

## Measurement of Radiation Exposure to Caregivers of Patients with Thyroid Diseases Treated with Iodine-131: A Review

Ali Abdulhasan Kadhim<sup>1</sup>, Peyman Sheikhzadeh<sup>2\*</sup> , Saeed Farzanefer<sup>2</sup>, Shima Yavari<sup>2</sup>, Majdi Mousa Jber<sup>1</sup>, Mohammad Reza Ay<sup>1,3</sup>

<sup>1</sup> Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup> Department of Nuclear Medicine, Vali-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Research Center for Molecular and Cellular Imaging, Tehran University of Medical Sciences, Tehran, Iran

\*Corresponding Author: Peyman Sheikhzadeh  
Email: [sheikhzadeh-p@razi.tums.ac.ir](mailto:sheikhzadeh-p@razi.tums.ac.ir)

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### Abstract

This review paper aimed to examine radiation safety issues related to relatives as well as caregivers of patients with thyroid diseases treated with radioiodine (I-131). During I-131 therapy for thyroid disorders such as hyperthyroidism, patients receiving I-131 doses (200-800 MBq) emit radioactive radiations which pose a prospective risk to other people. Critical groups are patients' visitors and families, especially children. Following the updated international guidelines, the doses received by members of the public as a proportion of the therapy of a patient have been decreased. The public annual dose limits are 1 mSv, although higher doses are permitted for adults in the patient's family, provided that the maximum 5 mSv is not surpassed for 5 years. Without compliance with the current recommendations, extended hospitalizations for patients are essential. Family members should therefore limit close interactions with an individual for some duration following thyroid therapy with I-131.

**Keywords:** Radioiodine; Hyperthyroidism; Iodine-131; Thyroid Cancer Treatment; Radioactive Radiations.

## 1. Introduction

John Livingood and Glenn Seaborg in 1938 made a discovery of a very crucial radioisotope named radioiodine (I-131). The half-life of I-131 is about 8 days for its radioactive decay. The various fields in which it is utilized include energy, industry as well as medical diagnosis and therapeutic aims.

In the treatment of diseases, as the beta decay from I-131, causes the death of diseased cells up to a few millimeters. Hence, higher doses of radioiodine are sometimes less perilous compared to lower doses, since they will, in general, eliminate tissues that would, in one way or the other, become malignant owing to radiation.

I-131 is one of the most commonly used tracers which emits gamma in addition to beta radiation. The hydraulic fracturing fluid is infused with the radioactive tracer's isotopes to decide the profile of infusion and area of breaks made by pressure-driven breaking [1]. Higher doses of I-131 than those utilized in therapeutic techniques, are assumed by certain examinations to be a major reason for expanded thyroid diseases after accidental atomic disasters. These investigations revealed that malignant growths occur from leftover tissue radiation damage brought about by I-131, even long after the decay cycle of I-131 [2, 3]. However, several studies did not discover this relationship [4, 5].

### 1.1. Applications of I-131

The thyroid gland is an endocrine organ and its hormones such as thyroxine (T4) and triiodothyronine (T3) play multifaceted roles in normal growth, neurological development and homeostasis.

For such cases whereby the thyroid becomes overactive, a condition commonly known as hyperthyroidism, one of the remedies is treatment with radioiodine (i.e. Radioactive Iodine-131). It is noteworthy that the main cause of hyperthyroidism is Graves' disease [6]. This disease is characterized by overactive glands or in some cases nodules created inside the gland become overactive and hence produce excessive amount of thyroid hormones [7].

The application of I-131 is also commonly utilized in the treatment of thyroid cancer [8]. Thus, as far as I-131 is concerned, it is a radio emitter iodine isotope which is used in multiple medical purposes. After administration (usually orally) of I-131, it flows through the bloodstream and is first absorbed in the Gastrointestinal (GI) tract. Thereafter, it flows through the blood and then gets trapped in the thyroid tissue, where the destruction of diseased cells occurs.

For treatment aims, it is recommended that I-131 be administered orally either in capsule or liquid form. The medicine once taken rapidly begins the destruction of cells in the thyroid tissue. It is important to note that medications containing radioactive substances are absorbed for a long time (ranging from days to months) in the body depending on the type of organ.

