بسم الله الرحمن الرحيم

Sudan University of Sciences and Technology

College of Graduate Studies

Study of Normal Thyroid Uptake using Technisium-99m

دراسة الإمتصاص الطبيعي للغدة الدرقية بإستخدام التكنيشيوم-99m

A thesis submitted for partial fulfillment of the requirement of M.Sc. Degree in Nuclear Medicine Technology

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2017

الآيـة

بسم الله الرحمن الرحيم

يقول الله عز وجل:

﴿وَمَا تَوْفِيقِي إِلَّا بِاللَّهِ عَلَيْهِ تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ﴾

[سورة هود : 88]

Dedication

To my parents ***(Salah &Wejdan)***

To my husband ***(Aymen)***

To my brothers ***(Mohamed & Omer)***

To my family

To my all friends

To my colleagues

To any one that help me in this research especially

(Mustafa&Eman)

Acknowledgment

First of all I would like to say Alhamdulillah for giving me the health and strength to finish this research.

Then I would like to thank my supervisor ***Dr. Mohamed Elfadil****for his sincere supervision ,advice and guidance from the very early stage of this research as well as giving me extraordinary experiences throughout the work , above all he provided by the encouragement.*

I would like to express my gratitude to college of medical radiological science members and staff, and the whole staff of the Radiotherapy department great help and support.

I would like to the staff of Radiation and Isotopes Center of Khartoum, especially the staff of Nuclear Medicine department for their help and cooperation to achieve my gall.

I would like to thanks my parents and my family for their great support to finish this project and they have been always there for me with encouragement, fostering ,empower me paving my way .

I would like to thank my husband ,thesis would be incomplete without a mention of the supported and encouraged given by my husband who kept my spirits up . I am greatly indebted to him for bearing with me during the past several months.

Finally I would like to thank everybody helped me prepare and finish this study.

Abstract

Thyroid gland is a vital endocrine gland in the body, estimation of its uptake and thyroid area are generally consider to be an important in several pathologic situations such as iodine deficiency, Goiter, thyroiditis, multi-nodular goiter and others. The aim of this study was to evaluate the normal range of thyroid uptake and determine the thyroid area in patients who has normal thyroid function test (T.F.T) and homogenous distribution of the radiotracer in Sudanese especially in Radiation & Isotope Center of Khartoum (RICK). This study includes 58 patients (91.5% Female, 8.5% Male) in different age, sex, center of origin and type of food and drink intake. For six months from Dec 2016 to May 2017. The most frequency of ages distribute as (25-35=31.03%, 15-25=29.3%), The thyroid uptake value in the gamma camera (mediso). The result of the study showed that the mean age was 33.6 ± 11 years old, the overall mean area of thyroid gland was 19.3 ± 3.78 cm^2. The mean area of right lobe was 7.7 ± 1.65 cm^2. The mean area of left lobe was 7.1 ± 1.84 cm^2. The right lobe area was significantly homogenous from left lobe area. Furthermore, a significant correlation was observed between thyroid area, weight and age of the subject. The normal range of thyroid uptake is in the range between (0.77% - 3.8%) and the thyroid area is in the range of (12.7 cm^2 to30.1 cm^2) there was a direct relationship between thyroid uptake and the thyroid area that when the area increase the uptake increase that shown in the following equation: $y= 0.054x + 0.89$ where x refers to thyroid area and y refers to uptake in percent. The result also shown that when thyroid weight increase the uptake increase as shown in the following equation: $y= 0.056x + 1.53$ where x refers to thyroid weight and y refers to uptake in percent. And the result shown that when BMI increase the uptake decrease as shown in the following equation: $y = - 0.033x + 2.82$ where x refers to BMI and y refers to uptake in percent. Finally the result also shown that when patient age increase the thyroid uptake decrease as shown in the following equation: $y = - 0.6x + 1.85$ where x refers to patient age and y refers to uptake in percent.

الخلاصه

الغدة الدرقية هي غدة صماء حيوية في الجسم، وتقدير امتصاصها ومساحتها يعتبر مهما في عدة حالات مرضية مثل نقص اليود، والدراق، التهاب الغدة الدرقية، عقيدات الغدة الدرقية وغيرها. كان الهدف من هذه الدراسة هو تقيم وتحديد المعدل الطبيعي لتشبع الغدة الدرقية بعنصر التكنيشيوم عند السودانيين الذين لديهم نتائج في المعدل الطبيعي لفحص وظائف الغدة الدرقية وتشيع متناسق في شكل الغدة وامتصاصها (خالية من الحبيبات والأكياس بنوعيها البارد والحار) بالإضافة لذلك يهدف البحث لمعرفة معدل المساحة الطبيعية للغدة الدرقية لهؤلاء المرضى، شملت هذه الدراسة 58 مريض (91.5% اناس و8.5% ذكور) بمختلف الاعمار والاجناس والولايات بالإضافة لاختلاف طبيعة الطعام والشراب عند هؤلاء المرضى. أجريت هذه الدراسة بالمركز القومي للعلاج بالأشعة والطب النووي الخرطوم قسم الطب النووي (القاما كاميرا/ مدسو) لمدة ستة أشهر من ديسمبر 2016 وحتى مايو 2017. أظهرت نتائج الدراسة أن متوسط سنوات العمر كان 33.6 ± 11 سنة، وكان متوسط مساحة الغدة الدرقية 19.3 ± 3.78 سم². بلغ متوسط مساحة الفص الأيمن 7.7 ± 1.65 سم²، ومتوسط مساحة الفص الايسر 7.1±1.84 سم². مساحة الفص الايمن متباين بشكل كبير من مساحة الفص الايسر. وعلاوة على ذلك ، لوحظ وجود ارتباط كبير بين مساحة الغدة الدرقية والوزن والعمر. كانت النتائج بالنسبة لمستوى التشبع الطبيعي للغدة الدرقية بعنصر التكنيشيوم في النسبة بين (0.77% الى 3.8%) وكانت مساحة الغدة الدرقية تتراوح ما بين (12.7سم² الى 30.1 سم²) كما إنه كلما زادت مساحة الغدة الدرقية يزيد تبعا لذلك كمية التشبع بعنصر التكنيشيوم كما في المعادلة التالية:

$$y = 0.054x + 0.89$$

كما وجد انه كلما زاد وزن الغدة الدرقية يزيد تبعا لذلك كمية التشبع كما في المعادلة :

$$y = 0.056x + 1.53$$

وكلما زادت كتلة الجسم قلت كمية التشبع بعنصر التكنيشيوم كما في المعادلة:

$$y = - 0.033x + 2.82$$

كما اثبتت الدراسة ان مستوى التشبع للغدة يتباين باختلاف العمر للمريض.

$$y = -0.6x +1.85$$

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List of Abbreviation

Abb	Name
RICK	Radiation & Isotope Center Khartoum
T4	Thyroxin
TFT	Thyroid Function Test
T3	Tri iodothyronine
TSH	Thyroid stimulating Hormone
NM	Nuclear Medicine
RIA	Radio Active Iodine
IRMA	Immuno-Radiometric assay
TG	Thymoglobulin
TPO	Thyroid Peroxides
GD	Graves' Disease
ATA	American Thyroid Association
T½	Half-Life
PTU	Propylene Thiouracil
TU	Thyroid Uptake
BG	Back Ground
ROI	Region of Interest
SPECT	Single Photon Emission Computer Tomography

Chapter One

Introduction

Chapter one

1.1 Introduction:

Thyroid gland is one of the important glands in human bodies that by playing great role in hormone function by producing thyroxin and tri-iodothyronin (T3 & T4).

The iodine trapping by thyroid is known in the nuclear medicine investigation by Thyroid Uptake (Brucer, 1989). Concerning the high incidence of thyroid disease, the normal range for thyroid hormones level and thyroid uptake have not been established yet for the Sudanese population.

Estimation of the thyroid gland volume is generally consider to be an important in several pathologic situations such as iodine deficiency, Goiter, thyroiditis, multinodular goiter and others (Zimmermann et al., 2001).

The thyroid gland function depend on the presence of iodine content in the blood, which is a form of minerals and like other chemicals content of the soil is affected by the climate and location. The main supply of the iodine for the thyroid gland is the food (fish as main) and water which is ultimately depend on the iodine content of the soil and water as the soil component and composition vary from area to another (Brucer, 1989).

The Sudan is the largest African country occupying an area of about 1 million square miles, it is extended from the Sahara in the Northern part down to the forest in its Southern part, and the altitude varies from high mountainous area at the red sea coast in the east and low altitude in the mid land. There are a number of mountains scattered throughout the country. The rain also varies from heavy rain in the South and the West and very drought areas in the North and middle of the country. The water resources also very from town to town and there is even great variation in the water resources and water content within the same town (Bafarag et al, 2004) .

Thyroid gland ultrasonography has proven a useful and practical method for assessment of thyroid volume various investigators over the world have measured the thyroid volume and have found different values of normal thyroid volume (Lee and Anzai, 2013). So this study was done to established the thyroid uptake ,volume and defining the 99mTc-pertechnetate uptake values in normal cases Sudanese from 13-60 years in RICK.

1.2 Problem of the study:

Most of regions internationally they have a reference number for thyroid volume against which normal thyroid dimension will be determined, therefore this study is an attempt to find normal thyroid volume in for Sudanese especially in Radiation and Isotopes Center – Khartoum (RICK) the huge number of thyroid dysfunction cases that referred for assessment of normal uptake which is varies among Sudanese native based on their residence areas.

1.3 Research Objectives:

1.3.1 General objectives:

The main objective of this research was to standardize a simple and fast methodology for performing Thyroid Uptake & Thyroid Area, and to determine the normal values for 99mTc-pertechnetate uptake.

1.3.2 Specific objectives:

- To determine the normal range of the thyroid uptake & Area
- To measure the thyroid Area, right lobe and left lobe Area for patients with homogenous distribution of radiotracer & normal thyroid function test (T.F.T)
- To correlate between the thyroid uptake to age, gender, body mass index (MBI) and thyroid area

- To correlate between the thyroid area to age and weight.

1.4 Research outlines

This study falls into five chapters, Chapter one which is an introduction, It presents the statement of the study problems, objectives and the overview of the study. Chapter two contains the background material. Specifically it discusses the anatomy and physiology as well as pathology of the thyroid gland. This chapter also includes a summary of previous work performed in this field. Chapter three describes the materials and a method used. Chapter four deals with the results and finally chapter five shows the discussion, conclusion and recommendations and references list.

Chapter 2

Literature Review

Chapter two

Literature Review

2.1 Background:

2.1.1 Anatomy of the thyroid gland:

The Thyroid gland is one of the important glands in human bodies that by playing great role in hormone function by producing thyroxin (T3) and tri-iodothyronin (T4). It is the largest of the endocrine glands (20-25 g). In humans, it has a "butterfly" shape, with two lateral lobes that are connected by a narrow section called the isthmus. It is located in the neck just below your Adam's apple, in close approximation to the first part of the trachea. Most animals, however, have two separate glands on either side of the trachea. Thyroid glands are brownish-red in color.

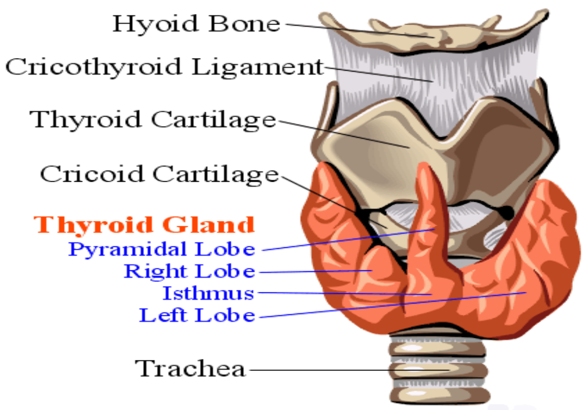

Figure 2.1: Human Thyroid Anatomy

2.1.2 Anatomical Variations

Hypoglossal Duct Cyst Thyroglossal duct fails to involute completely.

A thyroid Absence of Thyroid gland:

1. Pyramidal Lobe
2. Absence of Isthmus
3. Ectopic Gland

The average gland is 40 to 60 mm in length and 13 to 18 mm thick with the isthmus approximately 4 to 6 mm thick. A pyramidal lobe is present in 10% to 40% of it is a finger-like lobe of tissue which extends superiorly from the isthmus and is of variable height. The normal thyroid gland has a wide range of sizes. Normal variations in size occur with age, gender and nutrition: the gland is larger in youth, the well-nourished and in women - especially during menstruation and pregnancy.

