

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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Arnaud Guertin, Ferid Haddad, Cyrille Alliot, Anne-Cécile Bonraisin, Lèna Brionne, et al.. Are alpha beams of interest to produce medical radionuclides ?. The 28th International Nuclear Physics Conference (INPC 2022), Sep 2022, Le Cap, South Africa. hal-03834976

HAL Id: hal-03834976
https://hal.science/hal-03834976

Submitted on 31 Oct 2022

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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

Nantes Université

Subatech

ARRONAX

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

Isotopes in nuclear medicine

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

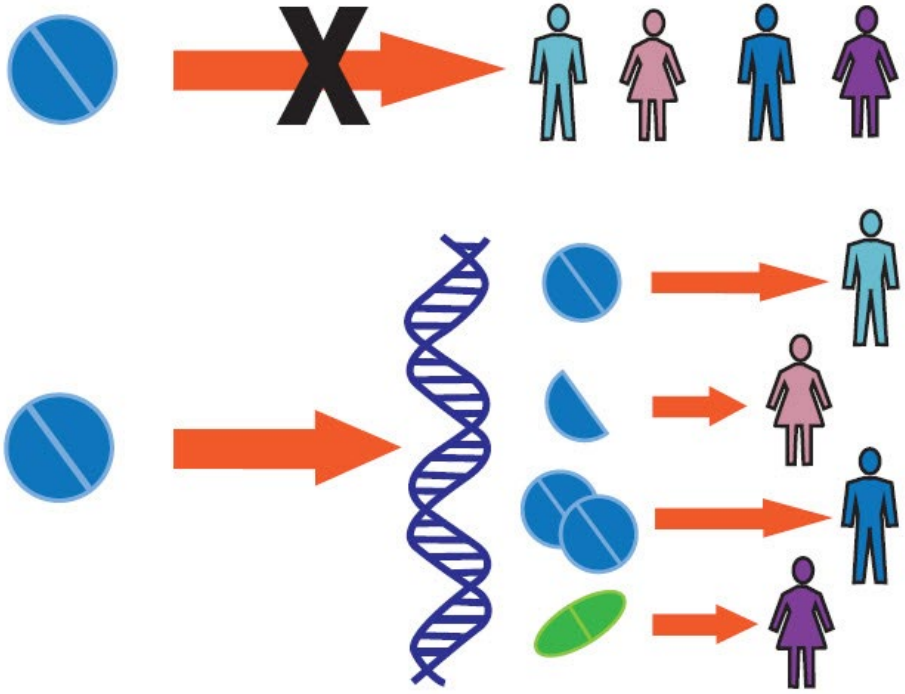
- Diagnosis (γ, β^+)	SPECT, TEP	^{99m}Tc, ^{18}F, ^{64}Cu …	Detecnet (^{64}Cu dotatate inj.)
- Therapy (β^-, α, e_{Auger})	TAT	^{117}Lu, ^{225}Ac …	Lutathera (^{177}Lu oxodotreotide)

Personalized nuclear medicine

Imaging and diagnosis

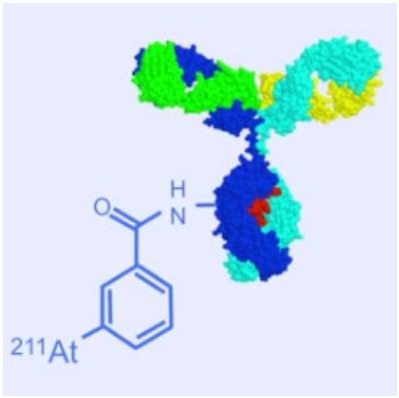
Choose the best treatment

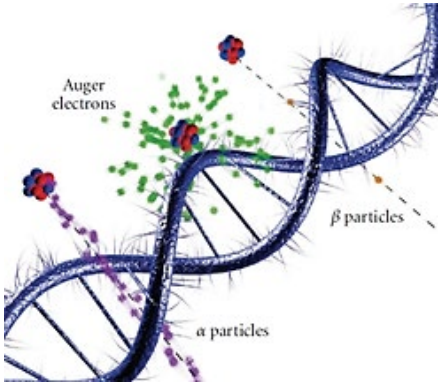
Evaluate its efficacy



Therapy

Destroy tumor cells



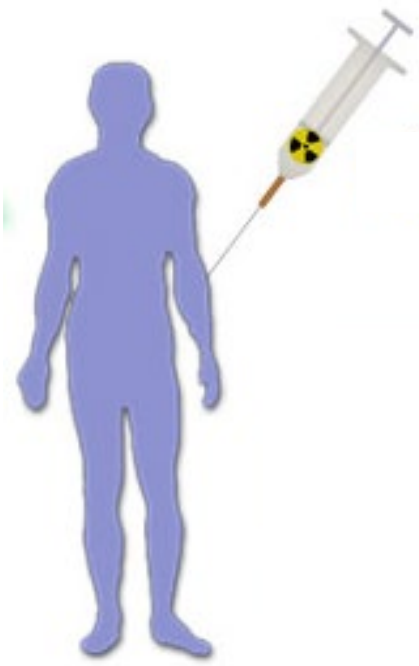


B.Q. LEE et al.

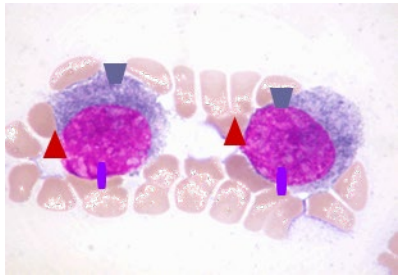
The Right Drug To The Right Patient For The Right Disease
At The Right Time With The Right Dosage

