Networks for Innovation in Nuclear Applications

Magazine 2019

Containing the results of the Networks for Nuclear Innovation projects during the World Nuclear University School on Radiation Technologies
The articles in this magazine were prepared during the WNU School on Radiation Technology 2019 by participants in the programme. Unless expressly stated otherwise, the findings, interpretations, views, and conclusions expressed in this book are those of the authors, and do not necessarily represent the views of the World Nuclear Association, World Nuclear University or any of the companies with which the participants are affiliated.
From World Nuclear University President

Radiation technologies are tangibly linked with the attainment of several UN Sustainable Development Goals, and are used to build a healthier and safer world. They have widespread beneficial impacts on a diverse range of fields, including agriculture, cultural heritage, medicine, and industry. This is well-demonstrated in the variety of topics explored in the NINA projects in this magazine: considering radionuclides with potential theranostic applications for patients with prostate cancer; investigating the current and future suppliers of Ac-225; developing a business plan for a food irradiation facility.

These projects represent the bright future of the fields of radiation technologies and radioisotope production, from the development and delivery of emerging technologies to ensuring the availability of existing technologies. The global nature of the issues addressed in these projects illustrates the need for effective international collaboration in the provision of such technologies. The authors of these reports now belong to a vibrant international network of professionals in the radiation technologies area, and I anticipate that they will carry the ideas generated in their NINA projects back to their respective 20 countries. I am excited to share the work completed by the Fellows, and fully believe in their future successes.

Agneta Rising
President, World Nuclear University

Acknowledgements

The Networks for Innovation in Nuclear Applications module of the WNU School on Radiation Technologies 2019 presented Fellows with timely and important topics in their professional areas. The quality of the information exchange and the subsequent reports produced was remarkable, and I would like to congratulate the Fellows on their accomplishments in their NINA projects. I would like to thank them for their enthusiasm, dedication, and impactful work which ensured the success of the module and the programme.

I would like to thank Rosatom for their collaboration in realizing the School on Radiation Technologies 2019. Their hard work and hospitality, as well as their fantastic resources and infrastructure, was greatly appreciated. I would also like to extend thanks to IAEA for their generous support of the programme.

I would like to acknowledge the dedication of the Mentors, and their valuable guidance and observations, for which WNU is extremely grateful. I would like to thank the NINA Magazine Editor, Sarah Cullen, for ensuring that the articles were correct and properly presented for their publication. The digital version of the NINA magazine can be found at world-nuclear-university.org.

I know that the articles in this magazine will be of immense interest and inspiration to anyone with any interest in radiation technologies or radioisotope production.

Patricia Wieland
Head, World Nuclear University
Foreword

The World Nuclear University is a worldwide network of nuclear education and research institutions, created in 2003. Since 2010, WNU has run a serial programme called the School on Radiation Technologies focused on developing leadership and communication skills, as well as knowledge and networks, for professionals in the fields of radiation technologies and radioisotope production. In 2019, WNU welcomed 28 Fellows from 20 countries to the School on Radiation Technologies in Obninsk, Russia. For the first time, an accompanying text (Advanced Radiation Technology 1st Edition) to the course was available, providing an authoritative overview of various radiation technology applications.

The aim of the Network for Innovation in Nuclear Applications (NINA) is for groups of Fellows to investigate and present an innovative approach to important global topics regarding radioisotopes and radiation technologies, guided by a mentor. The topics were chosen due to their significance in the future of the industry and their practical importance. They relate to the areas of radiopharmaceuticals, radioisotope production, and food irradiation.

Participants in the School on Radiation Technologies are selected in part due to their drive, expertise and enthusiasm in their professional fields. The diverse backgrounds and profiles of these exceptional participants contributed to the exchange of vanguard ideas and information, and the development of serious, innovative proposals.

The groups made presentations on their results, and compiled their work into articles. This magazine consists of these articles. They build upon existing research and discussions, and we expect that their publication will be of interest to anyone with a connection to these broad areas, and will spark further innovative ideas.

We hope that the reader will find value in the content of this magazine, and will enjoy reading it.

Sarah Cullen
Training Manager, World Nuclear University
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A Study of the Current and Potential Suppliers of Actinium-225 for Targeted Alpha Therapy

Quest for “The Rarest Drug on Earth”

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Abstract
Targeted Alpha Therapy (TAT) is one of the most important treatments for cancer cells. Ac-225 based radiotracers have shown very promising results over the last decades in this treatment. The positive results of Ac-225 radiopharmaceuticals for the treatment of brain tumors, neuroendocrine tumors, melanoma and prostate cancer has led to a demand for more production of Ac-225.

Currently, problems in the treatment of cancer using Ac-225 radiopharmaceuticals are the high price and significant gaps between demand and supply. The increasing demand for Ac-225 and the major production routes were discussed to produce a solution to the current problems. The advantages and disadvantages of each of the production methods are presented, as well as Ac-225 supply forecasts.

Medium energy proton accelerators remain the most promising option due to being the most cost effective, also ensuring a decentralized approach, as numerous facilities exist around the world. The scaled-up production of Ac-225 in commercial quantities is theoretically and technically feasible in many countries. The most promising in this regard are Canada, France and South Africa.

Introduction
With advancements in medical imaging, it is easier to detect and subsequently treat smaller tumours efficiently than it was many years ago. The use of beta emitters and gamma rays would lead to unnecessary irradiation of normal cells through entrance and exit doses. There is a need to find a way of delivering the dose to focus primarily on the target, minimizing normal tissue damage.

Furthermore, prostate cancer is the most common malignancy in men in the US, with an estimated 241,740 cases diagnosed in the US in 2012 [1]. Worldwide, 80,000 patients die from prostate-cancer each year. Focal therapy encompasses an approach to improve the therapeutic ratio by maximizing tumor control while minimizing side effects. The targeted treatment strategy has the potential to reduce the chance of injury to adjacent organs and resultant side effects while maintaining excellent oncologic outcomes.

Targeted peptide receptor alpha therapy (TAT) with Ac-225 has to date been clinically tested for treatment of brain tumors, neuroendocrine tumors, melanoma and prostate cancer. The treatment of cancer cells by the application of Ac-225 based radiotracers has shown promising results over the last decade. Ac-225 is a high-energy alpha-emitting radioisotope with therapeutic applications for the
treatment of certain cancers [3]. Alpha particle-emitting isotopes are being investigated in radio-immunotherapeutic applications because of their ability to selectively affect the cancer cells while minimizing the damage to normal tissues.

Currently there is an inadequate supply of this life-saving isotope, which is why Ac-225 has earned the title of “the rarest drug on earth”.

**Decay Characteristics of Actinium-225**

Ac-225 is a silvery radioactive metallic element. Actinium was derived from the Greek word aktis or aktinos, meaning ray or beam [2]. The element was discovered by Debierne in year 1899 and Giesel in 1902 [3]. Ac-225 is a radioactive element with a half-life of 9.9 days emitting alpha particles. It decays first into Francium-221, then successively in Astatine-217, Bismuth-213, Thallium-209 and Lead-209 before leading to the stable Bismuth-209 (FIG. 1).

![Decay scheme of Ac-225](image)

**FIG. 1: Decay scheme of Ac-225**

Ac-225 generates four alpha particle isotopes in a short decay chain to stable Bi-209, and as such, can be described as an alpha-particle nano-generator. The key properties of the alpha particles generated by Ac-225 are the following:

i) limited range in tissue of a few cell diameters,  
ii) high linear energy transfer leading to dense radiation damage along each alpha track,  
iii) a 10-day half-life, and  
iv) 4 alpha particles emitted per decay.

**Production Methods for Actinium-225**

**Radiochemical Extraction from Th-229**

Currently the production of Ac-225 is achieved by milking the decay product of stockpiled U-233. This stockpile of enriched U-233 was initially separated for the weapons program. The majority of U-233 was produced between 1954 and 1970 via neutron irradiation of Th-232.

FIG. 2 shows the decay scheme and production pathways for Ac-225. Since 1995, the decayed Th-232 has been chemically extracted [4].
The key advantage of this production method is that the final product is a pure Ac-225 free of other actinium isotopes. However, as discussed in Section 5, the total current production from this method is insufficient to meet the current global demand. As the use of Ac-225 is more widely adopted in the world for targeted alpha therapy, the current supply will become even more inadequate.

**Production Using High Energy Protons - Th-232 (p,xn) Ac-225**

High power cyclotrons with proton energies >65 MeV can be used to produce Ac-225. Examples of such facilities where this method can be used are TRIUMF, BNL, INR, Arronax, LANL and iThemba Labs. However, irradiation of Thorium targets with high-energy protons can result in the production of a number of isotopes including fissile isotopes such as Pu-239 and U-235, which can cause challenges in radiochemical separation. Another isotope that is produced through this method is the beta-emitting Ac-227 (T1/2 = 22 y) with 0.3% yield, which cannot be chemically separated from Ac-225. One option to produce pure Ac-225 using this method is to first separate the Ra-225 which is produced with a yield of 10 to 15% of the produced activity of Ac-225. Isotopically pure Ac-225 can then be obtained through elution [4]. The disadvantage of using the separation of Ra-225 is that it produces lower yields of Ac-225, but nonetheless, the final pure Ac-225 is suitable for radiopharmaceutical production.
Medium Energy Proton Acceleration - Ra-226 (p,2n) Ac-225

Another method producing Ac-225 is through irradiation of Ra-226 targets using medium energy proton accelerators. The production can be performed with high yields in a cost-effective manner in cyclotrons at proton energies around 20 MeV. This method of producing Ac-225 is regarded as the most promising process for large-scale production of Ac-225. The reported maximum cross-section for this nuclear reaction is 7.1x10^2 mb at 16.8 MeV proton energy [4]. A list of existing cyclotrons around the world that can potentially produce Ac-225 is provided in Table 1. The method produces pure Ac-225 that is free of other long-lived actinium isotopes such as Ac-227 (T1/2 = 22 y). Production of other short-lived isotopes such as Ac-226 (T1/2 = 29 h) and Ac-224 (T1/2 = 2.9 h) can occur but through selecting appropriate energy of incoming proton, the production of these isotopes can be minimized.

