Chapter One

Introduction

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1-1 Background:

Nowadays thyroid disorder is one of the most common health problems all over the world; about 200 million people in the world have some form of thyroid disease, thus the accurate and rapid diagnosis and treatment of thyroid diseases is a critical issue depending on the efficiency and rapidity of tools been used to conduct the diagnosis of thyroid disorders.

Radioimmunoassay, enzyme linked immunosorbent assay (ELISA) and imunoradiometric assay (IRMA) constitute the main tools for biochemical evaluation of thyroid functions. Thyroid radioactive $^{99m}TcO_4$ uptake study is a simple and cost effective method to investigate thyroid function and retains a confirmatory and clarifying status when the results of other tests are ambiguous or contradictory. $^{99m}TcO_4$ uptake by thyroid is also performed for calculation of therapeutic dose of iodine-131 in thyrotoxicosis. This study is trying to find out the correlation between thyroid uptake of $^{99m}TcO_4$ and thyroid hormone levels obtained by radioimmunoassay(RIA) (John 2003).

1-2 Problem of the study:

The problem of the study lies in the fact that the thyroid tests are done separately without trying to find correlation between them.

1.3 Objective of the study:

1.3.1 General objective:

To study relation between thyroid uptake of ^{99m}Tc and the levels of thyroid hormones in blood

1.3.2 Specific objectives:

- To find out the correlation between thyroid uptake of technetium pertechnetate and thyroid hormone levels (T3, T4 and TSH) obtained by radioimmunoassay (RIA).
- To measure the thyroid uptake on the sample patients using ^{99m}Tc.
- To measure the T3, T4 and TSH level and to find out the linear equations to estimate hormones levels mathematically from given uptake values, if the correlation is found to be strong enough.

1-4 Significance of the study:

This study will determine how much the thyroid uptake and function are correlated to each other, reflecting the sensitivity of the thyroid uptake scan to indicate the levels of thyroid hormones in patient's blood .This will make thyroid studies more accurate and reliable .

1-5 Overview of the study:

This study falls into five chapters as follows chapter one is an introduction which includes the problem, objectives, significance of the study, and an overview of the study. Chapter two includes the literature review, while chapter three demonstrates the research methodology, data collection, materials and methods which were used in this study. Chapter four includes presentation of results, chapter five includes discussion,conclusion and recommendations , and finally appendices and reference.

Chapter Two

Literature Review

Chapter two

Literature review

2-1 Theoretical background:

2-1-1 Anatomy of the Thyroid Gland

Thyroid gland is 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. Most animals, however, have two separate glands on either side of the trachea. Thyroid glands are brownish-red in color (Arthur 2003).

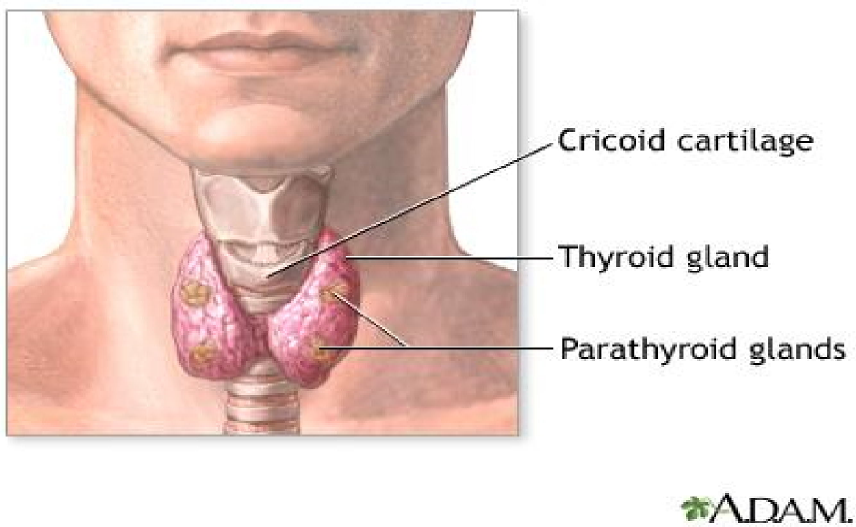

Figure 2-1: location of thyroid gland in the body

Close examination 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.

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. 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. In standard histologic preparations such as these, colloid stains pink (Arthur 2003).

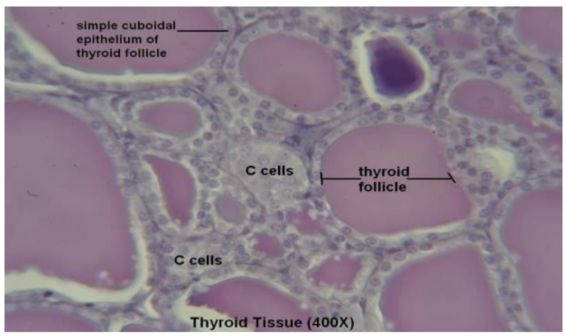

Figure 2-2 thyroid tissue

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. The image below shows a section of a feline parathyroid gland on the left, associated with thyroid gland (note the follicles) on the right.

2-1-2 Physiology of Thyroid Gland

2-1-2-1 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

2-1-2-2 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) (John 2003).

2-1-2-3 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, although only a handful of these are actually used to synthesize T4 and T3.

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

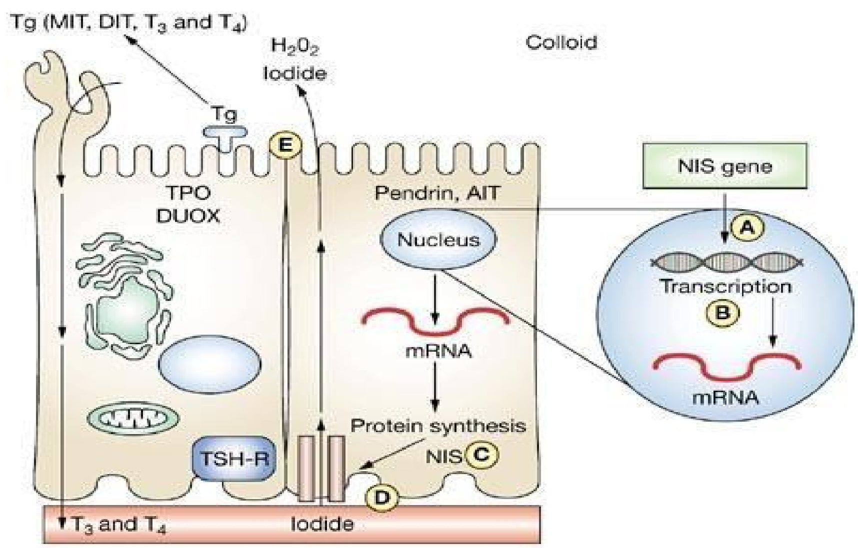

Figure 2-3 mechanism of thyroid hormones synthesis

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:

Iodination of tyrosines on thyroglobulin (also known as "organificationof 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 (Arthur 2003).

