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Are alpha beams of interest to produce medical radionuclides ?

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INPC2022
Cape Town, South Africa

IN2P3

Institut national de **physique nucléaire**
et de **physique des particules**

**Are alpha beams of interest to produce
medical radionuclides ?**

A. Guertin, Haddad F., C. Alliot, A.C. Bonraisin, L. Brionne, E. Nigron, T. Sounalet

Nuclear medicine

Many useful / potentially useful isotopes identified for applications in nuclear medicine

Cyclotrons and accelerators being used in an increasing number of countries along with reactors

A large set of radioisotopes with very different characteristics:

- Radiation type for the different applications
- Half-life to match the bio-distribution time
- Chemical properties to attach to the vector molecule

Over the last years, several radionuclides have emerged:

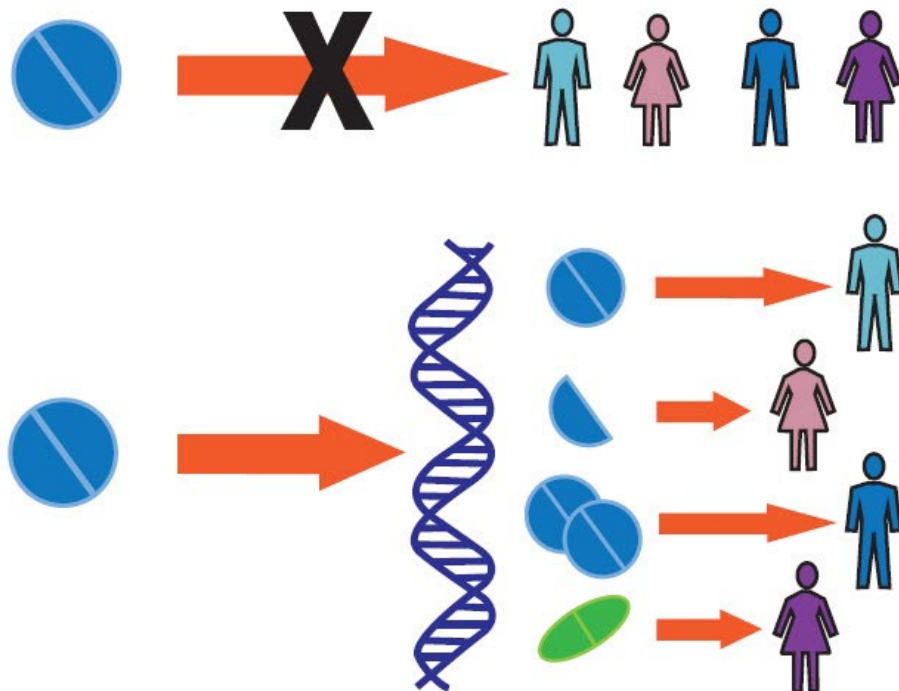
- β^+ : ^{64}Cu , ^{68}Ga , ^{89}Zr ...
- β^- : ^{166}Ho , ^{177}Lu ...
- Auger: $^{117\text{m}}\text{Sn}$, ^{155}Tb
- Theranostic: $^{44}\text{Sc}/^{47}\text{Sc}$, $^{64}\text{Cu}/^{67}\text{Cu}$, $^{68}\text{Ga}/^{177}\text{Lu}$...
- γ : $^{117\text{m}}\text{Sn}$...
- α : ^{211}At , ^{212}Bi , ^{213}Bi , ^{223}Ra , ^{225}Ac ...

- | | | | |
|---------------------------------------------------------|------------|-------------------------------------------------------------------|----------------------------------------------|
| - Diagnosis (γ , β^+) | SPECT, TEP | $^{99\text{m}}\text{Tc}$, ^{18}F , ^{64}Cu ... | Detecnet (^{64}Cu dotatate inj.) |
| - Therapy (β^- , α , e_{Auger}) | TAT | ^{117}Lu , ^{225}Ac ... | Lutathera (^{177}Lu oxodotreotide) |

Imaging and diagnosis

Choose the best treatment

Evaluate its efficacy



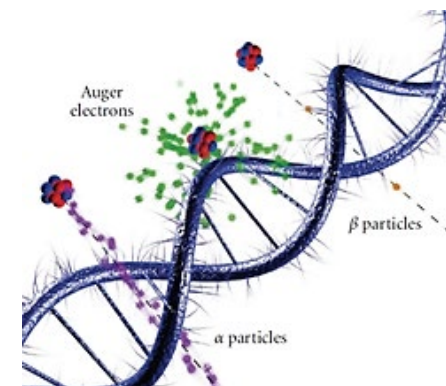
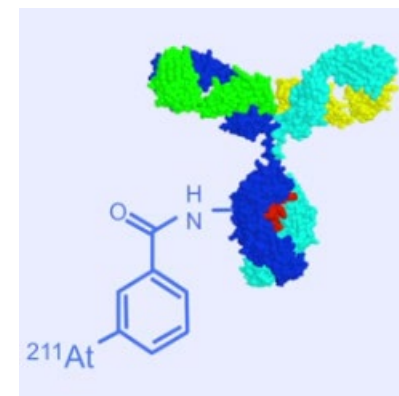
**The Right Drug
At The Right Time**

To The Right Patient

At The Right Time

Therapy

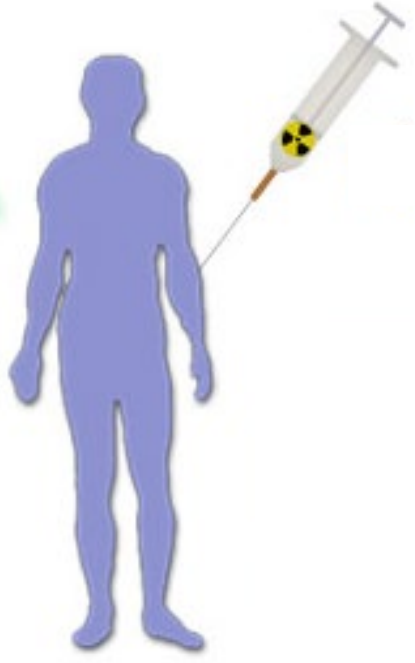
Destroy tumor cells



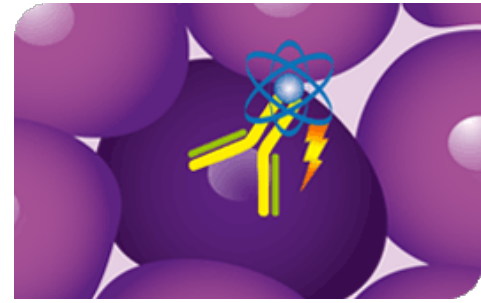
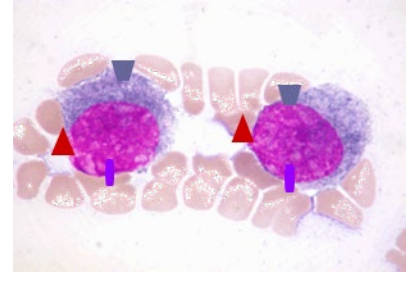
B.Q. LEE et al.

