Conference Paper

Application of ^{99m}Tc Radioisotope in Diagnostic Procedures and Internal Radiation Dose Estimation

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Abstract

At about 70% of nuclear medicine procedures have utilized ^{99m}Tc in their clinical practices. This has lead ^{99m}Tc becoming the most convenient radioisotope in nuclear medicine diagnostic. To estimate the internal radiation dose due to the administration of ^{99m}Tc to the patients, only few documents from International Commission of Radiation Protection (ICRP) have been available. However, the calculation usually has applied Caucasian data in Standard Reference Man as a model. The objective of this study was to review the application of ^{99m}Tc in Indonesia and to compare the internal dose estimation for ^{99m}Tc procedures by using Organ Level Internal Dose Assessment/Exponential Modeling (OLINDA/EXM) software. The result of calculation was compared between Adult Caucasian model and Asian Reference Man. The result shows that ^{99m}Tc has been well applied and developed for diagnostic procedures in Nuclear Medicine Department. Moreover, in most diagnostic procedures using ^{99m}Tc in Indonesia, adult patients will receive effective dose about 1-15% higher than adult patient in foreign countries which apply the Caucasian model. Hence, to estimate the similar stochastic risk from the same procedure, the maximum value in recommended administered dose should be avoided and need to be evaluated.

Keywords: ^{99m}Tc radioisotope, diagnostic procedures, internal radiation dose, OLINDA/EXM

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1. Introduction

^{99m}Tc has become the most convenient radioisotope for diagnostic procedures in nuclear medicine. It has been reported that approximately 70% nuclear medicine procedures have utilized ^{99m}Tc in their clinical practices using either gamma camera or single photon emission computed tomography (SPECT). Despite the emerging nuclear medicine equipment such as Photon Emission Tomography (PET) has lead the application of molecular imaging agents, the application of ^{99m}Tc seems still to be preferred choice due to the ease of supply process [1].

The application of ^{99m}Tc radioisotopes in the world have been supplied from available methods, such as uranium fission in the research reactors using both high enriched uranium (HEU) and low enriched uranium (LEU) targets, neutron activation of ^{98}Mo in a nuclear reactor, and ^{99m}Tc production with cyclotrons. From these available options, the ^{99m}Tc production based on uranium fission using HEU target is the favorable option regarding to consideration of several factors: the maturity of technology, production yield, available irradiation capacity, commercial compatibility, estimated unit cost, ease of nuclear regulatory approval, ease of health regulatory, and units required to supply world market [2].

With regard to its chemistry characteristic, ^{99m}Tc has major advantages for nuclear medicine procedures [3], since it has multiple oxidation states which make it is possible to be used in either single compound of ^{99m}Tc (pertechnate), or with a labeling compound, such as ^{99m}Tc -methylene diphosphonate (MDP) for bone studies and ^{99m}Tc -Diethyl Triamine Penta-Acetic (DTPA) for renal studies. Moreover, other applications of ^{99m}Tc have been expanded into next generation of ^{99m}Tc labeling process, due to the development of research in imaging agents for cardiovascular and brain studies, such as ^{99m}Tc Tetrofosmin and ^{99m}Tc Hexamethylpropyleneamine Oxime (HMPAO), respectively [4].

Since the administration of radiopharmaceutical in those procedures will lead the patients to receive internal radiation dose, internal dosimetry should be assessed either from calculation or reference documents published by International Atomic Energy Agency (IAEA), International Commission of Radiation Protection (ICRP) and/or national regulatory authorites [5]. For example, ICRP publications no. 53, 80, and 106 provides internal dosimetry assessment for patient due to radiopharmaceutical administration in human body [6-8]. However, those documents have referred Caucasian anatomical data for the reference model.

In general, the objective of this study is to investigate the application of ^{99m}Tc in Nuclear Medicine diagnostic procedure in Indonesia, and performing internal dose estimation from related procedures. The internal dose estimation will be performed based on the calculation using OLINDA/EXM, a software from Vanderbilt University for internal dosimetry calculation in nuclear medicine. The calculation in this study will adopt the organ weight of Asian Reference Man (ARM), to be compared with Standard Reference Man in OLINDA/EXM. The result of calculation will be utilized as a tool to compare the effective dose for adult male and female of both models. It will show when the same radiopharmaceutical will be administered, how Asian model will differ from Caucasian model in terms of internal dose estimation. This study will also verify an initial assumption that, with the similar administered dose for the same radiopharmaceuticals, Asian Group will receive higher internal radiation dose because the weight of Asian Reference Model is lower than the Standard Reference Model in ICRP.

