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

Arnaud Guertin, Ferid Haddad, Cyrille Alliot, Anne-Cécile Bonraisin, Lèna Brionne, Etienne Nigron, Thomas Sounalet

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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. Nigrone, 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:

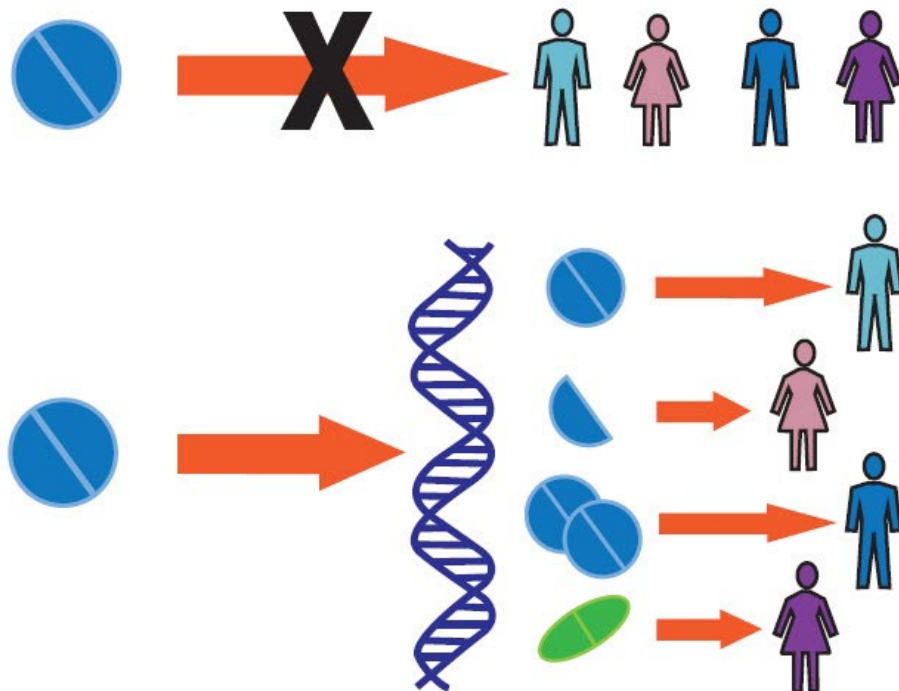
- $\beta^+$ :  $^{64}\text{Cu}$ ,  $^{68}\text{Ga}$ ,  $^{89}\text{Zr}$  ...
- $\beta^-$ :  $^{166}\text{Ho}$ ,  $^{177}\text{Lu}$  ...
- Auger:  $^{117\text{m}}\text{Sn}$ ,  $^{155}\text{Tb}$
- Theranostic:  $^{44}\text{Sc}/^{47}\text{Sc}$ ,  $^{64}\text{Cu}/^{67}\text{Cu}$ ,  $^{68}\text{Ga}/^{177}\text{Lu}$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

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

## Imaging and diagnosis

Choose the best treatment

Evaluate its efficacy



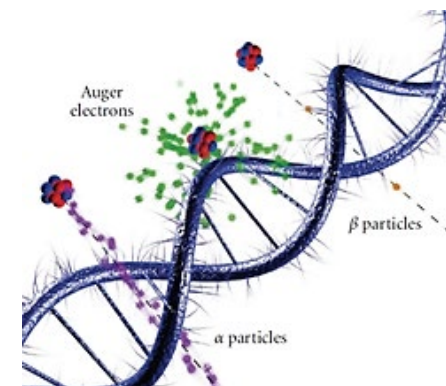
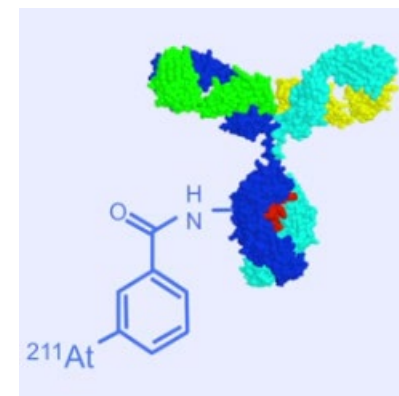
**The Right Drug  
At The Right Time**

**To The Right Patient**

**At The Right Time**

## Therapy

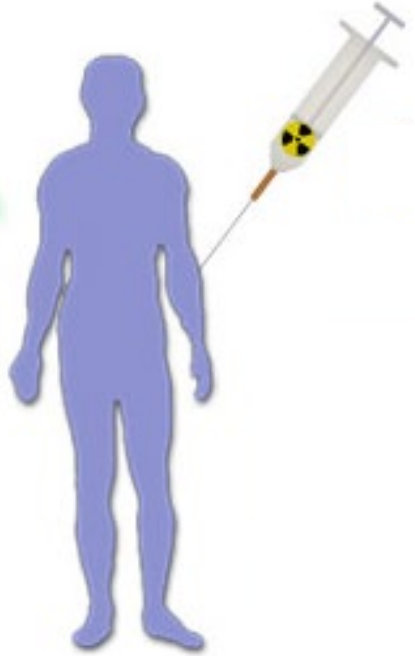
Destroy tumor cells



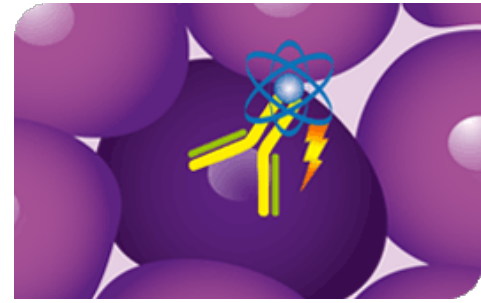
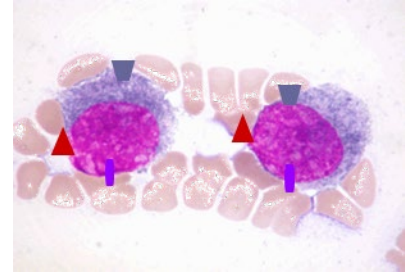
*B.Q. LEE et al.*

