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## Nuclear data for applications in nuclear medicine

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HAL Authorization

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CNRS Research Officer

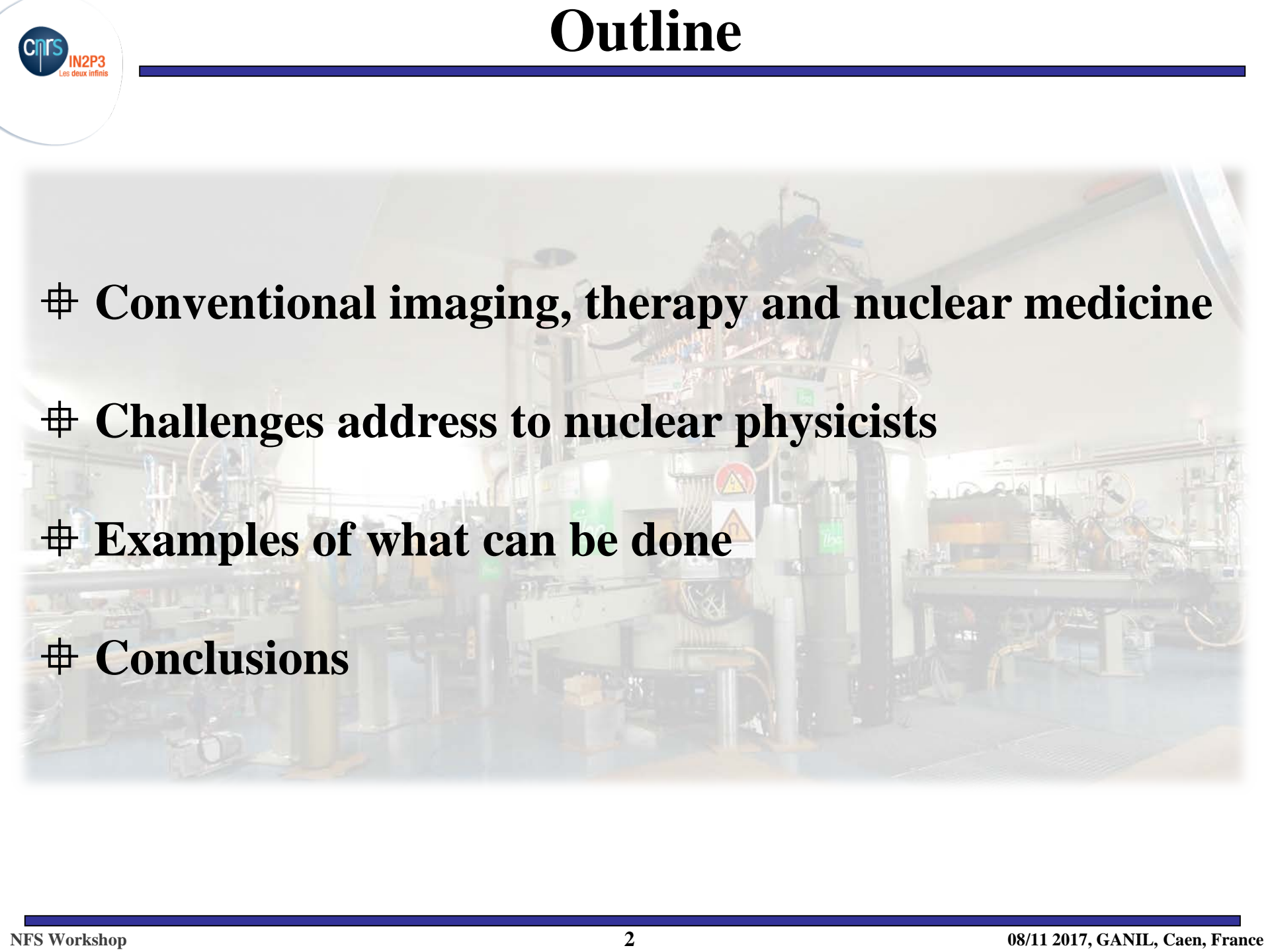


**IN2P3**

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

# **Nuclear data for applications in nuclear medicine**

**A. Guertin and F. Haddad**

- 
- # **Conventional imaging, therapy and nuclear medicine**
  - # **Challenges address to nuclear physicists**
  - # **Examples of what can be done**
  - # **Conclusions**

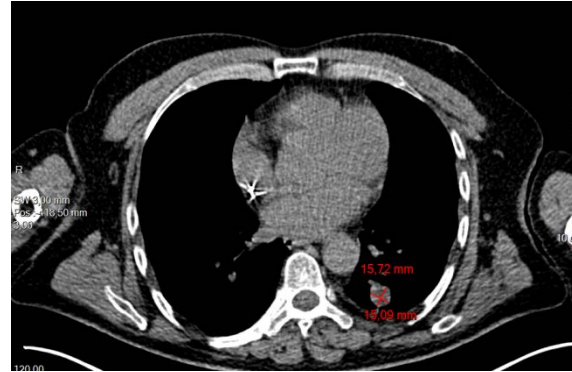
# Conventional imaging in oncology

**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**

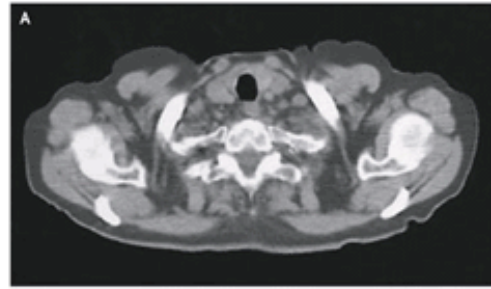
**A gain can be obtain by coupling them with nuclear medicine technique ( SPECT or PET) which gives these information**

# Great progress in the last ten years

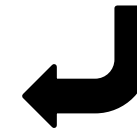
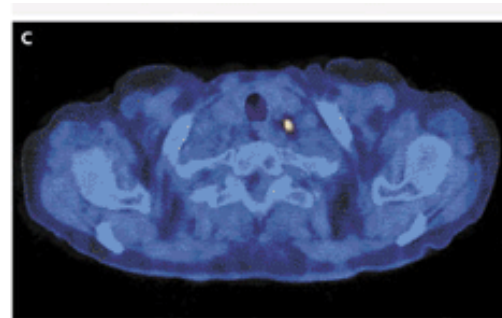
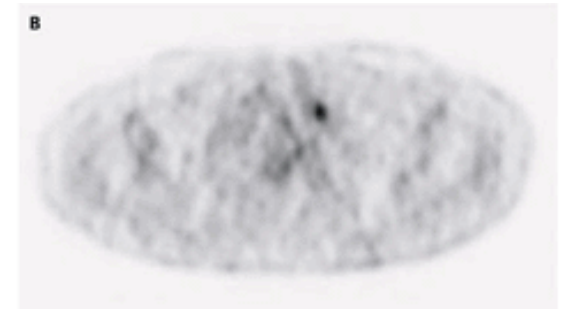
**<sup>18</sup>F FDG PET:** whole body 3D mapping of a biomarker, non invasive

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

Morphology



Metabolism

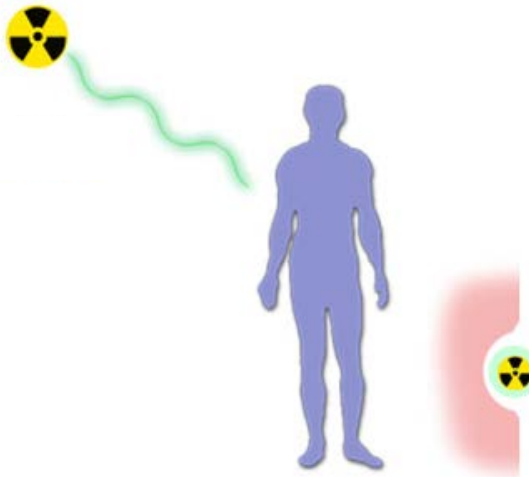


**New targets, tracers and radionuclides (béta+, béta-, Auger and alpha)**

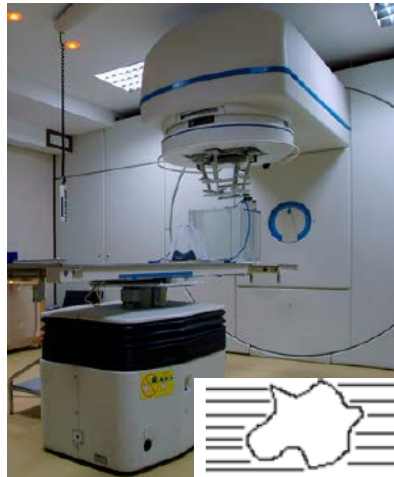
# Conventional radiotherapy

External beam radiotherapy:

- X rays, gamma, electrons
- Hadrontherapy



Brachytherapy  
 Curietherapy



*Institut de cancérologie de l'Ouest*



*ProteusOne, IBA*



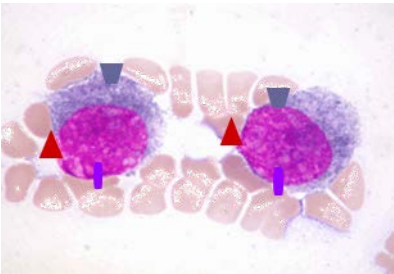
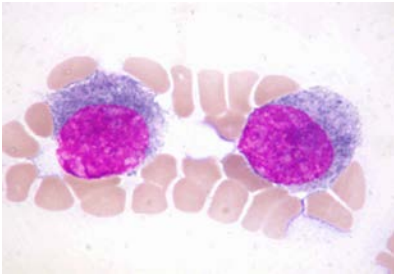
*Institut de cancérologie de l'Ouest*

**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**

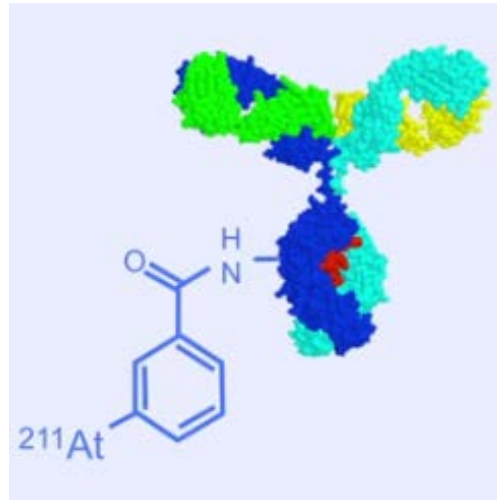
## Molecular targeting



From Pr Kraeber-Bodéré

- Receiver: SMS
- Antigen: CEA
- Carrier: GLUT1
- ...

## Radiopharmaceutical



GIP ARRONAX

- Peptide
- Antibody
- NorA analog
- Glucose
- ...



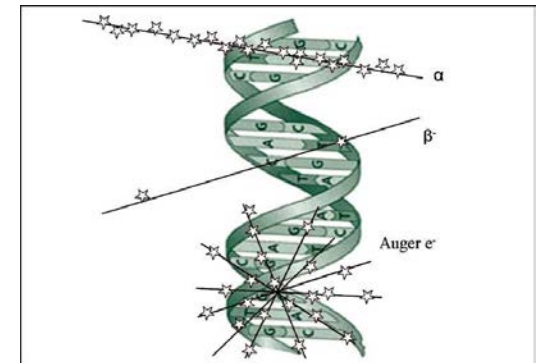
Siemens

Gamma: scint, SPECT/CT



General Electric

Béta +: PET, PET/CT

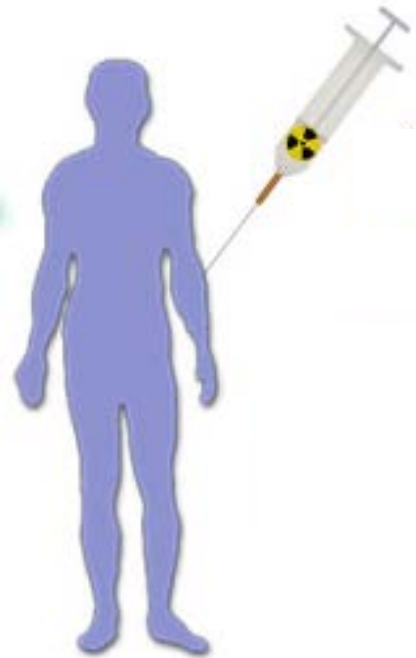


JCRT 6, 3, p. 239

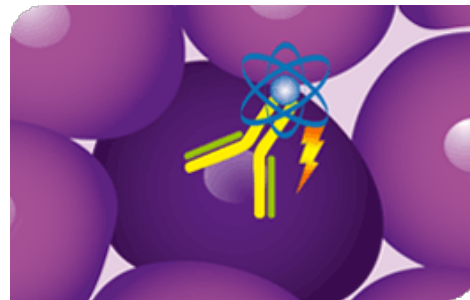
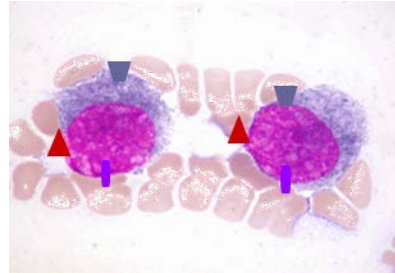
Alpha, béta-, Auger e-: therapy

