Disease

**Parathyroid** 

Journal of

**Mini-Review** 

# Evaluation of radiation side effects on thyroid function

DOI:10.34172/jpd.2022.9145

Kolsoum Teimouri<sup>10</sup>, Samaneh Pakravan<sup>20</sup>, Elham Rahmatinia<sup>30</sup>, Kamran Azadbakht<sup>3\*0</sup>

#### Abstract

The thyroid gland is a crucial component of the body's glandular system and metabolism, which is exposed to unnecessary radiation as an organ at risk in radiation therapy to the head, neck, and chest. Radiation can lead to thyroid dysfunction such as hypothyroidism and thyroid cancer.

Journal of Parathyroid Disease 2022,10, e9145

Keywords: Thyroid cancer, Radiation, Hypothyroidism, Absorption dose, Head and neck cancers

Please cite this paper as: Teimouri K, Pakravan S, Rahmatinia E, Azadbakht K. Examining the relationship between non-alcoholic fatty liver disease and hypothyroidism. J Parathyr Dis. 2022;10:e9145. doi:10.34172/jpd.2022.9145.

**Copyright** © 2022 The Author(s); Published by Nickan Research Institute. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## Introduction

The thyroid gland is one of the largest endocrine glands in the front of the neck that weighs(usually 15-20 g) (1). Thyroid hormones regulate the body's metabolic processes; these hormones control the body's vital functions such as nerve reflexes, heart rate, and body temperature; The thyroid gland affects a wide range of physiological functions of all organs of the body (2). Thyroid dysfunction occurs in patients who are exposed to radiation to the head, neck, and chest (3). Radiation damages the thyroid gland by destroying small blood vessels and, to some extent, direct damage to the follicles (4). When the thyroid gland is exposed to radiation, 40% to 67% of persons develop thyroid issues, the most common of which are hypothyroidism, as well as thyroid cancer (5). The ultimate goal in radiation therapy is to deliver the most radiation dosage to the tumor while delivering the lowest radiation damage to nearby healthy tissues. Emami et al estimated the tolerable radiation dose of the thyroid to be 45 gray (Gy) (6). Radiation therapy for cancer treatment in both childhood and adulthood has the potential to cause thyroid malfunction. In addition, hypothyroidism can occur during treatment or decades later (3). The objective of this study was to assess how radiation's adverse effects on thyroid function.

#### **Materials and Methods**

In this study, we review recently published article that examine the side effects of radiation on thyroid function. Articles were searched in PubMed, Google Scholar, and ScienceDirect databases with related keywords such as thyroid cancer, radiation, hypothyroidism, absorption dose, and head and neck cancers.

### **Thyroid gland**

The thyroid gland, a butterfly-shaped organ situated in the anterior part of the neck, has a variety of functions that have an impact on several physiological systems. The thyroid gland and its hormones play an important role in how the body grows as well as in controlling the body's basic physiological mechanisms. The thyroid gland controls the body's metabolism with several specific hormones, the most important of which are triiodothyronine (T3) and thyrotoxin (T4). From late fetal development to adulthood, the pituitary gland's production of thyroid-stimulating hormone is the primary regulator of thyroid growth and function (7).

## Hypothyroidism

Hypothyroidism is the most frequent side effect of radiation therapy in patients with lymphoma and head and neck cancers (HNCs), affecting 20% to 30% of these people; hypothyroidism usually occurs during the first 5 years after treatment. Head and neck radiation therapy results in significant doses of radiation to the thyroid gland (10-80 Gy) because all or a large part of the thyroid gland is inside or near its (8). Factors such as gender, age, and thyroid volume affect hypothyroidism after radiation therapy, but radiation exposure to the thyroid is a proven risk factor (9). Ionizing radiation to the neck is a known risk factor for hypothyroidism, especially when exposed to it in childhood (2).

