National Diagnostic Reference Levels for Nuclear Medicine in Kuwait

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The diagnostic reference level (DRL) is a patient-exposure optimization tool 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 in patient radiation exposure. This increase has encouraged international and national health-care organizations to take action and keep up with such changes to meet the expectation of increasing use of ionizing radiation in medicine. **Methods:** DRLs in Kuwait were established by investigating the administered activity of radiopharmaceuticals and CT radiation doses in hybrid imaging systems. The DRLs were determined on the basis of the 75th percentile of radiopharmaceutical administered activity distribution as recommended by the International Commission on Radiological Protection. **Results:** The DRLs determined in Kuwait agree well with other published DRLs in Europe, Japan, Korea, Australia, and the United States. **Conclusion:** This study presents the establishment process and the results of the first national DRLs for nuclear medicine procedures in Kuwait as a way to optimize radiation exposure.

Key Words: DRL; hybrid imaging; radiation exposure; ALARA dose optimization; radiation safety

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Over the past few decades, clinical use of diagnostic imaging procedures has been growing in an attempt to improve the accuracy of diagnosis and to resolve clinical dilemmas. This growth has included both the use of anatomic and radiologic modalities and the use of functional nuclear medicine modalities, including conventional and hybrid procedures such as SPECT/CT and PET/CT. Nearly 13.5 million nuclear medicine procedures were performed in the United States in 2016 (*1*). In Kuwait, more than 5,000 nuclear medicine procedures are performed every year. Unfortunately, the radiation dose to patients determined from the amount of administered radiopharmaceutical activity might vary by as much as 20-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 has encouraged national and international initiatives to standardize and optimize activities administered to patients.

More than 20 years ago, the International Commission on Radiological Protection (ICRP) established the concept of reference dose guidelines for different imaging modalities to reduce and manage patient radiation exposure (*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 procedure and to assess the effective dose to patients. The radiation metric used as a DRL quantity should be easily measured or available, such as volume CT dose index and dose–length product for CT and administered activity in nuclear medicine (*4*). In this context, when a hybrid imaging procedure is performed—that is, 2 imaging modalities are used together—it is appropriate to set and present DRLs 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, a nuclear medicine global initiative 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 fields throughout the world (*11*). One of the recommendations of this initiative was that countries with no current guidelines on administered nuclear medicine activities in children should either develop their own or officially adopt currently existing ones.

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Nuclear medicine and hybrid imaging procedures may also increase radiation exposure to the general public because of the characteristics of the administered radiopharmaceuticals compared with diagnostic radiology procedures. This potential increased exposure has raised many concerns about potential radiation risks (*12*). Subsequently, various methods to reduce patient radiation exposure and optimize doses were 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 the results of the first DRLs for nuclear medicine procedures in Kuwait.

MATERIALS AND METHODS

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

The amount of equipment and status of nuclear medicine in Kuwait were previously described and published by our academic group (*13*). The data were collected from 11 nuclear medicine departments as recommended by ICRP 135 to collect data from at least 10 facilities for the establishment of local DRLs. Each department was asked to enter the average administered activities used for nuclear medicine examinations. The number of reported protocols was 51 for general nuclear medicine and 4 for PET. Some protocols were conducted by only a few departments or were rarely used; hence, the DRL was calculated only if the protocol was used by more than 4 departments. Only 31 protocols met this condition. The Ministry of Health 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 were generated in terms of 25th percentile, 50th percentile, 75th percentile, minimum, maximum, SD, and effective dose. The third quartile (75th 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 on the basis of the dose coefficients extracted from ICRP 106 and the Society of Nuclear Medicine and Molecular Imaging radiation dose tool (*14,15*). The results were compared with other countries' DRLs as indicated in international references. The conversion factors for administered activities for the most common nuclear medicine procedures in Kuwait were determined on the basis of patient weight. The recommended pediatric DRLs based on the European Association of Nuclear Medicine dosage card for administered activities with reference to weight or age (<15 y) were also presented.