# Imaging and molecular radiotherapies

**Inject a tracer**



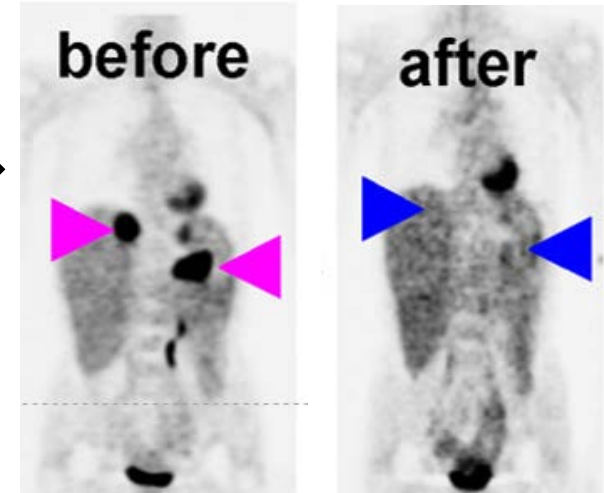
**Target a tumor marker**



*AREVA Med*

**Detect the disease**

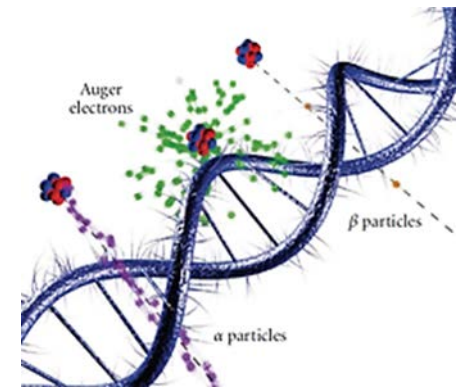
$\gamma, \beta^+$  →



*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

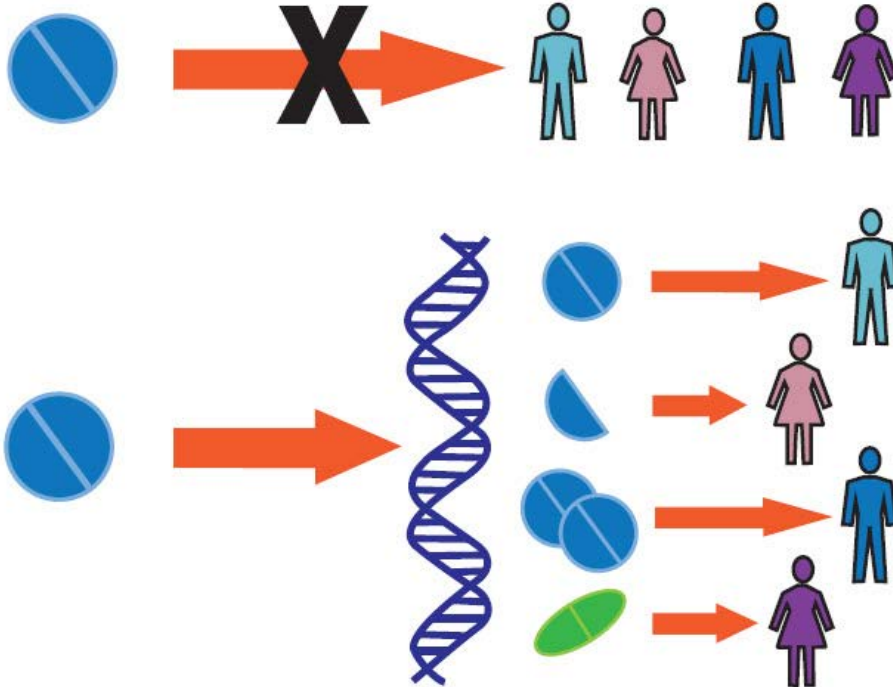
Pharmaceuticals 2017, 10(2), 56

# Personalized nuclear medicine

## Imaging and diagnosis

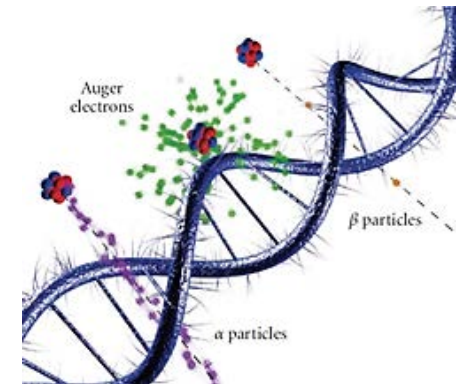
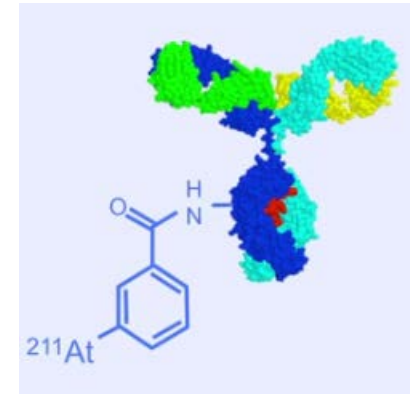
Choose the best treatment

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**

**$^{18}\text{F}$ FDG PET:** whole body 3D mapping of a biomarker, non invasive

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

In biology, **new vectors:** peptides, humanized antibodies, nanobodies ...

**New radionuclides** are needed to match with these new vectors

**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**
- Production capacities – to envisaged **large scale use**

## The nuclear physicist could have crucial contribution:

- Identify production route and define production process even large scale production (reactors, accelerators by spallation, fission or activation)
- Identify and quantify contaminants
- Define waste management process
- Help scientists working in a pluridisciplinary team (nuclear physicists are use to do that)
- Discuss with physicians to promote its use

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

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

**To do so, we possess facility (will possess) available for irradiations equipped with experimental techniques such as the stacked-foil technique**

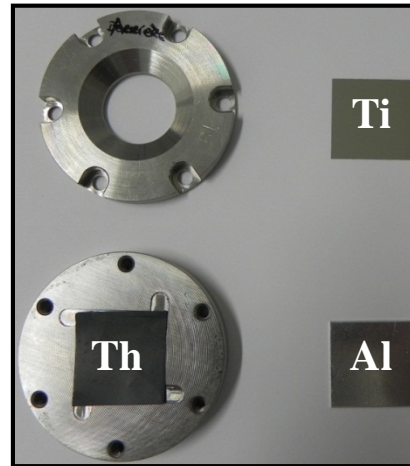
# Stacked-foil technique

## Stacked-foil technique:

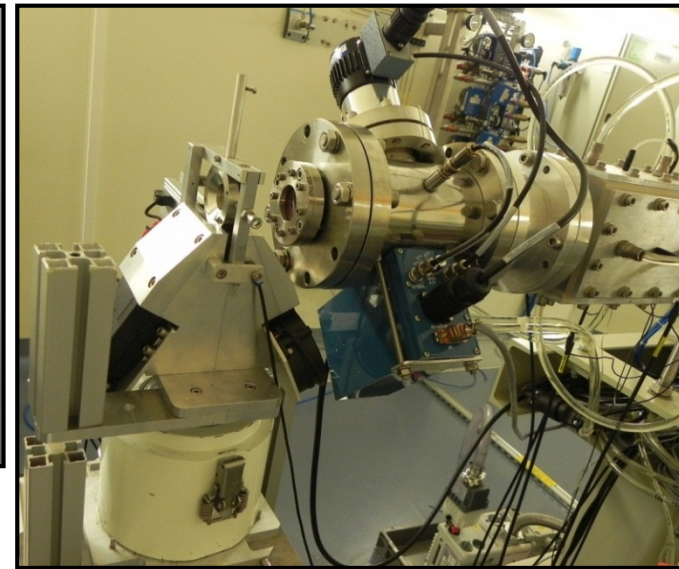
- Target/monitor/degrader **pattern**
- **Thin** foils:
  - E loss small and constant
- One cross section value per foil

## Activity and cross section:

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



Capsule and foils



Irradiation station and beam line

## 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

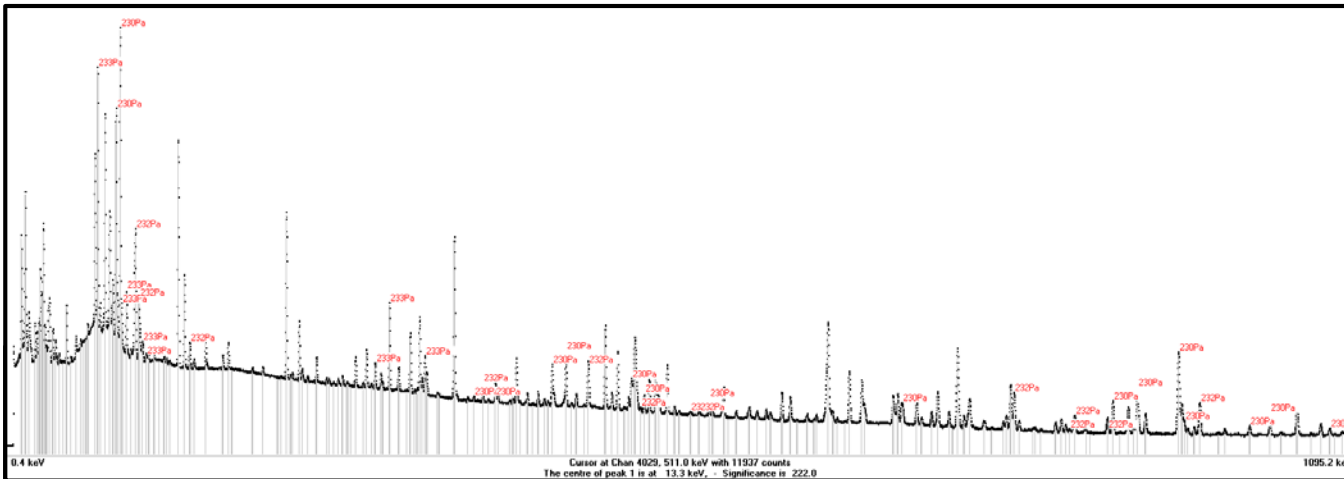
## IAEA recommended cross sections:

- 8 reactions available for protons  
 $^{27}\text{Al}$  (2),  $^{\text{nat}}\text{Ni}$ ,  $^{\text{nat}}\text{Ti}$  and  $^{\text{nat}}\text{Cu}$  (4)
- 5 reactions available for deuterons  
 $^{27}\text{Al}$  (2),  $^{\text{nat}}\text{Fe}$ ,  $^{\text{nat}}\text{Ni}$  and  $^{\text{nat}}\text{Ti}$
- 6 reactions available for alpha-particles  
 $^{27}\text{Al}$  (2),  $^{\text{nat}}\text{Ti}$  and  $^{\text{nat}}\text{Cu}$  (3)

