بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

Sudan University of Science and Technology

College of Graduate Studies

Estimation of Thyroid Nodules using Thyroid Function Test and Scintigraphy

تقدير عقيدات الغدة الدرقية باستخدام فحص وظائف الغدة و المسح الذري للغدة

Thesis submitted for the fulfilment of the requirements of the Master Degree in nuclear medicine sciences

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2020

الآية

يقول الله عز وجل:

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

(يهدي الله لنوره من يشاء)

الآية (35) من سورة النور

Dedication

To my family, families are like branches on a tree, we grow in different directions yet our roots remain as one.

Acknowledgment

Special thanks to my Godfather of technology science in sudan **Prof. Mohamed Elfadil** I am grateful to have you as guide.

To my friends **Dr.Hanadi Seid Mohamed**, **Malaz Yasir**, **Elaf Ahmed**, you will always be the sisters of my soul, the friends of my heart.

Abstract

This study consists of 51 patients with thyroid nodules of different ages, gander, weigh, and heights, the data of this study collected from patients who referred to the department of nuclear medicine at Khartoum hospital for oncology and nuclear medicine for thyroid scan and they done laboratory test of Thyroid function test (TFT) .in period from Mar 2018 to Feb 2020. After that they were divided into three groups according to number of nodules. Group A consisted of 44 patients with one nodule. Group B contained of 5 patients with two nodules, and Group C consisting of 2 patients with three or more. For data analysis we used SPSS.

This study aimed to find thyroid uptake and TFT values and evaluated the effects of thyroid uptake on TFT for patients with thyroid nodules. The result found that there is significant correlation between the thyroid uptake and T, where uptake can be estimated using T3. There is a possibilities of using TFT as a diagnostic method for thyroid nodules alone.

المستخلص

تتكون هذه الدراسة من 51 مريض يعانون من عقيدات الغدة الدرقية من مختلف الأعمار والأوزان . وقد تم جمع البيانات من المرضى الذين تم تحويلهم إلى قسم الطب النووي بمستشفى الخرطوم للأورام والطب النووي للمسح الذري للغدة الدرقية وقاموا بفحص وظائف الغدة TFT. في الفترة من مارس 2018 إلى مارس 2020. بعد ذلك تم تقسيمهم إلى ثلاث مجموعات حسب عدد العقيدات. المجموعة الأولى تتكون من 44 مريض يعانون من عقيدة واحدة. المجموعة الثانية تتكون من 5 مرضى مع عقيدتين. والمجموعة الثالثة تتكون من 2 مريض مع ثلاث أو أكثر من العقيدات. لتحليل البيانات استخدمنا . SPSS

هدف هذه الدراسة تقدير عقيدات الغدة الدرقية باستخدام فحص وظائف الغدة و المسح الذري للغدة وتقييم تأثيرات امتصاص الغدة الدرقية على فحص وظائف الغدة. وجدت النتيجة ان هناك ارتباطا كبيرا بين امتصاص الغدة الدرقية وفحص وظائف الغدة, حيث يمكن تقدير الامتصاص باستخدام T3 . هناك احتمالية لاستخدام فحص وظائف الغدة كطريقة تشخيص للعقيدات الدرقية وحده.

CHAPTER ONE

CHAPTER TWO

CHAPTER THREE

CHAPTER FOUR

CHAPTER FIVE

CHAPTER ONE

Introduction

1.1 Nuclear medicine

In nuclear medicine clinical information is derived from observing the distribution of a pharmaceutical administered to the patient. By incorporating a radionuclide into the pharmaceutical, measurements can be made of the distribution of this radiopharmaceutical by noting the amount of radioactivity present. These measurements may be carried out either in vivo or in vitro. In vivo imaging is the most common type of procedure in nuclear medicine, nearly all imaging being carried out with a gamma camera. Nuclear medicine is intrinsically an imaging technique showing the body's biochemistry, the particular aspect depending upon the choice of the radiopharmaceutical. This is in contrast to other commonly used imaging procedures whose main strengths are showing anatomy. Where a knowledge of the precise amount of activity present in an organ is required then positron emission tomography can provide this, although while its usage is increasing it still remains a specialized technique. If an image of the distribution is not essential, collimated scintillation probe detectors aligned with the organ of interest may be used. If the amount of radioactivity present is very low then high-sensitivity whole body counters, consisting of heavily shielded probe detectors, are necessary. In vitro measurements are made on samples of material taken from the patient, such as breath, blood, urine, and feces, to determine the amount of radiopharmaceutical present. Such measurements are made using the gamma- or beta-sample counting techniques discussed in Chapter 4. The diagnostic information is provided by the action of the pharmaceutical; the role of the radioactivity is purely a passive one, enabling the radiopharmaceutical to be

localized. For this reason it is possible to use low levels of radioactivity and so the potential hazard to the patient can be kept small. [Peter F. Sharp, Practical Nuclear Medicine]

1.2 Objective of the study

1.2.1 General Objectives:

• To estimate thyroid nodules with TFT and technetium-99m pertechnetate.

1.2.2 Specific Objectives:

- To find thyroid uptake and TFT values
- To measure the size of nodules in thyroid scan and uptake for each
- To find the effects of thyroid nodules on TFT values
- To classify the patient as class 1, class 2, class 3 as result of nodules presence using body character and TFT.
- To generate a discriminate analysis equation that can identify the classes of the patients.

CHAPTER TWO

2.1 Anatomy

The thyroid is a bilobed structure evolving from the fourth and fifth branchial pouches. It is initially attached to the ventral floor of the pharynx by the thyroglossal duct. Thyroid tissue may be found anywhere between the base of the tongue and the retrosternal anterior mediastinum (Figure 2.1). The fetal thyroid gland begins to concentrate iodine and synthesize thyroid hormones by approximately 10.5 weeks, which is pertinent when the administration of 131I to fertile women is contemplated. The two ellipsoid lobes of the adult thyroid are joined by a thin isthmus. Each lobe is approximately 2 cm in thickness and width and averages 4–4.5 cm in length. The thyroid gland, averaging approximately 20 grams in weight, resides in the neck at the level of the cricoid cartilage. A pyramidal lobe is present in approximately 30–50%, arising from either the isthmus or the superomedial aspect of either lobe; it undergoes progressive atrophy in adulthood but may be prominent in patients with Graves' disease. Although the right lobe tends to be somewhat larger than the left lobe, there is a great deal of variability in both size and shape of the normal gland. [Peter F. Sharp, Practical Nuclear Medicine]

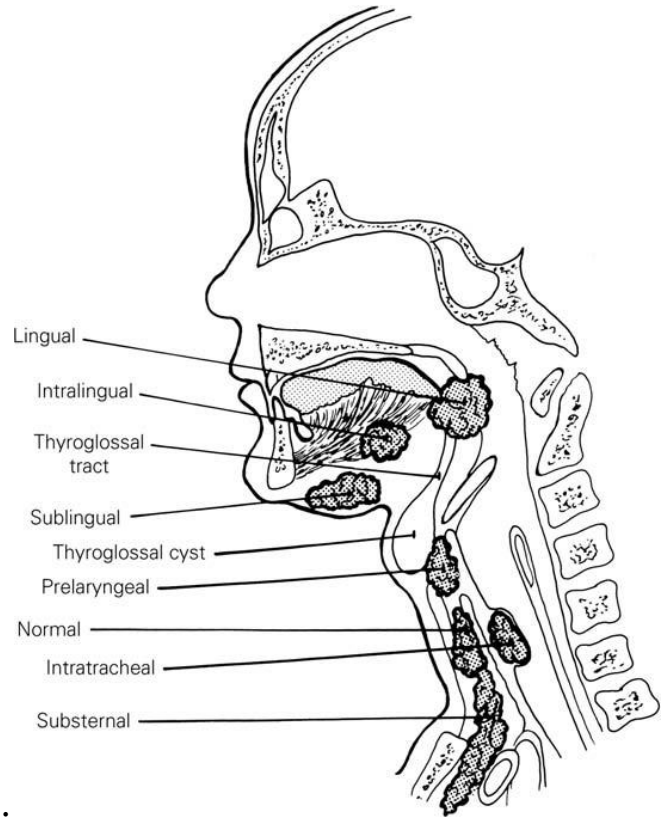


Figure 2.1 Normal and aberrant locations of thyroid tissue

[Peter F. Sharp, Practical Nuclear Medicine]

2.2 Physiology

An appreciation of thyroid physiology and pathophysiology is essential for the optimal management of thyroid disorders. The function of the thyroid gland includes the concentration of iodine, synthesis of thyroid hormones, storage of these hormones as part of the thyroglobulin (Tg) molecule in the colloid, and their secretion into the circulation as required. Over 99% of circulating thyroid hormones are bound to plasma proteins, primarily thyroxine-binding globulin (TBG). Only the unbound fraction of thyroid hormone is metabolically active and, for this reason, accurate assays of free thyroid hormone, “free T4” and “free T3”, have been developed. Dietary sources of iodine include seafood, milk, eggs, and

iodized products such as salt and bread. Approximately one-third of the absorbed dietary iodide is trapped by the thyroid, the remainder being excreted in the urine. Although gastric mucosa, salivary glands, and the lactating breast may also trap iodide, none of these organify it. The concentration of iodide by the thyroid gland, synthesis, and release of thyroid hormones are under the regulatory control of the hypothalamic-pituitary thyroid axis. Thyroid stimulating hormone (TSH) from the pituitary plays the major role in regulating thyroid function and this, in turn, is under the control of hypothalamic thyrotropin releasing hormone (TRH) secretion. The present third generation assay for circulating TSH is highly sensitive and represents the most sensitive biochemical indicator of both hypothyroidism and hyperthyroidism; the serum TSH is elevated to above 5 mIU/l with even subclinical primary hypothyroidism and is suppressed usually to undetectable levels with hyperthyroidism. Numerous exogenous factors such as systemic illness, nutritional status, thionamides, beta blockers, steroids, iodide, lithium, amiodarone, and anticonvulsants, may affect thyroid hormone secretion and metabolism. [Peter F. Sharp, Practical Nuclear Medicine]

2.3 Thyroid Nodules

Thyroid nodules are a common clinical problem. The prevalence of palpable thyroid nodules in adults is ashigh Solitary Thyroid Nodule [Hans-Jürgen Biersack, Clinical Nuclear Medicine] . They occur more often in women than men. The incidence of both benign and malignant nodules increases with age [Harvey A. Ziessman, Nuclear medicine: the requisites] Differentiating a benign versus malignant nodule is a common clinical problem [Harvey A. Ziessman, Nuclear medicine : the requisites]. The likelihood of malignancy occurring in a single nodule is 2–10%, but varies considerably from series to series, depending on

selection criteria. There is an increased risk of thyroid cancer associated with previous external radiation to the head or neck, although the clinical course of the cancer is the same as thyroid cancers found in other settings [Gary J.R. Cook, Clinical Nuclear Medicine]. The management of patients with a solitary thyroid nodule remains controversial, related to the high incidence of nodules, the infrequency of thyroid malignancy, and the relatively low morbidity and mortality associated with differentiated thyroid cancer (DTC) [2]. Thyroid nodules may contain normal thyroid tissue, benign hypofunctioning tissue (solid, cystic, or complex), hyperplastic or autonomously functioning benign tissue, or malignant neoplasm. [Peter F. Sharp, Practical Nuclear Medicine]