**For The Right Disease
With The Right Dosage**

Inject a tracer



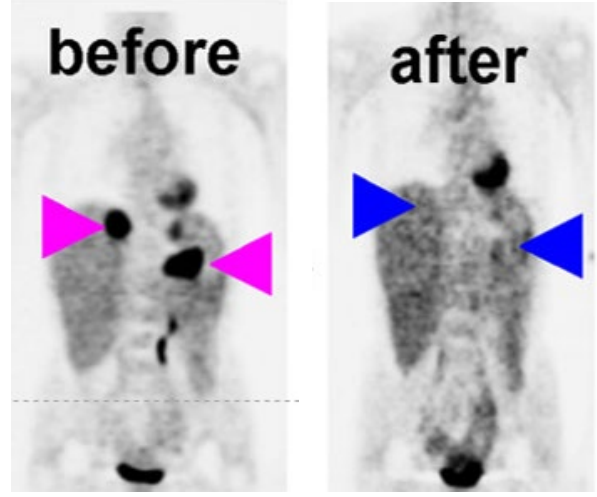
Target a tumor marker



AREVA Med

Detect the disease

γ, β^+ →

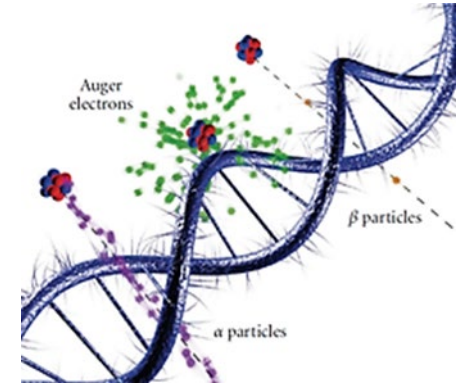


NIRS, Shiba, MIC



$\beta^-, \alpha,$
 e_{Auger} →

Treat the disease





**Predictive imaging,
companion diagnostic**



Targeted therapy

THERANOSTICS



M
L
E
C
U
L
E

WANTED

An adequate therapeutic nuclide

A corresponding positron emitter

= (Available matched) pair
of therapeutic and PET nuclides

WANTED

Molecules = targeting vectors

Identical or similar
radiolabelling chemistry

What you see is what you treat

Nuclear physicists could have crucial contributions:

- **Identify** reaction channel [spal., fis., act.]
- **Optimize** production process
- **Quantify** contaminants
- **Produce** the purest product
- **Define** waste management process
- **Discuss** with physicians to promote its use

Nuclear data

- **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

Nuclear codes

- 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

Beams

Many medical isotopes are produced using **neutron** induced reactions in reactors

Quick progress and achievements in production using charged particle induced reactions:

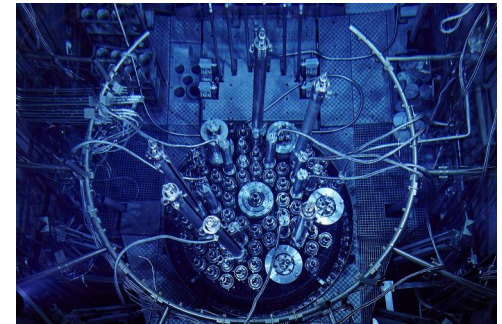
proton, deuteron, triton and alpha particle

Protons are more commonly available

Still limited applications for d, ^3He and alpha particle

Focus on some opportunities with alpha particle beams

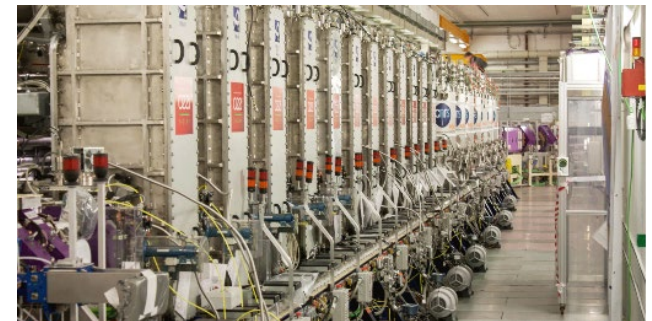
- ✓ **Avoid** radioactive target material
 ^{211}At , ^{97}Ru
- ✓ **Access** to a higher cross section
 ^{43}Sc
- ✓ **Reuse** an existing process : targetry, chemistry
 ^{67}Cu
- ✓ **Facilitate** target manufacturing
 $^{117\text{m}}\text{Sn}$
- ✓ **Use** a monoisotopic target
 ^{135}La



BR2 reactor @ SCK•CEN



C70XP @ ARRONAX



SPIRAL 2 @ GANIL

58% EC, 42% α $T_{1/2} = 7.3$ h
 α -targeted internal radiotherapy

Avoid radioactive target and use of a monoisotopic target

Z	^{207}At 1.81 H ϵ : 91.40% α : 8.60%	^{208}At 1.63 H ϵ : 99.45% α : 0.55%	^{209}At 5.42 H ϵ : 95.90% α : 4.10%	^{210}At 8.1 H ϵ : 99.82% α : 0.18%	^{211}At 7.214 H ϵ : 58.20% α : 41.80%	^{212}At 0.314 S α : 100.00% $\epsilon < 0.03\%$	^{213}At 125 NS α : 100.00%	^{214}At 558 NS α : 100.00%	^{215}At 0.10 MS α : 100.00%
84	^{206}Po 8.8 D ϵ : 94.55% α : 5.45%	^{207}Po 5.80 H ϵ : 99.98% α : 0.02%	^{208}Po 2.898 Y α : 100.00% ϵ : 4.0E-3%	^{209}Po 124 Y α : 99.55% ϵ : 0.45%	^{210}Po 138.376 D α : 100.00%	^{211}Po 0.516 S α : 100.00%	^{212}Po 0.299 μS α : 100.00%	^{213}Po 3.72 μS α : 100.00%	^{214}Po 163.6 μS α : 100.00%
83	^{205}Bi 15.31 D ϵ : 100.00%	^{206}Bi 6.243 D ϵ : 100.00%	^{207}Bi 31.55 Y ϵ : 100.00%	^{208}Bi 3.68E+5 Y ϵ : 100.00%	^{209}Bi 2.01E19 Y 100% α : 100.0%	^{210}Bi 5.012 D β^- : 100.00% α : 1.3E-4%	^{211}Bi 2.14 M α : 99.72% β^- : 0.28%	^{212}Bi 60.55 M β^- : 64.06% α : 35.94%	^{213}Bi 45.61 M β^- : 97.80% α : 2.20%