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.

2-1-2-4Thyroid 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 hormoneactivated 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.

2-1-2-5Receptor 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:

2-1-2-5-1A Tran's activation domain at the amino terminus that interacts with other transcription factors to form complexes that repress 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(John 2003).

2-1-2-5-2A DNA-binding domain that binds to sequences of promoter DNA known as hormone response elements.

2-1-2-5-3 A ligand -bindingand 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 ligand-binding domains. Most notably, the alpha-2 isoform has a unique carboxy-terminus and does not bind triiodothyronine (T3).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-knowneffects of thyroid hormones on development of the fetal and neonatal brain.

The presence of multiple forms of the thyroid hormone receptor, with tissue and stage-dependent differences in their expression, suggests an extraordinary level of complexity in the physiologic effects of thyroid hormone (Arthur 2003).

2-1-2-6Interaction 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 hormonereceptor complex activates transcription (Arthur 2003).

2-1-2-7 Ligand-free state: The transactivation domain of the T3-free receptor, as a heterodimer with RXR, assumes a conformation 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" conformation of chromatin. The net effect of recruiting these types of transcription factors is to repress transcription from affected genes.

2-1-2-8 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 gene

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.

2-1-2-9 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(Arthur 2003).

2-1-2-9-1 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:

2-1-2-9-2Lipid 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.

2-1-2-9-3 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 .

2-1-2-9-4Growth: 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.

2-1-2-9-5Development: 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.

2-1-2-9-6Other Effects: As mentioned above, there do not seem to be organs and tissues that are not affected by thyroid hormones. A few additional, welldocumented effects of thyroid hormones includes:

1-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.

2-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.

3-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(John 2003).

2-1-3Common 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:

1- Those concerning the production of hormone (too much, or too little).
2- Those due to increased growth of the thyroid causing compression of important neck structures or simply appearing as a mass in the neck.
3- The formation of nodules or lumps within the thyroid which are worrisome for the presence of thyroid cancer. And
4- Those which are cancerous.

2-1-3-1Goiters:

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 including 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.

2-1-3-2Thyroid Cancer :

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

2-1-3-3Solitary 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.

2-1-3-4Hyperthyroidism :

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:

1- Over activity of the thyroid gland (hyperthyroidism).

2- Inflammation of the tissues around the eyes causing swelling, and 3- 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)(Arthur 2003).

2-1-3-5Hypothyroidism :

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.

- **Symptoms of Hypothyroidism**

1-Fatigue

2-Weakness

3-Weight gain or increased difficulty losing weight

4-Coarse, dry hair

5-Dry, rough pale skin

6-Hair loss

7-Cold intolerance (can't tolerate the cold like those around you)

8-Muscle cramps and frequent muscle aches

9-Constipation

10-Depression

11-Irritability

12-Memory loss

13-Abnormal menstrual cycles

14-Decreased libido

- 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 a "compensatory goiter"). Outlines that a deficiency of thyroid hormone is a common cause of goiter formation. Left untreated, the symptoms of hypothyroidism will usually progress. Rarely, complications can result in severe life-threatening depression, heart failure or coma (Arthur 2003).

2-1-3-6Thyroiditis:

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.

2-1-3-6-1 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 takeup 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.

2-1-3-6-2 De Quervain's Thyroiditis: De Quervain's Thyroiditis (also called sub acute or granulomatous thyroiditis) was first described in 1904 and is much less common than Hashimoto'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(LAMB 2004).

2-1-3-6-3Silent 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 Quervain'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 exophthalmos (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 antithyroid medication is never needed. A few patients have become permanently hypothyroid and needed to be placed on thyroid hormone (LAMB 2004).

2-1-4 Diagnosis:

2-1-4-1 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.

2-1-4-2 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

2-1-4-3 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 (LAMB , 2004).

2-1-4-4 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.

2-1-4-5 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 anqinjection 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 values of thyroid lab investigations.

Test	**Abbreviation**	**Typical Ranges**
Serum thyroxin	T4	4.6-12 ug/dl
Free thyroxin fraction	FT4F	0.03-0.005%
Free Thyroxin	FT4	0.7-1.9 ng/dl
Thyroid hormones binding ratio	THBR	0.9-1.1

Free Thyroxin index	FT4I	4-11
Serum Triiodothyronine	T3	80-180 ng/dl
Free Triiodothyronine l	FT3	230-619 pg/d
Free T3 Index	FT3I	80-180
Radioactive iodine uptake	RAIU	10-30%
Serum thyrotropin	TSH	0.5-6 uU/ml
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 l	Tg	0-30 ng/m
Thyroid microsomal antibody titer	TMAb	Varies with method
Thyroglobulin antibody titer	TgAb	Varies with method

2-1-4-6 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. 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 (LAMB , 2004)

2-1-4-7 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. 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

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

2-1-4-8 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(LAMB 2004).

2-1-4-9Thyroid 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 (LAMB 2004).

2-1-4-10 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 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".

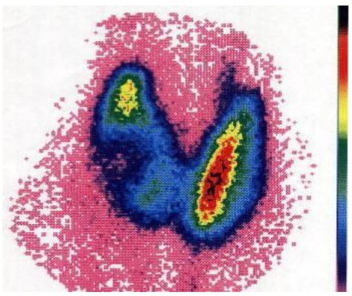

Figure 1-2 cold nodule image

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.

The following features favor a benign thyroid nodule:

-Family history of hashimoto's thyroiditis.

-Family history of benign thyroid nodule or goiter.

-Symptoms of hyperthyroidism or hypothyroidism.

-Pain or tenderness associated with a nodule.

-A soft, smooth, mobile nodule.

-Multinodular goiter Without a predominant nodule (lots of nodules, not one main nodule)

"warm" nodule on thyroid scan (produces normal amount of hormone) simple cyst on ultrasound

The following features increase the suspicion of a malignant nodule:

Age Less than 20.

