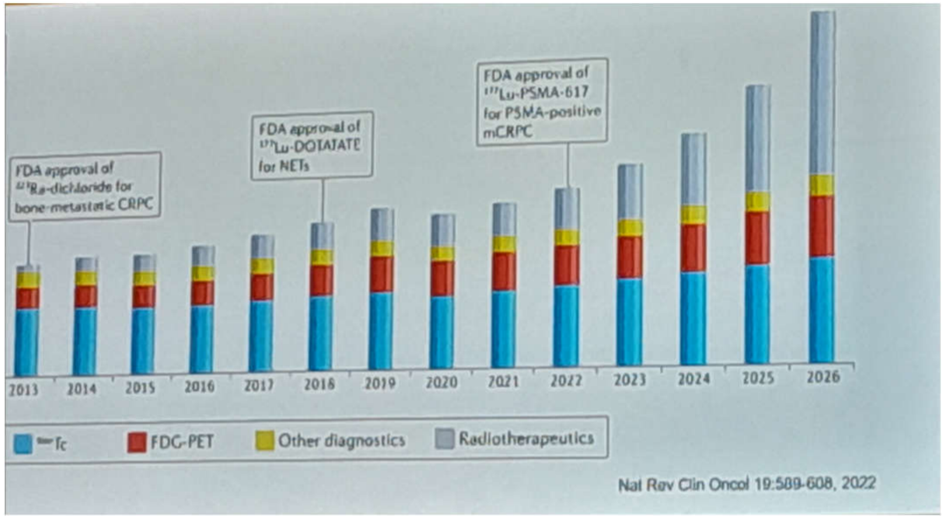
  → **90%** for diagnostic purpose

- **Rapid evolution** over the last 20 years:

  - **2000s**: FDG becomes gold standard for **PET imaging** in oncology
  - **2005**: FDA approval of **Zevalin** (^{90}Y-ibritumomab) for hematologic cancers
  - **2013**: FDA approval of first **alpha therapy** using **^{223}Ra**
  - **2017**: FDA approval of **^{177}Lu-DOTATATE** for neuroendocrine tumors
  - **2022**: FDA approval of **^{177}Lu-PSMA** for metastatic prostate cancer

- **Targeted radiotherapies** now available

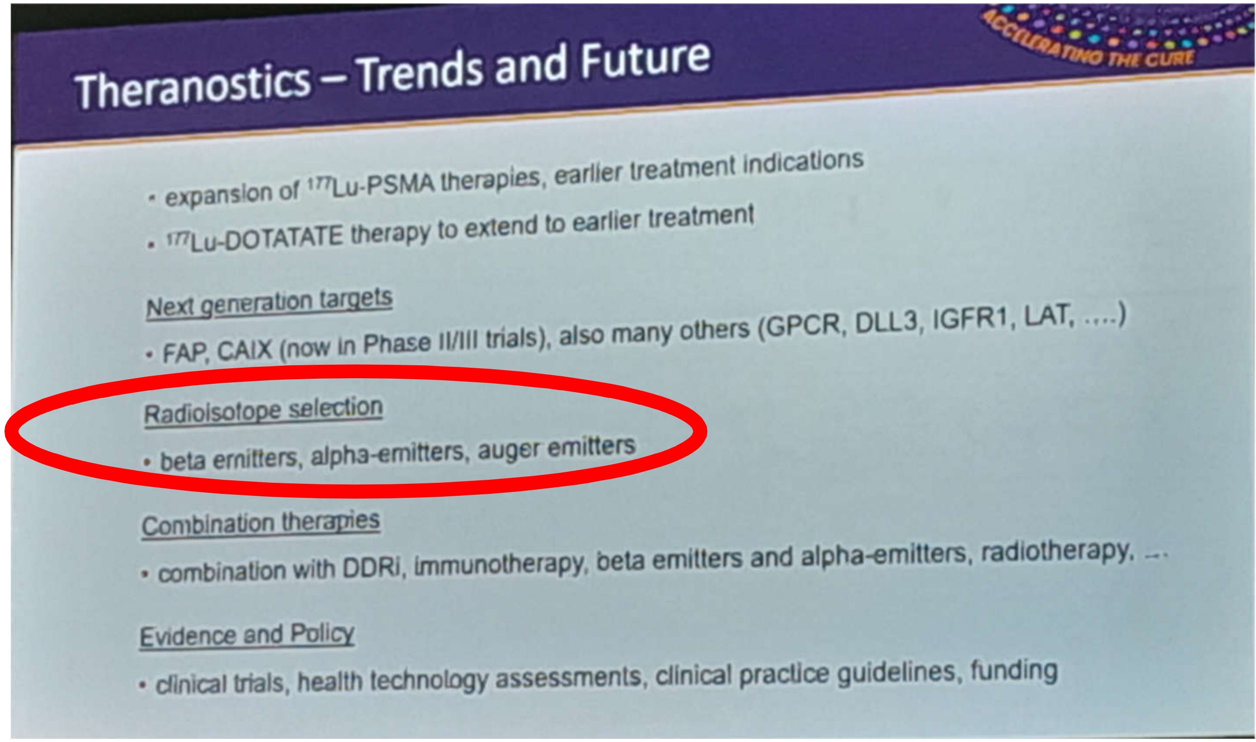
  → Most **pharmaceutical companies** have launched **nuclear medicine programs**