The main challenge in the production of Ac-225 using Ra-226 is that the process of target manufacturing is a complex one involving handling of highly radioactive materials. Furthermore, the daughter of Ra-226 is Radon, an inert radioactive gas. Currently, no facility is making Ra-226 targets.

Ac-225 Production Using Electron Accelerators - Ra-226 (γ,n) Ra-225

One option for producing Ac-225 is though the Ra-226 (γ,n) Ra-225 reaction. This method has been experimentally explored using old radium needles on electron linear accelerators. The method has the advantage of producing pure Ac-225 without coproduction of other Actinium isotopes. This method of production has a low yield of Ac-225. It is important to note, that while many medical linear accelerator facilities are capable of producing Ac-225, these facilities are primarily used for patient care and are not currently equipped with the infrastructure required for safe large-scale isotope production and processing. As mentioned above, similar challenges exist with respect to the Ra-226 target manufacturing.

Reactor Based Production of Ac-225

Reactor production of Ac-225 can be done through the Ra-226 (n,2n) Ra-225 reaction. The reaction requires high-energy neutrons (>6.4 MeV) found only near the tail end of the neutron spectrum in typical fast breeder reactors. Not only is this method of production expected to give a low yield of Ac-225, also due to the presence of higher probability of lower energy neutrons, there is a high likelihood of coproduction of longer lived Ac-227. Another reactor-based reaction, Th-228 (n, γ) Th-229, can produce Ac-225 parent product, however, this reaction is impractical due to low yields of Th-229 and coproduction of unwanted radioisotopes.

Clinical Experience with Actinium-225 in Targeted Alpha Therapy

Alpha emitting radionuclides Ac-225 may be more effective than beta-emitting radionuclides, due to higher rates of double-strand DNA breaks in prostate cancer cells, with less tissue penetration and minimal bystander effects in PSMA-negative cells. Beta particles have low linear energy transfer (LET) and energies between 0.05 -2.3 MeV which is suitable for large tumors; while alpha particles have high energy (5-9 MeV) and high LET which is suitable for specific targeting and killing of individual malignant cells, minimizing the toxicity to surrounding healthy tissue.

Thirty eight patients with neuroendocrine tumors and 200 patients with prostate cancer have been treated with Ac-225-DOTATOC and Ac-225-PSMA-617. For all aforementioned radiopharmaceuticals the beta-emitting counterparts based on Y-90 or Lu-177 are also available. Alpha-therapies consistently demonstrate a gradual and clinically valuable improvement of response rates (radiological and tumor markers). The prostate cancer cells express the prostate-specific membrane antigen (PSMA) on its surface. Higher level of PSMA expression is found in metastatic and castration-resistant forms of prostate cancer. PSMA has been targeted for imaging and therapy of prostate cancer. The earlier experience with PSMA-based radio-ligand therapy (RLT) was with the use of Lu-177, a beta emitter. The effectiveness of Lu-177-PSMA RLT has been shown in several
studies with tolerable side effects. However, up to about 30% of patients will not respond to Lu-177-PSMA RLT. A remarkable therapeutic efficacy has been demonstrated in heavily pre-treated metastatic castration-resistant prostate cancer (mCRPC) patients. Despite several new agents having been approved in the last several years, metastatic castration resistant prostate cancer (mCRPC) is still a major medical challenge. The beta-emitter Lu-177-PSMA RLT is applied under compassionate use in several countries but its antitumor effect can decrease over time. Preliminary data exists on the treatment with Ac-225-PSMA (Ac-225-PSMA) as an alpha-emitter.

PSMA-Ac-225 RLT resulted in remarkable clinical, biochemical and radiological responses in end-stage mCRPC pts, and may be considered a promising therapy for this type of cancer.

The Economics of Actinium-225

The current price of Ac-225 and the significant gap between demand and supply limits the widespread use of Ac-225 in targeted alpha therapy. Attention must be given to address these challenges. The assumption is that if the production of Ac-225 increases to same level with other targeted therapy radioisotopes, its price drops and Ac-225 can be more attractive in radiotherapy as indicated in Figure 3.

![FIG. 3: demand vs price chart](image)

Based on a discussion with an expert from the industry, it is discovered that 200mCi (7.4GBq) Targeted Beta Therapy Lu-177 costs USD 3,000 while that of targeted 10 MBq alpha therapy Ac-225 costs USD 8,000 in India. In comparison, Actinium is almost 3 times higher than Lutetium. Currently the total annual production is 63 GBq (see Section 5) versus the predicted need of 1,850 GBq per drug i.e., production is 30 times less than the need. If the production is increased to around 30 times more there would be a drastic decrease of the Ac-225 prices thus making it more attractive than other radioisotopes and the demand is likely to increase. There is a potential for increase in the demand for Ac-225 by several factors as there are several bio-molecules currently under clinical investigation.

Current and Potential Production of Actinium-225

While the majority of medical isotopes today are sourced from nuclear reactors, the potential for reactor-based Ac-225 production is limited. Currently there are three main producers of Ac-225, worldwide which delivered a total amount of 63 GBq produced from Th-229 through decay of U-233 stockpiles. It is important to mention that there are no specific reports mentioning the total production of Ac-225, but the total amount of Ac-225 can be calculated from the information available regarding the quantities of Th-229 currently available:

- 5.55 GBq, is obtained from Russia U-233 stockpiles exists at the Leipunskii Institute for Physics and Power Engineering (IPPE)Russia in Obninsk;
- ∼5.55 GBq, is obtained at Oak Ridge National Laboratory (ORNL, Oak Ridge, TN);
- 1.7 GBq transferred to the Institute for Transuranium Elements (ITU, Karlsruhe, Germany); [4]
Th-229 decays by alpha emissions with a half-life of 7917 years to Ra-225 with half-life of 14 days, and then to Ac-225 with a half-life 10 day. However, at every three months you get roughly the same amount of Ac-225 as Th-229 existed available. The milking process of Ac-225 is shown in Figure 4.

In conclusion it can be estimated that these three sources serve as generators of Ac-225 and its parent Ra-225 \((t_{1/2} = 14.9 \text{ d})\) and act as the major Ac-225 sources worldwide, producing approximately 63 GBq.

**Potential future sources of Ac-225**

The production of Ac-225 in commercial quantities is theoretically and technically feasible, thereby potentially reducing outdated therapies and displacing the need for expensive importation of Ac-225 from the three producers worldwide (USA, Germany and Russia) in the years ahead.

Scaled up production of Ac-225 could be achieved either by the use of a high and medium energy proton cyclotrons and linear accelerator.

Regarding potential for Ac-225 production via high-energy proton spallation of thorium, only a few existing accelerators can produce proton beams with a current and energy sufficient for large-scale Ac-225 production. The nuclear reaction of 226Ra (p,2n) turns out to be favourable for the direct cyclotron production of Ac-225 irradiation of the target Ra-226 with medium-energy protons being a very promising direction for the production of Ac-225 due to its large cross-section and the presence of hundreds of suitable cyclotron installations around the world. This method was first experimentally investigated at JRC Karlsruhe more than 15 years ago.

The IAEA estimates that there are currently a few kg of Ra-226 in the form of radium brachytherapy needles in the world. [5] In many countries, there are special programs to safely store these sources, and their treatment in Ra-226 production purposes can be very useful. These reserves could potentially be used as target in than 100 cyclotrons.

There are several countries able to apply these technologies, and already have installed necessary capacities. A list of some of these facilities is given in Table 1 along with estimates of the maximum amount of Ac-225 each could produce per month. [4], [6].
Many countries have medium energy cyclotron facilities suitable for production of Ac-225. As can be seen in Figure 6, the current production of Ac-225 is concentrated in the upper part of the map (Russia, USA, Germany). To ensure the normal provision of radiopharmaceuticals to all countries, it is necessary to establish the production of Ac-225 in Australia, Africa, South America, Europe and Central Asia. The most promising in this regard are Canada, France and South Africa.
Discussion and Concluding Remarks

The advancement in medical imaging, diagnosis and treatment of tumours at early stage requires ways of delivering the dose to volumes of tumours with minimal damage to the surrounding healthy tissues. Ac-225 is known to emit high-energy alpha particles of 5800 keV with short half-life ($t_{1/2} = 9.92$ days), high LET, short range of few cells in diameter and hence suitable for TAT. TAT with Ac-225 has been clinically tested and proven through numerous trials to be fit for the treatment of brain tumours, neuroendocrine tumours, melanoma and prostate cancer.

Several production methods exist for Ac-225 such as the radiochemical extraction from Th-229, high energy proton acceleration of Th-232 (p,xn) Ac-225, low energy proton acceleration of Ra-226 (p,2n) Ac-225, electron accelerators of Ra-226 ($\gamma$,n) Ra-225, and the reactor based method through Ra-226 (n,2n) Ra-225.