The CT component of hybrid systems was used for attenuation correction or localization purposes only. The CT data were collected for the most commonly used protocols for PET/CT and SPECT/CT procedures. The 75th percentiles of the average volume CT dose index and dose–length product for the scanner were used to establish DRLs for the CT component in hybrid examinations as described by the CT working group in the United Kingdom (*16*). To estimate the effective radiation dose from the CT component of hybrid imaging, the dose–length products from the scanner-generated dose reports were multiplied by a conversion factor (*17*). All data analyses were undertaken using Excel (Office Pro Plus 2019; Microsoft).

RESULTS

Completed surveys of current practice were received from nuclear medicine departments in Kuwait for the protocols that met the conditions. For each procedure, the statistical distributions of the administered activities, proposed DRLs, and estimated effective doses for adult patients derived from current practice were generated (Table 1).

The DRLs in Kuwait were compared with DRLs recently internationally reported (Table 2). Pediatric reference DRLs are generally based on adult DRLs multiplied by a correction factor that was adopted from the European Association of Nuclear Medicine dosage card (Table 3). The recommended conversion factors adopted from the European Association of Nuclear Medicine dosage card and the North American consensus guidelines for administered activities based on patient weight are presented in Table 4.

Regarding 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 the CT irradiation dose from PET/CT protocols for head and brain, vertex to thighs, and vertex to toes are listed in Table 6.

DISCUSSION

The ICRP introduced 3 principles that became a cornerstone in radiation protection. These principles evolved into 3 key words: justification, optimization, and limitation. Optimization aims to ensure that every exposure is performed with the lowest ionizing radiation needed to execute the procedure, following the "as low as reasonably achievable" principle. DRLs are considered an effective optimization tool for improving radiation protection in diagnostic medical imaging (*4*) and are not in any way dose limits or constraints, nor do they serve regulatory purposes. However, they aim to identify whether some common procedures present unusually high values, alerting the department to act accordingly by, for instance, reviewing procedures, protocols, or equipment.

The first national DRLs for commonly performed nuclear medicine imaging procedures in Kuwait, including hybrid imaging procedures such as PET/CT and SPECT/CT, were established in this study. Table 1 shows that there is a large variation in the reported administered activities. For instance, there is a dispersion (as variance) between the activities used for ^{99m}Tc-methyl diphosphonate bone scanning, as indicated by the large SD and the 3-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 adults can be categorized according to Towson and Smart (*18*) into the following: high-dose (>10 mSv) procedures (^{67}Ga for infection and ^{131}I

TABLE 1
DRLs for Most Common Procedures in Kuwait

Scan	Radiopharmaceutical	25th percentile	50th percentile	75th percentile	Maximum	Minimum	SD	DRL (MBq)	Effective dose (mSv)
PET tumor	^{18}F-FDG	222	228	230	231	185	18	230	4.4
PET brain	^{18}F-FDG	223	228	231	231	222	3.9	231	4.4
PET	^{18}F-NaF	185	220	230	231	185	22	230	6.2
PET	^{68}Ga (DOTATATE/PSMA)	150	150	217	231	150	38	217	0.9
Gated blood pool	^{99m}Tc-RBC	740	740	850	1,100	740	115	850	5.6
MPI rest	^{99m}Tc-tetrofosmin, MIBI	914	958	976	1,039	884	49	976	7.4
MPI stress	^{99m}Tc-tetrofosmin, MIBI	914	958	976	1,039	884	49	976	7.4
Renal	^{99m}Tc-DMSA	185	200	200	250	180	20	200	1.5
Renal	^{99m}Tc-DTPA (GFR)	73	85	90	100	60	14	90	0.7
Renal	^{99m}Tc-MAG3	204	260	370	407	185	90	370	2.8
Bone	^{99m}Tc-methyl diphosphonate	897	927	944	1,110	459	171	944	7.2
Brain	^{99m}Tc-HMPAO	828	850	893	900	800	39	893	6.8
Gastrointestinal	^{67}Ga-citrate	13	15	20	25	10	5	20	2.0
Esophageal reflux	^{99m}Tc-DTPA	36	40	40	40	30	3	40	0.3
Hepatobiliary	^{99m}Tc-HIDA	200	200	210	220	190	10	210	1.6
Lung perfusion	^{99m}Tc-MAA	200	204	218	220	190	11	218	1.7
Parathyroid	^{99m}Tc-MIBI, tetrofosmin	850	875	900	900	800	35	900	6.8
Salivary gland	^{99m}Tc-pertechnetate	186	190	200	200	180	8	200	1.5
Testicular	^{99m}Tc-pertechnetate	500	550	600	600	400	82	600	4.6
Thyroid	^{131}I-iodide	200	200	200	250	180	25	200	10.4
Thyroid	^{99m}Tc-pertechnetate	185	185	185	250	185	21	185	1.4
Gastric emptying	^{99m}Tc-DTPA	13	15	37	37	10	5	37	0.3
Meckel diverticulum	^{99m}Tc-pertechnetate	250	264	278	278	220	24	278	2.1
Salivary gland	^{99m}Tc-pertechnetate	194	197	200	200	10	59	200	1.5
Renal cystogram	^{99m}Tc-pertechnetate	91	94	94	100	90	4	94	0.7
Testicular	^{99m}Tc-pertechnetate	500	520	520	555	500	17	520	4.0
Infection	^{67}Ga-citrate	200	200	220	220	200	10	220	22.0
Infection	^{99m}Tc-WBC (colloid/HMPAO)	663	725	750	800	500	94	750	5.7
Lymphoscintigraphy	^{99m}Tc-nanocolloid	36	40	40	40	30	3	40	0.3
CSF leak	^{99m}Tc-DTPA	386	370	370	407	370	14.7	370	2.8
CSF shunt patency	^{99m}Tc-pertechnetate, DTPA	80	80	80	100	80	8	80	0.6

