International Conference on Nuclear Data for Science and Technology 2007
DOI: 10.1051/ndata:07153

Production of medically relevant radionuclides with medium energy deuterons

A. Hermanne[1,a], F. Tárkányi[2], and S. Takács[2]

[1] Vrije Universiteit Brussel, Brussels, Belgium
[2] Institute of Nuclear Research, Hungarian Academy of Sciences (ATOMKI), Debrecen, Hungary

Abstract. Radioisotopes used in medical practice and for industrial or research applications are often produced with charged particle induced reactions. Although mostly proton beams are used, the cross sections of deuteron induced reactions are sometimes higher and lead to higher thick target production rates. For 13 targets, ranging from mass 61 to 176, an experimental comparison between cross sections and TTY for (p,n) and (d,2n) reactions were made. Three examples, leading to ^{64}Cu, ^{103}Pd and ^{186}Re, respectively, are discussed in detail as well as the production of ^{99}Mo and ^{176}Lu by deuteron induced reactions.

1 Introduction

Neutron deficient radioisotopes are increasingly used in nuclear medicine, industry and research projects. Their production needs charged particle irradiations (CP) at accelerator sites. The CP radioisotopes are mostly produced in proton induced reactions because of the rather high cross sections of the processes involved and low stopping power of protons. Dedicated high beam power, cost effective and simple to operate ($^{-}$H,p) cyclotrons were commercially developed.

Applications of heavier CP beams are limited: heavy ion therapy, production of specific radioisotopes by α or ^{3}He.

Medium energy deuterons could play a role as some intrinsic properties are interesting: the stopping power not too large, simplicity of the cyclotron remains, high intensity beams available, additional reaction channels open. It is interesting to compare cross sections and thick target yields (TTY) for proton and deuteron reactions for given end-products because:

- cross sections for (d,2n) are often higher than for (p,n) processes, thick target yields could be doubled;
- the (d,p2n) channel has higher cross sections than (p,pn) due to the breakup and low Coulomb barrier;
- (d,p) reactions open access to products that can not be reached with proton irradiations;
- relying on (d,n) instead of (p,n) reactions allows use of enriched targets with higher isotopic abundance.

We present here a summary of our experimental investigations on proton and deuteron production routes for the 12 production pathways shown in table 1. Examples discussed in detail in this article are indicated in bold.

The planned medium energy, high intensity deuteron accelerator dedicated to neutron production (International Fusion Materials Irradiation Facility) could hence be very effective in radioisotope production.

A drawback is the rather poor performance of computercodes for prediction of deuteron reactions.

[a] Presenting author, e-mail: aherman@vub.ac.be

Table 1. Production routes studied.

^{64}Ni(p,n)^{64}Cu↔^{64}Ni(d,2n)^{64}Cu
^{61}Ni(p,n)^{61}Cu↔^{61,60}Ni(d,xn)^{61}Cu
^{103}Rh(p,n)^{103}Pd↔^{103}Rh(d,2n)^{103}Pd
^{111}Cd(p,n)^{111}In ↔^{111}Cd(d,2n)^{111}In
^{114}Cd(p,n)^{114m}In ↔^{114}Cd(d,2n)^{114m}In
^{110}Pd(p,n)110mAg ↔110Pd(d,2n)^{110m}Ag
^{165}Ho(p,n)^{165}Er↔^{165}Ho(d,2n)^{165}Er
^{170}Er(p,n)^{170}Tm ↔^{170}Er(d,2n)^{170}Tm
^{169}Tm(p,n)^{169}Yb↔^{169}Tm(d,2n)^{169}Yb
^{186}W(p,n)^{186}Re↔^{186}W(d,2n)^{186}Re
^{192}Os(p,n)^{192}Ir↔^{192}Os(d,2n)^{192}Ir
^{100}Mo(p,pn)^{99}Mo↔^{100}Mo(d,p2n)^{99}Mo
^{176}Yb(d,n)^{177}Lu;^{176}Yb(d,p)^{177}Yb-^{177}Lu

2 Experimental techniques

Nearly all results discussed here were published earlier by our group [1–8] and were obtained in irradiation campaigns using the external beams of the cyclotrons at the sites of Sendai (Japan), Atomki-Debrecen (Hungary), UCL-Louvain la Neuve and VUB-Brussels (both in Belgium). For all cross section determinations, the established technique of stacked foil experiments, with monitoring of the beam energy and beam current with standard reactions for which recommended excitation functions exist [9], was used.

