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

A. Guertin et al.
Conventional imaging in oncology

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

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

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

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

Morphology

Metabolism
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 ($\gamma$, $\beta^+$)
- 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
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:
- **$\beta^+$**: Cu-64, Ga-68, Zr-89 ...
- **$\gamma$**: Sn-117m ...
- **$\beta^-$**: 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 ...
- **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:

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

**Activity and cross section:**

\[
\sigma = \frac{\text{Act} \cdot A}{\chi \cdot \Phi \cdot N_A \cdot \rho \cdot e \cdot (1 - e^{-\lambda \cdot t})}
\]

**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': ≤ 1%
- error on t: negligible

**IAEA recommended cross sections:**

- 11 reactions available for protons
  
  $^{27}$Al (2), $^{\text{nat}}$Ni, $^{\text{nat}}$Ti (2), $^{\text{nat}}$Cu (5), $^{\text{nat}}$Mo

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

- 6 reactions available for alpha-particles
  
  $^{27}$Al (2), $^{\text{nat}}$Ti and $^{\text{nat}}$Cu (3)
Stacked-foil technique

Off line gamma spectroscopy

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

- $\gamma$ 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

$\gamma$ 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)  
Ra-223 from Th-232(p,x)  
Fission fragment distribution from Th-232(p,x)  
Monitor reactions on Ti, Ni and Cu

Deuteron induced reactions:

Sc-44 New data set for Ca-44(d,x)  
Tb-155 New data set for Gd-nat(d,x)  
Re-186g New data set for W-186(d,x)  
Th-226 New data set for Th-232(d,x)  
Fission fragment distribution from Th-232(d,x)  
Monitor reactions on Ti

“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($\alpha$,x)  
Monitor reactions on Cu, Ti, Ni

“Production of medically interesting $^{97}$Ru via natMo($\alpha$,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

\[ \text{1952, H, A, Tewes}^+ \]
\[ \text{1961, M, Lefort}^+ \]
\[ \text{1962, C, Brun}^+ \]
\[ \text{1981, A, Celler}^+ \]
\[ \text{1982, H, Kudo}^+ \]
\[ \text{1997, A, Roshchin}^+ \]
\[ \text{2001, C, U, Jost}^+ \]
\[ \text{2008, A, Morgenstern}^+ \]
\[ \text{2015, C, Duchemin} \]

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

α RIT for leukaemia treatment

4 α cascade of 27.7 MeV

TALYS

Code for the simulation of nuclear reactions

Many state-of-the-art nuclear models

Provide a complete description of all reactions channels and observables

Nuclear reactions

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

Energy: 1 keV to 1 GeV

Targets: Z = 3 to 110

Influence on the calculated production cross section values

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

Th-232(p,3n)Pa-230

- 1952, H, A, Tewes+
- 1961, M, Lefort+
- 1962, C, Brun+
- 1981, A, Celler+
- 1982, H, Kudo+
- 1997, A, Roshchin+
- 2001, C, U, Jost+
- 2008, A, Morgenstern+
- 2015, C, Duchemin

TALYS 1.9 Default
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, $^1$H, $^2$, $^3$H, $^2$, $^3$He, $^6$, $^7$Li, $^{10}$, $^{11}$B, $^8$Be, $^{14}$, $^{15}$N, $^{16}$O and $^{19}$F from ENDF/B-VII.1)
Pa-230 as a precursor of an $\alpha$ generator

Th-232(p,3n)Pa-230

- 1952, H, A, Tewes
- 1961, M, Lefort
- 1962, C, Brun
- 1981, A, Celler
- 1982, H, Kudo
- 1997, A, Roshchin
- 2001, C, U, Jost
- 2008, A, Morgenstern
- 2015, C, Duchemin

TENDL2015

TALYS 1.9 Default

Cross section (mb)

Proton energy (MeV)
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.

<table>
<thead>
<tr>
<th>Models</th>
<th>Projectile</th>
<th>Default</th>
<th>Adj.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>d (5)</td>
<td>S. Watanabe (1958)</td>
<td>Y. Han et al. (2006)</td>
</tr>
<tr>
<td></td>
<td>α (8)</td>
<td>V. Avrigeanu et al. (2014)</td>
<td>Demetriou et al. (2002)</td>
</tr>
<tr>
<td>Level density</td>
<td>All (6)</td>
<td>Constant temperature and Fermi gas model A.J. Koning et al. (2008)</td>
<td>Microscopic level density (Skyrme force) from Hilaire’s combinatorial tables Goriely et al. (2008)</td>
</tr>
</tbody>
</table>
Pa-230 as a precursor of an \(\alpha\) generator

\[
\text{Th-232(p,3n)Pa-230}
\]

- 1952, H, A, Tewes+
- 1961, M, Lefort+
- 1962, C, Brun+
- 1981, A, Celler+
- 1982, H, Kudo+
- 1997, A, Roshchin+
- 2001, C, U, Jost+
- 2008, A, Morgenstern+
- 2015, C, Duchemin

