

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



---

# Radiation Dosimetry in Thyroid Cancer Patients

---

Lebriz Uslu Beşli and Mustafa Demir

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/64087>

---

## Abstract

Radioactive iodine is utilized commonly for ablation of remnant thyroid tissue after thyroidectomy and treatment of persistent disease and metastases in differentiated thyroid cancer patients. As it involves ionizing radiation, it is important to ensure that the patients receive optimum amount of radiation to destruct the target tissue while keeping the radiation-related side effects to minimum. In clinical practice, standard activity doses are preferred for thyroid cancer patients, assuming that biokinetics are similar in all patients. Lately, many clinicians offered to individualise the radioactive iodine therapy by calculating the optimal amount of radioactivity using patient dosimetry. Radiation dosimetry is used to calculate the minimum effective and maximum tolerated absorbed dose for a successful radioactive iodine therapy. This approach enables to administer increased amount of therapeutic activity while minimizing the related side effects. This chapter presents some of the basic principles of patient dosimetry and radioiodine biokinetics following radioactive iodine administration in differentiated thyroid cancer patients.

Following radioactive iodine therapy, radiation protection measures are necessary to protect the public from ionizing radiation after discharge of the patient from hospital. Radiation exposure to patients, family members and caregivers and attempts to decrease the exposure during therapy are also going to be discussed.

**Keywords:** radiation dosimetry, radiation exposure, dose rate, radioiodine therapy

---

## 1. Introduction

Radioactive iodine is an important component in treatment approach of differentiated thyroid carcinoma patients. Following thyroidectomy, radioactive iodine is used for remnant tissue ablation and to destroy residual tumor foci or metastatic disease. Traditionally a fixed dose of

---

3700–7400 MBq (100–200 mCi) of radioiodine was recommended for treatment of residual disease [1]. However, concerns related with ionizing radiation led to a significant decrease in the administered dose recommended in the recent thyroid cancer management guidelines [2].

The optimum I-131 activity is controversial as the radioiodine biokinetics is different in each patient. Therefore, radiation dosimetry is preferred especially in the subgroup of patients, where selection of biologically effective dose is more crucial, such as patients with metastatic disease, especially with lung metastases or with comorbidities such as chronic kidney disease, as well as in pediatric and elderly population.

This chapter aims to present the basic principles of radiation dosimetry and common dosimetric methods, as well as main dosimetric approaches for radiation dose selection for thyroid carcinoma patients. Also, concerns about radiation exposure to patients, family members, and caregivers and attempts to decrease the exposure during therapy are discussed.

## 2. Basic principles of radiation dosimetry

Radiation dosimetry is a general term implying the approach for (1) calculation of the minimum amount of radiation activity necessary for successful treatment of a patient (i.e., therapeutic dose) for treatment planning using radionuclides or external beam radiotherapy, (2) assessment of the radiation dose received by a specific organ or tissue of a patient to ensure that radiation dose received by the patient would not exceed the tolerable limits of certain organs or tissues, (3) determining the total radiation dose received by patients, health care workers, or family members of patients to maintain radiation safety of individuals, (4) measurement of the instantaneous and cumulative radiation dose in the environment where ionizing radiation sources are used to ensure radiation safety of the workers and public, and (5) calculation of the total amount of dose received by the fetus, in case the mother is exposed to ionizing radiation during pregnancy. Radiation dosimetry for treatment planning of thyroid cancer patients involves calculating the minimum amount of I-131 activity to be given to the patient to ensure successful remnant thyroid tissue ablation or treatment of persistent disease and metastases, as well as measuring the radiation dose received by critical or dose-limiting organs to calculate the maximal safe dosage of I-131 that can be given to the patient.

There are two main approaches to determine the amount of I-131 to be given to the thyroid cancer patients after thyroidectomy operation: empirical fixed amount approach, and dosimetrically calculated amount approach. Empirical fixed amount approach is more widely used, as it is a more simple and convenient method. However, it lacks the ability to accurately incorporate the individual biological and physical features of patients, such as radioiodine uptake, release, and residual functioning volume of thyroid tissue. On the other hand, current individual dosimetric approaches are both demanding and inconvenient to calculate the exact uptake and kinetics for each patient. However, it is especially crucial in the subgroup of thyroid cancer patients, who require higher amount of radioiodine due to the presence of metastases or relapsing disease.

The tissue damage caused by ionizing radiation is dependent on many factors, such as the type of radiation emitted, its amount and energy, its biokinetics in the body, including its uptake and clearance in various organs, and the physical arrangement and location of organs emitting radiation. Therefore, unlike external radiation sources, the doses received from internal radiation sources used in nuclear medicine cannot be calculated exactly; rather several formulas and assumptions are used to predict the radiation dose applied to the body.

## 2.1. Internal radiation dosimetry

The main aim of internal radiation dosimetry is to calculate the *absorbed dose*, which is defined as the mean energy imparted to matter per unit mass by ionizing radiation. Absorbed dose ( $D$ ) is calculated using the following formula:

$$D = \frac{d\varepsilon}{dm} \quad (1)$$

where  $d\varepsilon$  is the mean energy imparted by ionizing radiation and  $dm$  is the matter of mass.