The generated activities were assessed with high purity Ge γ-spectrometry without any chemical separation.

For several reactions studied the experimental values were compared to data obtained from codes based on theoretical models and performed at IPPE-Obninsk (ALICE-IPPE, EMPIRE, GNASH). Calculations were done with a priori parameters, without adjustment for particular reactions. The comparison allows having an idea about the predictive quality of the codes for the different types of reactions and over a rather large range of masses.

For more details about specific experiments, data processing procedures, uncertainty estimation and discussion of the results of the computer codes we refer to the published articles [1–8] where also the references to works of other

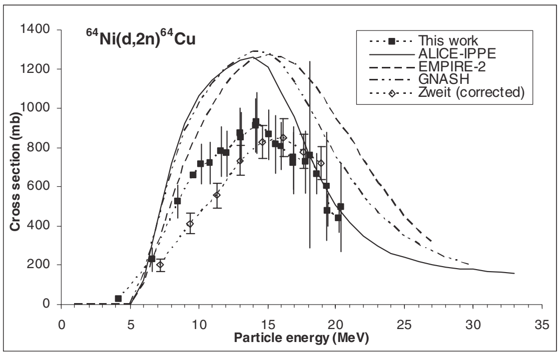

Fig. 1. Excitation function for ^{64}Ni(d,2n)^{64}Cu, comparison with literature and codes (fig. taken from [1]).

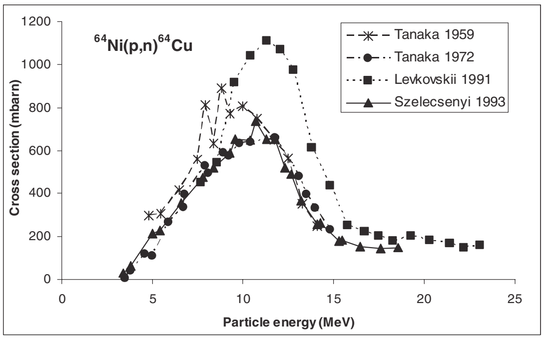

Fig. 2. Excitation functions for ^{64}Ni(p,n)^{64}Cu, data from literature (fig. taken from [1]).

authors can be found. Literature data were taken from the original publications or from the EXFOR database.

3 Comparison of proton and deuteron reactions

3.1 Production of ^{64}Cu/^{61}Cu from ^{64}Ni/^{61}Ni

Figure 1, showing the ^{64}Cu results for the deuteron induced reaction, is taken from our recent publication [1] where new experimental results are compared to model calculations and to the only existing literature value.

For proton induced reactions (fig. 2) values are taken from EXFOR where data over a larger energy range are given. For ^{64}Cu production the cross section for (d,2n) is only marginally larger than for the (p,n) reaction. All codes give serious deviations and energy shift for maximum between them. For ^{61}Cu production comparison is more difficult as for protons only (p,n) on ^{61}Ni (1.1%) is possible, while for deuterons also the (d,n) reaction on ^{60}Ni (26.1%) takes place. Problem of scaling can be resolved by taking into account that for ^{61}Ni(d,2n)^{61}Cu we find Q = −9.13 MeV and hence below 15 MeV only ^{60}Ni(d,n)^{61}Cu with a $\sigma_{\max}$ at 7 MeV of 310 mbarn occurs which is well below the $\sigma_{\max}$ = 600 mbarn for the (p,n) reaction.