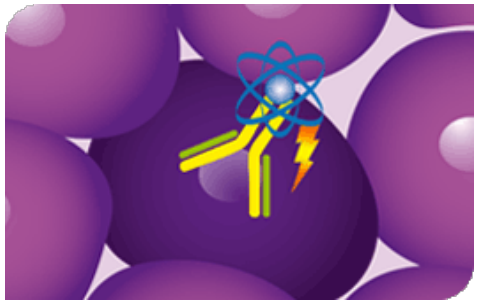
Imaging and molecular radiotherapies

Inject a tracer



Target a tumor marker

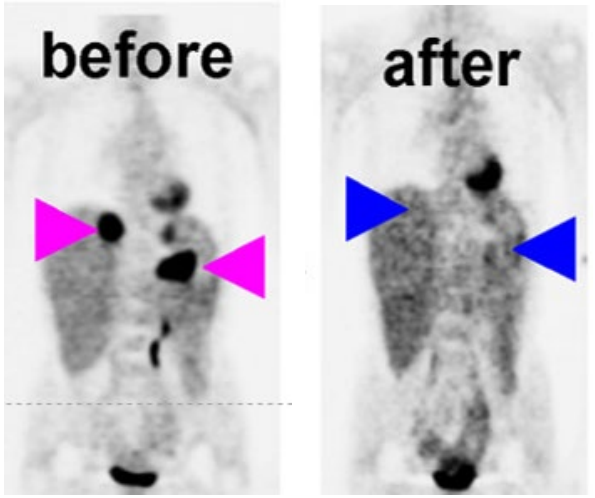




AREVA Med

Detect the disease

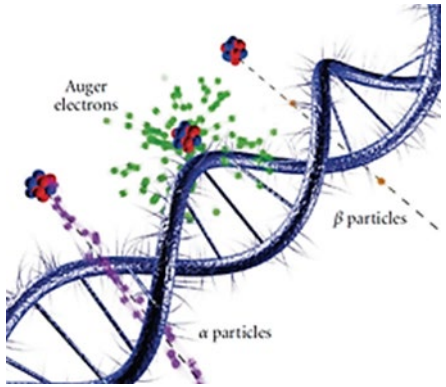
$\gamma, \beta+$ ➡



NIRS, Shiba, MIC

Treat the disease

$\beta-, \alpha, e_{Auger}$ ➡



Theranostic radiopharmaceuticals



Predictive imaging, companion diagnostic

Targeted therapy



THERANOSTICS MOLECULE

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

Pharmaceuticals 2017, 10(2), 56

What you see is what you treat

Motivations

Nuclear physicists could have crucial contributions:

- **Identify** reaction channel [spal., fis., act.]
- **Quantify** contaminants
- **Define** waste management process
- **Optimize** production process
- **Produce** the purest product
- **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

Motivations

Beams

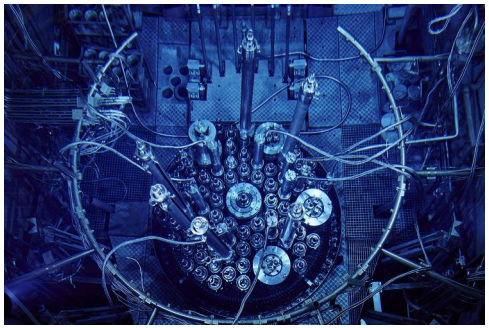
Many medical isotopes are produced using **neutron** induced reactions in reactors

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

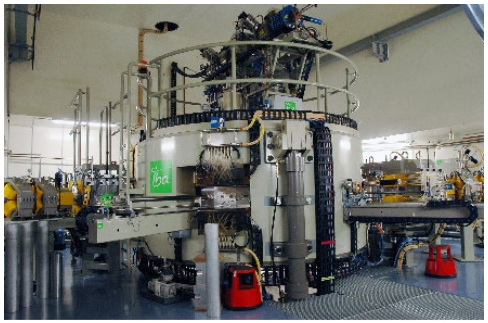
proton, **deuteron**, **triton** and **alpha particle**

Protons are more commonly available

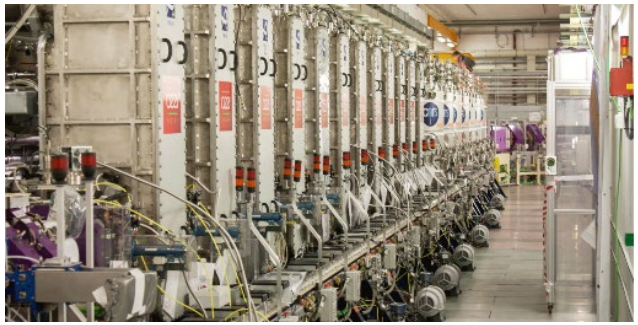
Still limited applications for d, ^{3}He and alpha particle



BR2 reactor @ SCK•CEN



C70XP @ ARRONAX



SPIRAL 2 @ GANIL

Focus on some opportunities with alpha particle beams

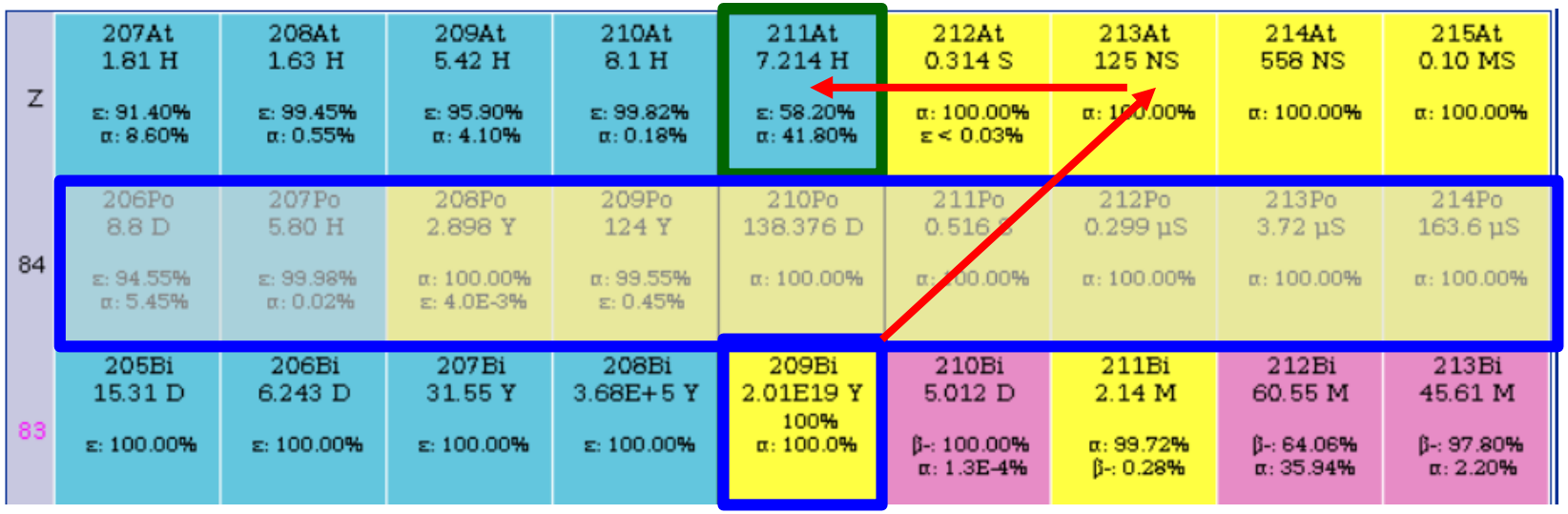
- ✓ **Avoid** radioactive target material
  ^{211}At, ^{97}Ru
- ✓ **Access** to a higher cross section
  ^{43}Sc
- ✓ **Reuse** an existing process : targetry, chemistry
  ^{67}Cu
- ✓ **Facilitate** target manufacturing
  ^{117}mSn
- ✓ **Use** a monoisotopic target
  ^{135}La