TENDL2015

TALYS 1.9 Default
TALYS 1.9 Adj
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

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

W-nat(d,x)Re-186g

- Cross section (mb)
- Deuteron energy (MeV)

- 1981, T, Zhenlan
- 2003, F, Tarkanyi
- 2002, N, S, Ishioka
- 2015, C, Duchemin

- IAEA
- TALYS 1.9 Default
Re-186g: deuteron production route

$W_{\text{nat}}(d,x)\text{Re-186g}$

Cross section (mb)

- 1981, T, Zhenlan
- 2003, F, Tarkanyi
- 2002, N, S, Ishioka
- 2015, C, Duchemin

- IAEA
- TALYS 1.9 Default
- TALYS 1.9 Adj.

Deuteron energy (MeV)
Novel therapeutic and imaging nuclide

Sn-117m ($T_{1/2} = 13.6$ d)
Conversion $\gamma$- emitter used for the palliation of painful bone metastases
158 keV gamma ray suitable for SPECT imaging

Novel therapeutic and imaging nuclide

Cd-nat(α,x)Sn-117m

Cross section (mb)

α particles energy (MeV)

1984,S,M,Qaim
2010,A,Hermanne
2016,C,Duchemin
TALYS 1.9 Default
Novel therapeutic and imaging nuclide

Cd-nat(α,x)Sn-117m

Cross section (mb)

α particles energy (MeV)

1984, S, M, Qaim
2010, A, Hermanne
2016, C, Duchemin
TALYS 1.9 Default
TALYS 1.9 Adj.
Terbium 155: theranostic isotope

$\text{Tb-155 (T}_{1/2} = 5.3 \text{ d})$

a theranostic isotope for SPECT imaging and Auger therapy

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

Gd-nat(d,x)Tb-155
Terbium 155

Gd-nat(d,x)Tb-155

- 2014, Tarkanyi
- 2016, C. Duchemin
- TALYS 1.9 Default

Cross section (mb)

Alpha particles energy (MeV)
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 particles energy (MeV)
Co-57 ($T_{1/2} = 271.79$ d)

EC process (100%) to stable Fe-57

Suitable for proton monitor reaction

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**Cu-nat(p,x)Co-57 (cum)**

1967, L.R., Williams+

1982, A., Grütter

1984, L.R., Greenwood+

1987, V.N., Aleksandrov+

1992, S.J., Mills+

1997, R., Michel+

2002, H., Yashima+

2015, M., Shahid+

2016, E., Garrido

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Monitor reaction
Monitor reaction

Cu-nat(p,x)Co-57 (cum)

- 1967, I.R. Williams
- 1982, A. Grütter
- 1984, L.R. Greenwood
- 1987, V.N. Aleksandrov
- 1992, S.J. Mills
- 1997, R. Michel
- 2002, H. Yashima
- 2015, M. Shahid
- 2016, E. Garrido
- TALYS 1.9 Default

Cross section (mb)

Proton energy (MeV)
Monitor reaction

Cu-nat(p,x)Co-57 (cum)

Cross section (mb)

Proton energy (MeV)

1967, I.R. Williams†
1982, A. Grütter
1984, L.R. Greenwood†
1987, V.N. Aleksandrov†
1992, S.J. Mills†
1997, R. Michel†
2002, H. Yashima†
2015, M. Shahid†
2016, E. Garrido

TALYS 1.9 Default
TALYS 1.9 Adj.
Monitor reaction

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

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

Suitable for PET imaging

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

Ni-nat(d,x)Cu-61

- 1991, J, Z, Zweit
- 1997, S, Takacs
- 2007, S, Takacs
- 2007, A, Hermanne
- 2015, C, Duchemin

Cross section (mb)

Deuteron energy (MeV)
Monitor reaction

Ni-nat(d,x)Cu-61

- 1991, J, Z, Zweit
- 1997, S, Takacs
- 2007, S, Takacs
- 2007, A, Hermann
- 2015, C, Duchemin

IAEA
TALYS 1.9 Default
TALYS 1.9 Adj.

Cross section (mb)

Deuteron energy (MeV)
Monitor reaction

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

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

Suitable for theranostic approach with the Sc-44

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**Ti-nat($\alpha,x$)Sc-47**

- 1983, R, Michel
- 1999, A, Hermann
- 2015, C, Duchemin

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

Ti-nat(α,x)Sc-47

1983, R, Michel
1999, A, Hermanne
2015, C, Duchemin

TALYS 1.9 Default

Cross section (mb)

α particle energy (MeV)
Monitor reaction

Ti-nat(α,x)Sc-47

- 1983, R, Michel
- 1999, A, Hermanne
- 2015, C, Duchemin

TALYS 1.9 Default

TALYS 1.9 Adj.

Cross section (mb)

α particle energy (MeV)
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
Thank you for your attention

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

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