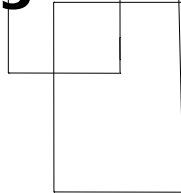


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Sudan University of Science and Technology

College of graduate studies



Assessment of Head and Neck Cancers Irradiation in Effects in Thyroid Function

تقدير آثار تشعيع سرطان الرأس والرقبة في وظيفة الغدة الدرقية

A thesis Submitted for the academic Requirements of M.Sc. Degree in Radiotherapy Technology

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بسم الله الرحمن الرحيم

قال تعالى

:

وَلَوْ بَسَطَ اللَّهُ الرِّزْقَ لِعِبَادِهِ لَبَغَوْا فِي الْأَرْضِ))

وَلَكِنْ يُنْزِلُ بِقَدَرٍ مَّا يَشَاءُ إِنَّهُ بِعِبَادِهِ

((خَبِيرٌ بِصِيرٌ

صدق الله العظيم

الايه رقم (57) سوره الشورى

Deductions

To

Parent

Husband

And friends

Acknowledgment

My Acknowledgment and gratefulness at the beginning and end to God who gave us the gift of mind.

Profound thanks and gratitude to every one who encouraged me to complete this work.

My gratitude is extended to my supervisor Dr /Mohammed Elfadil. All Radiation and Isotopes Center of Khartoum (RICK) for their helps. Their work have stimulated and fostered my efforts' in producing this research.

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Finally I would like to warmly thank of my long suffering family for never ending support .my almighty God bless them all.

Abstract:

The most important criterion of radiotherapy is accuracy in all planning stage and in delivery of the prescribed treatment. In head and neck tumour especially in radical irradiation, a high dose of radiation was delivered to the tumour site. Thyroid gland most of the time found inside the radiation field and hence might receive a substantial amount of radiation which may alter the function of thyroid. Out of 80 patient's who were received a radical radiation dose in range of 6000-6500cGy at radiation and isotopes center of Khartoum RICK and planned for conventional radiotherapy, Patients treated radically under isocentric cobalt 60, blood sample are taking from patient and RIA used to analyze level of thyroid hormones .Day's method used to calculate distant between thyroid and other organs. as assessment for thyroid hormones level T4, T3 and TSH have been studied after receiving average dose of 2653.33 cGy. Accordingly the analysis of the data showed that the thyroid hormones (T4 and T3) decrease as a result of irradiation and the reduction persists following radiation dose in a linear form by a factor of 0.0002nmol/cGy and 0.0074 nmol/cGy respectively, while the TSH increase following radiation dose increment and the increment factor was 0.0005 nmol/cGy. The researcher recommended; firstly assessment of thyroid hormones in head and neck cancer patient after complete treatment .Secondary using of CT simulator will reduce the amount of dose serviced by thyroid.

الخلاصة:-

إن المعيار الأهم في العلاج بالاشعة الدقة في كل مراحل المعالجة الإشعاعية من تخطيط وإعطاء الجرعة الإشعاعية الموصوفة . عند اعطاء جرعه إشعاعية كبيرة لمرضى- سرطان الراس والعنق غالبا ما تتأثر الهرمونات التي تفرزها الغدة الدرقية نظرا لتواجدها في حقل العلاج او قربه منه مما يؤثر تبعا لذلك في الوظيفة. تعرض ⁸⁰ من مرضى- سرطان الرأس والعنق لجرعة إشعاعية جذرية بمعدل 6500 - 6000cGy وذلك في المركز القومي للعلاج بالاشعة والطب النووي , باستخدام التخطيط التقليدي. اخذت عينة من دم المرضى- وحللت بواسطة جهاز التحليل الإشعاعي للهرمونات وطريقة داي لحساب المسافة بين الغدة الدرقية والاعضاء المجاوره المصابة , عند تقييم الهرمونات, TSH, T4, و T3 درسوا بعد تلقى جرعة إشعاعية بمعدل 2653.33cGy تبعا لتحليل البيانات وجد أن T4, T3 انخفض نتيجة لتلقي جرعة إشعاعية بمعدل 0.002nmol/cGy و 0.0074nmol/cGy على التوالي, بينما زاد TSH بمعدل 0.0005

تمثلت أهم نتائج البحث في: أولا يجب القيام بعملية فحص هرمونات الغدة الدرقية بعد الانتهاء من العلاج عند مرضى سرطان الراس والعنق

تانيا إستخدام الأجهزة الحديثه مثل جهاز المحاكه المقطعي يقلل من كميّه الإشعاع التي
تصل الى
الغدة الدرقية.

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List of Abbreviation

TSH	<u>thyroid-stimulatinghormone</u>
TFT	thyroid function test
T₃	<u>triiodothyronine</u>
T₄	<u>thyroxin</u>
Gy	gray
cGy	centgrey
Mev	megaelectron volt
r.p.m	rotation per minutesr
RTA	radioimmunoassay

TBI	total body irradiation
FT4	free thyroxin
TRHt	<u>hyrotropin-releasing hormone</u>
SRIH	<u>somatostatin</u>
PTH	<u>parathyroid hormone</u>
FNA	fine needle aspiration
RAIU	Radioactive iodine-123 uptake
PTC	papillary thyroid carcinomas
FTA	follicular thyroid adenomas
TPO	thyroid peroxides
PTH	parathyroid hormone
NCI	National Cancer Institute
FMTC	familial medullary thyroid cancer
CIAE	chine institute for Atomic Energy

CHAPTER ONE

Chapter one

1-1Introduction

Thyroid dysfunction commonly develops after ionizing radiation therapy at therapeutic doses. The reason for such dysfunction is usually the direct radiation injury of the thyroid gland, but sometimes it is due to radiation therapy to the pituitary. There are many proposed mechanisms to explain radiation injury of the thyroid gland. For example, radiation may inhibit the active follicular epithelium and reduce the number of functional follicles, it may reduce the vascular permeability or may trigger immunologic reactions leading to several clinical events. However, even these ‘perfect’ mechanisms cannot give clear information about the radiation injury. Primary hypothyroidism often develops as a result of radiotherapy to the cervical region in

therapeutic doses (30-70 Gy) in patients with head and neck cancer. Abnormally high serum thyroid stimulating hormone (TSH) and normal thyroxin (FT4) levels characterize subclinical hypothyroidism. Subclinical hypothyroidism is the laboratory finding most often encountered in periodic biochemical tests after radiotherapy. In overt or clinical hypothyroidism, there are classical symptoms such as weight gain, cold intolerance, dry skin, hair loss, a decrease in physical activity, muscle cramps and a decrease in mental functions associated with abnormally low FT4 and high TSH levels in serum. Periorbital edema, a decrease in deep tendon reflexes, cold and dry skin, peripheral edema, pleural and pericardial effusions are the findings in such cases. The published incidence of clinical and subclinical hypothyroidism may differ according to technic, dose, fractionation schedule of radiation and the duration of follow-up. Thyroid dysfunction develops after other treatment modalities. In the large series of [Diaz et al\(2010\)](#), children and adults with Hodgkin's lymphoma were followed for 27 years and the reported risk of subclinical or clinical hypothyroidism was as high as 47%. Partial thyroidectomy during neck dissection increases the risk of hypothyroidism. Tami et al. reported that the incidence of hypothyroidism in their patients with head and neck cancer was 68% in cases who had laryngectomy + partial thyroidectomy + radiotherapy but 29% in patients treated only with radiotherapy.