# Stacked-foil technique

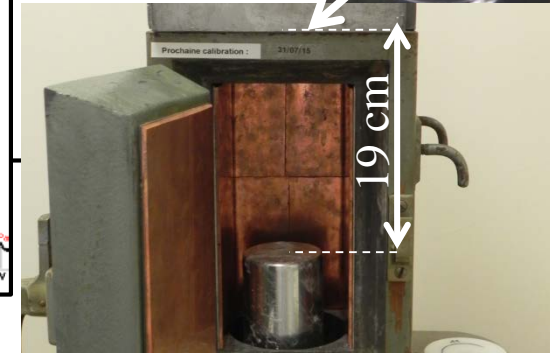
## Gamma spectroscopy

- **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

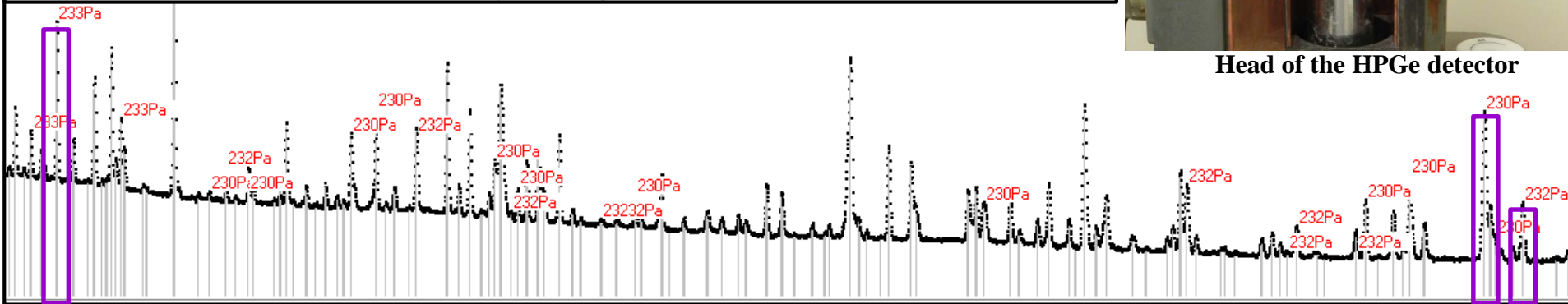


**Target and monitor:**

- ✓ counted twice
- ✓ during > 24 hrs
- ✓ 2 week delay

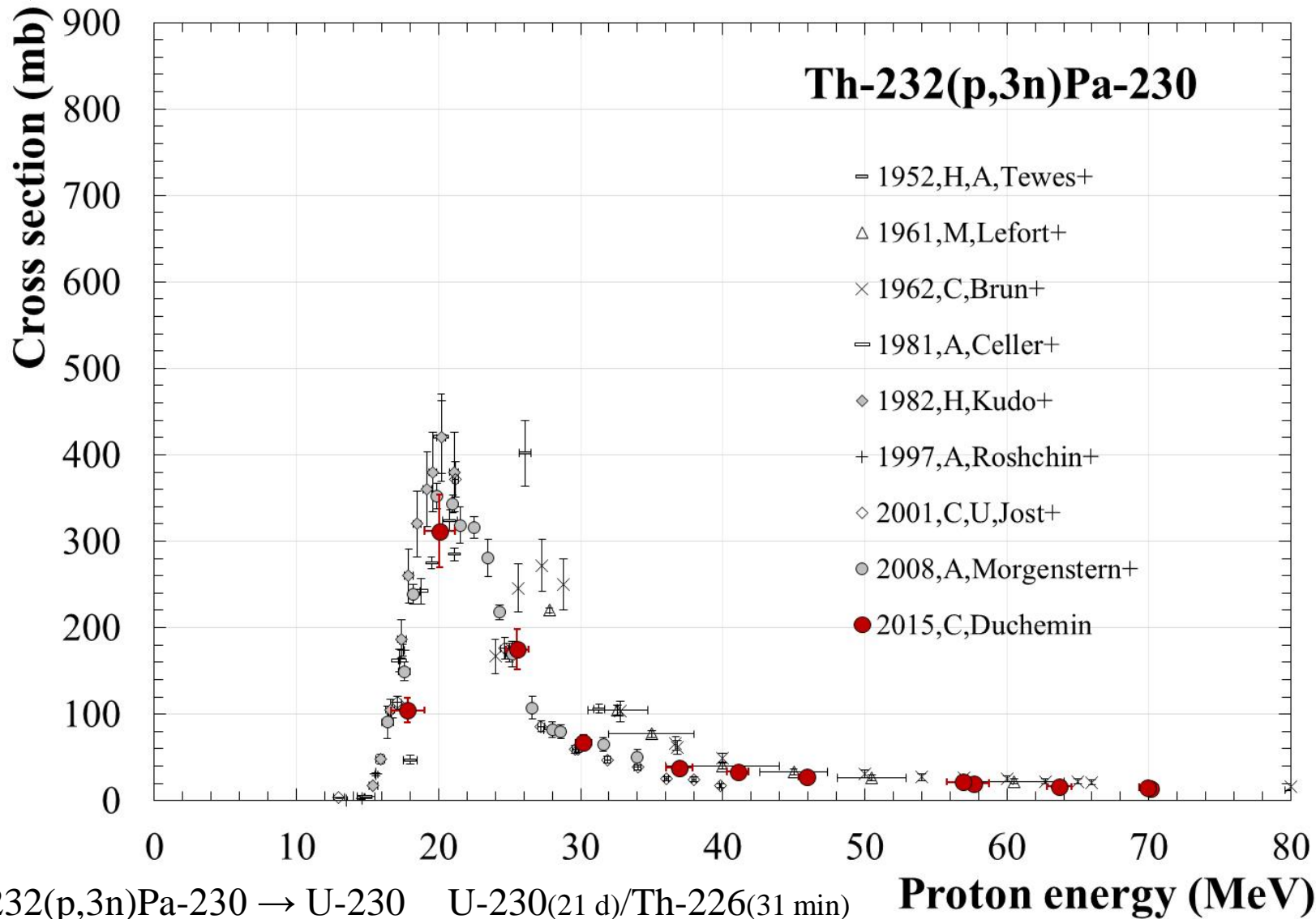


Head of the HPGe detector



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

# Novel therapeutic nuclide



α RIT for leukaemia treatment

4 α cascade of 27.7 MeV

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

Code for the simulation of nuclear reactions

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

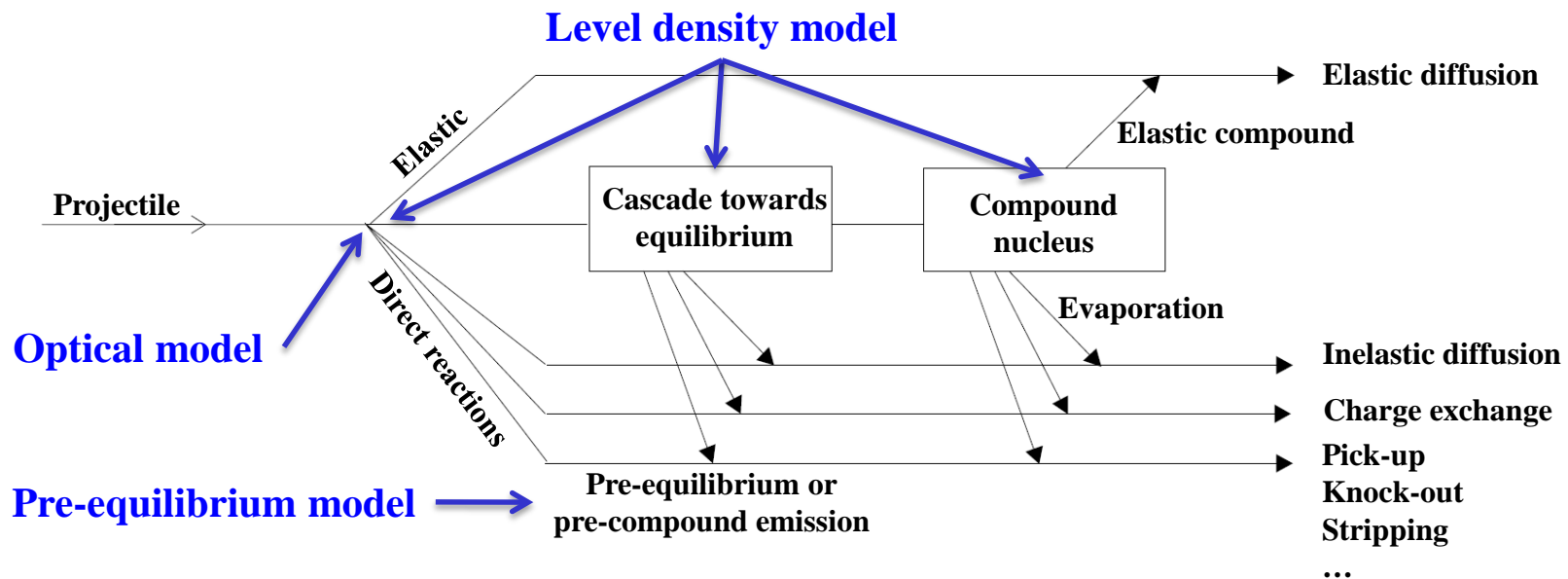
Many state-of-the-art nuclear models

Energy : 1 keV to 1 GeV

Provide a complete description of all reactions channels and observables

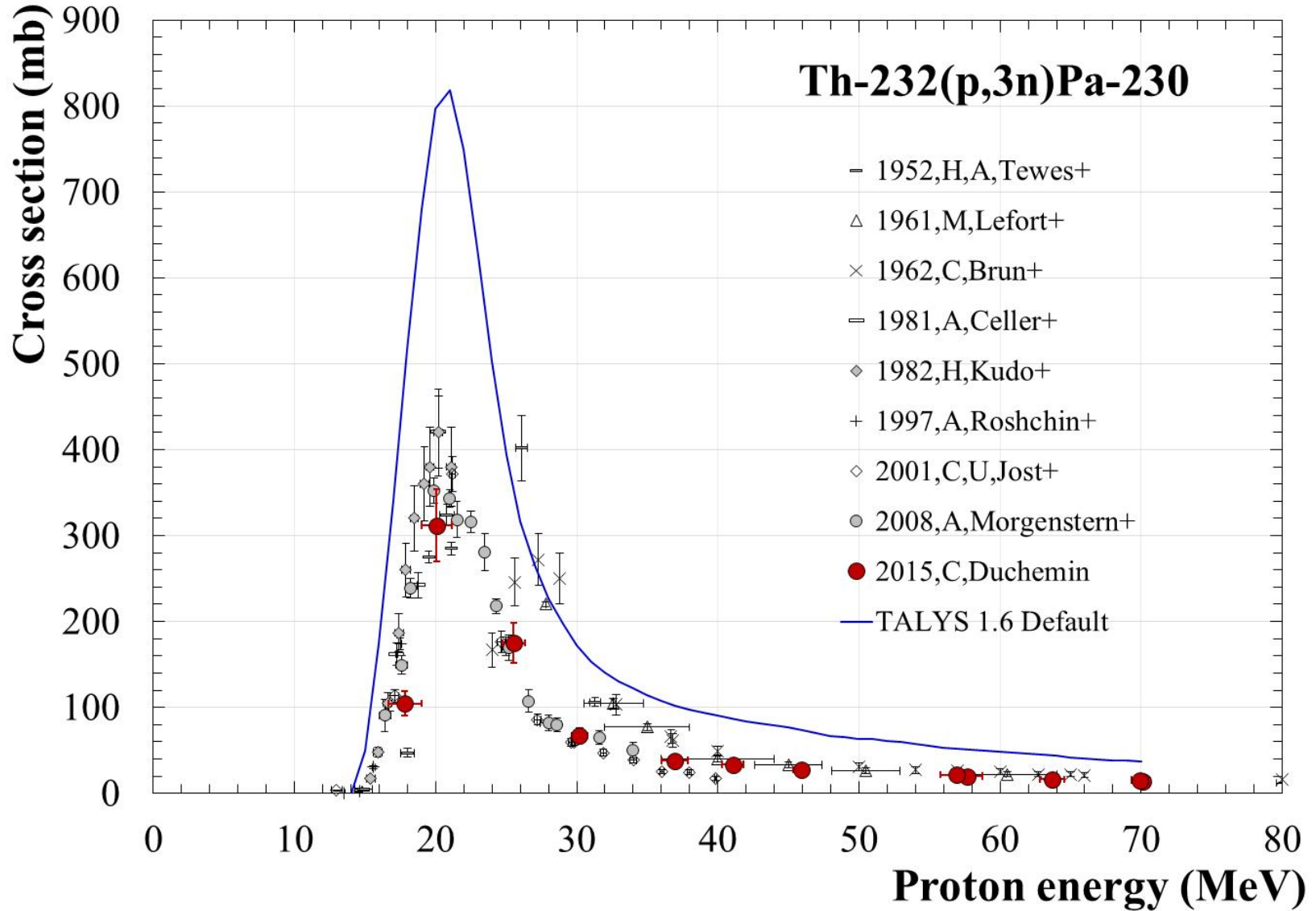
Targets :  $Z = 3$  to 110

### Nuclear reactions



⇒ Influence on the calculated production cross section values

# Novel therapeutic nuclide



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

## TENDL2015

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



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

<sup>1</sup> IAEA, <sup>2</sup> PSI, <sup>3</sup> JUKO Research, <sup>4</sup> CCFE, <sup>5</sup> Uppsala Univ., <sup>6</sup> NRG, <sup>7</sup> CEA, <sup>8</sup> Vattenfall, <sup>9</sup> NEA, <sup>10</sup> ULB, <sup>11</sup> VTT, <sup>12</sup> ATI, <sup>13</sup> IRMM, <sup>14</sup> NNLL.

TENDL2015 contains evaluations for :

seven types of incidents particles (n, p, d, t, He-3, alpha-particle, gamma ray)

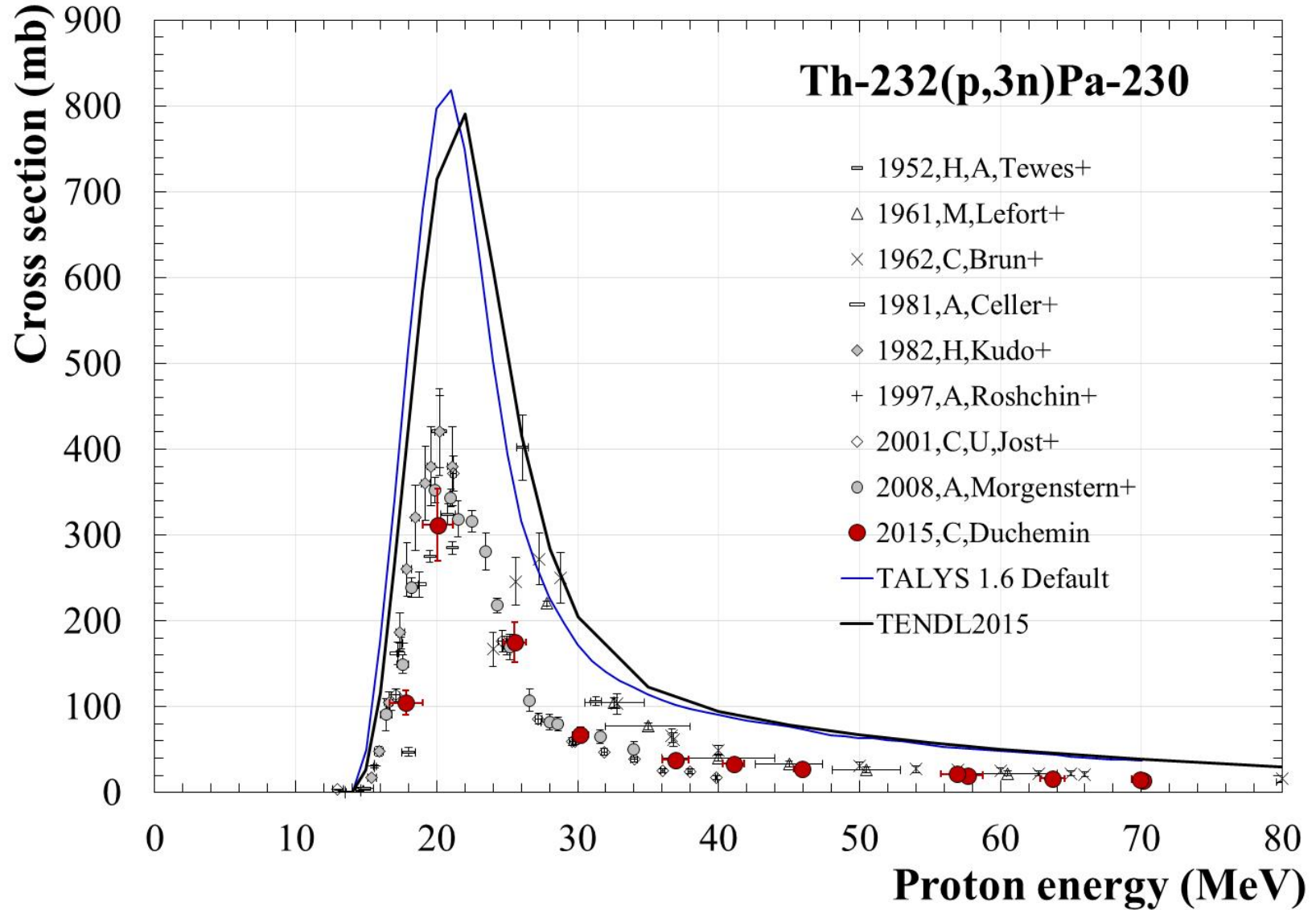
all isotopes living more than 1 second (~ 2800 isotopes)

all files are original except 15 (natural carbon from JENDL-4.0, <sup>1,2,3</sup>H, <sup>2,3</sup>He, <sup>6,7</sup>Li, <sup>10,11</sup>B, <sup>9</sup>Be, <sup>14,15</sup>N, <sup>16</sup>O and <sup>19</sup>F from ENDF/B-VII.1)

Koning A.J. et al., [https://tendl.web.psi.ch/tendl\\_2015/tendl2015.html](https://tendl.web.psi.ch/tendl_2015/tendl2015.html)

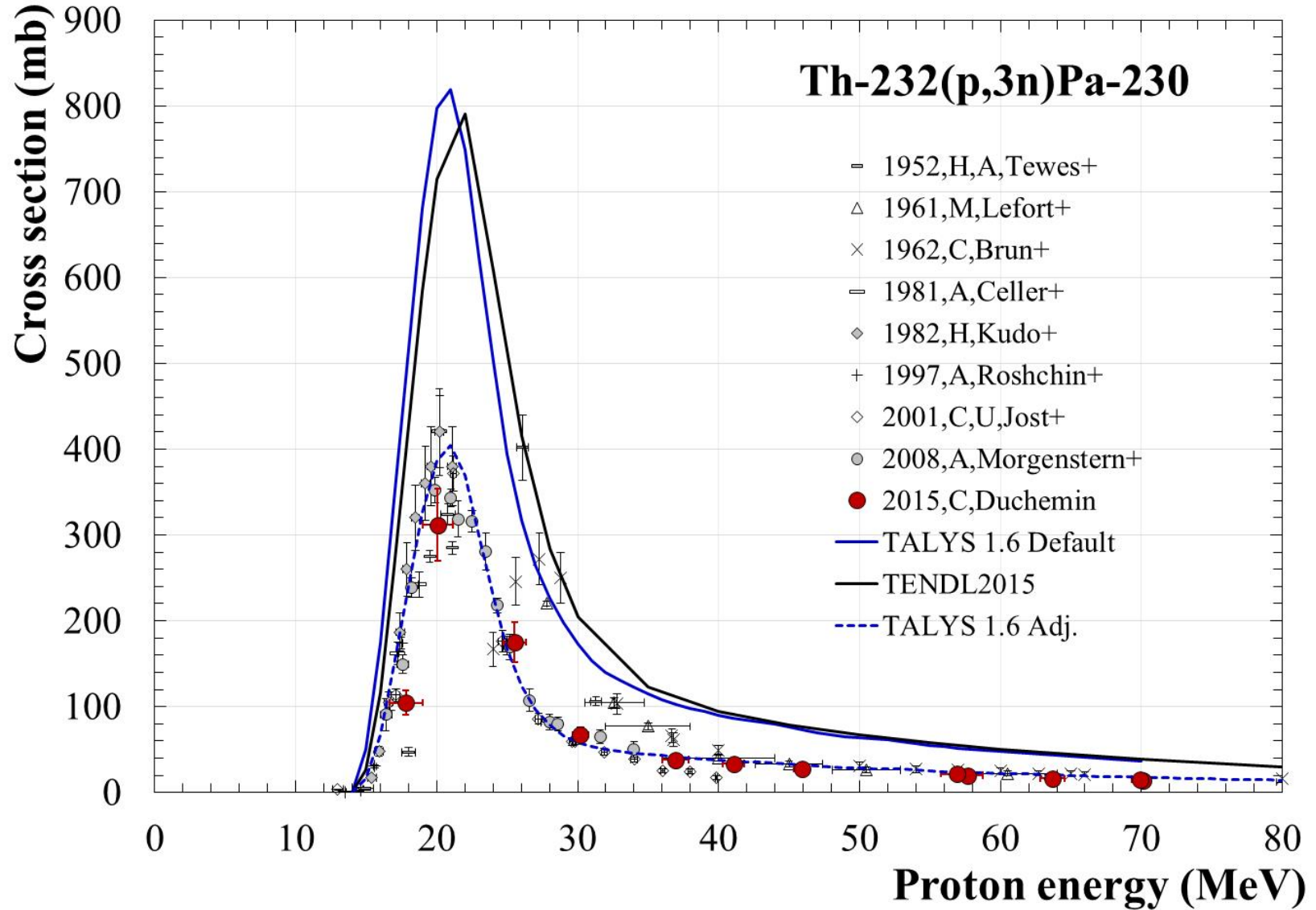
Koning A.J. and Rochman D., Nucl. Data Sheets, 113, 2012