2.1.3Thyroid tissue:

The microscopic structure of the thyroid is quite distinctive. Thyroid epithelial cells - the cells responsible for synthesis of thyroid hormones - are arranged in spheres called thyroid follicles. Follicles are filled with colloid, a proteinaceous depot of thyroid hormone precursor.

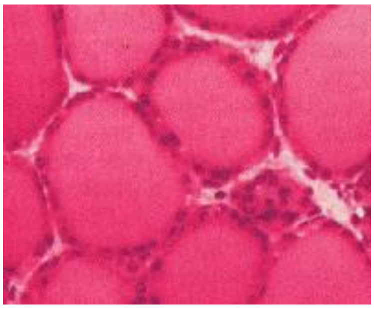

Figure 2.2: Thyroid tissue

In addition to thyroid epithelial cells, the thyroid gland houses one other important endocrine cell. Nestled in spaces between thyroid follicles are Para follicular or C cells, which secrete the hormone calcitonin. The structure of a parathyroid gland is distinctly different from a thyroid gland. The cells that synthesize and secrete parathyroid hormone are arranged in rather dense cords or nests around abundant capillaries. (Chwajink, 1995)

2.2 Physiology of the thyroid gland:

The thyroid gland located immediately below the larynx on each lobe of and anterior to the trachea, is one of the largest endocrine glands, normally weighting 15 to 20 grams in adults. The thyroid secrete two major hormones, thyroxin and tri iodothyroxine, commonly called T4 and T 3, respectively (Stathatos, 2012).both of these hormones profoundly increase the metabolic rate of the body. complete lack of thyroid secretion usually causes the basic metabolic rate to fall 40 to 50 per cent below normal, and extreme excesses of thyroid secretion can increase the basal metabolic rate to 60 to 100 per cent above normal. Thyroid secretion is controlled primarily by thyroid -stimulating hormone (TSH) secreted by the anterior thyroid pituitary gland. The thyroid gland also secretes calcitonin, an important hormone for calcium metabolism (Stathatos, 2012).

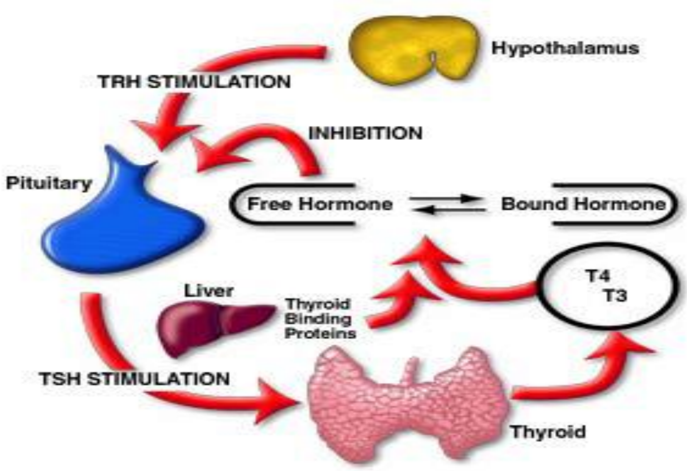

Figure 2.3 Thyroid Function

Synthesis and Secretion of the Thyroid Metabolic Hormone About 93 percent of the metabolically active hormones secreted by the thyroid gland is thyroxin, and 7 percent triiodothyroxine. However, almost all the thyroxin is eventually converted to triiodothyronine in the tissue, so that both are functionally important.

The functions of these two hormones are qualitatively the same, but they differ in rapidity and intensity of action. Triode threonine is about four times as potent as thyroxin, but it’s present in the blood in much smaller quantities and persists for much shorter time than thyroxin (Moleti et al., 2014).

Iodide Trapping is the first stage in the formation of thyroid hormone, it transport of iodides from the blood into the thyroid glandular cells and follicles. The basal membrane of the thyroid cell has the specific ability to pump the iodide actively to the anterior of the cell. This is called iodide trapping. In normal gland, the iodide pump concentrates the iodide to about 30 times its concentration in the blood. When the thyroid gland becomes maximally active, this concentration ratio can rise to as high as 250 times. The rate of iodide trapping by the thyroid is influenced by several factors, the most important being the concentration of TSH (Moleti et al., 2014).

Oxidation of the iodide ion is the first essential step in the formation of the thyroid hormone is conversion of the iodide ions to oxidized form iodine, either nascent iodine (10) or (13). That is then capable of combining directly with the amino acid tryosine. This oxidation of iodine is promoted by the enzyme peroxidase and its accompanying hydrogen peroxide, which provide potent system capable of oxidizing iodides. The peroxidase is either located in the apical membrane of the cell or attached to it, thus providing the oxidized iodine at exactly the point in the cell where the thyroglobulin molecule issues forth from the Golgi apparatus and through the cell membrane into the stored thyroid gland colloid (Moleti et al., 2014).

The binding of iodine with the thyroglobulin molecule is called organification of the thyrogloulin. Oxidized iodine even in the molecular form will bind directly but very slowly with the amino acid tyrosine. In the thyroid cell, however, the oxidized iodine is associated with an iodinase (Moleti et al., 2014).

Enzyme the process to occur within seconds or minute. Therefore, almost as rapidly as the thyroglobulin molecule is released from the golgi apparatus or as it is secreted through the apical cell membrane into the follicle, iodine binds with about one sixth of the tyrosine amino acids within the thyroglobulin molecule, the stage of iodination of tyrosine and final formation of the two important thyroid hormones, thyroxine and triiodothyronine (Mariotti and Beck-Peccoz, 2000).

Release of thyroxine and triiodothyronine from the thyroid Gland: Throglobulin itself is not released into the circulating blood in measurable amounts, instead, thyroxine and triiodothyronine must first be cleaved from the thyroglobulin molecule, and then these free hormones are released.

Daily Rate of Secretion of Thyroxine and Triiodothyronine about 93 per cent of thyroid hormone released from the thyroid gland is normally thyroxine and only 7 percent is triiodothyronine, about 35 micrograms of triiodothyronine per day.

The general effect of thyroid hormone is to activate nuclear transcription of large numbers of genes therefore, in virtually all cells of the body, great numbers of protein enzymes, the new result is generalized increase in functional activity throughout the body (Mariotti and Beck-Peccoz, 2000).

Thyroid hormones increase the number and activity of Mitochondria, when thyroxine or triiodothyronine is given to an animal, the mitochondria in most cells of the animals body increase in size as well as number. Furthermore, the total membrane surface area of the mitochondria increases almost directly in proportion of the increased metabolic rate of the whole animal. Therefore, one the principal functions of the thyroxine might be increases the rate of formation of adenosine triphosphate (ATP) to energize cellular function. However, the increase in the number and activity of the cell as well as the cause of the increase (Mariotti and Beck-Peccoz, 2000).

Thyroid Hormones Increase Active Transport of ions Through Cell Membranes:

One of the enzymes that increase its activity in response to thyroid hormone is Na+-Ka+-ATPase. this in turn increases the rate of transport of both sodium and potassium ions through the cell membranes of some tissues. Because this process uses energy and increases the amount of heat produced in the body, it has been suggested that this might be one of the mechanisms fact, thyroid hormone also causes the cell membrane of most cells to become leaky to sodium ions, which further activate the sodium pump and further increases heat production.

2.3 Thyroid Problems:

The suboptimum level of thyroid dysfunction could lead to some diseases or other pathological states in the human bodies such as (hyperthyroidism, hypothyroidism, thyrotoxicosis, thyroiditis ….. etc) (Brucer, 1989).

The thyroid gland is prone to several very distinct problems, some of which are extremely common. These problems can be broken down into:

• Those concerning the production of hormone (too much, or too little).

• Those due to increased growth of the thyroid causing compression of

important neck structures or simply appearing as a mass in the neck.

• The formation of nodules or lumps within the thyroid which are worrisome for the presence of thyroid cancer. And

• Those which are cancerous.

2.4 Pathology of the thyroid:

2.4.1 Goiter:

Any form of thyroid enlargement is called a goiter. The increase in volume is gradual and may be associated with normal thyroid function (euthyroid), decreased function (hypothyroidism) or increased hormonal production (hyperthyroidism). Euthyroid goiter is the most common and iodine deficiency is usually the cause (Cignini et al., 2012).

2.4.2 Nodules:

Many thyroid diseases can present with one or more thyroid nodules. Benign thyroid nodules outnumber malignant thyroid nodules approximately 500 to 1.

2.4.2.1 Solitary thyroid nodules:

There are several characteristics of solitary nodules of the thyroid which make them suspicious for malignancy. Although as many as 50% of the population will have a nodule somewhere in their thyroid, the overwhelming majority of these are benign. Occasionally, thyroid nodules can take on characteristics of malignancy and require either a needle biopsy or surgical excision.

2.4.3 Diffuse Colloid (Simple) Goiter:

Zones of glandular hyperplasia result in dilated follicles filled with colloid. These dilated follicles appear as cold nodules. They can undergo hemorrhage and necrosis. Colloid nodules are the most common type of thyroid nodule but thyroid function is normal.

Sonographically; the gland is symmetrically enlarged with normal echogenicity.

2.4.4 Adenomatous or Multinodular Goiters (MNG):

Sometimes hyperplasia and dilatation of follicles with colloid does not affect the thyroid uniformly and results in a multinodular goiter. Thyroid function is usually normal. The patient presents with an enlarged gland and pressure symptoms related to the trachea and esophagus. Multiple cold nodules are demonstrated on NM scans. MNG’s can grow to enormous sizes and are often asymmetrical due to nodule masses of various sizes (Cignini et al., 2012).

2.4.5 Hyperthyrodism:

Hyperthyroidism means too much thyroid hormone. Current methods used for treating a hyperthyroid patient are radioactive iodine, anti-thyroid drugs, or surgery. Each method has advantages and disadvantages and is selected for individual patients. Many times the situation will suggest that all three methods are appropriate, while other circumstances will dictate a single best therapeutic option. Surgery is the least common treatment selected for hyperthyroidism. There are different causes of hyperthyroidism but the most common underlying cause of hyperthyroidism is Graves' disease.

There are actually three distinct parts of Graves' disease:

- Over activity of the thyroid gland (hyperthyroidism)
- Inflammation of the tissues around the eyes causing swelling, and
- Thickening of the skin over the lower legs (pretibial myxedema)

2.4.5.1 Characteristics of Graves' Disease:

Graves' Disease effects women much more often than men (about 8.1 ratio, thus 8 women get Graves' Disease for every man that gets it. Graves' Disease is often called diffuse toxic goiter because the entire thyroid gland is enlarged, usually moderately enlarged, and sometimes quite big. Graves' Disease is uncommon over the age of 50 (more common in the 30's and 40's). Graves' Disease tends to run in families.

2.4.6 Hypothyrodism:

Hypothyroidism means too little thyroid hormone and is a common problem. In fact, hypothyroidism is often present for a number of years before it is recognized and treated. There are two fairly common causes of hypothyroidism:

The first is a result of previous (or currently ongoing) inflammation of the thyroid gland which leaves a large percentage of the cells of the thyroid damaged (or dead) and incapable of producing sufficient hormone. The most common cause of thyroid gland failure is called autoimmune thyroiditis (also called Hashimoto's thyroiditis), a form of thyroid inflammation caused by the patient's own immune system.

The second major cause is the broad category of medical treatments.

Hypothyroidism can even be associated with pregnancy. Treatment for all types of hypothyroidism is usually straightforward.

2.4.6.1 Symptoms of Hypothyroidism:

They are many symptoms of hypothyroidism: Fatigue, weakness, weight gain or increased difficulty losing weight, coarse, dry hair, dry, rough pale skin, hair loss, cold intolearance (can't tolerate the cold like those around you), muscle cramps and frequent muscle eaches, constipation, depression, irritability, memory loss, abnormal menstrual cycles and decreased libido.

2.4.6.2 Potential dangers of hypothyroidism:

Because the body is expecting a certain amount of thyroid hormone the pituitary will make additional thyroid stimulating hormone (TSH) in an attempt to entice the thyroid to produce more hormones. This constant bombardment with high levels of TSH may cause the thyroid gland to become enlarged and form a goiter (termed as "compensatory goiter"). The symptoms of hypothyroidism will usually progress. Rarely, complications can result in severe life-threatening depression, heart failure or coma.