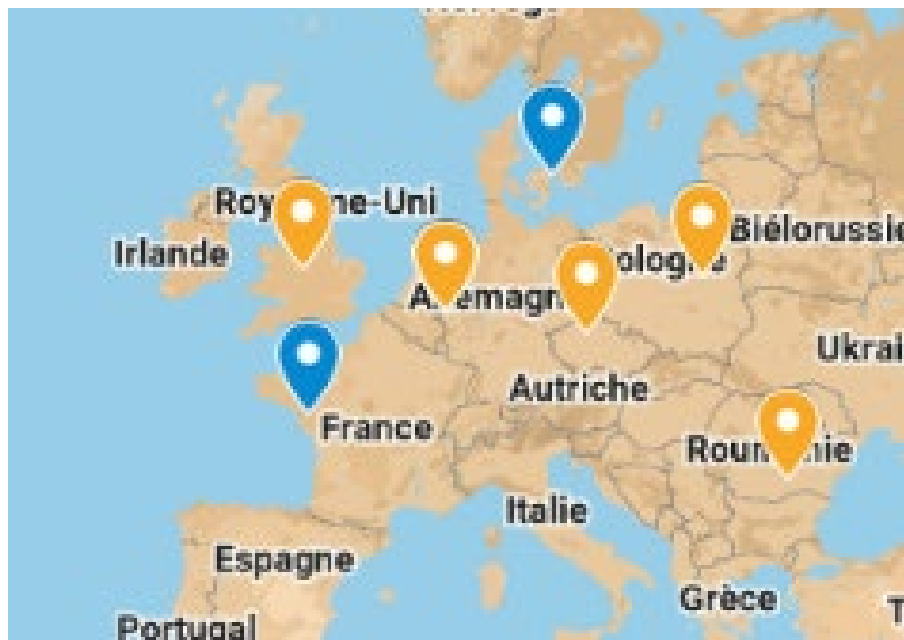
Spallation reaction

- ✓ lower yield
- ✓ higher level of impurity

$^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$

- ✓ monoisotopic target
- ✓ high radionuclidic purity
- ✓ GBq quantities

COST NOAR network: European Cooperation in Science & Technology
Network for Optimized Astatine labeled Radiopharmaceuticals



^{211}At production facilities in the world

- Running
- Potentially usable

Courtesy of F. Haddad – SUBATECH – GIP ARRONAX

Direct production with alpha particles

$\text{Bi-209}(\alpha, 2n)\text{At-211}$, 20.7 MeV

$\text{Bi-209}(\alpha, 3n)\text{At-210}$, 28.6 MeV \triangle

At-211 α particles

$\text{LET}_{\text{mean}} = 99 \text{ keV}/\mu\text{m}$

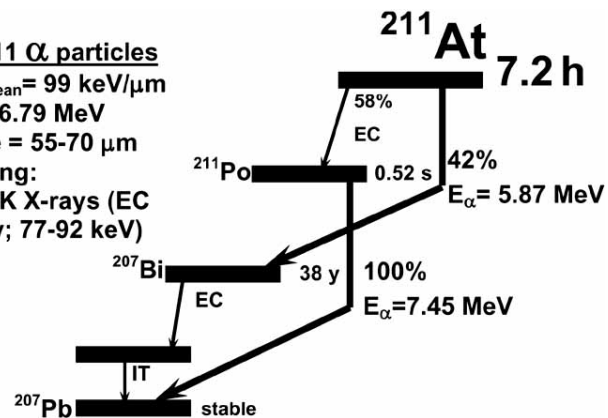
$E_{\text{ave}} = 6.79 \text{ MeV}$

range = 55-70 μm

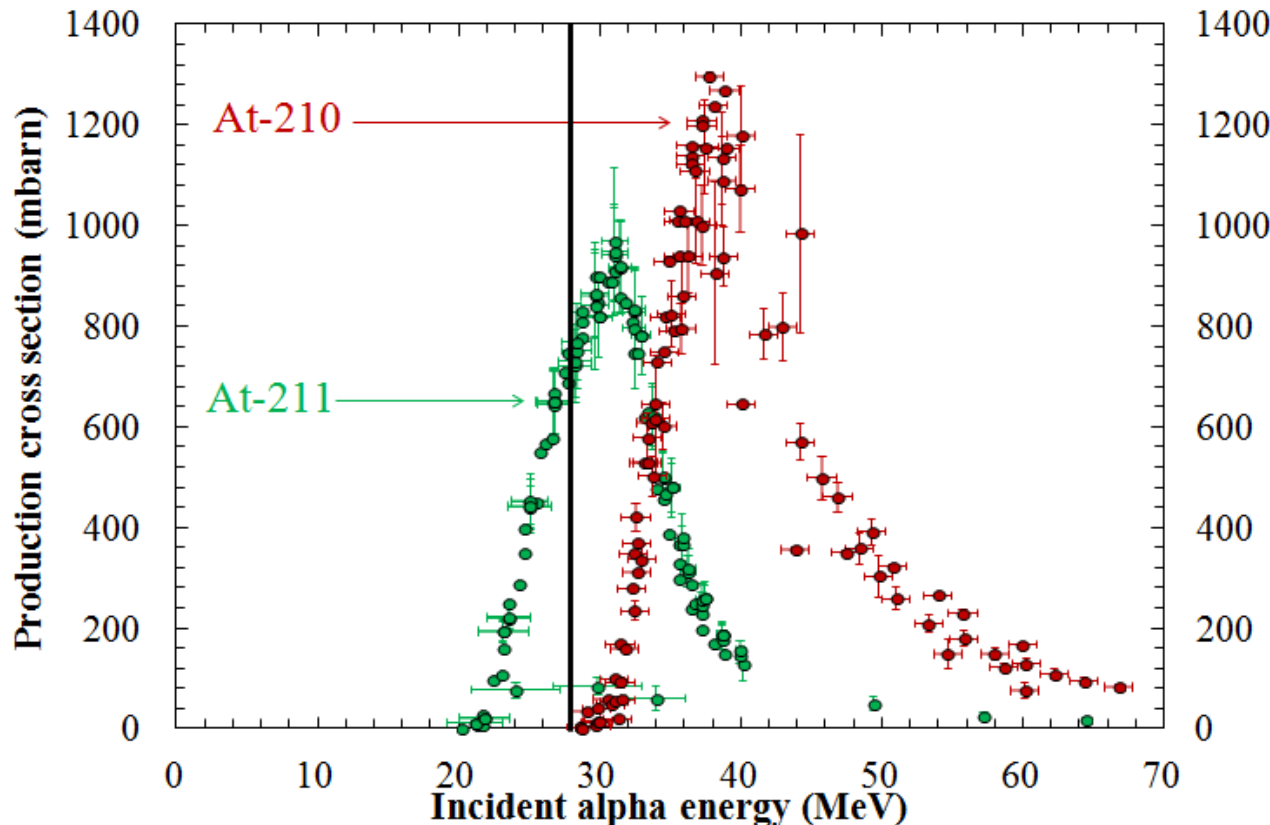
Imaging:

^{211}Po K X-rays (EC

decay; 77-92 keV)



At-210, $T_{1/2}$ 8.1 h
 decays at 99.8% by EC
 to **Po-210** (138.4 days)
 and at 0.2% by α emission
 to Bi-206 (6.2 days)



100% EC, no β^+

$T_{1/2} = 2.9 \text{ d}$

SPECT

Theranostic pair with ^{103}Ru $T_{1/2} = 39.26 \text{ d}$, decaying to $^{103\text{m}}\text{Rh}$ $T_{1/2} = 56.12 \text{ min}$ Auger emitter no γ