The current Ac-225 high prices are as a result of low production (63 GBq against estimated need of 1850 GBq) by only three producers worldwide (USA: ORNL, Germany: ITU and Russia: Obninsk). In comparison to the prices of Lu-177, the Ac-225 prices are 3 times higher. Increased production of Ac-225 would mean a likely drop in the prices, which would need to be balanced with the expected increase in demand of Ac-225 as TAT becomes more common.

The production of Ac-225 in commercial quantities is theoretically and technically feasible using scaled up production by establishing Ac-225 production in Australia, Africa, South America, Europe and Central Asia. The most promising in this regard are Canada, France and South Africa.

There is need for different governments and capable private entities to cooperate and ensure adequate production, low price and sustainable supply of Ac-225 radiopharmaceuticals. The high-energy accelerators need to scale up production to increase capacity. In addition, regional production units need to be initiated using the medium energy cyclotrons (accelerators) to ensure that the current demand is met.

However, some limitations are to be considered. More research is needed in the possibility of producing Ra-226 targets that can facilitate the production of Ac-225 as well as addressing the
challenges that exist with Ra-226 target production due to its high radioactivity. Additionally, further studies should be continued to investigate ways to make Ac-225 more attractive economically.

References

[5] IAEA, Conditioning and interim storage of spent radium sources
Installing a Food Irradiation Facility in Mexico: A Smart Business Plan

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Abstract
In a globalized world with increasing demands for food safety and security, food irradiation technology offers powerful solutions against foodborne diseases, waste and malnutrition. In this study, a business plan was proposed for the installation of a 5-10 MeV electron beam accelerator-based irradiation facility in the province of Jalisco, Mexico – a strategic region of fast growth in the fruit and vegetable production sector. A feasibility study was conducted through assessments of factors such as infrastructure, logistics, licensing and legislation, radiation safety, public outreach, marketing strategy, timeline and cost estimation. Based on the study results, the proposed plan represents a secure and promising investment, which may also serve as encouragement for technological innovation due to the projected partnerships with research institutes and universities. PIÑATA (Project for Irradiation as a New Accelerator Technology in Agriculture) represents an innovative approach to food irradiation services, by combining the ideals of financial success, social impact and respect for the environment – in consonance with sustainable development goals.

Introduction
Nuclear technologies are intrinsic to modern and daily life, contributing to continuous societal development through their applications on energy, health, agriculture and industrial fields. As populations grow and globalization presents itself as the new economic order, food safety and availability become a major concern for consumers and nations [1], [2].

In that context, food irradiation represents a powerful tool which not only facilitates worldwide trade but also helps prevent food shortage, food waste and related diseases. Because of the population growth the demand for food is expected to increase by 60 % by 2050. According to the World Health Organization over 420,000 people die annually due to foodborne disease (where children under 5 years of age represent 30% of that figure) [3] while Global Food Supply indicates that nearly one-third of the worldwide food production for human consumption (over 1.3 mega tons) is lost or wasted yearly [4].

As one of the few additive food treatment techniques able to maintain the nutritional and sensorial attributes of products, food irradiation technologies allow slow ripening, control spoilage and pathogenic microorganisms and prevent the spread of invasive insect pests – therefore promoting extended shelf life. And because these techniques can be applied to packaged products, chances of re-contamination are minimal [5].
Global irradiation market overview and trends

Increasing consumer acceptance of irradiated food products as well as awareness related to foodborne diseases are expected to boost the market in the next decade as estimated by Figure 1 [6][7]. But such industrial food irradiation facilities should be operated in a safe environment for workers, clients and the public. Towards this there must be licensed, regulated and inspected in terms of good manufacturing practices, quality control, radiation protection and security.

The global food irradiation market was valued at US$ 199.98 million in 2017 and is projected to exhibit a Compound Annual Growth Rate (CAGR) of 4.9% over the forecast period by 2026 [8].

Radiation processing methods account for 26% of the total sterilization market (2016), and by 2030 the market will grow to 37% [9] due to the abandonment of a number of chemical and gas processing methods. The growth rate of radiation technology will be 5% in average.

The gamma radiation segment occupied a significant market share in the global food irradiator market in 2017-2018. Though, as for the further development of the gamma technology, the market for gamma has entered a phase of maturity, while the highest growth rates are expected for electron and x-ray accelerators. The growing rates are expected to reach 11% annually, also due to the replacement of the gas sterilization methods.

North America is expected to account for significant market share of 56% in the global food irradiation market. Today, 40% of all irradiating facilities are located in the USA, the second place occupies China with 16%.

Over 40 countries allow irradiation of over 50 food types. It is estimated that over 450 kilotons are irradiated annually. In addition to the US, other countries using irradiated food include Japan,
Canada, France, Belgium, the Netherlands, Portugal, Israel, Thailand, Russia, China, South Africa and Brazil.

There are several approaches that are focused on elimination of microorganisms or extending of products' shelf-life. Among such processes, various irradiation techniques are prevalent that apply ionizing energy (radiation) depending on the effect required.

Apart from providing safe food for the local consumption, irradiated food also offers the possibility of export.

Food irradiation for export purposes

The key market drivers for exportation purposes are the following: a strong need for logistic efficiency, a strict requirement of pesticides or antibiotics appliance, and limitations of alternative solutions such as gas, steam or chemical treatment. In this context irradiation offers a big advantage.

In fact, veterinary and phytosanitary authorities from 69 countries have already joined the agreement on the safety of processing products with accelerated electrons.

In addition, the increased shelf life allows better logistics and distribution. Further, in many states, some products are banned from import without prior processing to ensure food safety. For example, it is forbidden to import unprocessed tropical fruits into the United States. Food irradiation improves the quality and safety of products and facilitates exports into such countries [10].

Key competitive advantages of food irradiation

In comparison with other types of food processing, food irradiation provides several competitor advantages for the food producer, such as:

- The key indicators on customers is economic viability: with an increase in the cost of raw materials by 3%, producer income increases by 7-10%.
- Irradiation is an efficient way to reduce losses caused by spoilage, bacteria and etc. due to shelf-life increasing and disinfection.
- The producers can reduce costs that are dedicated to efficiency of storage costs and energy supply for this storage, and efficient logistic.
- Food irradiation enables to meet international phytosanitary requirements in terms of pesticides or antibiotic use.

The key products with significant perspectives for exportations are the following. See Table 1.

<table>
<thead>
<tr>
<th>Product</th>
<th>Value USD per kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berries</td>
<td>3.5</td>
</tr>
<tr>
<td>Coffee</td>
<td>3</td>
</tr>
<tr>
<td>Tea</td>
<td>12</td>
</tr>
<tr>
<td>Chilli</td>
<td>6</td>
</tr>
<tr>
<td>Seafood</td>
<td>6.8</td>
</tr>
</tbody>
</table>

The objective of this study is to propose a business plan to install a food irradiation processing facility in a suitable location.

In this context, Mexico was considered to be an ideal location being currently the seventh largest producer of fruits and vegetables in the world with a total of 32 mega tons per year, with a solid growth rate.

Market analysis

Mexico is today one of the most dynamic fruit and vegetables producers/ exporters with an approach of productivity, competitiveness and sustainability. The existence of a network of 12 free
trade agreements with 46 countries and a potential market of approximately 1.5 billion people stimulate the search for new opportunities and better conditions for the sale of products of Mexico's agricultural, livestock and fishery origin in the International markets. For the fourth consecutive year (2018), the Agricultural and Agroindustrial Trade Balance presented a surplus of 5.8 billion dollars, being the largest positive balance in over 2 decades. Mexico’s 2018 balance increased in 10.9% (570 million dollars) from the previous year due to the increase in exports by 5.6% (1.8 billion dollars). For 2018, the value of Mexican agri-food exports was the highest reported in 26 years [12].

![Evolution of Mexican food exports (1993 - 2018)](image)

**FIG 3: Mexican food export values in the last 25 years [12]**

The dynamics presented by exports of agrifood goods and the level reached allowed the country to obtain currencies that exceed those achieved by sale of petroleum products in 3.6 billion dollars (12.0%) and foreign tourism in 11.7 billion dollars (52.2%), for instance. It is notable that 67.7% of the total currency for foreign sales of agri-food products of Mexican origin correspond to the top 20 products of commercial value. [13]

Since 2007, Mexico has been exporting irradiated foods such as mango, orange, grapefruit, tangerine, sweet lime, guava, manzano pepper, carambola or star fruit, pomegranate, fig and red pitaya to USA through an agreement. It is notable that in 2017, 17 kilotons of irradiated fruits were exported – a sharp increase in comparison to 265 ton of guavas exported in 2008.

There is still an unexploited large potential for food irradiation and exportation.

Among the various Mexican regions, Central-West generates the highest production volume, with 84.2 mega tons. This region comprising of Jalisco, Durango, Coahuila, Veracruz, Puebla and Guanajuato states present an annual production volume greater than 1.2 mega tons. An annual production growth of 2.6% is expected in this region by the end of 2019. In addition, the expectation of livestock production is 22.3 mega tons – 2.6% increase from 2018. The estimate of fisheries production points to 2 giga tons and sardine stands out in terms of production volume. In addition, Jalisco has established itself as the main food producer in the country due to the improvement of quality management systems in agriculture, livestock, fisheries and aquaculture. It's impressive to note that an area of 1 million 675 thousand hectares, which produces 106 mega tons, with a value of 57 billion Mexican pesos (MXN) and more than 100 different agricultural crops planted in this state.

