

A SURVEY ON THE USAGE AND DEMAND OF MEDICAL RADIOISOTOPE & RADIOPHARMACEUTICALS IN MALAYSIA

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ABSTRACT

Medical radioisotope is a small quantity of radioactive substance used in safe, cost effective, for the purpose of diagnostic and therapy of various diseases. In Malaysia, the emerging of new nuclear medicine centers or institutions in both government and private sectors rose abruptly for the past few years. Currently, there are no data available on the usage and demand of medial radioisotope or radiopharmaceuticals. Understanding the usage trending and demand of radiopharmaceuticals and medical radioisotope is essential when related to technology changes in order to meet the market size of these radiopharmaceuticals. Survey result found out that the highest demand and the highest usage among all radioisotopes are Technetium-99m and Radioiodine isotopes such as the Iodine-131, Iodine-131 MIBG, Iodine-123 and Iodine-123 MIBG. Currently, most of the medical isotopes and radiopharmaceuticals are currently imported. Technetium-99m is the backbone of nuclear medicine whereby more than 80% of Nuclear Medicine services utilize this radioisotope. Technetium-99m supply chain is unstable globally and in coming future, two main reactors (Canada & Holland) that produces 60% of world Molybdenum-99 will shut down the operation and supply of Molybdenum-99 will be disrupted. As for radioiodine services, currently, Iodine-123 can't be obtained in Malaysia and neighboring countries due to its short half-life. Iodine-123 is useful in diagnostic of thyroid related diseases. As for PET services, the highest demands are F-18 FDG and Gallium-68 Generator for the moment. However the survey data still did not include most of the PET centers in the Klang Valley, northern area (Penang) and the new upcoming PET center in Southern Region (Malacca and Johor). It is important for Malaysia to self-produced medical radioisotope and radiopharmaceuticals to meet the market and local demand of these medical isotopes.

ABSTRAK

Radioisotop perubatan adalah kuantiti kecil bahan radioaktif yang digunakan dalam keadaan selamat dan kos efektif, bagi tujuan diagnostik dan terapi pelbagai penyakit. Di Malaysia, penubuhan pusat-pusat perubatan nuklear baru atau institusi di kedua-dua sektor kerajaan dan swasta meningkat secara mendadak pada tahun-tahun kebelakangan ini. Pada masa ini, tiada data tersedia bagi mengetahui penggunaan dan permintaan radioisotop atau radiofarmaseutikal. Memahami trend penggunaan dan permintaan radiofarmaseutikal dan radioisotop perubatan adalah penting apabila berkaitan dengan perubahan teknologi untuk memenuhi saiz pasaran radiofarmaseutikal ini. Hasil kajian mendapati bahawa permintaan yang paling tinggi dan penggunaan yang tertinggi di kalangan semua radioisotop adalah isotop Technetium-99m dan radioiodin seperti Iodin-131, Iodin-131 MIBG, Iodin-123 dan Iodin-123 MIBG. Pada masa ini, sebahagian besar daripada isotop perubatan dan radiofarmaseutikal

diimport daripada luar negara. Technetium-99m merupakan tulang belakang kepada perubatan nuklear di mana lebih daripada 80% daripada perkhidmatan Perubatan Nuklear menggunakan radioisotop ini. Rangkaian bekalan Technetium-99m adalah tidak stabil di peringkat global dan pada masa akan datang, dua reaktor utama (Kanada & Holland) yang menghasilkan 60% daripada dunia Molybdenum-99 akan menutup operasi dan pembekalan Molybdenum-99 akan terganggu. Bagi perkhidmatan radioiodin, pada masa ini, Iodin-123 tidak boleh diperolehi di Malaysia dan negara-negara jiran disebabkan separuh hayatnya yang pendek. Iodin-123 adalah berguna dalam diagnosis penyakit berkaitan tiroid. Bagi perkhidmatan PET, permintaan tertinggi adalah F-18 FDG dan Gallium-68 Generator buat masa ini. Walau bagaimanapun data kaji selidik itu masih tidak termasuk kebanyakan PET pusat di Lembah Klang, kawasan utara (Pulau Pinang) dan pusat PET akan datang baru di Wilayah Selatan (Melaka dan Johor). Adalah penting bagi Malaysia untuk menghasilkan sendiri radioisotop perubatan dan radiofarmaseutikal untuk memenuhi permintaan pasaran tempatan.

Keywords: Radioisotope, Radio-pharmacy, PET, Isotope generator

INTRODUCTION

Radioisotopes and radiopharmaceuticals play an important role in nuclear medicine, where they are used routinely in the clinics for the non-invasive diagnosis and treatment of various diseases, including some of the most important and frequent ones, like cancers and cardiovascular diseases (R.J. Kowalsky and S.W. Falen, 2013). According to International Atomic Energy Agency (IAEA) database, currently, over 10 000 hospitals worldwide use radioisotopes in medicine. Currently more than 80% of the medical radioisotopes are produced by research reactors. The remaining isotopes are made by particle accelerators, mostly with cyclotrons and sometimes with linear accelerators or by other methods (Kahn and Laura H, 2008). These isotopes can be used in 2 forms: as sealed sources or as unsealed sources. Sealed sources are used essentially for the localised treatment of cancers, like prostate or breast cancer. This is called brachytherapy. Unsealed radio-isotopes are a crucial component of the radiopharmaceuticals that are widely used in a Nuclear Medicine field.

The emerging of new nuclear medicine centers or institutions in both government and private sectors rose abruptly for the past few years in Malaysia. Currently, there are no data available on the usage and demand of medial radioisotope or radiopharmaceuticals. Understanding the usage trending and demand of radiopharmaceuticals and medical radioisotope is essential when related to technology changes in order to meet the market size of these radiopharmaceuticals. The future technology changes in nuclear medicine are related with the demand and the readiness of the healthcare professionals. Besides that, it also limited to the availability of the imaging modalities, such as the gamma camera, SPECT-CT and PET-CT. Thus it is important to provide a data on the trending usage and demand of these medical radioisotope and radiopharmaceuticals in both private and government institutions within Malaysia.

MATERIALS AND METHOD

The study was conducted in centers or institutions that utilize Gamma Camera /SPECT/ PET CT or utilizes any medical radioisotopes in both government and private sector. A survey for a period of 3 months (between 14th February and 15th May 2015) was conducted across Malaysia. The questionnaire used in this study had been developed with all the expertise from the Medical Technology Division of Malaysian Nuclear Agency. The survey was distributed among healthcare professionals that involved working with medical radioisotope and

radiopharmaceuticals in private, government and university based hospitals or institutions and was distributed manually either by hand, mail or e-mail.

Inclusion criteria for the potential respondents are:

- i. Healthcare professionals working in Nuclear Medicine Department
- ii. Healthcare professionals working in any Imaging Department involve with the usage of PET/CT, SPECT/CT and Gamma Camera
- iii. Healthcare professionals dealing with therapeutic isotope
- iv. Healthcare professionals dealing with diagnostic isotope (both PET and SPECT isotope)
- v. Healthcare professionals that have the authority in making clinical decision

The questionnaire was divided into five (5) main part which include the profile of the respondents, the usage and demand of radioisotopes in General Nuclear Medicine Services, the usage and demand of radioisotopes in PET Nuclear Medicine Services, the usage and demand of isotopes in Radioiodine Services and the usage and demand of radioisotopes used in Therapeutic Radiopharmaceuticals. The values were expressed as actual numbers and corresponding percentages. Data is presented in either pie chart or bar chart.