These remarks on cross sections reflect on the TTY (fig. 3) calculated from spline fits to the excitation curves.

For ^{64}Cu production a small advantage for d over p exists above 15 MeV, rising with beam energy. For ^{61}Cu, even on highly enriched ^{60}Ni, the (d,n) yield is 3 times lower than for the (p,n) reaction on enriched ^{61}Ni, but at lower target cost.

3.2 Production of ^{103}Pd from ^{103}Rh

This radioisotope (0.022% γ-line at 357 keV and strong low energy X-lines around 20 keV, 64%), used in seeds for permanent interstitial brachytherapy, is presently produced in dedicated high power accelerators using ^{103}Rh (100%) targets and 18 MeV protons. We updated the older existing data for the (p,n) reaction [2] and measured the first cross sections for the deuteron induced reaction [3] yielding values that are 50% higher than for the proton reaction. The thick target yields derived from the fitted experimental excitation function agree well with those measured earlier and are nearly double at 20 MeV incident particle energy compared to those found for a proton irradiation (fig. 4).

3.3 Production of ^{186}Re from ^{186}W

The decay characteristics of ^{186}Re makes it very suitable for systemic radionuclide therapy after binding on peptides or monoclonal antibodies. As long as no accelerator routes were available, often ^{188}Re was used obtained from ^{188}W generators, produced by double (n,γ) caption on ^{186}W. To update and complement the older cross section data, a systematic investigation of the proton and deuteron reactions on ^{186}W was performed in our group [4,5]. As can be seen from

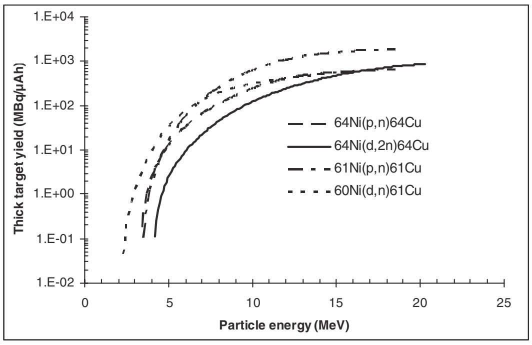

Fig. 3. Thick target yields (TTY) for ^{64}Cu and ^{61}Cu production (fig. taken from [1]).

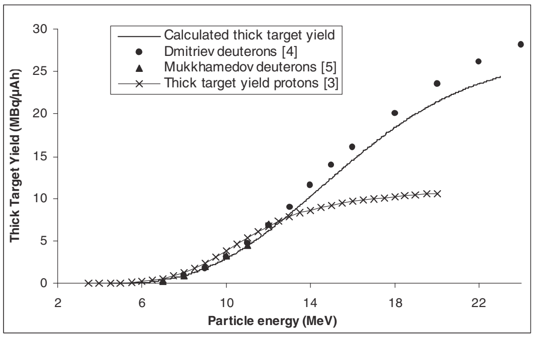

Fig. 4. Thick target yield for ^{103}Pd production: comparison of proton and deuteron induced reaction (fig. taken from [3]).

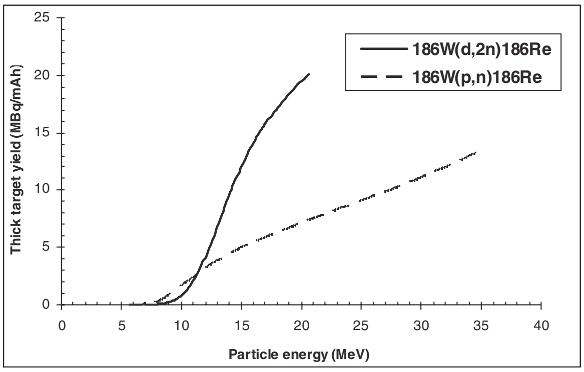

Fig. 5. Thick target yield for ^{186}Re production: comparison of proton and deuteron induced reactions (fig. taken from [5]).