2.4 Nuclear Medicine History

2.4.1 Fundamental Concepts

The science and clinical practice of nuclear medicine involve the administration of trace amounts of compounds labeled with radioactivity (radionuclides) that are used to provide diagnostic information in a wide range of disease states. Although radionuclides also have some therapeutic uses, with similar underlying physics principles, this book focuses on the diagnostic uses of radionuclides in modern medicine. In its most basic form, a nuclear medicine study involves injecting a compound, which is labeled with a gamma-ray-emitting or positron-emitting radionuclide, into the body. The radiolabeled compound is called a *radiopharmaceutical*, or more commonly, a *tracer* or *radiotracer*. When the radionuclide decays, gamma rays or high-energy photons are emitted. The energy of these gamma rays or photons is such that a significant number can exit the body without being scattered or attenuated. An external, position-sensitive gamma-ray

"camera" can detect the gamma rays or photons and form an image of the distribution of the radionuclide, and hence the compound (including radiolabeled products of reactions of that compound) to which it was attached. There are two broad classes of nuclear medicine imaging: *single photon imaging* [which includes single photon emission computed tomography (SPECT)] and *positron imaging* [positron emission tomography (PET)]. Single photon imaging uses radionuclides that decay by gamma-ray emission. A *planar* image is obtained by taking a picture of the radionuclide distribution in the patient from one particular angle. This results in an image with little depth information, but which can still be diagnostically useful (e.g., in bone scans, where there is not much tracer uptake in the tissue lying above and below the bones). For the tomographic mode of single photon imaging (SPECT), data are collected from many angles around the patient. This allows cross-sectional images of the distribution of the radionuclide to be reconstructed, thus providing the depth information missing from planar imaging. Positron imaging makes use of radio-nuclides that decay by positron emission. The emitted positron has a very short lifetime and, following annihilation with an electron, simultaneously produces two high-energy photons that subsequently are detected by an imaging camera. Once again, tomographic images are formed by collecting data from many angles around the patient, resulting in PET images.[Simon R. Cherry, Physics In Nuclear Medicine]

2.4.2 The Power Of Nuclear Medicine

The power of nuclear medicine lies in its ability to provide exquisitely sensitive measures of a wide range of biologic processes in the body. Other medical imaging modalities such as magnetic resonance imaging (MRI), x-ray imaging, and x-ray computed tomography (CT) provide outstanding anatomic images but are limited in their ability to provide biologic information. For example, magnetic resonance

methods generally have a lower limit of detection in the millimolar concentration range (≈â•›6 × 1017 molecules per mL tissue), whereas nuclear medicine studies routinely detect radio-labeled substances in the nanomolar (≈â•›6 × 1011 molecules per mL tissue) or picomolar (≈â•›6 × 108 molecules per mL tissue) range. This sensitivity advantage, together with the ever-growing selection of radiolabeled compounds, allows nuclear medicine studies to be targeted to the very specific biologic processes underlying disease. Examples of the diverse biologic processes that can be measured by nuclear medicine techniques include tissue perfusion, glucose metabolism, the somatostatin receptor status of tumors, the density of dopamine receptors in the brain, and gene expression. Because radiation detectors can easily detect very tiny amounts of radioactivity, and because radiochemists are able to label compounds with very high specific activity (a large fraction of the injected molecules are labeled with a radioactive atom), it is possible to form high-quality images even with nanomolar or picomolar concentrations of compounds. Thus trace amounts of a compound, typically many orders of magnitude below the millimolar to micromolar concentrations that generally are required for pharmacologic effects, can be injected and followed safely over time without perturbing the biologic system. Like CT, there is a small radiation dose associated with performing nuclear medicine studies, with specific doses to the different organs depending on the radionuclide, as well as the spatial and temporal distribution of the particular radiolabeled compound that is being studied. The safe dose for human studies is established through careful dosimetry for every new radiopharmaceutical that is approved for human use. .[Simon R. Cherry, Physics In Nuclear Medicine]

2.4.3 Historical Overview

As with the development of any field of science or medicine, the history of nuclear medicine is a complex topic, involving contributions from a large number of scientists, engineers, and physicians. A complete overview is well beyond the scope of this book; however, a few highlights serve to place the development of nuclear medicine in its appropriate historical context. The origins of nuclear medicine1 can be traced back to the last years of the 19th century and the discovery of radioactivity by Henri Becquerel (1896) and of radium by Marie Curie (1898). These developments came close on the heels of the discovery of x rays in 1895 by Wilhelm Roentgen. Both x rays and radium sources were quickly adopted for medical applications and were used to make shadow images in which the radiation was transmitted through the body and onto photographic plates. This allowed physicians to see "inside" the human body noninvasively for the first time and was particularly useful for the imaging of bone. X rays soon became the method of choice for producing "radiographs" because images could be obtained more quickly and with better contrast than those provided by radium or other naturally occurring radionuclides that were available at that time. Although the field of diagnostic x-ray imaging rapidly gained acceptance, nuclear medicine had to await further developments. The biologic foundations for nuclear medicine were laid down between 1910 and 1945. In 1913, Georg de Hevesy developed the principles of the tracer approach2 and was the first to apply them to a biologic system in 1923, studying the absorption and translocation of radioactive lead nitrate in plants.3 The first human study employing radioactive tracers was probably that of Blumgart and Weiss (1927),4 who injected an aqueous solution of radon intravenously and measured the transit time of the blood from one arm to the other using a cloud chamber as the radiation detector. In the 1930s, with the invention of the cyclotron by Lawrence, 5 it became possible to artificially produce new

radionuclides, thereby extending the range of biologic processes that could be studied. Once again, de Hevesy was at the forefront of using these new radionuclides to study biologic processes in plants and in red blood cells. Finally, at the end of the Second World War, the nuclear reactor facilities that were developed as part of the Manhattan Project started to be used for the production of radioactive isotopes in quantities sufficient for medical applications. The 1950s saw the development of technology that allowed one to obtain images of the distribution of radionuclides in the human body rather than just counting at a few measurement points. Major milestones included the development of the rectilinear scanner in 1951 by Benedict Cassen6 and the Anger camera, the forerunner of all modern nuclear medicine single-photon imaging systems, developed in 1958 by Hal Anger. 7 In 1951, the use of positron emitters and the advantageous imaging properties of these radionuclides also were described by Wrenn and coworkers.8 Until the early 1960s, the fledgling field of nuclear medicine primarily used 131I in the study and diagnosis of thyroid disorders and an assortment of other radionuclides that were individually suitable for only a few specific organs. The use of 99mTc for imaging in 1964 by Paul Harper and colleagues9 changed this and was a major turning point for the development of nuclear medicine. The gamma rays emitted by 99mTc had very good properties for imaging. It also proved to be very flexible for labeling a wide variety of compounds that could be used to study virtually every organ in the body. Equally important, it could be produced in a relatively long-lived generator form, allowing hospitals to have a readily available supply of the radionuclide. Today, 99mTc is the most widely used radionuclide in nuclear medicine. The final important development was the mathematics to reconstruct tomographic images from a set of angular views around the patient. This revolutionized the whole field of medical imaging (leading to CT, PET, SPECT and MRI) because it replaced the two-dimensional representation of

the three-dimensional radioactivity distribution, with a true three-dimensional representation. This allowed the development of PET by Phelps and colleagues10 and SPECT by Kuhl and colleagues11 during the 1970s and marked the start of the modern era of nuclear medicine. .[Simon R. Cherry, PHYSICS In NUCLEAR MEDICINE]

2.4.4 Current Practice Of Nuclear Medicine

Nuclear medicine is used for a wide variety of diagnostic tests. There were roughly 100 different diagnostic imaging procedures available in 2006.* These procedures use many different radiolabeled compounds, cover all the major organ systems in the body, and provide many different measures of biologic function. Table 1-1 lists some of the more common clinical procedures. As of 2008, more than 30 million nuclear medicine imaging procedures were performed on a global basis.† There are more than 20,000 nuclear medicine cameras capable of imaging gamma-ray-emitting radionuclides installed in hospitals across the world. Even many small hospitals have their own nuclear medicine clinic. There also were more than 3,000 PET scanners installed in the world performing on the order of 4 million procedures annually. The short half-lives of the most commonly used positron-emitting radionuclides require an onsite accelerator or delivery of PET radiopharmaceuticals from regional radiopharmacies. To meet this need, there is now a PET radiopharmacy within 100 miles of approximately 90% of the hospital beds in the United States. The growth of clinical PET has been driven by the utility of a metabolic tracer, 18F-fluorodeoxyglucose, which has widespread applications in cancer, heart disease, and neurologic disorders. One major paradigm shift that has occurred since the turn of the millennium has been toward multimodality instrumentation. Virtually all PET scanners, and a rapidly growing number of SPECT systems, are now integrated with a CT scanner in combined PET/ CT and

SPECT/CT configurations. These systems enable the facile correlation of structure (CT) and function (PET or SPECT), yielding better diagnostic insight in many clinical situations. The combination of nuclear medicine scanners with MRI systems also is under investigation, and as of 2011, first commercial PET/MRI systems were being delivered. In addition to its clinical role, PET (and to a certain extent, SPECT) continues to play a major role in the biomedical research community. PET has become an established and powerful research tool for quantitatively and noninvasively measuring the rates of biologic processes, both in the healthy and diseased state. In this research environment, the radiolabeled compounds and clinical nuclear medicine assays of the future are being developed. In preclinical, translational and clinical research, nuclear medicine has been at the forefront in developing new diagnostic opportunities in the field of molecular medicine, created by the merger of biology and medicine. A rapid growth is now occurring in the number and diversity of PET and SPECT molecular imaging tracers targeted to specific proteins and molecular pathways implicated in disease. These nuclear medicine technologies also have been embraced by the pharmaceutical and biotechnology industries to aid in drug development and validation. .[Simon R. Cherry, PHYSICS In NUCLEAR MEDICINE]

2.4.5 The Role Of Physics In Nuclear Medicine

Although the physics underlying nuclear medicine is not changing, the technology for producing radioactive tracers and for obtaining images of those tracer distributions most certainly is. We can expect to continue seeing major improvements in nuclear medicine technology, which will come from combining advances in detector and accelerator physics, electronics, signal processing, and computer technology with the underlying physics of nuclear medicine. Methods for accurately quantifying the concentrations of radio-labeled tracers in structures of

interest, measuring biologic processes, and then relaying this information to the physician in a clinically meaningful and biologically relevant format are also an important challenge for the future. Refinement in the models used in dosimetry will allow better characterization of radiation exposure and make nuclear medicine even safer than it already is. Physics therefore continues to play an important and continuing role in providing high-quality, cost-effective, quantitative, reliable, and safe biologic assays in living humans. .[Simon R. Cherry, PHYSICS In NUCLEAR MEDICINE]

2.5 The Gamma Camera System

The gamma camera is the principal instrument for imaging in nuclear medicine and is shown in **Figure 2.2.** As can be seen, it consists of a large detector in front of which the patient is positioned. Gamma cameras with more than one detector are Now common, allowing a higher throughput of patients by acquiring two or more views simultaneously. Every aspect of the modern gamma camera is under computer control, allowing the operator to select the study acquisition time, or the number of counts to be acquired, to set the pulse height analyzers to reject scattered radiation, control the detector and patient bed positions for SPECT and whole body procedures, and display the image. A typical gamma camera image is shown in **Figure 2.3.** All gamma camera manufactures sell associated computers and software to process and display the acquired images. The type of computer and the operating system upon which the software functions has, in the past, varied between manufacturers. This has led to a number of problems, which has hindered the transfer of data between systems. However, in recent years, driven by the demand for onscreen reporting of images by clinicians and the need to transfer data to picture archiving and communications systems (PACS), these problems have, in part, been overcome. The solution has been to develop an industry standard data

format (DICOM) which, when used with the correct software, will allowthe free movement of data between imaging systems. Although all manufacturers will promote their products as being fully DICOM compliant, unfortunately a number of specific problems remain. [Peter F. Sharp, Practical Nuclear Medicine]