In SI system, the unit for absorbed dose is joules per kilogram (J/kg) or ergs per gram (erg/g). The special units for absorbed dose are gray (Gy) and rad:

$$1 \text{ J/kg} = 1 \text{ Gy} = 100 \text{ rad} = 10^4 \text{ erg/g}$$

The term *equivalent dose* is derived from the absorbed dose to refer the different biological effects of different types of ionizing radiation. It is calculated by multiplying the absorbed dose by a radiation weighting factor ( $w_R$ ), which is dependent on the type and energy of radiation. The formula for the equivalent dose ( $H$ ) is therefore:

$$H = D \times w_R \quad (2)$$

The unit for equivalent dose is the same as absorbed dose, as the radiation weighting factor does not have a unit. However, special unit names are also defined for equivalent dose, which are *sievert* (Sv) and *rem*. Radiation weighting factor is dependent on the type of radiation. According to the International Commission on Radiological Protection (ICRP), alpha particles have radiation weighting factor of 20, whereas the factor for beta minus, beta plus (positron), gamma rays, and X-rays are 1:

$$1 \text{ Sv} = 100 \text{ rem}$$

Absorbed dose for a certain organ or tissue can be calculated when the energy absorbed per unit mass is identified. Several authors have established similar equations to calculate the absorbed dose, which are known as the Marinelli method [3], Quimby method, Medical

Internal Radiation Dose (MIRD) method [4], and International Commission on Radiological Protection (ICRP) method. For the scope of our chapter, only MIRD method is going to be explained in details, as it is the most commonly used method for radiation dosimetry calculations in nuclear medicine.

A generic equation for the absorbed dose ( $D$ ) in an organ or tissue has been established as [5, 6]:

$$D = \frac{k\tilde{A}\sum_i n_i E_i \phi_i}{m}$$

(3)

where  $k$  is the proportionality constant,  $\tilde{A}$  is the cumulated activity ( $\mu\text{Ci-h}$  or  $\text{MBq-s}$ ),  $n_i$  is the number of particles with energy  $E_i$  emitted per nuclear transition,  $E_i$  is the energy per particle ( $\text{MeV}$ ),  $\phi_i$  is the fraction of energy absorbed in the target, and  $m$  is the mass of the target region ( $\text{g}$  or  $\text{kg}$ ).

Source	Target	S-value
Bladder	Bladder	$1.2 \times 10^{-3}$
Stomach	Stomach	$9.7 \times 10^{-4}$
Kidney	Kidney	$1.5 \times 10^{-3}$
Kidney	Adrenal gland	$3.2 \times 10^{-5}$
Kidney	Spleen	$2.4 \times 10^{-5}$
Thyroid gland	Thyroid gland	$2.2 \times 10^{-2}$
Thyroid gland	Whole body	$9.5 \times 10^{-6}$
Thyroid gland	Lungs	$2.9 \times 10^{-6}$
Thyroid gland	Bone marrow	$2.4 \times 10^{-6}$

Table 1. Some S-factors for I-131.

2.2. Medical internal radiation dose (MIRD) method

MIRD method was established by the Society of Nuclear Medicine to assist radiation dose estimation to various organs using a simplified calculation method. Instead of using numerous variables, MIRD method has shortened the absorbed dose equation by using the “S-factor” for all the absorption parameters, which includes types and energy of radiation emitted, size and shape of the target organ and other related organs, and energy fraction of each emission absorbed in the target organ from radiation that originated in the source organ. S-factor is ascertained for common radiopharmaceuticals, including I-131. S-factors for I-131 and Tc-99m are given in **Tables 1** and **2**. Equation for the S-factor would be:

$$S = \frac{k \sum_i n_i E_i \Phi_i}{m} \quad (4)$$

where  $k$  is the proportionality constant ( $\approx 2.13$ ),  $n_i$  is the number of particles with energy  $E_i$  emitted per nuclear transition,  $E_i$  is the energy per particle (MeV),  $\Phi_i$  is the fraction of energy absorbed in the target, and  $m$  is the mass of the target region (g or kg).

Source	Target	S-value
Liver	Liver	$4.6 \times 10^{-7}$
Liver	Kidneys	$3.9 \times 10^{-6}$
Liver	Whole body	$2.2 \times 10^{-6}$
Liver	Bone marrow	$1.6 \times 10^{-6}$
Liver	Spleen	$9.2 \times 10^{-7}$
Spleen	Spleen	$3.3 \times 10^{-4}$
Spleen	Pancreas	$1.9 \times 10^{-5}$
Spleen	Stomach	$1.0 \times 10^{-5}$
Spleen	Whole body	$2.2 \times 10^{-6}$
Spleen	Bone marrow	$1.7 \times 10^{-6}$
Spleen	Liver	$9.8 \times 10^{-7}$
Bone marrow	Bone marrow	$3.1 \times 10^{-5}$
Bone marrow	Whole body	$2.2 \times 10^{-6}$
Bone marrow	Liver	$9.2 \times 10^{-7}$

**Table 2.** Some S-factors for Tc-99m.

Finally, MIRD equation is as follows:

$$D_t = \sum_s \tilde{A}_s S(t \rightarrow s) \quad (5)$$

$$\tilde{A} = A_0 \times \tau \quad (6)$$

where  $\tilde{A}_s$  is the cumulated activity in the source organ,  $t$  is the target organ,  $s$  is the source organ,  $A_0$  is the initial activity given, and  $\tau$  is the residence time.

