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ORIGINAL ARTICLE

Report of a nationwide survey on actual administered radioactivities of radiopharmaceuticals for diagnostic reference levels in Japan

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Abstract
Objective The optimization of medical exposure is one of the major issues regarding radiation protection in the world, and The International Committee of Radiological Protection and the International Atomic Energy Agency recommend establishing diagnostic reference levels (DRLs) as tools for dose optimization. Therefore, the development of DRLs based on the latest survey has been required for nuclear medicine-related societies and organizations. This prompted us to conduct a nationwide survey on the actual administered radioactivity to adults for the purpose of developing DRLs in nuclear medicine.
Methods A nationwide survey was conducted from November 25, 2014 to January 16, 2015. The questionnaire was sent to all of the 1249 nuclear medicine facilities in Japan, and the responses were collected on a website using an answered form.

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Results Responses were obtained from 516 facilities, for a response rate of 41 %. 75th percentile of ^{99m}Tc-MDP and ^{99m}Tc-HMDP: bone scintigraphy, ^{99m}Tc-HM-PAO, ^{99m}Tc-ECD and ^{123}I-IMP: cerebral blood flow scintigraphy, ^{99m}Tc-Tetrofosmin, ^{99m}Tc-MIBI and ^{201}Tl-Cl; myocardial perfusion scintigraphy and ^{18}F-FDG: oncology PET (in-house-produced or delivery) in representative diagnostic nuclear medicine scans were 932, 937, 763, 775, 200, 831, 818, 180, 235 and 252, respectively. More than 90 % of the facilities were within the range of 50 % from the median of these survey results in representative diagnostic nuclear medicine facilities in Japan. Responses of the administered radioactivities recommended by the package insert, texts and guidelines such as 740 MBq (^{99m}Tc-MDP and ^{99m}Tc-HMDP: bone scintigraphy), 740 MBq (^{99m}Tc-ECD and ^{99m}Tc-HM-PAO: cerebral blood flow scintigraphy) and 740 MBq (^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI: myocardial perfusion scintigraphy), etc. were numerous. The administered activity of many radiopharmaceuticals of bone scintigraphy (^{99m}Tc-MDP and ^{99m}Tc-HMDP), cerebral blood flow scintigraphy (^{99m}Tc-HM-PAO) and myocardial perfusion scintigraphy (^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI), etc. were within the range of the EU DRLs and almost none of the administered radioactivity in Japan exceeded the upper limit of SNMMI standard administered radioactivity.

Conclusions This survey indicated that the administered radioactivity in diagnostic nuclear medicine in Japan had been in the convergence zone and nuclear medicine facilities in Japan show a strong tendency to adhere to the texts and guidelines. Furthermore, the administered radioactivities in Japan were within the range of variation of the EU and the SNMMI administered radioactivities.

Keywords Survey · Diagnostic reference level · Radiopharmaceutical · Radioactivity · Optimization of dose

Introduction

The International Committee of Radiological Protection (ICRP) recommended three fundamental principles (justification, optimization of protection, and application of dose limits) for radiation protection. It should be noted that with regard to medical exposure of patients, it is not appropriate to apply dose limits or dose constraints, because such limits would often do more harm than good [1, 2]. Therefore, the justification and optimization of protection are very important in clinical practice. However, with the development of radiation medical technology increases in the medical exposure dose are of concern. The optimization of medical exposure is one of the major issues regarding radiation protection in the world, and the ICRP and the International Atomic Energy Agency (IAEA) recommended establishing diagnostic reference levels (DRLs) as tools for dose optimization [3, 4]. In Europe, the European Union (EU) required establishment of DRLs by Council Directive 97/43/Euratom in 1996 [5]. It is suggested that DRLs should be set by countries, regions, academic societies or associations and they have been defined in Europe and North America [6–12]. On the other hand, in Japan the Japanese Society of Nuclear Medicine (JSNM) or other research groups have recommended the standard administration radioactivity dose [13, 14]. The Japan Association of Radiological Technologists (JART) recommended the reduction target dose [15, 16] and the JART conducted a nationwide survey of radiopharmaceutical doses [17]. Unfortunately this survey was not strictly limited to "actual" administered doses but included radioactivity doses determined by the time and date of assay of radiopharmaceuticals. Until 2015, neither a nationwide survey of "actual" administered doses had been conducted nor had DRLs been proposed by any nuclear medicine-related societies or organizations.