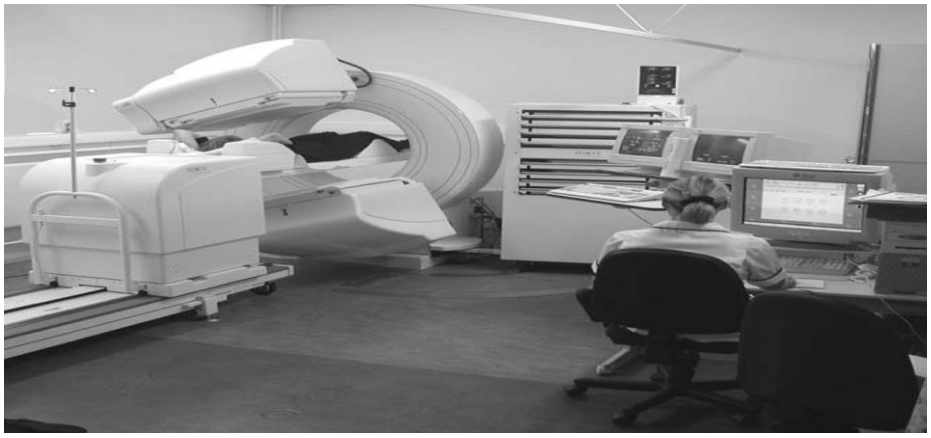


Figure 2.2 [Peter F. Sharp, Practical Nuclear Medicine]

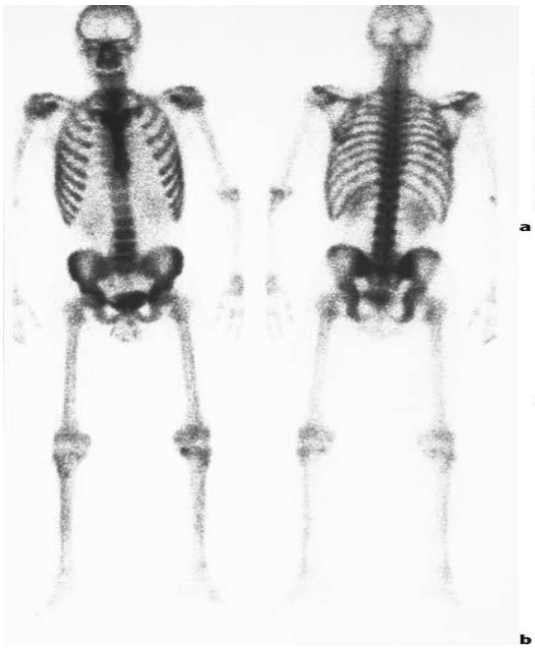


Figure 2.3

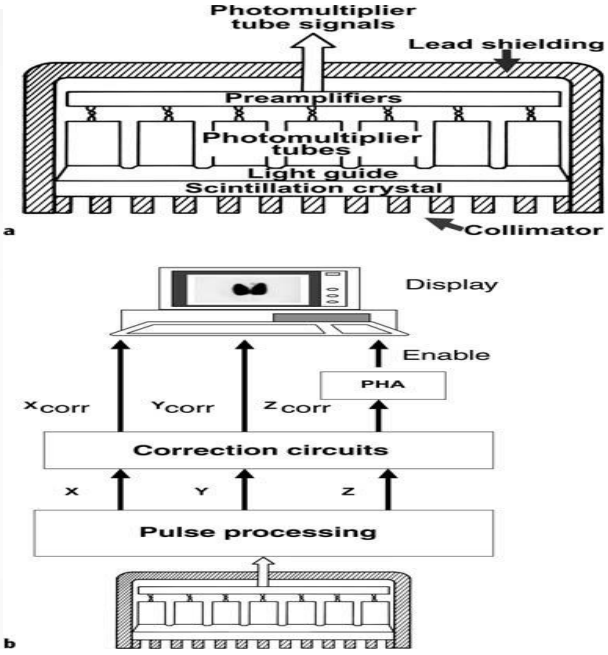


Figure 2.4

[Peter F. Sharp, Practical Nuclear Medicine]

2.6 Mode of Operation of the Gamma Camera

The basic principles of how a camera works are shown in **Figure 2.4.** The image of the distribution of the gamma-ray-emitting radiopharmaceutical is produced in the scintillation crystal by a collimator. The gamma rays, which are not visible to the eye, are converted into flashes of light by the scintillation crystal. This light is, in turn, transformed into electronic signals by an array of photomultiplier tubes (PMT) viewing the rear face of the crystal. After processing, the outputs from the PMTs are converted into three signals, two of which (X and Y) give the spatial location of the scintillation while the third (Z) represents the energy deposited in the crystal by the gamma ray. To improve their quality these signals then pass through correction circuits. The Z signal goes to a pulse height analyzer (PHA), which tests whether the energy of the gamma ray is within the range of values expected for the particular radionuclide being imaged. If the Z signal has an acceptable value, then a signal is sent instructing the display to record that there has been a gamma ray detected, the position being determined by the X and Y signals. The individual elements of the system will now be considered in more detail. [Peter F. Sharp, Practical Nuclear Medicine]

2.7 99Mo–99mTc Generator

The 99Mo radionuclide has a half-life of 66 hr and decays by b–emission; 87% of its decay goes ultimately to the metastable state 99mTc and the remaining 13% to the ground state 99Tc. It has photon transitions of 740 keV and 780 keV. The radionuclide 99mTc has a half-life of 6 hr and decays to 99Tc by isomeric transition of 140 keV. Approximately 10% of these transitions are via internal conversion. The ground state 99Tc has a half-life of 2:1 105 years and decays to stable 99Ru by b-emission. Because the half-lives of 99Mo and 99mTc di¤er by a factor of about 11, these two radionuclides lend themselves to the construction of a

useful generator. The extreme usefulness of this generator is due to the excellent radiation characteristics of 99mTc, namely its 6-hr half-life, very little electron emission, and a high yield of 140-keV g rays (90%), which are nearly ideal for the current generation of imaging devices in nuclear medicine. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.8 Solid Column Generator

The solvent extraction technique has been replaced by the solid column generator for obtaining 99mTc. The 99Mo–99mTc or ‘‘Moly’’ generator is constructed with alumina (Al2O3) loaded in a plastic or glass column. The Important Radionuclide Generators 67 amount of alumina used is of the order of 5 to 10 g, depending on the total activity of 99Mo. The 99Mo radioactivity is adsorbed on alumina in the chemical form MoO2-4 (molybdate) and in various amounts. The column is thoroughly washed with 0.9% NaCl solution to remove any undesirable activity. Currently, all generators are made with fission-produced 99Mo. The generator columns are shielded with lead for radiation protection. Some commercial firms use depleted uranium in lieu of lead for shielding high 99Mo activity generators (8.3–16.6 Ci or 307–614 GBq) because 238U has higher Z and therefore attenuates g rays more e‰ciently (depleted uranium is natural uranium from which 235U has been removed, leaving only 238U). After adsorption of 99Mo on alumina, 99mTc grows by the decay of 99Mo according to Eq. (2.10) until its maximum activity is reached after approximately four half-lives of 99mTc. At equilibrium and thereafter, the 99mTc radioactivity follows the half-life of 99Mo. The typical decay–growth relationship between 99Mo and 99mTc is illustrated in for a 100-mCi (3.7-GBq) generator. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

The 99mTc radionuclide is eluted as sodium pertechnetate (Na99mTcO4) with a 0.9% NaCl solution (saline without any additivies). After elution, the 99mTc radioactivity starts to grow again. Elution may be carried out, if needed, even before equilibrium is reached (a and b in Figure 5.2). The amount of 99mTc activity obtained in this case will depend on the time elapsed between the previous and present elutions. The 99Mo–99mTc generators are available from several commercial suppliers. In some commercial generators, isotonic saline is provided in a bottle that is placed inside the generator housing, and aliquots of saline are used up to elute 99mTc-pertechnetate (99mTcO4) using evacuated vials. Evacuated vials of di¤erent volumes are often supplied for elution in order to have approximately the same daily concentrations of 99mTc activity. Larger volume vials are used in the beginning of the week, and smaller volume vials are used in the latter part of the week. In other generators, vials with definite volumes of saline for each elution are provided. A commercial generator supplied by Mallinckrodt Medical, Inc. is shown in Figure 5.3. There are two types of Moly generators, wet column generators and dry column generators, supplied by di¤erent commercial firms. The di¤erence between the two types is that in a dry column generator after routine elution the leftover saline in the column is drawn out by using an evacuated vial without adding any more saline. The suggestion for a dry column generator came from the fact that radiation can cause radiolysis of water in a wet generator resulting in the formation of hydrogen peroxide (H2O2) and perhydroxyl free radical (HO2 :). These species are oxidants and, if present in the 99mTc eluate, can interfere with the technetium chemistry outlined in Chapter 6. The radiolysis of water is likely to be greater in the high activity generator. Also, in wet column generators, saline in the tubing may possibly freeze in extremely cold weather, thus preventing elution until thawed. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.9 Dose Calibrators

A dose calibrator is essentially a well-type ionization chamber that is used for assaying relatively large quantities (i.e., MBq range) of γ-ray-emitting radioactivity Figure 2.5. Dose calibrators are used for measuring or verifying the activity of generator eluates, patient preparations, shipments of radioactivity received from suppliers, and similar quantities of activity too large for assay with NaI(Tl) detector systems. The detector for a dose calibrator typically is an argon-filled chamber, sealed and pressurized to avoid variations in response with ambient barometric pressure Ionization chamberdose calibrators assay the total amount of activity present by measuring the total amount of ionization produced by the sample. Plug-in resistor modules, pushbuttons, or other selector mechanisms are used to adjust the electrometer readout to display the activity of the selected radionuclide directly in MBq or kBq units. Because ionization chambers have no inherent ability for energy discrimination, they cannot be used to select different γ-ray energies for measurement, as is possible with detectors having pulse-height analysis capabilities. One approach that is used to distinguish low-energy versus highenergy γ-ray emitters (e.g., 99mTc vs. 99Mo) is to measure the sample with and without a few millimeters of lead shielding around the source. Effectively, only the activity of the high-energy emitter is recorded with the shielding in place, whereas the total activity of both emitters is recorded with the shielding absent. This technique can be used to detect tens of kBq quantities of 99Mo in the presence of tens or even hundreds of MBq of 99mTc. As with the NaI(Tl) well counter, dose calibrators are subject to sample volume effects. These effects should be investigated experimentally when a new dose calibrator is acquired, so that correction factors can be applied in its use, if necessary. For example, a quantity of activity can be measured in a very small volume (e.g., 0.1mL in a 1-mL syringe),

and that activity can be diluted progressively to larger volumes in larger syringes and then in beakers, and so forth to determine the amount by which the instrument reading changes with sample volume. Another parameter worth evaluating is linearity of response versus sample activity. This may be determined conveniently by recording the reading for a 99mTc source of moderately high activity (e.g., 1 GBq, or whatever the approximate maximum amount of activity the dose calibrator will be used to assay), then recording the readings during a 24- to 48-hour period (4-8 half-lives) to determine whether they follow the expected decay curve for 99mTc. Deviations from the expected decay curve may indicate instrument electronic non- linearities requiring adjustment or correction of readings. In applying this technique, it is necessary to correct for 99Mo contamination using the shielding technique described earlier, especially after several 99mTc half-lives have elapsed. .[Simon R. Cherry, PHYSICS in NUCLEAR MEDICINE]

