Chapter One

1.1 Introduction

Scientific research is ever developing day after day especially that concerning with organ and glands in human bodies and there function to get diagnostic procedure tools as well as therapeutic if any disease affects them.

Geographical location-specific reference data for thyroid uptake of technetium-99m pertechnetate are rare and vary significantly[1-3]. Therefore, there is a need to establish reference values for each location.The purpose of this study was to evaluate the normal values for ^{99m}Tc- pertechnetate uptake in patients with normal thyroid function test (T.F.T) & homogenous distribution of the radiotracer in Sudan .

The thyroid gland is the most significant organs of the endocrine system and is located in front of the trachea and below the larynx. The main function of thyroid gland is the production of thyroid hormones. The major form of thyroid hormone in the blood is thyroxine (T4), which has a longer half-life than Triiodothyronine (T3). Thyroid hormones regulate the basal metabolic rate and also influence many bodily functions, such as physical growth and development, adolescence, organ function, fertility and body temperature. Thyroid hormones secreted from the gland are T4 is about 80-90% and T3 is about 10-20% [4, 5]. The thyroid gland uses iodine from food to make the hormones. According to the latest estimates, about 2.5 billion people worldwide (38% of the world's population) have insufficient iodine intake, of which 313 million are in the Southeastern Asian region that includes Bangladesh. The widespread severe iodine deficiency in all ecological zones indicates that the country as a whole is an iodine deficient region. An iodine deficiency thyroid disorder is still one of the major public health problems in Bangladesh. In 1993, a nationwide iodine deficiency disorders (IDD) survey of Bangladesh was conducted. This report showed that about 47.1% of our population had symptoms of goiter and nearly 69% population has biochemical iodine deficiency. Iodine deficiency remains the main cause of hypothyroidism worldwide [6,7].

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) (Yildirim M, 2006, 36). 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.

The suboptimum level of thyroid dysfunction could lead to some diseases or other pathological states in the human bodies such as (hyperthyroidism, hypothyroidism, thyrotoxicosis, thyroditis ... etc) Yildirim M, 2006, [20].

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)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. Yildirim M, 2006, [20].

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 areas 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 vary from town to town and there is even great variation in the water resources and water content within the same town. Yildirim M, 2006, [20].

1.2 Iodine deficiency in Sudan:

The Sudan has been reported as an endemic goiter area by woodman in *1982*. He described a small area inhabited by the Zandi group in southern Sudan near the border with Congo Democratic Republic (Zaire). He also described other neighboring areas with a high goiter incidence in the south of malakal among the Newir tribe around El-Darner in the Northern Province and in Dar-Fur Kambal completed an extensive survey in *2005* comprising 17470 people in Dar-Fur province (Western Sudan) and found that 57% were goiterous and that l8.5% of these have large goiter. In Khartoum 12.6% of 5566 subjects have goiter. Recently Eltom et al, *2010*, [112] have shown that the incidence of endemic goiter among school-children in Dar-Fur is 85 % and also in central of Sudan (Kosti) is considered as an area of Endemicity. Bafarag et al, *2011*, [43] have estimated that 14 million of the 25 million inhabitants of Sudan are at risk of having iodine deficiency which consequently leading to thyroid problem. Here in this research the discussion about the assessment of the normal range of thyroid uptake with homogenous distribution of the radiotracer in Sudan in a form of percentage will be highlighted At least 1 in 10 women could be expected to suffer from some sort of thyroid disorder during her lifetime, whether thyroid disorders strike at puberty, during peak reproductive years, during or after her pregnancy, around menopause, or after 60 years old, a women's body is uniquely and dramatically affected Cameron et al, 1992, [23]. However, the presence of hyperthyroidism or hypothyroidism favors a benign nodule (that's why a "warm" nodule or a "hot" nodule favors a benign condition). Thyroglobulin levels are useful tumor markers once the diagnosis of malignancy has been made, but are nonspecific in regard to differentiating a benign from a cancerous thyroid nodule.

Ultrasound accurately determines thyroid gland volume, number and size of nodules; separates thyroid from nonthyroidal masses; helps guide fine needle biopsy when necessary; and can identify solid nodules as small as 3 mm and cystic nodules as small as 2 mm. Although several ultrasound features favor the presence of a benign nodule, and other ultrasound features favor the presence of a cancerous nodule. Ultrasound alone cannot be used to differentiate benign from malignant nodules. And since 15 percent of cystic thyroid nodules are malignant, ultrasound determination that a nodule is cystic does not rule out thyroid cancer.

Nodules detected by thyroid scans are classified as cold, hot or warm. Eighty-five percent of thyroid nodules are cold, 10 percent are warm, and five percent are hot, but remember that 85 percent of cold nodules are benign, 90 percent of warm nodules are benign, and 95 percent of hot nodules are benign. Although thyroid scanning can give a probability that a nodule is benign or malignant, it cannot truly differentiate benign or malignant nodules and usually should not be used as the only basis for recommending treatment of the nodule, including thyroid surgery Cameron et al, 1992, [16].

1.2Diagnosis

1.2.1 Measurement of Serum Thyroid Hormones T4 by RIA:

The T4 measurement by RIA (radioimmunoassay) is the most used thyroid test of all.. 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.

1.2.2 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 tri iodothyronine 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.

1.2.3 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 13w 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). An interpretation of the TSH level depends upon the level of thyroid hormone; therefore, the TSN is usually used in combination with other thyroid tests such as the T4 R1A and T3 RIA Bracer, 1989, [25].

1.2.4 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 r 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 sand 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 Berman, 1988, [15].

1.2.5 Thyroid Ultrasound:

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.

1.2.6 Problem of the study:

Here in Sudan especially in Radiation and Isotopes Center - Khartoum & Elnelain Medical Center 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. Also in contrast with the European level (0.4 - 4.0%) Cameron.et 1992, [16] there is some differences, according to these the researchers is trying to obtain normative data for Sudanese.

1.2.7 **The general objective of this study is:**

• To estimate normal homogenous thyroid uptake for Sudanese.

The specific objectives of this study are:

• To measure the thyroid volume for patients with homogenous distribution of radiotracer & normal thyroid function test (T.F.T).

- To estimate the relationship between the thyroid uptake & thyroid volume.
- To evaluate the relationship between the thyroid uptake & age of patients.
- To evaluate the relationship between the thyroid uptake & TFT.

1.2.8 Thesis out line:

This study falls into 5 chapters with chapter one is an introduction which include the tools used for investigation of thyroid disorder, problem of the study, purpose of the study, objective of the study and the overview of the study. Chapter two include theoretical background and literature review, while chapter three demonstrate the method and material used in this study, chapter four include presentation of the result and finally chapter five include the discussion ,recommendation and references list.

Chapter Two

Literature review

2.1 Anatomy of the Thyroid Gland

Thyroid glands are located in the neck, in close approximation to the first part of the trachea. In humans, the thyroid gland has a "butterfly" shape, with two lateral lobes that are connected by a narrow section called the isthmus as shown in Figure (2.1). Most animals, however, have two separate glands on either side of the trachea. Thyroid glands are brownish-red in color.

