How nuclear data collected for medical radionuclides production at ARRONAX could constrain the TALYS code

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AccApp’17
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Motivation: study of the production of innovative radionuclides for nuclear medicine
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- **Diagnosis** → to reveal/localize the disease
  - Functional imaging (organs' activity, cells metabolism)
- **Therapy** → to treat the disease
  - $\alpha$ particle/electron emitters
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  - I-131 for therapy
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  - F-18 linked to a glucose analogue for PET imaging
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Since 2010: collaboration between the Subatech laboratory & ARRONAX in Nantes in France
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SUBATECH
Research lab

- Particle physics
- Nuclear physics
- Nuclear chemistry
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C70 Cyclotron build by IBA:
- 4 sectors isochron cyclotron
- 2 extraction methods: stripper or electrostatic deflector
- 6 beam lines
  one vault devoted to experiments

Extracted Energy Max. current
Extracted (MeV) (μA)
H⁺ 30 – 70 2 × 375
D⁺ 15 – 35 2 × 50
He²⁺ 68 70
HH⁺ 17 50

Accelerator for the Research in Radiochemistry and in Oncology at Nantes Atlantique X
2. Production process
1. Motivation  
2. Production process  
3. $\sigma$ determination  
4. Exp. Set-up  
5. RN of interest  
6. TALYS  
7. Results & discussion  
8. Conclusions
2. Particle flux

1. Target

3. radionuclide(s)

4. Exp. Set-up

5. RN of interest

6. TALYS

7. Results & discussion

8. Conclusions
Usual production routes

→ Accelerators: low energy protons
  F-18

→ Reactors: neutrons
  I-131, Mo-99

The production of a limited number of radionuclides can be assessed through these production routes.
Study of alternative production routes for the production of innovative radionuclides

1. Motivation
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2. Particle flux

1. Target

3. Radionuclide(s) produced

$\rightarrow$ High energy protons
$\rightarrow$ Deuterons
$\rightarrow$ $\alpha$ particles

$\rightarrow$ Fission process
Study of alternative production routes for the production of innovative radionuclides

- High energy protons
- Deuterons
- α particles
- Fission process

The production cross section is not known or only few experimental data are available

→ Needed to determine the best production pathway and the best irradiation conditions
3. Production cross section determination
Thin target approach

Few µm thick
Thin target approach

→ **Low energy loss** of the projectile through the target
Thin target approach

→ **Low energy loss** of the projectile through the target

→ **σ slightly changes** on this small energy range
Thin target approach

→ **Low energy loss** of the projectile through the target

→ **σ slightly changes** on this small energy range

→ for a mean energy value of the projectile crossing the target

  \[ \sigma \]

  =

  One experimental σ value
Thin target approach

→ **Low energy loss** of the projectile through the target

→ **σ slightly changes** on this small energy range

→ for a mean energy value of the projectile crossing the target

\[
\text{Act} = \sigma (E) \cdot \Phi \cdot \chi \cdot \frac{N_A \cdot \rho \cdot \text{ef}}{A} \cdot (1 - \exp(-\lambda \cdot t_{irr}))
\]

Produced radionuclide

Target

Irradiation conditions

1. Motivation
2. Production process
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Stack of foils made of a:

- **Target**: to produce the radionuclide
  for which the cross section will be determined
Stack of foils made of a:

→ **Target**: to produce the radionuclide for which the cross section will be determined

→ **Degrader**: to decrease the beam energy
Stack of foils made of a:

→ **Target:** to produce the radionuclide for which the cross section will be determined

→ **Degrader:** to decrease the beam energy

!! Particle flux measured at the end of the stack
Stack of foils made of a:

→ **Target**: to produce the radionuclide for which the cross section will be determined

→ **Monitor**: to produce a radionuclide with a cross section value of *reference*

→ **Degrader**: to decrease the beam energy
Monitor reactions

. Defined by the International Atomic Energy Agency (IAEA) 
  Coordinated Research Project F41029 
  « Nuclear Data for Charged-particle Monitor Reactions and Medical Isotope Production »
Monitor reactions