2. Theory

^{99m}Tc has been produced in a nuclear reactor as a fission product by irradiating enriched U-235. The product needs to be processed to purify ^{99}Mo from other impurities. The ^{99}Mo isotopes which are in aquous phase, then being adsorbed into alumina (Al_2O_3) column which is contained in a radiation-shielded equipment (Fig. 1), known as technetium generators. In the generator, ^{99m}Tc is eluted by a sterile saline solution (NaCl) to recover ^{99m}Tc [9]. The elution will generate ^{99m}TcO4 (pertechnate) in saline solution. The ^{99m}Tc is ready to be used either as pure pertechnate or combined with any others labeling compounds. A typical ^{99m}Tc generator produced by Australian National Science and Technology Organisation (ANSTO) is displayed in Fig. 1. The generator can be used several times in a week by re-passing saline solution into ^{99}Mo column until the activity of eluted ^{99m}Tc is very low and unable to be applied for any diagnostic procedure. The schematic of the generator is displayed in Fig. 2.

Figure 1: Gentech, a typical of ^{99m}Tc generator produced by ANSTO.

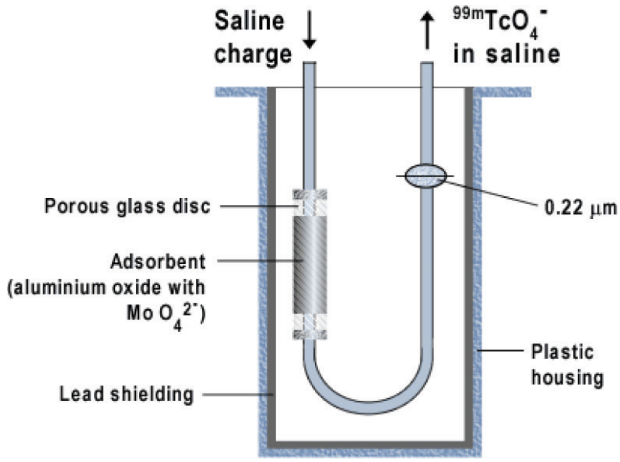

Figure 2: Schematic diagram of ^{99m}Tc generator [10].

^{99m}Tc Application for Diagnostic Procedures

^{99m}Tc application for diagnostic procedures is well known in worldwide, started from thyroid scintigrafi, perfusion studies, bone scan, and other diagnostic applications, due to its short half live, low energy, and economic consideration [11]. A report of application ^{99m}Tc in the United Stated has acknowledged that the application of nuclear medicine diagnostic in the US has increased approximately 6 million per year since early 1980 until about 20 millions in 2005. The increasing has been believed that it was due to to the application of ^{99m}Tc based agents which have replaced the use of ^{201}Tl in cardiac procedures from 1 % in 1973 to 57% in 2005 [12].

With regard to radiation safety practices, the administered dose of radiopharmaceutical in diagnostic procedures, ICRP has published the report regarding the administered dose to patients in ICRP Publication No. 17, then continued in 1987 by releasing the Publication No. 53: Radiation Dose to Patients from Radiopharmaceuticals, by contributing 120 radiopharmaceuticals, and the use of 71 radionuclides in 34 elements. Furthermore, with the increasing the number of new radiopharmaceuticals, the publication has been revised few times until third addendum in 2008 in Publication No.106 [8].

In 2002, IAEA has published Radiological Protection for Medical Exposure to Ionizing Radiation [5] and Nuclear Medicine Resources Manual [13], in which the administered dose of radiopharmaceuticals in diagnostic procedures have been recommended to optimize radiation protection to the patients. The first document [5] has listed the value of maximum dose to be administered to the patients in Nuclear Medicine Departments. Furthermore, the values have been adopted locally by National Nuclear Regulatory Agency (BAPETEN) into the Decree of BAPETEN head No. 17 year 2012, regarding Radiation Safety Guide in Nuclear Medicine Department in Indonesia [14]. Table 1 has presented the application ^{99m}Tc for diagnostic procedures and the standard activities of ^{99m}Tc radiopharmaceuticals [13].

Calculation of Internal Dosimetry Assessment

In previous paper, a basic concept of internal dosimetry estimation has presented a method from Medical Internal Radiation Dosimetry (MIRD) committee, which has been well applied in nuclear medicine communities [15]. Since the internal dosimetry assessment in diagnostic procedure may provide stochastic risk estimation, the assessment should be quantified to

Table 1: The list of ^{99m}Tc procedure and its standard activitiy [13].

