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**IN2P3**

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

## **Clean Production of $^{67}\text{Cu}$ using the $^{70}\text{Zn}(d,x)^{67}\text{Cu}$ Reaction Routes**

**A. Guertin, Nigron E., Sounalet T., Haddad F., Michel N., Métivier V., Servagent N.**

## 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

- Diagnosis ( $\gamma$ ,  $\beta^+$ )
- Therapy ( $\beta^-$ ,  $\alpha$ ,  $e_{\text{Auger}}$ )

## 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 data needs** addressed by successive:

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

## 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

## A large set of radioisotopes with very different characteristics is suitable:

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

## The nuclear physicist could have crucial contribution:

- Identify production route and define production process (spallation, fission or activation)
- Identify and quantify contaminants
- Produce the purest product
- Define waste management process
- Discuss with physicians to promote its use

## Over the last years, several radionuclides have emerged:

- $\beta^+$ : Cu-64, Ga-68, Zr-89 ...
- $\beta^-$ : Ho-166, Lu-177 ...
- $\gamma$ : Sn-117m ...
- $\alpha$ : At-211, Bi-212, Bi-213, Ra-223, Ac-225 ...
- **Theranostic**: Sc-44/Sc-47, Cu-64/Cu-67, Ga-68/Lu-177 ...
- **Auger**: Sn-117m, Tb-155
- Terbium quadruplet: Tb-149  $\alpha$ , 152 PET, 155 SPECT/Auger, 161  $\beta^-$

**To do so, we possess facility (will possess) available for irradiations equipped with experimental techniques**

# Experimental facility

Since 2010 Subatech & ARRONAX launched a program on production of innovative radionuclides



## C70 Cyclotron build by IBA:

- 4 sectors isochron cyclotron
- 2 multi-particle sources:
  - H<sup>-</sup>, D<sup>-</sup>: multicusp
  - He<sup>2+</sup>, HH<sup>+</sup>: supernanogan ECR
- 2 extraction lines:
  - stripper or electrostatic deflector

| Extracted        | Energy (MeV) | Max. current (μA) |
|------------------|--------------|-------------------|
| H <sup>+</sup>   | 30 – 70      | 2 x 375           |
| D <sup>+</sup>   | 15 – 35      | 2 x 50            |
| He <sup>2+</sup> | 68           | 70                |
| HH <sup>+</sup>  | 17           | 50                |

## Proton induced reactions:

Ac-225 from Th-232(p,x)

Ra-223 from Th-232(p,x)

C. Duchemin et al, Phys Med Biol **60** (2015) **931-946**

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)

Ga-67 from (p,2n), Ga-66 from (p,3n)

Cu-67 and Cu-64 from Zn-70(p,x)

Ga-67, Ga-66, Zn-65 and Zn-69m

G. Pupillo et al., Nucl Instr Meth Phys Res B 415 (2018)

**41-47**

G. Pupillo et al., Proceedings of the 15th International Conference on Nuclear Reaction Mechanisms **341**

Tb-149 from Gd-nat(p,x)

Tb-150,151,152,153,154,154m2,155,156

R. Formento Cavaier, PhD thesis (2019)

Monitor reactions on Ti, Ni and Cu

E. Garrido et al., Nucl Instr Meth Phys Res B **383** (2016) **191-212**

Sc-47,44mSc,44Sc from V-nat(p,x)

Sc-48,46,43, K43,42, V-48, Cr-51,49,48

G. Pupillo et al., Il Nuovo Cimnto **42 C** (2019) 139

Sc-47,44mSc,44Sc from Ti-48(p,x)

G. Pupillo et al., J Radioanal Nucl Chem (2019) **322**: 1711

## Alpha induced reactions:

**Mo-99** New data set from Zr-96( $\alpha$ ,n)

G. Pupillo et al., J. Radioanal. Nucl. Chem. **302** (2014), 2, **911-917**

**Sn-117m** New data set from Cd-116( $\alpha$ ,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( $\alpha$ ,x)

M. Sitarz et al, Instruments 2019, **3**, 7

## 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**

Re-186g New data set for W-186(d,x)

C. Duchemin et al, Appl Radiat Isot **97** (2015) **52-58**

Th-226 New data set for Th-232(d,x)

**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

Cu-67 New data set for Zn-70(d,x)

E. Nigron, PhD thesis 2019

## Properties

- Half-life to match the **bio-distribution** time: 61.8 hours
- Chemical properties to attach to the **vector molecule**:  
Copper as a well known chemistry
- **Radiation types, energies and intensities** suitable for applications:  
SPECT, vectorized internal radiation therapy, theranostic pair  $^{64}\text{Cu}/^{67}\text{Cu}$

| $\langle E_{\beta} \rangle$<br>(keV) | $E_{\beta\text{max}}$<br>(keV) | $I_{\beta}$ (%) |
|--------------------------------------|--------------------------------|-----------------|
| 121                                  | 377                            | 57              |
| 154                                  | 468                            | 22              |
| 189                                  | 562                            | 20              |

| $E_{\gamma}$<br>(keV) | $I_{\gamma}$ (%) |
|-----------------------|------------------|
| 91.3                  | 7.0              |
| 93.3                  | 16.1             |
| 184.6                 | 48.7             |

## Production routes

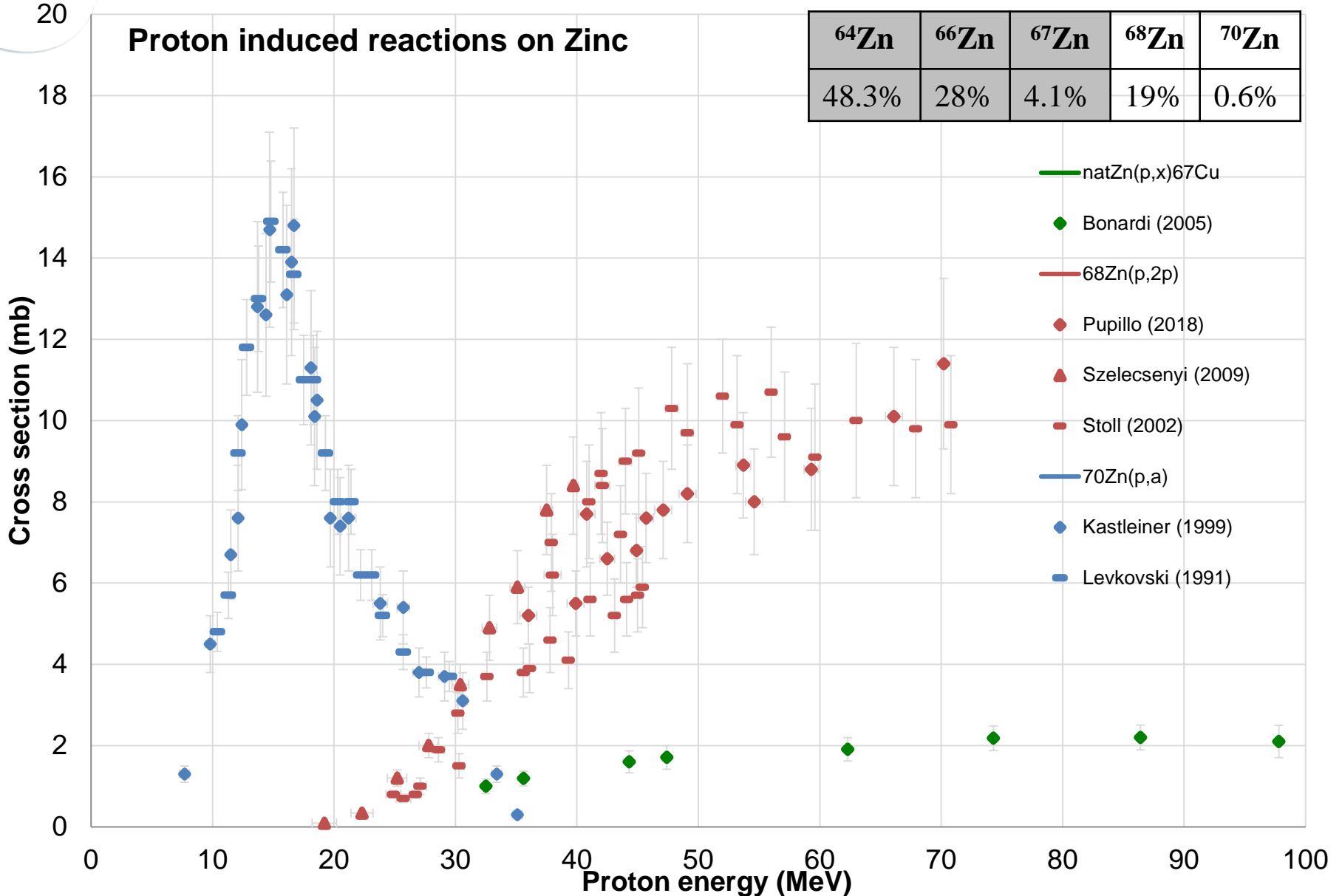
Balance between :

- Cross section
- Impurities coproduction : specific activity
  - Copper isotopes
  - Half lives
- Target manufacturing and chemistry

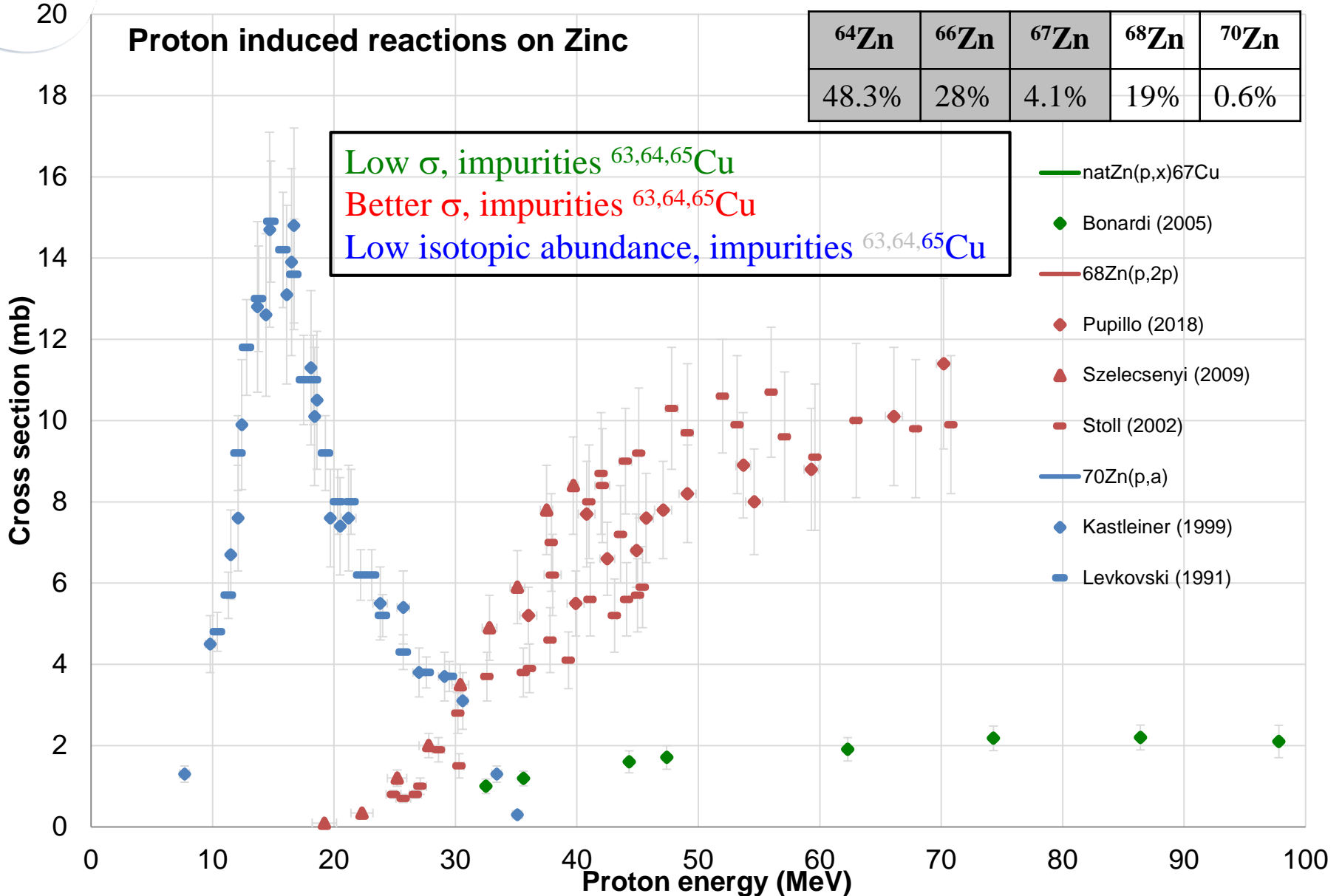
| 60      | 61     | 62     | 63     | 64     | 65     |
|---------|--------|--------|--------|--------|--------|
| 23.7 mn | 3.3 h  | 9.7 mn | Stable | 12.7 h | Stable |
| 66      | 67     | 68     | 68m    | 69     |        |
| 5.1 mn  | 61.8 h | 30.9 s | 3.7 mn | 2.9 mn |        |