Autoimmune thyroiditis is the most typical cause of radiation-induced hypothyroidism. Exposure to radiation

4School of Dentistry, Lorestan University of Medical Sciences, Khorramabad, Iran

\*Corresponding author: Kamran Azadbakht, Email: dr.kamran3519@gmail.com, Azadbakht.k@lums.ac.ir



Received: 28 June 2022, Accepted: 30 July 2022, ePublished: 16 August 2022

<sup>&</sup>lt;sup>1</sup>Department of Medical Physics, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran. <sup>2</sup>Department of Clinical Biochemistry, Faculty of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran. <sup>3</sup>Department of Medical Physiology, Faculty of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran.

# Implication for health policy/practice/research/ medical education

Hypothyroidism and non-alcoholic fatty liver disease have been recognized as two main public health complications. Early diagnosis of these diseases can delay the progress of the disease and thus increase the property of life of these patients.

can trigger autoimmune processes in which the body produces antibodies against the thyroid gland, which can lead to thyroid gland inflammation and hypothyroidism (10). A study found that individuals with average radiation exposure of more than 45 Gy were 4.9 times more likely to develop hypothyroidism than those with an average radiation dose of less radiation (11).

### **Thyroid cancer**

The majority of thyroid cancers, or 80% of cases, are papillary thyroid tumors (PTCs), the most prevalent kind. Follicular thyroid carcinoma (FTC), which accounts for 10% to 20% of all thyroid cancer cases, is the second most common kind of thyroid cancer. Medullary thyroid cancer, which develops from para-follicular cells, makes up 6% to 8% of all thyroid tumors. One of the fastestgrowing and most invasive malignancies is anaplastic thyroid carcinoma (12).

Thyroid cancer has no fixed etiologic cause, although radiation exposure has been a proven risk factor; Exposure to Hiroshima and Nagasaki atomic bomb radiation increased thyroid cancer during World War II (12).

Ionizing radiation exposure during childhood and adolescence has a strong carcinogenic effect on the thyroid gland, which is extremely sensitive to it. The first case of thyroid cancer with radiation exposure was documented in 1950 as a result of neonatal thymus radiotherapy. From 0.05 to 0.1 Gy, there is a much higher danger of thyroid radiation exposure. Malignant thyroid tumors account for one-third of radiation-induced thyroid tumors, and papillary thyroid carcinoma makes up the majority of these tumors (PTC). PTC happens between 5 to 10 years following irradiation (13).

Long-term radiation exposure has been proven to have particularly negative effects on the thyroid. Thyroid cancer incidence significantly rises when radiation exposure is excessive (14). Survivors' studies in Hiroshima and Nagasaki have shown that if exposure to ionizing radiation occurs in childhood, the risk of thyroid cancer is significantly higher (15).

### The absorbed dose of the thyroid gland

Shen et al examined 69 nasopharyngeal cancer (NPC) patients who were eligible for intensity-modulated radiotherapy (IMRT) in a study. These individuals received an average thyroid dosage of 41.79 Gy. A total of 24 patients (34.8%) experienced hypothyroidism twelve months following radiation therapy. The incidence of hypothyroidism in individuals with NPC following RT was significantly influenced by the thyroid gland's volume and mean dosage (Dmean) (9).

Lin et al. Examined 56 patients with NPC who underwent IMRT, the mean dose of the thyroid gland was 43.9 Gy. The incidence of hypothyroidism was reported to be between 2.6 and 10.7%. Which was observed between 6 and 30 months after radiation therapy (16).

Sommat et al in a research of 102 patients with NPC who underwent IMRT reported that after 48.8 months of follow-up (FU) 43.1% developed hypothyroidism. The mean thyroid dose was 55.3 Gy (17)

In a study, Fujiwara et al retrospectively analyzed data from 116 patients with HNC who underwent threedimensional conformal radiation therapy (3D-CRT). The mean FU period was 24 months. In total (38.6%) suffered from hypothyroidism due to radiation therapy. Dmean for the thyroid gland was 44.39 Gy (18).

