IOP Conference Series: Materials Science and Engineering

PAPER • OPEN ACCESS

Future of nuclear medicine- an overview

To cite this article: Siti Amira Othman *et al* 2019 *IOP Conf. Ser.: Mater. Sci. Eng.* **555** 012032

IOP Conf. Series: Materials Science and Engineering **555** (2019) 012032 doi:10.1088/1757-899X/555/1/012032

Future of nuclear medicine- an overview

Siti Amira Othman[1,a)], Nurul Fathihah Abu Bakar[1], Nor Farah Amirah Nor Azman[1] and Nurin Saqinah Jasrin[1]

[1]Faculty of Applied Sciences and Technology, Universiti Tun Hussein Onn Malaysia, Pagoh Educational Hub, KM 1, Jalan Panchor, 84000, Pagoh, Muar, Johor.

[a]sitiamira@uthm.edu.my

Abstract. The development of nuclear medicine has led to an entire subset of extremely effective strategies in diagnosis and disease therapy. The emerging advancements in nuclear medicine are vast and diverse. Nuclear medicine tests and treatments involve the use of small amounts of radioactive material in order to diagnose and determine the severity of a variety of conditions and diseases. Basically, nuclear medicine involves the use of the latest imaging facilities such as magnetic resonance imaging, computed tomography scans and positron emission tomography which will find in many modern medical institutions today. One significant advantage of using nuclear medicine is the ability to make complex medical procedures simpler and safer for patients. With this technology, physicians and medical professionals are able to examine in great detail the most sensitive areas. All examinations can happen without subjecting patients to possibly dangerous and invasive procedures and surgeries. This medical technology has enabled the development of treatment options for patients suffering from serious illnesses, such as cancer either through radiation or chemotherapy. Health care professionals now face many challenges in their profession such as new rules and the latest practices that enable them to learn new skills and new ways of practicing their daily tasks in nuclear medicine areas. As a result, they are confronted with new skills and new ways of practicing in nuclear medicine area every day.

1. Future of Nuclear Medicine

Nuclear Medicine is one of dominant part in medicine world that use unsealed radioactive substances for therapy and diagnosis. The substances consist small amount of radionuclides which known as radiopharmaceuticals. Based on history, radiopharmaceuticals have been existed in the middle of 1920-s. During that time German scientists had been working hard on one experiment on rats using radionuclides. Phosphorus-32 was the first radionuclides that have been used in the late 1930 to treat leukaemia disease. After 1946, Iodine-131 began to take a dominant lead in the field which it's has been used to treat thyroid cancer. The differences between therapy and diagnosis is diagnosis (radionuclides imaging) is one of the technique in medical instrument or device that has an ability to emits radiation from the injected radionuclides which the output result is detected by a special indicator or detector such as scintillation cameras (gamma cameras or positron emission tomography (PET) cameras). Usually the output result will be in detail or high resolution image to give real 3D image of the body. The result of image is due to the distribution of medically injected, inhaled, or ingested radionuclides within the body examples include bone scans, thyroid scans, renal scans, and many others as well. For therapeutic purposes, radiopharmaceuticals are administered to treat disease with curative (able to cure or cause to get better) or palliative intent (providing relief from the symptoms and stress of a serious illness). It relies on killing abnormal cells within body by high but

IOP Conf. Series: Materials Science and Engineering **555** (2019) 012032 doi:10.1088/1757-899X/555/1/012032

localized radiation exposure. Examples include I-131 therapies for thyroid disorders (hyperthyroidism and thyroid cancer), Strontium and Samarium bone palliation for osseous metastases and etc.

