"BABES-BOLYAI" UNIVERSITY

FACULTY OF PHYSICS

Laura Daraban

Production and characterization of new radionuclides used for medical applications

PhD Thesis Summary

Scientific Advisor

Prof. dr. Onuc Cozar

Cluj-Napoca
-2010-

Contents of the Thesis

List of publications

● ISI articles

1. A. Hermanne, M. Sonck, A. Fenyvesi, <u>Laura Daraban</u>, *Study on production of ^{103}Pd and characterisation of possible contaminants in the proton irradiation of ^{103}Rh up to 28 MeV,* Nuclear Instruments and Methods in Physics Research B **170**, 281-292 (2000) (impact factor: 0.955).
2. <u>Laura Daraban</u>, K. Abbas, F. Simonelli, N. Gibson, *Experimental study of excitation functions for deuteron particle induced reactions $^{64}Zn(d,2p)^{64}Cu$ and $^{64}Zn(d,\alpha n)^{61}Cu$ by the stack foil technique,* Applied Radiation and Isotopes **66**, 261-264 (2008) (impact factor: 1.147).
3. R. Adam Rebeles, A. Hermanne, P. Van den Winkel, F. Tarkanyi, S. Takacs, <u>Laura Daraban</u>, *Alpha induced reactions on ^{114}Cd and ^{116}Cd: an experimental study of excitation functions*, Nuclear Instruments and Methods in Physics Research B **266**, 4731- 4737 (2008) (impact factor: 0.999).
4. <u>Laura Daraban</u>, R. Adam Rebeles, A. Hermanne, F. Tarkanyi, S. Takacs, *Study of the excitation functions for ^{43}K, $^{43,44,44m}Sc$ and ^{44}Ti by proton irradiation on ^{45}Sc up to 37 MeV*, Nuclear Instruments and Methods in Physics Research B **267**, 755-759 (2009) (impact factor: 0.999).
5. <u>Laura Daraban</u>, R. Adam Rebeles, A. Hermanne, *Study of the excitation function for the deuteron induced reaction on $^{64}Ni(d,2n)$ for the production of the medical radioisotope ^{64}Cu*, Applied Radiation and Isotopes **67**, 506-510 (2009) (impact factor: 1.147).
6. A. Hermanne, <u>Laura Daraban</u>, F. Tarkanyi, S. Takacs, F. Ditroi, A. Ignatyuk, R. Adam Rebeles, *Excitation functions for some W, Ta and Hf radionuclides obtained by deuteron irradiation of ^{181}Ta up to 40 MeV*, Nuclear Instruments and Methods in Physics Research B **267**, 3293-3301 (2009) (impact factor: 0.999).
7. A. Hermanne, <u>Laura Daraban</u>, R. Adam Rebeles, A. Ignatyuk, F.Tarkanyi, S. Takacs, *Alpha induced reactions on ^{nat}Cd up to 38.5 MeV: experimental and theoretical studies of the excitation functions* (submitted to Nucl. Instr. and Meth. in Phys. Res. B 57155 (10.1016/j.nimb.2010.01.022, 2010) (impact factor: 0.999).

● Other articles

8. <u>Laura Daraban</u>, O. Cozar, G. Damian, L. Daraban, *ESR Dosimetry by some Detergents,* Studia Universitatis Babes-Bolyai, Physica, **50**, 4b, 587-590 (2005).
9. <u>Laura Daraban</u>, Onuc Cozar, Liviu Daraban, *The Production and Characterization of some Medically used Radioisotopes*, Studia Universitatis Babes-Bolyai, Physica, **51**, 2, 61-68 (2006).
10. L. Daraban, <u>Laura Daraban</u>, O. Cozar, R. Adam Rebeles, *The Use of Isotopic Neutron Sources for some Radionuclides Production in Nuclear Medicine and other Domains of Science,* The 5th International Conference on Isotopes, 25-29 Aprilie (2005), Bruxelles, Belgia, International Proceedings, 257-264.
11. <u>Laura Daraban</u>, O. Cozar, T. Fiat, L. Daraban, *The Production and characterization of some medically used radioisotopes*, International Physics Conference TIM-06, 24-27 Noembrie (2006), Timişoara, România, Abstract Book, 38-39.

Introduction

The radionuclides are often used in medicine for diagnosis, treatment and research. The radioactive tracers which emit gamma radiation can offer a large amount of information about the anatomy and the well functioning of different organs in the human body, as they are often used for tomography investigations (single photon emission computed tomography, PET scanning). Also, the radionuclides (gamma and beta emitters) have become a promising method for the treatment of some tumors.

This thesis is mainly focused on the production and characterization of some medically relevant radionuclides, the calculation of their activation cross section values for induced reactions with neutrons, protons, deuterons or alpha particles on thin targets in the energy range of 15- 40 MeV. The experimental data presented in this thesis have high reliability as they are measured relative to well known recommended monitor cross sections that were determined simultaneously [17]. Our results are compared with a number of earlier investigations [11-15, 20, 21, 22, 24, 26-36, 40, 46, 54, 56] and some discrepancies can be due to outdated nuclear data or different measuring techniques.

Chap.1 presents a short introduction of the preparation and production techniques of artificial radionuclides, methods of preparation of labeled compounds with radioisotopes and their applications in medicine (radiopharmaceuticals used in diagnosis and therapy).

Chap.2 presents the main techniques of production of radioisotopes used for medical applications by neutron activation and by charged particles irradiation and consists of 2 subchapters. Subchapter one presents the study of the radioisotopes production and their characterization by the neutron activation and some medical applications of radioisotopes produced by neutron reactions. The second subchapter describes the radioisotopes production and their characterization by charged particles irradiation at a cyclotron (the deuterons irradiations on ^{64}Zn targets at a cyclotron up to 19.5 MeV and the production and separation of a medically applied radioisotope ^{64}Cu).

Chap.3 presents the study of the excitation function for the deuteron induced reaction ^{64}Ni(d,2n) for the production of NCA^{64}Cu and some impurities (^{61}Cu candidate for radioimmunotherapy) up to 20.5 MeV.

Chap.4 presents the study of the excitation functions for the radioisotopes ^{43}K, ^{43,44,44m}Sc (NCA ^{44g}Sc) and ^{44}Ti, by protons irradiation on ^{45}Sc targets at energies up to 37 MeV.

Chap.5 presents the study of the production of ^{103}Pd used for brachytherapy, by protons irradiation on ^{103}Rh targets at energies up to 28 MeV.

Chap.6 consists of the study of the excitation functions for some radionuclides of W, Ta and Hf by deuterons irradiation on ^{181}Ta targets at energies up to 40 MeV.

Finally, Chap.7 presents an experimental study of the excitation functions and possible production pathways by induced alpha reactions on ^{nat}Cd targets at energies up to 38.5 MeV for radionuclides of medical interest such as: NCA^{117m}Sn, NCA^{114m}In and NCA^{111}In.

The general conclusions highlight the most important results obtained in these experiments, some of them studied for the first time, regardless to the production cross section values and the yield of some new radioisotopes used for medical applications.

Keywords: radionuclides, neutron activation, proton, deuteron, alpha induced reaction, cyclotron, thin target, stack foil method, HPGe detector, γ spectrometry, cross-section, excitation function, thick target yield.

Chap.1.1 The natural and artificial radioisotopes

The radioisotopes are the result of the nuclear reactions, the interaction between a projectile particle (neutron, proton, deuteron, alpha particle, photon) and an atomic nucleus. The probability of interaction between the nucleus and the bombarding particle is the cross section of the reaction.

The most often reaction by neutrons is the one in which the target element is irradiated by thermal neutrons (n,γ) and the radioisotope of the same element is obtained. A series of radioisotopes can be obtained by neutron irradiation in a neutron reactor or by charged particles at a cyclotron, this last one being more technologically profitable.

1.2 Applications of radioisotopes

The radiopharmaceuticals labeled with radiotracers are often used for diagnosis and therapy in nuclear medicine. They mainly have two compounds: the radionuclide and the pharmaceutical compound. The radionuclide is important for the detection or to release a radiation dose and the radiopharmaceutical product dictates the bio-distribution and the in vivo localization in the human body.

The radionuclides used in radiotherapy can be localized at the level of the target structure as well as those used in diagnosis, being attached to a chemical or biological compound. In the case of diagnosis, the radiopharmaceuticals are given to the patient and the emitted radiation inside the human body is then to be measured by using a gamma camera for the radiation detection (nuclear scintigraphy). In the case of therapy, the radiopharmaceuticals are given for the treatment of some diseases [7] and preferably they should contain only beta emitters with the energy of 0.5-1 MeV and to have a relative short half life as about 4 to 10 days and also, they should not present any toxicity for the human tissues [7]. The most recent diagnosis techniques are PET (Positron Emission Tomography) and SPECT (Single Photon Emission Computer Tomography), in which beta emitters radionuclides produced at a cyclotron are used, which provide information about the metabolism, neuronal transmission and blood circulation in the human body (Fig.1.2.4). A suitable PET candidate is the NCA^{64}Cu, a positron and a beta emitter, used for labeling a wide range of radiopharmaceuticals for both PET imaging, as well as immuno-radionuclide therapy of tumors [13]. Another interesting radionuclide is ^{103}Pd, used for the brachytherapy of tumors in the United States since 1986 and can be produced at a cyclotron by irradiation of rhodium targets.
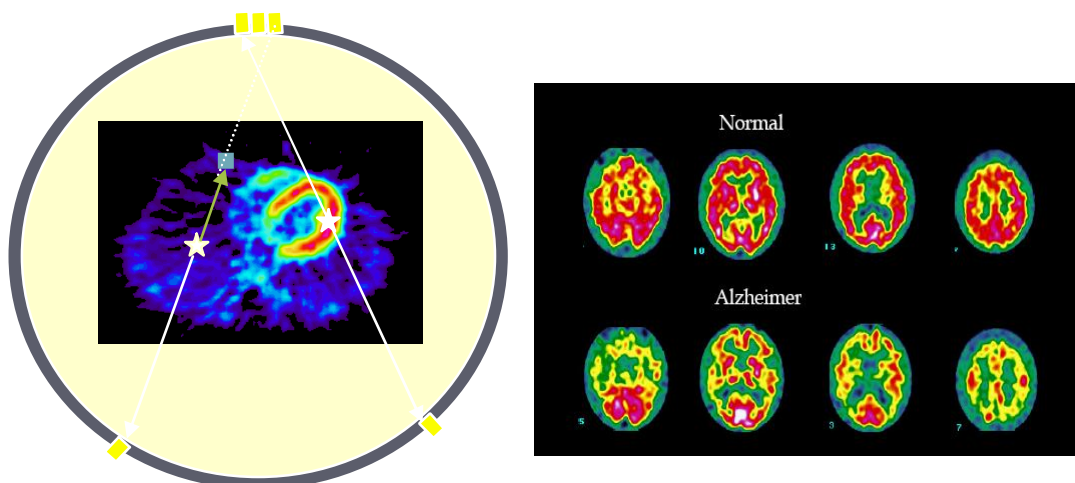

Fig.1.2.4 *Examples of PET and SPECT images using radionuclides*

Presently, approximately 100 radionuclides are used in medical and biological centers, from which about 30 are often used in therapy and diagnosis. It is well known that presently the applications of radiopharmaceuticals reflect the economical development degree of a particular country and that there is a strong connection between the industrialization and the radiopharmaceuticals consumption. In the United States this consumption became almost double to the one from the United Kingdom and 4 times more than the one from France in 1963.

