



Contribution ID: 170

Type: **Invited Oral**

## **Ion sources in medical isotope production - requirements, trends, and limitations**

*Monday, 8 September 2025 11:40 (30 minutes)*

Since the 1940s, when radioactive iodine was first used to treat hyperthyroidism and later thyroid cancer, the field of nuclear medicine has grown substantially, benefiting tremendously from technological advancements in physics, chemistry, and biology, as well as an increased understanding of disease mechanisms and immunology. From the early days of the cyclotron for radioisotope production and external beam radiation therapy to the discovery of the world's most commonly used radioisotope, metastable technetium-99m, for diagnostic imaging via gamma cameras, medical isotopes have played a significant role in disease diagnosis and treatment. This role became even more prominent with the development of Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET)—technologies that enhanced disease diagnosis and treatment, advanced knowledge of metabolic activity, and ultimately led to significant progress in the following decades with the introduction of targeted cancer therapies such as radioimmunotherapy and radiopharmaceutical therapy. Radiopharmaceutical therapy, in particular, is one of the most exciting and promising developments, offering the ability to administer highly tailored and localised radiation to specific cancer cells or tumour microenvironments while minimising damage to surrounding cells and organs-at-risk. While several key components make up a radiopharmaceutical and ultimately govern its success, the type of emitted radiation and the amount of energy transferred to surrounding material per unit distance are crucial to the treatment's efficacy. Radiopharmaceuticals labelled with the radioisotope lutetium-177—a beta (electron) emitter—have received widespread attention and obtained regulatory approval in the USA, Canada, and Europe for the treatment of neuroendocrine tumours and metastatic prostate cancer. Additionally, interest in expanding the application of lutetium-177-labelled radiopharmaceuticals to the treatment of other types of cancer continues to drive growing demand for this radioisotope. Among other beta emitters used in radiopharmaceutical therapy, terbium-161 is emerging as an attractive alternative to lutetium-177. Both lutetium-177 and terbium-161 are produced through neutron irradiation in a reactor, but their target materials and production pathways differ. A preferred pathway for lutetium-177 production involves the enrichment of stable ytterbium-176 isotope targets. These targets are subsequently neutron irradiated to produce ytterbium-177, which undergoes beta decay to form non-carrier-added lutetium-177. For terbium-161, enriched stable gadolinium-160 targets can be neutron irradiated to produce gadolinium-161, which subsequently decays to terbium-161. For both of these radioisotopes, enriched stable isotope targets can be produced via conventional electromagnetic isotope separation, provided a suitable ion source is paired with an appropriate electromagnet. Achieving the desired production, enrichment, and isotopic purity requirements is not trivial, however. This talk will discuss the experience at Kinectrics Canada in the production of highly enriched, chemically pure ytterbium-176 targets, with specific emphasis on ion beam generation, transport, and separation.

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**Session Classification:** Oral Session

**Track Classification:** Applications of ion sources