Age Greater than 70.

Male Gender.

New onset of swallowing difficulties.

New onset of hoarseness.

History of external neck irradiation during childhood.

Firm, irregular and fixed nodule.

Presence of cervical lymphadenopathy (Swollen Hard Lymph Nodes in the Neck).

Previous History of thyroid cancer.

Nodule that is "Cold" on scan (Shown in picture above, meaning the nodule Does not make hormone) , and solid or complex on ultrasound (LAMB).

2-1-4-11 Thyroid 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).

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.

2-2 Previous studies:

-(2008) Kamal Faisal Yusuf worked out a method to estimate the normal thyroid Uptake by using technisium-99m and found that the uptake of the thyroid gland For patients with normal thyroid function test (T.F.T) and homogenous distribution of the radiotracer in the

range of (0.4% to 4.5%).

-by measuring the thyroid volume in this study for patient that with homogenous distribution of the radiotracer and normal thyroid function test (T.F.T) (mean of normal range of these patients T3 0.8-3.0n mol/L, T4 60-160 n mo/L and TSH 0.7-5.0 mu/L) in RICK.

-(2009) Wadah Mohammed Ali worked out a method to evaluate the relationship between thyroid uptake and thyroid function test (T.F.T) and found that there is strong and significant correlation between thyroid uptake and T3 and T4 but insignificant between the uptake and TSH. The normal range for thyroid uptake in this study was ranged from 5.78 to 6.12%. The linear relationship between thyroid uptake and T3 showed a coefficient equal to 0.65 uptake%/(nmol\L) and a constant equal to 2.6 as shown in the following equation: uptake% = 0.647 T3 + 2.6859.

In case of T4 the coefficient equal to 0.04 uptake%/(nmol\L) with a constant equal to 3.6 as shown by the following equation: uptake% = 0.0365 T4nmol\L + 3.5861. This study indicates that thyroid uptake can be use only to show thyroid disorder because it can give indication about the level of hormones if it low, normal, or elevated.

-October(2010) Shimaa Hamid Mohammed worked out a method to assess the thyroid abnormalities by using ^{99m}Tc and RIA (comparative study) ,and found that there is higher incidence of thyroid abnormalities in females than males 4:1 ,while 50% of patients their age range from 21-40 with the mean age of 41.8-+15 .the shape of thyroid (i.e. regular and irregular) and homogeneity of radiotracer (i.e. homogenous and in homogenous) has no effects on the T3 ,T4,TSH and uptake between the two of each group . but these quantities were affected by the age factor in a linear fashion; inversely with the TSH and uptake, and directly with T3and T4. As well the thyroid uptake was linearly associated with T3and T4 inversely, while with TSH was directly.

-November (2010) DafallaEltayebHussien worked out a method to assess the thyroid hormones level in thyroid patients by using Radio Immune Assay (RIA) and found that subjects aged between 20-40 years old are the most commonly affected by one of the thyroid abnormalities (hyperthyroidism and hypothyroidism) .the subjects of (20-30) years old were approximately referred for investigation 1.5 times as those aged between (20-40) years old .also found that females were approximately four times as the number of males patients referred for thyroid investigation . A further conclusion is that the majority of the thyroid referred subject were complaining of hyperactivity of the thyroid gland.

Chapter Three

Materials andMethods

Chapter Three
Materials and Methods

3-1Materials

The materials which used for data collection were classified into two categories, Nuclear medicine, and Radioimmunoassay materials.

- A planar gamma camera (Siemens), a dualheaded SPECT camera, NUCINE TM (MEDISO), with LEGP collimators

- ^{99}MO/^{99m}Tc generator.

- shielded syringes.

- Dose calibrator.

- Na-^{99m}Tco radiopharmaceutical.

- Gamma counter (OAKFIED) running with IAEA software program.

- T3, T4, and TSH kits.

- Adjustable micropipettes (10-200µl).

- Polystyrene test tubes (disposable).

- Vortex mixer (single and multi-tubes).

- Multidose micropipette 25µl and 250µl.

- Magnetic base.

- Incubator.

- Centrifuge.

- Gamma counter

3-2 Methods:

This study was an Experimental correlational research, in whicha primary data consisting of 100 samples was statistically analyzed using descriptive, correlation, and regression statistics to find out and describe the correlation between thyroid uptakes and the levels of thyroid hormones in blood representing its function.

3-2-1Methods of data collection:

Data were collected from references, textbooks, internet sites .

3-2-2 Methods of data analysis:

Regression lines were computed and Correlation coefficients (r) were calculated and tested for statistical significance in the total data using Microsoft excel software , SPSS program.

3-2-3Area and duration of study:

The study was conducted at the Radiation and Isotopes Centre of Khartoum (RICK),during the period from 2016 – 2017.

3-2-4Study population:

patients who were referred to the Radiation and Isotopes Centre-Khartoum (RICK) during the period from 2016 to 2017, from various hospitals and private clinics to obtain Thyroid Function test (TFT) and Thyroid isotopes uptake .

3-2-5 Data size: A total of 100 adult patients in the age between 20 and 60 years, that included 92 females and 8 males.

3-2-6 Data design: Each sample included four variables:

(1) Thyroid uptake % (Estimated using thyroid $^{99m}TcO4$ uptake scan.)

(2) T3 hormone level (nmol/L).

(3) T4 hormone level (nmol/L). (Estimated using RIA techniques.)

(4) TSH hormone level (nmol/L).

3-2-7The RIA technique:

The radioimmunoassay used in this study are typical for RIA department in radiation and isotopes center of Khartoum, which include incubation of 5mL of patient blood and then follow the below procedure:

3-2-7-1: T3: Sufficient number of test tubes were labeled and in duplicate arranged in assay rack. 25 µl of standard solutions, QC samples and patients sample were added to each target tube. 100 µl of T3- I^{125} tracer and 100 µl anti-T3 antibody were added to each tube and mixed the tubes and incubated at ^{37}Co for one and half hour and then precipitate agent polyethylene glycol (PEG) was added and vortex well and then centrifuged to separate bound fraction, (liquid phase separation system) the supernatant was decanted and then each tube was placed in gamma counter.

