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A detailed investigation on Thyroid Nuclear Medicine Examinations and organ dose assessment: A Monte Carlo simulation study

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Abstract: The importance of radionuclide dosimetry was that as nuclear medicine grew to include new therapeutic and diagnostic techniques as well as new radiopharmaceutical products. Dosimetry of radionuclide should be used for the purpose of planning radionuclide therapy as the dosimetry for external radiotherapy is used. In order to achieve nuclear therapy treatment planning, it is important to understand and distinguish between biological and dosimetry factors. Therefore, continuing improvements in dosimetry and codes are crucial in nuclear medicine to ensure that the role of dosimetry can be adequately evaluated in relation to biological factors. In this study, the VMC general-purpose Monte Carlo code has been utilized for the evaluation of absorbed organ doses from Technetium-99m applied in the Thyroid Gland scan. For this aim, radioactivity amounts of Technetium-99m have been changed from 5 mCi to 10 mCi, respectively. In each simulation run, the absorbed dose amount was recorded. The outcomes of recent investigation can be useful for the assessment of Technetium-99m radioactivity utilization Thyroid Gland scan considering the potential risks, cancer history, and general condition of the patient.

Tiroid Nükleer Tıp Muayeneleri ve organ doz değerlendirmesi üzerine detaylı bir araştırma: Monte Carlo simülasyon çalışması

Anahtar Kelimeler
Tanısal görüntüleme,
Nükleer tıp,
Hasta,
Radyasyon dozu

Özet: Radyonüklid dozimetrisinin önemi, nükleer tıp ilerledikçe yeni terapatik ve diagnostik tekniklerin yanı sıra yeni radyofarmasötik ürünleri de kapsamasıydı. Harici radyoterapi için dozimetri kullanıldığı için radyonüklid tedavisinin planlanması amacıyla radyonüklid dozimetrisi kullanılmalıdır. Nükleer tedavi planlamasını gerçekleştirmek için biyolojik ve dozimetrik faktörleri anlamak ve ayırt etmek önemlidir. Bu nedenle dozimetri ve kodlarda devam eden gelişmeler, dozimetrinin biyolojik faktörlerle ilişkili olarak yeterince değerlendirilebilmesini sağlamak için nükleer tıpta çok önemlidir. Bu çalışmada, Tiroid Bezi taramasında uygulanan Technetium-99m'den absorbe edilen organ dozlarının değerlendirilmesi için VMC genel amaçlı Monte Carlo kodu kullanılmıştır. Bu amaçla Technetium-99m'nin radyoaktivite miktarları sırasıyla 5 mCi'den 10 mCi'ye değiştirilmiştir. Her simülasyon çalışmasında emilen doz miktarı kaydedilmiştir. Son araştırmanın sonuçları, Teknetyum-99m radyoaktivite kullanımının Tiroid Bezi taramasının potansiyel riskleri, kanser öyküsü ve hastanın genel durumu dikkate alınarak değerlendirilmesi için faydalı olabilir.

1. Introduction

Nuclear medicine (NM) techniques, such as Single Photon Emission Computed Tomography (SPECT), planar imaging, and Positron Emission Tomography (PET), developed in the second half of the 20th century, have become very complex and intensively included in diagnostic tests. The number of NM procedures increased from 23.5 to 37 million worldwide between 1980-1984 and 1997-2007 [1,2], while it increased from 7 to 18.6 million in the United States between 1980-1982 and 2006 [3,4]. As can be seen from the results, until 2006, half of the NM procedures in the world were carried out in the USA. The annual effective dose per capita expected from NM studies conducted in the United States increased from 0.14 mSv [5] between 1980 and 1982 by 5.5 times in 2006 from 0.77 mSv [6]. There are important technical developments that have affected diagnostic NM procedures over the past decade and have led to changes in absorbed doses over time. These developments are the development of the first molybdenum-99 / technetium-99m generator, the first synthesis of 18F-FDG and the development of the PET / CT scanner. The main purpose of NM therapy is to give the tumor a sufficient dose of radiation by minimizing the risk of toxicity in healthy tissues surrounding the lesion. The absorbed dose depends on the half-life of the radionuclide as well as the spatial-temporal distribution at the target. Typically, images obtained at different times after application of the radiopharmaceutical are used to obtain the temporal distribution. On the other hand, it is used to estimate the amount or concentration of radioactivity in a particular region.