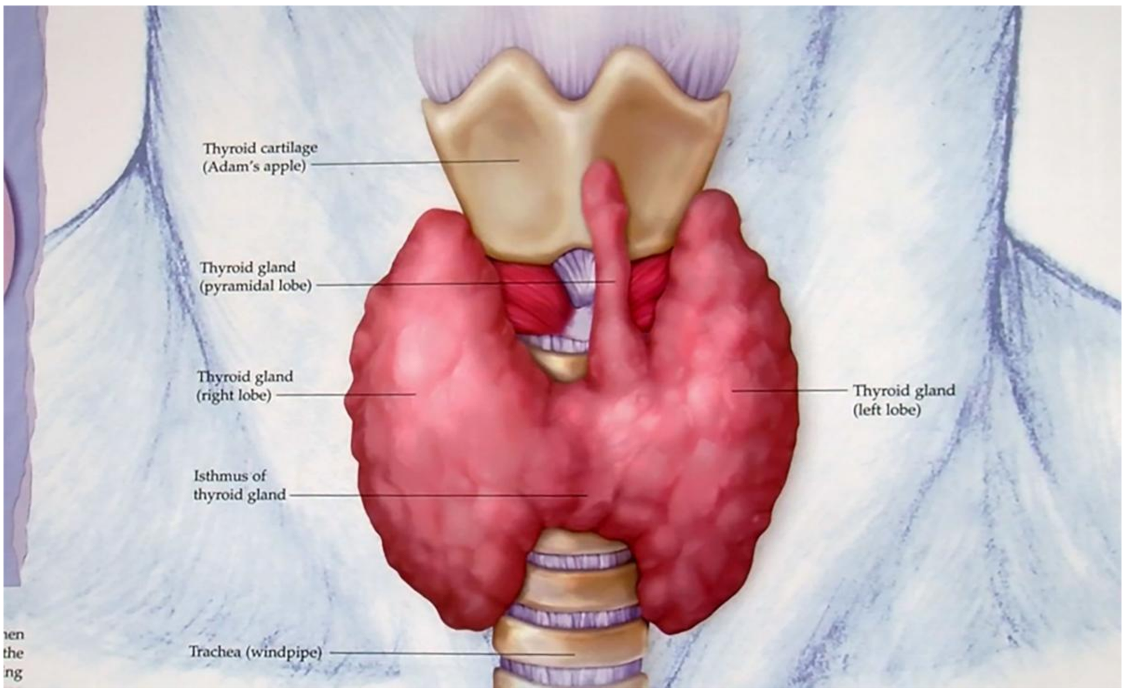

Figure 2.1: Human thyroid gland in the body

Anatomy of a thyroid gland will reveal one or more small, light-colored nodules on or protruding from its surface - these are parathyroid glands (meaning "beside the thyroid"). The image to the right shows a canine thyroid gland and one attached parathyroid gland. His 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. In the low (left) and high-magnification (right) images of a cat thyroid below, follicles are cut in cross section at different levels, appearing as roughly circular forms of varying size as shown in Figure (2.2). In standard histological preparations such as these, colloid stains pink.

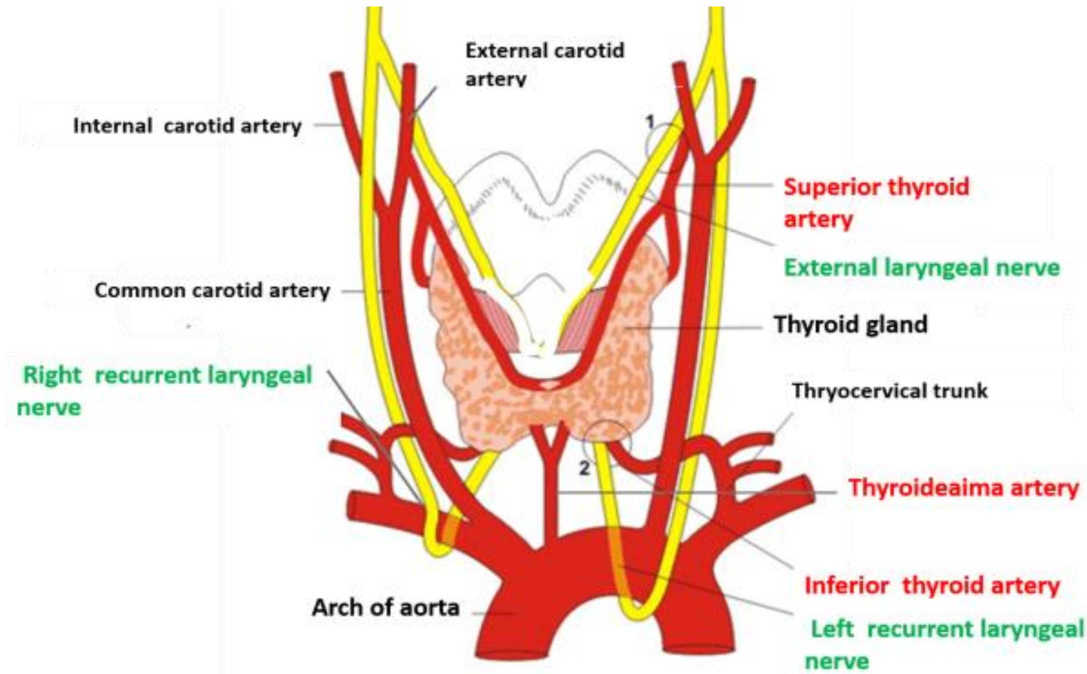

Figure 2.2: the blood supply for thyroid gland

2.1.1: Blood supply:

The arteries to the thyroid gland are (a) the superior thyroid artery, (b) the inferior thyroid artery, and sometimes (c) the thyroideaima. The arteries anastomose profusely with one another over the surface of the gland.

The superior thyroid artery, a branch of the external carotid artery, descends to the upper pole of each lobe, accompanied by the external laryngeal nerve. The inferior thyroid artery, a branch of the thyrocervical trunk, ascends behind the gland to the level of the cricoids cartilage. It then turns medially and downward to reach the posterior posterior border of the gland.

The recurrent laryngeal nerve crosses either in front of or behind the artery, or it may pass .between its branches.

The thyroidaema, if present, may arise from the brachiocephalic artery or the arch of the aorta. It ascends in front of the trachea to the isthmus.

The veins from the thyroid gland are (1) the superior thyroid, which drains into the internal jugular vein; (2) the middle thyroid, which drains into the internal jugular vein and (3) the inferior thyroid. The latter vein receives its tributaries from the isthmus and the lower poles of the gland. The inferior thyroid veins of the two sides anastomose with one another as they descend in front of the trachea. They drain into the left brachiocephalic vein in the thorax, such blood supply and verves trees are shown in Figure (2.2)

2.1.2: Lymph drainage:

The lymphatic follow the arteries from the upper pole they enter the anterior superior group of the deep cervical lymph nodes from the lymph pole they pass with the inferior thyroid artery back to its point of origin from the subclavian behind the carotid sheath into posterior inferior.

2.1.3: Nerve supply:

The bulk of the sympathetic (vasoconstrictor) supply is derived from the middle cervical ganglion and enters some fibers from the superior cervical ganglion.

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. The image below shows a section of a feline parathyroid gland on the left, associated with thyroid gland (note the follicles) on the right Barrere, *2000, [21]*

2.2 Physiology of Thyroid Gland

2.2.1 Synthesis and Secretion of Thyroid Hormones:-

Thyroid hormones are synthesized by mechanisms fundamentally different from what is seen in other endocrine systems. Thyroid follicles Serve as both factory and warehouse for production of thyroid hormones.

2.2.2 Constructing Thyroid Hormones:

The entire synthetic process occurs in three major steps, which are, at least in some ways, analogous to those used in the manufacture of integrated circuits (ICs): Production and accumulation of the raw materials (in the case of ICs, a large wafer of doped silicon) Fabrication or synthesis of the hormones on a backbone or scaffold of precursor (etching several ICs on the silicon wafer) Release of the free hormones from the scaffold and secretion into blood (cutting individual ICs out of the larger wafer and distributing them)

2.2.3 The recipe for making thyroid hormones calls for two **principle ?raw materials:** Tyrosine's are provided from a large glycoprotein scaffold called thyroglobulin, which is synthesized by thyroid epithelial cells and secreted into the lumen of the follicle - colloid is essentially a pool of thyroglobulin. A molecule of thyroglobulin contains 134 tyrosine, E although only a handful of these are actually used to synthesize T4 and T3.

