Depending Radionuclide Iodine for Diagnosis and Treatment Thyroid Cancer

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ABSTRACT

The fastest rising cancer in women is Thyroid cancer . Current treatment including surgery (total thyroidectomy) followed by thyroid hormone therapy. Radioactive iodine therapy is used in patients with an intermediate or higher risk of persistent or recurrent thyroid cancer. Radioactive iodine works as a “magic bullet” by getting taken up by both normal and cancerous thyroid cells and destroying them. Similarly, radioactive iodine can be used to destroy thyroid cancer cells if the cancer returns

Keywords: Radionuclide, Thyroid cancer, Iodine, magic bullet

Introduction

Follicular cell-derived thyroid carcinoma (FCTC), when it is well differentiated, is generally an indolent disease which can be managed by surgery alone in most patients; papillary thyroid carcinoma (PTC) represents 80- 85% of cases of FCTC and follicular thyroid carcinoma (FTC) typically 10-15% [1]. Poorly differentiated and undifferentiated (anaplastic) thyroid cancer will not be discussed in this review. The need for additional postoperative therapy increases with the aggressiveness of disease. Radioactive iodine (RAI) has long been known to have a role in the management of both PTC and FTC and the goals of RAI therapy have recently been defined as ablation of normal thyroid tissue (remnant ablation), adjuvant treatment , or treatment of known disease (gross residual, locoregional or distant spread) [2] Options for disease management teams to consider when managing PTC or FTC range from active surveillance, through conservative surgical resection or aggressive initial surgery with adjuvant RAI to the extreme end of the spectrum, i.e.

therapeutic RAI, external beam radiation and targeted therapies for the most advanced cases For the majority of cases, who present with localized disease confined to the neck, controversy surrounds deciding whether the patient is a candidate for adjuvant RAI. As a bilobar resection approach (whether near-total or total thyroidectomy) is necessary to optimize RAI uptake, the decision to perform more extensive surgery is critical for the surgeon, and guides primary surgical management, with potentially significant consequences for the patient. International guidelines now outline an approach to selection of patients for RAI based on potential for oncological benefit. owever, a decision regarding the extent of surgical intervention relies not only on such treatment-related indications, but also complex aspects of the patient and their tumour which affect decision making throughout. The aim of this review is to consider the optimal approach to surgical management and will initially consider the

evidence base supporting or opposing the use of adjuvant RAI. [3]

1.1 Literature Review:

In this section, some works that have used radioactive iodine in the treatment and diagnosis of thyroid tumors will be reviewed:

Study Stanley J. Goldsmith (2017) Radioactive Iodine Therapy of DifferentiatedThyroid Carcinoma Radioactive iodine therapy has evolved over the past 70 years from treatment of known metastatic thyroid carcinoma toinclude adjuvant use to decrease the incidence of recurrent disease and to ablation of normal remnant tissue following thyroidectomy, even for minimal tumor involvement. Advances in laboratory testing, development of drugs useful in radioiodine treatment, as well as advances in radiation detection and imaging instrumentation, have progressively improved the utility of radioiodine therapy of differentiated thyroid carcinoma. Guidelines have proliferatedand they have become more detailed and complex. This trend is likely to continue as the science and technology involved increases in sophisticationand efficacy.[4]

Study Mohammad M (2020) and et.al The Radioactive Iodine (I_{131}) Efficiency for the Treatment of Well-Differentiated Thyroid Cancer The aim of this study was to evaluate the

effectiveness of Radioactive iodine-131 therapy after complete thyroidectomy using Accumulated high doses of radioactive iodine (I_{131}). This study was a retrospective review of more than 141 patients 22 months between January 2018 and November2019In Al-Ahly Hospital, Hebron, Palestine. All patients after completion Thyroidectomy, thyroid remnant tissue confirmed by (I_{131}) Whole body examination afterthat, the high doses of accumulated iodine were performed for treatment. The results were the total effective rate of treatment 131I for the current study It was 87.9%. The recurrence rate was 12.1%. From 141 true thyroid gland Cancer patients, 114 female thyroid cancer patients (80.15%), 27 patients were male (19.85%). The repetitions were more It is more common in female patients with thyroid cancer than in male patients (17.55 vs. 11.11%, respectively).However, the middle age is 30-40 The age group was the most affected, while the age group was least affected It was 60-70. CONCLUSION: 131I provides an effective treatment for patients with Thyroid cancer after complete thyroidectomy. Thyroglobulin (Tg) Postoperative levels are a reliable indicator of the presence of residual [5]

