Production of innovative radionuclides for therapy or diagnostic: nuclear data measurements and comparison with TALYS code

Arnaud Guertin, Etienne Nigron, Mateusz Sitarz, Charlotte Duchemin, Ferid Haddad, Vincent Métivier

GUERTIN Arnaud
Subatech Laboratory – UMR 6457
CNRS Research Officer

IN2P3
Institut national de physique nucléaire et de physique des particules

Production of innovative radionuclides for therapy or diagnostic: nuclear data measurements and comparison with TALYS code

A. Guertin et al.

UNIVERSITÉ DE NANTES

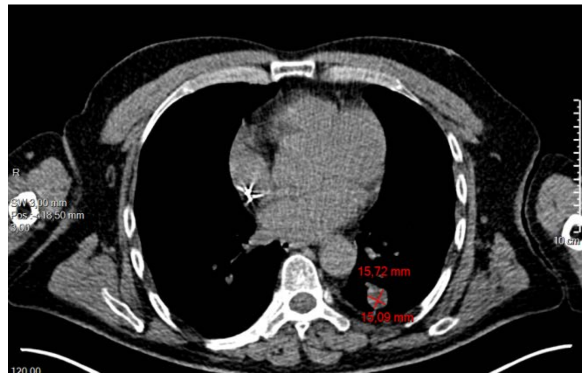
IMT Atlantique
Bretagne-Pays de la Loire
École Mines-Télécom

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

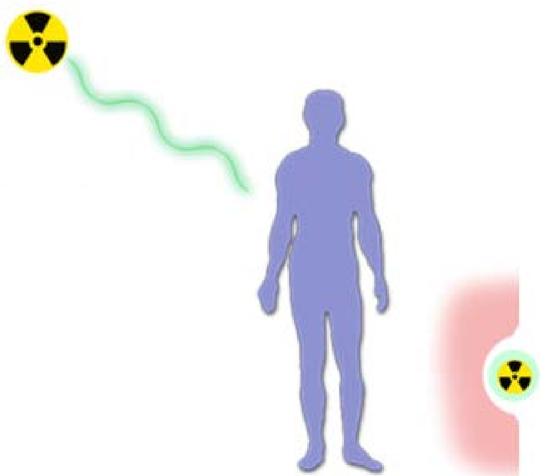
Magnetic Resonance Imaging

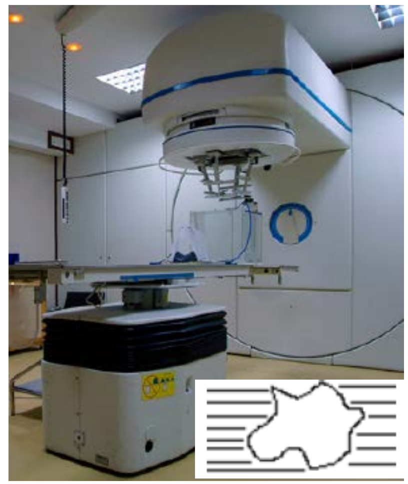
These techniques allow to get accurate information on the morphology but give limited information on the metabolism

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

Conventional radiotherapy

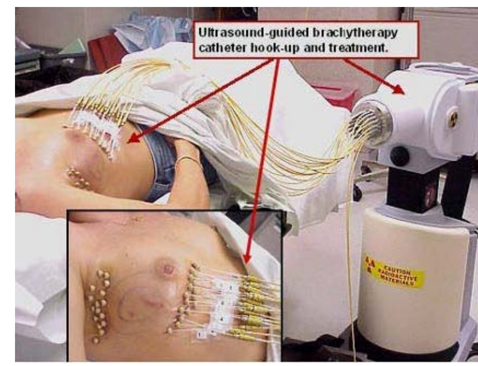
External beam radiotherapy:
- X rays, gamma, electrons
- Hadrontherapy





Institut de cancérologie de l'Ouest

ProteusOne, IBA



Institut de cancérologie de l'Ouest

Brachytherapy
Curietherapy

These techniques are very efficient to treat a localized disease

Limit: does not target disseminated disease or residual disease

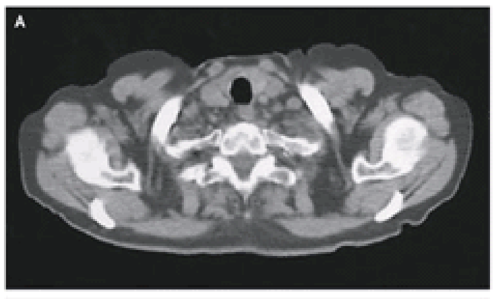
This can be address by nuclear medicine techniques

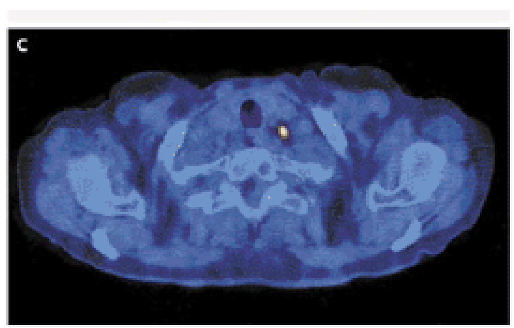
Great progress in the last ten years

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

Morphology

Metabolism





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

Motivations

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 (γ, β^+)
- Therapy (β^-, α, e_{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

Motivations

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**
- Production yields to get the **purest product**
- Prod. capacities to envisaged **large scale use**

The nuclear physicist could have crucial contribution:

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

Over the last years, several radionuclides have emerged:

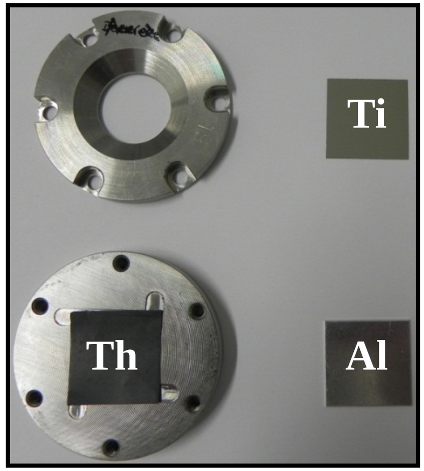
- β^+: Cu-64, Ga-68, Zr-89 …
- γ: Sn-117m …
- β^-: Ho-166, Lu-177 …
- α: At-211, Bi-212, Bi-213, Ra-223, Ac-225 ...
- **Theranostic**: Sc-44/Sc-47, Cu-64/Cu-67, Ga-68/Lu-177 …
- **Auger**: Sn-117m, Tb-155 (at the research level for the moment)
  Terbium quadruplet: Tb-149, 152, 155, 161

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

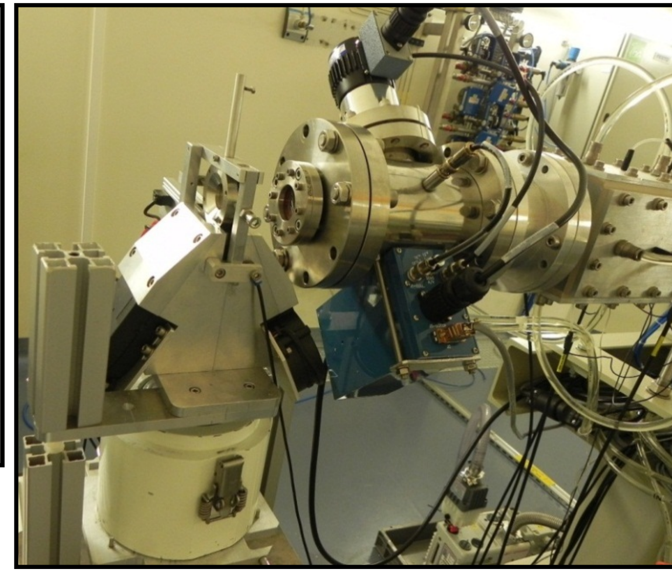
Stacked-foil technique

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:

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

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:

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

- error on e, e’: ≤ 1%
- error on t: negligible

IAEA recommended cross sections:

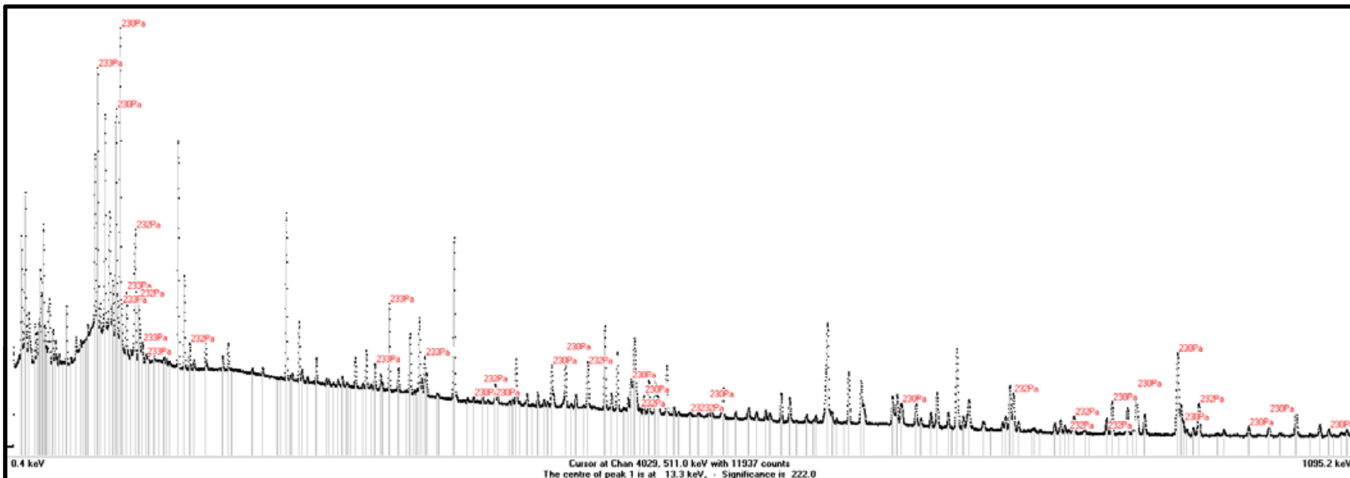
- 11 reactions available for protons
  ^{27}Al (2), ^{nat}Ni, ^{nat}Ti (2), ^{nat}Cu (5), ^{nat}Mo
- 11 reactions available for deuterons
  ^{27}Al (2), ^{nat}Fe, ^{nat}Ni(3), ^{nat}Cu (5), ^{nat}Ti(2)
- 6 reactions available for alpha-particles
  ^{27}Al (2), ^{nat}Ti and ^{nat}Cu (3)

Stacked-foil technique

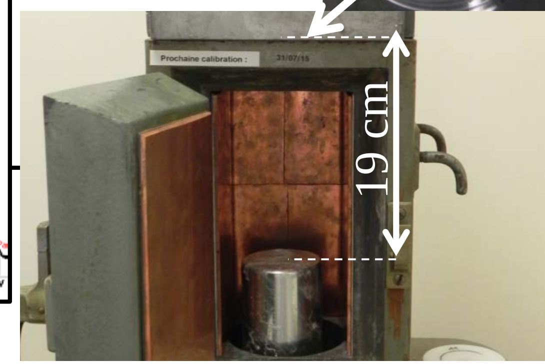
Off line gamma spectroscopy

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

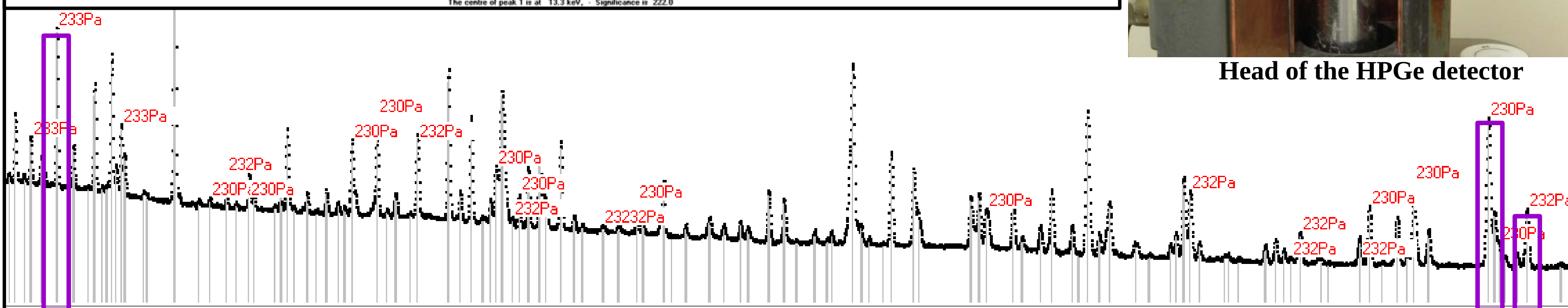
- γ spectra recorded on **8192 channels**
- FWHM: 1.04 keV at 122 keV (^{57}Co)
1.97 keV at 1332 keV (^{60}Co)
- Energy and efficiency calibrations: Co and Eu



Target and monitor:
- ✓ counted twice
- ✓ during > 24 hrs
- ✓ 2 week delay



Head of the HPGe detector



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

Collected data sets

Proton induced reactions:

Ac-225 from Th-232(p,x) — C. Duchemin et al, Phys Med Biol **60** (2015) **931-946**

Ra-223 from Th-232(p,x) — 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**

Monitor reactions on Ti, Ni and Cu — E. Garrido et al., Nucl Instr Meth Phys Res B **383** (2016) **191-212**

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 — C. Duchemin et al, Appl Radiat Isot **103** (2015)**160-165**

"Production cross section of ^{197m}Hg induced by deuterons on natural gold target", Etienne Nigron, Friday morning, deuteron induced reaction