^{211}At for α-targeted internal radiotherapy

58% EC, 42% α $T_{1/2}$ = 7.3 h

α-targeted internal radiotherapy

Avoid radioactive target and use of a monoisotopic target



Spallation reaction

- ✓ lower yield
- ✓ higher level of impurity

^{209}Bi(α,2n)^{211}At

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

^{211}At for α-targeted internal radiotherapy

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







^{211}At production facilities in the world

- Running
- Potentially usable

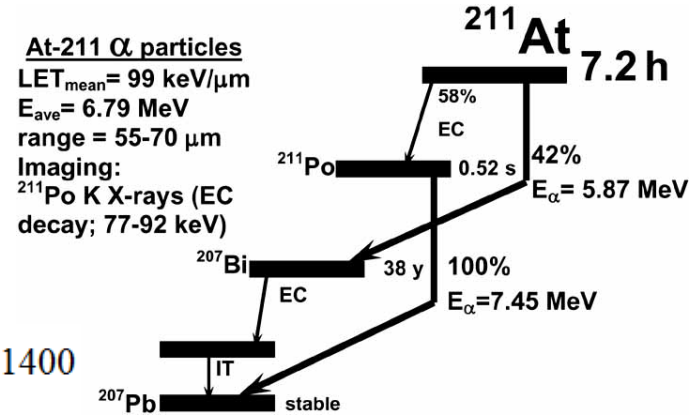
Courtesy of F. Haddad – SUBATECH – GIP ARRONAX

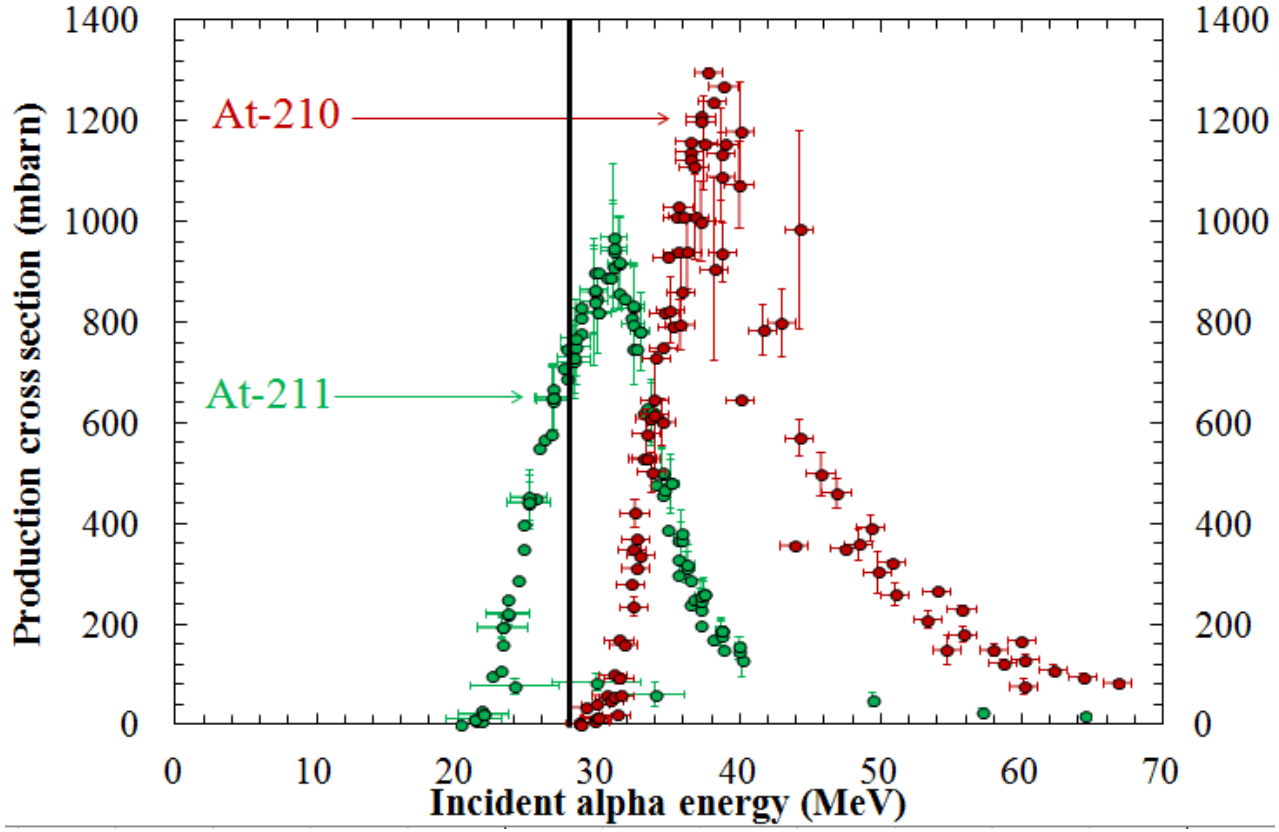
^{211}At for α-targeted internal radiotherapy

Direct production with alpha particles

Bi-209(α,2n)At-211, 20.7 MeV

Bi-209(α,3n)At-210, 28.6 MeV ⚠





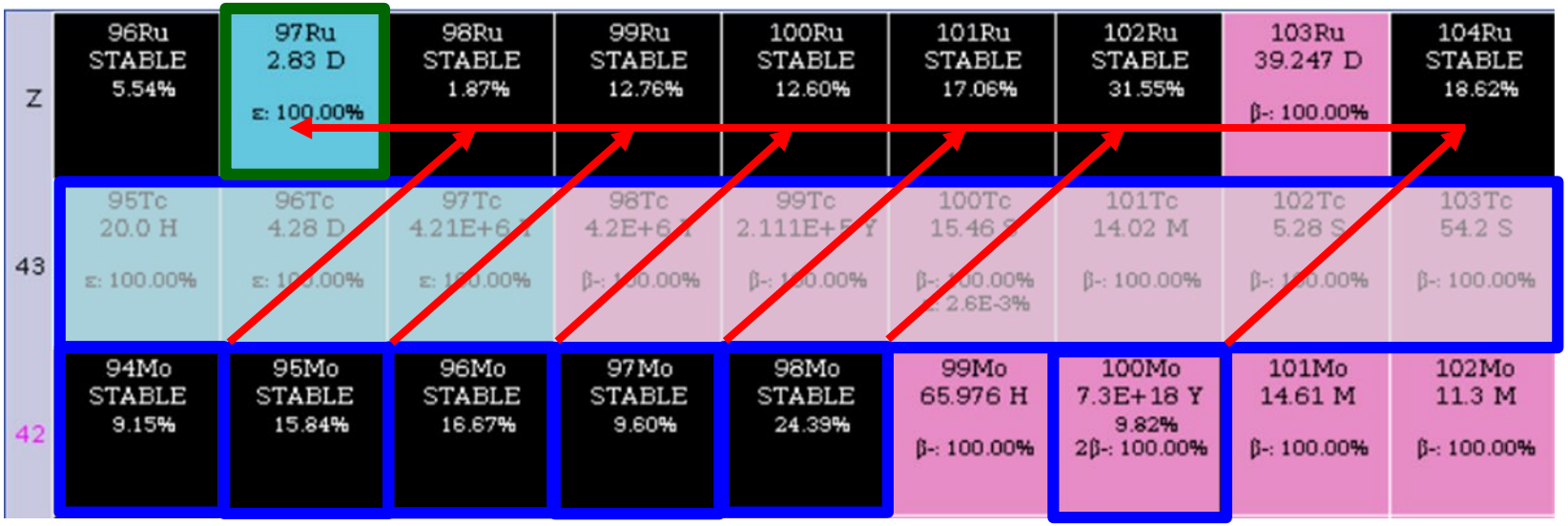
At-210, $T_{1/2}$ 8.1 h decays at 99.8% by EC to **Po-210** (138.4 days) and at 0.2% by α emission to Bi-206 (6.2 days)