Technetium-99m and iodine-131 are two of the most commonly used radioisotopes in medicine. Gamma emitting technetium-99m is originally used to display the skeleton and heart, it is also used to display brain, thyroid, lungs, liver, spleen, kidney, gallbladder, bone marrow and infections, and other special medical studies. Iodine-131 is widely employed in the treatment and vision of thyroid glands and thyroid cancer. The regular, irregular function of organs and structures is often studied using radioisotopes in medical science. Comprehensive and early diagnosis information is given by radioisotopes, which increases patient care, and also leads to a shift in therapy. Furthermore, radioisotopes treat all visible and invisible areas of the organism in a targeted manner. In comparison with traditional radiology, nuclear diagnostics is essentially a physiological process of functional imaging, while traditional radiology aims at obtaining anatomic images that mainly reflect form and structure. Radionuclides are used in a range of diagnostic and therapeutic procedures in nuclear medicine. In the determination of nuclear medicine radiation dosimetry, individual doses of organ absorption (physical quantity, in Gy) or equivalent doses (derived quantity, in Sv) must be considered, which includes the highest exposed (sometimes called critically) organ, as well as other tissue-related doses such as active red marrow. The energy absorbed by the tissue (absorbed dose) is one factor that strongly affects the intensity or probability of radiation effects and can only be carried out when you know the radiation doses which are delivered to other organisms.

In nuclear medicine procedures, it is almost impossible to measure the radiation dose directly using any kind of radiation detector. Absorbed doses are estimated using standardized reference models of the human body this has to be calculated by using a variety of physical and biological data and mathematical equations specially developed for this purpose. Voxel simulation that discriminates between absorbed dose in the particular section of the organ, such as thyroid can achieve a spatial dose distribution. Such change will lead to improved deterministic effects on the organs of radiation. The importance of radionuclide dosimetry was that as nuclear medicine grew to include new therapeutic and diagnostic techniques as well as new radiopharmaceutical products. Dosimetry of radionuclide should be used for the purpose of planning radionuclide therapy as the dosimetry for external radiotherapy is used. In order to achieve nuclear therapy treatment planning, it is important to understand and distinguish between biological and dosimetry factors. Therefore, continuing improvements in dosimetry and codes are crucial in nuclear medicine to ensure that the role of dosimetry can be adequately evaluated in relation to biological factors. In this study, the VMC general-purpose Monte Carlo code has been utilized for the evaluation of absorbed organ doses from Technetium-99m applied in the Thyroid Gland scan. For this aim, radioactivity amounts of Technetium-99m have been changed from 5 mCi to 10 mCi, respectively. In each simulation run, the absorbed dose amount was recorded. The outcomes of recent investigation can be useful for the assessment of Technetium-99m radioactivity utilization Thyroid Gland scan considering the potential risks, cancer history, and general condition of the patient.

2. Materials and Methods

2.1. Technetium-99m

In 1957, the 99Mo-99mTc generator in Brookhaven National laboratory was developed and introduced to nuclear medicine. Widespread use of 99 mTc is the option of radionuclides based primarily on their physical properties for a number of nuclear medicine imaging processes. These properties include a t1/2 of 6 hours; a 140-keV photon (88% abundance) which provides good tissue penetration and imaging. Additionally, there is no beta emission which reduces radiation absorbed dose, and Tc-99m is available from the 99Mo-99mTc generator, although as of this writing (2010), reactor shut-downs in Europe and Canada have led to shortages of 99Mo for this

generator system, and consequently has limited the number of gamma scintigraphy and SPECT procedures using 99mTc. Technetium is obtained from a generator in normal saline (0.9% NaCl) as the pertechnetate ion, 99mTcO4−. In this form, Tc is in the +7 valence state as pertechnetate and has all seven of the outer electrons involved in covalent bonding. This is the most stable of all valence states of technetium in aqueous solution. The only RaPh containing technetium possibly in a+7 valence state is technetium sulfur colloid (99mTc-SC). The99mTc-SC is rapidly cleared from the blood. The mechanism of action is phagocytosis, cells of the reticuloendothelial system (RES) engulf the colloidal particles.