Table 3-1 T3 Radioimmunoassay analysis technique:

	Total	Standards	Unknowns
Standard Serum	-	50 µl	-
Unknowns serums	-	-	50 µl
^{125}I-T3	500 µl	500µl	500µl
T3 antibodies suspension	-	500µl	500µl

Vortex mix

Incubated at 37°C for 60 min

Magnetic separation

Supernatant is discarded

Counting

3-2-7-2: T4

Sufficient (polystyrene) test tubes were labeled in duplicates and arranged in assay rack, and then 25 µl was pipetted into each tube of the standards, quality control sample and patient's sample. And 250 µl anti T4 antibody added to each tube, and mixed well, to the STD and QC and samples250 µl of tracer was added.

After mixing well incubated at ^{37} Co for 45 minutes, then the rack was placed in the magnetic base for 10 minutes, to separate the bound fraction free from the free fractions by decant the supernatant. Lastly each tube was counted in the gamma counter to evaluate the gamma emission per minutes, and binding percent was plotted vs. the concentration, to get standard calibration curve, and from the curve obtained the concentration of Thyroxin in the patient's samples was evaluated. This method is bioassay method, (Radioimmunoassay), Using radioactive isotope of iodine. (I^{125}) which is gamma emitter

Table 3-2: T4 Radioimmunoassay analysis technique:

	Total	Standards	Unknowns
Standard Serum	-	50 µl	-
Unknowns serums	-	-	50 µl
^{125}I-T4	500 µl	500µl	500µl
T4 antibodies suspension	-	500µl	500µl

Vortex mix

Incubated at 37°C for 45 min

Magnetic separation

Supernatant is discarded

Counting

3-2-7-3: TSH

Sufficient test tubes were labeled and arranged in assay rack in duplicates,100 µl of STD and QC and sample was pipetted in target tube and 25 µl tracer (anti TSH labeled by I125)was added to each tube and vortexed then incubated at ^{37}Co in the incubator for one hour 250 µl of anti TSH (antibody coupled to magnetic particles) was added to each tube and mixed well and incubated at ^{25}Co for one hour then the racks were placed in the magnetic bases for 10 minutes and the supernatant was separated by decantation.

A wash buffer was diluted by adding water (1:9), and then 500 µl of the diluent was added to each tube and then vortexed well and then placed again in the magnetic base, the wash step was repeated and all the tubes were counted in the gamma counter, to evaluate the concentration of TSH in the patient sample.

The quantitative analysis of TSH is achieved by the above method, which is immunoradiometric method and it is noncompetitive method in which the radioactive compound (tracer) is TSH antibody, we have two antibodies react with the TSH in the analyte to get a sandwich complex.

Table 3-3: TSH Radioimmunoassay analysis technique:

	Total	Standards	Unknowns
Standard Serum	-	200 µl	-
Unknowns serums	-	-	200 µl
$_{125}$I-TSH	50 µl	50µl	50µl
Incubated at 37 ℃ for 1 hour			
TSH-Ab suspension	-	500µl	500µl
Incubated at room temp (18-25℃) for 1 hour			
Magnetic separation			
Wash buffer			
Reseperation followed by rewashing			
Counting			

3-2-7 Thyroid uptake technique:

3-2-7-1 patient preparation:

All patients were prepared by discontinuing thyroid medications for certain recommended periods of four weeks for Thyroxin medications and for two weeks for Neomercazole medications,

Female patients were inspected for pregnancy and breastfeeding, in case of breast feeding the patients were instructed to stop feeding for 24 hours after the exam during which the milk should be discarded three times the last one of them at ten minutes before restart breastfeeding.

The clinical history of the patient should be considered, and the clinical condition should be noted. The related study must be available, which is help full in diagnosis.

3-2-7-2: Technique:

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 3-5 mCi of $^{99m}TcO_4$ – 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, the patient waits for 15 to 20 minute, for maximum concentration of technetium sodium pertechnetate. 60 seconds' image for the empty syringe was taken.

Firstly 60 seconds image 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.

Take AP for thyroid gland with 300,000 counts, which gives good statistic image of radioactive distribution within the gland.

If there an enlarged in the thyroid gland marker with point source ^{99m}Tc or ^{57}Co will be used in the suprasternal 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 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

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Chapter four

Results

Chapter four

Results

Table 4.1: Thyroid uptake frequencies

Uptake range (%)	Frequency
normal	52
abnormal	48
total	100

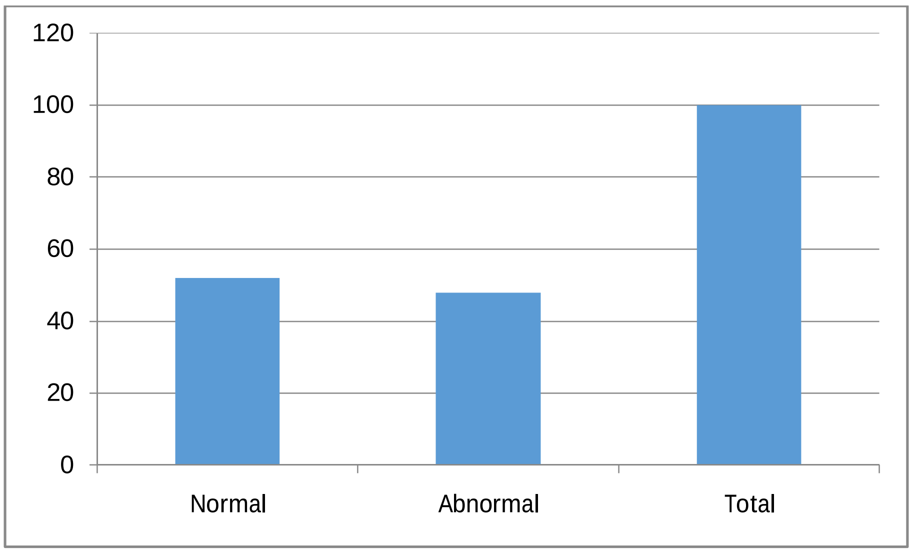

Figure 4.1: Thyroid uptake frequencies

Table 4.2show:T3 hormone levels

nmol/L	Frequency
0-0.5	3
0.51-1	9
1.01-1.5	23
1.51-2	18
2.01-2.5	7
2.51-3	4
3.01-3.5	4
3.51-4	4
More	28