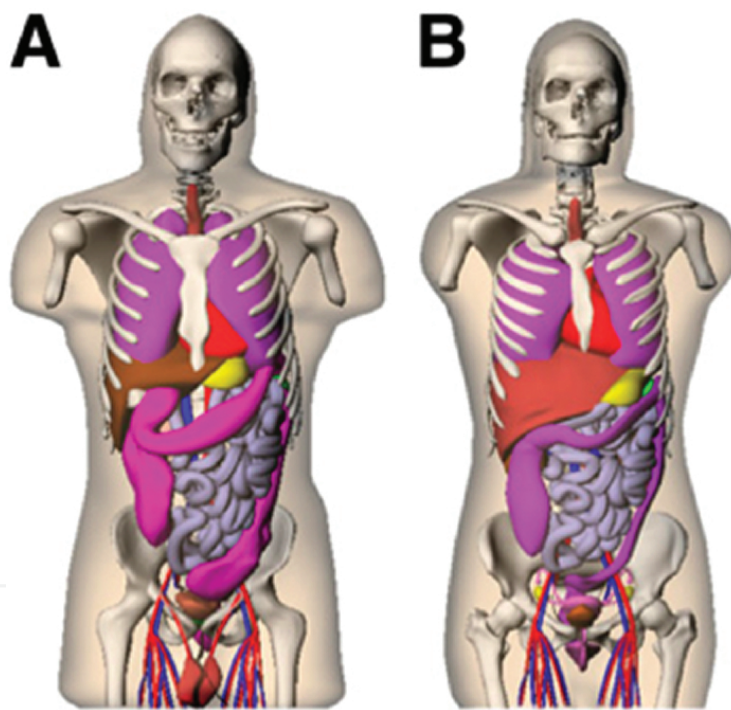
For the MIRD equation, various body phantoms, which represent human body and enable accurate measurement of absorbed fractions, organ masses, and relationship of organs, were established to determine the cumulated activity. Either external probes, such as thyroid uptake device, or time-activity curves obtained from scintigraphic imaging are used to calculate the



cumulative activity. Using MIRD equation, the calculation of radiation dose of patients after radiopharmaceutical application is possible, but MIRD equation is not suitable for establishment of radiation dose received by radiation workers and family members.

Following the establishment of MIRD phantom, various other phantoms were introduced representing human body more realistically, such as female and male phantoms, pregnant female phantom [7], family phantoms including pediatric phantom series [8], and bone and marrow phantom [9]. The data obtained using these phantoms are inserted in special software programs dedicated for internal dose calculations, such as MIRDOSE [10] and OLINDA/EXM 1.0 [11].

The recent development in computer and anatomical imaging technologies led to the creation of more realistic voxel phantoms, which include three-dimensional digital images of internal organs and hybrid phantoms enabling a realistic and rapid modeling of human body (**Figure 1**) [12, 13].



**Figure 1.** Adult male (A) and adult female (B) phantom by Segars [13]. There are also different age-specific phantoms for dose evaluation in pediatric patients.

### 3. Dosimetric approaches for thyroid carcinoma

There are two main dosimetric approaches for administration of radioiodine for the treatment of thyroid carcinoma: bone marrow-based approach, which aims to limit the radiation dose to be within safe limits for bone marrow, and lesion-based approach, which aims to give at least the minimum amount of radiation dose to destroy the lesions.

### 3.1. Bone marrow-based dosimetric approach

Bone marrow depression is one of the most important complications of radioiodine therapy as bone marrow is susceptible to ionizing radiation. Bone marrow-based dosimetry aims to calculate the maximum amount of radiation that bone marrow can tolerate for radioiodine treatment. This method was first developed by Benua et al. and it allows estimating the radiation dose received by the hematopoietic system from each unit (GBq or mCi) of I-131 activity given to the patient [14]. The procedure involves an initial administration of a tracer activity of I-131 to the patient, followed by serial blood sampling and whole-body activity measurement for at least 4 days to follow the clearance of radioiodine from the body. Although the name of this approach is bone marrow based, the calculations involve whole blood compartment, not only the bone marrow. In the study by Benua et al., the group of patients that received a whole blood dose of more than 200 cGy showed serious complications related to ionizing radiation, whereas the group of patients that received less than 200 cGy to the blood did not have serious side effects. Therefore, 2 Gy limit was proposed to be the safety limit for bone marrow.

I-131 has both gamma ( $\gamma$ ) and beta minus ( $\beta$ ) radiation; so both radiation types are included in radiation dose calculations. I-131 activity to be administered to the patient is calculated as combined absorbed doses for gamma and beta radiation and is within safety limits for bone marrow, which is accepted as 2 Gy:

$$A_{\text{administered}} (\text{MBq}) = \frac{2 \text{ Gy}}{D_{\beta} (\text{Gy} / \text{MBq}) + D_{\gamma} (\text{Gy} / \text{MBq})} \quad (7)$$

According to the original Benua protocol, a standard tracer I-131 activity was given to the patient before the therapy and measurement of serial blood samples in a gamma counter is performed for the detection of  $\beta$ -radiation dose ( $D_{\beta}$ ), whereas radiation dose for  $\gamma$ -radiation ( $D_{\gamma}$ ) is calculated either by serial measurement of the whole body of the patient using a gamma probe or by measurement of the periodic urine collection.

After the introduction of the Benua protocol, several studies were performed with different modifications to the original protocol, such as using gamma camera instead of gamma probe [15], using geometric mean of the body activity counts instead of anterior measurement, delaying the onset of whole body counting to 2 hours, and elimination of urine collection. EANM Dosimetry Committee has also published a detailed guideline providing most recent recommendations on how to perform blood- and bone marrow-based dosimetry in thyroid cancer patients [16].

