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Original Article

Comparison of awareness of radiation protection, dose levels, and complications of radiation exposure in imaging procedures between radiology residents/undergraduate students and radiology staff: A cross-sectional study

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Abstract

Introduction

Radiographic tools are one of the most instruments in hospitals. The ionizing radiation process occurs in radiographic instruments. The ionizing radiation causes side effects in the users. Lack of knowledge of staff and students radiology regarding radiation risks, protection, and dose levels in medical imaging procedures causes complications in them. Therefore, this study was conducted to compare the awareness of radiology staff and students regarding radiation risks, protection, and dose levels in medical imaging procedures.

Methods

In this analytical cross-sectional study with the participation of 180 participants include 62 students and 118 radiology staff were done by convenience sampling from the hospitals of Tehran university of medical sciences, in 2020 from February to September. The structural and valid gathering tool including 3 sections: baseline data, radiation protection awareness and dose assessment knowledge questionnaire were used.

Results

Approximately 82 % of students chose a dose of lumbar X-ray exams between 1 and 50 times the (posterior – anterior (PA)) chest, and only 9 % answered the question correctly. However, 27% of the staff chose the correct answer. Students on the average dose of mammography had more choice (1-10 times) of a PA chest test, while staff preferred 100-500. The crew performed better on the dose resulting from a PET-CT test as well as the dose estimate from a nuclear medicine heart scan, and selected 36% correct response (more than 500 times the PA chest), while students had a lower rating (1-10 times) than others. Overall, 45% of students and staff had any training or retraining after completing their training at the university.

Conclusion

In self-reporting, most students and staff believed that they had a suitable or sufficient level of awareness of ionizing radiation. Radiology students had a better level of knowledge about radiation protection than radiology staffs, while radiology staffs had a better estimate in discussing dose assessment.

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Introduction

Radiographic tools are one of the most practical instruments in hospitals, which are utilizable



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in diagnostic imaging procedures [1]. The ionizing radiation process occurs in radiographic instruments. Today, the interpretation of radiographic images is one of the most important and practical tools in the diagnosis of diseases by the treatment team. In the early years of the use of radiology, simple radiography was the only available and eligible image that was used as a primary key by a physician due to its great convenience, high speed “procedures,” and relatively low expenditure. For illustration, using computer tomography (CT), which has more radiation exposure than conventional radiography, has increased effectively over the last 30 years (1-3). Although CT scan contains about 50% of the total radiation burden, it plays an important role in the medical field; it causes some concerns about the dangers of cancer. In the science of physics, ionizing radiation is radiation that has sufficient energy to separate an electron from an atom or molecule, it is called ionization [4]. Research has recognized significant numbers of unpleasant and negative effects of radiation, such as causing the occurrence of cancer, the possibility of causing disorders such as goiter, lung and breast cancer, cataract, infertility and leukemia (even in a low-level dose of radiation). Moreover, according to the statement of control and preventing disease centers, “exposure to the radiation” especially during the second to fifteenth weeks of pregnancy can be leading to irreversible effects such as sorts of the raucous, unnatural function of heart and brain,

and lack of growth [5,6]. Taking the foregoing into account, the full awareness of radiation protection issues and proper knowledge of the radiation doses delivered by the various imaging modalities should be considered as an essential concern [7]. A general principle of radiation protection is based on three principles: justification, optimization (as low as reasonably achievable), and dose limitation. This is the foundation of radiation protection strategies. The main principles for radiation protection are time, distance, and shielding which should be carefully controlled [8,9]. If an equal measure of radiation reaches each organ of the body, The greatest danger is for particular organs such as the thyroid gland, marrow, and genitals, which are called critical organs. Boshang explains that the most specific factors in protection against radiation are: 1- raising the distance 2- decreasing the time 3- using the guided shields [10-12]. By considering the third factor and also improving the awareness of staff for using leaden shields such as thyroid and gonad shields, we can prevent injuries to the mentioned critical organs. An overall review of the previous studies indicates that radiologists and technologists who are employed in different sections have inadequate information about ionizing beams, or they underestimate its harms [13-16]. At the same time, another study claims that reducing the dose level in X-Ray examinations is possible if imaging center staff get appropriate training [17]. Today, by spreading information, clienteles of imaging centers inquire