# Proton induced reactions

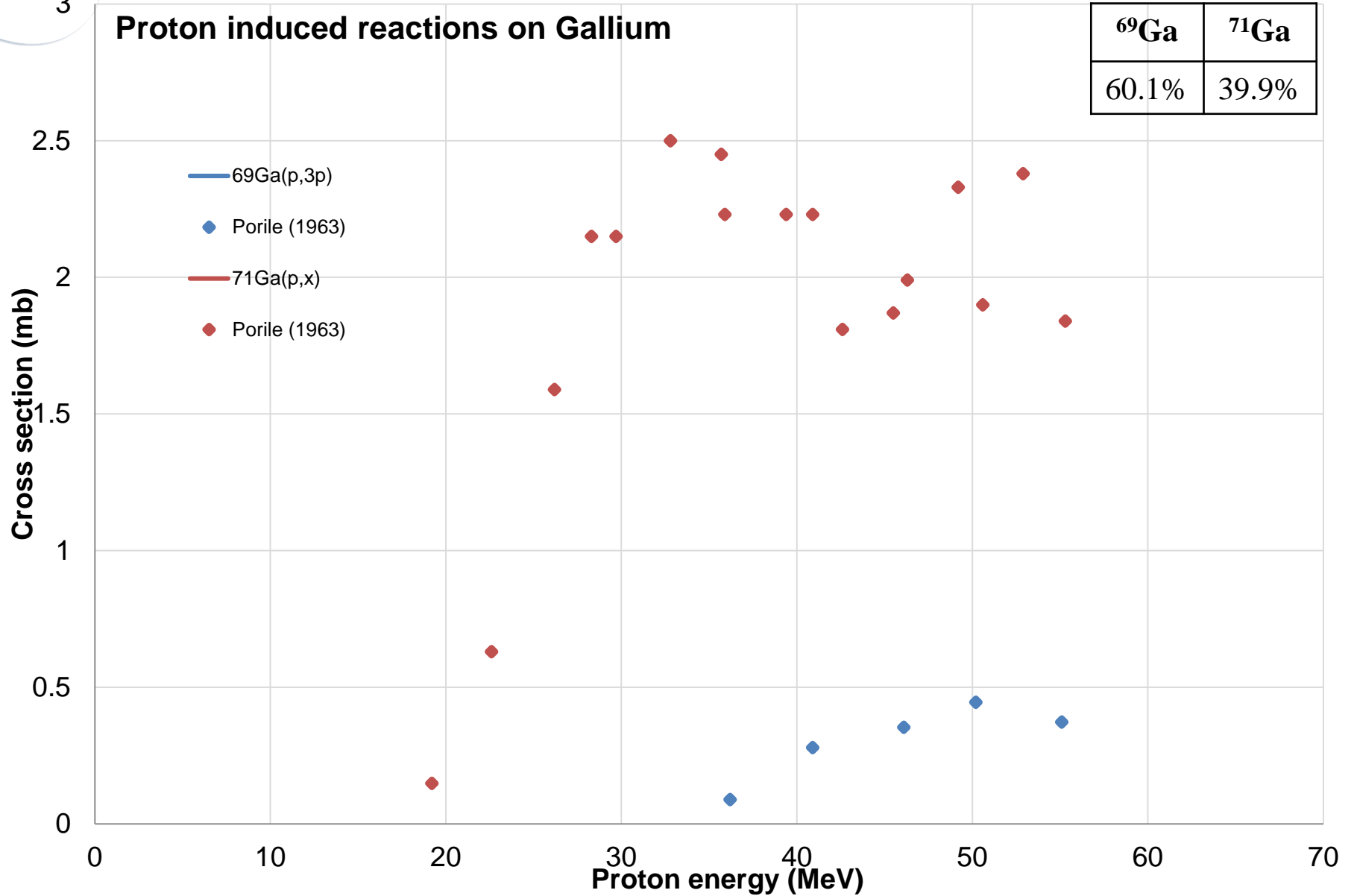


# Proton induced reactions



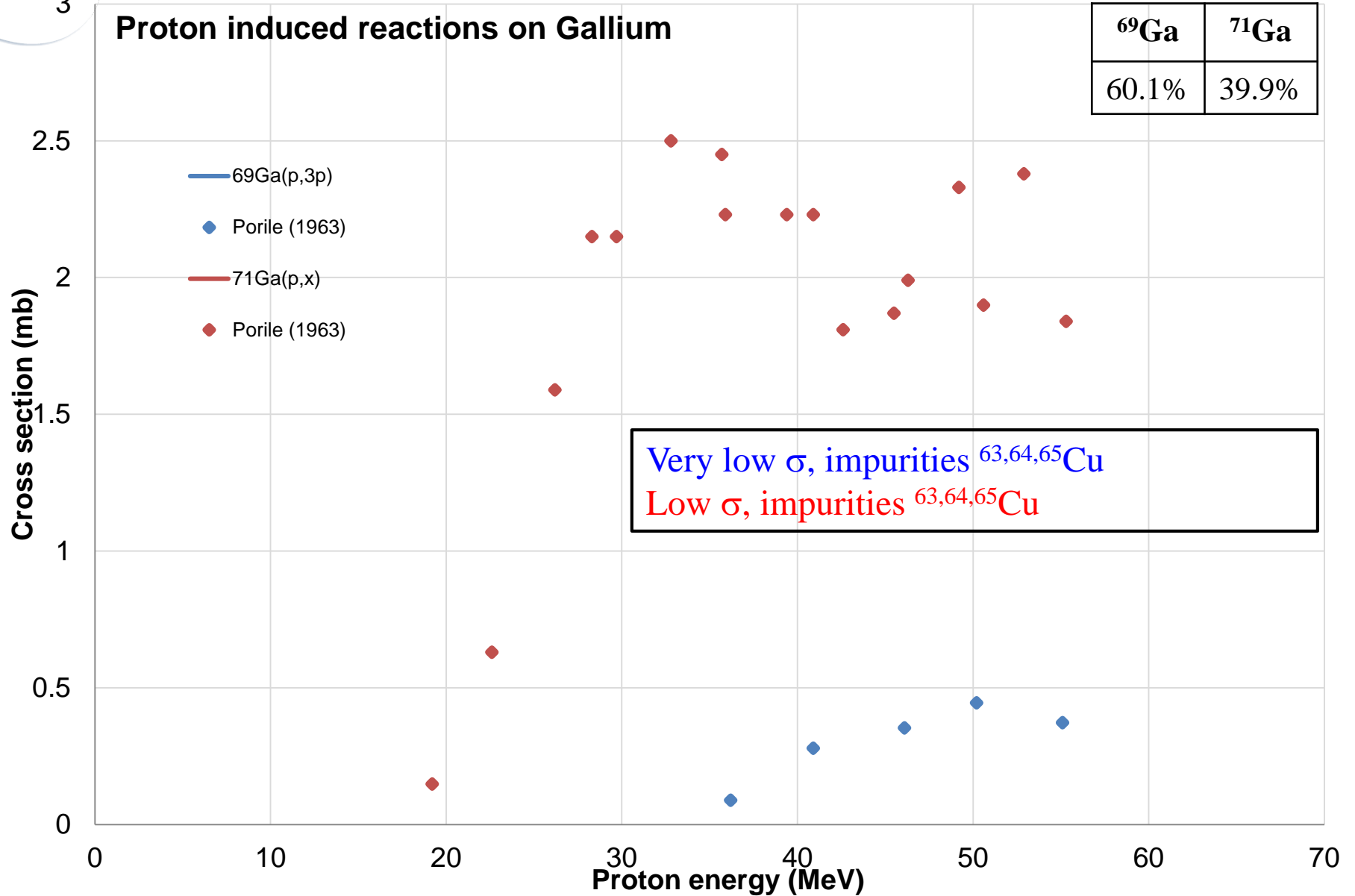
# Proton induced reactions

3

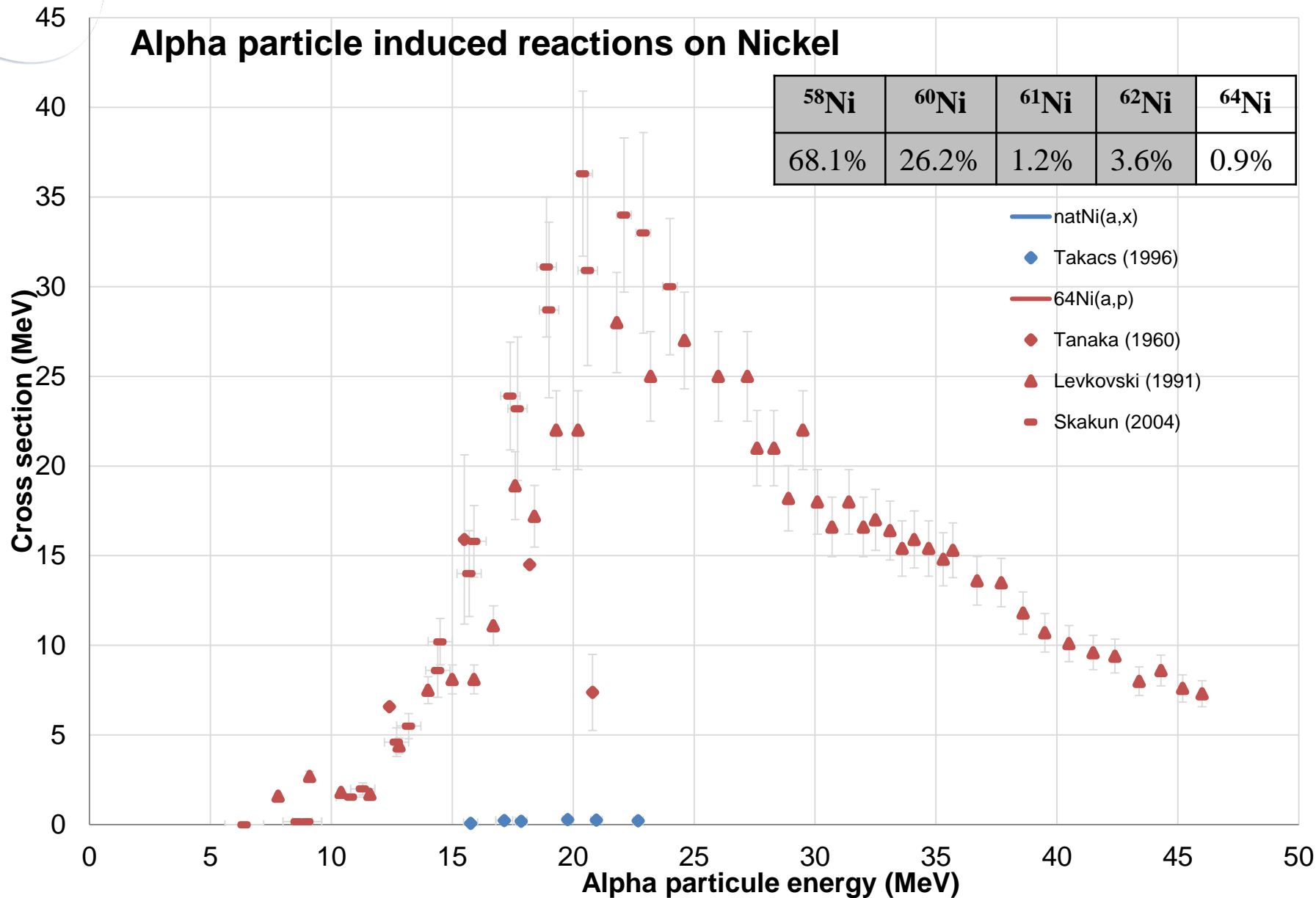


# Proton induced reactions

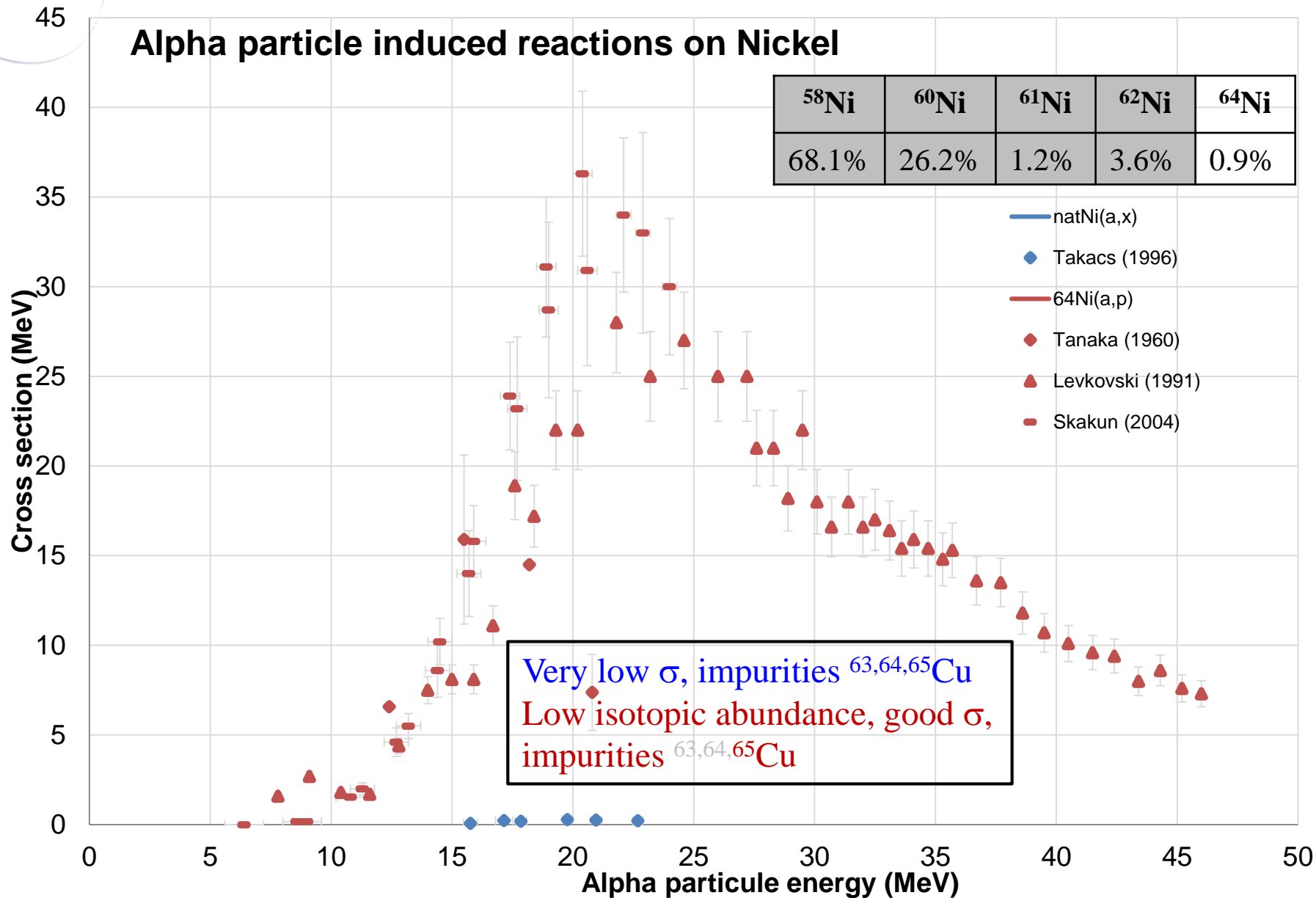
3



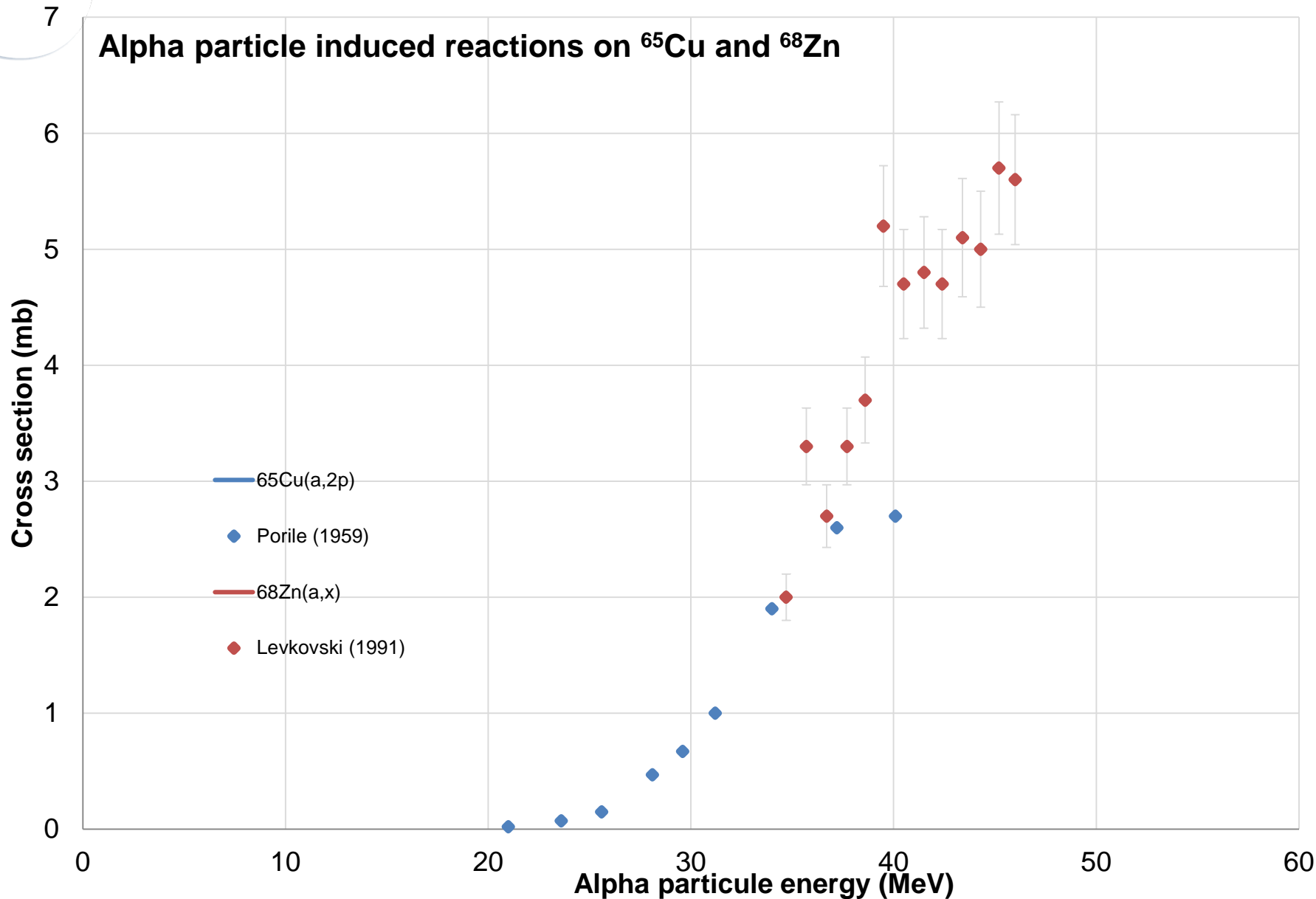
# Alpha particle induced reaction



# Alpha particle induced reaction



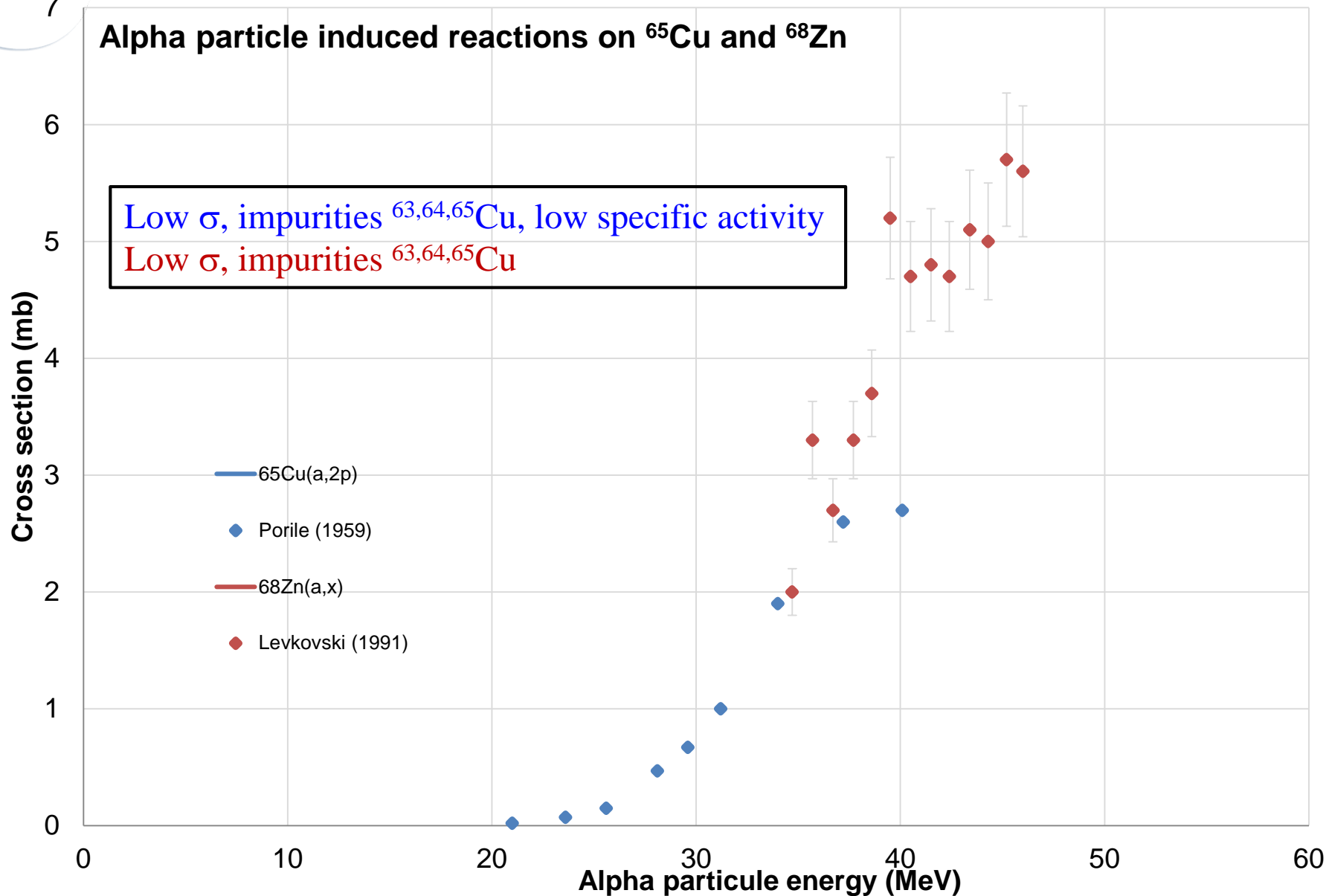
# Alpha particle induced reaction



# Alpha particle induced reaction

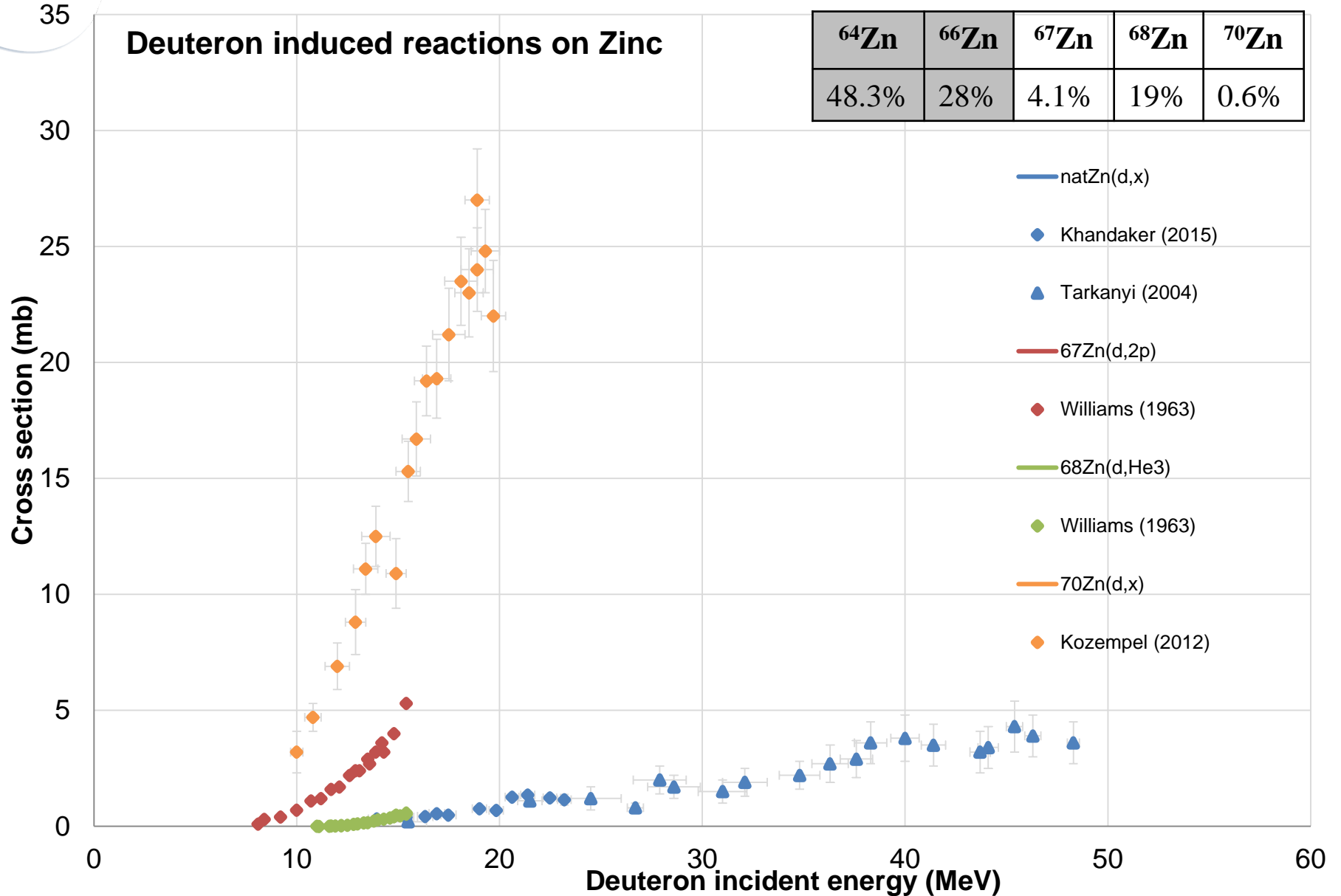
7

## Alpha particle induced reactions on $^{65}\text{Cu}$ and $^{68}\text{Zn}$

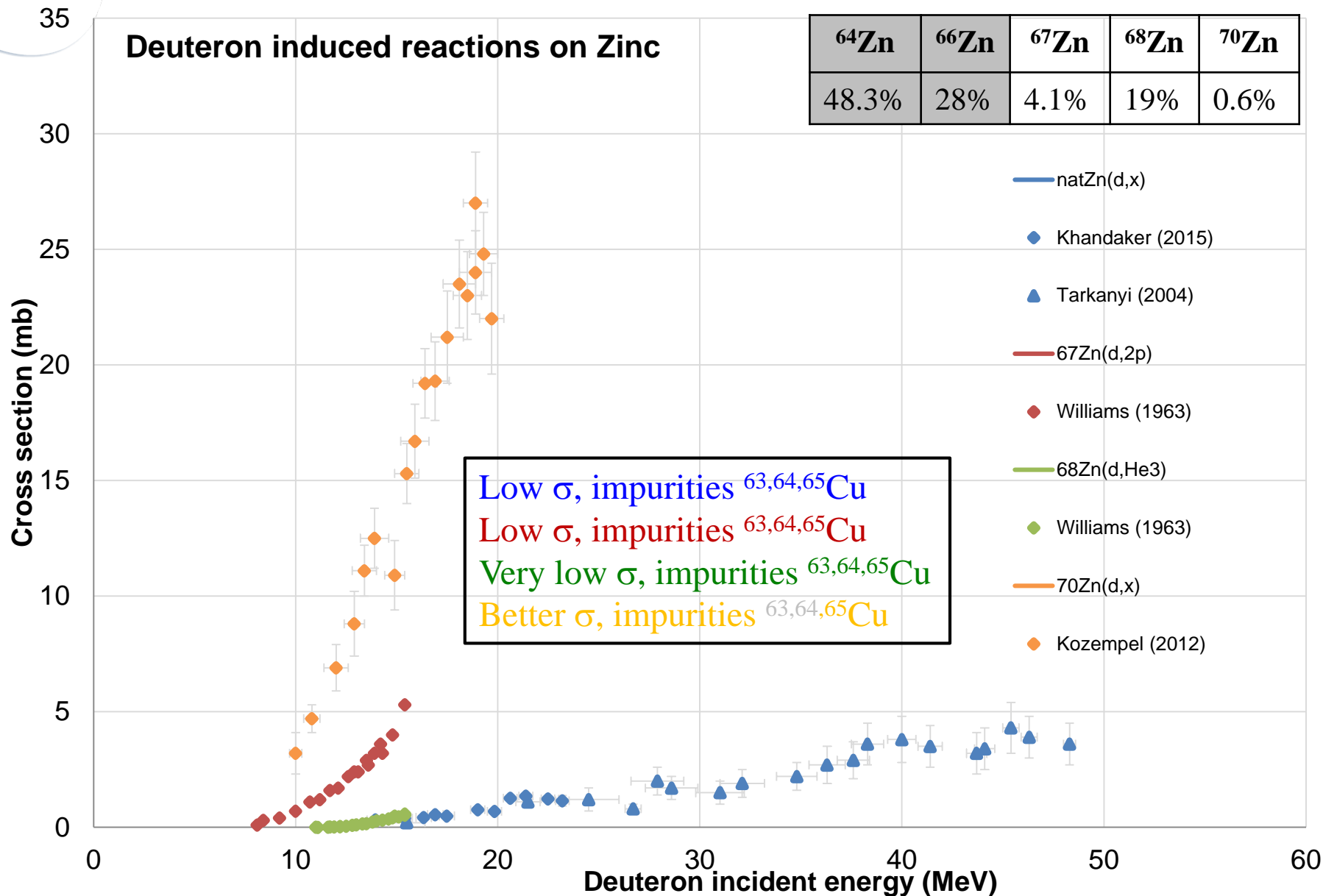




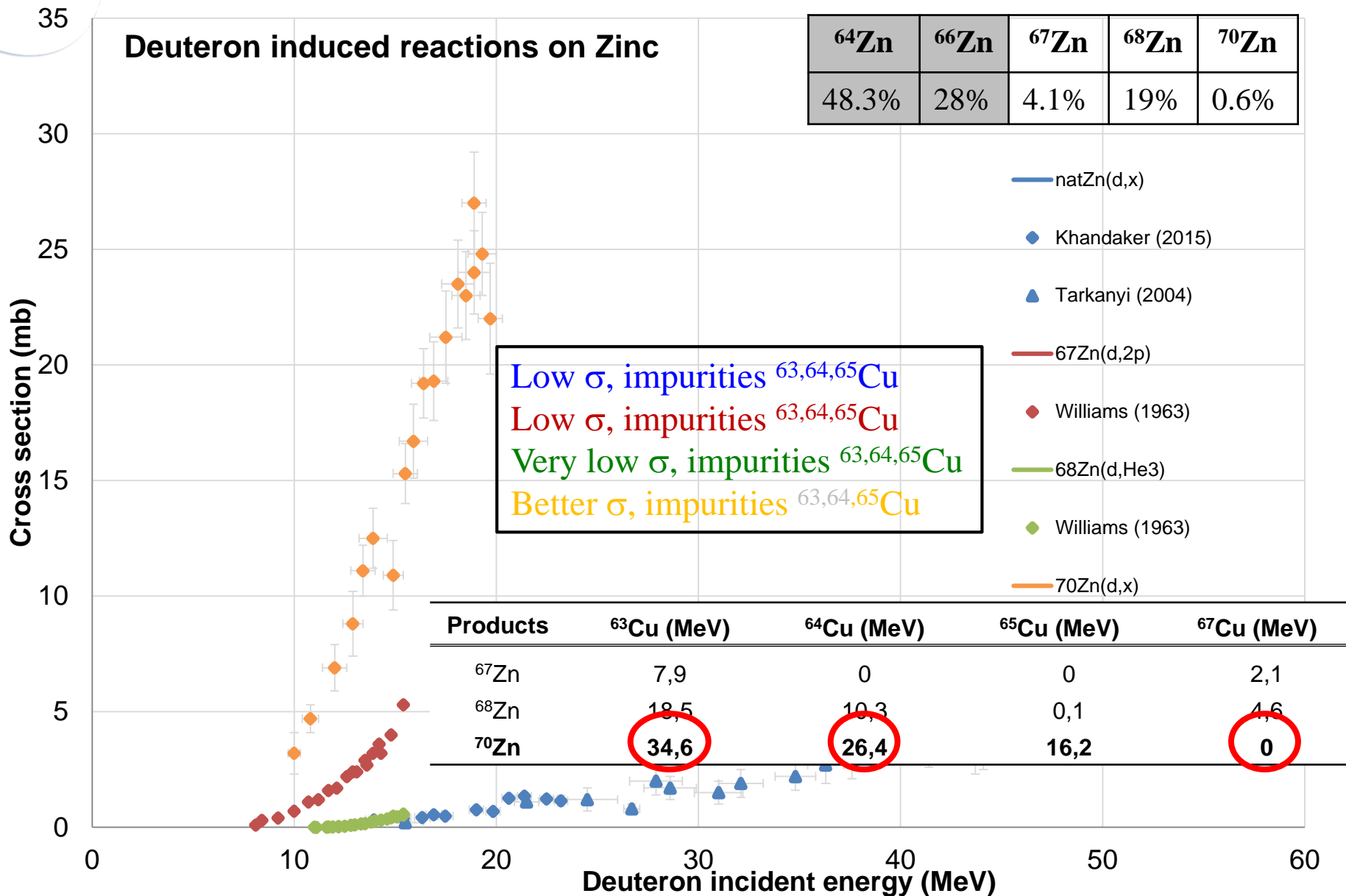
# Deuteron induced reaction



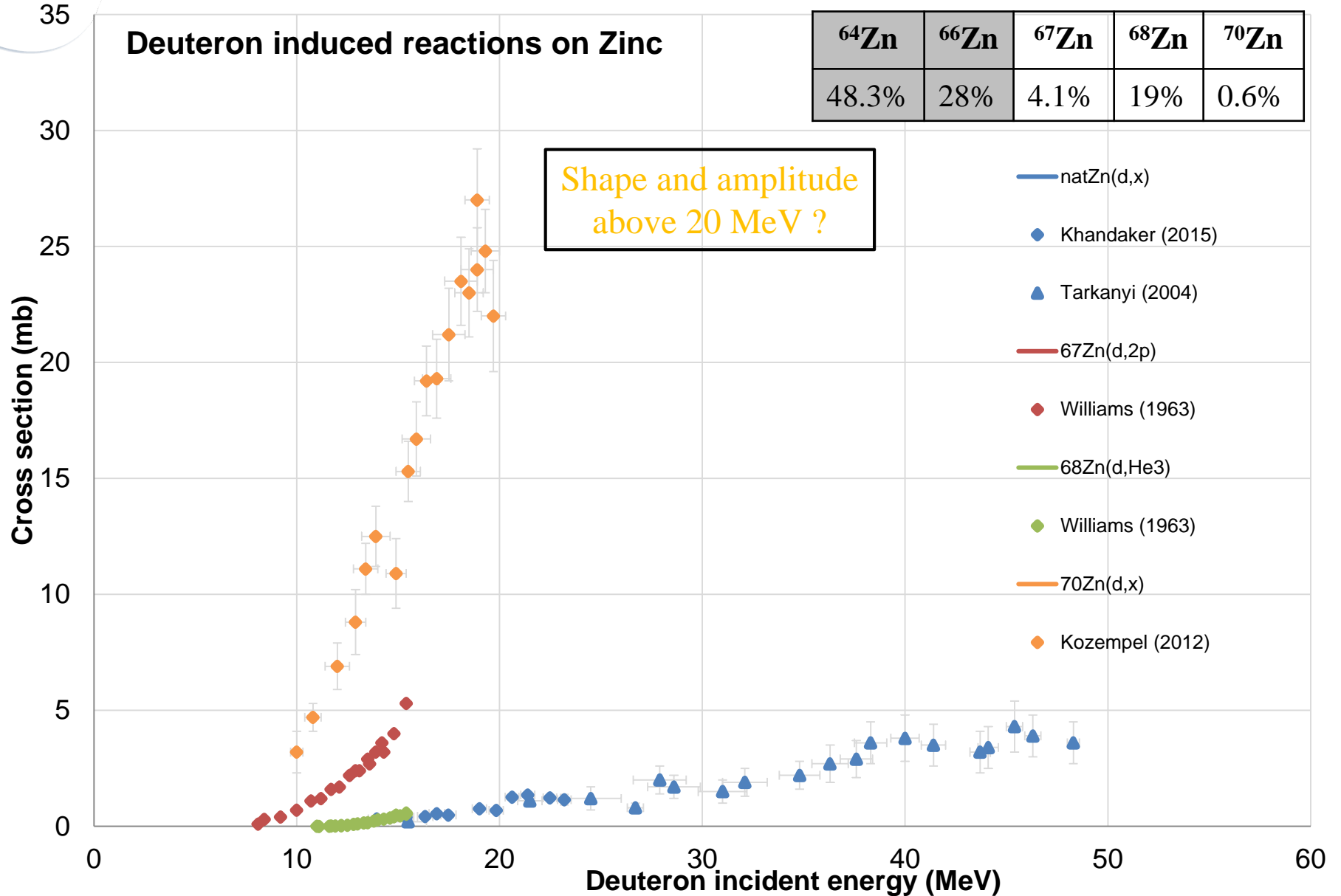
# Deuteron induced reaction



# Deuteron induced reaction



# Deuteron induced reaction

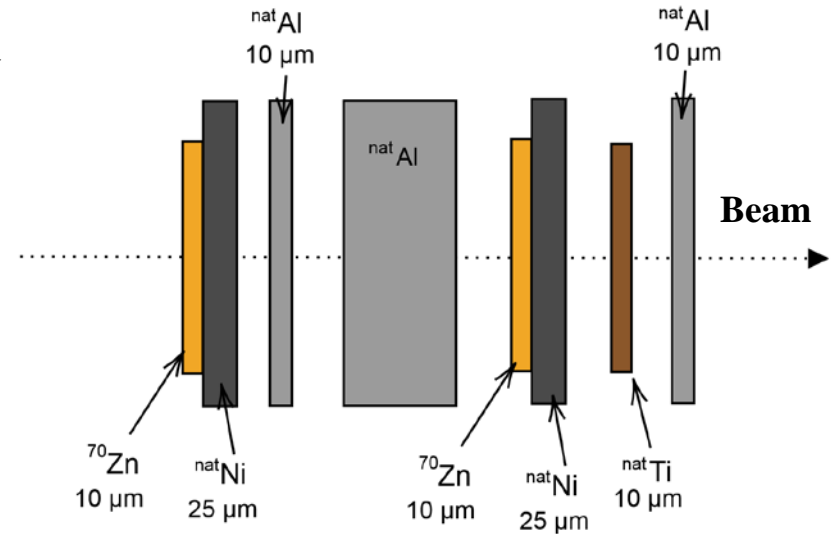


# Target preparation & experiments

Electrodeposition of  $^{70}\text{Zn}$  from ISOFLUX company on a  $^{\text{nat}}\text{Ni}$  sheet @ GIP ARRONAX by T. Sounalet, PRISMA team

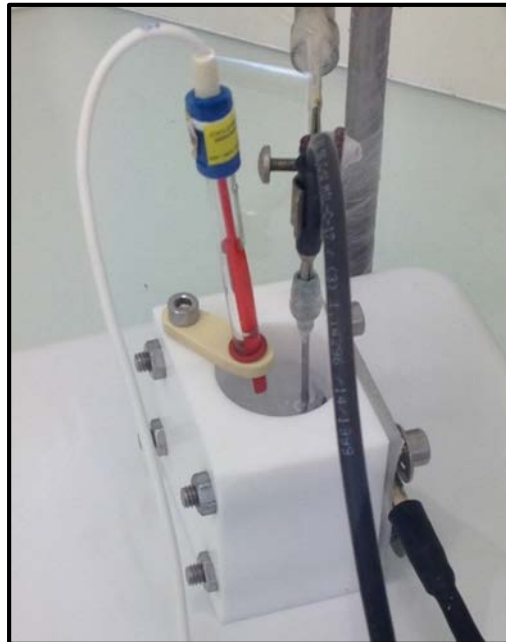
Surface: 20x20 mm Thickness: approx. 10  $\mu\text{m}$

| $^{64}\text{Zn}$ | $^{66}\text{Zn}$ | $^{67}\text{Zn}$ | $^{68}\text{Zn}$ | $^{70}\text{Zn}$ |
|------------------|------------------|------------------|------------------|------------------|
| 48.3%            | 28%              | 4.1%             | 19%              | 0.6%             |
| 0.1%             | 0.1%             | 0.1%             | 2.2%             | 97.5%            |

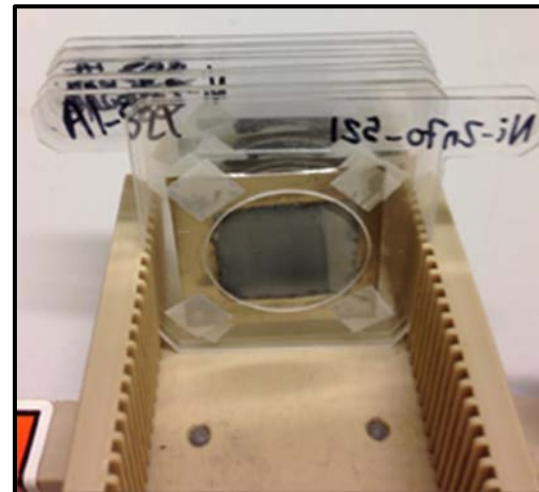


**Stack**

- 6 irradiations of 2 patterns
- under vacuum
- Faraday cup used for flux measurements
- 12 cross section values



**Electrodeposition setup**



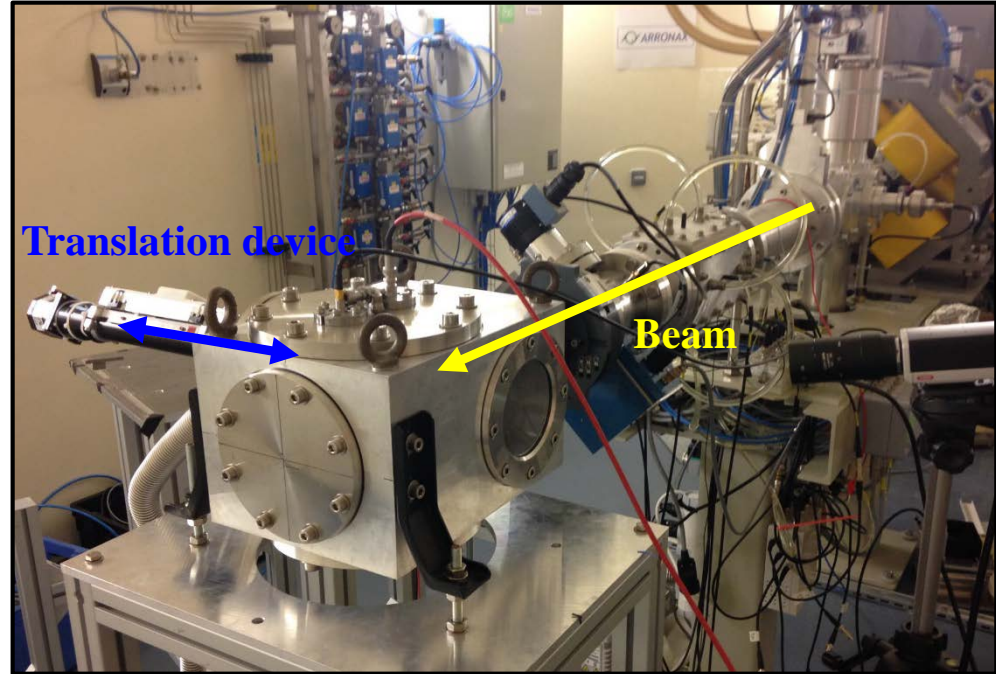
# Stacked foils under vacuum

## Activity and cross section:

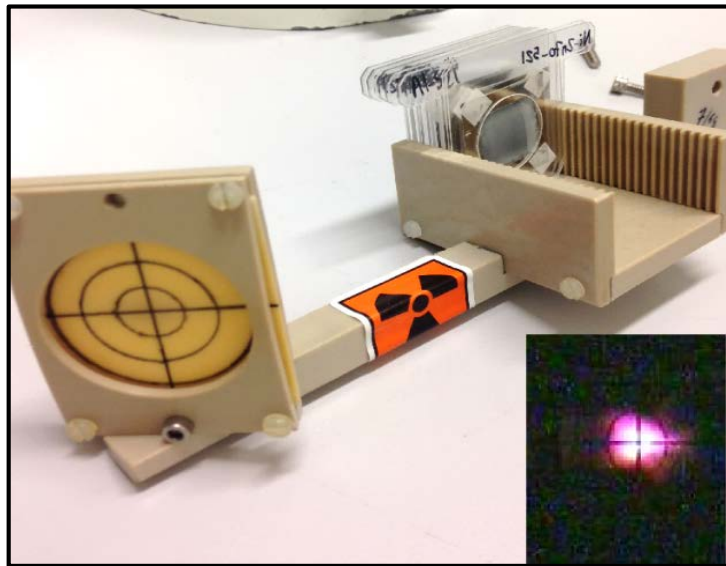
$$\sigma = \frac{\text{Act} \cdot A}{\chi \cdot \Phi \cdot \mathcal{N}_A \cdot \rho \cdot e \cdot (1 - e^{-\lambda \cdot t})}$$

