J of Nuclear Medicine Technology, first published online September 28, 2021 as doi:10.2967/jnmt.121.262175

NATIONAL DIAGNOSTIC REFERENCE LEVELS FOR NUCLEAR MEDICINE IN KUWAIT

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The diagnostic reference level (DRL) is an optimization tool of patients exposure used to evaluate and provide guidance for radiation doses in medical imaging. In the past few decades, there has been a global increase in the number of diagnostic imaging procedures, including nuclear medicine procedures, and consequently the patient radiation exposure. This has encouraged international and national healthcare organizations to take actions and keep up with such changes to meet the expectations of an increasing use of ionizing radiation in medicine. The DRL in Kuwait was established by investigating the administered activity of radiopharmaceuticals and computed tomography (CT) radiation doses in hybrid imaging systems. The DRL were determined based on the 75th percentile of radiopharmaceuticals administered activity distribution as recommended by the international commission on radiation protection (ICRP). This study presents the establishment process and results of the first national DRLs for nuclear medicine procedures in Kuwait as a way to optimize radiation exposure. The DRLs determined in Kuwait are in good agreement with other published DRLs in Europe, Japan, Korea, Australia and the US.

Word count: 4294
Financial Support: None
Keywords: DRL; hybrid imaging; radiation exposure; ALARA dose optimization; radiation safety.
Disclosure: The authors declare that they have no conflict of interest.
Running title: Optimizing Patients Radiation Exposure from NM Procedures

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ABSTRACT

The diagnostic reference level (DRL) is an optimization tool of patients exposure used to evaluate and provide guidance for radiation doses in medical imaging. In the past few decades, there has been a global increase in the number of diagnostic imaging procedures, including nuclear medicine procedures, and consequently the patient radiation exposure. This has encouraged international and national healthcare organizations to take actions and keep up with such changes to meet the expectations of an increasing use of ionizing radiation in medicine. The DRL in Kuwait was established by investigating the administered activity of radiopharmaceuticals and computed tomography (CT) radiation doses in hybrid imaging systems. The DRL were determined based on the 75^{th} percentile of radiopharmaceuticals administered activity distribution as recommended by the International Commission on Radiological Protection (ICRP). This study presents the establishment process and results of the first national DRLs for nuclear medicine procedures in Kuwait as a way to optimize radiation exposure. The DRLs determined in Kuwait are in good agreement with other published DRLs in Europe, Japan, Korea, Australia and the US.

INTRODUCTION

Over the past few decades, there has been a growing clinical use of diagnostic imaging procedures in an attempt to improve the accuracy of disease diagnosis and to resolve clinical dilemmas. This included the use of both anatomical and radiological modalities and functional nuclear medicine (NM) modalities, including conventional and hybrid procedures like SPECT/CT and PETC/CT. Nearly 13.5 million nuclear medicine procedures were performed in the US in 2016 *(1).* In Kuwait, there are more than five thousand NM procedures performed every year. Unfortunately, the radiation dose to patients determined from the amount of administered radiopharmaceutical activities might vary by as much as twenty-fold among different nuclear medicine departments *(2).* At the moment, no information is available on dose reference levels for nuclear medicine in Kuwait and there is a similar lack of information from neighboring countries in the region. Therefore, the International Atomic Energy Agency (IAEA) encouraged national and international initiatives to standardize and optimize patient administered activities.

The International Commission on Radiological Protection (ICRP) established the concept of reference doses guidelines for different imaging modalities in order to reduce and manage patient's radiation exposure since more than 20 years *(3,4).* The diagnostic reference level (DRL) is an effective tool for protection optimization in patient radiation exposure, particularly as dose limits are not applicable in medical exposure. DRL quantities should evaluate the amount of ionizing radiation used to perform a diagnostic, interventional or nuclear medicine procedures and to assess the effective dose (ED) to patients. The radiation metric used as a DRL quantity should be easily measured or available, such as volume computed tomography (CT) dose index (CTDIvol) and dose–length product (DLP) for CT and administered activity in nuclear

medicine *(4).* In this context, when a hybrid imaging procedure is performed, i.e. two imaging modalities are used together, it is appropriate to set and present DRL values for both modalities independently. Two major guidelines for the recommended administered activities for nuclear medicine have been developed in Europe *(5)* and North America *(6).* Recent studies published in reputed medical journals have demonstrated multiple national initiatives to establish DRLs for nuclear medicine as a tool to control and reduce patient radiation exposure *(7–10).*

In 2012, nuclear medicine global initiative (NMGI) was established that aims to promote human health by advancing the fields of nuclear medicine and molecular imaging, to encourage global collaboration in education and to harmonize procedure guidelines and other policies that ultimately lead to improvements in quality and safety in the field throughout the world *(11).* One of the recommendations of this initiative was that countries with no current paediatric nuclear medicine administered activities guidelines should either develop their own or officially adopt currently existing ones.