Defined by the International Atomic Energy Agency (IAEA) Coordinated Research Project F41029 « Nuclear Data for Charged-particle Monitor Reactions and Medical Isotope Production »

→ Analysis of the $\sigma$ exp. data and related articles
→ Adjustment of the selected data
→ Determination of recommended/reference values

\[
\text{Act} = \sigma (E) \cdot \Phi \cdot \chi \cdot \frac{N_A \cdot \rho \cdot \text{ef}}{A} \cdot (1 - \exp(-\lambda \cdot t_{irr}))
\]
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\]

\[
\Phi = \frac{\text{Act} \cdot A}{\sigma(E) \cdot \chi \cdot N_A \cdot \rho \cdot \text{ef} \cdot (1 - \exp(-\lambda \cdot t_{irr}))}
\]

\[
\Phi' = \frac{\text{Act}' \cdot A'}{\sigma'(E') \cdot \chi' \cdot N_A \cdot \rho' \cdot \text{ef}' \cdot (1 - \exp(-\lambda' \cdot t_{irr}))}
\]
\[ \text{Act} = \sigma(E) \cdot \phi \cdot \chi \cdot \frac{N_A \cdot \rho \cdot \text{ef}}{A} \cdot (1 - \exp(-\lambda t_{irr})) \]

\[ \phi_{\text{Target}} = \frac{\text{Act} \cdot A}{\sigma(E) \cdot \chi \cdot N_A \cdot \rho \cdot \text{ef} \cdot (1 - \exp(-\lambda t_{irr}))} \]

\[ \phi'_{\text{Monitor}} = \frac{\text{Act}' \cdot A'}{\sigma'(E') \cdot \chi' \cdot N_A \cdot \rho' \cdot \text{ef}' \cdot (1 - \exp(-\lambda' t_{irr}))} \]

Condition: \( \phi = \phi' \)
\[ \text{Act} = \sigma (E) \cdot \Phi \cdot \chi \cdot \frac{N_A \cdot \rho \cdot \text{ef}}{A} \cdot (1-\exp(-\lambda t_{\text{irr}})) \]

\[ \Phi = \frac{\text{Act} \cdot A}{\sigma (E) \cdot \chi \cdot N_A \cdot \rho \cdot \text{ef} \cdot (1-\exp(-\lambda t_{\text{irr}}))} \]

\[ \Phi' = \frac{\text{Act}' \cdot A'}{\sigma'(E') \cdot \chi' \cdot N_A \cdot \rho' \cdot \text{ef}' \cdot (1-\exp(-\lambda' t_{\text{irr}}))} \]

Condition: \( \Phi = \Phi' \)

\[ \sigma(E) = \frac{\sigma'(E') \cdot \text{Act} \cdot A \cdot \chi' \cdot \rho' \cdot \text{ef}' \cdot (1-\exp(-\lambda' t_{\text{irr}})) \cdot \text{Act}' \cdot A' \cdot \chi \cdot \rho \cdot \text{ef} \cdot (1-\exp(-\lambda t_{\text{irr}}))}{\text{Act} \cdot A' \cdot \chi \cdot \rho \cdot \text{ef} \cdot (1-\exp(-\lambda t_{\text{irr}}))} \]

Recommended cross section values from the IAEA

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4. Experimental set-up
Stacked-foils technique

1. Motivation
2. Production process
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Stacked-foils technique

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Stacked-foils technique

Capsule

Beam line under vacuum

Kapton© foil

Alumina target under irradiation


Stacked-foils technique

Capsule

Target Monitor Degrader

Beam line under vacuum

Kapton© foil

Thin foil after irradiation

Gamma-spectrometry

19 cm

Target

Alumina target under irradiation

HPGe
5. Radionuclides of interest for nuclear medicine

*Production cross section study*
positron emitters $e^+$

$^{44}\text{Sc}$

$T_{1/2} = 3.97\text{ h}$

$+\gamma (1.157\text{ MeV})$

Of interest for PET

Of interest for the 3 $\gamma$ imaging technique developed at the SUBATECH lab (Xenon group)