## Use of a Faraday cup:

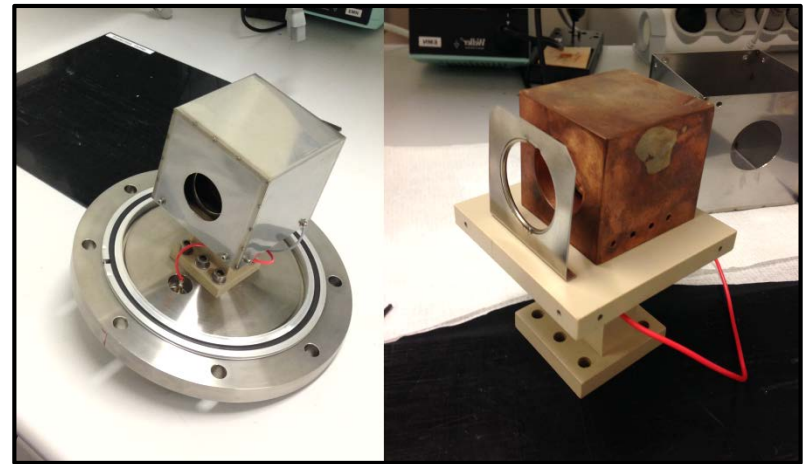
- Placed at the end of the stack to measure the intensity during the irradiation



Irradiation station and beam line

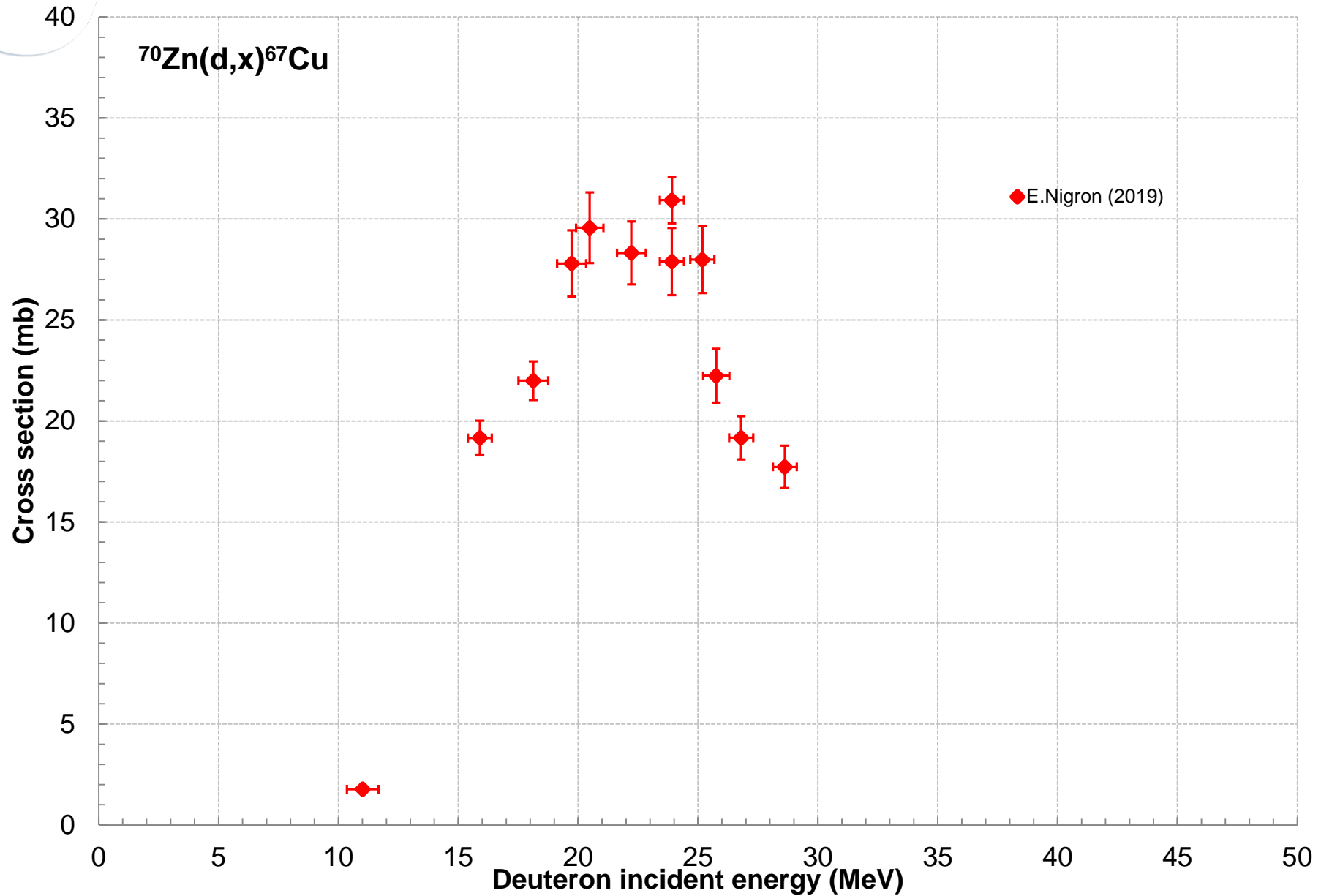


Translation device : stack, empty,  $\text{Al}_2\text{O}_3$

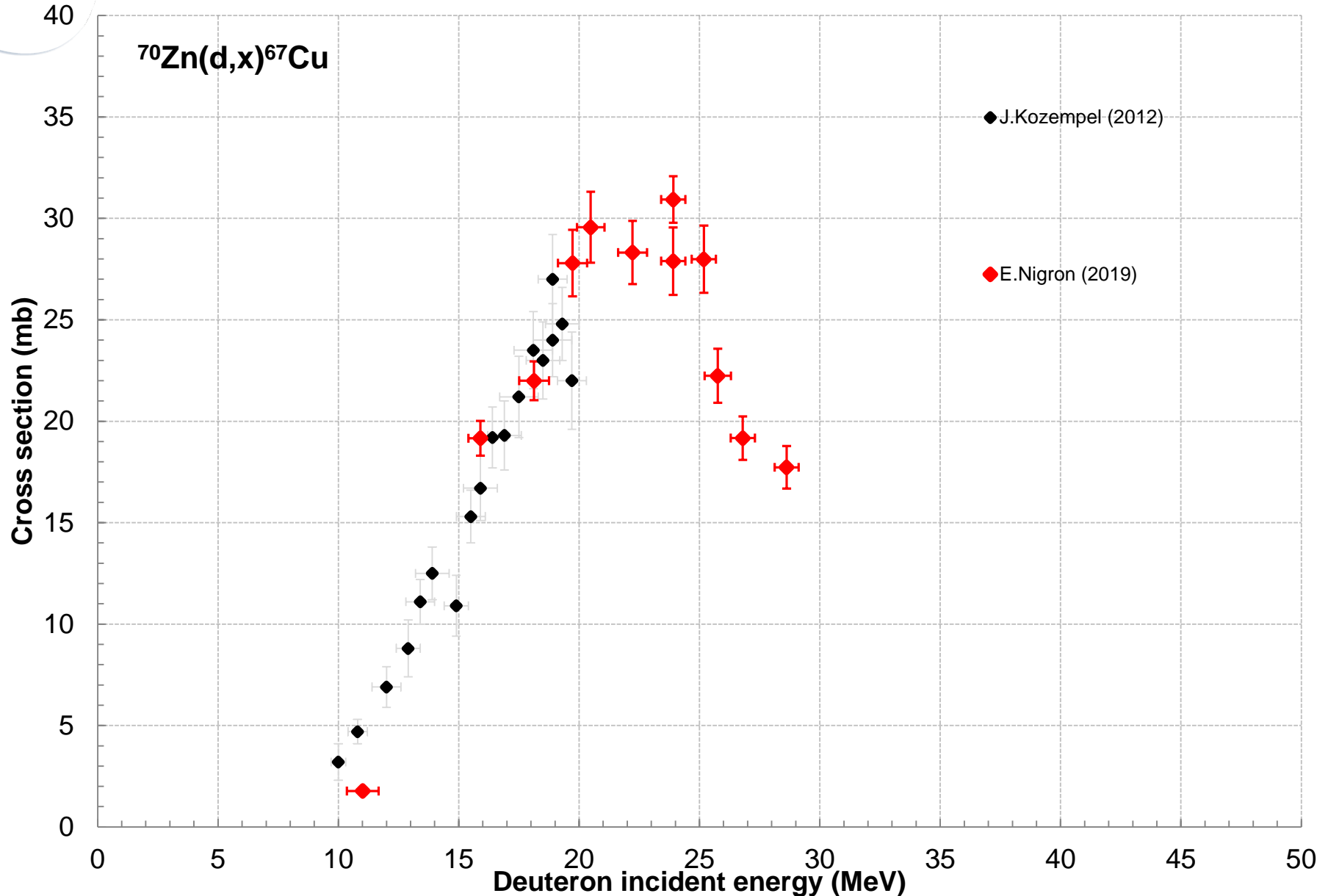


Faraday Cup

# $^{67}\text{Cu}$ production cross section

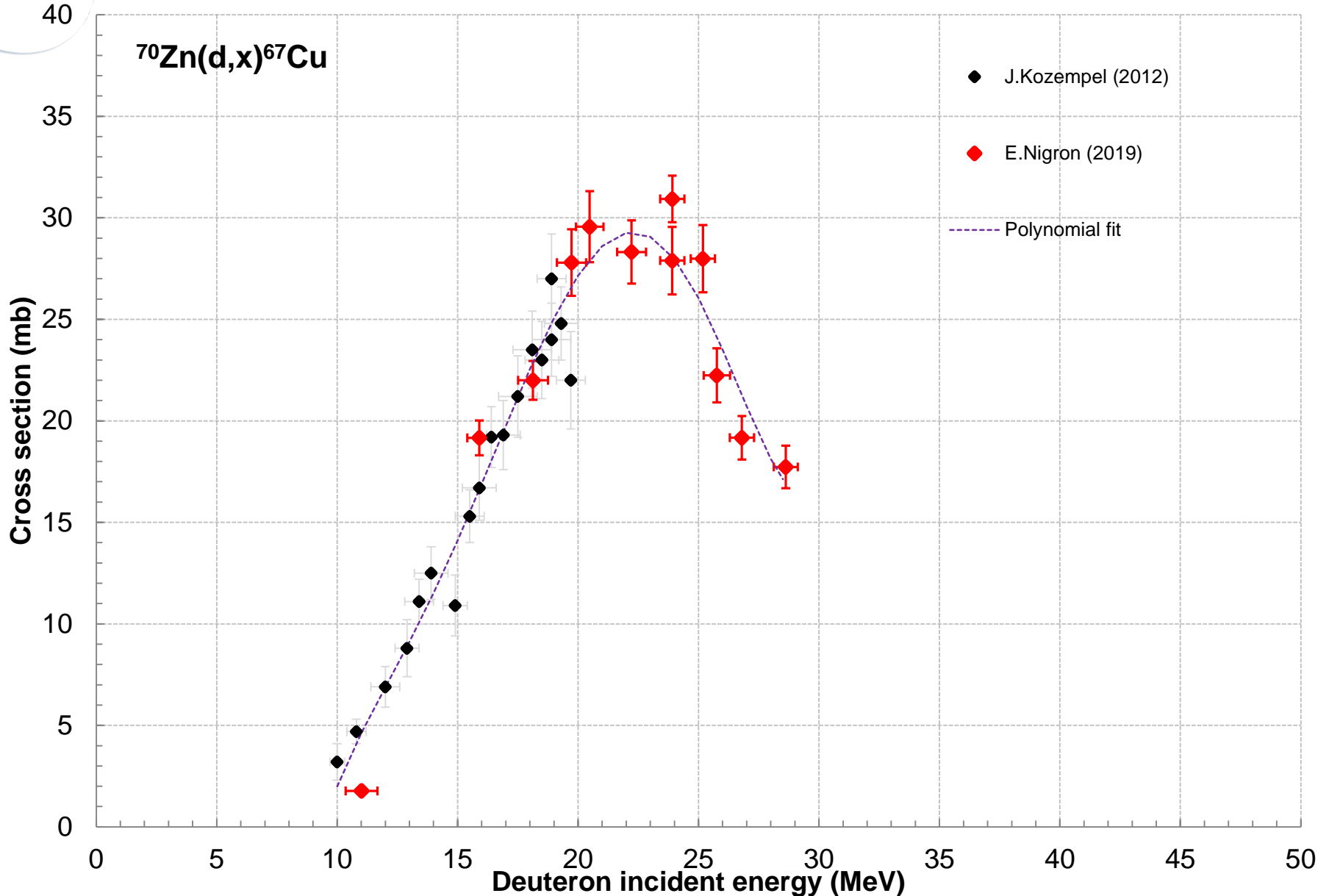


# Comparison with existing data



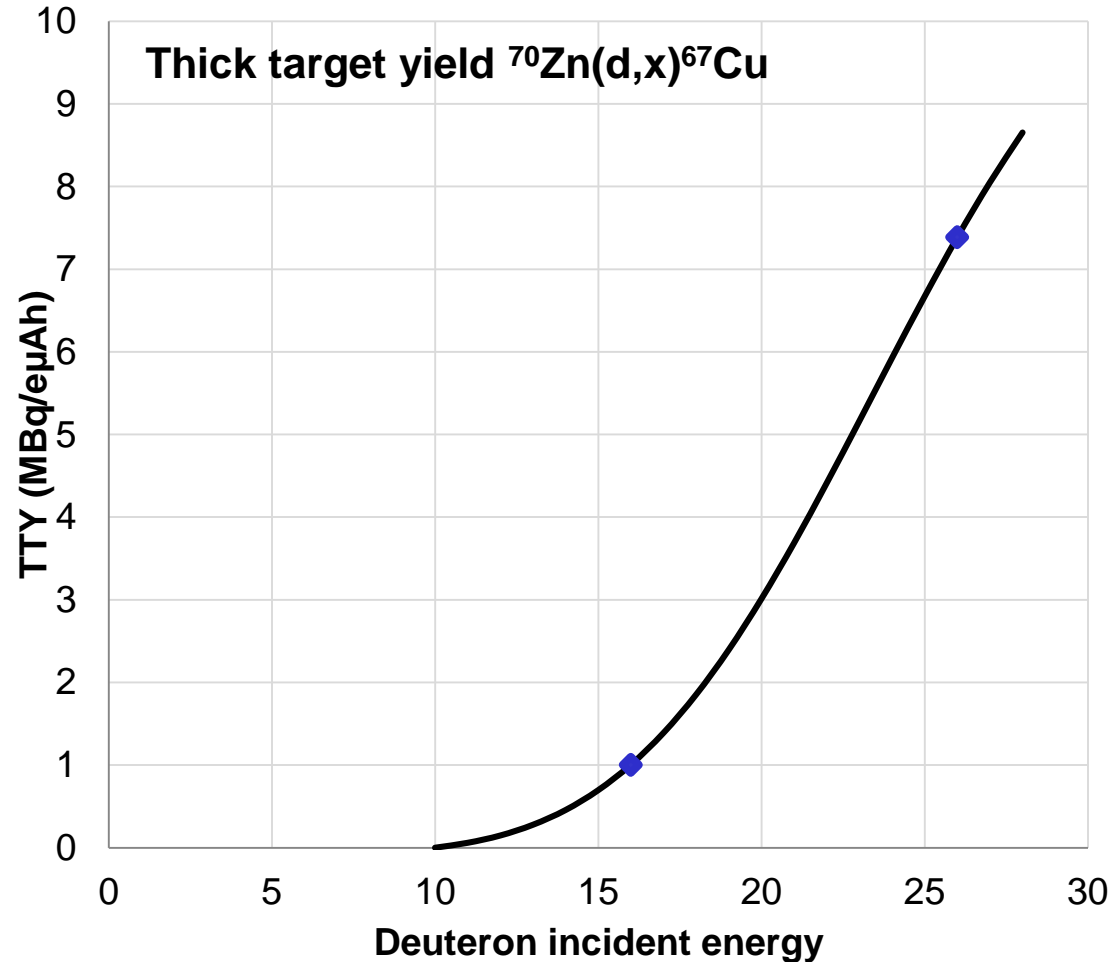


# Thick Target Yield



# Thick Target Yield

To optimise production, the energy range from 16 to 26 MeV is chosen, corresponding to a thickness of 575  $\mu\text{m}$  of  $^{70}\text{Zn}$



For:

- A beam intensity of 1  $\mu\text{A}$
- 97.5% target purity
- One hour of irradiation
- TTY = **6.2 MBq EOB**

Irradiation scenario C70:

- A beam intensity of 100  $\mu\text{A}$
- 97.5% target purity
- 72 hours of irradiation
- TTY = **30.9 GBq EOB**
- Clinical trials possible

Irradiation scenario SPIRAL2:

- A beam intensity of 5 mA
- 97.5% target purity
- 72 hours of irradiation
- TTY  $\approx$  **1.54 TBq EOB**
- Therapy possible

TTY calculations done with RYC developed @ GIP ARRONAX by M. Sitarz,  
<https://www.arronax-nantes.fr/outil-telechargement/outils-radionuclide-yield-calculator/>

**New data set** for  $^{70}\text{Zn}(d,x)^{67}\text{Cu}$  has been obtained

**Impurities production is limited** for a **better specific activity** of the final product

TTY has been calculated for 3 days of irradiation at 100  $\mu\text{A}$  : clinical trials could be envisaged

## **Nuclear medicine**

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

- Personalized medicine

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

## **Nuclear data**

**A large set of data have been collected** using the stacked-foil technique at ARRONAX

- with different type of projectiles (proton, deuteron and alpha particles)
- for materials all over the mass range
- for diagnosis and therapy purposes in nuclear medicine

To achieve:

- optimum production of specific radionuclides
- minimization or elimination of impurities
- realistic dose calculations

# Session D1: Manufacturing

Thank you for your attention

Acknowledgments to the 10<sup>th</sup> International Conference on Isotopes  
organization committee

**“Clean Production of  $^{67}\text{Cu}$  using the  $^{70}\text{Zn}(d,x)^{67}\text{Cu}$  Reaction Routes”**

**Guertin A.<sup>1\*</sup>, Nigrón E.<sup>1</sup>, Sounalet T.<sup>1</sup>, Haddad F.<sup>1,2</sup>, Michel N.<sup>1,2</sup>, Métivier V.<sup>1</sup>, Servagent N.<sup>1</sup>**

1 SUBATECH, CNRS/IN2P3, IMT Atlantique, Université de Nantes, Nantes, France

2 GIP ARRONAX, 1 rue Aronnax, 44817 Saint-Herblain cedex – France

\* [Arnaud.Guertin@subatech.in2p3.fr](mailto:Arnaud.Guertin@subatech.in2p3.fr)



**Some backup slides**

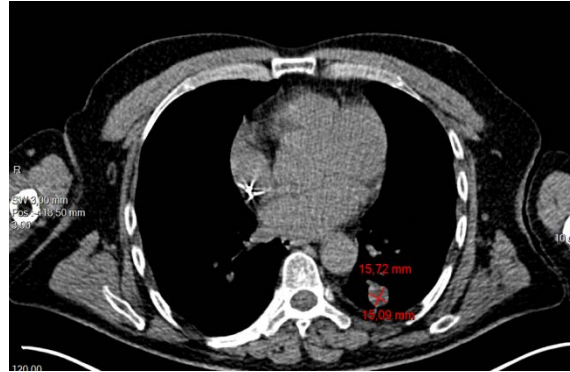
# Conventional imaging in oncology

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



*Centre François Baclesse*

Radiography



*Centre René Gauducheau*

Computerized Tomography  
Scanner



*Institut Roi Albert II*

Magnetic Resonance  
Imaging

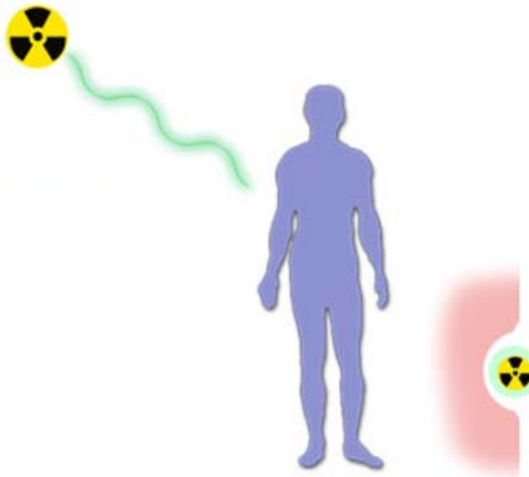
**These techniques allow to get accurate information on the morphology  
but give limited information on the metabolism**

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

# Conventional radiotherapy

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**

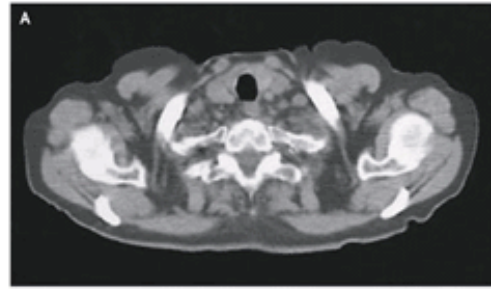
**Limit:** does not target disseminated disease or residual disease

**This can be address by nuclear medicine techniques**

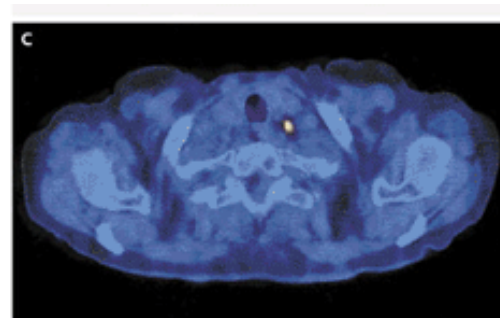
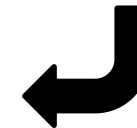
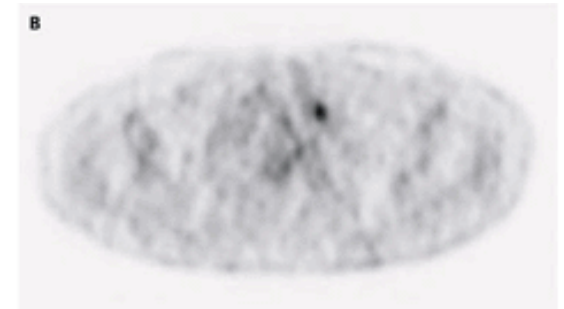
# Great progress in the last ten years

**Multimodality:** SPECT/CT, PET/CT then PET/MR

**Morphology**



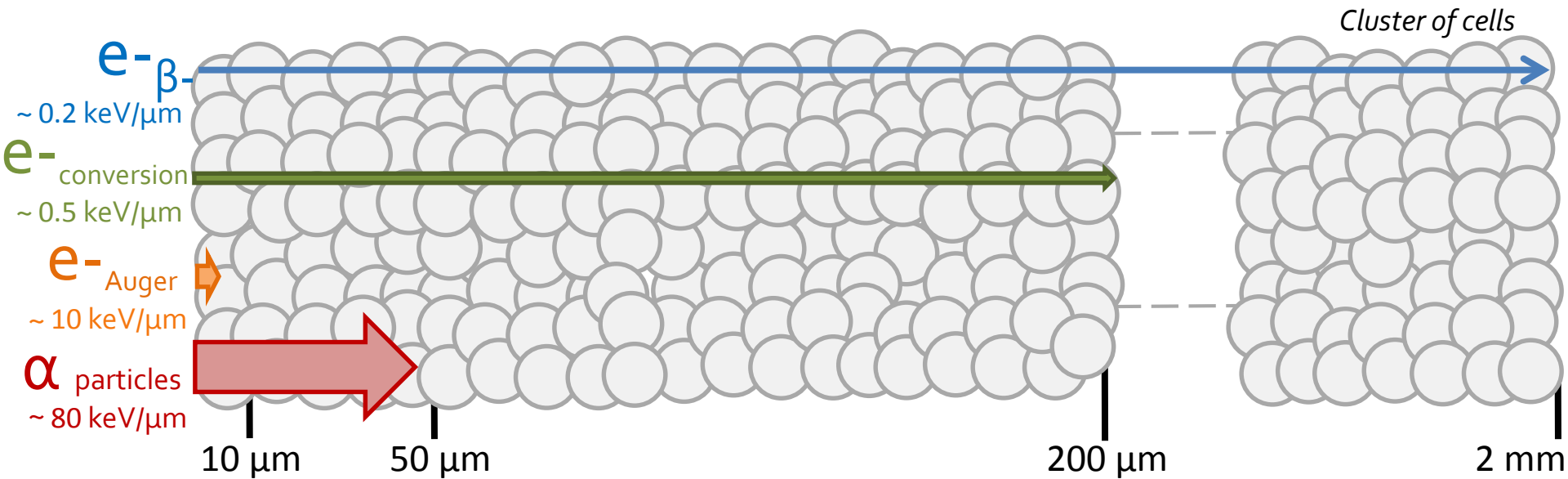
**Metabolism**



**New targets, tracers and radionuclides (béta+, béta-, Auger and alpha)**



# Targeted therapy and LET



From C. Duchemin PhD defense

# A high intensity cyclotron for medical applications



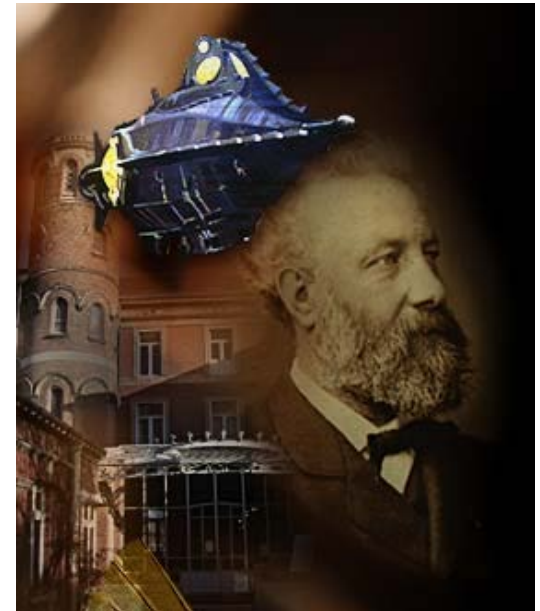
# What is ARRONAX ?