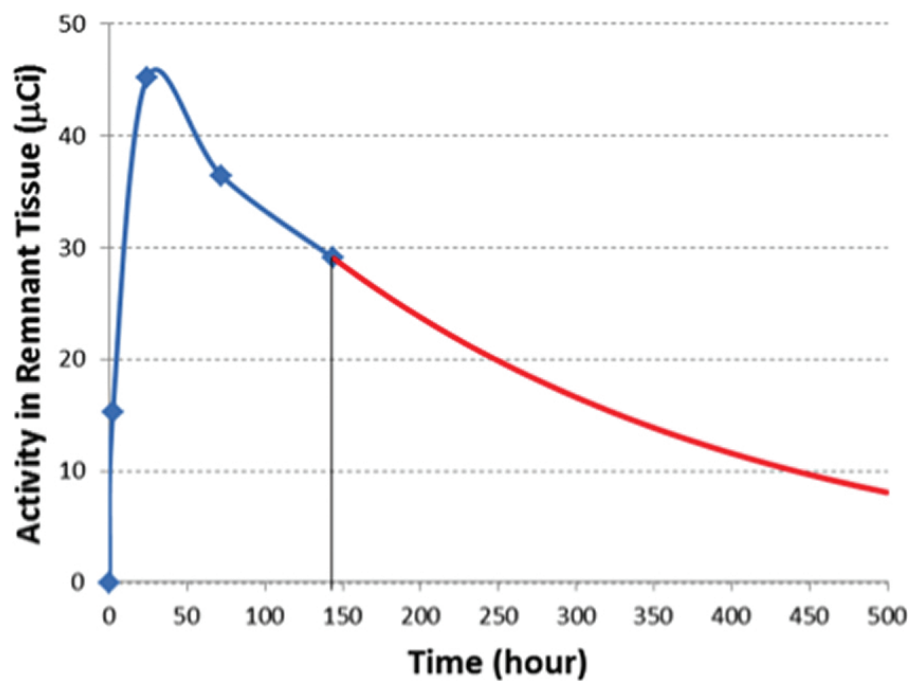
Further studies revealed that serious bone marrow toxicity is avoided in radiation doses of less than 3 Gy; so 3 Gy is accepted today as bone marrow safety limit and it is used generally for treatment of thyroid carcinoma patients with multiple metastases. Bone marrow dosimetry is not recommended for patients with extended bone metastases, as blood-based absorbed dose calculation could underestimate the absorbed dose to bone marrow [16]. Also, in the



presence of multiple pulmonary micrometastasis, lung would be the critical organ instead of bone marrow, therefore, bone marrow dosimetry would not be appropriate in those patients.

### 3.2. Lesion-based dosimetric approach

Bone marrow-based dosimetry aims to give the maximum safe amount of I-131, ignoring the absorbed dose in the tumor, which may end up with giving a higher amount of radioiodine than the actual therapeutic amount. Lesion-based dosimetric approach aims to calculate the therapeutic amount of radioiodine that provides the minimum necessary radiation dose to the residual thyroid tissue and metastatic foci. For lesion-based dosimetry, uptake and clearance of I-131 from residual thyroid tissue and all metastatic foci are needed to be calculated.



**Figure 2.** Time-activity curve obtained from series of scintigraphic images of a thyroid cancer patient. Series of whole body scintigraphy with empty bladder and rectum were acquired at different time points following tracer radioiodine administration.

The lesion-based dosimetric approach was first described by Maxon et al. in 1983 in a study with 76 thyroid carcinoma patients. Clinical response was detected in the group of patients that received minimum 300 Gy radiation dose to residual thyroid tissue and 80 Gy to metastatic foci, whereas less values were found to be inadequate for treatment [17].

The equation for assessment of lesion dose is as follows [18]:

$$Dose(cGy) = 0.63 \times C_0 (\mu Ci / g) \times T_{1/2 \text{ lesion}} (h) \quad (8)$$

where  $C_0$  is the initial concentration of I-131 in the lesion and  $T_{1/2 \text{ lesion}}$  is the effective half-life of the lesion activity.

To obtain the initial concentration of I-131 in the lesion, either serial whole body scintigraphic imaging or radioiodine uptake test are performed after the administration of an initial tracer I-131 activity. Using scintigraphic images, region of interest is drawn around the residual thyroid tissue and all metastatic foci and time-activity curves are obtained to calculate the initial activity and the effective half-life (**Figure 2**). Measurements were performed at the 2nd, 6th, 24th, 48th, 72nd, and 96th hours following radioiodine administration and additional measurements are performed if the excretion is delayed. Also, the lesion mass is calculated either using the gamma camera images or using radiological imaging tools, such as computerized tomography (CT) or ultrasonography (USG).

Selection of optimum administered dose is challenging in the presence of chronic renal failure, as delayed excretion of radioiodine in these patients lead to increased radiation exposure of the whole body including the critical dose limiting organs such as bone marrow. Dosimetry is therefore recommended for these patients to refrain from radiation-related side effects and to limit the exposure of the healthcare providers [19, 20].