PSMA = prostate-specific membrane antigen; RBC = red blood cell; MPI = myocardial perfusion imaging; MIBI = methoxyisobutylisonitrile; DMSA = dimercaptosuccinic acid; DTPA = diethylenetriamine pentaacetic acid; GFR = glomerular filtration rate; MAG3 = mercaptoacetyltriglycine; HMPAO = hexamethylpropyleneamine oxime; HIDA = hepatobiliary iminodiacetic acid; WBC = white blood cell; MAA = macroaggregated albumin; CSF = cerebrospinal fluid.

Dose distributions are presented in terms of 25th percentile, 50th percentile, 75th percentile, maximum, minimum, SD and effective dose associated with DRL of administered activity.

for thyroid cancer), moderate-dose (<10 mSv) procedures (^{18}F-NaF for bone imaging; ^{18}F-FDG for tumor and brain imaging; and ^{99m}Tc for bone, cardiac, brain, renal, lung, hepatobiliary, salivary, thyroid, and parathyroid scans), and low-dose (<1 mSv) procedures (the rest of the procedures).

It is noteworthy that the average reduction in effective doses when using DRLs in routine work is up to 25%. The impact of dose reduction is estimated by comparing the maximum to the DRL-recommended activities and is stronger when applied to high-dose procedures involving ^{67}Ga and ^{131}I radioisotopes. Additionally, the DRLs can also have a lower value, that is, the 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 of 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 DRLs, which allow identification of unusually high or low activities compared with the national distribution.

Table 2 shows that the DRLs in Kuwait are comparable to, and agree well with, those reported from other countries. The DRL in Kuwait for ^{18}F-FDG tumor imaging is generally lower than those in the United States, the United Kingdom, Australia. The large differences between the ^{18}F-FDG DRL in Kuwait and those reported for other countries could reflect the fact that the data in this study were gathered recently (many years later than other reported data), at a time when scanners with more advanced imaging technology and sophisticated dose-saving technologies have been used; since that time, a greater awareness of the need for optimization may have come about.

For myocardial perfusion scans, especially rest studies, the DRLs tend to be higher than other values presented in Table 2. The higher DRLs could be due to the fact that the stress and rest parts of the study are performed on 2 different days and that the 1-d protocol is not routinely performed in Kuwait. Optimization of radiopharmaceutical activities for myocardial perfusion scans has been widely promoted by the establishment of the national DRLs.