# Novel therapeutic nuclide



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

# Novel therapeutic nuclide



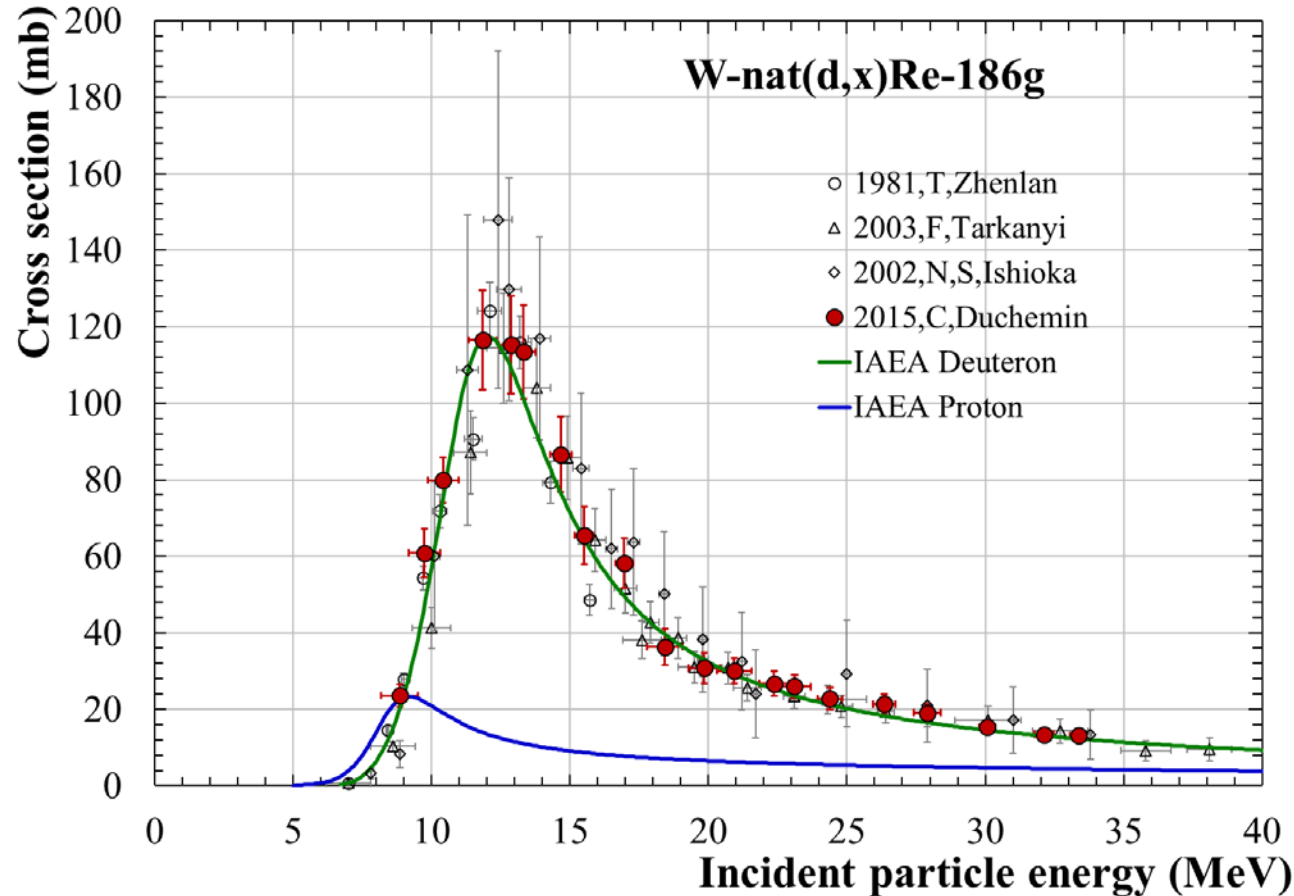
*C. Duchemin et al., Phys. Med. Biol. 60 (2015) 931-946*

# 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

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



# At-211: direct / indirect production

## Targeted alpha-particle radiotherapy

### Direct production with alpha particles

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

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

At-211  $\alpha$  particles

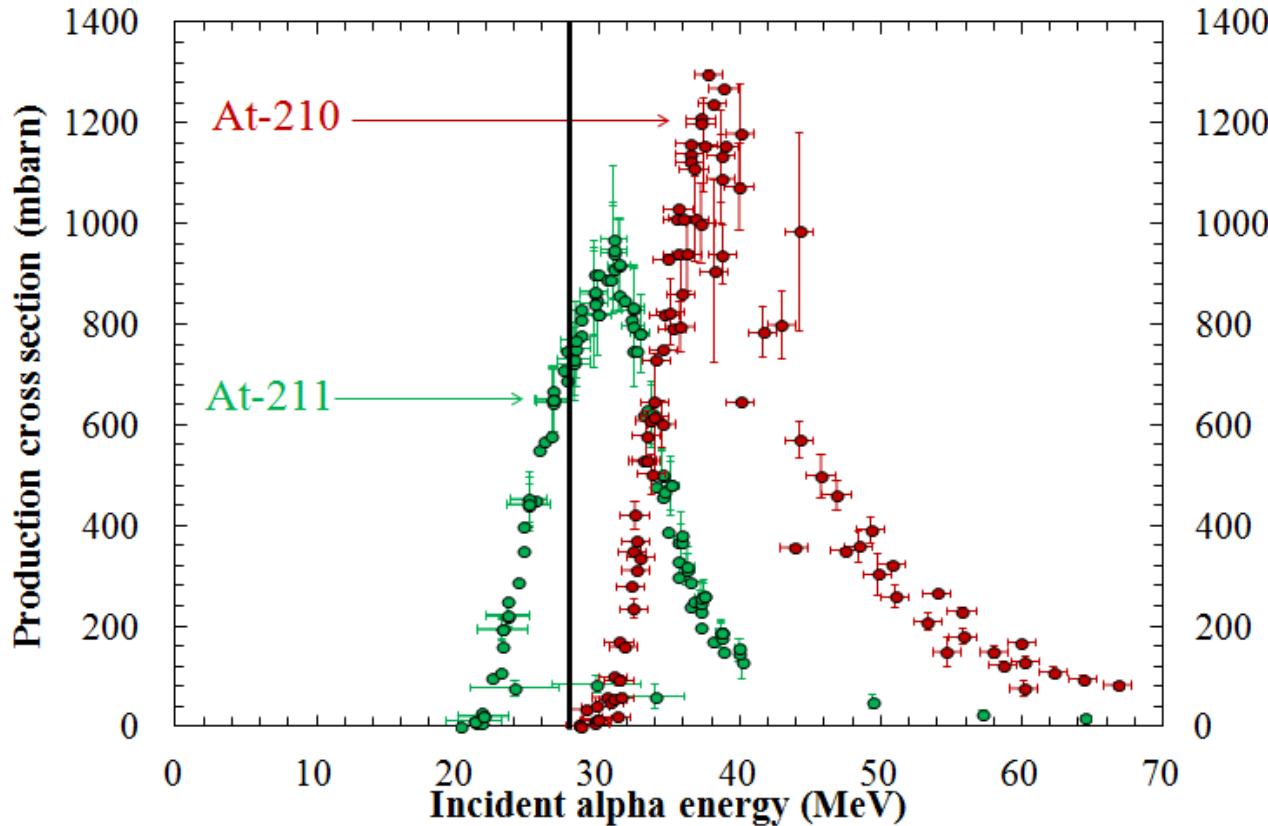
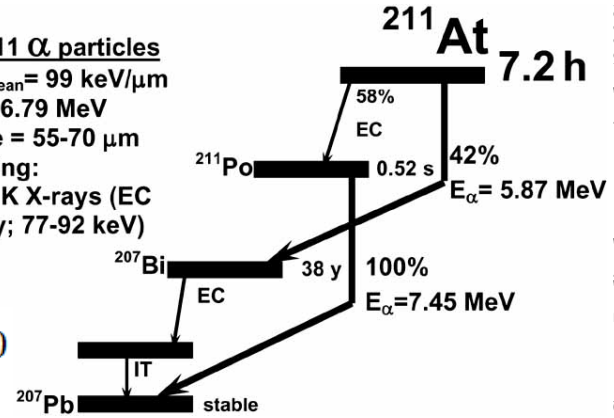
LET<sub>mean</sub> = 99 keV/ $\mu$ m

E<sub>ave</sub> = 6.79 MeV

range = 55-70  $\mu$ m

Imaging:

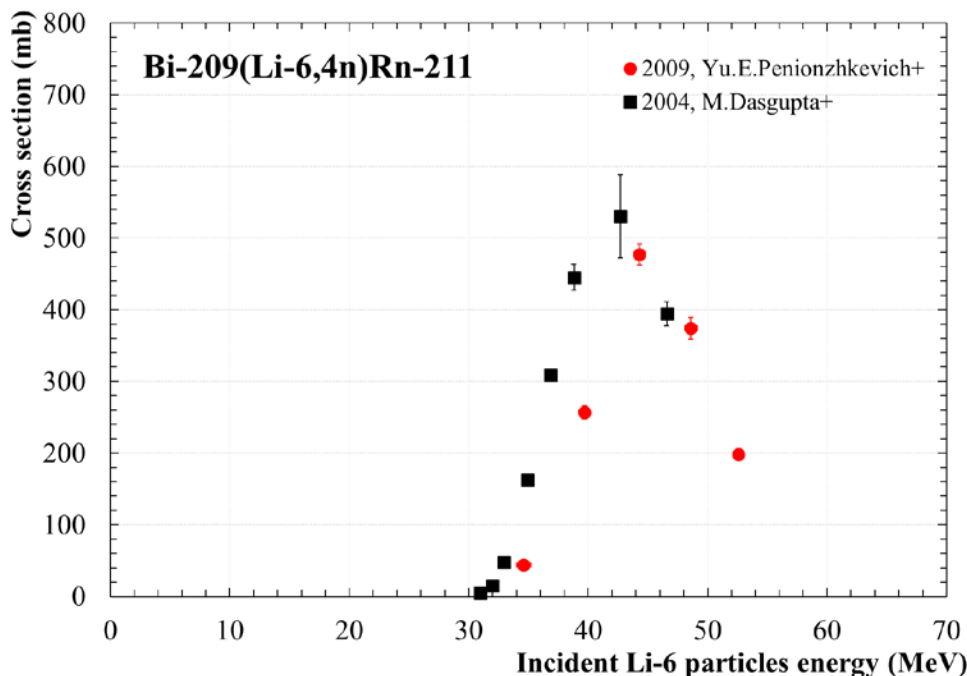
<sup>211</sup>Po K X-rays (EC decay; 77-92 keV)



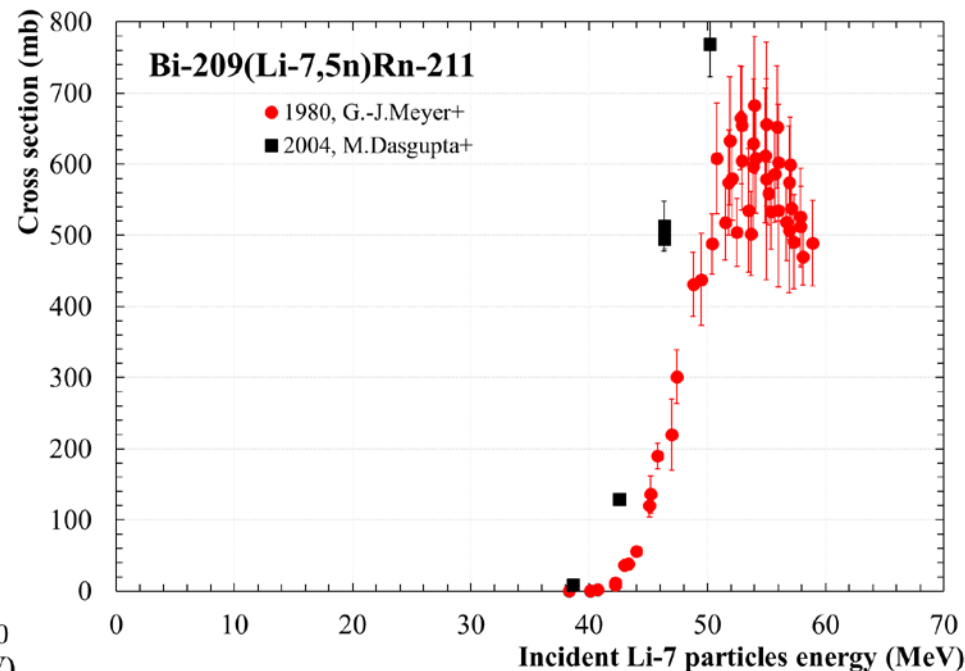
At-210, T<sub>1/2</sub> 8.1 h  
 decays at 99.8% by EC  
 to **Po-210** (138.4 days)  
 and at 0.2% by  $\alpha$  emission  
 to Bi-206 (6.2 days)