2.4.7 Thyroiditis:

Thyroiditis is an inflammatory process ongoing within the thyroid gland. Thyroiditis can present with a number of symptoms such as fever and pain, but it can also present as subtle findings of hypo or hyper-thyroidism. There are a number of causes, some more common than others. Thyroiditis is an inflammation (not an infection) of the thyroid gland. Several types of thyroiditis exits and the treatment is different for each.

2.4.7.1 Hashimoto's thyroiditis:

Hashimoto's Thyroiditis (also called autoimmune or chronic lymphocytic thyroiditis) is the most common type of thyroiditis. It is named after the Japanese physician, Hakaru Hashimoto that first described it in 1912. The thyroid gland is always enlarged, although only one side may be enlarged enough to feel. During the course of this disease, the cells of the thyroid becomes inefficient in converting iodine into thyroid hormone and "compensates" by enlarging the radioactive iodine uptake may be paradoxically high while the patient is hypothyroid because the gland retains the ability to take-up or "trap" iodine even after it has lost its ability to produce thyroid hormone. As the disease progresses, the TSH increases since the pituitary is trying to induce the thyroid to make more hormone, the T4 falls since the thyroid can't make it, and the patient becomes hypothyroid. The sequence of events can occur over a relatively short span of a few weeks or may take several years.

It is more common in young and middle aged women. NM studies show little or no uptake of isotope.

2.4.7.2 De Quatrain's Thyroiditis: (also called Subacute Hashimoto's thyroiditis or granulomatous thyroiditis) was first described in 1904 and is much less common than Hashimoto's. the thyroid gland generally swells rapidly and is very painful and tender. The gland discharges thyroid hormone into the blood and the patients become hyperthyroid; however the gland quits taking up iodine (radioactive iodine uptake is very low) and the hyperthyroidism generally resolves over the next several weeks.

Subacute Hashimoto's thyroiditis is believed to be caused by a virus rather than autoimmunity and is also more common in women. The gland is swollen and painful usually 2-3 weeks after an upper respiratory infection. Severe destruction of the gland releases hormone, resulting in a period of hyperthyroidism, followed by a short period of hypothyroidism caused by hormone depletion. Most patients recover fully (Zhang et al., 2016).

2.4.7.3 Silent Thyroiditis:

Silent thyroiditis is the third and least common type of thyroiditis. It was not recognized until the 1970's although it probably existed and was treated as Graves' disease before that. This type of thyroiditis resembles in part Hashimoto's Thyroiditis and in part De Quatrain's Thyroiditis. The blood thyroid test are high and the radioactive iodine uptake is low (like De Quatrain's Thyroiditis), but there is no pain and needle biopsy resembles Hashimoto's Thyroiditis. The majority of patients have been young women following pregnancy. The disease usually needs no treatment and 80% of patients show complete recovery and return of thee thyroid gland to normal after three months. Symptoms are similar to Graves' Disease except milder. The thyroid gland is only slightly enlarged and expophthalamoses' (development of "bug eyes") does not occur. Treatment is usually bed rest with beta blockers to control palpitations (drugs to prevent rapid heart rates).

Radioactive iodine, surgery, or anti thyroid medication is never needed. A few patients have become permanently hypothyroid and needed to be placed on thyroid hormone (Chwajink, 1995).

2.4.8 Thyroid cancer:

Thyroid cancer is a fairly common malignancy; however, the vast majorities have excellent long term survival.

2.4.8.1 Adenomas and Carcinomas:

Evaluation of thyroid nodules is particularly annoying because thyroid nodules are exceedingly common and US detects most of them, even as small as 1-2 mm, but can rarely unequivocally differentiate benign from malignant nodules. US is used to evaluate nodules and indicate whether a biopsy is necessary. It is also used to direct aspiration biopsies of thyroid nodules and to guide alcohol ablation of thyroid lesions (Zhang et al., 2016).

Adenomas are benign tumors of thyroid follicles. Usually the adenoma is a solitary, well encapsulated lesion. The remainder of the gland appears normal. Occasionally adenomas are hyperfunctioning and result in hyperthyroidism with suppression of the rest of the gland. Hyperfunctioning adenomas usually result in "hot" lesions on radioisotope nuclear medicine scans.

Sonographically most adenomas are solitary, solid, homogeneous lesions with regular margins and an oval or round shape. Adenomas can be hypoechoic, isoechoic or hyperechoic to the normal thyroid tissue. They tend to undergo cystic degeneration. An anechoic peripheral halo may be seen with adenomas however, it may also be present with malignant lesions and is therefore nonspecific. Adenomas may have localized peripheral calcification or may be entirely calcified resembling a calculus (Zhang et al., 2016).

Carcinomas is the most common malignancy of the endocrine glands, it remains a rare disease accounting for less than 1% of all malignancy, and is the cause of death in only 0.005% of the United States population. Most thyroid cancers are relatively nonaggressive and have a good prognosis with 90% 10-year survival for early disease. Thyroid carcinoma is 2-3 times more common in women. Neck irradiation, especially as a child, is a major risk factor, greatest 20 years after radiation. The most common age for developing papillary carcinoma is 30 years of age and for follicular carcinoma, 45 year of age. A thyroid nodule found in a very young or very old patient is probably malignant. The most common presentation is an asymptomatic neck lump. The ultrasound appearances of thyroid cancer are highly variable.

2.4.9 Colloid Cysts:

Are collections of colloid in large thyroid follicles which appear as tiny cysts (<5mm in size) with no solid component. They are benign, can be considered a normal finding and are of no clinical significance.

Simple cysts of the thyroid are rare. Most thyroid cysts are complex and represent degeneration of either an adenoma or a colloid nodule.

Because of the rare occurrence of pure simple thyroid cysts and because both benign and malignant lesions can have cystic components, doing a thyroid ultrasound scan to distinguish a cyst from a solid mass is generally not of much clinical value (Zhang et al., 2016).

Hemorrhagic cysts are most often the result of acute hemorrhage within a follicular adenoma according to pathologic analysis. These lesions appear complex (cystic and solid). Septations and fluid-fluid levels can sometimes be seen in the cystic component. Fluid in a thyroid nodule is most consistent with a degenerating adenoma however, malignancy cannot be excluded.

2.5 Thyroid function tests

2.5.1 Definition:

Thyroid function tests are blood tests used to evaluate how effectively the thyroid gland is working . The thyroid gland function depend on the presence of iodine content Is the most popular test .Because thyroid is the only organ in the body that takes up and uses iodine These tests include the thyroid-stimulating hormone test (TSH), the thyroxine test (T4), the triiodothyronine test (T3), the thyroxine-binding globulin test (TBG), the triiodothyronine resin uptake test (T3RU), and the longacting thyroid stimulator test (LATS).

2.5.2 Purpose:

Thyroid function tests are used to:

• help diagnose an underactive thyroid(hypothyroidism) and an overactive thyroid(hyperthyrodism)

• evaluate thyroid gland activity

• monitor response to thyroid therapy

2.5.3 Precautions

• Thyroid treatment must be stopped one month before blood is drawn for a thyroxine (T4) test.

• Steroids, propranolol (Inderal), cholestyramine (Questran), and other medications that may influence thyroid activity are usually stopped before a triiodothyronine (T3) test.

• Estrogens, anabolic steroids, phenytoin, and thyroid medications may be discontinued prior to a thyroxine-binding globulin (TBG) test. The laboratory analyzing the blood sample must be told if the patient cannot stop taking any of these medications. Some patients will be told to take these medications as usual so that the doctor can determine how they affect thyroxine-binding globulin.

• Patients are asked not to take estrogens, androgens, phenytoin (Dilantin), salicylates, and thyroid medications before having a triiodothyronine resin uptake (T3RU) test.

• Prior to taking a long-acting thyroid stimulant (LATS) test, the patient will probably be told to stop taking all drugs that could affect test results.

2.6 Other test used to diagnose thyroid gland:

2.6.1 Measurement of Serum Thyroid Hormones T4 by RIA: T4 by RIA (radioimmunoassay) is the most used thyroid test of all. It is frequently referred to as a T7 which means that a resin T3 uptake (RT3u) has been done to correct for certain medications such as birth control pills, other hormones, seizure medication, cardiac drugs, or even aspirin that may alter the routine T4 test. The T4 reflects the amount of thyroxin in the blood. If the patient does not take any type of thyroid medication, this test is usually a good measure of thyroid function.

2.6.2 Measurement of Serum Thyroid Hormones T3 by RIA: As stated on our thyroid hormone production page, thyroxin (T4) represents 80% of the thyroid hormone produced by the normal gland and generally represents the overall function of the gland. The other 20% is triiodothyronine measured as T3 by RIA. Sometimes the diseased thyroid gland will start producing very high levels of T3 but still produce normal levels of T4. Therefore measurement of both hormones provides an even more accurate evaluation of thyroid function

2.6.3 Thyroid Binding Globulin: Most of the thyroid hormones in the blood are attached to a protein called thyroid binding globulin (TBG). If there is an excess or deficiency of this protein it alters the T4 or T3 measurement but does not affect the action of the hormone. If a patient appears to have normal thyroid function, but an unexplained high or low T4, or T3, it may be due to an increase or decrease of TBG. Direct measurement of TBG can be done and will explain the abnormal value. Excess TBG or low levels of TBG are found in some families as in hereditary trait. It causes no problem except falsely elevating or lowering the T4 level. These people are frequently misdiagnosed as being hyperthyroid or hypothyroid, but they have no thyroid problem and need no treatment.

2.6.4 Measurement of Pituitary Production of TSH: Pituitary production of TSH is measured by a method referred to as IRMA (immunoradiometric assay). Normally, low levels (less than 5 units) of TSH are sufficient to keep the normal thyroid gland functioning properly. when the thyroid gland becomes inefficient such as in early hypothyroidism, the TSH becomes elevated even though the T4 and T3 may still be within the "normal" range. This rise in TSH represents the pituitary gland's response to a drop in circulating thyroid hormone; it is usually the first indication of thyroid gland failure. Since TSH is normally low when the thyroid gland is functioning properly, the failure of TSH to rise when circulating thyroid hormones are low is an indication of impaired pituitary function. The new "sensitive" TSH test will show very low levels of TSH when the thyroid is overactive (as a normal response of the pituitary to try to decrease thyroid stimulation). interpretations of the TSH level depends upon the level of thyroid hormone; therefore, the TSH is usually used in combination with other thyroid tests such as the T4 RIA and T3 RIA.

2.6.4 TRH Test: In normal people TSH secretion from the pituitary can be increased by giving a shot containing TSH Releasing Hormone (TRH...the hormone released by the hypothalamus which tells the pituitary to produce TSH). A baseline TSH of 5 or less usually goes up to 10-20 after giving an injection of TRH. Patients with too much thyroid hormone (thyroxin or triiodothyronine) will not show a rise in TSH when given TRH. This "TRH test" is presently the most sensitive test in detecting early hyperthyroidism. Patients who show too much response to TRH (TSH rises greater than 40) may be hypothyroid. This test is also used in cancer patients who are taking thyroid replacement to see if they are on sufficient medication. It is sometimes used to measure if the pituitary gland is functioning. The new "sensitive" TSH test (above) has eliminated the necessity of performing a TRH test in most clinical situations.

Table 2.1: shows the normal value of thyroid lab investigation.

Test	Abbreviation	Typical Ranges
Free thyroxin fraction	FT4F	0.03-0.005%
Free Thyroxin	FT4	0.7-1.9 ng/dl
Thyroid hormone binding ratio	THBR	0.9-1.1
Free Thyroxin index	FT4I	4-11

Serum Triiodothyronine	T3	80-180 ng/dl
Serum thyroxin	T4	4.6-12 ug/dl
Serum thyrotropin	TSH	0.5-6 uU/ml
Free Triiodothyronine 1	FT3	230-619 pg/d
Free T3 Index	FT3I	80-180
Radioactive iodine uptake	RAIU	10-30%
Thyroxin-binding globulin	TBG	12-20 ug/dl T4 +1.8 ugm
TRH stimulation test Peak	TSH	9-30 uIU/ml at 20-30 min
Serum thyroglobulin 1	Tg	0-30 ng/m
Thyroid microsomal antibody titer	TMAb	Varies with method
Thyroglobulin antibody titer	TgAb	Varies with method

2.6.5 Thyroid Uptake Test: A means of measuring thyroid function is to measure how much iodine is taken up by the thyroid gland (RAI uptake). Remember, cells of the thyroid normally absorb iodine from our blood stream (obtained from foods we eat) and use it to make thyroid hormone (described on our thyroid function page). Hypothyroid patients usually take up too little iodine and hyperthyroid patients take up too much iodine. The test is performed by giving a dose of radioactive iodine on an empty stomach. The iodine is concentrated in the thyroid gland or excreted in the urine over the next few hours. The amount of iodine that goes into the thyroid gland can be measured by a "Thyroid Uptake". Of course, patients who are taking thyroid medication will not take up as much iodine in their thyroid gland because their own thyroid gland is turned off and is not functioning. At other times the gland will concentrate iodine normally but will be unable to convert the iodine into thyroid hormone; therefore, interpretation of the iodine uptake is usually done in conjunction with blood tests.