During the therapy period, radiation exposure to caregivers or relatives who are in contact with the patient is almost inevitable. Hence, there is always a fear that these people receive some amount of radiation.

The current study aimed to review previous researches involving radioiodine I-131 for treatment of different illnesses with regards to the radiation doses received by caregivers as well as relatives who are in contact with the patients.

## 2. Review of Previous Researches

There are numerous researches wherein we find the application of I-131 therapy for treatment of patients suffering from Graves' disease, toxic nodular and multi-nodular goiters etc. [9-14].

The utilization of I-131 for treatment of thyroid-related disorders is widely practiced all around the world. It is true that the advantages to patients treated with I-131 are remarkable but at the same time, much attention should also be paid to the relatives or caregivers who are exposed to radiation following the utilization of I-131. Advantages to patients following treatment with I-131 must be adjusted against radiation exposure to caregivers whose effort in ensuring that patients receive adequate support after administration of the radioiodine cannot be overemphasized.

There is no proof, however, that the safety of caregivers has been compromised, following quality of patient's care becoming more convenient and cost-effective. The present international guidelines are far less rigid than those involving I-131 therapies in countries in which this therapeutic method is being utilized. On the other hand, exposure to radiation from new procedures has been remained as a source of concern of the international community.

The International Atomic Energy Agency (IAEA) has set a few benchmarks, which aimed at ensuring that the safeties of individuals in contact with radioactive materials, for example I-131, for various aims, including treatment, are not compromised. Their standard states that patients receiving treatment with radioactive substances with doses less than 1100 MBq do not require hospitalization [15]. In any case, treatments with higher doses of radioiodine may pose hazards to both clinical staff and patient's family members; hence, it necessitates the need for these guidelines [16-20].

Cappelen *et al.* [21] investigated the radiation doses that relatives have been exposed to in the event of those patients who have been treated for thyrotoxicosis with I-131 (Table 1). For this investigation, they gathered information from 76 relatives of 42 patients of different ages. The relatives, whether older or younger, were approached to wear Thermoluminescent Dosimeters (TLD) in their wrist for about 14 days. At the end of this period, it was discovered that their radiation levels were within the acceptable limits. The only exception was found on account of a 13-year old child. The radiation doses to relatives under the prescribed limits for thyrotoxic patients being treated with I-131 was up to 600 MBq.

Mulazimoglu *et al.* [22] examined the aftereffects of external exposure to caregivers of patients hospitalized in two distinct gatherings of 3-4 administered radioiodine treatment for Hyperthyroidism (HT) and Thyroid Cancer (TC). A total of 1989 patients were assessed, from which 1517 patients had TC and 472 had HT. Dose rates were measured at clinical release time from a distance of 1 m at the stomach level. The dose rates for 99.7 % of patients were  $<30 \mu\text{Sv h}^{-1}$  and that for 0.3 % of patients were  $>30 \mu\text{Sv h}^{-1}$ . The outcomes between patient gatherings with TC and HT at the third and fourth days, and the disparity of

estimation results at the third and fourth days in all outpatients, without separating the day distinction, was significant albeit 3-day isolation period for  $30 \mu\text{Sv h}^{-1}$  was acceptable.

A study by D'Alessio *et al.* [23] was conducted to evaluate the prospective entry of alien radioactivity from patients treated with I-131 therapies for embolization of the remaining thyroid cancer and metastases, to the level of continuous assessments of dosage levels. Estimates of administration rate were made around the outside of every treatment patient at 1 m and 5 cm when the patients were released. The proportion estimates based on the projected levels of implementation and those based on logical Line-Source (LSM) and Point Source (PSM) Models were compared. Feasible  $D(\infty)$  parts were measured using conventional gamma factor (protons) and physical half-life, or characteristics derived from valuable data from researchers, associates, and accomplices. Until the implementation at 1 m was below the 0.010 mSv limit, 700 patients were investigated. Patients received I-131 doses ranging from 1.85 to 11 GBq (median: 3.7 GBq). With the PSM test, a mixture of 2.60/20.65, 0.32/2.53, 0.96/7.59 and 0.57/4.50 mSv, the intermediate and perhaps most severely assessed doses to infinity ( $\infty$ ) were observed for family members as well as peers. The LSM and 0.57/4.42 mSv values were used in the  $D(\infty)$  value of 2.41/19.15, 0.32/2.50 and 0.83/6.62, respectively. Their results showed a fairly accurate estimate of doses to infinity  $D(\infty)$  after patient's discharge, and therefore may be utilized by physicians and emergency staff to obtain information about patient's doses prior to discharge as well as giving adequate precautions for post-discharge following I-131 treatments.