A Growing Demand in Nuclear Medicine

➢ **Radionuclide Production: A Key Future Challenge**

- ❑ Rising need for isotopes
- ❑ supply
- ❑ Strategic challenge



Lecture @SNMMI 2025

Applications in Nuclear Medicine

- **Imaging and diagnosis** (X-rays, γ-rays , β^+ emitters)

  (e.g., PET, SPECT)

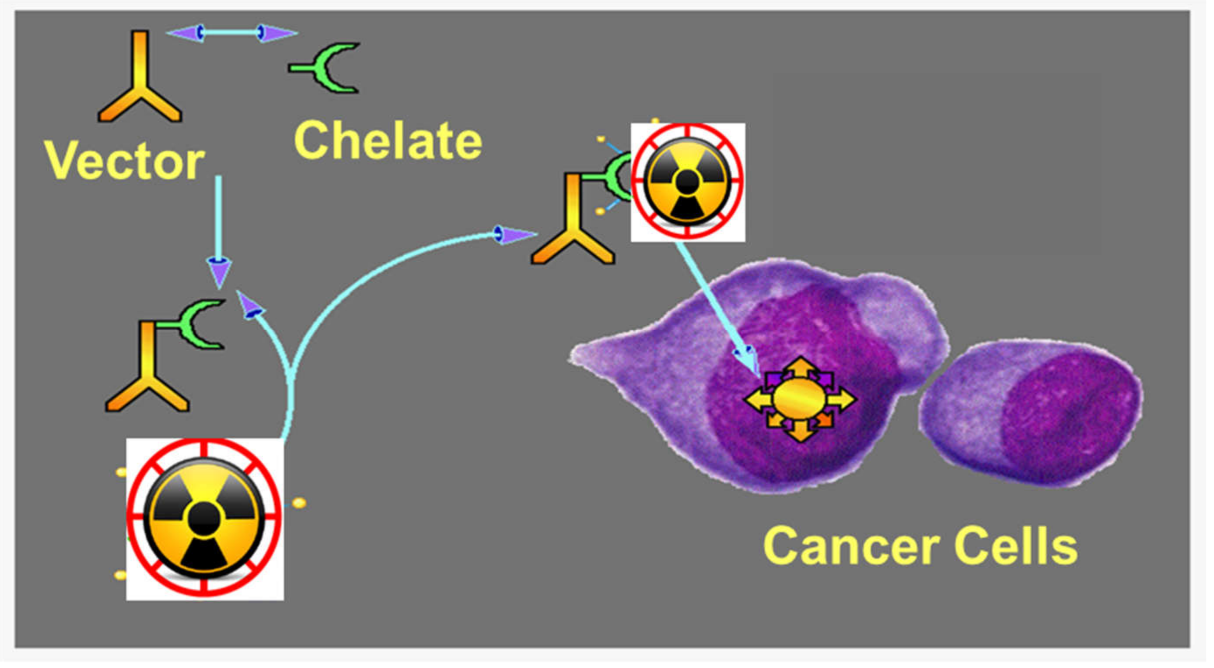
- **Therapy** (α particles, β^- particles , Auger electrons)

- **Targeted Radionuclide Therapy** (TRT)

Targeting Strategy

➢ **Targeting Strategy**

In most cases, **a vector molecule (**e.g., antibody, peptide, small molecule) **is needed** to specifically target the cells or tissues of interest.