### 3.3. Dosimetry using I-124

Traditionally, dosimetric methods for thyroid carcinoma involve use of low dose of I-131. However, concerns about the stunning effect of I-131 limit its usage and lead to search for alternative radionuclides, such as I-123 or I-124. I-123 is a cyclotron product with a half-life of 13 h. Being a pure gamma emitter, it is more favorable for diagnostic imaging but its supply is limited. I-124 is also produced in a cyclotron, but it has a longer half-life of 4.18 days and it is a positron emitter, which makes the isotope a promising tool for imaging of the residual disease using PET/CT, for detection of patients who would benefit from radioiodine therapy and for dosimetry of lesions especially for patients who require higher amount of radioiodine [21].

I-124 PET-based dosimetry protocol involves serial PET/CT imaging starting 2–4 h after oral administration of I-124 until 72–96 h. There are also simplified protocols proposed involving imaging only at the 24th and 96th hours for lesion dosimetry [22]. Data obtained from I-124 PET/CT image can also be used to simplify the blood dose protocol, reducing the number of blood sampling [23].

I-124 PET/CT was reported to provide a better assessment of lesion dosimetry in thyroid cancer patients as it enables to determine the concentration of radionuclide in the lesion, providing higher spatial resolution and imaging sensitivity than images acquired using gamma cameras [24, 25]. Also, it allows estimating the lesion absorbed dose per administered I-131 activity for each radioiodine positive tumor foci [24]. In a study investigating the relationship between the absorbed radiation dose detected by I-124 PET and lesion response after I-131 administration, similar response rates were found for thyroid remnant tissue compared to the historical data of Maxon et al., who used planar I-131 scintigraphy to detect absorbed radiation dose [23]. It was shown that I-124 PET/CT lesion dosimetry could be used as a prognostic tool to predict lesion-based I-131 response [26]. Moreover, I-124 PET was found to be promising for detection of radioiodine avidity of the remnant thyroid tissue and metastatic foci [27, 28]. However, high

false negative rate of I-124 PET/CT was also reported in patients who had received rhTSH stimulation [29].

4. Radiation safety

Increased usage of radiation in science, technology, and medicine led to a need for establishment of an international organization to provide recommendations on radiation protection. International Commission on Radiological Protection (ICRP, former name “International X-ray and Radium Protection Committee”) is an international, nongovernmental organization that was founded in 1928 in Sweden to provide recommendations and guidance on radiation protection.

4.1. Biological effects of radiation

Biological effects of radiation can be divided into two categories: deterministic effects and stochastic effects.

Tissue/organ	Effects	Equivalent dose for single exposure (Sv)	Equivalent dose rate for prolonged exposure (Sv/year)
Testis	Temporary infertility	0.15	0.4
	Permanent infertility	>3.5	2.0
Ovaries	Permanent infertility	>2.5	>0.2
Lens of the eye	Detectable opacities	>0.5	>0.1
	Cataract	>2.0	>0.15
Bone marrow	Impairment of blood cell production	>0.5	>0.4

Table 3. Threshold for deterministic for different tissues and organs by ICRP [30].

Deterministic effects can be seen in medium to high radiation doses. The effects related with radiation are seen only above a certain threshold, when there is loss of tissue function and the damage will increase with the absorbed dose. Bone marrow, testis, and lens of the eye are the most sensitive tissues for radiation; therefore, deterministic effects such as pancytopenia, infertility, and cataract are first seen in those tissues. Although skin is not one of the most sensitive organs for radiation, erythema is another common deterministic effect, which occurs due to accidental skin contamination. Doses of radionuclides used for nuclear medicine imaging procedures are below the threshold for deterministic effects. During radionuclide therapy, including I-131 therapy for thyroid cancer, doses are selected that exceed the deterministic threshold only for the thyroid tissue, preserving the other tissues. ICRP has published recommendations including the thresholds for deterministic effects of different tissues and organs (Table 3) [30].

Stochastic effects can be seen in low level of exposure, there is not a certain threshold for the effects and the severity is not dependent on the absorbed dose. The name stochastic is given to refer that the effects can be seen by chance and the proportion of the population that are effected can be predicted statistically but the exact persons that will be affected cannot be foreseen. Stochastic effects occur when radiation does not kill the cell but modifies its DNA. Radiation-related cancers and hereditary disorders are examples for stochastic effects of radiation.

#### 4.2. Practical dosimetry

Despite many advantages of radiation dosimetry, it is difficult to be performed for all thyroid carcinoma patients undergoing radioiodine therapy. Some information, on the other hand, obtained from dosimetry principles can guide clinicians in treatment planning of patients. Retention of radioiodine can be easily determined using a standard uptake probe and if high radioiodine retention is detected, prescribed radioiodine dose could be decreased to ensure safety [31]. On the contrary, if radioiodine retention is low, then prescribed dose of I-131 could be increased to optimize the efficacy. Bone marrow is the dose-limiting organ for radioiodine therapy, as the bone marrow depression is one of the most important complications of the therapy. Radiation to blood and to bone marrow is correlated with body retention. Also, increased serum thyroxine concentration in the blood in the absence of thyroid hormone medication can be used as an indicator of increased blood radiation and reduction of prescribed activity could be taken into consideration. Thyroid carcinomas, which are at least 1 cm in diameter but are not visible on scintigraphic image, usually cannot be eliminated with a usual therapeutic I-131 dose of 3700–7400 MBq (100–200 mCi); therefore, either dose increase or dosimetric approaches should be considered for those patients [31]. Presence of radiation-related side effects after the first radioiodine therapy, such as bone marrow toxicity, sialadenitis, and lacrimal gland dysfunction, should be assessed prior further therapy planning to avoid cumulative radiation toxicity.