Chap.2.1 Techniques of radioisotopes production used for medical applications

2.1 The study of the radioisotopes production and their characterization by the neutron activation

Some radioisotopes with medical applications can be produced by different nuclear reactions, which can take place in nuclear reactors or in accelerators. The production method of radionuclides by neutron irradiation consists in bombarding some elements with neutrons at different energies [9, 11], obtained with neutron isotopic sources type (α,n) ($^{241}Am-^{9}Be$ of 5 Ci and $^{239}Pu-^{9}Be$ of 33 Ci). It was thus noticed that by using neutron isotopic sources, some important radioisotopes with applications in nuclear medicine can be produced at the place of their application in clinical laboratories, such as: ^{116m}In, ^{198}Au, ^{56}Mn, ^{64}Cu as presented in Table1. The samples containing the target isotopes, were irradiated with neutron sources and their spectra were acquired with the help of a Ge(Li) detector type CANBERRA, coupled at a multichannel analyzer and a software GENIE 2000 for data acquisition.

Table.1 *The specific activity and spectral chracteristics of some radionuclides produced by neutron activation*

Radionuclide	Nuclear reaction	Main γ emission (keV) (Abundance %)	Specific activity at saturation (Ci/g)
^{198}Au $T_{1/2}$ = 2.70 d	^{197}Au(n,γ)^{198}Au	411.80 (96)	8
^{56}Mn $T_{1/2}$ = 2.58 h	^{55}Mn(n,γ)^{56}Mn	846.77 (98.9) 1810.77 (27.2) 2113.12 (14.3)	3.9
^{116m}In $T_{1/2}$ = 54 min	^{115}In(n,γ)^{116m}In	416.86(27.7) 818.71 (11.5) 1097.32 (56.2) 1293.55 (84.4) 1507.67 (10.0)	21
^{64}Cu $T_{1/2}$ = 12.70 h ^{66}Cu $T_{1/2}$ = 5.15 min	^{63}Cu(n,γ)^{64}Cu ^{65}Cu(n,γ)^{66}Cu	1345.84 (0.473) 1039.23 (9.0)	0.79

By analyzing each gamma spectrum, it was able to determine the new produced radioisotopes and also their half life from the disintegration curve, especially if they interfere on the annihilation peak at 511 keV, such as the copper isotopes [15] ^{64}Cu (T$_{1/2}$ = 12.70 h, β⁻ 578 keV EP, 38 %, β⁺, 653 keV EP, 18 %; γ at 1345.84 keV, 0.473 % [23], Fig.2.1.12). Its properties ensure this radionuclide a great potential to serve a dual function in order to develop new molecular agents used for the positron emission tomography (PET) and radiopharmaceuticals used for the radioimmunotherapy in oncology [12, 14, 24].
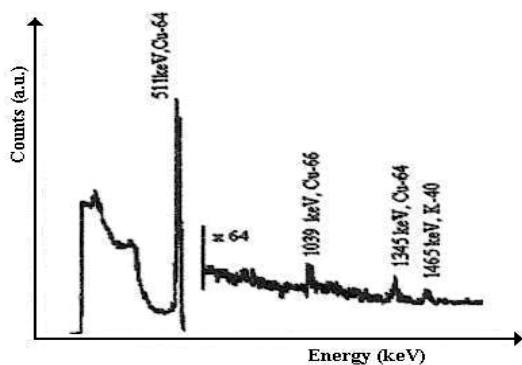
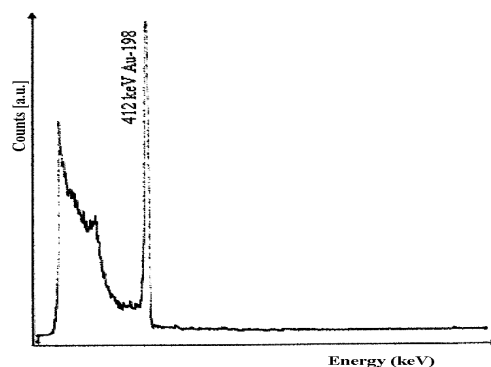

Fig.2.1.12 Characteristic spectrum of ^{64}Cu   *Fig.2.1.7 Characteristic spectrum of ^{198}Au*

Another radionuclide ^{198}Au (Fig.2.1.7) is often used as agent in the nuclear medicine for clinical applications (rheumatoid arthritis) and also for the SPECT technique or as implants for the brachytherapy for the treatment of prostate cancer [41]. Recent studies [42] show that the ^{56}Mn from manganese superoxide dismutase (MnSOD) is a proper candidate for the treatment of prostate tumors by brachytherapy. Also, ^{116m}In is used for the scintigraphy of carotid tumors [43].

2.2. The study of the radioisotopes production and their characterization by charged particles irradiation at a cyclotron

Radionuclides are often used as radiotracers to follow processes in different systems, such as the radiotracers applied for diagnosis in medicine, clinical chemistry, molecular biology, different problems that occur in industry and research [29]. The radionuclides low in neutrons, produced by irradiation with charged particles at a cyclotron offer a special advantage because they are often *No Carrier Added* (NCA) and have a high activity, which makes them useful to be used as radiopharmaceuticals [27].

2.2.3 The experimental study of deuteron irradiations on natural Zn and ^{64}Zn targets at the JRC Ispra cyclotron

The production method is based on the study of the experimental excitation function for the deuterons induced reactions ^{64}Zn(d,2p)^{64}Cu and ^{64}Zn(d,αn)^{61}Cu, irradiating thin Zn targets (the stack foil technique) at a cyclotron up to 19.5 MeV. The NCA^{64}Cu is therefore produced together with other impurities such as: ^{61}Cu, ^{69m}Zn, ^{65}Zn, ^{67}Ga, ^{66}Ga [14, 19] as presented in Table 2 and Fig.2.2.19, which can be chemically separated in the final product used for PET.

Table. 2 *Main induced nuclear reactions by deuterons irradiation on zinc targets and the spectral characteristics of the produced radionuclides*

Radionuclide	Nuclear reaction	Main γ emission (keV) (Abundence %)	Thick target yield (MBq/μA.h)
^{64}Cu T $_{1/2}$ = 12.70 h	^{64}Zn(d,2p) ^{66}Zn(d,α) ^{67}Zn(d,αn) ^{68}Zn(d,α2n)	1345.84 (0.473)	14.12 8.60 3.36 0.01 sum: 26.09
^{61}Cu T $_{1/2}$ = 3.33 h	^{64}Zn(d,αn)	656.01 (10.77)	179.20
^{67}Ga T $_{1/2}$ = 3.26 d	^{66}Zn(d,n) ^{67}Zn(d,2n) ^{68}Zn(d,3n)	184.58 (21.2) 300.22 (16.8) 393.53 (4.68)	15.28 3.78 0.21 sum: 19.27
^{66}Ga T $_{1/2}$ = 9.49 h	^{66}Zn(d,2n) ^{67}Zn(d,3n)	833.50 (5.896) 1039.35 (37.00)	109.12 0.29 sum: 109.41
^{69m}Zn T $_{1/2}$ = 13.76 h	^{68}Zn(d,p) ^{70}Zn(d,pn)	438.63 (94.77)	28.06
^{65}Zn T$_{1/2}$ = 244.26 d	^{64}Zn(d,p) ^{66}Zn(d,p2n) ^{64}Zn(d,n)+ decay	1115.55 (50.6)	0.29 ~ 0 ~ 0 sum: 0.29

The activities produced in the irradiated samples were then measured by gamma spectrometry at HPGe detectors type CANBERRA and EG&G ORTEC USA, with the help of the acquisition softwares Gamma Vision (Model A66-B32, Version 5.10) and GENIE 2000. The detectors were calibrated in energy and efficiency with standard sources of ^{152}Eu (1μCi, 10μCi), ^{241}Am, ^{137}Cs, ^{60}Co (ENEA Italy, DAMRI and CERCA France). For the production of the radioisotope ^{64}Cu, only the γ line at 1345.84 keV (0.473 %) [19, 24] was used for the activity estimation with a good resolution (Fig.2.2.18).
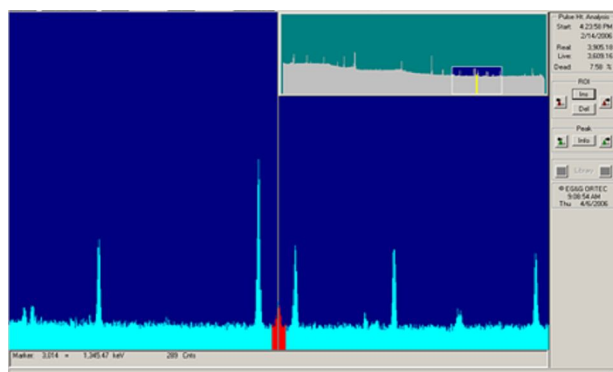