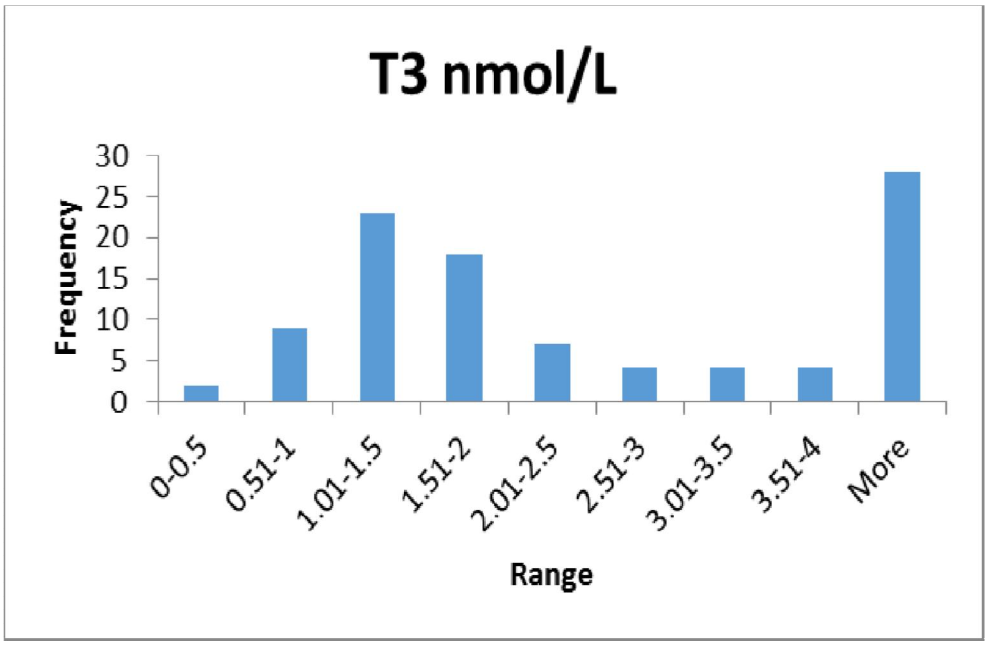

Figure 4.2: T3 hormone levels frequencies

Table 4.3: T4 hormone levels

nmol/L	Frequency
20-40	2
40-60	6
60-80	8
80-100	15
100-120	24
120-140	4
140-160	7
160-180	4
180-200	5
>200	25

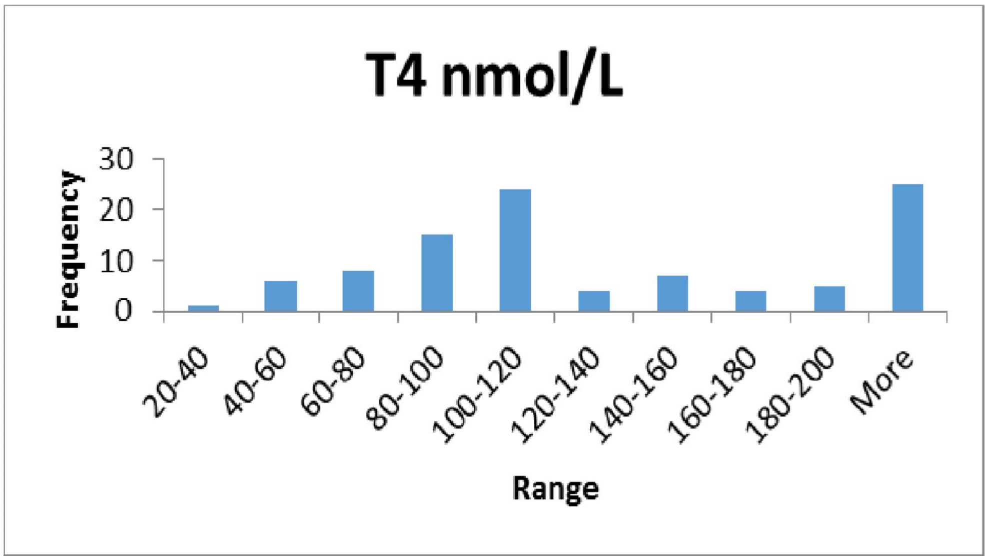

Figure 4.3: T4 hormone levels frequencies

Table 4.4: Frequencies of TSH levels

nmol/L	Frequency
0.5 – 1.0	43
1.0 - 1.5	10
1.5 – 2.0	11
2.0 - 2.5	15
2.5 - 3.0	4
3.0 - 3.5	9
>3.5	8