In a study of 40 breast cancer patients receiving 3D-CRT, Tunio et al showed that the typical radiation dose to the thyroid gland was 25.8 Gy. After 52 months of FU, 10% of patients developed hypothyroidism (8).

Kim et al examined a total of 114 patients with HNCs receiving external beam radiation therapy (3D-CRT and IMRT). The mean FU period was 25 months. 56% of patients developed hypothyroidism. The mean thyroid dose was 31.78 Gy (19).

Huang et al reviewed data from 98 patients with NPC who underwent IMRT. The mean FU period was 17 months. The findings revealed that the mean thyroid dose was 49.72 Gy and the incidence of hypothyroidism was 33.7% (20). Table 1 contains a summary of these studies.

Table 1. Studies on the prevalence of radiation-induced hypothyroidism

	No. of Patients	Median FU	Tumor types	Dmean (Gy)	Rate of HT(%)
Study					
Shen (9)	69	12 months	NPC	41.79	34.8
Lin (16)	56	6-30 months	NPC	43.9	2.6-10.7
Sommat (17)	102	48.8 months	NPC	55.3	43.1
Fujiwara (18)	116	24 months	HNC	44.39	38.6
Tunio (8)	40	52 months	BC	25.8	10
Kim (19)	114	25 months	HNC	31.78	6
Huang (20)	98	17 months	NPC	49.72	33.7

HT, hypothyroidism; NPC, nasopharyngeal cancer; HNC, head and neck cancer; BC, breast cancer.

# Conclusion

In radiation therapy for HNCs, exposure to non-target tissues such as the thyroid cannot be prevented. In radiation therapy for head, neck, and chest tumors, the thyroid gland ought to be viewed as a high-risk organ. Hypothyroidism and thyroid cancer are related to decreased quality of life. It is important to consider this risk when planning radiation therapy. The typical radiation dose to the thyroid gland is a key factor in causing hypothyroidism and thyroid cancer. Every effort should be made to avoid exposure to radiation in childhood. In any case, FU of thyroid function after radiation therapy is mandatory.

#### **Authors' contribution**

Conceptualization: KT and SP. Methodology: KT and SP. Investigation: KT, SP, KA, and ER. Resources: KT, SP, KA, and ER. Data Curation: KT, SP, KA, and ER. Writing—Original Draft Preparation: KT, SP, KA, and ER. Writing—Review and Editing: KT, SP, KA, and ER. Supervision: KT, SP, KA, and ER. Project Administration: KT, SP, KA, and ER.

#### **Conflicts of interest**

There are no conflicts of interest declared by the authors.

#### **Ethical issues**

Ethical concerns (including plagiarism, data fabrication, and double publication) are fully respected by the authors.

#### **Funding/Support**

No financing from any source

#### References

- Nagayama Y. Radiation-related thyroid autoimmunity and dysfunction. J Radiat Res. 2018;59:ii98-ii107. doi: 10.1093/ jrr/rrx054.
- 2. Hartmann K. Thyroid Disorders in the Oncology Patient. J Adv Pract Oncol. 2015;6:99-106. doi: 10.6004/jadpro.2015.6.2.2.
- Gebauer J, Higham C, Langer T, Denzer C, Brabant G. Long-Term Endocrine and Metabolic Consequences of Cancer Treatment: A Systematic Review. Endocr Rev. 2019;40:711-67. doi: 10.1210/er.2018-00092.
- Boomsma MJ, Bijl HP, Langendijk JA. Radiation-induced hypothyroidism in head and neck cancer patients: a systematic review. Radiother Oncol. 2011;99:1-5. doi: 10.1016/j. radonc.2011.03.002.
- Koo E, Henderson MA, Dwyer M, Skandarajah AR. Radiation-Associated Thyroid Cancer Surveillance and Management in a Cohort of Late Effects Patients. World J Surg. 2020;44:3028-35. doi: 10.1007/s00268-020-05547-6.
- Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, et al. Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys. 1991;21:109-22. doi: 10.1016/0360-3016(91)90171-y.
- Nilsson M, Fagman H. Development of the thyroid gland. Development. 2017;144:2123-40. doi: 10.1242/dev.145615.

