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Development of Cyclotron Radionuclides for Medical Applications: From Fundamental Nuclear Data to Sophisticated Production Technology

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Introduction and Historical

Soon after the discovery of radioactivity it was shown that radionuclides can be used both for diagnostic and therapeutic studies, depending on the characteristic radiations emitted by them. By 1960's the radionuclide production technology using nuclear reactors was well established. In early 1970's a renaissance of the cyclotrons occurred because many of the neutron deficient radionuclides could only be produced using irradiations with charged particles, like protons, deuterons, α-particles, etc. Initially, interest was directed towards radioactive gases for inhalation studies and other radionuclides for scintigraphy. Later, with the advent of emission tomography, i.e. Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET), the emphasis shifted to ^{123}I and positron emitters [cf. 1–3], and tremendous progress ensued. In order to keep abreast of the fast developments, a Symposium was organized at the Brookhaven National Laboratory (BNL), USA, in 1976, with the title "Radiopharmaceutical Chemistry". This became a biennial event, with alternate meetings in North America and Europe. It included all aspects of radionuclide and radiopharmaceutical research. About a decade later, however, it was realized that for discussion of technical aspects, a separate forum would be more appropriate. A group of experts therefore convened the first Targetry Workshop in Heidelberg in 1985. Thereafter it was established as a recurring Workshop, with its scope enlargened to include also nuclear and radiochemical problems. Today, the major conference on Radiopharmaceutical Sciences and the specialist International Workshop on Targetry and Target Chemistry are held in alternate years. The present Workshop is No. 15 in the series and it is being jointly held by the research groups in Dresden and Prague, both of which have a long tradition of cyclotron production of radionuclides. In this talk, some personal reminiscences and impressions of the historical developments in the field over the last 40 years will be briefly described.

Development Steps

The development of cyclotron radionuclides involves work in three major directions [cf. 4,5]:

a) Nuclear data studies.
b) High-current targetry.
c) Chemical separations and quality assurance.

A brief review of the developments and achievements in each direction is presented.

Nuclear data studies

An accurate knowledge of nuclear data is a prerequisite for developing a production route. Data measurements related to cyclotron radionuclides are much more demanding than in the case of reactor produced radionuclides [cf. 6]. Extensive excitation function measurements using highly enriched target material and high-resolution γ- or X-ray spectrometry are mandatory. Special attention needs to be paid to determination of charged particle flux and energy degradation in the target constituents. To date both gaseous and solid targets have been used for nuclear reaction cross section measurements. The techniques have reached a certain degree of perfection and, in recent years, the uncertainties in properly measured cross sections have been considerably reduced. A few typical examples of recent nuclear data measurements will be shown [cf. 7]. Some attention has also been paid to standardization, evaluation and validation of data for commonly used radionuclides through the use of nuclear model calculations, statistical fitting procedures and integral yield measurement [cf. 8,9]. The status of data will be discussed.

High-current targetry

Development of high-current targets has been one of the major challenges in large scale production of cyclotron radionuclides. Often a nuclear reaction with a relatively low yield may be chosen for production, if targetry is easier. Since often enriched material is irradiated, economic considerations play an important role in target design and construction [cf. 10].

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All three forms of materials, viz. solid, liquid and gas, have been finding application. Whereas in irradiation of gaseous and liquid targets a perpendicular collimated beam is used and the target is operated under high pressure to keep the change in the target density within controlled limits, in case of solid targets a broadened and wobbled slanting beam is often employed. An efficient heat transfer from the target is mandatory. In general, for the production of commonly used short-lived PET radionuclides (^{11}C, ^{13}N, ^{15}O, ^{18}F) at dedicated small-sized cyclotrons, gaseous or liquid targets are used. A spherical water target has proven to be very effective for large scale production of ^{18}F, the most important PET-radionuclide. Also in the production of the SPECT-radionuclide ^{123}I at a medium-sized cyclotron, high-class gas target technology is utilized. In most of the other cases, e.g. metallic SPECT, PET and therapeutic radionuclides, both at small and medium-sized cyclotrons, solid targets are used. As a result of constant developments [for review, cf. 4, 11], sophisticated target systems are now available.