Radiopharmaceutical	Study	Standard Activity (MBq)
^{99m}Tc-pertechnetate	Thyroid scintigraphy	80 - 200
^{99m}Tc- diethylene triamine penta acetic acid (DTPA)	Glomerular Filtration Rate	200
	Liquor Cerebro Spinalis system	185 - 370
	Gatric emptying time (liquid)	18-37
	Esophageal Reflux	37 - 74
	Esophageal Transit Time	37 - 74
	Vesico urethral Reflux	200
^{99m}Tc - 2-methoxyisobutyl isonitrile (MIBI	Myocardial Perfusion Scintigraphy	1000 - 1110
	Tumor Imaging	555 - 740
^{99m}Tc - tetrofosmin	Myocardial Perfusion Scintigraphy	1000 - 1110
	Tumor Imaging	555 - 740
^{99m}Tc - Methylene diphosphonate (MDP)	Bone Scintigraphy	740 - 1110
^{99m}Tc – Red Blood Cell (RBC)	Ventriculography	555 - 1100
	Gastrointestinal Bleeding	370 - 1110
^{99m}Tc - macroaggregated albumin (MAA)	Pulmonary Perfusion Imaging	40 - 150
^{99m}Tc- diethylene triamine penta acetic acid (DTPA-aerosol	Pulmonary Ventilation Imaging	900 - 1300
^{99m}Tc - nanocolloid	Lymphoscintigraphy	15 - 35
	Sentinel Node Imaging	15 - 35
^{99m}Tc - mercapto acetyl tri glycine (MAG3)	Renal Excretion	100
^{99m}Tc - Sulfur colloid	Gastric Emptying Time (solid)	7,4 - 14,8
	Liver scintigraphy	110 - 220
^{99m}Tc-2,6-dimethyl phenyl carbamoyl methyl) – iminodi acetic acid (HIDA)	Biliary Tract Imaging	50 - 200

estimate the effective dose for the patients [16]. Moreover, a calculation of effective dose can be done by applying a voxel based model dosimetry in computer codes, such as MIRDOSE and OLINDA/EXM. Both MIRDOSE and OLINDA/EXM have applied the organ mass in Standard Reference Man, which is adopted from Caucasian Model. Unfortunately, the distribution of MIRDOSE3 has been withdrawn and has been being replaced by The OLINDA/EXM, since it provides more radioisotope data, modification of the organ mass, and the fitting of kinetic data [17]. The software has been approved by the Federal and Drug Administration of the USA, for internal dosimetry calculation in nuclear medicine. Since OLINDA/EXM provides a menu for organ mass modification, hence it can be used to calculate another reference model. In this study Asian Reference model has been adopted by referring the organ mass in Asian Reference Man [19].

3. Materials and Method

To calculate internal dose of ^{99m}Tc in diagnostic procedures using OLINDA/EXM, it needs the kinetic data from Technetium and the labeled compounds. These data can be found from ICRP publications, such as ICRP 53, 80 and 103 [6-8]. Other input data are the name of nuclide, chosen body phantoms (adult male, adult female, 15 year-old, 10-year old, 5 year-old, 1-year-old, newborn, 6 month pregnant woman, 6 month pregnant woman, 9 month pregnant woman), and the kinetic data. Figure 3 shows the main menu of OLINDA/EXM.

