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Use of Cyclotron for Radionuclide Production in SPECT Diagnostics at Nuclear Medicine Installation

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Abstract

The development of cyclotron technology in the healthcare industry became important after the production of several radioisotopes with short half-lives were used. Single Photon Emission Computed Tomography (SPECT) became one of the important diagnostic methods, especially in the visualization and functional analysis of internal organs. In Indonesia, cyclotron is only available in a few hospitals and is not fully optimized in the production of radionuclides for SPECT. By involving cyclotron technology in the production of radionuclides for SPECT, it is hoped that this research can make a contribution in advancing the field of nuclear medicine, opening up new opportunities for diagnostic research, and improving the healthcare quality by providing more accurate and timely information to medical practitioners. Relatively low-energy cyclotrons are required to produce PET radionuclides such as 18F, 11C, 13N, 64Cu, and 124I with energies between 2.7 and 5.6 MeV. Medium cyclotrons capable of accelerating protons greater than 10 MeV are required for the production of SPECT radionuclides such as 99mTc, 123I, 201Tl, 111In and 67Ga.

Keywords*: Cyclotron; Nuclear Cross-section; Production Efficiency; Radionuclide Production;, Single Photon Emission Computed Tomography (SPECT).*

Introduction

Accelerator physics is a branch of applied physics where technological developments have brought new developments to particle physics research. Accelerator physics itself studies the interaction between charged particles and electromagnetic fields. Accelerators can be found in many areas of science and technology, medicine, and industrial processes. Accelerators can be divided into two types according to the nature of the particle field motion, namely accelerators that work with direct particle motion (better known as linear accelerators) and circular particle motion accelerators (magnetic accelerators), among others: Betatron, cyclotron, EULIMA, and HIMAC neutron generators (Anum, n.d.).

A cyclotron is a type of circular accelerator and is used to accelerate electrically charged particles. The cyclotron is circular and uses a magnetic field to keep charged ions (usually protons) in orbit. The development of cyclotron technology in the healthcare industry became important after the production of several radioisotopes with short half-lives were used, as the main basis for the use of PET (*Positron Emission*

Tomography) (Nuttens et al., 2010).

The main components of a cyclotron are a high-frequency source to generate alternating voltage, a large electromagnet to generate a uniform field and a pair of small hollow made of a highly conductive material called Dees. The Dees are placed face-to-face between the electromagnetic poles and the magnetic flux of the electromagnet cuts the Dees perpendicularly. The charged particles accelerate along a spiral path away from the center, a static magnetic field holds them in the spiral path, and a rapidly changing electric field accelerates them. Cyclotrons are used to accelerate charged particles or ions to high energy, study atomic structure, produce medical radioisotopes, and treat cancer with particle therapy. Cyclotrons are widely used in engineering, physics, and medicine. A cyclotron has several main parts (Anum, n.d.):

1. A high-frequency source for generating alternating voltage.
2. A very large electromagnet a uniform magnetic field.
3. A pair of small hollow half-cylinders composed of a highly conductive material called Dees.
4. RF System
5. Ion source system
6. File monitor monitor extractor system

The development of cyclotrons in Indonesia has been developed in several institutions, including BATAN and BRIN. Its development at the Center for Accelerator Science and Technology (PSTA), the National Nuclear Energy Agency (BATAN) Yogyakarta is often called DECY-13, which stands for Development of Experimental Cyclotron in Yogyakarta, which is designed to be able to produce protons with 13 MeV energy is a form of cyclotron development in Indonesia. Protons with such energy will later be used to produce F-18 radioisotopes for cancer diagnosis using *Positron Emission Tomography* (PET) scans.

Currently, the DECY-13 Cyclotron is under the completion of installation stage. It is expected that the specific year, testing, commissioning and operation can begin. At the testing stage, modifications, and revitalization of the devices that make up the cyclotron system are required. This is also the case for the long term. After the testing phase is completed, there is still an opportunity to develop the cyclotron system, especially in improving its quality.