Choosing the right radionuclide

➢ **Key Constraints**

- Matching radionuclide half-life ($T_1/_2$) with vector pharmacokinetics

- Purity

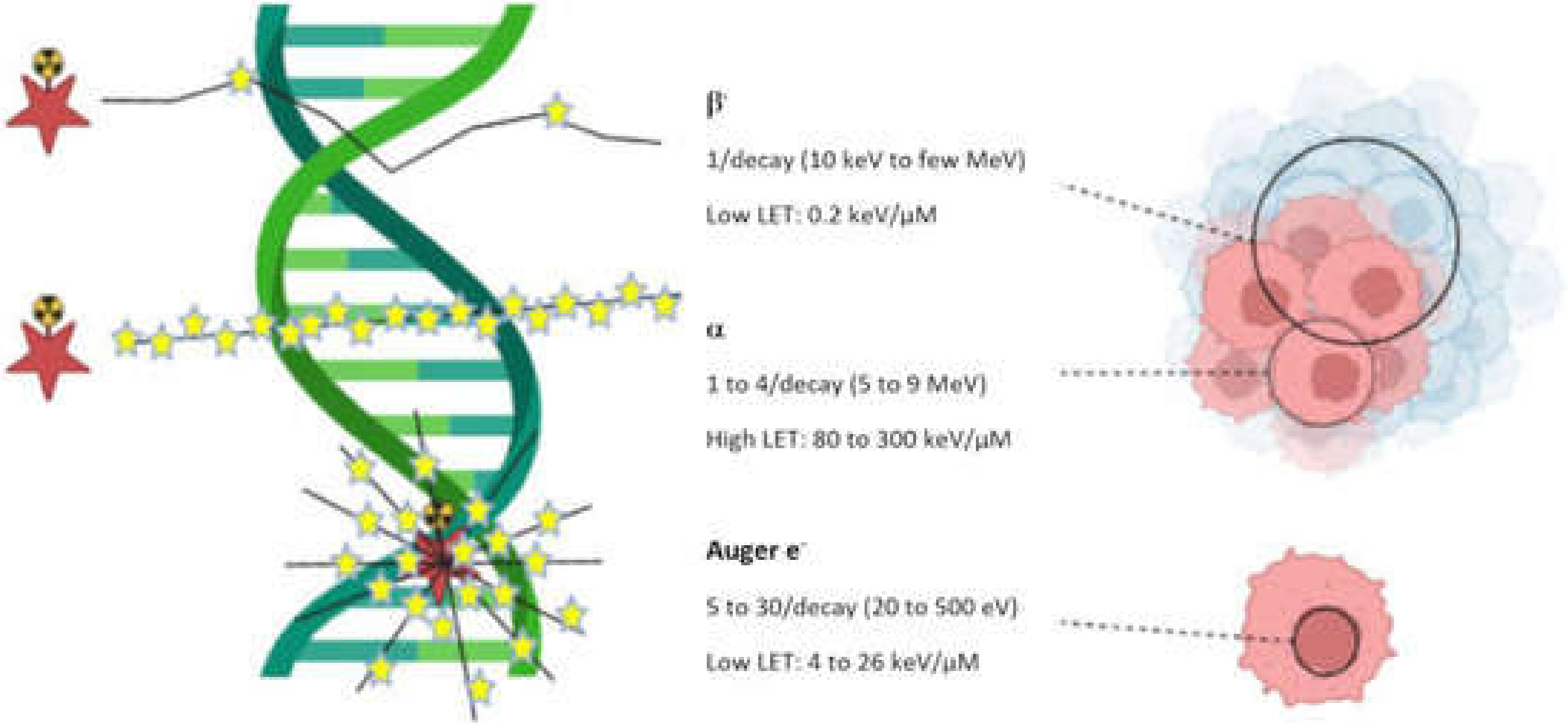
- Logistics

- Optimizing radiation type based on Linear Energy Transfer (LET)

Radionuclide	Half-life (h)	decay mode
Ac-225	10 d	4α(2β-)
At-211	7,2 h	1α
Bi-213	45 m	1α (2β-)
Ra-223	11,4 d	4α (2β-)
Lu-177	6,65 d	β-
F-18	110 min	β+
Cu-64	12,7 h	(β-, EC)/β+
Zr-89	78,4 h	EC/β+

Radiation Type and LET

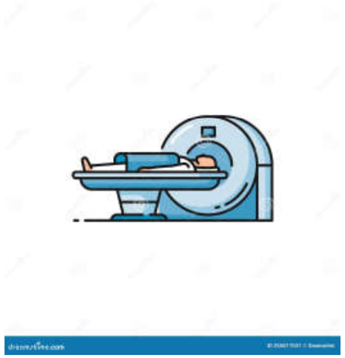
- **High LET** (α, Auger): localized, high-damage potential
- **Low LET** (β^-): effective for diffuse or larger targets