Study Department of Medical Imaging, Division of Nuclear Medicine, McGill University Health Centre (2020) and et.al Radioactive iodine therapy (RAIT)was firstused nearly 80years ago to treat hyperthyroidism and thyroid cancer. Today, it still plays a central role in the management of differentiated thyroid cancer (DTC). Person- alized management of DTC is becoming more common in clinical practice. The conceptualization and implementation of risk stratification systems account for thispara- digm shift. Estimating DTC recurrence risk and mortality aids in guiding initial therapy and subsequent surveillance. Clinical out- come prediction ultimately defines the most appropriate management. An update on RAIT would thus be incomplete without an overview of risk stratification. This article will review the key factors to consider when planning RAIT for DTC.[6]

Study Michele Klain (2021) and et.al Advances in Functional Imaging of Differentiated Thyroid Cancer The present review provides a description of recent advances in the field of functional imaging that takes advantage of the functional characteristics of thyroid neoplastic cells (such as radioiodine uptake and FDG uptake) and theragnostic approach of differentiated thyroid cancer (DTC). Physical and biological characteristics of available radiopharmaceuticals and their use with state-of-the-art technologies for diagnosis, treatment, and follow-up of DTC patients are depicted. Radioactive iodine is used mostly with

a therapeutic intent, while PET/CT with 18F-FDG emerges as a useful tool in the diagnostic management and complements the use of radioactive iodine. Beyond 18F-FDG PET/CT, other tracers including I_{124}, 18F-TFB and 68Ga-PSMA, and new methods such as PET/MR, might offer new opportunities in selecting patients with DTC for specific imaging modalities or treatments.[7].

Study Antonio De la Vieja (2021) and et.at Radio-Iodide Treatment: From Molecular Aspects to the Clinical View They analyzed key questions when facing treatment, such as: (1) How to integrate Radioactive iodine occurs in normal, tumor and metastaticthyroid cells and how they are regulated; (2) Pros Disadvantages of Thyroid Hormone Deprivation vs. Recombinant Human Thyroid Stimulating Hormone (rhTSH) radioactive iodine survival time, treatment efficacy, thyroglobulin levels and composition, And its effect on diagnostic imaging tests and treatment of metastases. and (3) the stun effect and possible causes. We discuss the possibility of merging massive sequence data into files Clinical practice, and we conclude with a socioeconomic and clinical view of the above aspects.[8].

Jaume .Cap , and other (2022) study Molecular diagnosis and targeted treatment of advanced follicular cell-derived thyroid cancer in the precision medicine era where Most malignant thyroid tumours are initially treated with surgery or a combination of surgery and radioactive iodine (RAI) therapy. However, in patients with metastatic disease, many tumours become refractory to RAI, and these patients require alternative treatments, such as locoregional therapies and/or systemic treatment with multikinase inhibitors. Improvements in our understanding of the genetic alterations that occur in thyroid cancer have led to the discovery of several targeted therapies with clinical efficacy. These alterations include NTRK (neurotrophic tyrosine receptor kinase) gene fusions, with the tropomyosin receptor kinase inhibitors larotrectinib and entrectinib both approved by the European Medicines Agency and in other markets worldwide. Inhibitors of aberrant proteins resulting from alterations in RET (rearranged during transfection) and BRAF (B-Raf proto-oncogene) have also shown promising efficacy, and so far have receivedapproval by the US Food and Drug Administration. Selpercatinib, a RET kinase inhibitor,was approved for use in Europe in early 2021.[9].

Kodia Nishi and other (2023) study Reduction of thyroid radioactive iodine exposure by oral administration of cyclic oligosaccharides This study clarified the inhibition of radioactive iodine absorption by the oral administration of α-cyclodextrin in a murine model

using direct measurement of single photon emission computed tomography. The uptake of radioactive iodine into the thyroid gland in mice administered with radioactive iodine and an α-cyclodextrin solution was approximately 40% lower after 24 h. The finding that oral uptake of α-cyclodextrin has an inhibitory effect on the transfer of radioactive iodine to the thyroid gland has potential for application in many fields such as food, pharmaceuticals, nuclear emergency preparedness, and medicine.[10]

1.2 Research aims:

The aim of this study is to evaluate the effectiveness of Radioactive iodine therapy and use The accumulated high doses of radioactive iodine and the extent of its effect on the patient and the side effects that occur.