2.6.6 Thyroid Scan: Taking a "picture" of how well the thyroid gland is functioning requires giving a radioisotope to the patient and letting the thyroid gland concentrate the isotope (just like the iodine uptake scan above). Therefore, it is usually done at the same time that the iodine uptake test is performed. Although other isotopes, such as technetium, will be concentrated by the thyroid gland; these isotopes will not measure iodine uptake which is what we really want to know because the production of thyroid hormone is dependent upon absorbing iodine. It has also been found that thyroid nodules that concentrate iodine are rarely cancerous; this is not true if the scan is done with technetium. Therefore, all scans are now done with radioactive iodine. Both of the scans above show normal sized thyroid glands, but the one on the left has a "HOT" nodule in the lower aspect of the right lobe, while the scan on the right has a "COLD" nodule in the lower aspect of the left lobe (outlined in red and yellow).

Pregnant women should not have thyroid scans performed because the iodine can cause development troubles within the baby's thyroid gland .two types of thyroid scans are available. A camera scan is performed most commonly which uses a gamma camera operating in a fixed position viewing the entire thyroid gland at once. This type of scan takes only five to ten minutes. In the 1990's, a new scanner called a Computerized Rectilinear Thyroid (CRT) scanner was introduced. The CRT scanner utilizes computer technology to improve the clarity of thyroid scans and enhance thyroid nodules. It measures both thyroid function and thyroid size. A life-sized 1:1 color scan of the thyroid is obtained giving the size in square centimeters and the weight in grams. The precise size and activity of nodules in relation to the rest of the gland is also measured. CTS of the normal thyroid gland In addition to making thyroid diagnosis more accurate, the CRT scanner improves the results of thyroid biopsy. The accurate sizing of the thyroid gland aids in the follow-up of nodules to see if they are growing or getting smaller in size. Knowing the weight of the thyroid gland allows more accurate radioactive treatment in patients who have Graves' disease. Specifically thyroid Scans are used for the following reasons:

• Identifying Nodules and Determining If They Are "Hot" Or "Cold".

• Measuring the size of the goiter prior to treatment.

• Follow-up of thyroid cancer patients after surgery.

• Locating thyroid tissue outside the neck, i.e. base of the tongue or in the chest.

2.6.7 Thyroid Ultrasound scans: Thyroid ultrasound refers to the use of high frequency sound waves to obtain an image of the thyroid gland and identify nodules. It tells if a nodule is "solid" or a fluid-filled cyst, but it will not tell if a nodule is benign or malignant. Ultrasound allows accurate measurement of a nodule's size and can determine if a nodule is getting smaller or is growing larger during treatment.

Ultrasound aids in performing thyroid needle biopsy by improving accuracy if the nodule cannot be felt easily on examination.

2.6.8 Thyroid Antibodies: The body normally produces antibodies to foreign substances such as bacteria; however, some people are found to have antibodies against their own thyroid tissue. A condition known as Hashimoto's Thyroiditis is associated with a high level of these thyroid antibodies in the blood. Whether the antibodies cause the disease or whether the disease causes the antibodies is not known; however, the finding of a high level of thyroid antibodies is strong evidence of this disease. Occasionally, low levels of thyroid antibodies are found with other types of thyroid disease. When Hashimoto's thyroiditis presents as a thyroid nodule rather than a diffuse goiter, the thyroid antibodies may not be present.

2.6.9 Thyroid Needle Biopsy: This has become the most reliable test to differentiate the "cold" nodule that is cancer from the "cold" nodule that is benign ("hot" nodules are rarely cancerous). It provides information that no other thyroid test will provide. While not perfect, it will provide definitive information in 75% of the nodules biopsied. Thyroid nodules increase with age and are present in almost ten percent of the adult population. Autopsy studies reveal the presence of thyroid nodules in 50 percent of the population, so they are fairly common. Ninety-five percent of solitary thyroid nodules are benign, and therefore, only five percent of thyroid nodules are malignant. Common types of the benign thyroid nodules are adenomas (overgrowths of "normal" thyroid tissue), thyroid cysts, and Hashimoto's thyroiditis. Uncommon types of benign thyroid nodules are due to sub-acute thyroiditis, painless thyroiditis, unilateral lobe agenesis, or Riedel's struma. As noted on previous pages, those few nodules which are cancerous are usually due to the most common types of thyroid cancers which are the differentiated" thyroid cancers. Papillary carcinoma accounts for 60 percent, follicular carcinoma accounts for 12 percent, and the follicular variant of papillary carcinoma accounting for six percent. These well differentiated thyroid cancers are usually curable, but they must be found first. Fine needle biopsy is a safe, effective, and easy way to determine if a nodule is cancerous.

Thyroid cancers typically present as a dominant solitary thyroid nodule which can be felt by the patient or even seen as a lump in the neck by his/her family and friends. This is illustrated in the picture above. As pointed out on our page introducing thyroid nodules, we must differentiate benign nodules from cancerous solitary thyroid nodules. While history, examination by a physician, laboratory tests, ultrasound, and thyroid scans (shown in the picture below) can all provide information regarding a solitary thyroid nodule, the only test which can differentiate benign from cancerous thyroid nodules is a biopsy (the term biopsy means to obtain a sample of the tissue and examine it under the microscope to see if the cells have taken on the characteristics of cancer cells). Thyroid cancer is no different in this situation from all other tissues of the body...the only way to see if something is cancerous is to biopsy it. However, thyroid tissues are easily accessible to needles, so rather than operating to remove a chunk of tissue with a knife, we can stick a very small needle into it and remove cells for microscopic examination. This method of biopsy is called a fine needle aspiration biopsy, or "FNA". Cold nodule: Thyroid cells absorb iodine so they can make thyroid hormone out of it. When radioactive iodine is given, a butterfly image will be obtained on x-ray film showing the outline of the thyroid. If a nodule is composed of cells which do not make thyroid hormone (don't absorb iodine) then it will appear "cold" on the x-ray film. A nodule which is producing too much hormone will show up darker and is called "hot". The evaluation of a solitary thyroid nodule should always include history and examination by a physician. Certain aspects of the history and physical exam will suggest a benign or malignant condition. Remember, a biopsy of some sort is the only way to tell for sure.

2.6.10Thyroid fine needle aspiration (FNA) biopsy: is the only non-surgical method which can differentiate malignant and benign nodules in most, but not all, cases. The needle is placed into the nodule several times and cells are aspirated into a syringe. The cells are placed on a microscope slide, stained, and examined by a pathologist. The nodule is then classified as no diagnostic, benign, suspicious or malignant.

No diagnostic indicates that there are an insufficient number of thyroid cells in the aspirate and no diagnosis is possible. A no diagnostic aspirate should be repeated, as a diagnostic aspirate will be obtained approximately 50 percent of the time when the aspirate is repeated. Overall, five to 10 percent of biopsies are no diagnostic, and the patient should then undergo either an ultrasound or a thyroid scan for further evaluation.

Benign thyroid aspirations are the most common (as we would suspect since most nodules are benign) and consist of benign follicular epithelium with a variable amount of thyroid hormone protein (colloid).

2.7 Malignant thyroid aspirations can diagnose the following thyroid cancer types:

papillary, follicular variant of papillary, medullary, anaplastic, thyroid lymphoma, and metastases to the thyroid. Follicular carcinoma and Hurthle cell carcinoma cannot be diagnosed by FNA biopsy. This is an important point. Since benign follicular adenomas cannot be differentiated from follicular cancer (~12% of all thyroid cancers) these patients often end up needing a formal surgical biopsy, which usually entails removal of the thyroid lobe which harbors the nodule. Suspicious cytologies make up approximately 10 percent of FNA's. The thyroid cells on these aspirates are neither clearly benign nor malignant. Twenty five percent of suspicious lesions are found to be malignant when these patients undergo thyroid surgery. These are usually follicular or Hurthle cell cancers. Therefore, surgery is recommended for the treatment of thyroid nodules from which a suspicious aspiration has been obtained. FNA is the first, and in the vast majority of cases, the only test required for the evaluation of a solitary thyroid nodule. (A TSH value should also be obtained to evaluate thyroid function.) Thyroid ultrasound and thyroid scans are usually not required for evaluation of a solitary thyroid nodule. FNA has reduced the cost for evaluation and treatment of thyroid nodules, and has improved yield of cancer found at thyroid surgery. Although a solitary thyroid nodule can enlarge or shrink over time, the natural history of solitary nodules reveals that most nodules change little with it.

2.8 Previous study

- In the study carried by Kamal, (2010), to evaluate the normal range of thyroid uptake and determined the thyroid volume in patients who has normal thyroid function test (T. F.T) & homogenous distribution of the radiotracer in Sudanese especially in Radiation & Isotope Center Khartoum (RICK) &Elnelain Medical Diagnostic Center. This study includes 100 patients (85% female, 15% male) in different age, sex, center of origin and type of food and drink intake, for nine months from May 2009 to Apr 2010. The most frequency of ages distribute as (22-26=15%, 26-30=15%) the thyroid uptake value in the gamma camera (mediso) & (simens), the result of this study showed that, the normal range of thyroid uptake is the range between (0.4% - 4.5%) & the thyroid volume is in the range of (20 cm^2 to 40 cm^2) there was a direct relationship between thyroid uptake and the thyroid volume that when the volume increase the uptake increase that shown in the following equation: $y = -0.33x + 6.07$ where x refers to patient weight in kg and y refers to uptake in percent.

  The result shown that high uptake young patient in age between 18 – 26 years and slightly stable (reasonable high and low) under fifty, then increase to be high again. The increasing of high uptake in age 18 – 26 years known area of changes in hormonal activity to be stable, then it becomes slightly stable till below 50 and after that go to increase.

- The study consisted of 47 normal individuals, 30 women and 17 men, with ages ranging from 19 to 61years (mean of 33 years). The laboratory assessment of thyroid function consisted of serum dosages of ultra-sensitive thyroxin and thyrotrophin. Twenty minutes after an intravenous injection of 10 mCi (370MBq) of ^{99m}Tc-pertechnetate, the images were obtained on a computerized scintillation camera equipped with a low-energy high-resolution parallel holes collimator. All the individuals were euthyroid both on clinical and laboratory evaluation. The baseline thyroid ^{99m}Tc-pertechnetate uptake ranged from 0.4 to 1.7%. the uptake values obtained in these normal individuals showed that 95% presented a thyroid uptake that ranged from 0.4 to 1.5% of the injected dose. The assessment of thyroid structure and function using ^{99m}Tc-pertechnetate is a simple, fast and efficient method, which could easily become a part of the routine studies in nuclear medicine laboratories (Crespo, 1996).