The municipality of Zapotlán el Grande (situated in the province of Jalisco) leads the agro-industrial production and it is located 170 km from Manzanillo – one of the most important seaports in Mexico as shown in Figure 4. This strategic location has enabled trade with Japan, South Korea, China, Singapore and Malaysia, while recent markets the Arab Emirates, Qatar, Dubai, Saudi Arabia and Kuwait [14].
Based on the discussions above, the Jalisco region was chosen for the installation of the irradiation facility. The two most common options for food irradiation are Co-60 gamma source and e-beam accelerator as irradiation facilities. The advantages and disadvantages are given in Table 2.

Table 2: Comparison between Co-60 gamma source and e-beam accelerator as irradiation facilities

<table>
<thead>
<tr>
<th>Source</th>
<th>Co-60 gamma source</th>
<th>e-beam accelerator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensing</td>
<td>Higher requirements for licensing</td>
<td>Less requirements for licensing</td>
</tr>
<tr>
<td>Operation costs</td>
<td>Medium</td>
<td>Higher</td>
</tr>
<tr>
<td>Operation &amp; Maintenance</td>
<td>Less specialized</td>
<td>More specialized</td>
</tr>
<tr>
<td>Human Recourses</td>
<td>Less specialized stuff</td>
<td>Higher specialized stuff</td>
</tr>
<tr>
<td>Security infrastructure</td>
<td>Higher requirements</td>
<td>Lower requirements</td>
</tr>
<tr>
<td>Waste Disposal</td>
<td>Requires</td>
<td>No need</td>
</tr>
<tr>
<td>Electricity</td>
<td>No permanent electricity supply required</td>
<td>Reliable supply required</td>
</tr>
<tr>
<td>Price</td>
<td>Lower</td>
<td>Higher</td>
</tr>
</tbody>
</table>

Based on efficiency, cost safety aspects and considering the variety of foodstuff to be treated, the e-beam accelerator with capacity between 5 and 10 MeV was considered the best choice for this business endeavor.

It was recognized that such a facility has multiple factors that need to be addressed in terms of resources, services, infrastructure, safety aspects, regulatory aspects, business strategy and implementation timelines, costs and stakeholder engagement.

**Infrastructure, resources and services**

In order to install the proposed food irradiation facility, the following resources and services must be acquired and implemented [15]:

---

**World Nuclear University School on Radiation Technologies 2019**
— Physical building: The location of the building will be easy to access for farmers and business partners. The building will have all the features for a production environment and should be easily accessible for delivery of building material and equipment.
— Type of equipment: 2 EBM (4.5 -10 MeV)
— Bought-in mechanical and electrical installation: Motor Control Center (MCC), pricing require input from an in-house electrical engineer (PCs, PLCs, DCS and supervisory Computers).
— They will be done by Installers, the pipe work, bracketry, supports with additional skilled labor required to fix and mechanical commissioning the mechanical bought-in items.
— Software and instrumentation: This will be provided by in-house, by a combination of MCC suppliers or installation contractor, or a specialist can be used to install and commission instruments, program PLCs and setup supervisory control and data acquisition (SCADA), Distributed Control Systems (DCS) and Remote telemetry and such systems.
— Design consultants: Process design engineers will be used at a cost of $250 per hour
— Project programming: Professional engineer produce a schedule or program of events that set out the time scale (section 4) for the key elements of the design- construction-commissioning phases and allocates resources against each of the tasks required. This will confirm the pricing of those items whose cost are based on entirely on their duration of use (e.g. hired trailers, mobile cranes, etc). The schedule highlights hours which will be required by each discipline. This may be in-house or external resources.
— Man-hours estimation: The proposal engineers will have produced their estimates of how many hours of each discipline will be required to do the job, but the discipline managers within a company will also want to give their estimates of how long it will take to complete their projects. Since the discipline managers are the ones who have to deliver the project, and the proposals engineer for winning the work, discipline manager estimates tend to be high side and proposal engineer’s on the lower side. There should be negotiations from both sides.
— Pricing risk: Once the price for all the goods and services required to install until to operate the plant, assured is required that the allocated money is available for the chances of process, financial, legal, and political or other risks that are going against the company. Might need to buy Insurance known as Performance bond until the project is complete.
— Margins: Margins vary greatly from Industry to Industry (Civil and Building).
— Infrastructure implementation requires several assessments:
  • Load bearing capacity of the facility: It is important that the site will have the capacity to bear the heavy load of shielding; this will need to be ensured by engaging appropriate specialists.
  • Compliance with all the regulatory requirements, such as [16][17]:
    o To be at an appropriate distance from residential area
    o compliance with General Law of Ecological Balance and Environmental Protection Association (LGEEPA) standards; with Clean Air Act; Hazardous Air Pollutants law; Mexican General Ecology Law; Resources Conservation and Recovery Act; CICOPLAFEST (Inter-secretarial Commission for the Control of Pesticide, Fertilizers and Toxic substances);
    o Compliance with Mexico’s Industrials health and Safety Regulations
    o Compliance with the laws of Secretariat of Labor and Social Welfare
  • Activity analysis:
    o Description of the process activities which will include anticipated production rate and costs. Figure 7
    o Assessment of risks and Hazards- Microbial, Cross-contamination, Radiation, Product mix-up and manual handling.
  • User Requirements Specification:
    o The construction costs will be outlined in Figure 7
    o Ensure facility requirements will be met.
    o Ensure cost comparison between bidders’ proposal are valid;
Ensure a high degree of price certainty;
- Environmental Performance standards are met.
- Air handling requirements are met.
- Finishes of clean rooms envelopes fixtures are met.
- Individual items of equipment per room are listed.
- Services power, data telecom, etc. are available and listed.
- Contractors design proposal refined accepted/ contracts sign off at fixed price.
- Functional Design Specification (FDS) developed
- Design Qualification specified;
- FDS refined, construction drawings accepted and signed off.

- GMP Standards Documents:
  - EU GMP, BSEN 14644; Health building Note: HBN 14-01;
  - HTM (Health Technical memorandum, e.g. HTM 03-01

- Initial Planning Considerations:
  - project team appointed;
  - Knowledge; skills and Experience identified at the planning stage (Engineers; architects, clean room designers; clean room builders; ventilation specialist, installation specialist).
  - Additional resources identified,
  - Foot print envelop – floor square meter, shape of the facility and structure already specified.
  - Project costs: include Facility, HVAC, equipment plus validation, professional fees, enabling works, backfilling, build-in services, relocation, cranes, trucks, personnel, etc.

- Public Participation Forum: In Mexico public participation to be held when ready to build is mandatory

**Legislation**

The irradiation facility will operate under Mexican legislation and according to required quality control and assurance, by complying with the following [18][19]:

- Regulations associated with installation, use of ionizing radiation generating devices - particle accelerators with energies equal to or greater than 10 MeV, in accordance with the General Regulation of Radiological Safety, and official standards corresponding Mexican.
- Official Mexican Standard NOM-022-FITO-1995, Establishing the characteristics and specifications for the notice of commencement of operation and certification.
- Technical standards and standards applicable to the plant.
- Ministry of Agriculture, Livestock and Rural Development.
- General Law of Ecological Balance and Environmental Protection in Environmental Impact
- Regulation during the development such as NOM-001-STPS-2008 Buildings, premises and facilities
- Regulation in environmental matters on the measurement of concentrations in environmental matters such as Official Mexican Standard NOM-020-SSA1-1993, Environmental Health. Criteria for assessing the quality of ambient air, with respect to ozone (O3). Regulated value for the concentration of ozone (O3) in the ambient air, as a measure of protection of the population's health; and Official Mexican Standard NOM-156-SEMARNAT-2012, Establishment and operation of air quality monitoring systems.
- American Society of Testing Materials (ASTM) such as E2628 Standard Practice for Dosimetry in Radiation Processing; and F1640 Standard Guide for Packaging Materials for Foods to Be Irradiated.
Radiation safety

As required, the business plan foresees a structured radiation protection program, which will include a top level policy document supported by detailed and specific procedures and a comprehensive system of records. These components will consist on the following [20]:

— A policy document specifying objectives, responsibilities, training, safety assessment and quality management.
— Procedures covering operation (e.g. access control, start-up and shutdown procedures), individual monitoring, training, testing of radiation monitors, audits and safety assessments by a qualified expert, response to visible and audible alarms; incident reporting and investigation and emergency response.
— A system of records covering: documentation of authorization and any correspondence between the operating organization and the regulatory body; name of the authorized person responsible for the radiation protection program; safety assessment reports; operation logbook; routine checks of safety systems by a radiation protection officer; individual doses (current and prior work history); results of workplace monitoring; radiation monitor test reports; reports on investigations of incidents and accidents; audits and reviews of the radiation safety program (by a qualified expert); installation, maintenance and repair work; facility modifications and training provided (initial and refresher).

Licenses

The entire licencing process will be in accordance with national regulatory requirements and IAEA Safety Standards. The regulator will be notified if any changes in the original project occur in any stages of the construction phase.

The operation of the irradiator in accordance with regulatory requirements implies obtaining a licence from the regulatory body for the siting, design, construction, acquisition, storage and operation of the irradiator.