Avoid radioactive target

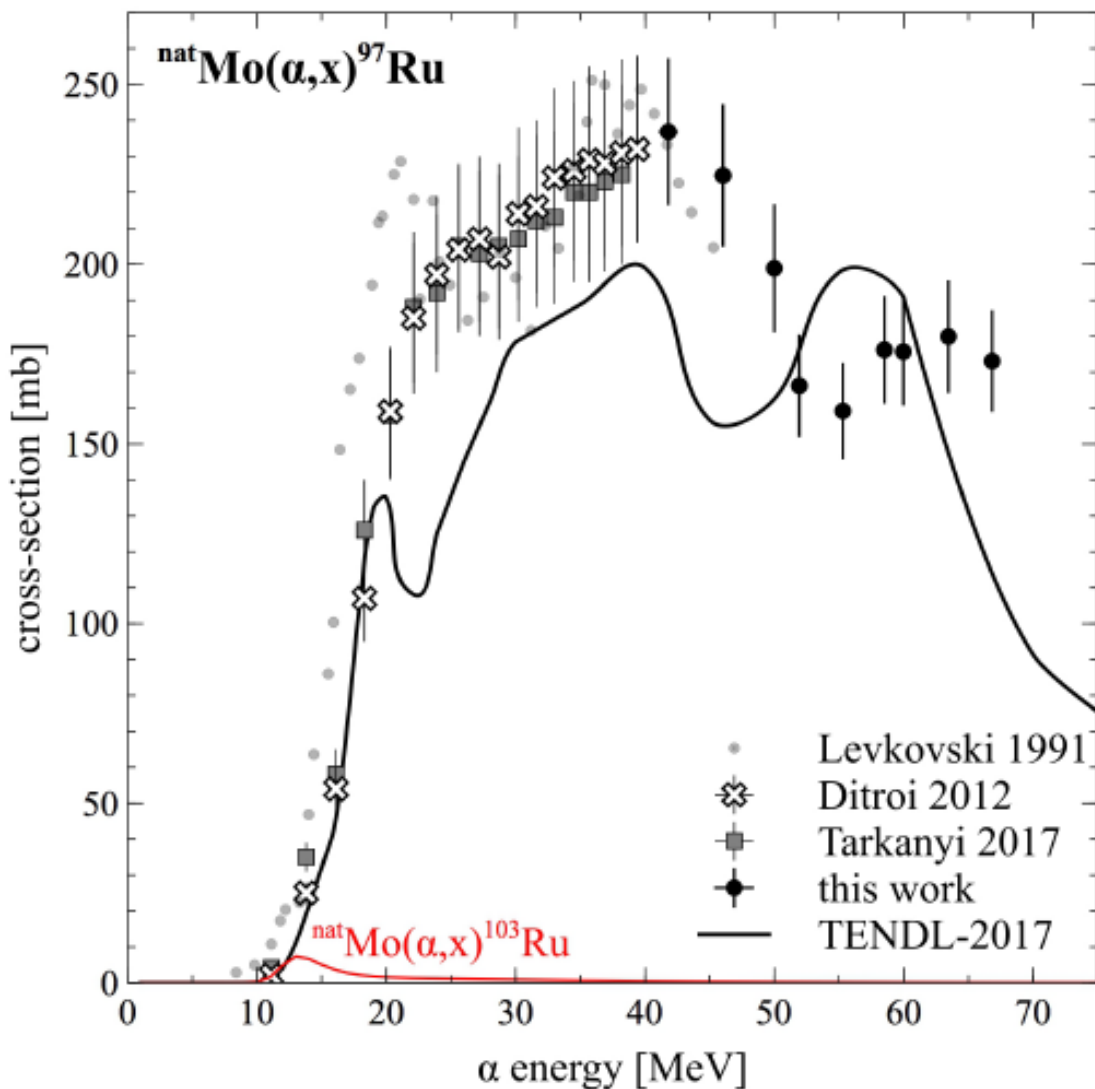
Z	^{96}Ru STABLE 5.54%	^{97}Ru 2.83 D $\epsilon: 100.00\%$	^{98}Ru STABLE 1.87%	^{99}Ru STABLE 12.76%	^{100}Ru STABLE 12.60%	^{101}Ru STABLE 17.06%	^{102}Ru STABLE 31.55%	^{103}Ru 39.247 D $\beta^-: 100.00\%$	^{104}Ru STABLE 18.62%
43	^{95}Tc 20.0 H $\epsilon: 100.00\%$	^{96}Tc 4.28 D $\epsilon: 100.00\%$	^{97}Tc 4.21E+6 Y $\epsilon: 100.00\%$	^{98}Tc 4.2E+6 Y $\beta^-: 100.00\%$	^{99}Tc 2.111E+5 Y $\beta^-: 100.00\%$	^{100}Tc 15.46 S $\beta^-: 100.00\%$ $\epsilon: 2.6E-3\%$	^{101}Tc 14.02 M $\beta^-: 100.00\%$	^{102}Tc 5.28 S $\beta^-: 100.00\%$	^{103}Tc 54.2 S $\beta^-: 100.00\%$
42	^{94}Mo STABLE 9.15%	^{95}Mo STABLE 15.84%	^{96}Mo STABLE 16.67%	^{97}Mo STABLE 9.60%	^{98}Mo STABLE 24.39%	^{99}Mo 65.976 H $\beta^-: 100.00\%$	^{100}Mo 7.3E+18 Y 9.82% $2\beta^-: 100.00\%$	^{101}Mo 14.61 M $\beta^-: 100.00\%$	^{102}Mo 11.3 M $\beta^-: 100.00\%$

Polyisotopic target of Mo

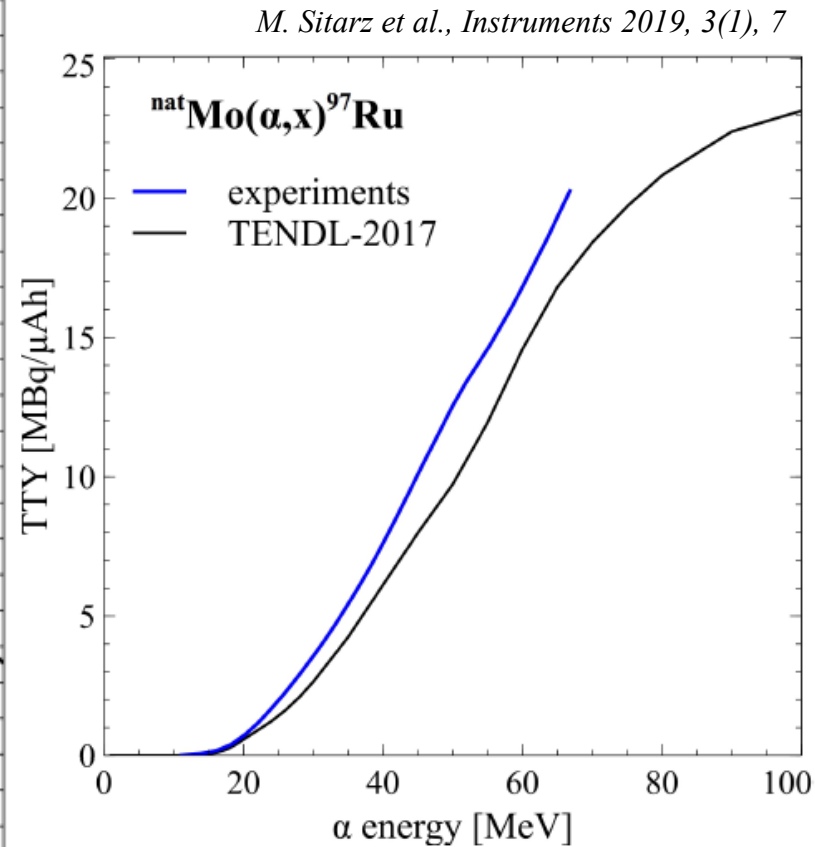
Decaying time to increase specific activity