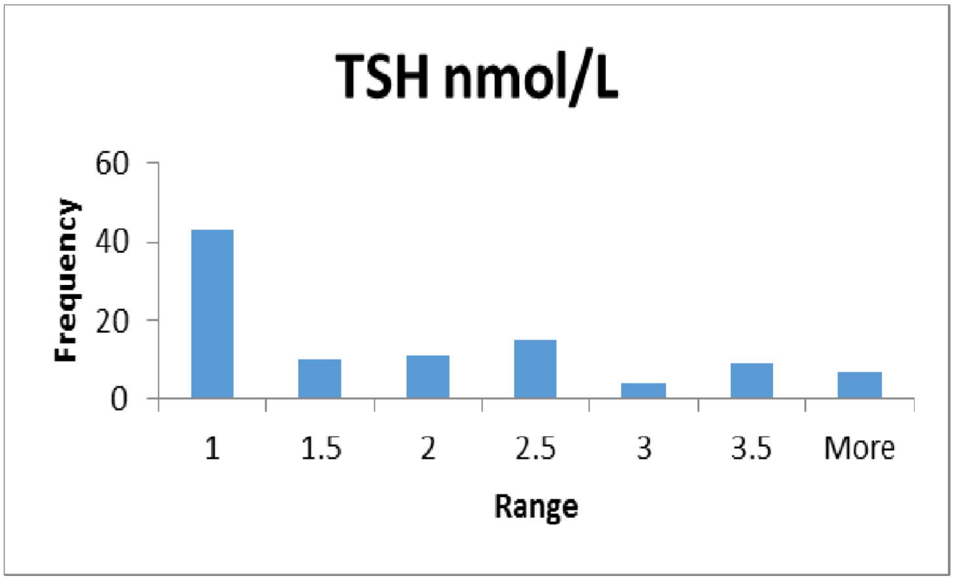

Figure 4.4: TSH hormone levels frequencies

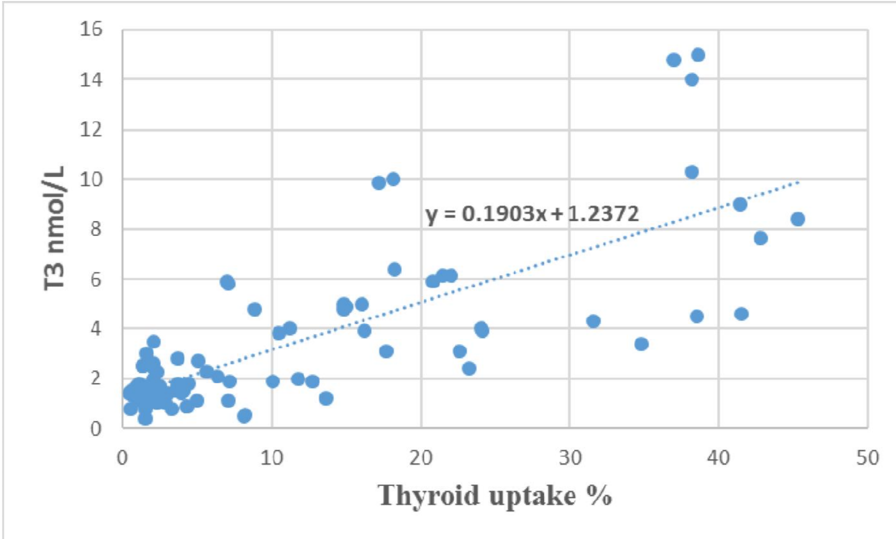

Figure 4.5: Scatter plot shows linear association between Thyroid uptake and T3 hormone level

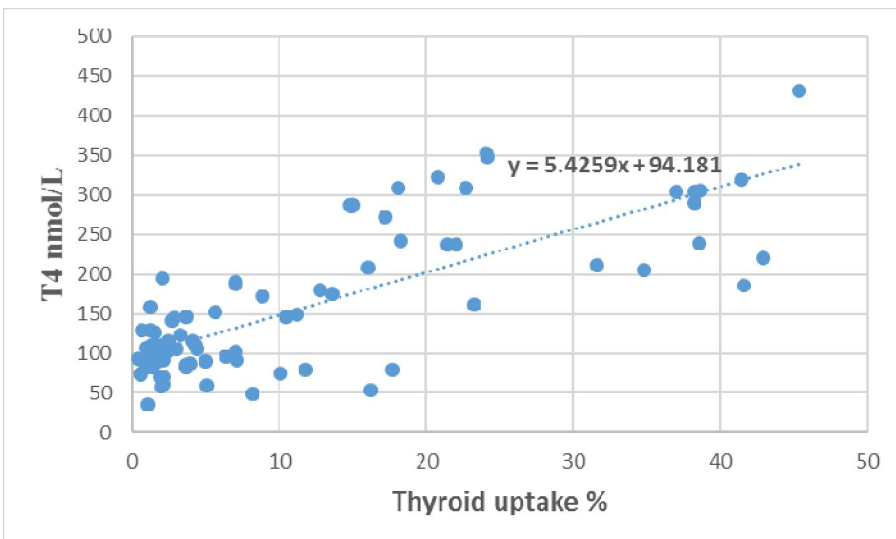

Figure 4-6: Scatter plot shows linear association between the thyroid ($^{99m}TcO4$) uptake and T4 hormone level

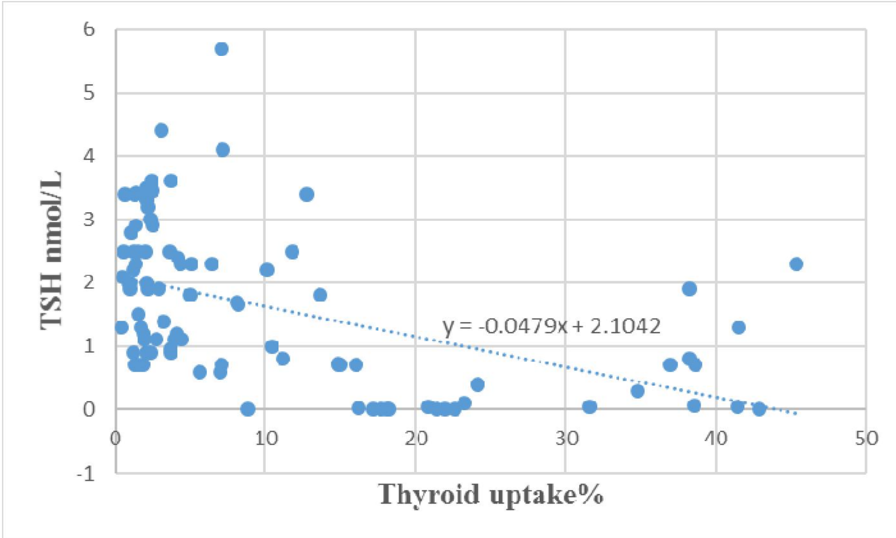

Figure 4.7: Scatter plot shows linear association between the thyroid ($^{99m}TcO_4$) uptake and TSH hormone level.

Table 4.5: Correlation coefficients of T3, T4, and TSH RIA with Thyroid uptake of $^{99m}TcO_4$

r(T3)	r(T4)	r(TSH)
0.536 (P-value=0.0001)	0.644 (P-value=0.004)	- 0.4398 (P-value=0.13)