$^{44}\text{Ca}(d,2n)$
### Functional imaging/Diagnosis

**Positron emitters $e^+$**

- **$^{44}$Sc**
  - $T_{1/2} = 3.97\ h$
  - Of interest for PET
  - + $\gamma$ (1.157 MeV)
  - Of interest for the 3 $\gamma$ imaging technique developed at the SUBATECH lab (Xenon group)

- **$^{44}$Ca** ($^{44}$Ca(d,2n))

**Photon emitters $\gamma$**

- **$^{99m}$Tc**
  - $T_{1/2} = 6.01\ h$
  - Widely used in functional imaging (SPECT)
  - $^{99m}$Tc "crisis"

### Therapy

**Ca-44(d,2n)**

- **Th-232(d,f) and Th-232(p,f)**
**Functional imaging/Diagnosis**

- **Positron emitters e⁺**
  - Sc-44 ($T_{1/2} = 3.97$ h)
  - Of interest for PET
  - Of interest for the 3 γ imaging technique developed at the SUBATECH lab (Xenon group)
  - Ca-44(d,2n)

- **Photon emitters γ**
  - Tc-99m ($T_{1/2} = 6.01$ h)
  - Widely used in functional imaging (SPECT)
  - Tc-99m "crisis"

**Therapy**

- **Electrons emitters e⁻**
  - Re-186g → β⁻, used in clinical trials palliative therapy for painful metastases
  - W-nat(d,xn)
  - Tb-155 ($T_{1/2} = 5.32$ d)
  - Auger e⁻ / γ for imaging
  - Gd-nat(d,xn)
  - Sn-117m → Conversion e⁻, used in clinical trials cardiovascular diseases
  - Cd-116(α,3n)

- **Th-232(d,f) and Th-232(p,f)**
Functional imaging/Diagnosis

**Positron emitters** $e^+$

- **Sc-44**
  - $T_{1/2} = 3.97\ h$
  - Of interest for PET
  - Of interest for the 3 $\gamma$ imaging technique developed at the SUBATECH lab (Xenon group)

- **Ca-44(d,2n)**

**Electrons emitters** $e^-$

- **Re-186g**
  - $T_{1/2} = 3.72\ d$
  - $\beta^-$, used in clinical trials
  - Palliative therapy for painful metastases

- **Tb-155**
  - $T_{1/2} = 5.32\ d$
  - Auger $e^-$ / $\gamma$ for imaging

- **Sn-117m**
  - $T_{1/2} = 13.60\ d$
  - Conversion $e^-$, used in clinical trials

- **Th-232(d,f) and Th-232(p,f)**

**Photon emitters** $\gamma$

- **Tc-99m**
  - $T_{1/2} = 6.01\ h$
  - Widely used in functional imaging (SPECT)
  - Tc-99m "crisis"

- **Th-226**
  - $T_{1/2} = 30.57\ m$
  - High cell destruction power (4 part. $\alpha$)

- **Ac-225**
  - $T_{1/2} = 10.0\ d$
  - High cell destruction power (3 part. $\alpha$)

- **Ra-223**
  - $T_{1/2} = 11.44\ d$
  - Xofigo© radiopharmaceutical

Th-232(d,x) and Th-232(p,x)

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6. The TALYS code
Code for the simulation of nuclear reactions

**Code for the simulation of nuclear reactions**

**TALYS**

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

- **Projectiles:** n, p, d, t, He-3, α particles
- **Energy:** 1 keV to 1 GeV
- **Targets:** Z = 3 to 110

1. Motivation  
2. Production process  
3. σ determination  
4. Exp. Set-up  
5. RN of interest  
6. TALYS  
7. Results & discussion  
8. Conclusions
Code for the simulation of nuclear reactions

- Includes several nuclear models to cover the main reaction mechanisms
- Provides a description of all the reactions channels and observables

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

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Targets: $Z = 3$ to 110
Study with the TALYS code version 1.6

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 1.6 Default
Study with the TALYS code version 1.6

. 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 1.6 Default

. One combination of models that best describes our whole set of data for proton, deuteron, alpha particles as projectile (and literature data) has been defined during this study.