^{95}Ru $T_{1/2} = 1.66 \text{ h}$

^{94}Ru $T_{1/2} = 51.8 \text{ m}$



M. Sitarz et al., Instruments 2019, 3(1), 7

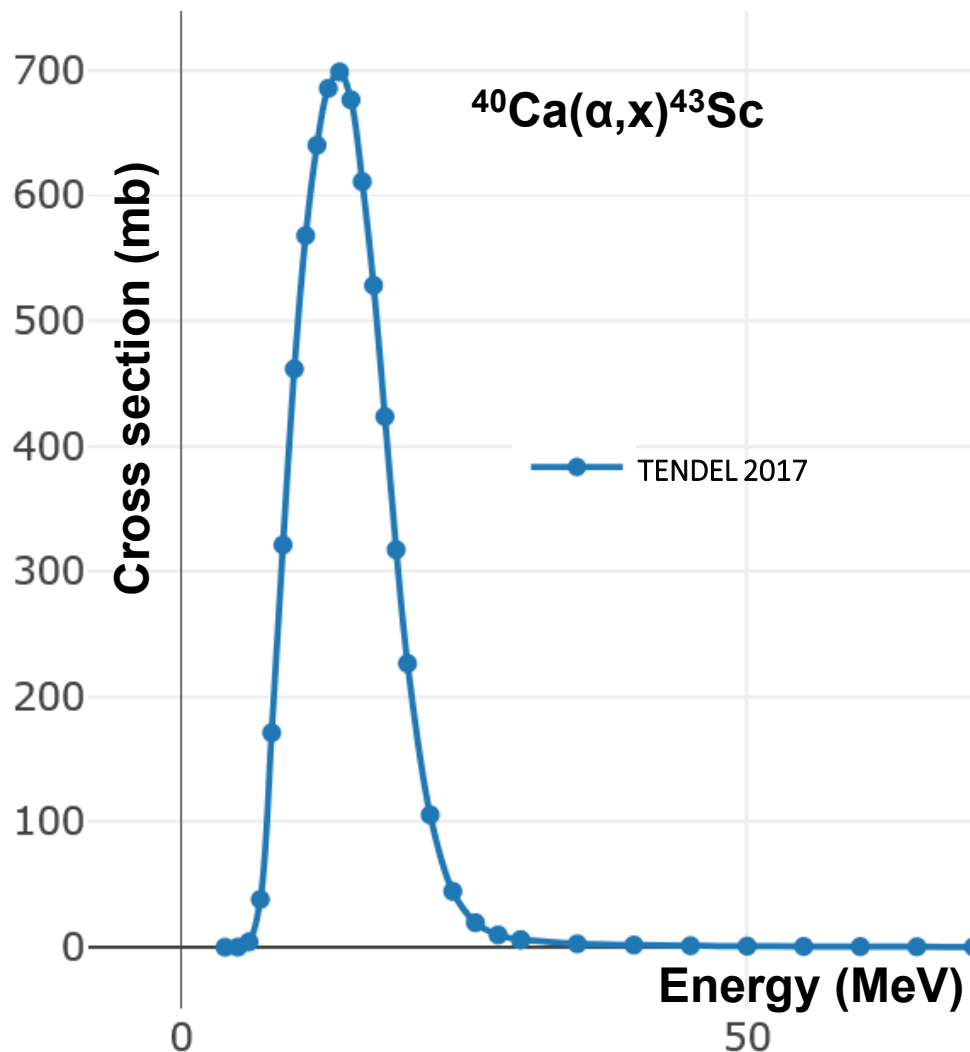
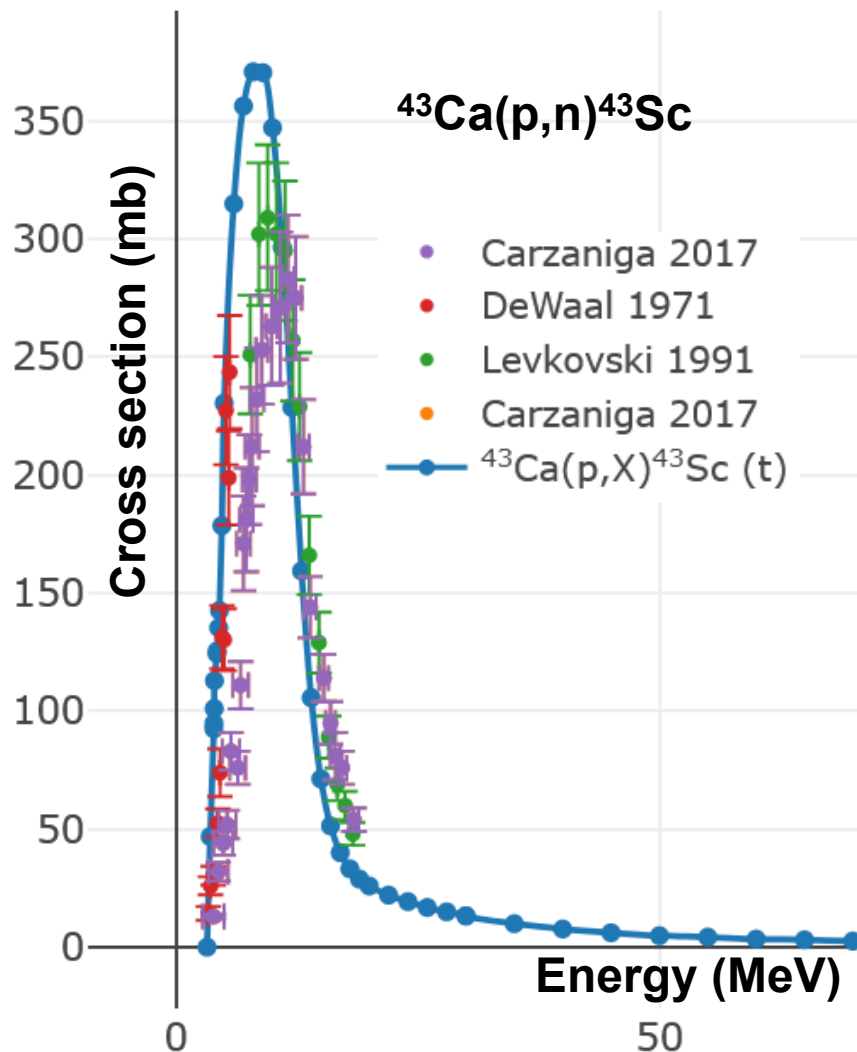


Few tens of MBq/ μAh
Increase possible : duration, intensity,
enriched $^{95,96}\text{Mo}$ target