Concerning pediatric nuclear medicine, the European Association of Nuclear Medicine (EANM) dosage card has been proposed and developed by the Pediatric Task Group EANM in Europe [18–21] and consensus guidelines have been proposed and developed by the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in North America [22–26]. In 2014, the Japanese consensus guidelines for pediatric nuclear medicine were provided by JSNM in Japan [27].

The Japan Network for Research and Information on Medical Exposures (J-RIME) was established in 2010 with the cooperation of related academic societies [28]. The J-RIME decided to establish the first DRLs (Japan DRLs) of common modality as all medical radiation-related societies and organizations at the annual meeting held in 2013. Therefore, the establishment of DRLs based on the latest survey results was required by nuclear medicine-related societies and organizations. This survey was performed voluntarily by medical radiation-related societies and organizations but was not forced by national offices.

The JSNM and JSNMT conducted a nationwide survey on the actual administered radioactivity in adults for the purpose of establishing DRL in nuclear medicine.

In Japan there is a unique system for delivered radiopharmaceuticals. When radiopharmaceuticals are provided from radiopharmaceutical manufacturers to nuclear medicine facilities, the radioactivity dose has been determined by the time and date of assay of radiopharmaceuticals. For example, in the case of ^{99m}Tc and ^{123}I agents, the radiopharmaceutical to be delivered to the nuclear medicine facility has been assayed as the assay radioactivity

(radioactivity at 12 am) of the delivery date (examination date). In addition, in the case of ^{201}Tl and ^{67}Ga agents, radioactivity in the two days after the delivery date is delivered (radioactivity at the delivery day is about 1.6 times the assay radioactivity). That is, the assay radioactivity does not actually mean the true administered radioactivity.

Methods

Distribution, collection, and contents of the questionnaire

A nationwide survey on the actual administered radioactivity of adults for the purpose of providing DRLs in nuclear medicine was conducted from November 25, 2014 to January 16, 2015. The questionnaire was sent to all 1249 facilities where nuclear medicine examinations are performed in Japan, and the responses were sent to a website.

The questionnaire included items such as the average administered radioactivity dose of an adult for each diagnostic nuclear medicine examination, number of scanners, number of staff members, number of board certified nuclear medicine physicians and nuclear medicine radiological technicians.

How to calculate or evaluate the average administered radioactivity in each facility

The average administered radioactivity was obtained from the responses following this questionnaire.

1. The average value of the actually measured doses at the administered time or the average value of the assay dose that was corrected for the administered time.
2. The average administered radioactivity per week or the average administered radioactivity of several dozen times.
3. When the administered time is set at the facility, the average dose at that time.
4. The target administered radioactivity.
5. In the case of rare nuclear medicine examinations, the average administered radioactivity for several months or 1 year, or, the administered radioactivity in standard procedures.
6. For positron emission tomography (PET), the above 2 or 3 are used as a reference. The estimated radioactivity when using an automatic injecting machine for ^{18}F-FDG.

When calculating the average doses, responses that appeared clearly erroneous were excluded.

Results and discussion

Response rate and the distribution of administered radioactivity

Replies were obtained from 516 facilities (response rate 41 %). The average, 75th, 80th and 90th percentile of each administered radioactivity are shown in Table 1.

The 75th percentile of ^{99m}Tc-MDP, ^{99m}Tc-HMDP (bone scintigraphy), ^{99m}Tc-HM-PAO, ^{99m}Tc-ECD, ^{123}I-IMP (cerebral blood flow scintigraphy), ^{99m}Tc-Tetrofosmin, ^{99m}Tc-MIBI, ^{201}Tl-Cl (myocardial perfusion scintigraphy) and ^{18}F-FDG for oncology (in-house-produced and delivery) administered radioactivity were 932, 937, 763, 775, 200, 831, 818, 180, 235 and 252, respectively.

Distribution of administered radioactivity in a representative diagnostic nuclear medicine examination

The administered radioactivity distributions of bone scintigraphy, cerebral blood flow scintigraphy, myocardial perfusion scintigraphy for single photon emission computed tomography (SPECT) and ^{18}F-fluorodeoxyglucose (FDG) tumor scintigraphy in PET are shown in Figs. 1, 2, 3, 4, 5, 6 and 7. It should be noted that in Figs. 1, 2, 4 and 6 the numbers of different response facilities are adjusted.