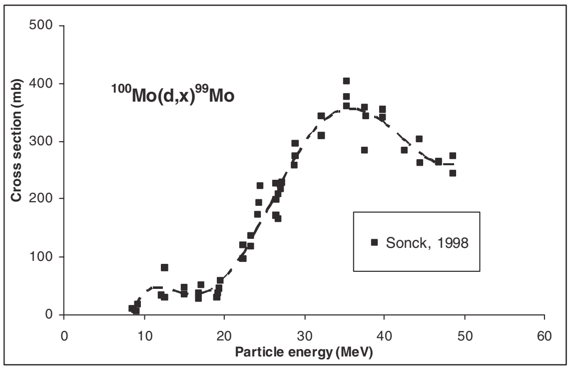

Fig. 7. Excitation function for ^{100}Mo(d,x)^{99}Mo (fig. taken from [7]).

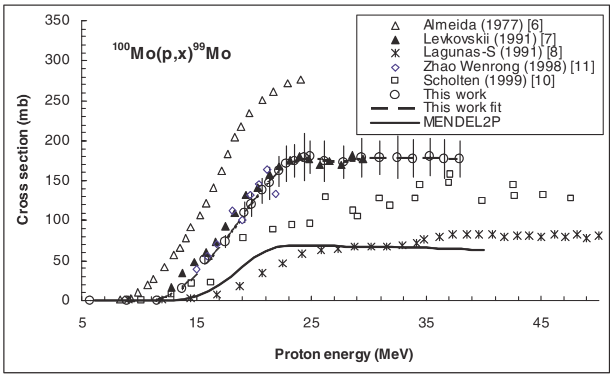

Fig. 6. Excitation function for ^{100}Mo(p,x)^{99}Mo, comparison with literature and codes (fig. taken from [6]).

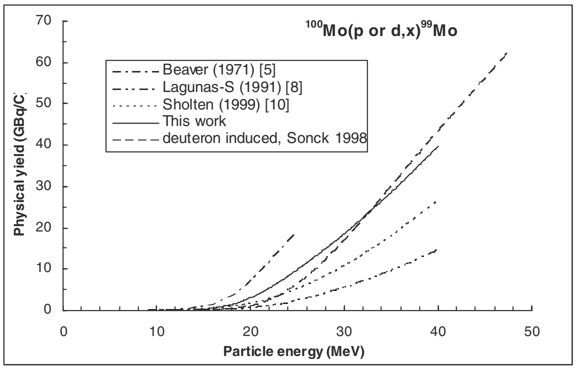

Fig. 8. Thick target yield for ^{99}Mo production: comparison of proton and deuteron induced reactions (fig. taken from [7]).

the calculated thick target yields in figure 7, the deuteron reaction presents a factor 3 advantage over proton production at 20 MeV. The advantage of the extension of the deuteron excitation function to higher energies is limited by the onset of the (d,4n) reaction resulting in an ^{184}Re contamination.

4 Accelerator production of ^{99}Mo

A vast majority of nuclear medicine investigations is presently relying on the ^{99}Mo – ^{99m}Tc generator where ^{99}Mo is a fission product recovered from research reactors. In the 90's progressive closure of the reactors was foreseen and possible accelerator production was studied. In [6, 7] we presented our results for proton and deuteron induced reactions on ^{100}Mo resulting in ^{99}Mo (figs. 6 and 7).

The advantages of the (d,p2n) over (p,pn) reaction can clearly be seen on figures 6 and 7 as the cross sections for d induced are more than double compared to p induced but the maximum occurs at higher energy. As both excitation functions remain high over a broad energy range, higher energy deuteron machines are needed to take advantage of the increased TTY (fig. 8). An upper limit is imposed by possible contaminants production, especially ^{96}Tc reached by (d,6n) with Q = −35.6 MeV. Direct production of ^{99m}Tc by (p,2n) and (d,3n) on ^{100}Mo or by ^{98}Mo(d,n) could be other alternative, not requiring recycling of the expensive enriched target material.