Our policy will be designed to meet the radiation safety objectives as: i) providing human and material resources necessary to ensure safe working conditions and compliance with regulatory requirements; ii) establish and maintain a radiation protection program focused on the protection of workers as provided in IAEA recommendations (which will ensure that doses received by workers and members of the public will be kept below the relevant dose limits specified in Basic Safety Standards [21])

Meeting specific safety requirements of the regulatory body pertaining to site selection and evaluation, construction, installation, operation, maintenance and decommissioning is also important. This will be achieved by:

— Using a qualified expert in radiation safety who is accredited according to criteria specified by the regulatory body and who is knowledgeable about the safe design of irradiation facilities.
— Ensuring that the following items are provided:
  • A detailed description of the design and operation of the safety systems, including control circuit diagrams.
  • Detailed operating procedures and maintenance procedures, including the type and frequency of checks of safety and control systems, routine monitoring and radiation surveys.
  • Safety assessments using formal methods of analysis appropriate to the level of risk associated with the facility. The operating organization should also carry out a safety assessment on the basis of information provided by the supplier and the operating organization’s own administrative rules.
  • Instructions and procedures to be followed in an emergency

According to IAEA recommendations we will ensure that information on both normal and abnormal operations significant to protection and safety is disseminated or made available, as appropriate, to the regulatory body and to manufacturers and/or suppliers, as specified by the
regulatory body. This information would cover, for example, maintenance data, descriptions of events, information regarding defects in materials and equipment, weaknesses in operating procedures and corrective actions. In addition, procedures of risk analysis in facilities and activities that involve the management of radioactive material will be in place.

Organization structure

The irradiation facility will have the structure presented on Figure 5 composing a staff of 30 people among managers, operators and assistants. It is noteworthy to mention the essential role of the radiation protection department in complying with the appropriate safety standard requirements for operations involving radiation sources. The business plan also will have a microbiology laboratory that will conduct further and innovative research and development studies in radiation processing of agricultural raw materials and food products. The lab will also be accountable for quality control in terms of product pollution and taxonomic composition of microorganisms belonging to the E. coli group; mesophilic aerobic and facultative anaerobic microorganisms; fungi and yeast; bactericidal and antioxidant environmental properties of plant products. It is finally important to point out the additional role of the marketing department in communicating the benefits of the use of irradiation technologies on food processing to clients (especially the small farmers) as a way to prevent misconceptions in terms of radiation and risks.

Public outreach

An extensive list of medical and scientific organizations supporting or supporting food irradiation should be widely used to convince retailers and the public of their broad support for food irradiation. Food Irradiation is already approved by the World Health Organization (WHO), Centres for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), United States Department of Agriculture (USDA), American Medical Association, and European Commission Scientific Committee on Food.

Thus, hundreds of credible groups support irradiation as the most efficient and safe way to ensure food safety, however a very limited number of groups are opposing this technology, relying on uncreditable outdated information. This brings risks to create unreasonable suspicion to the technology and do not let irradiation of food as a public health measure has not yet reached its full potential and achieved widespread consumer acceptance. Thus, efficient public outreach is required. Among the instruments that are efficient to be applied are:
— Conducting seminars on public acceptance of food irradiation for farmers;
— Conducting social media and mass media activities;
— Arrange tours to the facility.

What is also important is to ensure that the public outreach campaigns are developing as an ongoing process with long-term perspective.

**Cooperation opportunities**

**Domestic:**

To ensure efficient communication it is vital to build solid partnerships with stakeholders among local agro holdings, associations of producers or local authorities. For example: Association of Irradiated Fruit Packers (Asociacion de Empacadoras de Frutas Irradiadas de Mexico), Mexico’s Secretariat of Agriculture, Livestock, Rural Development, Fisheries and Food (SAGARPA), etc.

**International:**

- Membership in IIA (International Irradiation Association), FIPA (Food Irradiation Processing Alliance) will ensure continuous access to the most accurate and updated information on irradiation sector development.
- IAEA and FAO, World Health Organization (WHO).
- Potential investors: The World Bank Group, Economic and Trade Associations, APEC (Asia-Pacific Economic Cooperation)
- Educational organizations that can send students and young professionals for training courses, workshops and internships: World Nuclear University (WNU), The U.S. Particle Accelerator School (USPAS), Consejo Nacional de Ciencia y Tecnología (the National Council of Science and Technology) (abbreviated CONACYT)

**Marketing**

The target market for PINATA food irradiation facility is local farmers’ community and associations that are focusing on increasing exportations to foreign markets. Among the key clients are expected to be local small or medium producers that are uniting into associations or large agro holdings that are focusing of producing and exportation of such products as fresh fruits, berries, coffee and tea, seafood and vegetables.

**Competition**


Mexico has an experience in applying irradiation technologies. Apart from Industrial gamma irradiator (1980 – 1983, ININ) and semi-industrial gamma irradiator (1986) and E-Beam irradiator for sterilization of medical devices (2017), there are two facilities that provide services of food processing:
— Multipurpose gamma irradiator constructed by Sterigenics in 2000.
— Sterigenics is the only vertically integrated company on the market. It provide services for sterilization of various range of objects: food, agricultural products, medical products, polymers. Sterigenics, in addition to radiation technologies, actively uses the gas method. The company owns 49 product processing centres in 13 countries. The number of employees of Sterigenics is around 1.6 thousand people. The plant in Mexico is focused on product irradiation for the United States market.
— Multipurpose gamma irradiator and Phytosanitary control called Benebion that was built in 2011. Benebion was Mexico’s first irradiation facility devoted entirely to food, based in Matehuala,
San Luis Potosi and played essential role for ensuring entry of Mexican fruit exports to the US. Thus, it is not full covers exportations to European or Asian markets.

Taking into consideration that Benebion and Sterigenics facilities is focused on the US market, the location of the new e-beam irradiation plant in South-East of Mexico seems viable and efficient.

Advertising and promotion

Marketing communications

To ensure that the target market is aware of all competitive advantages that has food irradiation as well as information on new business opportunities for exportations, it is required to build direct communication with farmers.

Among the key instruments are:

— Providing the opportunity to bring samples of the products for trial processing to the facility. The microbiological information is to be provided for the product.
— Providing information in an interactive way on opportunities to be provided for their businesses: 10% increase in revenues [22].

Strategy and implementation timeline

The Implementation Timeline presented below on Figure 6 will be used to plan and track key milestones during the implementation process. Some items will occur in sequence, while others will occur concurrently. The template has been designed for alteration and site specific modifications. It may be added to, or subtracted from, as the implementation team requires so [23].

![Implementation timeline](image)

**FIG. 6: Implementation timeline - schedule of activities to be accomplished**

Costs and revenues

Assessments indicate that the cost of irradiating food could differ by up to 20 times. This wide range results from the many variables involved in any one irradiation operation. Among them are the dose of radiation employed (which can vary widely depending on the purpose of the treatment), the volume and type of product being irradiated, the type and efficiency of the radiation source, whether the facility handles one or a variety of food products, the cost of transporting food to and from the irradiator, special packaging of the food, and the cost of supplementary processing such as freezing or heating. [24].
Table 3 presents data on the per-unit costs for irradiation and methyl bromide treatments for selected crops. Although irradiation is more expensive than fumigating with methyl bromide, the cost of irradiation may be offset by its many benefits, including reduced damage to fruits and vegetables and an extended shelf life [25].

Table 3: Comparison of estimated post-harvest treatment costs for selected crops [26]

<table>
<thead>
<tr>
<th>Crop</th>
<th>Methyl Bromide (cents per pound)</th>
<th>Irradiation (cents per pound)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strawberries</td>
<td>1.56 to 1.66</td>
<td>4.43 to 14.34</td>
</tr>
<tr>
<td>Papaya</td>
<td>1.56 to 1.66</td>
<td>1.6 to 7.43</td>
</tr>
<tr>
<td>Mango</td>
<td>1.56 to 1.66</td>
<td>Data not available</td>
</tr>
</tbody>
</table>

Recalculated taking into account the Inflation rate of 77% (Jan 1993 – Dec 2018).

According to the statistics from private companies in the food irradiation field, it is reasonable to infer that the future complex should have the following properties:

- Capacity: 30 000 tons/year (up to 8 tons/hour);
- Equipment: 2 EBM (4.5 – 10 MEV);
- Capital expenditures – $ 15 million;
- The cost of the accelerator complex is about 30% ($ 5 million);
- Added value to irradiated food products – 3 - 5%;
- The return on investment –5 years;
- The tariff for electricity in the Mexico in 2019 – 8 cents/ kW-h.
- Average salary – $ 1500/month
- Average total economic effect: with an increase in the cost of raw materials by 3%, producer income increases by 7-10%.
- Annual income – $ 1 080 000
- Salary –540 000 $ (50%)
- Other (Electricity, consultancy, repair works, component parts) - 540 000 (50%)
- Annual working time of EBM – $ 4 160 h (5 days a week, 16 hours daily)
- Cost price for 1 hour EBM – 260 $
- Price for 1 hour EBM for clients – 980 $
- Price for kilo (average loading 4t/hour) – 0.25 $
- Price for kilo (maximum loading 8t/hour) – 0.125 $

**FIG. 7: Costs distribution for the proposed facility**

**Discussion and conclusion**

Based on the assessments conducted in the aspects of technology, marketing, safety, logistics, cost estimation and public awareness, the proposed business plan foresees great potential for
implementation. A strategic and successful e-beam food irradiation facility in the Latin American region will enable reliable products and services, thus representing a secure investment in a globalized economy. In addition, the proposed endeavour will enable the development of new technologies and approaches to food irradiation through enriching partnerships with universities and research institutions, thus stimulating innovation. PINATA represents an innovative approach to food irradiation services, by bringing together financial success, social impact and respect for the environment, all in harmony with sustainable development goals.