#### 4.3. Radiation-related risks in thyroid cancer patients

The risk of radioiodine-related secondary cancer in thyroid cancer patients is controversial. There are several long-term follow-up studies investigating the secondary malignancies in thyroid cancer patients and only a very low associated risk of malignancy could be found. Therefore, recent thyroid cancer management guidelines do not recommend any specific screening after radioiodine administration in thyroid cancer patients [2]. The risk of secondary cancers is dose related and generally seen in patients who receive cumulative I-131 activity of more than 22,200 MBq (600 mCi) and there is no direct evidence of increased risk in patients who have received 1110–3700 MBq (30–100 mCi) radioiodine in a single session [32]. In a meta-analysis including 16,502 patients from two distinct multicenter studies, overall risk of secondary cancer was shown to be increased by 1.2 (95% CI: 1.04–1.36;  $p < 0.01$ ) [33]. The most significant risk increase was reported to be in leukemias, with a relative risk of 2.5 (95% CI: 1.13–5.53;  $p < 0.024$ ) [33]. Other cancers reported to have increased risk are bone and soft tissue cancers, breast cancer, colorectal cancer, salivary gland tumors, and kidney cancer [32, 34, 35].

There are also several other studies that show increased risk of secondary malignancies in thyroid cancer patients, that is not associated with radioiodine administration [36, 37].

4.4. Radiation safety precautions for family members and public

Three of basic elements of radiation safety are distance, shielding, and time. Distance is the most important and simple way to ensure radiation safety. For point sources, the intensity of radiation is inversely related with the square of distance (inverse square law). For nonpoint sources, such as the patients, this law is not as accurate as in point sources, but still the exposure decreases as the distance in between increases. Shielding is another important parameter to ensure radiation safety. During radioiodine therapy, protection against beta and gamma radiation of I-131 is necessary. Beta radiation can be absorbed in a few centimeters of wood and they cannot penetrate out of patient body. Gamma rays are absorbed by atoms with heavy nuclei, such as lead. Reducing the exposure time reduces the cumulative dose proportionally. So the shorter time patients spend with their family, the smaller the radiation dose the family members receive.

ICRP and International Atomic Energy Agency (IAEA) recommend a dose limit of 1 mSv/year to the general public and 5 mSv/year to family members and caregivers of patients who have received radionuclide therapy (Table 4) [30, 38]. According to the European Atomic Energy Community (EURATOM), patients are allowed to be discharged after a radiation dose rate limit of 20 µSv/h at 1 m is achieved. After discharge, patients are advised to take further precautions at home.

Organ or tissue	Radiation worker (mSv/year)	Public (mSv/year)
Whole body	20	1
Gonads	50	5
Bone marrow	50	5
Bone	500	50
Skin	500	50
Thyroid gland	500	50
Extremities	500	75

Table 4. Dose limits to radiation workers and public recommended by ICRP.

Patients undergoing radioiodine therapy for thyroid cancer treatment and ablation are hospitalized in radionuclide therapy units to ensure proper shielding and waste control. Special precautions are taken in design of the patient rooms: The walls are lead lined to limit the gamma ray exposure of the health care workers and other patients. Also, lead lined tanks are used to store the waste of patients for decay to limit the release of I-131 to public sewage system. After discharge, patients are advised to maximize their distance from pregnant women and children, sleep in separate beds, to avoid spending extended time in public places, and to



limit travel for some time depending on the amount of radioiodine given [39, 40]. Also, several attempts are being discussed to decrease the radiation-related side effects of the patient, such as increased amount of daily water intake, frequent urination to decrease the absorbed dose to kidneys and bladder, and chewing-gum stimulation to decrease the absorbed dose to salivary glands [41]. Pregnancy is contra-indicated for radioiodine administration and according to ICRP female patients are advised to refrain from pregnancy for at least 4 months following radioiodine administration. Also, breast-feeding is not allowed after radioiodine administration.

## Author details

Lebriz Uslu Beşli and Mustafa Demir\*

\*Address all correspondence to: [demirm@istanbul.edu.tr](mailto:demirm@istanbul.edu.tr)

Department of Nuclear Medicine, Istanbul University Cerrahpaşa Medical Faculty, Istanbul, Turkey

## References

- [1] Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid: Official Journal of the American Thyroid Association*. 2009;19:1167–1214. doi: 10.1089/thy.2009.0110.
- [2] Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid: Official Journal of the American Thyroid Association*. 2016;26:1–133. doi: 10.1089/thy.2015.0020.
- [3] Marinelli LD, Quimby EH, Hine GJ. Dosage determination with radioactive isotopes; biological considerations and practical applications. *Nucleonics*. 1948;2:44–49.
- [4] Zanzonico PB. Internal radionuclide radiation dosimetry: a review of basic concepts and recent developments. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 2000;41:297–308.
- [5] Toohey RE, Stabin MG, Watson EE. The AAPM/RSNA physics tutorial for residents: internal radiation dosimetry: principles and applications. *Radiographics: A Review Publication of the Radiological Society of North America, Inc*. 2000;20:533–546; quiz 1–2. doi: 10.1148/radiographics.20.2.g00mc33533.