β^+ with no co-emitted high energy γ rays
 Promising candidates for PET imaging

$T_{1/2} = 3.89\text{h}$
 Theranostic pair with ^{47}Sc or ^{177}Lu

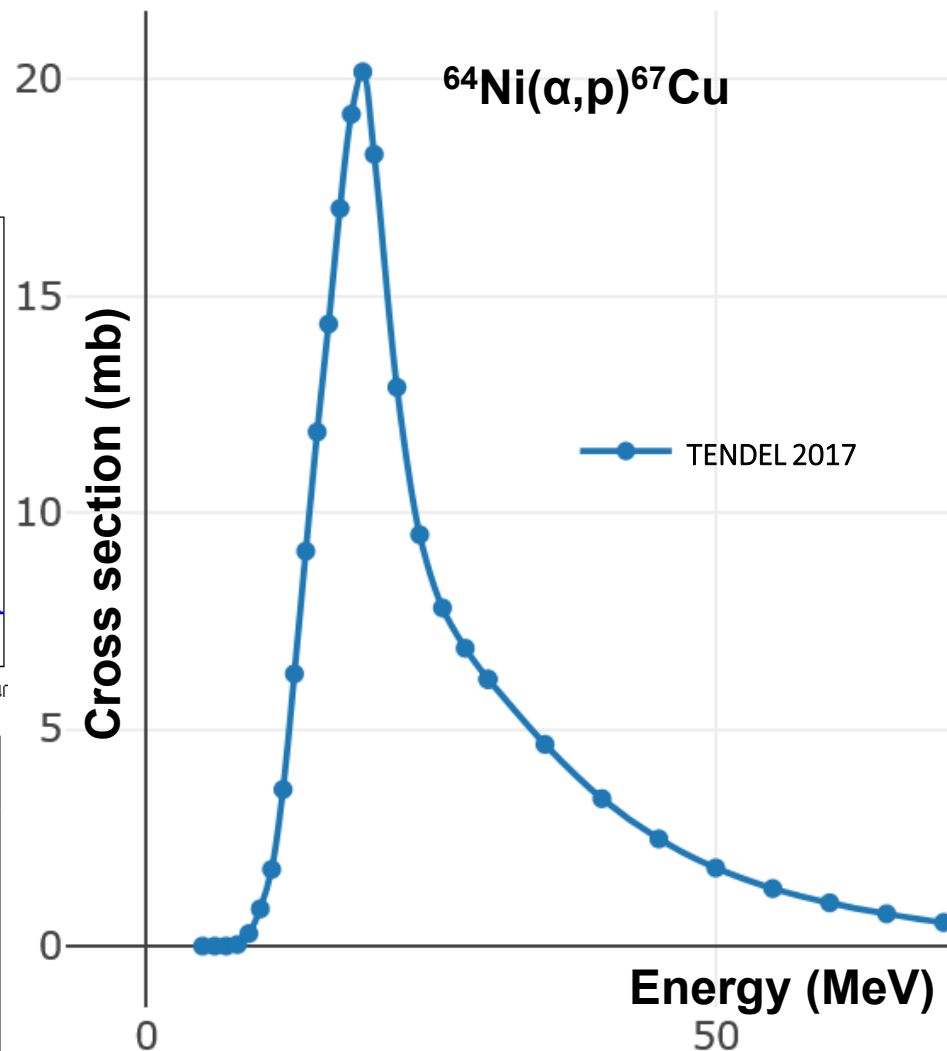
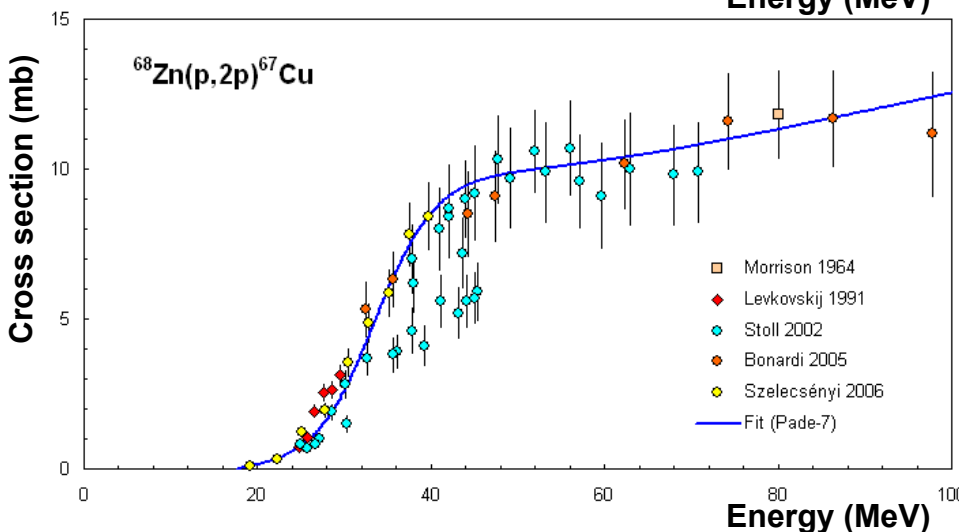
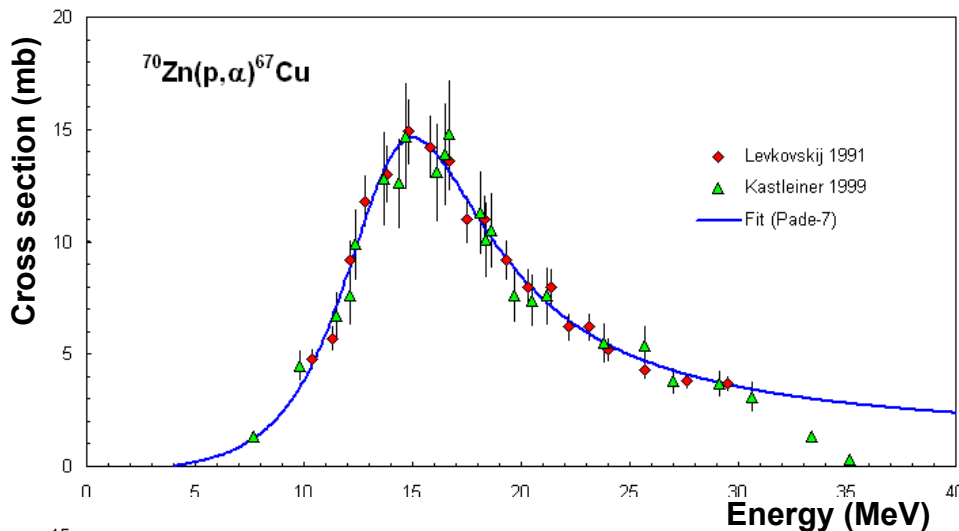
Access to a higher cross section and a higher natural abundance: ^{43}Ca 0.135%, ^{40}Ca 96.941%



67Cu for theranostic approach

β^- $T_{1/2} = 61.9$ h
 Theranostic pair with 64Cu

Reuse of an existing efficient process



Same target for ^{64}Cu production @ARRONAX
 Same chemistry
 Recycling of ^{64}Ni [0.926% natural abundance]