RESULTS

General Information of Respondent

The survey questionnaire was distributed to 21 centers (hospitals and institutions) that met the criteria as above. Out of the 21 centers, only 13 centers responded and participated in this survey. The respondent rate was 61.9% as in Table 1 below. In general, out of that 13 centers that participated in this survey, 38% was from hospitals under the Ministry of Health, while the both Private Hospitals and University Hospitals was 31% as can be shown in Figure 1. The distribution of the imaging modalities among the centers was identified based on types of camera involved in Nuclear Medicine Imaging; either Positron Emission Tomography-CT Scan (PET-CT) and Single Photon Emission Computed Tomography (SPECT) or Gamma Camera. The distribution was, out of 13 centers responded, 69% of them having only Gamma Camera or SPECT, 8% of them having only PET-CT while 23% of the centers having both SPECT and PET-CT. The distribution is detailed out in Figure 2.

Table 1: Respondent Rate

No. of Questionnaire Distributed (Hospitals / institution / Centers)	No. of Respondent (Hospitals / institution / Centers)	Respondent Rate (%)
21	13	61.9%

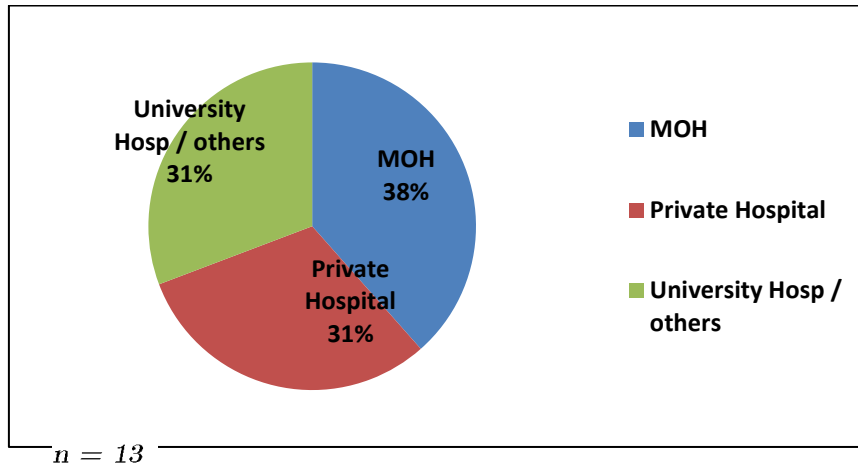


Figure 1: Percentage Distribution of Respondent

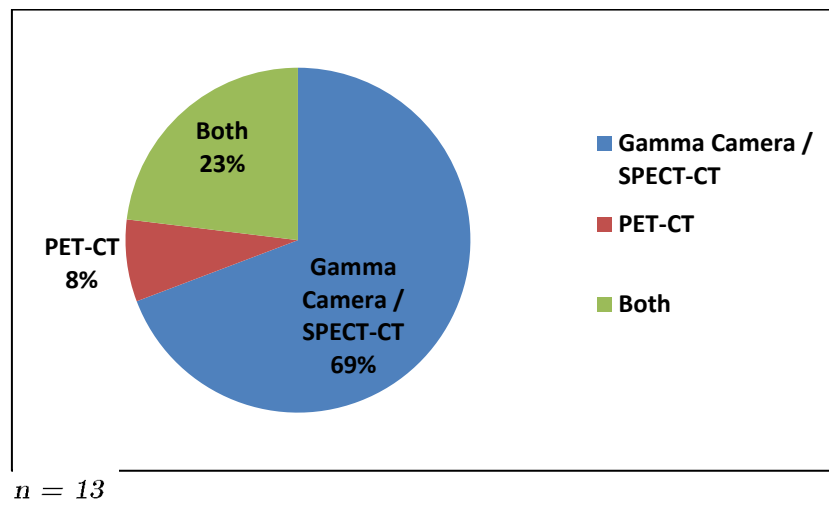


Figure 2: Percentage Distribution of imaging Modalities

A total number of 23 healthcare professionals participated in this survey and 52% of them are Nuclear Medicine Physician /Specialist / Medical Officer, 31% of them are pharmacist (radiopharmacist) while 17% of them are from other groups either technologist, radiographer or medical physicist. Result can be shown in Figure 3.

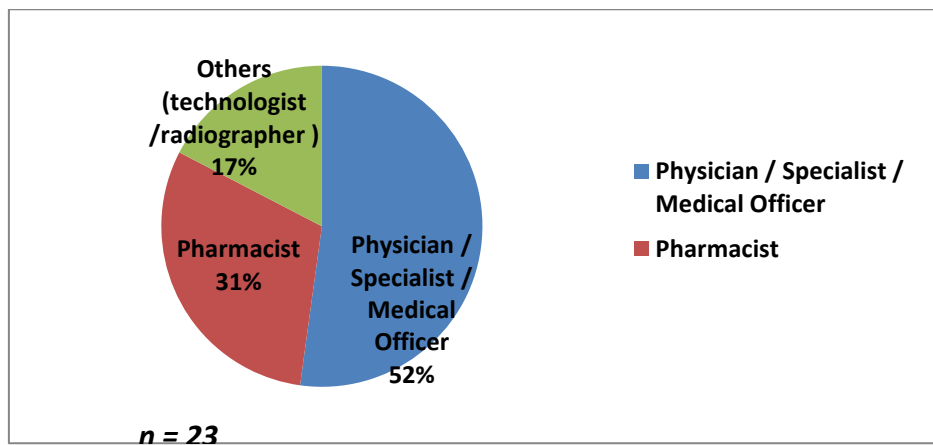


Figure 3: Percentage Distribution of Expertise Involved In the Survey

Medical Radioisotope and Radiopharmaceutical Trending Usage

General Nuclear Medicine Services

Figure 4 shows the usage of medical radioisotope in General Nuclear Medicine Services (that involved in Gamma Camera / SPECT Scan). Currently, there are 3 types of medical radioisotope used in General Nuclear Medicine that are; Technetium-99m (Tc-99m), Gallium-67 (Ga-67) and Chromium-51 (Cr-51). The highest usage is Tc-99m, where 8 centers currently utilize this radioisotope, followed by Cr-51 whereby 2 centers involved in the utilization of it and lastly Ga-67 whereby only 1 center use this radioisotope.

The average Technetium-99m Generator order on weekly basis among the 8 centers was assessed. Figure 5 shows that 7 centers ordered an average of 500-1000mCi activity of Tc-99m generator per week with an average cost of RM 52 500 per week, while only 1 center ordered a Tc-99m generator with an activity of more than 1000mCi per week with an average cost of RM 7 500 per week.

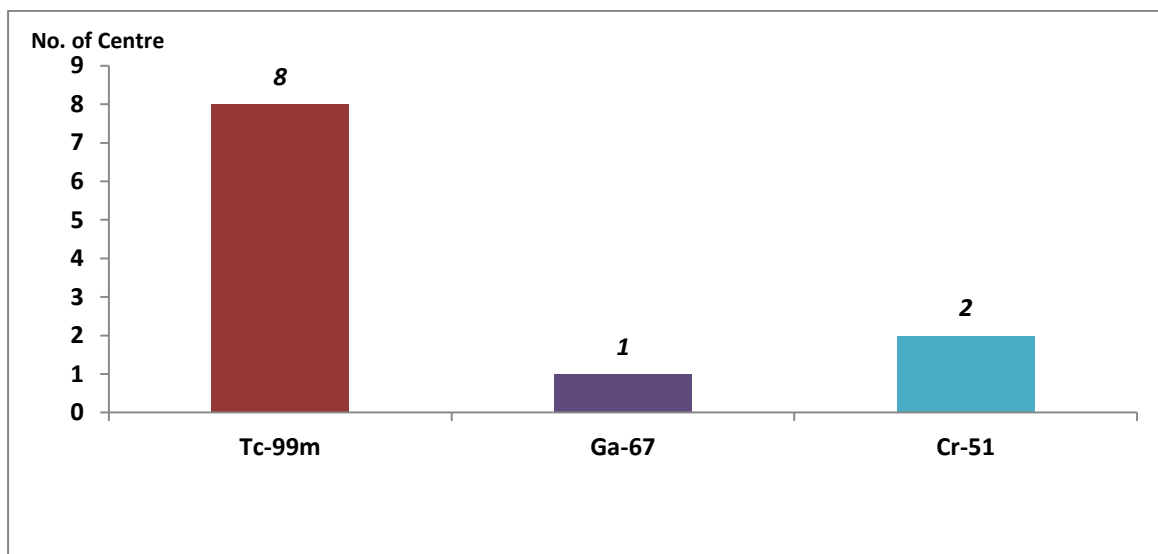


Figure 4: Response to “What type of radioisotope do you currently used at your center?”