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

**Inject a tracer**



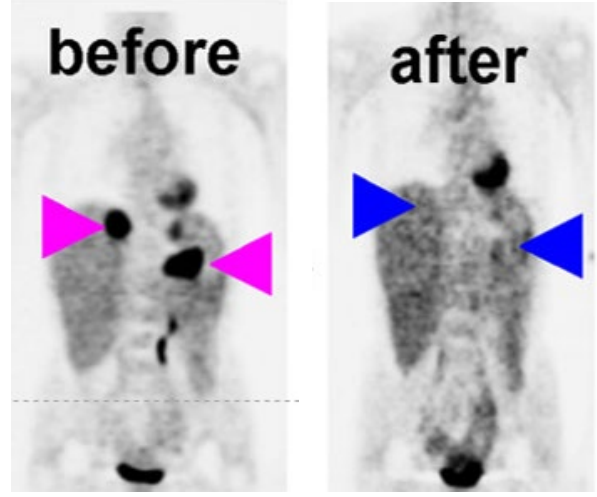
**Target a tumor marker**



*AREVA Med*

**Detect the disease**

$\gamma, \beta^+$  →

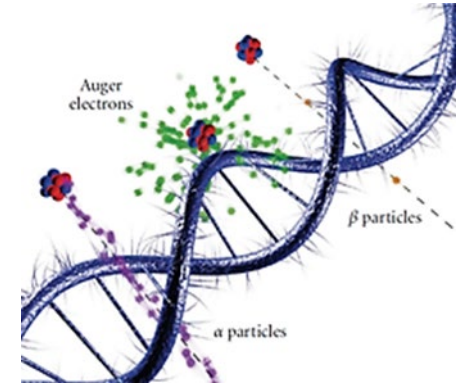


*NIRS, Shiba, MIC*



$\beta^-, \alpha,$   
 $e_{\text{Auger}}$  →

**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:

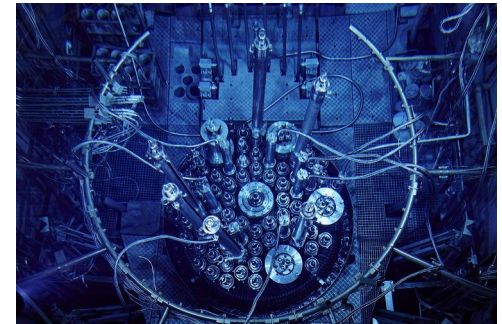
**proton, deuteron, triton and alpha particle**

Protons are more commonly available

Still limited applications for d,  $^3\text{He}$  and alpha particle

## Focus on some opportunities with alpha particle beams

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



BR2 reactor @ SCK•CEN



C70XP @ ARRANAX



SPIRAL 2 @ GANIL



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

**Avoid radioactive target and use of a monoisotopic target**

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



$^{211}\text{At}$  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  $\alpha$  particles

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

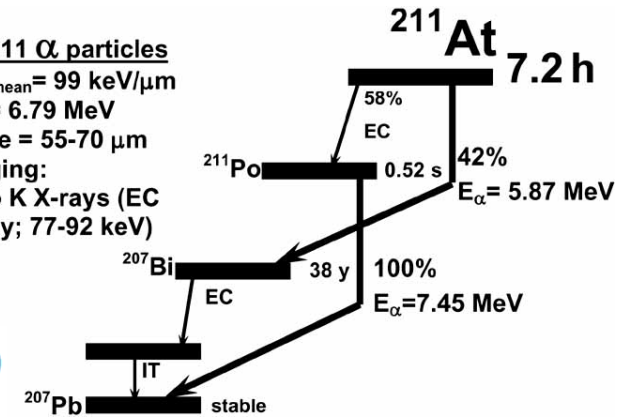
$E_{\text{ave}} = 6.79 \text{ MeV}$

range = 55-70  $\mu\text{m}$

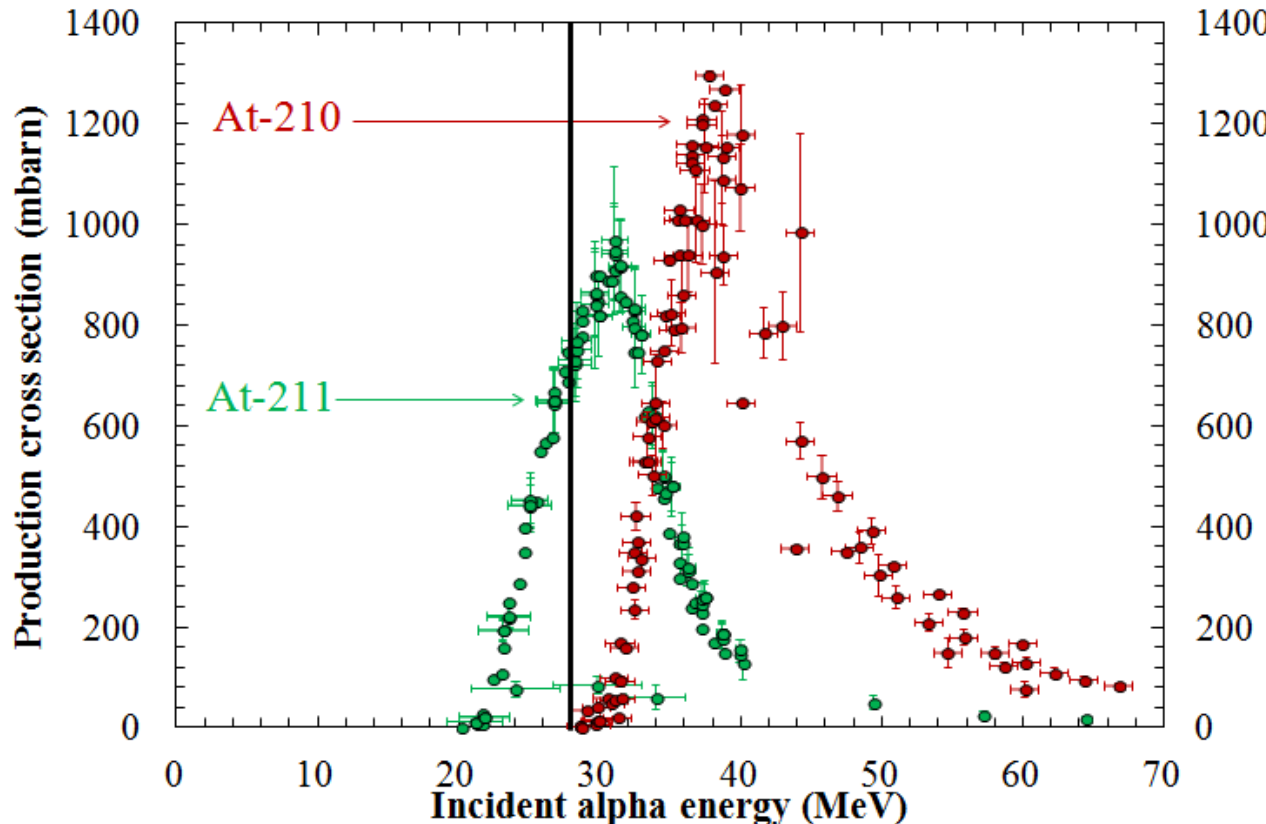
Imaging:

$^{211}\text{Po}$  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  $\alpha$  emission  
 to Bi-206 (6.2 days)



100% EC, no  $\beta^+$

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

SPECT

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

**Avoid radioactive target**

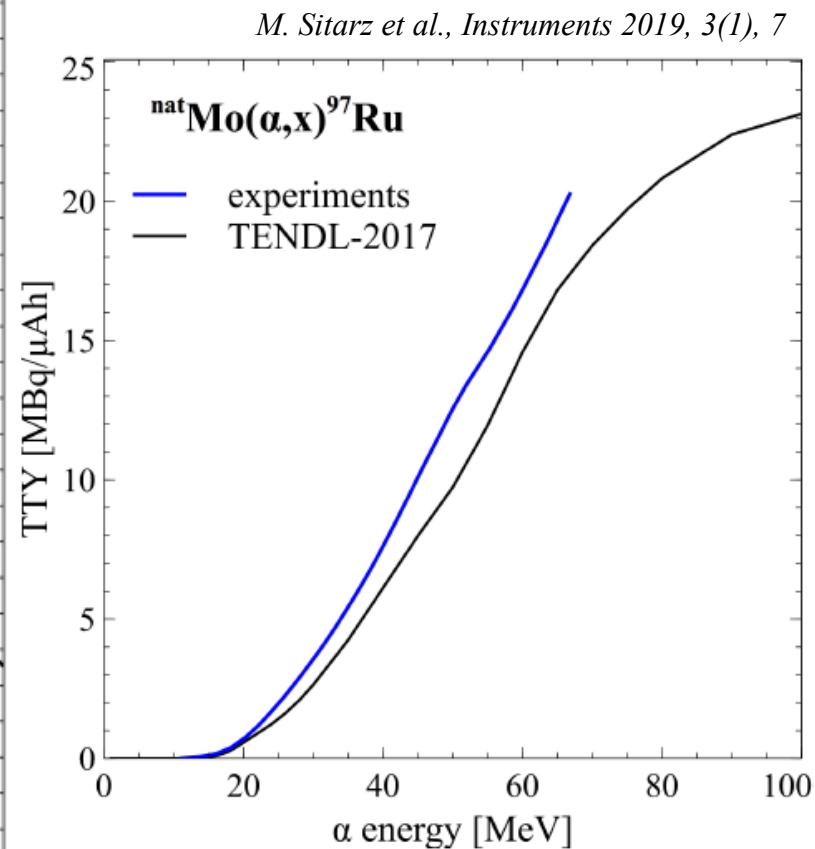
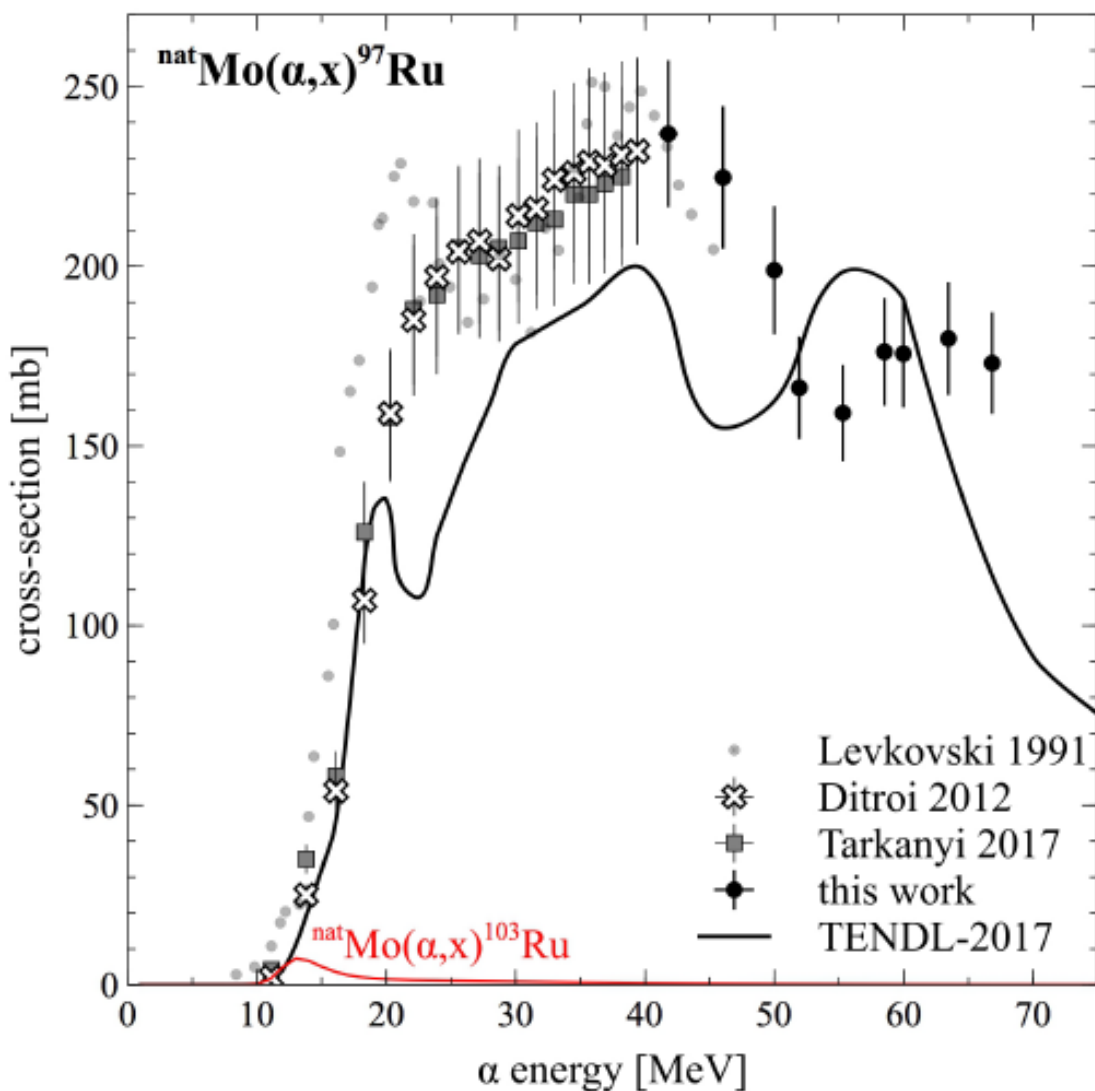
Z	$^{96}\text{Ru}$ STABLE 5.54%	$^{97}\text{Ru}$ 2.83 D $\epsilon: 100.00\%$	$^{98}\text{Ru}$ STABLE 1.87%	$^{99}\text{Ru}$ STABLE 12.76%	$^{100}\text{Ru}$ STABLE 12.60%	$^{101}\text{Ru}$ STABLE 17.06%	$^{102}\text{Ru}$ STABLE 31.55%	$^{103}\text{Ru}$ 39.247 D $\beta^-: 100.00\%$	$^{104}\text{Ru}$ STABLE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