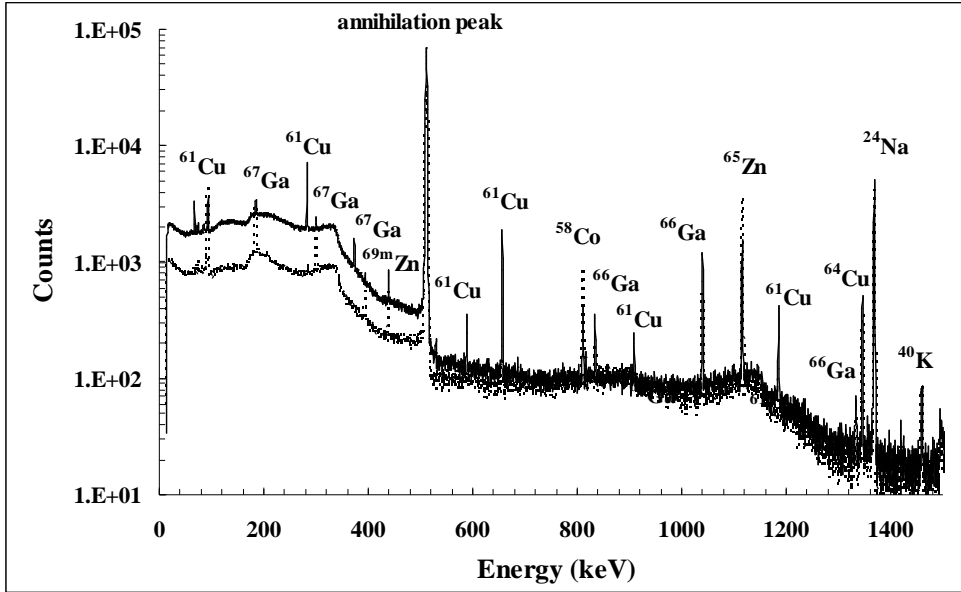*Fig.2.2.18* *Spectrum counts/channel vs. gamma energy (keV) for the peak of* ^{64}*Cu*

Fig.2.2.19 *Spectrum counts/channel vs. energy (keV) for ^{64}Cu and impurities, measured in a stack of ^{64}Zn foils after one day and respectively two days from the end of irradiation*

The transmitted deuteron energies through the stack of Zn foils were calculated with the help of the SRIM code 2006 [15, 16], taking in consideration the errors of the thickness of different foils in the stack. The cross-section values for each foil in the stack were determined by using the activities measured and other constant parameters by using the *activation formula* (as for the production of ^{64}Cu) [19]:

$$\Lambda_0 = \rho \cdot N_{Avog} \cdot f \cdot I \cdot (1 - e^{-\lambda t}) \cdot \sigma (E) / M \cdot d$$

$\rho = 8.92000 \cdot 10^{-3}$ g/mm^3 (the density of the obtained Cu isotope)
M = 63.54 u.a.m. (the atomic mass of the target Zn isotope)
f = 1 the isotopic abundance of the target (^{64}Zn)
N_{Avog} = 6.02300 $\cdot 10^{+23}$ atoms
t = the irradiation time (3 h)
I = the measured current in the irradiated foil (0.3 μA)
1 μA = 6.2500 $\cdot 10^{+12}$ p/s
d = the thickness of the irradiated Zn foil (0.14 mm)
$\lambda = \ln2 \cdot t / T_{1/2}$, $T_{1/2}$ = the half life of the radioisotope ^{64}Cu (12.7 h)
$\Lambda = \Lambda_0 \cdot e^{-\lambda t}$ = the measured activity of the produced radioisotope in the Zn foil
$\sigma (E)$ = the measured cross section.

The experimental excitation functions for the deuteron induced reactions ^{64}Zn(d,2p)^{64}Cu and ^{64}Zn(d,αn)^{61}Cu were then compared with theoretical estimations made with the help of the theoretical codes EMPIRE and AliceMC [19, 44, 45]. Fig.2.2.24 presents the experimental excitation function for the reaction ^{64}Zn(d,2p)^{64}Cu up to 19.5 MeV, compared with the theoretical estimation made with the theoretical codes AliceMC and EMPIRE and shows a good agreement. Fig.2.2.25 presents the experimental excitation function for the reaction ^{64}Zn(d,αn)^{61}Cu, here the theoretical values follow the trend of the experimental curve and are higher than the experimental values, compared also with other data from literature measured for this reaction.
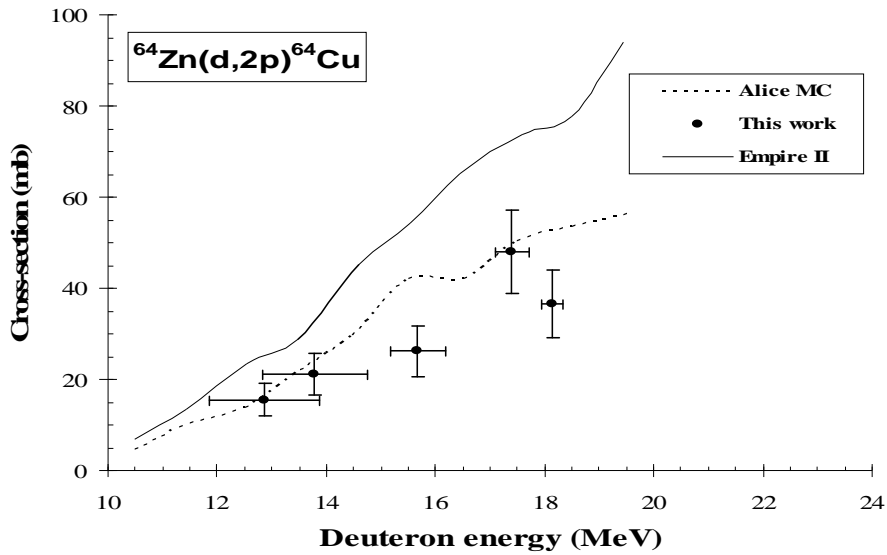
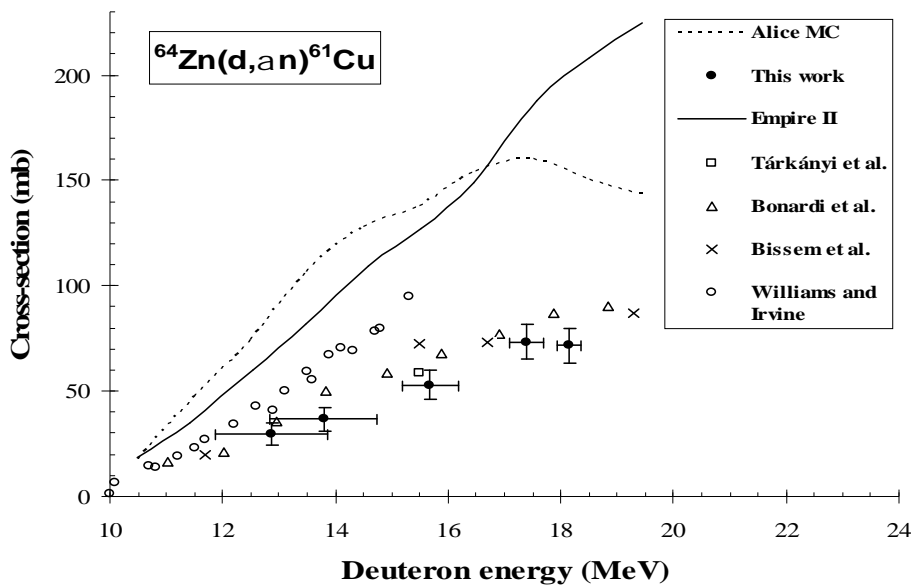**Fig.2.2.24** *The excitation function for the reaction $^{64}Zn(d,2p)^{64}Cu$ in a stack of ^{64}Zn foils*

Fig.2.2.25 *The excitation function for the reaction $^{64}Zn(d,\alpha n)^{61}Cu$ in a stack of ^{64}Zn foils*

Cap.3 Study of the excitation function for the deuterons induced reaction $^{64}Ni(d,2n)$ for the production of ^{64}Cu used for medical applications

The production of ^{64}Cu was studied also via the reaction $^{64}Ni(d,2n)^{64}Cu$ using the stack foil technique. Several stacks, each containing 8 foils of enriched ^{64}Ni (96.1 %, impurities ^{58}Ni 1.95 %, ^{60}Ni 1.31 %, ^{61}Ni 0.13 %, ^{62}Ni 0.51 %) were irradiated by deuterons up to 20.5 MeV at the VUB CGR-560 cyclotron. The ^{64}Ni targets were obtained by electrodeposition on foils of Au (99.95 %). The cross section values for the reaction $^{64}Ni(d,2n)^{64}Cu$ were calculated with the help of the activation formula and are presented in Fig.3.3.29, as being a single set of values from two different irradiations. The excitation function is also compared with results previously obtained

for this reaction by the group from VUB Brussels (Hermanne et al. and values from literature [20, 26]) and show a good agreement.
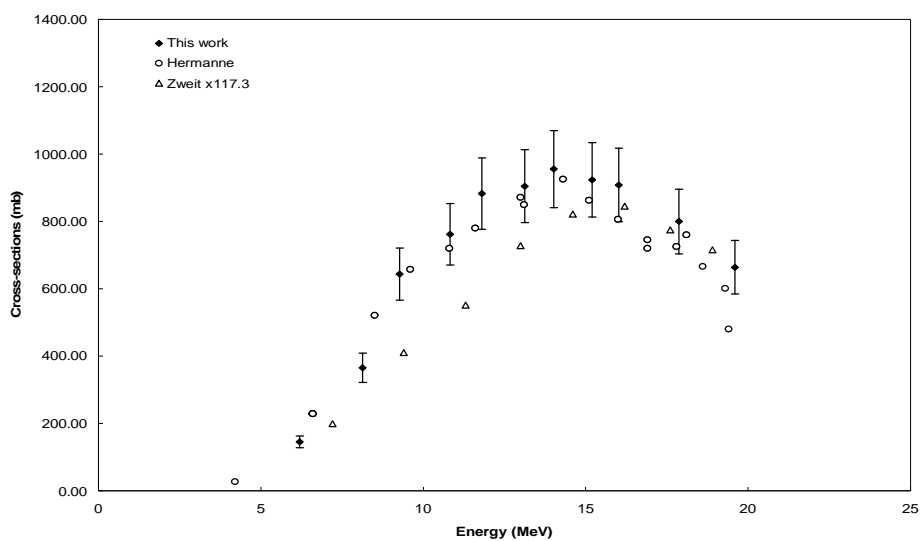