The link between external radiation during childhood and thyroid cancer has been known since 1950 (Duffy & Fitzgerald 1950); until recently this was the only demonstrated etiological risk factor for thyroid cancers Marjolein et al(2011). A higher incidence of thyroid cancer has been reported in epidemiological studies after either internal or external exposure to radiation Ron et al(1989). A pooled analysis of seven studies established that the excess relative risk of thyroid cancer in subjects irradiated at a young age was very high – 7.7 per Gray (Gy) – the risk being significant for radiation doses as low as 0.1Gy and increasing linearly with increasing doses Ron et al (1989). It has been estimated that 88% of thyroid carcinomas occurring in subjects exposed to radiation doses equal to 1Gy during childhood are radiation-induced. The risk of developing a thyroid carcinoma is the highest 15-30 years after exposure, but is still present after more than 40 years Ron et al (1989) In parallel, a

worldwide increase in thyroid tumors, mainly PTC, has been observed over the last 30 years Stephen et al(1980). This has led to debate concerning a potential link with changes in environmental exposure linked to nuclear tests, the nuclear industry, and, in Western Europe, Chernobyl disaster fallout. Some data suggest that this increase is at least partly related to the routine screening of thyroid nodules using neck ultrasound and fine needle biopsy, which permit the detection of small papillary carcinomas that would otherwise have gone undetected Tell et al(2004). This high prevalence of such small cancers had already been reported in autopsy studies Dianaf et al(1978). However, it is not possible to exclude the possibility that some of these thyroid tumors could have been radiation-induced. Radiation-induced thyroid tumors have no specific histological characteristics Laway et al(2011) They are either follicular thyroid adenomas (FTA) or papillary thyroid carcinomas (PTC). These histological subtypes are also the most frequent sporadic thyroid tumors. For these reasons, it is of major interest to identify specific fingerprints of thyroid cancer developing after thyroid radiation exposure that would indicate, with a high probability, the etiology of any tumor. Molecular differences between sporadic and radiation-induced thyroid tumors were sought using microarray transcriptome analysis. The first study, including sporadic and post-Chernobyl PTC, did not show any specific radiation-induced gene expression signature Ron et al(1989). However, the authors were able to classify their series of tumors by using a signature that was previously found to discriminate between irradiated- and hydrogen-peroxide-treated lymphocytes (Detours et al. 2007). Others studies found radiation-induced signatures in post-Chernobyl PTC, Stein et al. , but without blind validation of the signature. A recent study compared cell cycle protein expression in sporadic and post-radiotherapy PTC, but none of the tested markers could be associated with the etiology (Achille et al. 2009), while combinations of protein markers such as matrix metalloproteinases, cathepsins, and neurotrophic tyrosine kinase receptor 1 allowed discrimination of post-Chernobyl PTC as a function of etiology by immunostaining (Boltze et al. 2009). Together, these studies must be considered as preliminary and others should be

analyzed to establish a robust characterization of the gene expression differences between sporadic and radiation-induced PTC (rPTC).

1.2 Problem of the study

In head and neck tumour especially in radical irradiation, a high dose of radiation was delivered to the tumour site. Thyroid gland most of the time found inside the radiation field and hence might receive a substantial amount of radiation which may alter the function of thyroid, therefore investigation of thyroid hormone is mandatory.

1.3 Objectives of the study:

1.3.1 General objective

The main objective of this study is to assess the level of thyroid hormones after head and neck radical irradiation.

1.3.2 Specific objective

To relate the amount of dose received by the thyroid of the hormone effect.

To evaluate function of thyroid gland hormones.

To assess the effect of brain irradiation in TSH.

To compare the level of thyroid hormone after head and neck irradiation with standard.

1.4 Significant of the study

This study provides information about change in the thyroid gland hormones production in patients treated radically by ionizing radiations in head and neck ,and the possible relation between the given dose and irradiated area .

1.5 Over view of the study

This study fall into five chapters, chapter one, which is an introduction, deals with theoretical frame work of study, it presents the statement of the study problem, objectives of the study, chapter two, is divided

into sections, section one deals with Thyroid Dysfunction, Hyperthyroidism, Hypothyroidism, section two deal with literature review (previous study), chapter three deal with material and method, chapter four deal with (results) and data presentations, chapter five discusses the data (disruption), analysis, conclusion, recommendation and references.

CHAPTER TWO

2.1 Anatomy

The thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings, *lobus dexter* (right lobe) and *lobus sinister* (left lobe), connected via the [isthmus](#). The organ is situated on the anterior side of the neck, lying against and around the [larynx](#) and [trachea](#), reaching posteriorly the [oesophagus](#) and [carotid sheath](#). It starts cranially at the oblique line on the [thyroid cartilage](#) (just below the laryngeal prominence, or '[Adam's Apple](#)'), and extends inferiorly to approximately the fifth or sixth [tracheal ring](#).

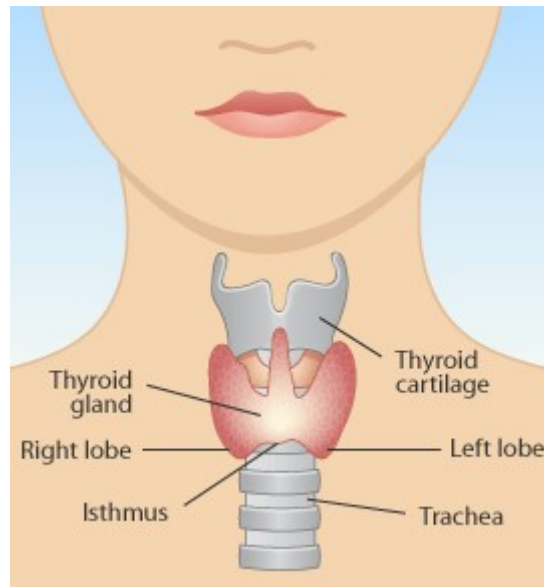


Figure 2.1 anatomy of thyroid

The thyroid is supplied with arterial blood from the [superior thyroid artery](#), a branch of the [external carotid artery](#), and the [inferior thyroid artery](#), a branch of the [thyrocervical trunk](#), and sometimes by the [thyroid artery](#), branching directly from the brachiocephalic trunk. The venous blood is drained via [superior thyroid veins](#), draining in the [internal jugular vein](#), and via [inferior thyroid veins](#), draining via the *plexus thyroideus impar* in the left [brachiocephalic vein](#) (Irvi et al 1985). Lymphatic drainage passes frequently the [lateral deep cervical lymph nodes](#) and the [pre- and paratracheal lymph nodes](#). The gland is supplied by [parasympathetic](#) nerve input from the [superior laryngeal nerve](#) and the [recurrent laryngeal nerve](#). (Irvi et al 1985)

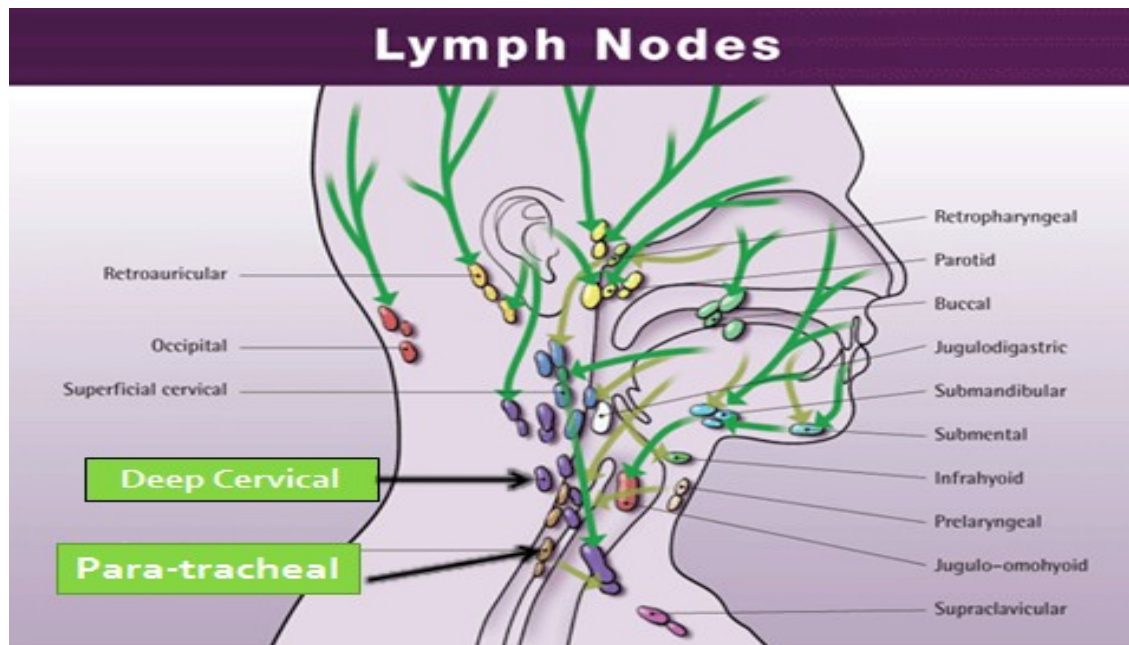


Figure 2.2 lymphatic drainage of the thyroid

2.2 Physiology

The primary function of the thyroid is production of the hormones [triiodothyronine](#) (T_3), [thyroxine](#) (T_4), and [calcitonin](#). Up to 80% of the T_4 is converted to T_3 by peripheral organs such as the [liver](#), [kidney](#) and [spleen](#). T_3 is several times more powerful than T_4 , which is largely a [prohormone](#), perhaps four or even ten times more active. Irvi et al 1985

2.3 T_3 and T_4 production and action

Thyroxine (T_4) is synthesised by the follicular cells from free tyrosine and on the tyrosine residues of the protein called thyroglobulin (Tg). Iodine is captured with the "iodine trap" by the hydrogen peroxide generated by the enzyme thyroid peroxidase (TPO) and linked to the 3' and 5' sites of the benzene ring of the tyrosine residues on Tg, and on free tyrosine. Upon stimulation by the thyroid-stimulating hormone (TSH), the follicular cells reabsorb Tg and cleave the iodinated tyrosines from Tg in lysosomes, forming T_4 and T_3 (in T_3 , one iodine atom is absent compared to T_4), and releasing them into the blood. Deiodinase enzymes convert T_4 to T_3 . Thyroid hormone secreted from the gland is about 80-90% T_4 and about 10-20% T_3 .