## Indirect production with lithium beams

Bi-209(Li-6,4n)Rn-211, 28.5 MeV



Bi-209(Li-7,5n)Rn-211, 36.1 MeV

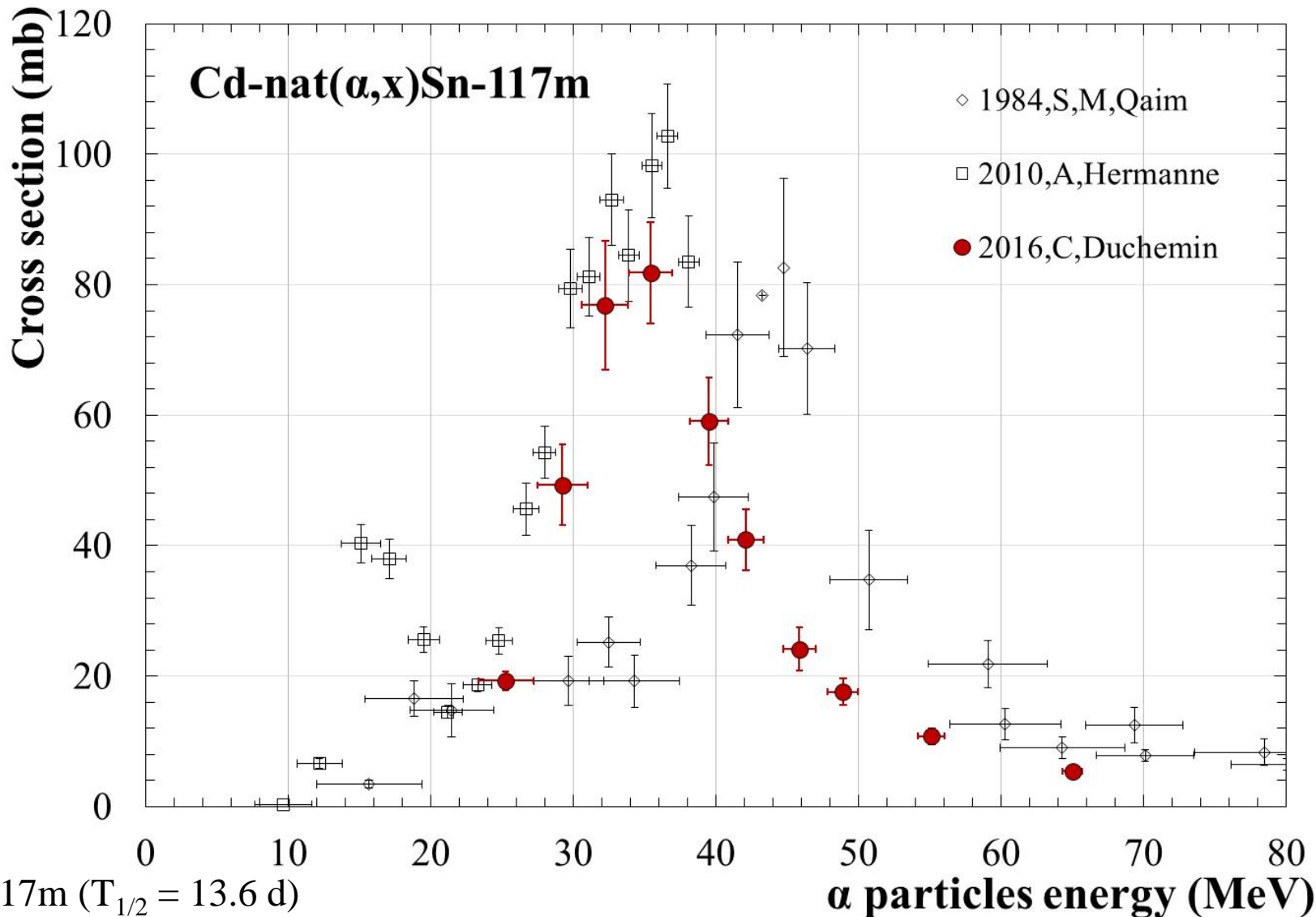


Rn-211 decays at 72.6% by EC to At-211 and by  $\alpha$  decay to Po-207 with a 14.6 h half-life

Rn-210 decays at 3% by EC to **At-210** and at 96% by  $\alpha$  decay to Po-206,  $T_{1/2}$  8.8 d  $\triangle!$

**Astatine can be also available through the Rn211/At211 generator**

# Novel therapeutic and imaging nuclide



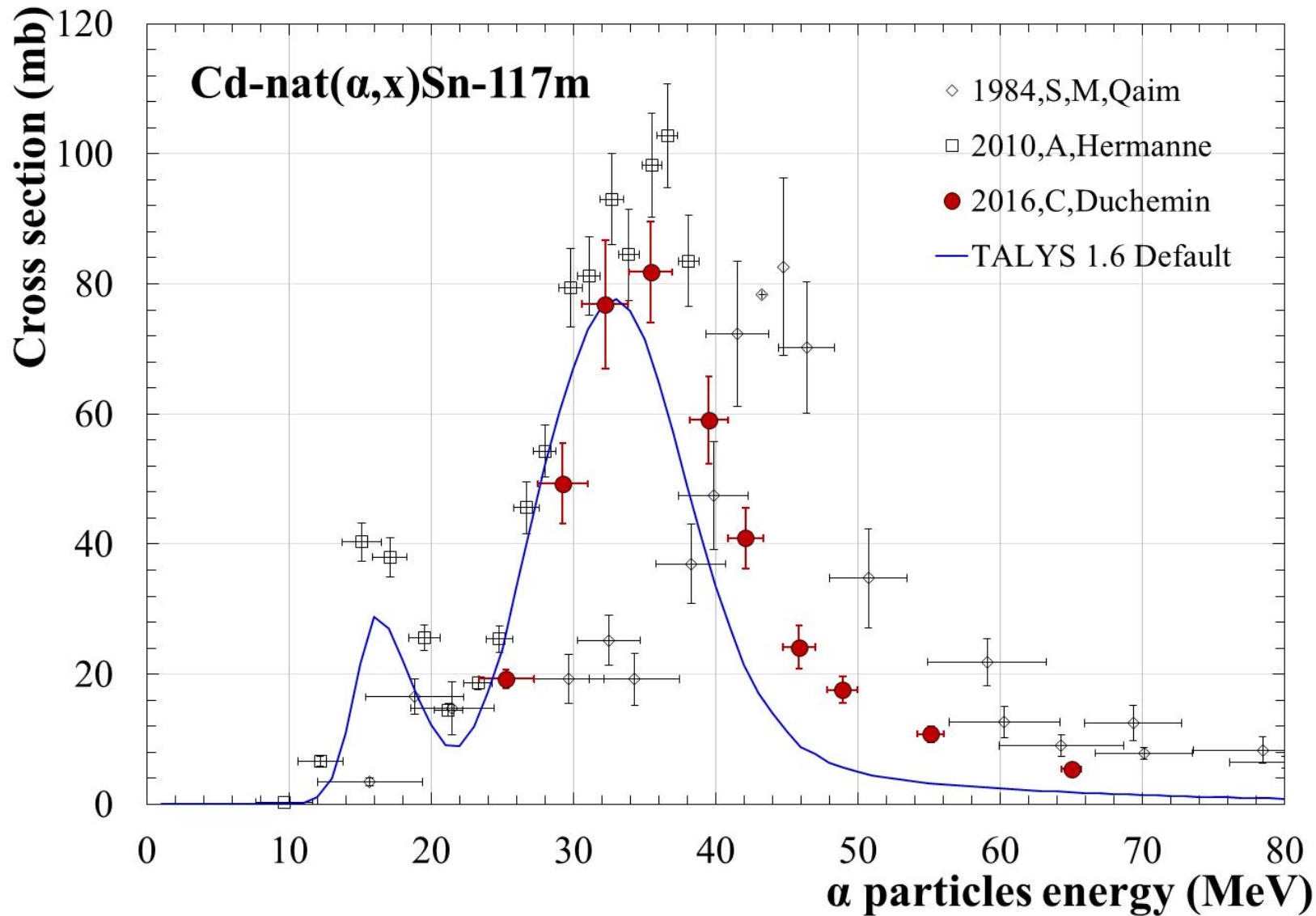
Sn-117m ( $T_{1/2} = 13.6$  d)

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

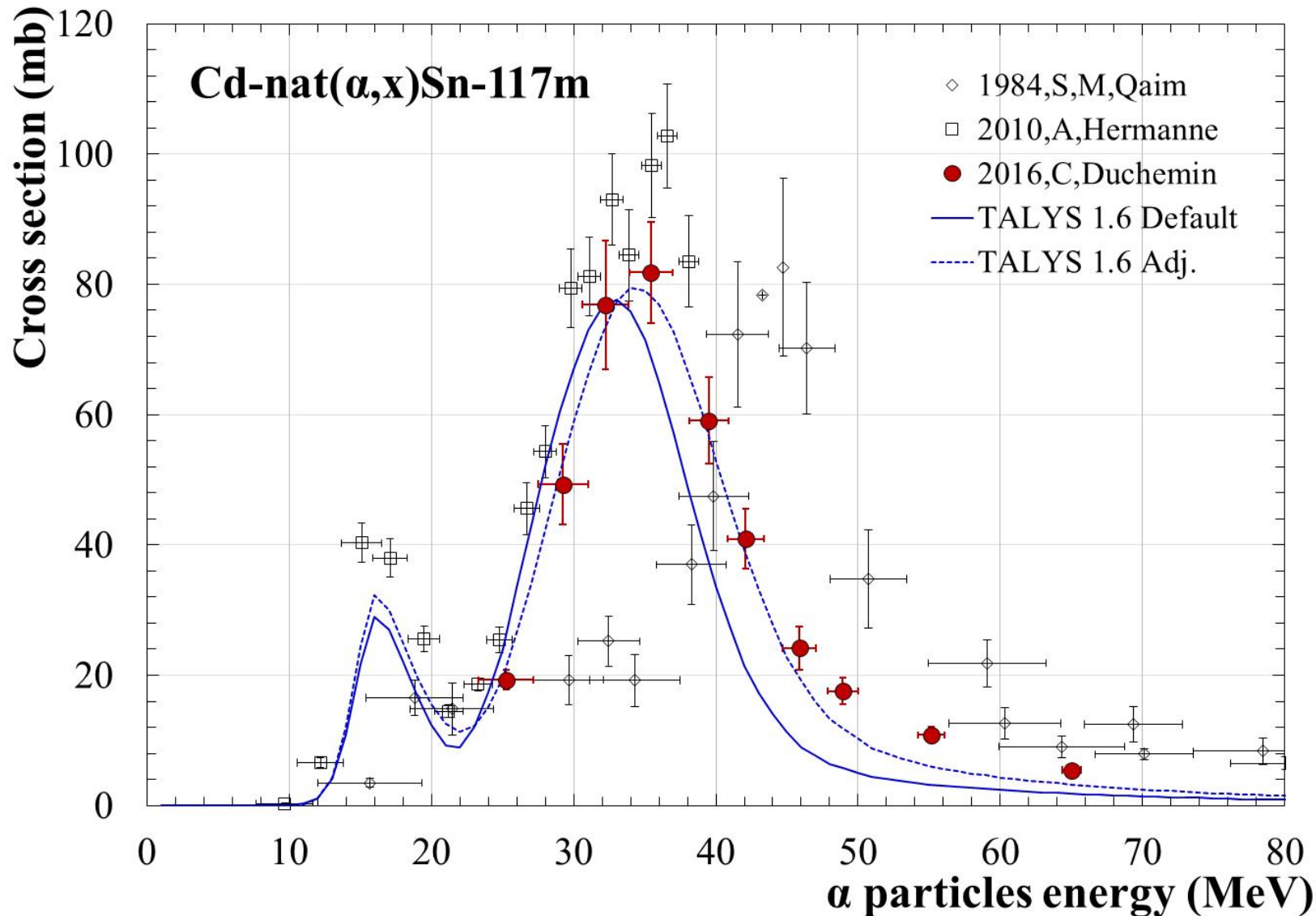
158 keV gamma ray suitable for SPECT imaging

