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REVIEW

Of Mateusz Sitarz doctoral thesis entitled:

"Research on production of new medical radioisotopes with cyclotron"

Nuclear medicine is developing rapidly during few last decades introducing new radioisotopes for labelling different chemical compounds or biological molecules for both, therapy or diagnosis purposes. Cyclotrons with various accelerated particles and their energies are widely used as very convenient tools for production of radioisotopes for nuclear medicine. The main advantage of radioisotopes obtained by cyclotron production is their feature of being carrier free. This is easy to obtain in some way for free with charged particle activation since during such processes a change of nuclei charge occurs, so obtained radionuclide is isotope of different element than target was. It is different to what happens during neutron activation when neutron capture usually does not change charge of nuclei, so activated product is just another isotope of irradiated element. Moreover, in cyclotron the activation conditions are relatively easy to modify. The energy and kind of accelerated particle as well as construction of target including isotopic enriched materials are main steps of freedom which are subject of optimization. To do such optimization the production conditions of given radioisotope must be studied for different particles, targets and a wide range of beam energies. This is the field of research described by Mr. Mateusz Sitarz, MSc, in his doctoral thesis. The manuscript was written under supervise of Professor Tomasz Matulewicz from Faculty of Physics of Warsaw University from Polish side and Professor Ferid Haddad from GIP ARRONAX & University of Nantes from French side. As co-supervisor acted also Dr. Agnieszka Trzcińska from Warsaw University.

The thesis is organized in five chapters followed by three appendixes containing some supplementary data. The really impressive set of literature containing 519 titles is closing the thesis.

The First Chapter ("Introduction") contains very brief history of nuclear medicine and description of aim of the thesis. The radionuclides of interest are defined as ^{97}Ru, ^{105}Rh and ^{43,44g,m,47}Sc. It is said there, that "The aim of these studies is to confirm the efficient production routes offered by cyclotrons for above mentioned (and other) medical radioisotopes. Additionally, a software for the calculation of Thick Target Yield is developed…". Three cyclotrons (two in Poland and one in France) are quoted as used in experimental work done for thesis.

Chapter 2 is entitled "Theoretical Background" contains a brief description of structure of nucleus including discussion of conditions for stability and radioactivity. The main concepts and definitions are presented. The Chapter contains also short description of nuclear reactions and problems with radionuclides production using cyclotron. It contains also description of interaction of nuclear radiation with matter. The following sub-chapter is devoted to nuclear medicine. Presented is characterization of medical radioisotopes, basic methods of their production including different construction of targets and separation processes. Chapter ends with description of SPECT, PET diagnostic techniques as well as description of radioisotopes used for radiotherapy and the most modern concept of theranostics, ie. use of pair of radionuclides for simultaneous therapy and diagnosis functions.

Chapter 3 is devoted to experimental procedures used in research described in thesis. Namely, the used cyclotrons, gamma spectrometers and methods applied for data analyses.

Chapter 4, entitled "Projects and experiments" contains description of details of conducted experiments. The chapter starts with presentation of ^{97}Ru production with alpha particles beam including presentation and wide discussion of obtained results. Next, similar presentation is devoted to experiments on ^{105}Rh with use of deuteron beams. The third part of this chapter is of similar construction and presents production of scandium radioisotopes with proton and deuteron beams. In sub-chapters presented and discussed are production of ^{43}Sc, $^{44g.m}$Sc and ^{47}Sc. The final part of this Chapter presents method of reconstruction of reaction cross-section from results obtained for thick targets. An analytical form of total thick target yield function (TTY) was assumed and its free parameters (constant) are obtained from fit. This allows to get formula for cross-section dependence on beam energy as function of derivate product: dTTY(E)/dE and dE/dx . The values of the latest factor (ie. dE/dx for target material) are obtained from existing literature what allows to get value of differential cross section from thick target measurement.

Short Chapter 5 "Conclusions and summary" on only about a half of page summarize work and obtained results. It is concluded, that production of all radionuclides of interest (with applied cyclotrons) are promising and the optimum values of irradiation were found. It is however stated also, that the actual usefulness of subjected radioisotopes is a different story and was not subject of the thesis.

As was already said the thesis contains also three Appendixes. In Appendix the Radionuclide Yield Calculator (RYC) software is presented and its use is described. It is not said "explicite" that it was written by the thesis Author on his own solely, however the leading role of him here is suggested in words "it is a GUI software developed during this thesis". Maybe this is to modest phrase only. I hope to get more clear explanation of the role of Mr. M.Sitarz in writing RYC later, maybe on a public defend of thesis.. Anyway, I think that creation of such software is one the most interesting scientific achievement of the thesis. In experimental obtaining of cross-sections used targets have defined thickness, so in general sense they are always "thick". Therefore I think that the created here software RYC will be very useful tool for long time and many various experiments.

The Appendix B contains description of relatively novel concept of beta plus-gamma (three photons) coincidence PET method. There is rather extensive description of long list of radionuclides, which are suitable for implementation of this method.

The third Appendix, "C" contains what Author named directly the "Suplementary data": there are figures of cross section for monitor reactions, two gamma spectra, isotopic compositions of targets, values of cross sections and thick target yields. This is followed by list of abbreviation, list of symbols, physical constants, list of figures and tables.

The whole thesis is well written and organized. However I may say that for me this organizing of text would not be worse if the first two Appendixes will be included in main part of thesis, as separate Chapters. The Appendix B tells a lot on radionuclides currently considered for possible applications for future development of nuclear medicine. Appendix A describes very useful tool developed for getting better the thesis results. But still, removing those parts from main body of thesis makes it perhaps better for following and more clear, so I understand likely the reason why they were shifted to Appendixes.

Obtained results are important and useful, the methodology of work is proper and my general impression is very good. However, some criticism is required in a review like that. What I missed in thesis was for example a comment on a cascade summing problem on gamma sources used for gamma spectrometer calibration. In Table 3.2 at least two radionuclides (^{133}Be and ^{152}Eu) which are well known for cascade summing problems are quoted as used for calibration.

The construction of targets (p. 23) is restricted only to solid state ones, despite a wide use of liquid and rarely gaseous targets in modern nuclear medicine.

Some abbreviation like for example TENDL (p. 44-49) are not explained nor quoted in list of abbreviations. By the way – the reasons for discrepancies between TENDL predictions and experimental data presented in Fig. 4.11 – 4-15 are not explained sufficiently for me.

The data presented in Tables C1-C4 has no unit. I can guess, what perhaps is obvious, that it is [%] but it should be written anyway.

Those few minor critical remarks presented above do not affect my general very high rank of presented Mr. Mateusz Sitarz thesis The whole text present him as a researcher who finds right way to solve complex scientific problems and draws correct conclusions using proper modern and advanced techniques. It my opinion the thesis fulfils all the requirements which might be addressed to PhD thesis and therefore I am pleased to recommend Mr Mateusz Sitarz for the further steps in her way to obtain the PhD degree. Moreover, since the thesis brings very interesting and unique results and especially it brought the development of new very useful tool (the RYC software) I recommend Mr. Mateusz Sitarz doctoral work for distinction.

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