Cells of the developing brain are a major target for the thyroid hormones T_3 and T_4 . Thyroid hormones play a particularly crucial role in brain maturation during fetal development. A transport protein that seems to be important for T_4 transport across the blood-brain barrier (OATP1C1) has been identified. A second transport protein (MCT8) is important for T_3 transport across brain cell membranes.

Non-genomic actions of T_4 are those that are not initiated by liganding of the hormone to intranuclear thyroid receptor. These may begin at the plasma membrane or within cytoplasm. Plasma membrane-initiated actions begin at a receptor on the integrin $\alpha V \beta 3$ that activates ERK1/2. This binding culminates in local membrane actions on ion transport systems such as the $Na(+)/H(+)$ exchanger or complex cellular events including cell proliferation. These integrins are concentrated on cells of the vasculature and on some types of tumor cells, which in part explains the proangiogenic effects of iodothyronines and proliferative actions of thyroid hormone on some cancers including gliomas. T_4 also acts on the mitochondrial genome via imported isoforms of nuclear thyroid receptors to affect several mitochondrial transcription factors. Regulation of actin polymerization by T_4 is critical to cell migration in neurons and glial cells and is imT_3 can activate phosphatidylinositol 3-kinase by a mechanism that may be cytoplasmic in origin or may begin at integrin $\alpha V \beta 3$.

In the blood, T_4 and T_3 are partially bound to thyroxine-binding globulin (TBG), transthyretin, and albumin. Only a very small fraction of the circulating hormone is free (unbound) - T_4 0.03% and T_3 0.3%. Only the free fraction has hormonal activity. As with the steroid hormones and retinoic acid, thyroid hormones cross the cell membrane and bind to intracellular receptors (α_1 , α_2 , β_1 and β_2), which act alone, in pairs or together with the retinoid X-receptor as transcription factors to modulate DNA transcription. Atahan et al[53]

2.4 T_3 and T_4 regulation

The production of thyroxine and triiodothyronine is regulated by thyroid-stimulating hormone (TSH), released by the [anterior pituitary](#). The thyroid and [thyrotropes](#) form a [negative feedback loop](#): TSH production is suppressed when the T_4 levels are high. The TSH production itself is modulated by [thyrotropin-releasing hormone](#) (TRH), which is produced by the [hypothalamus](#) and secreted at an increased rate in situations such as cold exposure (to stimulate [thermogenesis](#)). TSH production is blunted by [somatostatin](#) (SRIH), rising levels of [glucocorticoids](#) and [sex hormones](#) ([estrogen](#) and [testosterone](#)), and excessively high blood iodide concentration.

An additional hormone produced by the thyroid contributes to the regulation of blood [calcium](#) levels. [Parafollicular cells](#) produce [calcitonin](#) in response to [hypercalcemia](#). Calcitonin stimulates movement of calcium into [bone](#), in opposition to the effects of [parathyroid hormone](#) (PTH). However, calcitonin seems far less essential than PTH, as calcium metabolism remains clinically normal after removal of the thyroid ([thyroidectomy](#)), but not the [parathyroids](#). Atahan et al[53]

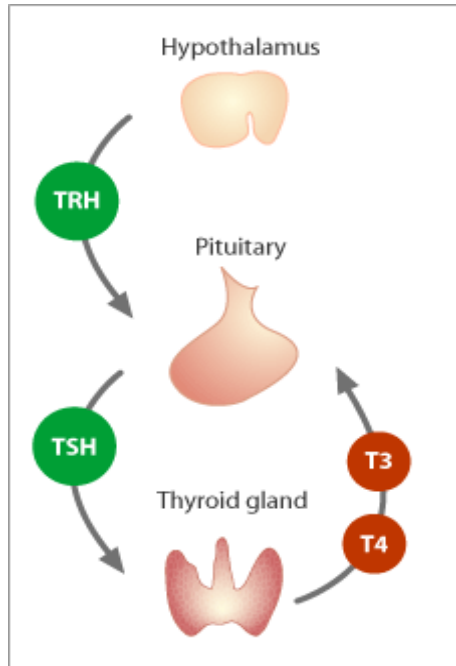


Figure 2.3 T₃ and T₄ regulation

2.5 Disorders

Thyroid disorders include [hyperthyroidism](#) (abnormally increased activity), [hypothyroidism](#) (abnormally decreased activity) and [thyroid nodules](#), which are generally benign [thyroid neoplasms](#), but may be [thyroid cancers](#). All these disorders may give rise to [goiter](#), that is, an enlarged thyroid. (Atahan et al 1998)

2.6 Hyperthyroidism

[Hyperthyroidism](#), or overactive thyroid, is the overproduction of the thyroid hormones T₃ and T₄, and is most commonly caused by the development of [Graves' disease](#), an autoimmune disease in which antibodies are produced which stimulate the thyroid to secrete excessive quantities of thyroid hormones. The disease can result in the formation of a toxic [goiter](#) as a result of thyroid growth in response to a lack of [negative feedback](#) mechanisms. It presents with symptoms such as a thyroid goiter, protruding eyes ([exophthalmos](#)), [palpitations](#), excess [sweating](#), [diarrhea](#), [weight loss](#), [muscle weakness](#) and unusual sensitivity to heat. The [appetite](#) is often increased. Atahan et al [53]

2.7 Hypothyroidism

[Hypothyroidism](#) is the underproduction of the thyroid hormones T₃ and T₄. Hypothyroid disorders may occur as a result of congenital thyroid abnormalities, autoimmune

disorders such as [Hashimoto's thyroiditis](#), [iodine deficiency](#) (more likely in poorer countries) or the removal of the thyroid following surgery to treat severe hyperthyroidism and/or thyroid [cancer](#). Typical symptoms are abnormal weight gain, tiredness, baldness, cold intolerance, and [bradycardia](#). Hypothyroidism is treated with [hormone replacement therapy](#), such as [levothyroxine](#), which is typically required for the rest of the patient's life. Thyroid hormone treatment is given under the care of a [physician](#) and may take a few weeks to become effective. [Negative feedback](#) mechanisms result in growth of the thyroid gland when thyroid hormones are being produced in sufficiently low quantities as a means of increasing the thyroid output; however, where the hypothyroidism is caused by iodine insufficiency, the thyroid is unable to produce T₃ and T₄ and as a result, the thyroid may continue to grow to form a non-toxic [goiter](#). It is termed non-toxic as it does not produce toxic quantities of thyroid hormones, despite its size. Atahan et al[53]

2.8 Cancers

In most cases, the thyroid cancer presents as a painless mass in the neck. It is very unusual for the thyroid cancers to present with symptoms, unless it has been neglected. One may be able to feel a hard nodule in the neck. Diagnosis is made using a needle biopsy and various radiological studies.

2.8.1 Different Types of Thyroid Cancer:

The National Cancer Institute (NCI) describes the major types of thyroid cancer as follows:

2.8.1.1 papillary and follicular thyroid cancer

These two types of thyroid cancer account for 80 percent to 90 percent of all thyroid cancers. Papillary thyroid cancer is the more common of the two types. Both types begin in the follicular cells of the thyroid and tend to grow slowly.

2.8.1.2 follicular thyroid cancer

This type of thyroid cancer occurs most often among elderly patients and accounts for about 15 percent of thyroid cancer cases. This type of thyroid cancer is more aggressive and tends to spread through the bloodstream to other parts of the body.

2.8.1.3 medullary thyroid cancer

This type of thyroid cancer accounts for 5 percent to 10 percent of all thyroid cancers. Medullary thyroid cancer is the only thyroid cancer that begins in the C cells. This type of thyroid cancer is easier to control if it is found and treated early, before it spreads to other parts

of the body. There are two types of medullary thyroid cancer: sporadic medullary thyroid cancer and familial medullary thyroid cancer (FMTC). Because familial medullary thyroid cancer tends to run in families, screening tests for genetic abnormalities in the blood cells may be conducted.