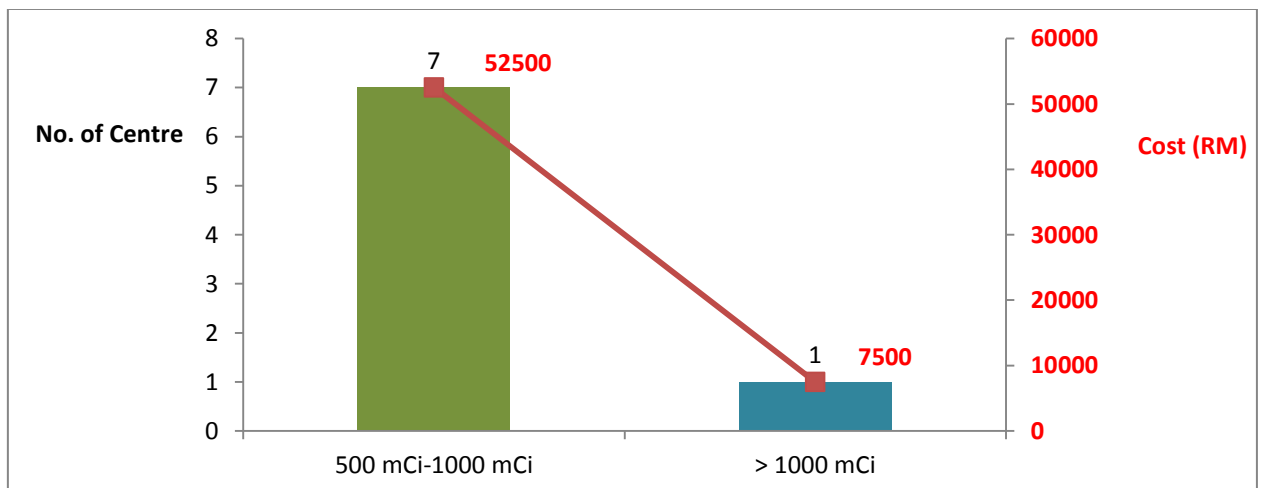


Figure 5: Response to “What is the minimum activity of generator do you order on a weekly basis and how much cost (in Ringgit Malaysia) on average to obtain these radioisotope?”

Positron Emission Tomography (PET) Nuclear Medicine Services

As for PET Nuclear Medicine Services (that involved with PET-CT Scan Services), only two medical radioisotope and radiopharmaceutical is currently in use that are Flourine-18 FDG and Gallium-68 Generator. Figure 6 shows that 4 centres involved in the usage of Flourine-18 FDG while only 1 centre use Gallium-68 Generator.

Flourine-18 FDG utilization was assessed among these centers. Figure 7 show that 2 centers utilize Flourine-18 FDG with an average activity of 100-200 mCi per order. While only 1 center utilizes Flourine-18 FDG with an average activity of 200-500 mCi per order. The average total cost were around RM 6 000 and RM 7 500 per order.

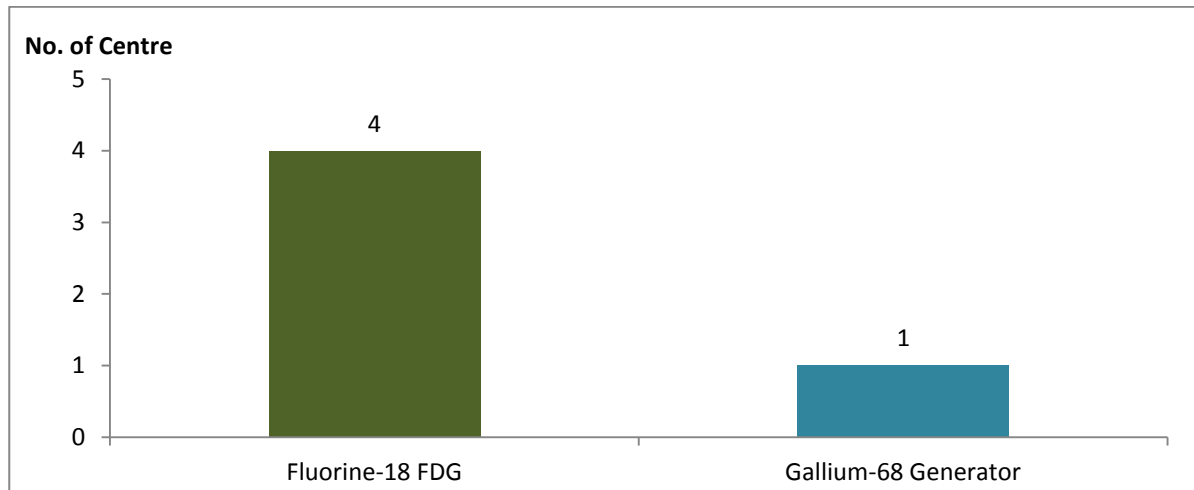


Figure 6: Response to “What type of PET radioisotope do you currently used at your center?”

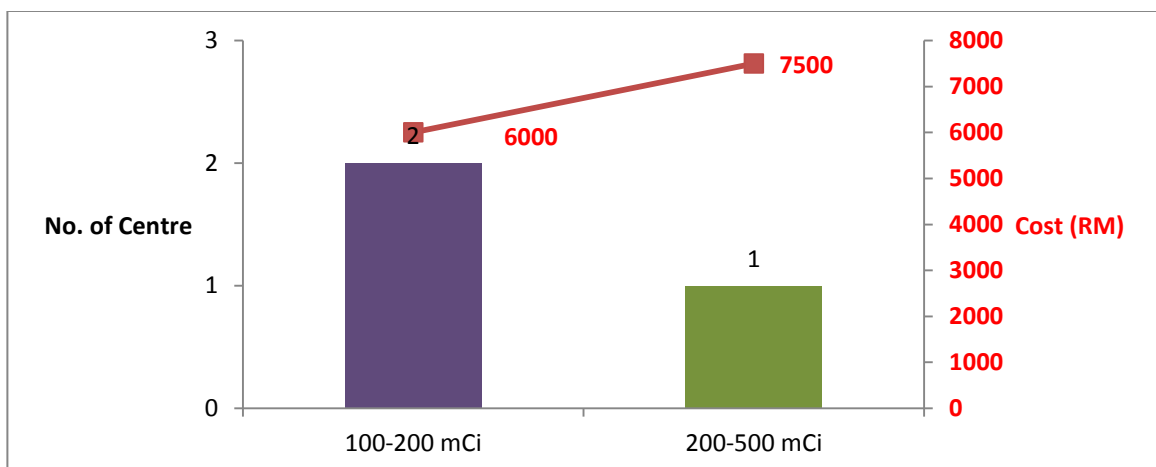


Figure 7: Response to “What is the minimum ¹⁸F-FDG activity do your order and how much cost (in Ringgit Malaysia) to obtain the ¹⁸F-FDG injection (RM/mCi)?”