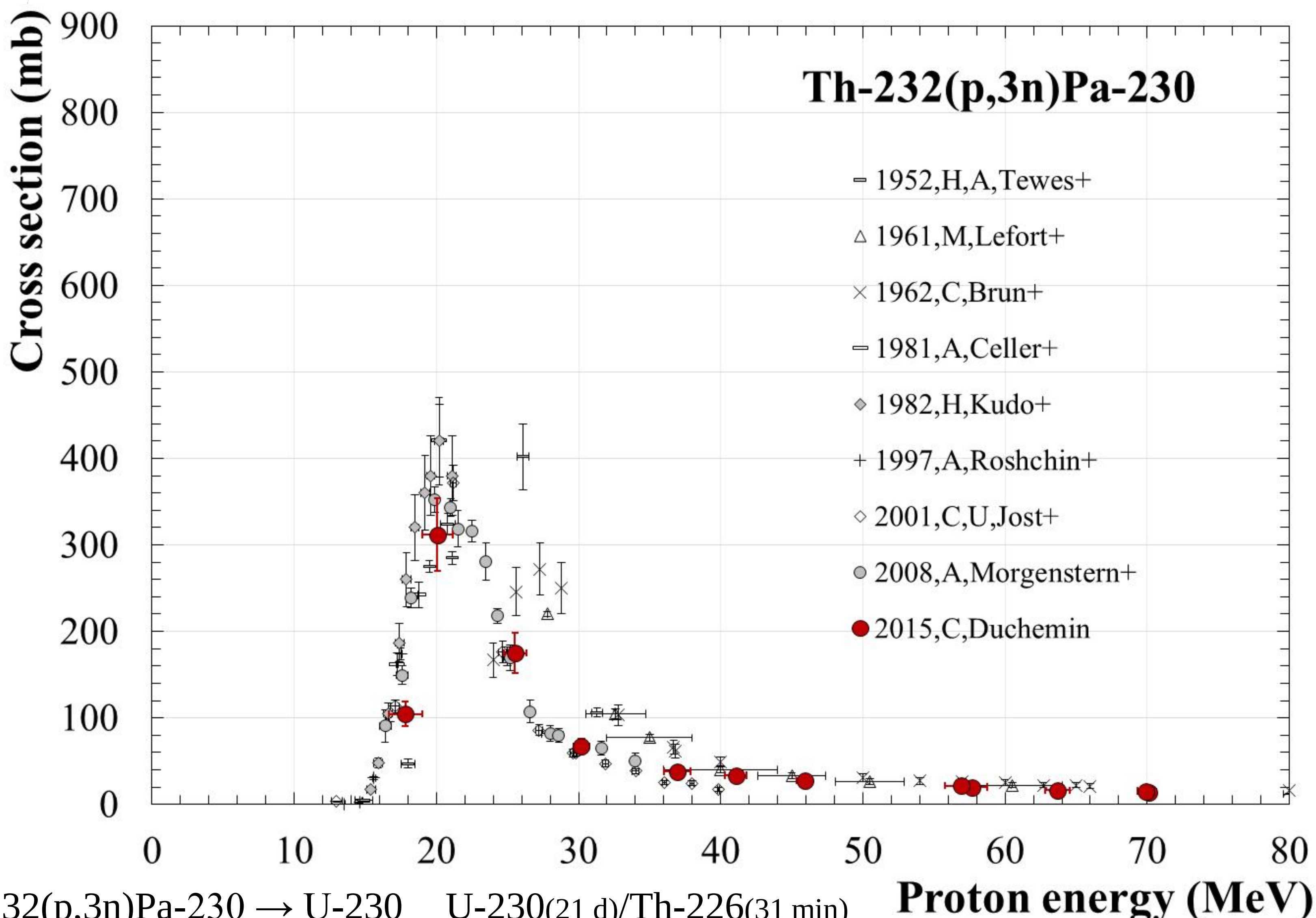
Alpha induced reactions:

Sn-117m from Cd-116(α,x) — C.Duchemin et al, Appl Radiat Isot **115** (2016) **113-124**

Monitor reactions on Cu, Ti, Ni

"Production of medically interesting ^{97}Ru via ^{nat}Mo(alpha,x) above 40 MeV at ARRONAX", Mateusz Sitarz, today, in this session medical radioisotopes

Pa-230 as a precursor of an α generator



Th-232(p,3n)Pa-230 → U-230 U-230(21 d)/Th-226(31 min)

α RIT for leukaemia treatment 4 α cascade of 27.7 MeV *C. Duchemin et al., Phys. Med. Biol. 60 (2015) 931-946*

TALYS

TALYS

Code for the simulation of nuclear reactions

Projectiles : n, p, d, t, He-3, α particles

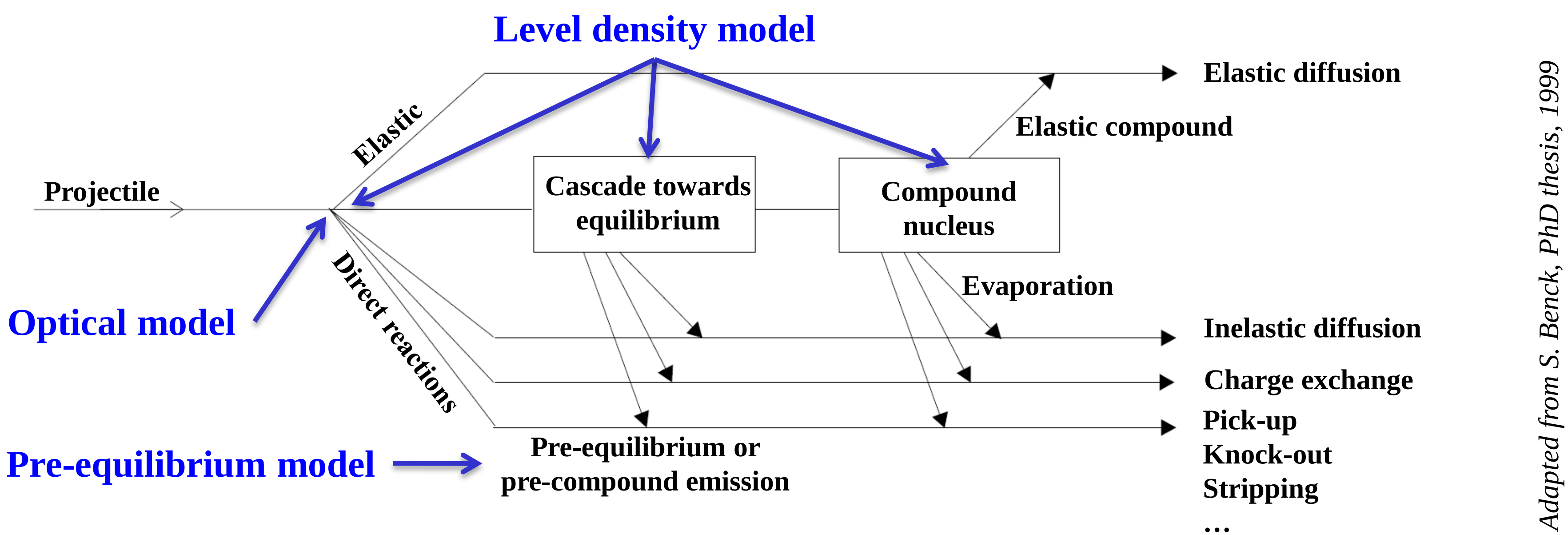
Many state-of-the-art nuclear models

Energy : 1 keV to 1 GeV

Provide a complete description of all reactions channels and observables

Targets : Z = 3 to 110

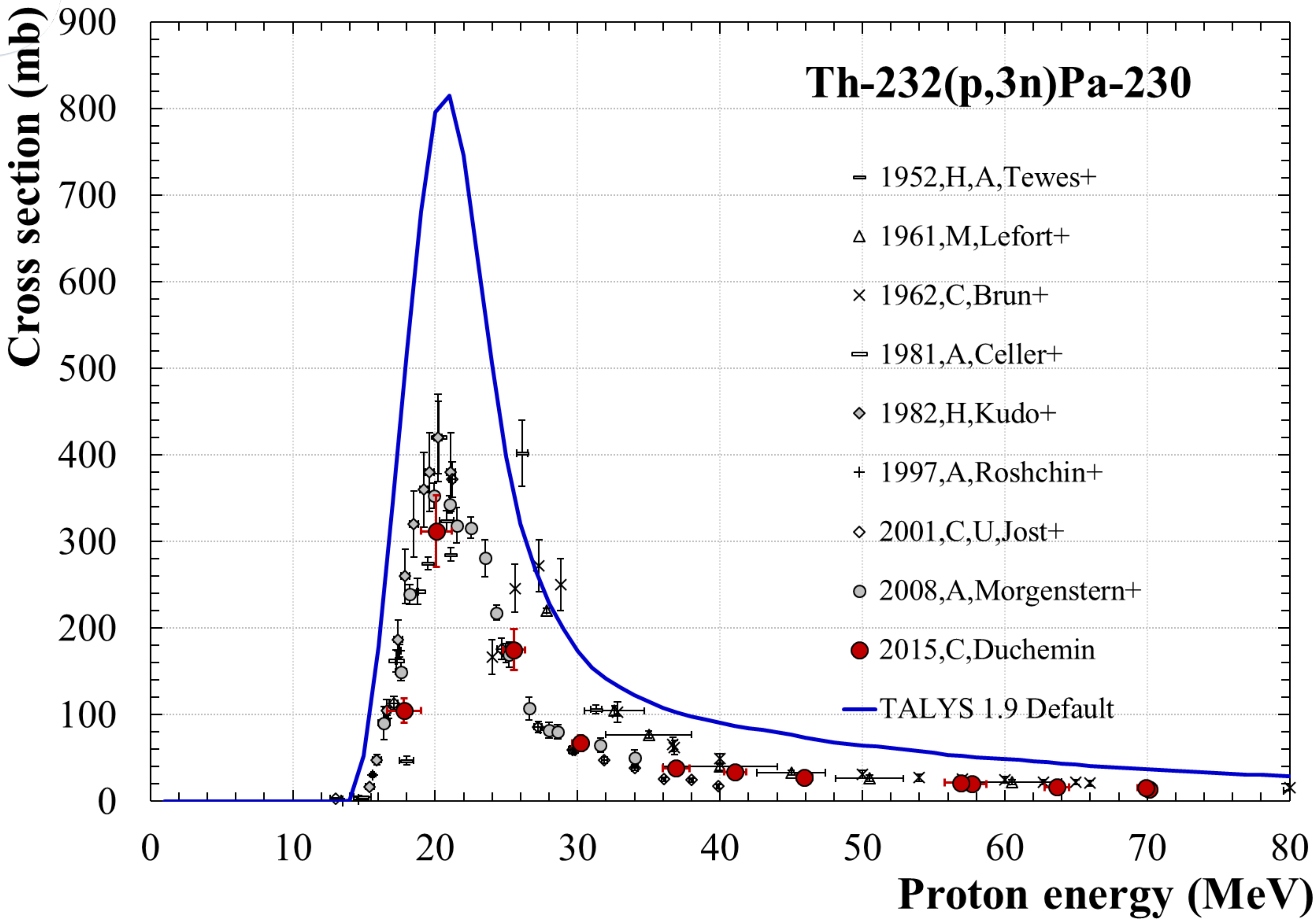
Nuclear reactions



⇨ Influence on the calculated production cross section values

Koning A.J. and Rochman D., Nucl. Data Sheets, 113, 2012

Pa-230 as a precursor of an α generator



TENDL2015

TENDL2015

Nuclear data library based on both default and adjusted TALYS calculations and data from other sources

By A.J. Koning[1], D. Rochman[2], J. Kopecky[3], J.Ch. Sublet[4], M. Fleming[4], E. Bauge[7], S. Hilaire[7], P. Romain[7], B. Morillon[7], H. Duarte[7], S.C van der Marck[6], S. Pomp[5], H. Sjostrand[5], R. Forrest[1], H. Henriksson[8], O. Cabellos[9], S. Goriely[10], J. Leppanen[11], H. Leeb[12], A. Plompen[13], and R. Mills[14]