- The uptake of ^{99m}Tc has been recommended as an alternative to a ^{131}I uptake test for the purpose of evaluating thyroid function, one advantage being that ^{99m}Tc, compared with ^{131}I, give a very low radiation dose to the thyroid. The uptake of ^{99m}Tc by the thyroid was measured in 18 normal volunteers and in 22 patients with thyrotoxicosis. Ten of the thyroitoxic patients has not been given any treatment. The remainders were treated with carbimazole for periods varying between one and six months and some of them had also been taking L-thyroxin 0.3 mg daily . the test was usually carried out a few days after the drugs had been discontinued. ^{99m}Tc uptake was also measured in four hypothyroid patients and in ten patients with non-toxic goiter. Scans were carried out with dual detector scanner 9cm diameter sodium iodide crystals of 7-6cm thickness and 19 holes focusing collimators, the collimator focal distance being 15 cm. the collimators were separated by a distance being 15 cm. the collimators were separated by a distance of 30 cm and a thin aluminum filter of 1mm thickness is placed in front of the anterior detector to obtain a depth independent system. In such a system, the count rate per time recorded by the counting equipment depends only on the neck thickness and is independent of the position of the source of radiation at any point between 0.5 – 5.0 cm deep to the anterior surface of the neck. The dose of ^{99m}Tc (0.5 -1.0 mCi) and a standard of between 5% and 10% of the dose were dispensed in 2 ml. syringes and the ratio of the activities between the dose and standard is determined by counting each, using one of the scanner detectors with the collimator removed. The test dose is given intravenously and the scan is started 20 minutes later. The scanning speed is 1-5 cm per second and the scan is completed within 5 minutes. A coloured dot scan and a punch paper tape record of the position of each dot of the scan is obtained. On completion of the scan the antero-posterior neck thickness in the region of the thyroid was measured. The contents of the standard syringe were transferred to a model thyroid gland which is then placed in a tank (20x20x15 cm) containing water to a depth equivalent to 1cm less than the thickness of the neck (see next section). The standard was scanned using the same operating conditions as for scanning the patient and the net number of dots in the standard scan is then determined. The result showed that the mean % of thyroid uptake for hypothyroid, normal, non-toxic goiter, thyrotoxic treated, thyrotoxic untreated were 0.64%, 1.62%, 2.81%, 10% and 11.7% respectively (A tkins and Richards, 1968; Degrossi et al, 1965).

- In this study they compared the thyroid uptake measurement obtained from a gamma camera fitted with a low-energy general –purpose (LEGP) collimator to those obtained from a thyroid uptake probe and gamma camera fitted with a pinhole (PH) collimator. Thirty-one patients (27 female and 4 male patients) were studied for comparison between a probe and a gamma camera fitted with LEGP collimators. A different group of 25 patients (20 female and 5 male patients) were studied for comparsion between LEGP and HP collimators. The patients were given 7.4-11 MBq (200-300 μCi) ^{123}I capsule orally. Uptake with both the probe and the gamma camera was measured at 5h and 24h. the uptake measurements by these 3 methods were compared. Comparison of all the camera uptake values with the probe system correlated well with correlation coefficient values ranging from

0.912 to 0.988. the probe system yielded uptake ratios slightly higher than those measured by the gamma camera with LEGP collimator. Comparison between LEGP and PH uptake values resulted in a correlation coefficient of 0.979 and 0.931 for 24h uptake. Thyroid uptake with a gamma camera fitted with a LEGP collimator can accurately and consistently be used to determine the thyroid uptake of radioactive materials if proper ROIs are applied. In this study researcher used the LEGP collimator with accurate ROI drawing as in RICK protocol and this is good finding (Berman, 1988).

- IAEA (1989) has put forward a number of recommendations for standard uptake measurement. In these recommendation the optimum working distance for uptake measurement has been recommended to be between 20 and 30 cm, which is measured from the surface the NaI (TL) detector to the skin above the isthmus of the gland. The result of the measurement were accurate only when the distance in minimum. Wellman et al, (2005) worked out a method to improve the sensitivity of the uptake system by keeping the detector in contact with the neck and making a correction for the depth. SchuHz and Rollo 2005 described a double distance method for correcting for the depth of the thyroid gland. So a simple method has been suggested for correcting for the depth of thyroid. The counting equipment used in this study was medical sepectrometer (MDS 26) and thyroid uptake probe made by electronic corporation of India Itd, neck phantom of different diameter 8.0, 9.5, 13.0 and 15.5 . these phantom were filled with water to a height of 15 cm to simulate the neck. A Perspex vial of 3cm diameter, and containing 30ml of ^{131}I. solution was supported from the top with a slotted Perspex strip resting horizontally on the polythene bottle. The Perspex vial containing the activity simulate the thyroid gland, and it is depth in the phantom can be varied with a sliding arrangement along the slotted Perspex strips. The percentage decrease in the photo-peak count rate with the increase in the effective depth, the count rate is normalized to 100% at an effective depth of 2.25cm. the ideal distance for accurate uptake measurement is to be 25cm.

- AUGUST, (1972) the study collected Forty-four scans were rejected leaving 256 cases available for analysis. In these 256 patients, the thyroid gland was normal in size by palpation in 159, whereas 97 were felt to have diffuse goiter or a palpably enlarged thyroid mass. It was found that the range of the longitudinal length of the lobes in normal glands varied from 2 to 9 cm. on the right and from 1.5 to 8 cm. on the left. However, in 8o per cent of the cases, the lengths were between 4 to 5.5 cm. The mean length and the standard deviation of the distribution were calculated to be 4.8 ±0.9 cm. on the right and .7 ± 1.0 cm. on the left. In enlarged lobes, the measurements ranged from 4.0 to 11.5 cm. on the right lobe and between 3.5 and 12 cm. on the left lobe. The mean length and standard deviation of the distribution were 6.6 ± 1.3 cm.and 6.4 ± I .4 cm. on the right and left lobes, respectively. The width of the whole gland in the normal size thyroid ranged from 3.5 to 8.o cm. with a mean and standard deviation of 5.2 ±0.7 cm. In enlarged glands, the measurements ranged from 4.5 to 12.5 cm., with the mean and standard deviation of the distribution being 6.5 ± 1.7 cm. Measurements of the widths of the lobes, the height of the isthmus, and axial angle for normal and enlarged glands were found to overlap in most instances. The mean and standard deviation of the measurements are found in Table I. (American Journal of Roentgenology 1972.115:706-708).

Chapter 3

Material and Methods

Chapter Three

Material and Methods

3.1 Materials:

3.1.1 Machine used:

The material used to collect the data were categorized into, nuclear medicine an instrument which is dual head SPECT and whole body gamma camera,NUCINE Spirit (DHV), manufactured by MEDISO company Hungary at 2005. Collimator used low energy general purpose (LEGP), window: 20% and the radiopharmaceutical used the Tc-99m injected intravenously, dose: 5mci (185Mbq) (+,- depending on extremes of body weight).

3.1.2 Radiopharmaceutical uses:

Thyroid gland function and structure can be evaluated using uptake and Scintigraphy studies.

Technetium-99m, in the chemical form of pertechnetate (99m TcO4-), is also used for thyroid Scintigraphy and uptake the similarity of volume and charge between the iodide and pertechnetate ions is the explanation for the uptake of 99m Tc-pertechnetate by the thyroid gland. 99mTc-pertechnetate has been used worldwide to study the thyroid function because of a number of advantage, such as a short half-life (6 hours), short retention in the gland, and no ß- radiation, thus providing low dosimetry to the thyroid gland (10,000 times less than that of ^{131}I-iodide) , as well as to the body as a whole. its gamma photon of 140 kev is ideal for imaging using scintillation cameras and in addition it has low cost and is readily available.

There is an international consensus that the radiopharmaceuticals of choice for thyroid gland imaging are 99m Tc-pertechnetate or ^{123}I-iodide. Although the thyroid does not organify 99mTc- pertechnetate, in the majority of cases the uptake and imaging data provide all the information needed for accurate diagnosis.

in rare instances, ^{123}I-iodide can subsequently be used for assessment of organification defects.

Despite these recommendations, most nuclear medicine laboratories in Brazil choose the radiopharmaceutical ^{131}I-iodide to study the thyroid gland. This practice can in part be explained by the fact that there is a lack of standard values for 99mTc- pertechnetate uptake by the thyroid gland. This study had the aim of standardizing a simple and fast method for performing thyroid uptake and Scintigraphy and defining the 99mTc- pertechnetate uptake values in normal individual (IAEA, 1995).

3.2 Method:

3.2.1 Design of the study:

This is a descriptive study where the data collected prospectively

3.2.2 Population of the study

Adult Sudanese male and female with normal thyroid that showed no sign of abnormality T.F.T in RICK their age ranged from 13 to 60 years old. The sample of this study were consisted of 58 patients with thyroid problem referred to RICK from different hospitals and private clinics in Sudan. The sample includes different tribes and ethnic groups because RICK is the biggest central hospital in Sudan. All the investigations was done in radiation and isotopes center of Khartoum (RICK) including T.F.T and thyroid uptake in the period from December 2016 to May 2017.

Exclusion criteria: All subjects with anterior neck swelling or if there is any clinical evidence of thyroid disease, high or low uptake, non-homogenous of shape or T.F.T abnormal.

3.2.3 Sample size and type

The sample of this study were consisted of 58 patients (54 female and 4 male) their age ranged from 13 to 60 years old with thyroid problem referred to RICK from different hospitals and private clinics in Sudan. The sample includes different tribes and ethnic groups because RICK is the biggest central hospital in Sudan.

3.2.4 Method of data collection:

3.2.4.1 Technique and methods of thyroid uptake:

3.2.4.1.1 Patient preparations:

The patient was prepared according to the following points: patient should stop thyroid media, patient also should stop taking any food contain iodine. If the patient is female, will be inspected if she is pregnancy, the patient will return to their physicians. In case of breast feeding, the patient will be asked to stop feeding for a while until the radioactive substance been execrated from the body. The history of the patient should be taking into account, and the clinical condition should be noted. The related study must be available, which is help full in diagnosis.

3.2.4.1.2 Technique of uptake:

Before the injection of the radioactive dose it must be measure accurately in the dose calibrator, and take a 60 seconds image of the full syringe in the gamma camera. Then inject the dose of 5.0 mci of 99mTcO4 – for adult patient. The dose can be minimizing in case of children or low weight patient using different calculation methods. (it is also can be used to maximize the dose in case of high weight patients). After the injection, 60 seconds image for the empty syringe was taken.The patient waits for 15 minutes, for maximum concentration of sodium pertecnetate.

Firstly 330 K. counts image AP was taken in supine position with pillow under the shoulder and chin hyper extended for good visualizations of thyroid gland; this image is used in calculation of thyroid uptake.

If there an enlarged in the thyroid gland marker with point source 99mTc or 57Co will be used in the supra-sternal notch (S.S.N) to determine the extension of the gland.

If there is suspicious of any disorder in the first image, additional images (RAO, LAO) will be done, or by using the marker in the location of abnormality.

Lastly ROI was drawn around full syringe, empty syringe and AP patient image, the computer program will automatically measure the actual activity injected to the patient by subtract the empty activity from the full, after that it can measure the thyroid uptake using special nuclear medicine program.

The method for the calculation of thyroid uptake, based on images of the gland and syringe counts before and after radiopharmaceutical injection, was previously described by simplified for routine use. The number of counts present in the thyroid (T) was determined by an automatic region of interest (ROI) draw around the borders of the gland. Another ROI was drawn by the same process just below the gland for background subtraction (BG). The counts in the syringe before and after radiopharmaceutical injection were obtained directly from the images. All counts were corrected for the acquisition time and decay of technetium-9m. the thyroid uptake (TU) was calculated automatically by subtraction before & after injection of the radioactive isotopes & background of surround tissues according to the software of the machine in a form of percentage. Berman, M (1988).

3.2.4.2 Variable of data collection:

The data in in this study were collected using the following variable: Age, gender, height, weight, BMI, thyroid uptake, thyroid weight, area of lobes measurement; and thyroid area as well as isthmus.

Table 3.1: Simple Example of Master Data Sheet

Age	Gender	Height	Weight	BMI	Th. Uptake	Th. area	Th. weight	A of Rt. lo	A of Lt. lo

3.2.5 Method of data analysis:

Data will be analyzed by using of Excels Microsoft program, SPSS version 21.0 under windows and Qlik view program, where the mean dimension of each lobe was measured and significant differences between male and female as well as sample was made including the difference between the area of thyroid and BMI. Also correlation and linear relationship between thyroid measurements and body characteristics were investigated.

3.3 Ethical approval:

The study has been approved by college research board and participant were verbally agreed to participate in the study.

Chapter Four

Result

Chapter Four
Results

The following tables and figures presented the data obtained from 58 patients (54 female & 4 male) Sudanese , aged from 13 to 60 years old , all were examined by Thyroid Scintigraphy.