Currently, cyclotrons in Indonesia are only available in four hospitals, namely RS Gading Pluit, MRCCC Siloam Hospital, Dharmais Cancer Hospital, all three of which are in the city of Jakarta, and RSUD Abdul Wahab Sjahranie in Samarinda, as well as one hospital that is still being construction of the cyclotron at RSPAD Gatot Soebroto. However, although the cyclotron offers great potential, its use in radionuclide production for SPECT has yet to be fully optimized. By involving cyclotron technology in the production of radionuclides for SPECT, it is hoped that this research can make a real contribution to advancing the field of nuclear medicine, opening up new opportunities for diagnostic research, and ultimately, improving the quality of healthcare by providing more accurate and timely information to medical practitioners. Therefore, in-depth research into the use of cyclotrons in this context can make an important contribution to improving the efficiency and availability of radionuclides used in SPECT (Saktia, 2013).

Methods

The research method that was being used in this research was literature review. The stages of making this journal begin by looking for problems that will be selected and then looking for references that will be used to be able to make this journal. The number of articles used in this study is nine references. The selection of cyclotrons is based on the need for radioactive substances in large nuclear medicine installations.

Result and Discussion

Radionuclide production with accelerators requires the particle beam to be delivered with two specific characteristics. The particle beam must have sufficient energy to produce the necessary nuclear reactions and sufficient current beam to give practical results. The basic characteristics of all cyclotrons are the same. There is an ion source to generate ions, an acceleration chamber to accelerate the ions, and a magnet to hold the ions on a circular path. A typical modern cyclotron construction is shown in **Figure 1.**

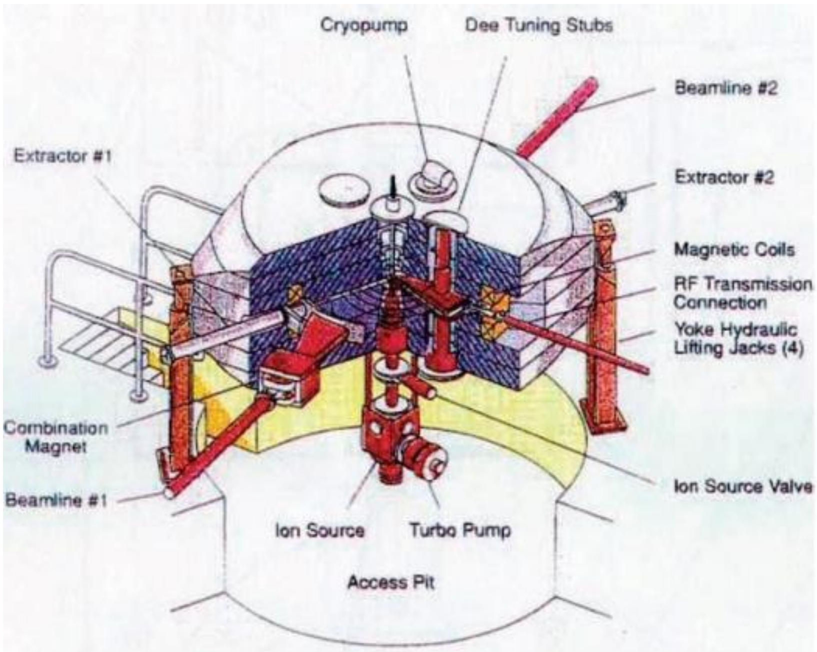

Figure 1. Cyclotron (Evans, 1955)

Nuclear Reaction

When energetic charged particles pass through matter there is a chance that they will interact with nuclei along their path. They can either be scattered from the nucleus or, if the energy of the particles is high enough upon collision, they can combine to form compound nuclei that can decay in the nucleus.

The incoming particle must have enough energy to overcome two potential barriers. The first barrier is the electrostatic repulsion between the positively charged particle and the positively charged nucleus or the Coulomb barrier. The second barrier depends on whether the reaction is exothermic or endothermic, and is referred to as the Q value. The Q value is the mass difference between the compound nucleus and the incoming particles. If a reaction occurs, the nucleus of the compound is usually highly excited because the absorbed particles carry some of the kinetic energy and the energy of the mass difference.