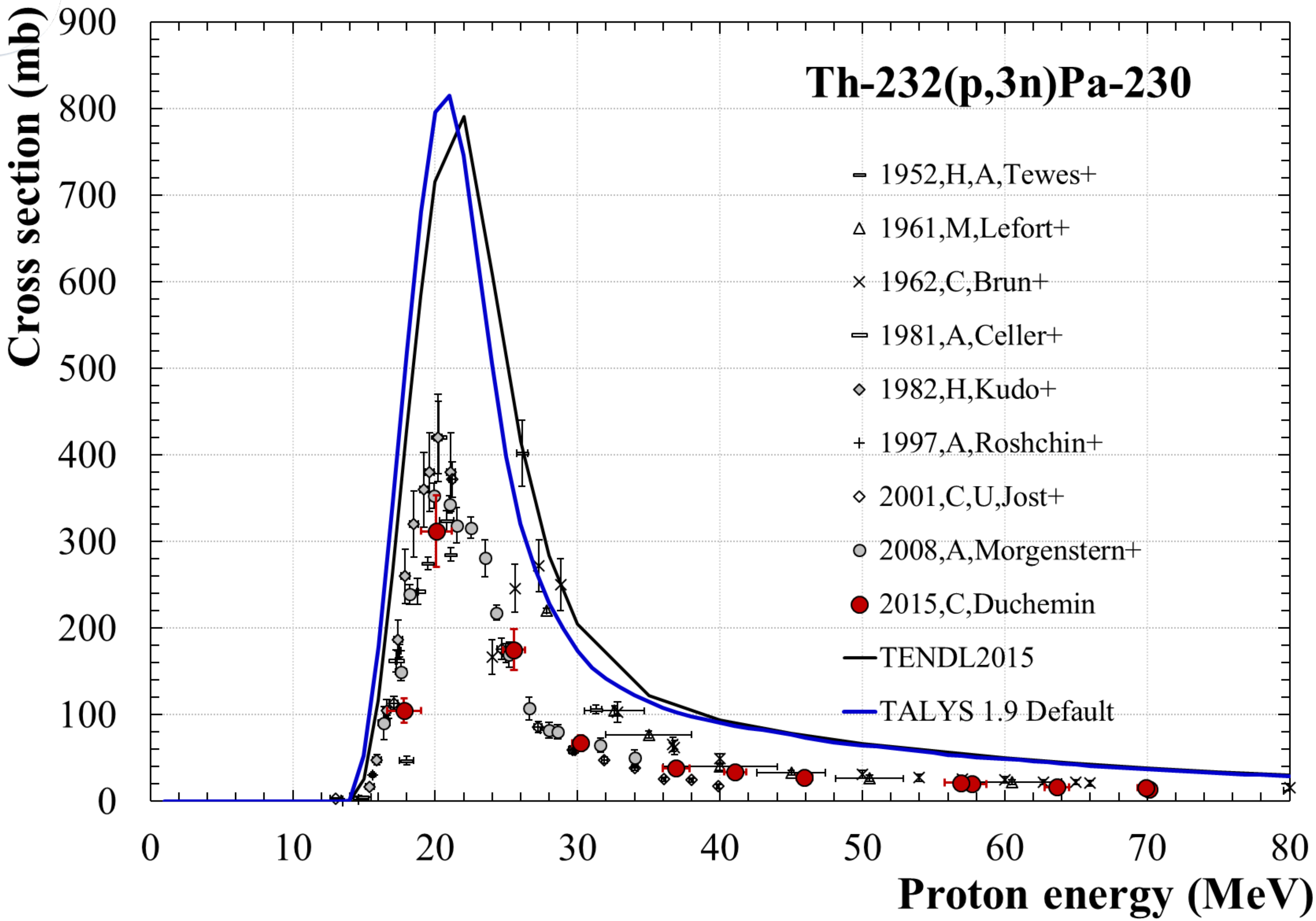
[1] IAEA, [2] PSI, [3] JUKO Research, [4]CCFE, [5]Uppsala Univ., [6]NRG, [7]CEA, [8]Vattenfall, [9]NEA, [10]ULB, [11]VTT, [12]ATI, [13]IRMM, [14]NNL.

TENDL2015 contains evaluations for :

- seven types of incidents particles (n, p, d, t, He-3, alpha-particle, gamma ray)
- all isotopes living more than 1 second (~ 2800 isotopes)
- all files are original except 15 (natural carbon from JENDL-4.0, ^{1,2,3}H, ^{2,3}He, ^{6,7}Li, ^{10,11}B, ^{9}Be, ^{14,15}N, ^{16}O and ^{19}F from ENDF/B-VII.1)

Koning A.J. et al., https://tendl.web.psi.ch/tendl_2015/tendl2015.html
Koning A.J. and Rochman D., Nucl. Data Sheets, 113, 2012

Pa-230 as a precursor of an α generator



TALYS

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

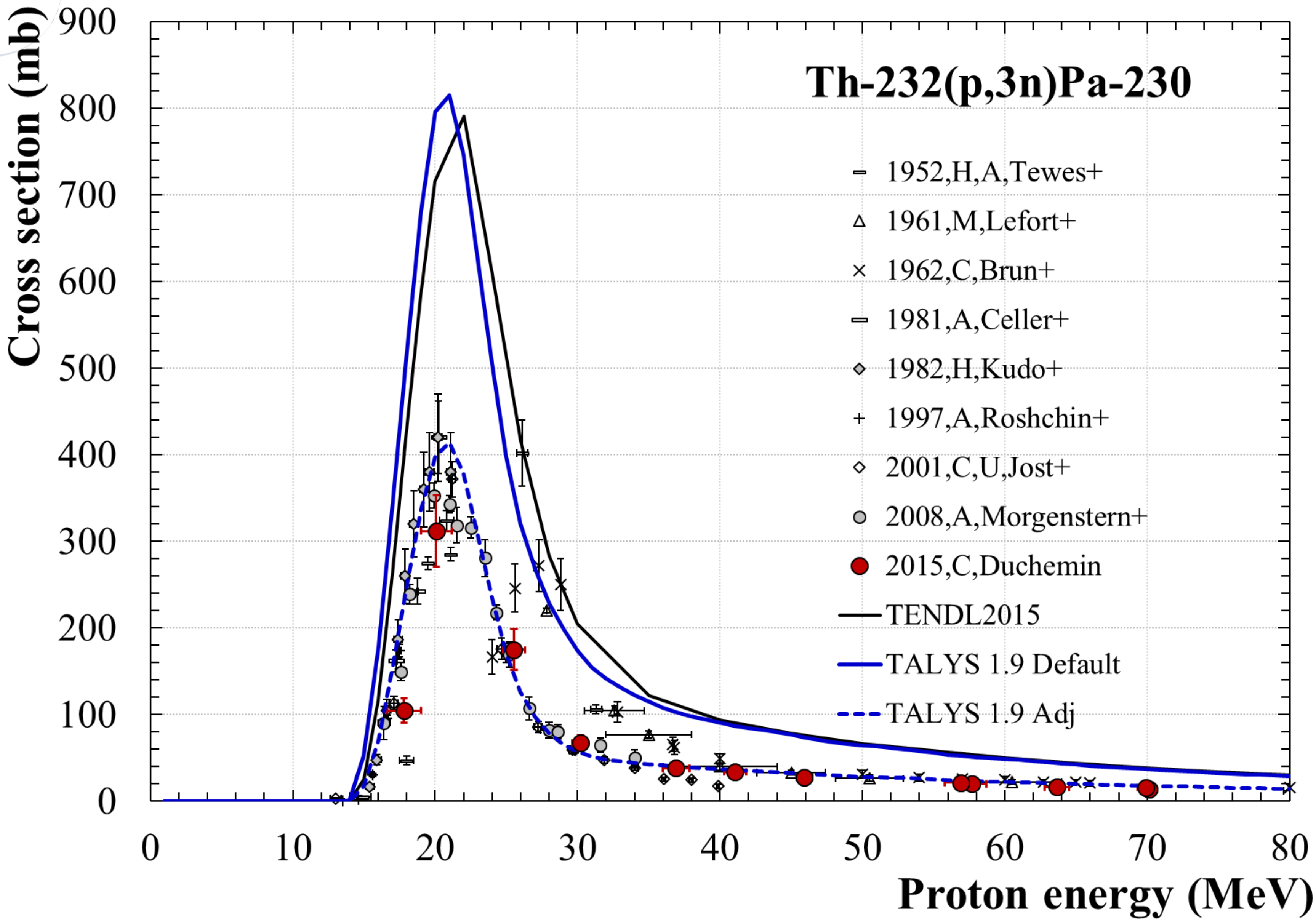
⇨TALYS 1.9 Default

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)
	α (8)	V. Avrigeanu et al. (2014)	Demetriou et al. (2002)
Pre-equilibrium	All (4)	Two-component exciton model Numerical transition rates with E-dependent matrix element A.J. Koning and M.C. Duijvestijn (2004)	Two –component exciton model Numerical transition rates with optical model for collision probabilities A.J. Koning and M.C. Duijvestijn (2004)
Level density	All (6)	Constant temperature and Fermi gas model A.J. Koning et al. (2008)	Microscopic level density (Skyrme force) from Hilaire's combinatorial tables Goriely et al. (2008)

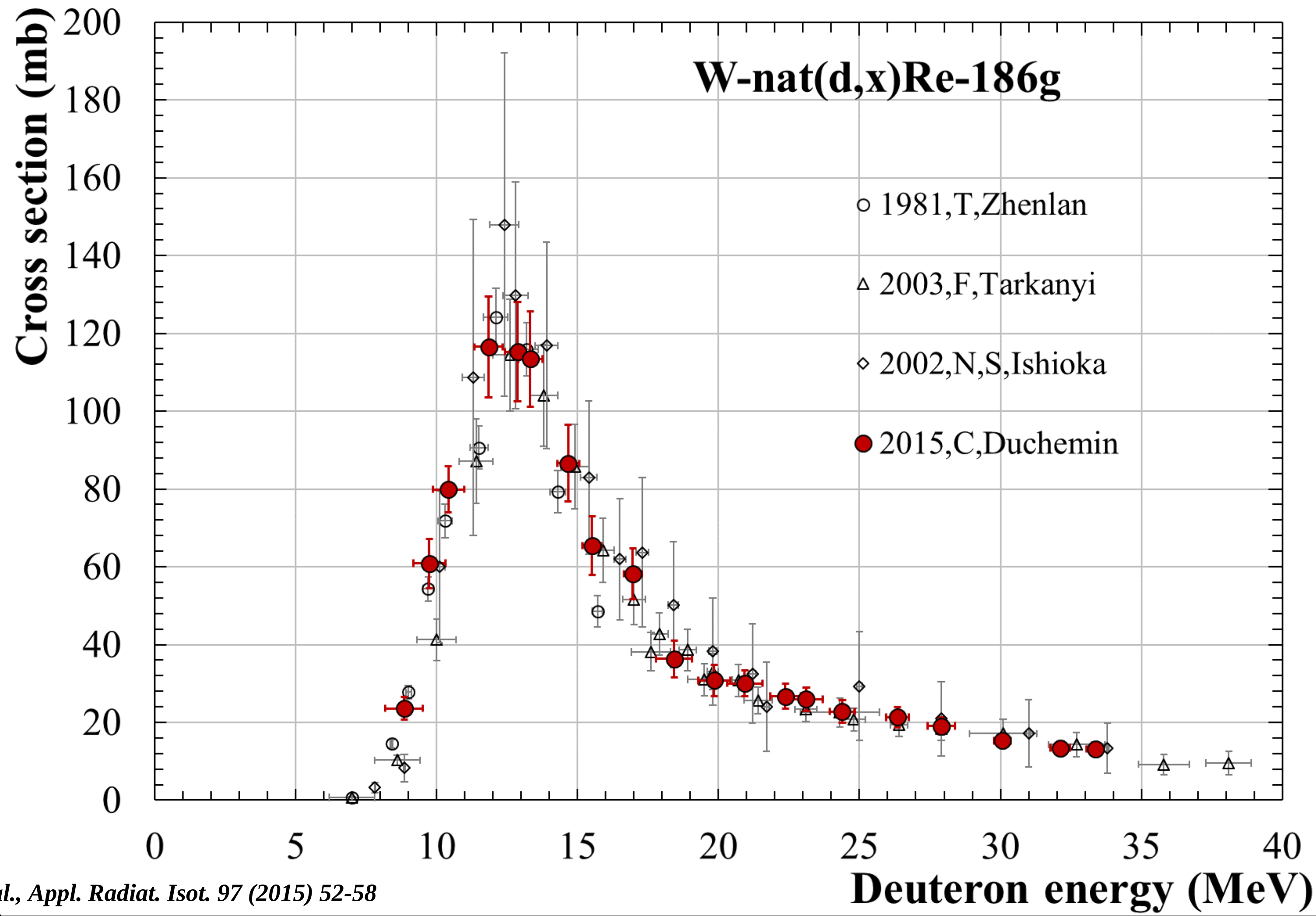
Pa-230 as a precursor of an α generator



Re-186g: proton/deuteron production route

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

β- emitter used in clinical trials for the palliation of painful bone metastases resulting from prostate and breast cancer