It has been shown that I-131 therapy is very effective for hyperthyroidism [24]. However, this therapy involves important issues related to radiation safety during and after the administration. Some amount of radiations could be observed in the saliva, urine, perspiration, blood, and breast-milk [25] due to exposure to I-131. Those at increased danger of exposure to radiations are individuals and family members with whom the patients may come in close contact. Children are considered to be of highest risk as they would have a longer duration of contact than

elders; also, their tissues are more sensitive to radiation [26]. In the first days after treatment, contamination with radioactive secretions is generally avoided by reducing body contact with children. Therefore, any radiation doses in the air, even if they are low, are dangerous and should be avoided [27-28].

Almost any outpatient dose of radioiodine (up to 30 mCi) is administered and following patients proceed with their everyday life. Whilst also radioactive I-131 for these patients is suggested, patients may take measures to prevent the spread of radiation contamination among their family members as well as other persons they are in contact with. After therapeutic quantities would be administered, contamination through urinary secretion, respiration, blood, and saliva may be related to domestic radioactive iodine intake by family members or individuals coming in contact [29]. The domestic spread of radiation to other individuals in the family can be minimized by patients following careful instructions, including proper hygiene, eating practices and observing radiation safety guidelines [30].

The duration of stay for prescribed radioiodine individuals relies exclusively on the assessment of their exposure rates [31] by reducing their dose to others [32]. The dose restrictions indicated in the latest European Commission guidelines are age-related and are designed to take radioactive contamination from other human sources into consideration [33]. For families, such as children older than 10 years, with a larger-dose dose limit of 15 mSv for family members above 60 years old, a dose limit of 3 mSv per-treatment was recommended.

For children under the age of 10, the dose limit is 1 mSv. For the general public such as fellow passengers, a dose stipulation of 0.3 mSv was defined. The way such dose restrictions are currently being implemented in Europe is significant in vastly different ways [34, 35]. In countries such as Switzerland, Germany, and Czech Republic, hyperthyroidism patients are treated based on the same recommendations as that of cancer patients (in which patients are admitted to the hospital). However, other European countries and the United States give outpatient care with recommendations to minimize future close contacts with other people. If revised, dose constraints cannot be accomplished during

outpatient therapy. Therefore, admitting these countries will lead to a substantial rise in medical costs.

In recent times, several investigations of Radioiodine Therapy (RIT) for treatment of cancerous and non-cancerous thyroid diseases have proposed several precautionary standards for radiation exposure [36-38]. The proposed patient behaviors and limitations differ considerably in the literature that were presented in [39, 40]. This was due to many variables such as the fact that nurses involved in the treatment team for thyrotoxicosis have not had extensive knowledge about the biokinetics of radioiodine and different radioactivity precautionary strategies.

One of the key variables in evaluating the aggregate doses and developing radioactive exposure protections to the public is patient-specific biokinetics for I-131. In view of the complexity of this process, few hospitals depend on personal measures for patient-specific iodine biokinetics, thereby providing protection to radioactive iodine-treated patients. In the context of radioimmunotherapy [41] and I-131 thyroid therapy [42], the importance of the use of real biokinetics in successive doses and radioactive contamination precautionary notations have been shown.