Figure 1 shows the administered radioactivity distribution of ^{99m}Tc-methylene diphosphonate (MDP) and ^{99m}Tc-Hydroxymethylene diphosphonate (HMDP). In Japan, ^{99m}Tc-MDP and ^{99m}Tc-HMDP have been used in bone scintigraphy as radiopharmaceuticals and there are two methods of on-site preparation of kits and ready-to-use radiopharmaceuticals. Two manufacturers have provided radiopharmaceuticals for bone scintigraphy. One has 555 and 740 MBq and the other has 370, 555, 740 and 925 MBq as assay radioactivity for one patient. For the present survey, information regarding whether kits were prepared on-site or ready-to-use radiopharmaceuticals was not obtained. The administered radioactivity distribution of ^{99m}Tc-MDP and ^{99m}Tc-HMDP was almost the same, and, the numbers of 740 MBq in both agents were the highest because administration of radioactivity of 555–740 MBq is recommended by the package insert, texts and guidelines as a standard administration activity in Japan. The percentages of response rates in the range of 740 MBq ± 5 % of ^{99m}Tc-MDP and ^{99m}Tc-HMDP were 30 and 31 %, respectively. The latter is around 930 MBq because the dose of 930 MBq corresponds to the case of administration of 740 MBq (assay activity at 12 am) at 10 am. Two radiopharmaceuticals for bone scintigraphy are recommended to be scanned from 2 to 3 h after administration.

Table 1 Nationwide survey results and diagnostic reference levels (DRLs) in Japan

Procedure and radiopharmaceutical	Average dosage in % value of nationwide survey results (MBq)			DRLs (MBq)[a]
	75 %	80 %	90 %	
Bone: ^{99m}Tc-MDP	932	962	1045	950
Bone: ^{99m}Tc-HMDP	937	963	1045	950
Bone marrow: ^{111}I *n*-Cl	125	125	125	120
Cerebral blood flow: ^{99m}Tc-HM-PAO (rest or stress)	763	800	932	800
Cerebral blood flow: ^{99m}Tc-HM-PAO (rest and stress)	1155	1280	1464	1200
Cerebral blood flow: ^{99m}Tc-ECD (rest or stress)	775	800	848	800
Cerebral blood flow: ^{99m}Tc-ECD (rest and stress)	1007	1068	1130	1100
Cerebral blood flow: ^{123}I-IMP (rest or stress)	200	211	236	200
Cerebral blood flow: ^{123}I-IMP (rest and stress)	287	310	340	300
Cerebral blood flow: Iomazenil (^{123}I)	193	195	244	200
Dopamine transporter: Ioflupane (^{123}I)	186	189	195	190
Cisternography: ^{111}I *n*-DTPA	63	63	72	70
Thyroid imaging: ^{123}I-NaI	9	9	13	10
Thyroid imaging: ^{99m}Tc-pertechnetate	261	370	370	300
Parathyroid: ^{201}Tl-Cl	120	120	175	120
Parathyroid: ^{99m}Tc-pertechnetate	300	370	391	300
Parathyroid: ^{99m}Tc-MIBI	784	824	848	800
Lung ventilation: ^{81m}Kgas	185	185	288	200
Lung ventilation: ^{133}Xe gas	468	480	489	480
Lung perfusion: ^{99m}Tc-MAA	260	261	370	260
Venography: ^{99m}Tc-MAA	459	555	740	500
Liver and spleen: ^{99m}Tc-phytate	185	197	228	200
Liver function: ^{99m}Tc-GSA	251	260	261	260
Hepatobiliary: ^{99m}Tc-PMT	252	260	261	260
Liver and spleen: ^{99m}Tc-Sn colloid	157	185	185	180
Myocardial perfusion: ^{201}Tl-Cl	180	180	196	180
Myocardial perfusion: ^{99m}Tc-tetrofosmin (rest or stress)	831	880	951	900
Myocardial perfusion: ^{99m}Tc-tetrofosmin (rest and stress)	1110	1130	1247	1200
Myocardial perfusion: ^{99m}Tc-MIBI (rest or stress)	818	848	900	900
Myocardial perfusion: ^{99m}Tc-MIBI (rest and stress)	1110	1125	1221	1200
Myocardial fatty acid metabolism: ^{123}I-BMIPP	130	130	159	130
Cardiac sympathetic nerve imaging: ^{123}I-MIBG	129	130	130	130
Cardiac blood pool: ^{99m}Tc-HSA	931	932	1045	1000
Cardiac blood pool: ^{99m}Tc-HSA-D	944	997	1045	1000
Myocardial infarction: ^{99m}Tc-PYP	750	925	1001	800
Salivary gland: ^{99m}Tc-pertechnetate	370	370	466	370
Meckel's diverticulum: ^{99m}Tc-pertechnetate	466	523	740	500
Gastrointestinal bleeding: ^{99m}Tc-HSA-D	1036	1045	1046	1040
Renal imaging (static): ^{99m}Tc-DMSA	210	230	261	210
Renal imaging (dynamic): ^{99m}Tc-MAG3	390	400	424	400
Renal imaging (dynamic): 99mTc-DTPA	380	400	502	400
Adrenal cortex: ^{131}I-Adosterol	44	44	44	44
Adrenal medulla: ^{131}I-MIBG	40	40	48	45
Adrenal medulla: ^{123}I-MIBG	130	130	170	130
Tumor: ^{201}Tl-Cl	178	180	180	180
Tumor and inflammation: ^{67}Ga-citrate	174	174	208	200