about potential perils of “imaging procedures” (One out of every four patients or 25.3%), whereas studies have reported the lack of ability to answer correctly to common questions of patients [18-20]. On the other hand, as shown by several studies, this increasing use of medical radiation can be partly explained by the inaccurate and often inadequate knowledge among professionals about radiation protection issues and radiation doses of commonly performed imaging procedures [16,21,22]. Despite lack of correct information to patients which is inverse to professional and ethical principles, the awareness of ionizing radiation dangers amongst medical staff in imaging centers is essential to plan for accomplishing diagnostic procedures of disease; moreover, it correlates with improving the protection against radiation which is all the primary purpose of the forwarding study. In Iran, there is little information about radiation protection among professional staff and students. This study aimed to compare the awareness of radiation protection, dose levels, and complications of radiation exposure in imaging procedures between radiology residents/ undergraduate students and radiology staff.

Methods

This analytical cross-sectional study is done in Tehran province in Iran, in 2020 from February to September. This study involved 180 participants, including 62 radiology residents and undergraduate radiology students, and

118 radiologists and radiographers. All the participants of the study who have passed the radiation protection course (academic course) and have filled out the questionnaire completely were enrolled in the study. For measuring their awareness, a validated structural questionnaire was used. The validity and reliability of the questionnaire were reported by F. Polcchi and et. al [23]. At first, this questionnaire was translated by two people into Persian whose mother tongue was Persian; then, the back-translation was done by two English language experts. Finally, another expert in both languages adapted the present questionnaire to the main questionnaire and the disagreements were resolved. Our goal in this study was to use this tool to measure awareness and knowledge. At the same time, the validity of the form and its content were measured by a panel of experts, which was acceptable. The questionnaire has acceptable internal reliability ($\alpha = 0.780$; 95% CI: 0.762 - 0.852) in total. Also, the questionnaire has acceptable internal reliability ($\alpha = 0.760$; 95% CI: 0.746 - 0.796) and ($\alpha = 0.727$; 95% CI: 0.688 - 0.744) in the radiation protection and radiation dose levels awareness respectively. The questionnaire was divided into three sections including demographics data (questions in this part consist of age, gender, work experience and positioning of the person (student, staff), 2) radiation protection awareness (Questions in this part have assessed in 7 categories: 1- The necessity informing patients against dangers of ionizing



Table 1. Comparison of baseline data (age, gender, duration of education /work experience, training and level of radiation protection awareness).

Variable	Radiology students (n=62)	Radiology staff (n=118)	P-value* ¹
Age, y (mean± SD)	22.5±2.8	35.6±6.8	<0.001
Gender, male,	25 (45.5)	37 (34.6)	0.177
Duration of education /work experience			
<4 y	62 (100)	24 (20.1)	<0.001
≥4 y	0	94 (79.10)	
Training experience			
Frequently	11 (17.7)	19 (16.5)	0.978
Rarely	28 (45.2)	53 (46.1)	
Never	23 (37.1)	43 (37.4)	
Perceived knowledge, (Self-declaration)			
Excellent	4 (6.6)	12 (10.3)	0.306
Good	22 (36.1)	47 (40.5)	
Sufficient	25 (41.0)	48 (41.4)	
Insufficient	10 (16.40)	9 (7.8)	

radiation 2- Sensitivity of people against radiation was divided into four groups and the questions were asked. 3- Assessing information about an expert who is legally responsible for unreasonable exposures to patients. 4- Assessing awareness of an expert who has the most contact with radiation. 5- Assessing information about the sensitivity of different tissues against radiation. 6- Be aware of probable diseases from pollution. 7- Being mindful of dose optimization. 7- Assessing radiation dose levels (This part has nine questions which they investigate the knowledge of radiologists about dose levels).