References


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Promising Options for Prostate Cancer Using Theranostic Radionuclides: Future Solution for an Old Problem

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Abstract
Prostate cancer continues to be the most common type of male cancer and has the fifth highest fatality rate of all cancers worldwide. Prostate cancer recurrence after primary treatment is marked by increasing Prostate Specific Antigen (PSA) levels in the blood. A radiopharmaceutical consisting of a radionuclide and a biological tracer can be used in the diagnosis and treatment of prostate cancer. Different biological tracers such as Choline, PSMA and FACBC have the advantage of being able to detect recurrence prostate cancer at very low PSA levels. PSMA is the superior tool with detection levels as low as PSA levels of 2 ng/ml. Radionuclides can be classified into two main groups: the first group comprises of diagnostic radionuclides such as $^{68}$Ga and $^{18}$F, and the second group therapeutic ones such as $^{177}$Lu and $^{225}$Ac. This article provides a summary on the importance of currently used radiotracers as an effective option for the development of the diagnosis and the treatment of the prostate cancer process, delivers key challenges for the availability and affordability of the radiotracers, and outlines new ideas which can be applied in the near future.

Introduction
Prostate cancer is one of the most common malignancies affecting men around the World, and the fifth leading cause of death worldwide [1, 2]. Based on GLOBOCAN 2018, the estimates are found to be around 1.2 million worldwide [2]. The five years survival rate of localized prostate cancer is satisfactory. However, the metastatic disease is associated with poor outcomes [3]. Cancer can be developed when there is an unbalance between mutated cells proliferation and inability of the body's immune system to keep them under check. Normally, prostate cancer has no clear symptoms until at a very advanced stage. Its common symptoms are: difficulty with urination, increased frequency of urination, nucturia, and the presence of blood in urine or semen. More advanced stage may appear with urinary retention and back pains, which strongly correlate with the site of bone metastases [2, 4]. The factors that increases prostate cancer risk at old age (>65 years of age) are ethnicity (African-American men), strong family history with prostate cancer, and high doses of vitamin E [2, 4]. Prostate cancer diagnosis can be done by Prostate-Specific Antigen test (PSA > 4 ng/ml), rectal examination, and trans-rectal ultrasound. In addition to the tissue biopsy which clearly proves if a patient has a true prostate cancer [2, 4].
Methodology

This article provides a review and analysis of the currently available and promising potential PET radiotracers for theranostic use in patients with prostate cancer, which will be helpful in decreasing the morbidity and mortality of patients with this life-threatening disease. In addition, it provides an innovative solution to the availability of the radiotracers from any potential hurdle of its market accessibility to the prostate cancer patients across a range of economic status. A literature survey was performed using electronic database, including Pubmed, Medline and Google Scholar. The Search keywords were the following: prostate cancer, prostate cancer treatment, prostate cancer prevalence/incidence, choline, FACBC, PSMA, $^{68}$Ga, $^{64}$Cu, $^{177}$Lu, $^{11}$C or $^{18}$F. PET radiotracers were then categorized into two groups that display their uses in diagnostic and therapeutic aspects. Finally, a review and analysis of currently available and promising potential PET radiotracers for theranostic in patients with prostate cancer was done regarding its potential use in clinical settings, associated risks, and the potential barriers to their uptake, including non-technical aspects.

Prostate Cancer

Background

The World Health Organisation (WHO) estimates that 75% of all prostate tumours are found in the peripheral zone, which is close to the rectum area, and can therefore be easily detected during the digital rectal examination and subsequent prostate biopsy procedure. Tumours which lie within the transitional and central zones, are difficult to detect using this procedure and are usually diagnosed using Prostate Specific Antigen (PSA) testing. Early detection is of utmost importance as studies show a direct correlation between stage of detection and survival rate. Tc-99m scans are also done mostly for the staging of the cancer. Advances in Magnetic Resonance Imaging (MRI) and CT scans have showed that these techniques revolutionize the diagnostic scene.

Prostate Cancer Staging & Treatment

There are five stages that a prostate cancer diagnosis can be classified under. These stages and their characteristics are as follows:

- **Stage 0**: No evidence of tumour in the prostate; PSA < 3 ng/ml [7];
- **Stage I**: Early stage development. Tumour cannot be felt through physical examinations. PSA levels are still fairly low <10 ng/ml [7];
- **Stage II A/B/C**: Tumour is localised within the prostate. PSA levels range from low ~10 ng/ml to medium<20 ng/ml with a risk of the cancer growing and spreading. Tumour is large enough to be felt during physical examination [7];
- **Stage III A/B/C**: The PSA level is high > 20 ng/ml. The cancer has spread ranging from beyond the outer layer of the prostate into nearby tissues to invading nearby organs [7].
- **Stage IV A/B**: Wide ranging metastasis i.e. lymph nodes, bones etc. with PSA levels > 30 ng/ml and sometimes as high as > 100 ng/ml with Gleason scores on the upper end of the range 8, 9 and 10 [7].

The treatment of prostate cancer depends on various factors such as aggressiveness of tumor (Gleasons score), stage of the cancer, PSA levels, and the patient age [4]. Early stage cancer, ranging from Stage 0 to Stage II, which is still confined to the prostate gland is predominantly diagnosed via the use of PSA blood tests and Digital Rectum Examination (DRE) tests and a subsequent biopsy. Should a PSA level above 20 be detected during the PSA test, this indicates a probable case of metastasis requiring the use of nuclear medicine or MRI for a more precise prognosis. A Gleason score towards the highest rating of 10 also indicates an aggressive type of cancer that will spread rapidly [4]. Patient with this high-risk prostate cancer will have prostate gland surgically removed, and then undergo combination of radiotherapy and chemotherapy coupled with
surveillance of PSA level and bone scintigraphy or PET-CT whole body scan [5]. The rise in PSA value usually signals the recurrence of the disease. There are promising advances in prostate cancer management and these involve the use of radionuclides or tracers for diagnosis and treatment.

Radioisotopes and Biological Tracers

Tables analyzing different types of radioisotopes and biological tracers are included as Table 1 and 2.

Production Methods

The **Electron Linear Accelerator** technology is based on the use of high energies resulting from accelerated electron beam conversion. It uses microwave technology to accelerate electrons, in a section of the machine called the waveguide. These electrons collide with heavy metal targets and as a result produce high energy photons that can be used to activate stable isotopes.

**Cyclotrons** are the more commonly used systems to produce short-lived radioisotopes after nuclear reactors. Cyclotrons with proton energies less than 20 MeV are used for the production of positron emitting radioisotopes whilst those with energies above 20 MeV can be used to produce a wider range of radioisotopes with various applications.

The other irradiation option remains the neutron activation route inside a **Nuclear Reactor**. It makes use of High Enriched Uranium fuel plates that provide a neutron flux that can be used to activate stable isotopes such as Low Enriched Uranium. This reaction is referred to as a “fission reaction” and usually results in a large number of fission products that have to be further processed and separated to recover the products of interest.

Types of Radiation

There are different types of ionizing radiation that can be emitted from active radioisotopes. Some of these and their characteristics are mentioned below:

- **Alpha (α)** – Alpha radiation is ionizing in nature with very high energies (5-9 MeV) and short wavelengths. It is therefore very effective in the treatment of metastatic Prostate Cancer.
- **Beta (β)** – Beta electrons or positrons is also ionizing radiation with energy levels ranging from 0.05 MeV to 2.3 MeV. It has long wavelengths and usually used in the therapy of cancer that has metastasized to soft tissues.
- **Gamma (γ)** – Gamma radiation is made up of photons and is highly penetrative. This type of radiation is therefore used as a diagnostic tool and can be detected and interpreted using a Gamma camera/SPECT.
- **Auger** – Radiation has low energy levels and very short wavelengths.

Biological Tracers

A biological tracer is a molecule with specific characteristics able to transport the radionuclide to the receptor site. The specific bioactive molecules of receptors that can be fractions of antibodies, peptides, mimetic peptides, DNA analogs, oligonucleotides antisense (antisense) and non-peptide ligands. In recent years, several studies provide information about potential biological tracers such as PSMA, Choline, and Fluciclovine that can be used in the diagnostic and treatment of prostate cancer. The characteristics, advantages, and disadvantages are summarized in Table 2.

Potential “Theranostic” Pairs

In order to ascertain the best diagnostic and therapeutic combination, a comparative exercise was carried out between high-potential diagnostic and therapy tools.
68Ga-PSMA-11/18F Fluciclovine/11C-Choline/18F-PSMA-1007

There is an increasing need for biological tracers with a high detection sensitivity towards low PSA limits to allow for the early detection of recurrence prostate cancer after primary treatment. If a comparison was done between Choline and PSMA as biological tracers that can be radiolabeled with diagnostic radioisotopes, PSMA shows better detection levels at PSA levels as low as 2 ng/ml [8]. PSA levels are also found in high expressions in the prostate gland allowing a PSA specific targeting tracer such as PSMA to have better targeting in the prostate gland even at low PSA levels. Choline has a disadvantage of being consumed by other cells due to its increased cell membrane synthesis and proliferation [9].