Theranostics: From Diagnosis to Therapy

THERAPEUTIC + DIAGNOSTICS

THERANOSTICS



Diagnosis → **SAME VECTOR** → **Therapy**

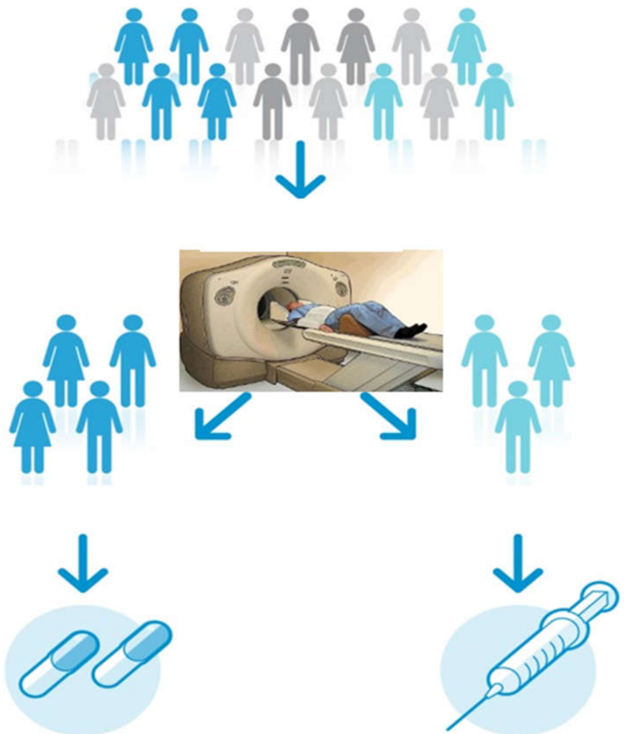
PET / SPECT
Patient selection

Targeted irradiation
Dose delivery

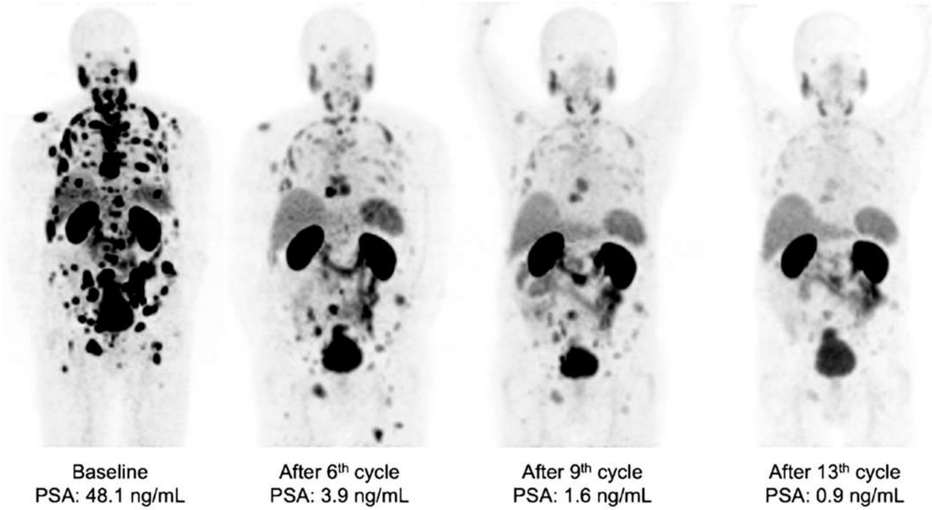
Examples: ^{68}Ga / ^{177}Lu | ^{64}Cu / ^{67}Cu

Clinical objectives

- ❑ Patient selection
- ❑ Dosimetry
- ❑ Response evaluation



Examples



From left to right: MIP of [^{68}Ga]Ga-PSMA-11 PET images of a patient with disseminated bone metastases and local disease responding to the standard treatment with six cycles and showing further response to the extended RLT. Treatment was discontinued due to insufficient PSMA-expressing residual disease after 13 cycles of [^{177}Lu]Lu-PSMA RLT (PFS: 58 months)

Eur J Nucl Med Mol Imaging **50**, 1811–1821 (2023)