5 Accelerator production of ^{177}Lu

The radionuclide ^{177}Lu (β^- emission of 497 keV, 78.6%, $T_{1/2}$ = 6.7 days) has excellent properties for applications in therapy and the emitted photons are also ideally suited for imaging with gamma cameras. At present, ^{177}Lu is predominantly produced in reactors by neutron-capture on ^{nat}Lu or enriched ^{176}Lu. Since efficient labelling of the biomolecules requires very high specific activity, production is confined to high-flux reactors. The accelerator based ^{176}Yb(d,x) route was studied as an alternative carrier free, high specific activity production pathway [8]. From a time sequence of measurements it is shown that the main contributing channel is indirect ^{176}Yb(d,p)$^{177m+g}$Yb→^{177g}Lu production and not ^{176}Yb(d,n)^{177g}Lu.

Predominance of (d,p) over (d,n) is understood from the Coulomb barrier for the Yb + d interaction (13 MeV). Only above that energy a possible contribution exists for (d,n) reaction where the proton has to penetrate into the nucleus.

The correspondence between the experimentally determined cross section values and the predictions of the ALICE-IPPE code is not good, especially for the direct production of ^{177}Yb. It shows again that the model used is inadequate for describing stripping reactions such as the (d,p) channel.

The favourable ratio of half-lives (saturation of $^{177m+g}$Yb and decay during irradiation) permits obtaining carrier-free ^{177g}Lu on Yb targets in irradiations of several days, followed by chemical separation. Batches of 60 GBq of ^{177}Lu could

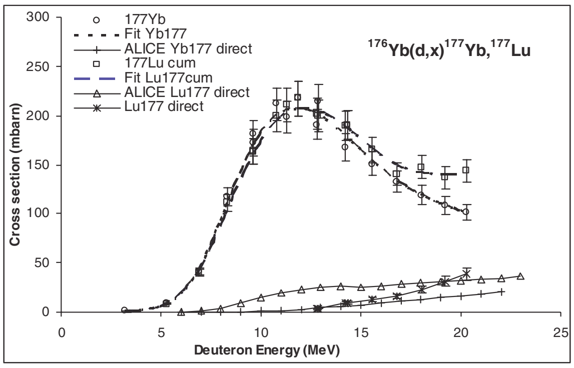

Fig. 9. Excitation function for ^{176}Yb(d,x)^{177}Yb, ^{177}Lu, comparison with code (fig. taken from [8]).

be produced in 72 h irradiations with 21 MeV deuterons, at 100 μA beam intensities on 100 mm thick, enriched ^{176}Yb targets. This value does not compare favourably with production at high flux reactors, where batches of 3700 GBq using ^{nat}Lu are reported (7 days irradiation at a thermal flux of 3×10^{13} n/cm^2/s, using 100 mg of material, the cross section for ^{176}Lu(n,γ)^{177}Lu being 2100 barn). However, the advent of ion-accelerators delivering beam intensities in the mA range, will progressively diminish this advantage.

The a priori possible production of the annoying long lived ^{177m}Lu contaminant was assessed by 24 hours measurements at EOB + 240 days, but no significant intensities of the characteristic γ-lines were detected.

6 Overview of thick target yields

In table 2 a comparison of thick target yields over energy ranges of maximal production (not necessarily optimal for radio-nuclidic purity) is given. For most reactions considered the results for deuterons are clearly more advantageous than for protons even if higher incident proton energies are considered. For some reactions (^{99}Mo production) higher energy deuterons are needed to take advantage of the increased cross sections. Some experiments on enriched targets still have to be performed before definitive conclusions for specific reactions can be drawn.