⇒ TALYS 1.6 Adj.
Study with the TALYS code version 1.6

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

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⇒ TALYS 1.6 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>
</tbody>
</table>
7. Comparison between the experimental results and the TALYS code
→ α particles as projectiles
→ α particles as projectiles

Used in clinical trials
cardiovascular diseases
→ α particles as projectiles

![Cd-nat(α,x)Sn-110](image)

- Cross section (mb)
- Incident α particles energy (MeV)

Legend:
- 2010, A, Hermaße+
- 2015, This work
- TALYS 1.6 Default
- TALYS 1.6 Adj.
→ \( \alpha \) particles as projectiles

Of interest for PET imaging
protons as projectiles
→ protons as projectiles

Produces Th-226
Candidate for alpha immunotherapy

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+

This work

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TALYS 1.6 Default
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TALYS 1.6 Adj.
protons as projectiles

Th-232(p,f)Mo-99

Cross section (mb)

0 5 10 15 20 25 30 35 40 45 50 55

0 10 20 30 40 50 60 70 80

Incident proton energy (MeV)

1971 G.R. Choppin+
1982 H. Kudo+
2012 K. Abbas+
This work
TALYS 1.6 Default
TALYS 1.6 Adj.

Produces Tc-99m
For SPECT
Monitoring reaction

Ni-nat(p,x)Ni-57

Cross section (mb)

Incident proton energy (MeV)

- 1975, J.N. Barrandon+
- 1980, R. Michel+
- 1987, V.N. Aleksandrov+
- 1991, F. Tarkanyi+
- 1998, M. Sonck+
- 2002, S. Takaes+
- 2011, A.A. Alharbi+
- 2011, Yu.E. Titarenko+
- 1976, F.J. Haasbroek+
- 1983, R. Michel+
- 1990, M. Furukawa+
- 1997, R. Michel+
- 2001, F. Szeleczenyi+
- 2007, F.S. Al-Saleh+
- 2011, M.U. Khandaker+
- This work

TALYS 1.6 Default

TALYS 1.6 Adj.

IAEA Recommendation
→ **deuterons** as projectiles
→ deuterons as projectiles

### used in clinical trials

**Palliative therapy for painful metastases**
→ deuterons as projectiles

Produces Th-226
Candidate for alpha immunotherapy
→ deuterons as projectiles

Ni-nat(d,x)Co-55

Cross section (mb)

0 10 20 30
0 5 10 15 20 25 30 35 40 45 50
Incident deuteron energy (MeV)

Of interest for PET imaging
8. Conclusions
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 on a wide mass range
- On radionuclides for diagnosis and therapy purposes in nuclear medicine
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Three main mechanisms have been studied:
- optical potential
- level density description
- preequilibrium model

A set of models have been found to allow a better description of our collected data, different from the suggested default models.
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Three main mechanisms have been studied:
- optical potential
- level density description
- preequilibrium model

A set of models have been found to allow a better description of our collected data, different from the suggested default models.

Further investigations are ongoing on other mechanisms that can affect the computation of the production cross sections.

- Charlotte DUCHEMIN¹*, Arnaud GUERTIN¹, Férid HADDAD¹², Nathalie MICHEL² and Vincent MÉTIVIER¹

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List of publications related to the topic

Nucl. Med. and Biol. 49 (2017) 30-37  
Appl. Rad. And Isot. 118 (2016) 281-89  
NIMB 383 (2016) 191-212  
Frontiers in Medicine 2 (2015) 31  
Press article Medical Physics Web Feb 16, 2015  
Nucl. Med. and Biol. 41 (2014) e16–e18  
Nuclear Data Sheets 119 (2014) 267–269  