Fig.3.3.29 *The excitation function for the reaction $^{64}Ni(d,2n)^{64}Cu$, comparison with literature values*

By making a fit over all cross section values, the thick target yields were calculated for different deuteron energies (Fig.3.3.31), extrapolating our experimental values up to 25 MeV, the thick target yield can increase up to 30 %.
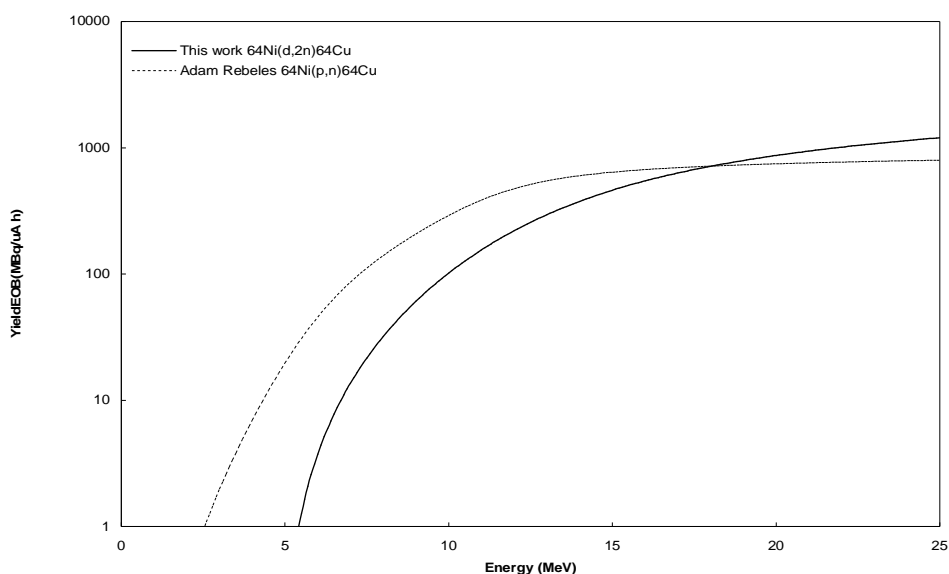
Fig.3.3.31 *The thick target yields for the reactions $^{64}Ni(d,2n)^{64}Cu$ and $^{64}Ni(p,n)^{64}Cu$*

By comparing our results with thick target yield values obtained by protons irradiation on enriched ^{64}Ni targets (Adam Rebeles et al. [20]), it is obvious that the deuterons induced reaction becomes more profitable than the protons reaction in the same energy range higher than 18 MeV. Possible contaminants of Ni and Co in the final product NCA^{64}Cu can be chemically separated, necessary also in order to recycle the expensive target material of Ni.

Cap.4 The study of the excitation functions for ^{43}K, ^{43,44,44m}Sc and ^{44}Ti by protons irradiation on ^{45}Sc targets at energies up to 37 MeV

In the nuclear medicine for the positron emission tomography (PET), the injected positron emitter leads to two back-to-back 511 keV γ-rays, detected by crystals in most commercial cameras. The number of β$^+$ γ emitters is quite large, but it can be restricted to those that have some useful properties. One of the most promising radionuclide is ^{44}Sc, it has a good β$^+$ γ yield (94.3 %) and there is only one additional γ-ray with energy of 1157 keV. Its radionuclidic properties, its facile labeling chemistry and the lack of specific in vivo trapping make it an attractive candidate for RAIT (radioimmunotheraphy) [65].

In this experiment, the main purpose was to investigate the excitation functions for the reactions ^{45}Sc(p,2n)^{44}Ti and ^{45}Sc(p,pn)^{44g}Sc, but also the results about possible contaminants such as ^{43}K, ^{43}Sc and ^{44m}Sc. The β$^+$ emitter radionuclide ^{44g}Sc can be directly produced by protons irradiation on Sc targets, but also it can be obtained from a generating system such as the daughter radionuclide with long half life ^{44}Ti of 60 years (can also be produced in meteorites through cosmic-ray interactions), obtained from the same irradiation, giving the possibility to hospitals and laboratories to have this certified tracer always at disposal.

The cross section values for protons induced reactions on natural Sc (^{45}Sc 100 %) at energies up to 37 MeV, were determined by using the stack foil technique. Several palletes containing powder of Sc$_2$O$_3$ (99.5 %), enclosed in two Al foils, together with monitor foils of ^{nat}Ti (99 %) were irradiated in the external beam of the VUB CGR-560 cyclotron. The cross section values for the produced radionuclides ^{43}Sc, ^{44m}Sc, ^{44g}Sc and ^{44}Ti were calculated from activity measurements and their spectral characteristics are presented in Table 3.

Table. 3 Main induced nuclear reactions by protons irradiation on Sc targets and their spectral characteristics

RADIONUCLIDE	NUCLEAR REACTION	E_{TH} (MEV)	MAIN γ EMISSION (KEV) (ABUNDANCE %)
^{43}K T$_{1/2}$ = 22.3 h	^{45}Sc(p,3p)^{43}K	19.47	372.76 (86.8 %) 617.49 (79.2 %)
^{43}Sc T$_{1/2}$ = 3.89 h	^{45}Sc(p,2np)^{43}Sc	21.49	372.9 (22.5 %)
^{44m}Sc T$_{1/2}$ = 2.4 d	^{45}Sc(p,np)^{44m}Sc	11.57	271.13 (86.74 %) 1157.002 (1.2 %)
^{44g}Sc T$_{1/2}$ = 3.9 h	^{45}Sc(p,np)^{44g}Sc	11.57	1157.02 (99.9 %)
^{44}Ti T$_{1/2}$ = 60 y	^{45}Sc(p,2n)^{44}Ti	12.65	1157.02 (99.9 %) (disint. of ^{44g}Sc daughter)

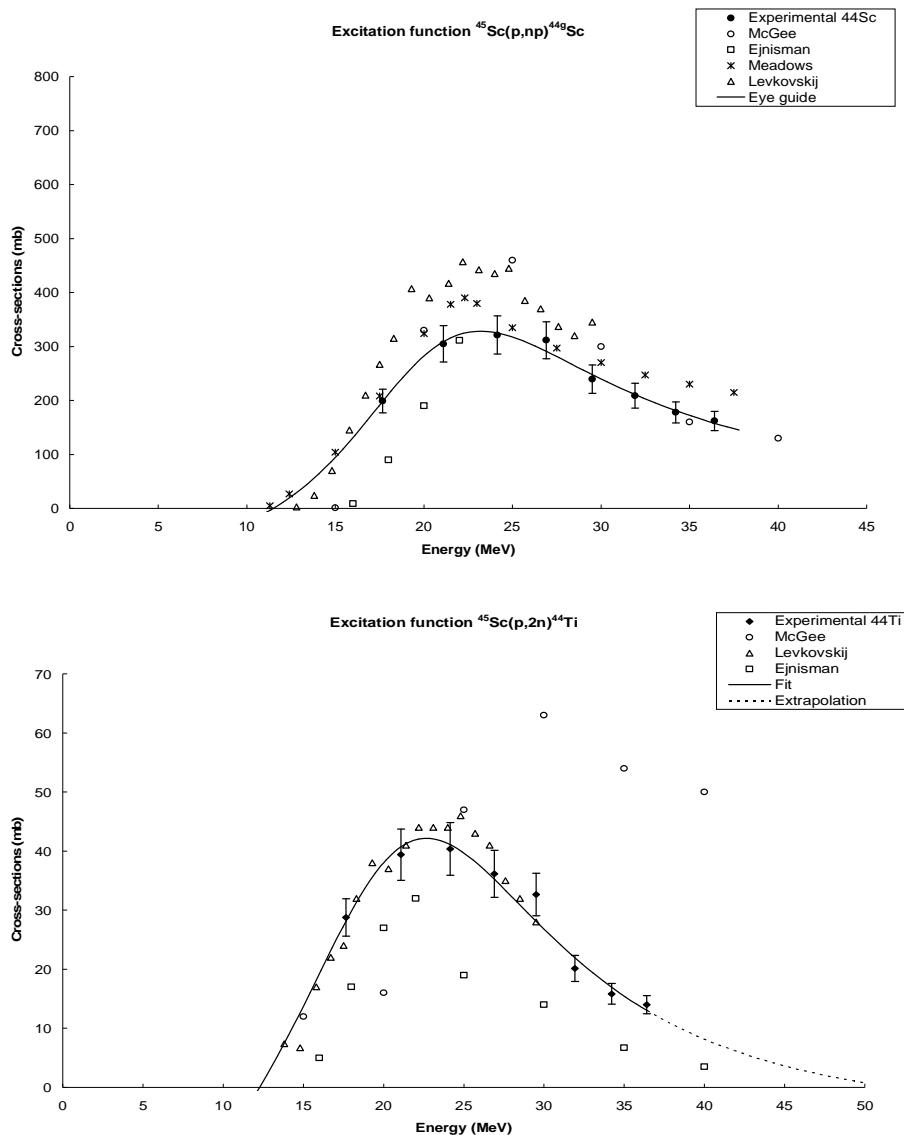**Fig.4.3.35** *The excitation function for the reactions $^{45}Sc(p,np)^{44g}Sc$ and $^{45}Sc(p,2n)^{44}Ti$, comparison with literature values*