ARRONAX is the acronym for

“Accelerator for **R**esearch in **R**adiochemistry and **O**ncology at **N**antes **A**tlantique”

It is both the name of the accelerator and of the facility (GIP ARRONAX)

The name ARRONAX is a tribute to the famous novel writer **Jules Verne** which was born in Nantes in 1828. **Aronnax** is the name of the Professor in the novel « *Twenty Thousand Leagues Under the Sea: A Tour of the Underwater World* » published in 1870



# What is ARRONAX ?

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Arronax is a “Groupement d'Intérêt Public (GIP)”. It is a mixed economy organization\*

Stakeholders are :

– **Research organizations:**

- Centre national de la recherche scientifique (CNRS)
- Institut national de la santé et de la recherche médicale (Inserm)

– **Health institutions:**

- Nantes University Hospital
- Institut de Cancérologie de l'Ouest (ICO), Saint-Herblain

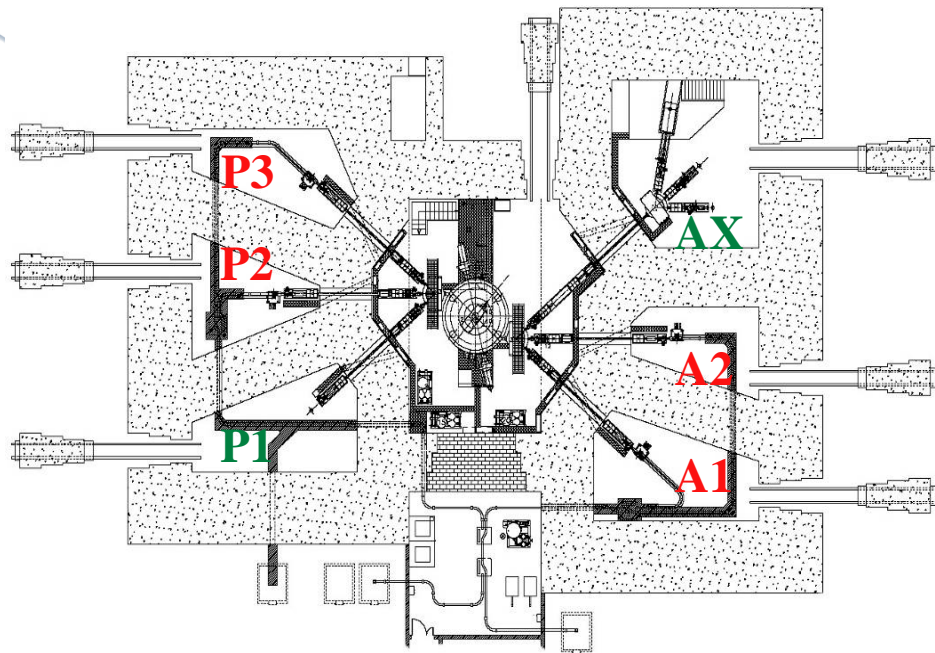
– **Educational institutions:**

- Nantes University
- Mines-Telecom Atlantique

– **Other institutions:**

- The State (Ministère de la Recherche et de l'Enseignement Supérieur)
- Pays de la Loire Regional Council

\*legally a governmental entity allowing personnel procurement by the GIP members runs as a company with a private accounting system and private contracts for additional hired staff members

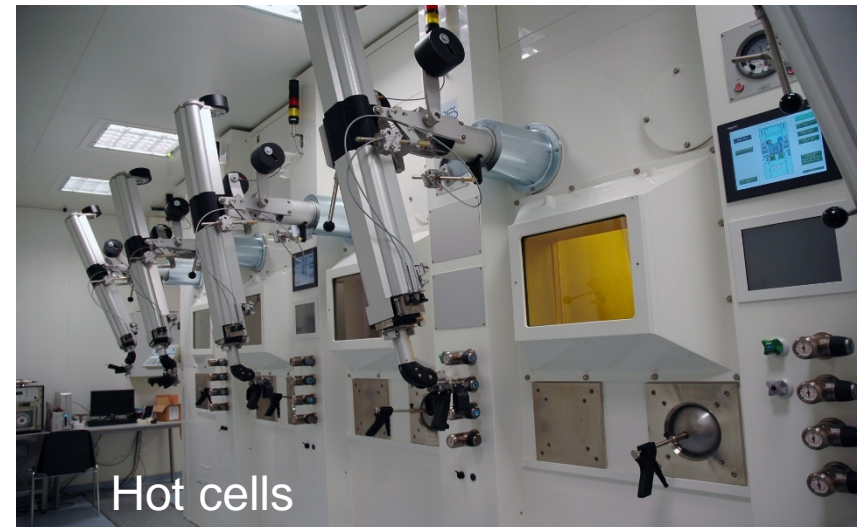


6 experimental vaults

4 vaults connected through a **pneumatic system** to the hot-cells

5 lines of hot cells

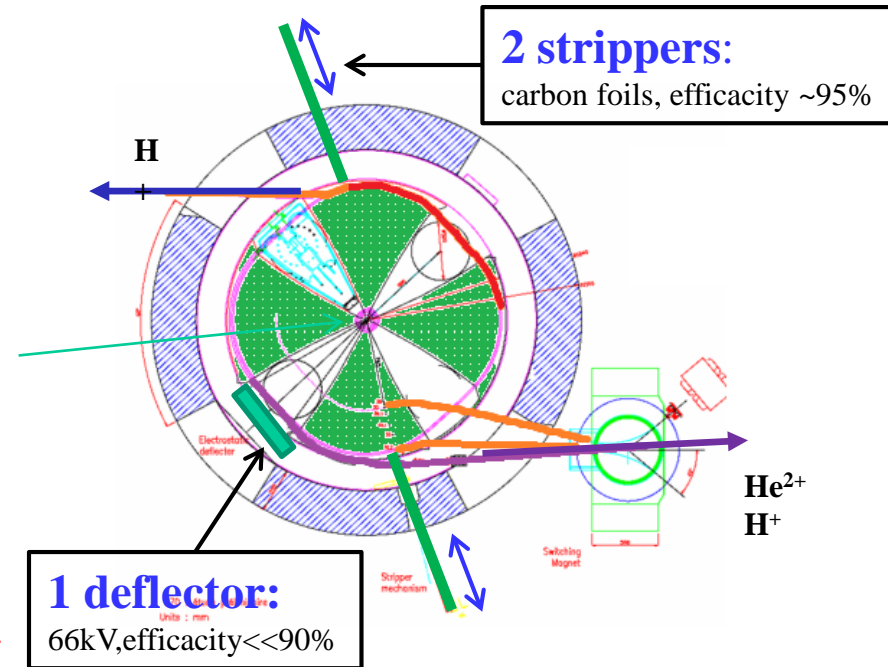
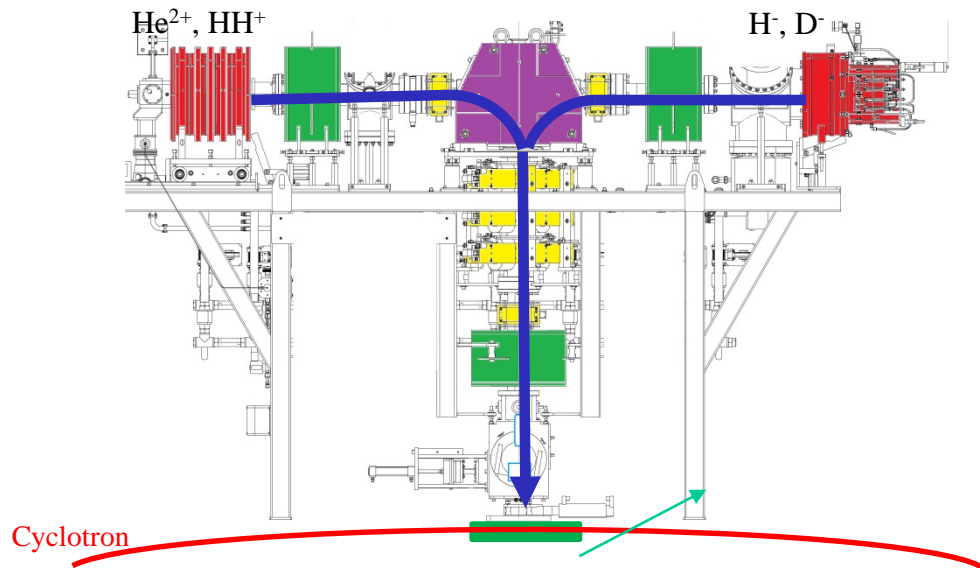
2 lines in a sterile environment



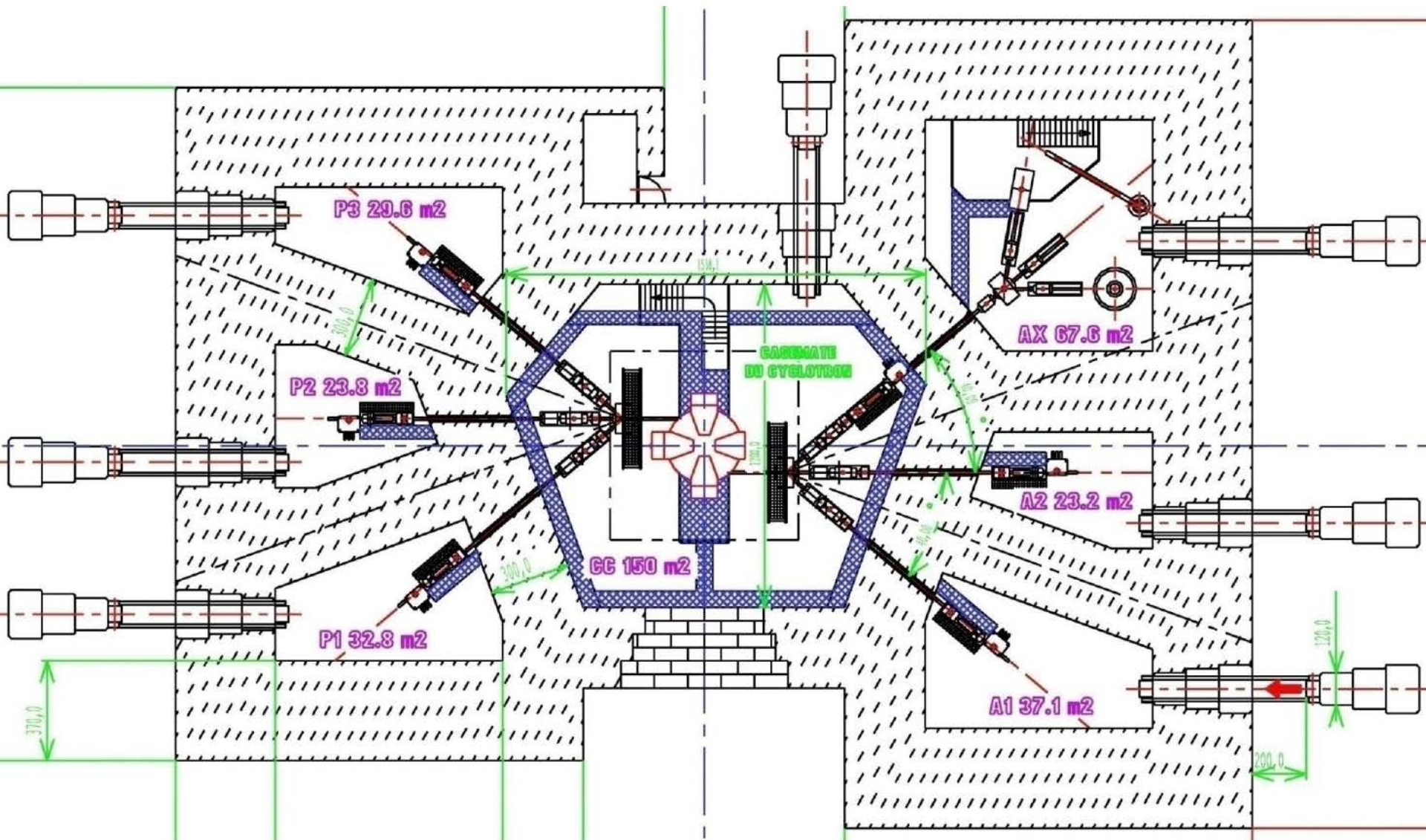
## C70 Cyclotron build by IBA:

- **4 sectors isochron cyclotron** (~ 4m of diameter)
  - RF: 30.45 MHz
  - Acceleration Voltage: 65 kV
  - Max magn. field : 1.6 T
  - Max kin. energy/n: 30-70 MeV
- **2 multi-particle sources:**
  - H<sup>-</sup>, D<sup>-</sup>: multicusp, 5 mA max.
  - He<sup>2+</sup>, HH<sup>+</sup>: supernanogan ECR
- Extraction: stripper (-) or electrostatic deflector (+)

| Extracted        | Energy (MeV) | Max. current (μA) |
|------------------|--------------|-------------------|
| H <sup>+</sup>   | 30 – 70      | 2 x 375           |
| D <sup>+</sup>   | 15 – 35      | 2 x 50            |
| He <sup>2+</sup> | 68           | 70                |
| HH <sup>+</sup>  | 17           | 50                |



# ARRONAX facility



– **Radionuclide targeted therapy:**

$^{211}\text{At}$  ( $\alpha$  emitter)

$^{67}\text{Cu}$ ,  $^{47}\text{Sc}$  ( $\beta^-$  emitters)

– **Theranostic radionuclides:**

Radionuclide pairs  $\beta^+/\beta^-$  :  $^{64/67}\text{Cu}$ ,  $^{44/47}\text{Sc}$

– **Imaging:**

Cardiology:  $^{82}\text{Sr}/^{82}\text{Rb}$

Oncology:  $^{68}\text{Ge}/^{68}\text{Ga}$

Hypoxia :  $^{64}\text{Cu}$  + ATSM

Immuno-PET ( $^{64}\text{Cu}$ ,  $^{44}\text{Sc}$ , ...)

**GMP production  
Approved by FDA & ANSM**

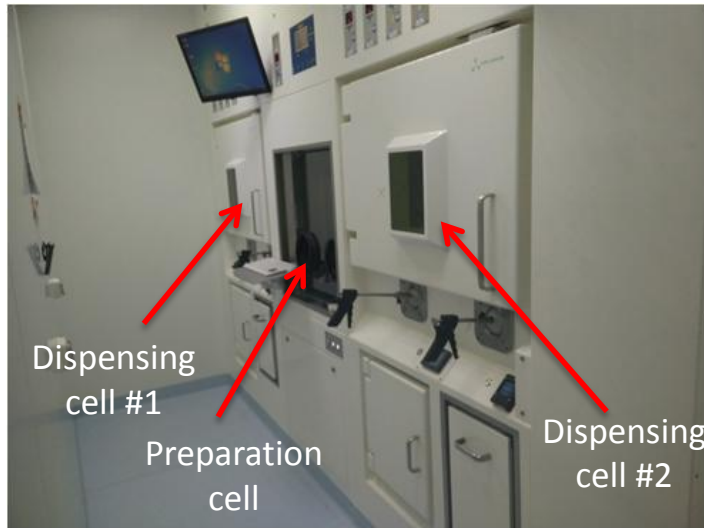
– **Neutron production for particle activation:**

$^{166}\text{Ho}$



**Goal:** produce radiopharmaceuticals for clinical trials (with the Nantes CHU)

- **New hot cells in a sterile environment**



Automates for radio-synthesis and aseptic dispensing

Authorization obtained **from ARS: Feb. 2017**

Funding obtained for 4 clinical trials: 2 with Lu-177, 2 with Cu-64

other under studies with both At-211 and Cu-64

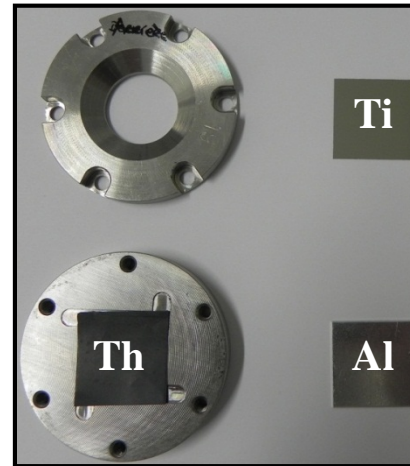
Investigational Medicinal Product Dossiers (IMPD) ongoing.

→ First patient expected May 2018

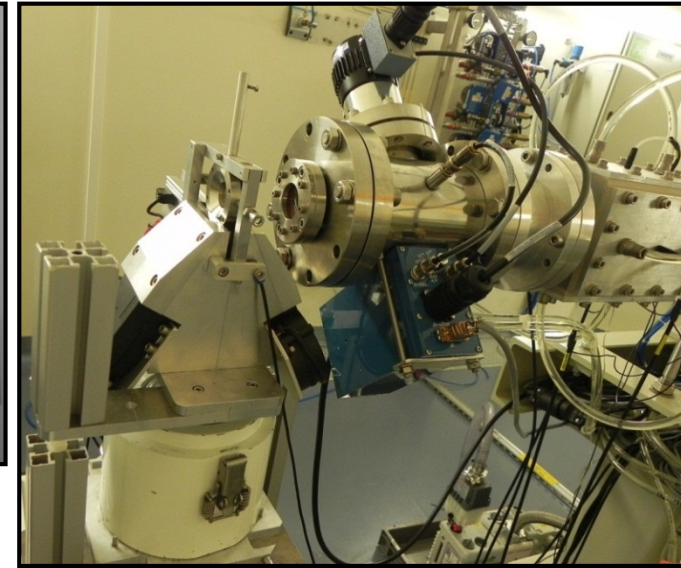
# Stacked-foil technique

## 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:

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

## 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:

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

- error on e, e':  $\leq 1\%$
- error on t: negligible

## IAEA recommended cross sections:

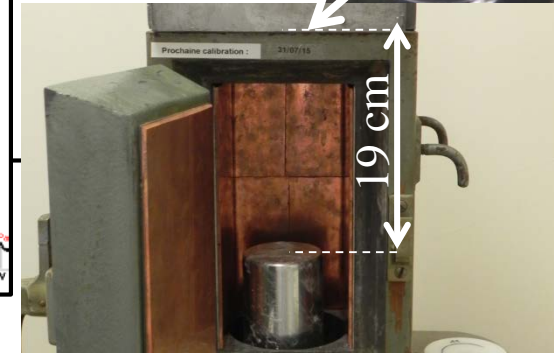
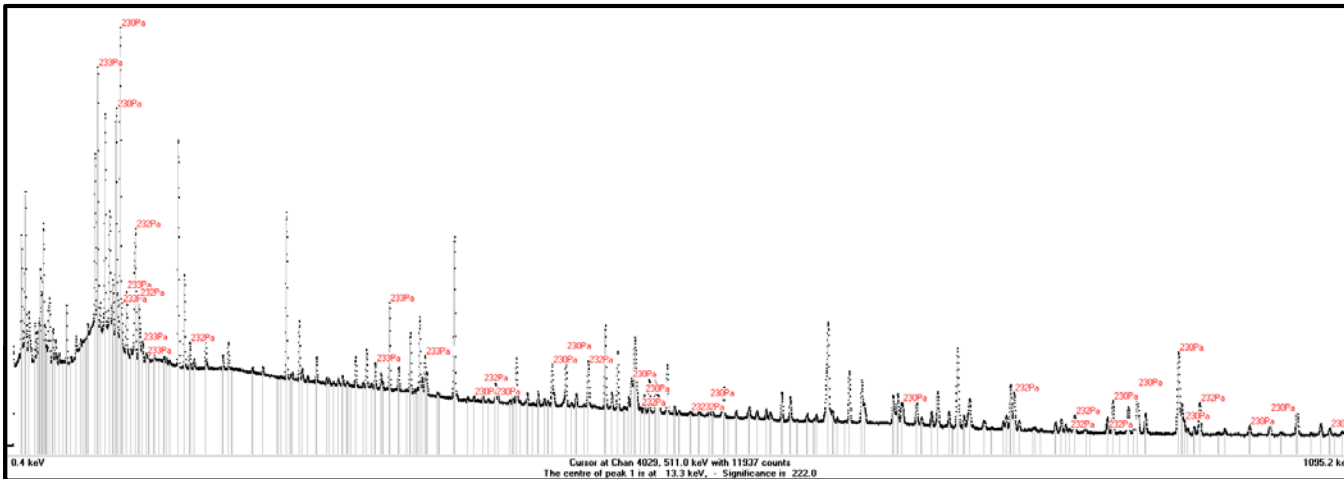
- 11 reactions available for protons  
 $^{27}\text{Al}$  (2),  $^{\text{nat}}\text{Ni}$ ,  $^{\text{nat}}\text{Ti}$  (2),  $^{\text{nat}}\text{Cu}$  (5),  $^{\text{nat}}\text{Mo}$
- 11 reactions available for deuterons  
 $^{27}\text{Al}$  (2),  $^{\text{nat}}\text{Fe}$ ,  $^{\text{nat}}\text{Ni}$ (3),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

# Stacked-foil technique

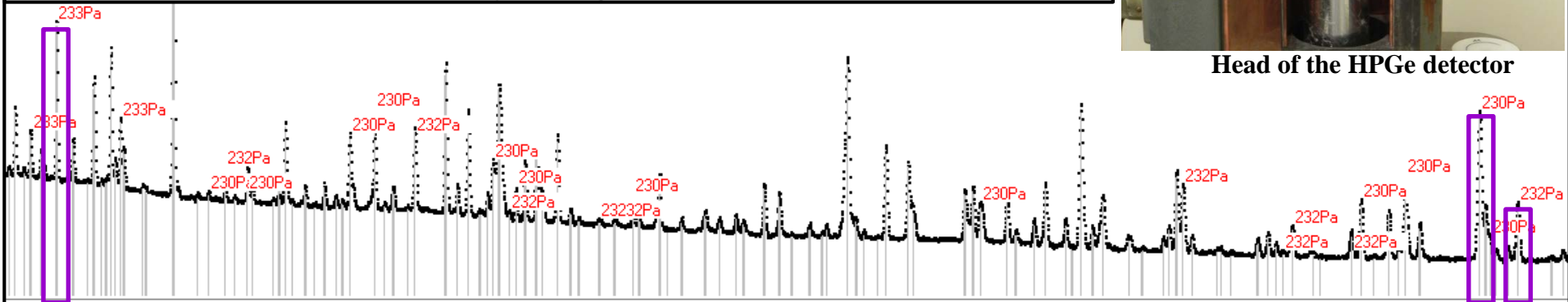
## Off line gamma spectroscopy

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

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

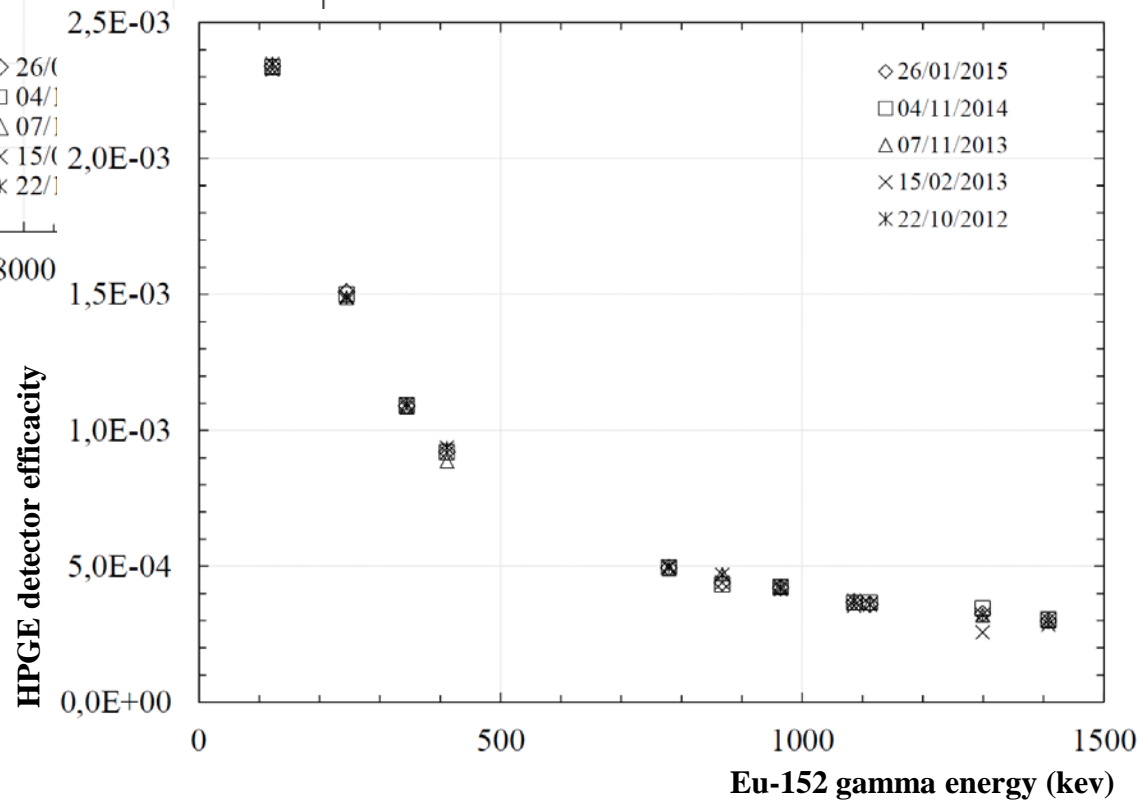
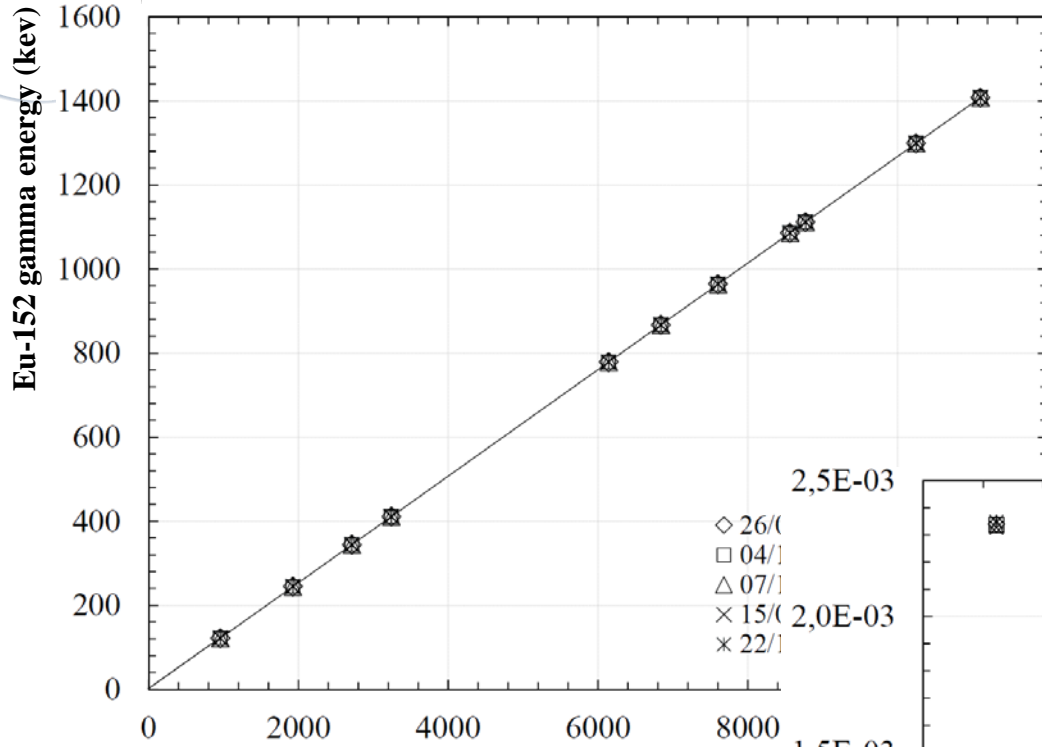


Head of the HPGe detector



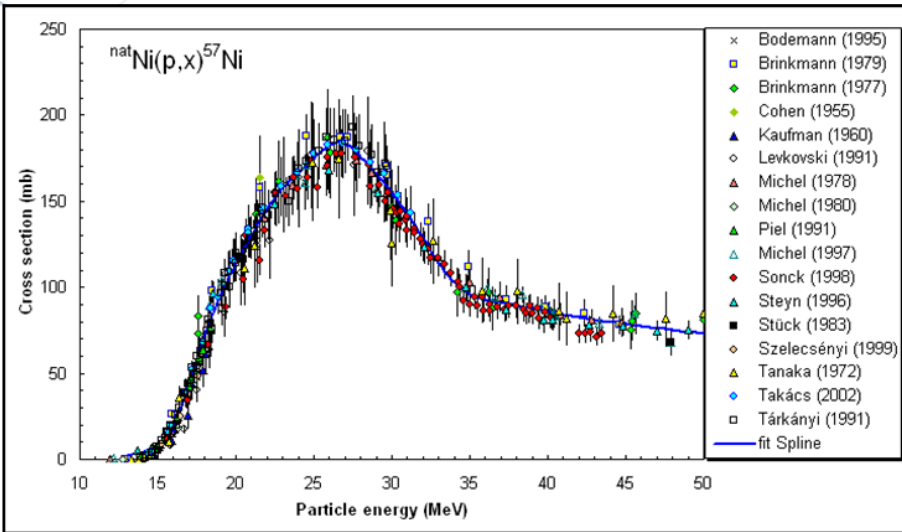
$\gamma$  rays used to extract production cross section of  $^{230,232,233}\text{Pa}$