^{97}Ru for SPECT and theranostic approach

100% EC, no β+ $T_{1/2}$ = 2.9 d SPECT

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

Avoid radioactive target

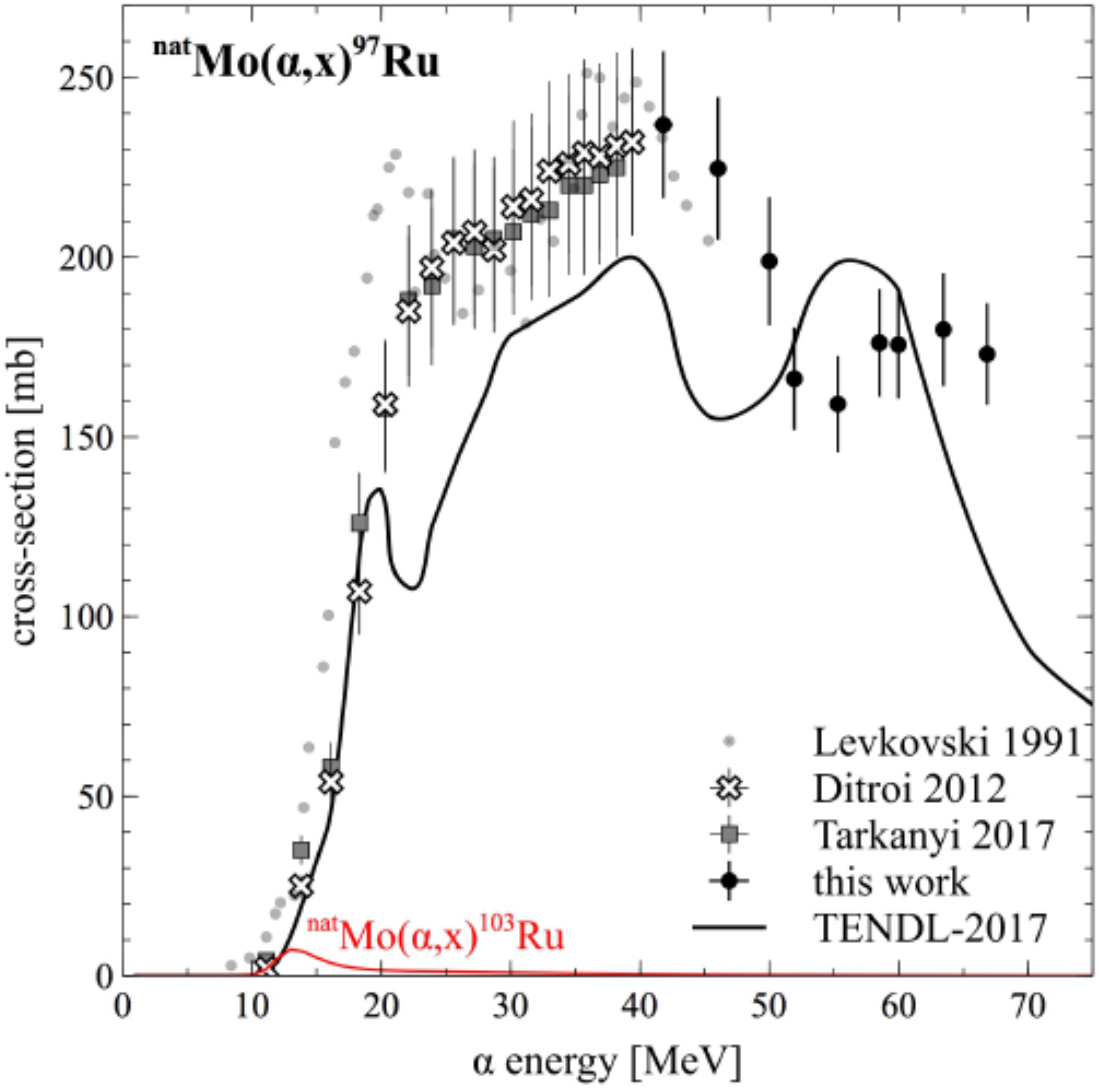


Polyisotopic target of Mo

Decaying time to increase specific activity

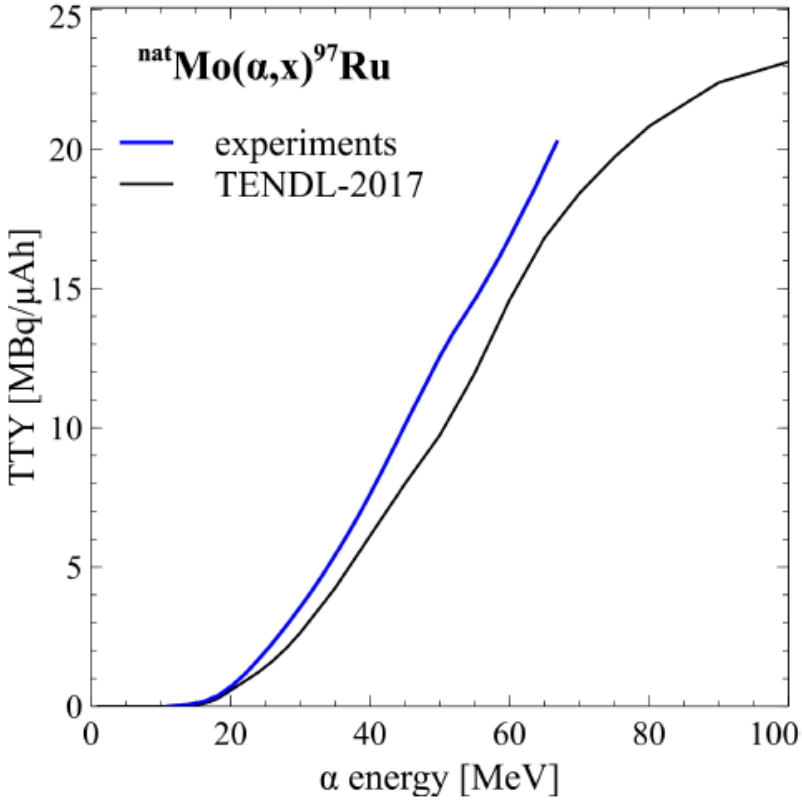
^{95}Ru $T_{1/2}$ = 1.66 h ^{94}Ru $T_{1/2}$ = 51.8 m