2.8.1.4 anaplastic thyroid cancer

This rare type of thyroid cancer accounts for about 1percent to 2 percent of all thyroid cancers. Anaplastic thyroid cancer begins in the follicular cells and tends to grow and spread very quickly.

2.8.2 Non-cancerous nodules

Many individuals may find the presence of [thyroid nodules](#) in the neck. The majority of these thyroid nodules are [benign](#) (non cancerous). The presence of a thyroid nodule does not mean that one has thyroid disease. Most thyroid nodules do not cause any symptoms, and most are discovered on an incidental examination. Doctors usually perform a [needle aspiration biopsy](#) of the thyroid to determine the status of the nodules. Atahan et al[53]

2.9-Thyroid function tests:

Several thyroid function tests (TFTs) are used to evaluate thyroid status. The development of sensitive TSH testing has been an important advance since the early 1990s. Before the sensitive TSH test was available, there was a gray zone between normal and abnormal thyroid function. The sensitive TSH test clearly defines thyroid disease and allows for precise titration of thyroid replacement therapy.

Thyroid-Stimulating Hormone:

Assays to measure TSH are conducted using an extremely sensitive radioimmunoassay. The origin of hypothyroidism-whether at the level of the pituitary gland, hypothalamus, or thyroid gland-can be determined by using the test for TSH. Levels of TSH are used to diagnose or screen for hypothyroidism and to evaluate adequacy of replacement therapy.

T3 and T4 Levels:

Both T3 and T4 are measured by radioimmunoassay. Tests are available to directly or indirectly measure both bound and unbound hormone. The resin T3 and T4 uptake tests (RT3U and RT4U) estimate binding capacity to TBG and are used to calculate free T3 and T4 levels. The free T3 index (FT3I) and the free T4 index (FT4I), which can

be calculated in several different ways, are used to correct for alterations in TBG.

Antibodies:

Autoantibodies of clinical interest in thyroid disease include thyroid-stimulating antibodies (TSAb), TSH receptor-binding inhibitory immunoglobulins (TBII), antithyroglobulin antibodies (Anti-Tg Ab) and the antithyroid peroxidase antibody (Anti-TPO Ab). Elevated levels of Anti-TPO A are found in virtually all cases of Hashimoto's thyroiditis and in approximately 85 percent of Graves' disease cases. Also, approximately 10 percent of asymptomatic individuals have elevated levels of Anti-TPO Ab that may suggest a predisposition to thyroid autoimmune diseases. Historically, Anti-TG Ab determinations were used in tandem with antimicrosomal Ab determinations to maximize the probability of a positive result in patients with autoimmune disease. Although the prevalence of Anti-TG Abs in thyroid autoimmune disease is significant (85 percent and 30 percent in Hashimoto's thyroiditis and Graves' disease, respectively), it is much lower than the prevalence of the Anti-TPO Abs. Thyroid-stimulating antibodies (TSAb) are present in more than 90% of Grave's disease, and TSH receptor-binding inhibitory immunoglobulins (TBII) are present in atrophic form of Hashimoto's Disease, in maternal serum of pregnant women (predictive of congenital hypothyroidism) and myxedema

Radioactive Iodine Uptake (RAIU):

The RAIU test indicates iodine use by the thyroid gland but not hormone synthesis capacity or activity. A tracer dose of radioactive iodine (¹³¹I or ¹²³I) is administered intravenously, and the thyroid gland is scanned for iodine uptake. A normal test result is 5% to 15% of the dose taken up within 5 hours and 15% to 35% within 24 hours. This test is primarily used for diagnosis of Graves' disease (increased uptake). In patients who are iodine deficient, results indicate a greater uptake of iodine, and in those with an iodine excess, lesser uptake. Additionally, after the administration of radioactive iodine, a thyroid scan can reveal "hot" or "cold" spots indicating areas of increased or decreased iodine uptake, which can be useful in the detection of thyroid carcinoma. Atahan et al[53]

2.10 Head and neck cancer irradiation

The anatomy of the head and neck are complex, as a result target volumes are irregular in shape and close to other normal structures, and thus irradiation of the head and neck tumors could affect the amount of hormones produce by thyroid gland.

2.10.1 Example for some cases

Brain cancer

Treatment technique

Parallel opposed lateral fields cover whole brain.

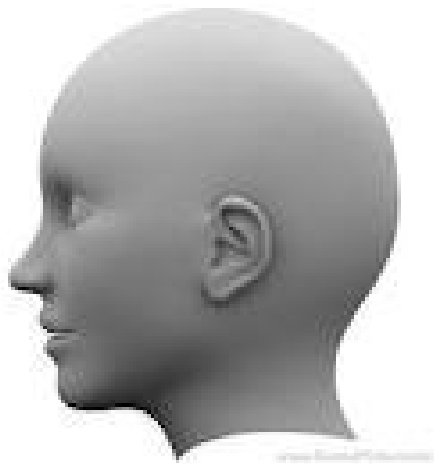


Figure2.4 border of brain cancer

Nasopharyngeal carcinoma

Treatment technique

Parallel opposed lateral fields; extend from base of the brain to thyroid cartilage.

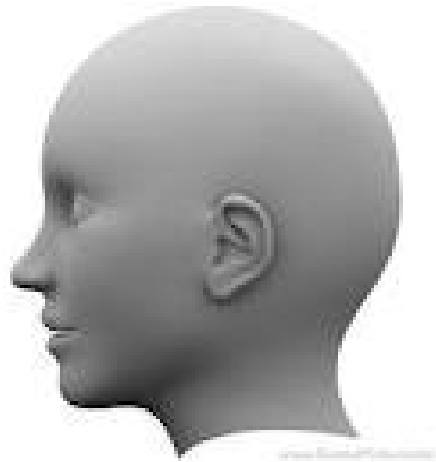


Figure2.5 border of Nasopharyngeal carcinoma

Carcinoma of the upper part of oesophagus

Treatment technique

Parallel opposed lateral fields, or arterial and arterial oblique fields.

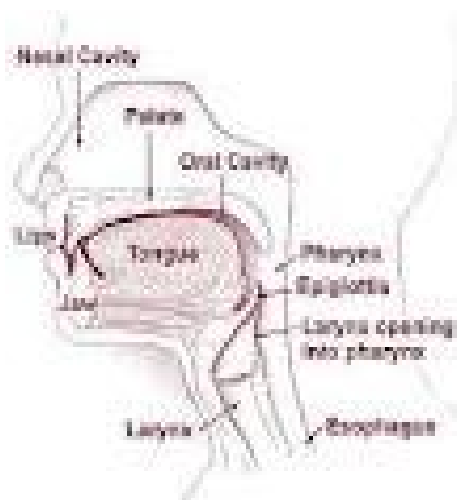


Figure2.6 border of Carcinoma of the upper part of oesophagus

Secondary neck nodes

Single arterial field extend from mastoid presses to the inferior border of the medial end of the clavicle.

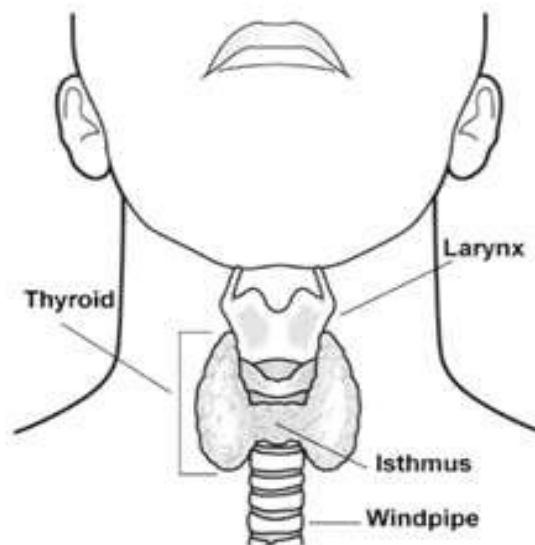


Figure 2.7 border of Secondary neck nodes

2.11 The possible late effects

The thyroid is generally not affected by chemotherapy. If damage occurs, radiation is usually the culprit. Several types of thyroid problems can develop after radiation.

Primary hypothyroidism (primary = damage at the thyroid gland; hypo = low; thyroidism = disease of the thyroid) can occur from damage to the thyroid gland caused by radiation. In this type of hypothyroidism, the TSH is elevated because the brain is trying to make the thyroid produce more T_3 and T_4 . If patient received more than 1500 cGy of radiation to the neck or more than 750 cGy total body irradiation (TBI), he/she will become at risk. This includes survivors of Hodgkin's disease, non-Hodgkin's lymphoma, head and neck tumors, or those who had TBI prior to a bone marrow transplant. Hypothyroidism sometimes occurs in patients treated with cranial or craniospinal radiation for leukemia.