Nuclear medicine and hybrid imaging procedures could also increase radiation exposure to the general public due to the characteristics of the administered radiopharmaceuticals compared to diagnostic radiology procedures. This has raised many concerns for the potential radiation risks *(12).* Subsequently, various methods to reduce patients radiation exposure and dose optimization was developed such as reference levels. In addition, there is a need to assess, monitor and regularly review patient radiation doses during medical exposure. This study presents the establishment process and results of the first DRLs for nuclear medicine procedures in Kuwait.

MATERIALS AND METHODS

The study was carried out with Kuwait's Ministry of Health (MOH) initiative to collect information about nuclear medicine studies radiation doses and to setup a national DRLs. A committee was formed by the MOH in 2016 to conduct a nationwide survey on the type of exams commonly performed, radiopharmaceutical administered activities, types of imaging equipment available, quality control records and the standard procedures used to determine patient doses for nuclear medicine imaging studies as explained by the ICRP publication 135 *(4).*

The number of equipment and status of nuclear medicine in Kuwait was described and published by our academic group *(13).* The data was collected from 11 NM departments as recommended by the ICRP 135 to at least collect data from 10 facilities for the establishment of local DRLs. Each department was asked to enter the average value of administered activities used for nuclear medicine examinations. The number of reported general NM protocols were 51 and 4 PET protocols. Some protocols were conducted by few departments or rarely used, hence, the DRL was calculated only if the protocol is used by more than four departments. Only 31 protocols met this condition. The MOH Ethics Committee approved this retrospective study and the requirement to obtain informed consent was waived.

For each protocol, the dose distributions derived from current practice in terms of (25^{th} percentile, 50^{th} percentile, 75^{th} percentile, minimum, maximum, standard deviation (SD) and effective dose (ED)) were generated. The third quartile (75^{th} percentile) of the average dose distribution reported by survey participants was used to establish national DRLs. The effective radiation dose received by patients from nuclear medicine procedures was estimated based on the dose coefficients extracted from the ICRP 106 and SNMMI radiation dose tool *(14,15).* The results were compared to other countries

DRLs indicated in international references. The conversion factors for administered activities based on patient weights for the most common NM procedures in Kuwait were determined. The recommended pediatric DRL values based on the European Association of Nuclear Medicine (EANM) dosage card for administered activities with reference to weight or age (< 15 years) were also presented.

The CT component of hybrid systems was used for attenuation correction (AC) and/or localization purposes only. The CT data were collected for the most commonly used protocols of PET/CT and SPECT/CT procedures. The 75^{th} percentile values of scanner average $CTDI_{vol}$ and DLP were used to establish DRLs of CT component in hybrid examinations as described by the CT working group in the UK *(16).* To estimate the effective radiation dose from CT component of hybrid imaging, the DLP values from the scanner-generated dose reports were multiplied by a conversion factor *(17).* All data analyses were undertaken using Microsoft Excel (Microsoft Office Pro Plus 2019).

RESULTS

Completed surveys of current practice were received from NM departments in Kuwait for the protocols that met the conditions. For each procedure, the statistical distributions of the administered activities, proposed DRL values and estimated effective dose for adult patients derived from current practice were generated as shown in Table 1.

The DRL values in Kuwait were compared with recently internationally reported DRL values as shown in Table 2. Pediatric reference DRL are generally based on adults based DRL activities multiplied by a correction factor that was adopted from the EANM dosage card as presented in Table 3. The recommended conversion factors adopted from the EANM dosage card and the north American consensus guidelines for administered activities based on patient weight are presented in Table 4.

For hybrid imaging examinations, the DRLs of the CT component of SPECT/CT are listed in Table 5 for most commonly used protocols. The DRLs for CT irradiation dose from PET/CT imagining for head/brain, vertex- thighs and vertex- toes protocols are listed in Table 6.