Table 1 continued

Procedure and radiopharmaceutical	Average dosage in % value of nationwide survey results (MBq)			DRLs (MBq)[a]
	75 %	80 %	90 %	
Lymphatic system: ^{99m}Tc-HSA-D (not covered with health insurance)	928	932	1045	950
Sentinel lymph node: ^{99m}Tc colloid	111	111	156	120
Sentinel lymph node: ^{99m}Tc-phytate	93	105	127	120
RI angiography: ^{99m}Tc-HSA-D	943	987	1046	1000
Tumor: ^{18}F-FDG (in-house-produced)	235	240	260	240
Tumor: ^{18}F-FDG (delivery)	252	260	280	240
Brain: ^{18}F-FDG (in-house-produced)	227	233	248	240
Brain: ^{18}F-FDG (delivery)	255	259	295	240
^{15}O-CO_2 gas: 2D	7500	7700	8100	8000
^{15}O-O_2 gas: 2D	4500	5400	8360	6000
^{15}O-CO gas: 2D	3000	3000	3800	3000
^{15}O-CO_2 gas: 3D	2888	2910	2955	2900
^{15}O-O_2 gas: 3D	6600	7300	7400	7000
^{15}O-CO gas: 3D	7125	7500	7750	7500
Myocardial metabolism: ^{18}F-FDG (in-house-produced)	221	223	236	240
Myocardial metabolism: ^{18}F-FDG (delivery)	251	258	287	240
Myocardial perfusion: ^{13}N-NH_3	718	–	740	720

[a] Adult dosage (MBq)

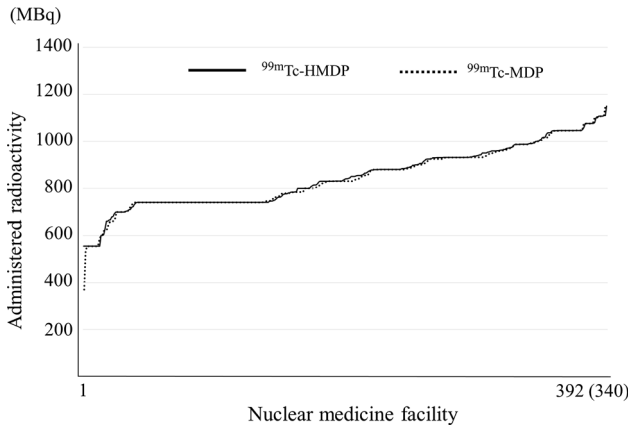

Fig. 1 Bone: ^{99m}Tc-HMDP and ^{99m}Tc-MDP. Note: They are arranged in decreasing order to separate the nuclear medicine facilities with more from those with less radioactivity. Numbers responding for ^{99m}Tc-HMDP and ^{99m}Tc-MDP were 392 and 340, respectively

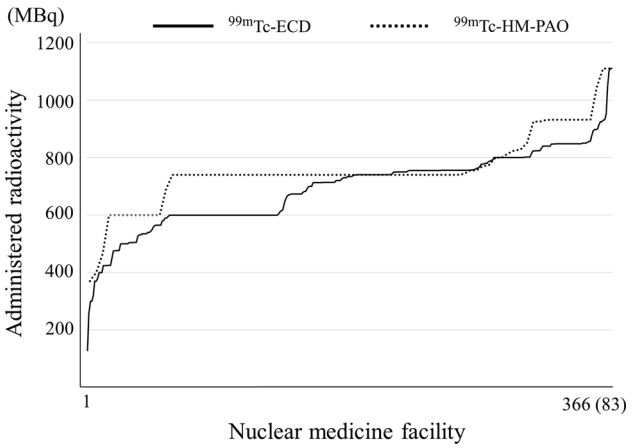

Fig. 2 Cerebral blood flow: ^{99m}Tc-ECD and ^{99m}Tc-HM-PAO. Note: They are arranged in decreasing order to separate the nuclear medicine facilities with more from those with less radioactivity. Numbers responding for ^{99m}Tc-ECD and ^{99m}Tc-HM-PAO were 366 and 83, respectively

This may reflect the reality that many nuclear facilities are imaging at 1 pm after administration at 10 am using an assay radioactivity of 740 MBq (ready-to-use radiopharmaceuticals).