- [6] Stabin MG. Dosimetric and radiobiologic considerations. In: Ell PJ, Gambhir SS, editors. *Nuclear Medicine in Clinical Diagnosis and Treatment*. 3rd edition. Churchill Livingstone, New York; 2004. Pp 363–373.
- [7] Stabin MG. Mathematical models and specific absorbed fractions of photon energy in the nonpregnant adult females and at the end of each trimester of pregnancy. Oak Ridge, TN: Oak Ridge National Laboratory; 1995.
- [8] Cristy M. Development of mathematical pediatric phantoms for internal dose calculations: designs, limitations, and prospects. In: Watson EE, Stelson A, Coffey J, Cloutier R, editors. *Proceedings of the Third International Radiopharmaceutical Dosimetry Symposium (FDA 81–8166)*. Oak Ridge, TN: Oak Ridge Associated Universities; 1981. Pp. 496–517.
- [9] Eckerman K. Aspects of the dosimetry of radionuclides in the skeleton with particular emphasis on the active marrow. In: Stelson A, Watson E, editors. *Proceedings of the Fourth International Radiopharmaceutical Dosimetry Symposium (CONF-851113)*. Oak Ridge, TN: Oak Ridge Associated Universities; 1986. Pp. 514–534.
- [10] Stabin MG. MIRDOSE: personal computer software for internal dose assessment in nuclear medicine. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 1996;37:538–546.
- [11] Stabin MG, Sparks RB, Crowe E. OLINDA/EXM: the second-generation personal computer software for internal dose assessment in nuclear medicine. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 2005;46:1023–1027.
- [12] Zaidi H, Xu XG. Computational anthropomorphic models of the human anatomy: the path to realistic Monte Carlo modeling in radiological sciences. *Annual Review of Biomedical Engineering*. 2007;9:471–500. doi:10.1146/annurev.bioeng.9.060906.151934.
- [13] Stabin MG, Emmons MA, Segars WP, Fernald MJ. Realistic reference adult and paediatric phantom series for internal and external dosimetry. *Radiation Protection Dosimetry*. 2012;149:56–59. doi:10.1093/rpd/ncr383.
- [14] Benua RS, Cicale NR, Sonenberg M, Rawson RW. The relation of radioiodine dosimetry to results and complications in the treatment of metastatic thyroid cancer. *The American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine*. 1962;87:171–182.
- [15] Wahl RL, Kroll S, Zasadny KR. Patient-specific whole-body dosimetry: principles and a simplified method for clinical implementation. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 1998;39:14s–20s.
- [16] Lassmann M, Hanscheid H, Chiesa C, Hindorf C, Flux G, Luster M. EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy. *European*

Journal of Nuclear Medicine and Molecular Imaging. 2008;35:1405–1412. doi:10.1007/s00259-008-0761-x.

- [17] Maxon HR, Thomas SR, Hertzberg VS, Kereiakes JG, Chen IW, Sperling MI, et al. Relation between effective radiation dose and outcome of radioiodine therapy for thyroid cancer. *The New England Journal of Medicine*. 1983;309:937–941. doi:10.1056/nejm198310203091601.
- [18] Atkins FB, Van Nostrand D, Wartofsky L. Dosimetrically-determined prescribed activity of radioiodine for the treatment of metastatic thyroid carcinoma. In: Wartofsky L, Van Nostrand D, editors. *Thyroid Cancer: A Comprehensive Guide to Clinical Management*. 2nd edition. Humana Press, Totowa, New Jersey; 2006. Pp. 433–446.
- [19] Alevizaki C, Molfetas M, Samartzis A, Vlassopoulou B, Vassilopoulos C, Rondogianni P, et al. Iodine 131 treatment for differentiated thyroid carcinoma in patients with end stage renal failure: dosimetric, radiation safety, and practical considerations. *Hormones (Athens, Greece)*. 2006;5:276–287.
- [20] Yeyin N, Cavdar I, Uslu L, Abuqbeitah M, Demir M. Effects of hemodialysis on iodine-131 biokinetics in thyroid carcinoma patients with end-stage chronic renal failure. *Nuclear Medicine Communications*. 2016;37:283–287. doi: 10.1097/mnm.0000000000000439.
- [21] Lassmann M, Reiners C, Luster M. Dosimetry and thyroid cancer: the individual dosage of radioiodine. *Endocrine-Related Cancer*. 2010;17:R161–R172. doi: 10.1677/erc-10-0071.
- [22] Jentzen W, Freudenberg L, Eising EG, Sonnenschein W, Knust J, Bockisch A. Optimized <sup>124</sup>I PET dosimetry protocol for radioiodine therapy of differentiated thyroid cancer. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 2008;49:1017–1023. doi: 10.2967/jnumed.107.047159.
- [23] Jentzen W, Bockisch A, Ruhlmann M. Assessment of simplified blood dose protocols for the estimation of the maximum tolerable activity in thyroid cancer patients undergoing radioiodine therapy using <sup>124</sup>I. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 2015;56:832–838. doi: 10.2967/jnumed.114.153031.
- [24] Freudenberg LS, Jentzen W, Stahl A, Bockisch A, Rosenbaum-Krumme SJ. Clinical applications of <sup>124</sup>I-PET/CT in patients with differentiated thyroid cancer. *European Journal of Nuclear Medicine and Molecular Imaging*. 2011;38(Suppl 1):S48–S56. doi: 10.1007/s00259-011-1773-5.
- [25] Chen MK, Cheng DW. What is the role of dosimetry in patients with advanced thyroid cancer? *Current Opinion in Oncology*. 2015;27:33–37. doi: 10.1097/cco.0000000000000145.
- [26] Wierts R, Brans B, Havekes B, Kemerink G, Halders S, Schaper N, et al. Dose–response relationship in differentiated thyroid cancer patients undergoing radioiodine treatment