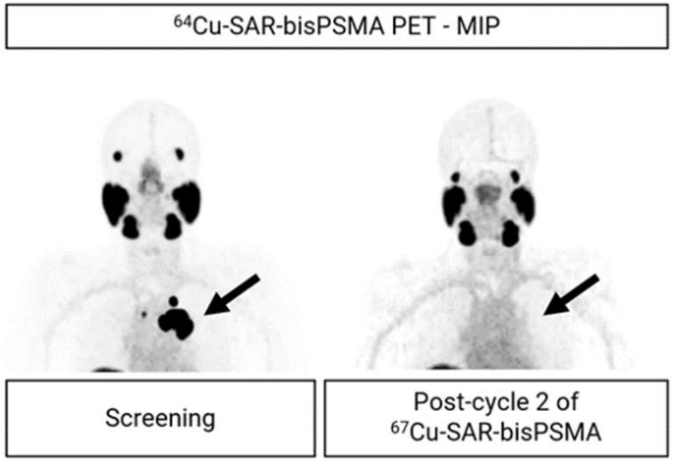


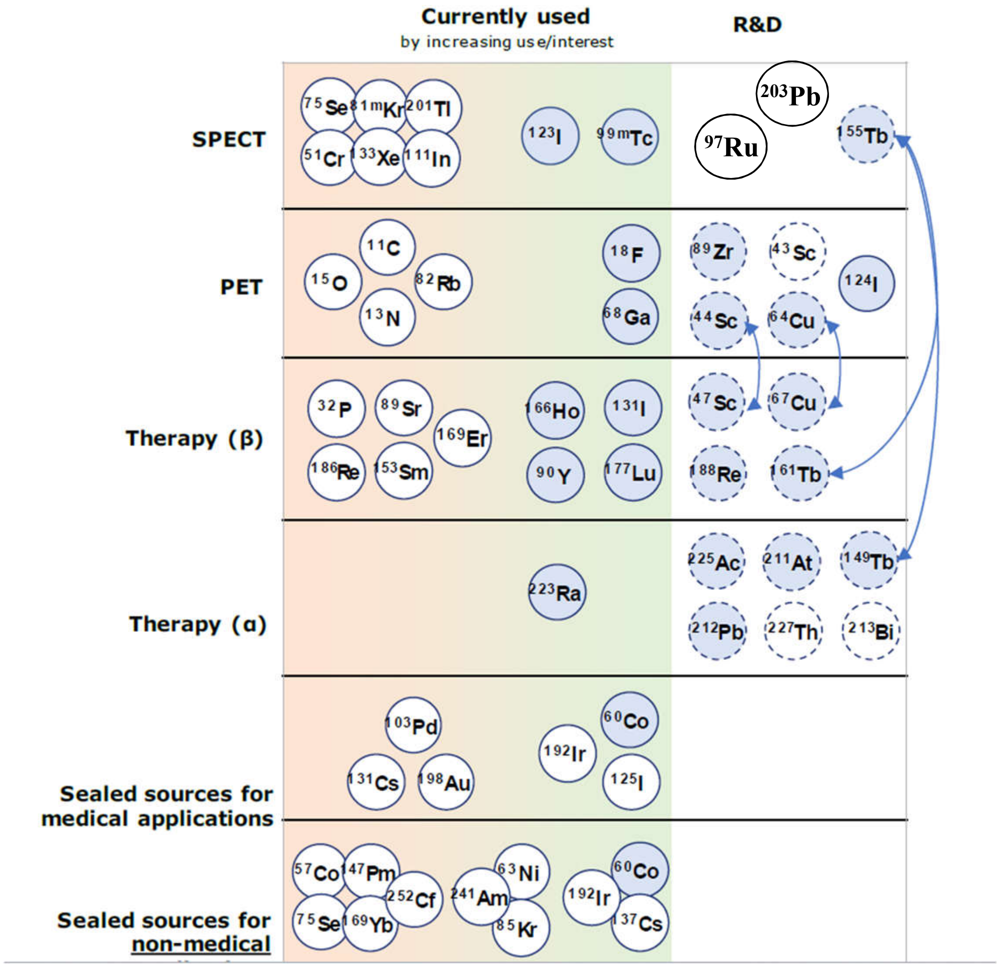
***Figure 2**. PET images showing uptake of ^{64}Cu-SAR-bisPSMA in prostate cancer lesions at screening (arrow, left image; maximum standardised uptake value [SUVmax] 140.1). Image post-treatment show no ^{64}Cu-SAR-bisPSMA uptake (arrow, right image). Images shown as maximum intensity projection.*

From clarity pharmaceuticals

^{68}Ga/ ^{177}Lu

^{64} Cu/ ^{67}Cu

A Critical Need for Radionuclides



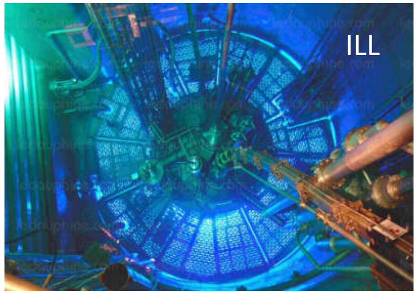
- Limited supply
- Increasing demand
- Need for new production routes

Adapted from « co-ordinated Approach to Development and supply of radionuclides in the EU » N°ENER/D3/2019-231