Statistical analysis

Categorical variables were expressed as number (percentage), and continuous variables as mean and standard deviation, respectively. Non-normality data were expressed as median, interquartile ranges (IQR). T-test and Chi-square test were applied for analyzing the data. For non-

normality data, the Mann-Whitney U test was used. A P-value of less than 0.05 was set as a threshold for statistical significance. Statistical analysis was carried out via SPSS for Windows, Version 16.0. Chicago, SPSS Inc.

Results

All 180 participants completed the questionnaire. In this study, 45.5% of the participants were students. The mean age of participants was 31.08 ± 5.74 and most of them (n=100, 55.6 %) were female. Most of the responses (n=73, 40.6) about the knowledge of radiation protection were at good level and 45.0% had training. Table 1 demonstrates the demographics of participants such as age and gender, the knowledge of radiation protection in 4 levels (excellent, good, sufficient, and insufficient), and relative training. The mean age of radiology students and radiography staff was 22.5 ± 2.8 and 35.6 ± 6.8 , respectively.

¹Data were presented as Mean ±SD or number (%) for continuous and categorical variables respectively . P-value extract from T-test and Chi-square

There was no significant difference between the two groups according to the sex ($P=0.177$). Regarding perceived knowledge in participants, it has shown that radiology staff had the most information in good level (40.5%) compared to radiology students (36.1%); moreover, their knowledge in the excellent level was by far the lowest amount 6.6% for radiology students and 10.3% for radiology staff. In fact, 41% of radiology residents had sufficient information ($P < 0.05$). Figure 1 indicates the total questionnaire scores in different charts. Chart A illustrates the scores of radiation protection knowledge in which radiology students scored between 3 to 4 out of 5 while radiology staff scored approximately between 1.8 to 2.8 out of 4 ($P < 0.001$). Chart B shows the amount of dose level assessment. The count of dose level assessment reported 4.5 out of 8.5 for radiology staff while for radiology students it was approximately 2.5 out of the maximum of 8. ($P < 0.001$). Regarding chart C, the overall knowledge among both groups was as followed: about 7.7 out of more than 12.5 and 5.7 out of 11.7 for radiology staff and radiology students respectively, ($P < 0.001$).

Radiation protection knowledge

Figure 2 describes the statistics of radiology staff and radiology students' education to survey questions about general radiation protection issues. Considering chart 2, it shows that the majority of radiology students (79.1%) and radiology staff (about 87%) were aware of the necessity to inform