Chemical separations

For separation of desired radionuclides from cyclotron irradiated targets, both dry and wet chemical processing methods have been attempted [for review, cf. 4,5]. The dry distillation process may be optimized to obtain the purified radionuclide in a very small volume of the solvent. A variation of the process, termed as thermochromatography, leads only to a removal of the desired activity from the strong matrix, which is generally followed by a more refined separation method. The wet chemical processing, on the other hand, may involve all types of separation techniques, such as ion-chromatography, solvent extraction, electrolysis, etc. Many of the techniques have been very well developed. Examples relevant to the production of a few novel radionuclides like ^{124}I, ^{64}Cu, ^{55}Co, etc. will be given. Some special precautions needed to assure good specific activity will be discussed.

Conclusions and Perspectives

As a result of vast research and development work in all the areas discussed above, dispersed over a span of several decades, the radionuclide production technology at a cyclotron has now reached a level of high sophistication. The impetus has also come through the development of dedicated high-powered cyclotrons and high-resolution imaging devices. In the case of short-lived positron emitters, for example, full production units, consisting of a cyclotron, set of suitable targets and apparatus for chemical separation and synthesis can be commercially obtained. Yet it is vital that research and development work continues. In particular, if the supply chain of some established radionuclides is jeopardized, alternative routes of production need to be developed.

The present emphasis with regard to cyclotron production of medical radionuclides is on longer lived positron emitters and highly-ionizing low-range emitting therapeutic radionuclides. Some other emerging areas of interest [cf. 12] include a combination of PET and Magnetic Resonance Imaging (MRI) as well as of radioactivity and nanotechnology. The future perspectives of some radionuclides, potentially useful in those areas of applications, will be considered. The increasing significance of intermediate energy, multi-particle cyclotrons in production of some radionuclides will be outlined.

References

1. H. N. Wellman, V. J. Sodd, J. F. Mack: *Production and clinical development of a new ideal radioisotope of iodine – Iodine-123*. In: Frontiers of Nuclear Medicine, W. Horst (Editor), Springer Verlag, p. 19, 1971.
2. S. M. Qaim, G. Stöcklin, R. Weinreich (Editors): Iodine-123 in Western Europe (Production, Application, Distribution), *JÜL-Conf.-20*, 1976.
3. G. Stöcklin, V.W. Pike (Editors): *Radiopharmaceuticals for Positron Emission Tomography* (Methodological Aspects), Kluwer, pp. 1–178, 1993.
4. S.M. Qaim: *Cyclotron production of medical radionuclides*. In: Handbook of Nuclear Chemistry, Vol. 4, A. Vertes, S. Nagy, Z. Klencsár, R.G. Lovas, F. Rösch (Editors), Springer Verlag, pp. 1903–1933, 2011.
5. S.M. Qaim: *Radiochim. Acta* **99**, pp. 611–625, 2011.
6. S.M. Qaim: *Radiochim. Acta* **30**, pp. 147–162, 1982.
7. S.M. Qaim: *Radiochim. Acta* **101**, pp. 473–480, 2013.
8. K. Gul, A. Hermanne, M.G. Mustafa, F.M. Nortier, P. Oblozinsky, S.M. Qaim, B. Scholten, Yu. Shubin, S. Takács, F.T. Tárkányi, Y.Zhuang: *Charged Particle Cross Section Database for Medical Radioisotope Production: Diagnostic Radioisotopes and Monitor Reactions*. *IAEA-TECTOC-1211*, pp. 1–285, 2001.
9. S.M. Qaim, F. Tárkányi, R. Capote (Editors): *Nuclear Data for the Production of Therapeutic Radionuclides. IAEA Tech. Rep. Ser. No. 473*, pp. 1–358, 2011.
10. S.M. Qaim: *Nucl. Instr. Methods A* **282**, pp. 289–295, 1989.

11. *Proceedings of Int. Workshops on Targetry and Target Chemistry*, held every two years (1985–2012).
12. S.M. Qaim: *Radiochim. Acta* **100**, pp. 635–651, 2012.