Set-up of a commercial ^{225}Ac production facility

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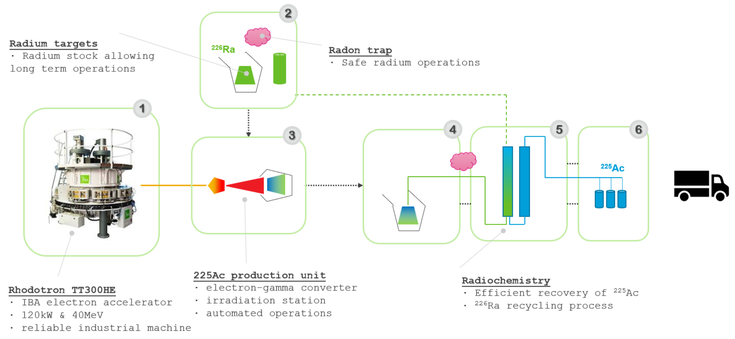
Abstract: Many clinical studies have demonstrated all the therapeutic potential of alpha-emitting Actinium-225. Today, SCK CEN and IBA are joining their forces to enable large-scale and high-quality production of this promising radioisotope.

Introduction

Nuclear medicine has evolved considerably over recent years with the emergence of radiotheranostics, a modality which combines targeted diagnosis and therapy with radioisotopes, offering an important alternative in the treatment of many cancers[1-3]. Radiotheranostics is based on the use of radioisotopes which, when they disintegrate, emit radiation that enables cancer cells to be precisely located and/or destroyed.

Among these isotopes, one of the most promising is alpha-emitting Actinium-225 (^{225}Ac). Alpha emitters present high LET (linear energy transfer- about 100 KeV/µm) and short path length in (50-100 µm) which results in high cytotoxic potency limited to few cancerous cells while sparing surrounding healthy tissues[4]. In addition, ^{225}Ac has an appropriate half-life (10 days) which facilitate smooth logistics process and a centralized industrial distribution scheme. One of the main challenges for worldwide patient access is to ensure the availability of high-quality ^{225}Ac in large quantities. By joining their unique expertise and resources, SCK CEN and IBA will be able to work towards the large-scale production of ^{225}Ac.



Methods and materials

SCK CEN and IBA have considered the two following reactions to produce Actinium-225 (^{225}Ac):

- ^{226}Ra (p,2n) ^{225}Ac: “the proton route”
- ^{226}Ra(g,n) ^{225}Ra à ^{225}Ac: “the gamma route”

Given the objective of IBA and SCK-CEN to supply large-scale amounts, the gamma route was selected and will translate into the set-up of a commercial production facility located in Belgium.

To enable the large-scale and high-quality production via the gamma route, several challenges must be addressed:

- The source material ^{226}Ra has very limited availability.
- The overall process efficiency must be high to allow long-term operation and avoid Radium losses
- The cross-section of the gamma route reaction is low, so the gamma flux on the Radium target and Radium quantity in the target must be high to enable commercial production of ^{225}Ac.
- Handling of ^{226}Ra target material which is radioactive and releases radioactive Radon-222
- The end-product quality must respond to pharmaceutical drug quality standards.

An overview of the complete process is shown on Figure 1

a) *Powerful electron beam accelerator – Rhodotron® TT300HE*

The facility is powered by the IBA Rhodotron® TT300HE. This unique compact accelerator allows the production of a 40MeV electron beam with power up to 120kW. The Rhodotron® is a very compact accelerator that enables seamless and continuous operations with reduced energy consumption when compared to standard linear accelerators.

b) 120kW electron-gamma converter

The electrons need to be converted into a gamma flux. Several challenges are faced when trying to maximize the amounts of gammas that hit the isotope target, especially to handle to high power density deposited in a small volume. The designed system allows to limit the energy deposition in the converter material so that water cooling is possible. The power dissipated in the isotope target remains limited to a few kW which can also be cooled down with water.

c) Radon trap system

Considering the properties of ^{226}Ra and its ^{222}Rn daughter, handling large quantities of Radium requires specific systems to ensure safety of operations. Between 1968 and 1973, SCK CEN was involved in the production of ^{227}Ac for space application (radioisotope power generation).

This project involved the irradiation of large quantities (tens of grams) of 226Ra in the BR2 reactor. Back then, SCK CEN had designed a Radon trapping system to safely manipulate the decay nuclides of Radium. Today, SCK CEN has developed a new Radon trapping system, much more compact, that will be connected to the ventilation system of all the hotcells where radon is expected to be trapped. This will guarantee safety and ensure operation continuity.

d) Radiochemistry system

Radium scarcity is at the center of all initiatives to produce of 225Ac via medium-energy cyclotrons or via the gamma route. Consequently, it is crucial that the production process is extremely efficient and prevents any Radium losses during the manipulation steps. Moreover, the cost of contaminated Radium waste treatment is prohibitive. Therefore, the overall process efficiency has been set to 99.9% per cycle which will guarantee the long-term operations of the center.

Results & Discussion

The commercial production facility aims at producing, with an electron beam accelerator, large quantities of purified ^{225}Ac enabling commercial distribution. The process described should lead to the cumulated production of more than 100Ci of ^{225}Ac per year and per accelerator. Several production lines could be added to supply a growing demand.

Conclusions

As clinical trials are progressing, the demand for ^{225}Ac is continuously increasing. It has been estimated that the worldwide demand could easily reach several hundreds of Ci per year as soon as the first commercial products reach the market (around 2026). It is essential that the radioisotope supply community provides confidence to the pharmaceutical companies that a high-quantity, high-quality and reliable ^{225}Ac supply chain will be achieved. Pantera is a clear illustration of the commitment to make this supply chain a reality.

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