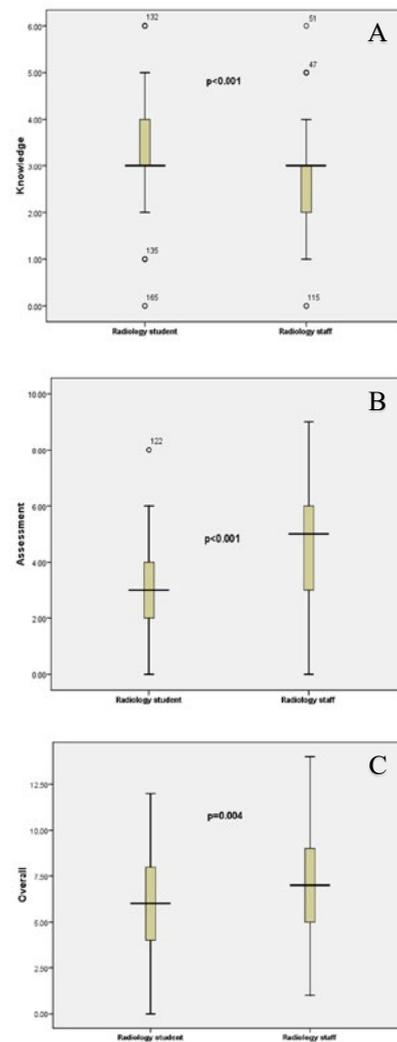


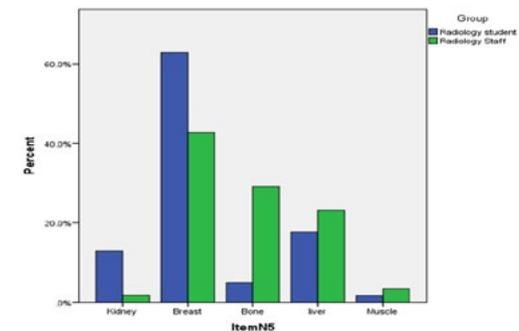
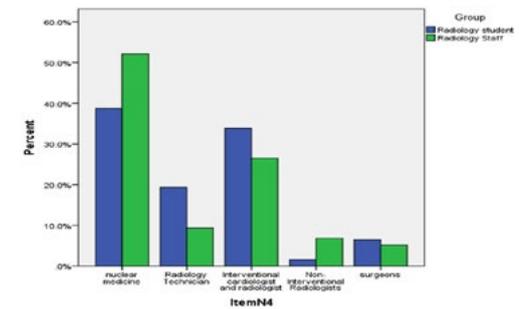
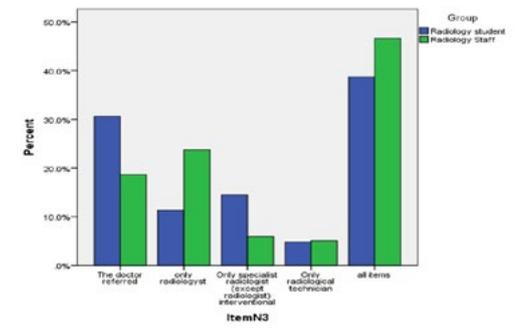
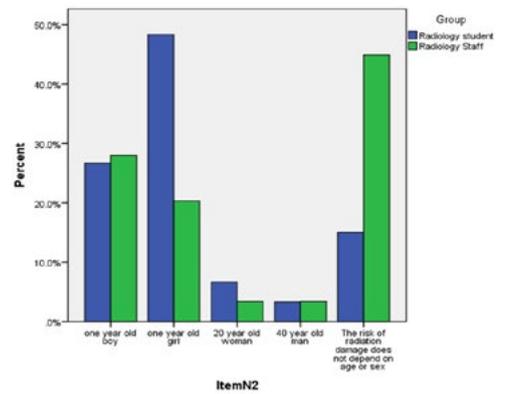
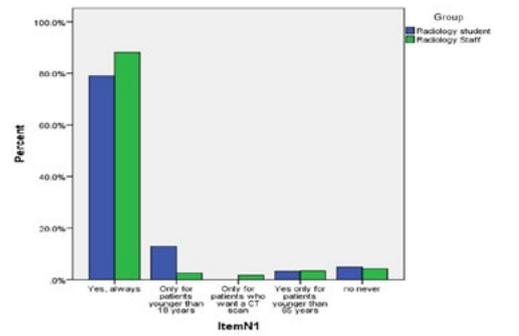
Figure 1. Distribution of scores related to knowledge of radiation protection (a), dose level assessment (b), and overall knowledge (i.e. radiation protection and dose level assessment) among radiology residents, and radiography staff (c). Box plot diagrams show

patients about the dangers of radiation exposure. As can be seen, the highest percentage of the responses to the question of “which patients have the most sensitivity to ionizing radiation?” was reported for radiology students (slightly less than 50%) as a one-year-old girl while around 45% of radiology staff answered that the risk of radiation damage does not depend on age or sex. A high