Production Methods

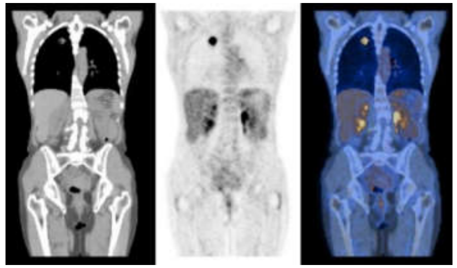
- Nuclear reactors
- Particle accelerators
- Neutron / gamma source

Nuclear reactor



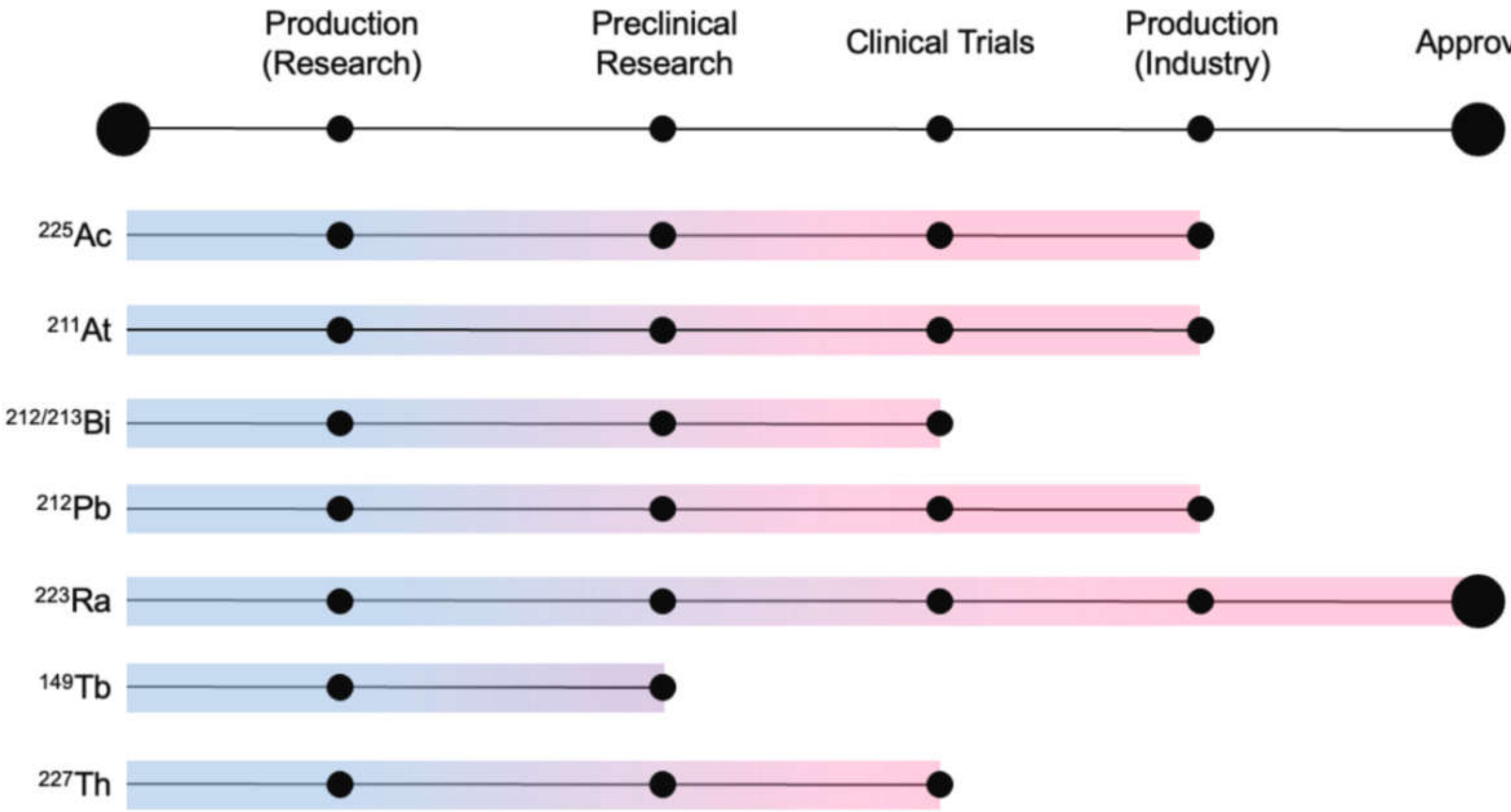
Particle accelerator

From Production to patient



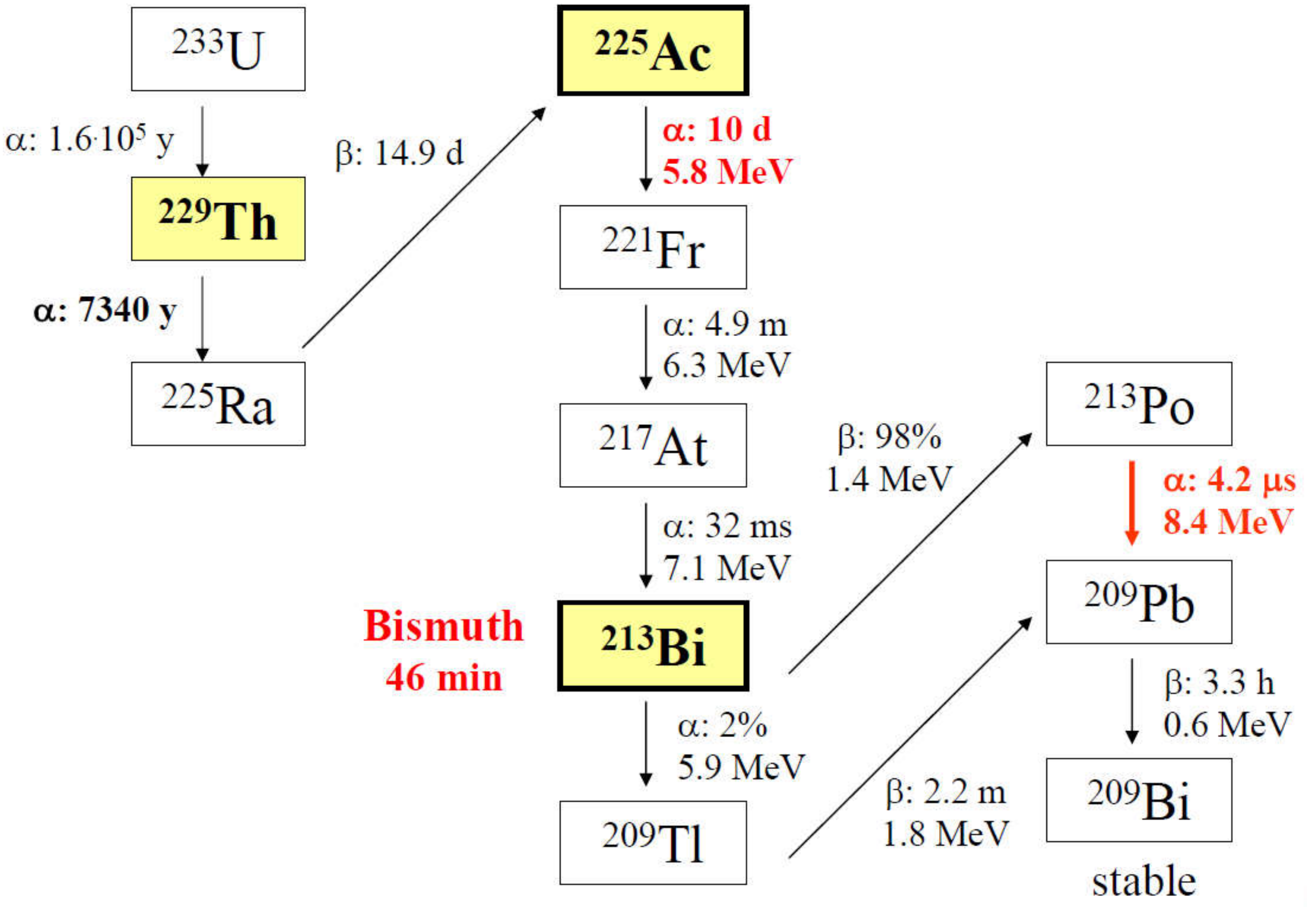
Target → Irradiation → Separation → Radiolabeling → Patient

Case Study: Targeted Alpha Therapy with Ac-225



Du laboratoire au patient : parcours de développement des émetteurs α

(Tosato et al Nuclear Medicine and Biology 142–143; 2025; 108990)



- High LET α-emitter → highly localized damage
- Promising results in oncology
- Limited availability

Challenges:

- Production routes
- Separation of daughter nuclides
- Radiolysis

Actinium-225 Production Routes – Summary Table

Production Route	Target Material	Nuclear Reaction / Process	Maturity Level	Yield	Isotopic Purity	Main Limitations
Generator from ^{229}Th	thorium-229	Decay chain ($^{229}Th \rightarrow ^{225}Ac$)	Mature	Low	Excellent	Very limited global stock
Cyclotron (protons on ^{226}Ra)	radium-226	$^{226}Ra(p,2n)^{225}Ac$	Advanced development	Moderate to high	Good	Handling of Ra (radiotoxic, radon release)
Spallation of ^{232}Th	thorium-232	high-energy proton-induced spallation	Advanced	High (potential)	Moderate	Complex separation, co-production of ^{227}Ac
Neutron irradiation (reactor)	thorium-232	$^{232}Th(n,\gamma) \rightarrow \ldots \rightarrow ^{229}Th \rightarrow ^{225}Ac$	Developing	Low	Good	Long production time, low efficiency
Photonuclear production	Th or U targets	(γ,xn) reactions using high-energy photons	Emerging	Low	Potentially good	Technology not yet mature