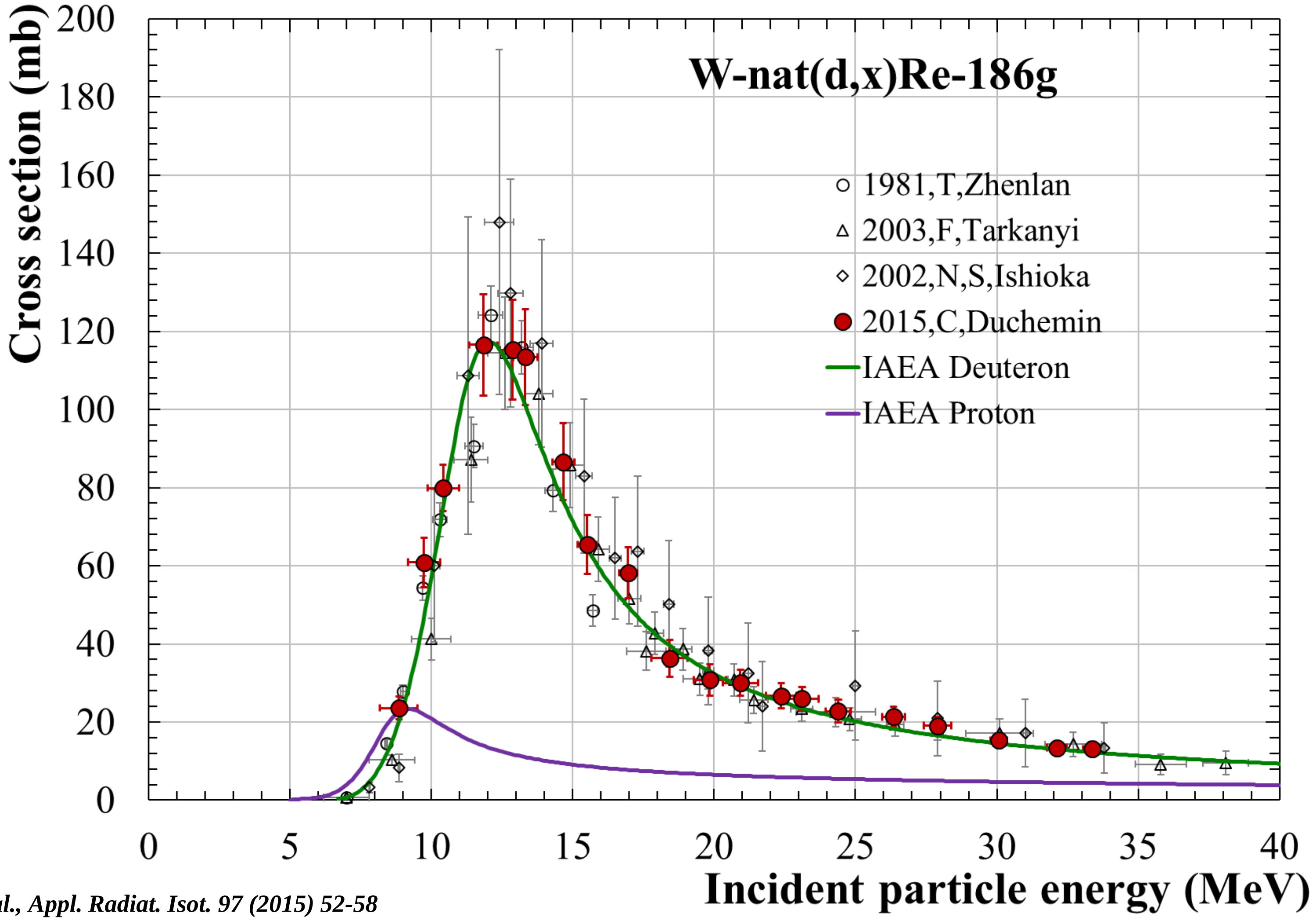


C. Duchemin et al., Appl. Radiat. Isot. 97 (2015) 52-58

Re-186g: proton/deuteron production route

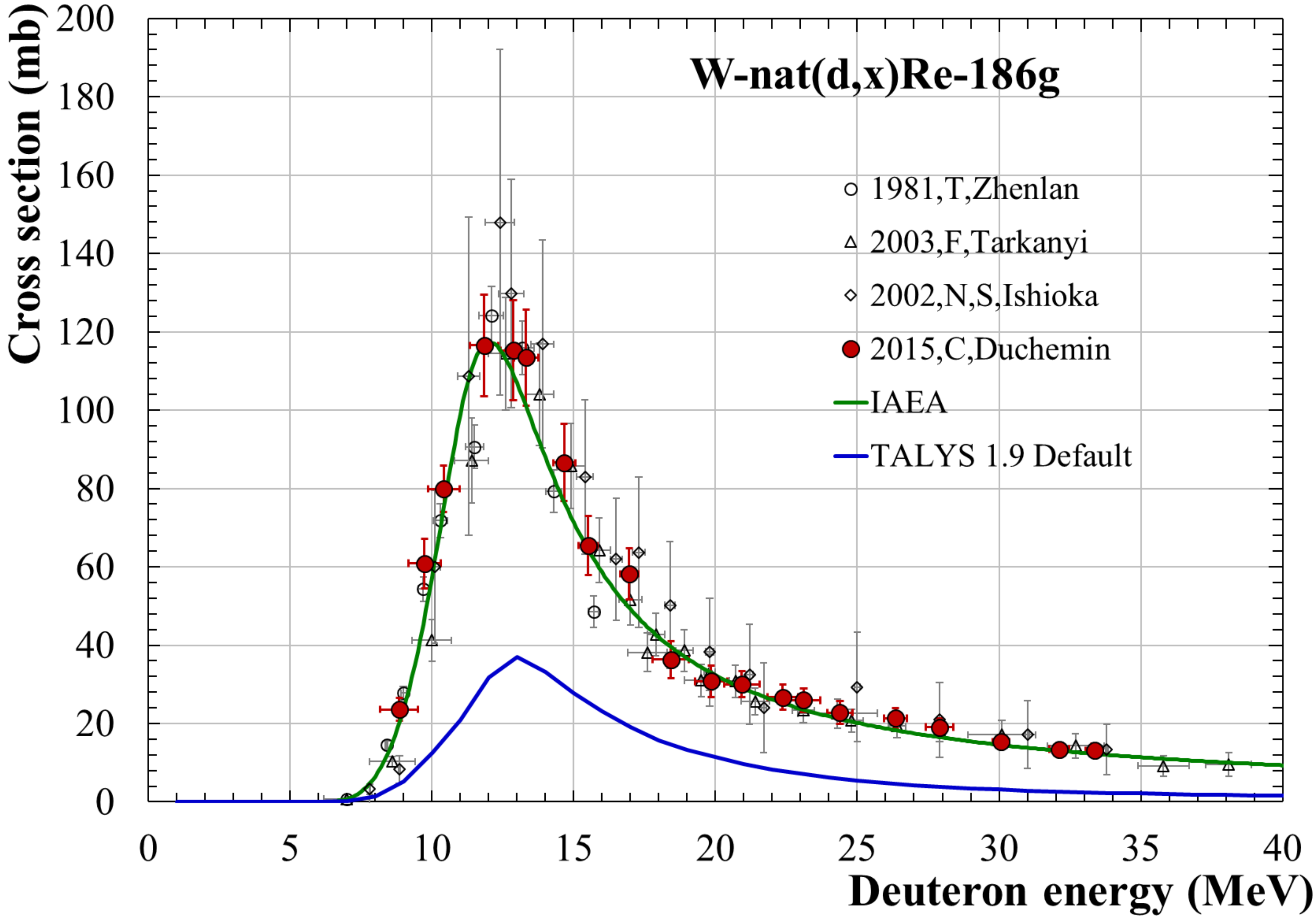
Re-186g ($T_{1/2}$ = 3.7 d)