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

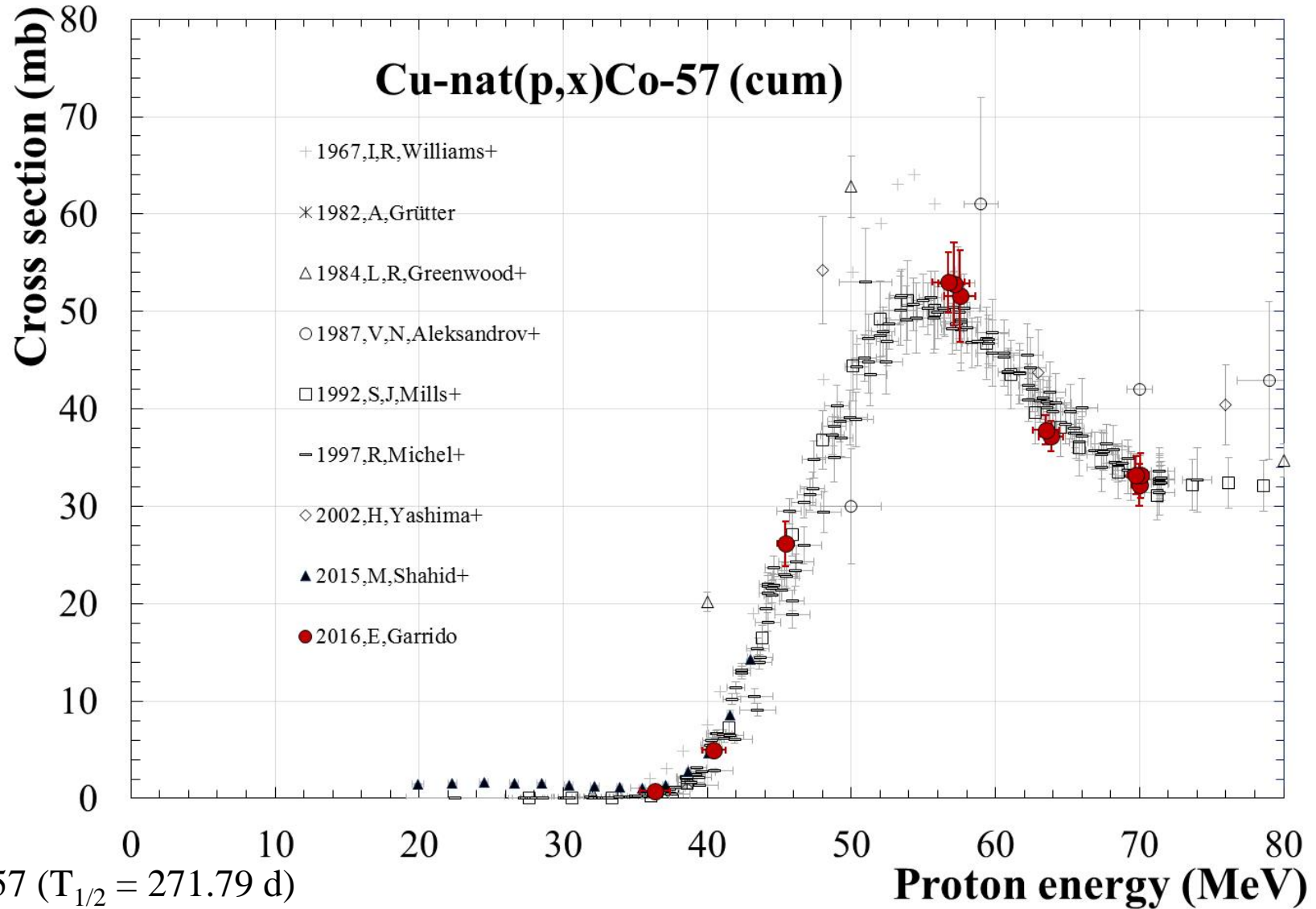
# Novel therapeutic and imaging nuclide



# Novel therapeutic and imaging nuclide



# Monitor reaction



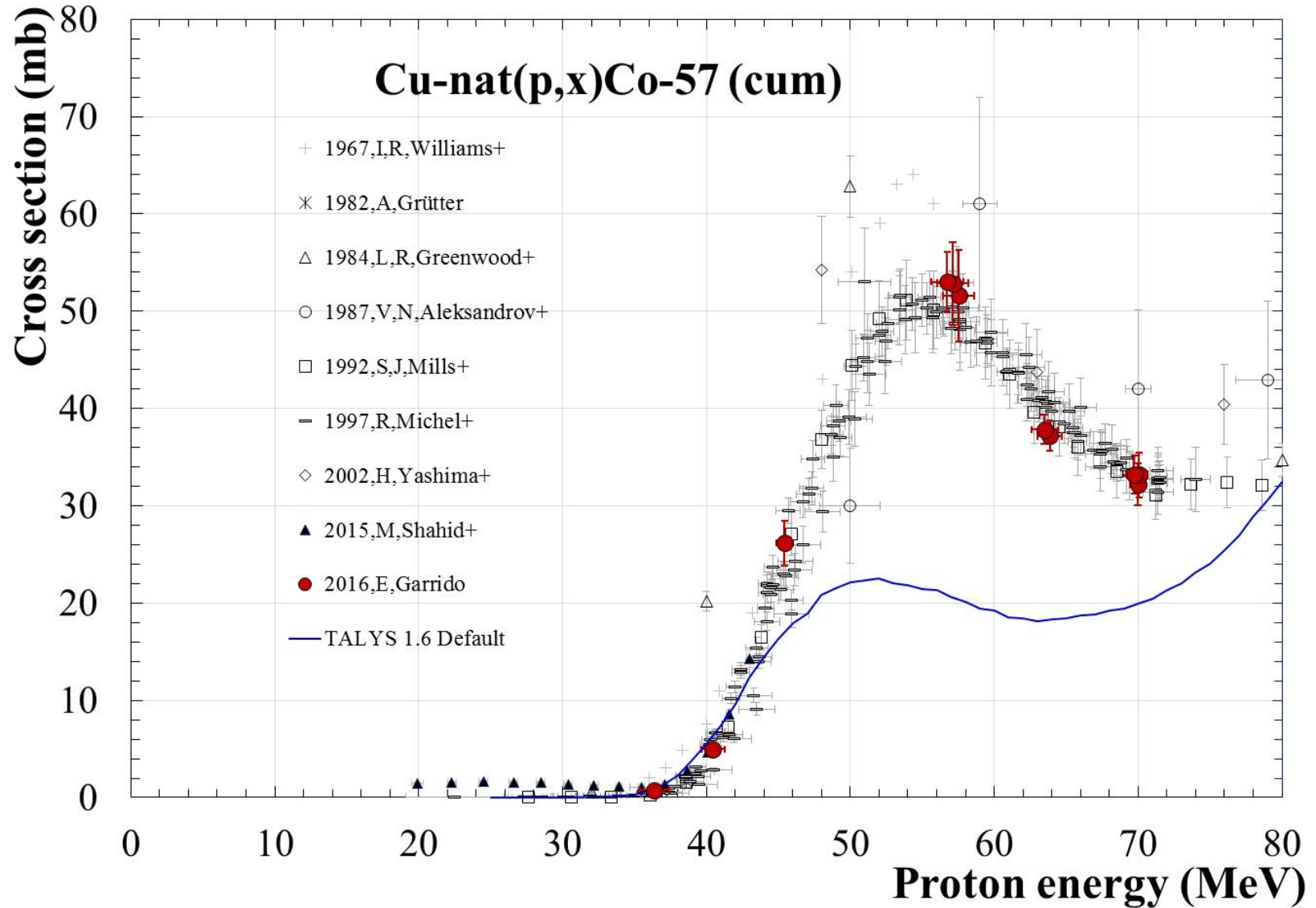
Co-57 ( $T_{1/2} = 271.79$  d)

EC process (100%) to stable Fe-57

Suitable for proton monitor reaction

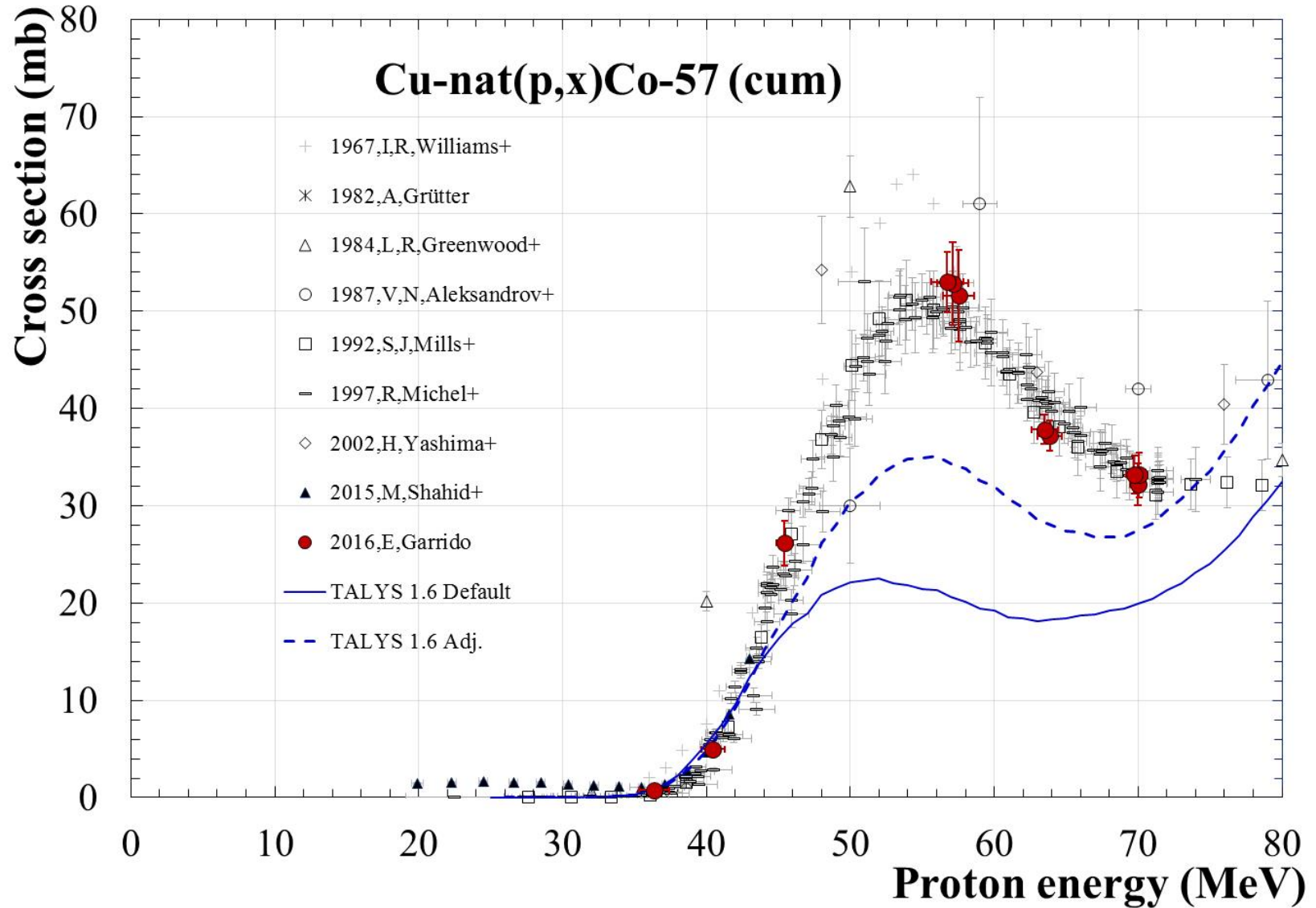
*E. Garrido et al., Nucl. Instr. Meth. Phys. Res. B 383 (2016) 191-212*

# Monitor reaction



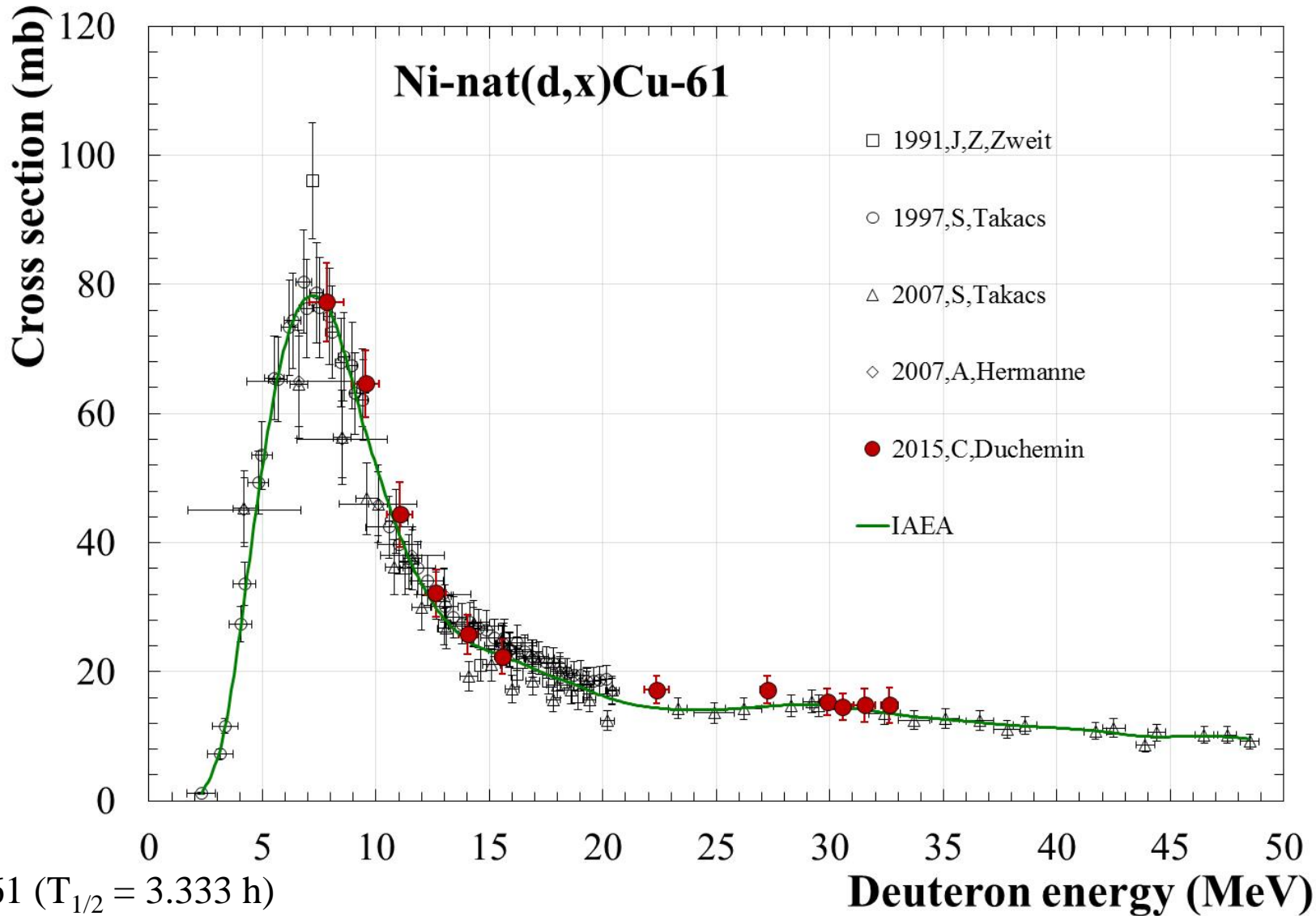
*E. Garrido et al., Nucl. Instr. Meth. Phys. Res. B 383 (2016) 191-212*

# Monitor reaction



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

# Monitor reaction



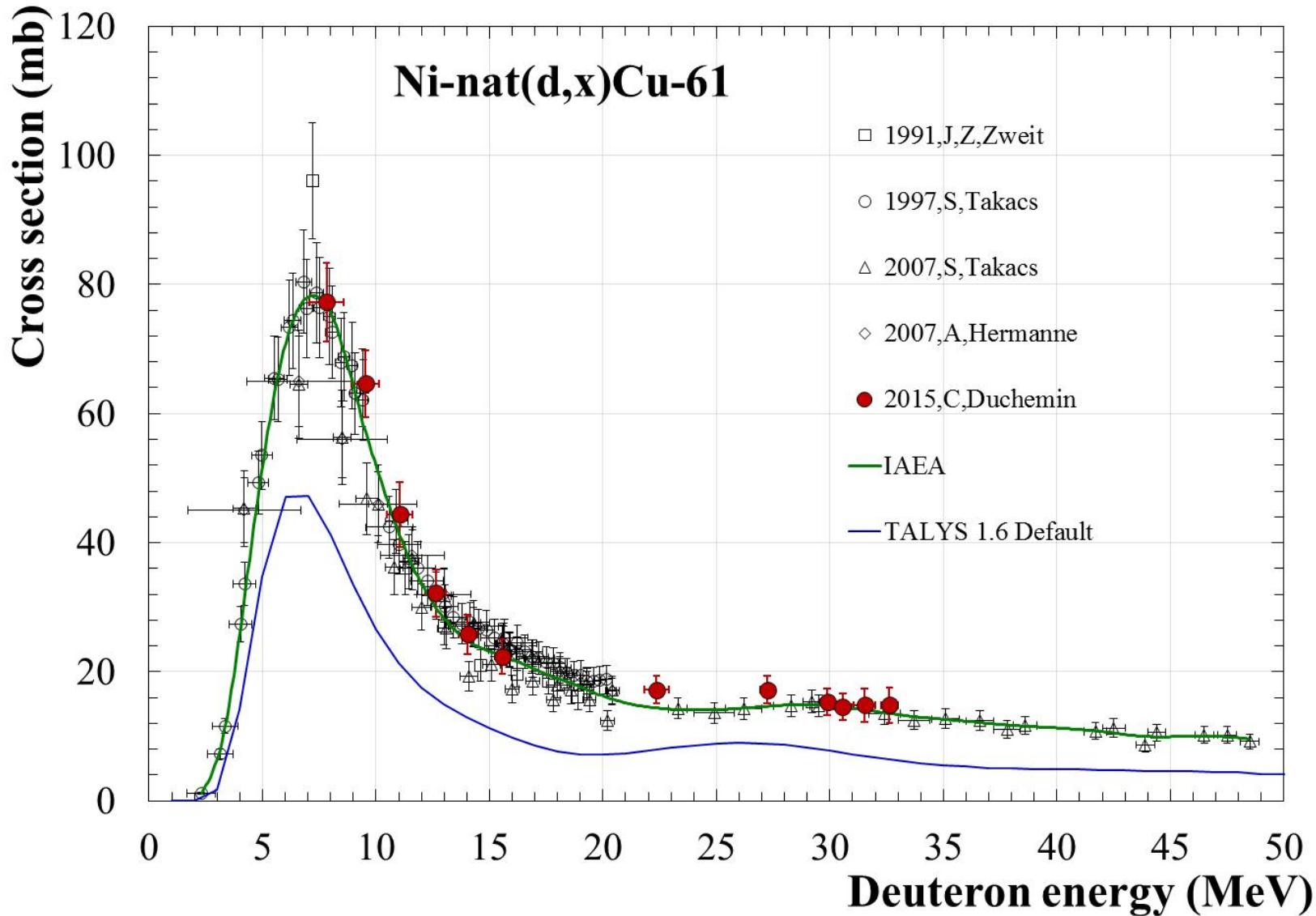
Cu-61 ( $T_{1/2} = 3.333$  h)