- assessed by means of  $^{124}\text{I}$  PET/CT. *Journal of Nuclear Medicine: Official Publication, Society of Nuclear Medicine*. 2016. doi: 10.2967/jnumed.115.168799.
- [27] Pettinato C, Spezi E, Nanni C, Grassetto G, Monari F, Allegri V, et al. Pretherapeutic dosimetry in patients affected by metastatic thyroid cancer using  $^{124}\text{I}$  PET/CT sequential scans for  $^{131}\text{I}$  treatment planning. *Clinical Nuclear Medicine*. 2014;39:e367-74. doi: 10.1097/rlu.0000000000000490.
- [28] Pettinato C, Monari F, Nanni C, Allegri V, Marcatili S, Civollani S, et al. Usefulness of  $^{124}\text{I}$  PET/CT imaging to predict absorbed doses in patients affected by metastatic thyroid cancer and treated with  $^{131}\text{I}$ . *The Quarterly Journal of Nuclear Medicine and Molecular Imaging: Official Publication of the Italian Association of Nuclear Medicine (AIMN) [and] the International Association of Radiopharmacology (IAR), [and] Section of the Society of Radiopharmaceutical Chemistry and Biology*. 2012;56:509–514.
- [29] Kist JW, de Keizer B, van der Vlies M, Brouwers AH, Huysmans DA, van der Zant FM, et al.  $^{124}\text{I}$  PET/CT to predict the outcome of blind  $^{131}\text{I}$  treatment in patients with biochemical recurrence of differentiated thyroid cancer: Results of a multicenter diagnostic cohort study (THYROPET). *J Nucl Med*. 2016;57(5):701–7.
- [30] International Commission on Radiological Protection. 1990 Recommendations of the International Commission on Radiological Protection. *Annals of the ICRP*. ICRP Publication 60 ed. Oxford: Pergamon Press; 1991. Pp. 1–201.
- [31] Sisson JC. Practical dosimetry of  $^{131}\text{I}$  in patients with thyroid carcinoma. *Cancer Biotherapy & Radiopharmaceuticals*. 2002;17:101–105. doi: 10.1089/10849780252824118.
- [32] Rubino C, de Vathaire F, Dottorini ME, Hall P, Schwartz C, Couette JE, et al. Second primary malignancies in thyroid cancer patients. *British Journal of Cancer*. 2003;89:1638–1644. doi: 10.1038/sj.bjc.6601319.
- [33] Sawka AM, Thabane L, Parlea L, Ibrahim-Zada I, Tsang RW, Brierley JD, et al. Second primary malignancy risk after radioactive iodine treatment for thyroid cancer: a systematic review and meta-analysis. *Thyroid: Official Journal of the American Thyroid Association*. 2009;19:451–457. doi: 10.1089/thy.2008.0392.
- [34] Brown AP, Chen J, Hitchcock YJ, Szabo A, Shrieve DC, Tward JD. The risk of second primary malignancies up to three decades after the treatment of differentiated thyroid cancer. *The Journal of Clinical Endocrinology and Metabolism*. 2008;93:504–515. doi: 10.1210/jc.2007-1154.
- [35] Chen AY, Levy L, Goepfert H, Brown BW, Spitz MR, Vassilopoulou-Sellin R. The development of breast carcinoma in women with thyroid carcinoma. *Cancer*. 2001;92:225–231.

- [36] Berthe E, Henry-Amar M, Michels JJ, Rame JP, Berthet P, Babin E, et al. Risk of second primary cancer following differentiated thyroid cancer. *European Journal of Nuclear Medicine and Molecular Imaging*. 2004;31:685–691. doi: 10.1007/s00259-003-1448-y.
- [37] Sandeep TC, Strachan MW, Reynolds RM, Brewster DH, Scelo G, Pukkala E, et al. Second primary cancers in thyroid cancer patients: a multinational record linkage study. *The Journal of Clinical Endocrinology and Metabolism*. 2006;91:1819–1825. doi: 10.1210/jc.2005-2009.
- [38] International Atomic Energy Agency. *Radiological Protection for Medical Exposure to Ionizing Radiation*. Vienna: IAEA; 2002.
- [39] Sisson JC, Freitas J, McDougall IR, Dauer LT, Hurley JR, Brierley JD, et al. Radiation safety in the treatment of patients with thyroid diseases by radioiodine  $^{131}\text{I}$ : practice recommendations of the American Thyroid Association. *Thyroid: Official Journal of the American Thyroid Association*. 2011;21:335–346. doi: 10.1089/thy.2010.0403.
- [40] Barrington SF, Kettle AG, O'Doherty MJ, Wells CP, Somer EJ, Coakley AJ. Radiation dose rates from patients receiving iodine-131 therapy for carcinoma of the thyroid. *European Journal of Nuclear Medicine*. 1996;23:123–130.
- [41] Jentzen W, Richter M, Nagarajah J, Poeppel TD, Brandau W, Dawes C, et al. Chewing-gum stimulation did not reduce the absorbed dose to salivary glands during radioiodine treatment of thyroid cancer as inferred from pre-therapy (124)I PET/CT imaging. *EJNMMI Physics*. 2014;1:100. doi: 10.1186/s40658-014-0100-1.

