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Nuclear data for production and medical application of radionuclides: Present status and future needs☆

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ABSTRACT

Introduction: The significance of nuclear data in the choice and medical application of a radionuclide is considered: the decay data determine its suitability for organ imaging or internal therapy and the reaction cross section data allow optimisation of its production route. A brief discussion of reaction cross sections and yields is given.
Standard radionuclides: The standard SPECT, PET and therapeutic radionuclides are enumerated and their decay and production data are considered. The status of nuclear data is generally good. Some existing discrepancies are outlined. A few promising alternative production routes of ^{99m}Tc and ^{68}Ga are discussed.
Research-oriented radionuclides: The increasing significance of non-standard positron emitters in organ imaging and of low-energy highly-ionizing radiation emitters in internal therapy is discussed, their nuclear data are considered and a brief review of their status is presented. Some other related nuclear data issues are also mentioned.
Production of radionuclides using newer technologies: The data needs arising from new directions in radionuclide applications (multimode imaging, theranostic approach, radionanoparticles, etc.) are considered. The future needs of data associated with possible utilization of newer irradiation technologies (intermediate energy cyclotron, high-intensity photon accelerator, spallation neutron source, etc.) are outlined.
Conclusion: Except for a few small discrepancies, the available nuclear data are sufficient for routine production and application of radionuclides. Considerable data needs exist for developing novel radionuclides for applications. The developing future technologies for radionuclide production will demand further data-related activities.

1. Introduction

1.1. Significance and overview

Radionuclides find application in many fields, their major use being in nuclear medicine, both in diagnosis and internal radiotherapy [1]. Each application, however, demands a special type of radionuclide, the choice being dependent on its decay properties. The two major physical considerations in internal use of radionuclides are:

(a) suitability for imaging.
(b) radiation dose caused to the patient.

The underlying principle in diagnostic nuclear medicine is that the radiation dose to the patient is as low as possible, compatible with the required quality of imaging and the diagnostic advantage in comparison to non-radioactive methods. In internal radionuclide therapy, on the other hand, a localized, well-defined radiation dose needs to be deposited in a malignant or inflammatory tissue to achieve the desired therapeutic effect. Thus, for in vivo diagnostic investigations involving organ imaging, radionuclides are required that do not cause much radiation dose and can be efficiently detected from outside of the body. To this end, short-lived γ-ray emitters, like ^{99m}Tc and ^{123}I, and positron emitters, like ^{11}C and ^{18}F, are commonly used, the former finding application in single photon emission computed tomography (SPECT) and the latter in positron emission tomography (PET). Regarding the radiation dose, attention has to be paid to the emitted corpuscular radiation. The spectrum of radionuclides required in internal radionuclide therapy (endotherapy) is therefore very broad. In general, radionuclides emitting low-range highly-ionizing radiation, i.e. α or β^- particles, conversion and/or Auger electrons, are of great interest. Thus a complete set of decay data of a radionuclide is required to be able to calculate the radiation dose in a diagnostic or therapeutic medical application.

Besides the physical considerations mentioned above, the quality and availability of a radionuclide play an important role in its broad application. In this regard the production data, i.e. the nuclear reaction cross section data, are of great significance. As it is well known, the production of radionuclides is carried out using nuclear reactors as well as accelerators/cyclotrons. The reactor production generally leads to

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neutron excess radionuclides. They mostly decay by β^- emission and are therefore especially suited for radiotherapy. The cyclotron produced radionuclides, on the other hand, are mainly neutron deficient and decay by electron capture (EC) or β^+ emission. They are therefore particularly useful for diagnostic studies. The positron emitters can be produced only at cyclotrons. For production of some nuclides both nuclear reactors and cyclotrons are extensively used. In other words, their roles are to be regarded as complementary [2]. In reactor production of radionuclides the nuclear reactions (n,γ), (n,f) and (n,p) are commonly utilized, and in cyclotron production, proton, deuteron, ^{3}He or α-particle induced reactions find application, though the use of proton induced reactions is more common. In recent years some attention has also been devoted to photon-induced reactions like (γ,n) and (γ,p).

The optimization of a production route is strongly dependent on an accurate knowledge of the relevant nuclear reaction cross section data. The major aim of optimization is to maximize the yield of the desired product and to minimize the impurity level. The latter is the most important criterion, and nuclear reaction data play a very important role in achieving a high radionuclidic purity of the product. Whereas non-isotopic impurities can be chemically removed, the change in the ratio of the desired radionuclide to an isotopic radioactive impurity is achieved only through the choice of a proper energy range of the projectile within the target material. Another consideration is the specific activity (which is defined as the radioactivity per unit mass of the element) of the radionuclide. Charged particle induced reactions generally lead to products of high specific activity whereas in neutron and photon induced reactions, particularly in (n,γ) and (γ,n) reactions, special techniques (e.g. use of precursor/generator system, Szilard Chalmer's process, etc.) are needed to increase the specific activity. The former involves the separation and use of the daughter radionuclide formed via β^- or EC decay of the nuclear reaction product. In the latter case, some of the recoiling radioactive atoms, following a nuclear reaction, are separated (from the bulk of the inactive target material) because of their occurrence in a different valence state as compared to the target atoms. The specific activity of the separated species is thus high but its yield amounts to only a small fraction of the total activity.