2.2. Technetium-99m applied in Thyroid Gland scan

Thyroid imaging, most commonly done with the Technetium-99 m pertechnetate, is entangled with the thyroid in the same way as iodide, and is thus not coordinated over time. Its short six-hour physical half-life and 140-keV main gamma energy are ideal for gamma imagery (greater than 90% efficiency with a ½-inch-thick crystal). The physical characteristics and effectiveness for the thyroid scanning are distinct advantages. The low absorbed thyroid intake often allows higher doses to be given so that the glans can be imaged more easily with minimal motion. Thus 99mTc-pertechnetate provides excellent quality images at great convenience to the nuclear medicine service and the patient and is currently widely used for thyroid imaging. These images identify the size and location of thyroid tissue. Images are obtained 15 to 20 minutes after injection. The concern that because 99mTc-pertechnetate is trapped but not organized, it might provide misleading information about whether a nodule is hot or cold is not relevant because thyroid carcinoma characteristically traps poorly compared to normal thyroid. This is the basis for the cold nodule. In patients with thyroid carcinoma, 99mTc-pertechnetate used to image the thyroid bed remnant after surgery, but it is not useful to detect metastatic disease because its short physical and biological half-life in the thyroid makes detection difficult when combined with the fact that trapping itself is often reduced in thyroid carcinoma compared to normal thyroid tissue.

3. Results

To know the absorbed dose amount from the clinical applications are not always possible. Some techniques and prediction methods can be utilized only with entrance skin dose (ESD) calculations. In nuclear medicine procedures, it is almost impossible to measure the radiation dose directly using any kind of radiation detector. Therefore, risk assessments and optimization studies can be performed only with mathematical phantoms and different types of simulation methods. For this study, we used the VMC Monte Carlo simulation code [15-26]. A Monte Carlo simulation imitates the human body as a phantom with a certain number of pixels and simulates the interaction of the photons and the absorption of the radiopharmaceutical in the organ and then calculates the absorbed dose by the neighbor organs, through the use of mathematical equations on a computer, reproduces as closely as possible the real interactions suffered by the photons, the numerical outcome depends on the following factors (height, weight, age, scan type, used radioactivity level, type of radiopharmaceutical, average exposure time, imaging time).

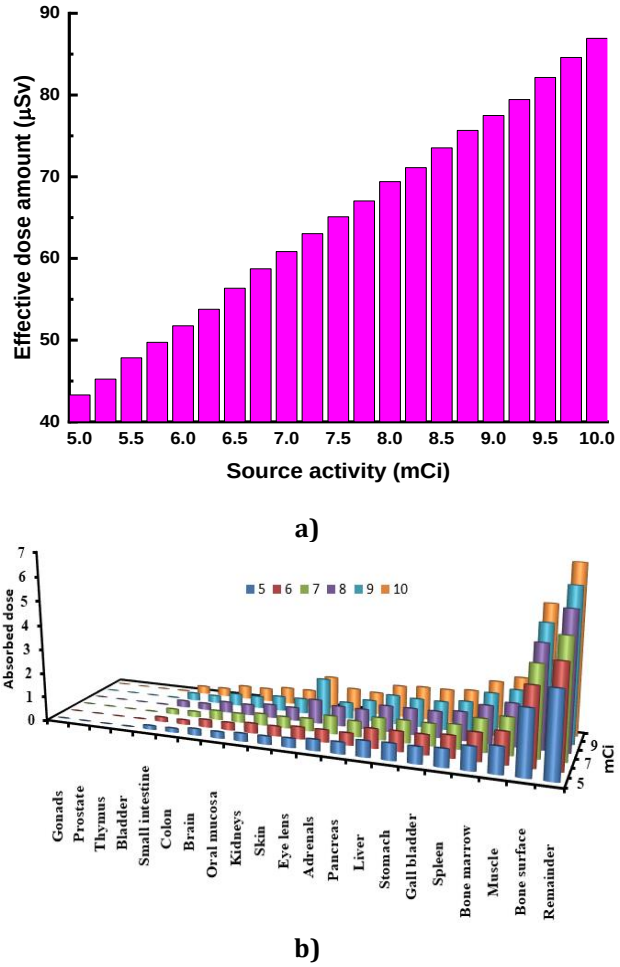

Figure 1. Total effective (a) and Absorbed (b) dose amounts against different source radioactivity levels

