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TO WHOM IT MAY CONCERN

Review of the Ph.D. thesis of Mateusz Sitarz entitled "Research of production of new medical radioisotopes with cyclotron"

This thesis is organized in 5 chapters starting with a brief introduction summarizing the development of nuclear medicine from the discovery of X-ray by W Röntgen in 1895 until today and the developments of innovative radioisotopes to diagnose and treat diseases, in particular cancers. This introduction ends with a presentation of the thesis goal, namely the study of the production routes of several radioisotopes of potential interest for nuclear medicine (^{97}Ru, ^{105}Rh, ^{43,44g,m,47}Sc) using a cyclotron in three different laboratories (HIL Warsaw, ARRONAX Nantes, NCNR Swierk). These studies are based on the measurements and calculations of cross-sections as well as Thick Target production Yields (TTY). The second chapter describes the basis to understand what are the concepts and observables used in the thesis starting with the required background on the structure of the nucleus, its various possible decay modes and how a radioisotope can be produced. The equations leading to the determination of the main quantities (activity at the end of bombardment, A_{EOB}, TTY and cross-sections) are clearly presented and established. This is followed by a section on the various interactions of radiations with matters, and concluded with a section on the important criteria, which need to be carefully investigated in order to evaluate the relevance of a given radioisotope in a nuclear medicine context (production routes, targetry and target processing, association with biomolecules, imaging, therapy and theranostics).

The experimental procedures used to produce the radioisotopes of interest, to control the machines parameters and to analyze the data are described in the third chapter. The various quantities required to evaluate a given radioisotope (and any possible contaminant) are measured using the detection of characteristic gamma-ray lines. These measurements are performed using Hyper Pure germanium detectors (HPGe). The determination of their main characteristics (efficiency and energy calibrations) are presented as well as the way to analyze the measured spectra to extract the interesting quantities (activities, minimum detectable activity, cross-sections and TTY). The method to control beam energy and intensity is also explained in this chapter.

Chapter 4 contains the results and discussions of the work. It is divided in four sections namely: 1) the production of ^{97}Ru with an alpha beam, 2) production of ^{105}Rh using a deuteron beam, 3) production of Sc isotopes using proton and deuteron beams and, 4) the reconstruction of Sc production cross-sections from TTY measurements. Sections 1 to 3 are organized in the same way with an introduction specific to the measured radioisotope, followed by sections associated to targets, experimental results, discussion and a

summary/conclusion. Each introduction presents the interest, state of the art, production routes and contaminants associated to the isotope of interest. In the target subsections the stacked target technique to build excitation functions is described as well as purity and beam monitoring aspects using a well-known cross-section as recommended by the AIEA and explained in section 3. The results subsections present the measured cross-sections and/or TTY. The measurements from this work are compared with existing data and TENDL extracted cross-sections. In the discussion part, M Sitarz introduces a software called RYC (for Radionuclide Yield Calculator) he developed himself to calculate production yield (providing the knowledge of the excitation function) and TTYs (this software is described in Appendix A). A short executive summary concludes each section. The fourth section of chapter 4 is dedicated to the determination of the cross-section of Sc isotopes. For these radioisotopes, only TTYs could be measured due to the difficulty to produce thin self-supported Ca targets. To do so, an analytical function is chosen so that a least square fit to the TTY data leads to the determination of three parameters of the chosen function, the derivative of which yielding eventually the cross-sections. The cross-sections extracted this way for the various Sc isotopes are shown together with published data and the measured TTYs.

Chapter 5 is a short conclusion and summary of the whole thesis work. Finally, apart from Appendix A already mentioned and presenting the RYC software developed by M Sitarz, two other appendixes describe the technique of β^+–γ coincidences for PET imaging and the various possible isotopes for this technique (Appendix B), and a compilation of all the experimental data that are used in the thesis (Appendix C).

The document is very well organized and well written. It is easy, pleasant to read, and it is self-consistent so that the reader can easily find any information required to get a full understanding of the results and discussions. The chosen radioisotopes (^{97}Ru, ^{105}Rh, ^{43,44g,m,47}Sc) are uncommon (not necessarily new) or emerging in nuclear medicine. They all have interesting specific properties, which make them attractive candidates for imaging, therapy or both (the theranostic approach). Studying the cyclotron route to produce them is therefore potentially very interesting. The disagreement observed when comparing the cross-sections measured in this work and TENDL predictions clearly demonstrates the needs for more measurements. The obtained results indicate that it might be worth pursuing research in the various fields leading to the radiopharmaceuticals. However, as pointed out in the conclusion, these emerging radioisotopes should also be evaluated in view of existing ones.

M Sitarz has clearly accomplished an important amount of work designing experiments, running them in various laboratories, developing software tools to analyze his data and publishing results.

I therefore recommend granting the candidate with the permission to defend his PhD thesis work.

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