DISCUSSION

The ICRP introduced three principles that became a cornerstone in radiation protection. These principles evolved into three keywords: justification, optimization and limitation. Optimization aims to ensure that every exposure is performed with the least amount of ionizing radiation possible to execute the procedure, following the ”As low as reasonably achievable (ALARA)” principle. The DRLs were considered as an effective optimization tool for improving radiation protection in diagnostic medical imaging *(4)*. DRLs are not in any way dose limits or constraints, nor do they serve regulatory purposes. However, they aim to identify if some common procedures present unusually high values alerting the department to act accordingly by for instance reviewing procedures, protocols and/or equipment.

The first national DRLs for commonly performed nuclear medicine imaging procedures in Kuwait, including hybrid imaging procedures like PET/CT and SPECT/CT, were established in this study. The results in Table 1 show that there is a large variation in the reported administered activities. For instance, there is dispersion between the activities used for ^{99m}Tc-MDP bone scan which is indicated by the large SD and the three-fold difference between the maximum and minimum values. Thus, there is a need for reference levels and standardization of activities. The effective radiation doses for average weight adult patient can be categorized according to Towson et al. *(18)* into the following:

- High dose procedures (> 10 mSv)
    - ^{67}Ga - infection
    - ^{131}I - thyroid cancer
- Moderate dose procedures (< 10 mSv)
    - ^{18}F NaF, ^{18}F FDG –tumor and brain imaging
    - ^{99m}Tc bone, cardiac, brain, renal, lung, hepatobiliary, salivary, thyroid and parathyroid scans
- Low dose procedures (< 1 mSv)
    - Rest of the procedures

It is noteworthy that the average reduction in the effective doses when using the DRL values in routine work is up to 25%. The impact of dose reduction is estimated by comparing the maximum to the DRL recommended activities and it is more effective when applied to high dose procedures involving ^{67}Ga and ^{131}I radioisotopes. Additionally, the DRLs can also have a lower value, i.e. 25th percentile as shown in Table 1, indicating that below a certain dose, the resulting image quality could be diagnostically insufficient. Thus, the 25th percentile is an indicator for the minimum dose that can be used to achieve acceptable image quality. As described by Korpela et al. *(19)* the first step in optimizing medical exposure is the establishment of national DRL where using unusually high or low activities compared with the national distribution can be identified.

The results in Table 2 show that the DRL values in Kuwait are comparable and in good consensus with DRL values reported from other countries. The DRL value in Kuwait for ^{18}F-FDG tumor imaging is generally lower than the US, UK and Australian DRLs. The large differences between ^{18}F-FDG DRL in Kuwait compared with other countries reported DRLs could reflect the fact that the data in this study was gathered recently

(many years later than other reported data), during which scanners with more advanced imaging technology and sophisticated dose saving technologies have been utilized, and there may have become a greater awareness of the need for optimization.

For myocardial perfusion scans, especially for the rest studies, the DRL values tend to be higher than other values presented in Table 2. This could be due to the fact that the stress and rest parts of the study are performed on two different days and the one-day protocol is not routinely performed in Kuwait. The optimization of radiopharmaceutical activities used for myocardial perfusion scans has been widely promoted by the establishment of the national DRLs.

Recently, there has been several reviews of children and adolescence administered activities that led to development of paediatric guidelines in nuclear medicine *(20,21).* Table 3 shows the pediatric minimum recommended administered activities that can be used to minimize the variations in the practice of paediatric nuclear medicine in Kuwait. These calculated activities are weight and age based. Table 4 shows the recommended conversion factors for administered activities based on patient's weight. These factors can be used for children, adolescence and adult patients who weigh more than average weight.

CT scanning in hybrid imaging procedures is performed for different purposes which ranges from obtaining diagnostic quality high dose images to ultra-low-dose images for attenuation-correction protocols *(22).* The variations between CT radiation doses delivered to the patient in hybrid imaging examinations is mainly due to the varied types of equipment settings and acquisition protocols. A detailed analysis of current practice in Kuwait for CT in hybrid imaging studies is demonstrated in reported national dose audit *(23).* The DRL values of the CT portion associated with hybrid imaging procedures performed for attenuation correction and localization purposes in

Kuwait are presented in Table 5 and 6. CT dose can be optimized for PET/CT examinations by further investigating the CT protocol parameters that contribute to the dose received by patients.