Iodine, or more accurately iodide (1-), is avidly taken up from blood by thyroid epithelial cells, which have on their outer plasma membrane a sodium-iodide symporter or "iodine trap". Once inside the cell, iodide is transported into the lumen of the follicle along with thyroglobulin as shown in Figure (2.3)

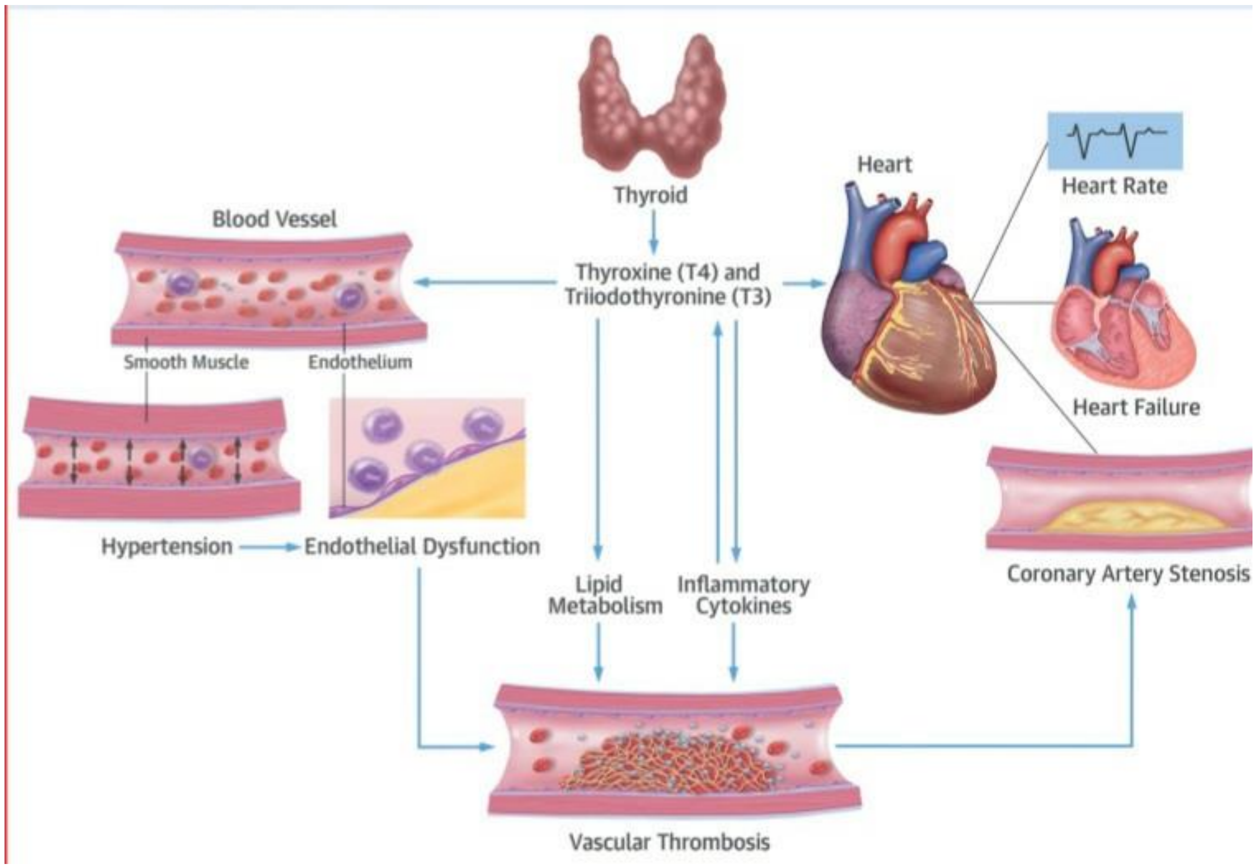

Figure 2.3 mechanism of thyroid hormones synthesis

Fabrication of thyroid hormones is conducted by the enzyme thyroid peroxides, an integral membrane protein present in the apical (colloid-facing) plasma membrane of thyroid epithelial cells. Thyroid peroxides catalyzes two sequential reactions:

lodination of tyrosines on thyroglobulin (also known as “organification of iodide”).

Through the action of thyroid peroxidase, thyroid hormones accumulate in colloid, on the surface of thyroid epithelial cells. Remember that hormone is still tied up in molecules of thyroglobulin - the task remaining is to liberate it. from the scaffold and secrete free hormone into blood.

Thyroid hormones are excised from their thyroglobulin scaffold by digestion in lysosomes of thyroid epithelial cells. This final act in thyroid hormone synthesis proceeds in the following steps:

Thyroid epithelial cells ingest colloid by endocytosis from their apical borders - that colloid contains thyroglobulin decorated with thyroid hormone.

Colloid-laden endosomes fuse with lysosomes, which contain hydrolytic enzymes that digest thyroglobluin, thereby liberating free thyroid hormones.

Finally, free thyroid hormones apparently diffuse out of lysosomes, through the. basal plasma membrane of the cell, and into blood where they quickly bind to carrier proteins for transport to target cells.

2.2.4Thyroid Hormone Receptors:

Receptors for thyroid hormones are members of a large family of nuclear receptors that include those of the steroid hormones. They function as hormone-activated transcription factors and thereby act by modulating gene expression. In contrast to steroid hormone receptors, thyroid hormone receptors bind DNA in the absence of hormone, usually leading to transcriptional repression. Hormone binding is associated with a conformational change in the receptor that causes it to function as a transcriptional activator.

2.2.5 Receptor Structure:

Mammalian thyroid hormone receptors are encoded by two genes, designated alpha and beta. Further, the primary transcript for each gene can be alternatively spliced, generating different alpha and beta receptor isoforms. Currently, four different thyroid hormone : receptors are recognized: alpha-1, alpha-2, beta-1 and beta-2, Like other members of the nuclear receptor super family, thyroid hormone receptors encapsulate three functional domains:

2.2.5.1A Tran’s activation domain:

At the amino terminus that interacts with other transcription factors to form complexes: that suppress or activate transcription. There is considerable divergence in sequence of the Tran activation domains of alpha and beta isoforms and between the two beta isoforms of the receptor.

2.2.5.2A DNA-binding domain:

DNA-binding domain which binds to sequences of promoter DNA is known as hormone response elements.

2.2.5.3 A ligand -binding and dimerization domain at the carboxy-terminus.

As depicted in the figure below, the DNA-binding domains of the different receptor isoforms are very similar, but there is considerable divergence among Tran activation and 1igand-binding domains. Most notably, the alpha-2 isoform has a unique carboxy-terminus and does not bind triiodothyronine (T3).