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

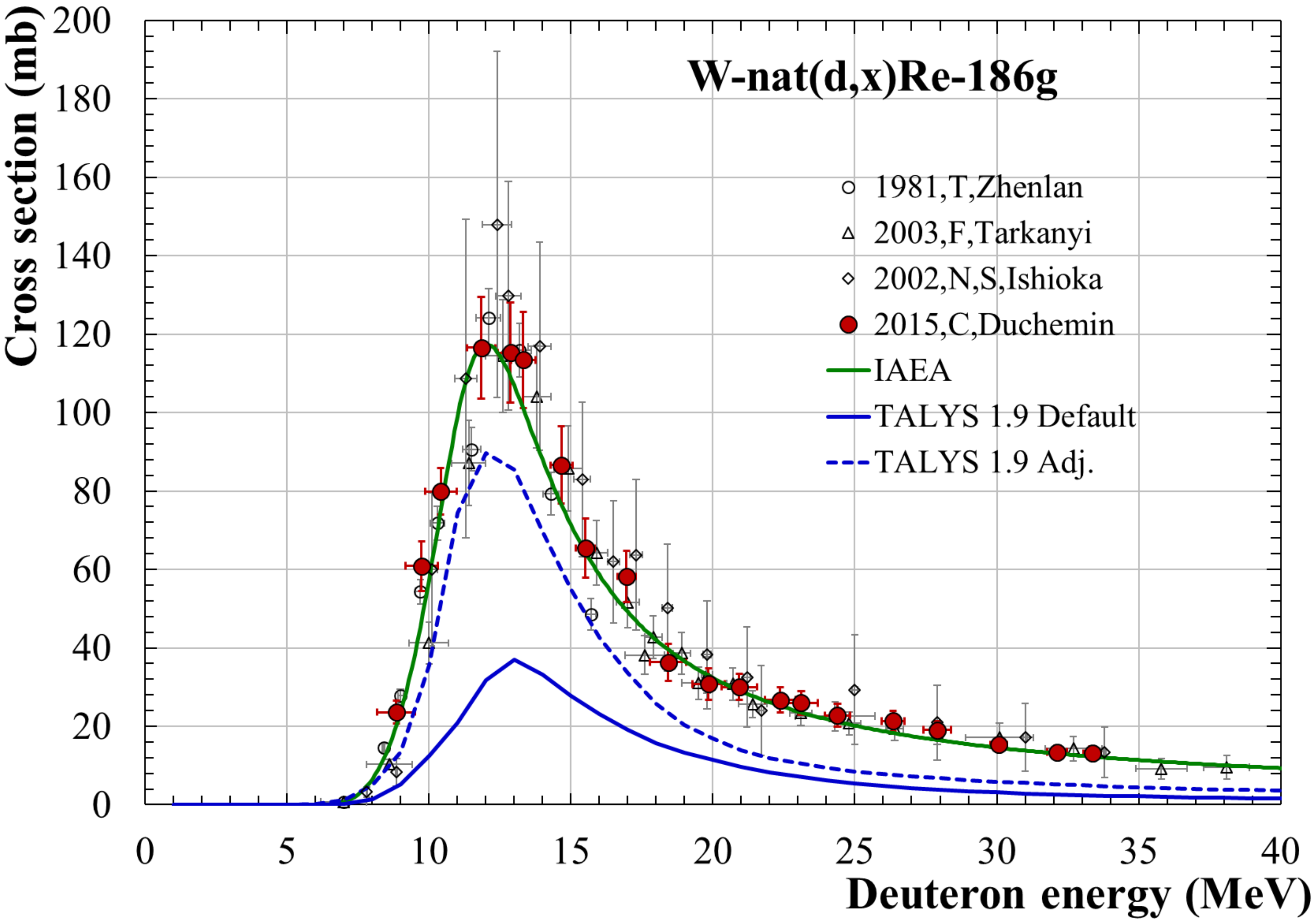


C. Duchemin et al., Appl. Radiat. Isot. 97 (2015) 52-58

Re-186g: deuteron production route



Re-186g: deuteron production route

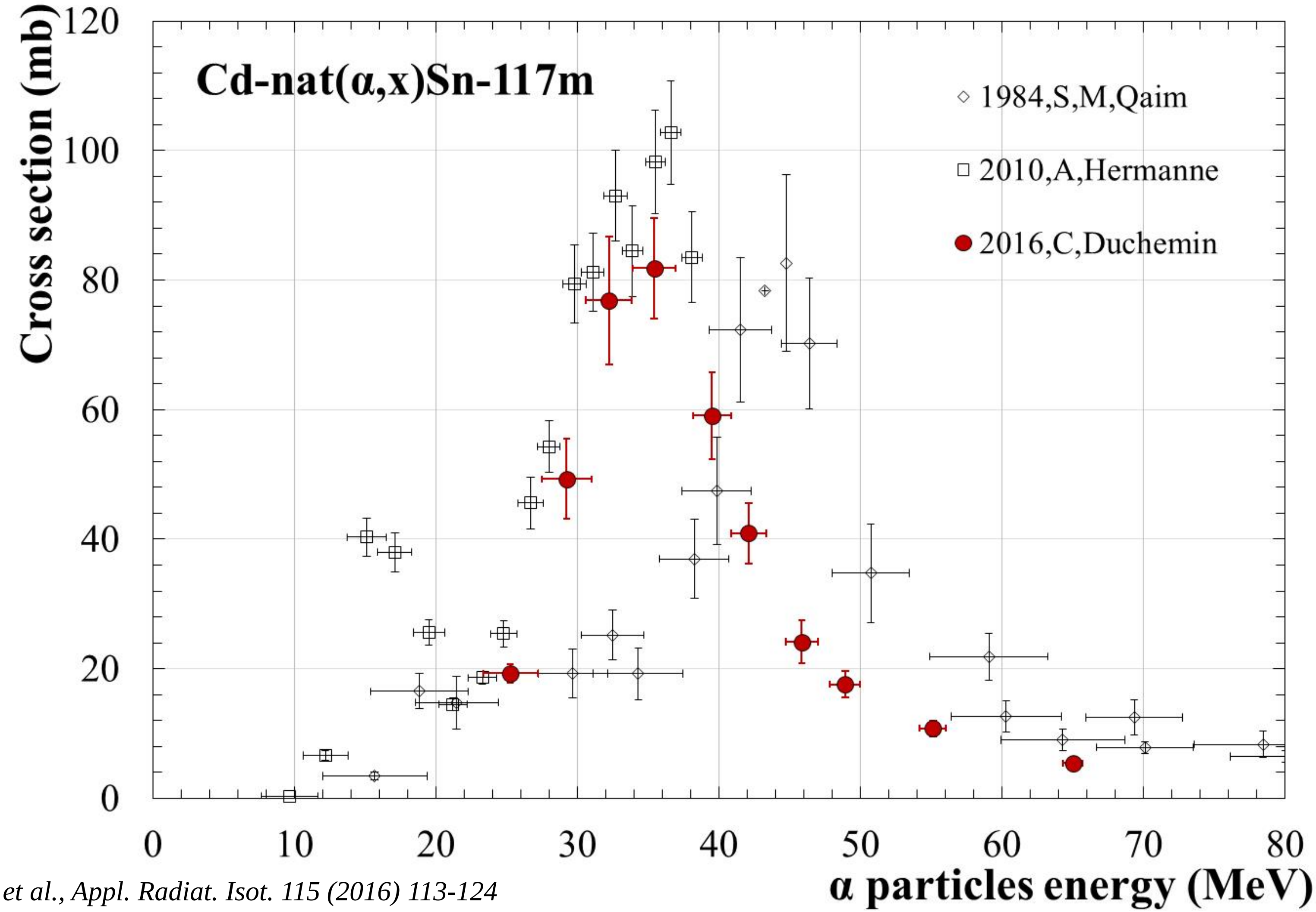


Novel therapeutic and imaging nuclide

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

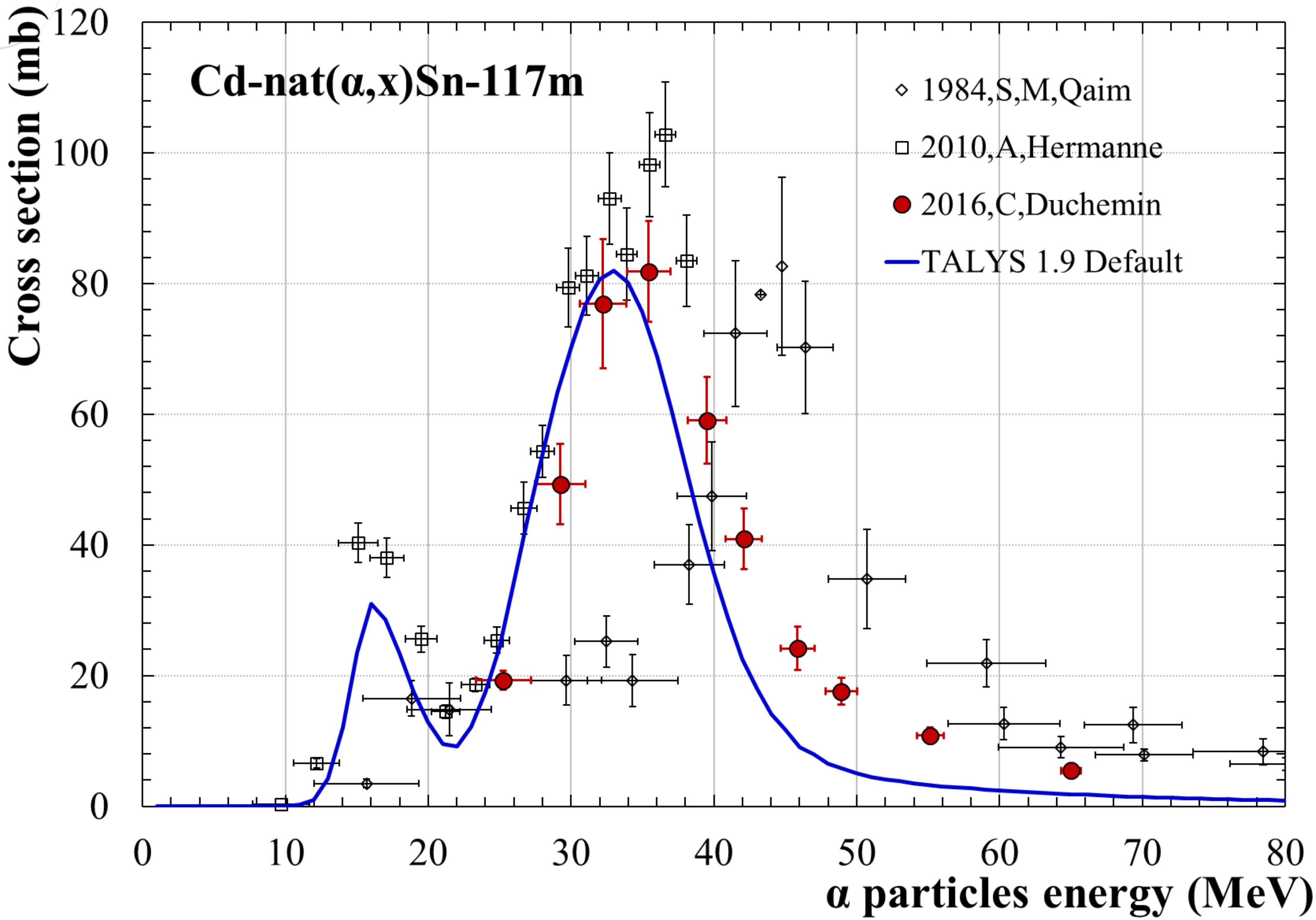
Conversion e- emitter used for the palliation of painful bone metastases

158 keV gamma ray suitable for SPECT imaging

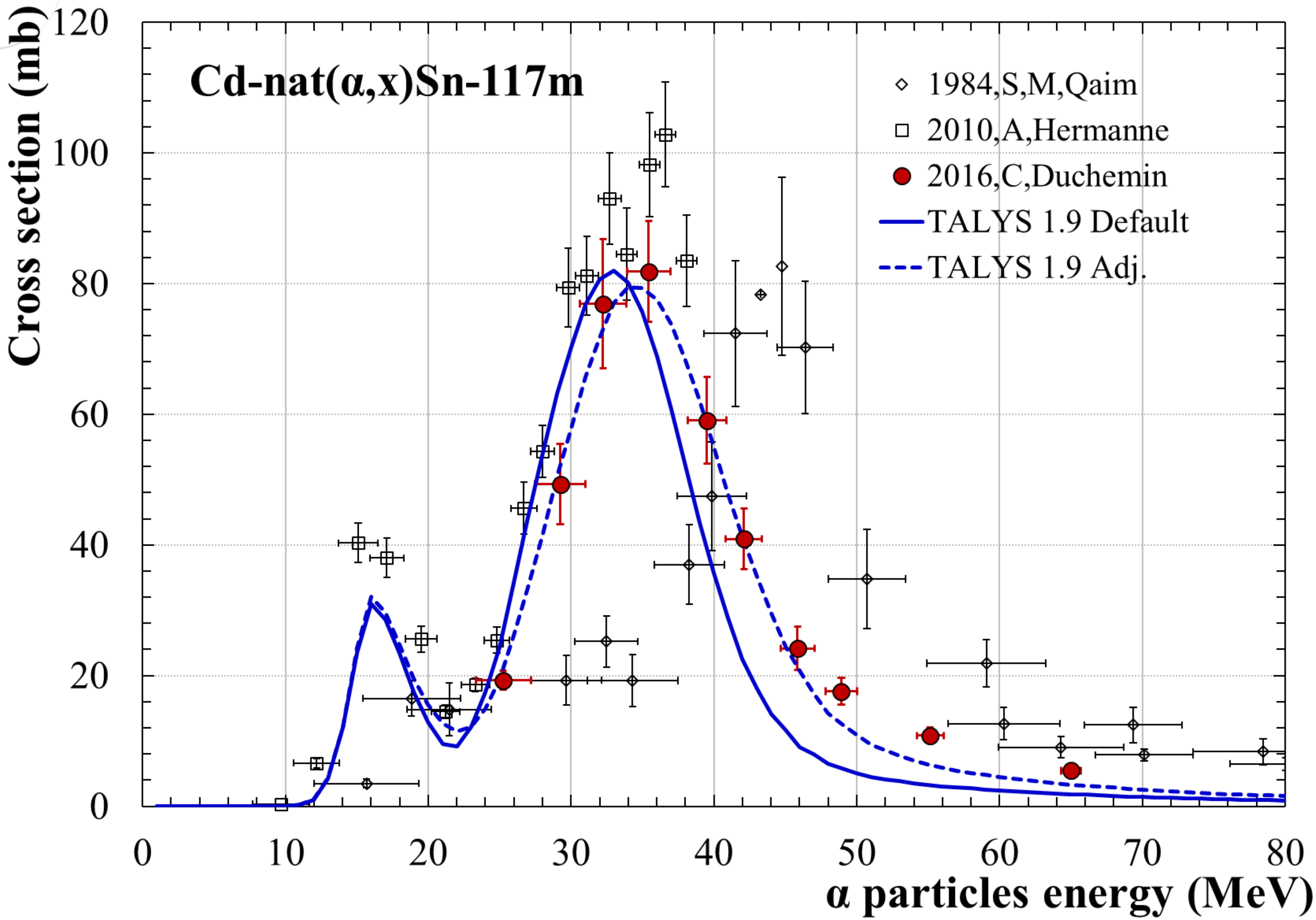


C. Duchemin et al., Appl. Radiat. Isot. 115 (2016) 113-124

Novel therapeutic and imaging nuclide



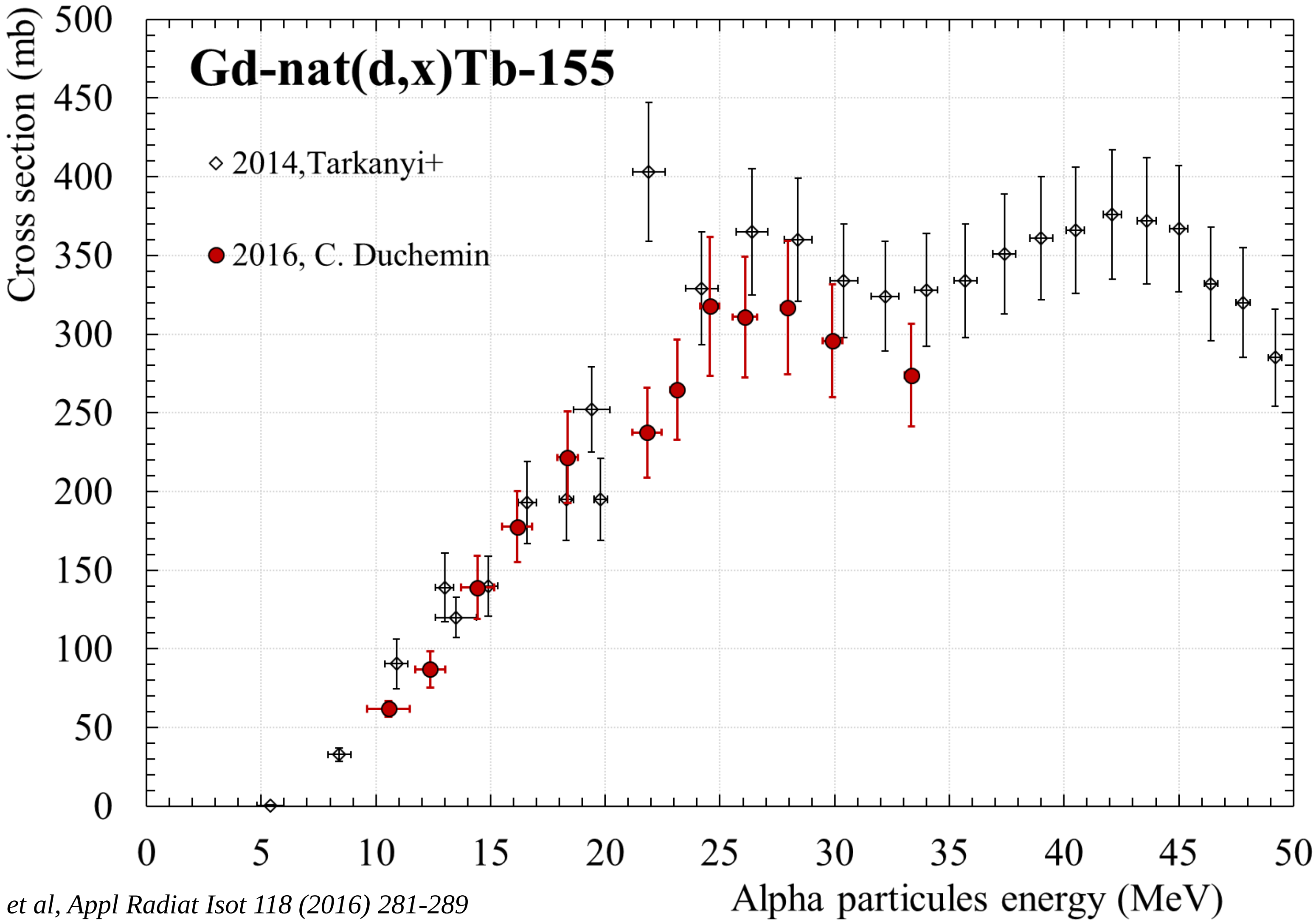
Novel therapeutic and imaging nuclide



Terbium 155: theranostic isotope

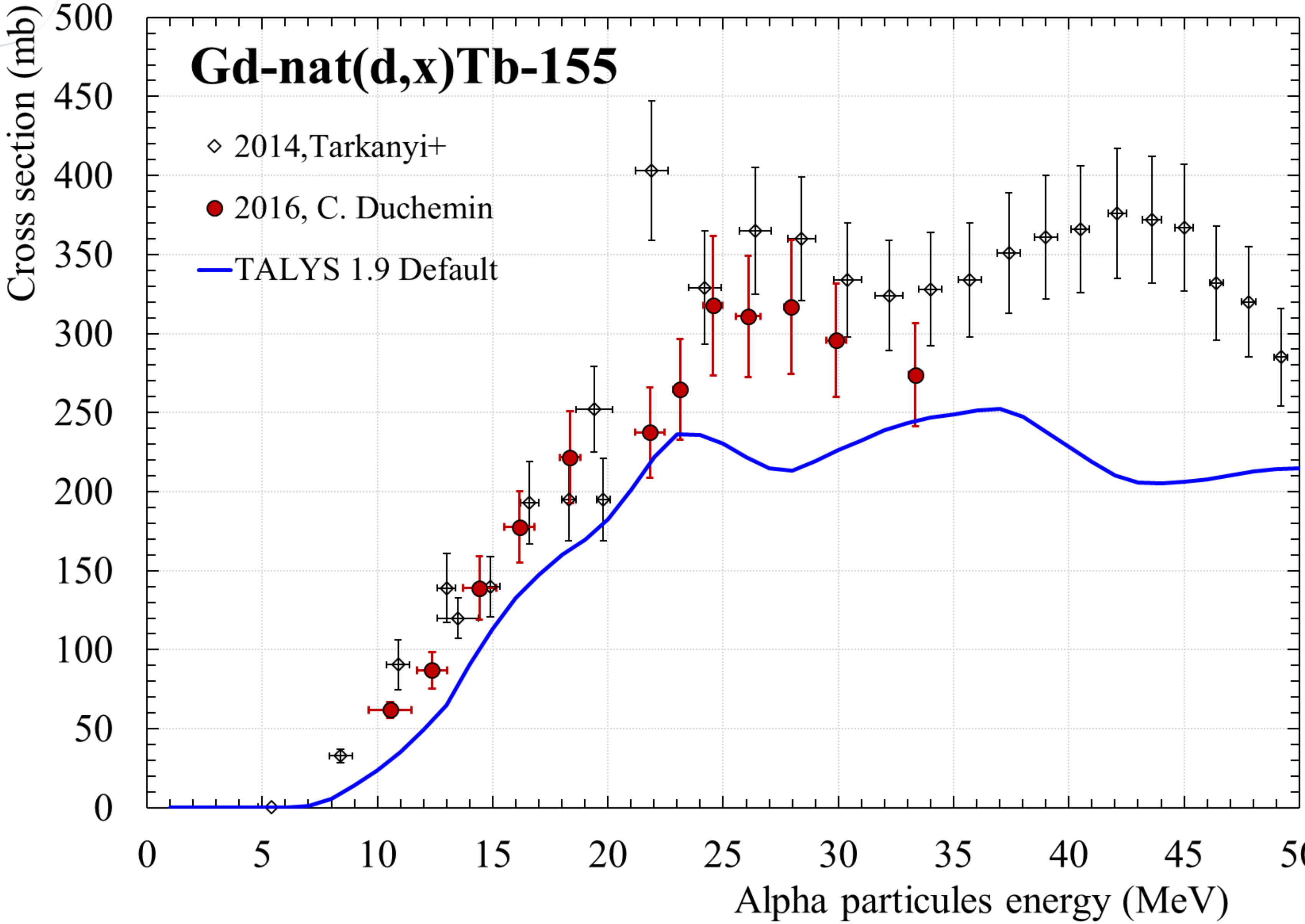
Tb-155 ($T_{1/2}$ = 5.3 d)