^{97}Ru for SPECT and theranostic approach



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

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



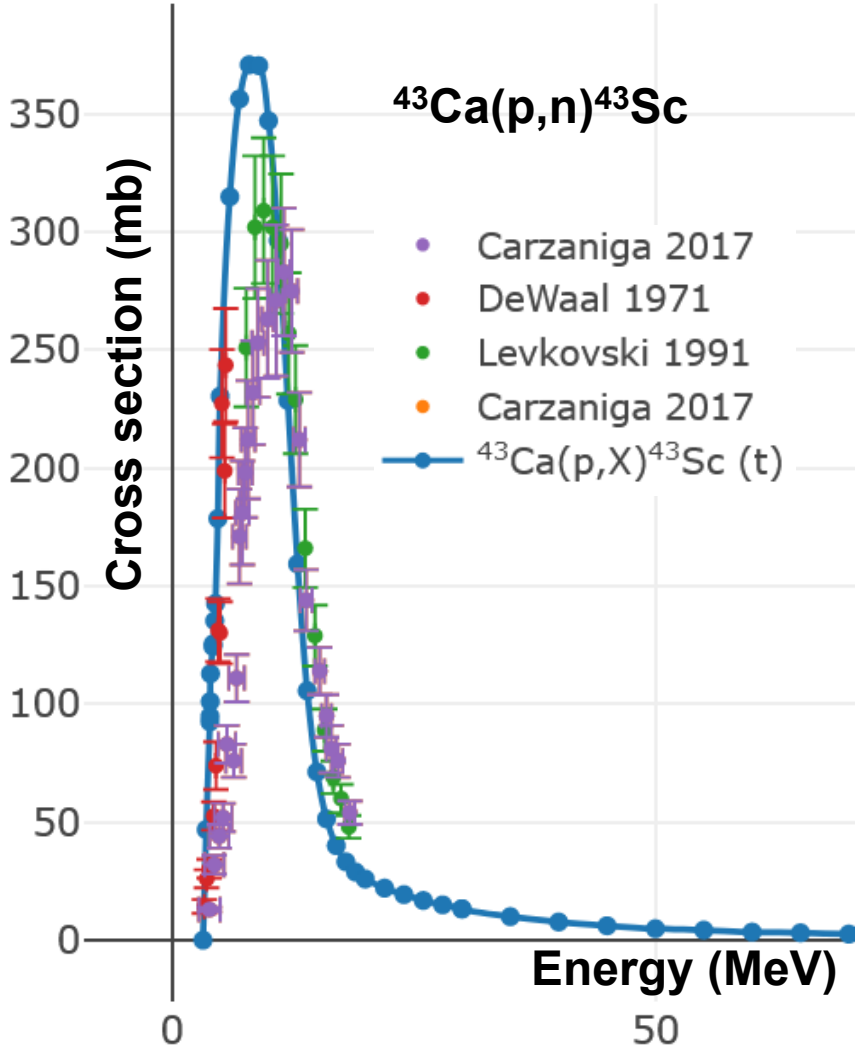
Few tens of MBq/μAh
Increase possible : duration, intensity, enriched ^{95,96}Mo target

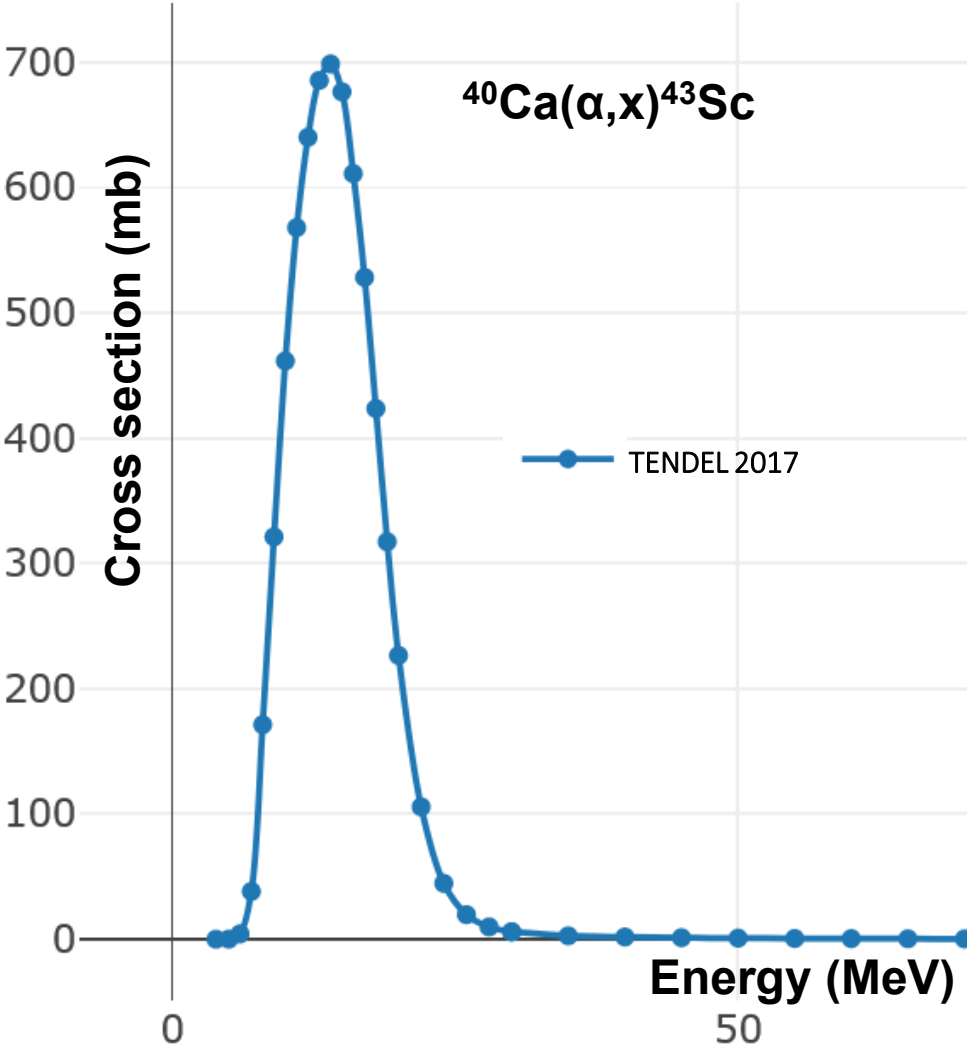
^{43}Sc for PET and theranostic approach