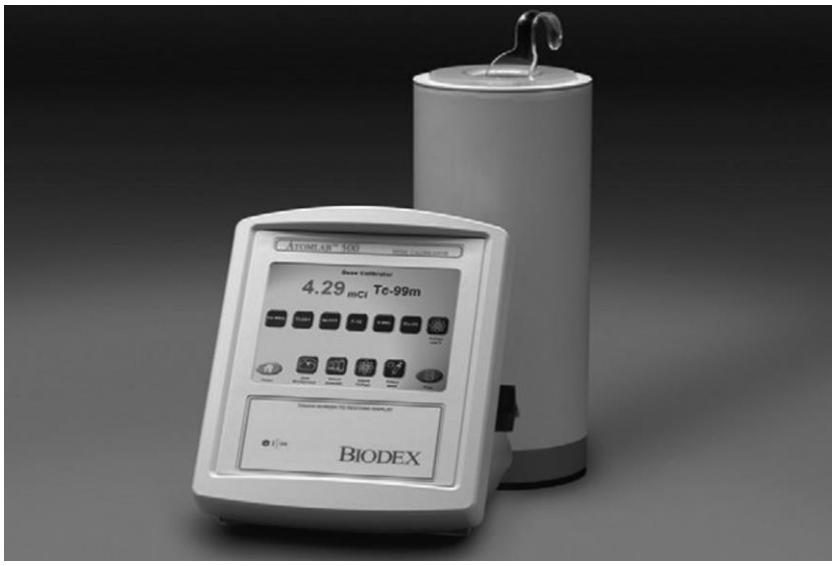


FIGURE 2.5 An ionization chamber dose calibrator. Samples are inserted into the well in the sealed ionization chamber. The current is measured and displayed on a digital readout. (*Courtesy Biodex Medical Systems, Shirley, NY.*)

2.10 Thyroid Scintigraphy

With the development of fine needle aspiration biopsy (FNA) for evaluation of nodular disease combined with the exquisite anatomic detail provided by sonography, CT, and MRI, the use of thyroid scintigraphy has decreased appropriately. However, it will continue to play an important role in the functional evaluation of a variety of thyroid disorders aswell as the detection of metastatic thyroid cancer. Technetium-99m pertechnetate is the most readily available radionuclide employed for thyroid imaging. Pertechnetate ions (TcO^{-}_{4}) are trapped by the thyroid in the same manner as iodine through an active iodine transporter, but pertechnetate ions are not organified. 123Iodine is both trapped and organified by the thyroid gland, allowing overall assessment of thyroid function. Since 123I is cyclotron-produced and has a relatively short half-life of 13.6 hours, it is more expensive and advance notice is necessary for imaging. Because of its inferior image quality and the high thyroid and total body radiation dose from its β-emission, 131I is not used for routine thyroid imaging other than for metastatic thyroid cancer assessment. Due primarily to less background activity, 123I imaging provides somewhat higher quality images than 99mTc, but the diagnostic information provided by each is roughly equivalent. 123I imaging is used in specific situations, such as retrosternal goiter. The normal thyroid scintigram is shown in Figure 13.2. High-resolution images are obtained by using a pinhole collimator, thus permitting the detection of nodules as small as 5mmin diameter. The oblique views permit detection of small nodules obscured by overlying or underlying physiological activity. Pinhole SPECT has been used to better detect subtle abnormalities. With pertechnetate, salivary glands, gastric mucosa, esophagus, and blood pool background are seen in addition to thyroid activity. Due to delayed imaging, salivary gland activity is often absent with 123I imaging. In

the euthyroid gland, thyroid activity should be greater than that of the salivary glands. Ectopia is typically associated with hypothyroidism. Significant concavity of the lateral margin should be considered suspicious of a hypofunctioning nodule, and exaggerated convexity is often seen with diffuse goiters. The pyramidal lobe, a remnant of the distal thyroglossal duct, is identified in less than 10% of euthyroid patients, but is visualized in as many as 43% of patients with Graves' disease. Extrathyroidal accumulation of the radiopharmaceutical usually represents ectopic thyroid tissue or metastatic thyroid carcinoma if gastroesophageal and salivary gland activity can be excluded. [Peter F. Sharp, Practical Nuclear Medicine]

2.11 Thyroid Function Test

2.11.1 Free Thyroxine (FT4)

The normal values for FT4 in adults range from 1.0 to 3.0 ng/dL (13 to 39 pmol/L). A minute amount of thyroid hormone circulates in the blood in a free form, not bound to serum proteins. It is in reversible equilibrium with the bound hormone and represents the diffusible fraction of the hormone capable of traversing cellular membranes to exert its effects on body tissues. Although changes in serum hormone-binding proteins affect both the total hormone concentration and the corresponding fraction circulating free in the euthyroid person, the absolute concentration of free hormone remains constant and correlates with the tissue hormone level and its biologic effect. Serum FT4 may be suppressed in the patients with thyroidal illness and transiently rise in acute thyroidal illness, when thyroid-binding protein frequently falls. Thyroid function tests:a review G.Shivaraj, B.Desai Prakash, V.Sonal, K.Shruthi, H.Vinayak, M.Avinash.

2.11.2 Free Triiodothyronine (FT3)

The normal adult reference value is 0.25-0.65 ng/dL (3.8-10 nmol/L). Free triiodothyronine (FT3) measures the very tiny amount of T3 that circulates unbound. It is useful in looking for hyperthyroidism or thyroxine overplacement in women who are pregnant or taking any effective drugs that varies the TBG like estrogen. More consistently, patients with a variety of non-thyroidal illnesses have low FT3 levels1. This decrease is characteristic of all conditions associated with depressed serum TT3 concentrations due to a diminished conversion of T4 to T3 in peripheral tissues. Marked elevations in both FT4 and FT3 concentrations in the absence of hypermetabolism are typical of patients with resistance to thyroid hormone. The FT3 concentration is usually normal or even high in hypothyroid persons living in areas of severe endemic iodine deficiency and their FT4 levels are, however, normal or low. Information concerning this value can be the most important parameter in evaluation of thyroid function because it relates to patients status although other mechanisms exists for cell to control the active amount of the thyroid hormone by autoregulation of receptor and regulation of deiodinase activity. Rarely, a defect in thyroid hormone transport in the cells would abolish the free hormone and metabolic effect co-relation. The free hormone concentration is high in thyrotoxicosis, low in hypothyroidism,and normal in euthyroidism. Thyroid function tests:a review G.Shivaraj, B.Desai Prakash, V.Sonal, K.Shruthi, H.Vinayak, M.Avinash.

2.11.3 Thyrotropin or Thyroid Stimulating Hormone (TSH)

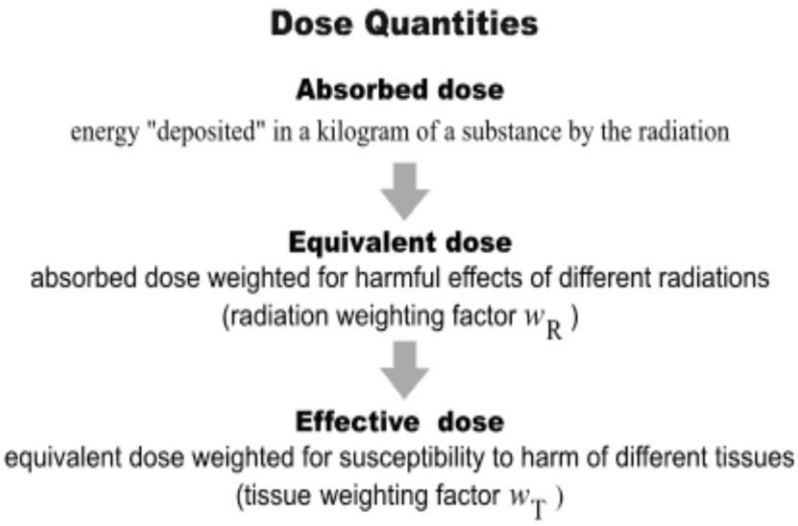
Likely to all pituitary hormones, TSH is secreted pulsately and has a circadian rhythm. Serum TSH concentrations are highest in the evening at 23 hours, during the first hours of sleep. The serum TSH values vary as the age changes. Normal range is approximately 0.5-4.5 mU/L1. The American Association of Clinical

Endocrinologists (AACE) has revised these guidelines as of early 2003, narrowing the range 0.3-3.0 mU/L. The majority of practitioners including endocrinologists and the physicians who specialize in thyroid disease rely solely on the TSH test as the primary test, for diagnosing and managing most thyroid conditions. Moreover, to minimize the cost of a TFT the study was aimed to determine if TSH or FT4 alone as a first-line test would be adequate in assessing the thyroid hormone status of patients. Analyzed TFT records from January 1996 to May 2000 in the Port Moresby General Hospital was done. The biochemical status of 95% of patients will be appropriately categorized as euthyroidism, hypothyroidism or hyperthyroidism with only 5% discrepant (i.e., normal TSH with abnormal FT4) results. In contrast, using FT4 alone as a firstline test correctly classifies only 84% of TFTs. Euthyroid status is observed in 50% of patients and FT4 assays on these samples will be excluded appropriately if a TSH-only protocol is adopted. This will save a quarter of the yearly cost of Thyroid Function Test (TFT) on reagents alone by performing TSH only. Hence TSH alone is an adequate first-line thyroid function test, when it is normal no further FT4 test is necessary unless clinically indicated. Thyroid function tests:a review G.Shivaraj, B.Desai Prakash, V.Sonal, K.Shruthi, H.Vinayak, M.Avinash

2.12 Radiation Protection

In the United States, radiation absorbed dose, dose equivalent, and exposure are often measured and stated in the older units called rad, rem, or roentgen (R). For practical purposes with gamma and x rays, these units of measure for exposure or dose are considered equal. This exposure can be from an external source irradiating the whole body, an extremity, or other organ or tissue resulting in an external radiation dose. Alternately, internally deposited radioactive material may cause an internal radiation dose to the whole body or other organ or tissue. Smaller fractions

of these measured quantities often have a prefix, such as, milli (m) means 1/1,000. For example, 1 rad = 1,000 mrad. Micro (μ) means 1/1,000,000. So, 1,000,000 μrad = 1 rad, or 10 μR = 0.000010 R. The "System International" of units (SI system) for radiation measurement is now the official system of measurement and uses the "gray" (Gy) and "sievert" (Sv) for absorbed dose and equivalent dose respectively. Conversions are as follows: (1 Gy = 100 rad /1 mGy = 100 mrad / 1 Sv = 100 rem / 1 mSv = 100 mrem) With radiation counting systems, radioactive transformation events can be measured in units of "disintegrations per minute" (dpm) and, because instruments are not 100% efficient, "counts per minute" (cpm). Background radiation levels are typically less than 10 μR per hour, but due to differences in detector size and efficiency, the cpm reading on fixed monitors and various handheld survey meters will vary considerably. The information and material posted on this website is intended as general reference information only. Specific facts and circumstances may alter the concepts and applications of materials and information described herein. The information provided is not a substitute for professional advice and should not be relied upon in the absence of such professional advice specific to whatever facts and circumstances are presented in any given situation. Answers are correct at the time they are posted on the Website. Be advised that over time, some requirements could change, new data could be made available, or Internet links could change. For answers that have been posted for several months or longer, please check the current status of the posted information prior to using the responses for specific. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]