Polyisotopic target of Mo

Decaying time to increase specific activity

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

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



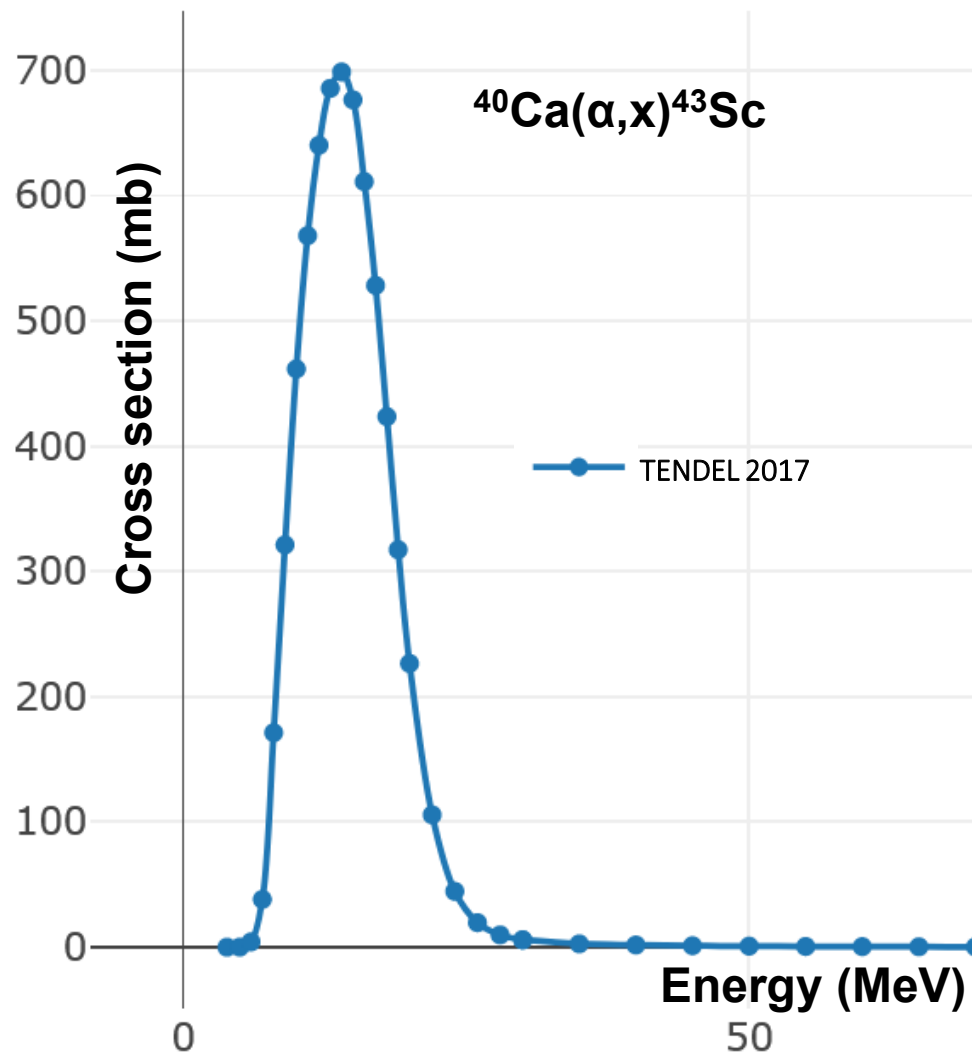
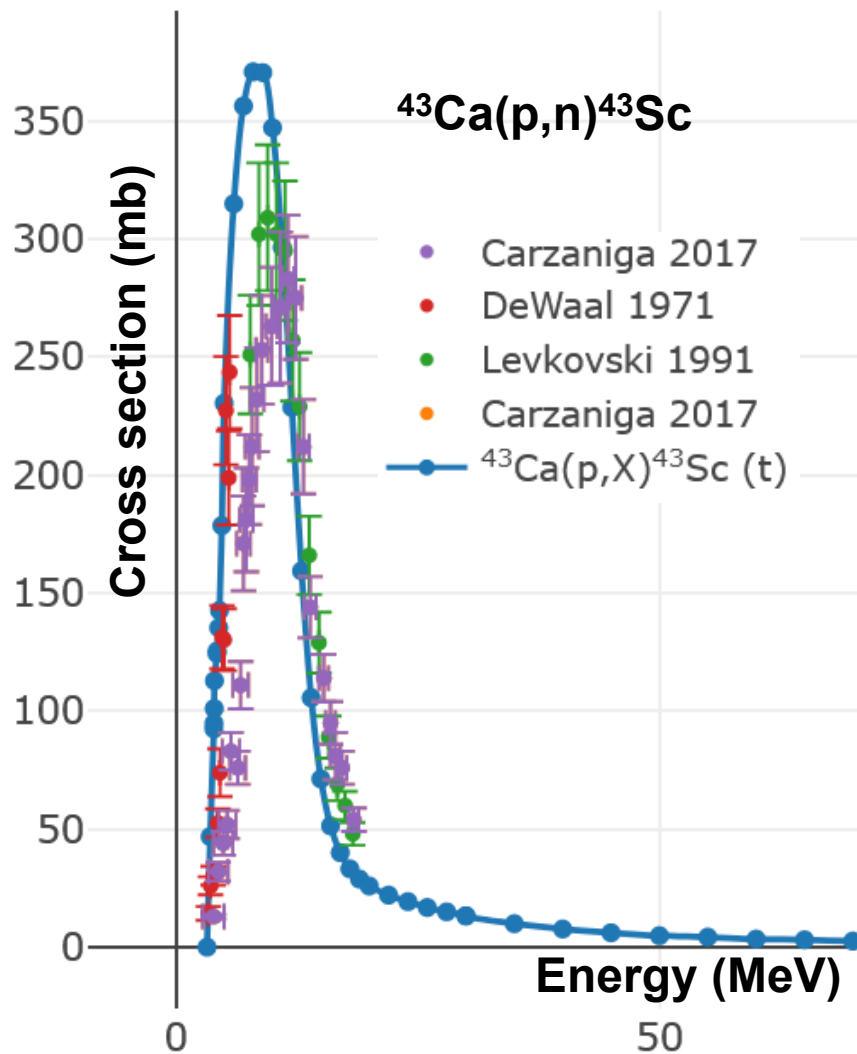
Few tens of MBq/ $\mu\text{Ah}$   
 Increase possible : duration, intensity,  
 enriched  $^{95,96}\text{Mo}$  target