The experimental excitation functions were calculated with the help of the activation formula and compared with literature values on the same reactions (Fig.4.3.35). By making a fit over the cross section values measured for ^{44}Ti, the thick target yield for the same radionuclide was calculated. The thick target yield for proton energies from 15 MeV up to 50 MeV is presented in Fig.4.4.38. In the range 22-15 MeV, the measured thick target yield values are in good agreement with values previously measured by Dmitriev [32]. Our values were obtained by extrapolation on the fitted curve at energies up to 50 MeV of the excitation function measured up to 36.4 MeV (Fig.4.4.38).
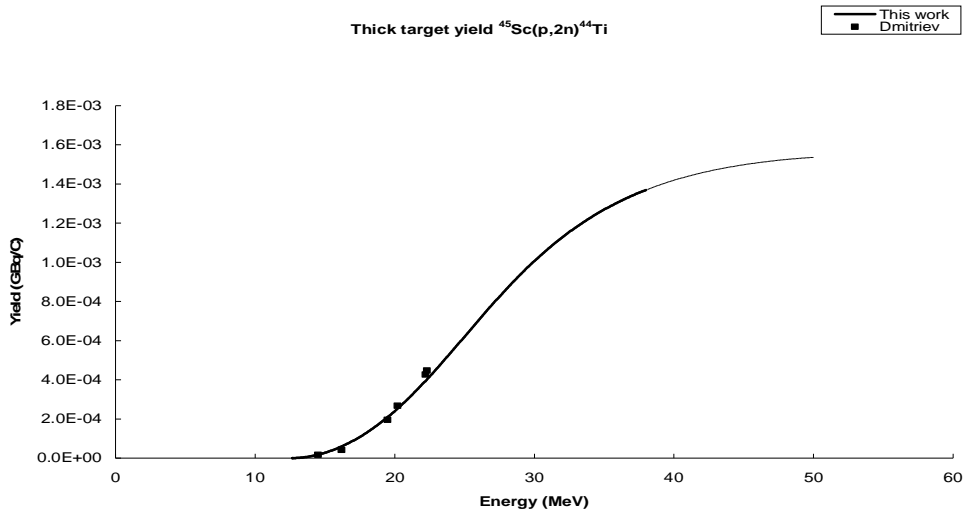
Fig.4.4.38 *The thick target yield for the reaction $^{45}Sc(p,2n)^{44}Ti$*

Cap.5 The study of the production of ^{103}Pd by protons irradiation on ^{103}Rh targets at energies up to 28 MeV

^{103}Pd with a $T_{1/2}= 17$ d, is a photon emitter at low energies often used as permanent implants for the brachytherapy for the treatment of prostate tumors since 1986 in the USA. The production method is based on the proton irradiation on rhodium metal targets via the reaction $^{103}Rh(p,n)^{103}Pd$, followed by a chemical separation of the radionuclide from the expensive target material.

The cross section values were determined by using the stack foil technique, 7 stacks contai ning Rh foils (99 %) together with monitor foils of Ti, Cu and Ni were irradiated in the external beam of the VUB CGR-560 cyclotron at energies up to 28 MeV. In Fig.5.2.40, a fit of our experimental data for the production of ^{103}Pd (cross section values derived from X and γ lines and data from Harper et al. [37]) is presented. The values are compared also with those measured directly by Dmitriev [32] and are in good agreement. The thick target yield at energies up to 16.7 MeV (9.9 MBq/µAh) is higher than the value of 8.1 MBq/µAh calculated by Harper et al. [37].
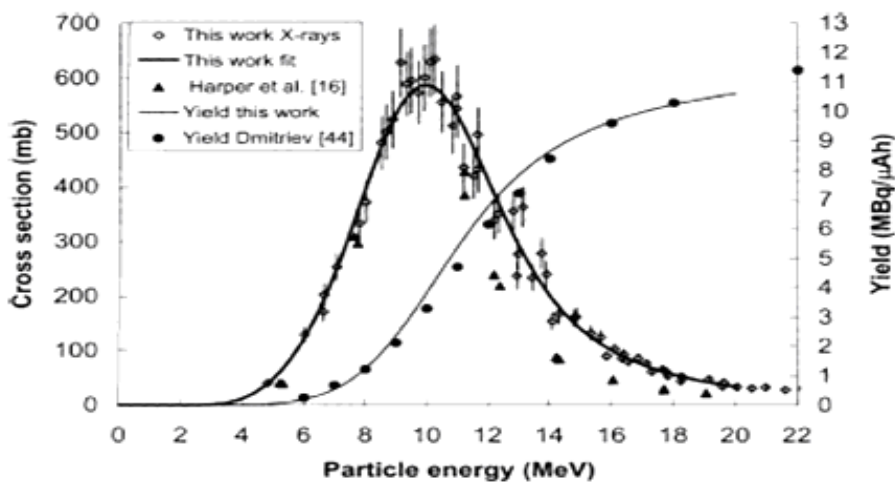

Fig.5.2.40 *The excitation function fit for the reaction $^{103}Rh(p,n)^{103}Pd$ and the thick target yield*

Cap.6 The study of the excitation functions for W, Ta and Hf by deuterons irradiation on ^{181}Ta targets at energies up to 40 MeV

A few tantalum radio-isotopes have found medical applications. ^{182}Ta wires were implanted for radiotherapy of prostate neoplasms [39] and in head and neck tumors [40], while several studies on bio-distribution in tumors were published [41]. The ^{178}W- ^{178}Ta generator received even recently a lot of attention in angiographic studies [42].

The metal tantalum has a very special composition as it consists of two isotopes: for more than 99.98 % it is formed by stable ^{181}Ta and ^{180m}Ta occurring for 0.012 % but it is the only element in nature that contains a very long lived metastable state (^{180m}Ta: half life over 1.2 10^{15} years). The main radionuclides of W, Ta and Hf produced by deuterons irradiations on ^{181}Ta targets are presented in Table 4.

Table.4 *Main induced nuclear reactions on ^{181}Ta targets and their spectral chracteristics and the Q values*

Radionuclide	$T_{1/2}$	Main γ emission (keV)	I (%)	Nuclear reaction	Q Value (MeV)
^{177g}Ta	56.6 h	112.95	7.2	^{181}Ta(d,p5n)	-31.23
^{178g}Ta	2.25 h	331.6	31.2	^{181}Ta(d,p4n)	-24.37
^{180g}Ta	8.1 h	93	4.5	^{181}Ta(d,p2n)	-9.8
		103.8			
^{182g}Ta	114 d	1121	35	^{181}Ta(d,p)	3.8
		1231	11.5		
		59.31	18		
		57.98	10.5		
		67.75	41.2		
^{181}W	121.2 d	56.28	18.7	^{181}Ta(d,2n)	-3.2
		57.53	32		
		65.14	11		
		67.25	2.8		
^{180m}Hf	5.5 h	332.3	94.1	^{181}Ta(d,2pn)	-8.16
		443.1	81.9		
^{179m}Hf	25 d	453.4	68	^{181}Ta(d,2p2n)	-15.5

The excitation functions for the reactions ^{181}Ta(d,x) were measured at VUB cyclotron in Brussels, Belgium and also at the CYRIC cyclotron at the Tohoku University in Sendai, Japan. Also, in order to understand better the contributions of the individual reactions, some theoretical codes such as ALICE-IPPE [44] and EMPIRE [45] were used for the comparison of the experimental cross section values (Fig. 6.5.43 and 6.5.44).
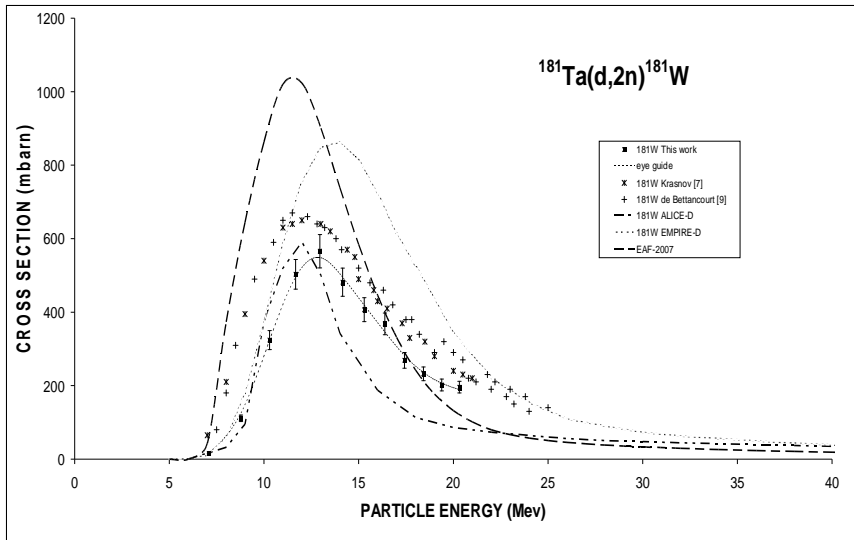
Fig.6.5.43 *The excitation function for the reaction $^{181}Ta(d,2n)^{181}W$, comparison with literature values and theoretical codes calculation*
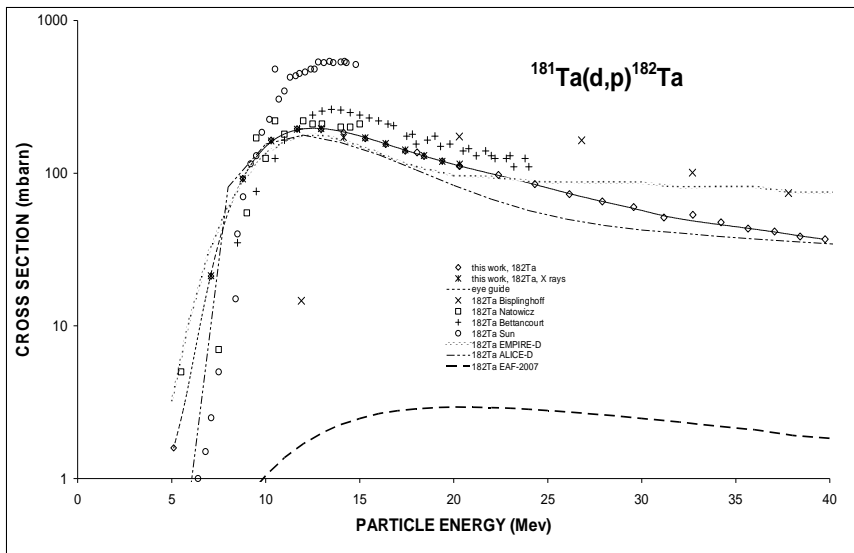

Fig.6.5.44 *The excitation function for the reaction $^{181}Ta(d,p)^{182}Ta$, comparison with literature values and theoretical codes calculation*