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

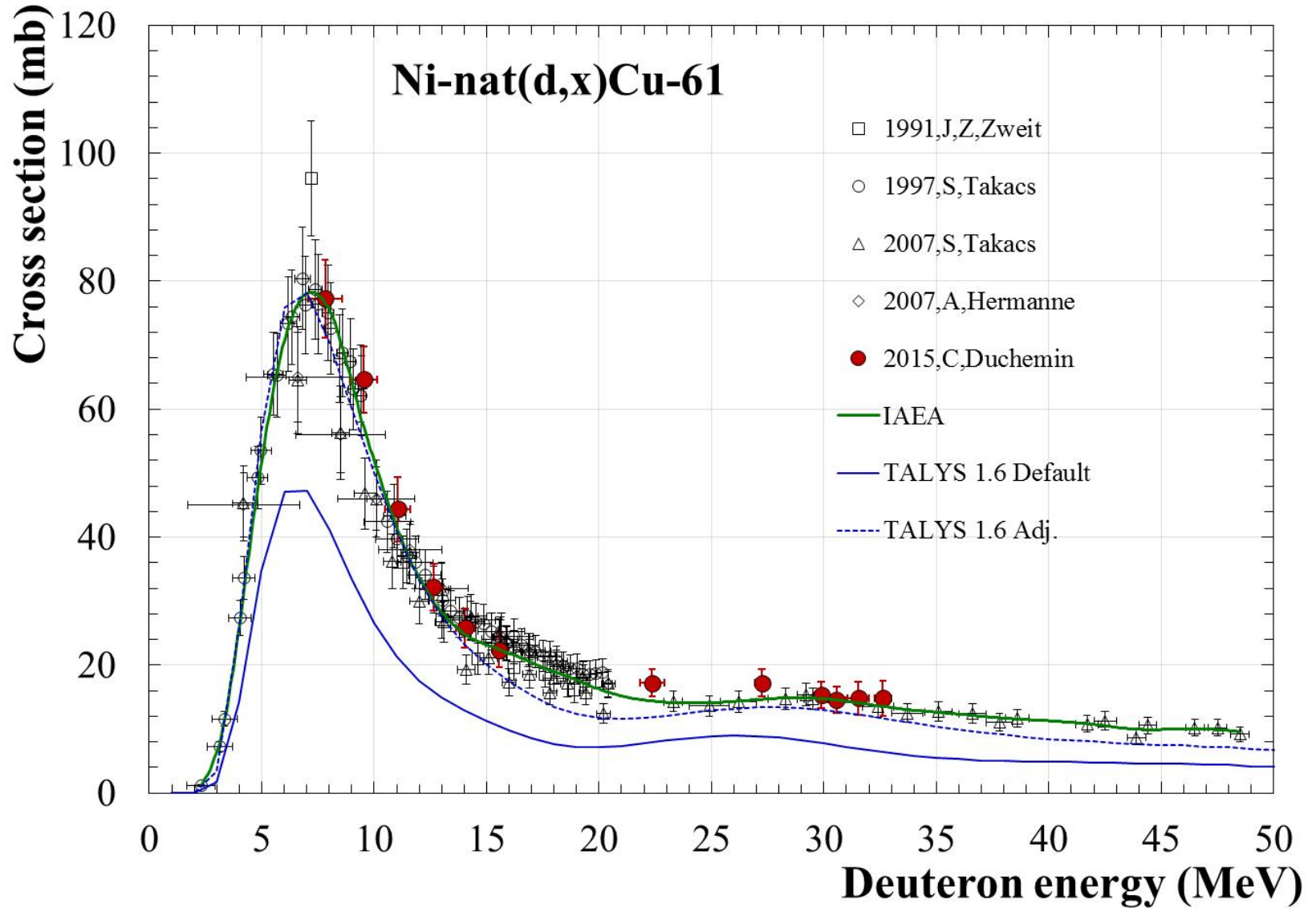
Suitable for PET imaging

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

# Monitor reaction

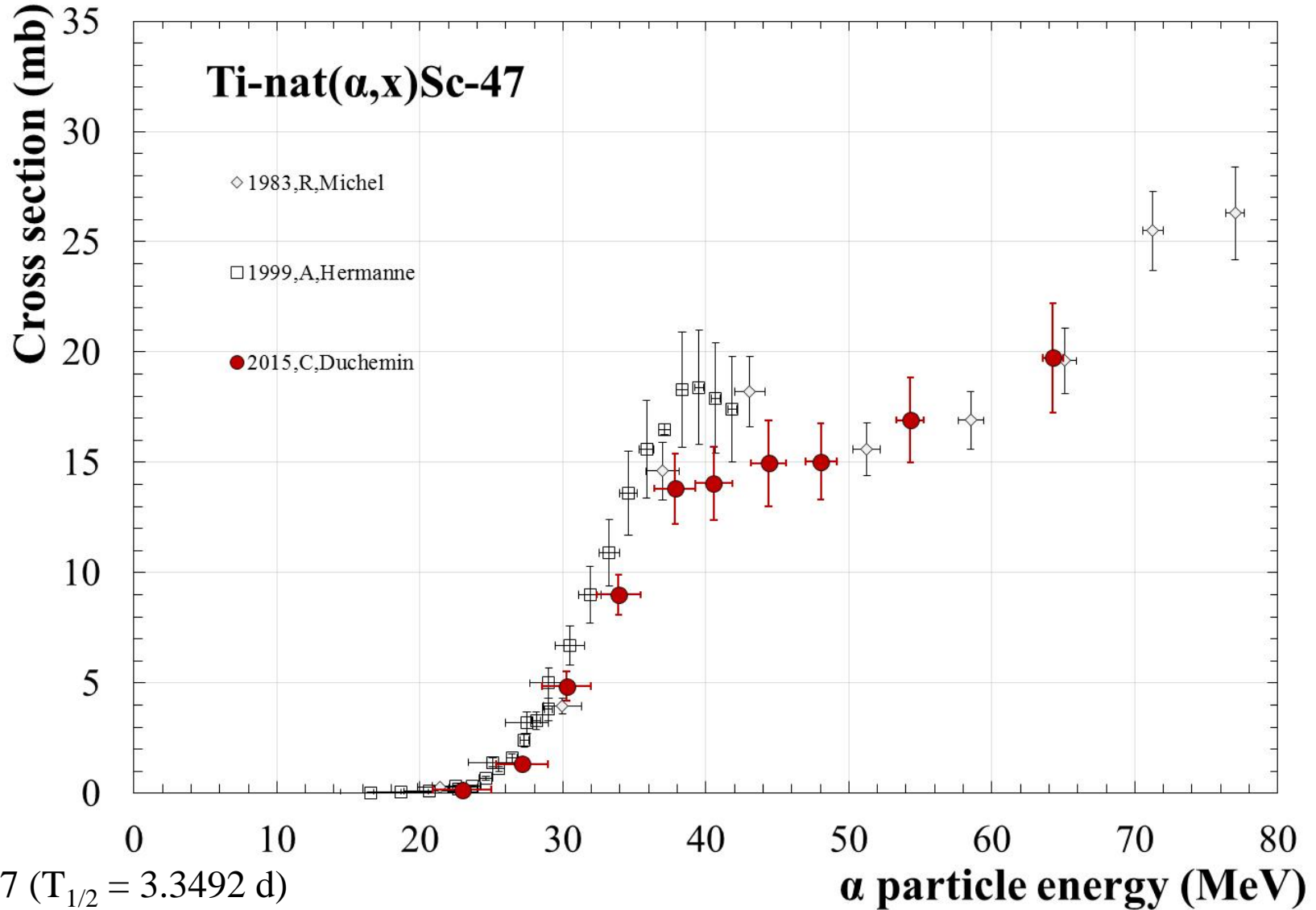


# Monitor reaction



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

# Monitor reaction

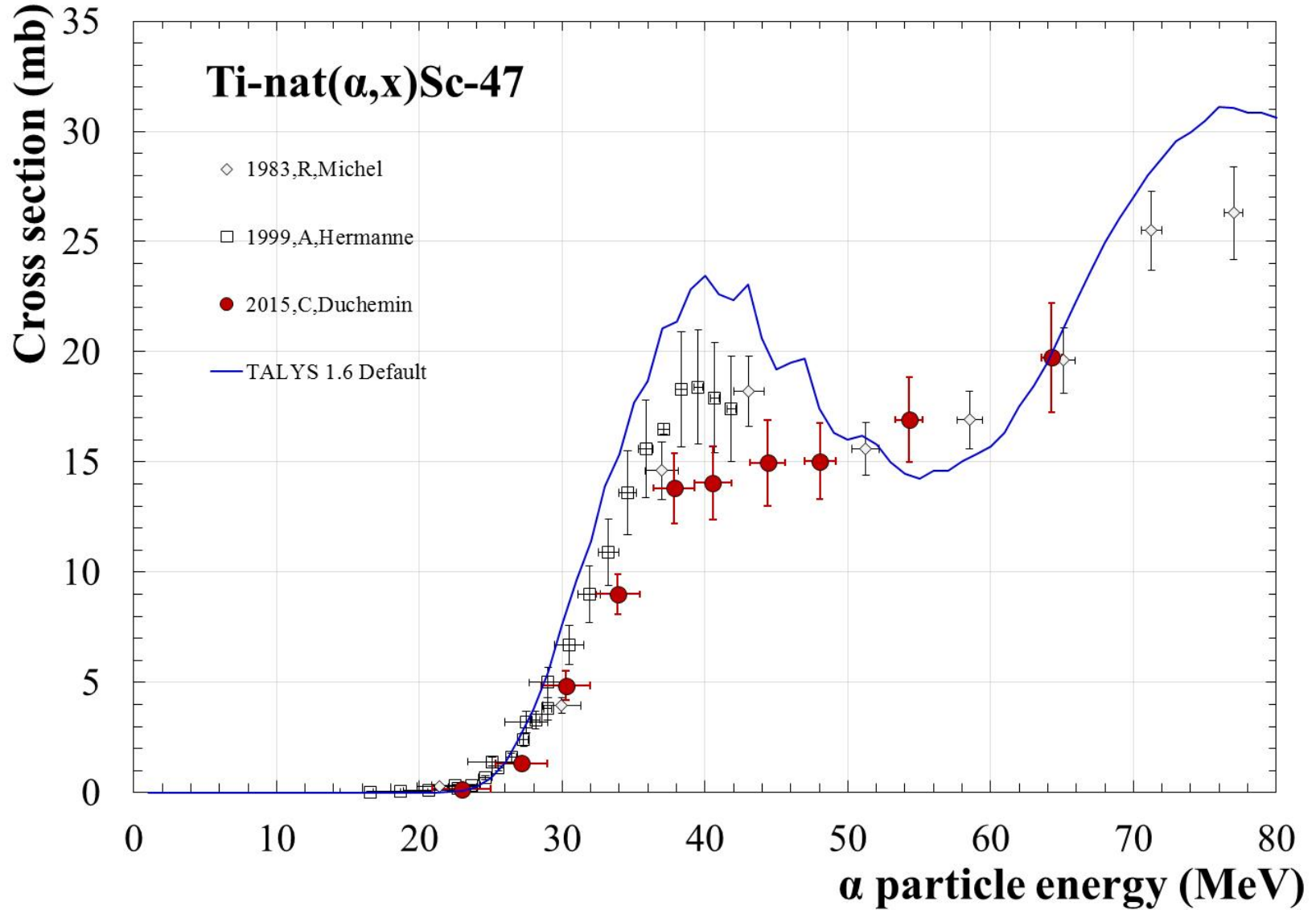


Sc-47 ( $T_{1/2} = 3.3492$  d)  
 $\beta^-$  (100%) to stable Ti-47

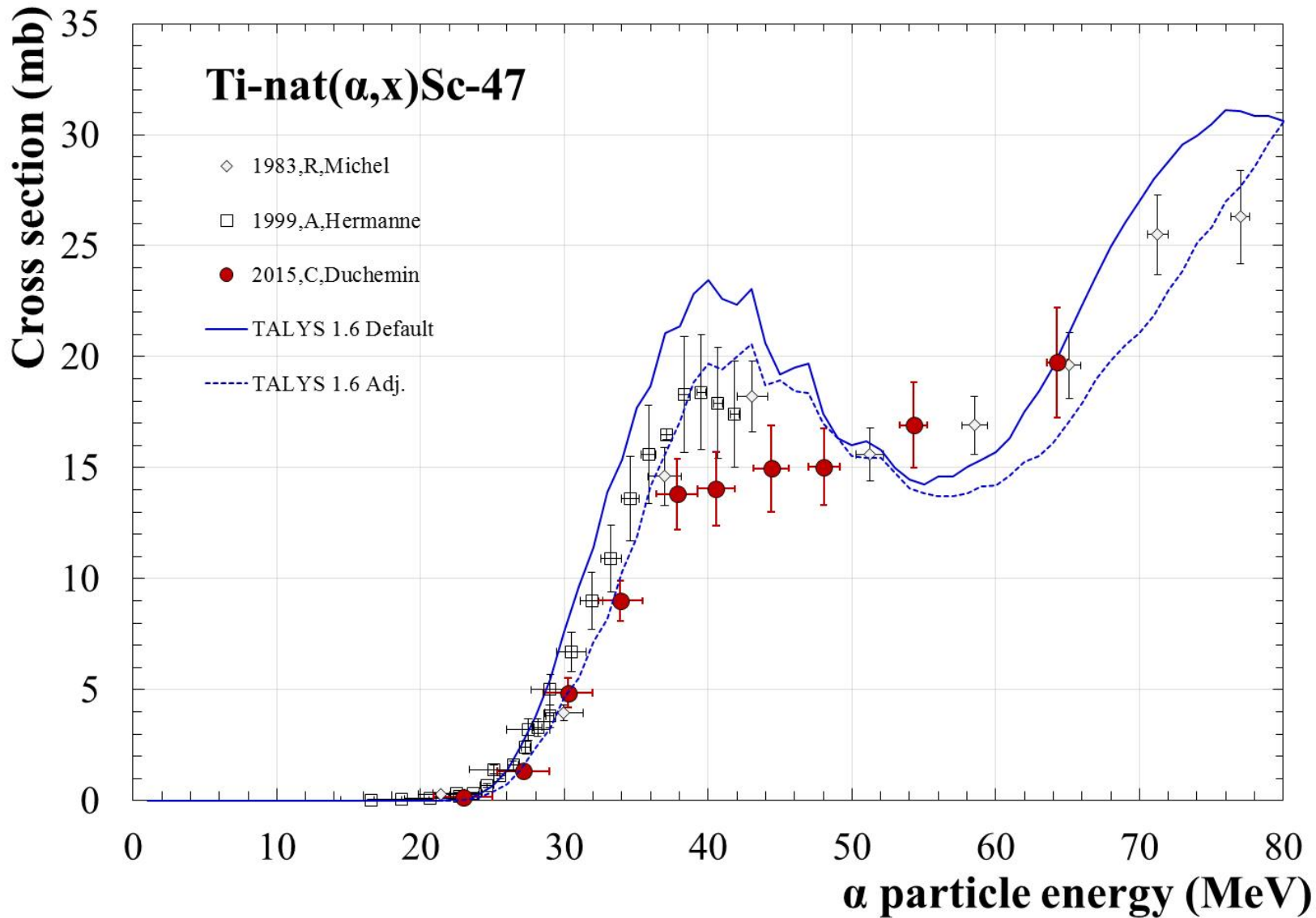
Suitable for theranostic approach with the Sc-44