The appearance of the utilized human phantom can be seen in **Figure 1**. In our simulation study, the radionuclide type was selected as Tc-99m in the code database. Next, source geometry has been defined as an internal source in the thyroid gland. In addition, activity and time parameters were defined, respectively. The dose entered into the mathematical equation has varied between 5 mCi up to 10 mCi, We started with 5 mCi and kept increasing the dose by +0.25 mCi, it ran for 1million per minute. The results obtained showed the normal high uptake of the thyroid in addition to the dose uptake of the esophagus, lungs, bone marrow, and eye lens (See **Table 1** and **Table 2**). The focus of this study was

Table 1. Organs and absorbed dose amounts against different source radioactivity levels

Organs /Source Activity	5.00 mCi	5.25 mCi	5.50 mCi	5.75 mCi	6.00 mCi	6.25 mCi	6.50 mCi	6.75 mCi	7.00 mCi	7.25 mCi
Bone marrow	0.96	1	1.07	1.1	1.15	1.2	1.24	1.3	1.35	1.39
Colon	0.17	0.17	0.18	0.19	0.19	0.21	0.21	0.23	0.23	0.24
Lung	4.66	4.89	5.14	5.39	5.59	5.86	6.03	6.31	6.55	6.76
Stomach	0.69	0.67	0.75	0.76	0.82	0.79	0.88	0.91	0.92	0.96
Remainder	3.46	3.61	3.82	4.01	4.16	4.33	4.49	4.67	4.84	5.02
Gonads	0	0	0	0	0	0.01	0	0	0	0
Bladder	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02
Oesophagus	23.65	24.41	26.07	27.48	28.53	29.31	30.64	31.82	32.91	34.2
Liver	0.66	0.7	0.73	0.75	0.8	0.84	0.85	0.9	0.9	0.95
Thyroid	925.9	968.03	1,023.47	1,063.34	1,106.61	1,150.26	1,205.69	1,256.58	1,301.91	1,348.69
Bone surface	2.64	2.77	2.9	3.04	3.17	3.29	3.43	3.56	3.7	3.83
Brain	0.27	0.29	0.31	0.32	0.32	0.34	0.36	0.37	0.38	0.4
Salivary glands	11.96	12.35	13.19	13.9	14.43	14.82	15.5	16.09	16.64	17.3
Skin	0.34	0.36	0.37	0.39	0.41	0.42	0.44	0.46	0.47	0.49
Adrenals	0.46	0.58	0.49	0.51	0.51	0.71	0.65	0.57	0.74	0.71
Extrathor airways	23.65	24.41	26.07	27.48	28.53	29.31	30.64	31.82	32.91	34.2
Gall bladder	0.69	0.67	0.75	0.76	0.82	0.79	0.88	0.91	0.92	0.96
Heart	6.84	7.19	7.55	7.91	8.21	8.6	8.86	9.28	9.63	9.93
Kidneys	0.33	0.36	0.39	0.39	0.41	0.42	0.43	0.45	0.48	0.47
Lymphatic nodes	6.84	7.19	7.55	7.91	8.21	8.6	8.86	9.28	9.63	9.93
Muscle	1.09	1.15	1.2	1.26	1.31	1.37	1.42	1.47	1.53	1.58
Oral mucosa	0.27	0.29	0.31	0.32	0.32	0.34	0.36	0.37	0.38	0.4
Pancreas	0.48	0.52	0.56	0.56	0.5	0.61	0.6	0.7	0.65	0.75
Prostate	0	0	0	0	0	0.01	0	0	0	0
Small intestine	0.16	0.18	0.18	0.2	0.19	0.21	0.21	0.23	0.22	0.24
Spleen	0.74	0.76	0.81	0.83	0.91	0.96	0.96	0.97	1	1.03
Thymus	0	0	0	0	0	0	0	0	0	0
Eye lens	0.38	0.37	0.33	0.93	0.5	0.89	0.84	0.51	0.52	0.92
Effective dose (microSv)	43.29	45.24	47.84	49.74	51.76	53.78	56.35	58.73	60.84	63.03

Table 2. Organs and absorbed dose amounts against different source radioactivity levels-continued

