

19 Isotope Production for Medical Applications

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19.1 Introduction

The use of radiation for medical imaging and therapy has a long history, originating almost immediately in the earliest days of the X-rays discovered by W.C. Röntgen in 1895, and the subsequent discovery of natural radioactivity by Becquerel in 1896 and the separate isolation of radium by Pierre and Marie Curie in 1898. The use of radioactive materials was limited to natural radioisotopes until the demonstration of induced nuclear transformations using an accelerated beam by Cockcroft and Walton [1]. Despite the relatively widespread use of accelerators in the following decade for radioisotope production, these early machines were quite limited in the amount of useful radioactive material they could produce.

The field quickly evolved with the advent of nuclear reactors and improved charged-particle accelerators as part of the weapons programs in the Second World War. By far the most prolific source of man-made radioisotopes was from the energetic neutrons from nuclear reactors. While medical applications of these isotopes quickly evolved, the scarcity of reactor sources and the nature of neutron-induced reactions generally limited the field to the use of long-lived, neutron-rich nuclei. These isotopes and subsequent procedures are by far the most widely used in nuclear medicine today. There are numerous biological applications using reactor-produced radionuclides such as ^{14}C and ^{32}P . Medical applications include in vivo photon imaging (SPECT, single-photon-emission computed tomography) of source compounds labeled with ^{125}I , ^{99}Tc and many other isotopes. Other reactor-produced isotopes have found uses in radiotherapy, taking advantage of the local cell-killing capabilities of heavy-particle disintegration, particularly α -particles.

While the application of reactor-produced isotopes for medical purposes continues to be important, it was quickly realized that there are advantages to using accelerator-produced isotopes. First, the flexibility of using beams of well-defined energy allows for controlled selection of nuclear reactions. Next, the use of positively charged beams, typically of protons, deuterons or helium nuclei, allows the selective production of proton-rich radioisotopes, greatly

expanding the choice of isotopes available for medical use. More importantly, for imaging applications, radioisotopes can be produced in this manner with a change in proton number, facilitating easier chemical separation of the reaction products from the starting material. This can be crucial in the synthesis of compounds suitable for medical use, allowing complex radiochemistry to be performed, and efficient removal of the often toxic bulk material.

A further need for charged-particle-produced radioisotopes is in the imaging application of PET (positron emission tomography). Isotopes that decay by positron emission can be located using pairs of coincidence scintillators tuned to the characteristic 511 keV gamma rays emitted at near 180° upon positron–electron annihilation. By using rings of detector pairs, three-dimensional distributions of PET radioisotopes can be quantitatively imaged. In addition to the true three-dimensional distribution quantitation, there are significant advantages of using PET radioisotopes in medical studies, including the availability of chemical compounds labeled with naturally occurring light radioisotopes such as ^{15}O , ^{13}N and ^{11}C , and lifetimes well matched to the imaging requirements of physiological pathways of interest, seconds to hours rather than years.

While much of the early development work on isotope production originated out of nuclear-physics laboratories using electrostatic accelerators, most recent installations use commercially available small cyclotrons. The main beam requirements are energy and current, and the precise energy definition required for nuclear-physics experiments is less important. Nonetheless, isotope production with tandems still has a role in the field. The accelerator technology is well established, robust and comparatively inexpensive, and in some cases may be a matter of necessity, for example through collaboration with established physics or engineering tandem facilities. Furthermore, few commercial production cyclotrons allow much tuning of the beam shape and energy, hampering some basic development work on isotope production. Finally, most commercial cyclotrons require costly technological additions to provide different particle beams (protons vs. deuterons, typically), a feature readily available with the electrostatic tandem.

19.2 Historical Perspective

Since its initial development in the 1930s [2], the electrostatic accelerator, insulated under high pressure, has dominated the field of nuclear investigations. This was the direct result of the exquisite control of such beam variables as:

- energy, with an achievable resolution of $\delta E/E \approx 10^{-6}$ [3]
- geometry, with microbeams of μm dimensions [4]
- polarization [5, 6]
- heavy-ion capability, with the tandem today acting as the second accelerator in radioactive-ion-beam experiments [7].