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

$\beta^+$  with no co-emitted high energy  $\gamma$  rays  
 Promising candidates for PET imaging

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

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

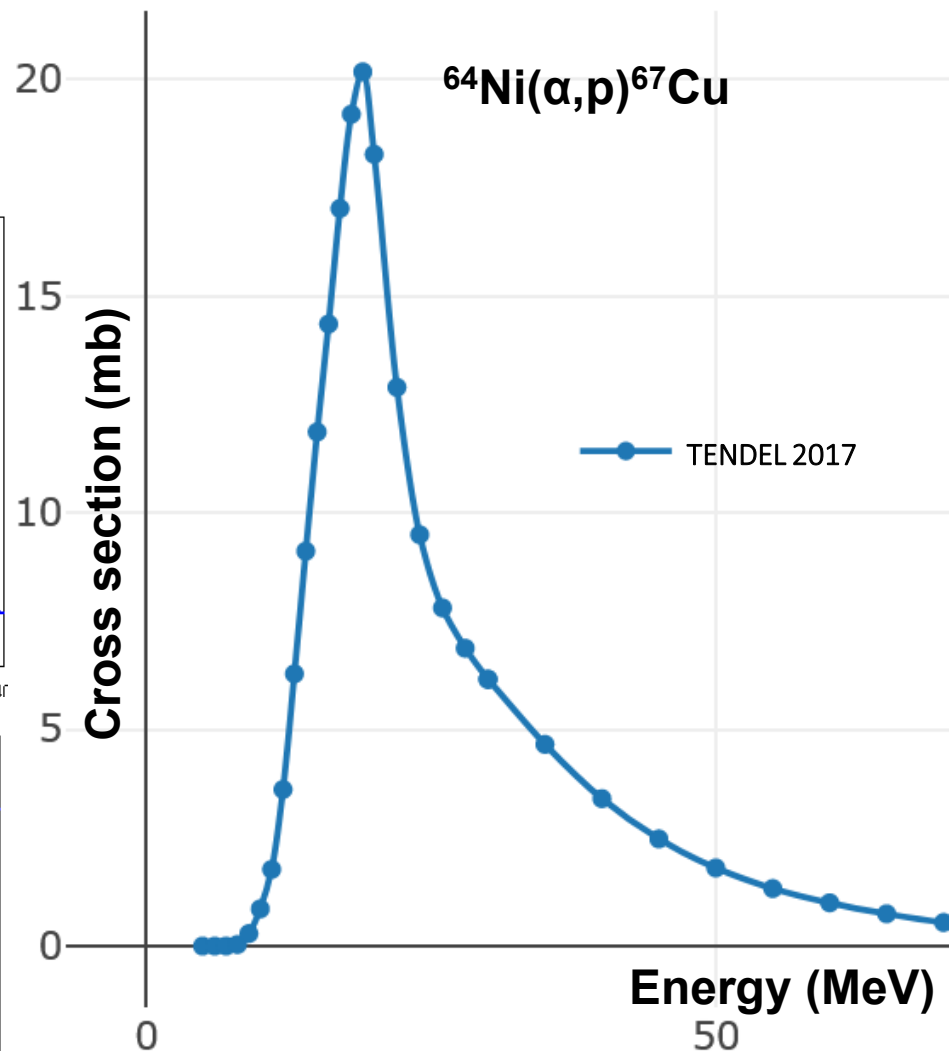
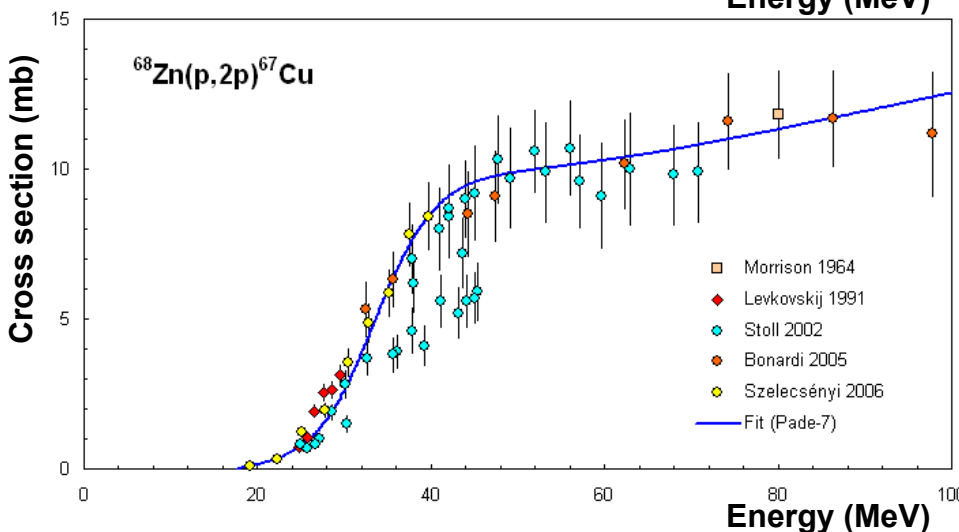
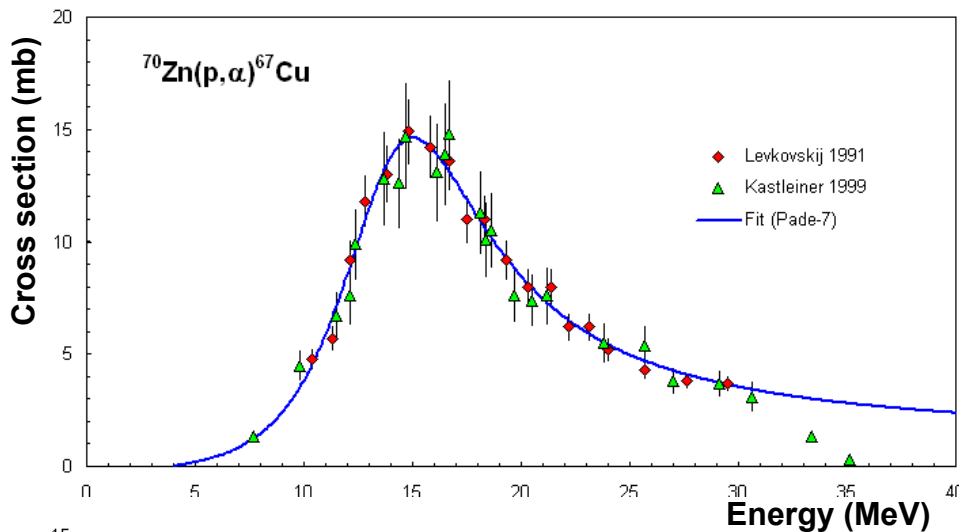