Organs/ Source Activity	7.50 mCi	7.75 mCi	8.00 mCi	8.25 mCi	8.50 mCi	8.75 mCi	9.00 mCi	9.25 mCi	9.50 mCi	9.75 mCi	10.00 mCi
Bone marrow	1.44	1.49	1.55	1.59	1.63	1.67	1.74	1.79	1.8	1.89	1.92
Colon	0.25	0.26	0.27	0.28	0.29	0.29	0.3	0.31	0.31	0.33	0.34
Lung	6.98	7.22	7.48	7.68	7.86	8.18	8.41	8.67	8.92	9.08	9.35
Stomach	1.01	1.07	1.08	1.09	1.18	1.16	1.16	1.23	1.27	1.32	1.36
Remainder	5.19	5.39	5.6	5.66	5.8	6.05	6.27	6.43	6.65	6.79	6.96
Gonads	0.01	0	0	0	0	0	0	0.01	0	0	0
Bladder	0.01	0.01	0.01	0.01	0.02	0.02	0.01	0.01	0.02	0.02	0.02
Oesophagus	35.24	36.92	38.35	38.68	39.25	40.9	43.18	43.64	44.99	46.51	47.72
Liver	0.99	1.03	1.07	1.09	1.13	1.14	1.2	1.22	1.27	1.26	1.3
Thyroid	1,393.11	1,433.37	1,483.65	1,521.33	1,573.99	1,619.10	1,656.13	1,698.45	1,756.80	1,809.23	1,859.13
Bone surface	3.95	4.09	4.22	4.35	4.48	4.62	4.75	4.88	4.99	5.15	5.28
Brain	0.42	0.42	0.44	0.45	0.47	0.48	0.49	0.5	0.5	0.51	0.54
Salivary glands	17.83	18.67	19.39	19.57	19.86	20.69	21.84	22.07	22.74	23.51	24.13
Skin	0.51	0.53	0.54	0.56	0.58	0.6	0.61	0.63	0.65	0.66	0.68
Adrenals	0.94	0.66	0.82	0.54	0.7	1.13	0.67	0.98	1.38	0.94	0.96
Extrathor airways	35.24	36.92	38.35	38.68	39.25	40.9	43.18	43.64	44.99	46.51	47.72
Gall bladder	1.01	1.07	1.08	1.09	1.18	1.16	1.16	1.23	1.27	1.32	1.36
Heart	10.25	10.61	10.99	11.28	11.55	12.02	12.36	12.74	13.1	13.33	13.74
Kidneys	0.5	0.52	0.55	0.56	0.57	0.55	0.6	0.61	0.66	0.63	0.67
Lymphatic nodes	10.25	10.61	10.99	11.28	11.55	12.02	12.36	12.74	13.1	13.33	13.74
Muscle	1.64	1.69	1.75	1.8	1.86	1.91	1.97	2.02	2.08	2.14	2.18
Oral mucosa	0.42	0.42	0.44	0.45	0.47	0.48	0.49	0.5	0.5	0.51	0.54
Pancreas	0.69	0.78	0.81	0.82	0.94	0.84	0.87	1.01	1	0.98	0.9
Prostate	0.01	0	0	0	0	0	0	0.01	0	0	0
Small intestine	0.25	0.25	0.27	0.27	0.28	0.29	0.31	0.31	0.32	0.33	0.32
Spleen	1.14	1.16	1.18	1.17	1.23	1.26	1.28	1.37	1.35	1.45	1.44
Thymus	0	0	0	0	0	0	0	0	0	0	0
Eye lens	0.56	1.17	0.98	0.74	1.24	1.37	1.56	0.66	0.84	1.11	1.36
Effective dose (microSv)	65.1	67.04	69.4	71.11	73.53	75.67	77.49	79.45	82.15	84.6	86.93

mainly on the thyroid scan because it's very common, the radionuclide used was Tc-99.
The results showed that there is a linear relationship between total effective dose amount and different source radioactivity levels (See **Figure 1**). Of course, this situation is expectable since internal exposure amount and absorbed radiation dose amount has a direct relationship due to the quantity of internal source. However, regular increment (+0.25 mCi) of source radioactivity levels from 5 mCi to 10 mCi has caused different rage of increments in the organs