The above discussion shows that both radioactive decay data and reaction cross section data play important roles in the production and application of radionuclides in medicine. It should also be explicitly mentioned that the chemical form of the radionuclide and its biochemical behavior are perhaps of greater significance regarding the application. The scope of this review, however, is limited to nuclear data related to medical radionuclides. This subject has been treated during the last 30 years in many compilations, evaluations and review articles. In general, the decay data of medical radionuclides are being constantly improved under the auspices of the Society of Nuclear Medicine (SNM) of the USA and the standard publication MRID 2007 [3] encompasses about 500 radionuclides. Furthermore, the evaluated decay data files of the National Nuclear Data Center (NNDC), USA, describe the data for almost all the known radionuclides [4]. Nonetheless, some discrepancies and deficiencies still exist in individual cases.

Regarding the production data, a huge amount of information exists on neutron induced reactions [5], mainly due to their potential energy-related applications. Those data are very useful also for production of radionuclides in a nuclear reactor. In comparison, the database for charged-particle induced reactions, needed in cyclotron production of radionuclides, is not strong. Although during the last three decades extensive measurements have been reported from several laboratories around the world [6] and the database has been considerably strengthened, several critical reviews carried out periodically by this author [7–13] demonstrate the need of continuous charged-particle data work in relation to medical radionuclide development and applications, in particular because it is a dynamic field. As far as photon-induced reactions for medical radionuclide production are concerned, their database is weak [14].

1.2. Cross sections and yields

The formation of a radioactive product in irradiation of a target is described by the activation equation given below (in a simplified form):

$$A = N\,\Phi\,\sigma\left(1-e^{-\lambda t}\right)$$

where A is the absolute activity of the reaction product (Bq) at the end of irradiation, N the number of target nuclei, Φ the projectile flux density ($cm^{-2}\,s^{-1}$), σ the reaction cross section (cm^2), λ the decay constant, and t is the time of irradiation (s). The number of nuclei exposed to projectiles is calculated from the mass of the target used, the irradiation time is properly chosen and λ is a constant. Thus using the above equation, both the cross section of a reaction and the projectile flux can be determined, provided one of them is accurately known. In each case, however, the absolute activity of the product needs to be determined.

The quantitative assay of the induced radioactivity is commonly carried out by using one or more well-defined γ-rays (or other characteristic radiation) of the radionuclide, whereby the efficiency of the detector and the intensity of the γ-ray (or other radiation) used play vital roles. In particular, if a weak γ-ray with a large uncertainty in the intensity is used, the measured absolute activity (i.e. the disintegration rate) and therefore the calculated reaction cross section may entail large uncertainty. In fact the determination of the projectile flux and the measurement of the product radioactivity constitute the two major sources of uncertainty in the experimentally determined cross section of a nuclear reaction.

The techniques involved in neutron and photon induced reaction cross section measurements are somewhat similar. The charged-particle induced reaction cross section measurement, however, is more challenging [7] due to the following two reasons:

a) rapid loss of energy of the charged particle in the target (range–energy relationship).
b) rapid change of the reaction cross section with energy (excitation function).

The technique therefore consists of irradiation of a stack of thin samples of the target material (often of high isotopic enrichment, with thickness of each sample amounting to only a few μm) with a few monitor reaction foils inserted in between to determine the beam current (for more details [7]). The induced radioactivity in the target material as well as in the monitor foil is determined as described above. The loss of the projectile energy in the stack is calculated by a well-established code but uncertainties in the calculation influence both the energy scale and the cross section. Thus rather than using an average cross section, the individual cross sections effective over small energy ranges are considered. Due to the use of thin targets, the number of target nuclei in the path of the beam is relatively small but it must be known accurately, not only for obtaining high accuracy in the cross section but also in the projectile energy degradation calculation. The total uncertainty involved in charged-particle induced reaction cross section measurements is thus generally higher than in the neutron cross section work.

In charged-particle production of radionuclides the yield A (in Bq) for a certain energy range (E_1 to E_2) is calculated by a modified form of the activation equation given below [7]:

$$A = \frac{N_L \cdot H}{M}\, I\left(1-e^{-\lambda t}\right)\int_{E_1}^{E_2}\left(\frac{dE}{d(\rho\chi)}\right)^{-1}\sigma(E)\,dE$$

where N_L is the Avogadro number, H the enrichment (or isotopic abundance) of the target nuclide, M the mass number of the target element, I the projectile current (particles s^{-1}), $\left(\frac{dE}{d(\rho\chi)}\right)$ the amount of the target material needed to decrease the projectile energy over a small range