The DRL values in Kuwait are consistent with the values presented in the literature for NM centers around the world. It is recommended to periodically review DRL values e.g. every 5 years. Periodic review of DRL values is required because imaging technologies and radiopharmaceuticals are rapidly advancing which can result in reducing radiation doses to the patients. The concept of comparing with reference values like the DRLs is an effective tool to alert professionals in some departments where the ALARA principle of dose optimization was not fully implemented *(24)*.

As DRL is supposed to be the activity needed for diagnosable good image quality, evaluating the patient doses and setting the DRLs based on only the administrated activities regardless of the image quality is not enough. The introduction of reference doses including image quality criteria and the acceptable quality dose has been proposed *(25)*. Thus, efforts are needed to develop reliable patient specific method to objectively analyze image quality in relation to dose. There are some large variations in the subjective analysis of image quality due to differences in physicians preferences in determining diagnosable image qualities. Some approaches are used to evaluates image quality that need further evaluation as demonstrated by the Japanese Society Of Nuclear Medicine Technology *(26)*.

CONCLUSIONS

In this study, the first DRL for nuclear medicine imaging studies in Kuwait for adults and pediatrics has been established. The values should be periodically reviewed and updated as recommended by the ICRP. The DRL is an effective tool that can be used in order to reduce unnecessary patient exposure and for the optimization of radiation protection in the field of nuclear medicine imaging.

ACKNOWLEDGMENTS

The authors thank the medical imaging council and nuclear medicine units who participated in this study for their contributions.

KEY POINTS:

- In this study, we report the first national diagnostic reference levels for nuclear medicine in Kuwait to be use as a tool to alert professionals where the ALARA principle of dose optimization is not fully implemented.
- The established national DRLs were used to identify variations in administered activities used for nuclear medicine imaging procedures and to reduce unnecessary patient radiation exposure. The findings show that the average reduction in radiation dose used for nuclear medicine examinations based on national DRLs is up to 25% compared to the range of doses observed previously in clinical practice.
- the DRLs concept is a key component for radiation protection and optimization of patient imaging in the field of nuclear medicine.

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Table 1. DRL (MBq) for most common procedures in Kuwait. The dose distributions in terms of 25th percentile, 50th percentile, 75th percentile, maximum, minimum, standard deviation and effective dose associated with the DRL of administered activity are presented.

Procedure Name	Radiopharmaceuticals	25th Percentile	50th Percentile	75th Percentile	Max	Min	SD	DRLs	ED (mSv)
PET (Tumor)	F^{18} FDG	222	228	230	231	185	18	230	4.4
PET (Brain)	F^{18} FDG	223	228	231	231	222	3.9	231	4.4
PET	F^{18} NAF	185	220	230	231	185	22	230	6.2
PET	Ga^{68} (Dotatate/PSMA)	150	150	217	231	150	38	217	0.9
Gated blood pool scan	Tc^{99m} RBC	740	740	850	1100	740	115	850	5.6
MPI - Rest	Tc^{99m} Tetrofosmin, MIBI	914	958	976	1039	884	49	976	7.4
MPI - Stress	Tc^{99m} Tetrofosmin, MIBI	914	958	976	1039	884	49	976	7.4
Renal scan	Tc^{99m} DMSA	185	200	200	250	180	20	200	1.5
Renal scan	Tc^{99m} DTPA (GFR)	73	85	90	100	60	14	90	0.7
Renal scan	Tc^{99m} MAG3	204	260	370	407	185	90	370	2.8
Bone Scan	TC^{99m}MDP	897	927	944	1110	459	171	944	7.2
Brain	Tc^{99m} HMPAO	828	850	893	900	800	39	893	6.8
Gastrointestinal	Ga^{67} Citrate	13	15	20	25	10	5	20	2.0
Esophageal reflux	TC^{99m}DTPA	36	40	40	40	30	3	40	0.3
Hepatobiliary	TC^{99m} HIDA	200	200	210	220	190	10	210	1.6
Infection	Tc^{99m} WBC(colloid/HMPAO)	663	725	750	800	500	94	750	5.7
Lung perfusion	Tc^{99m} MAA	200	204	218	220	190	11	218	1.7
Parathyroid	Tc^{99m} MIBI, Tetrofosmin	850	875	900	900	800	35	900	6.8
Salivary glands	Tc^{99m} pertechnetate	186	190	200	200	180	8	200	1.5
Testicular scan	Tc^{99m} pertechnetate	500	550	600	600	400	82	600	4.6
Thyroid scan	I^{131} iodide	200	200	200	250	180	25	200	10.4
Thyroid scan	Tc^{99m} pertechnetate	185	185	185	250	185	21	185	1.4
Gastric emptying	Tc^{99m} DTPA	13	15	37	37	10	5	37	0.3