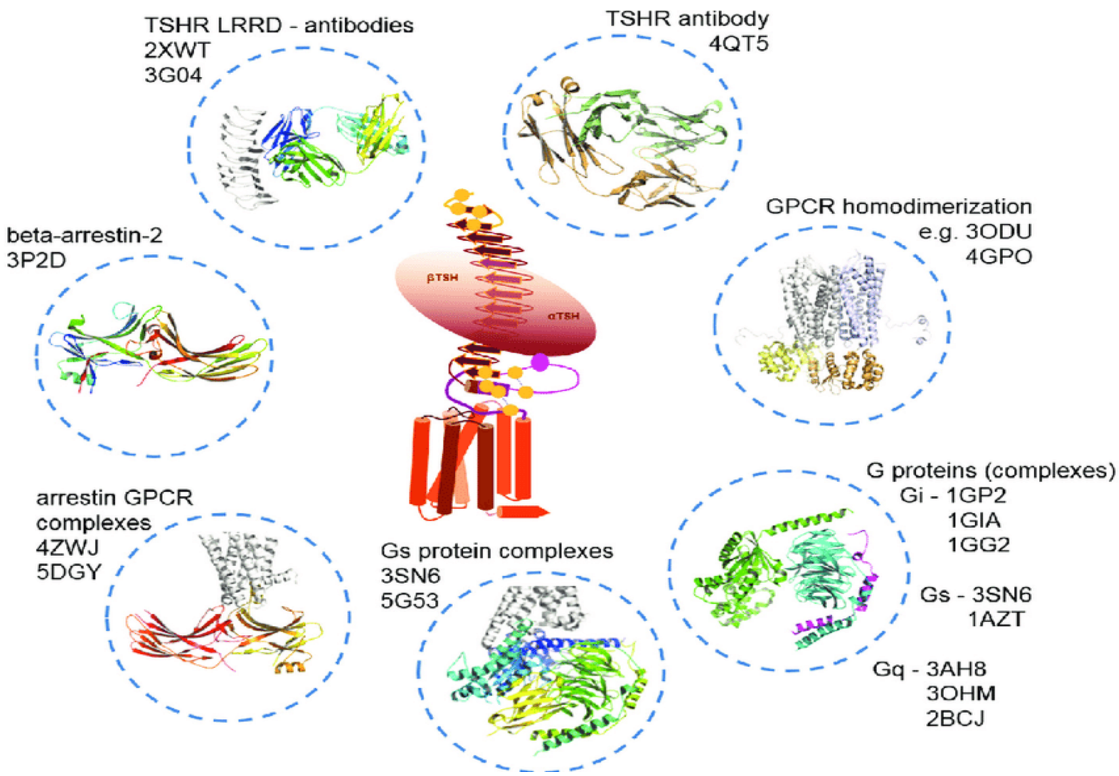

Figure *2.4* thyroid receptor structures

The different forms of thyroid receptors have patterns of expression that vary by tissue and by developmental stage. For example, almost all tissues express the alpha-1, alpha-2 and beta-1 isoforms, but beta-2 is synthesized almost exclusively in hypothalamus, anterior pituitary and developing ear. Receptor alpha-1 is the first isoform expressed in the conceptus, and there is a profound increase in expression of beta receptors in brain shortly after birth. Interestingly, the beta receptor preferentially activates expression from several genes known to be important in brain development (e.g. myelin basic protein), and up regulation of this particular receptor may thus be critical to the well known effects of thyroid hormones on development of the fetal and neonatal brain.

Figure 2.6 shows the actions of thyroid hormone

The presence of multiple forms of the thyroid hormone receptor, with tissue and staged dependent differences in their expression, suggests an extraordinary level of complexity in the physiologic effects of thyroid hormone.

2.2.6 Interaction of Thyroid Hormone Receptors with DNA:

Thyroid hormone receptors bind to short, repeated sequences of DNA called thyroid or T3 response elements (TREs), a type of hormone response element. A TRE is composed of two AGGTCA "half sites" separated by four nucleotides. The half sites of a TRE can be arranged as direct repeats, pallindromes or inverted repeats, The DNA-binding domain of the receptor contains two sets of four cysteine residues, and each set chelates a zinc ion, forming loops known as "zinc fingers". A part of the first zinc finger interacts directly with nucleotides in the major groove of TRE DNA, while residues in the second finger
interact with nucleotides in the minor groove of the TRE. Thus, the zinc fingers mediate: specificity in binding to TREs, Thyroid hormone receptors can bind to a TRE as monomers, as homodimers or as heterodimers with the retinoid X receptor (RXR), another member of the nuclear receptor superfamily that binds 9-cis retinoic acid. The heterodimer affords the highest affinity binding, and is thought to represent the major functional form of the receptor. Thyroid hormone receptors bind to TRE DNA regardless of whether they are occupied by T3. However, the biological effects of. TRE binding by the unoccupied versus the occupied receptor are dramatically different. In general, binding of thyroid hormone receptor alone to DNA leads to repression of transcription, whereas binding of the thyroid hormone-receptor complex activates transcription.

2.2.7 Ligand-free state:

The transactivation domain of the T3-free receptor, as a heterodimer with RXR, assumes a confirmation that promotes interaction with a group of transcriptional corepressor molecules. A part of this corepressor complex has histone deacetylase activity (HDA), which is associated with formation of a compact, 'turned-off' confirmation of chromatin. The net effect of recruiting these types of transcription factors is to repress transcription from affected genes.

2.2.8 Ligand-bound state:

Binding of T3 to its receptor induces a conformational change in the receptor that makes it incompetent to bind the co repressor complex, but competent to bind a group of co activator proteins. The co activator complex contains histone transacetylase (HAT) activity, which imposes an open configuration on adjacent chromatin. The co activator complex associated with the T3-bound receptor functions to activate transcription from linked genes.

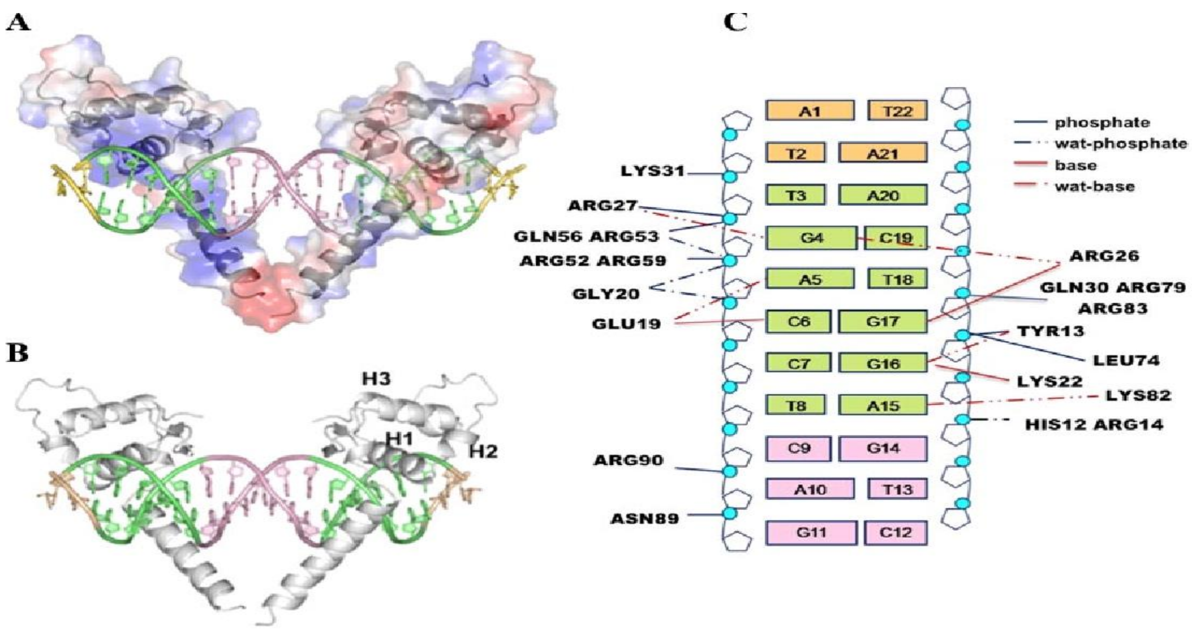

Figure 2.5 co activator complexes

A growing number of specific proteins have been identified as members of the co repressor and co activator complexes described. It should also be mentioned that there are several exceptions to the scheme described above. As mentioned, the alpha-2 receptor is unable to bind T3 and acts as similarly to a dominant-negative mutant of the receptor, but its carboxy-terminus can be differentially phosphorylated, which affects DNA binding and. dimerization. Also, the beta-2 isoform apparently fails to function as a repressor in the absence of T3.

2.2.9 Physiologic Effects of Thyroid Hormones

It is likely that all cells in the body are targets for thyroid hormones. While not strictly necessary for life, thyroid hormones have profound effects on many “big time” physiologic processes, such as development, growth and metabolism. Many of the effects of thyroid hormone have been delineated by study of deficiency and excess states, as discussed briefly below.

2.2.9.1 Metabolism:

Thyroid hormones stimulate diverse metabolic activities most tissues, leading to an increase in basal metabolic rate. One consequence of this activity is to increase body heat production, which seems to result, at least in part, from increased oxygen consumption and rates of ATP hydrolysis. By way of analogy, the action of thyroid hormones is akin to blowing on a smoldering fire. A few examples of specific metabolic effects of thyroid hormones include:

2.2.9 2Lipid metabolism:

Increased thyroid hormone levels stimulate fat mobilization, leading to increased concentrations of fatty acids in plasma. They also enhance oxidation of fatty acids in many tissues. Finally, plasma concentrations of cholesterol and triglycerides are inversely correlated with thyroid hormone levels - one diagnostic indiction of hypothyroidism ‘is increased blood cholesterol concentration.

2.2.9.3 Carbohydrate metabolism:

Thyroid hormones stimulate almost all aspects of carbohydrate metabolism, including enhancement of insulin-dependent entry of glucose into cells and increased gluconeogenesis and glycogenolysis to generate free glucose.