Radiopharmaceutical has developed into more crucial field of medicine. The application of global pharmaceutical in market is estimated to increase from $4.9 billion dollar in 2010 to 7.9 billion dollar in 2011. There is a significant increase in the global demand in radiopharmaceutical field, with the increase of disease related to cardiac, neurological and cancer disease. Radiopharmaceutical consists of drug component and a radioactive component or substances such as radioisotope and molecules labelled with radioisotopes, which are currently use in both diagnosis and therapy. Radionuclides refer to substances that have same number of protons but different number of neutrons. Unstable radionuclide causes their nuclei to undergo rearrangement while changing to a stable state and energy is give off. Most radionuclides contain a component that emits gamma radiation. Radiopharmaceuticals are the main component of nuclear medicine practice, where it was administered in diagnosing, managing and treating various types of diseases.

The obvious distinction between radiopharmaceuticals and traditional drugs is the lack of effect of pharmacological activity on human bodies as the part of pharmaceutical. Various radiopharmaceuticals have been developed that have different targeting mechanisms or routes. Some are given in the simplest salt form as non-invasive diagnostic imaging agents to provide functional and structural information about organs and diseased tissues. This became their main advantage, which is by allowing non-invasive external monitoring or targeted therapeutic irradiation, the effect on the biological processes in the body was minimized. Radiopharmaceutical was recorded as having an excellent safety record and their incidence of side effects is extremely low. They may be given to the patients in several ways such as orally or placed into the eyes or the bladder. Radioisotopes may be used internally or externally in intensive purposes of radiopharmaceutical, which have been used widely as tracers of physiologic processes. If the radioisotope were implanted in sealed capsules in a tissue, was applied externally; the dose could be terminated by the removal of the sources. If the radioisotope were implanted in an unsealed capsule, was applied internally; the dose cannot be stopped by the removal of the sources, and the dose tend to possess higher energy. Radiopharmaceutical are widely used in diagnostic and therapeutic area of human diseases, nearly 95% of pharmaceutical are used for diagnostic purposes, while the other 5% are usually used as therapeutic purposes. Since radiopharmaceutical was usually used as tracer, it has no pharmacological effects.

There are several examples that prostrate the use of radiopharmaceutical in therapeutic procedures such as Non-Hodgkin's Lymphoma Therapy. In therapeutic treatments for Non-Hodgkin's Lymphoma Therapy, a radioisotope called radioimmunotherapy (RIT) is given and attached it to an antibody in order to deliver radioactivity to specific cells. Rhenium 186 (3.8 d) is used for pain relief in bone cancer. Beta emitter with weak gamma for imaging Iridium 192 (74 d) is supplied in wire form for use as an internal radiotherapy source for cancer treatment (used then removed). Palladium 103 (17 d) is used to make brachytherapy permanent implant seeds for early stage prostate cancer. Yttrium 90 (64 h) is used for cancer brachytherapy and as silicate colloid for the relieving.

2. Application of nuclear medicine

2.1. Nitrogen-13

In producing nitrogen-13-ammonia in usable quantities with least contamination, a method has been developed in order to realise the statement. The system involves a device to produce a proton beam which travels along the selected path and strikes the target material in a target chamber. The process will produce nitrogen-13 atoms and alpha particles. In the early production of N-13-ammonia it was produced from alpha particle irradiation and heating of boron nitride in sodium hydroxide [1]. Then, it was produced by deuteron irradiation of methane gas or metal carbides, but somehow gave low yields. This shows that, this method was not too efficient. Thus another method was developed which is the proton irradiation of natural water target that involves oxygen bombarded with proton that producing nitrogen-13 and alpha particle [2][3]. This is due to the hydrogen abstraction from the target water matrix.

Another method to produce N-13 was found around year 1991 by Wieland *et al.* They produced the N-13 directly in the water by adding free radical scavengers like ethanol, acetic acid and hydrogen to avoid the formation of the oxo anions. The method is involving the use of pressurized, dilute aqueous solutions of acetic acid and ethanol. Previous study has stated that combination of hydrogen and ethanol was more effective rather stand alone at high beam doses [6][7]. However, it has limiting factor which is the nuclear reaction has very small cross-section of the reaction which requires accelerators or cyclotrons with energies that higher than 11 MeV. By using cyclotron, it produced radionuclide by irradiation reaction with 11 MeV protons. It bombards oxygen-16 with protons and emits alpha particles and nitrogen-13 as final product [5].