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

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

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



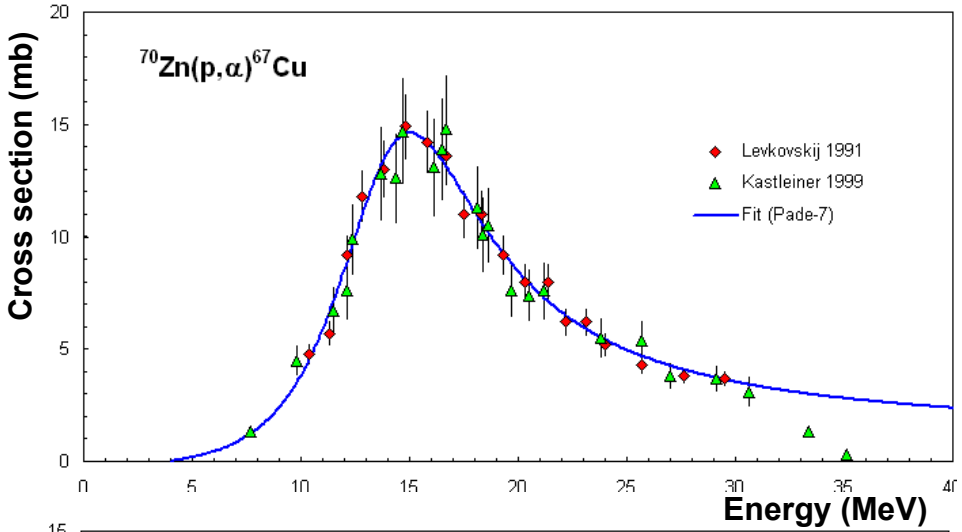


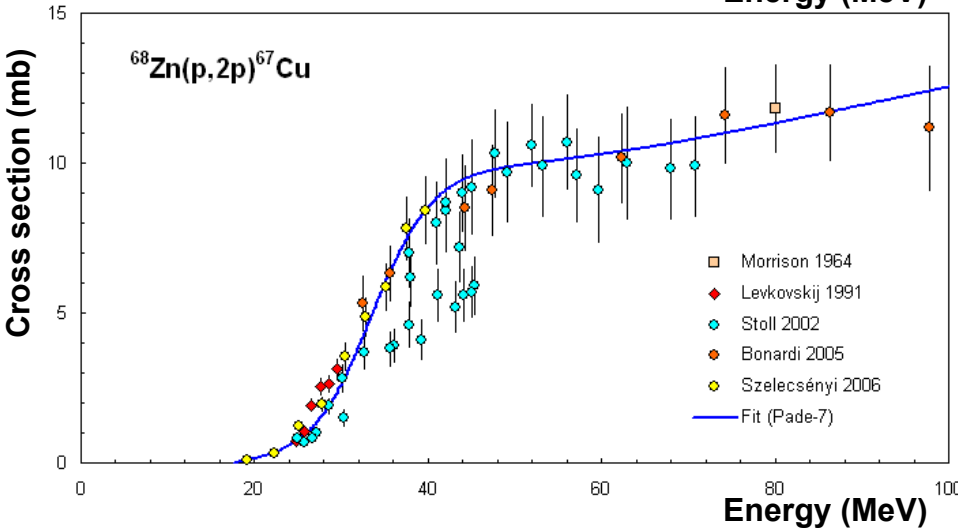
67Cu for theranostic approach

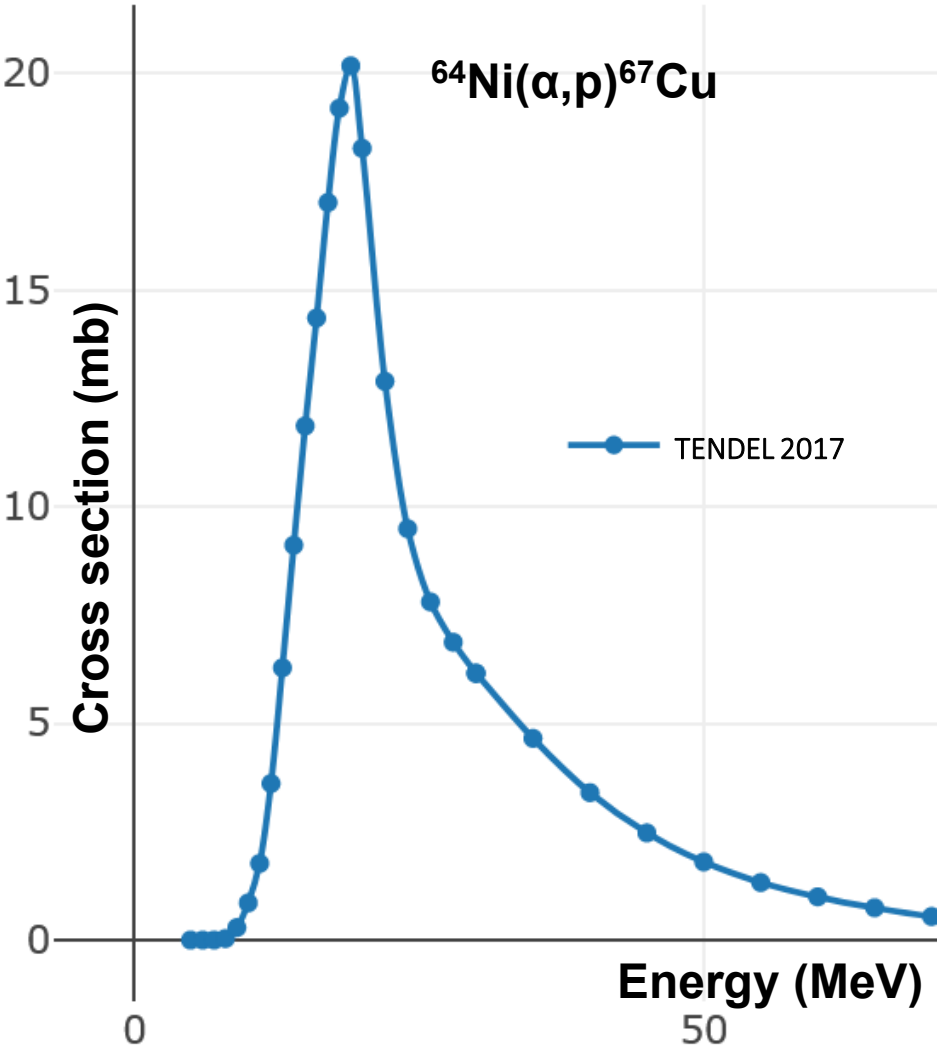
β- $T_{1/2} = 61.9$ h

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 abondance]