2.2.9.4 Growth:

Thyroid hormones are clearly necessary for normal growth in children and young animals, as evidenced by the growth-retardation observed in thyroid deficiency. Not surprisingly, the growth-promoting effect of thyroid hormones is intimately intertwined with that of growth hormone, a clear indication that complex physiologic processes like growth depend upon multiple endocrine controls.

2.2.9.5 Development:

A classical experiment in endocrinology was the demonstration that tadpoles deprived of thyroid hormone failed to undergo metamorphosis into frogs. Of critical importance in mammals is the fact that normal levels of thyroid hormone are essential to the development of the fetal and neonatal brain.

2.2.9.6 Other Effects:

As mentioned above, there do not seem to be organs and tissues that are not affected by thyroid hormones. A few additional, well-documented effects of thyroid hormones include:

- Cardiovascular system: Thyroid hormones increases heart rate, cardiac contractility and cardiac output. They also promote vasodilation, which leads to enhanced blood flow to many organs.

- Central nervous system: Both decreased and increased concentrations of thyroid hormones lead to alterations in mental state. Too little thyroid hormone and the individual tend to feel mentally sluggish, while too much induces anxiety and nervousness.

- Reproductive system: Normal reproductive behavior and physiology is dependent on having essentially normal levels of thyroid hormone. Hypothyroidism in particular is commonly associated with infertility.

2.3 Common Thyroid Problems:

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.

2.3. l Goiters:

A thyroid goiter is a dramatic enlargement of the thyroid gland. Goiters are often removed because of cosmetic reasons or, more commonly, because they compress other vital structures of the neck include the trachea and the esophagus making breathing and swallowing difficult. Sometimes goiters will actually grow into the chest where they can cause trouble as well. Several nice x-rays will help explain all types of thyroid goiter problems.

2.3.2Thyroid Cancer:

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

2.3.3Solitary 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.

2.3.4 Hyperthyroidism:

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 Jill 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).

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 (not known why).

2.3.5Hypothyroidism:

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.

2.3.5.1 Symptoms of Hypothyroidism

- Fatigue
- Weakness
- Weight gain or increased difficulty losing weight
- Coarse, dry hair
- Dry, rough pale skin
- Hair loss
- Cold intolerance (can’t tolerate the cold like those around you)
- Muscle cramps and frequent muscle aches
- Constipation
- Depression
- Irritability
- Memory loss
- Abnormal menstrual cycles
- Decreased libido

2.3.5.2 **Potentia1 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.

2.3.6 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 exist and the treatment is different for each.

2.3.6.1 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.

2.3.6.2 De Quatrain’s Thyroiditis:

De Quatrain's Thyroiditis (also called sub acute or granulomatous thyroiditis) was first described in 1904 and is much less common than Flashimoto's Thyroiditis. 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.

2.3.6.3 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 Quervain'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 the thyroid gland to normal after three months. Symptoms are similar to Graves' Disease except milder. The thyroid gland is only slightly enlarged and exophthalmoses' (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 Barrere, *2000, [21]*.

2.4 Previous Study

The uptake of ^{99}m Tc has been recommended as an alternative to a ^{131}I uptake test for the purpose of evaluating thyroid function; one advantage being that ^{99}mTc**,** compared with ^{131}I gives a very low radiation dose to the thyroid. The uptake of ^{99}mTc by the thyroid was measured in 18 normal volunteers and in 22 patients with thyrotoxicosis. Ten of the thyrotoxic patients had 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.99mTc uptake was also measured in four hypothyroid patients and in ten patients with non-toxic goitre. Scans were carried out with dual detector scanner 9 cm diameter sodium iodide crystals of 7-6 cm thickness and 19 holes focusing collimators, the collimator focal distance being 15 cm. The collimators were separated by a distance of 30 cm and a thin aluminum filter of 1 mm 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 99mTc (4.0-5.0 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 (20x20x 15 cm) containing water to a depth equivalent to 1 cm 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, thyiotoxic untreated were 0.64%, 1.62%, 2.81%, 10% and 11.7% respectively Atkins and Richards, 2008; Degrossi et al, 2010, [17] saied.

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 comparison between LEGP and PH collimators. The patients were given 7.4—11 MBq (200—3 00 uCi) 1231 capsules orally. Uptake with both the probe and the gamma camera was measured at 5 h and 24 h. 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 LEOP collimator. Comparison between LEGP and PH uptake values resulted in a correlation coefficient of 0.979 and 0.931 for 24 h 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 Knudsen N, 2002, [38] saied.

IEA (2016) 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 patients neck size matches with the neck phantom used and the error in the effective distance is minimum. Wellman at.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 spectrometer (MDS 26) and thyroid uptake probe made by electronic corporation of India ltd, neck phantom of different diameter 8.0, 9.5, 13.0 and l5.5.these phantom were filled with water to a height of 15Cm to simulate the neck. Aperspex vial of 3 cm diameter ,and containing 30mL of 1311 .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 photpeake 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.

The study consisted of 47 normal individuals, 30 women and 17 men, with ages ranging from 19 to 61 years (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 5 mCi (185 MBq) of 99mTc-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 99mTc-pertechnetate uptake ranged from 0.4 to 4.5%. The uptake values obtained in these normal individuals showed that *95%* presented a thyroid uptake that ranged from 0.4 to 4.5% of the injected dose. The assessment of thyroid structure and function using 99mTc-pertechnetate is a simple, fast and efficient method, which could easily become a part of the routine studies in nuclear medicine laboratories Crespo, 1996, [26].

This study was to evaluate the normal range of thyroid uptake and determine 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 2012 to Feb 2013. The most frequency of ages distribute as (22-2615%, 26-3015%)the thyroid uptake value in the gamma camera (mediso) & (simens), the result of this study showed that, the normal range of thyroid uptake is in the range between (0.4% —4.5%) & the thyroid volume is in the range of (20cm2 to 40cm2) 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: $y = 0.59x + 2.7$ where x refers to thyroid volume and y refers to uptake in percent.

The result also shown that when weight increase the uptake decrease as shown in the following equation: $y = -0.33x + 6.07$ where x refers to patient weight in Kg and y refers to up take 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. Degrossi, 1995, [13].

Despite historical reports on deviating normal thyroid uptake values (emphasising the importance of establishing local normal reference values), the relevant Namibian authorities have never revised these reference values, nor have local reference values been established. The aim of this study was to establish the normal reference values for thyroid uptake of technetium-99m pertechnetate in the Namibian population. Participants who were considered to be euthyroid completed a questionnaire designed to exclude individuals with thyroid pathologies, as well as those with renal or heart disease.

The study cohort consisted of 76 participants (58 women and 18 men), ranging in age from 39-81 years. The participants were of mixed ethnicity, consisting of Hereros, Ovambos, Damaras, Namas, Coloureds, Caucasians and other (non-Namibian immigrants), and were from Windhoek, Namibia. Studies were performed at the Windhoek Central Hospital.
Outcome measures:
Blood was drawn for thyroid hormone assessment. Participants were then given 185 MBq of technetium-99m pertechnetate intravenously, and their percentage thyroid uptake recorded after 20 minutes.
In this study, thyroid-stimulating hormone, triiodothyronine, and thyroxine levels were found to be 1.7 µIU/ml, 4.9 pmol/ml and 10.3 pmol/ml, respectively. Analysis of the empirical data showed that the normal reference uptake value for technetium-99m pertechnetate in the studied population ranged between 0.04% and 4.0%.

These results provide new evidence which supports the importance of periodical evaluation of normal thyroid uptake reference values for technetium-99m pertechnetate.(JEMDSA, 2013).

The aim of this study was to describe the thyroid volume in healthy adults by ultrasound and to correlate this volume with some anthropometric measures and other differentiated thyroid cancer risk factors

Thyroid volume and anthropometric measures were recorded in a sample of 100 healthy adults, including 21 men and 79 women aged 18-50 years, living in a non-iodine-deficient area of Havana city

The result of average thyroid volume was 6.6 ± 0.26 ml; it was higher in men (7.3 ml) than in women (6.4 ml; $p = 0.15$). In the univariate analysis, thyroid volume was correlated with all anthropometric measures, but in the multivariate analysis, body surface area was found to be the only significant anthropometric parameter. Thyroid volume was also higher in current or former smokers and in persons with blood group AB or B.