The nitrogen-13-ammonia is produced from the reduction process of nitrogen-13-nitrates and nitrites. It is converted into N-13-ammonia in aqueous medium which involving exothermic reaction. The application of nitrogen-13 as radiotracer is very essential in myocardial perfusion imaging. It is a nuclear medicine procedure that illustrates the function of heart muscle (myocardium) [1]. It is first developed by Dr. Herrmann Blumgart to measure cardiac strength by injecting patients with a radioactive compound known as Radium C. The substance was injected into venous system and pass through the right heart into the lungs then into left heart and out into arterial system where it then detected by Wilson chamber. The chamber monitor the circulation time of the radioactivity produced. It is concluded from the procedures that the longer the circulation time, the weaker the heart. The role of radioactive substance, like nitrogen-13 is important in order to determine the cardiac physiology (function).

2.2. Technetium- 99m

Technetium-99m is extensively used in medical application. The higher energy of gamma ray about 140keV is appropriate to be used in diagnosis as radioactive tracer. The techenetium-99m is not only used for skeleton image but also able to apply for brain, thyroid, lungs, liver, spleen, gall bladder and bone marrow. Technetium-99m is a radioisotope which emitting gamma rays. This allows Technetium-99m to be used for single photon emission computed tomography (SPECT). SPECT is a nuclear imaging technique which used gamma to be detected by the gamma camera. When the radioisotope injected in the patient body and the concentrated will attach to the organ of interest and give a signal for gamma camera to detect it. The gamma camera needs to be rotated every three to six degree of patient body until reach 360^{o} for recording the detectable data. This projection takes about 15-20 minutes to finish.

Technetium-99m also has been used widely in bone and brain scans. Bone scans can be used directly to heal the skeletal injury and some cases are allowing the Techenetium-99m to react with tumour of the bones. It is also able to detect strokes by brain scanning [7]. The property of Technetium-99m radioisotope is able to identify the lymph nodes drain cancer such as breast cancer. The radioisotope will be used together with antimony sulphide colloid as radioactive maker in our body to detect the abnormal activity of lymph nodes. This radioactive maker is injected by shielding syringe to lymph node drain area and the area spotted with abnormal activity as the area of cancer growth.

Next, the immunoscintigraphy is a process to detect hard-to-find cancers by injected the Technetium-99m into monoclonal antibody. Monoclonal antibody is one of the immune system proteins that are capable to binding with cancer cells. Medical equipment will detect the gamma ray that is emitted by Technetium-99m and diagnose that the higher concentration indicates the location of tumours. It usually relates with intestine organ treatment. Other than that, Technetium-99m is incorporate with tin compound to detect gastrointestinal bleeding sites. The detection occurs by binding them with red blood cells and maps the circulatory system disorders.

2.3 Rubidium-82

Biomarkers have the potential to aid in the risk assessment, diagnosis, early detection, prognosis and prevention of the breast cancer which is important and, numerous reports have been made on biomarkers, but only a few have been practiced and used in clinical. For the breast cancer risk especially for woman, shows a genetic risk factors. The food content of Rubidium was inversely associated with cancer incidence in early 1974 was found among Hopi Indians [8]. Tumour volume was significantly reduced in vivo study after the administration of Rubidium Carbonate in mice. Levels of Rubidium in tumour tissue were significantly higher than in the normal tissue or particularly breast tumour tissues. Due of that, Rubidium is used in tumour through intake of rubidium in form of food with control dose.