Figure 2 shows the distribution of ^{99m}Tc-hexamethyl-propylene amine oxime (HM-PAO) and ^{99m}Tc-ethyl cysteinate dimer (ECD). In Japan, ^{99m}Tc-HM-PAO and ^{99m}Tc-ECD are used for cerebral blood flow scintigraphy of ^{99m}Tc agents as a radiopharmaceutical. ^{99m}Tc-HM-PAO is used only by on-site preparation of kits and ^{99m}Tc-ECD either by on-site preparation of kits or ready-to-use

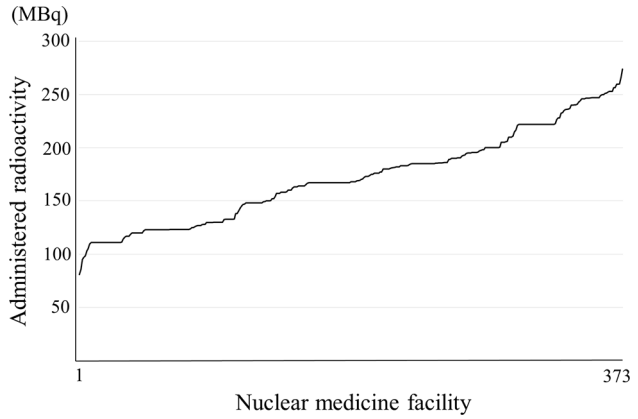

Fig. 3 Cerebral blood flow: ^{123}I-IMP. Note: They are arranged in decreasing order to separate the nuclear medicine facilities with more from those with less radioactivity. Number responding was 373

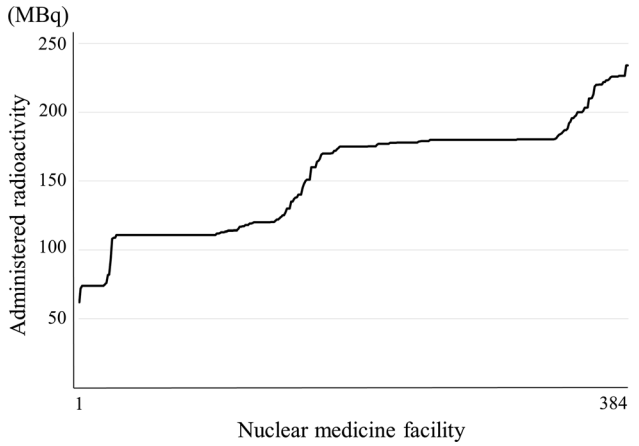

Fig. 5 Myocardial perfusion: ^{201}Tl-Cl. Note: They are arranged in decreasing order to separate the nuclear medicine facilities with more from those with less radioactivity. Number responding was 384

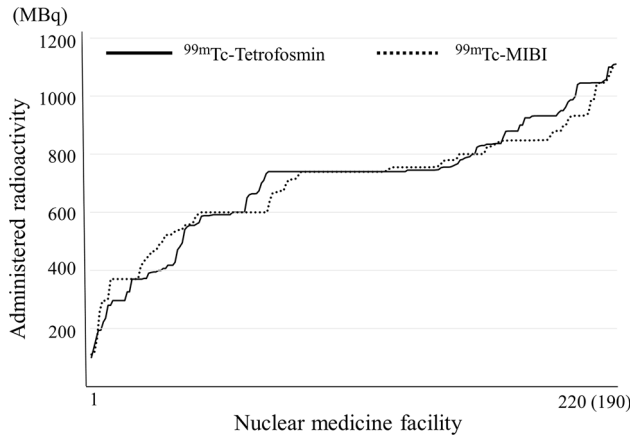

Fig. 4 Myocardial perfusion: ^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI. Note: They are arranged in decreasing order to separate the nuclear medicine facilities with more from those with less radioactivity. Numbers responding for ^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI were 220 and 190, respectively