The thick target yield was calculated by fitting the experimental curves for 4 radionuclides with practical importance: $^{178,180g,182}Ta$ and ^{181}W. While for the short lived radionuclides ^{178}Ta and ^{180}Ta high activities can be produced, for the long lived radionuclides ^{181}W and ^{182}Ta, these activities are much lower (on a scale of 1000 in Fig.6.6.48).
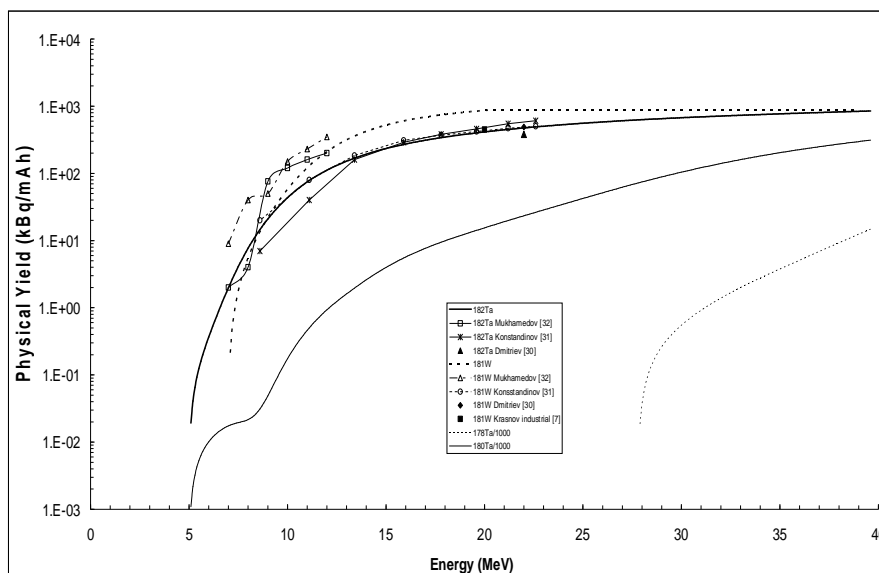
17

Fig.6.6.48 *The thick target yield for selected radionuclides produced by irradiation on Ta targets, comparison with literature values*

Cap.7 Induced alpha reactions on ^{nat}Cd targets at energies up to 38.5 MeV: experimental and theoretical studies of the excitation functions

Standardization of different production routes of medical important isotopes by means of charged particle activation requires investigation of the activation cross-section of certain reactions. Moreover, where the isotopes are produced by irradiation with high energy charged particles, special care must be employed in order to diminish the percentage of impurities in the end product. This can be done, where applicable, by chemical separation or by proper choice of the irradiation parameters such as type and incident energy of charged particle, thickness of target layer, decay time between end of bombardment and start of chemical processing based on different half lives of all induced isotopes. The discussion above is for instance applicable to the radioisotopes ^{114m}In ($T_{1/2}$= 49.5 d, 96.7 % IT, to be used in radio-immunotherapy) and ^{117m}Sn ($T_{1/2}$= 13.6 d, 100 % IT, bone cancer therapy and pain palliation [147-53]), which are available in a NCA form by protons, deuterons or alpha particles induced reactions on natural or enriched Cd or Sn targets, as reported earlier in [54, 55]. Also, the clinically proven ^{111}In used for SPECT (IAEA TECDOC 1211 [17]) and ^{110,109}In, possible PET candidates, are also present in the samples (Table 5).

18

Radionuclide	Nuclear reaction	Et (MeV)	Main γ emission (keV) (Abundance %)
^{117m}Sn	^{116}Cd(α,3n)^{117m}Sn	20.8	158.56 (86.4 %)
T ½ = 13.76 d	^{114}Cd(α,n)^{117m}Sn	5.4	
^{111g}In	^{108}Cd(α,p)^{111m}In	5.9	171.28 (90 %)
T ½ = 2.8 d			245.39 (94 %)
	^{109}Cd(α,pn)^{111m}In	13.5	
	^{110}Cd(α,p2n)^{111m}In	23	
	^{111}Cd(α,p3n)^{111m}In	31	
^{110g}In	^{108}Cd(α,pn)^{110}In	16.3	657.76 (98 %)
T ½ = 69.1 min			884.68 (92.9 %)
^{110m}In	^{110}Cd(α,p3n)^{110}In	34.1	
T ½ = 4.9 h	^{111}Cd(α,p)^{114m}In	5.7	190.27 (15.56 %)
^{114m}In	^{112}Cd(α,pn)^{114m}In	15.4	
T ½ = 49.51 d	^{113}Cd(α,p2n)^{114m}In	22.24	
	^{114}Cd(α,p3n)^{114m}In	31.6	
^{109g}In	^{108}Cd(α,p2n)^{109g}In	24.6	203.5 (74 %)
T ½ = 4.16 h	^{109}Cd(α,p3n)^{109g}In	32.2	

The cross section values for reactions type tip (α,2pxn), (α,pxn) and (α,xn) on all stable isotopes of ^{nat}Cd, were calculated over the entire energy range by using also theoretical codes such as ALICE-IPPE [57], GNASH [58] and EMPIRE-II [59] and compared with the experimental cross section values and literature values for the same reactions (Fig. 7.3.52, 7.3.58, 7.3.60 and 7.3.63).
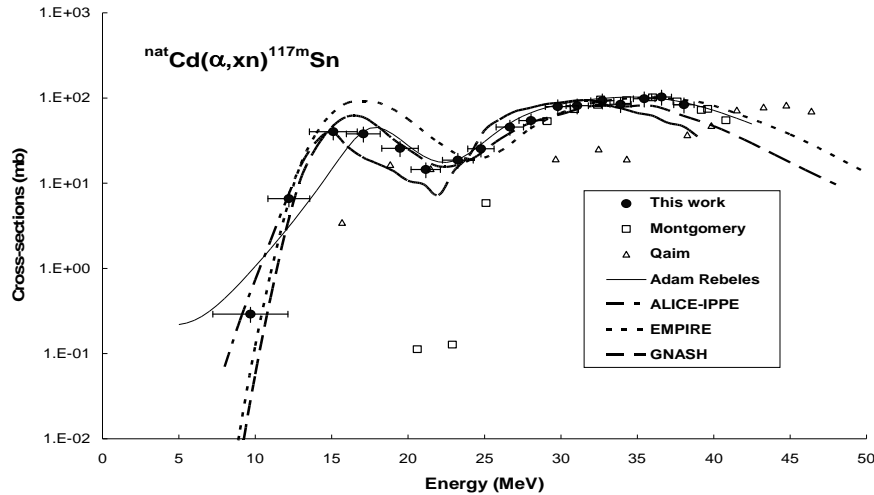

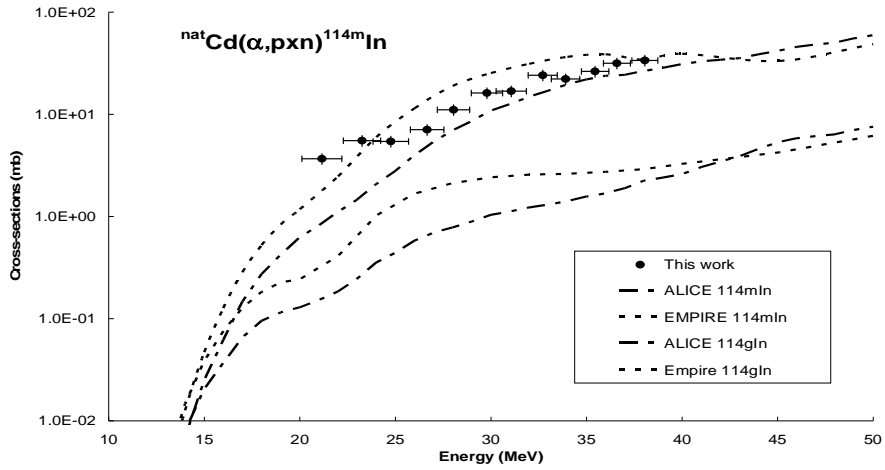**Fig.7.3.52** *The excitation function for the reaction ^{nat}Cd(α,xn)^{117m}Sn*

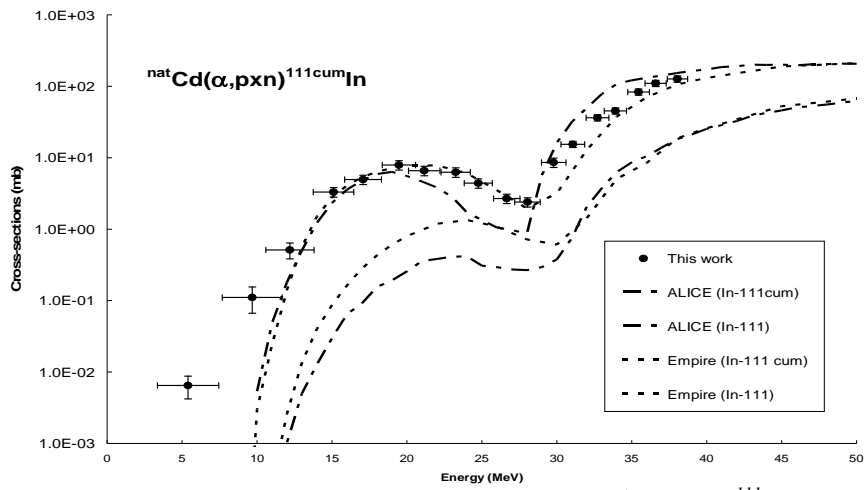**Fig.7.3.58** *The excitation function for the reaction* $^{nat}Cd(\alpha,pxn)^{114m}In$

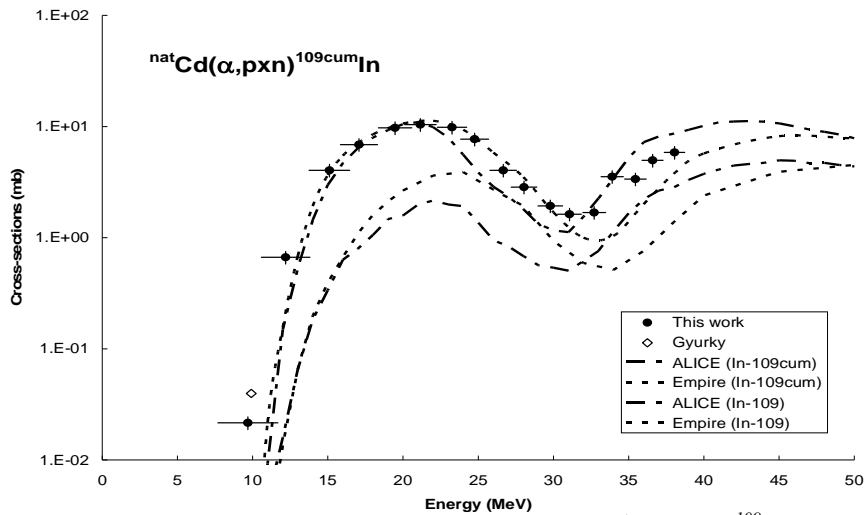**Fig.7.3.60** *The excitation function for the reaction* $^{nat}Cd(\alpha,pxn)^{111g}In$

Fig.7.3.63 *The excitation function for the reaction* $^{nat}Cd(\alpha,xnp)^{109g}In$

General conclusions

In this thesis, some production methods of medically relevant radionuclides for the nuclear medicine are presented, mainly based on experimental studies of the excitation functions of different types of induced reactions with charged particles and neutrons.