Table 4.1: show the frequency of gender

Gender	Frequency
Male	4
Female	54
Total	58

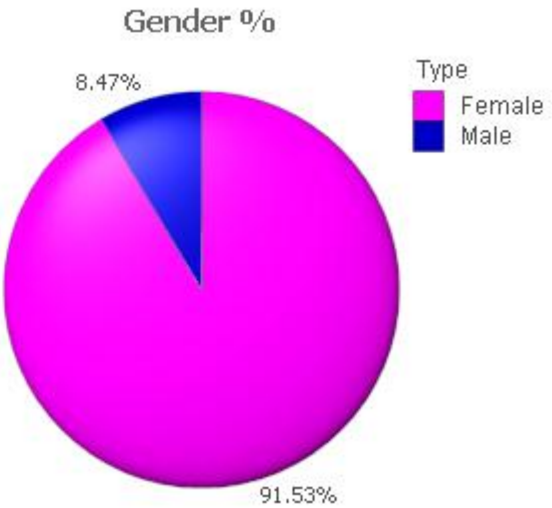

Figure 4.1: a pie graph shows the frequency distribution of male to female percentage

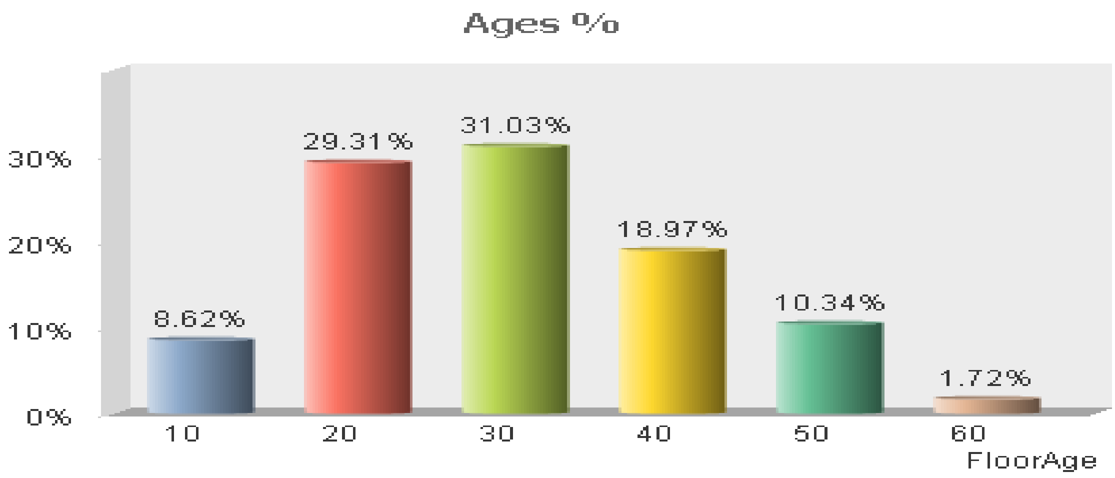

Figure 4.2: par graph show the frequency distribution of patient age

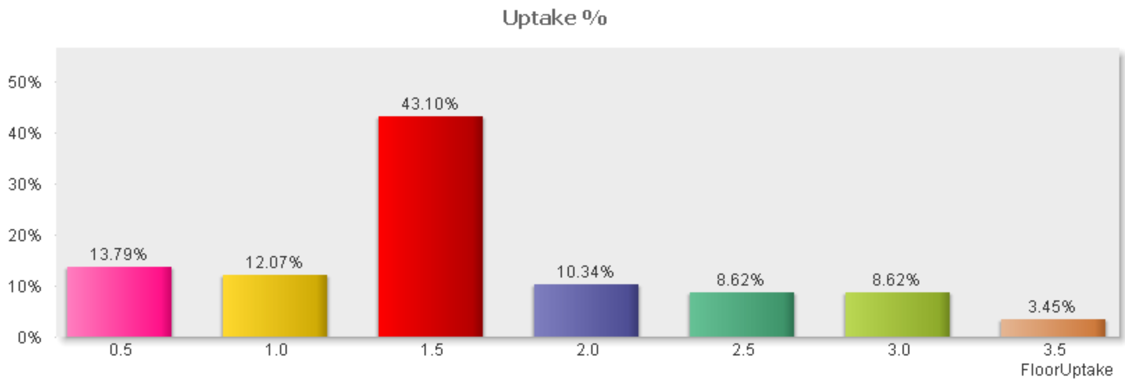

Figure 4.3:shows the frequency distribution of Thyroid uptake

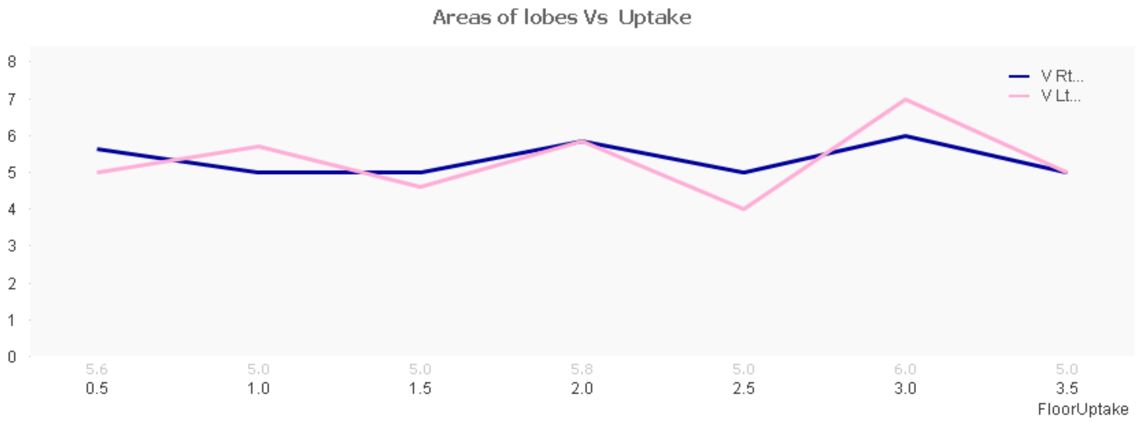

Figure 4.4: line chart shows the relation between the Areas of Rt. & Lt. lobes VS Thyroid Uptake

Table 4.2:showthe Minimum, Maximum, median and mean ± SD of the variables.

Variables	Minimum	Maximum	Median	Mean ± SD
Age	13	60	32	33.6±11
Weight	29	125	70	70.9±19.6
Height	147	180	160	160.6±6.97
BMI	12.1	40.4	27.39	26.7±7.92
Thyroid Uptake	0.77	3.77	1.85	1.93±0.76
Thyroid Area	12.7	30.1	19.05	19.3±3.78
Thyroid Weight	2.6	17.5	6.20	7.04±3.09
Area of Rt lobe	4.8	12	7.40	7.7±1.65
Area of Lt lobe	3.3	12.7	6.75	7.1±1.84

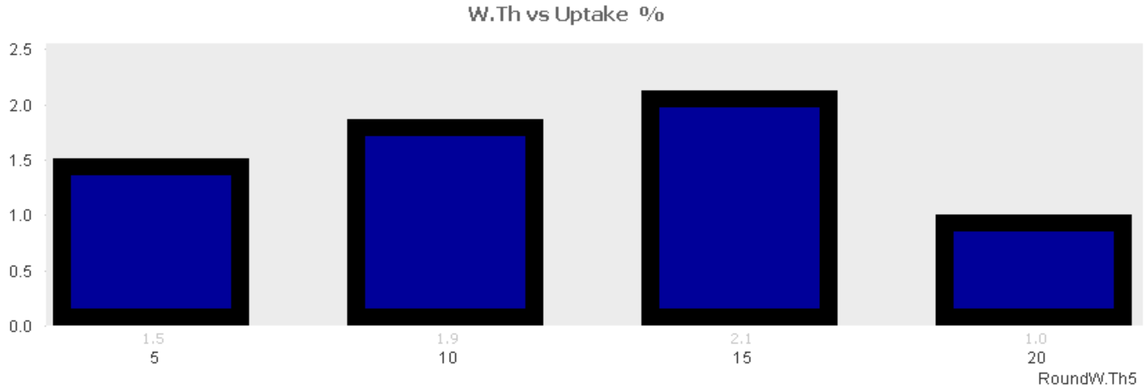

Figure 4.5:shows the distribution between Thyroid Weight & Uptake

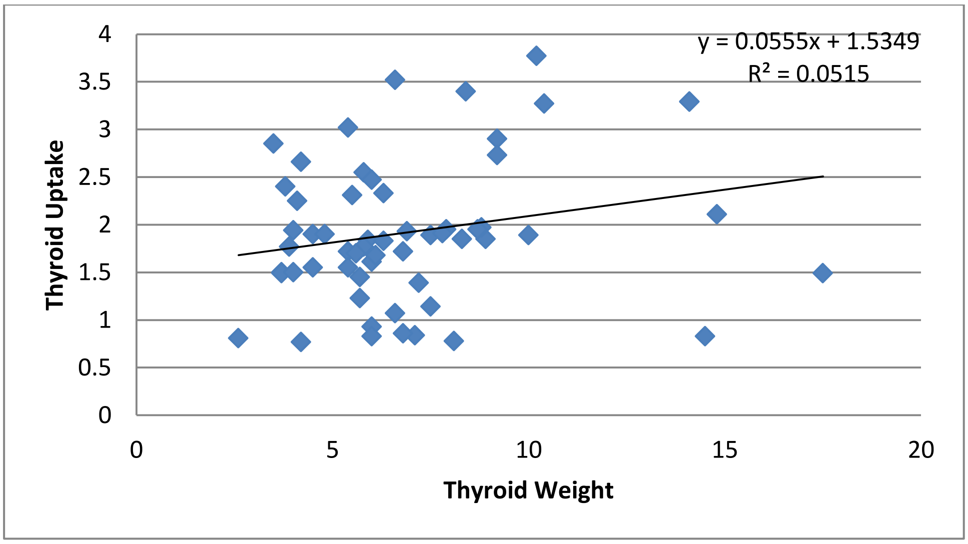

Figure 4.6: scatter plot shows Thyroid Weight of the linear relationships between Thyroid Uptake & Thyroid Weight.