4. Discussion

In the studies conducted, the biological effects of radiation have been examined in two groups as cytocratic and deterministic effects [7-10]. Cytocratic effects; There are effects occurring years after exposure to radiation, and no threshold dose has been reported for its development (since the radiation dose taken in the study is low, we can mention that it is beneficial to use lower doses in the long term to avoid this effect). Cytocratic effects; Cancers such as thyroid cancer, skin cancer, and genetic effects [11]. Cancers evaluated within cytocystic effects may be spontaneous or related to the mutation caused by radiation [11]. There are no fully resistant cells to radiation. The sensitivity of each cell to radiation is different. While the sensitivity of frequently dividing and slightly differentiating cells (ovarian and testicular germinal cells, hematopoietic system cells, gastrointestinal system epithelial cells) is high, the sensitivity of non-dividing and upper differentiating cells (Liver, kidney, muscle, nerve cells) is less. The aim of Radiation Protection is to prevent deterministic effects causing tissue damage and to limit the probability of occurrence of Stochastic effects to an acceptable level. A healthy person is unlikely to experience any effects for several tissues and organs, up to a few hundred and sometimes thousands of mSv (millisievert) doses. The tissues of the liver, kidney, muscle, bone, cartilage, and connective tissues are resistant to radiation since they are differentiated in adult life and do not divide. The dividing cells of the bone marrow, ovaries and testicles (organs of reproductive organs), and epithelial cells in the gastrointestinal and skin are sensitive. Gonads, eyepieces, and bone marrow have higher sensitivity. Late effects of radiation include radiation-induced cancer development, a genetic mutation in later generations, late organ effects (typical vascular changes, fibrous atrophy, and thyroid dysfunction), cataracts, and infertility. The Biological Effects of Ionizing Radiation Committee (BEIR VII, 2006) has developed mathematical risk models related to the late effects of radiation (Linear non-threshold) (LNT). the model has been reported [12]. According to the LNT model, while the late effects at zero radiation dose approach zero, this risk increases linearly with increasing radiation dose. After the atomic bombs dropped on Hiroshima and Nagasaki in 1945, there was a statistically increase in all types of leukemia except for chronic lymphocytic leukemia. In addition, an increase in radiation was detected in breast, thyroid, colon, stomach, and ovarian cancers. In esophagus, liver, skin, bladder, central nervous system (CNS) cancers, and multiple myeloma and lymphoma, there is a significant increase in the frequency of radiation-induced cancer [12-14]. In the BEIR VII report, 43 of every 100 people in the USA are expected to develop cancer in their lifetime. In another prediction, it is predicted that cancer, which occurs in 1 out of 43 people receiving 100 mSv (10 rem) dose, will develop due to radiation. The risk increase for deterministic effects above and below the threshold value (0.5-0.75 Sv) shows linear behavior [12]. According to the BEIR VII report, radiation-induced cancer can develop in 1 (100%) of 100 individuals receiving 0.1 Sv (10 10% / Sv) dose at one time. Since this patient will have cancer with a probability of ≈ 50% for life, the risk of extra risk due to radiation is calculated as ≈ 1%, and the total risk associated with it is 51%. In general, the risk of extra-fatal cancer due to radiation is accepted as 5 5% / Sv under radiation exposure on background values [12]. Apart from cancer, radiation has other late effects. These include cataracts, hyperparathyroidism, and weakening of the immune system, especially in the posterior capsule of the lens. In children exposed to intrauterine radiation, microcephaly, mental retardation, growth and development retardation, mental retardation and low school performance can be observed. When the threshold value in cataract formation is accepted as approximately 2 Gy (this value is higher in fractional doses), it is predicted that cataract will develop in approximately 100% of cases between 2 months and 35 years if 40 Gy dose is taken in the eye. In general, the latent period is shortened in the development of cataracts with increasing radiation dose.

5. Conclusion

An extensive organ dose assessment from VMC general-purpose Monte Carlo code has been utilized for the evaluation of absorbed organ doses from Technetium-99m applied in the Thyroid Gland scan. For this aim, radioactivity amounts of Technetium-99m have been changed from 5 mCi to 10 mCi, respectively. It can be concluded that the absorbed dose amount of each organ should be evaluated separately since there is no linear relationship between utilized source radioactivity amount and absorbed organ dose. On the other hand, the results showed that the total effective dose is directly related to the use of radioactivity amounts. Therefore, it can be concluded that minimum source radioactivity should be used during the Thyroid Gland scans by considering the ALARA (As low as reasonably achievable) principle.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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