rate of radiology students and radiology staff has correctly answered that all items in bar chart 3 are responsible for unnecessary patient exposure and lack of optimization. Considerably about 6% of both groups (lowest percent) responded that only radiological staffs are responsible for this matter ($P < 0.05$). Interventional radiologists and cardiologists accounted for the second-highest number of exposed professionals, at the same time, nuclear medicine has answered as the most exposed category with the percentage of approximately 38 and just above 50 for radiology students and radiology staff, respectively. About 64% of radiology students and 40% of radiology staff considered the breast as the most sensitive tissue. Regarding the question of "which of the following diseases may be a result of stochastic radiation damage?" the percentages of those who answered all times (dermatitis, leukemia, alopecia, and cataract) were the highest ratio slightly more than 40% and around 50% for radiology students and staff respectively. The final question, which is described in bar chart number 7, is about the meaning of dose optimization. As can be seen, the above rates of answers were reported for radiology staff (around 60%). All students' answers matched the correct answers (Fisher's exact test, $P < 0.05$).

Knowledge of recommended radiation dose levels for the main imaging procedures

Table 2, gives a breakdown of the percentage of answers to the questions about the dose of natural



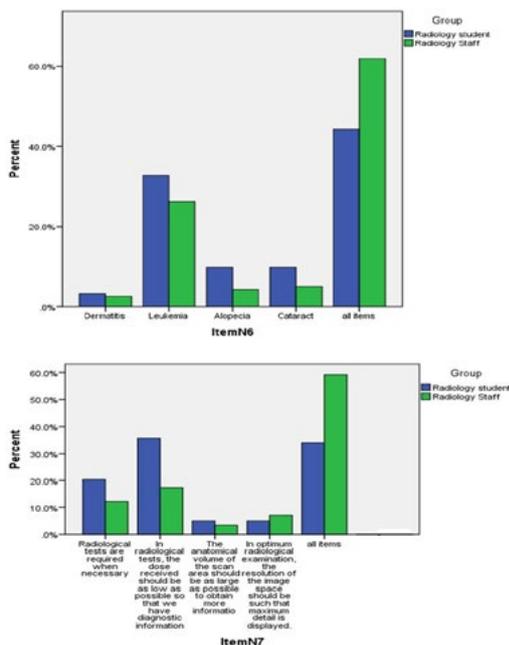


Figure 2. Descriptive statistics of radiology staff and radiography students' answers to survey questions about general radiation protection issues (a, questions from 1 to 4; b, questions from 5 to 7 of Section 2 of the survey questionnaire).

background, commonly performed imaging examinations given by radiology students and staff. The two examined groups estimated the average dose for a PA chest radiograph, 0.01 – 0.1 mSv in this way: 29% and 49.5% of radiology students and radiology staff, respectively ($P < 0.05$). 6.6% of radiography students and significantly less than that, 2.9% of radiology staff in Iran answered the average dose of the natural background radiation correctly. Regarding the average dose due to a lumbar X-Ray examination, 9.8 % of radiography students and around three times more than that, 27.7% of radiology staff gave the correct dose value. The average dose due to mammography was known by 19.7% of radiography students and 17.8% of radiology staff; all the same, 10.1 in

Table 2. Distributions of answers to questions about the dose of natural background radiation and commonly performed imaging examinations given by radiology student and staff. Values are expressed in terms of equivalent number of chest radiographs. Correct answers are indicated with “C” sign.