It was shown that, by using neutron isotopic sources, some radionuclides can be produced at the place of their applications in clinical laboratories, such as: ^{116m}In, ^{198}Au, ^{56}Mn and ^{64}Cu. Several studies on thin targets irradiated with charged particles at the cyclotron were performed, by making a calculation of the cross section values in each foil of the stacks (the stack foil technique) and their thick target yield. The cross section values for deuterons irradiation on ^{64}Zn targets up to 19.5 MeV were calculated for the radionuclides ^{64}Cu and ^{61}Cu, isotopes than generates a considerable interest for medical applications. The excitation functions for the reactions ^{64}Zn(d,2p)^{64}Cu, studied for the first time and ^{64}Zn(d,αn)^{61}Cu, were estimated by using the activation formula and show a good agreement with literature values [13, 14, 15] and theoretical calculations.

As an alternative production method, the activation cross section values for the reaction ^{64}Ni(d,2n)^{64}Cu for the production of the NCA ^{64}Cu by deuterons irradiation, were estimated in the energy range 5- 20.5 MeV. It was shown that above 18 MeV, the deuteron energy for the (d,2n) reaction is more interesting for the comercial production of ^{64}Cu than the (p,n) reaction in the same energy range.

In this study, several cross section values for induced proton reactions on scandium targets were studied in the energy range 17– 37 MeV by different reactions ^{45}Sc(p,x), leading to the formation of some radionuclides with medical applications, such as: ^{43}Sc, ^{44m}Sc, ^{44g}Sc and ^{44}Ti. The radionuclides ^{43}Sc and ^{44m}Sc will always be present in the samples in small quantities, ^{43}Sc is a β^+ emitter and will capture the signal in the positron direction, while the long lived radionuclide ^{44m}Sc behaves as an internal generator, which would allow kinetic PET studies over a few days period of time. Our results were also compared with some earlier investigations of other groups [27-29], some differences are due to some old nuclear data or different measurement techniques.

Another experiment presents the production of a medically important radionuclide ^{103}Pd, succesfully used for the brachytherapy of tumors. It can be produced by protons irradiation on Rh targets, the results of the excitation function and thick target yield for this radionuclide show a good agreement with literature values up to 18 MeV.

The excitation functions for the production of some radionuclides such as ^{177,178g,180g,182}Ta, ^{181}W and ^{179m,180m}Hf were determined by deuterons irradiation on ^{nat}Ta targets at energies up to 40 MeV. Also, some comparisons with literature values and different theoretical values calculated with the codes ALICE and EMPIRE, were performed and show a relative good agreement.

Finally, the excitation functions for the production of some radionuclides such as ^{110,113g,117m}Sn, ^{108m,g,109g,110m,110g,113m,114m,115m,116m,117m,g}In and ^{111m,115g}Cd, produced by irradiation with alpha particles on ^{nat}Cd targets, were presented here for the first time in the energy range 6- 38 MeV. Some of these radionuclides are important for medical applications, such as NCA^{117m}Sn, NCA^{114m}In, ^{111}In and can be produced in high doses at high energies. The comparison of the measured cross section values with literature values and theoretical values, obtained with theoretical codes EMPIRE [58], ALICE [57] and GNASH [59], show a relative good agreement as well.

Selected references

1. P. Sandru, Aurelia Topa, *Radionuclizii*, p.83, **93**, Ed. Academiei Romane (1968).

2. Perkins A.C., *Nuclear Medicine* (1995).

3. Firestone et al., *Table of Isotopes*, New York, USA (1998).

4. De Soete D., Gijbels R., Hoste J., *Neutron Activation Analysis*, p. 123, Wiley-Interscience, London, New York, Sydney, Toronto (1972).

5. I.E. Teodorescu, *Generatoare de neutroni. Principii si utilizari,* p.352, Ed. Academiei Romane, Bucuresti (1969).

6. S.F Mughabghab, M. Divadeenam, N.E. Holden, *Neutron Cross Sections from Neutron Resonance Parameters and Thermal Cross Sections,* Academic Press (1981).

7. J. J. M. de Goeij, *Nuclear, physical and chemical aspects in cyclotron production of radionuclides*, Nuclear Instruments and Methods in Physics Ressearch B **139**, 91-97 (1998).

8. S. M. Qaim et al., *Nuclear data relevant to the production and application of diagnostic radionuclides*, Radiochim. Acta. **89**, 223-232 (2001).

9. Laura Daraban, K. Abbas, F. Simonelli, N. Gibson, *Experimental study of excitation functions for deuteron particle induced reactions $^{64}Zn(d,2p)^{64}Cu$ and $^{64}Zn(d,\alpha n)^{61}Cu$ by the stack foil technique,* Applied Radiation and Isotopes **66**, 261-264 (2008).

10. Laura Daraban, Onuc Cozar, Liviu Daraban, *The Production and Characterization of some medically used Radioisotopes*, Studia Universitatis Babes-Bolyai, **51**, 2, 61 – 68 (2006).

11. F. Tarkanyi et al., *Excitation functions of deuteron induced nuclear reactions on natural zinc up to 50 MeV*, Nuclear Instruments and Methods in Physics Research B **217**, 531-550 (2004).

12. A. Hermanne et al., *Experimental study of excitation functions for some reactions induced by deuterons (10-50 MeV) on natural Fe and Ti*, Nuclear Instruments and Methods in Physics Research B **161-163**, 178-185 (2000).

13. F. Szelecsenyi et al., *Investigation of the $^{66}Zn(p,2pn)^{64}Cu$ and $^{68}Zn(p,x)^{64}Cu$ nuclear processes up to 100 MeV: Production of ^{64}Cu*, Nuclear Instruments and Methods in Physics Research B **240**, 625-637 (2005).

14. T. Stoll et al., Radiochim. Acta **90**, 309 (2002).

15. K. Hilgers et al., *Cross-section measurements of the nuclear reactions $^{nat}Zn(d,x)^{64}Cu$, $^{66}Zn(d,\alpha)^{64}Cu$ and $^{68}Zn(p,\alpha n)^{64}Cu$ for production of ^{64}Cu,* Applied Radiation and Isotopes **59**, 343-351 (2003).

16. F. Ziegler, SRIM 2006 code, Available from www.srim.org.

17. F. Tarkanyi, S. Takacs, K. Gul, A. Hermanne, M.G. Mustafa, M. Nortier, P. Oblozinsky, S. M. Qaim, B. Scholten, Yu. Shubin, Z. Youxiang, IAEA-TECDOC-1211, *Beam monitors reactions. In: Charged particles cross-sections database for medical radioisotope production*, Co-ordinated Research Project, IAEA, Vienna, p. 77-80. Updated Version January (2007). Available from http://www-nds.iaea.org/medical

18. Laura Daraban, R. Adam Rebeles, A. Hermanne, *Study of the excitation function for the deuteron induced reaction on $^{64}Ni(d,2n)$ for the production of the medical radioisotope ^{64}Cu,* Appl. Radiat. Isot. **67**, 506-510 (2009).

19. K. Abbas, J. Kozempel, M. L. Bonardi, F. Groppi, A. Alfarano, U. Holzwarth, F. Simonelli, H. Hofman, W. Horstmann, E. Menapace, L. Leseticky, N. Gibson, *Cyclotron production of ^{64}Cu by deuteron irradiation of ^{64}Zn*, Appl. Radiat. Isot. **64**, 1001-1005 (2006).

20. R. Adam Rebeles, *New measurement and evaluation of the excitation function of $^{64}Ni(p,n)$ reaction for the production of ^{64}Cu*, Private communication, Manuscript submitted to Nucl. Instr. and Meth. B. (2008).

21. A. Aydin, B. Sarer, E. Tel, *New calculation of excitation functions of proton-induced reactions in some medical isotopes of Cu, Z, and Ga,* Appl. Radiat. Isotopes **65,** 65-370 (2007).

22. V. N. Levkovskij, *Activation cross section nuclides of average masses (A= 40- 100) by proton and alpha particles with average energy (E= 50- 100 MeV)*, Inter Vesi, Moscow, EXFOR A0510 (1991).

23. NUDAT2, Levels and Gamma, National Nuclear Data Center, Brookhaven National Laboratory. Available from http://www.nndc.bnl.gov/nudat2.

24. A. Obata, S. Kasamatsu, D. McCarthy, M. Welch, H. Saji, Y. Yonekura, Y. Fujibayashi, *Production of therapeutic quantities of ^{64}Cu using a 12 MeV cyclotron*, Nucl. Med. Biol. **30**, 535 (2003).

25. Laura Daraban, R. Adam Rebeles, A. Hermanne, F. Tarkanyi, S. Takacs, *Study of the excitation functions for ^{43}K, $^{43,44,44m}Sc$ and ^{44}Ti by proton irradiation on ^{45}Sc up to 37 MeV*, Nucl. Instr. and Meth. B **267**, 755-759 (2009).