Specific reference values of thyroid volume as a function of body surface area could be used for evaluating thyroid volume in clinical practice. The relation between body surface area and thyroid volume is coherent with what is known about the relation of thyroid volume to thyroid cancer risk, but the same is not true about the relation between thyroid volume and smoking habit. Willum, 2014, [14].

Uptake & weight of patientsSmall variations in weight in persons with normal thyroid function can affect levels of thyroid hormones have found. "In euthyroid patients, weight loss lowers TSH and T3, while weight gain raises TSH and T3," Dr. Kitahara.,Dec 16, 2019, [25].

Thyroid gland is avital 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, multinodular 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% to 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 yrefers 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. Ahmed, 2010, [11].

In the study carried by OMER, (2013), 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 Elnelain Medical Diagnostic Center. This study includes 150 patients (85% female, 15% male) in different age, sex, center of origin and type of food and drink intake, for nine months from May 2011 to Apr 2013.
The most frequency of ages distribute as (22-26=15%, 26-30=15%) the thyroid uptake value in the gamma camera (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 to 40cm^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. Omer,2013, [24]

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 29 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 individu also showed that 95% presented a thyroid uptake that ranged from 0.4 to 4.0% 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. HINE, G. J, 1997 [24].

^{m}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 (5.0 -7.0 mCi) and a standard of between 5% and 10% of the dose were dispensed in 2 ml. syringes and the 31ratio 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 colored 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. Atkins and Richards, 2005; Degrossi et al, 2006, [7].

^{m}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 Lthyroxin 0.3 mg daily . the test was usually carried out a few days after the drugs had been discontinued.
^{m}Tc uptake was also measured in four hypothyroid patients and in tenpatients 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 (1.5 - 4.0 mCi) and a standard of between 5% and 10% of the dose were dispensed in 2 ml. syringes and the 31 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 . 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%, 3.62%, 2.81%, 10% and 11.7% respectively A tkins and Richards, 2005; Degrossi et al, [11].

The purpose of this study was to standardize a simple and fast methodology for performing thyroid uptake and scintigraphy and to determine the normal values for ^{99m}Tc- pertechnetate uptake. Prospective, non-randomized. Division of Nuclear Medicine, Department of Radiology, School of Medical Sciences, Campinas State University.
The study consisted of 47 normal individuals, 30 women and 17 men, with ages ranging from 19 to 61 years (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 (370 MBq) of ^{99m}Tc-pertechnetate, the images were obtained on a computerized scintillation camera

equipped with a low-energy high-resolution parallel hole collimator.
The result individuals were euthyroid both on clinical and laboratory evaluation. The baseline thyroid ^{99m}Tc-pertechnetate uptake ranged from 0.4 to 4.7%. The uptake values obtained in these normal individuals showed that 95% presented a thyroid uptake that ranged from 0.4 to 4.5% 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.

Chapter Three

Method & Material

3.1 Radio pharmaceutical uses:

Thyroid gland function and structure can be evaluated using uptake and scintigraphy studies. 1311-iodide, which was introduced in the late thirties, was the first radio pharmaceutical used for measuring thyroid uptake, and for many years it was the main study agent used in the evaluation of thyroid function. 1 Despite the fact that the sensitivity and specificity of in vitro tests for evaluation of thyroid function have evolved, thyroid uptake and scintigraphy still play an important role in various clinical situations, such as the detection of ectopic thyroid tissue in neck masses, functional assessment of single or multiple nodules, increasing the likelihood of detecting hyperthyroidism in difficult cases, identification of other causes of thyrotoxicosis and calculation of therapeutic doses of 1311-iodide.2

Studies with 1311-iodide have the serious disadvantage of high radiation doses to the gland (1-3 rad /m*Ci* administered) caused by its long half-life and 3- particle emission. Its main gamma photon has high energy (364 keV) that is inadequately collimated by most conventional scintillation cameras, and therefore poor quality images are produced. In the United States, the use of 1311-iodide for thyroid imaging has been prohibited and its use restricted to staging and follow-up of patients with differentiated thyroid carcinoma.2,3

Iodine-123 is a good substitute for iodine-131 because it has a shorter half-life (13hours), a gamma photon suitable for imaging using conventional scintillation cameras (159 keV) and no El-radiation. However, its main limitations are its high cost and reduced availability, due to its expensive and complex production in a cyclotron. In addition, depending on the production process chosen, contaminants such as 124I-iodide and 125I- iodide may be formed increasing the dosimetry and image degradation.4,5

Technetium 99m, in the chemical form of pertechnetate (99mTcO4-), is also used for thyroid scintigraphy and uptake.6-17 The similarity of volume and charge between the iodide and pertechnetate ions is the explanation for the uptake of 99mTc-pertechnetate by the thyroid gland.9, 10 99mTc-pertechnetate has been used worldwide to study the thyroid function because of a number of advantages, such as a short half-life (6 hours), short retention in the gland, and no f- radiation, thus providing low dosimetry to the thyroid gland (10,000 times less than that of

1311-iodide),10 as well as to the body as a whole. 10. Its gamma photon of 140 keV is ideal for imaging using scintillation cameras and in addition it has low cost and is readily available. 11

There is an international consensus that the radiopharmaceuticals of choice for thyroid gland imaging are 99mTc-pertechnetate or 1231-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. 17 In rare instances, 1231- iodide can subsequently be used for assessment of organification defects.

Despite these recommendations, most nuclear medicine laboratories in Brazil choose the radiopharmaceutical 1311-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, 2016, [22].

3.2 Patients:

No:	Pt. weight (kg)	Height (cm)	Gender	Age	Dose (mCi)	Uptake %	Volume (Cm^2)	T3 pmol/L	T4 pmol/L	TSH miU/L
1	62	178	F	35	4.0	5.3	22.6	3.1	11.0	0.3
2	50	177	F	24	4.0	4.6	25.4	3.4	14.4	2.6
3	74	155	F	22	4.0	4.6	25.4	5.2	15.6	5.5
4	62	162	F	23	4.0	1.1	20.3	3.3	10.4	3.6
5	77	179	F	41	4.0	5.3	25.2	4.2	16	5.2
6	61	180	F	30	4.0	1.4	36.6	4.0	22.4	1.6
7	78	165	F	18	4.0	3.0	32.1	6.0	13.6	2.8
8	78	155	F	34	4.0	4.4	30.5	6.5	20.0	0.4
9	75	177	F	36	4.0	4.5	36.6	3.3	11.9	0.6
10	60	179	F	44	4.0	2.0	32.1	5.3	17.4	2.6
11	55	178	F	52	4.0	2.4	30.5	3.6	22.3	3.7
12	53	170	F	61	4.0	1.1	36.6	4.5	14.4	4.8
13	70	182	M	39	4.0	4.6	36.6	5.4	16.7	2.9
14	61	166	F	25	4.0	5.0	27.7	3.6	21.0	5.2
15	59	178	F	35	4.0	1.0	26.9	4.6	13.9	3.6
16	78	181	F	22	4.0	3.1	19.4	4.2	16.9	2.4
17	70	181	M	27	4.0	3.9	24.4	5.1	14.6	05
18	55	170	F	29	4.0	2.7	21.4	6.0	18.4	1.4
19	76	176	F	24	4.0	3.1	14.3	3.2	13.6	1.6
20	66	172	F	21	4.0	1.9	14.0	3.7	14.5	4.2
21	82	178	F	20	4.0	4.4	36.7	5.2	23.4	4.1
22	71	175	F	19	4.0	2.0	20.5	4.6	24.5	3.2
23	70	178	F	57	4.0	4.1	12.8	3.7	14.7	2.8
24	66	162	F	47	4.0	2.3	16.4	4.2	13.5	4.1
25	59	166	F	42	4.0	3.9	22.2	3.9	15.7	3.6
26	76	164	M	33	4.0	4.6	29.5	5.3	11.8	1.4
27	55	184	F	38	4.0	4.6	22.1	4.4	19.6	1.3
28	62	166	F	36	4.0	1.1	21.3	4.2	13.6	3.8
29	71	177	F	25	4.0	5.3	24.4	3.5	23.4	2.8
30	70	175	F	24	4.0	1.4	24.9	5.6	11.8	1.6
31	59	179	F	29	4.0	1.9	20.9	6.2	17.3	1.9
32	62	180	F	42	4.0	3.8	23.1	3.4	14.8	2.0
33	78	178	M	49	4.0	4.5	20.1	4.8	16.6	3.9
34	66	174	F	21	4.0	2.2	23.2	3.6	15.7	4.2
35	64	179	F	27	4.0	3.6	24.4	4.2	14.7	5.2
36	70	178	F	35	4.0	5.0	25.5	5.1	14.6	2.6
37	59	174	F	38	4.0	4.0	18.6	6.0	18.4	3.7
38	63	179	F	40	4.0	3.1	36.7	3.2	13.6	4.8
39	52	177	F	49	4.0	3.9	23.7	3.7	16.7	2.9
40	71	164	M	21	4.0	1.1	23.7	5.2	22.8	5.2
41	74	178	M	37	4.0	3.3	12.4	4.6	15.8	3.6
42	64	178	F	40	4.0	2.6	11.9	3.7	16.7	4.2
43	71	166	F	49	4.0	3.4	24.8	4.2	24.5	4.1
44	54	162	F	47	4.0	3.1	24.8	3.9	14.7	1.9
45	60	159	F	55	4.0	1.2	22.3	5.3	18.4	2.0