- Tunio MA, Al Asiri M, Bayoumi Y, Stanciu LG, Al Johani N, Al Saeed EF. Is thyroid gland an organ at risk in breast cancer patients treated with locoregional radiotherapy? Results of a pilot study. J Cancer Res Ther. 2015;11:684-9. doi: 10.4103/0973-1482.167613.
- Shen G, Peng Y, Li J, Wu H, Zhang G, Zhao C, et al. Multivariate NTCP Model of Hypothyroidism After Intensity-Modulated Radiotherapy for Nasopharyngeal Carcinoma. Front Oncol. 2021;11:714536. doi: 10.3389/fonc.2021.714536.
- Reiners C, Drozd V, Yamashita S. Hypothyroidism after radiation exposure: brief narrative review. J Neural Transm (Vienna). 2020;127:1455-66. doi: 10.1007/s00702-020-02260-5.
- Zhai RP, Kong FF, Du CR, Hu CS, Ying HM. Radiationinduced hypothyroidism after IMRT for nasopharyngeal carcinoma: Clinical and dosimetric predictors in a prospective cohort study. Oral Oncol. 2017;68:44-9. doi: 10.1016/j. oraloncology.2017.03.005.
- Schneider DF, Chen H. New developments in the diagnosis and treatment of thyroid cancer. CA Cancer J Clin. 2013;63:374-94. doi: 10.3322/caac.21195.
- Iglesias ML, Schmidt A, Ghuzlan AA, Lacroix L, Vathaire F, Chevillard S, et al. Radiation exposure and thyroid cancer: a review. Arch Endocrinol Metab. 2017;61:180-7. doi: 10.1590/2359-3997000000257.
- Albi E, Cataldi S, Lazzarini A, Codini M, Beccari T, Ambesi-Impiombato FS, et al. Radiation and Thyroid Cancer. Int J Mol Sci. 2017;18. doi: 10.3390/ijms18050911.
- Cahoon EK, Nadyrov EA, Polyanskaya ON, Yauseyenka VV, Veyalkin IV, Yeudachkova TI, et al. Risk of Thyroid Nodules in Residents of Belarus Exposed to Chernobyl Fallout as Children and Adolescents. J Clin Endocrinol Metab. 2017;102:2207-17. doi: 10.1210/jc.2016-3842.
- Lin Z, Yang Z, He B, Wang D, Gao X, Tam SY, et al. Pattern of radiation-induced thyroid gland changes in nasopharyngeal carcinoma patients in 48 months after radiotherapy. PLoS One. 2018;13:e0200310. doi: 10.1371/journal.pone.0200310.
- Sommat K, Ong WS, Hussain A, Soong YL, Tan T, Wee J, et al. Thyroid V40 Predicts Primary Hypothyroidism After Intensity Modulated Radiation Therapy for Nasopharyngeal Carcinoma. Int J Radiat Oncol Biol Phys. 2017;98:574-80. doi: 10.1016/j. ijrobp.2017.03.007.
- Fujiwara M, Kamikonya N, Odawara S, Suzuki H, Niwa Y, Takada Y, et al. The threshold of hypothyroidism after radiation therapy for head and neck cancer: a retrospective analysis of 116 cases. J Radiat Res. 2015;56:577-82. doi: 10.1093/jrr/ rv006.
- Kim MY, Yu T, Wu HG. Dose-volumetric parameters for predicting hypothyroidism after radiotherapy for head and neck cancer. Jpn J Clin Oncol. 2014;44:331-7. doi: 10.1093/ jjco/hyt235.
- 20. Huang S, Wang X, Hu C, Ying H. Hypothalamic-pituitarythyroid dysfunction induced by intensity-modulated radiotherapy (IMRT) for adult patients with nasopharyngeal carcinoma. Med Oncol. 2013;30:710. doi: 10.1007/s12032-013-0710-9.