Absorbed Dose Radiation exposure is measured in an international (SI) unit called the gray (Gy). The radiation exposure is equivalent to the energy "deposited" in a kilogram of a substance by the radiation. Exposure is also referred to as absorbed dose. The important concept is that exposure is measured by what radiation does to substances, not anything particular about the radiation itself. This allows us to unify the measurement of different types of radiation (i.e., particles and wave) by measuring what they do to materials. The gray is a large unit and for normal radiation protection levels a series of prefixes are used: " nanogray (nGy) is one thousand millionth of a gray (1/1,000,000,000)" " microgray (μGy) is one millionth of a gray (1/1,000,000)" " milligray (mGy) is one thousandth of a gray (1/1,000)" Equivalent Dose Often we are interested in the effect of radiation exposure on human tissue. Enter a quantity called equivalent dose. This relates the absorbed dose in human tissue to the effective biological damage of the radiation. Not all radiation has the same biological effect, even for the same amount of absorbed dose. Equivalent dose is measured in an international (SI) unit called the Sievert (Sv). Like the gray, the sievert is a large unit and for normal radiation protection levels a series of prefixes are used: " nanoSievert (nSv) is one thousand

millionth of a Sievert (1/1,000,000,000)" " microSievert (μSv) is one millionth of a Sievert (1/1,000,000)" " milliSievert (mSv) is one thousandth of a Sievert (1/1,000)" To determine equivalent dose (Sv), you multiply absorbed dose (Gy) by a radiation weighting factor that is unique to the type of radiation. The radiation weighting factor WR takes into account that some kinds of radiation are inherently more dangerous to biological tissue, even if their "energy deposition" levels are the same. For x-rays and gamma rays and electrons absorbed by human tissue, WR is 1. For alpha particles it is 20. To compute Sieverts from Grays, simply multiply by WR. This is obviously a simplification. The radiation weighting factor WR approximates what otherwise would be very complicated computations. The values for WR change periodically as new research refines the approximations. Exposure occurs over time, of course. The more Sieverts absorbed in a unit of time, the more intense the exposure. And so we express actual exposure as an amount over a specific time period, such as 5 millisieverts per year. This is called the "dosage rate". In Australia the dosage rate from background radiation, the sum of all natural radiation, is about 2 millisieverts per year. Effective Dose The probability of a harmful effect from radiation exposure depends on what part or parts of the body are exposed. Some organs are more sensitive to radiation than others. A tissue weighting factor is used to take this into account. When an equivalent dose to an organ is multiplied by the tissue weighting factor for that organ the result is the effective dose to that organ. The unit of effective dose is the sievert (Sv). If more than one organ is exposed then the effective dose, E, is the sum of the effective doses to all exposed organs. Radiation area is an area in which an individual could receive from a radiation source a dose equivalent in excess of 5 mrem (0.05 mSv) in 1 hr at 30 cm from the source. High radiation area is an area in which an individual could receive from a radiation source a dose equivalent in excess of 100 mrem (1 mSv) in 1 hr at 30 cm from the source. Very high radiation area is an area

in which an individual could receive from radiation sources an absorbed dose in excess of 500 rad (5 Gy) in 1 hr at 1 m from the source. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.1 Caution Signs and Labels

The NRC requires that specific signs, symbols, and labels be used to warn people of possible danger from the presence of radiations. These signs use magenta, purple, and black colors on a yellow background. Caution: Radiation Area: This sign must be posted in radiation areas. Caution: High Radiation Area or Danger: High Radiation Area: This sign must be posted in high radiation areas. Caution: Radioactive Material or Danger: Radioactive Material: This sign is posted in areas or rooms in which 10 times the quantity or more of any licensed material specified are used or stored. All containers with quantities of licensed materials exceeding those specified should be labeled with this sign. These labels must be removed or defaced prior to disposal of the container in the unrestricted areas. Caution signs are not required in rooms storing the sealed sources, provided the radiation exposure at 1 foot (30 cm) from the surface of the source reads less than 5 mrem (0.05 mSv) per hr. Caution signs are not needed in rooms where radioactive materials are handled for less than 8 hr, during which time the materials are constantly attended. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.2 Occupational Dose Limits

The annual limit of the occupational dose to an individual adult is the more limiting of (a) TEDE of 5 rem (0.05 Sv) or (b) the sum of the deep-dose equivalent and the committed dose equivalent to any individual organ or tissue other than the lens of the eye being equal to 50 rem (0.5 Sv). It should be noted that there is no lifetime cumulative dose limit in the revised 10CFR20, although the NCRP

recommends a lifetime cumulative dose of 1 rem (0.01 Sv) age in years. The annual limit on the occupational dose to the lens of the eye is 15 rem (0.15 Sv). The annual limit on the occupational dose to the skin and other extremities is the shallow-dose equivalent of 50 rem (0.5 Sv). Depending on the license conditions, both internal and external doses have to be summed to comply with the limits. A licensee may authorize under planned special procedures an adult worker to receive additional dose in excess of the prescribed annual limits, provided no alternative procedure is available. The total dose from all planned procedures plus all doses in excess of the limits must not exceed the dose limit (5 rem or 0.05 Sv) in a given year, nor must it exceed five times the annual dose limits in the individual's lifetime. The annual occupational dose limits for minors are 10% of the annual dose limits for the adults. The dose limit to the fetus/embryo during the entire pregnancy (gestation period) due to occupational exposure of a declared pregnant woman is 0.5 rem (0.005 Sv). The total e¤ective dose equivalent to individual members of the public is 0.1 rem (0.001 Sv) per year. However, this limit can be increased to 0.5 rem (0.005 Sv) provided the need for such a higher limit is demonstrated. The dose in an unrestricted area from an external source is 2 mrem (0.02 mSv) in an hour. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.3 ALARA Program

The dose limits are the upper limits for radiation exposure to individuals. The NRC has instituted the ALARA (as low as reasonably achievable) concept to reduce radiation exposure to individuals. The ALARA concept calls for a reasonable e¤ort to maintain individual and collective doses as low as possible. Under this concept, techniques, equipment, and procedures are all critically evaluated. According to Regulatory Guide NUREG-1556, volume 9, under the ALARA concept, when the exposure to a radiation worker exceeds 10% of the occupational exposure in a

quarter (Action level I), an investigation by the RSO takes place and the report is reviewed by the radiation safety committee (RSC). When the occupational exposure exceeds 30% of the occupational exposure (Action level II), corrective actions are taken or the institution must justify a higher dose level for ALARA in that particular situation. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.4 Principles of Radiation Protection

Of the various types of radiation, the a particle is most damaging due to its great charge and mass, followed by the b particle and the g rays. Heavier particles have shorter ranges and therefore deposit more energy per unit path length in the absorber, causing more damage. These are called nonpenetrating radiations. On the other hand, g and x rays have no charge and mass and therefore have a much longer range in matter. These electromagnetic radiations are called penetrating radiations. Knowledge of the type and energy of radiations is essential in understanding the principles of radiation protection. The cardinal principles of radiation protection from external sources are based on four factors: time, distance, shielding, and activity. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.4.1 Time

The total radiation exposure to an individual is directly proportional to the time the person is exposed to the radiation source. The longer the exposure, the higher the radiation dose. Therefore, it is wise to spend no more time than necessary near radiation sources. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.4.2 Distance

The intensity of a radiation source, and hence the radiation exposure, varies inversely as the square of the distance. It is recommended that an individual

remains as far away as possible from the radiation source. Procedures and radiation areas should be designed such that only minimum exposure takes place to individuals doing the procedures or staying in or near the radiation areas. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.4.3 Shielding

Various high atomic number (Z) materials that absorb radiations can be used to provide radiation protection. Since the ranges of a and b particles are short in matter, the containers themselves act as shields for these radiations. However, g radiations are highly penetrating, and therefore highly absorbing material must be used for shielding of g-emitting sources. For economic reasons, lead is most commonly used for this purpose. The concept of half-value layer (HVL) of an absorbing material for penetrating radiations is important in the design of shielding for radiation protection. It is defined as the thickness of shielding that reduces the exposure from a radiation source by one half. Thus, an HVL of an absorber placed around a source of radiation with an exposure rate of 100 mR/hr will reduce the exposure rate to 50 mR/hr. The HVL is dependent on both the energy of the radiation and the atomic number of the absorbing material. The HVL value is greater for high-energy radiations and smaller for high Z materials. The greater the HVL of any material for a radiation, the larger the amount of material necessary to shield the radiation. Obviously, shielding is an important means of protection from radiation. Radionuclides should be stored in a shielded area. The dosages for patients should be transported in lead containers, and injected using syringe shield. Radionuclides emitting b particles should be stored in containers of low Z material such as aluminum and plastic because in high Z material such as lead they produce highly penetrating bremsstrahlung radiation. For example, 32P should be stored in

plastic containers instead of lead containers. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.12.5 Personnel Monitoring

Personnel monitoring is required under the following conditions:

1. Occupational workers including minors and pregnant women likely to receive in 1 year a dose in excess of 10% of the annual limit from the external radiation source.

2. Individuals entering high or very high radiation areas.

Monitoring for occupational intake of radioactive material is also required if the annual intake by an individual is likely to exceed 10% of the ALls in Table 1, Appendix B of 10CFR20, and if the minors and pregnant women are likely to receive a committed effective dose equivalent in excess of 0.05 rem (0.5 mSv) in 1 year. Three devices are used to measure the exposure of ionizing radiations received by an individual: the pocket dosimeter, the film badge, and the thermoluminescent dosimeter. The pocket dosimeter works on the principle of a charged electroscope **Fig. 2.6** provided with a scale inside. The scale is so designed that when the dosimeter is fully charged it reads zero, and as the charge is reduced by radiation, the reading on the viewable scale increases. The dosimeter is initially charged to read zero. Ionizing radiation discharges the dosimeter by ionization in the sensitive volume of the chamber and the amount of exposure can be read from the scale. The dosimeter has the advantage of giving an immediate reading, but it requires frequent charging for reuse. Because the charge leaks over time, the cumulative reading over a long period of time can be erroneous. These dosimeters are available in full-scale readings of 200 mR, 500 mR, and 1 R. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

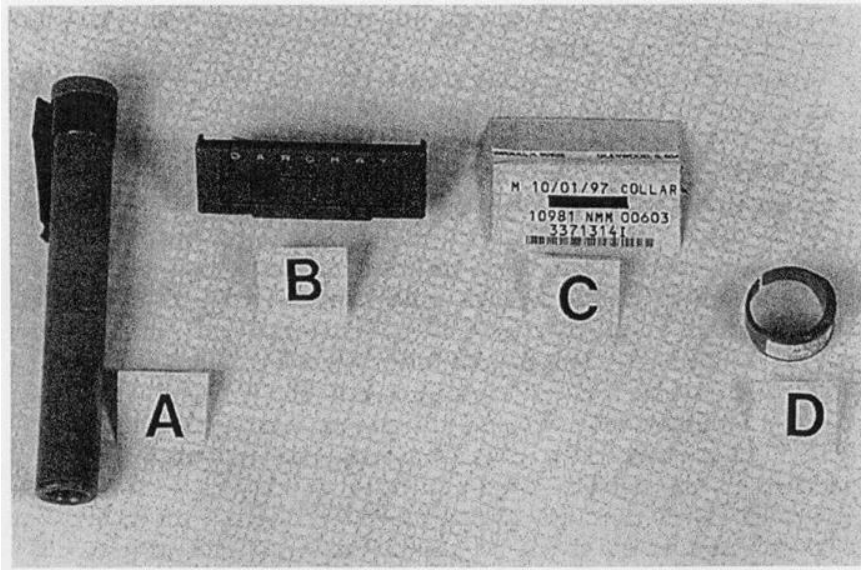


Figure 2.6 Devices to measure personnel radiation exposure. A: Pocket dosimeter. (Courtesy of Nuclear Associates, Division of Victoreen, Inc., 100 Voice Rd, Carle Place, New York.) B: Film badge holder. C: Film badge. D: Thermoluminescent chip in finger badge.