1-Which is the average dose for a PA chest radiograph? (mSv)							
Participants	<0.01	0.01–0.1 ⓐ	0.1–1	1–10	10-100	>100	P value
Radiography students	10 (16.1)	18 (29.0)	21 (33.9)	9 (14.5)	4 (6.5)	0 (0)	<0.001
Radiology staff	31 (29.0)	53 (49.5)	7 (6.5)	13 (12.1)	3 (2.8)	0 (0)	
2- If a PA chest radiograph counts as 1 unit, how much is the average dose due to natural background radiation in Iran?							
	0	1–10	10–50	50–100	100–500 ⓐ	>500	P value
Radiography students	9 (14.8)	28 (45.9)	13 (21.3)	7 (11.5)	4 (6.6)	0 (0)	0.711
Radiology staff	19 (18.6)	43 (42.2)	27 (26.5)	10 (9.8)	3 (2.9)	0 (0)	
3- PA chest radiograph counts as 1 unit; how much is the average dose due to a lumbar x-ray examination?							
	0	1–10	10–50	50–100 ⓐ	100–500	>500	P value
Radiography students	0 (0)	28 (45.9)	22 (36.1)	6 (9.8)	5 (8.2)	0 (0)	0.008
Radiology staff	1 (1.0)	28 (27.7)	38 (37.6)	28 (27.7)	3 (3.0)	3 (3.0)	
4- If a PA chest radiograph counts as 1 unit, how much is the average dose due to mammography (bilateral, two projections each, i.e. four images in total)?							
	0	1–10	10–50	50–100 ⓐ	100–500	>500	P value
Radiography students	5 (8.2)	32 (52.5)	12 (19.7)	12 (19.7)	0 (0)	0 (0)	<0.001
Radiology staff	2 (2.0)	24 (23.8)	18 (17.8)	25 (24.8)	31 (30.7)	1 (1.0)	
5- If a PA chest radiograph counts as 1 unit, how much is the average dose due to a noncontrast chest CT examination?							
	0	1–10	10–50	50–100	100–500 ⓐ	>500	P value
Radiography students	0 (0)	5 (8.2)	9 (14.8)	16 (26.2)	24 (45.9)	3 (4.9)	0.029
Radiology staff	1 (1.0)	7 (6.9)	20 (19.6)	10 (9.8)	46 (45.1)	18 (17.6)	
6-If a PA chest radiograph counts as 1 unit, how much is the average dose due to a pelvis MRI examination?							
	0 ⓐ	1–10	10–50	50–100	100–500	>500	P value
Radiography students	38 (62.3)	3 (4.9)	3 (4.9)	11(18.0)	4 (6.6)	2 (3.3)	<0.001
Radiology staff	92 (88.5)	3 (2.9)	7 (6.7)	1 (1.0)	1 (1.0)	0 (0)	
7-If a PA chest radiograph counts as 1 unit, how much is the average dose due to a whole body PET-CT examination?							
	0	1–10	10–50	50–100	100–500	>500 ⓐ	P value
Radiography students	2 (3.3)	6 (10.0)	24 (40.0)	5 (8.3)	11 (18.3)	12 (20.0)	<0.001
Radiology staff	2 (2.0)	7 (7.1)	8 (8.2)	12 (12.2)	33 (33.7)	36 (36.7)	
8- If a PA chest radiograph counts as 1 unit, how much is the average dose due to an abdominal ultrasound examination?							
	0 ⓐ	1–10	10–50	50–100	100–500	>500	P value
Radiography students	32 (53.3)	6 (10.0)	11 (18.3)	8 (13.3)	2 (3.3)	1 (1.7)	0.522
Radiology staff	60 (61.9)	6 (6.2)	11 (11.3)	10 (10.3)	8 (8.2)	2 (2.1)	
9- If a PA chest radiograph counts as 1 unit, how much is the average dose due to a myocardial scintigraphy (2-day protocol with 99mTc-sestamibi)?							
	0	1–10	10–50	50–100	100–500	>500 ⓐ	P value
Radiography students	1 (1.7)	14 (23.3)	9 (15.0)	13 (21.7)	13 (21.7)	10 (16.7)	<0.001
Radiology staff	0 (0)	6 (6.2)	11 (11.3)	14 (14.4)	12 (12.4)	54 (55.7)	

