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**Referee report on doctoral thesis
of Arshiya Anees Ahmed**

“Production of $^{99m}\text{Tc}/^{99}\text{Mo}$ radioisotopes using proton and electron beams”

The doctoral dissertation of Mrs. Arshiya Anees Ahmed addresses very important problem of contemporary nuclear medicine, namely the availability of the radioisotopes used for diagnostic and therapeutic purposes. Among them the meta-stable isotope of Technetium-99m (^{99m}Tc) and its parent nucleus - Molybdenum-99 (^{99}Mo) are the most commonly exploited. The ^{99m}Tc is used in 85% of nuclear medicine procedures. These radioisotopes have to be produced artificially with the use of reactors or particle accelerators. In the view of the decommissioning of some nuclear facilities providing these isotopes, which took place in the recent years and is still foreseen in the close future, the search for the new production methods of ^{99m}Tc and ^{99}Mo are of special importance. When invented, the new production schemes should permit the deployment of the small production centers around the World, providing local sources of the medical radioisotopes, upon the short delivery time and at the reasonable price. The former is particularly important in view of the short lifetimes of ^{99m}Tc and ^{99}Mo radioisotopes.

Mrs. Arshiya Anees Ahmed in her thesis examines the production of the ^{99m}Tc and ^{99}Mo with the use of proton and photon beams. The novelty of her approach consists in utilizing the small scientific facilities like cyclotrons or electron accelerators instead of large reactor-based radioisotope factories, which dominated the production of medical radionuclides in recent decades.

The dissertation has been completed at the Institute of Physics of the Jagiellonian University, Cracow whereas the experimental research has been performed in Institute of Nuclear Physics, Polish Academy of Sciences (IFJ PAN) in Cracow and in the National Synchrotron Radiation Centre SOLARIS of the Jagiellonian University (UJ). The thesis is composed of 7 chapters and extensive bibliography of the relevant research literature. The material contained in the thesis, to great extent, have been already published in the three reviewed scientific papers where Mrs. A. A. Ahmed is the first author.

Introduction to the thesis provides necessary scientific medical and physical background as well as informs about the contemporary technological and organizational issues related to production and availability of medical radioisotopes.

In chapter 2 Mrs. A. A. Ahmed introduces and explains the necessary theoretical formalism and notions like the “sample activity at the end of irradiation” or the “target yield”, and their relation to the particular reaction cross-section, lifetimes of resulting isotopes and the specific conditions of the production process.

Both experimental facilities where the experimental research has been performed are presented in chapter 3. The energy degraded proton beam from AIC-144 cyclotron of IFJ PAN have been used for proton irradiation whereas the photons for gamma irradiation were created by means of bremsstrahlung of electron beam at linac injector of SOLARIS Synchrotron of UJ. Moreover, in this chapter, the experimental methods and tools are explained including the high purity Germanium detectors utilized for gamma rays measurements, their energy calibration and efficiency calculation. The short information about the radionuclide identification by means of gamma spectroscopy is given as well.

The experimental setups for target irradiation with protons and photons are presented in chapter 4 along with their optimization methods. With the proton beam the activation of both a single- and the stack of multiple targets was done. In this chapter Mrs. A. A. Ahmed describes also the spectroscopic measurements demanded after the target irradiation in order to identify the resulting radionuclide composition of the samples. The examples of gamma spectra of ^{nat}Mo target bombarded with protons and with photons are shown.

Chapter 5 contains the description of the data analysis schemes. The identification of registered gamma lines is performed. Then the partial isotopic activities are calculated and their time decline is observed. The beam intensity is concluded from the parallel measurements of the monitoring reactions. For this aim the monitoring foils were installed in vicinity of the irradiated targets. The registered activities induced in the monitoring foils are used as well to cross-check (together with performed simulations) the actual energies of particles bombarding the samples. The data analysis results in establishing of the value of energy dependent cross-section for production of specific isotope of interest and for the so-called target yields which provide the measure of achievable activity of the sample for irradiation with given beam current and during specific time period. Besides of production cross-sections and target yields for medical radioisotopes of interest, this kind of analysis allows as well the determination of kinds and the yields of radioactive impurities in the sample created during irradiation.

The same analysis scheme has been used both for data obtained with proton and photon irradiation. Due to the lack of data for gamma-induced monitoring reactions the energy dependence of the photon flux activating the target had to be established only by means of Geant4 simulations.