The film badge is most popular and cost-effective for personnel monitoring and gives reasonably accurate readings of exposures from b, g, and x radiations. The film badge consists of a radiation-sensitive film held in a plastic holder. Filters of different materials (aluminum, copper, and cadmium) are attached to the holder in front of the film to differentiate exposures from radiations of different types and energies. The optical density of the developed film after exposure is measured by a densitometer and compared with that of a calibrated film exposed to known radiations. Film badges are usually changed by radiation workers on a monthly basis and give an integrated dose for each individual for a month. The main disadvantage of the film badge is the long waiting period before the exposed personnel know about their exposure. The film badge also tends to develop fog due to heat and humidity, particularly when in storage for a long time, and this may obscure the actual exposure reading. In many institutions the film badges of all

workers are sent to a commercial firm approved by National Voluntary Laboratory Accredition Program (NVLAP) of the National Institute of Standards and Technology that develops and reads the density of the films and sends the report of exposure to the institution. When an individual is employed at a radiation facility, a record of his accumulated dose must be retrieved from previous employers and added to his present dose account. A thermoluminescent dosimeter (TLD) consists of inorganic crystals (chips) such as lithium fluoride (LiF) and manganese-activated calcium fluoride (CaF2 :Mn) held in holders like the film badges or finger rings. When these crystals are exposed to radiations, electrons from the valence band are excited and trapped by the impurities in the forbidden band. If the radiation-exposed crystal is heated to 300to 400C, the trapped electrons are raised to the conduction band, wherefrom they fall back into the valence band, emitting light. The amount of light emitted is proportional to the amount of radiation energy absorbed in the TLD. The light is measured and read as the amount of radiation exposure by a TLD reader, a device that heats the crystal and reads the exposure as well. The TLD gives an accurate exposure reading and can be reused after proper heating (annealing). It should be noted that exposures to radiation due to medical procedures and background radiation are not included in occupational dose limits. Therefore, radiation workers should wear film badges or dosimeters only at work. These devices should be taken o¤ during any medical procedures involving radiation such as radiographic procedures and dental examinations, and also when leaving after the day's work

- Dos and Don'ts in Radiation Protection Practice
- Do post radiation signs in radiation areas.
- Do wear laboratory coats and gloves when working with radioactive materials.

- Do work in a ventilated fumehood when working with radioactive gases.
- Do cover the trays and workbench with absorbent paper.
- Do store and transport radioactive material in lead containers.
- Do wear a film badge while working in the radiation laboratory.
- Do identify all radionuclides and dates of assay on the containers.
- Do survey work areas for any contamination as frequently as possible.
- Do clean up spills promptly, and survey the area after cleaning.
- Do not eat, drink, or smoke in the radiation laboratory.
- Do not pipette any radioactive material by mouth.
- Do monitor hands and feet after the day's work.
- Do notify the RSO in case of any major spill or other emergencies related to radiation. [Gopal B. Saha, Fundamentals of Nuclear Pharmacy]

2.13 Literature review

2.13.1 Walter MA, Christ-Crain M, Müller B, Müller-Brand J. et al(2007). Compared radioiodine uptake and thyroid hormone levels on or off simultaneous carbimazole medication; a prospective paired comparison. The aim was to allow radioiodine (RAI) treatment in patients with need for anti-thyroid drug medication and low RAI uptakes we investigated the feasibility of discontinuing carbimazole for 3 days to enhance the RAI uptake without concurrent exacerbation of hyperthyroidism. The method was prospectively investigated RAI dynamics and thyroid hormone concentration in 12 patients with low RAI uptake (<30%) under simultaneous carbimazole medication and 3 days after discontinuation. At both time points FT4, T3 and TSH were monitored. The result showed that discontinuation of carbimazole for 3 days led to a significant increase of RAI uptake in all patients. We found an enhancement up to 4.9-fold compared to the

measurement on carbimazole. The mean RAI uptake increased from 15.2 +/- 4.4% to 50.1 +/- 15.5% ($p<0.001$). The intrapersonal radioiodine half-life increased from 4.2 +/- 1.6 days to 5.4 +/- 0.7 days ($p = 0.13$). Mean thyroid hormone concentration was not affected by the three day withdrawal of anti-thyroid drugs and no patient suffered from an aggravation of biochemical hyperthyroidism. The conclusion was a withdrawal of carbimazole for 3 days is long enough to provide sufficiently high RAI uptakes for RAI treatment in patients with low RAI uptakes and short enough to avoid the risk of exacerbation of hyperthyroidism.

2.13.2 M. Faruk Hossain. et al.(2017). Correlated Serum T4, T3 and TSH Levels with Radioiodine Thyroid Uptakes. 240 studies including serum T4, T3, TSH and thyroid uptake at 2 and 24 hrs. were performed in 48 Bangladeshi adult individuals (52% female and 48% male). The aim of the present study was to make a correlation between thyroid serum levels and radioiodine thyroid uptake values of same individuals. Serum T4 and T3 were assessed with commercially available radioimmunoassay kits and TSH with a highly sensitive immunoradiometric assay kits (Beijing Atom Hightech Co. Ltd., China). The uptake study was consisted of oral administration of 6 – 10 μCi of 131I as sodium-iodide. Correlation coefficients (r) were calculated and tested for statistical significance. Radioiodine thyroid uptake values measured in this study show a statistically significant positive correlation with T4 and T3 levels and negative correlation with serum TSH levels. The present results were also compared with the experimental data available in literature and found to be in fairly good agreement. Conclusion: A total of 48 adult patients including 25 female and 23 male, referred to the Institute of Nuclear Medicine and Allied Sciences (INMAS), Dhaka for thyroid function tests were evaluated to study the correlation of serum T4, T3, TSH levels with 24 and 2 hrs. thyroid RAIU values. The present results revealed a positive and statistically

significant correlation of serum T4 and T3 levels with RAIU values. Serum TSH levels, on the other hand, showed an expected negative correlation with uptake values. The results obtained in this study were also found to be in fairly good agreement with the reported data. However, the positive correlation of serum T4 and T3 RIA values with 24 and 2 hrs RAIU, in this study, is not a perfect one because correlation coefficient (r) though greater than zero ($r > 0$) is less than one ($r < 1$). The present study, therefore, suggests that thyroid RAIU cannot be recommended as the sole diagnostic investigation for thyroid function tests.

2.13.3 Hadeel S. et al.(2017). Studied of Normal Thyroid Uptake using Technisium-99m. Thyroid gland is a vital endocrine gland in the body, estimation of its uptake and thyroid area are generally consider to be an important in several pathologic situations such as iodine deficiency, Goiter, thyroiditis, multi-nodular goiter and others. The aim of this study was to evaluate the normal range of thyroid uptake and determine the thyroid area in patients who has normal thyroid function test (T.F.T) and homogenous distribution of the radiotracer in Sudanese especially in Radiation & Isotope Center of Khartoum (RICK). This study includes 58 patients (91.5% Female, 8.5% Male) in different age, sex, center of origin and type of food and drink intake. For six months from Dec 2016 to May 2017. The most frequency of ages distribute as (25-35=31.03%, 15-25=29.3%), The thyroid uptake value in the gamma camera (mediso). The result of the study showed that the mean age was 33.6 ± 11 years old, the overall mean area of thyroid gland was 19.3 ± 3.78 cm^2. The mean area of right lobe was 7.7 ± 1.65 cm^2. The mean area of left lobe was 7.1 ± 1.84 cm^2. The right lobe area was significantly homogenous from left lobe area. Furthermore, a significant correlation was observed between thyroid area, weight and age of the subject. The normal range of thyroid uptake is in the range between (0.77% - 3.8%) and the thyroid area is in the range of (12.7 cm^2

to30.1 cm^2) there was a direct relationship between thyroid uptake and the thyroid area that when the area increase the uptake increase that shown in the following equation: y= 0.054x + 0.89 where x refers to thyroid area and y refers to uptake in percent. The result also shown that when thyroid weight increase the uptake increase as shown in the following equation: y= 0.056x + 1.53 where x refers to thyroid weight and y refers to uptake in percent. And the result shown that when BMI increase the uptake decrease as shown in the following equation: y = - 0.033x + 2.82 where x refers to BMI and y refers to uptake in percent. Finally the result also shown that when patient age increase the thyroid uptake decrease as shown in the following equation: y = - 0.6x + 1.85 where x refers to patient age and y refers to uptake in percent.

2.13.4 Correlation of Thyroid Hormone Levels with Radioactive *99mTc*Thyroid Uptakes Waddah M. Ali, Objective: This study aimed to study the relationship between thyroid function test and thyroid uptake using 99mTc and to determine of the normal range of the thyroid uptake in Sudanese as well as the possibility of replacing the TFT test by thyroid uptake.

Methods: Out of the 77 patients (6.2%)males and (93.5%) females who referred to the department of nuclear medicine at radio isotope center Khartoum (RICK) for thyroid function test and thyroid scan in the period fromMay to Aug 2009, were included in this study.Simple sensitive RIA wasused for the measurement of thyroid related hormones (T4, T3and TSH), and thyroid uptake value in the gamma camera (mediso).

Results: The results showed that mean±SD values for T3, T4, TSH and thyroid uptake were 5.6±3.6, 79.8±6.5, 6.7±0.8 and 6.3±2.4 respectively. The normal range for thyroid uptake in this study was ranged from 5.78 to 6.12% at 20 min

after injected with a dose of 3mCi 99mTc. As well as the results showed that there is strong and significant correlation at p = 0.05 between the thyroid uptake versus T3 and T4. Whereas in low uptake the correlation coefficient r = 0.87 and 0.81 for T4 and T3 respectively, and in elevated group r = 0.94 for T4 and 0.96 for T3. While in the normal uptake group r = 0.99 and 0.88 for T4 and T3 respectively. This study concluded that there was relationship between thyroid uptake and the level of the thyroid related hormones The percentage of thyroid uptake was ranging between 1.2 and 8.0

Conclusion: There were possibilities of using thyroid uptake only as a diagnostic tool for thyroid activity

CHAPTER THREE

3.1 Materials

Gamma Camera: MEDISO Nucline Spirit Dual head at RCIH, KEV high resolution at NMDC).

3.2 Pharmaceutical agent

99-m TC

3.3 Type of study

This study was a descriptive analytical study.