Radioiodine Services

Figure 8 shows the trending of radioiodine usage in Malaysia. Iodine-131 has the highest usage among centers where 8 centers involve in the utilization of it, while only 2 centers utilizes Iodine-131 MIBG

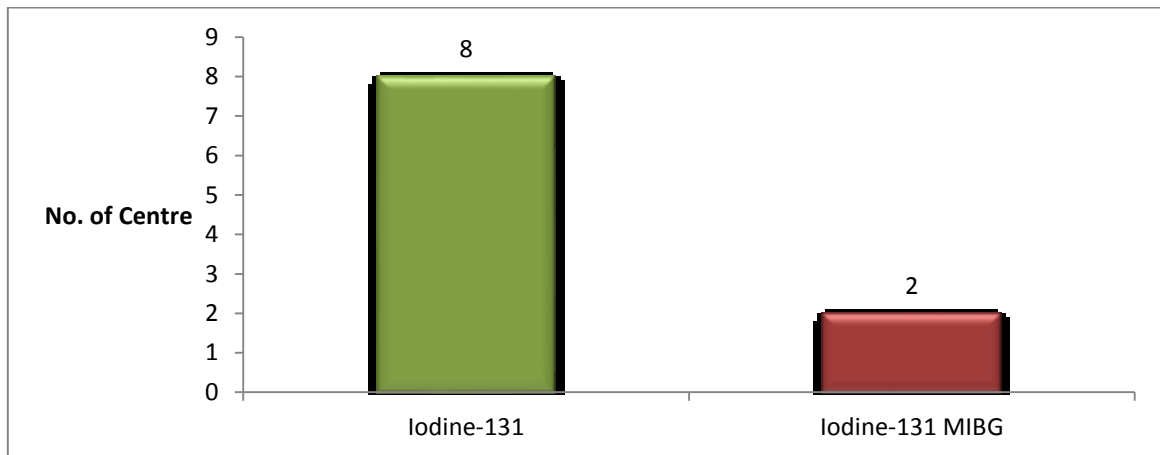


Figure 8: Response to “What type of radioiodine isotope do you currently used at your center?”

The average Iodine-131 and Iodine-131 MIBG ordered on weekly basis were 4 200 mCi and 4.5 mCi. The average cost were RM 84 000 per week and RM 15 750 per week for Iodine-131 and Iodine-131 MIBG as in Figure 9.

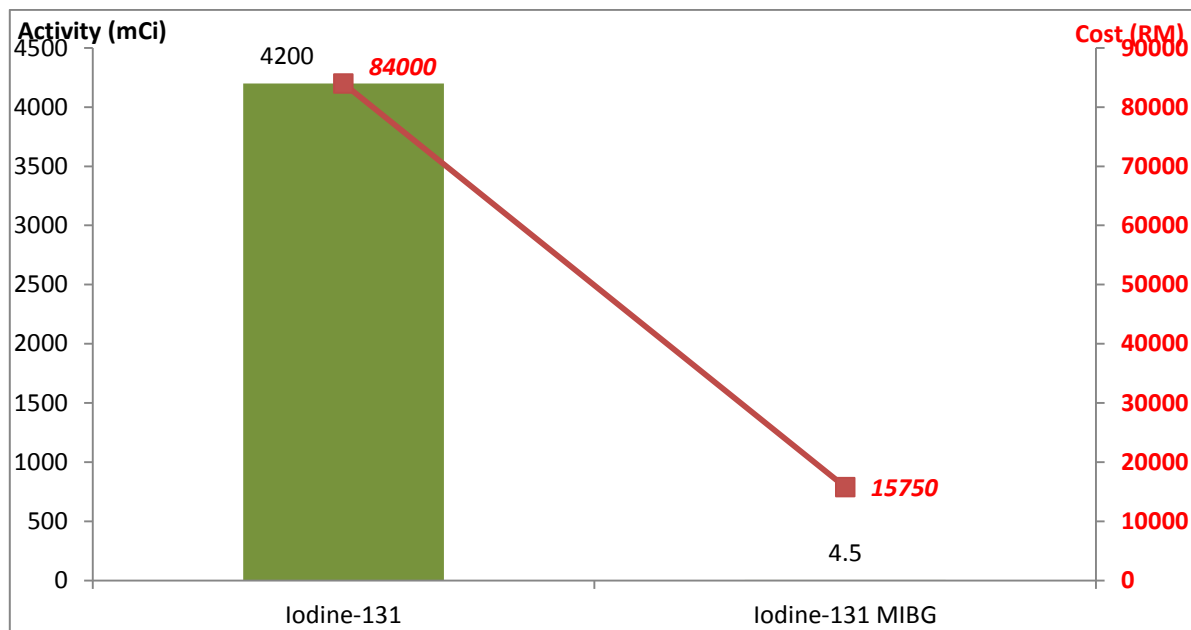


Figure 9: Response to “What is the minimum activity of radioiodine do you order on a weekly basis and how much cost (in Ringgit Malaysia) on average to obtain these radioisotope?”

Therapeutic Radiopharmaceutical Services

Figure 10 shows the usage of therapeutic radiopharmaceuticals among centers in Malaysia. The lists of therapeutic radiopharmaceuticals are Yterium-90 (Y-90) Microspheres, Yterium-90 (Y-90) Synovectomy, Rhenium-186 (Re-186), Irridium-192 (Ir-192) and Samarium-153 (Sm-153).

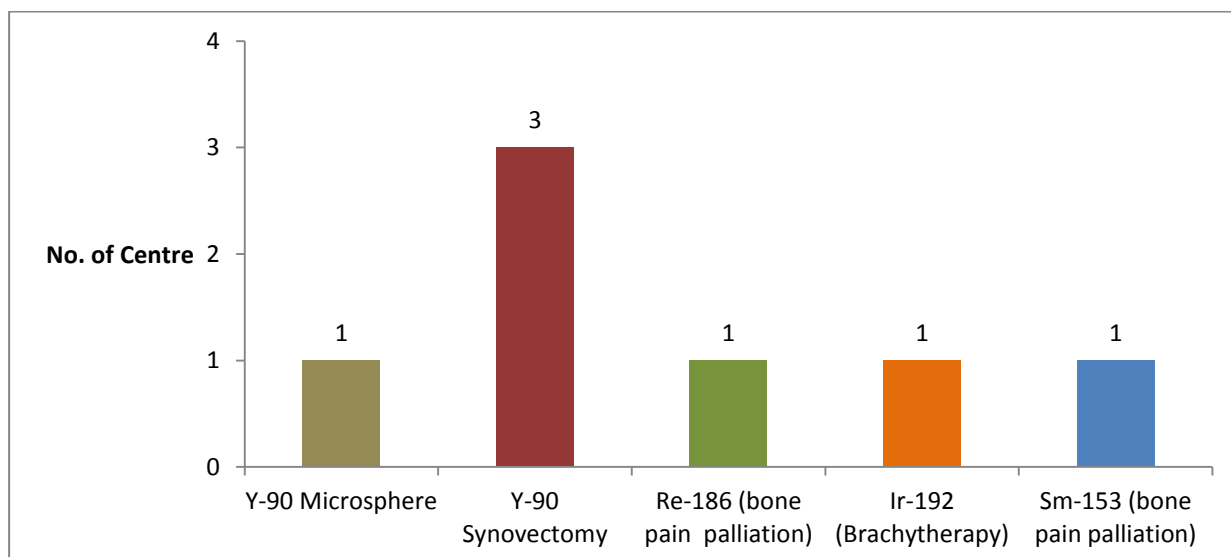


Figure 10: Response to “What type of therapeutic radiopharmaceutical do you currently used at your center?”

The average numbers of patients in the year2014 indicated for these therapeutic radiopharmaceuticals are as in Figure 11. 21 patients indicated for Yterium-90 Microsphere, 51 patients indicated for Yterium-90 Synovectomy, 5 patients indicated for Rhenium-186 for bone pain palliation, 4 patients indicated for brachytherapy using Irridium-192 while 2 patients indicated for Samarium-153 for bone pain palliation.