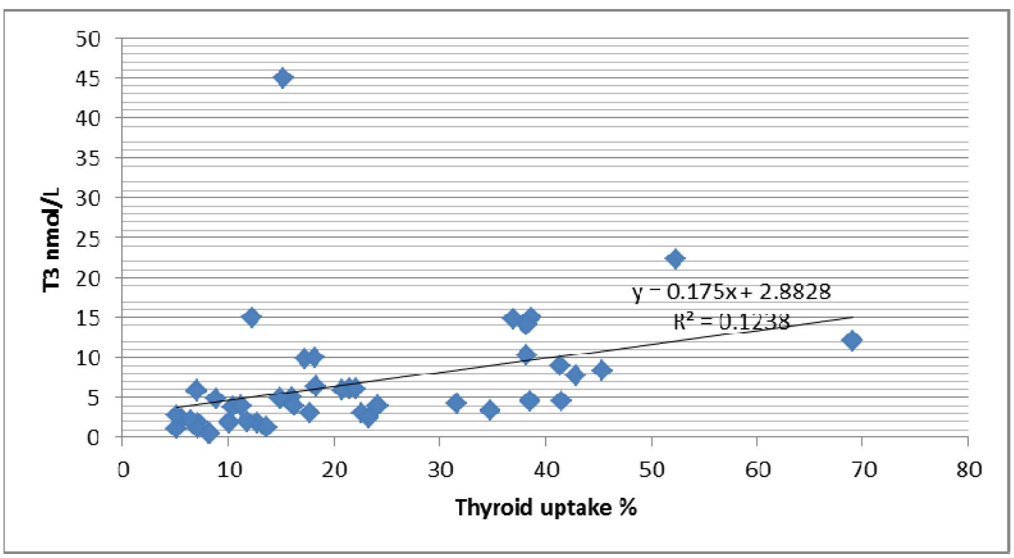

Figure 4.8: Scatter plot shows cross tabulation between higher thyroid uptake ($^{99m}TcO_4$) and T3 hormone level.

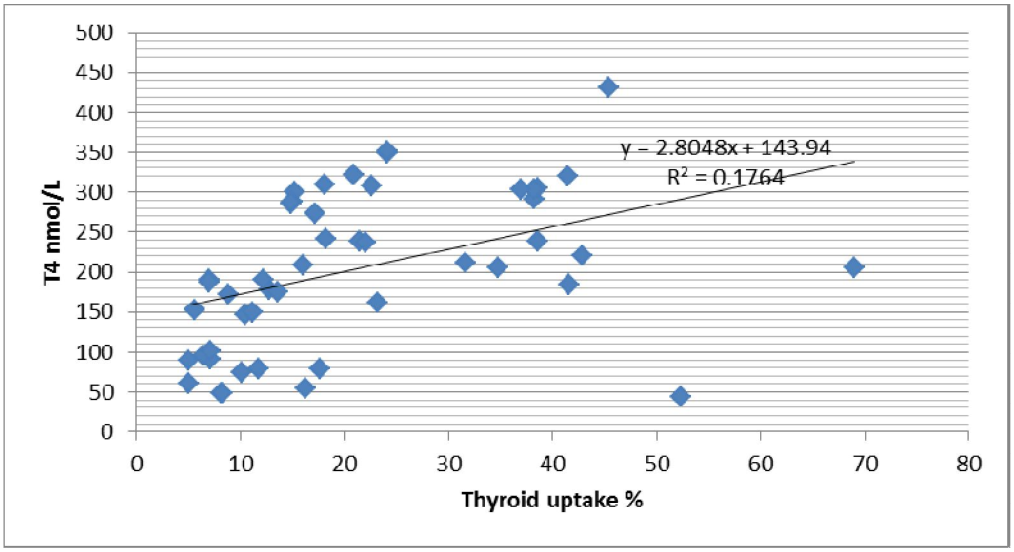

Figure 4.9: Scatter plot shows cross tabulation between higher thyroid uptake (^{99m}TcO4) and T4 hormone level.

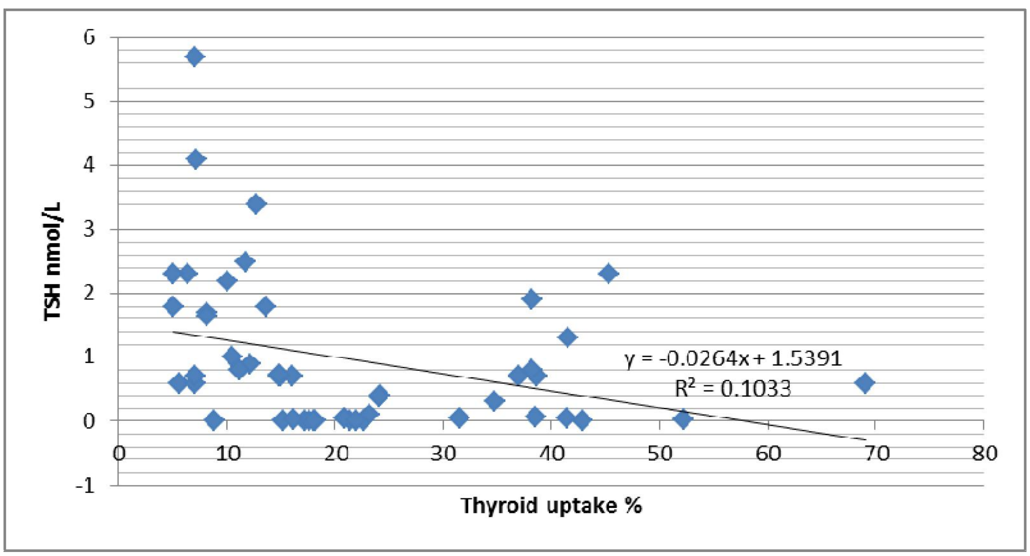

Figure 4.10: Scatter plot shows cross tabulation between higher thyroid uptake (^{99m}TcO4) and TSH hormone level.

Chapter Five

Discussion, conclusion and recommendations

Chapter Five

Discussion, conclusion and recommendations

5-1 Discussion:

The sample of this study included 100 patients with normal and abnormal results of thyroid uptake using gamma camera, where the main objective was to study the thyroid uptake of technetium pertechnetate and thyroid hormone levels (T3, T4 and TSH) obtained by radioimmunoassay (RIA) and to find out the correlation between them.

Physiologically it was expected that there will be a strong correlation between the values of thyroid ($^{99m}TcO_4$) uptakes and the levels of thyroid hormones (T3 &T4) in blood; since hormones synthesis by the thyroid gland is totally depending on its ability to extract iodide species from blood (uptake), but as what in the present study a moderate _not strong enough_ correlation was observed between the results of the TFT levels, and the uptake values of thyroid, as shown on table 4.5 .

In the present study, no doubt, a significant correlation between T3, T4 RIA values and thyroid uptake of $^{99m}TcO4$ was observed but it was weak ($0< r <1$) as shown on table 4.5 .This weak correlation may be attributed to non-thyroidal factors which have an influence on the Pertechnetate hemodynamics and uptake; therefore, estimating the thyroid hormones levels in blood from a given thyroid uptake values will not be applicable based on their correlational relationship.

Figures4.5 , 4.6 and 4.7 showed a linear association between thyroid uptake and T3,T4 and TSH hormone level using person product moment analysis .