3.4 Duration of study

Mar 2018 to Mar 2020.

3.5 Place of study

This study conducted at Khartoum hospital for oncology and nuclear medicine.

3.6 Analysis of data

All patients parameters registered from Data collection sheet, and used as input to the Microsoft excel and SPSS software for analysis.

A	B	C	D	E	F	G	H	I	J	K
Age	Gend	W	H	T3	T4	TSH	Thyroid uptak	Thyroid Size	Nodules no.	Nodules size

3.7 Technique procedures

started our procedures with patient preparation, make sure that patient to discontinue thyroid medications and avoid contrast material. Refrain from eating foods containing iodine such as cabbage, greens, seafood, or large amounts of table salt. Administer injection to patient 2–5 mCi of 99mTcO4. wait 15 to 20 minutes before imaging. Give patient water (optional lemon to clear salivary glands). Place patient in supine position with pillow under shoulders and chin up (Water's position). Using the LEAP collimator, obtain anterior views (300 seconds or 100,000 depending on protocol) with and without markers as per protocol (thyroid cartilage and suprasternal, marker strip, right side, etc.). [Nuclear Medicine Technology: Procedures and Quick Reference Second Edition Pete Shackett, BA, ARRT[N], CNMT]

CHAPTER FOUR

Table 4.1: Descriptive statistic for body character and TFT and thyroid uptake& size and nodules size (maximum, minimum, mean, Std. Deviation)

	Mean± SD	Minimum	Maximum
Age	43.7± 13.5	17	70
W	68.3± 16.2	42	100
H	162.3± 7.8	150	182
T3	5.8± 2.8	2.82	22.85
T4	16.1± 8.1	2.24	53.13
TSH	1.3± 1.1	0.005	6.07
Thyroid uptake	3.3± 2.6	0.83	16.84
Thyroid size	36.1± 12.5	16.4	74.4
Nodules size	6.9± 3.8	1.3	19

variables	Mean± SD	Mean± SD	Mean± SD
	Group A	Group B	Group C
Age	42.4± 13.6	56.8± 8	41.5± 0.7
T3 pmol/L	5.1 ± 1.4	4.7± 2.4	14.1± 12.3
T4 pmol/L	14.9± 7.4	14.3± 3.2	31.1± 21.2
TSH mIU/L	1.3± 1.1	0.7± 0.6	0.3± 0.4
Thyroid Uptake %	2.7± 1.6	3.3± 2.7	9.1± 10.8
Thyroid SIZE cm2	33.4± 11	47.2± 16.6	48.4± 3.3
Nodules size cm2	6.7± 3.6	7.9± 5.5	3.7± 0.3