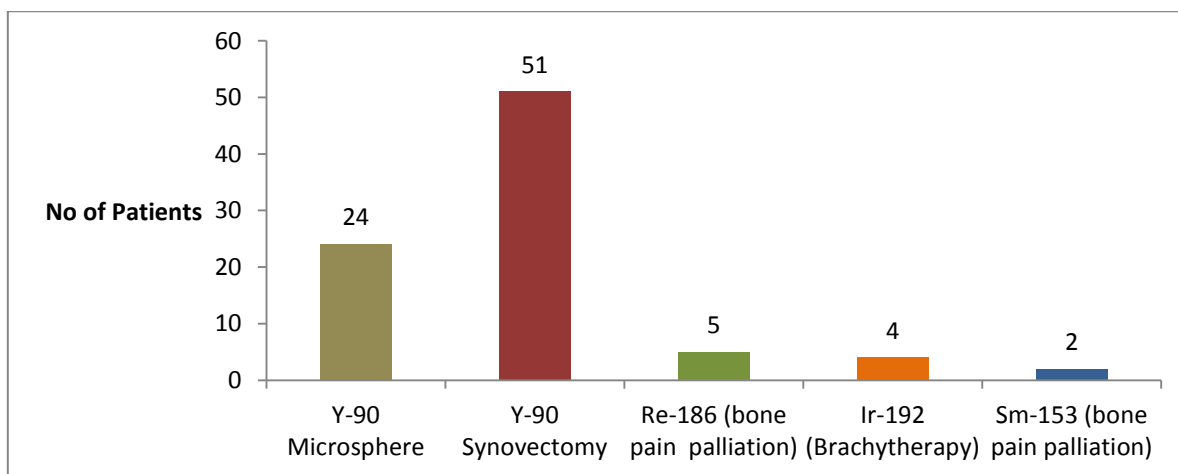


Figure 11: Response to “What is the average number of patients undergoing the above therapeutic radiopharmaceutical on yearly basis?”

Medical Radioisotope and Radiopharmaceutical Demand

General Nuclear Medicine Services

Demand in medical radioisotope among General Nuclear Medicine Services as shown in Figure 12. Among the radioisotope in demand are Technetium-99m (Tc-99m), Indium-111 (In-111), Gallium-67 (Ga-67) and Chromium-51 (Cr-51). The highest demand are Technetium-99m (8 centers) followed by Chromium-51 (5 centers), Gallium-67 (4 centers) and lastly Indium-111 (2 centers).

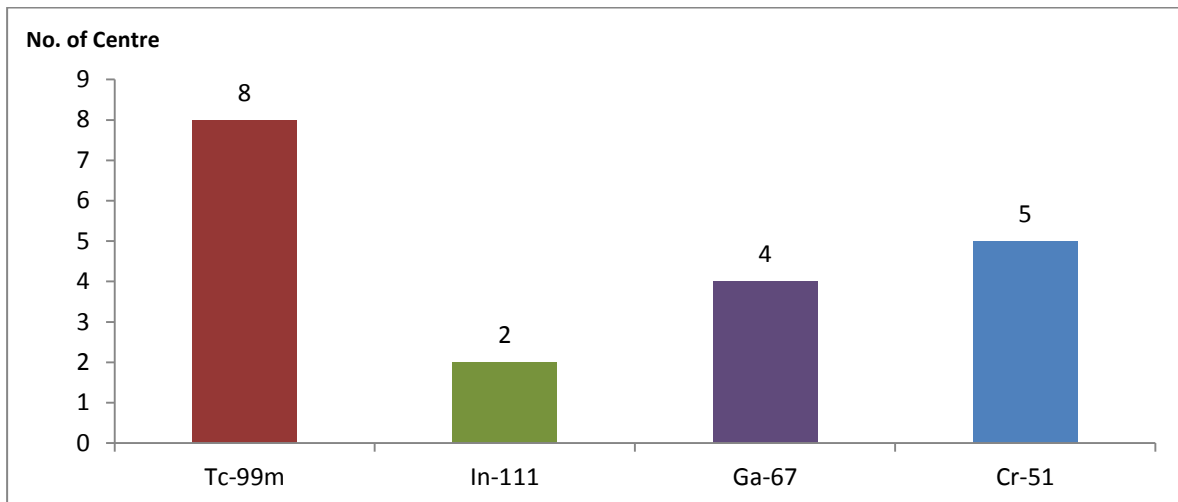


Figure 12: Response to “What type of radioisotope that is most needed at your center?”

Positron Emission Tomography (PET) Nuclear Medicine Services

Figure 13 shows the demand in PET radioisotope and radiopharmaceutical among centers in Malaysia. There are 4 Fluorine-18 Based radiopharmaceuticals in demand which is Fluorine-18 FDG, Fluorine-18 FDOPA, Fluorine-18 FCholine and Fluorine-18 Sodium Fluoride. While 2 Carbon-11 based radiopharmaceuticals which is Carbon-11 Choline and Carbon-11 Acetate. The other PET radiopharmaceuticals that are in demand is Gallium-68 Generator, Zirconium-89 Labeled Antibody and Copper-64.

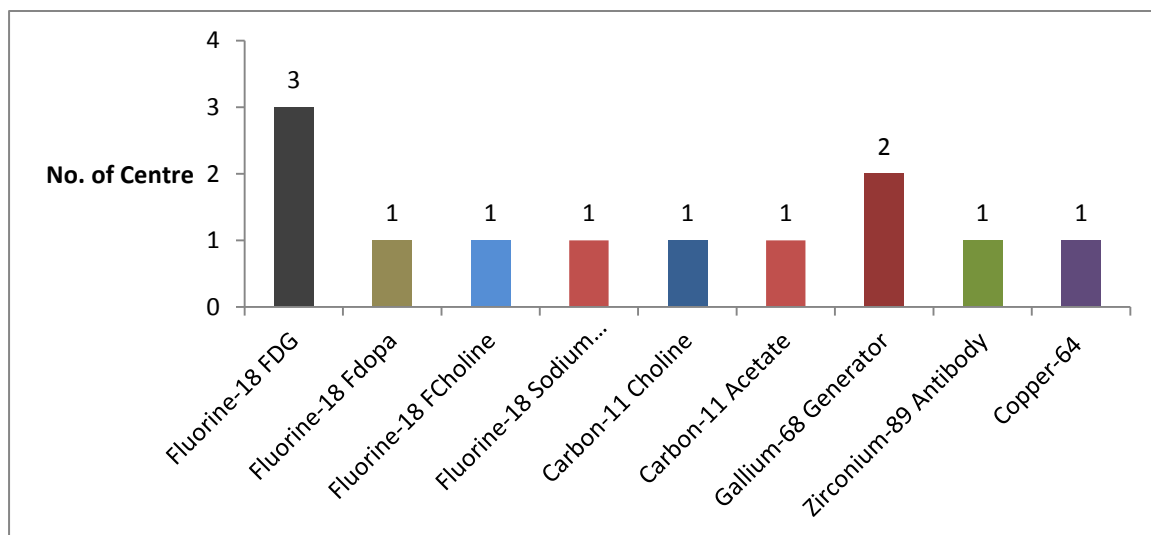


Figure 13: Response to “What type of PET radioisotope that is most needed at your center?”

Radioiodine Services

Figure 14 shows the demand in types of radioiodine among centres. Iodine-131 and Iodine-123 shows high demand where 8 centers require both of the radioiodine. While 5 centers demand for Iodine-123 Meta-Iodobenzylguanidine. There other types of radioiodine only 1 center in demand of it which is Iodine-124, Iodine-123 Orto Iodo-hippurate and Iodine-123 Iodobenzofuran.