While less than one percent of children with leukemia treated with 1800 cGy of cranial radiation develop hypothyroidism, 40 to 90 percent of Hodgkin's patients who receive mantle radiation and up to 50 percent of bone marrow transplant patients do. Treatment at a young age may also increase the likelihood of developing a thyroid problem.

Thyroid dysfunction (dys = abnormal) can occur soon after radiation, but generally does not occur until several years later.

Secondary hypothyroidism (secondary = damage in the pituitary gland/brain) is an uncommon late effect caused by radiation damage to the pituitary gland which results in a decreased production of TSH. Thus, in this type of hypothyroidism, the TSH and T_4 levels are low.

Compensated hypothyroidism. A mildly elevated TSH and normal T_4 may occur if the thyroid is working too hard. There are usually no symptoms. An overstimulated gland is at increased risk for developing tumors, both benign and malignant. Survivors with

compensated hypothyroidism are sometimes given supplemental thyroid hormone to allow the gland to rest.

Hyperthyroidism (hyper = high) occurs when too much T₃ or T₄ are produced causing the body to use energy faster than it should. This late effect is not well understood but has been found in very small numbers of survivors who were treated with neck radiation.

Thyroid cancer. Radiation to the neck can result in thyroid cancer later in life so all survivors at risk need life-long evaluation of thyroid function.

Signs and symptoms of an underactive thyroid (hypothyroidism) can include:

Fatigue or lethargy
Hoarseness
Difficulty concentrating
Depression or mood changes
Constipation
Weakness
Intolerance to cold
Swelling around the eyes
Poor growth
Delayed puberty
Puffy face and hands
Weight gain
Dry or rough skin
Brittle hair
Joint or muscle aches
Slow heart rate
Low blood pressure
High cholesterol
Decreased tolerance for exercise

The signs and symptoms of an overactive thyroid (hyperthyroidism) can include:

Nervousness or anxiety
Difficulty concentrating
Fatigue
Muscle weakness or tremor
Rapid or irregular heartbeat
Excessive perspiration
Heat intolerance
Diarrhea
Weight loss
Menstrual irregularities

Protruding eyes

Tenderness in the neck

Decreased tolerance for exercise

Signs and symptoms of thyroid cancer:

Thyroid cancer is generally a slow growing cancer without a lot of signs or symptoms. Usually, a painless, hard mass (lump) in the thyroid gland can be felt. One might also experience hoarseness, problems with swallowing, enlarged lymph nodes in the neck and difficulty breathing.

2.11.1 follow up needed for those at risk

T₄ and TSH levels should be checked every year after radiation to the chest, neck, or head and any time symptoms develop. These are simple blood tests. And during this time, thyroid should be palpated (felt by hand) and growth should be plotted on a chart.

In some facilities, radioactive iodine uptake by the thyroid is measured. The benefit of screening with periodic ultrasound of the thyroid every 1 to 3 years is controversial and is currently being studied. Thyroid problems can occur years or decades after treatment for cancer, so a yearly check is necessary for the rest of life if the patients are at risk. If any abnormalities are detected during an examination, referral and follow-up by an endocrinologist or surgeon may be necessary.

2.11.2 Treatment of thyroid damage

Although thyroid problems are common in survivors who had radiation to the head and neck, treatment generally is easy and effective.

Primary hypothyroidism (high TSH, low or normal T₄): To make one euthyroid (normal thyroid level), a daily pill of levothyroxine, a synthetic form of thyroxine, is used to replace what the thyroid gland is not making. Common brand names of this medication include Synthroid, Levoxyl, Levothyroid, and L-thyroxine. Treatment is for life!!! Some survivors do not want to avoid taking medications, and so get tired of taking a daily pill. Stopping the medication will result in redeveloping the symptoms of hypothyroidism.

Compensated hypothyroidism (mildly elevated TSH, normal T₄): Daily pill of levothyroxine may be used to suppress excessive gland activity.

Thyroid-stimulating hormone deficiency (low TSH, low T₄): Daily levothyroxine.

Hyperthyroidism (low TSH, high T₃ or T₄): The overproduction of the thyroid hormones, T₃ or T₄, can cause life threatening changes to the body, so more aggressive therapies are required to make the thyroid produce less or no thyroid hormone. There are three options to treat hyperthyroidism: (1) surgery to remove most of the thyroid gland; (2) a medication to cause the thyroid to be unable to make as much thyroid hormone (generally only a temporary treatment); and (3) drinking a radioactive liquid called I¹³¹ which is taken up by the thyroid gland and causes it to 'scar' over. The goal of treatment of hyperthyroidism is to make the patient either euthyroid (normal thyroid level) or hypothyroid, which can then simply be treated with a daily pill of levothyroxine.

Thyroid nodules: Patients with nodules detected by palpation should be further tested. This is generally done with a special type of needle biopsy called a fine needle aspiration (FNA). A thyroid scan and/or an ultrasound of the thyroid is sometimes done as part of the evaluation.

Thyroid cancer: Thyroid cancer is usually very treatable. Depending upon the type and stage of thyroid cancer, treatment generally includes a subtotal thyroidectomy (surgery to remove almost all of the thyroid) followed by taking a large dose of I^{131} intended to ablate (destroy) any of the remaining thyroid tissue and cancer cells. The patient is then placed on levothyroxine and followed on a regular basis.

2.12 Previous studies :

Fuks Z,et al. (1976) assessed long-term effects of external radiation therapy on the pituitary and thyroid glands. Histological evidence for radiation damage has been produced in normal thyroids irradiated externally with doses ranging from 225 cGy to 4300 cGy, in 41 patients followed for more than 10 years after treatment for

carcinoma of the larynx and hypopharynx. The incidence of established hypothyroidism was 7.3%. However, the 24-hour ¹³¹I uptake following TSH stimulation was decreased in all 41 patients, indicating thyroid dysfunction in all treated patients. The incidence of hypothyroidism seems to increase in patients who have a hemithyroidectomy following radiation. So external irradiation of the normal pituitary and thyroid glands delivered incidentally during radiotherapy of neoplasms of the head and neck may produce a wide spectrum of radiation-induced syndromes. Clinical damage is usually manifested months to years after treatment. Careful exclusion of the pituitary and the thyroid from radiation treatment fields is recommended whenever possible.

Mini et al. (2001) studied in Pretreatment prevalence of hypothyroidism in patients with head and neck carcinoma. Serum thyroid-stimulating hormone, free T4, and total T3 levels were recorded in 110 patients with non thyroid HNC prior to treatment in a prospective, controlled study. The mean patient age (\pm standard deviation) was 65 years \pm 13.8 years, and 82% of patients had squamous cell carcinoma. A diagnosis of hypothyroidism already was established in 4.5% of patients, and subclinical hypothyroidism was discovered in an additional 6.4% of patients. Sixteen patients had other equivocal anomalies in thyroid function and were referred for further endocrine evaluation. Hypothyroidism after treatment for head and neck carcinoma stems from the effects of treatment. The need for pretreatment evaluation of thyroid function should be considered.

Koc M. et al (2009) evaluated the early and late changes in thyroid dysfunction after radiation therapy for head and neck cancer. Sixty-three patients receiving neck irradiation including the thyroid gland were recruited in the study, and radiotherapy was the primary treatment in 27 patients. Of 63 patients, 24 (38%) were diagnosed with hypothyroidism (HT), 8 (12.7%) with clinical HT, and 16 (25.4%) with subclinical HT. The median time to the development of clinical HT was 15 months (range, 0-36 months) and subclinical HT was 3 months (range, 0-24 months). Eleven (17.5%) of the patients were diagnosed with subclinical hyperthyroidism. The median time to the development of the subclinical hyperthyroidism was 0 months (completion of radiation therapy) (range, 0-3 months). Univariate analysis of clinical HT revealed that the elevated pre-radiation therapy thyroid-stimulating hormone level was significant factor ($P = 0.021$). HT associated with head and neck irradiation.

Cetinayak et al (2008) assessed thyroid dysfunction in head and neck cancer patients who have received external beam radiotherapy according to radiotherapy fields and dose, tumor site and other local or systemic treatments retrospectively and prospectively and propose a follow-up schedule. A total of 378 patients was classified into two groups. Group I (n = 345) consisted of surgically treated 153 laryngeal, 80 nasopharyngeal and 112 oral cavity/oropharyngeal carcinoma patients;. Group II included 33 patients with head and neck cancer who were evaluated prospectively. Thyroid function tests were performed at the beginning of the radiotherapy and every three months after the radiotherapy course. In Group II, 1 (3%) patient was found to have thyroid dysfunction postoperatively prior to radiotherapy. At the time of analysis, 29 (87.8%) patients were euthyroidic, 2 (6.1%) patients had subclinical and 2 (6.1%) patients had clinical hypothyroidism. We recommend thyroid function tests in these patients prior to and once every 3-6 months after the radiotherapy course.