Table 4.2 shows the mean and standard deviation for all groups

Gender	Frequency	Percent
Female	43	82%
Male	9	18%

Table 4.3 show the frequency of Gender

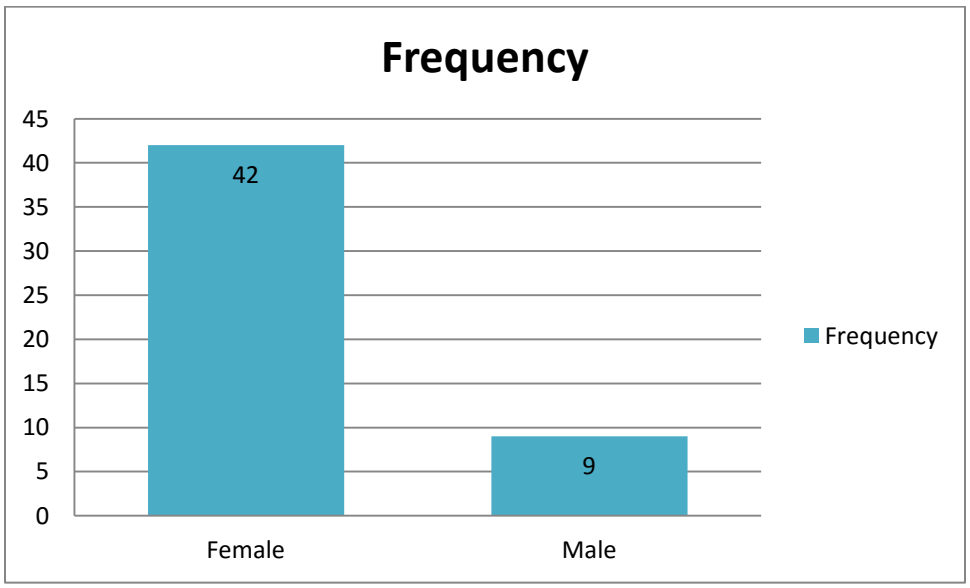


Figure 4.1show the distribution of Gender

Nodules no.	Frequency	Percent
Group A	44	86%
Group B	5	10%
Group C	2	4%

Table 4.4 show the frequency of Nodules number

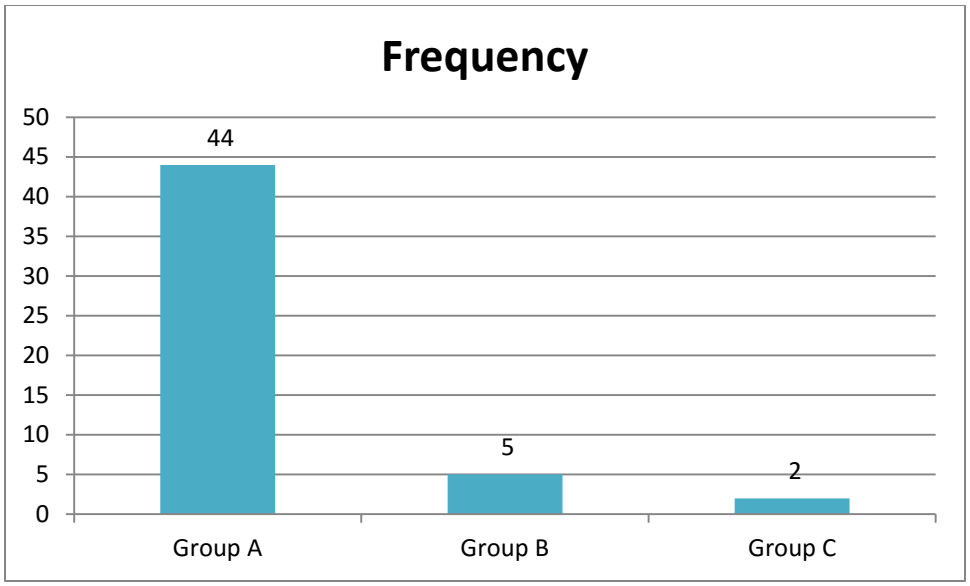


Figure 4.2 show the distribution of Nodules number

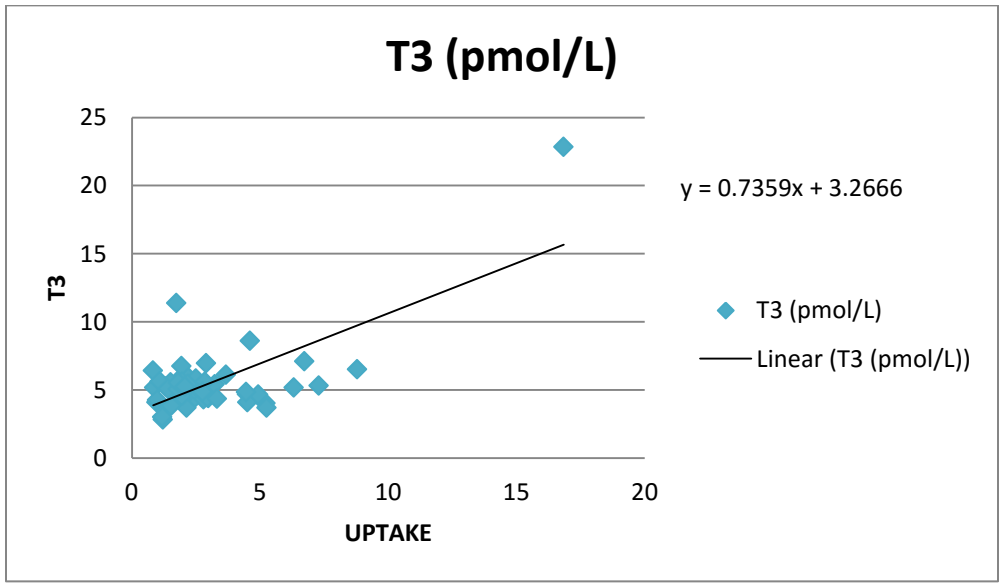


Figure 4.8 show the correlation relationship between T3 and thyroid uptake

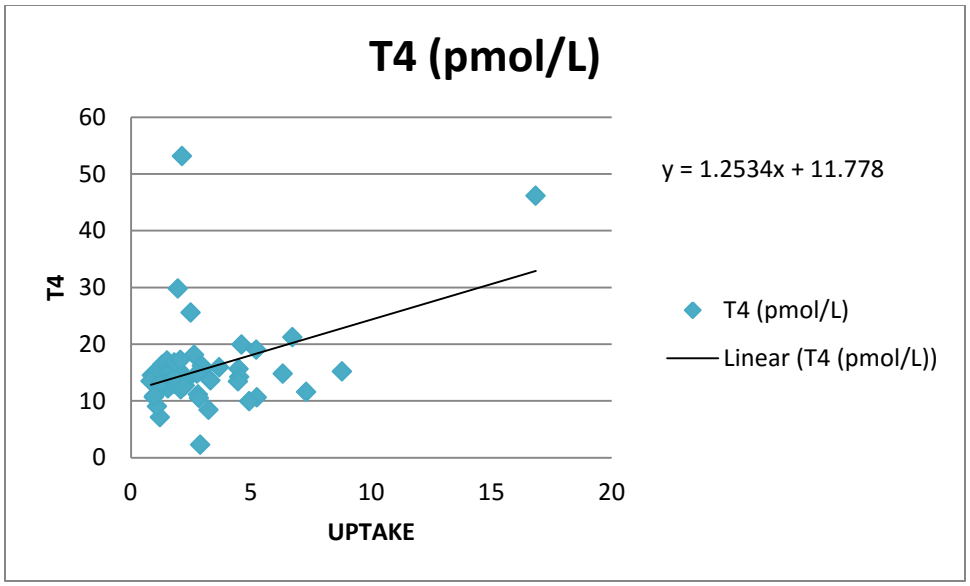


Figure 4.9 show the correlation relationship between T4 and thyroid uptake

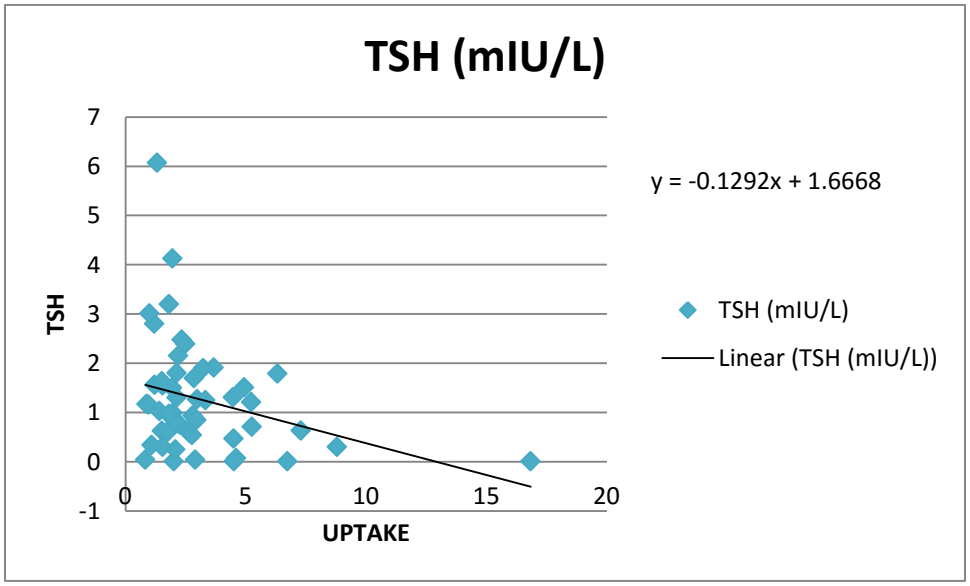


Figure 4.10 show the correlation relationship between TSH and thyroid uptake

CHAPTER FIVE

1.5 Discussion

- The data divided according to nodules number into three group, Group A patient with one nodule 44 patients 86% , Group B patient with two nodules 5 patients 10% , Group C patient with three or more number of nodules 2 patients 4% .
- The study found that the correlation between T3 and thyroid uptake show that the rate of change T3 increase with value 0.735 .
- The correlation between T4 and thyroid uptake show that the rate of change T4 increase with value 1.253.
- The correlation between TSH and thyroid uptake show that the rate of change TSH decrease with value -0.129.
- The nodules size in group A, B, C (6.7± 3.6, 7.9± 5.5, 3.7± 0.3)
- The estimate of the patients class using the following equations **Group A = (Gender* 33.98) + (T3* 1.79) – 22.79. Group B = (Gender* 39.04) + (T3*1.9)-28.9. Group C = (Gender*57.35) +(T3* 3.6) – 69.6. (Note : Gender 1= female, 2= male)** and the determination of patients class from the equation, the high value from the three equation determine the patient class.

2.5 conclusion

Estimation of Thyroid Nodules using TFT and Scintigraphy, what we found more than halve of the patients were female 82%. According to the study of epidemiology of thyroid nodules, nodules incidence increased in woman.

The significant correlation between the T3, T4 and thyroid up take was expected because the uptake of thyroid gland physiologically, has direct proportionality with the amount of thyroid hormones syntheses by the thyroid gland. Therefore in case of low hormones level the uptake of thyroid is low due to the smallest number of thyroid gland cells act in trapping and syntheses of thyroid hormones, while at elevated hormones level mean that the number of thyroid cell act as syntheses increase so the uptake was increased. There were insignificant correlation between the thyroid uptake and TSH level; this is because a lot of patients have no problem in thyroid stimulating hormones TSH but the problem within thyroid cells mainly due to iodine deficiency. Therefore there is no obvious linear association between TSH and uptake, as the one shown by T3 and T4, which is compatible the study of the correlation of thyroid hormone levels with radioactive Tc99m thyroid uptakes.

APPENDICES

ALARA as low as reasonably achievable

cpm counts per minute

CT computed tomography

dpm disintegrations per minute

DTC differentiated thyroid cancer

FNA fine needle aspiration

FT3 Free Triiodothyronine

FT4 Free Thyroxine

Gy gray

HVL half-value layer

LiF lithium fluoride

mGy milligray

MRI magnetic resonance imaging

mSv milliSievert

nGy nanogray

nSv nanoSievert

NVLAP National Voluntary Laboratory Accredition Program

PACS picture archiving and communications systems

PET positron emission tomography

PHA pulse height analyzer

PMT photomultiplier tubes

R RONTAGE

SPECT single photon emission computed tomography

Sv sievert

T3 Triiodothyronine

T4 Thyroxine

TBG thyroxine-binding globulin

TFT Thyroid function test

Tg thyroglobulin

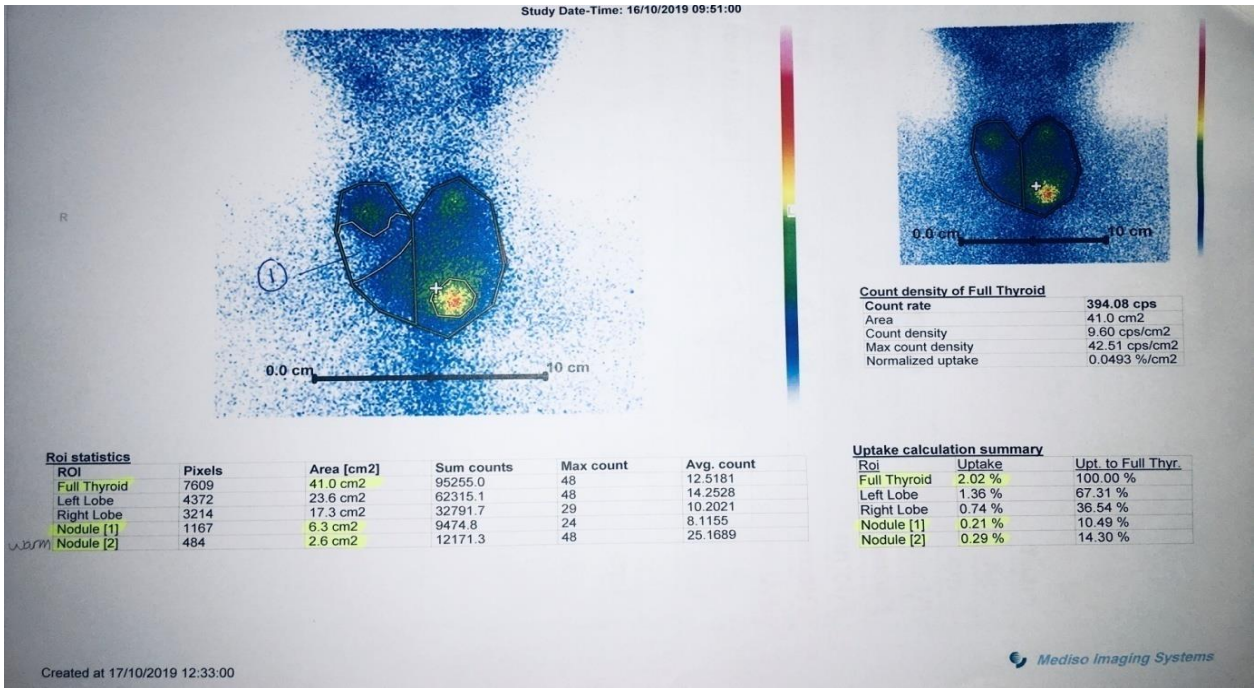
TLD thermoluminescent dosimeter

TRH thyrotropinreleasing hormone

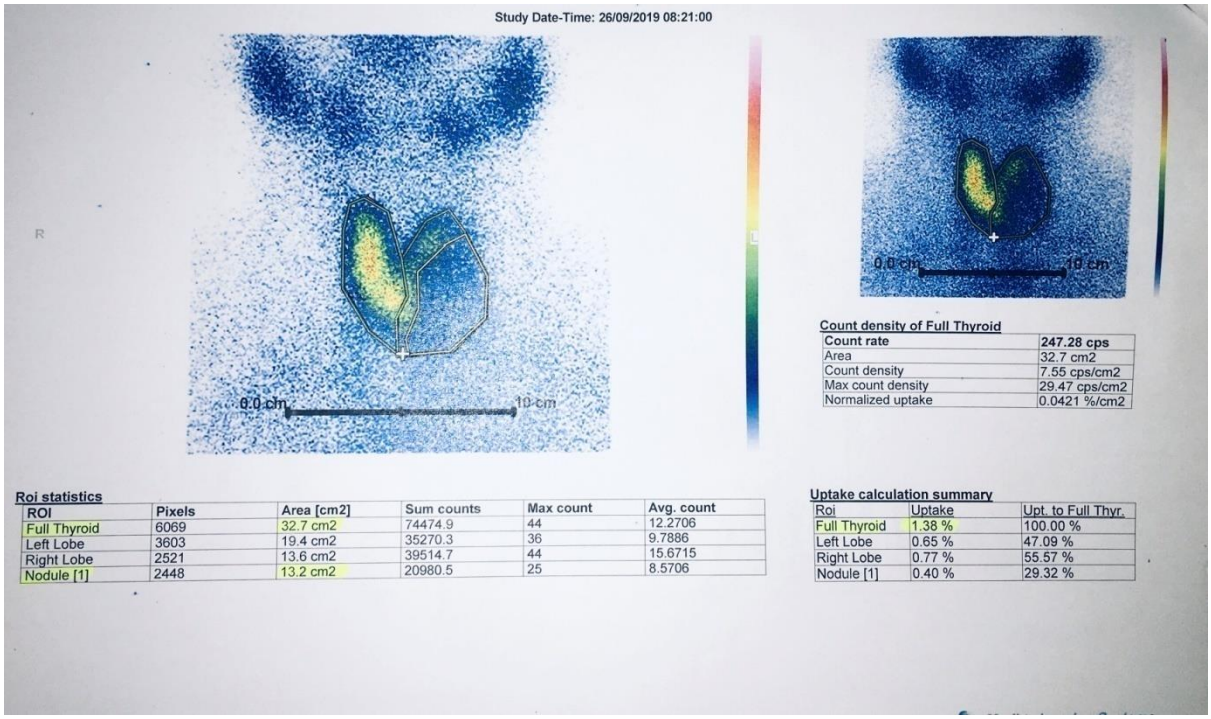
TSH Thyroid stimulating hormone

µGy microgray

µSv microSievert



Age	51	Years
Weight	56	Kg
Height	152	cm
T3 Total	[redacted]	nmol/L
T3 Free	(W) 6.07	pmol/L
T4 Total	[redacted]	nmol/L
T4 Free	(W) 15.40	pmol/L
TSH	.005	mIU/L
Thyroid Uptake	(W) 2.02	%
Thyroid Size	41	cm2
Nodules No.	TWO (.21%) (.29%)	
Nodules Size	6.3 – 2.6	cm2
U/S	Cold – warm	



No	Age	Gender	W	H	T3 (pmol/L)	T4 (pmol/L)	TSH (mIU/L)	Th.uptak	Th. Size (cm2)	Nod no.	Nod size (cm2)
1	51	1	56	152	6.07	15.4	0.005	2.02	41	2	4.45
2	65	1	64	158	6.03	53.13	1.3	2.14	36.9	1	11.6
3	23	1	51	162	5.17	14.77	1.79	6.33	25.7	1	6.6
4	51	1	92	150	4.95	12.18	1.55	1.55	24	1	5.2
5	45	1	85	165	4.4	15.56	1.27	2.99	53.7	1	8.9
6	45	1	42	156	4.68	15.63	0.468	4.5	39.8	1	7.9
7	55	1	61	160	6.11	15.91	1.91	3.68	49	2	4.6
8	45	1	56	157	8.6	19.9	0.07	4.61	37.2	1	5.1
9	48	1	59	156	4.73	13.8	2.48	2.35	19.9	1	3.8
10	27	1	59	162	4.94	18.09	0.591	2.65	36.6	1	6.3
11	26	1	65	153	4.3	11.1	0.94	2.8	42.9	1	13.2
12	17	1	48	154	6.75	15.28	1.5	1.95	24.1	1	5.5
13	67	1	60	160	4.03	12.67	0.754	2.26	40.2	1	7.8
14	39	1	52	165	4.01	19.02	1.21	5.23	33.7	1	3.8

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