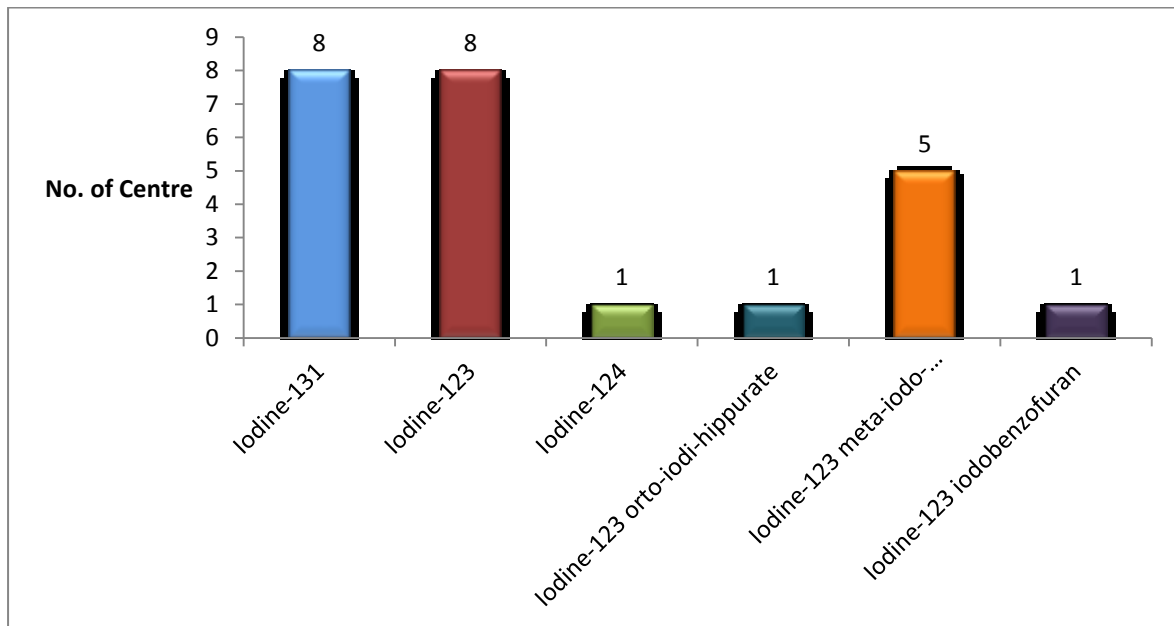


Figure 14: Response to “What type of radioiodine that is most needed at your center?”

Therapeutic Radiopharmaceutical Services

Figure 15 shows the list of therapeutic radiopharmaceutical in demand among centers in Malaysia. The lists of therapeutic radiopharmaceutical in demand are Yterium-90 Zevalin, Lutetium-177 Octreotate, Yterium-90 Microsphere, Rhenium-186 for bone pain palliation, Irridium-192 for Brachytherapy, Samarium-153 for Bone pain Palliation and Yterium-90 for Synovectomy.

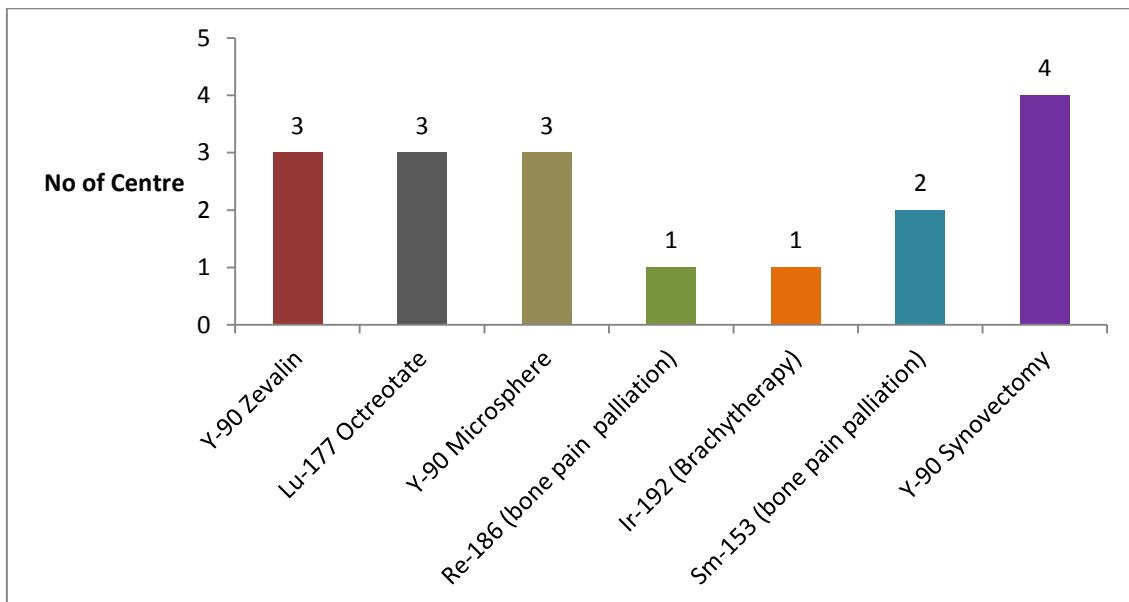


Figure 15: Response to “What type of therapeutic radioisotope / radiopharmaceutical that is most needed at your center?”

Average Cost

Table 1 shows the average cost of some medical radioisotope and radiopharmaceutical.

Table 1: Average Cost (RM/unit) for Medical Radioisotope in Malaysia

Radioisotope	Cost (RM)
Technetium-99m Generator	RM 7500 /each
Gallium-67	RM 4000 / 5 mCi
Chromium-51	RM 3000 / mCi
Fluorine-18 FDG	RM 15 / mCi
Gallium-68 Generator	RM 70 000 – 12 0000 / each
Iodine-131 MIBG	RM 3500/ mCi
Iodine-131	RM 20/ mCi
Yterium-90 Microspheres	RM 24 000 / patient

DISCUSSION

General Information of the Respondent

38% respondents in this survey are from the Ministry of Health Hospitals with a Nuclear Medicine Services. Currently, under the Ministry of Health, there are only 6 government hospitals that provide Nuclear Medicine Services that are Kuala Lumpur Hospital, National Cancer Institute Putrajaya, Penang General Hospital, Sultanah Aminah Hospital Johor Bahru, Sarawak General Hospital and Likas Hospital (Hospital Wanita dan Kanak-Kanak, Sabah). Others respondent were from the Private Hospitals or Institutions and University Hospitals. Most of the expertise groups that involve in this survey are from the Nuclear Medicine Physician / Specialist and Medical officer group which is 52%, while 31% of them are from the pharmacist group. The pharmacist was specifically chosen from those that working in the Nuclear Medicine Department or involve at least in the procurement, preparation, quality control and dispensing of medical radioisotope & radiopharmaceuticals to patient. In other words, they are best known as a Radiopharmacist or a Nuclear Pharmacist.

The imaging modalities among these centers was assessed and most of the centers having either gamma camera or SPECT-CT or both, as their imaging modalities. Only a few centers own a PET-CT Scan. Currently under the Ministry of Health, there are only two centers having a PET-CT Scan that are National Cancer Institute Putrajaya and Penang Hospitals. While the remaining are from the private and university hospitals.

Medical Isotope and Radiopharmaceutical Trending Usage and Demand

General Nuclear Medicine Services

In general nuclear medicine services, the most common medical radioisotope use is the Technetium-99m. Technetium-99m is the backbone of nuclear medicine where almost all procedure in Nuclear Medicine involves Technetium-99m such as the bone scan, brain scan, renal scan, and heart scan.

Two centers utilize Chromium-51 and mainly used to measure the glomerular filtration rate (GFR) to assess the renal function. Where else, only one center utilizes Gallium-67 and it is commonly used in the infection and inflammation imaging.