7 Conclusions

For several reactions leading to production of medically relevant radionuclides, deuteron induced channels have higher thick target yields for the same incident energy than proton reactions or are the only realistic pathway for CP production. This should be an incentive for developing dedicated high power commercial 30 MeV deuteron accelerators. The planned medium energy, high intensity deuteron accelerator

Table 2. Comparison of thick target yields.

Target/ Product	Protons energy range (MeV)	Protons TTY MBq/mAh	Deuterons energy range (MeV)	Deuterons TTY MBq/mAh
^{64}Ni/^{64}Cu	19 → 8	650	21 → 8	900
^{61}Ni/^{61}Cu	20 → 8	1890	20 → 8 [^{60}**Ni(d,n)**]	720
^{103}Rh/^{103}Pd	20 → 8	12	20 → 8	22
^{186}W/^{186}Re	30 → 8	11	20 → 10	19
^{111}Cd/^{111}In	30 → 8	95	20 → 8 (^{nat}**Cd**)	20
^{114}Cd/^{114m}In	30 → 8	2,2	20 → 9	3,6
^{nat}Er/^{170}Tm	30 → 9	0,065	20 → 9	0,055
^{169}Tm/^{169}Yb	30 → 9	2,2	20 → 9	3,74
^{192}Os/^{192}Ir	20 → 9	0,18	20 → 9	0,88
^{100}Mo/^{99}Mo	40 → 8	14,3	40 → 20	16,2
^{176}Yb/^{177}Lu	NA	NA	20 → 8	1,02

dedicated to neutron production (International Fusion Materials Irradiation Facility) could hence be very effective in medical radioisotope production.

The agreement with ALICE-IPPE and other numerical codes is often poor especially when stripping reactions are important. An effort for improving the description of deuteron induced reactions in theoretical codes is hence needed.

The Hungarian Academy of Sciences, the Fund for Scientific Research (FWO-Vlaanderen), and the OZR-VUB financially supported the different parts of this study.

References

1. A. Hermanne, F. Tarkanyi, S. Takacs, Nucl. Instrum. Meth. B (2007) (in press).
2. A. Hermanne, M., Sonck, A. Fenivesy, L. Daraban., Nucl. Instrum. Meth. B **170**, 281 (2000).
3. A. Hermanne, M. Sonck, S. Takács, F. Tárkányi, Y. Shubin, Nucl. Instrum. Meth. B **187**, 3 (2002).
4. F. Tarkanyi, F. Ditroi, S. takacs, F. Szelecsenyi, A. Hermanne, M. Sonck, Nucl. Instrum. Meth. B **211**, 319 (2003).
5. F. Tarkanyi, S. Takacs, F. Szelecsenyi, F. Ditroi, A. Hermanne, M. Sonck, Nucl. Instrum. Meth. B **252**, 160 (2006).
6. S. Takacs, Z. Szucs, F. Tarkanyi, A. Hermanne, M. Sonck, J. Radioanal. Nucl. Chem. **257**, 1957 (2003).
7. M. Sonck, S. Takacs, F. Szelecsenyi, A. Hermanne, F. Tarkanyi. AIP Conf. Proc. **475**, edited by Duggan and Morgan, (1999), p. 987.
8. A. Hermanne, S. Takacs, M. Goldberg, Y.N. Shubin, S.F. Kovalev, Nucl. Instrum. Meth. B **247**, 223 (2006).
9. F. Tarkanyi, K. Gul, A. Hermanne, M.G. Mustafa, M. Nortier, P. Oblozinsky, S.M. Qaim, B. Scholten, Yu.N. Shubin, S. Takács, Zhuang Youxiang, *Charged-Particle Cross-Section Database for Medical Radioisotope Production. Beam Monitor Reactions (Ch. 4),* IAEA-TECDOC-1211 (International Atomic Energy Agency, 2001), pp. 49–152, URL: http:/www-nds.iaea.org/medical.