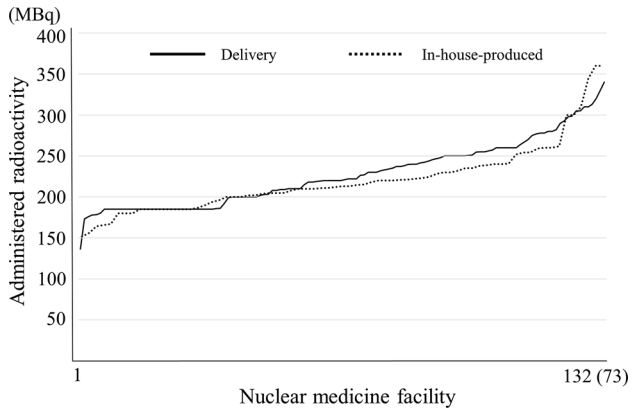

Fig. 6 Tumor: ^{18}F-FDG. Note: They are arranged in decreasing order to separate the nuclear medicine facility with more from those with less radioactivity. Numbers of delivery and in-house-produced were 132 and 73, respectively

radiopharmaceuticals. The assay radioactivities of ^{99m}Tc-ECD are 400 and 600 MBq for one patient. Concerning ^{99m}Tc-HM-PAO, the number of the responses of 740 MBq was the highest because administration radioactivity of 370–740 MBq is recommended by the package insert, texts and guidelines as a standard administration radioactivity in Japan. For ^{99m}Tc-ECD, the number of responses of around 740 MBq was the most because an administration dose of around 370–740 MBq is highest by the package insert, texts and guidelines as a standard administration dose as well as ^{99m}Tc-ECD. The percentages of response rates in the range of 740 MBq ± 5 % of ^{99m}Tc-HM-PAO and ^{99m}Tc-ECD were 61 and 33 %, respectively.

Figure 3 shows the results of the distribution of *N*-isopropyl-*p*-[^{123}I]iodoamphetamine (IMP). In Japan, for cerebral blood flow scintigraphy ^{123}I-IMP is provided by only delivery. ^{123}I-IMP has more kinds of assay radioactivities than other radiopharmaceuticals. One manufacturer has 111, 148, 167, 185 and 222 MBq and another has 111, 167 and 222 MBq as assay radioactivity for one patient. In addition, for ^{123}I-IMP, a wide range of administration doses of 111–222 MBq is recommended by the package insert, texts and guidelines as a standard administration dose. In particular, a wide range of administration radioactivity (37–222 MBq) is recommended in the package insert. Thus, the distribution of radioactivity of ^{123}I-IMP is scattered, which may reflect the various uses to which it is put at individual facilities. The response rate in the range of 111 MBq ± 5 % of ^{123}I-IMP was 7 %.

Figure 4 shows the distribution of ^{99m}Tc-Tetrofosmin and ^{99m}Tc-hexakis-2-methoxyisobutylisonitrile (MIBI). In Japan, ^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI have been used for myocardial perfusion scintigraphy as ^{99m}Tc agents, and,

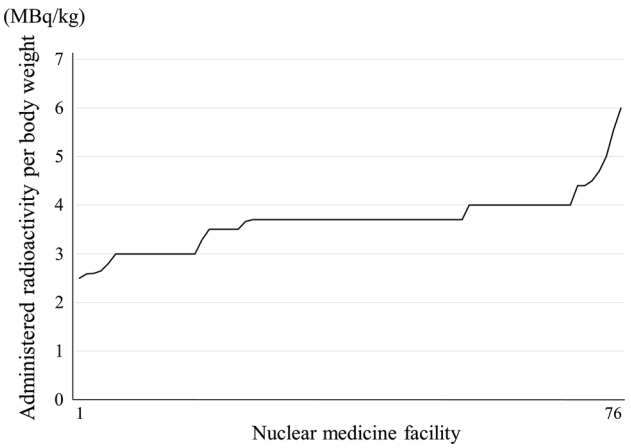

Fig. 7 Tumor: ^{18}F-FDG, administered activity per body weight. Note: They are arranged in decreasing order to separate the nuclear medicine facilities with more from those with less radioactivity. Number responding was 76

both agents have two methods of on-site preparation of kits and ready-to-use radiopharmaceuticals. ^{99m}Tc-Tetrofosmin has 296, 592 and 740 MBq and ^{99m}Tc-MIBI has 370, 600 and 740 MBq for one patient as the assay radioactivity. The response of around 740 MBq was the most common because an administration dose of 370–740 MBq is recommended by the package insert, texts and guidelines as a standard administration dose. The response rates in the range of 740 MBq ± 5 % of ^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI were 37 and 30 %, respectively.