The average cost of Technetium-99m generator ordered on weekly basis was currently RM 52 500 for a generator capacity of 500 mCi – 1000 mCi among the 7 centers while only 1 center used Technetium-99m generator with an activity of more than 1000 mCi per week which amount to RM 7 500.

The highest demand of medical radioisotope in General Nuclear Medicine Services is Technetium-99m. In this survey, 69% of Nuclear Medicine Centers utilizes Gamma Camera or SPECT for diagnostic procedure and the radioisotope mainly used with the Gamma Camera or SPECT are Technetium-99m. As been mentioned before, Technetium-99m is an established radioisotope with multiple uses and is a backbone of a Nuclear Medicine Services. Currently the Technetium-99m Generator is being imported. But the Technetium-99m supply chain is unstable globally. Lately, there are several forums and seminars held internationally addressing the issue on the market supply of the Molybdenum-99 which is the parent of Technetium-99m. There are two main reactors (Canada & Holland) that produces 60% of world Molybdenum-99 and in upcoming years, both reactors will be shut down and supply of Mo-99 will be disrupted. This is why several countries look for an alternative way of producing Technetium-99m. Among them is Canada which they took a lead in producing the Technetium-99m using a Cyclotron instead of a Nuclear Reactor. The cyclotron produced Technetium-99m uses Molybdenum-100 as a target material while reactor produced uses Molybdenum-99. The monograph of cyclotron produced Technetium-99m is still not yet available.

Other medical radioisotopes that are in demand are Indium-111 (In-111), Gallium-67 (Ga-67) and Chromium-51 (Cr-51). Indium-111 is commonly used in Octreotide scan, to detect tumour with a somatostatin receptor, although it still can be used in infection imaging but less likely. Chromium-51 and Gallium-67 is actually is in higher demand as compared to the current usage; five centers for Chromium-51 and four centers for Gallium-67. The main reason why the usage for Chromium-51 and Gallium-67 is low while the demand is there is because the cost of these medical radioisotopes is quite expensive and is currently imported. The average cost for Gallium-67 and Chromium-51 are RM 4000 / 5 mCi and RM 3000 /mCi each.

Positron Emission Tomography (PET) Nuclear Medicine Services

Currently in Malaysia, the Positron Emission Tomography (PET) radioisotope and radiopharmaceutical that are currently in used are Fluorine-18 Deoxyglucose (F-18 FDG) and Gallium-68 generator. F-18 FDG is the most use PET radiopharmaceutical in diagnosis of cancer, inflammation and neurodegenerative brain disease. F-18 FDG is produced by a cyclotron and has a short half-life of 109.7 minutes. Currently there are 4 cyclotrons operating in Malaysia. The details as in table 2. Cyclotron and PET Radiopharmaceutical Preparation Facility need to be Good Manufacturing Practice (GMP) certified and the product manufactured need to be registered with the Ministry of Health before it can be marketed out. Unlike the general nuclear medicine services, such as the Technetium-99m, Chromium-51 and Indium-111, which only involve with the preparation of radiopharmaceuticals, PET Cyclotron center need to comply with the cGMP requirement as it involve with the manufacturing of radiopharmaceuticals. Moreover, the classifications of radiopharmaceuticals for diagnosis are being move from Over the Counter (OTC) category to Poison category. Thus the registration of the radiopharmaceuticals product is more stringent in to meet the requirement of the regulatory body; National Pharmaceutical Control Bureau (NPCB), Ministry of Health.

Table 2: Types of Cyclotron Available in Malaysia

Facility	Model	Manufacturer	Beam Type	Energy	Radioisotope Produced
National Cancer Institute, Putrajaya	GE PETtrace	GE Healthcare	H ⁺ / d ⁻	16.5 MeV (H) 8.5 MeV (d)	F-18 FDG
BioMolecular Industry	Cyclone	IBA	H ⁺ / d ⁻	18 MeV (H) 9 MeV (d)	F-18 FDG
Beacon International Medical Centre	RDS 111	Siemens / CTI	H ⁺	11 MeV (H)	F-18 FDG
Austral-Euro Diagnostic	370V	Sumitomo	H ⁺ / d ⁻	18 MeV (H) 9.5 MeV (d)	F-18 FDG

Beside PET Radioisotope F-18 FDG, only one center utilizes Gallium-68. Gallium-68 is used in labeling with peptides either DOTA-(Tyr³)-octreotate (DOTA-TATE) or DOTA-(Tyr³)-octreotide (DOTA-TOC), where both are used in the diagnosis of neuroendocrine tumor. Gallium-68 doesn't need a cyclotron to produce it as it is eluted from a ⁶⁸Germanium/⁶⁸Gallium generator. Gallium-68 has a half-life of 68 minutes and the parent radionuclide is Germanium-68 which has a half-life of 271 days. The generator can last up to a year where the elution of Gallium-68 can be done every 4-5 hours after each elution. For each elution of Gallium-68 from the generator, is enough for 3 to 5 patients to perform DOTA-TOC or DOTA-TATE PET/CT scan, depending on the generator activity. The labeling of Gallium-68 with peptides is done within several minutes and it can be done either manually or automated but radiation safety issue and the product sterility must not be compromised. Commonly, Gallium-68 radiolabelling is done under laminar air flow which provides a clean environment with final filtration to ensure the sterility of the product is intact. Preparation and radiolabeling of Gallium-68 doesn't need to comply with GMP requirement and the products are not required to be registered as it is use in-house. Due to the short half-life of Gallium-68 (68 minutes), it is impossible for Gallium-68 labeled peptides to be commercial out. However, the preparation of Gallium-68 in a Nuclear Medicine Facility is still need to comply with the Good Preparation Practice (GPP) requirement as the product is intended for human use.

The average price of F-18 FDG spend was calculated per order basis. For two PET/CT centers, the average price was RM 6 000 with an average activity usage of around 100-200 mCi per day. Meanwhile, one PET/CT center utilizes F-18 FDG with an activity between 200-500 mCi per day and the average cost is around RM 7 500 per day. Commonly, the PET/CT scan does not operate every day. Some PET/CT center does the scan 3 days in a week while some does less depend on each center. The average price for F-18 FDG spends was calculated based on three PET/CT centers and there are still remaining PET/CT center that did not include in this survey due to the non-responsive. The average cost of ⁶⁸Germanium/⁶⁸Gallium generator is in a range of RM 70 000 to RM 120 000 each depends on the generator activity and the manufacturer.

As for the PET medical radioisotope / radiopharmaceutical demand, Fluorine-18 based radiopharmaceutical is still in demand. Besides F-18 FDG, the demand of F-18 based radiopharmaceuticals is Fluorine-18 FDopa for brain imaging, F-18 FCholine for prostate cancer imaging and F-18 Sodium Fluoride for bone imaging. While Carbon-11 based radiopharmaceuticals that are in demand are Carbon-11 Choline and Carbon-11 Acetate both for prostate cancer imaging. However, currently in Malaysia, there is no cyclotron available with a Carbon-11 target. Most cyclotron center in Malaysia currently has Fluorine-18 and Nitrogen-13 target. ⁶⁸Germanium/⁶⁸Gallium generator is also among the PET radiopharmaceuticals that are in demand followed by Zirconium-89 and Copper-64. Zirconium-89 has a half-life of 3.3 days and commonly Zirconium-89 is being used to label it with monoclonal antibody for detecting various disease; commonly cancer.

Radioiodine Services

As for radioiodine services, only two types of Iodine that are currently use that are Iodine-131 and Iodine-131 MIBG (meta-iodobenzylguanidine). In Malaysia, the highest usage is Iodine-131 as it is readily available with a half-life of 8.02 days and it is currently used for both diagnosis and treatment of thyroid related disease. The average utilization of Iodine-131 among 8 centers is 4200 mCi per week with an average cost of RM 84 000 while the utilization of Iodine-131 MIBG for 2 centers is 4.5 mCi per week with an average cost of RM 15 750.