TABLE 2
DRLs (MBq) in Kuwait Compared with Other Countries as Reported in the Literature

Scan	Radiopharmaceutical	Kuwait	Korea	Japan	Australia	U.K.	Brazil	United States (*27*)	European Union (*28*)
Tumor	^{18}F-FDG	230	370	240	310	400	370	461–710	200–400
Brain	^{18}F-FDG	231	370	240	250	250	350	—	—
Bone	^{99m}Tc-diphosphonate	944	925	950	920	600	1,110	848–1,185	500–1,110
Leukocyte	^{99m}Tc-HMPAO-WBC	892.5	888	—	800	200	—	—	300–600
Thyroid	^{99m}Tc-pertechnetate	185	217	300	215	80	444	—	75–222
Thyroid carcinoma	^{131}I-NaI	200	185	—	185	400	185	—	90–400
Parathyroid	^{99m}Tc-MIBI	900	740	800	900	900	740	—	400–900
Brain	^{99m}Tc-HMPAO	892.5	925	800	750	750	1,203	887–1,294	500–1,110
Cardiac	^{99m}Tc-MIBI or TF (MPI, rest)	976	555	900	620	800	444	519–1,153	560
Cardiac	^{99m}Tc-MIBI or TF (MPI, stress)	976	1,110	1,200	1,520	800	1,110	945–1,402	1,100
Cardiac	^{99m}Tc-RBC	740	740	—	1,030	800	—	916–1,301	600–1,000
Lung perfusion	^{99m}Tc-MAA	217.5	222	260	240	100	333	147–226	100–296
Lymphangioscintigraphy	^{99m}Tc-phytate	40	148		52	40	74	—	74–150
Hepatobiliary	^{99m}Tc-phytate	210	185	200	200	80	370	110–259	—
Salivary	^{99m}Tc-pertechnetate	370	370	370	200	80	555	—	—
Gastric emptying	^{99m}Tc-DTPA	37	111	—	44	12	—	31–50	150–540
Renal dynamic	^{99m}Tc-DTPA	90	555	400	500	300	449	407–587	—
Renal dynamic	^{99m}Tc-MAG3	370	500	400	305	100	—	283–379	100–370
Renal static	^{99m}Tc-DMSA	200	185	210	200	80	185	189–289	70–183
Radionuclide cystography	^{99m}Tc-pertechnetate	94	74	—	94	25	—	—	—

Recently, there have been several reviews of child and adolescent administered activities that led to development of pediatric guidelines in nuclear medicine (*20,21*). Table 3 shows the minimum recommended pediatric administered activities that can be used to minimize variations in the practice of pediatric 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 weight. These factors can be used for children, adolescents, and adults who weigh more than average.

CT scanning in hybrid imaging procedures is performed for different purposes, ranging 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 due mainly to the varied types of equipment settings and acquisition protocols. A detailed analysis of current practice in Kuwait for CT in hybrid imaging studies was demonstrated in a reported national dose audit (*23*). The DRLs of the CT portion associated with hybrid imaging procedures performed for attenuation correction and localization purposes in Kuwait are presented in Tables 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 DRLs in Kuwait are consistent with those presented in the literature for nuclear medicine centers around the world. It is recommended that DRLs be reviewed periodically—for example, every 5 years. Periodic review of DRLs is required because imaging technologies and radiopharmaceuticals are rapidly advancing, and these advances can result in reducing the radiation doses to patients. Comparison with reference values such as DRLs is an effective tool to alert professionals in some departments that have not fully implemented the "as low as reasonably achievable" principle of dose optimization (*24*).

Because a DRL is supposed to be the activity needed for good, diagnosable image quality, it is not enough to evaluate

TABLE 3
Pediatric Minimum Recommended Administered Activities (5)

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

Data are in megabecquerels.

TABLE 4
Recommended Weight-Based Dosing Guidance on Administered Activities Based on Patient Weight