Fluciclovine on the other hand has limited target potential due to its accumulation in other major sites of amino acid metabolism such as the liver and pancreas. This limits the radioactivity that is ultimately delivered to the prostate gland. PSMA similar structure to the molecule of target makes it the most appropriate biotracer for this application.

Looking at the radioisotopes of choice, $^{11}$C with very short half-life of 20.4 min limits its applicability as an imaging tool as sufficient time should be allowed for the radioisotopes to be metabolized by the cancer cells to allow for effective imaging. $^{18}$F with a half-life of 1 hour 50 minutes and its rapid uptake by the cells allows for sufficient imaging time. Generator based 68Ga however provides the most flexible option due to its ability to be made available to distant locations. $^{18}$F does not have a generator option and has to be utilized in close proximity to the generation site which requires a cyclotron.
Table 2: Assessment of available Radionuclides

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Function</th>
<th>Production</th>
<th>Availability/suppliers</th>
<th>Cost $/dose</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-11</td>
<td>Positron $\beta^+ \ (PET\ base\ diagnosis)$</td>
<td>• Cyclotron produced using Nitrogen: $^{14}\text{N}(\alpha,\gamma)^{11}\text{C}$</td>
<td>No information available.</td>
<td>No information available</td>
<td>20.36 min</td>
</tr>
<tr>
<td>Flourine-18</td>
<td>Positron $\beta^+ \ (PET\ base\ diagnosis)$</td>
<td>• Cyclotron produced using oxygen enriched water: $^{18}\text{O}(\text{n,}\alpha)^{16}\text{F}$</td>
<td>Limitless</td>
<td>428 (10 mCi)</td>
<td>1 hour 50 min</td>
</tr>
</tbody>
</table>
| Gallium-68   | Positron $\beta^+ \ (PET\ base\ diagnosis)$ | • Cyclotron produced using Gallium metal.  
• Generator based: $^{68}\text{Ge} \rightarrow^{68}\text{Ga}$  
Requires an 18 MeV and above size generator. | ITG, Eckert & Ziegler, iThemba labs, IRE, JSE Isotopes, | 1214 (312 MBq-8mCi) | $^{68}\text{Ga} \ (68 \text{ min})$ Generator (6 months-1 year) |
| Lutetium-177 | Beta $\beta^+ \ (Therapy)$; Gamma $\gamma$ (SPECT based diagnostic) | Nuclear reactor based production: $^{176}\text{Yt} \rightarrow^{177}\text{Lu (n.c.a).}$ n.c.a has a higher activity (4800 GBq/mg vs 800 GBq/mg for c.a due to the non-formation of meta-stable $^{177}\text{Lu}$.) | ITG, NTP, IRE, JSE Isotopes, | 48000 (4000 MBq-108mCi) | 6 days |
| Actinium-225 | Alpha $\alpha \ (Therapy)$ | • Natural production route: $^{235}\text{U} \rightarrow^{229}\text{Th} \rightarrow^{225}\text{Ac}$  
• Insufficient supply for commercial use. Companies are investigating a cyclotron based production route: $^{225}\text{Ra(p,2n)}^{225}\text{Ac}$  
• Challenges with irradiating a gas target ($^{226}\text{Ra}$). | ITG, JSC isotope, US department of energy | No information available | 10 days |
| Radium-223   | Alpha $\alpha \ (Therapy)$ | • Produced from Nuclear reactor ($^{222}\text{Ra} \rightarrow^{222}\text{Ac} \rightarrow^{222}\text{Th} \rightarrow^{223}\text{Ra}$)  
• Generator based.  
• Use of gas targets is a challenge. | Bayer Patent (Xofigo)- expires in 2021. | 25465 (216 mCi) | $^{223}\text{Ra} \ (11 \text{ days})$ Generator (21 years) |
| Palladium-103 | Brachytherapy Prostate Cancer | Cyclotron based production: $^{103}\text{Rh(p,}\alpha)^{103}\text{Pd}$ | JSC isotope Cyclotron Co Ltd | No information available | 16.9 days |
| Strontium-89 | Beta $\beta^- \ (Therapy)$; Palliative care | Nuclear reactor based irradiation: $^{89}\text{Y(n,}\gamma)^{90}\text{Sr}$ | National Isotope Development Center (NIDO), ISTC, Drugbank | No information available | 50.5 days |

*Information from various on-line sources
### Table 3: Assessment of available radionuclides

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Function</th>
<th>Production</th>
<th>Availability/suppliers</th>
<th>Cost $/dose</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molybdenum-99</strong></td>
<td>Gamma (SPECT based diagnosis)</td>
<td><img src="#" alt="Production equations" /></td>
<td>Nuclear reactors: HFR (Netherlands), BR-2 (Belgium), OPAL (Australia), Maria (Poland), SAFARI-1 (South Africa) Generator suppliers: NTP, IBA, GE, Monrol, ANSTO. Alternative tech suppliers: North Star, Triumph Canadian Linear Accelerator (Canada).</td>
<td>20 (10 mCi)</td>
<td>99Mo (66 hours), 99mTc (6 hours) Generator (1-2 weeks)</td>
</tr>
<tr>
<td><strong>Scandium-47</strong></td>
<td>Beta (Therapy)</td>
<td><img src="#" alt="Production equation" /></td>
<td>Research phase</td>
<td>No information available</td>
<td>3 days</td>
</tr>
<tr>
<td><strong>Copper-67</strong></td>
<td>Positron (PET based diagnosis)</td>
<td><img src="#" alt="Production equation" /></td>
<td>US department of energy (Brookhaven National Laboratory)</td>
<td>No information available</td>
<td>62 days</td>
</tr>
<tr>
<td><strong>Copper-64</strong></td>
<td>Beta (Therapy)</td>
<td><img src="#" alt="Production equation" /></td>
<td>Research Phase: Julich Institute &amp; The Hevesy Laboratory.</td>
<td>No information available</td>
<td>12.7 hours</td>
</tr>
<tr>
<td><strong>Y-90</strong></td>
<td>Beta (Therapy)</td>
<td><img src="#" alt="Production equation" /></td>
<td>No information available</td>
<td>No information available</td>
<td>64 h</td>
</tr>
<tr>
<td><strong>Iodine-125</strong></td>
<td>Brachytherapy (Seed)</td>
<td><img src="#" alt="Production equations" /></td>
<td>Canada Reactors: McMaster University's Reactor National Research Universal (NRU) reactor.</td>
<td>No information available</td>
<td>59.4 days</td>
</tr>
<tr>
<td><strong>Caesium-132</strong></td>
<td>Brachytherapy</td>
<td><img src="#" alt="Production equation" /></td>
<td>No information available</td>
<td>No information available</td>
<td>9.7 days</td>
</tr>
<tr>
<td><strong>Iridium-192</strong></td>
<td>Brachytherapy</td>
<td><img src="#" alt="Production equation" /></td>
<td>Research Reactor ISOFLEX</td>
<td>No information available</td>
<td>73.8 days</td>
</tr>
</tbody>
</table>

*Information from various on-line sources*
<table>
<thead>
<tr>
<th>Biotracer</th>
<th>Characteristics</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Approx. Cost *</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSMA</td>
<td>PSMA is a folate hydrolase cell surface glycoprotein.</td>
<td>• PSMA is highly overexpressed in prostate cancer cells as a transmembrane protein.</td>
<td>• It is expressed in different tissue types, including other cancers and benign conditions [8]</td>
<td>1000 – 1500 EUR (10 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• PSMA is widespread in most prostate tumors even when PSA staining is negative or weak.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• PSMA expression may increase as tumor grade and castrate resistance increases [8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• It is expressed in a different tissue types, including other cancers and benign conditions [8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Preclinical data conflict on the theory of augmented choline use by the cell because of increased cell membrane synthesis and proliferation [8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choline</td>
<td>Choline is a water-soluble organic compound.</td>
<td>• A higher intake or status of choline in plasma and tissues has been related to higher cancer risks.</td>
<td></td>
<td>2000 – 2500 EUR (10 mg)</td>
</tr>
<tr>
<td></td>
<td>It is classified as an essential nutrient.</td>
<td>• Choline metabolism, provides promising therapeutic opportunities for tumor growth arrest [9]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>It is involved in the synthesis of phospholipids and other structural components.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Preclinical data conflict on the theory of augmented choline use by the cell because of increased cell membrane synthesis and proliferation [8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluciclovine</td>
<td>Fluciclovine is a synthetic amino acid analog.</td>
<td>• Fluciclovine enters the cell via amino acid transporters, which are upregulated in prostate cancer cells, permitting the identification of malignancy</td>
<td>• Has limited target potential due to its accumulation in other major sites of amino acid metabolism such as the liver and pancreas. This limits the radioactivity that is ultimately delivered to the prostate gland.</td>
<td>2750 – 3250 EUR (10 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Approval by FDA.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Information from various on-line sources*
Based on the arguments presented above, $^{18}$F-PSMA-1007 is a better choice due to its superior targeting characteristics as opposed to non-PSMA-1007 based tracers. It was also chosen over $^{68}$Ga-PSMA-11 due to its rapid clearance from non-target tissue, high detection rate and limited nephrotoxicity or hepatotoxicity side effects. $^{68}$Ga-PSMA-11 is also rapidly excreted via the bladder which can result in ambiguous images as the bladder is situated in front of the prostate gland. This ambiguity is eliminated with the use of $^{18}$F-PSMA-1007. In conclusion, cited in a number of comparative trials carried out by various institutions, $^{18}$F-PSMA-1007 PET was able to detect a considerably higher number of lesions with increased PSMA-ligand uptake attributed to benign lesions as compared to $^{68}$Ga-PSMA-11 PET. However, it is highly recommended that the production of $^{68}$Ga-PSMA-11 not be ceased as this tool allows countries which do not have access to a cyclotron to access it due to its generator based characteristic. A $^{68}$Ge/$^{68}$Ga generator has a shelf life ranging from 6 to 12 months. Table 4 below shows how the diagnostic tools were ranked with 1 indicating poor performance and 5 indicating high performance in the specific indicator:

<table>
<thead>
<tr>
<th>Diagnostic tool</th>
<th>High Targeting precision</th>
<th>High specific Activity</th>
<th>Long shelf-life</th>
<th>Cost effective</th>
<th>Non-ambiguous images</th>
<th>Total score</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}$F-PSMA-1007</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>21</td>
<td>Winner</td>
</tr>
<tr>
<td>$^{68}$Ga-PSMA-11</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>19</td>
<td>Recommended</td>
</tr>
<tr>
<td>$^{18}$F-Fluciclovine</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>14</td>
<td>Lost</td>
</tr>
<tr>
<td>$^{18}$F-Choline</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>14</td>
<td>Lost</td>
</tr>
</tbody>
</table>

Table 4: Ranking table

Figure 1 represents the schematic chemical formulas for the two most promising diagnostic tools [13]:

![Chemical formulas](image)

$^{225}$Ac-PSMA-617/$^{177}$Lu-PSMA-617/$^{90}$Y-PMSA-617/$^{47}$Sc-PSMA-617

The next step was to analyze potential theranostic pairs with specific attention to their ability to perform as true "theranostic": be able to provide therapy and images for the monitoring of the efficacy of the therapy. This means that the radioisotopes needs to be able to produce radiation for diagnostic and therapeutic purposes respectively i.e. $\gamma$ and $\beta$ or $\gamma$ and $\alpha$. 

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The following points represent the type of radiation energies emitted by the various radioisotopes:

- $^{225}$Ac: 100% decay via $\alpha$ radiation. Total energy
- $^{90}$Y: 100% decay via $\beta^-$ radiation. Total energy
- $^{47}$Sc: 94.7 and 5.73% decay via $\beta$ and $\gamma$ radiation respectively.
- $^{177}$Lu: 78.6 and 21% decay via $\beta$ and $\gamma$ radiation respectively.

Based on this information above, $^{225}$Ac and $^{90}$Y do not make the cut as theranostic tools due to the fact that they only produce radiation for therapy purposes and will thus not enable the monitoring of the disease progression. This leaves $^{47}$Sc and $^{177}$Lu as potential theranostic potential elements. One of the most promising tools currently on the market for this treatment is $^{177}$Lu-PSMA-617.

There are many factors which make $^{177}$Lu a good candidate but some of the most prominent reason includes its decay into both $\gamma$ and $\beta$ radiation and its long half-life of 6.65 days. This allows for $^{177}$Lu to deliver therapeutic treatment to the cancer site via its $\beta$ radiation and allow for monitoring and tracking of progress due to its $\gamma$ radiation.

$^{177}$Lu is also already included on various guidelines as a treatment method making it more likely to be recommended. $^{47}$Sc on the other hand is still at a research and development stage and still has some time to go before it can be commercialized. It is for these reasons that $^{177}$Lu-PSMA-617 is recommend as the theranostic tool of choice. It is imperative to note however that $^{177}$Lu-PSMA-617 is more effective at the early stages where the degree of metastasis is still restricted to soft-tissue, for cases of hard tissue (bone) metastasis, $^{225}$Ac-PSMA-617 becomes a better intervention due to its $\alpha$ radiation.

Our final recommendation therefore is $^{177}$Lu-PSMA-617 with the option of using $^{225}$Ac-PSMA-617 for severe cases of metastasis. $^{225}$Ac-PSMA-617 also has more side-effects such as xerostomia and should preferably be used only for severe cases of metastasis. The schematic diagrams of $^{225}$Ac-PSMA-617 and $^{177}$Lu-PSMA-617 are shown in Figure 2 [13]:

![225Ac-PSMA-617](image1)
![177Lu-PSMA-617](image2)

**FIG 2: chemical formulas of 225Ac-PSMA-617 and 177Lu-PSMA-617**

As reported by Louise Emmett, Kathy Willowson et al (2017), $^{177}$Lu PSMA is showing interesting treatment responses in men with Metastatic castration-resistant, however, in some cases patients could have serious side effects like dry mouth, fatigue, nausea and Hematological toxicity [13, 14]. Additionally, $^{177}$Lu-PSMA has not been approved by the U.S. Food and Drug Administration.
Proposed Solution

The proposed solution is therefore the following pair:

- **Diagnostics:** $^{18}$F-PSMA-1007, and
- **Theranostic:** $^{177}$Lu-PSMA-617.

Figure 3 shows how $^{177}$Lu-PSMA-617 functions as a theranostics. Therapy is administered via the $\beta$ radiation whilst the efficacy of the treatment and progression of the disease are monitored via the $\gamma$ radiation using a SPECT scanner.

![FIG. 3: Schematic diagram of 177Lu as a theranostic [15]](image)

The final choice of the suitable radionuclide for the radiolabeling process was based on a number of factors such as:

- Simplicity of the production process and availability;
- Reasonable half-life: $^{18}$F and $^{177}$Lu have a suitable half-lifes which give a vital advantage during the diagnosis and treatment processes.
- Satisfactory cost: the radionuclides should be competitive not only in the production amount but also in the final cost for the end user. $^{18}$F and $^{177}$Lu have a lower production cost comparing to the other proposed radioisotopes.

Regulatory & Safety Requirements

Radiation protection must be considered as a crucial issue to the business that providing medical service and patient care. The facility or person which perform nuclear medicine procedures is required to have an appropriate authorization from the radiation protection regulatory body. In addition, there are some suggestions which could help in minimizing the personnel exposure for both occupational persons and patients:

- Adequate radiation protection program: PET/CT should be conducted within well-established radiation protection program, which includes the individual responsibilities of staff members, a radiopharmacist, nursing and other supporting staff who will be exposed as part of their routine activities [17].
- Shielding: Radiopharmaceutical should be stored and transported in suitable lead containers designed to limit external radiation levels from higher energy PET radionuclides [17].
Continuous radiation monitoring: Each facility should have a monitor to check staff hand and feet on a regular basis. Also, radiation monitoring devices in the hot lab and injection room should be used [17].

Radiation exposures of patients in medicine require an approach that differs from the radiological protection in other planned exposure situations. The exposure is intentional and for the direct benefit of the patient. In diagnostic, this means avoiding unnecessary exposures [16]. Safety and efficacy of targeted radionuclide therapies can be improved with the use of patient-specific dosimetry, which may guide successful tumor dosing and act as an early indicator of organ toxicity [18].

The security system needs to establish to prevent theft, loss, unauthorized use or damage to the radioactive source. It should include all steps from ordering and delivery to disposal of spent sources. Routine records of all steps should be kept. The security system should include emergency procedure on the basis of event identified by the safety assessment. The procedures should be clear and concise.

Future Developments

Nanoparticle Nuclear Medicine Technology

Developing a nanoparticle based concept for the theranostic solution will result in the following benefits:

- Decreased radiation exposure to unwanted tissue by decreasing the dose of the radionuclide thus reduced side-effects;
- Decrease in overall cost of treatment: Therapeutic nanoparticles for radionuclides can be design and created to match the sizes of tumor vasculature and gave optimal therapeutic payloads with minimum wastage [19].

Using the Same Radioisotope for Diagnosis and Therapy

Most current methods are based on using different pairs of radionuclides such as: $^{68}$Ga/$^{177}$Lu; $^{18}$F/$^{177}$Lu, which allowed a combination of PET and internal radiotherapy. For future development work, it is proposed to focus on developing radionuclides that can be used for both diagnostic and therapeutic purposes i.e. $^{44}$Sc/$^{47}$Sc; $^{64}$Cu/$^{67}$Cu; $^{86}$Y/$^{90}$Y. Basing this on the same element will result in the reduction of complications experienced in moving from diagnosis to therapy [20].

Alternative Production Methods

The production of $^{68}$Ga can also be explored using a cyclotron base via $^{68}$Zn instead of generator base. If this technology matures, it will drastically decreased cost of radiopharmaceuticals and offer a very advantage to those centres with existing cyclotron [17].

Conclusions

In conclusion, it would be better to highlight the importance of the creation of new medical radioisotopes for diagnosis and therapy as they are essential for the development and implementation of a personalized patient treatment. Early detection of prostate cancer results in earlier introduction of disease management solutions and prolongs the life-span of the patient. It is important to make use of targeted diagnostic tools which will be able to diagnose with higher precision and therapeutic tools that will be able to treat with greater efficacy. Finally, Theranostics combined with images and dosimetry will allow better treatment planning, leading to a personalization of medical practice.
References

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We would like to acknowledge the World Nuclear University for organizing this very informative programme, the IAEA for funding Fellows’ attendance and Rosatom Technical Academy for making their facilities and training experts available to us. We would also like to acknowledge our mentor Mr Ibrahim Duhaini for his guidance and advice.