[Chougule A](#) et al.(2011) evaluated Thyroid dysfunction following therapeutic external radiation to head and neck cancer. This prospective study was conducted on ninety patients with non-thyroid head and neck cancer who were referred to the department of radiotherapy. Thyroid function tests were conducted before, midway during and after EBRT, with follow up at monthly intervals up to 6 months after the completion of therapy. Serum T3 and T4 levels were decreased at completion of EBRT and remained so after 6 months follow up. However, serum TSH levels did not significantly vary. EBRT to the neck region for treatment of head and neck cancer induces hypothyroidism and therefore care must be taken to exclude the thyroid from radiation beams without sparing the tumor as far as possible. The clinical protocol in such cases should include monitoring of T3, T4 and TSH levels during and after the EBRT.

Laway BA et al (2012) assessed incidence of primary hypothyroidism in cancer patients, who were exposed to the therapeutic external beam radiation, where radiation portals include a part or whole of the thyroid gland. This non-randomized, prospective study was conducted for a period of 2 years in which thyroid function was assessed in 59 patients (cases) of head and neck cancer, breast cancer, and other malignancies, who had received radiotherapy to the neck region. 59 euthyroid healthy patients (controls) were also taken, who had not

received the neck irradiation. These patients/controls were assessed periodically for 2 years. The incidence of hypothyroidism after external beam radiation therapy (EBRT) to neck where radiation portals include part or whole of the thyroid gland was 16.94%, seven cases had subclinical hypothyroidism (11.86%) and three cases had clinical hypothyroidism (5.08%). Mean time for development of hypothyroidism was 4.5 months. In summary, we found that thyroid dysfunction is a prevalent, yet easily treatable source of morbidity in patients undergoing radiation therapy to neck where radiation portals include a part or whole of the thyroid gland.

Robison et al. (1996) studied induction of thyroid dysfunction after radiation therapy for Hodgkin's disease in Childhood. Eighty-nine pediatric and young adult patients (less than 21 years old at diagnosis) with Hodgkin's disease who were treated with radiation. And found that. The median age at diagnosis was 14 years, and the median duration of follow up was 11 years. Of 89 patients evaluable for thyroid abnormalities, 51 patients developed biochemical hypothyroidism. The median time to development of hypothyroidism was six years. The estimated actuarial risk of developing hypothyroidism was 60% at 11 years. Radiation to the thyroid region was associated with an elevated risk of development of hypothyroidism (relative risk = 9.9), with patients receiving mantle irradiation alone developing hypothyroidism earlier (median time 2.5 years) than patients receiving combined modality treatment (median time 6 years; $p = 0.001$). Dose of radiation was the chief correlate for the development of hypothyroidism, The mean dose of radiation was 43.8 Gy for patients with mantle radiation alone (midplane central axis), Four patients were diagnosed with thyroid nodules, (diagnosed 7.6 to 14.3 years after treatment of Hodgkin's disease), with histology showing multinodular goiter (2), single colloid nodule (1) and papillary carcinoma (1). Transient hyperthyroidism developed in two patients 8 and 13 months after treatment for Hodgkin's disease.

KhooVS , et al. (1998) studied develop Thyroid dysfunction in patients with Hodgkin's disease who are treated with mantle irradiation. During the period 1970-89, the records of 320 patients who received mantle irradiation and who had thyroid function tests (TFT) were retrospectively reviewed. The median age was 30 years (range, 7-69 years). The median mantle and thyroid dose was 36 Gy (range, 30-40 Gy) and 39.8 Gy (range, 32-65 Gy), respectively. Overall thyroid dysfunction was present in 39% of the patients. Clinical

hypothyroidism was seen in 10%, and hyperthyroidism was found in 4% of patients. Thyroid nodules had developed in six patients (2%), of which those in four patients were malignant. The narrow dose range prevented, (27.0%) of the 37 patients with thyroid cancer as a second tumor had earlier been irradiated with the treatment dose including the thyroid gland as compared with 34 (24.5%) of the 139 control patients. Eight of the ten cases with previous irradiation of the thyroid gland had papillary cancer. The median latency was 13 years. The estimated radiation dose in the thyroid varied between 3 and 40 Gy. External radiotherapy gave a crude odds ratio of 1.1 with 95% confidence interval = 0.5-2.8 for thyroid cancer. The weighted odds ratio was calculated to 2.3 with confidence interval = 0.5-8.9. This case-control study gave a non significantly increased odds ratio for thyroid cancer in patients with external radiotherapy including the thyroid gland.

Hallquist [A](#) et al. (1993) studied previous radiotherapy of malignant diseases as a risk factor for thyroid cancer. a total of 1056 cases of thyroid cancer were identified. Of these 37 had another previous malignant disease and they constituted the cases in this study. As controls four persons with at least two malignant diseases, thyroid cancer excluded, were selected for each case from the same cancer registry. Ten (27.0%) of the 37 patients with thyroid cancer as a second tumor had earlier been irradiated with the treatment dose including the thyroid gland as compared with 34 (24.5%) of the 139 control patients. Eight of the ten cases with previous irradiation of the thyroid gland had papillary cancer. The median latency was 13 years. The estimated radiation dose in the thyroid varied between 3 and 40 Gy. External radiotherapy gave a crude odds ratio of 1.1 with 95% confidence interval = 0.5-2.8 for thyroid cancer. The weighted odds ratio was calculated to 2.3 with confidence interval = 0.5-8.9. This case-control study gave a non significantly increased odds ratio for thyroid cancer in patients with external radiotherapy including the thyroid gland.

[Aich RK](#) et al. (2005) investigated hypothyroidism after external beam radiotherapy to the head & neck malignancies. 187 patients with head-neck malignancies were treated with external beam radiotherapy whose radiation portals included part or whole of the thyroid gland. Thyroid function tests were done at the beginning of treatment, at six weeks after completion of radiotherapy and

thereafter at six weeks interval for two years. Out of 187 patients, five were excluded from the study as they were found to be hypothyroid before the initiation of treatment. Of the patients attending the follow up clinic, 17.8 % and 21.8 % were found to have clinical and sub-clinical hypothyroidism at two year. As a significant number of patients develop hypothyroidism following radiotherapy to the neck, thyroid function tests should be included in the routine follow up protocol of such patients.

[Helen M](#) et al. (2002) assessed Thyroid neoplasia following irradiation in adolescent and young adult survivors of childhood cancer. 142 patients who had received irradiation to the thyroid. 49 subjects (24 of 65 patients who received scatter irradiation to the thyroid and 25 of 78 patients who received direct irradiation). Of these, 12 in the scatter and six in the direct irradiation group were found to have thyroid malignancy. Having a palpable thyroid was predictive of malignancy, but age at original diagnosis, sex, current age, time since irradiation, radiation dose, nodule type and nodal involvement were not. There is a significant risk of cancer in thyroid glands exposed to radiation as part of therapy for childhood cancer. This risk is greater for patients who received scatter (versus direct) irradiation.

Munyo-Estefan A .et al (2009) Studied the incidence of hypothyroidism in patients with Head and Neck Cancer who have undergone neck radiotherapy justifies the inclusion of thyroid function monitoring in the pre-operative and follow-up evaluation protocols. A total of 550 case records were analyzed. Of the 550 patients, 188 were excluded due to the fact they had not received radiotherapy as part of their treatment and 362 were included in the study. Of these, 55 patients had thyroid stimulating hormone (TSH) level determination after treatment with radiation therapy. Hypothyroidism was defined as a TSH value greater than or equal to 4.5 mIU/L, regardless of whether or not any symptoms were presented. 36.4% of the patients were diagnosed as having clinical or sub-clinical hypothyroidism. The type of treatment carried out, particularly whether or not surgical resection was performed, was found to be the most significant predictive factor for the development of hypothyroidism ($P=0.054$). Monitoring of the thyroid function on a six-month or annual basis, at least during the first 5 post-treatment years, has to be included in the follow-up and control protocols of every patient undergoing neck RT, and patients with TSH values over 4.5 mIU/L should be referred to the

endocrinologist for hormone replacement, whether they present symptoms or not.