Meckel's diverticulum	Tc^{99m} pertechnetate	250	264	278	278	220	24	278	2.1
Salivary glands	Tc^{99m} pertechnetate	194	197	200	200	10	59	200	1.5
Renal cystogram	Tc^{99m} pertechnetate	91	94	94	100	90	4	94	0.7
Testicular scan	Tc^{99m} pertechnetate	500	520	520	555	500	17	520	4.0
Infection	Ga^{67} Citrate	200	200	220	220	200	10	220	22.0
Lymphoscintigraphy	Tc^{99m} Nanocolloid	36	40	40	40	30	3	40	0.3
CSF leak	TC^{99m}DTPA	386	370	370	407	370	14.7	370	2.8
CSF shunt patency	Tc^{99m} pertechnetate	80	80	80	100	80	8	80	0.6

* PET, positron emission tomography; FDG, fluorodeoxyglucose; NAF, Sodium Fluoride; PSMA, Prostate-Specific Membrane Antigen; MDP, methyl diphosphonate; HMPAO, hexamethylpropyleneamine oxime; WBC, white blood cell; MIBI, methoxy-isobutyl-isonitrile; MPI, myocardial perfusion imaging RBC, red blood cell; SPECT, single-photon emission computed tomography; MAA, macroaggregated albumin; DTPA, diethylenetriamine pentaacetic acid; HIDA, hepatobiliary iminodiacetic acid; MAG3, mercaptoacetyltriglycine; DMSA, dimercaptosuccinic acid; MIBG, methyliodobenzylguanidine; GFR, Glomerular filtration rate; CSF, Cerebrospinal fluid.

Table 2. DRL (MBq) in Kuwait compared to other countries DRLs reported in the literature

Radiopharmaceuticals	procedures	Kuwait	Korea	Japan	Australia	UK	Brazil	US*	EU**
^{18}F-FDG	Tumor	230	370	240	310	400	370	461–710	200–400
^{18}F-FDG	Brain	231	370	240	250	250	350	-	-
^{99m}Tc-diphosphonate	Bone	944	925	950	920	600	1110	848–1185	500–1110
^{99m}Tc-HMPAO-WBC	Leukocyte	892.5	888	-	800	200	-	-	300–600
^{99m}Tc-pertechnetate	Thyroid	185	217	300	215	80	444	-	75–222
^{131}I-NaI	Thyroid ca	200	185	-	185	400	185	-	90–400
^{99m}Tc-MIBI	Parathyroid	900	740	800	900	900	740	-	400–900
^{99m}Tc-HMPAO	Brain	892.5	925	800	750	750	1203	887–1294	500–1110
^{99m}Tc-MIBI or TF (MPI, rest)	Cardiac	976	555	900	620	800	444	519-1153	560
^{99m}Tc-MIBI or TF (MPI, stress)	Cardiac	976	1110	1200	1520	800	1110	945-1402	1100
^{99m}Tc-RBC	Cardiac	740	740	-	1030	800	-	916–1301	600–1000
^{99m}Tc-MAA	Lung perfusion	217.5	222	260	240	100	333	147–226	100–296
^{99m}Tc-phytate	Lymphangioscintigraphy	40	148		52	40	74	-	74–150
^{99m}Tc-phytate	Hepatobiliary	210	185	200	200	80	370	110–259	-
^{99m}Tc-pertechnetate	Salivary	370	370	370	200	80	555	-	-
^{99m}Tc-DTPA	Gastric emptying	37	111	-	44	12	-	31–50	150–540
^{99m}Tc-DTPA	Renal dynamic	90	555	400	500	300	449	407–587	-
^{99m}Tc-MAG3	Renal dynamic	370	500	400	305	100	-	283–379	100–370
^{99m}Tc-DMSA	Renal static	200	185	210	200	80	185	189–289	70–183
^{99m}Tc-pertechnetate	Radionuclide cystography	94	74	-	94	25	-	-	-