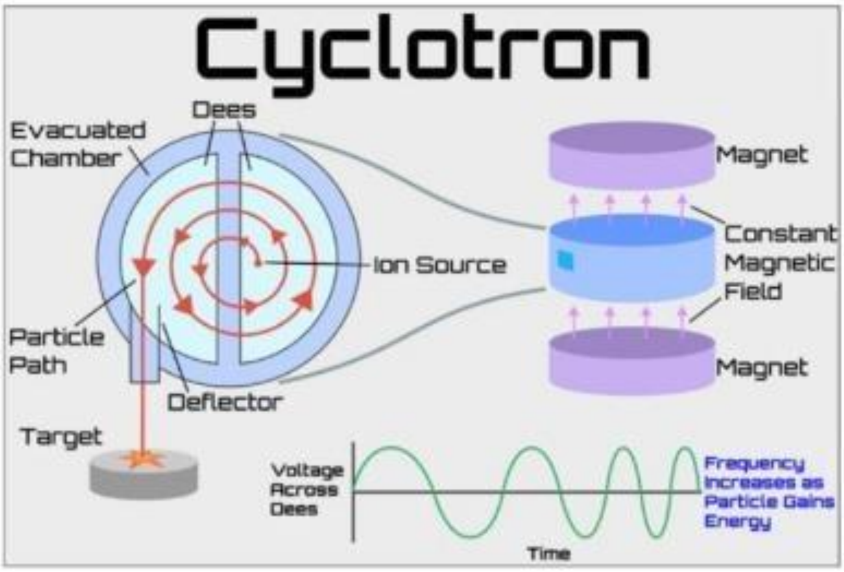

Figure 2. Components of a cyclotron (Anum, n.d.)

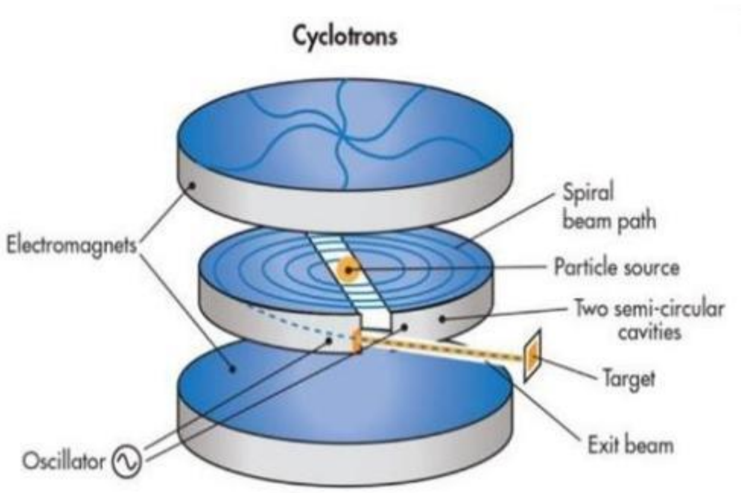

Figure 3. A pair of magnetic fields and two dees (Anum, n.d.)

Coulomb Barrier

In the classical sense, a reaction between a charged particle and a nucleus cannot occur if the center-of-mass energy of both particles is smaller than the Coulomb barrier. In the case applicable to radionuclide production with a cyclotron, the Coulomb barrier implies that the charged particle must have an energy greater than the electrostatic repulsion, which is given (Evans, 1955) by the following equation:

$$B = \frac{Zze^2}{R}$$

With :
B = reaction barrier
Z & z = atomic numbers of the two elements
e = electric charge
R = distance between two species (cm)

In any nuclear reaction, the total energy must be conserved, i.e. the total energy including the residual mass of the reactants must be equal to the total energy including the residual mass of the products. Any increase in kinetic energy must be accompanied by an equal decrease in the rest mass. The Q value of a nuclear reaction can be positive or negative. If the residual mass of the reactants exceeds the residual mass of the products, the Q value of the reaction is positive, with the decrease in residual mass being converted into an increase in kinetic energy. The energy equivalent to the mass deficit Q is given by:

$$Q(MeV) = 931.4\Delta M$$

with

$$\Delta M = (m_p + M_T) + (m_q - M_R)$$

m_P = particle mass
M_t = target mass
m_q = mass of product
M_r = mass of emitted particles

If Q < 0, the reaction is called an endotherm. However, if Q > 0, the reaction is said to be exothermic. If the reaction is exothermic, the amount of energy greater than Q must be provided the reaction be continued. The threshold is the Coulomb barrier plus the difference Q. If the reaction is exothermic, the threshold energy will only be the Coulomb barrier.