Table 4.5 showed a significant positive correlation ($r=0.536$, $p < 0.01$) with T3, values assessed by radioimmunoassay (RIA). The thyroid $^{99m}TcO4$-uptake values studied in data of the same patients also revealed a medium positive and statistically significant correlation ($r = 0.644$, $p < 0.01$) with the T4, values assessed by RIA. The thyroid $^{99m}TcO4$-uptake total values showed an expected negative statistically insignificant correlation ($r= - 0.4398$ $p > 0.01$) with the TSH values.

Figure 4.8 , 4.9 , 4.10 show cross tabulation between higher thyroid uptake and T3 , T4 ,TSH hormone levels respectively which show ……

Determination of the statistical significance in this study was based on (Tail-2) probability value (P-value < 0.01).

This study is agreed with American thyroid association result (www.thyroid .org)

5-2 Conclusion:

Thyroid uptake study using radioactive $^{99m}TcO_4$ is a simple and cost effective method to investigate the functional status of thyroid gland and retains a corroborative and clarifying status in situations where the results of other tests are ambiguous or contradictory. According to the given results of correlation coefficients between the Thyroid uptakes and hormones levels, the thyroid uptake using radioactive $^{99m}TcO_4$ cannot be used to estimate the levels of the thyroid hormones in the blood; as the positive correlation between T3, T4 RIA values and the thyroid uptake is not statistically significant ($r < 1$). This study has come out with some recommendations and proposals which may be useful in determining the thyroid disorders in an accurate and reliable fashion.

Recommendations:

- More concern should be given to thyroid patient in sudan.

- Modern equipment (SPECT&PET)should be procured to Sudan for thyroid investigations to have precise results .
- Radiation protection for patient and staff at the nuclear medicine departments should always be considered .
- Regular training to the nuclear medicine staff should be planed to keep pacewith the developments in this field .
- Further studies are recommended to be conducted in future with more accuracy in criteria of data selection including gender criterion; for more equivalency between males and females' subjects, in addition to criteria of acquisition specifications (administered dose, time before acquisition, and distance from collimator).

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Appendices

Appendices:

Appendix (A):

Master data sheet

N	Uptake%	T3 nmol/L	T4 nmol/L	TSH nmol/L
1	3.97	1.4	87	1.1
2	2.05	2.4	105	2.5
3	1.34	2.5	110	0.7
4	7.15	1.9	91	4.1
5	0.6	1.5	73	2.5
6	1.1	1.8	36	7.6
7	3.26	0.8	123	1.4
8	2.09	3.5	195	0.9
9	3.71	2.8	86	3.6
10	5.66	2.3	152	0.6
11	1.4	1.5	83	2.3
12	2.1	2	62	3.3
13	0.95	1.7	107	1.9
14	5.03	1.1	90	1.8
15	2.33	2.3	107	3
16	1.38	2.5	110	0.7
17	2.1	2.6	97	2
18	2.17	1.2	70	1.9
19	2.15	1.4	92	3.2
20	1.52	0.8	89	1.5
21	7.02	5.9	190	0.6
22	1.33	1.5	104	3.4
23	0.94	1.5	83	2
24	2.08	2	108	3.5
25	2.47	1.7	113	3.6
26	3.69	1.7	83	0.9
27	1.61	1.6	89	0.7
28	1.09	1.3	90	2.8
29	16.04	5	209	0.7
30	2.72	1.4	142	1.1
31	1.23	1.7	129	0.9
32	1.87	1.6	70	0.7
33	4.12	1.5	116	1.2
34	1.93	1.8	58	1.1
35	1.21	1.6	159	2.2

36	1.85	1.4	110	1.2
37	1.72	1	104	1.3
38	3.65	1.5	146	2.5
39	4.45	1.8	106	1.1
40	1.42	1.1	102	2.9
41	2.34	1	102	0.9
42	0.43	1.4	93	1.3
43	1.21	1.1	104	2.5
44	6.4	2.1	96	2.3
45	1.59	3	126	8.6
46	0.54	0.8	75	2.1
47	3.04	1.4	105	4.4
48	1.53	0.4	106	2.5
49	0.7	1.3	130	3.4
50	2.49	1.5	116	2.9
51	7.08	1.1	102	5.7
52	2.89	1	145	1.9
53	22.66	3.1	308	0.01
54	31.61	4.3	212	0.05
55	17.2	9.88	273	0.005
56	38.57	4.5	239	0.07
57	15.2	45	299.7	0.01
58	12.74	1.9	179	3.4
59	45.38	8.4	432	2.3
60	34.82	3.4	205	0.3
61	38.24	10.3	291	1.9
62	12.21	15	191	0.9
63	16.21	3.9	54	0.024
64	13.62	1.2	175	1.8
65	11.8	2	79	2.5
66	14.88	4.8	286	0.7
67	10.47	3.8	147	1
68	24.18	3.9	348	0.4
69	21.46	6.12	238	0.009
70	17.7	3.1	79.24	0.005
71	42.87	7.66	220	0.005

72	18.23	6.4	242	0.005
73	38.63	15	305	0.7
74	8.16	0.5	49	1.7
75	8.86	4.8	172	0.006
76	4.36	0.9	110	2.3
77	18.14	10	309	0.005
78	5.07	2.7	60	2.3
79	20.83	5.9	322	0.05
80	10.09	1.9	75	2.2
81	41.43	9	320	0.05
82	69.04	12.1	206.1	0.6
83	23.24	2.4	162	0.1
84	41.56	4.6	185	1.3
85	52.31	22.33	44.5	0.028
86	38.22	14	304	0.8
87	4.23	0.9	111	2.4
88	37	14.8	304	0.7
89	8.23	0.56	49	1.65
90	15	4.9	288	0.7
91	11.2	4	150	0.8
92	24.11	4.01	352	0.38
93	22.02	6.14	237	0.008
94	7.06	5.8	188	0.7
95	1.35	1.35	105	3.42
96	0.95	1.4	82	1.99
97	2.07	1.98	107	3.34
98	2.49	1.5	114	3.46
99	3.7	1.8	84	0.96
100	14.86	5	287	0.72

Appendix (B):

Image (1) show $MO^{99}/^{99m}Tc$generator :

Image (2) show different type of radiopharmaceutical:

Image (3) showed RIA kits:


cisbio
ACTION IS EVERYTHING