# Gamma spectroscopy

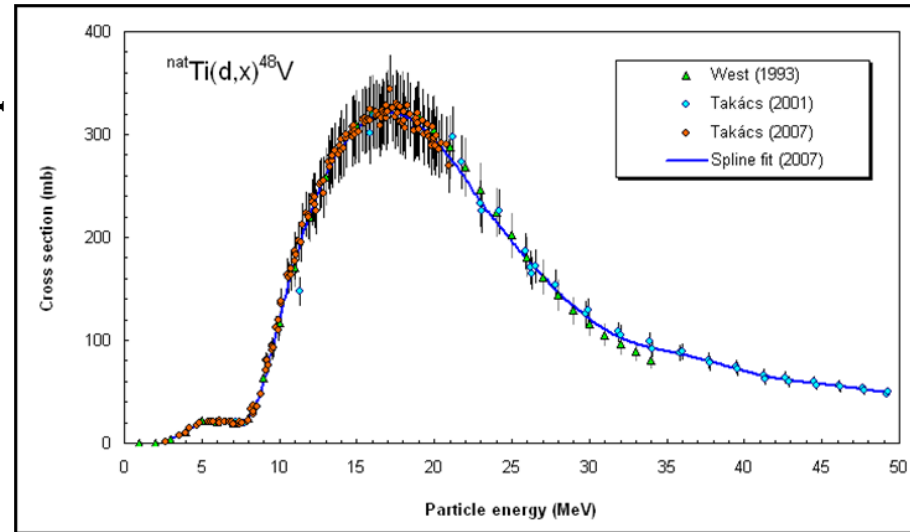


Good reproductibility for both energy calibration and efficiency calibration

## IAEA recommended monitor reactions used:



From NDS-IEAE medical portal



### Protons:

- ${}^{\text{nat}}\text{Ti}(p,x){}^{48}\text{V}$ ,  $E < 15 \text{ MeV}$
- ${}^{\text{nat}}\text{Ni}(p,x){}^{57}\text{Ni}$ ,  $15 \text{ MeV} < E < 50 \text{ MeV}$
- ${}^{\text{nat}}\text{Cu}(p,x){}^{62}\text{Zn}$ ,  $50 \text{ MeV} < E < 60 \text{ MeV}$
- ${}^{\text{nat}}\text{Cu}(p,x){}^{56}\text{Co}$ ,  $60 \text{ MeV} < E$

### Deuterons:

- ${}^{\text{nat}}\text{Ti}(d,x){}^{48}\text{V}$ ,  $E < 35 \text{ MeV}$

Objective: measure the activity of the  $^{67}\text{Cu}$

Interferences :

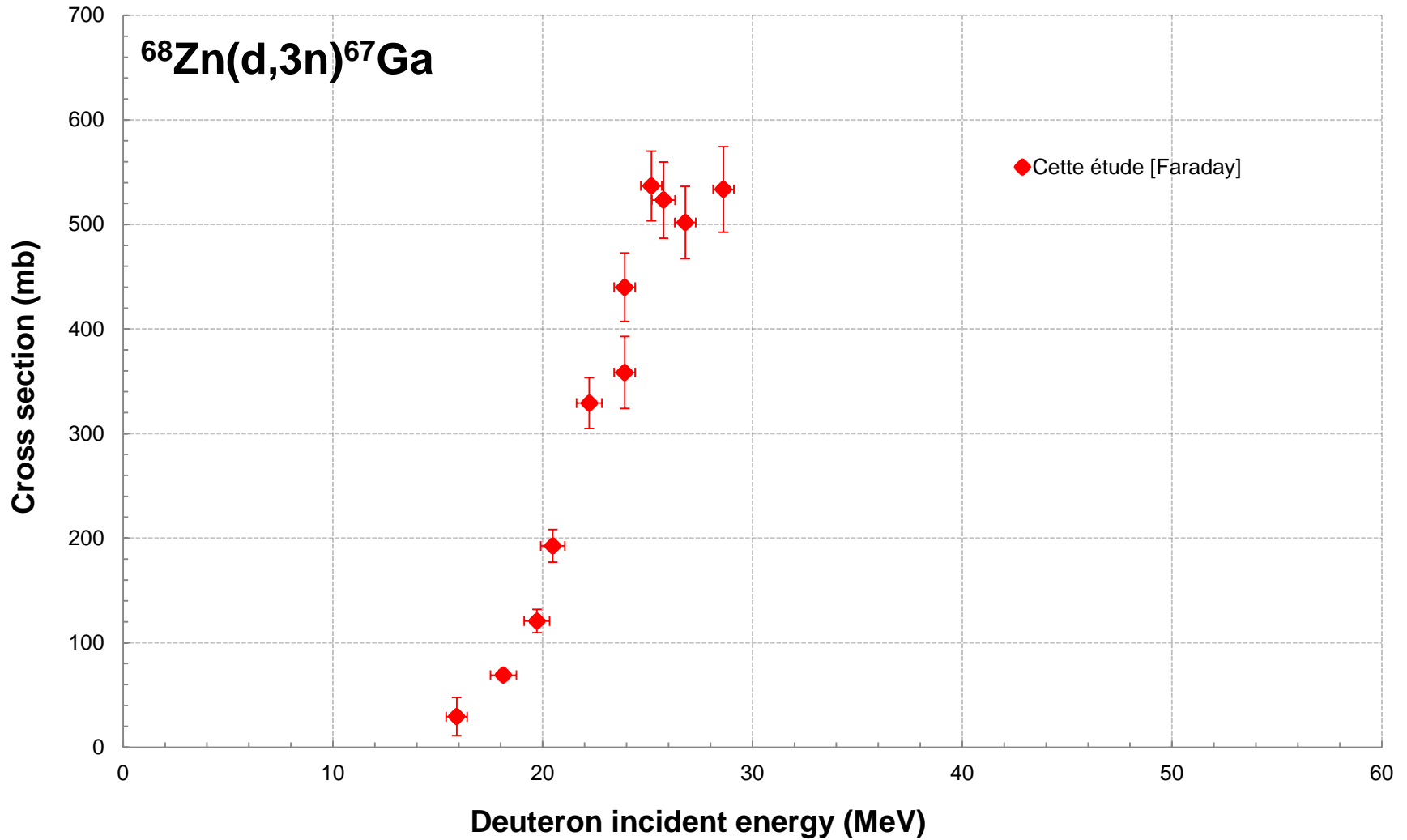


| Radionucléide    | $T_{1/2}$ | Gamma émis keV (%) |
|------------------|-----------|--------------------|
| $^{67}\text{Cu}$ | 61,8 h    | 91,3 (7,0)         |
|                  |           | 93,3 (16,1)        |
|                  |           | 184,6 (48,7)       |
|                  |           | 300,2 (0,8)        |
|                  |           | 393,5 (0,2)        |
| $^{67}\text{Ga}$ | 78,3 h    | 91,3 (3,1)         |
|                  |           | 93,3 (38,8)        |
|                  |           | 184,6 (21,4)       |
|                  |           | 300,2 (16,6)       |
|                  |           | 393,5 (4,56)       |

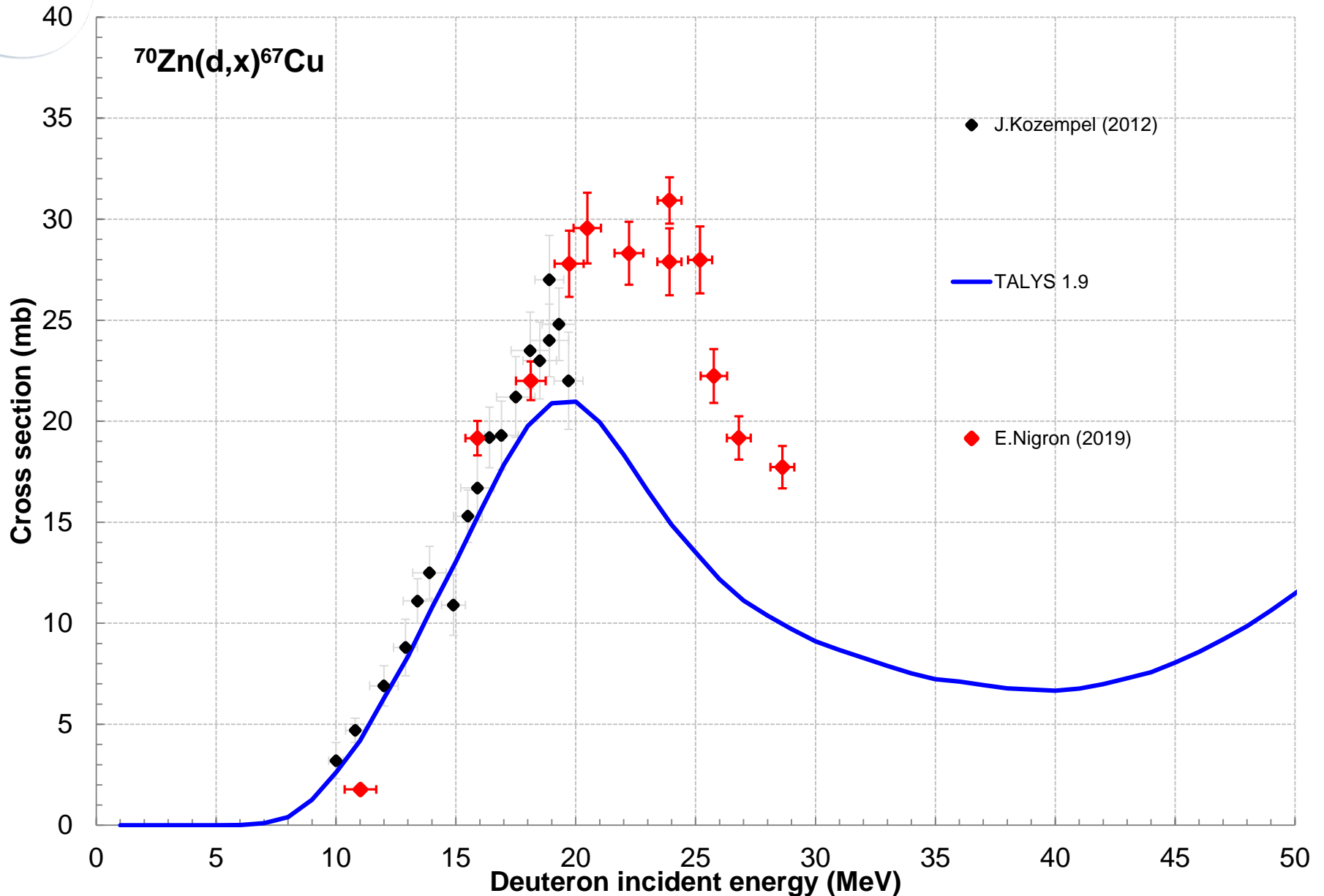
$^{67}\text{Cu}$  (62 h)/ $^{67}\text{Ga}$  (78h)

- No emission specific to any of the radionuclides
- Impossibility to play on  $T_{1/2}$
- 2-equation system: linking the total number of gammas collected, branching ratios and radionuclide activity.

# $^{67}\text{Ga}$ production cross section



# Comparison with TALYS 1.9





Code for the simulation of nuclear reactions

Projectiles : n, p, d, t, He-3,  $\alpha$  particles

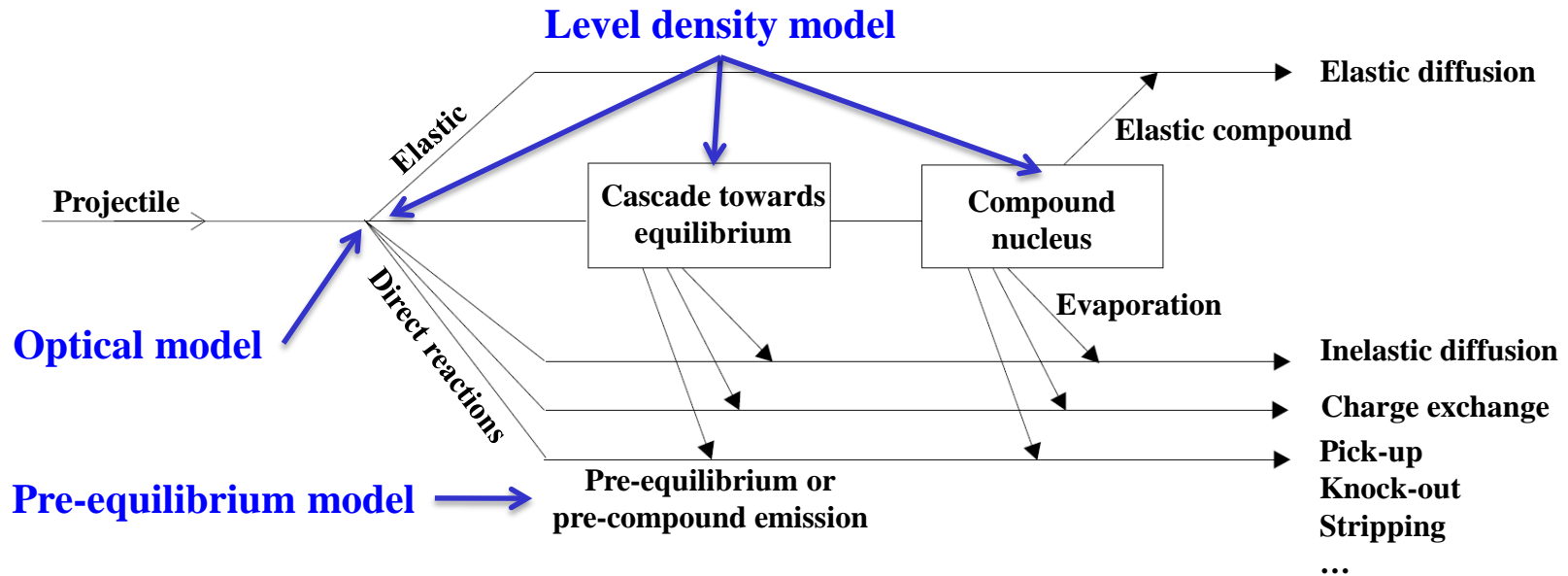
Many state-of-the-art nuclear models

Energy : 1 keV to 1 GeV

Provide a complete description of all reactions channels and observables

Targets :  $Z = 3$  to 110

## Nuclear reactions



Adapted from S. Benck, PhD thesis, 1999

⇒ Influence on the calculated production cross section values

## TALYS default and adjusted calculations

TALYS code version 1.9

the combination of models that best describes the whole set of available data for all projectiles, targets and incident energies defined by the TALYS authors

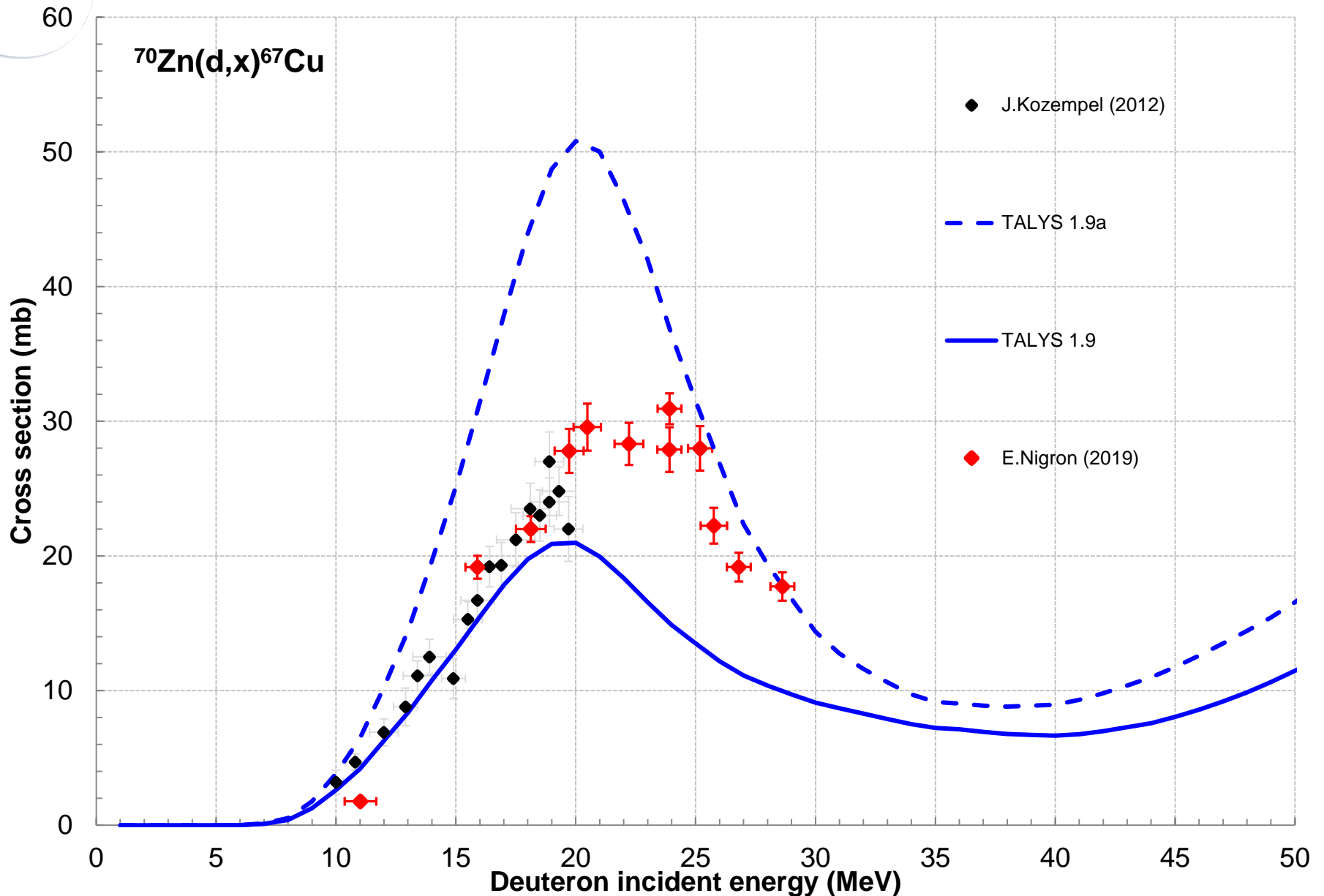
⇒ TALYS 1.9 Default

One combination of models that best describes our whole set of data for proton, deuteron, alpha particles as projectile (and also some literature data) has been defined by A. Guertin et al.

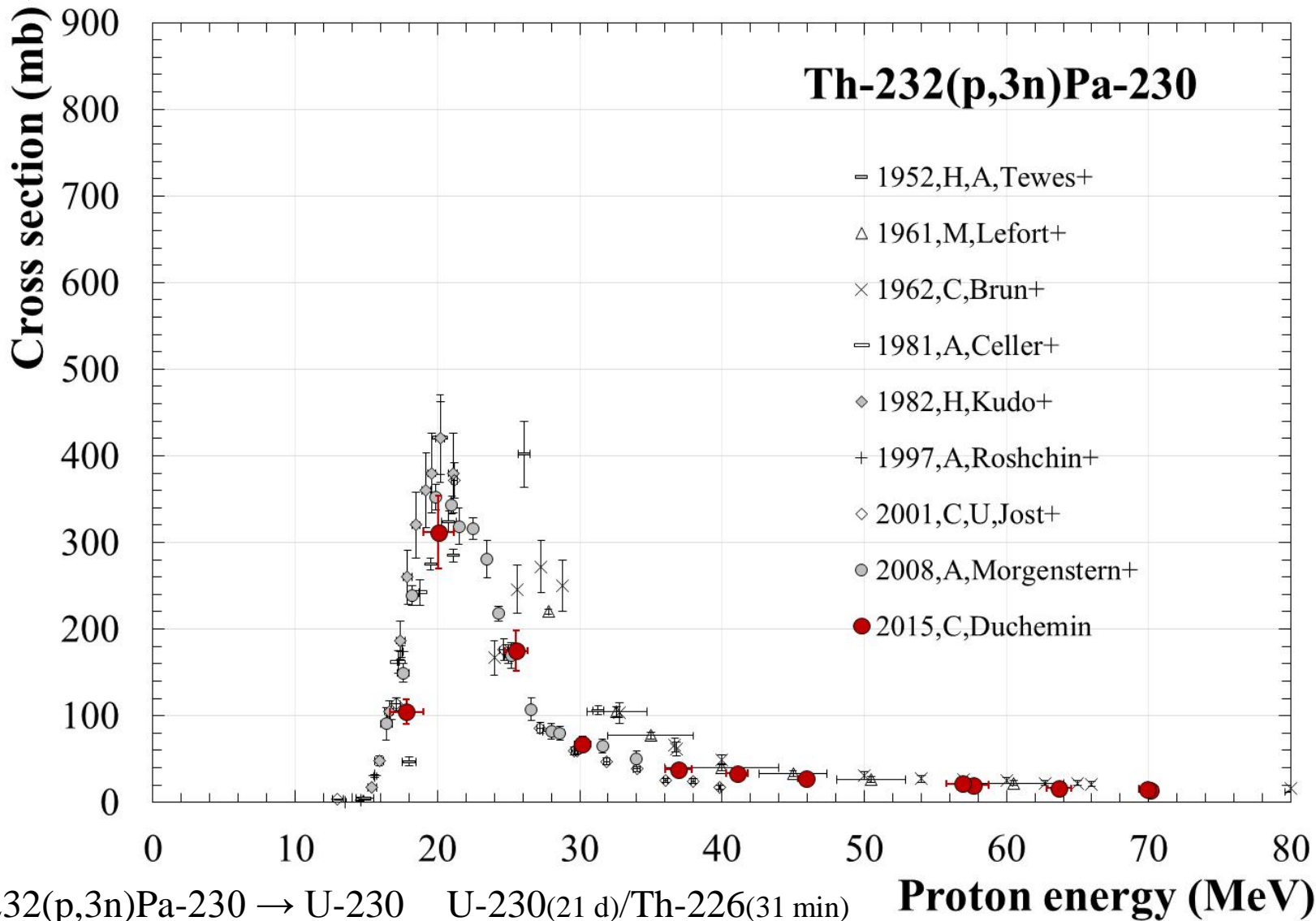
⇒ TALYS 1.9 Adj.

| Models          | Projectile   | Default  | Adj.   |
|-----------------|--------------|--|--|
| Optical         | p (1)        | A.J. Koning and J.P. Delaroche (2003)  | A.J. Koning and J.P. Delaroche (2003)  |
|                 | d (5)        | S. Watanabe (1958)   | Y. Han et al. (2006)   |
|                 | $\alpha$ (8) | V. Avrigeanu et al. (2014)   | Demetriou et al. (2002)  |
| Pre-equilibrium | All (4)      | Two-component exciton model<br>Numerical transition rates with E-dependent matrix element<br>A.J. Koning and M.C. Duijvestijn (2004) | Two –component exciton model<br>Numerical transition rates with optical model for collision probabilities<br>A.J. Koning and M.C. Duijvestijn (2004) |
| Level density   | All (6)      | Constant temperature and Fermi gas model<br>A.J. Koning et al. (2008)  | Microscopic level density (Skyrme force) from Hilaire’s combinatorial tables<br>Goriely et al. (2008)  |