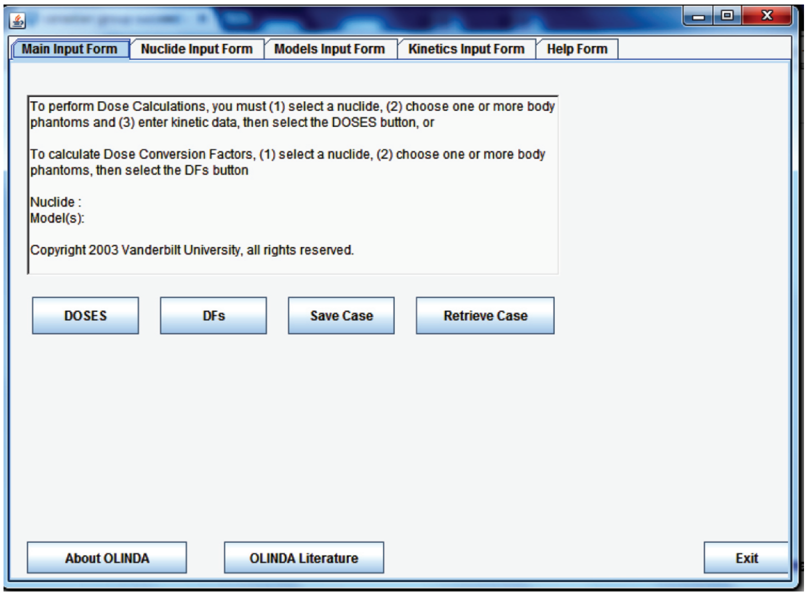

Figure 3: A sample of displayed main menu in OLINDA/EXM [18].

Tc

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Phosphonates

BIOKINETIC MODELS AND DATA

Biokinetic Data

Organ (S)	$\tilde{A}_S/A_0$
(1) Normal uptake and excretion	
Total body (excluding bladder contents)	4.06 hr
Bone	3.01 hr
Kidneys	7.5 min
Bladder contents	1.15 hr
(2) High bone uptake and/or severely impaired kidney function	
Total body	8.69 hr
Bone	5.84 hr

Figure 4: A sample of biokinetic data provided by ICRP [6].

In this work, the organs were selected depending on the referred organs on the kinetic data from each procedure. For example in bone scan procedure using ^{99m}Tc-MDP, the kinetic data which are available are bone, kidney, bladder and total body (Fig. 4). After the dose calculation has been done for Caucasian models [19], the effective dose due to the administration of radioisotope in those procedures can be displayed for both male and female. Furthermore, to calculate internal dose for Asian group, few organ masses need to be adopted from Asian Reference Man (ARM) [20], then it will give the effective dose. The difference of organ weight between Standard Reference Man and Asian Reference Man has been displayed on Table 2.

Table 2: The list of organ weights in Standard and Asian Reference Man.

ORGAN	Weight: adult male (gr)		Weight: adult female (gr)	
	SRM	ARM	SRFM	ARFM
Adrenals	16.3	14	14	13
Brain	1420	1470	1200	1320
Breasts	25	22	360	300
GB	10.5	8	8	6
LLI	167	150	160	120
SI	677	590	600	450
Stomach	158	140	140	110
ULI	220	180	200	140
Heart	316	380	240	320
Kidneys	299	320	275	280
Liver	1910	1600	1400	1400
Lungs	1000	1200	800	910
Muscle	28000	25000	17000	28000
Muscle	28000	25000	17000	28000
Pancreas	94.3	130	85	110
Red Marrow	1120	1000	1300	780
Osteogenic cells	120	120	90	90
Skin	3010	2400	1790	1800
Spleen	183	140	150	120
Testes	39.1	37	0	0
Thymus	20.9	30	20	29
Bladder	47.6	40	35.9	30
Uterus / Prostate	8	8	80	70
Fetus	0		0	0
Placenta	0		0	0
Total body	73700	60000	56912	51000

4. Result and Discussion

The purpose of this work was to review the application of ^{99m}Tc radiopharmaceutical in nuclear medicine diagnostic procedures in Indonesia, and to evaluate the internal radiation dose for ^{99m}Tc radiopharmaceuticals in related procedures. The evidences have shown that the application of ^{99m}Tc in Nuclear Medicine procedures has grown quickly in accordance with the development of research and production in radiopharmaceuticals, so that ^{99m}Tc becomes the most convenient radioisotope for diagnostic procedures in Nuclear Medicine Department due its simple characteristic to be labeled with other compounds. For example, the application of ^{99m}Tc for cardiac perfusion study, has been extended for early breast cancer detection [20] and it has shown that the early diagnosis of breast cancer using ^{99m}Tc is less painful than using mammography.

In terms of internal dose estimation, the study was intended to evaluate whether adult Standard (Caucasian) or adult Asian will receive the same number of internal radiation when the similar procedures will be given, by applying internal dose calculation using OLINDA/EXM. As a result, in OLINDA/EXM, effective dose is produced as a unit of mSv/MBq or mSv/mCi. The result can be copied and saved in txt files for later review. This is important since an evaluation is needed to verify that the input of radionuclide, models, kinetic data, and organ weights are correct and producing an accurate result. The summary of calculation in this study has been displayed on Table 3.