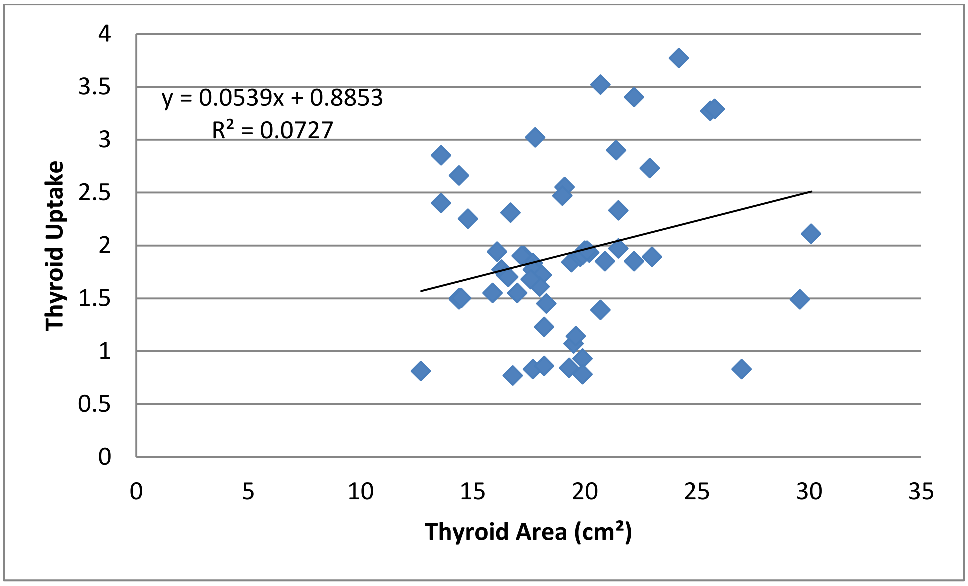

Figure 4.7 shows the correlation between Thyroid Uptake & Thyroid Area

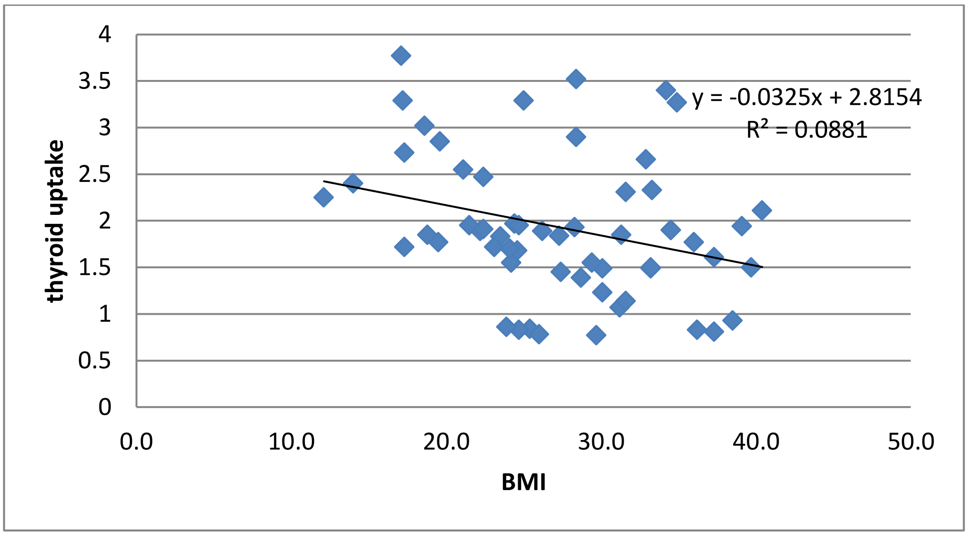

Figure 4.8 shows the correlation between Thyroid Uptake & BMI

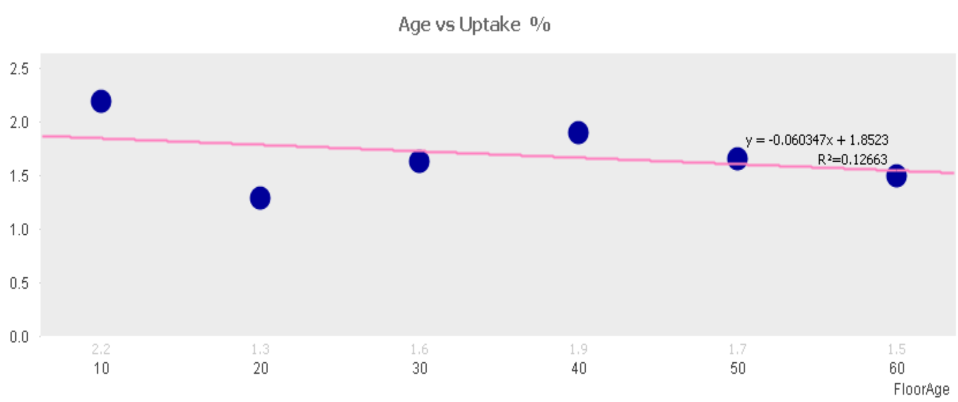

Figure 4.9 shows the correlation between Thyroid Uptake & Age

Table 4.3: show the BMI, frequency & AVG uptake

BMI	Center of class	Frequency	AVG uptake
12--16	14	2	2.33
17-21	19	9	2.62
22-26	24	17	1.71
27-31	29	12	1.75
32-36	34	12	2.04
37-41	39	6	1.48

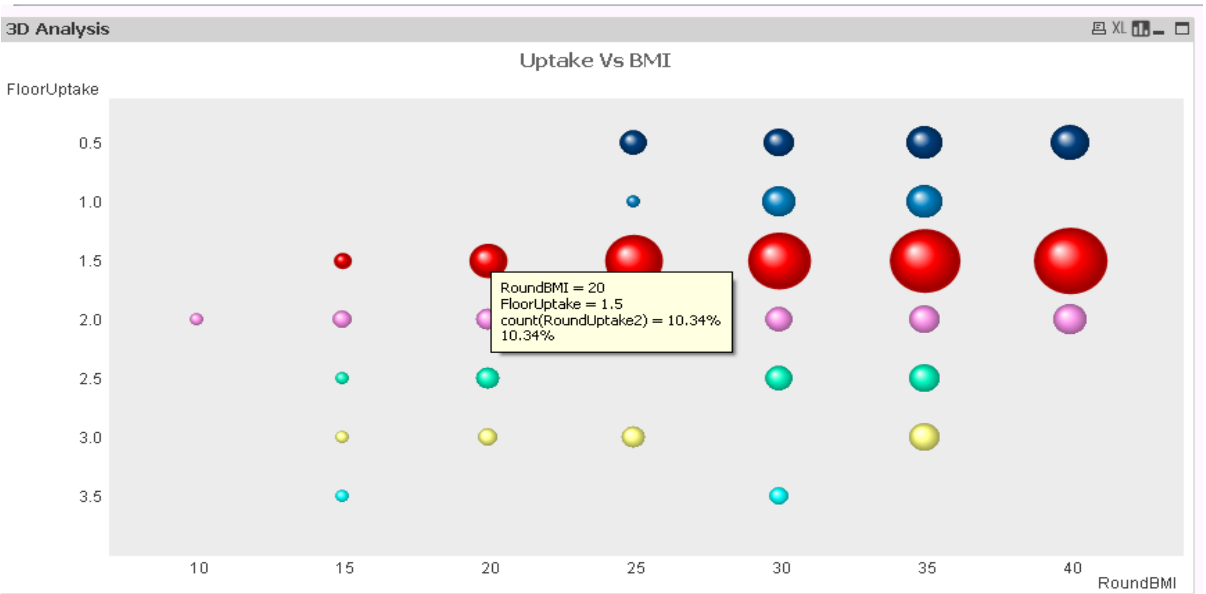

Figure 4.10 shows the distribution between Uptake & BMI & count of uptake%

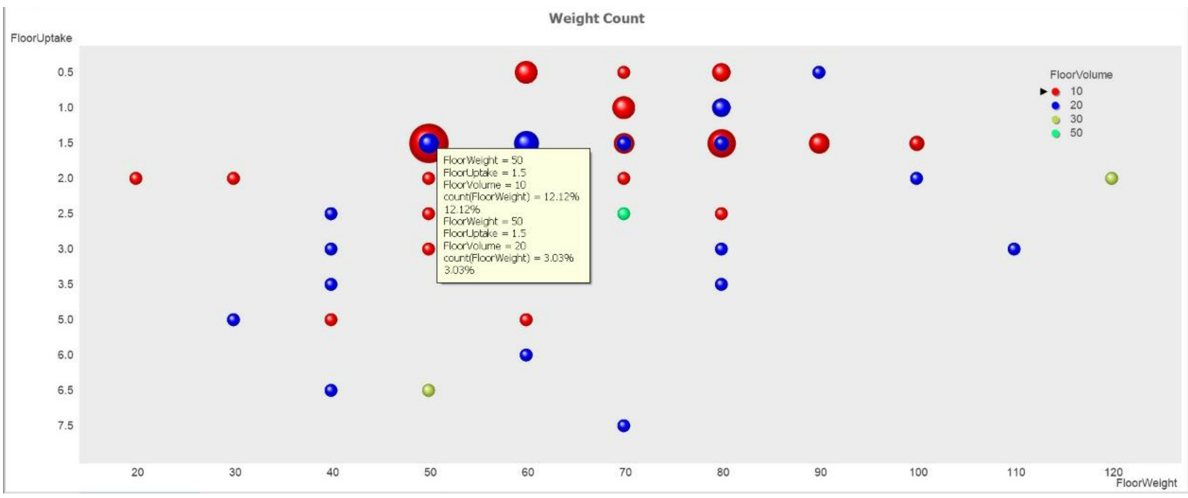

Figure 4.11 shows the distribution between Uptake, weight of patient, thyroid area & count of uptake%

Chapter Five

Discussion, Conclusion and Recommendation

Chapter Five

Discussion, Conclusion and Recommendation

5.1 Discussion:

The aim of this study was to estimate the reference values of total thyroid Area based on uptake measurements of thyroid gland for patient found T.F.T normal , to standardize a simple and fast methodology for performing Thyroid Uptake & Thyroid Area, and to determine the normal values for 99mTc-pertechnetate uptake.

The result of this study showed in figure 4.1 shows the distribution of sample based on their gender. Such study reveal that 91.5% of the sample under study were female relative to 8.5% as male, the high incidence of thyroid problems among female expected due to hormones disturbance in female rather than male (John Peter, 1996). Also this result is in agreement with study done by (Alexander, 2006).

Figure 4.2 shows the frequency distribution of age of patients within the sample of study, as shown that the high incidence of thyroid disorder was among the ages of 25-35 year about 31%. The high incidence among the age groups of 22-38 year is due to thyroid hormone problem in the young patient and binding that with the activities which done in this level of age (Berman, 1988)

Figure 4.4 shows the right lobe area was significantly homogenous from left lobe area VS Thyroid uptake

Figure 4.6 shows the relationship between the thyroid uptake and the thyroid weight. The study reveals that the thyroid uptake increases with increasing of thyroid weight. The correlation could be fitted in the following equation : $y = 0.056x + 1.53$ where x refers to thyroid weight and y refers to uptake in percent.

Figure 4.7 shows the relationship between the thyroid uptake and the thyroid area. The study reveals that the thyroid uptake increases with increasing of thyroid size,because the enlargement of thyroid area which means a lot off trapping of iodineion in human body (Berman, 1988). The correlation could be fitted in the following equation : $y = 0.054x + 0.89$ where x refers to thyroid area and y refers to uptake in percent.

Figure 4.8 which distribute the relationship between the thyroid uptake and Body Mass Index of the patients. The data showed that: the uptake of thyroid increase by decrease BMI in inverse relation and correlation could be fitted in the following equation : $y = -0.033x + 2.82$ where x refers to BMI in kg and y refers to uptake in percent.

Figure 4.9 which distribute the relationship between the thyroid uptake and age of the patients. The data showed that: the uptake of thyroid decrease by increase age in inverse relation and correlation could be fitted in the following equation : $y = -0.06x + 1.85$ where x refers to age in kg and y refers to uptake in percent.

The study also show that thyroid area was best correlated with body weight, BMI and with age.

The results support the notion that iodine insufficiency, in the county of Sudan, has been substantially improved over the last decade. This especially after the recent household salt iodization took place.

5.2 Conclusion

The thyroid gland affected by the presence or absent of iodine, according to amount of iodine in the body the gland cells can be depresses or enlargement. This situation of gland cells can be investigated with thyroid uptake test which measure the amount of iodine trapped by thyroid cells. This study includes 58 patients the patients (54 female and 4 male) with homogenous distribution of the radiotracer in the result of uptake and normal thyroid function test (T.F.T) in the age between 13 to 60 years and dose of 5 mci were investigated via thyroid uptake by using gamma camera SPECT system with ^{99m}Tc- pertechnetate.

The result of this study showed that the uptake of thyroid gland for patient with normal thyroid function test (T.F.T) and homogenous distribution of the radiotracer is in the range of 0.77% to 3.8%; by measuring the thyroid Area in this study for patients that with homogenous distribution of the radiotracer & normal thyroid function test (T.F.T) (mean of normal range of these patients T3 80 -180 ng/dl, T4 4.6-12 ug/dl & TSH 0.5-6.0 nu/L) in Radiation and Isotope Center Khartoum (RICK) and is in range of (12.7 cm^2 - 30.1 cm^2).

5.3 Recommendation:

This study would like to highlight some points in a form of recommendation as follow:-

- ❖ Further study should do with very larger sample to explain the normal range of thyroid uptake as well as to these result in thyroid with homogenous distribution of radiotracer (without nodules).
- ❖ Care must be taken in bringing of Gamma Camera machine about capability of uptake measurement and distribution.
- ❖ The dose of ^{99m}Tc must be accurately adjusted suing Q.C passed dose calibrator with constant factor for radioactive decay.
- ❖ The dose also can be exceeded up to 4.0 mci to evaluate the uptake.
- ❖ The distance between the patient head and gamma camera detector must be constant.
- ❖ The time between patient injection and imaging must be constant at 20 min for all subject that may include in other studies.
- ❖ Measurement of thyroid area should consider the iodine deficiency. Larger thyroid further study with larger size, sample size and duration should be done to assess thyroid area for Sudanese female.