# Comparison with TALYS 1.9



# Pa-230 as a precursor of an $\alpha$ generator

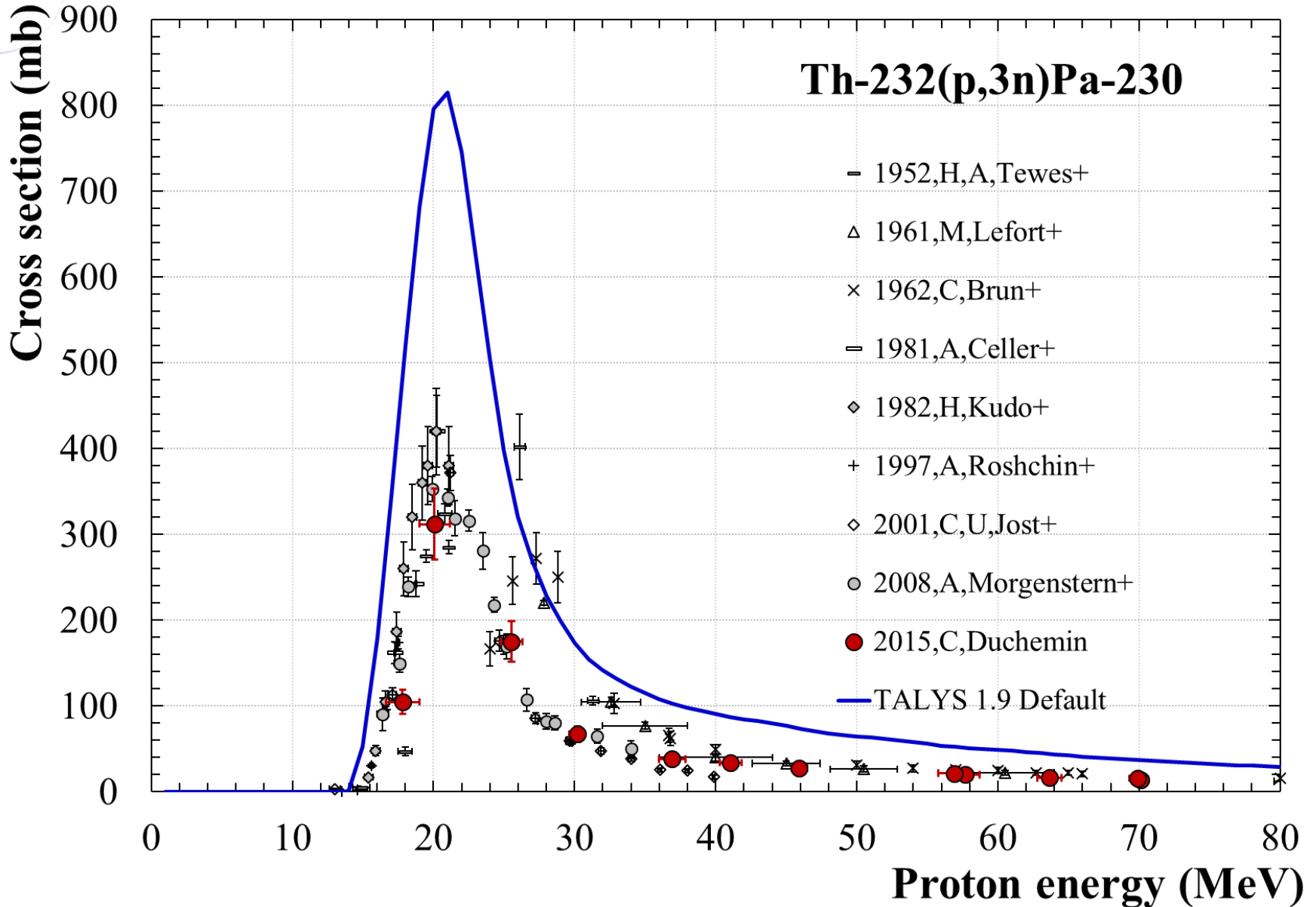


$\alpha$  RIT for leukaemia treatment

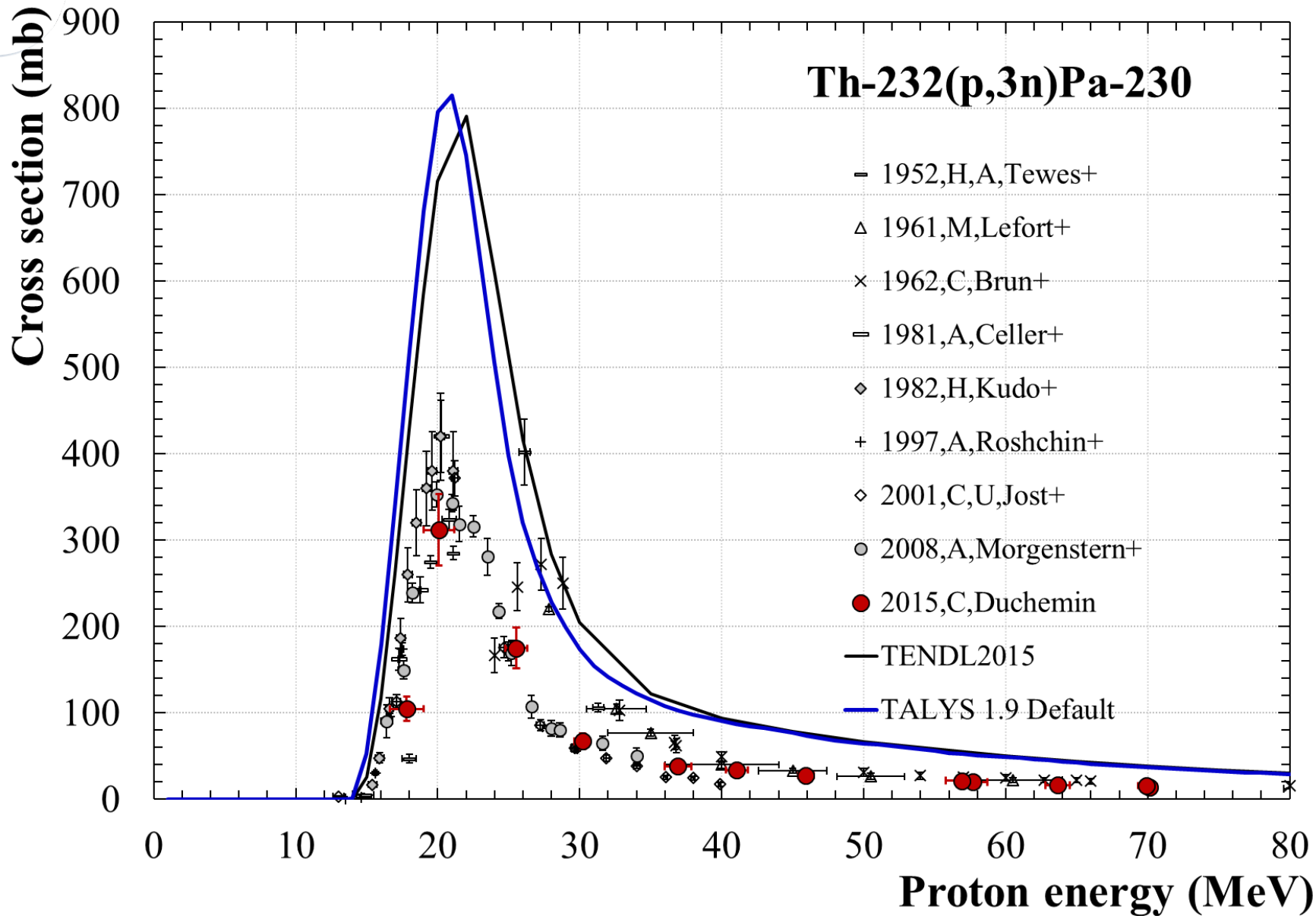
4  $\alpha$  cascade of 27.7 MeV

*C. Duchemin et al., Phys. Med. Biol. 60 (2015) 931-946*

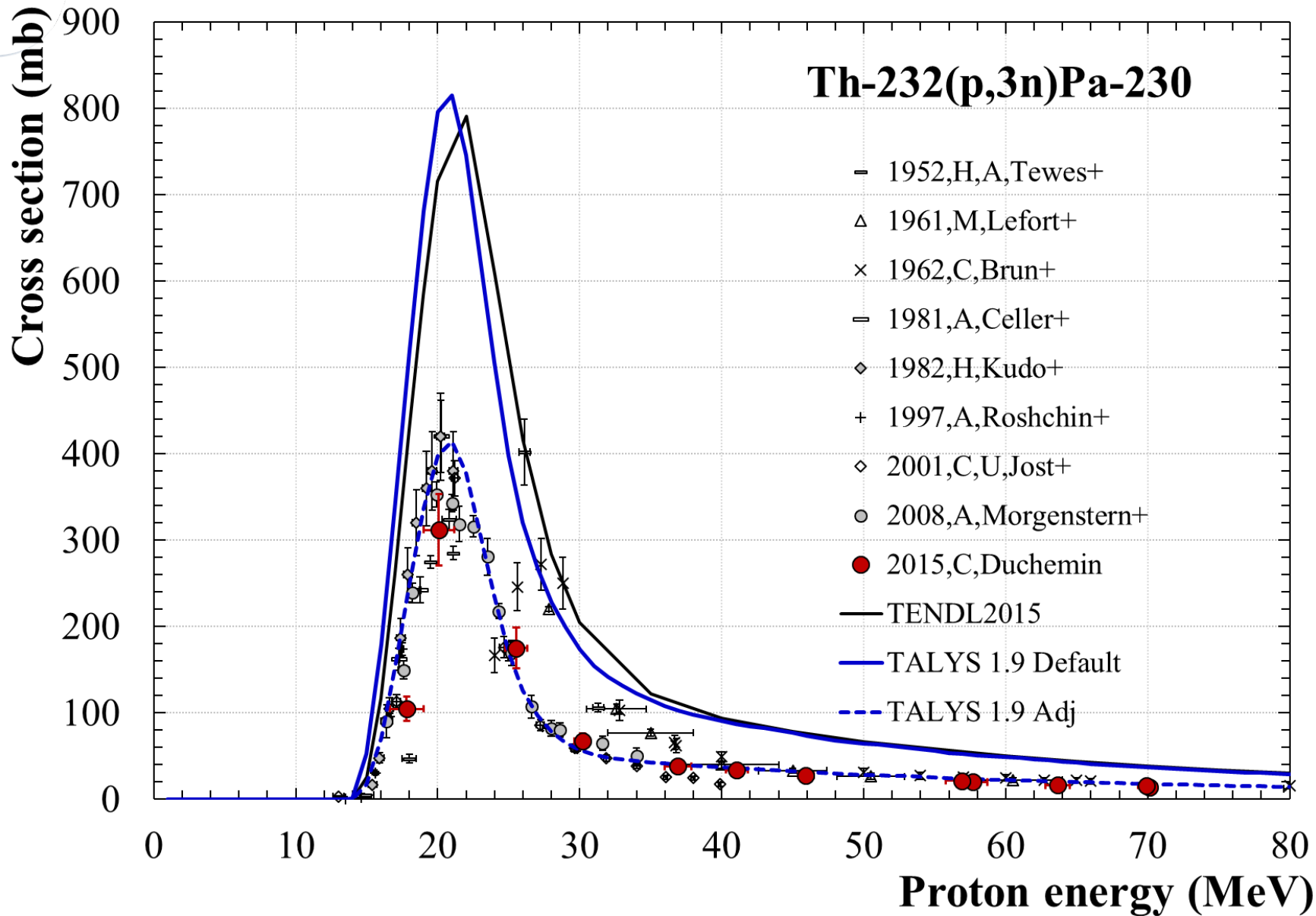
# Pa-230 as a precursor of an $\alpha$ generator



# Pa-230 as a precursor of an $\alpha$ generator



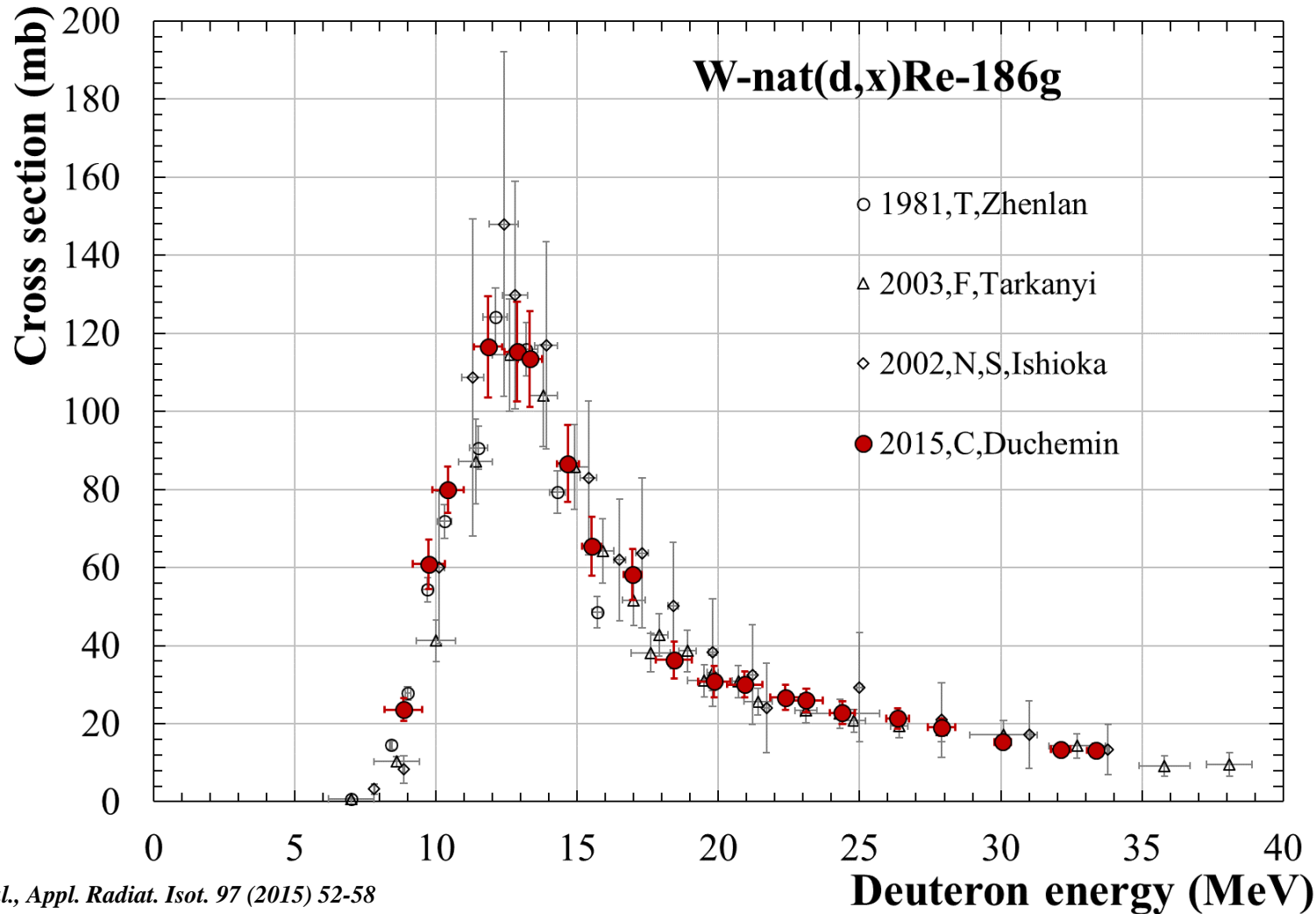
# Pa-230 as a precursor of an $\alpha$ generator



# Re-186g: proton/deuteron production route

**Re-186g ( $T_{1/2} = 3.7$  d)**

$\beta^-$  emitter used in clinical trials for the palliation of painful bone metastases resulting from prostate and breast cancer

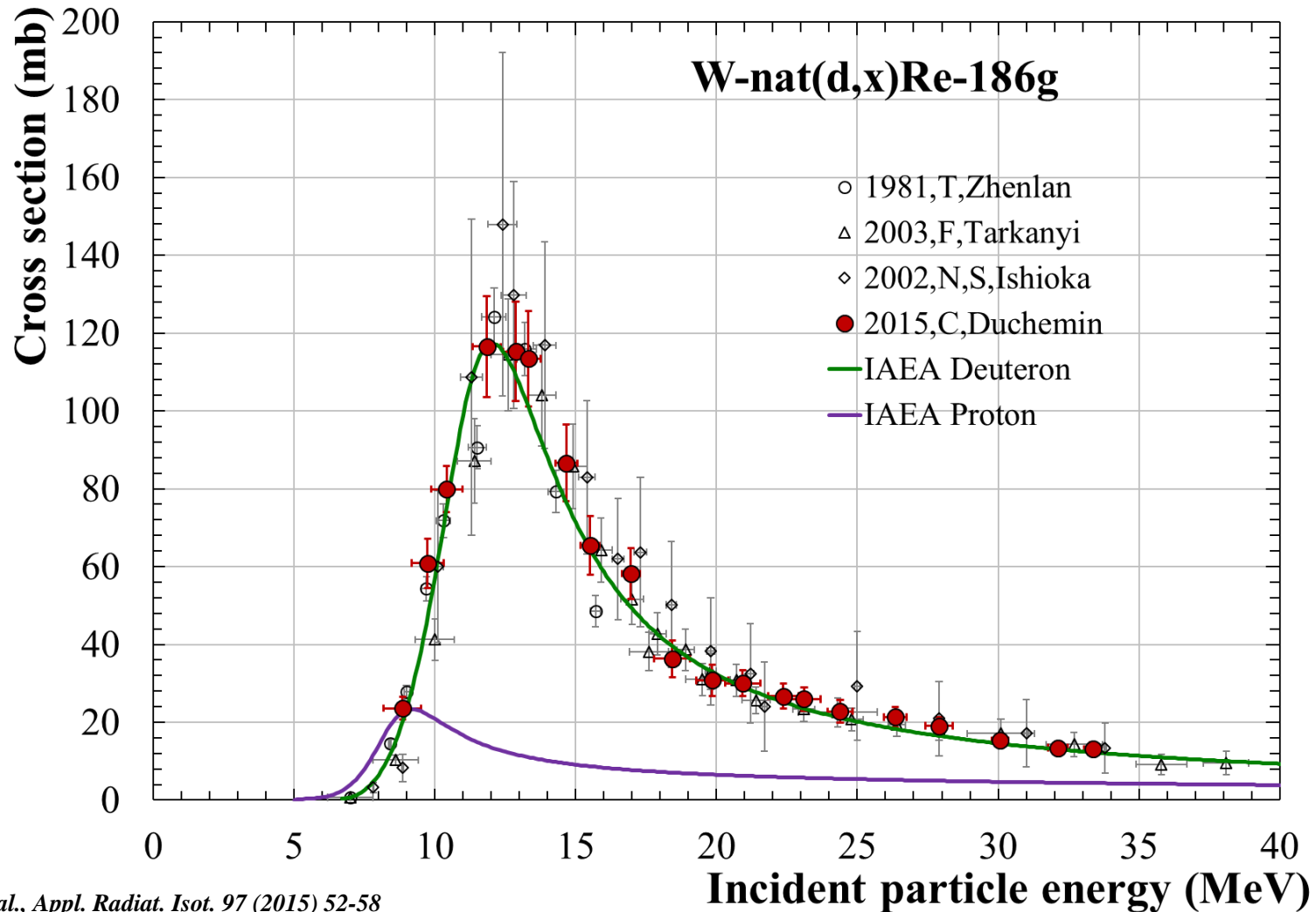




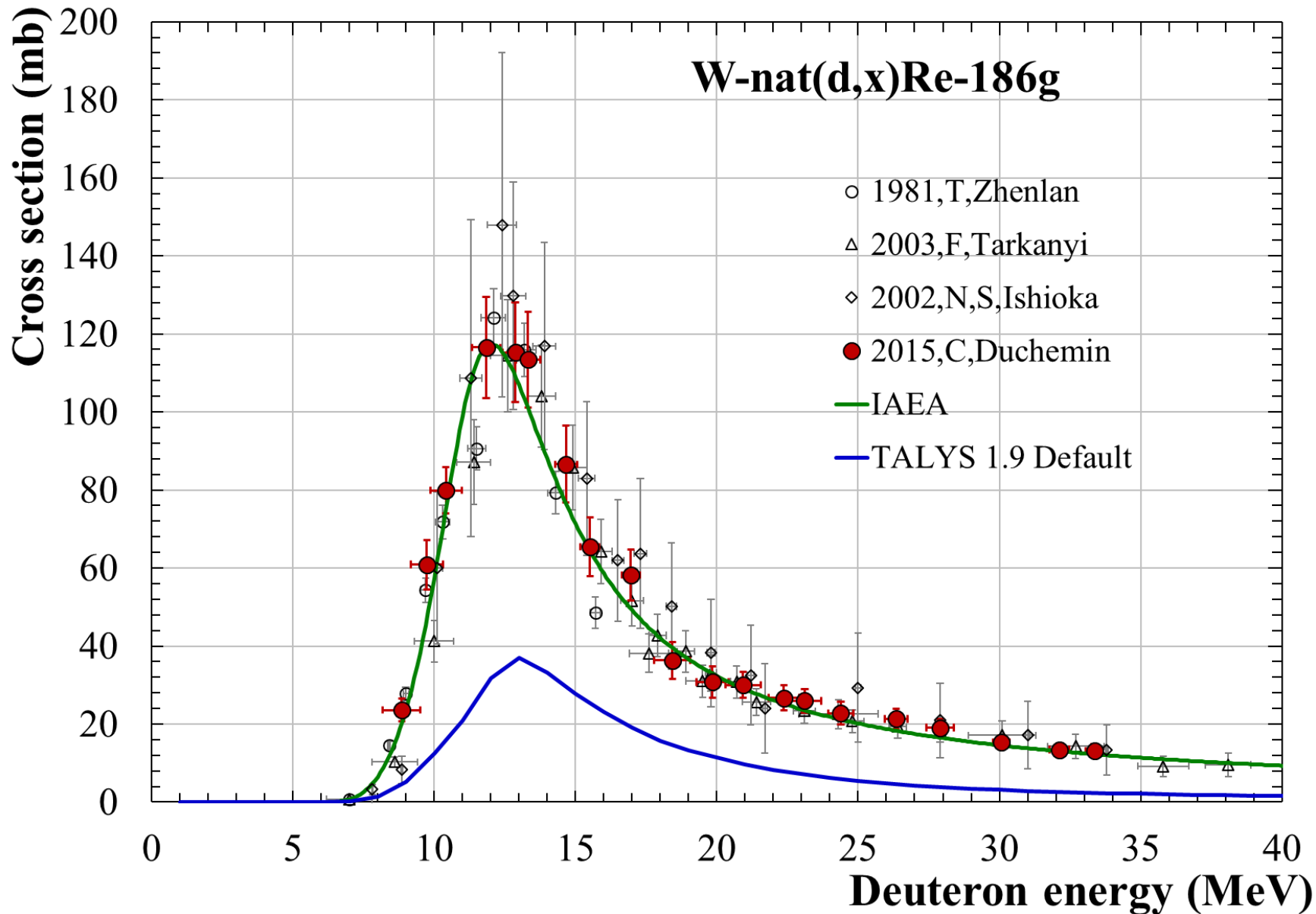
# Re-186g: proton/deuteron production route

Re-186g ( $T_{1/2} = 3.7$  d)

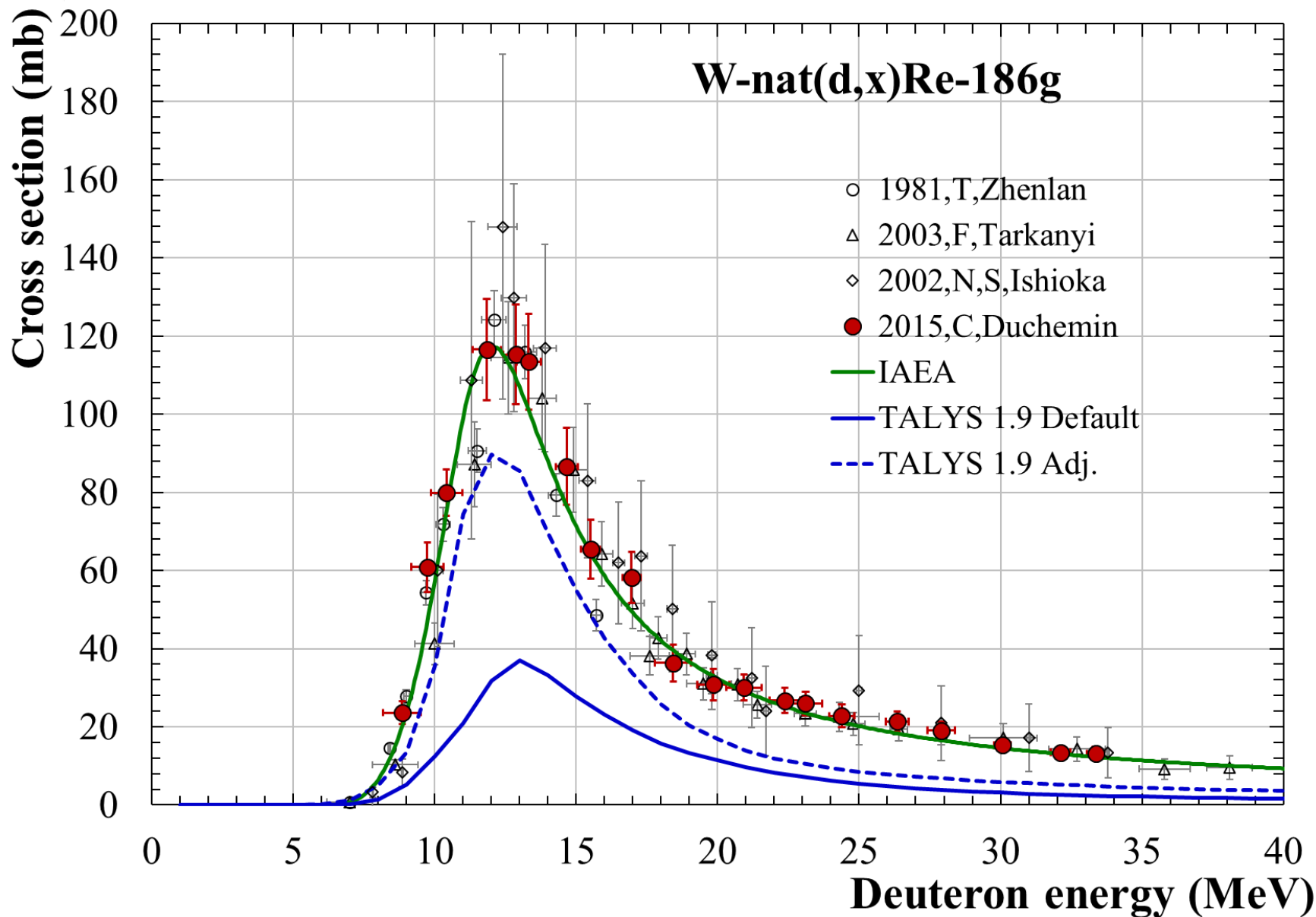
Deuteron induced reaction has clearly a highest Re-186g production cross section



# Re-186g: deuteron production route



# Re-186g: deuteron production route

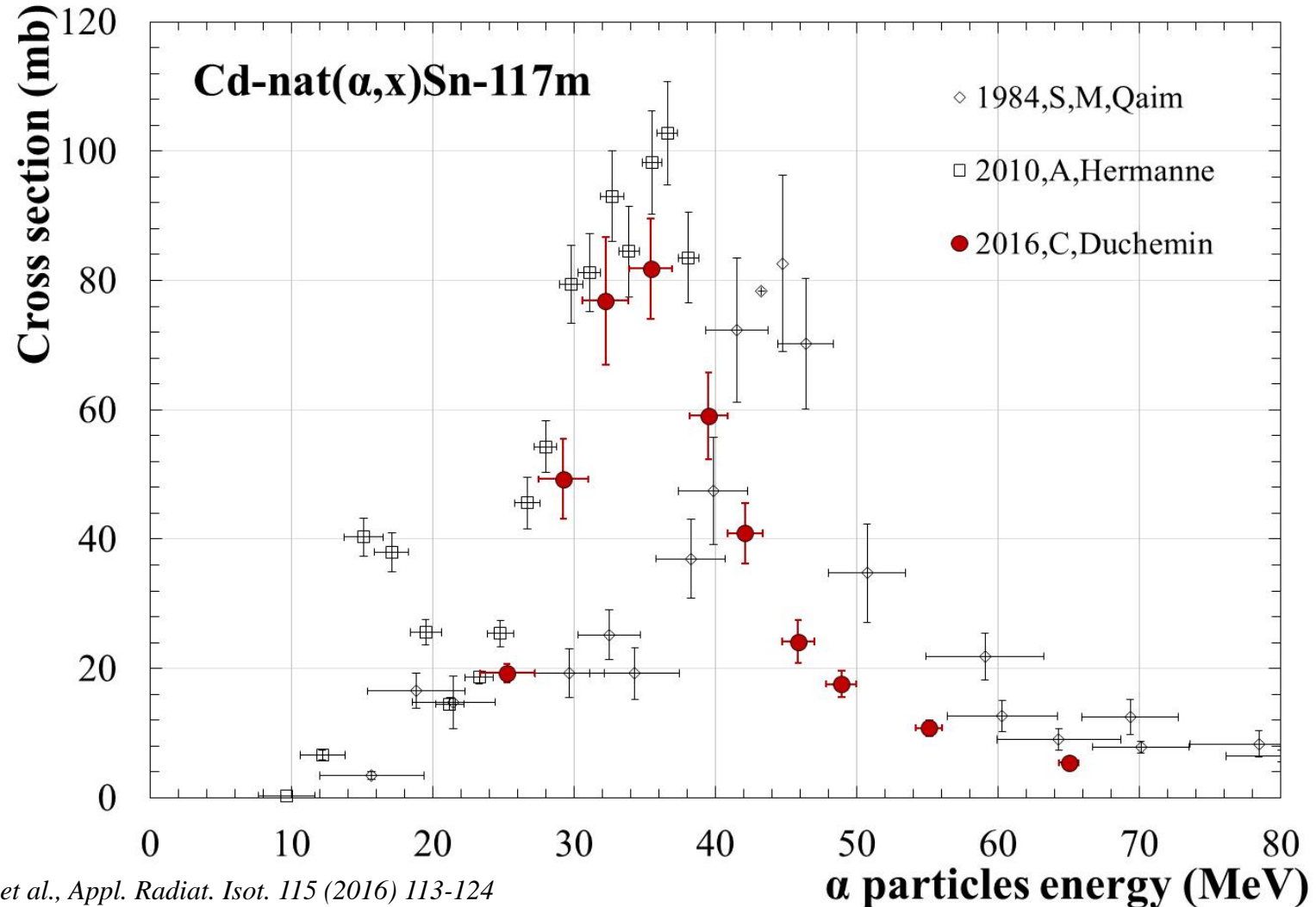


# Novel therapeutic and imaging nuclide

## Sn-117m ( $T_{1/2} = 13.6$ d)

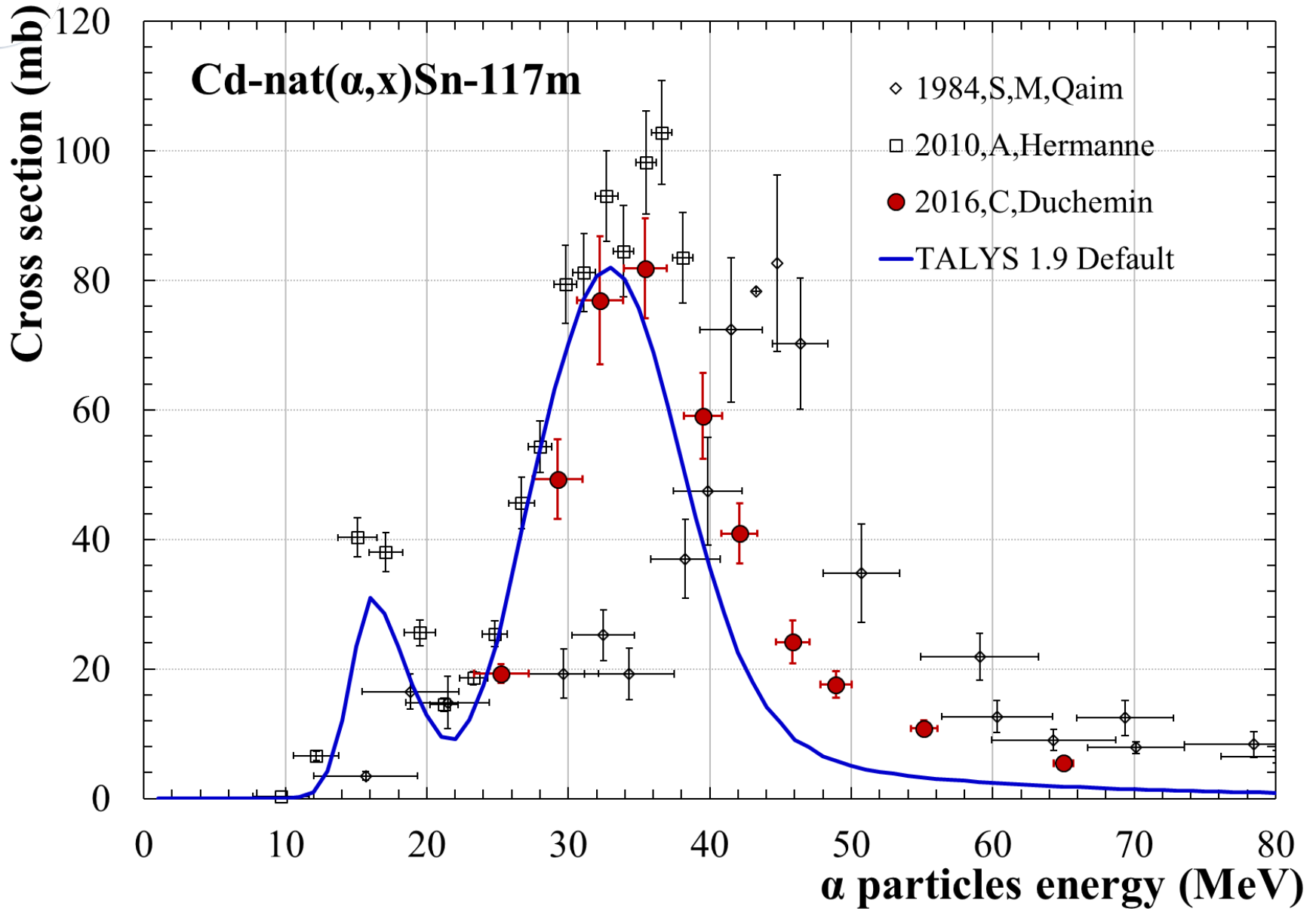
Conversion e- emitter used for the palliation of painful bone metastases