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

# Monitor reaction



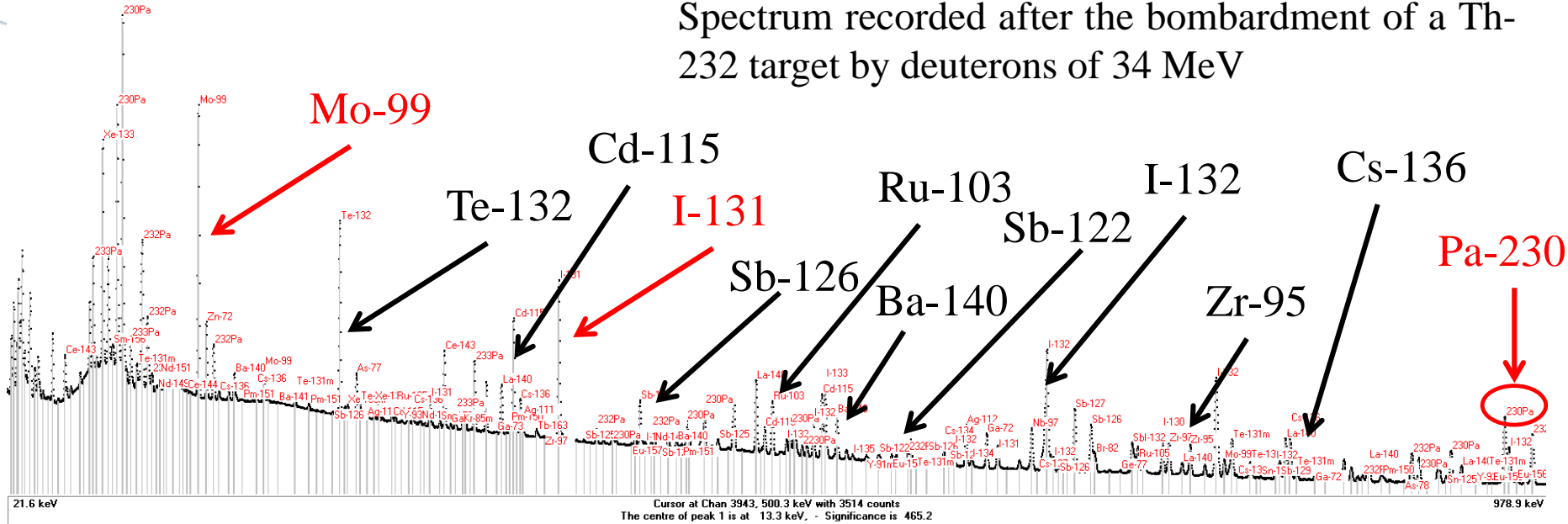
# Monitor reaction



# Th-232 induced fission

## Fission products

Spectrum recorded after the bombardment of a Th-232 target by deuterons of 34 MeV



## Alpha emitters

U-230/Th-226

Ac-225/Bi-213

Th-227/Ra-223

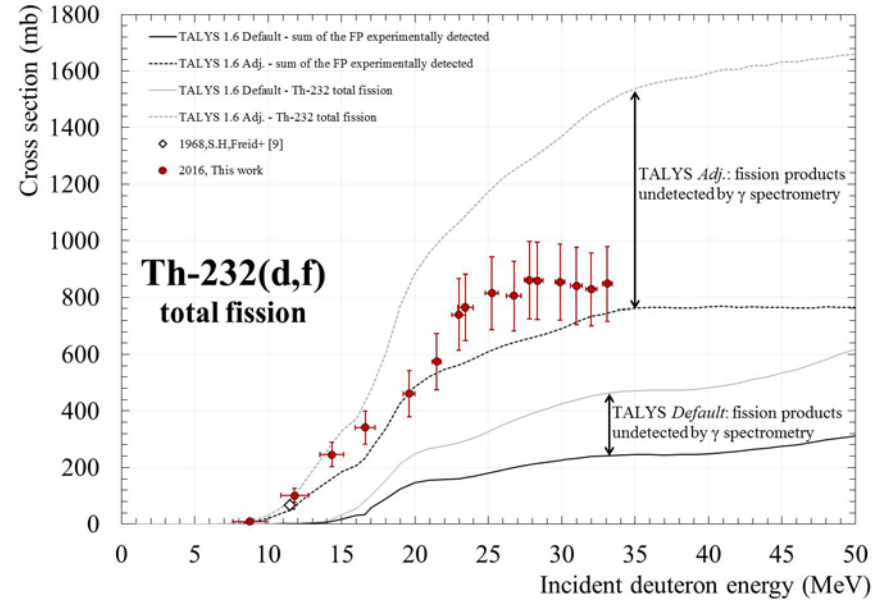
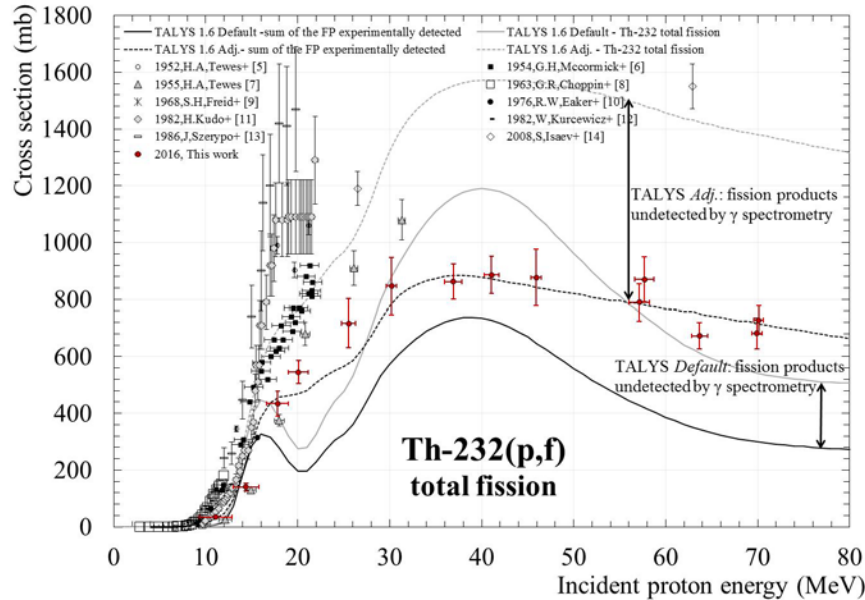
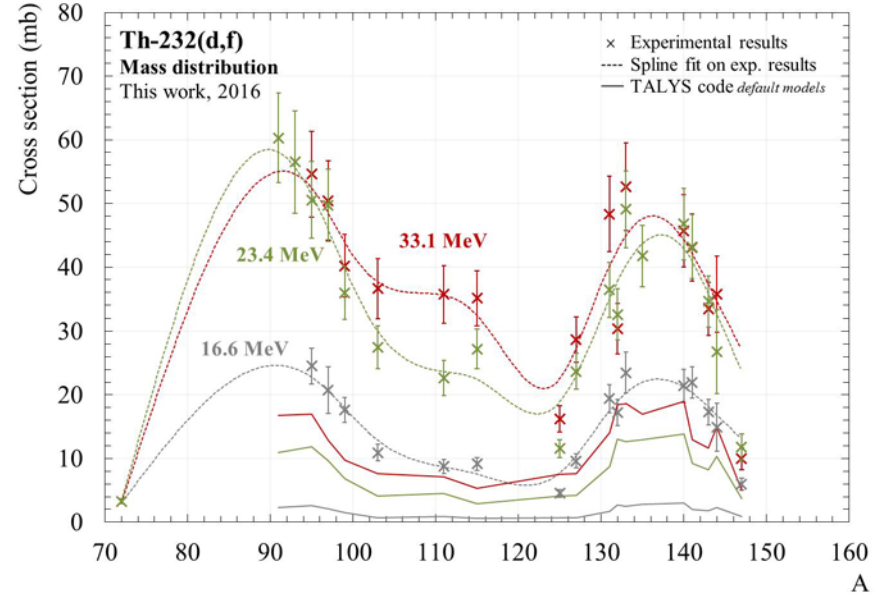
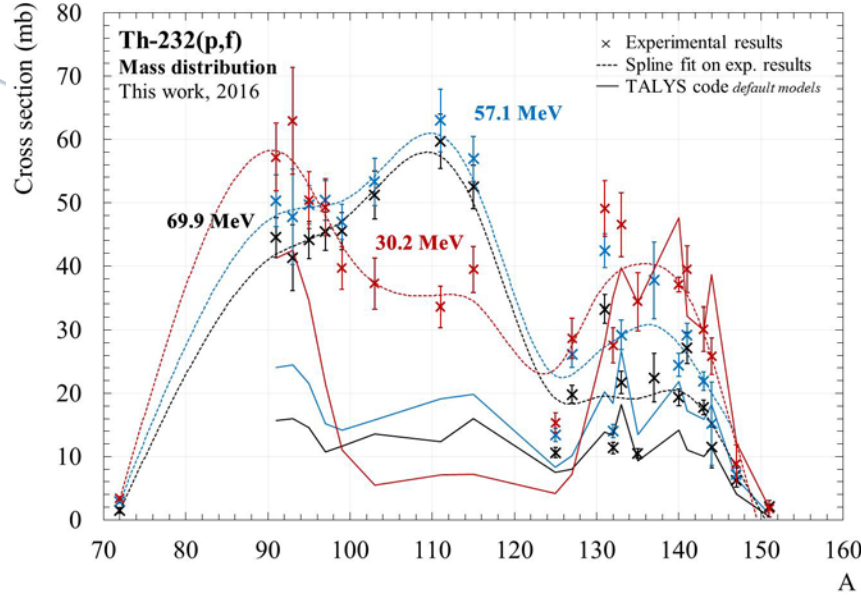
Proton beam

$E_{\text{proton}} > 70 \text{ MeV}$

Radionuclide	$T_{1/2}$	$\alpha$ particle emitted during the disintegration cascade
Bi-213	46 mn	1
Ra-223	11 d	3
Ac-225	10 d	4
Th-226	30 mn	4
Th-227	19 d	4

From C. Duchemin

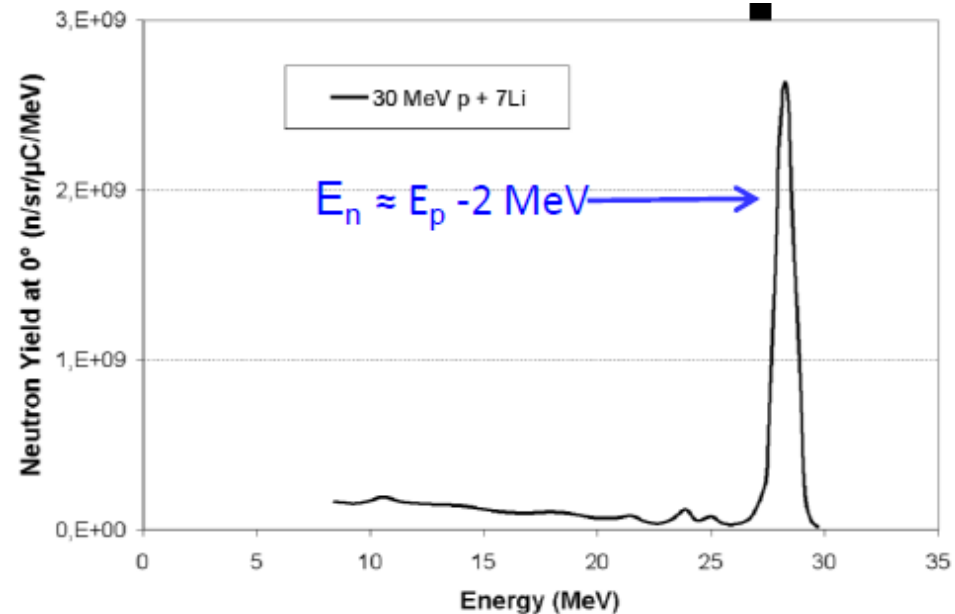
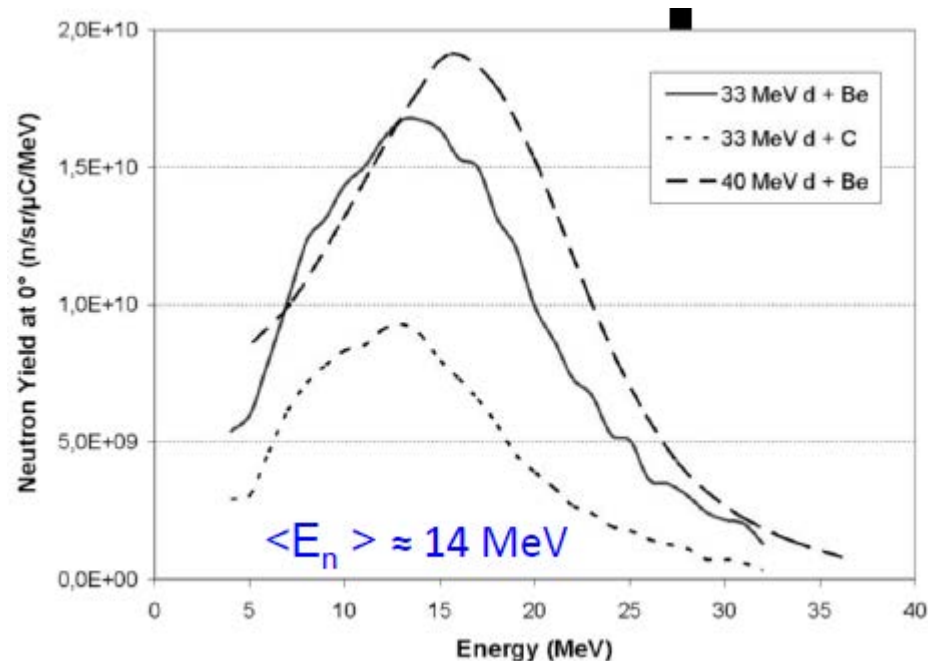
# Th-232 induced fission



# NFS beams

beam	P+	D+	ions	ions
A/Q	1	2	<3	<6 or 7
Max. I (mA)	5	5	1	1
Min. output E (MeV/A)	2	2	2	2
Max output E (MeV/A)	33	20	14.5	8
Max. beam power (kW)	165	200	44	48

*P. Bertrand, Proceedings of HB2014*



*X. Ledoux, SPIRAL2 Training 2015*

## Nuclear medicine

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

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

**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

- **Accurate and reliable** sets of data  
Statistical + systematic errors < 10%
- Well defined **production routes and decay properties**  
neutron, light charged particules and ions
- **Optimum production of specific radionuclides**, minimization / elimination of **impurities**, realistic dose calculations, monitor reactions

## 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

**Thank you for your attention**

Acknowledgments to the NFS Workshop organization committee

**“Nuclear data for applications in nuclear medicine”**

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