In human, Rubidium is natural substances and micronutrient like Selenium, for evaluating its anticancer efficacy, it would be meaningful to compare rubidium levels in biological samples between cancer patients and normal control patients and it is also important to know the application of the Rubidium as a biomarker in the risk assessment. Through urine, Rubidium is excreted and urine concentration is a good indicator for the exposure of the Rubidium. The acid toxins leaking out of the tumour mass were neutralized and render them to become nontoxic. This is because the presence of Rubidium salts in the body fluids neutralized the toxin. In the colorectal patients, the concentrations of the Rubidium in whole blood are much lower than the patients in healthy controls. The Rubidium was sequestered by the tumour so the levels of rubidium in patient's serum and urine is low.

Since the late 1950, Rubidium used in the context of myocardial perfusion have been studied [9]. In relation to myocardial perfusion, the Rubidium is extracted from blood and is taken up myocardium which requires high of energy. Similar to conventional single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), Rubidium-82 can generate a clear perfusion image because it is an extractable tracer and it can identify viable myocardium when the cell membrane was disruption during the rapid washout of Rb-82 from the tissue. The radiation exposures for patients is limited around (5.5mSv for 60mCi) because it has short half-life, the total study time can be reduced as the image acquisition requires is short after tracer administration. Rb-82 has lower extract fraction which may affect the hyperemic flow measurements and this will make the image resolution reduced.

However, data support with flow quantification of Rb-82 will be feasible, accurate and reproducible because of Rubidium activity can be infused over a longer interval to reduce the peak dead time-losses and the PET imaging will be displayed in three dimensional modes. When using Rubidium in PET, quick reconstruction of the rest uptake frame can often detected while the patient is still on the bed, and can be resolved by instructing the patient to eat or drink water before repeating the image acquisition [9]. PET also provides reliable images, particularly in large patients even though the patient with large breast and arm present in the field of view. By using Rubidium in PET, we can see our heart's image and show how much blood enters the heart muscle either during rest or exercise.

3. Conclusion

Nuclear Medicine is a promising area in the foreseeable future. The incorporation of molecular imaging and radiopharmaceutical will represent a significant paradigm shift for the specialty of this area.

4. References

[1] Boogers M J., Fukushima K, Bengel F M and Bax J J 2011 The role of nuclear imaging in the failing heart: myocardial sympathetic innervation and future applications *Heart Failure Reviews* p 411- 423.

[2] Joliot F, Curie I 1934 Artificial production of a new kind of radio-element *Nature* **133** p 201-202.

[3] Vaalburg W, Kamphuis J A, Beerling-Vander Molen H D *et al.* 1975 An improved method for the cyclotron production of 13n-labelled Ammonia. Int. J. Appl. Radiat. Isot. p 316-318.

[4] Wieland B, Bida G, Padgett H *et al.* 1991 In target production of [13n] Ammonia via proton irradiation of dilute aqueous ethanol and acetic acid mixtures *Int. J. Rad. Appl. Instrum. A* p 1095-1098.

[5] Berridge M S, Landmeier B J 1993 In-target production of [13n] Ammonia: target design, products, and operating parameters *Appl. Radiat. Isot.* p 1433-1441.

[6] Monahan W G, Tilbury R S, Laughlin J S 1972 *Uptake of 13n-labeled Ammonia* J. Nucl. Med. p 274-277 (Pub: Med).

[7] Smith E M 1964 Properties, uses, radiochemical purity and calibration of Tc-99m *J. of Nucl. Med.* p 871- 882.
[8] Brewer A K, Clarke B J, Greenberg M and Rothkopf N 1979 The effects of Rubidium on mammary tumour growth in C57blk/ 6J mice *Cytobios* p 99- 101.
[9] Yoshinaga K, Klein R and Tamaki N 2010 Generator produced Rubidium-82 positron emission tomography myocardial perfusion imaging- from basic aspects to clinical applications *J. of Cardiology* p 163- 173.

Acknowledgements
The authors would like to thank the Applied Physics Programme, Faculty of Applied Sciences and Technology Universiti Tun Hussein Onn Malaysia for facilities provided and gratefully acknowledged the financial support a research grant (H074) that make the research possible.