3.3 instrumentation:

The instruments used to collect the data were categorized into, nuclear medicine a instrument which is dual head SPECT and whole body gamma camera, NUC1EFE TM, manufactured by MEDISO company. Meager at 2006 and gamma camera SPECT sigle head, manufactured by SIMENS Company. German at 2008 .The sample of this study were consisted of 400 patients *(340* female and 60 male) with thyroid problem referred to 1JCK (radiation and isotopes center of Khartoum) & Elnelain Medical Diagnostic Center (KHARTOUM) 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 TFT (thyroid function test) and thyroid uptake in the period from May 2017 to May 2020.

3.3.1 quality control of the gamma camera:

anger scintillation camera was invented by Hall Hanger of donor laboratory university of California at Berkeley, in the latel95O.pictures of two modern scintillation cameras are the most commonly used imaging instrument in nuclear medicine today.

The complete camera system consists of a lead collimator .

*Collimators:

A collimator is typically al\2 to 2 in thick piece of lead with algometrical array of holes, the lead between each hole is called a septum; collectively the lead represents septa.

The patient and scintillation crystal by only a allowing those photons traveling in an appropriate direction to interact with the crystal .collimators thus discriminate based on direction of flight onto on whether the photons are scattered or not. Several types of collimators are used with anger cameras: parallel hole; converging; diverging.

The parallel holes collimator which consist of an array of parallel holes essentially Perpendicular to the crystal faces and thus presents areal- size image to the detector. The resolution of parallel hole collimator is best at the collimator surface the sensitivity is independent of the distance between the source and the collimator in most clinical applications.

Converging collimators have an array of tapered holes that aim at appoint at some distance in front of the collimator this point is called the focal point.

Converging collimators have their best resolution at the surface of the collimator.

The sensitivity of converging collimators slowly increases as the source is moved from the collimator face back to the focal plane and then decreases. diverging collimators are essentially upside down converging

Collimators they have an array of tapered holes that diverge from a hypothetical focal point behind the crystal the image presented to the crystal face is minified image of the real object. Converging and diverging collimators are simply flipped versions of each other way. Pin holes collimators are thick conical collimators with a single 2 to 5mm hole in the bottom center. As a source is moved away from the surface of pin holes collimators the camera image gets smaller. Other types of collimator have more specialized.

- Crystal

The properties of thallium activated sodium iodide crystal as scintillation detectors were described earlier as with crystal used in scintillation spectrometry. Those used in anger cameras are sensitive moisture and are sealed in an aluminum housing. The crystal used in anger cameras vary from 7in to more than 25in.

The photomultiplier tubes and the light pipe that is generally used to optically couple the two crystals that are l\4in thick have about l mm better intrinsic resolution than crystals that are l\2 thick.

- Positioning logic circuit

Anger cameras have an array of photomultiplier tubes optically coupled to the back of the scintillation crystal the actual number of tubes is determined by the size and shape of both the crystal and each individual photomultiplier tube.

- Approaches to camera quality control

When embarking on a scintillation camera quality program, department must make several decision regarding methods and apparatus to be used. Three major decisions have to be made.

- Intrinsic testing

Involves measuring the performance of the system without the collimator small volume or 13int source of the chosen radionuclide in positioned at a distance of five time that maximum dimension of the cameras useful field of view to give a uniform radiation flux across the crystal.

- Quality control phantoms

Many transmission phantoms have been developed for resolution and linearity testing; with several gaining the widest acceptance and spacing of the hole or bars of the phantom selected should stress the maximum resolving capability of the instrument.
Second: the same size patties of holes or bars should be used to cover the entire camera field of view.
Three: the parallel line equal space phantom consists of lead bars Lucite. Two transmission image acquired at an angle of 9odegrees relative to each other provide the assessment of spatial resolution linearity and spatial distortion for the entire detector area.
Four: different widths of bar and spaces are used in the quadrant bar phantoms. Are used in the quadrant are arranged so that each set of bars is oriented 90 degrees from the set adjective quadrant.
In general these transmission phantoms should only be used for intrinsic testing without collimator first attesting of system energy preferably high resolution collimator.
Used of the phantom with a collimator can produce armoire type of artifact because of inter faience phantom pattern with the pattern of holes in the collimator. Second it is also important to note that when acquiring transmission phantom image by computer the digital acquisition matrix can act a pattern. These types of image must be acquired with large matrix.

- Routine camera quality control procedures

Phantoms have been discussed and decisions have been made a daily quality program for scintillation camera can be established. One of the keys to a reliable quality control program is the standarelize performance of the quality control procedures.

- *Photo peak settings*

The correct energy window radionuclide being used must be selected and the peak must be centered in the window.

- *Intensity*

Daily use of the same CRT intensity setting and image size to produce filed uniformity images should result in a comparable daily image density.

- *Image size*

The size of an image can have a significant impact on interpretation of the image. For this reason care must be taken to use the format and intensity each time.

- *Uniformity*

Use one of the following methods daily.

Extrinsic method

Collimator is installed and planar source with account rate and planar source with account rate that does not exceed 30.000 counts\sec is centered over the detector. Covering the collimator surface with a plastic cover or enclosing the flood phantom in a plastic bag helps prevent contamination of the collimator.

1\ Acquire a flood image that contains at least 3 million counts for a camera with a circular field of view and 5million counts for a camera with a larger rectangular field of view.

2\ If the camera has microprocessor system for detector uniformity correction that can be turned off. Daily flood filed image are acquired with and without microprocessor correction. 3\ Evaluate and compare the image with previous images of uniformity that were acquired.

4 Record the data photo peak setting CTR intensity total counts and elapsed imaging time.

5\ Place the image in the appropriate file.

- **SPECT**

Principles of single photon emission computed tomography (SPECT) imaging:

Clinicians use planar images in the diagnosis of many types of disease .x-ray images show the distribution of materials of different densities in the body by imaging the attenuation of the photons passing through the body.

Clinicians use planar images in the diagnosis of many type of disease .x-ray images show the distribution of materials of different densities in the body by imaging the attenuation of photon passing through the body.

centigrams produced by a scintillation camera are planar images of the distribution of a photon emitting radioactive tracer administered to a patient.

Single photon emission computed tomography produce images of gamma rays entitled by a radioactive tracer.

Positron emission tomography (PET) images the two 511 key photon produced when a position comes into contact with an electron.