Scan	Radiopharmaceutical	MBq/kg
PET (tumor)	^{18}F-FDG	5.18
PET (brain)	^{18}F-FDG	3.7
PET	^{18}F-NaF	2.22
PET	^{68}Ga (DOTATATE/PSMA)	1.85
Gated blood pool	^{99m}Tc-RBC	8.14
MPI rest	^{99m}Tc-tetrofosmin, MIBI	10.73
MPI stress	^{99m}Tc-tetrofosmin, MIBI	10.73
Renal	^{99m}Tc-DMSA	1.85
Renal	^{99m}Tc-DTPA (GFR)	2.59
Renal	^{99m}Tc-MAG3	3.7
Bone	^{99m}Tc-methyl diphosphonate	9.25
Brain	^{99m}Tc-HMPAO	2.775
Gastrointestinal	^{67}Ga-citrate	1.85
Esophageal reflux	^{99m}Tc-DTPA	0.37
Hepatobiliary	^{99m}Tc-HIDA	1.85
Lung perfusion	^{99m}Tc-MAA	2.59
Parathyroid	^{99m}Tc-MIBI, tetrofosmin	5.55
Salivary gland	^{99m}Tc-pertechnetate	1.11
Testicular	^{99m}Tc-pertechnetate	7.4
Thyroid	^{131}I-iodide	0.555
Thyroid	^{99m}Tc-pertechnetate	1.11
Gastric emptying	^{99m}Tc-DTPA	0.37
Meckel diverticulum	^{99m}Tc-pertechnetate	1.85
Renal cystogram	^{99m}Tc-pertechnetate	0.37
Infection	^{67}Ga-citrate	1.11
Infection	^{99m}Tc-WBC (colloid/HMPAO)	27.75
Lymphoscintigraphy	^{99m}Tc-nanocolloid	0.259
CSF leak	^{99m}Tc-DTPA	2.59
CSF shunt patency	^{99m}Tc-pertechnetate + ^{99m}Tc, DTPA	0.259

PSMA = prostate-specific membrane antigen; RBC = red blood cell; MPI = myocardial perfusion imaging; MIBI = methoxyisobutylisonitrile; DMSA = dimercaptosuccinic acid; DTPA = diethylenetriamine pentaacetic acid; GFR = glomerular filtration rate; MAG3 = mercaptoacetyltriglycine; HMPAO = hexamethylpropyleneamine oxime; HIDA = hepatobiliary iminodiacetic acid; WBC = white blood cell; MAA = macroaggregated albumin; CSF = cerebrospinal fluid.

TABLE 5
DRLs for CT Used for Attenuation Correction and Localization in SPECT Scans in Terms of Volume CT Dose Index and Dose–Length Product and Effective Dose Associated with Hybrid CT of SPECT/CT

SPECT/CT protocol	Volume CT dose index (mGy)	Dose–length product (mGy·cm)	Effective dose (mSv)
Brain	5.6	163	2.44
Head and neck	4.5	181	2.74
Lung	2.1	69	1.03
Cardiac	1.2	32	0.48
Abdomen	1.7	65	0.98
Bone, general	2.7	166	2.49
Bone, extremities	2	169	2.53

TABLE 6
DRLs for CT Used for Attenuation Correction and Localization in PET Scans in Terms of Volume CT Dose Index and Dose–Length Product and Effective Dose Associated with Hybrid CT of PET/CT

PET/CT protocol	Volume CT dose index (mGy)	Dose–length product (mGy·cm)	Effective dose (mSv)
Brain	5.7	211	3.16
Oncology, vertex to mid thigh	4.2	677	5.66
Oncology, whole body (head to toe)	4.4	616	6.10

patient doses and set DRLs on the basis of only administrated activity regardless of image quality. Introduction of reference doses, including image quality criteria and the acceptable-quality dose (AQD principle), has been proposed (*25*). Thus, efforts are needed to develop reliable patient-specific methods 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 physician preferences on what constitutes an image of diagnosable quality. Some of the approaches used to evaluate image quality need further evaluation, as demonstrated by the Japanese Society of Nuclear Medicine Technology (*26*).

CONCLUSION

This study established the first DRLs for adult and pediatric nuclear medicine imaging studies in Kuwait. The values should be periodically reviewed and updated as recommended by the ICRP. DRLs are an effective tool that can be used to reduce unnecessary patient exposure and to optimize radiation protection in the field of nuclear medicine imaging.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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KEY POINTS

QUESTION: Can national DRLs be established for nuclear medicine in Kuwait, to be used as a tool to alert professionals when the "as low as reasonably achievable" principle of dose optimization is not fully implemented?

PERTINENT FINDINGS: National DRLs were established and used to identify variations in administered activities for nuclear medicine imaging procedures and to reduce unnecessary patient radiation exposure. The findings showed that the average reduction in radiation dose for nuclear medicine examinations based on national DRLs is up to 25%, compared with the range of doses observed previously in clinical practice.

IMPLICATIONS FOR PATIENT CARE: The DRL concept is a key component of radiation protection and optimization of patient imaging in the field of nuclear medicine.

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