158 keV gamma ray suitable for SPECT imaging

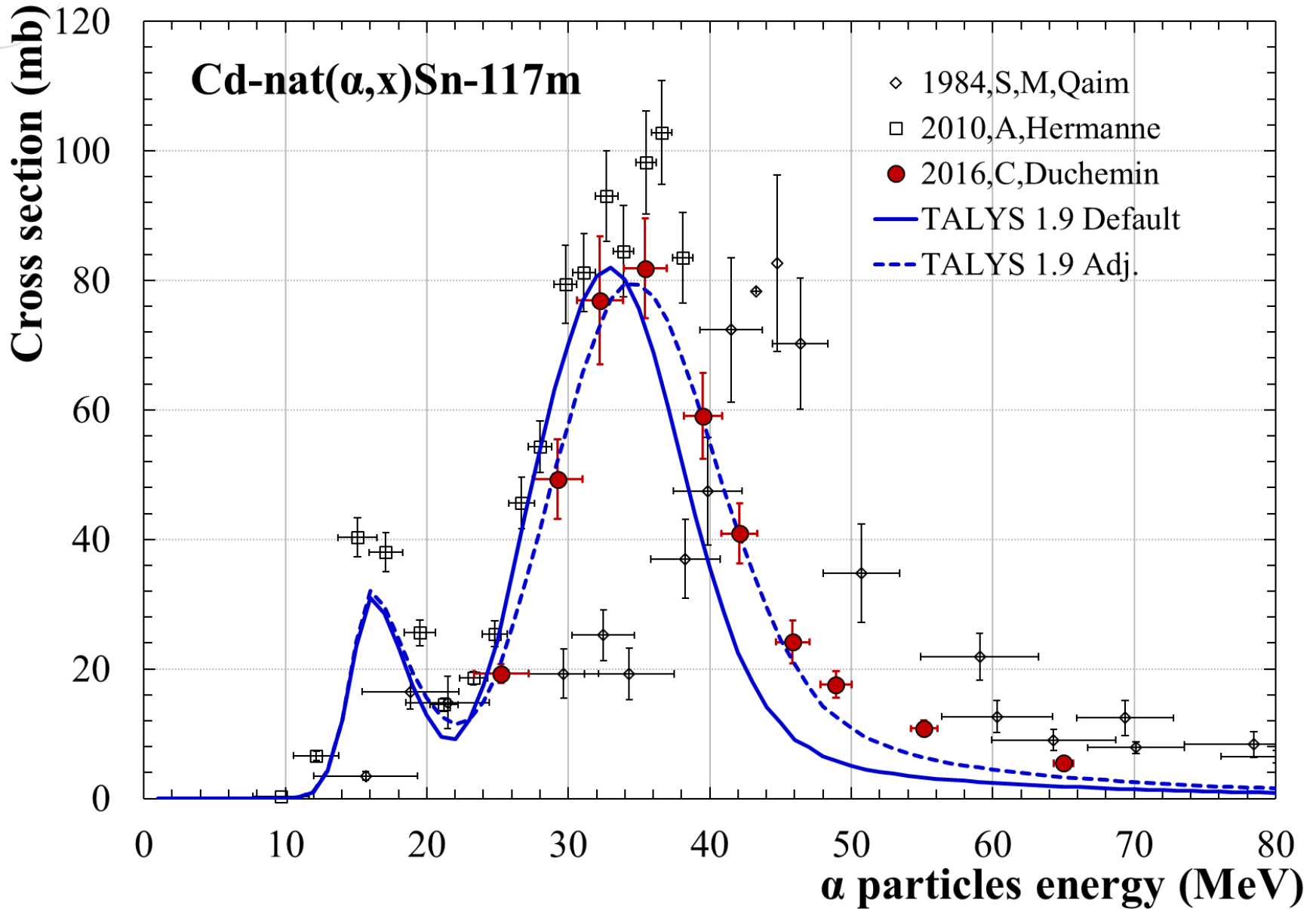


C. Duchemin et al., *Appl. Radiat. Isot.* 115 (2016) 113-124

# Novel therapeutic and imaging nuclide



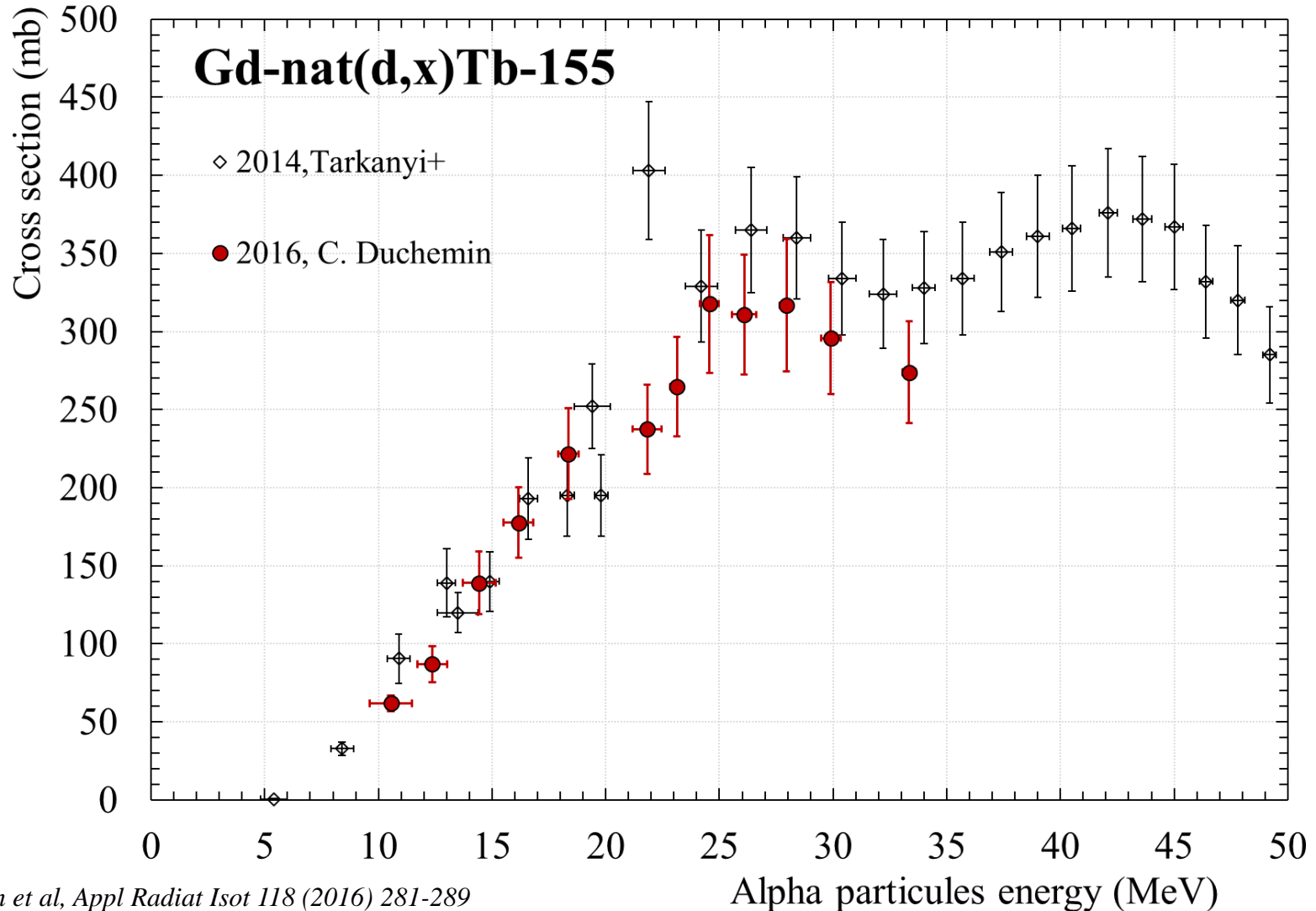
# Novel therapeutic and imaging nuclide



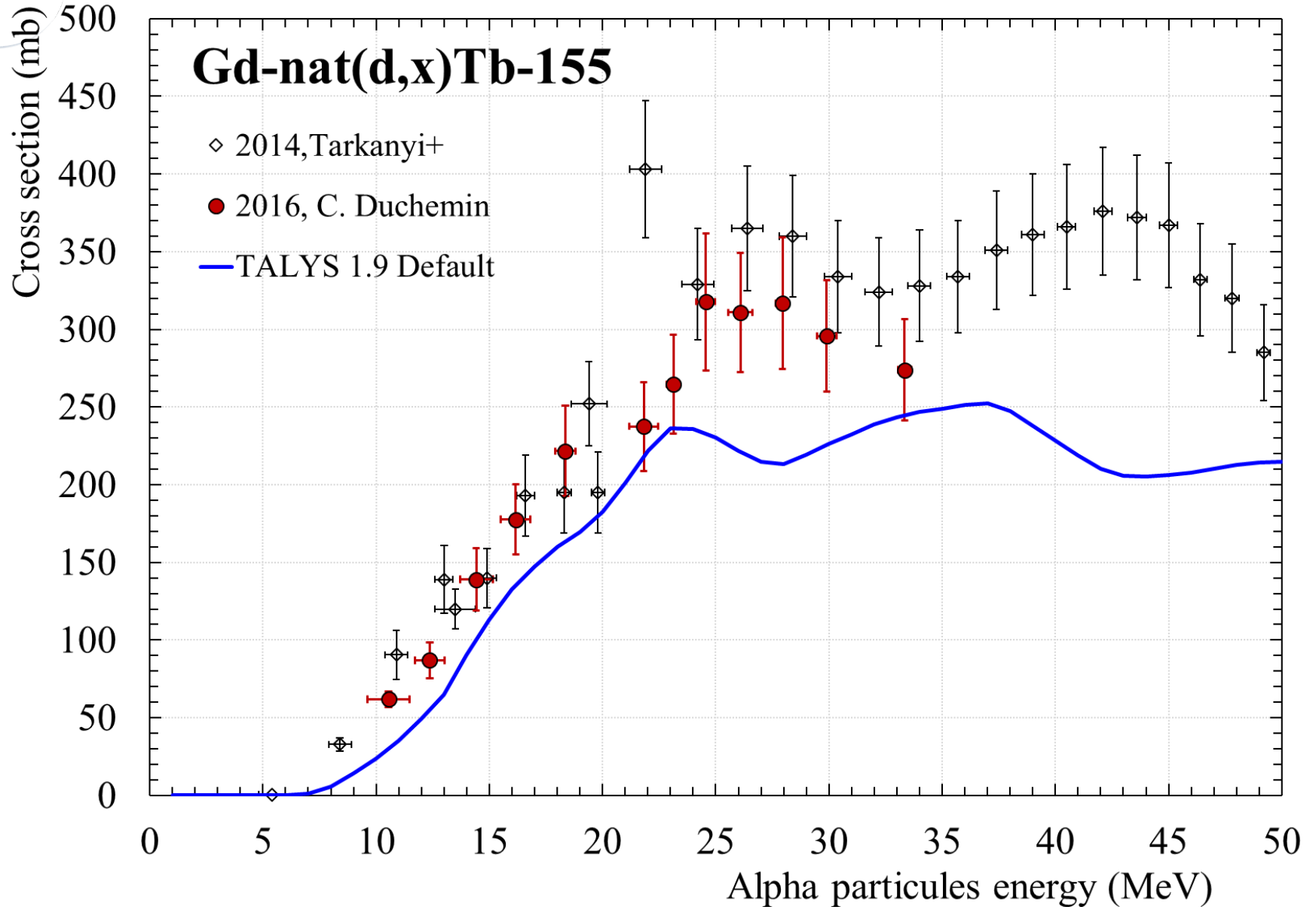
# Terbium 155: theranostic isotope

**Tb-155 ( $T_{1/2} = 5.3$  d)**

a theranostic isotope for SPECT imaging and Auger therapy

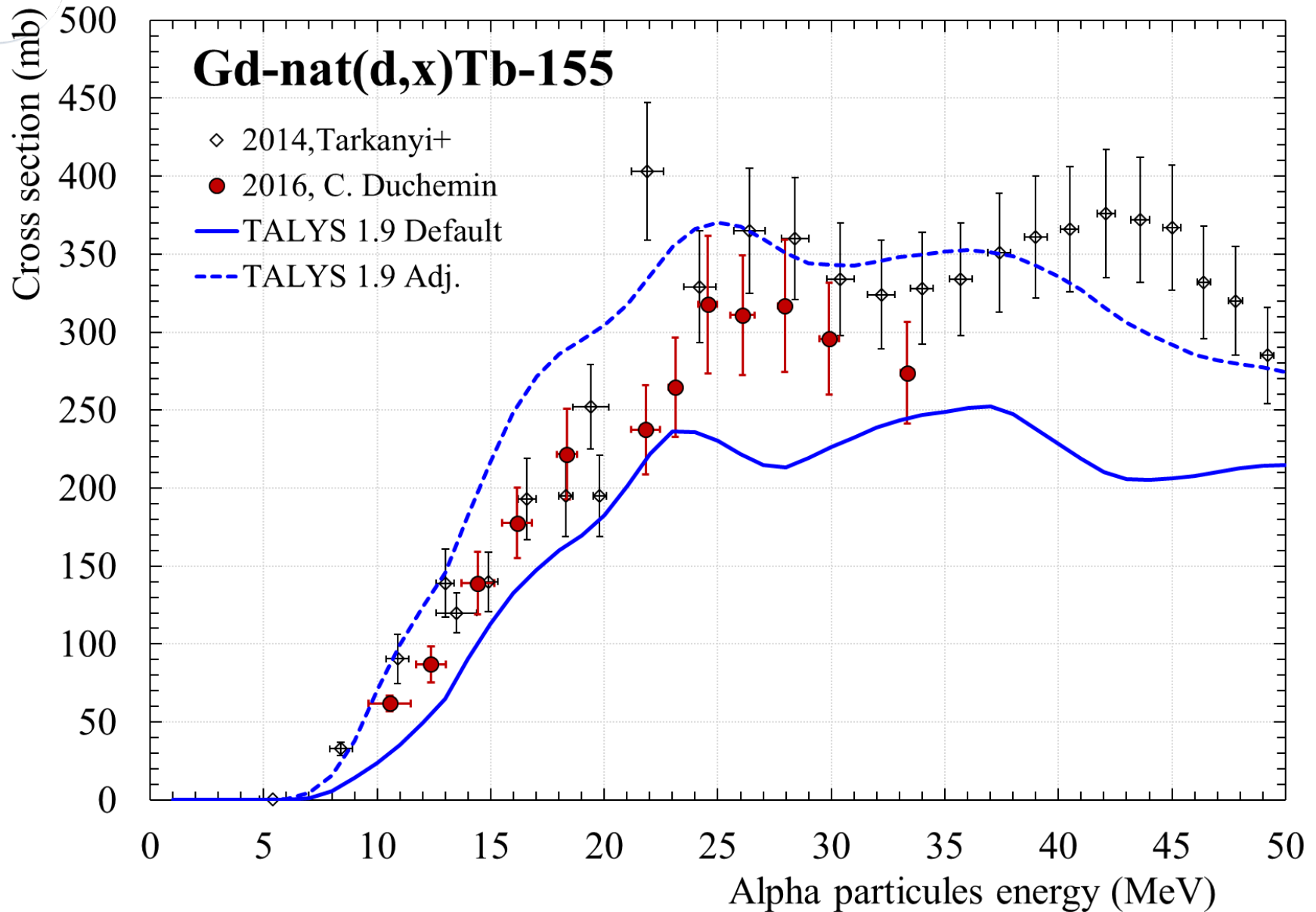


# Terbium 155





# Terbium 155

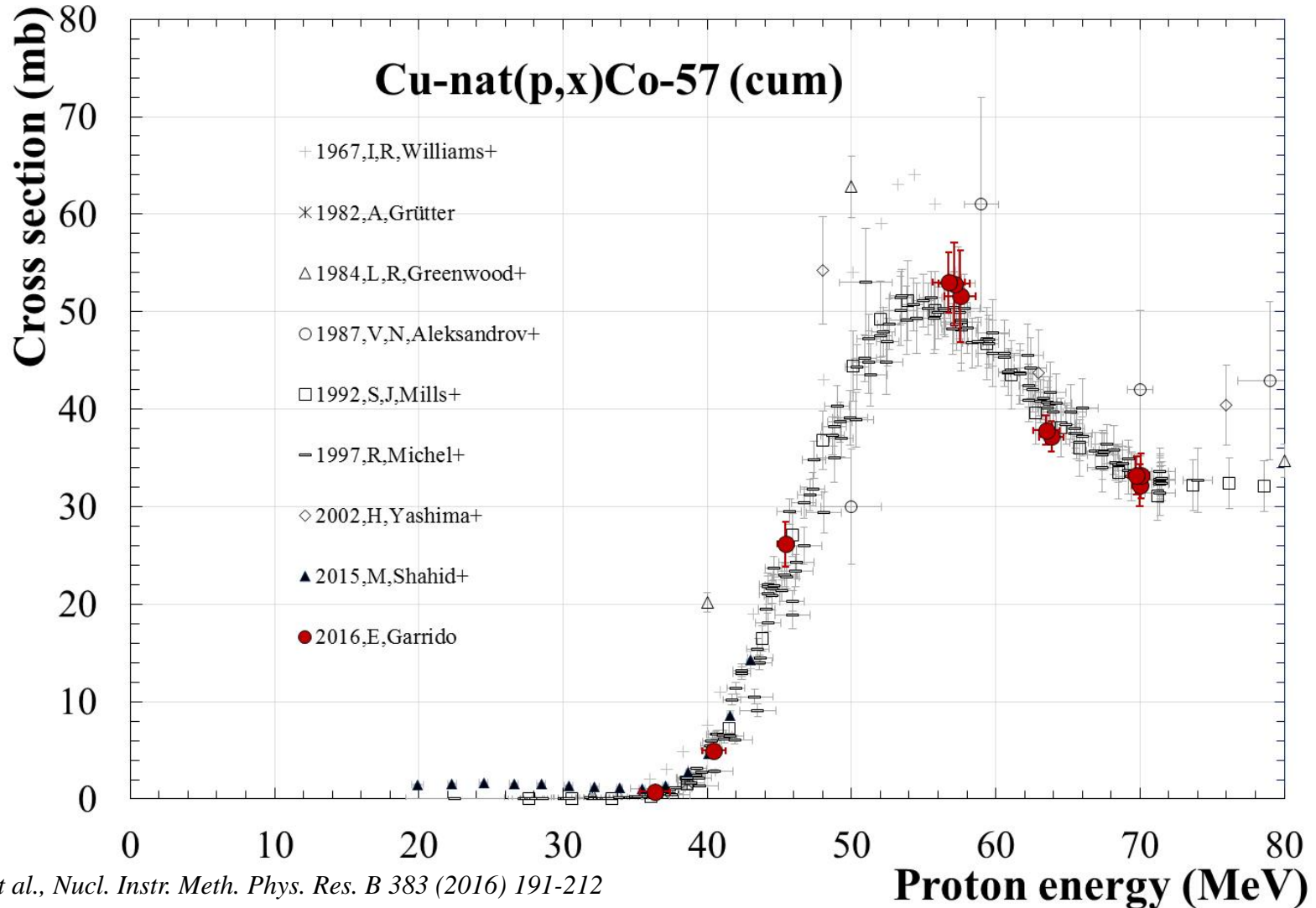


# Monitor reaction

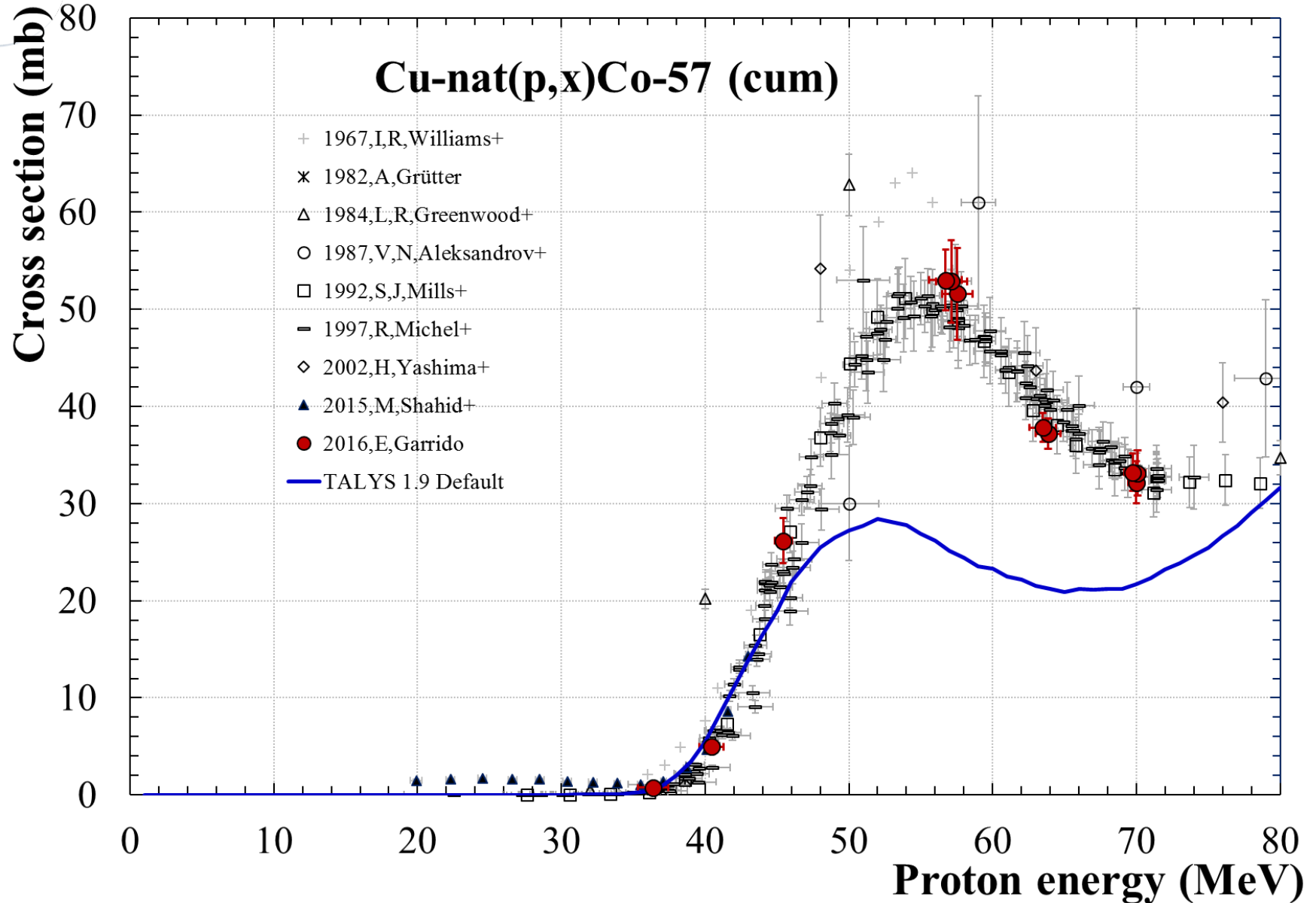
**Co-57 ( $T_{1/2} = 271.79$  d)**

EC process (100%) to stable Fe-57

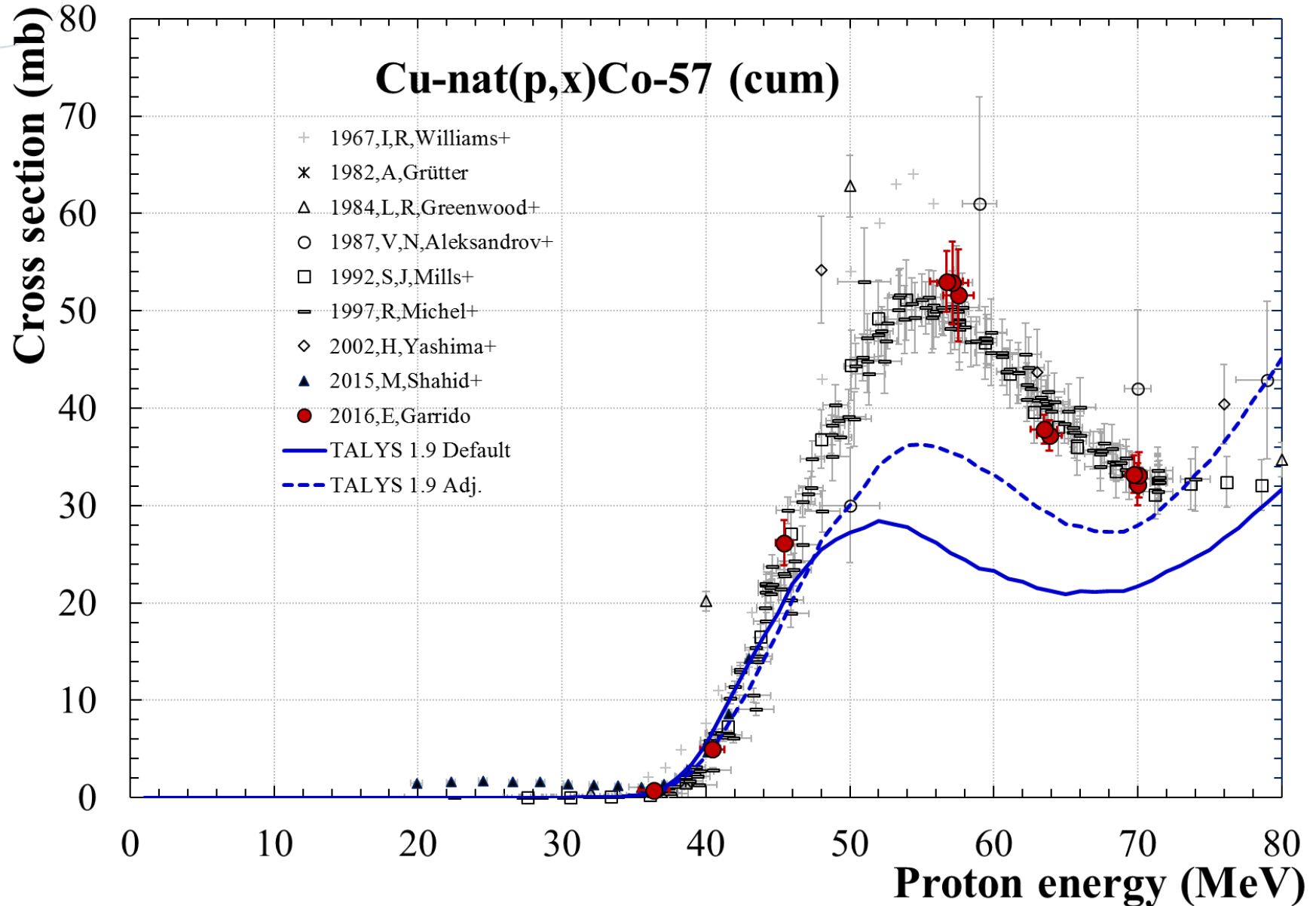
Suitable for proton monitor reaction



# Monitor reaction



# Monitor reaction

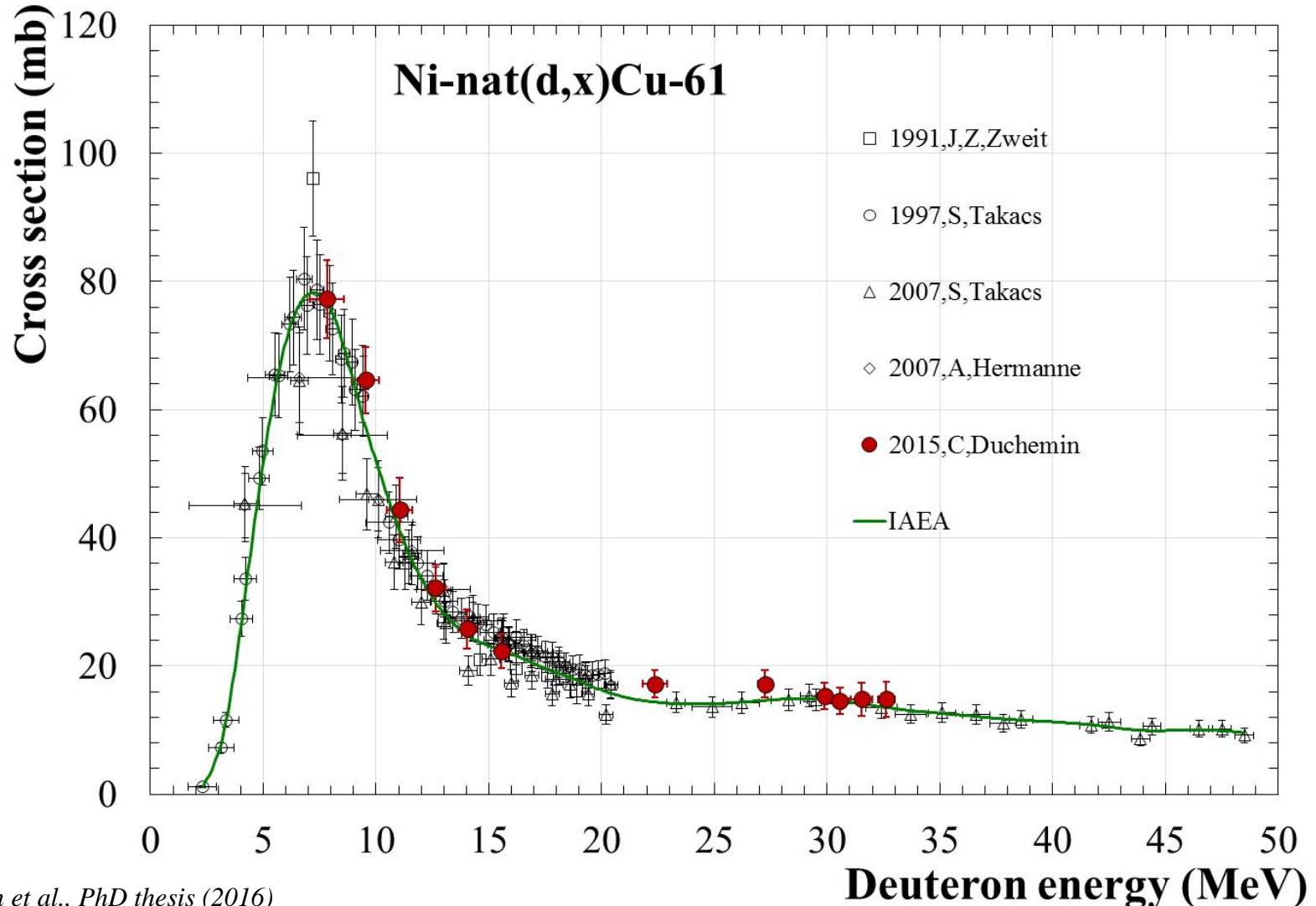


# Monitor reaction

**Cu-61 ( $T_{1/2} = 3.333$  h)**

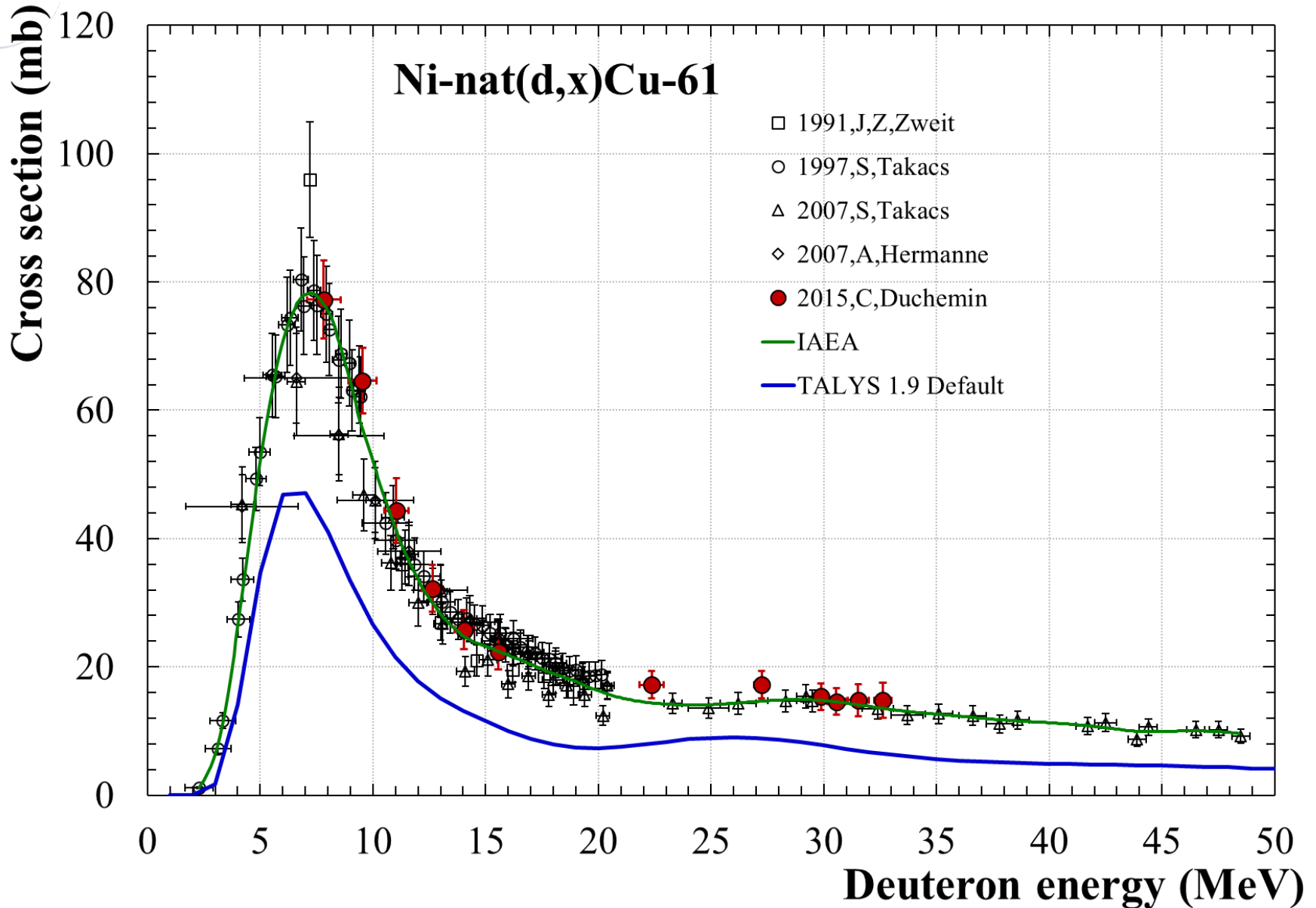
EC  $\beta^+$  processes to stable Ni-61

Suitable for PET imaging

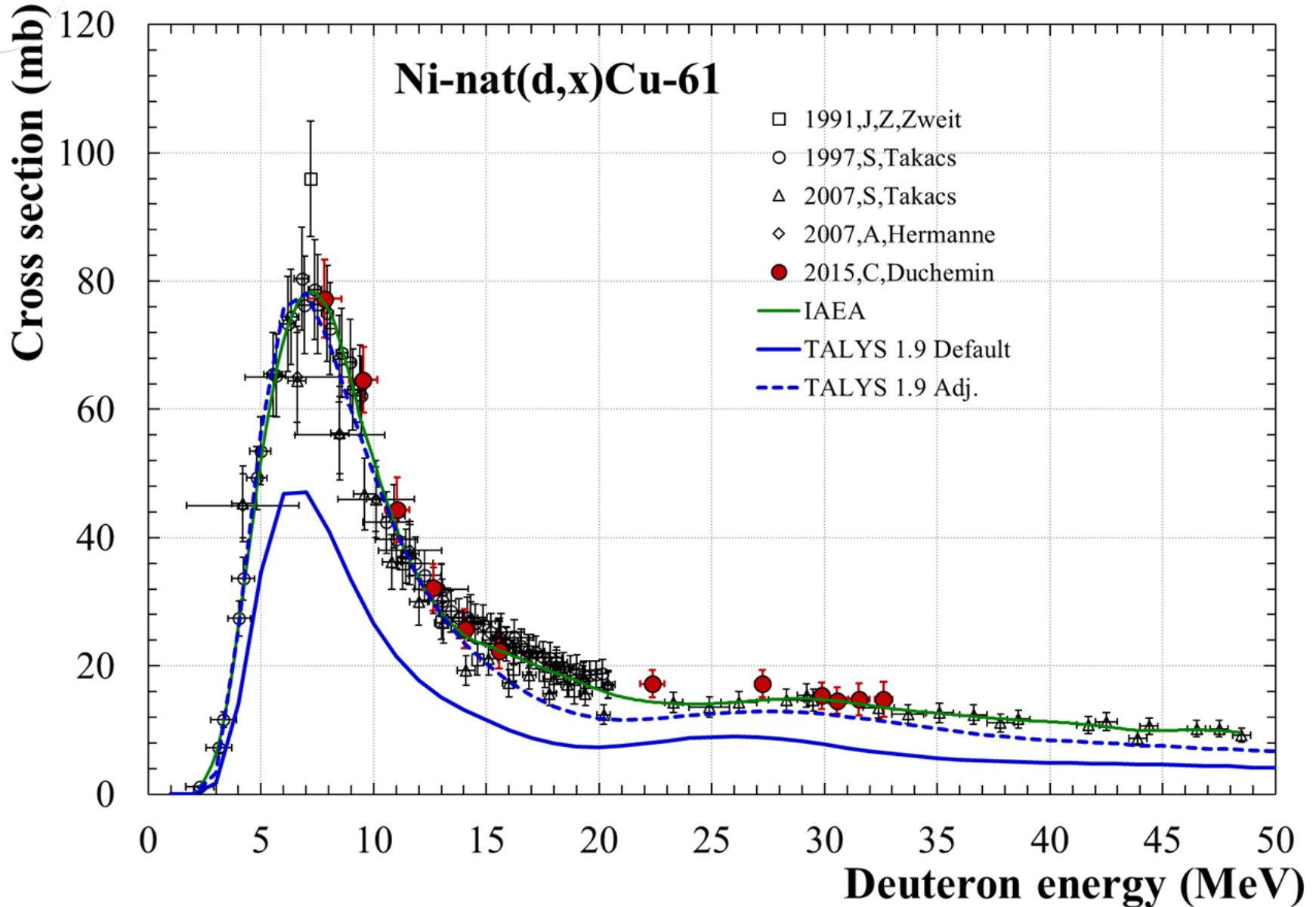


C. Duchemin et al., PhD thesis (2016)

# Monitor reaction



# Monitor reaction

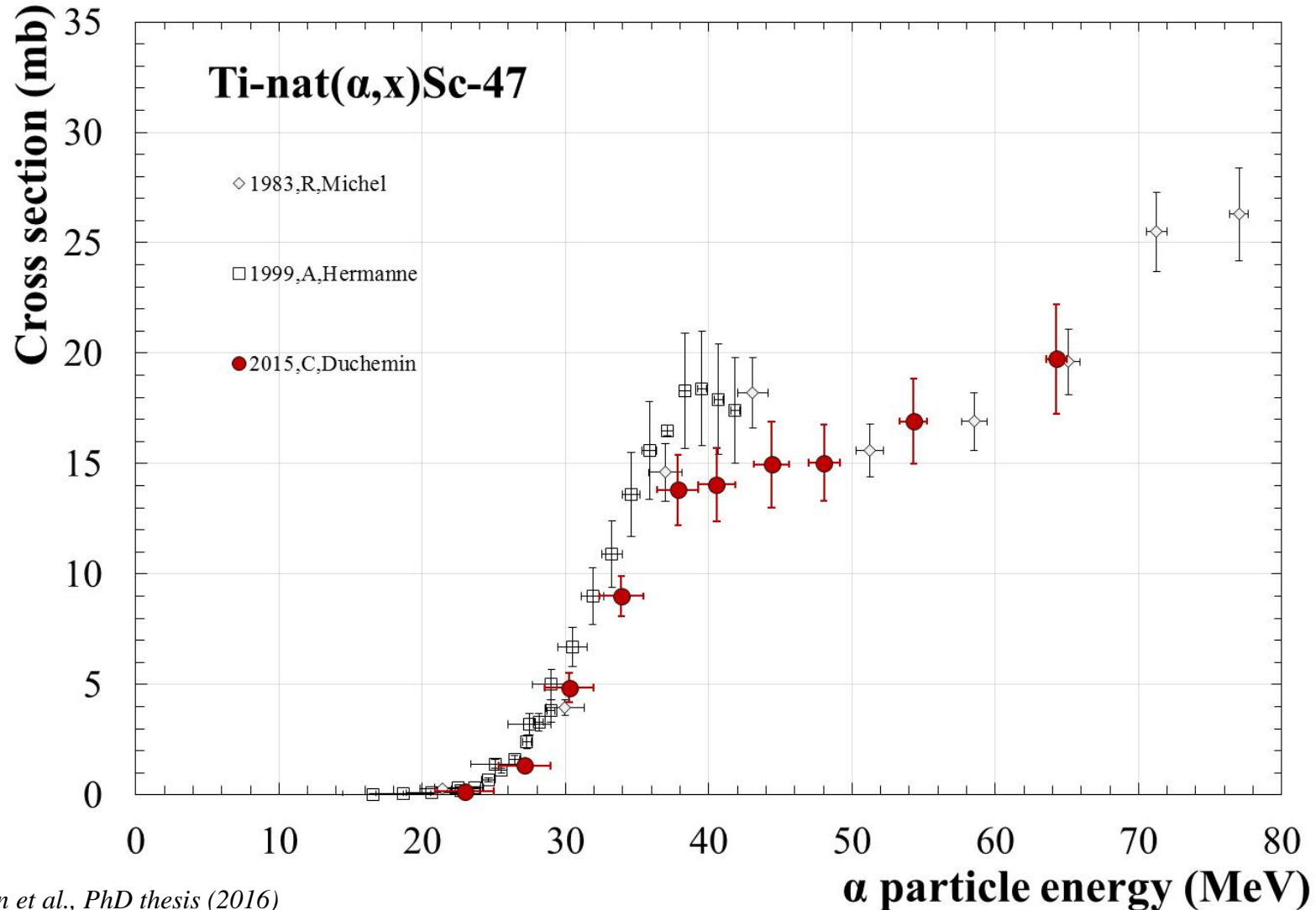


# Monitor reaction

**Sc-47 ( $T_{1/2} = 3.3492$  d)**

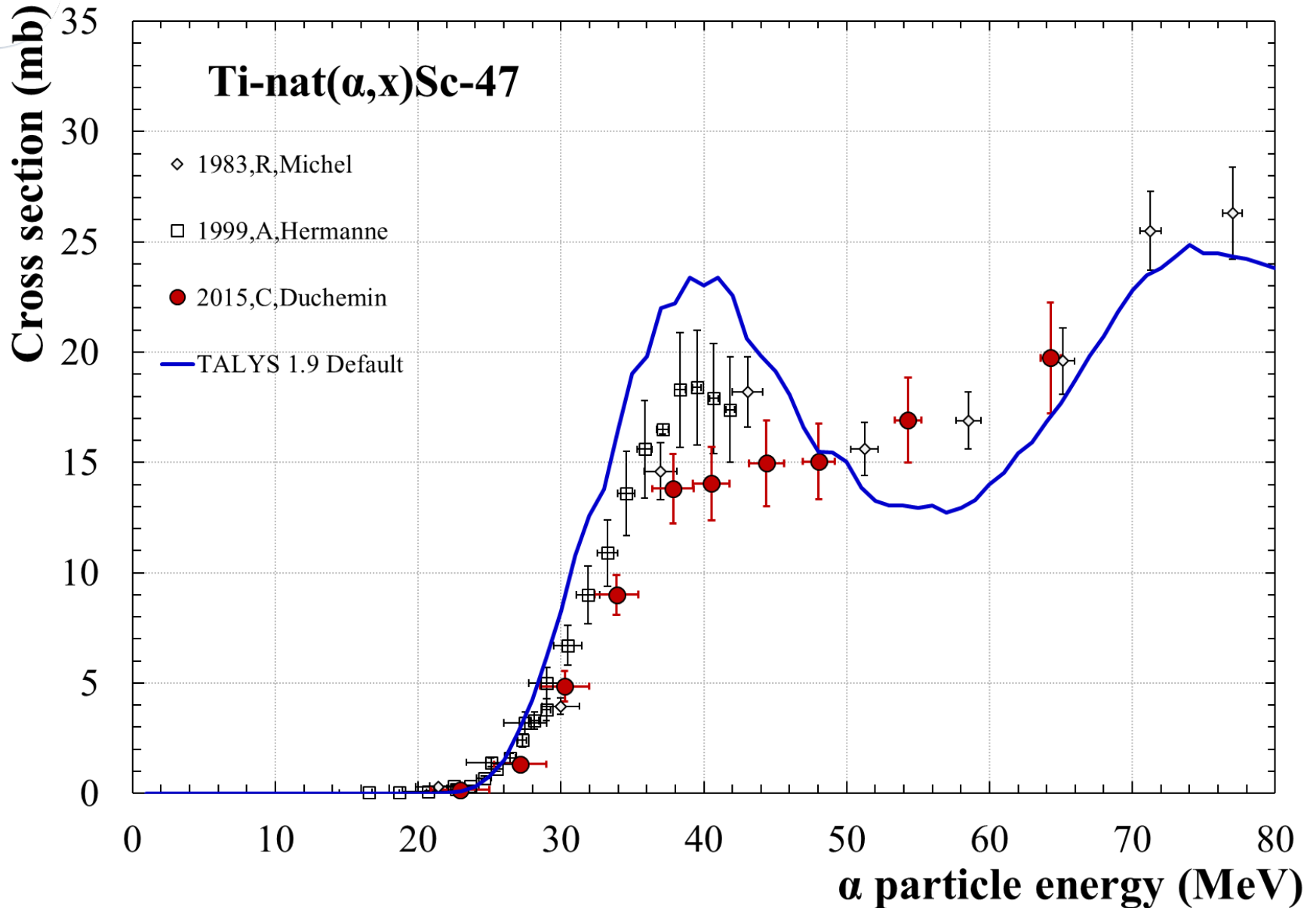
$\beta^-$  (100%) to stable Ti-47

Suitable for theranostic approach with the Sc-44

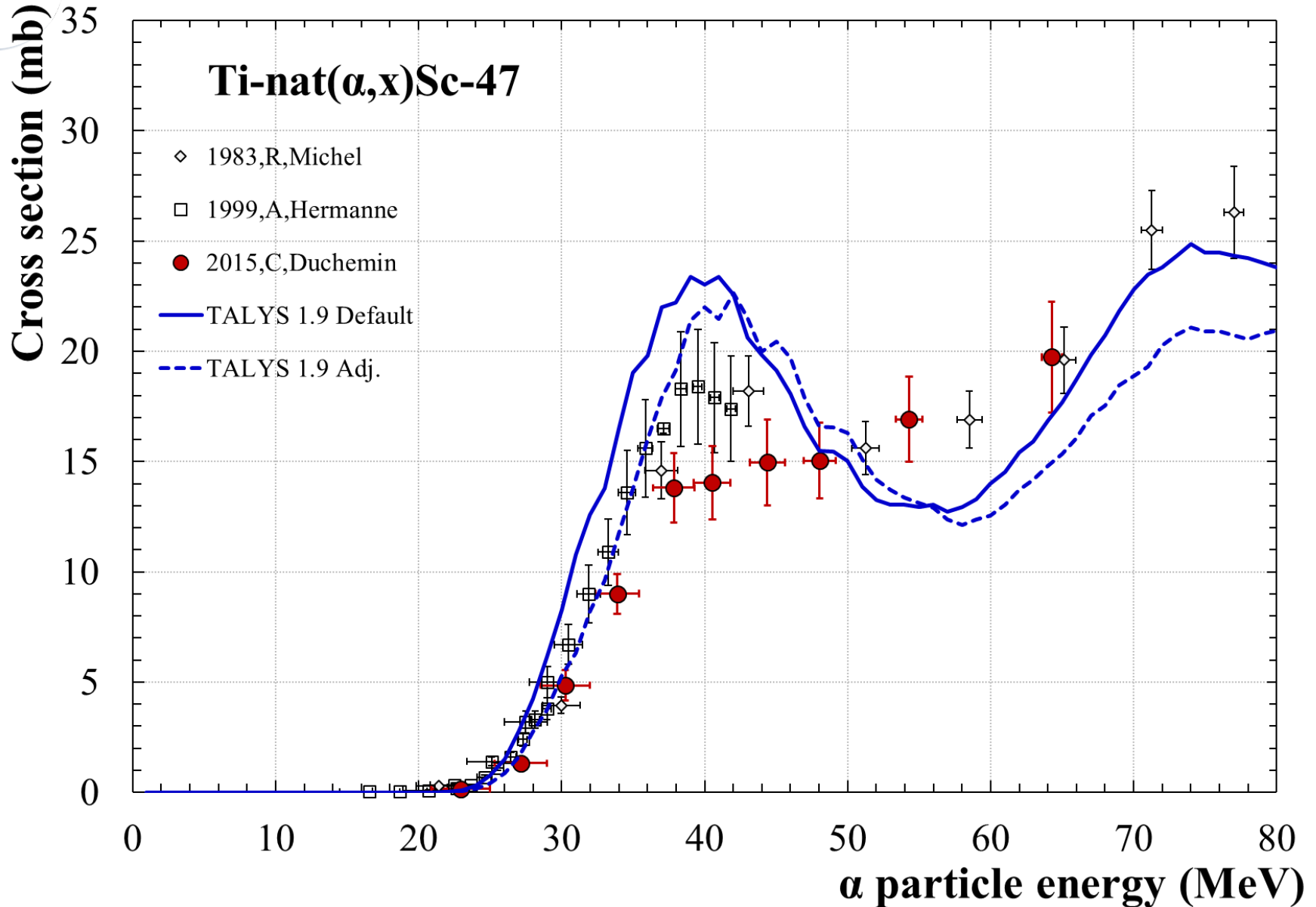




# Monitor reaction

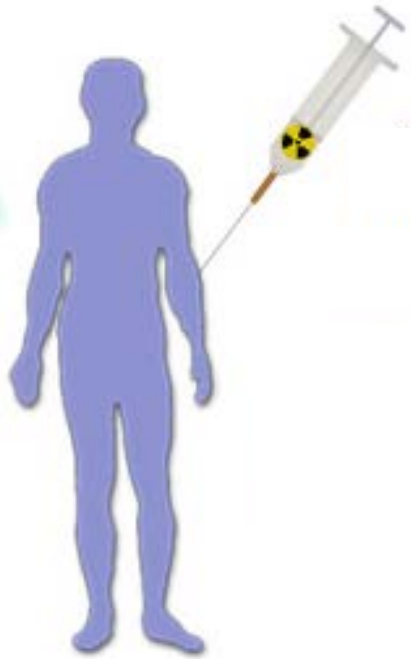