# 67Cu for theranostic approach

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

## Reuse of an existing efficient process



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

Conversion e- emitter

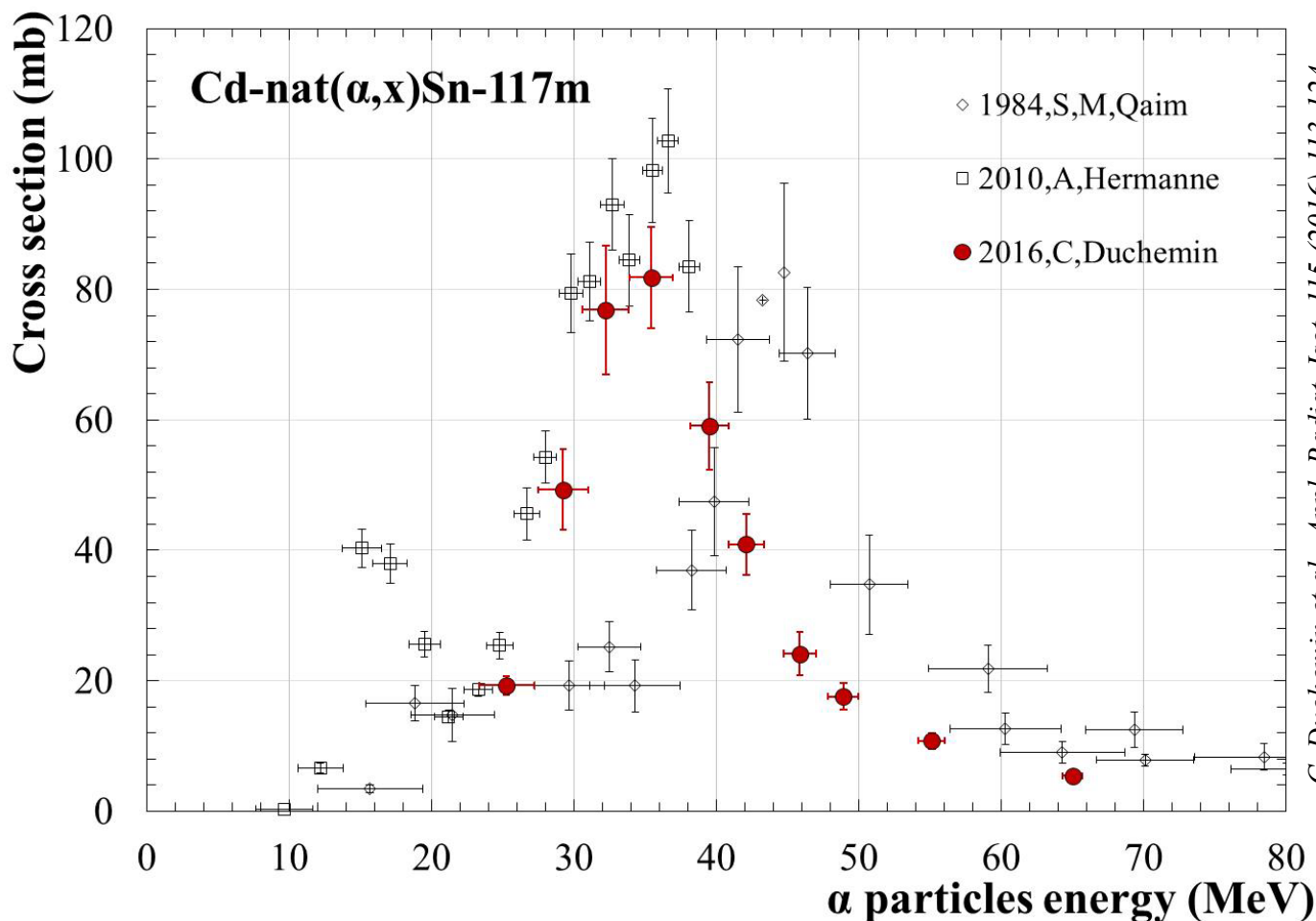
$T_{1/2} = 13.6 \text{ d}$

Used for the palliation of painful bone metastases