In chapter 6 Mrs. Arshiya A. Ahmed presents and discusses her results. The cross-sections derived both from a single- as well as from the multiple target irradiation with protons are presented. The effort were made to find the actual proton energy distribution in the targets. Thus, the cross-sections can be determined for narrow energy bins. Results of A. A. Ahmed are compared to the outcomes reported by other experimental groups. Cross-sections for ^{99}Mo and ^{99m}Tc are compared also to the results of two theoretical models. Both for ^{99m}Tc and ^{99}Mo isotopes and those which are in this case the impurities (other identified Tc isotopes), cross-sections provided by Mrs. A. A. Ahmed agree well with the values originating from other measurements. The same is observed when ^{99m}Tc and ^{99}Mo cross-sections are compared to the theoretical calculations. Very satisfactory agreement of obtained target yields with those derived from the literature is also confirmed. These facts prove the correctness of the experimental method and analysis scheme proposed in the thesis and confirm the feasibility of ^{99m}Tc and ^{99}Mo generation with the use of conventional low energy proton beams.

For isotope production method utilizing the photon irradiation of the ^{nat}Mo target the observables provided by Mrs. A. A. Ahmed are the activity of the specific isotope at the end of irradiation time and the yield of this isotope for the given beam/target conditions. The measured activities of the identified radioisotopes are compared with the model simulation (TALYS + Geant4). A discrepancies of the order of 20-50% are observed. But taking into account the systematic uncertainties of the model simulations

the obtained agreement is satisfactory. Mrs. A. A. Ahmed discusses the beam energy dependence of the resulting activity ratios for ^{99}Mo and radioisotopes, which are treated as the impurities of the sample. She realized that the most favorable electron beam energy for bremsstrahlung photons irradiation would be about 100 MeV.

The work is summarized in chapter 7 where also the suggestions of the further development and improvement of the $^{99\text{m}}\text{Tc}$ and ^{99}Mo production by irradiation of natural or enriched molybdenum targets with protons and photons are given.

The advantages of the thesis of Mrs. A. A. Ahmed are as follows:

- 1) the undertaken subject is very important for availability and development of the patients treatment methods in the nuclear medicine;
- 2) it provides important experimental quantities (cross-sections, activities, target yields) and the description of verified experimental procedures. They all are needed for development of new methods for large scale production of medical radioisotopes with the use of proton and photon beams;
- 3) the cross-sections for proton induced radionuclide production are determined for narrow energy bins;
- 4) the feasibility of ^{99}Mo production by means of photon beams of conventional scientific electron linac facilities is shown;
- 5) reported are the first ever obtained experimental results for ^{99}Mo production in irradiation of natural molybdenum with the 100 MeV and 200 MeV photons;
- 6) the clear structure of the thesis allows the reader to follow the reasoning of the Author and easily find the searched subtopics.

The text is written concisely, what should be an asset. But at a few places more details would be advisable.

First of all the discussion of experimental uncertainties is missing. The reader is referred to the original papers where one can learn about the sources and magnitudes of errors. But for the completeness of the thesis such information are needed also there.

In the description of advantages of used in this work HPGe detectors the Author compare them to other kind of detectors. But it is not clear if She always means the gaseous or scintillating detectors or rather other types of semiconductor detectors as well.

From fig. 3.6 one can learn that the detection efficiency of one of the used HPGe detectors, at the energy of the higher photopeak of ^{60}Co (1332.5 keV) is less than half of pro-mile (?). But in the next sub-chapter it is written that "relative efficiency" of this detector, for gammas of this energy is equal to 25% (!). Earlier the "relative efficiency" is referred as the detection efficiency taking into account the

relative intensities of the different peaks. Not clear relations between these "efficiencies" is shown and the large discrepancy between both reported values is not explained.

A few inconsistencies in description of the formulas or apparent typos are noticed. In general the text of the thesis reveals the signs of a certain rush, in which it was probably completed. The referee cannot avoid a remark of the geographic and political nature and point out that the Ontario belongs to the provinces of Canada, and not, as mistakenly written in the introduction, to the United States of America.

The indicated above shortcomings of the thesis do not change the very positive opinion about the work done by Mrs. A. A. Ahmed and the whole research group She belongs to. The important problem related to physics, medicine and technology was identified. The appropriate experimental research have been undertaken. Obtained results are important, to great extent original, and most likely will be utilized in practical applications.

In my opinion, dissertation of Mrs. Arshiya Anees Ahmed is of large scientific value. It satisfies as well the formal requirements for doctoral theses. I recommend admission of Mrs. Arshiya Anees Ahmed for the subsequent stages of the procedure, including the public defense.

A handwritten signature in blue ink, appearing to be 'Arshiya Anees Ahmed', is written in a cursive style.