Iodine-131 is mainly used as a therapy in the treatment of thyroid cancers, specifically papillary and follicular thyroid cancer. In current practice, a low dose of Iodine-131 is also being used as for diagnostic purposes. It is due to unavailability of diagnostic radioiodine; Iodine-123; in the local market. Iodine-131 labeled with MIBG or also known as I-131-MIBG therapy is used in the treatment of tumors that specifically take up MIBG such as neuroblastoma and pheochromocytoma.

The limitation of radioiodine isotope usage depends on mainly two factors that are:

i. Availability of Radioiodine isotope

Not all radioiodine isotopes are readily available in Malaysia such as Iodine-123 and Iodine-124. Currently, the isotope of iodine that is being used is iodine-131.

ii. Radioiodine Preparation Facility

Preparation facility for oral radioiodine is only required if liquid dosage forms are being used. Preparation facility is not needed for radioiodine capsule. The parameter to be considered when handling liquid radioiodine is the dispensing area. At least two rooms are required for dispensing of radioiodine to outpatient to ensure there is always a room available if spillage (e.g.; patient vomiting) occurred in the other room. Centralized radioiodine preparation area and dedicated air conditioning shall be considered. The preparation of radioiodine shall be carried out in a negative pressure control area with a positive pressure airlock. At least, the radioiodine facility shall have dedicated rooms for Radioiodine Preparation Room, Personnel Changing Room / Positive Airlock, Dispensing Room and Radioactive Waste Room / Area. Not all Nuclear Medicine centers in Malaysia have a proper radioiodine preparation facility.

The highest demand for radioiodine isotopes are Iodine-131 and Iodine-123. Iodine-131 is to be used mainly for treatment of thyroid disorder while iodine-123 is to be used for diagnostic purposes. Iodine-123 is not available in Malaysia due to its relatively short half-life of 13.22 hours and no neighboring countries are capable of producing Iodine-123. The nearest country producing Iodine-123 are Korea and Japan. Other demand is Iodine-124 which is to be used with a PET CT Scan. Iodine-124 has a half-life of 4.18 days and it is mainly for diagnostic purposes. The usage of PET-CT camera for radioiodine cases is interesting as the image resolution is higher than the ordinary Gamma Camera or SPECT. Other radioiodine carriers that are in demand are for Iodine-123 Meta-Iodobenzylguanidine (MIBG) which is use in diagnosis for the location of tumors such as phaeochromocytomas and neuroblastomas, Iodine-123 Orto Iodo-hippurate to be used in renography and Iodine-123 Iodobenzofuran (IBF) which is to be used in imaging of dopamine receptors.

Therapeutic Radiopharmaceutical Services

Among the therapeutic radioisotope or radiopharmaceuticals that is currently being used among Nuclear Medicine Centers in Malaysia are Yterium-90 (Y-90) Microspheres, Yterium-90 (Y-90) Synovectomy, Rhenium-186 (Re-186), Iridium-192 (Ir-192) and Samarium-153 (Sm-153).

Yterium-90 Microsphere is used in the treatment of hepatocellular carcinoma or carcinoma of the liver. The embolization of the microsphere within the cancer cells and the compound will then emit the radiation dose to kill the cancer cell. There are two brand of Yterium-90 microspheres in the market that are SIR-Spheres (Y-90 resin microsphere) from Sirtex Medical limited and Therasphere from BTG International Ltd. The difference between SIR-Spheres and Therasphere is that SIR-Spheres use biocompatible resin microspheres with size range between 20 to 60 μm while Therasphere use small glass microspheres with a size range between 20 to 30 μm .

Yterium-90 Synovectomy is being used mainly in the treatment of joint synovitis. Synovitis means inflammation of the connective tissue lining a joint cavity or synovium. The radiopharmaceutical is administered via joint puncture.

Samarium-153 is one of the radioisotopes that are approved in the USA and Europe for the palliation of pain from metastatic bone cancer, whereas rhenium-186 is famously used by other countries.

A brachytherapy is known as a radioactive seeds that are placed in or near the tumor, which will then give a high radiation dose to the tumor in order to kill the cancer cells. In other words it is in a form of a sealed source. The radioisotope that is currently used in Malaysia for brachytherapy is the Iridium-192 in which its decay is in β radiation.

The average numbers of patients undergone Yterium-90 Synovectomy is the highest among the therapeutic radiopharmaceuticals in which is around 51 patients per year and followed by Yterium-90 Microsphere for hepatocellular carcinoma which is around 24 patients per year. The usage of therapeutic radiopharmaceuticals is not as high as the diagnostic radiopharmaceuticals are due to the cost. The cost to obtain therapeutic radiopharmaceuticals is expensive and all are being imported. For example the average cost of Yterium-90 Microsphere therapy is around RM 24 000 per patient.

As for the demand, the highest are the Yterium-90 for Synovectomy, Yterium-90 Zevalin, Lutetium-177 Octreotate and Yterium-90 Microsphere. Yterium-90 Zevalin or Yterium-90 Ibritumomab tiuxetan is to be used in the treatment of non-Hodgkin's Lymphoma (NHL) while Lutetium-177 Octreotate to be used in the treatment of neuroendocrine tumour. There are two types of Lutetium-177 that are available worldwide, one is carrier added and the other is the non-carrier added. The non-carrier added Lutetium-177 is currently being favor as for its high specific activity (up to 3000 GBq/mg), high radionuclide purity and most important is there is no long-lived isomer of Lutetium-177m despite its expensive cost.

CONCLUSION

The highest demand and the highest usage among all radioisotopes are Technetium-99m and Radioiodine isotopes such as the Iodine-131, Iodine-131 MIBG, Iodine-123 and Iodine-123 MIBG. Currently, most of the medical isotopes and radiopharmaceuticals are currently imported. Technetium-99m is the backbone of nuclear medicine whereby more than 80% of Nuclear Medicine services utilize this radioisotope. Technetium-99m supply chain is unstable globally and in coming future, two main reactors (Canada & Holland) that produces 60% of world Molybdenum-99 will shut down the operation and supply of Molybdenum-99 will be disrupted (OECD 2011). As for radioiodine services, currently, Iodine-123 can't be obtained in Malaysia and neighboring countries due to its short half-life. Iodine-123 is useful in diagnostic of thyroid related diseases. As for PET services, the highest demands are F-18 FDG and Gallium-68 Generator for the moment. However the survey data still did not include most of the PET centers in the Klang Valley, northern area (Penang) and the new upcoming PET center in Southern Region (Malacca and Johor). It is important for Malaysia to self-produced

medical radioisotope and radiopharmaceuticals to meet the market and local demand of these medical isotopes. More importantly, the emerging of new centers that offers nuclear medicine services and also the expansion of the services of the existing nuclear medicine centers shall be taken into account.

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REFERENCES

- Kahn, Laura H.; The potential dangers in medical isotope production. Bulletin of the Atomic Scientists, 2008:
<http://www.isotopeworld.com/filestore/Danger%20Medical%20Isotope%20pdf.pdf>
- naweb.iaea.org/napc/physics/research_reactors/database/RR%20Data%20Base/datasets/category/status_operational_reactors.htm
- OECD 2011, Nuclear Energy Agency organization For Economic Co-Operation and Development, The Supply of Medical Radioisotopes: An Assessment of Long-term Global Demand for Technetium-99m
- R.J. Kowalsky and S.W. Falen, 2013 , Radiopharmaceuticals in Nuclear Pharmacy and Nuclear Medicine *J Nucl Med* February 1 vol. 54 no. 2 324-325