Figure 5 shows the distribution of ^{201}Tl-Cl. In Japan, ^{201}Tl-Cl for myocardial perfusion scintigraphy has been made available only by delivery. The assay radioactivities of ^{201}Tl-Cl are 74, 11, 148 MBq for one patient provided by two manufacturers. The responses of 111 and 180 MBq were the most common. In Japan the manufacturers usually provide ^{201}Tl-Cl to the nuclear medicine facility within 2 days before the assay date; therefore, 180 MBq corresponds to the radioactivity 2 days before the assay radioactivity 111 MBq. The administration radioactivity of around 74–111 MBq is recommended by the package insert, texts and guidelines as a standard administration activity for ^{201}Tl-Cl. This study indicated that many nuclear medicine facilities administered the assay radioactivity 111 MBq for one patient in Japan (actual administered radioactivity is 180 MBq). The response rate in the range of 180 MBq ± 5 % of ^{201}Tl-Cl was 43 %.

The distribution of administered radioactivity for ^{18}F-FDG oncology PET is shown in Fig. 6 and the responses of 185 MBq were the greatest. In Japan, nuclear medicine facilities have two methods, in-housed-produced and delivery for ^{18}F-FDG oncology PET. Provided manufacture of ^{18}F-FDG is one and it has an assay radioactivity of only 185 MBq for one patient. For these reasons, it is presumed that the responses of 185 MBq were diverse. The response rate in the range of 185 MBq ± 5 % of ^{18}F-FDG in-housed-produced and delivery were 19 and 27 %, respectively. In addition, the administered radioactivity per body weight (MBq/kg) was also investigated (Fig. 7). However, whether in-housed-produced or delivery was not distinguished by the survey items. An administered radioactivity per body weight of 2–5 MBq/kg (three dimensional collection) is recommended by the guidelines [29] and it was found that most of the facilities administered within the recommended radioactivity doses per body weight. Furthermore, the numbers of responses of 3.0, 3.7 and 4.0 MBq/kg were the highest, and the administered radioactivity dose per body weight was considered is be determined in accordance with the guidelines.

This survey reveals that many nuclear facilities determined the administered radioactivity dose according to the package insert, texts and guidelines.

Comparison with EU and North America

Basically DRLs are determined based on 75th percentile of the survey results. To compare the administered radioactivity between Japan and EU, a summary of Japanese and EU DRLs for diagnostic nuclear medicine is shown in Table 2 following a list of the EU DRLs [9]. Many DRL doses of radiopharmaceuticals: bone scintigraphy (^{99m}Tc-MDP and ^{99m}Tc-HMDP), cerebral blood flow scintigraphy (^{99m}Tc-HM-PAO) and myocardial perfusion scintigraphy (^{99m}Tc-Tetrofosmin and ^{99m}Tc-MIBI), etc. were within the range of the EU DRLs. Concerning ^{201}Tl-Cl (myocardial perfusion scintigraphy), Japan DRL 180 MBq exceeds the range of the EU DRL (75–150 MBq). For ^{99m}Tc-pertechnetate (thyroid scintigraphy), Japan DRL 300 MBq exceeded the range of the EU DRLs (75–222 MBq). However, in the ^{18}F-FDG for oncology PET and ^{123}I-NaI for thyroid scintigraphy, Japan DRLs were at the lowest level in the range of the EU DRLs. These variations reflect the situation of each country, and so it is not considered that Japan DRLs are particularly high as compared with those of EU. Next, the results of this study were compared with SNMMI standard administered radioactivity in representative diagnostic nuclear medicine procedures: the upper limit of SNMMI standard administration radioactivity (bone scintigraphy: 1110 MBq [30], cerebral blood flow scintigraphy: 1110 MBq [31], myocardial perfusion ^{99m}Tc agents: 1110 MBq, ^{201}Tl-Cl: 148 MBq [32], ^{18}F-FDG oncology PET: 740 MBq [33]) following facilities were bone scintigraphy (^{99m}Tc-MDP: 99.4 %, ^{99m}Tc-HMDP: 99.7 %), cerebral blood flow scintigraphy (^{99m}Tc-HM-PAO: 100 %, ^{99m}Tc-ECD: 100 %), myocardial perfusion (^{99m}Tc-Tetrofosmin: 100 %, ^{99m}Tc-MIBI: 100 %, ^{201}Tl-Cl: 41 %) and oncology PET (^{18}F-FDG of both in-

Table 2 Comparisons of diagnostic reference levels (DRLs) between European Union (EU) and Japan