Bakhshandeh M. et al (2013) determined the dose-response relationship of the thyroid for radiation-induced hypothyroidism in head-and-neck radiation therapy. Sixty-five patients treated with primary or postoperative radiation therapy for various cancers in the head-and-neck region were prospectively evaluated. Patient serum samples (tri-iodothyronine, thyroxine, thyroid-stimulating hormone [TSH], free tri-iodothyronine, and free thyroxine) were measured before and at regular time intervals until 1 year after the completion of radiation therapy. Hypothyroidism was defined as increased TSH (subclinical hypothyroidism) or increased TSH in combination with decreased free thyroxine and thyroxine (clinical hypothyroidism). Twenty-nine patients (44.6%) experienced hypothyroidism.

CHAPTER THREE

Chapter three

3.1 Material and method

The following study has been carried out on a sample consist of 80 head and neck cancer patients; who were received a radical radiation dose in the range of 6000-6500 cGy at radiation and isotopes center of Khartoum RICK.

3.1.1 study variable

These include Patients treated radically in head and neck area, and exclusion

Patients treated in other area, abdomen, chest, pelvic etc...).And palliative treatment.

3.1.2 Area of the study

The study was carried out in Radioisotope center in Khartoum /Sudan in the period from march 2012 to august 2013.

3.1.3 Method of Data collection

Five ml of venous blood collected in dry tubes allowed to clot and immediately centrifuged at 2000 r.p.m for 5minutes and separated sera were stored at 20C° until analyzed.

3.1.4 Method of data analyses

Correlation between the amount of dose received by the thyroid and the T3,T4 and TSH as well as the association between the body characteristics (weight , height, age) with the TFT.

3.1.5 Ethical Issue:

Permission of Radiotherapy Department and patients raised at the area of the study should be taken to use the patients data.

No patients details were

3.2. Material

3.2.1 Cobalt60 unit

An isocentric cobalt60 unit is extremely simple in design consisting of a radioactive isotopes, a source housing and method of collimation, and an isocentric mechanism. Cobalt60 is an isotope produce by bombarding it's stable form, Co60 with neutron. Co60 then attempts to gain stability by the emission of beta and gamma radiation $\text{Co60} \rightarrow \text{excited Ni60} + \beta (0.31 \text{ Mev})$ $\text{Excited Ni60} \rightarrow \text{stable Ni60} + \delta (1.17 \text{ Mev}) + \delta (1.33 \text{ Mev})$. The energy of a cobalt unite is usually quoted as 1.25 Mev, and it has a half life of 5.26 years.

3.2.2 RIA tools

Specific Reagents, All radioimmunoassay specific reagents for the measurement of thyroid hormones were obtained from chine institute for Atomic Energy [CIAE], Department of isotopes, the reagents include tracer standard and antibodies and separating agents for the different hormones.

3.2.3 Day's methods for calculating depth dose distribution

It is possible to calculate depth dose distributions at any point within the field or outside the field using, Day's has proposed a particularly simple calculation method for rectangular fields. In this method, percent depth dose can be calculated at any point within the medium using the central axis data. (khan 2003)

A. Point Off-Axis.

To calculate dose at any point Q, the field is imagined to be divided into four sections (Fig.) and their contribution is computed separately. Thus the dose at depth d along the axis through Q is given by $\frac{1}{4}(\text{sum of central axis dose at depth d for fields } 2a \times 2b, 2a \times 2c, 2d \times 2b, \text{ and } 2d \times 2c)$. Suppose the dose in free space on the central axis through P at SSD + dm is 100 cGy (rad) and its value at a corresponding point over Q is $KQ \times 100$, where KQ is the off-axis ratio determined in air from the primary beam profile. If the

BSF and central axis %DD for rectangular fields are available, the dose at depth d along the axis through Q will be.
given

by:

$$\frac{K_Q \times 100}{4} (\text{sum of BSF} \times \%DD \text{ at depth } d \text{ for fields } 2a \times 2b, 2a \times 2c, 2d \times 2b, \text{ and } 2d \times 2c)$$

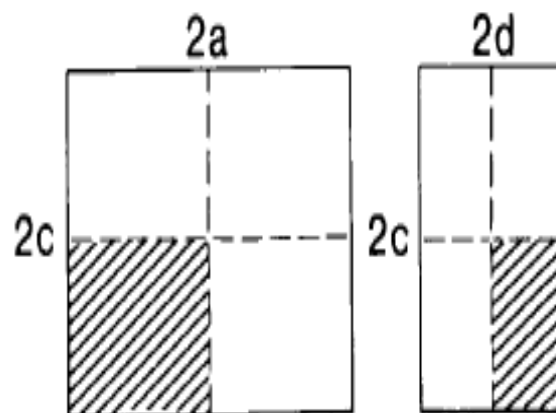
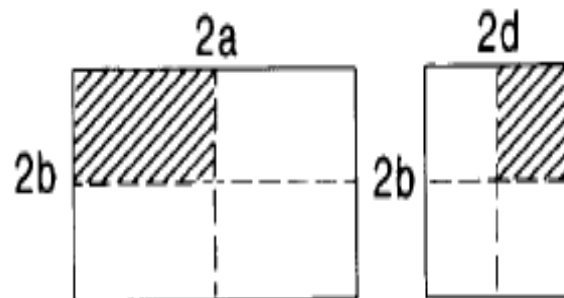
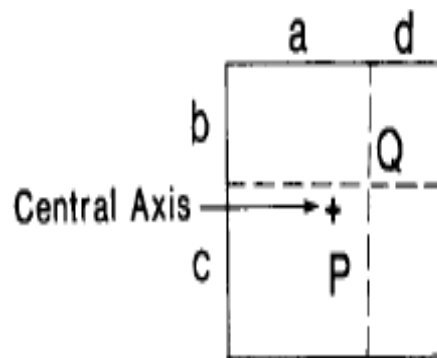


Figure 3.3.. Day's method of calculating dose at any point Q in a rectangular field

Since the D , at P is $100 \times \text{BSF}[(a + d) \times (b + c)]$, the percent depth dose at depth

D along the axis through Q, relative to $D_{m,,}$ at Z? will be given by:

$$\frac{K_Q}{4 \times \text{BSF}[(a + d) \times (b + c)]} \left(\text{sum of BSF} \right. \\ \left. \times \%DD \text{ at depth } d \text{ for fields } 2a \times 2b, 2a \times 2c, 2d \times 2b, \text{ and } 2d \times 2c \right)$$

B. Point Outside the Field

Day's method can be extended also to the case of determining dose distribution at points

outside the field limits. In Fig, a rectangular field of dimensions $a \times b$ is shown with the central axis passing through P. Suppose Q is a point outside the field at a distance c from the field border. Imagine a rectangle adjacent to the field such that it contains point Q and has dimensions $2c \times b$. Place another rectangle of dimensions $a \times b$ on the other side of Q such that the field on the right of Q is a mirror image of the field on the left, as shown in the figure. The dose at point Q at depth d is then given by subtracting the depth dose at Q for field $2c \times b$ from that for field $(2a + 2c) \times b$ and dividing by 2

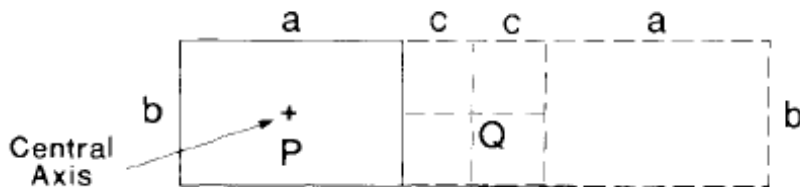


Figure 3.4. Calculation of depth dose outside a rectangular field

CHAPTER FOUR

Chapter four

Results

Table 4-1 number of patient treated in head and neck area

Gender	No. of patient
Male	33
Female	47
Total	80

Figure 4-1 number of patient treated in head and neck area.

Table 4-2 show Diagnosis :

Male	Female	Diagnosis
0	30	Ca breast
19	15	Ca nasopharynx
4	2	Ca hypopharynx
2	0	Ca tongue
0	2	Ca maxillary antrum
3	1	Ca larynx
0	2	Ca parotid

28

52

80

Figure 4-2 show diagnosis.

Figure 4- 3 shows the Mean and Std.Dev of T4.

Figure 4- 4 shows the Mean and Std.Dev of T3 .

Figure 4- 5 shows the Mean and Std.Dev of TSH .

Figure 4.6 . illustrate a direct linear association between T3 level and dose received by thyroid gland .

Figure 4.7. illustrate a direct linear association between T4 level and dose received by thyroid gland.

Figure 4.8 . illustrate a direct linear association between TSH level and dose received by thyroid gland.

Figure 4- 9 shows the Mean and Std.Dev of dose received by thyroid.

Figure 4.10 . illustrate a direct linear association between distance and dose received by thyroid gland

Figure 4- 11 shows the Mean and Std.Dev of given dose.