The nuclear reaction cross section or excitation function represents the total probability that a compound nucleus will form and then decay along a particular channel. This function determines the number of radionuclides that can be made on a given cyclotron, and the level of contamination of other radioisotopes that may be present in the target material. In the *'touching spheres'* nuclear reaction model, there are two spheres that approach each other. If the two spheres touch, a reaction will occur, and if they do not touch, no reaction will occur. In this visualization, the probability of reaction is proportional to the cross-sectional area of the two spheres. The total reaction cross-sectional area is given by the following equation:

$$\sigma_R = \pi r_o^2 (A_p^{\frac{1}{3}} + A_T^{\frac{1}{3}})$$

Nuclear reactions will not occur unless through the tunnel effect if the minimum energy is below the energy required to overcome the Coulomb barrier and the reaction Q value is negative. Particles with energy below this barrier have a very low probability of reacting. The energy required to induce a nuclear reaction increases as the Z value of the target material increases. For many low-Z materials, it is possible to use low-energy accelerators, but for high-Z materials, it is necessary to increase the particle energy (Deconninck, 1978).

Over the past few decades, nuclear technology has offered methods to diagnose cancer and other metabolic disorders. There are two nuclear or radio diagnostic modalities namely Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). PET and SPECT modalities require a radioactive source (radionuclide) for analysis. Radionuclides that emit positrons are used in PET-based diagnosis, while radionuclides that emit gamma rays are used in SPECT-based diagnosis.

At high energies (usually greater than 5 MeV), protons can penetrate the nucleus of the target atom resulting in a nuclear reaction that produces new radionuclides. Most of the radionuclides produced are short-lived, making them suitable for medical purposes. Cyclotron-based radionuclide production requires a thorough understanding of nuclear cross-sections or excitation functions, nuclear reactions, threshold energies, irradiation parameters and other requirements, theoretically and experimentally (Kambali, 2019). Cyclotrons are one of the most important radionuclide sources used in biomedical applications. The production of SPECT radionuclides using a cyclotron generally requires a high-energy proton beam as most can be generated via (p,2n), (p,3n) and several other nuclear reaction modes (Kambali, 2019).

Several other potential radionuclides for PET and SPECT can be produced using a cyclotron such as in the table above. Usually, relatively low-energy cyclotrons are required to produce PET radionuclides such as 18F, 11C, 13N, 64Cu, and 124I due to their relatively low nuclear threshold energy (between 2.7 and 5.6 MeV). However, medium cyclotrons capable of accelerating protons greater than 10 MeV are required for the production of SPECT radionuclides such as 99mTc, 123I, 201Tl, 111In, and 67Ga. These SPECT radionuclides can potentially be produced using the three available cyclotrons. A continuous supply of radionuclides is essential as they are useful for cancer diagnosis and other research. The radioisotopes produced by the cyclotron are shown in **Table 2**.

Table 2. Cyclotron Production Results

Radioisotopes	Specifications		
	Time Beak	Usability	Methods Decay
Gallium - 67	3,26 Day	Detection of neoplasm location	Gallium-67 decays to stabilize at 67Zn by electron capture. This decay produces emission in the form of 93.3 keV gamma rays (37%), 183.6 keV (20.4%), and 300.2 keV (16.6%).
Iodine 123	13,2 Hours	Diagnostics	Iodine-123 decays completely by electron capture and produces 0.028 gamma rays and 0.160 MeV.
Thallium 201	73,06 Hours	Diagnostics	Thalium-201 decays by electron capture with gamma-ray emission of 167 and 135 keV where it is ideally for gamma-ray cameras
Technetium 99m	6 Hours	Diagnostics and Therapy	Nuclear reaction equation on Technetium-99m is: ^{100}Mo(p, 2n) Tc^{99m} with Mo-100 as target material

Conclusion

Although cyclotrons have been implemented in several hospitals in Indonesia, their use in the production of radionuclides for *Single Photon Emission Computed Tomography* (SPECT) is still not fully optimized. In this study, a literature review was conducted to investigate the potential of cyclotrons in producing radionuclides for SPECT, with the hope of making a significant contribution to advancing the field of nuclear medicine. The results and discussion highlight technical aspects of radionuclide production with accelerators, including basic cyclotron characteristics, nuclear reactions, threshold energies, and other parameters. The focus on nuclear cross-sections, nuclear reactions, and threshold energies are key elements in understanding and improving the efficiency of radionuclide production using cyclotrons. With the development of cyclotron technology, especially in the context of radionuclide production for SPECT, it is expected to make an important contribution to improving efficiency, radionuclide availability, and accuracy of medical diagnosis. Although cyclotrons have become an integral part of several hospitals in Indonesia, further research and development of cyclotron technology could open up new opportunities for diagnostic research and improve the quality of healthcare with more accurate and timely information.

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