SPECT image are superior to planar images in contrast but at same cost to resolution because each image represent a slice through the patient. Much of the background activity is eliminated increasing the contrast resolution decreases with distance form a scintillation camera because the camera must view the patient from all angle.

- Instrumentation

The main components of SPECT system are the scintillation camera the gantry and the computer systems (hardware and soft ware) these components work together to acquire and reconstruct the homographic images.

- Scintillation camera

The basic components of a scintillation camera are a collimator a sodium iodide (SPECT) crystal. Photomultiplier tubes pulse height analyzers and spatial positioning circuitry. Gamma rays (photon) pass through the collimator and cause a scintillation event in the crystal.

- Gantry

The frame that supports the scintillation camera used for SPECT must be able to rotate and position the camera precisely. Making size and stability important factors size is practical issue because the gantry is largest part of the SPECT system.

- Collimators

The collimators is the focusing device of a SPECT camera gamma rays have too much energy to be focused by a lens in the same way that visible light photons are in film or digital camera. Instead collimators are made up of an array of long narrow. Collimators are rated by their sensitivity and resolution. In general the sensitivity and resolution of a collimator are inversely related a very high sensitivity collimator has low resolution and a very high resolution collimator has low sensitivity.

Parallel holes collimators are most commonly used to SPECT but increased sensitivity can be obtained with converging collimators in which the hole converge on a line (fan beam) or appoint (cone beam)

Converging collimators require more complex setup procedures than do parallel hole collimators if used for SPECT and once the images have been acquired they require special image reconstruction software that may result in much longer reconstruction times. Converging collimators allow more of the crystal to be used which increases sensitivity; is realized with a decrease in the size of the field of view.

Converging collimators pose a problem for cardiac SPECT because the field of view does not necessarily covers the entire Thorax.

SPECT reconstruction

Methods of reconstruction the radionuclide distribution from planar projections have been the subject of investigation sir ice the possibility was proven by l. Radon in 1917 the advent of computers a accelerated research into different methods of image reconstruction and many have been proposed these reconstruction algorithms fall into two categories: interactive methods and analytic methods. Analytic methods are based on exact mathematical solution to the image reconstruction problem where as interactive methods estimate the distribution through successive approximation

- Filtering of S images

In SPECT filter are used either to enhance or to remove the high frequency components of the image high frequency image Reconstruction shown in figure 3.1.

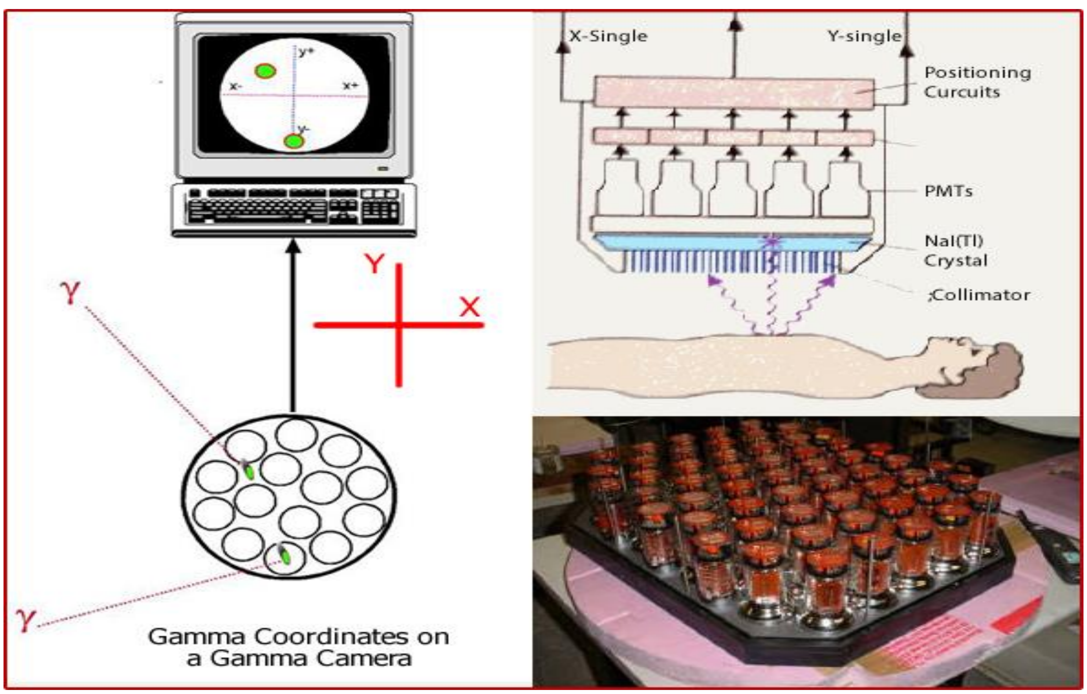

Figure 3.1 shows travel of gamma rays through the collimator

• Gamma Cameras

• Scintillation type Gamma Cameras

• Collimators

• Lead (tungsten or platinum)

• Excludes erroneous

• gamma rays (focus camera)

• Spatial Resolution

• Detection efficiency ratio

• Gamma Cameras

•NaI(T1) crystals

  - Produce lower frequency photons

• Photomultiplier tubes

  - Transform photons to electrical signals

  -Using photocathode.

  -These entire components appeared as whole machine in figure 3.2

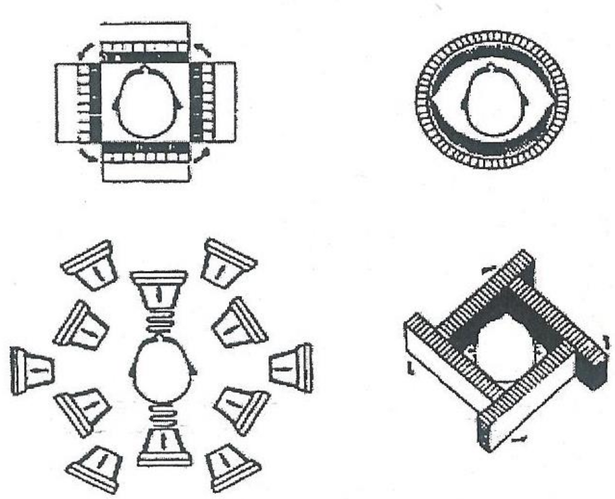

Figure 3.3 shows methods of camera rotation

• Image Reconstruction

•Gamma rays counted into matrix

•Filtering

• Convolution Method (9 point smoothing)

• Fourier Method

• Digital vs. Analog

• Too few pixels

• Too few bytes per pixel

• Technological Advances

• Problems with SPECT:

• Long scan times

• Low resolution

• Attenuation

• Solutions:

• Triple headed cameras drastically reduce scan times

• Improved cameras and computers enhance resolution

• Visual Tracking Systems to monitor patient movement and correct images accordingly

•Attenuation Correction software

• Clinical Applications

• In the 70's & 80's, SPECT was largely replaced by CAT and MRI scans because they provided superior resolution.

• Recently, SPECT has returned to prominent use, especial lly in diagnosing cardiac and nurologica1 abnormalities.

• While CAT and MRI scans only provide images of static brain anatomy, SPECT offers clues to brain function by tracing blood allocation.

• Diagnosis of Neurological and Psychiatric Disorders with SPECT Robins RJ, 2005, [17]

3.4 Technique and methods of thyroid uptake

3.4.1 patient preparations:

The patient was prepared according to the following points: Patient should stop thyroid medication for will before the investigation, Should prevent from any iodinated contrast 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 there physicians. In case of breast feeding, the patient will be asked to stop feeding for awhile 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.

3.4.2: 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 4.0 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 300 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 subrasternal notch (S.S.N) to determine the extension of the gland.

If there is suspicion 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 measured 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.7.The number of counts present in the thyroid (T) was determined by an automatic region of interest (ROI) drawn around the borders of the gland. Another ROT 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-99m. The thyroid uptake (TU) was calculated automatically by subtraction before & after injection of the radioactive isotopes & background of surround tissues according to the soft ware of the machine in a form of percentage. Crespo, 1996, [26].