Procedure and radiopharmaceutical	DRLs in EU[a] (MBq)		DRLs in Japan (MBq)
	Most common value	Range	
Bone: ^{99m}Tc-MDP and HMDP	600	500–1110	950
Myocardial perfusion: ^{201}Tl-Cl	110	75–150	180
Myocardial perfusion: ^{99m}Tc-tetrofosmin (rest or stress)	1200	300–1500	900
Myocardial perfusion: ^{99m}Tc-MIBI (rest or stress)	1200	300–1480	900
Tumor: ^{18}F-FDG (in-housed-produced and delivery)	–	200–400	240
Thyroid: ^{99m}Tc-pertechnetate	80	75–222	300
Thyroid: ^{123}I-NaI	20	10–37	10
Lung perfusion: ^{99m}Tc-MAA	150	100–296	260
Renal imaging (static): ^{99m}Tc-DMSA	–	70–183	210
Renal imaging (dynamic): ^{99m}Tc-MAG3	100	100–370	400
Renal imaging (dynamic): ^{99m}Tc-DTPA	–	150–540	400
Parathyroid: ^{99m}Tc-MIBI	–	400–900	800
Cerebral blood flow: ^{99m}Tc-HM-PAO (rest or stress)	500	500–1110	800
Tumor and inflammation: ^{67}Ga-citrate	–	110–370	200

[a] European Commission, 2010, DDM2 project report part 2: diagnostic reference levels (DRLs) in Europe

housed-produced and delivery: 100 %), respectively. Almost none of the administered radioactivity doses in Japan exceeded the upper limit of SNMMI standard administration radioactivity except for ^{201}Tl-Cl for myocardial perfusion. In ^{18}F-FDG for oncology PET, none of the doses at any of the facilities (100 %) exceeded the lower limit of SNMMI recommended administered radioactivity.

Convergence rate of the administered radioactivity, and the role of academic societies and experts

Table 3 shows the percentage of facilities that were within the range (25, 30 and 50 %) from the median of representative diagnostic nuclear medicine examinations in Japan. More than half of the facilities were within the range of 25 %. In addition, more than 90 % of the facilities were within the range of 50 %. In particular, the percentage of facilities was greater than 95 % in the range of 50 % in representative diagnostic nuclear medicine procedures except for the ^{99m}Tc-Tetrofosmin (myocardial perfusion scintigraphy) and ^{201}Tl-Cl (myocardial perfusion scintigraphy). Our findings indicate that the administered radioactivity for diagnostic nuclear medicine has been in convergence zones in Japan.

Table 3 Range from median value in this study results of representative administered radiopharmaceuticals

Procedure and radiopharmaceutical
Bone: ^{99m}Tc-MDP
Bone: ^{99m}Tc-HMDP
Cerebral blood flow: ^{99m}Tc-HM-PAO
Cerebral blood flow: ^{99m}Tc-ECD
Cerebral blood flow: ^{123}I-IMP
Myocardial perfusion: ^{99m}Tc-Tetrofosmin
Myocardial perfusion: ^{99m}Tc-MIBI
Myocardial perfusion: ^{201}Tl-Cl
Tumor: ^{18}F-FDG (in-house-produced)
Tumor: ^{18}F-FDG (delivery)

Essentially, optimization of the dose by DRL is performed at each facility, and is believed to lead to optimization in the whole country or region. However, nuclear medicine facilities have a strong tendency to adhere to the texts and guidelines in Japan. Therefore, in the optimization of radiopharmaceutical doses in Japan, a greater role of societies and organizations or experts is needed. As the finding of this study shows and the current state of Japan, to optimize radiopharmaceutical doses, Achievable Doses (ADs) [10, 12] might be useful, too.

Development of Japan DRLs

Based on the results of this study, a draft of Japan DRLs was prepared by the JSNM radiological protection committee.

Subsequently, it was approved by the JSNM board of directors, board of directors of the societies and organizations that performed the collaboration investigation,

J-RIME general meeting and J-RIME constituent bodies, respectively, and Japan DRLs were officially published on June 7, 2015 [34].

Limitation

Although the actual administered radioactivity doses to a standard body weight patient were obtained, the weight of the patients was not specified. It is necessary to pay attention to determine doses for DRLs when the standard body weight is different, because it is likely that the standard weight differs between Westerners and Asians.

Conclusions

For the first time a nationwide survey by nuclear medicine-related societies and organizations for the development of the Japanese DRLs of nuclear medicine was conducted in Japan. This study demonstrated that the administered radioactivity in diagnostic nuclear medicine in Japan has been in the convergence zone. Nuclear medicine facilities in Japan show a strong tendency to adhere to the package insert, texts and guidelines. Furthermore, the Japan administered radioactivities were within the range of variation of the EU and the SNMMI administration radioactivities. Whether nuclear facilities can optimize the dose, or whether this is required, depends on the role of the academic societies and experts.

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