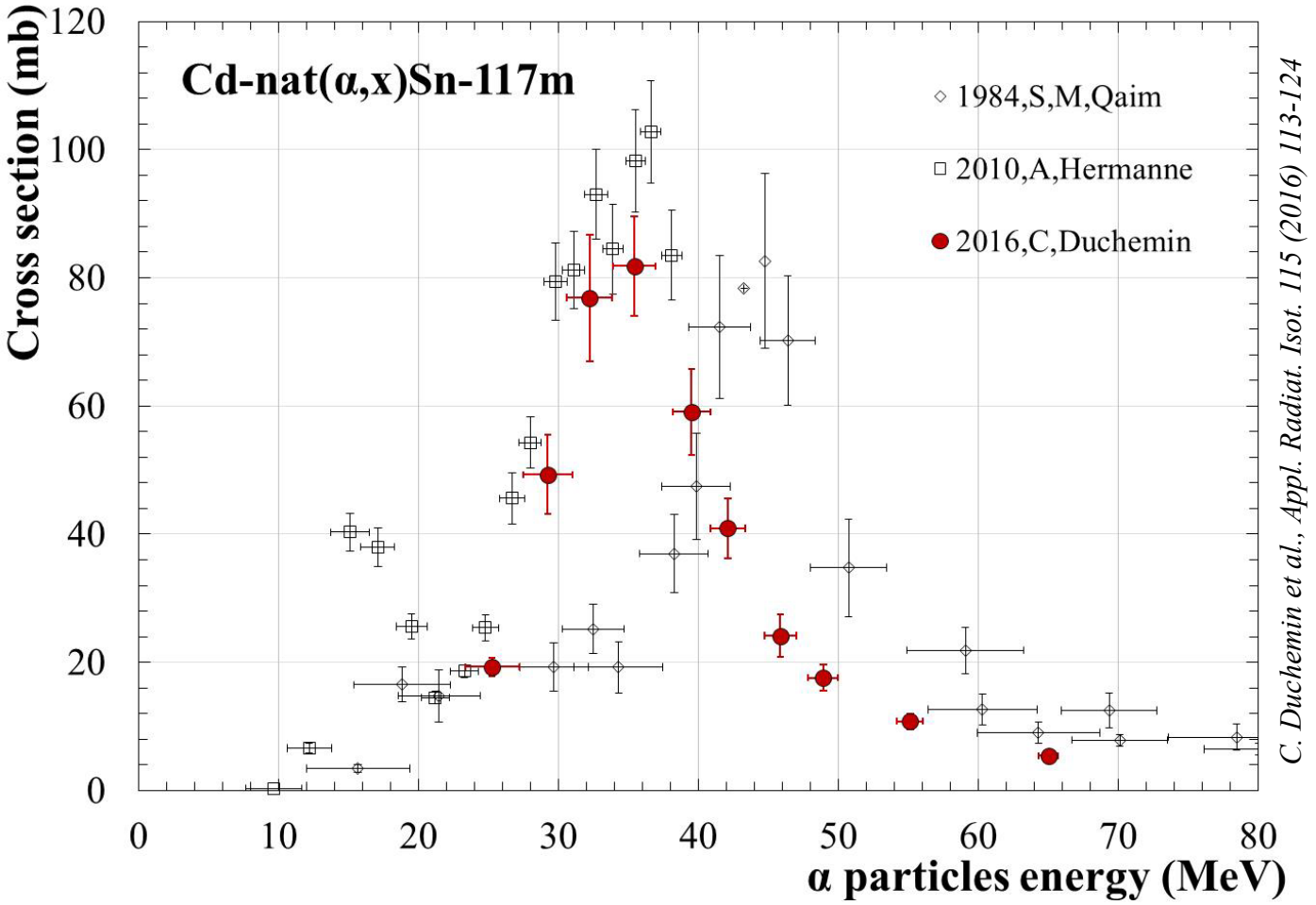
^{117m}Sn for therapy and imaging

Conversion e- emitter $T_{1/2}$ = 13.6 d

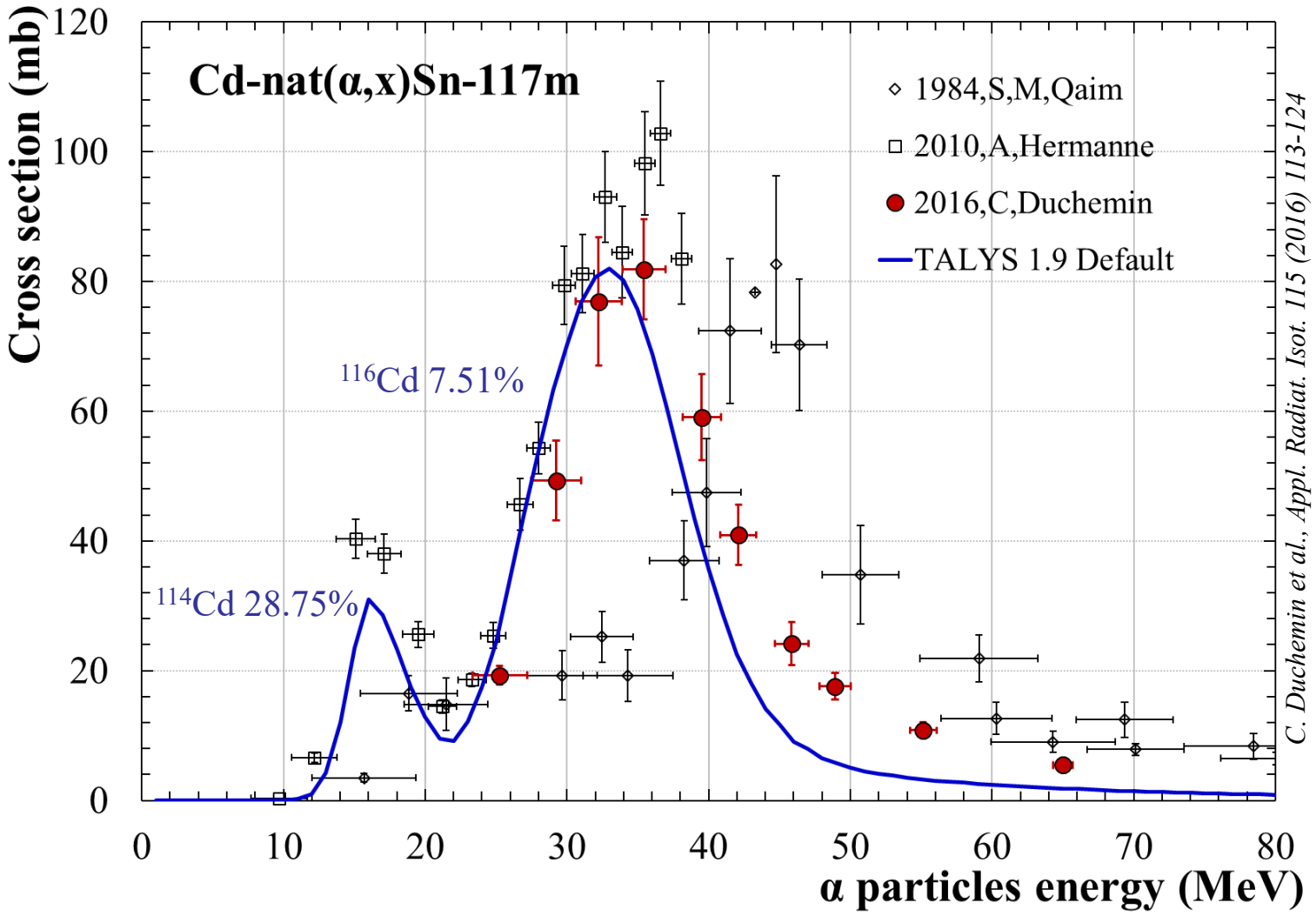
Used for the palliation of painful bone metastases 158 keV γ ray ideal for SPECT