From the calculation, in each MBq of ^{99m}Tc administered dose, adult Asian model receive higher effective dose than adult Caucasian model. The number is between 1% and 15% depends on the procedures has been given. This is true because each procedures has different labeled compound which means it has different biokinetic characteristic, source and target organs. Therefore, it will produce different absorbed doses in related organs and finally it will give the different effective doses. For example, in ^{99m}Tc pertechnate for thyroid study, the effective dose estimation for adult Asian male is about 5% higher than that in adult Caucasian male. Furthermore, in ^{99m}Tc sulfur colloid for Liver scintigraphy, the difference between adult Caucasian male and adult Asian male will be about 15%. In the report of Marine, et al, it has been stated that the change of body size will result the different exposure from the targeted organ as a source and the self-absorption dose from the organ [21].

Table 3: The comparison of effective dose calculation for ^{99m}Tc radiopharmaceuticals for adult Asian and adult Caucasian in Standard Reference Man.

Radio-pharmaceutical	Effective Dose (mSv)/MBq					
	SRM	ARM	ARM/ SRM	SRFM	ARFM	ARFM/ SRFM
^{99m}Tc-pertechnetate	0.0087	0.0092	105%	0.0106	0.0119	112%
^{99m}Tc-DTPA	0.0052	0.0055	105%	0.0071	0.0077	109%
^{99m}Tc-MIBI	0.0074	0.0081	110%	0.0090	0.0098	109%
^{99m}Tc-tetrofosmin	0.0089	0.0094	105%	0.0110	0.0118	107%
^{99m}Tc-MDP	0.0060	0.0063	105%	0.0078	0.0089	114%
^{99m}Tc-RBC	0.0004	0.0005	105%	0.0006	0.0006	107%
^{99m}Tc-MAA	0.0108	0.0113	105%	0.0169	0.0184	109%
^{99m}Tc-DTPA (aerosol)	0.0060	0.0064	106%	0.0080	0.0081	101%
^{99m}Tc-nanocolloid	0.0091	0.0102	112%	0.0096	0.0103	107%
^{99m}Tc-MAG3	0.0132	0.0141	107%	0.0175	0.0193	110%
^{99m}Tc-Sulfur colloid	0.0045	0.0051	115%	0.0052	0.0054	102%
^{99m}Tc-HIDA	0.0150	0.0155	103%	0.0180	0.0194	108%

SRM : Standard Reference Man-Male, ARM : Asian Reference Man-Male,
SRFM : Standard Reference Man-Female, ARFM : Asian Reference Man-Female

A similar study of internal dose estimation for diagnostic radiopharmaceuticals such as ^{18}F-FDG, ^{123}I-ioflupane and ^{99m}Tc-tetrofosmin has been performed to investigate the difference of internal dose across Asian model [22]. The study has presented the variation organ size within adult Chinese, Indian, Caucasian and the Caucasian female, and it has been stated that the effective dose of Caucasian female group is almost similar to the male patient in Asian group.

The finding of study has also showed that, if the administered dose for the patients has been by referring the value of administered dose from IAEA which has been adopted by BAPETEN, it will give higher effective dose to the patients in Indonesia, which means it will increase the stochastic risk. Hence, it would be better if the maximum administered dose in the Decree of BAPETEN Head No.17 year 2012 need to be either avoided or be reduced until at least, less than 15% of maximum dose to reduce the probability of stochastic risk for the patients in Nuclear Medicine Department in Indonesia.

For the future study, it would be better if the organ weight in Asian Reference Man in this study will be replaced by organ weight from of Indonesian. Then the result of study will be directly applied as Indonesian model. However, at the moment, it is hard to find the standard of anatomical data for Indonesian, since the Indonesian Reference Man has not been established yet. There was a report of anatomical data for Indonesian under IAEA project coordination, but it was not enough to represent the population [19]. Hence, temporarily, the result of this study might be useful for estimating the internal radiation dose for particular procedures in nuclear medicine despite it uses Asian Reference Man. The internal dose estimation for patients who undergo nuclear medicine diagnostic procedures will be more important when a patient also receive more radiation dose from other diagnostic modalities such as CT scan and fluoroscopy, which might add the effective dose to the patients.

5. Conclusion

The result shows that the application ^{99m}Tc has grown tremendously in accordance with the new presence of radiopharmaceutical production as well as the research in the application of 99mTc. Moreover, in most diagnostic procedures using ^{99m}Tc in Indonesia, adult patients will receive effective dose about 1-15% higher than adult patient in foreign countries which apply Caucasian model. Hence, to estimate the similar stochastic risk from the same procedure, the maximum value in recommended administered dose should be avoided and need to be evaluated.

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