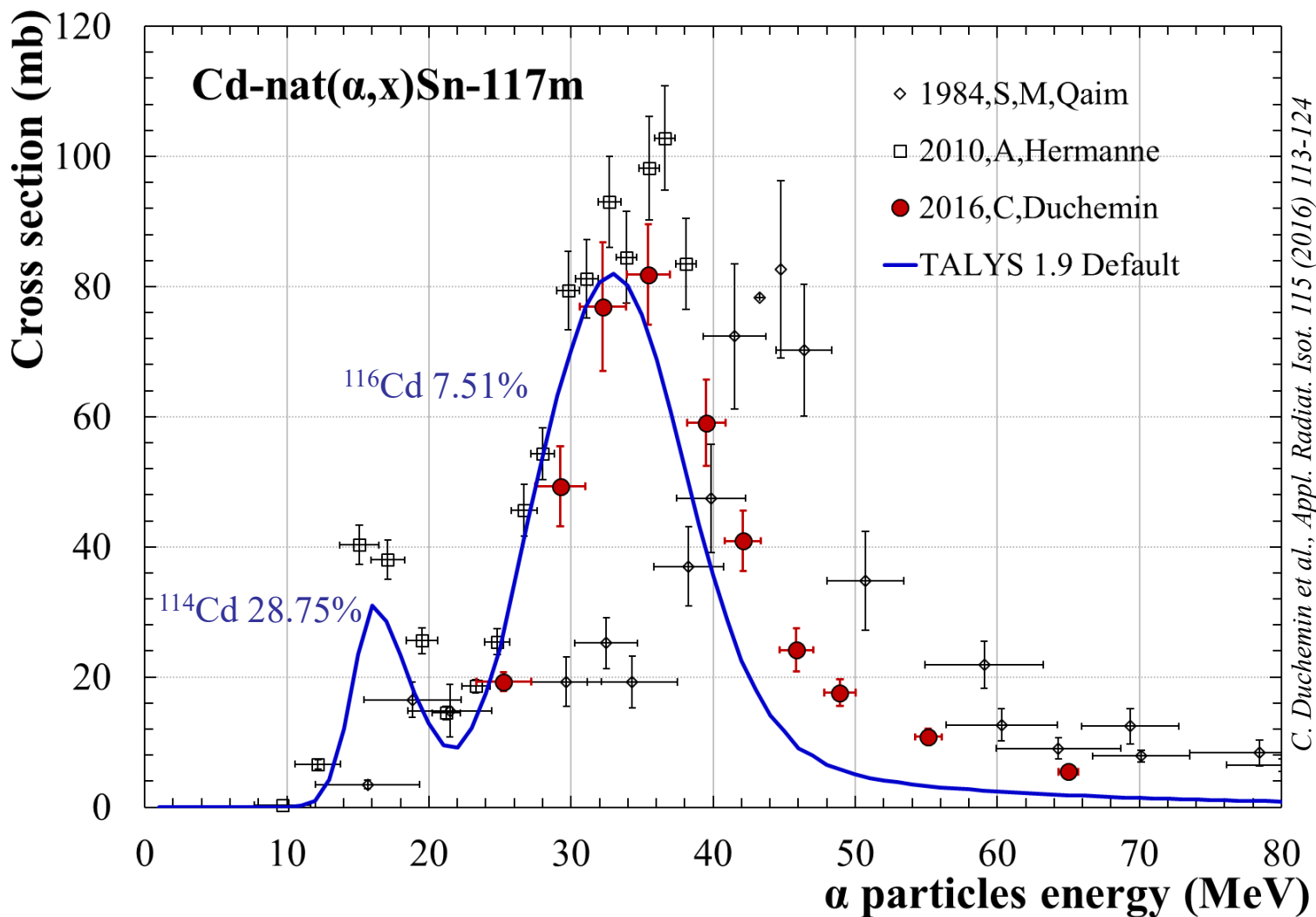
158 keV  $\gamma$  ray ideal for SPECT

## Facilitate target manufacturing

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



C. Duchemin et al., Appl. Radiat. Isot. 115 (2016) 113-124



More efficient enriched  $^{116}\text{Cd}$  target ( $\alpha$ ,3n) natural abundance 7.512%