Usually, TLD is the standard practice tool for measuring the radiation doses received by caregivers. This approach has been implemented in many studies. Pant *et al.* [43] assessed the effective doses to relatives of thyroid cancer patients treated with 0.9-7.4 GBq I-131. Their TLD measurements showed that 76% of relatives were exposed to less than 1.0 mSv, with an average dose of 0.7 mSv. In another study by Carvalho *et al.* to assess compliance with radiation protection recommendations for caregivers, the measured TLD doses of caregivers were well within the acceptable limits [44]. Tonnonchiang *et al.* [45] also utilized TLD in addition to *in vivo* bioassay in measuring caregivers' effective doses, with results showing a range of 0.033-1.92 mSv.

In some cases, when patients are discharged after treatment with I-131, getting access to their caregivers for monitoring their effective doses could be challenging and unrealistic. Moreover, if dose monitoring is done, it is usually for a short period of

time. Thus, in recent years, several approaches aiming at estimating radiation doses to caregivers have been proposed. The extent of the relationship between patients and caregivers has been shown to have an effect on radiation doses received by the caregivers. Jeong *et al.* [46] proposed the “engagement factor” (K) which gives a reflection on the degree of engagement of the caregiver to the patient and thus can be used in estimating caregivers’ effective doses. Their results using this approach showed that caregivers’ effective doses were approximately 2.5% of the 5 mSv limit. This approach was further evaluated in a study by Lee *et al.* [47] involving thyroid cancer patients treated with high and low activities of I-131. Their results showed that to limit the doses received by caregivers, patients receiving high-activity I-131 can be released after 24 h of isolation, while outpatients treated with low-activity I-131 should be isolated for at least 12 h. Thus, caregivers who have extremely close relationship to the patients will tend to have higher effective doses. This is even more expected in cases whereby caregivers are spouses, since spouses would normally have more interactions and also more personal contact.

Ebrahimi *et al.* [48] utilized neural network predicted effective doses to caregivers. This study involved caregivers of 52 thyroid cancer patients treated with I-131. Their results showed that the mean effective dose received by caregivers was 0.45 mSv. Furthermore, with a mean square error of 0.142, this approach seems promising.

In order to predict or estimate the effective doses to caregivers for an infinite time, the Nuclear Regulatory Commission’s (NRC) equation [49] has been utilized in several studies. This analytical approach was utilized in studies by Leslie *et al.* [50] and Ebrahimi *et al.* [51] and was compared to measured results from TLD. Their results showed that analytical calculations were higher than those of TLD. This could be attributed to the fact that analytical calculations give a rough estimate of caregivers’ effective doses at a fixed distance and also because it does not take into consideration the caregivers’ self-absorption. Therefore, it is important to have in mind that analytical results are rough estimates and not exact. For instance, in a study by Siegel *et al.* [52], even though their analytical results were within the

internationally acceptable limits, it differed in measured results by about 60%. Ebrahimi *et al.* [51] suggested that analytical calculations using the NRC equation may give a better estimation at half-lives greater than 17 h.

A study by Nantajit *et al.* [53] opined that a major determinant of the radiation doses received by caregivers was the amount of time spent by those caregivers with the patients within the vehicle while returning home. Moreover, in that study, caregivers who had received more than 0.1 mSv, had travelled home with the patients and had spent a substantial amount of time with them.

Caregivers’ educational level has been shown to have no significant correlation with their received effective doses. This was confirmed in studies by Salman *et al.* [54], Kuo *et al.* [55] and Martin *et al.* [56] showing no effect of literacy. These studies further highlight the necessity of educating both patients and caregivers on the importance of following Radiation Safety Instructions (RSI). In these studies, the fact that both patients and caregivers attended RSI sessions was evident as shown in terms of lower effective doses to the caregivers. This emphasizes the value of attending those RSI education sessions given by qualified professionals in the field of radiation protection by both patients and caregivers and more importantly ensuring their ability to comply with those instructions and to apply them in a proper way. Studies by Almaskery and Bererhi [57] and Nantajit *et al.* [53] have alluded to this. The latter stated that outpatient treatment with I-131 is a safe therapeutic modality, provided that both patients and caregivers are provided with detailed instructions and guidelines, while the former emphasized the value of properly understanding the given RSI that should be taken seriously by both patients and caregivers. It was stated by Martin *et al.* [56] that the presence of a well-informed patient and caregiver about RSI will minimize the risk of radiation exposure following treatment with I-131, as a set of clearly understood rules for hygiene and proper isolation precautions are followed. According to review article done by Stefanoyiannis *et al.* about radiation exposure to caregivers from patients treated with radionuclide all were in the range recommended by International Commission on Radiological Protection, thus, they