* NCRP Report No. 172 – Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States
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Table 3. Pediatric minimum recommended administered activities in MBq*

Radiopharmaceuticals	procedures	1 yr	5 yr	10 yr	15 yr
		10 kg	19 kg	32 kg	≥ 55 kg
^{18}F-FDG	Tumor	70	120	189	200
^{18}F-FDG	Brain	70	70	102	180
^{99m}Tc-diphosphonate	Bone	80	162	255	408
^{18}F-NaF	Bone	70	70	102	163
^{99m}Tc-MAA	Lung perfusion	15	26	41	65
^{99m}Tc-phytate	Hepatobiliary	28	49	77	122
^{99m}Tc-MAG3	Renal dynamic	23	33	45	61
^{99m}Tc-DMSA	Renal static	33	48	64	87
^{99m}Tc-pertechnetate	Radionuclide cystography	20	20	20	20
^{99m}Tc-pertechnetate	Meckel scan	20	26	41	65
^{99m}Tc-sulfur colloid	Gastric emptying	10	13	20	33

* Adopted from EANM pediatric Dosage card *(5)*

Table 4. Recommended weight-based dosing guidance on administered activities based on patient's weights (MBq/kg)

Procedure Name	Radiopharmaceuticals	MBq/kg
PET (Tumor)	F^{18} FDG	5.18
PET (Brain)	F^{18} FDG	3.7
PET	F^{18} NAF	2.22
PET	Ga^{68} (Dotatate/PSMA)	1.85
Gated blood pool scan	Tc^{99m} RBC	8.14
MPI Rest	Tc^{99m} Tetrofosmin, MIBI	10.73
MPI Stress	Tc^{99m} Tetrofosmin, MIBI	10.73
Renal scan	Tc^{99m} DMSA	1.85
Renal scan	Tc^{99m} DTPA (GFR)	2.59
Renal scan	Tc^{99m} MAG3	3.7
Bone Scan	TC^{99m} MDP	9.25
Brain	Tc^{99m} HMPAO	2.775
Gastrointestinal	Ga^{67} Citrate	1.85
Esophageal reflux	TC^{99m} DTPA	0.37
Hepatobiliary	TC^{99m} HIDA	1.85
Infection	Tc^{99m} WBC (colloid/HMPAO)	27.75
Lung perfusion	Tc^{99m} MAA	2.59
Parathyroid	Tc^{99m} MIBI, tetrofosmin	5.55
Salivary glands	Tc^{99m} pertechnetate	1.11
Testicular scan	Tc^{99m} pertechnetate	7.4
Thyroid scan	I^{131} iodide	0.555
Thyroid scan	Tc^{99m} pertechnetate	1.11
Gastric emptying	Tc^{99m} DTPA	0.37
Meckel's diverticulum	Tc^{99m} pertechnetate	1.85
Renal cystogram	Tc^{99m} pertechnetate	0.37
Infection	Ga^{67} Citrate	1.11
Lymphoscintigraphy	Tc^{99m} Nanocolloid	0.259
CSF leak	TC^{99m} DTPA	2.59
CSF shunt patency	Tc^{99m} pertechnetate + DTPA	0.259

Table 5. the DRL for CT used for AC and Localization in SPECT scans in terms of the volume computed tomography dose index and dose-length product and effective dose associated with hybrid CT of SPECT/CT.

Protocol	$CTDI_{vol}$ (mGy)	DLP (mGy.cm)	ED (mSv)
SPECT/CT brain	5.6	163	2.44
SPECT/CT head and neck	4.5	181	2.74
SPECT/CT lung	2.1	69	1.03
SPECT/CT cardiac	1.2	32	0.48
SPECT/CT abdomen	1.7	65	0.98
SPECT/CT bone general	2.7	166	2.49
SPECT/CT bone extremities	2	169	2.53

Table 6. the DRL for CT used for AC and Localization in PET scans in terms of the volume computed tomography dose index and dose-length product and effective dose associated with hybrid CT of PET/CT.

Protocol	$CTDI_{vol}$ (mGy)	DLP (mGy.cm)	ED (mSv)
PET/CT Brain	5.7	211	3.16
PET/CT Oncology (vertex to mid-thigh)	4.2	677	5.66
PET/CT Oncology WB (head to toe)	4.4	616	6.10

*WB, whole body

Graphical Abstract