Conversion e- emitter

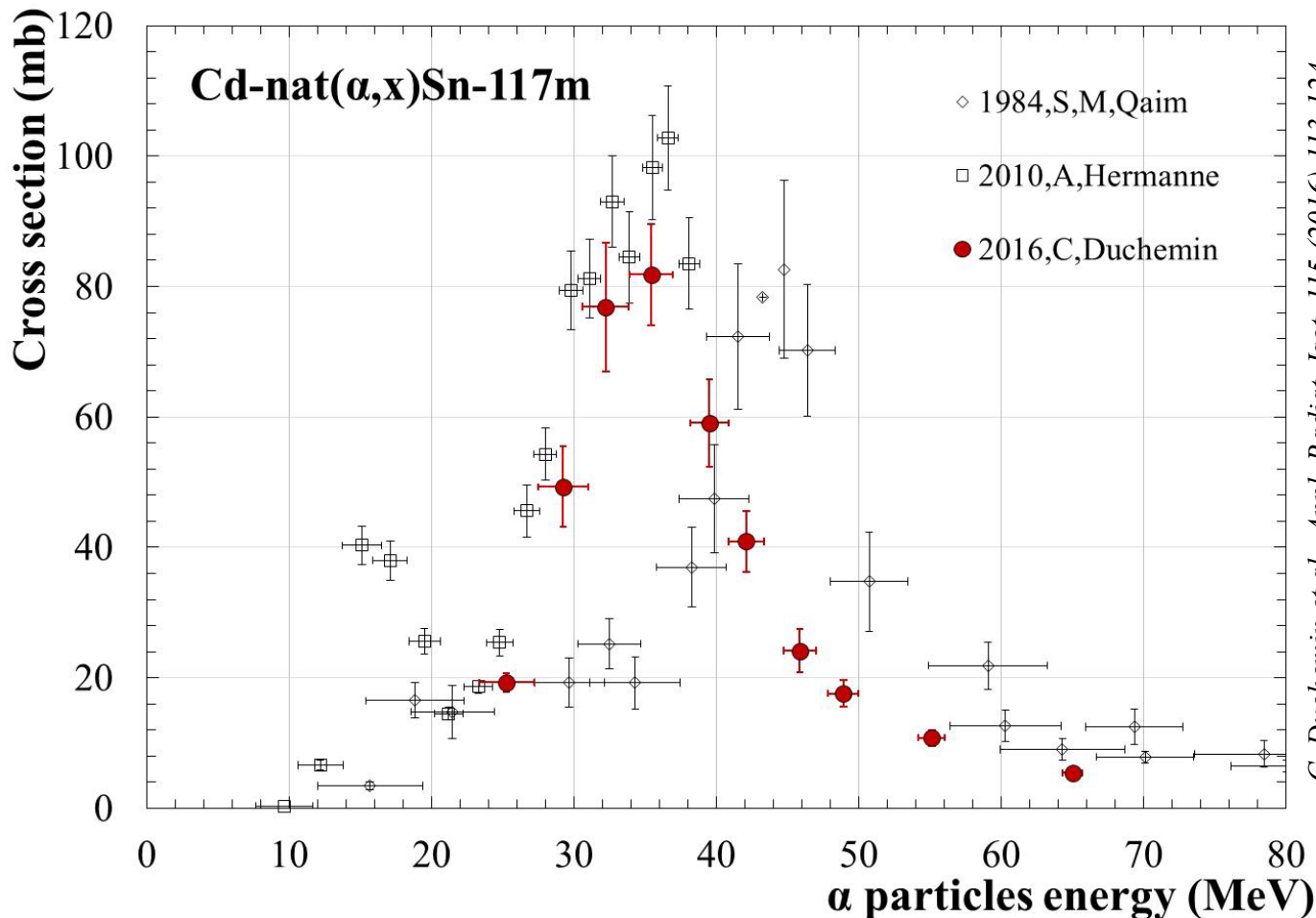
$T_{1/2} = 13.6 \text{ d}$

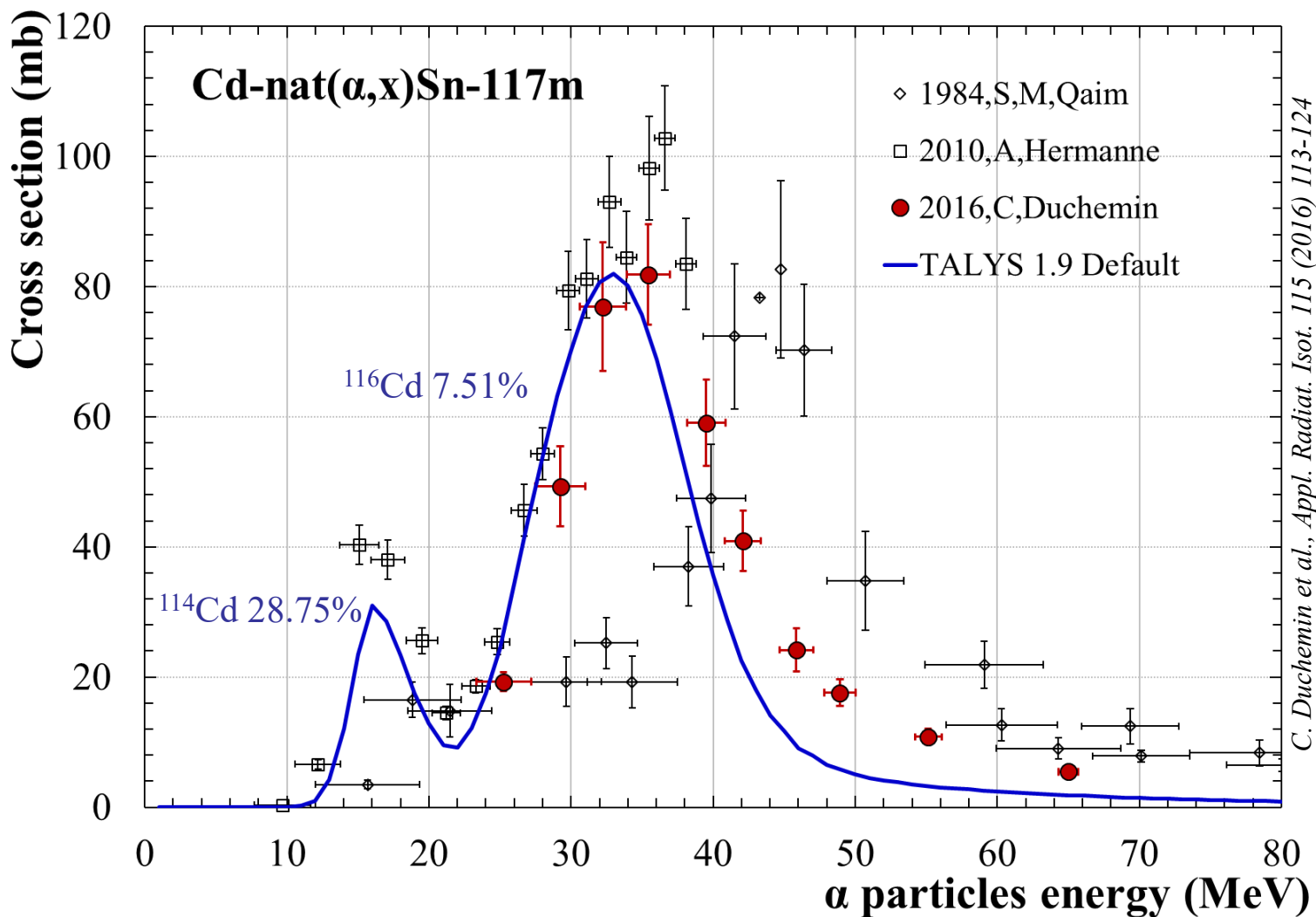
Used for the palliation of painful bone metastases

158 keV γ ray ideal for SPECT

Facilitate target manufacturing

Reaction routes by neutronic activation or using charged particles like protons or alpha particles