4- If a PA chest radiograph counts as 1 unit, how much is the average dose due to mammography (bilateral, two projections each, i.e. four images in total)?							
	0	1-10	10-50	50-100 ⊙	100-500	>500	P value
Radiography students	5 (8.2)	32 (52.5)	12 (19.7)	12 (19.7)	0 (0)	0 (0)	<0.001
Radiology staff	2 (2.0)	24 (23.8)	18 (17.8)	25 (24.8)	31 (30.7)	1 (1.0)	
5- If a PA chest radiograph counts as 1 unit, how much is the average dose due to a noncontrast chest CT examination?							
	0	1-10	10-50	50-100	100-500 ⊙	>500	P value
Radiography students	0 (0)	5 (8.2)	9 (14.8)	16 (26.2)	24 (45.9)	3 (4.9)	0.029
Radiology staff	1 (1.0)	7 (6.9)	20 (19.6)	10 (9.8)	46 (45.1)	18 (17.6)	
6- If a PA chest radiograph counts as 1 unit, how much is the average dose due to a pelvis MRI examination?							
	0 ⊙	1-10	10-50	50-100	100-500	>500	P value
Radiography students	38 (62.3)	3 (4.9)	3 (4.9)	11(18.0)	4 (6.6)	2 (3.3)	<0.001
Radiology staff	92 (88.5)	3 (2.9)	7 (6.7)	1 (1.0)	1 (1.0)	0 (0)	
7- If a PA chest radiograph counts as 1 unit, how much is the average dose due to a whole body PET-CT examination?							
	0	1-10	10-50	50-100	100-500	>500 ⊙	P value
Radiography students	2 (3.3)	6 (10.0)	24 (40.0)	5 (8.3)	11 (18.3)	12 (20.0)	<0.001
Radiology staff	2 (2.0)	7 (7.1)	8 (8.2)	12 (12.2)	33 (33.7)	36 (36.7)	
8- If a PA chest radiograph counts as 1 unit, how much is the average dose due to an abdominal ultrasound examination?							
	0 ⊙	1-10	10-50	50-100	100-500	>500	P value
Radiography students	32 (53.3)	6 (10.0)	11 (18.3)	8 (13.3)	2 (3.3)	1 (1.7)	0.522
Radiology staff	60 (61.9)	6 (6.2)	11 (11.3)	10 (10.3)	8 (8.2)	2 (2.1)	
9- If a PA chest radiograph counts as 1 unit, how much is the average dose due to a myocardial scintigraphy (2-day protocol with 99mTc-sestamibi)?							
	0	1-10	10-50	50-100	100-500	>500 ⊙	P value
Radiography students	1 (1.7)	14 (23.3)	9 (15.0)	13 (21.7)	13 (21.7)	10 (16.7)	<0.001
Radiology staff	0 (0)	6 (6.2)	11 (11.3)	14 (14.4)	12 (12.4)	54 (55.7)	

total consider mammography as a radiation-free procedure which should be a matter of concern (8.1 % of radiography students and 2% of radiology staff). The next figure shows the average dose because of the non-contrast chest CT examinations in which it was correctly estimated by 45.9% and slightly less 45.1% for radiography students and radiology residents, respectively. Considerably for radiography students and radiology staff, those who answered that CT involves no radiation exposure, the ratio is 0% for the former survey respondents and 1% for the latter. The MRI examination was correctly identified as radiation-free by 62.3% of radiography students and significantly 88.5% of radiology staff. As for nuclear medicine procedures, the correct estimation ratio for the radiation dose of PET-CT examinations was 20%

of radiography students and 36.7% of radiology staff; ($P < 0.05$); however, the average dose due to myocardial scintigraphy has estimated by 16.7 % of the former respondents and 55.7% for the later; ($P < 0.05$). Furthermore, as can be seen, 3.4% of radiology students about PET-CT examinations and exactly half of that (1.7%) for myocardial scintigraphy thought that these examinations are not associated with radiation exposure, this ratio for radiology staff was 2% for the former analysis and 0% for the later.