26. J. Zweit, A. Smith, S. Downey, H. Sharma, Excitation functions for induced reactions on natural nickel: Production of non-carrier-added ^{64}Cu from enriched ^{64}Ni targets for positron emission tomograph, Appl. Radiat. Isotopes **42**, 193 (1991).

27. T. McGee, C.L. Rao, G.B. Saha, L. Yaffe, Nucl. Phys. A **150,** 11 (1970).

28. J.W. Meadows, R.M. Diamond, R.A. Sharp, Phys. Rev. **102,** 190 (1956).

29. B. Levkovskij, *Cross-section of medium mass nuclide activation (A = 40–100) by medium energy protons and alpha particles*, Inter-vesi, Moscow, USSR (1991).

30. S. Takacs, F. Tarkanyi, M. Sonck, A. Hermanne, Nucl. Instr. and Meth. B **198,** 183 (2002).

31. E.B. Norman, E. Brown, Y.D. Chan, I.D. Goldman, R.M. Larimer, K.T. Lesko, M. Nelson, F.E. Wietfeldt, I. Zlimen, Phys. Rev. C **57** 2010 (1998).

32. P.P. Dmitriev, G.A. Molin, N.N. Krasnov, Sov. At. Energy **34,** 497 (1973).

33. F. Haddad, L. Ferrer, A. Guertin, T. Carlier, N. Michel, J. Barbet, J.F. Chatal, Eur. J. Nucl. Med. Mol. Imaging **35,** 1377 (2008).

34. A. Hermanne, M. Sonck, A. Fenyvesi, <u>Laura Daraban</u>, *Study on production of ^{103}Pd and characterisation of possible contaminants in the proton irradiation of ^{103}Rh up to 28 MeV,* Nuclear Instruments and Methods in Physics Research B **170**, 281-292 (2000).

35. C.H. Johnson, A.Galonsky, C.N. Inskeep, ORNL-2910 Report 25 (Exfor: B0068), (1960).

36. J.P. Blaser, F. Boehm, P. Marmier, P. Scherrer, Helvetica Acta **24** (441 (Exfor: P0033) (1951).

37. P. Harper, K. Lathrop, J.L. Need, ORNL-LR-DWG 51564 124 (1961).

38. A. Hermanne, <u>Laura Daraban</u>, F. Tarkanyi, S. Takacs, F. Ditroi, A. Ignatyuk, R. Adam Rebeles, M. Baba, *Excitation functions for some W, Ta and Hf radionuclides obtained by deuteron irradiation of ^{181}Ta up to 40 MeV,* Nuclear Instruments and Methods B **267**, 3293-3301 (2009).

39. S. Takai, G. Yamashita, K. Igawa, T. Wada, T. Tamiya, *Radiation therapy of prostatic cancer*, Tumor Res. **1**, 77-102 (1966).

40. Y.H. Son and G.R. Ramsby, *Percatuneous tantalum- 182 wire implantation using a guiding needle-needle technique for head and neck tumors,* Am. J. Roentgenol Radium Ther Nucl Med **96**, 37-44 (1966).

41. A. Ando, I. Ando, S. Sanada, T. Hiraki, T. Takeuchi, K. Hisada, N. Tonami, *Relationship between the biodistribution of radioactive metal nuclides in tumor tissue and the physicochemical properties of these metal ions,* Annales of Nuclear Medicine **13**, 83-88 (1999).

42. J. Heo, T. Htay, D. Mehta, L. Sun, J. Lacy, A.E. Iskandrian, *Assesment of left ventricular function during upright treadmill exercise with tantalum 178 and multi-wire gamma camera*, Nucl Cardiol **12**, 560-566 (2005).

43. IFMIF Conceptual Design Activity, Final Report, IFMIF CDA Team, ENEA Frascati Report RT/ERG/FUS/96/11 edited by M.Martone, (December 1996), Home page of IFMIF project, http://www.frascati.enea.it/ifmif.

44. A.I. Dityuk, A.Yu. Konobeyev, V.P. Lunev, Y. Shubin, *New version of the advanced computer code ALICE-IPPE*, Report INDC (CCP)-410, IAEA, Vienna, 1998.

45. M. Herman, R. Capote, B. Carlson, P. Oblozinsky, M. Sin, A. Trkov, V. Zerkin, *EMPIRE modular system for nuclear reaction calculations Version 2.19*, International Atomic Energy Agency, Vienna, Austria (2005) available in CD and web http://www-nds.iaea.or.at/empire/index.html

46. P.P. Dmitriev, M.N. Krasnov, G.A. Molin, *Radioactive yields for thick target at 22 MeV deuteron energy*, Yadernia Konstanti **34,** 38 (EXFOR A0194) (1982).

47. A. Hermanne, <u>Laura Daraban</u>, R. Adam Rebeles, A. Ignatyuk, F.Tarkanyi, S. Takacs, *Alpha induced reactions on ^{nat}Cd up to 38.5 MeV: experimental and theoretical studies of the excitation functions,* submitted to Nucl. Instr. And Meth. B (2010).

48. A. Bishayee, D. V. Rao, S. C. Srivastava, L. G. Bouchet, W. E. Bolch, R. W. Howell, *Marrow-sparing effects of ^{117m}Sn (+4) diethylenetriaminepentaacid for nuclide therapy of bone cancer*, Journal of Nuclear Medicine **41,** 2043-2050 (2000).

49. Y. Kvinnsland, A. Skretting, O. S. Bruland, *Radionuclide therapy with bone seeking compunds: Monte Carlo calculations of dose-volume histograms for bone marrow in trabecular bone*, Physics in Medicine and Biology **46,** 1149-1161 (2001).

50. J. R. Zeevaart, W. K. Louw, Z. I. Kolar, E. Killian, I. C. Dormehl, *Biodistribution and pharmacokinetics of variously molecular sized $^{117m}Sn(II)$-polyethyleneiminomethyl phosphonate complexes in the normal primate model as potential selective therapeutic bone agents*, Arzneimittelforschung **54,** 340-347 (2004).

51. Y. Yang, S. Luo, M. Pu, W. Wang, J. He, G. Lin, W. Bing, H. Wei, *Labeling conditions, in vitro properties and biodistributions of various Sn-label complexes,* Applied Radiation and Isotopes **62,** 597-603 (2005).

52. L. F. Mausner, K. L. Kolsky, V. Joshi, S. C. Srivastava, *Radionuclide development at BNL for Nuclear Medicine Therapy*, Applied Radiation and Isotopes **49**, 4, 285-294 (1998).

53. L. G. Bouchet, W. E. Bolch, S. M. Goddu, R. W. Howell, D. V. Rao, *Considerations in the selection of radiopharmaceuticals for palliation of bone pain from metastatic osseuous lesions,* Journal of Nuclear Medicine **41,** 688-691 (2000).

54. F. Tarkanyi, S. Takacs, A. Hermanne, P. Van den Winkel, R. Van der Zwart, Yu. A. Skakun, Yu. N. Shubin, S. F. Kovalev, *Investigation of the production of the therapeutic radioisotope ^{114m}In through proton and deuteron induced nuclear reactions on cadmium*, Radiochimica Acta **93,** 1 (2005).

55. R. Adam Rebeles, A. Hermanne, S. Takacs, F. Tarkanyi, S. F. Kovalev, A. Ignatyuk, *Alpha induced reactions on ^{nat}Sn: an experimental study of excitation functions and possible production pathways*, Nuclear Instruments and Methods in Physics Research B **260,** 672-684 (2007).

56. R. Adam Rebeles, A. Hermanne, P. Van den Winkel, F. Tarkanyi, S. Takacs, <u>Laura Daraban</u>, *Alpha induced reactions on ^{114}Cd and ^{116}Cd. An experimental study of excitation functions,* Nuclear Instruments and Methods in Physics Research B 266, 4731- 4737 (2008).

57. A. I. Dituyk, A. Yu. Konobeyev, V. P. Lunev, Yu. N. Shubin, *New advanced version of computer code ALICE-IPPE*, Report INDC(CCP)-410, International Atomic Energy Agency, Vienna (1998).

58. M. Herman, R. Capote, B. Carlson, P. Oblozinsky, M. Sin, A. Trkov, V. Zerkin, *EMPIRE Modular System for Nuclear Reaction Calculations, Version 2.19*, International Atomic Energy Agency, Vienna, Austria, 2005. Available in CD and Web <http://www-nds.iaea.or.at/empire/index.html>

59. P.G. Young, E.D. Arthur, M.B. Chadwick, Comprehensive nuclear model calculations: theory and use of the GNASH code, in: A.Gandini, G. Reffo (Eds.), *Proceedings of the IAEA Workshop on Nuclear Reaction Data and Nuclear Reactors: Physics,* Design and Safety-Trieste, Italy, April 15–May 17, 1996, World Scientific Publishing, Ltd., Singapore, pp. 227–404 (1998).

60. A. Hermanne, F. Tarkanyi, S. Takacs, P. Van den Winkel, R. Adam Rebeles, A. Ignatyuk, S.F. Kovalev, *Production of the therapeutic radioisotope^{114m}In through the ^{116}Cd(p,3n)^{114m}In reaction,* Applied Radiation and Isotopes, **68**, 14-17 (2010).

61. S. M. Qaim, H. Doehler, *Production of Carrier-free ^{117m}Sn,* Int. J. Applied Radiation and Isotopes, Vol. **35,** No. 7, 645- 650 (1984).

62. A. Hermanne, F. Tarkanyi, S. Takacs, P. Van den Winkel, R. Adam Rebeles, A. Ignatyuk, S.F. Kovalev, *Production of the therapeutic radioisotope^{114m}In through the ^{116}Cd(p,3n)^{114m}In reaction,* Applied Radiation and Isotopes, **68**, 14-17 (2010).

63. Laura Daraban, O. Cozar, G. Damian, L. Daraban, *ESR Dosimetry by some Detergents,* Studia Universitatis Babes-Bolyai, Physica, **50**, 4b, 587-590 (2005).

64. L. Daraban, Laura Daraban, O. Cozar, R. Adam Rebeles, *The Use of Isotopic Neutron Sources for some Radionuclides Production in Nuclear Medicine and other Domains of Science,* Book of Abstracts, The 5th International Conference on Isotopes, 25-29 April (2005), Bruxelles, Belgium, International Proceedings, 257-264.

Acknowledgments