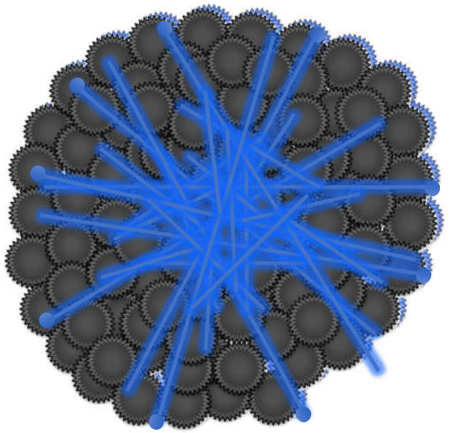
"Limited availability remains the main bottleneck for clinical deployment"

Why are we interested in α emitters?

Alpha and beta particles are complementary

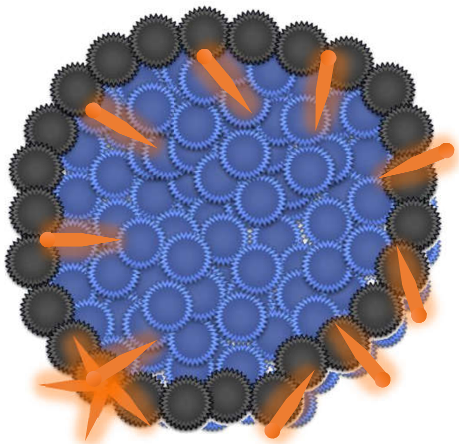
β^- emitter

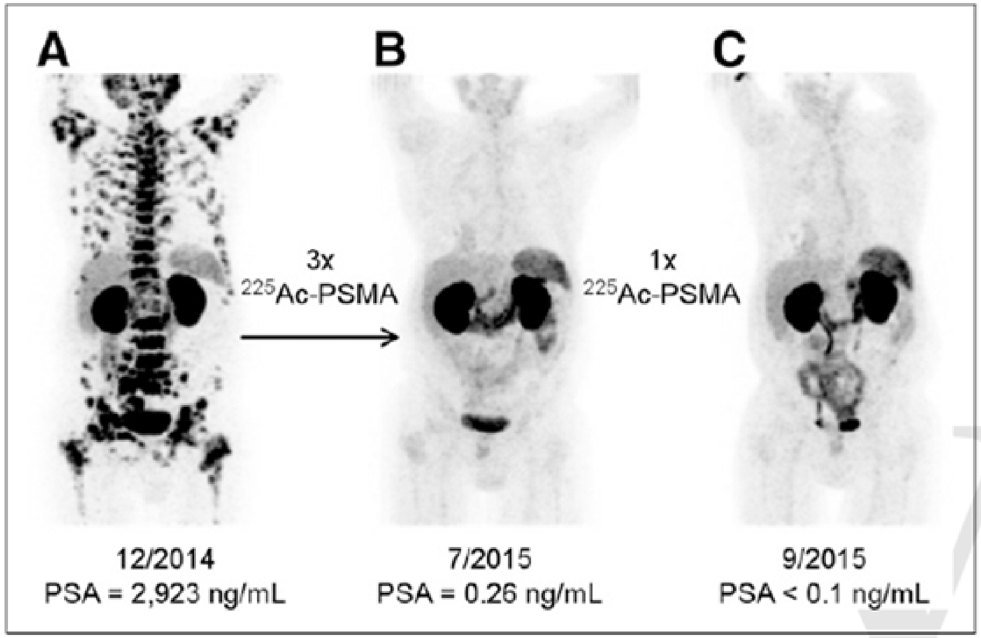
- Long range
- Crossfire



α emitter

- Short range
- High LET





Kratochwil et al. J Nucl Med 2016; 57:1-4

Take-home message

- Growing demand for radionuclides
- Production is a key challenge
- From physics to patient: an integrated chain

"Producing the right radionuclide is often more challenging than using it"

Future prospects and needs

- α (~30 MeV) & deuterons → new production routes
- 20–40 MeV → critical gap
- Bottleneck: intensity + targets
- Future: purity (mass separation?)
- → Flexible, high-intensity accelerators

Thank you for your attention