concluded that the radiation risks to caregiver were negligible [58]. Based on the American Thyroid Association Taskforce on Radioiodine Safety, Sisson et al, complying with recommendations of Nuclear Regulatory Commission regulations and consistent with guidelines and promoted by the National Council on Radiation Protection and Measurement (NCRP-155) can help in radiation safety related to RIT of patients with thyroid diseases [59]. Rutar et al. conducted a research into radiation exposure to family members of outpatient treated with I-131-anti-B1 antibody; they measured the received dose of 26 caregivers of patients that received activity ranging between 0.94 to 4.77GBq (25-129 mCi). Their result showed that the patients can be released immediately after the administration that doses to other individuals are below the 5-mSv [60].

Radiation safety officers play key roles in reducing radiation exposures to both patients and caregivers. The radiation safety officer is a technically qualified individual who can provide unbiased technical information on the measures that need to be taken to minimize radiation exposure to staff, patients and caregivers. They are also in charge of administering Radiation Safety Instructions (RSI). Those RSI on being well understood by patients as well as caregivers and subsequently being properly applied, the exposure to caregivers should not exceed the established annual radiation exposure constraints and supposed to be of much less values, aimed at achieving the “As Low As Reasonably Achievable” (ALARA) principle.

**Table 1.** Summary of reviewed studies

Reference	Number of Patients	Patient Condition	Administered I-131 Activity (mCi)	Number of Caregivers	Caregivers' Effective Doses (mSv)	Method of Dose Measurements
Cappelen et al. [21]	76	Thyrotoxicosis (TH)	7.02 - 16.2	42	0.07 - 3.04	TLD
Pant et al. [43]	NR	TH and Thyroid cancer (TC)	TH: 5 - 13.5 TC: 25 - 200	TH: 45 TC: 297	TH: 0 - 2.4 TC: 0 - 5	TLD
Carvalho et al. [44]	20	TC	100 and 150	26	0.2 - 2.8	TLD
Tonnonchiang et al. [45]	20	TC	150 and 200	20	$176 * 10^{-7}$ - 0.333	TLD
Jeong et al. [46]	NR	TC	100 - 200	70	0.02 - 0.5	TLD and K-Factor
Lee et al. [47]	Outpatients: 31 Inpatients: 33	TC	30 100 - 200	31 33	0.01 - 2.17 0.01 - 1.88	TLD and K-Factor
Ebrahimi et al. [48]	57	TC	100 - 200	99	0.1 - 3.64	TLD and Neural Network
Ebrahimi et al. [51]	51	TC	100 - 200	85	0.1 - 3.75	TLD and Analytical Calculations
Nantajit et al. [53]	10	TC	100 - 150	10	0.021 - 0.672	TLD
Salman et al. [54]	23	Graves' disease	10 - 20	39	0.079 - 0.992	TLD

NR: Not Reported, TLD: thermoluminescence dosimeter, K-factor: engagement factor which describes the degree of closeness between patients and caregiver.

### 3. Conclusion

Findings from the reviewed studies showed that the radiation doses to caregivers of patients with thyroid diseases treated with I-131 were generally low and within the acceptable international recommendations of 5 mSv [49]. It was also observed that dose measurements to caregivers were mostly conducted using TLD. Although calculation methods exist, they give overestimated dose values [51]. Thus, the TLD approach remains the most accurate method of assessing dose values. Another important finding from these studies is that higher effective doses were observed for caregivers who had more intimate relationship (such as spouses) with the patients compared to others. This was evaluated using a term called the “k-factor” [46, 47]. The reviewed studies also highlight the importance of educating both patients and caregivers on the importance of following RSI. This was evident as shown in terms of the low effective doses received by the caregivers. Thus, this emphasizes the value of strict adherence to RSI as well as the importance of having qualified professionals in the field of radiation protection to administer these RSI to both patients and caregivers.

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