# Monitor reaction

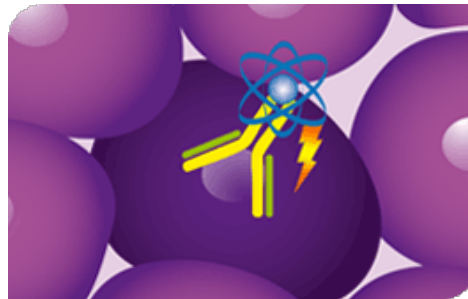
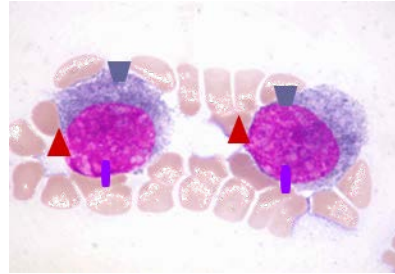


# Imaging and molecular radiotherapies

**Inject a tracer**



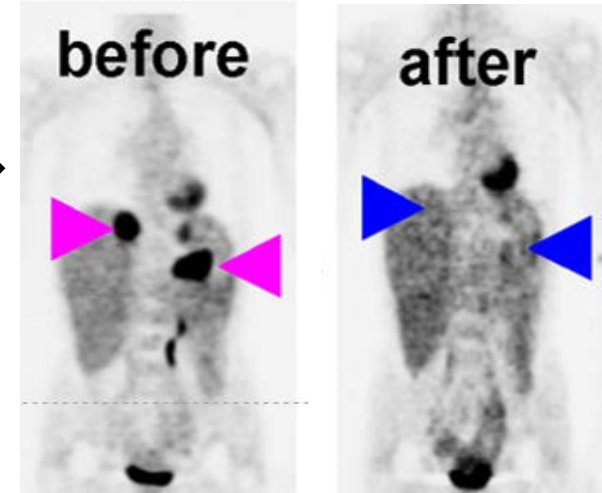
**Target a tumor marker**



*AREVA Med*

**Detect the disease**

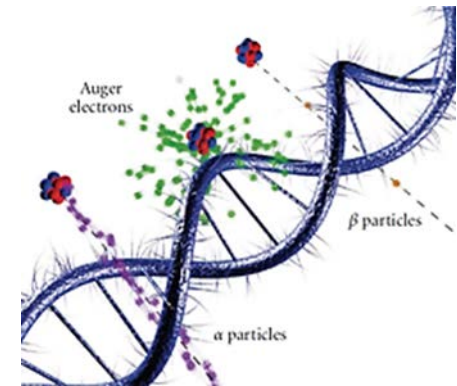
$\gamma, \beta^+$  →



*NIRS, Shiba, MIC*

**Treat the disease**

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



*B.Q. LEE et al.*

# Theranostic radiopharmaceuticals



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

Pharmaceuticals 2017, 10(2), 56

# Personalized nuclear medicine

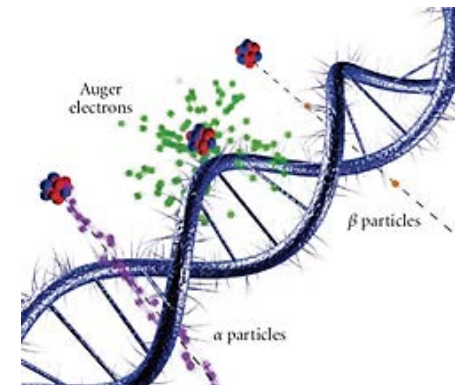
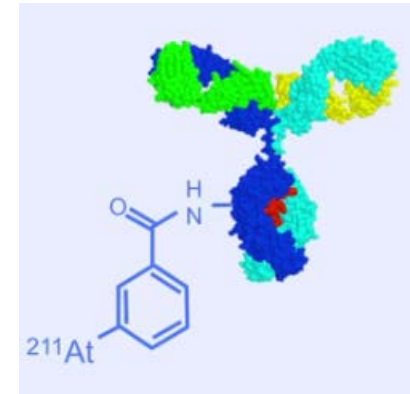
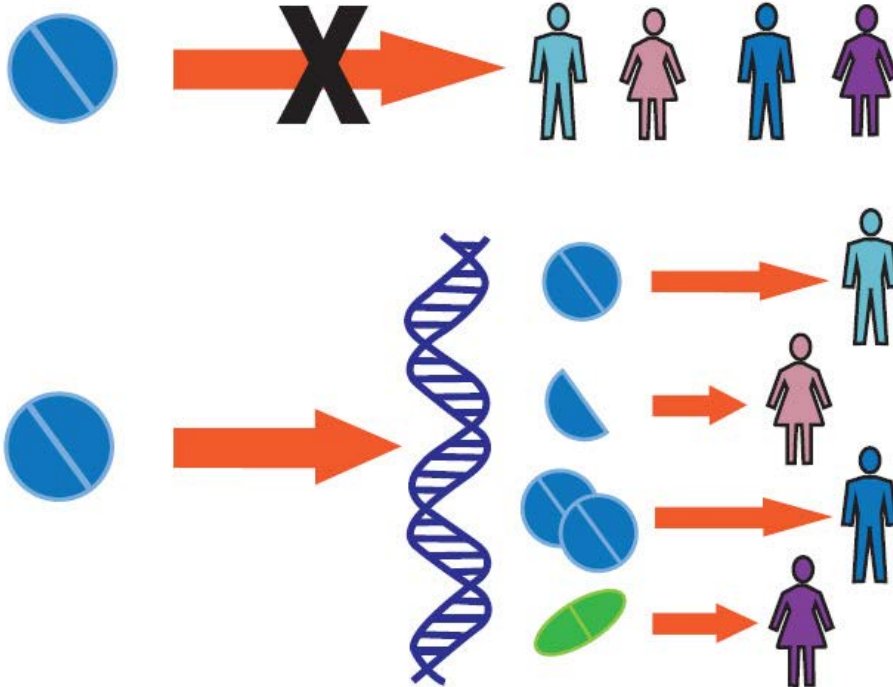
## Imaging and diagnosis

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**

## Imagery

### For SPECT

$\gamma$  emitters (100 – 250 keV)

$^{99m}\text{Tc}$ ,  $^{123}\text{I}$ ,  $^{201}\text{Tl}$

### For PET

$\beta^+$  emitters

$^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{18}\text{F}$ ,

$^{68}\text{Ge}$  ( $^{68}\text{Ga}$ ),  $^{82}\text{Sr}$  ( $^{82}\text{Rb}$ )

$^{64}\text{Cu}$ ,  $^{124}\text{I}$

## Therapy

$\beta^-$  emitters ( $^{32}\text{P}$ ,  $^{90}\text{Y}$ ,  $^{131}\text{I}$ ,  $^{153}\text{Sm}$ ,  $^{177}\text{Lu}$ )

$\alpha$  emitter ( $^{211}\text{At}$ )

Auger electron emitters ( $^{67}\text{Ga}$ ,  $^{111}\text{In}$ ,  $^{125}\text{I}$ )

X-ray emitter ( $^{103}\text{Pd}$ )