Few MBq/ $\mu\text{Ah}$

# $^{135}\text{La}$ for Auger-based targeted therapy

CE 100%

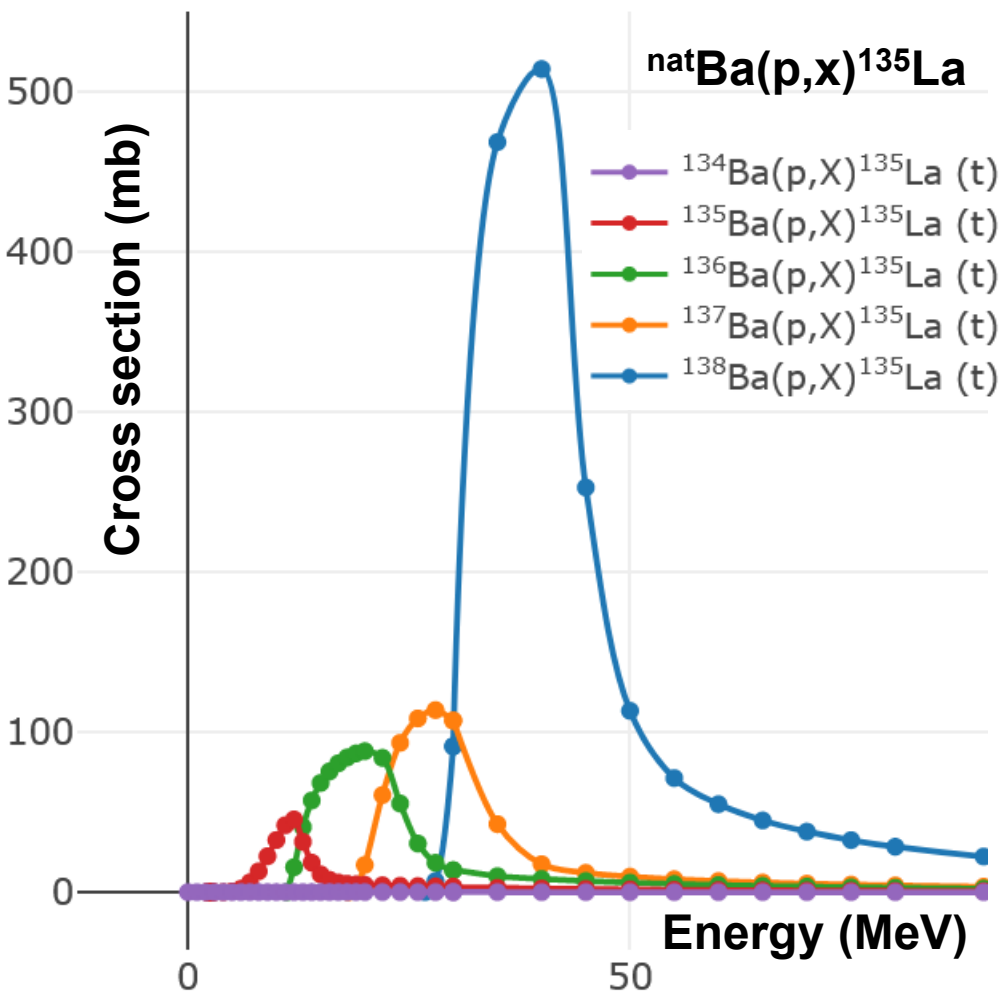
Auger electron emitter

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

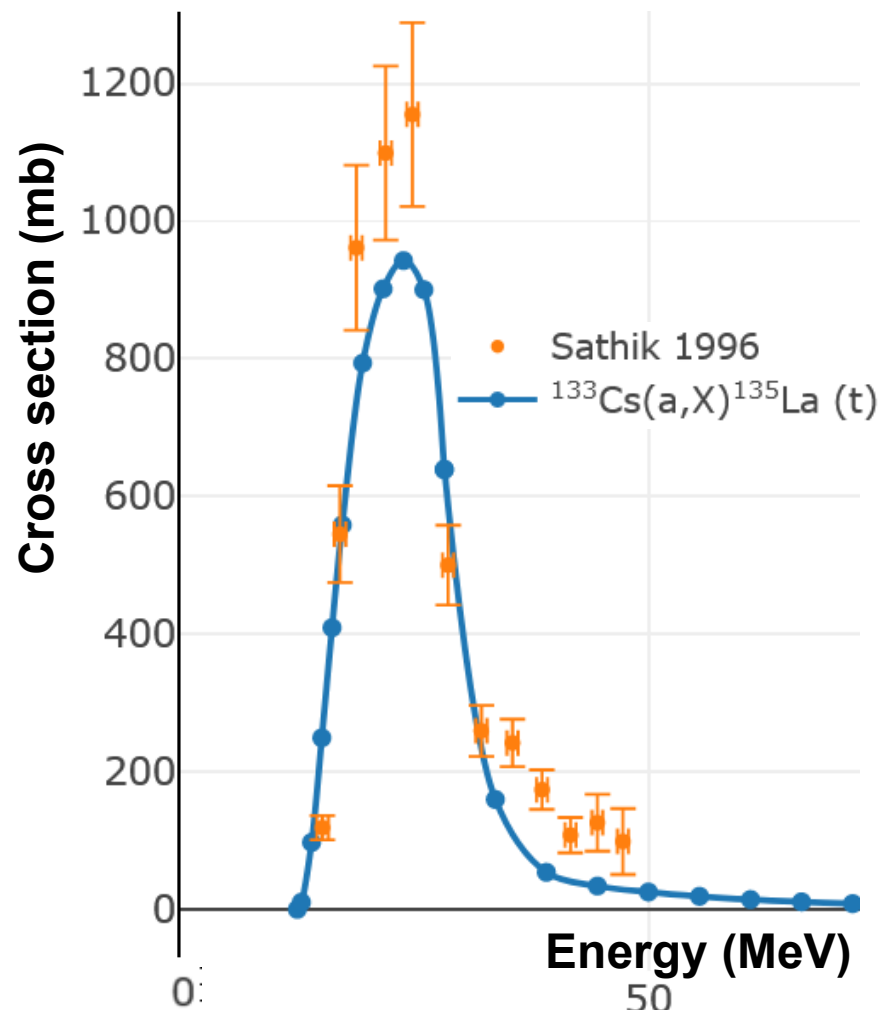
Auger-based targeted internal radiotherapy

Theranostic pair with  $^{133}\text{La}$

Use a monoisotopic target



Ba: thermal conductivity low



Cs: alkaline but  $^{82}\text{Rb}$  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 28<sup>th</sup> International Nuclear Physics Conference  
organization committee

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

**Guertin A.<sup>1\*</sup>, Haddad F.<sup>1,2</sup>, Alliot C.<sup>2</sup>, Bonraisin A.C.<sup>2</sup>, Brionne L.<sup>2</sup>, Nigrone E.<sup>2</sup>, Sounalet T.<sup>1</sup>**

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