a theranostic isotope for SPECT imaging and Auger therapy

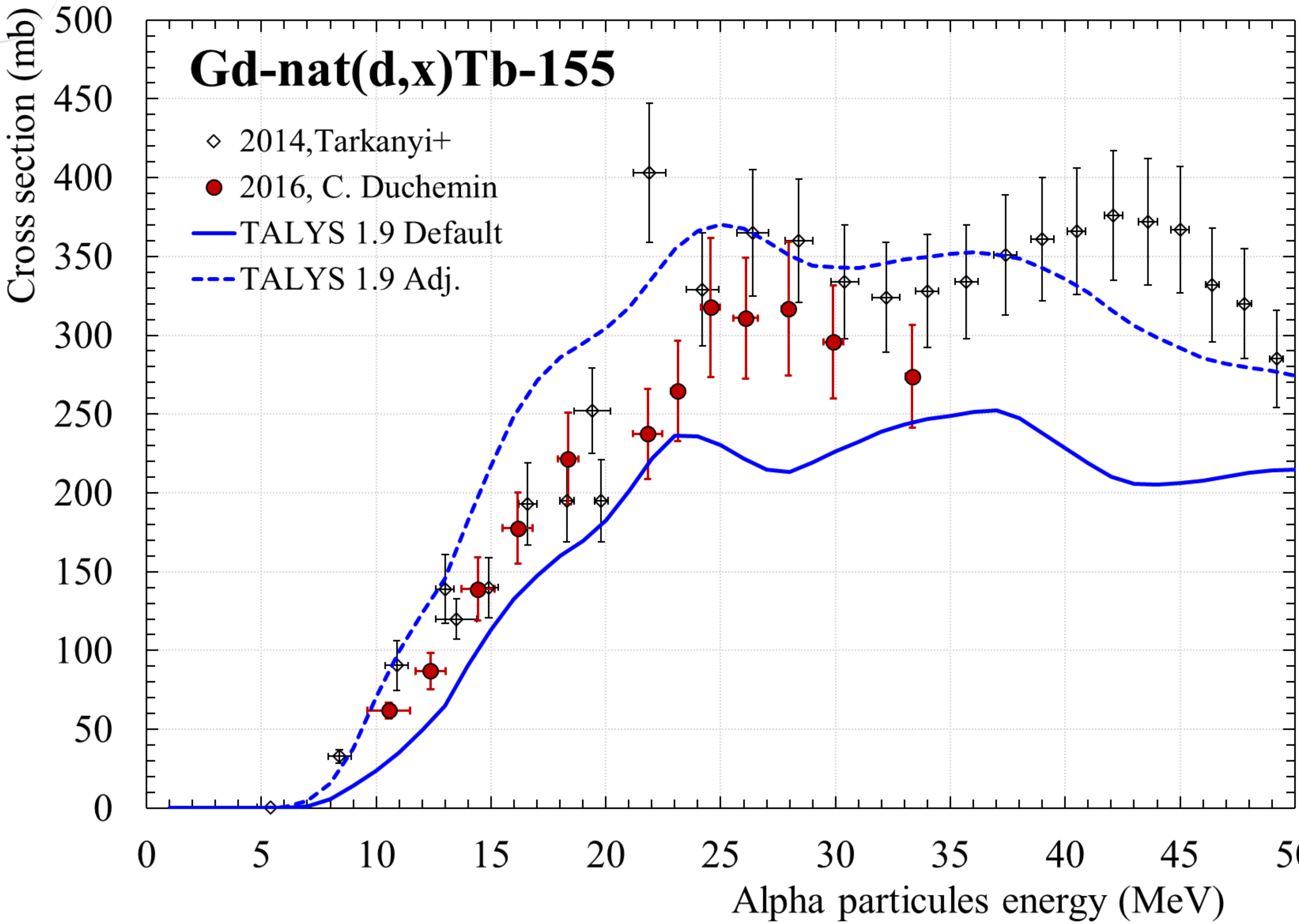


C. Duchemin et al, Appl Radiat Isot 118 (2016) 281-289

Terbium 155


Gd-nat(d,x)Tb-155
2014,Tarkanyi+
2016, C. Duchemin
TALYS 1.9 Default
Cross section (mb)
Alpha particules energy (MeV)
0
50
100
150
200
250
300
350
400
450
500
0
5
10
15
20
25
30
35
40
45
50

Terbium 155



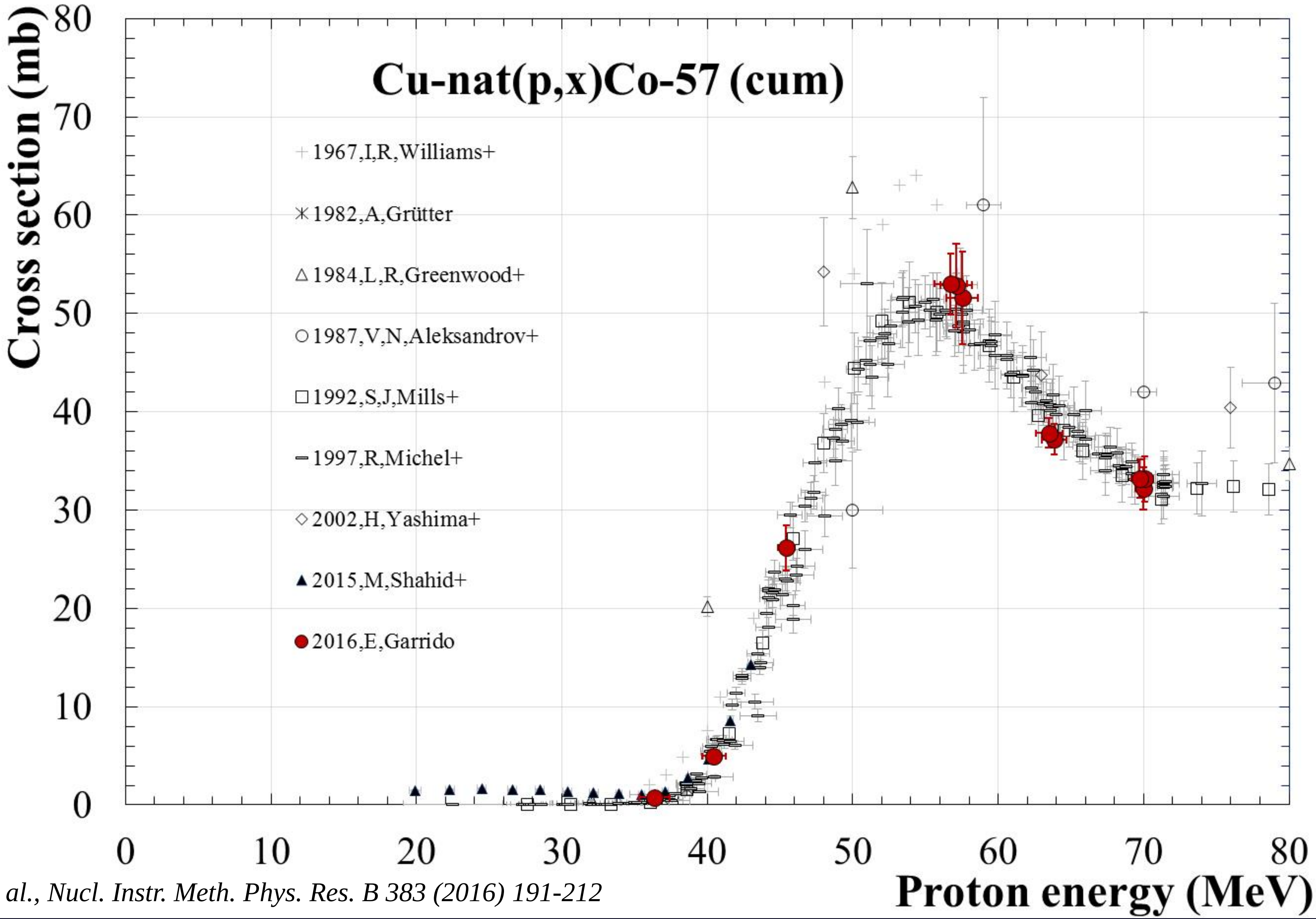
Gd-nat(d,x)Tb-155
2014,Tarkanyi+
2016, C. Duchemin
TALYS 1.9 Default
TALYS 1.9 Adj.
Cross section (mb)
Alpha particules energy (MeV)
0
50
100
150
200
250
300
350
400
450
500
0
5
10
15
20
25
30
35
40
45
50