More efficient enriched ^{116}Cd target (α ,3n) natural abundance 7.512%

Few MBq/ μAh

^{135}La for Auger-based targeted therapy

CE 100%

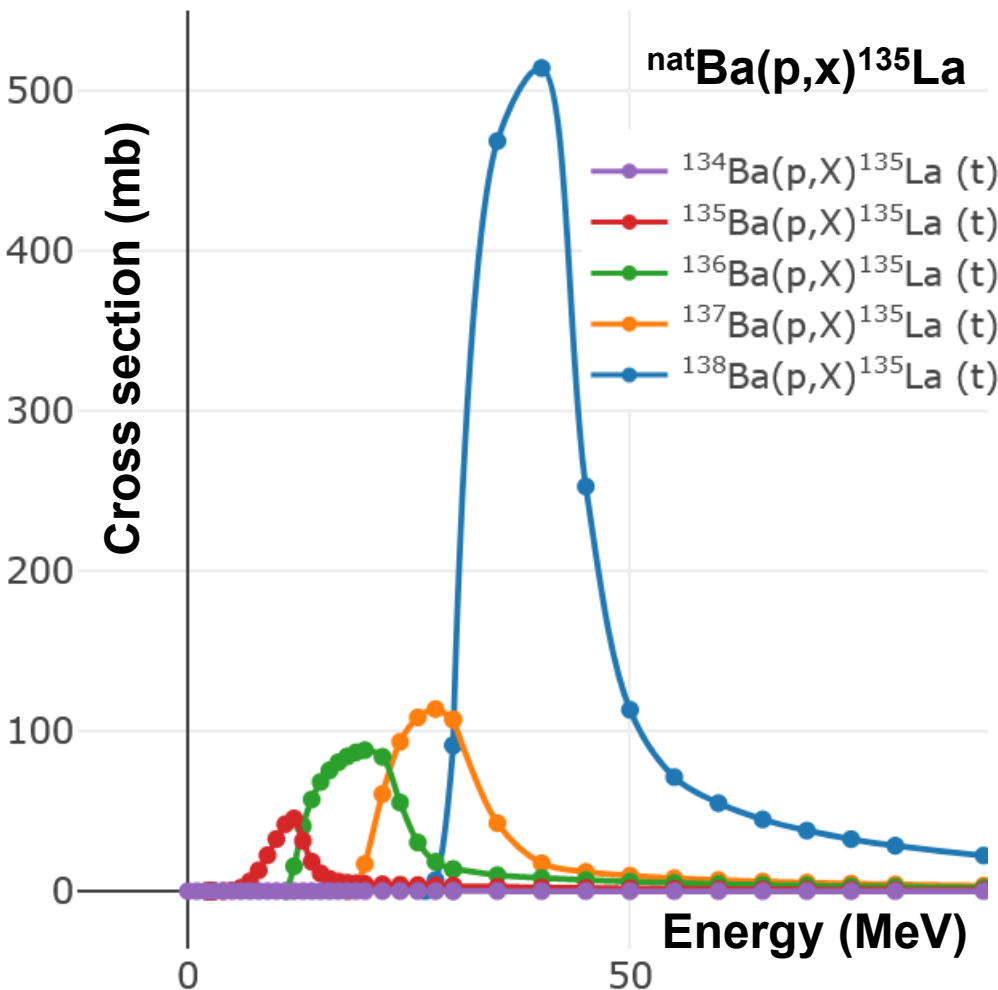
Auger electron emitter

$T_{1/2} = 19.4 \text{ h}$

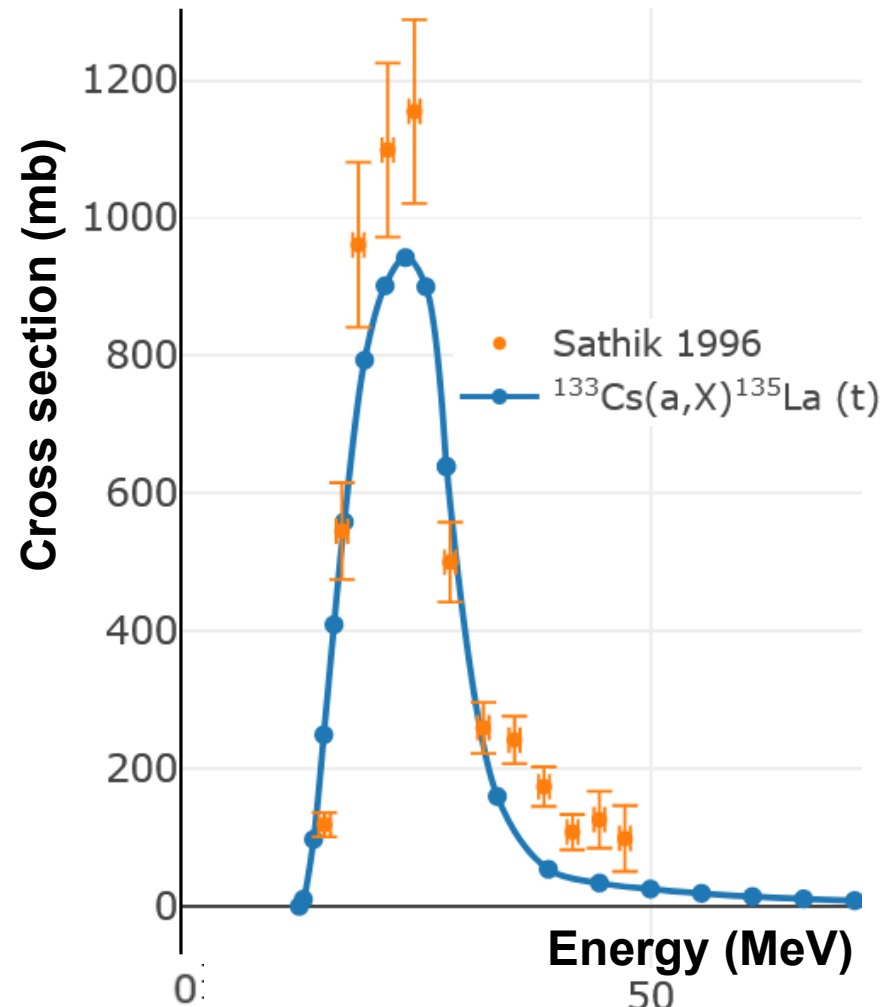
Auger-based targeted internal radiotherapy

Theranostic pair with ^{133}La

Use a monoisotopic target



Ba: thermal conductivity low



Cs: alkaline but ^{82}Rb produce with an alkaline

Medicine: production of medical interest isotopes

- ✓ Avoid radioactive target material
- ✓ Access to a higher cross section
- ✓ Reuse an existing process : targetry, chemistry
- ✓ Facilitate target manufacturing
- ✓ Use a monoisotopic target

Non-standard positron emitters, alpha-targeted internal radiotherapy ...

Personalized medicine:

- Developed the set of isotopes available and
- Produce sufficient quantities for applications in diagnostic and therapy

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

Activation of materials for both fundamental and applied research

- ✓ Nuclear data: cross section measurements, comparison with nuclear model calculations
 - Reaction mechanism, excitation function, isomeric cross section
 - Optimum production, minimization of impurities
 - Realistic dose calculation
- ✓ Nuclear structure data: high-spin level
- ✓ Astrophysics: r process



Thank you for your attention

Acknowledgments to the 28th International Nuclear Physics Conference organization committee

“Are alpha beams of interest to produce medical radionuclides ?”

Guertin A.^{1*}, Haddad F.^{1,2}, Alliot C.², Bonraisin A.C.², Brionne L.², Nigrón E.², Sounalet T.¹

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