Figure 4-12 illustrate a direct linear association between given dose and dose received by thyroid.

CHAPTER FIVE

Chapter five

Dissociation conclusion and recommendation

5-1 Discussion

This study designed to evaluate thyroid hormone level in cancer patients receive radiation on organ adjacent to thyroid gland and to study the amount of the dose which produces these effects .The study include 80 patient with different cancer cases, the result showed that the

amount of T3 hormone decrease with mean 1.85 (figure 4) as dose to the thyroid increased the amount of T4 hormone decrease with mean 152.36 (figure 5) as dose to the thyroid increased, as a result of that TSH hormone has normal elevation with mean 0.96. (figure 6), where the T3, T4 reduce by 0.0002 nmol/cGy and 0.0074 nmol/cGy respectively, in thyroid dose range from 2000 cGy to 8000 cGy. the mean given dose was 4858.9 (figure 9) and thyroid received 2653.3 of that dose, Arun Chougule, et al [35] the mean serum T3 & T4 levels were found to be decreased during EBRT significantly ($p < 0.001$, $p < 0.005$, Garcia-Serra A et al [27], Head and neck irradiation results in biochemical hypothyroidism in at least 50% of patients, IRVIN et al [11] Decreased thyroid function have been reported following external irradiation. Khoo et al [12] The median mantle and thyroid dose was 36 Gy (range, 30-40 Gy) and 39.8 Gy (range, 32-65 Gy), respectively. Overall thyroid dysfunction was present in 39% of the patients. The effect to the thyroid can reduce by increases the distance between thyroid and target area as possible this appear clearly in (figure 2), so that all patient treated in neck have early thyroid problem Robison et al [10] Radiation to the thyroid region was associated with an elevated risk of development of hypothyroidism (relative risk = 9.9), with patients receiving mantle irradiation alone developing hypothyroidism earlier (median time 2.5 years) than patients receiving combined modality treatment (median time 6 years; $p = 0.001$). if the height of the radiation field was ≥ 7 cm, or the patient had been operated. Hypothyroidism was less common if less than a half of the thyroid bed was irradiated. . Dose increased to thyroid gland as the given dose increased. EBRT to the neck region for treatment of head and neck cancer induces hypothyroidism and therefore care must be taken to exclude the thyroid from radiation beams without sparing the tumor as far as possible

5-2 Conclusion

Radiotherapy of the head and neck cancer have accompanied with serious complication in the vital organs structure and the physiological state, in this view the thyroid hormones(T3 and T4) have been reduced and the TSH increases due to irradiation of

head and neck radiation, and such consequences have been commonly with conventional radiation therapy.

5-3 Recommendation

Assessments of thyroid hormone level one time after patient treatment .

planning patient by simulator or CT simulator.

Shielding vital organs using different shield to avoid unnecessary dose.

Further study should be done to evaluate the dose received by the critical organ in case of head and neck treatment since high dose were delivered and IMRT and other precise protocols for localization were not established yet.

References

[Aich RK](#), [Ranjan DA](#), [Pal S](#), [Naha BL](#), [Amitabh R](#). (2005). Iatrogenic hypothyroidism: a consequence of external beam radiotherapy to the head & neck malignancies. [J Cancer Res Ther.](#);1(3):142-6.

[Atahan IL](#), [Yildiz F](#), [Ozyar E](#), [Uzal D](#). (1998) . Thyroid dysfunction in children receiving neck irradiation for Hodgkin's disease. [Radiat Med](#);16(5):359-61.

[Bakhshandeh M](#) , [Hashemi B](#), [Nikoofar A](#), [Vasheghani M](#), [Kazemnejad A](#). (2013). Normal Tissue Complication Probability Modeling of Radiation-Induced Hypothyroidism After Head-and-Neck Radiation Therapy, [international Journal of Radiation Oncology](#) [85, 2](#) , 514-521,

[Cetinayak O](#), [Akman F](#), [Kentli S](#), [Duzen M](#), [Eyiler F](#), [Sen M](#), and [Kinay M](#). Assessment of treatment-related thyroid dysfunction in patients with head and neck cancer. 2008. [Tumori](#), 94: 19-23.

[Chougule A](#), [Kochar B](#). (2011). Thyroid dysfunction following therapeutic external radiation to head and neck cancer. [Asian Pac J Cancer Prev.](#);12(2):443-5.

[Dianaf](#) , [Nelson K](#), [Eddym V](#), [Roberte](#) , [O'mara](#), and [Ubin ph](#). (1978). Thyroid abnormalities following neck irradiation for hodgkin's disease. [cancer](#) 42:2553-2562.

[Diaz R](#), [Jerry J. Jaboin](#), [Morales-Paliza M](#), [Koehler E](#), [John G. Phillips](#), [Stinson S](#), [Gilbert J](#), [Christine H. Chung](#), [Barbara A. Murphy](#), [Wendell G. Yarbrough](#), [Patrick B. Murphy](#), [Shyr Y](#), [Anthony J. Cmelak](#), (2010). Hypothyroidism as a Consequence of Intensity-Modulated Radiotherapy With Concurrent Taxane-Based Chemotherapy for Locally Advanced Head-and-Neck Cancer. [International Journal of Radiation Oncology](#) [77, 2](#) , 468-476,

[Fuks Z](#), [Glatstein E](#), [Gerald W](#) , [marsa](#), [malcolma](#), [ragshaw](#), and [henry. laplan](#) . (1976). long-term effects of external radiation on the pituitary and thyroid glands. [Cancer](#) 37:1152-1161.

[Hallquist A](#), [Hardell L](#), [Löfroth PO](#). (1993). External radiotherapy prior to thyroid cancer: a case-control study. [Int J Radiat Oncol Biol Phys.](#)1;27(5):1085-9.

[Helen M](#) , [Somerville](#), [Albert H Lam](#), [Michael M Stevens](#), [Kate S Steinbeck](#), [Stevens G](#) and [Leigh W Delbridge](#) . (2002). Thyroid neoplasia following irradiation in adolescent and young adult survivors of childhood cancer . [Med J Aus t](#); 176 (12): 584-587.

[Khoo VS](#), [Liew KH](#), [Crennan EC](#), [D'Costa IM](#), [Quong G](#). (1998). Thyroid dysfunction after mantle irradiation of Hodgkin's disease patients. [Australas Radiol.](#) 42(1):52-7.

Koc M, Capoglu I . (2009),Thyroid dysfunction in patients treated with radiotherapy for neck. American Journal of Clinical Oncology 32(2):150-153.

Laway BA, Shafi KM, Majid S, Lone MM, Afroz F, Khan S, Roohi R. (2012). Incidence of primary hypothyroidism in patients exposed to therapeutic external beam radiation, where radiation portals include a part or whole of the thyroid gland. Indian J Endocr Metab;16:329-31

[Marjolein J. Boomsma](#). 2011. Radiation-induced hypothyroidism in head and neck cancer patients: A systematic review. Radiotherapy & Oncology [99.1](#) . 1-5.

Munyo-Estefan A, López-Paullier M, Charlone-Granucci R, Peña-Rehbein JL, d'Albora-Rivas R, Schiavo-Viviani L. (2009). Thyroid function alteration in patients with radiation therapy of the neck Acta Otorrinolaringol Esp.;60(4):268-71.

[Robison](#) ,[Bhatia](#) S, [Norma K.C](#), [Ramsay](#), [John P](#) ,[Ann B Mertens](#) ,[Leslie L](#). (1996).Thyroid Abnormalities after Therapy for Hodgkin's Disease in Childhood.The Oncologist . 2: 62-67 .

Ron E, Modan B, Preston D, Alfandary E, Stovall M, Boice JD Jr. (1989).Thyroid neoplasia following low-dose radiation in childhood. Radiat Res;120(3):516-31.

Stephen C. Schimpff, Charles H. Diggs, John G. Wiswell, Paula C. Salvatore; And Peter H. Wiernik .(1980). Radiation-Related Thyroid Dysfunction: Implications For The Treatment Of Hodgkin's .Disease . .Ann Intern Med. 92(1):91-98 .

Tell R, Lundell G, Nilsson B, Sjödin H, Lewin F, Lewensohn R . (2004). Long-Term Incidence Of Hypothyroidism After Radiotherapy In Patients With Head-And-Neck Cancer.**International Journal Of Radiation Oncology** . 2 , 395-400.

Appendix

Appendix A

Data collection sheet

table.1-A data collection sheet

Patient gender	Patient height (cm)	Patient age	Diagnosis	Field size
Tumour dose cGy/min	Out put cGy/min	Treatment time (min)	Given dose (Gy)	