Monitor reaction

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

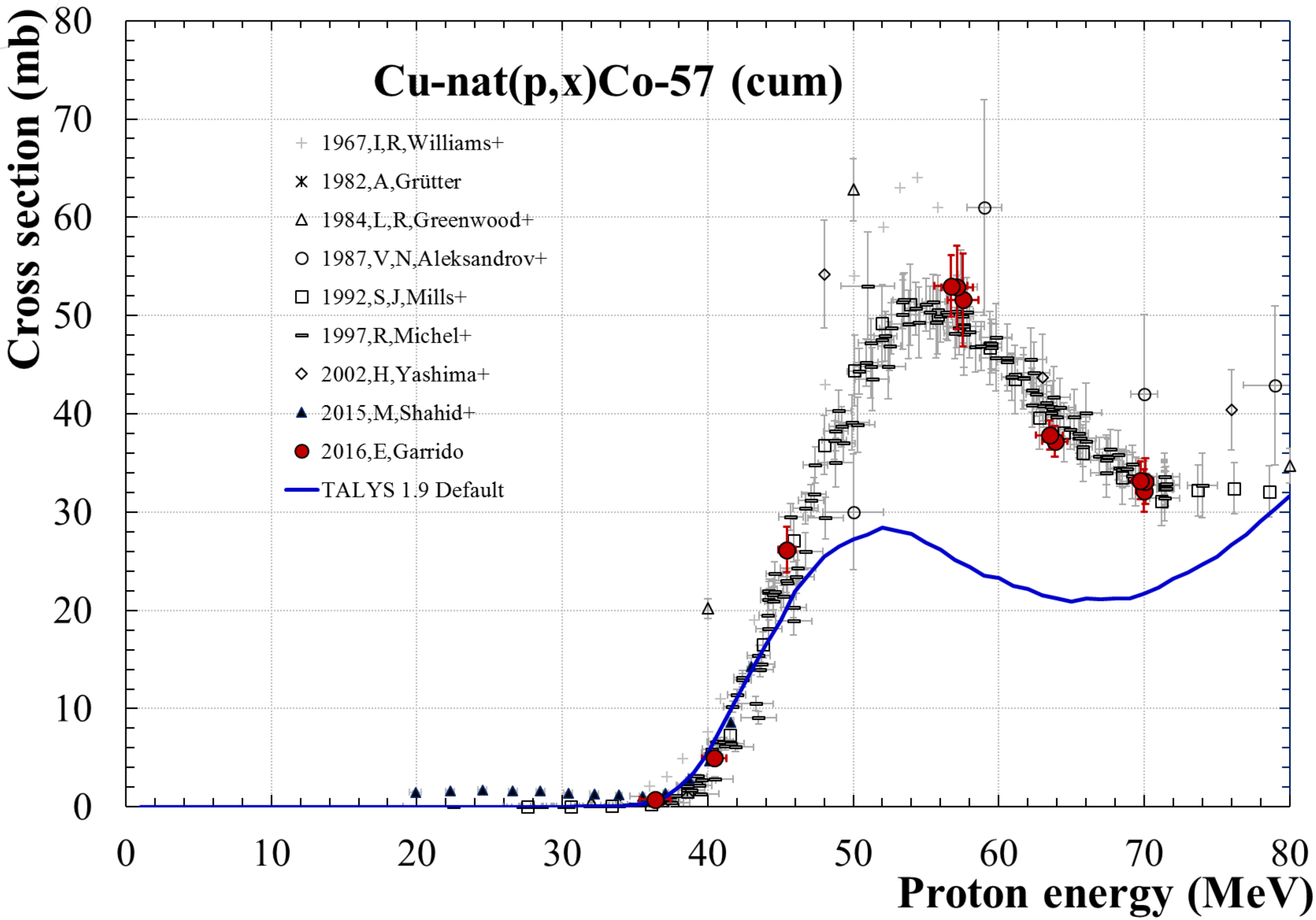
EC process (100%) to stable Fe-57

Suitable for proton monitor reaction

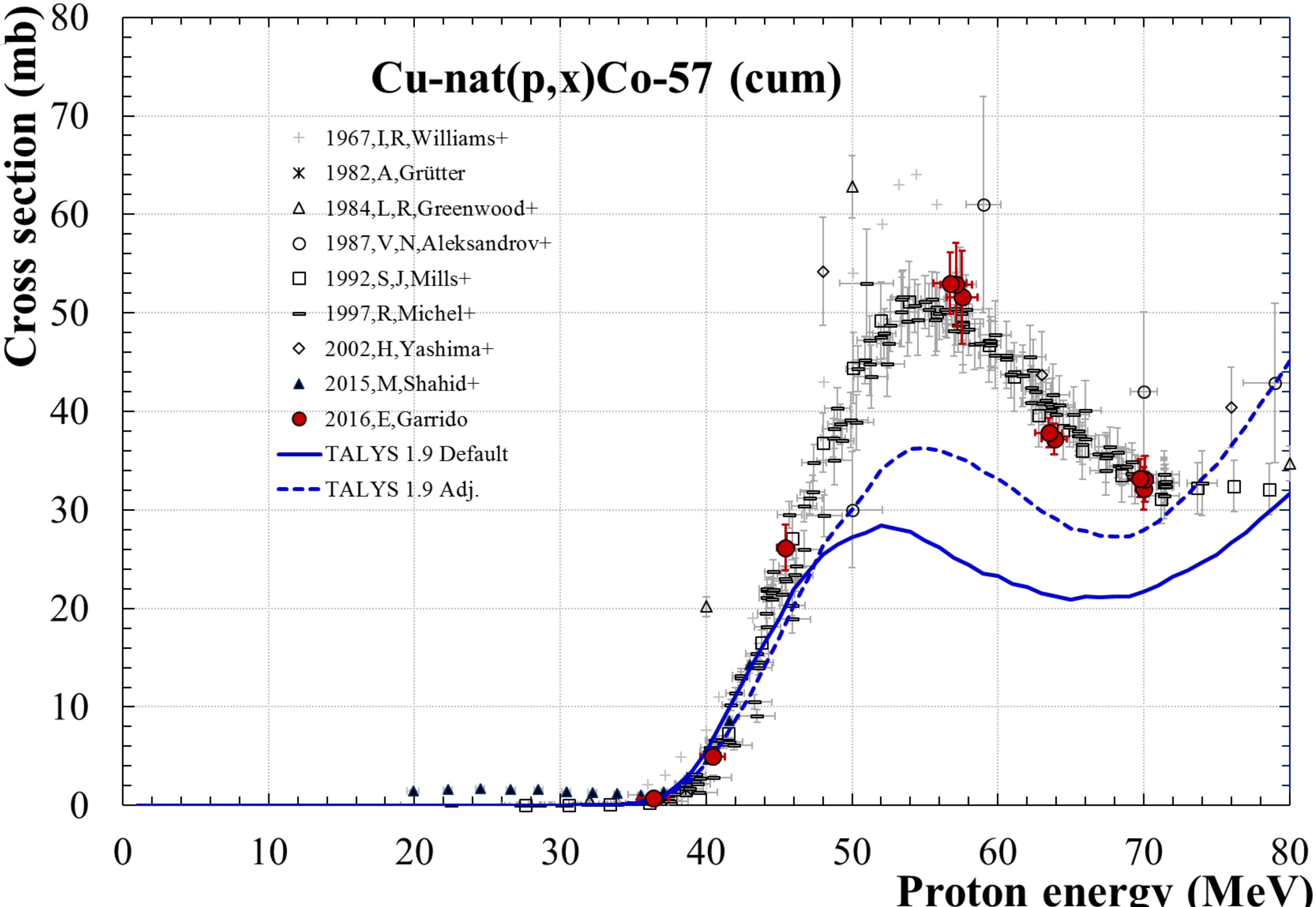


E. Garrido et al., Nucl. Instr. Meth. Phys. Res. B 383 (2016) 191-212

Monitor reaction



Monitor reaction

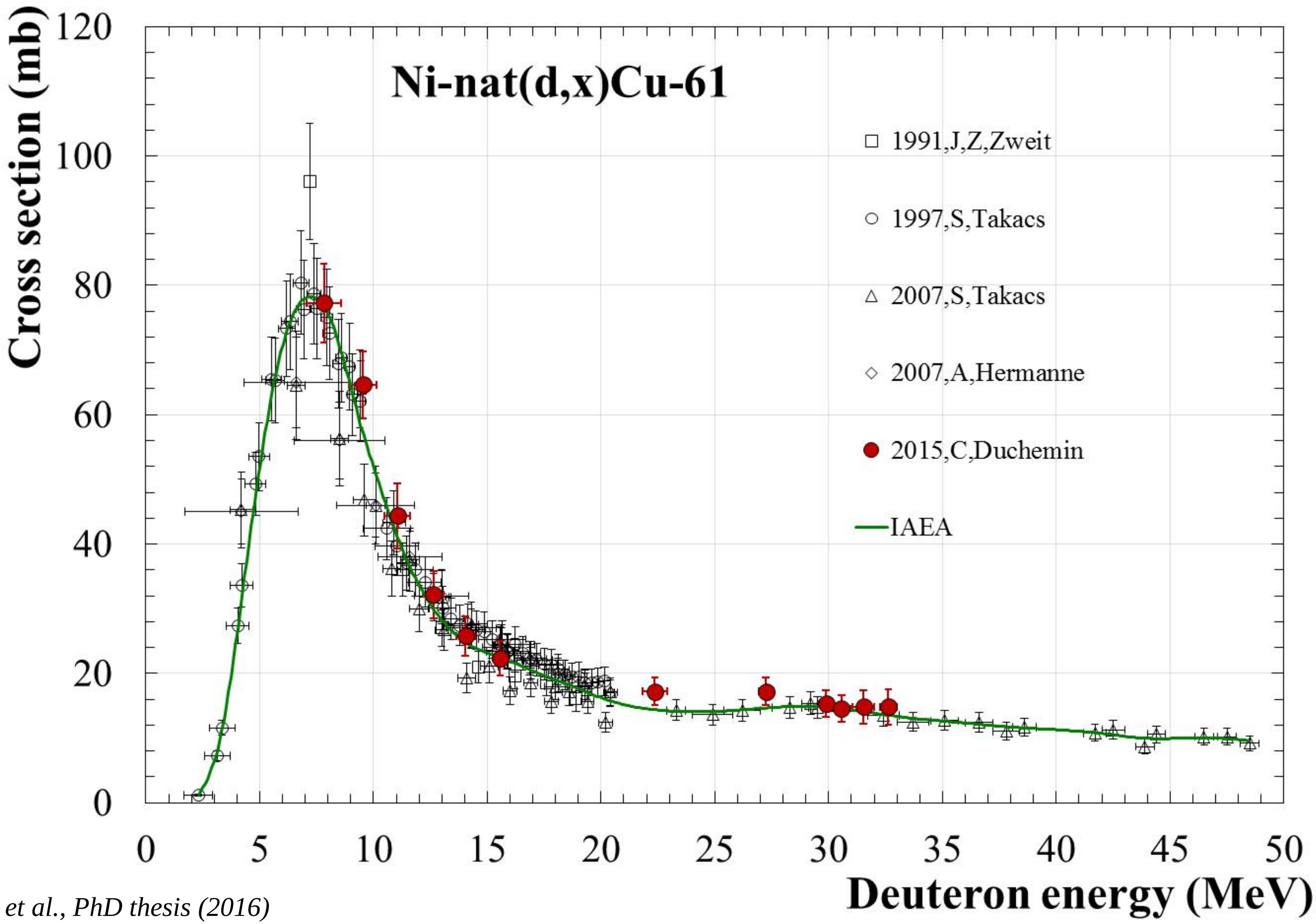


Monitor reaction

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

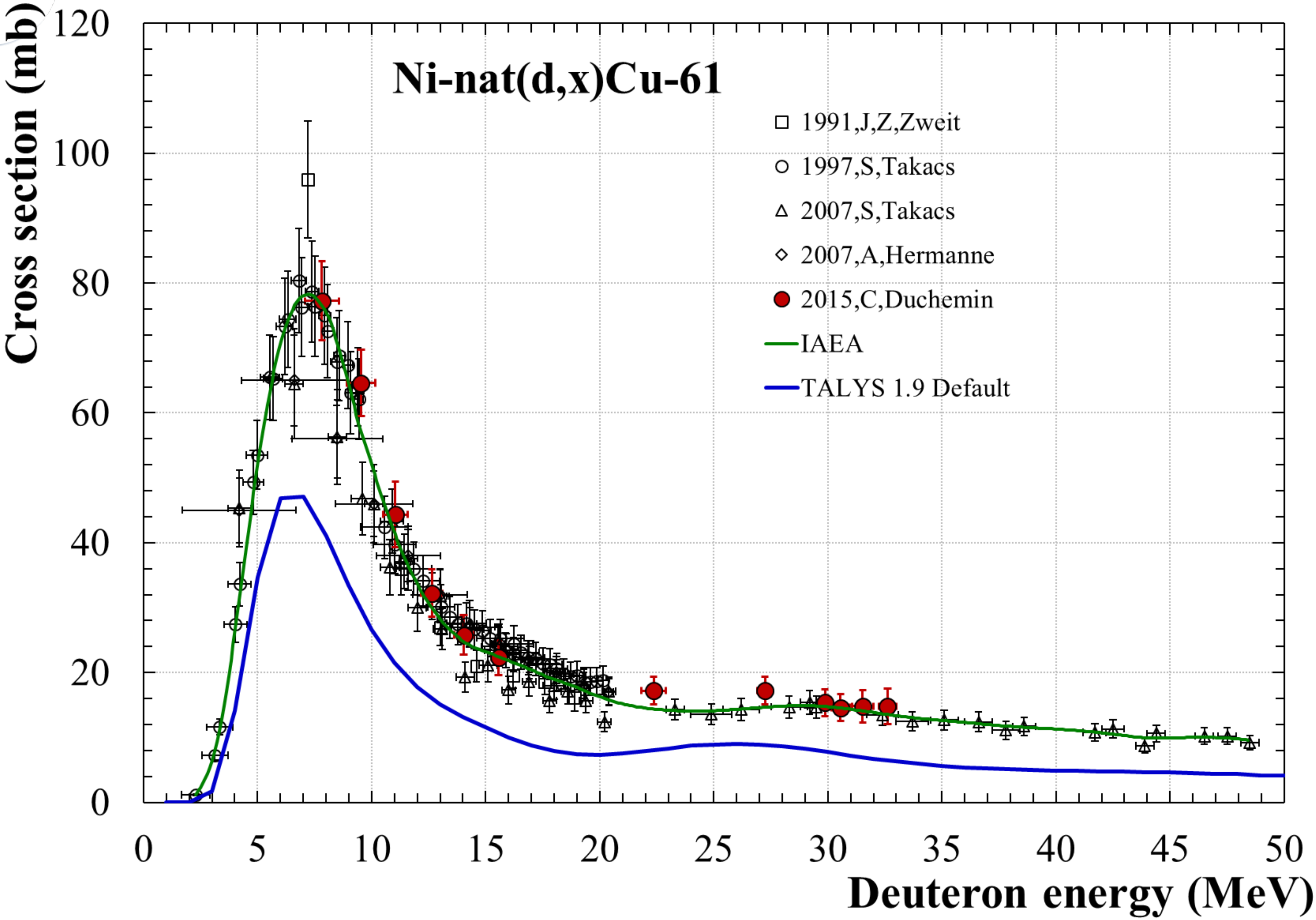
EC β^+ processes to stable Ni-61

Suitable for PET imaging

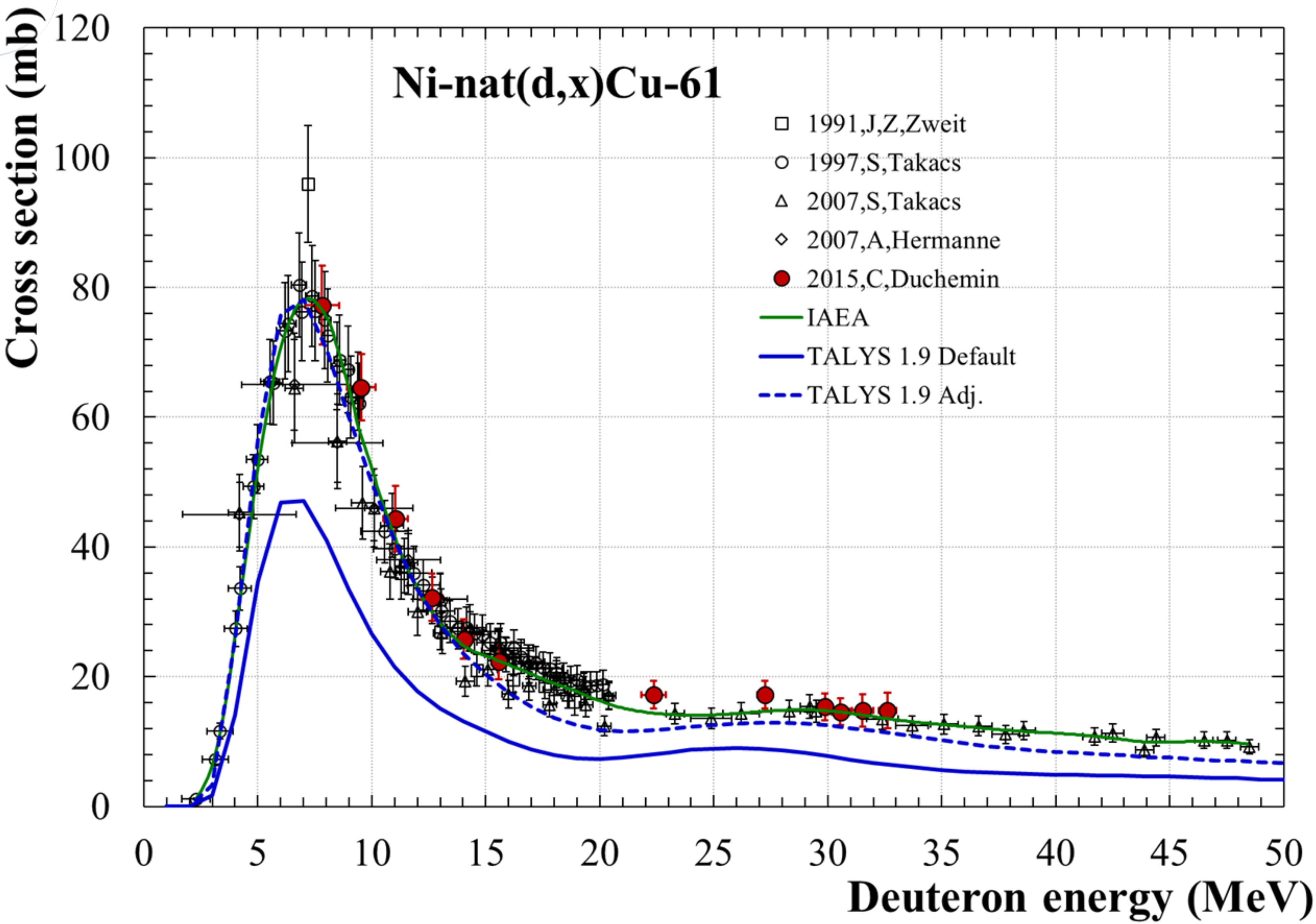


C. Duchemin et al., PhD thesis (2016)

Monitor reaction



Monitor reaction

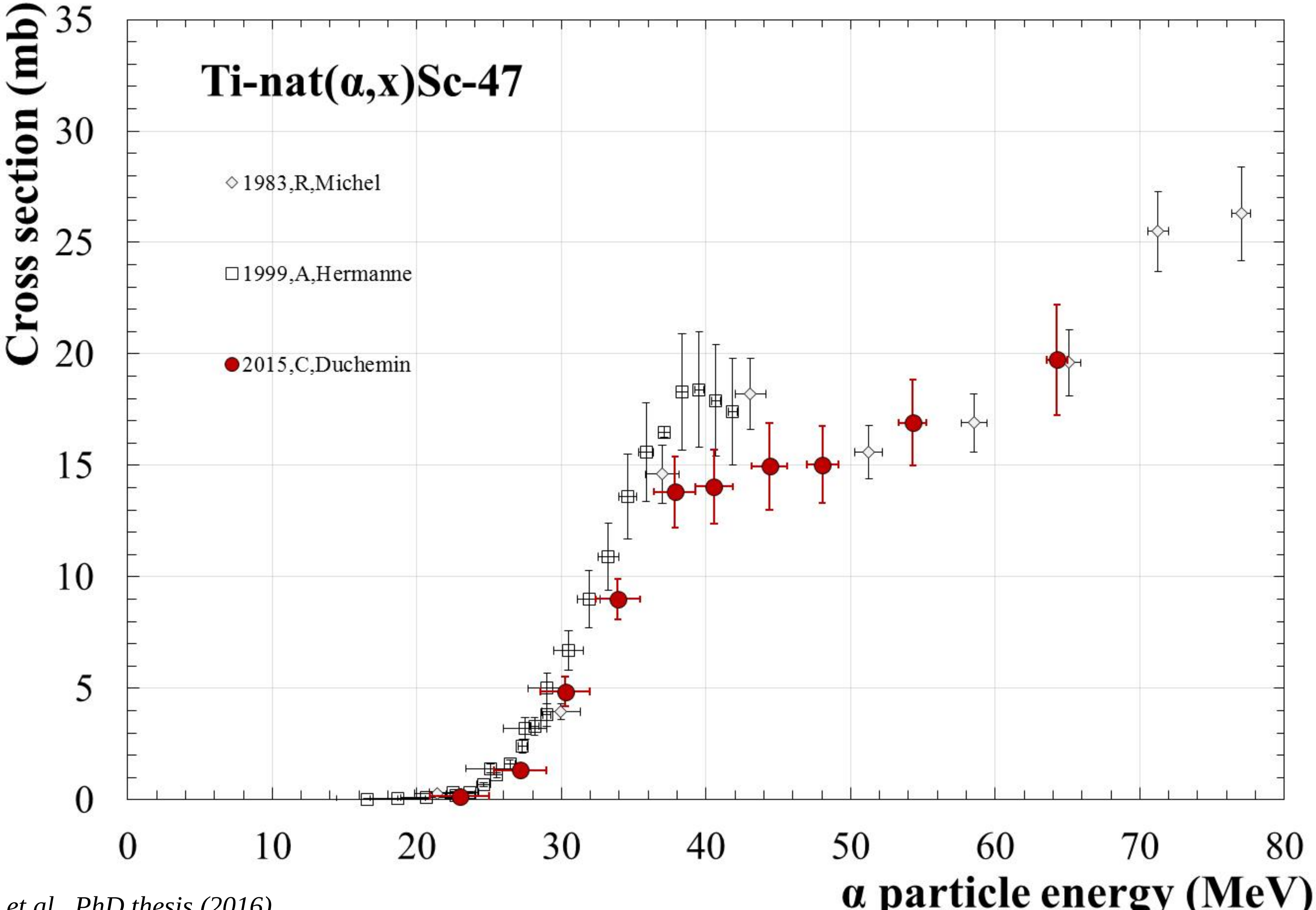


Monitor reaction

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

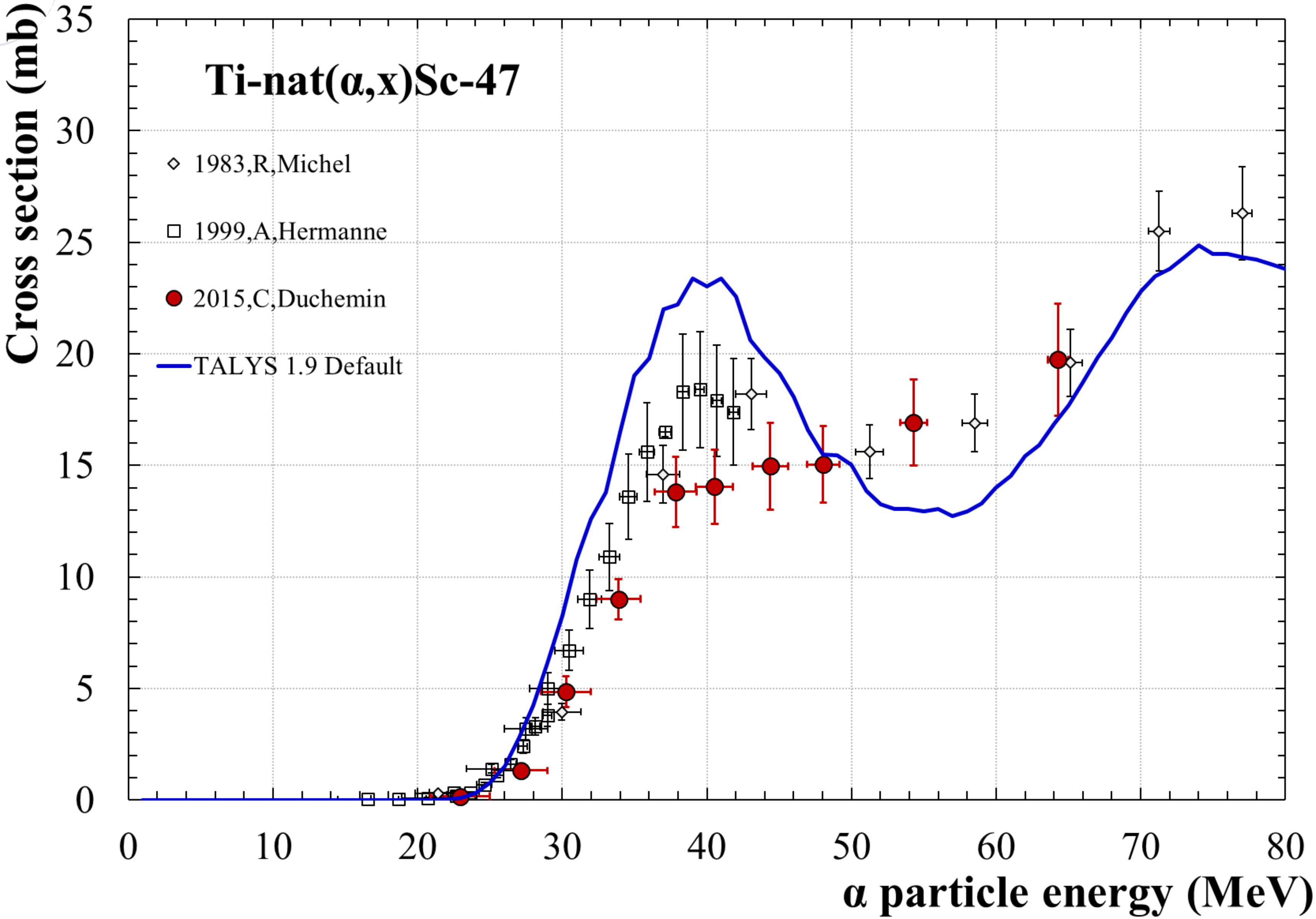
β^- (100%) to stable Ti-47

Suitable for theranostic approach with the Sc-44

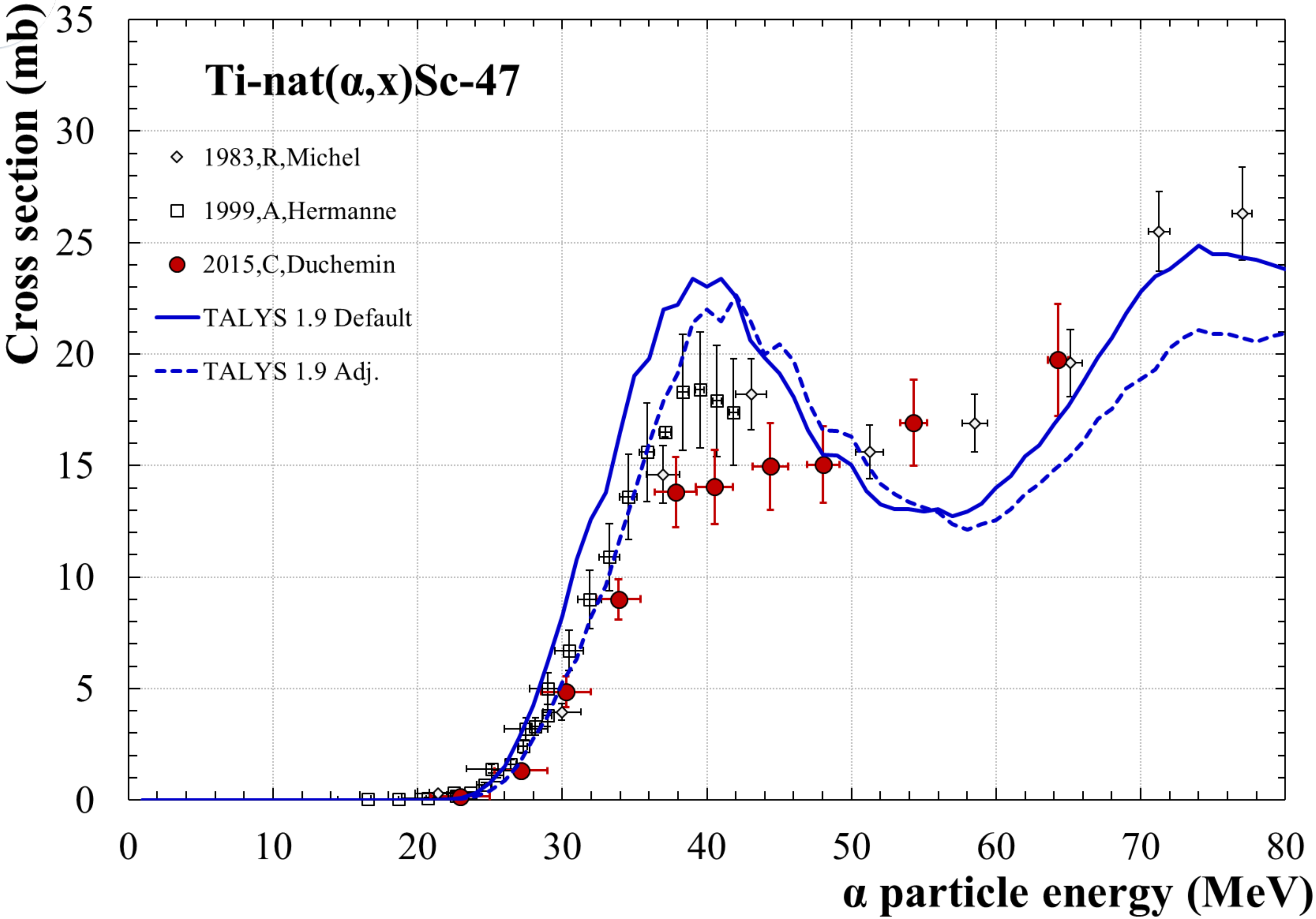


C. Duchemin et al., PhD thesis (2016)

Monitor reaction



Monitor reaction



Conclusions

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

Comparisons have been performed systematically with the **TALYS 1.9 code**

- state of the art models included
- possibility to combine models to better describe data
- a set of models have been found to allow a **good description of all our collected data**

Medical radioisotopes session

Thank you for your attention

Acknowledgments to the 15th Varenna International Conference organization committee

"Production of innovative radionuclides for therapy or diagnostic: nuclear data measurements and comparison with TALYS code"

Guertin A.[1], Nigron E.[1], Sitarz M.[2,3], Duchemin C.[1], Haddad F.[1,2], Métivier V.[1]
1 SUBATECH, CNRS/IN2P3, IMT Atlantique, Université de Nantes, Nantes, France
2 GIP ARRONAX, 1 rue Aronnax, 44817 Saint-Herblain cedex – France
3 University of Warsaw, 00-927 Warszawa, Poland