Discussion

Our study found that most staff and students believe that awareness of the dangers of radiation to patients is essential. It also turned out that doctors were not aware of the dangers of radiation. Studies by Dunlap et al. and, Shiralkar et al. also found that physicians require radiation training (3,1). On the other hand, some studies indicated that the knowledge of radiation experts was also low (17,23,24). Based on our study and confirmation of studies by Briggs- Kamara et al. and Ria et al., it was found that patients' awareness was deficient (17,13). It should be noted that in our study, most radiation students and staff thought they were well aware and did not need to undergo training. However, in some studies, it was found that training reduces radiation risks and increases radiation awareness (23,25). Several cases raise the level of radiation knowledge in staff, patients, and physicians. Continuous beam training increases radiation safety and reduces fear of radiation [19,

23, 25], as well as determining radiation levels and dose level references for each region [12,26-27] and monitoring personnel radiation measures are two other effective strategies [28]. In our study, it was demonstrated that the dose received in nuclear medicine tests (more than 500 times that of Chest PA) increased the risk of cancer in younger people, especially in vulnerable tissues. Research by Huang et al. has also pointed out that although PET / CT facilitates the diagnosis, it also increases the risk of cancer. Therefore, these examinations should be justified, and appropriate measures should be taken to reduce the dose received [29-31]. More than 50% of our subjects have erroneous dose assessment data on CT scans, which has been found in other studies [8, 25]. It may imply that ionizing imaging may give physicians very high precision, still, physicians neither do they give patients information about the risk of a CT scan nor are they able to estimate the exact dose of imaging for specific anatomical areas. A study by Zhou et al. also acknowledged that about 55% did not estimate the radiation dose level for correct radiology tests, and also, about 60% underestimated the risk of cancer from the Abdominal CT scan (lack of radiation knowledge) [32]. He also came to this conclusion in his study that about 11% and 25% believed that MRI and ultrasound had ionizing radiation (lack of radiation knowledge), in comparison, about 10% of the subjects considered radiation knowledge to be irrelevant. And it should be noted that this study

clearly (about 40%) among radiology students and (10%) among radiology staff considered MRI tests with ionizing radiation [32-33]. Another study found that people with less radiation knowledge had higher self-esteem. This issue led to poor self-esteem among medical students, which may be one of the psychological factors for inattention to learn about the subject of radiation knowledge [24-25,34]. L. Borgen and his colleagues have found that radiology experts and residents have more radiation and shielding information from physicians due to the specialized nature of their units, which confirms our results [14, 35-38]. In their study, Dehghani and colleagues found that only 6% of the subjects were well aware that this result is very similar to our results, although it should be noted that our statistical population was much larger [26, 39-41].

Conclusion

Knowledge of radiation protection is important for both students and staff. Lack of this knowledge leads to irreparable complications in patients, staff, and students. Therefore, the necessary training related to radiation protection should be given when starting work in radiology departments. On the other hand, in-service training should not be neglected. After conducting this study, we provided the necessary framework for radiation protection education for both students and staff to the University Radiology Department.



Abbreviation

CT: computed tomography

PA: posterior-anterior

MRI: magnetic resonance imaging

PET: positron emission tomography

IQR: interquartile ranges

Declarations

Ethics approval and consent to participate

This study was reviewed by the Ethics Committee of Behbahan School of Medical Sciences. Therefore, the Ethics Committee of Behbahan Paramedical School stated that this study does not require ethical approval. Informed consent was obtained from participants' information. The results of this study were provided to the participants.

Consent for publication

All participants included in this research gave written informed consent to publish the data contained within this study. In this study, informed consent was obtained from all participants.

Availability of data and material

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Competing interests

We declare that we have no significant competing financial, professional, or personal interests that might have influenced the performance or presentation of the work described

in this manuscript. We have described our potential competing for financial, professional, and/or personal interests in this space.

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Authors' contributions

O A, L D, M SH, P F, A A, M A, P H, and Z H conceived and planned the experiments. O A, L D, M SH and Z H carried out the experiments. O A, L D, and M SH planned and carried out the simulations. P F, A A, M A, P H, and Z H participated in the gathering. O A, L D, M SH and Z H contributed to sample preparation. O A, L D, M SH and Z H contributed to the interpretation of the results. O A and M SH took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript. All authors read and approved the final manuscript.

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