Facilitate target manufacturing

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



^{117m}Sn for therapy and imaging



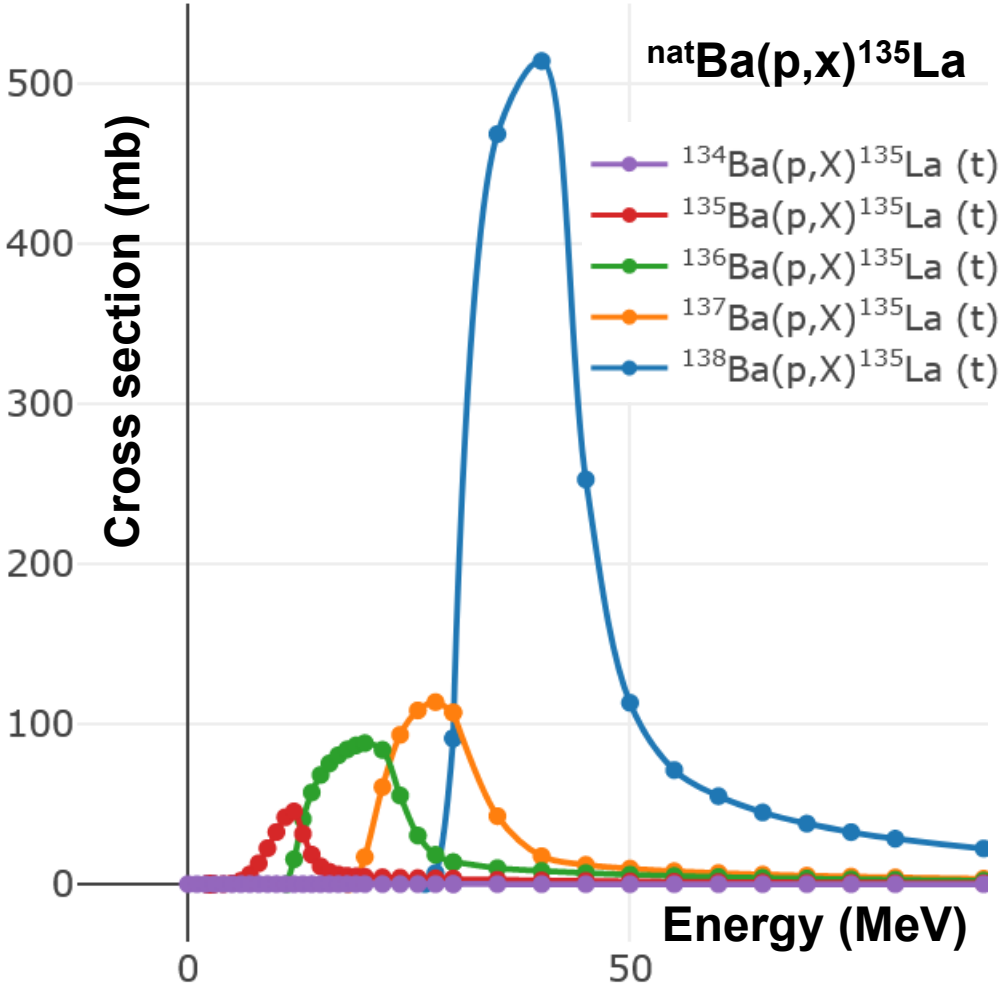
More efficient enriched ^{116}Cd target (alpha,3n) natural abundance 7.512%
Few MBq/µAh

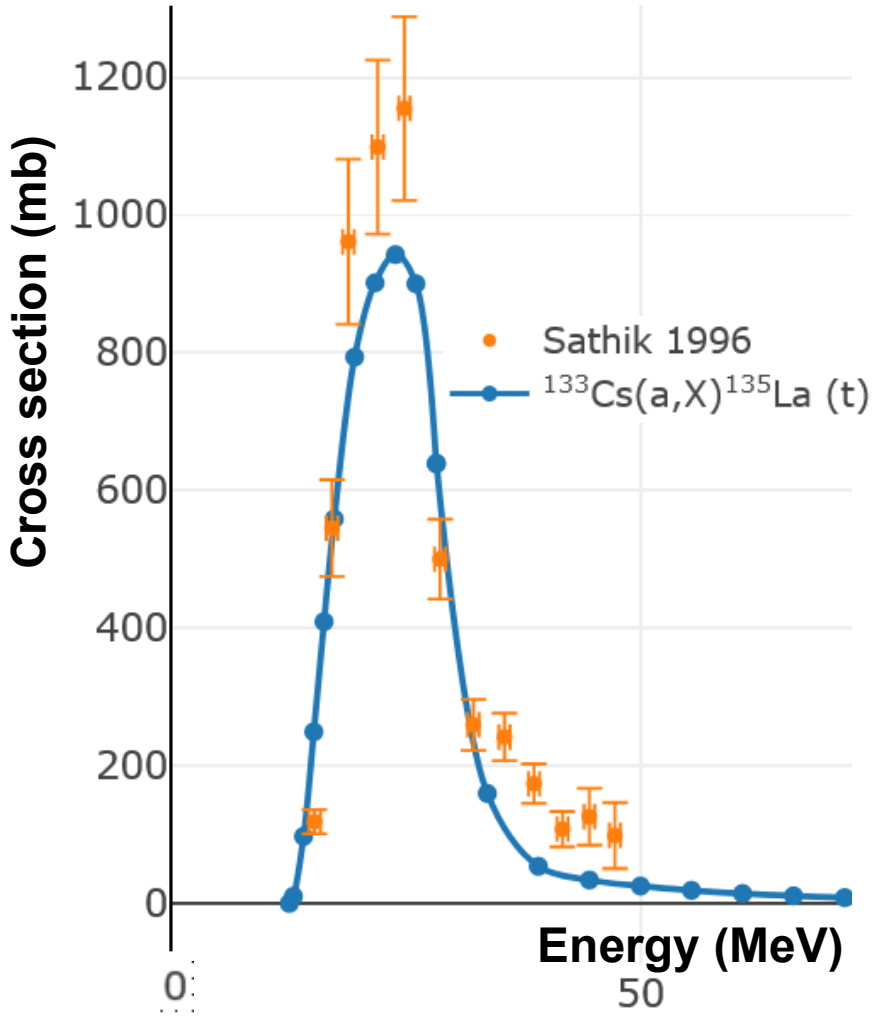
^{135}La for Auger-based targeted therapy

CE 100% Auger electron emitter $T_{1/2}$ = 19.4 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

In Conclusion α beams could help

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

Theme: Applications – Nuclear medicine

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], Nigron E.[2], Sounalet T.[1]
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