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Appendix

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HOSPITAL NAME
Hospital address

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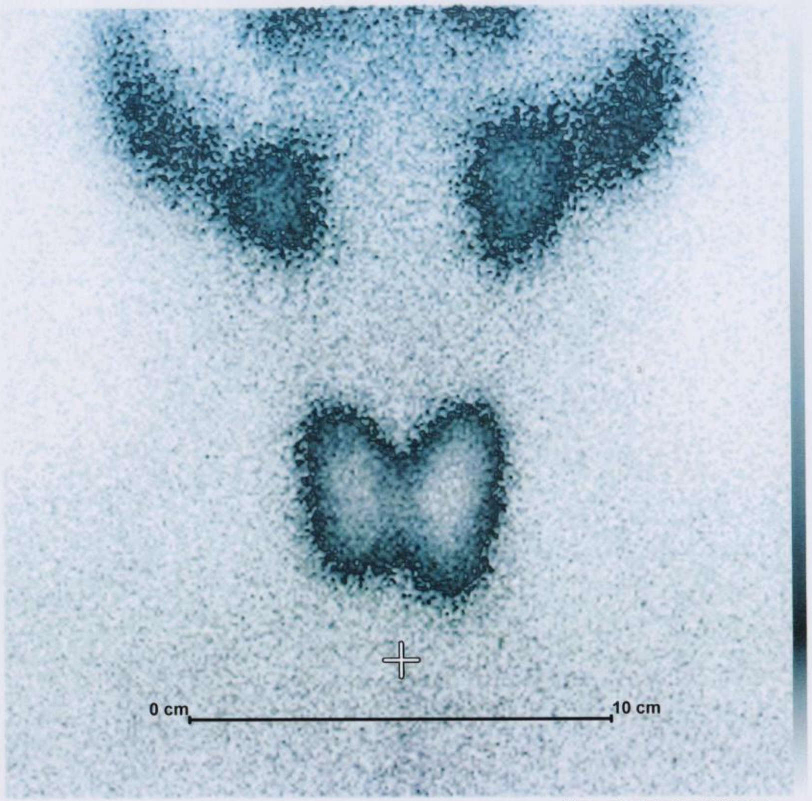

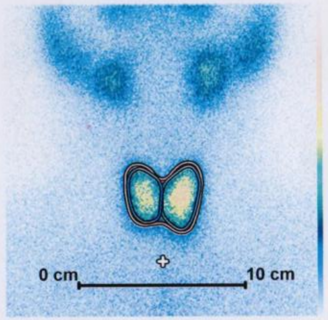

Count density of Full Thyroid

Count rate	**248.47 cps**
Area	15.5 cm2
Count density	16.01 cps/cm2
Max count density	46.01 cps/cm2
Normalized uptake	0.0997 %/cm2

Size estimation summary

Thyroid weight	**5.0 g**
Area of Full Thyroid	15.5 cm2
Area of Left Lobe	6.9 cm2
Area of Right Lobe	5.5 cm2

Uptake calculation summary

Roi	Uptake	Upt. to Full Thyr.
Full Thyroid	1.55 %	100.00 %
Left Lobe	0.81 %	52.22 %
Right Lobe	0.58 %	37.47 %

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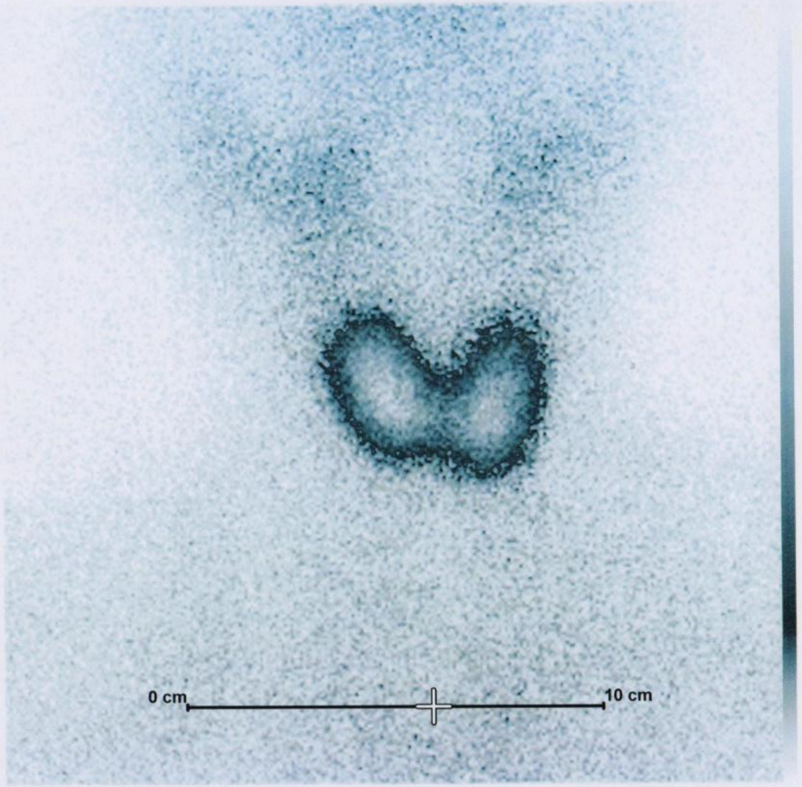
Delay after injection: 20.0 min

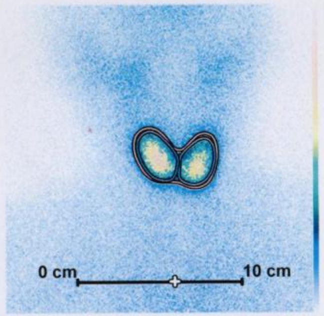
Mediso Imaging Systems

Patients [1] - Patient Name:

HOSPITAL NAME
Hospital address

Acquisition date: 5/8/2017 12:17:00 PM





Size estimation summary

Thyroid weight	**3.8 g**
Area of Full Thyroid	13.6 cm2
Area of Left Lobe	5.1 cm2
Area of Right Lobe	5.6 cm2

Uptake calculation summary

Roi	Uptake	Upt. to Full Thyr.
Full Thyroid	2.40 %	100.00 %
Left Lobe	0.97 %	40.25 %
Right Lobe	1.17 %	48.82 %

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Delay after injection: 25.0 min

Mediso Imaging Systems

Patients [1] - Patient Name: [illegible]

HOSPITAL NAME
Hospital address

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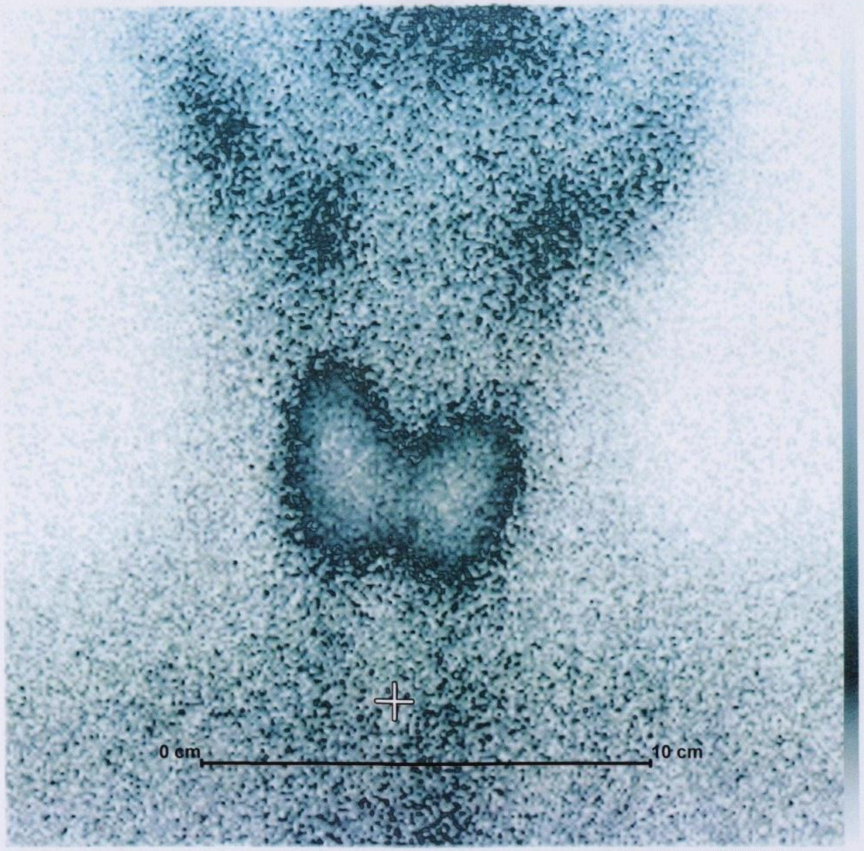

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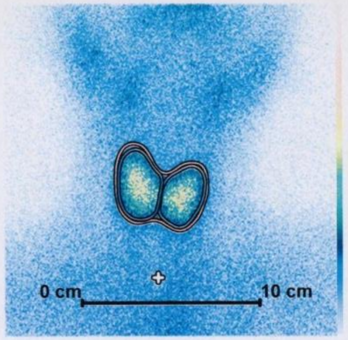


Size estimation summary

Thyroid weight	**6.5 g**
Area of Full Thyroid	18.3 cm2
Area of Left Lobe	7.0 cm2
Area of Right Lobe	8.0 cm2

Uptake calculation summary

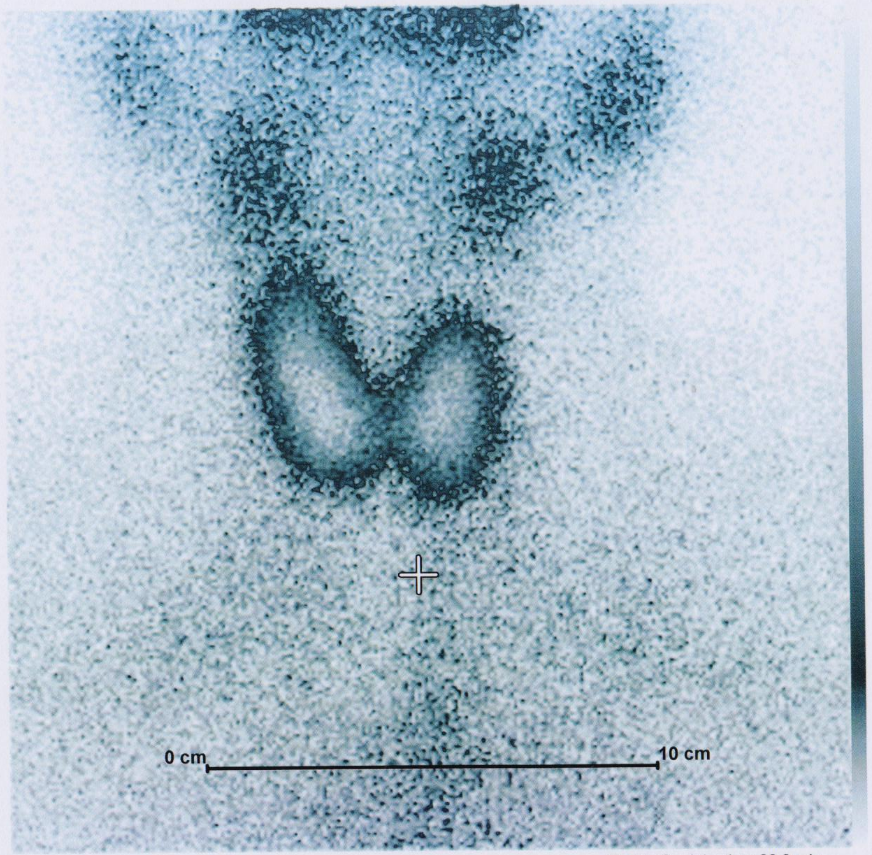
Roi	Uptake	Upt. to Full Thyr.
Full Thyroid	0.95 %	100.00 %
Left Lobe	0.39 %	41.35 %
Right Lobe	0.47 %	49.28 %

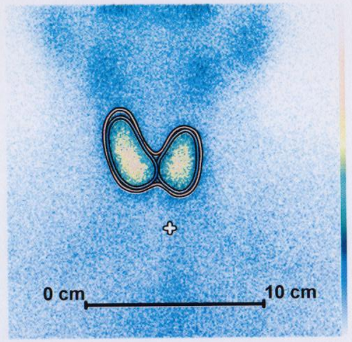
Mediso Imaging Systems

Patients [1] - Patient Name:

HOSPITAL NAME
Hospital address

Acquisition date: 5/8/2017 12:17:00 PM





Size estimation summary

Thyroid weight	**6.1 g**
Area of Full Thyroid	17.6 cm2
Area of Left Lobe	6.2 cm2
Area of Right Lobe	7.7 cm2

Uptake calculation summary

Roi	Uptake	Upt. to Full Thyr.
Full Thyroid	1.74 %	100.00 %
Left Lobe	0.67 %	38.35 %
Right Lobe	0.89 %	50.99 %

Delay after injection: 20.0 min

System - Current Date-Time: 5/10/2017 4:28:55 PM

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