1.3 Research problem:

One of the most important problems to improve patient management, such as As a preoperative treatment method (th-deprivation or rhTSH), the amount of radioactiveiodine Used, short and long-term responses to treatment. Massive sequencing techniques Allowing a more accurate classification of traditional thyroid tumor types. This will allowTo improve treatment selection and predict patient response Psychiatric treatment. Inturn, it will also help in predicting RAI refractory tumors more accurately and To access alternative treatments without the unnecessary use of radioactive iodine, or better yet
Allow re- differentiation in tumor therapy so that the patient can then be successful Treat with radioactive iodine. Although there are still some challenges to be faced, thistreatment It poses greater patient benefits and relatively minor side effects compared to others.

2.1-Radioactive materials:

Radioactive sources are used throughout the world for a wide variety of peaceful purposes in industry, medicine, agriculture, research and education; and they are alsoused in military applications. The International Basic Safety Standards provide an internationally harmonized basis for ensuring the safe and secure use of sources of ionizing radiation. Because of the wide variety of uses and activities of radiation sources, a categorization

system is necessary so that the controls that are applied to the sources arecommensurate with the radiological risks. [11]

2.2 Radiation and confiscation

Radiation is energy in the form of waves or streams of particles. There are many kinds of radiation all around us. When people hear the word radiation, they often think of atomic energy, nuclear power and radioactivity, but radiation has many other forms. Sound and visible light are familiar forms of radiation; other types include ultraviolet radiation (that produces a suntan), infrared radiation (a form of heat energy), and radio and television signals. Figure(2.1) presents an overview of the electromagnetic spectrum; section 3 will go into greater detail on the different types of radiation.[10]

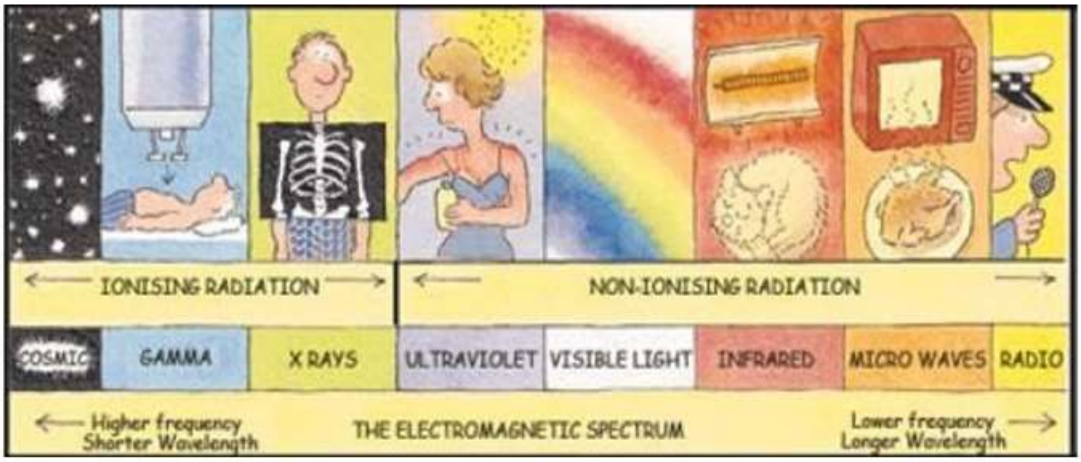


Figure (2.1): The electromagnetic spectrum [10]

Uncontrolled use of man-made radiation carries a potential risk to the health and safety of workers and the public. This is where the Canadian Nuclear Safety Commission (CNSC) comes in. The CNSC regulates the use of nuclear energy and materials to protectthe health, safety and security of Canadians and the environment from the effects of radiation.[11] The purpose of this document is to provide clear and simple information about radiation: what it is, where it comes from and how it is used. It also presents information on radiation health effects, radiation doses and how the CNSC ensures the safety of the Canadian nuclear sector through its comprehensive regulatory framework and vigilant oversight.

2.3 Introduction to Radiation :

All life has evolved in an environment filled with radiation. The forces at work in radiation are revealed upon examining the structure of atoms. Atoms are a million times thinner than a single strand of human hair,[12] and are composed of even smaller particles – some of which are electrically charged. Sections 2.1 to 2.3 discuss atoms in more detail, along with basic radiation-related principles. form the basic building blocks of all matter. In other words, all matter in the world begins

1- Atoms:

Where all matter begins Atoms with atoms – they are elements like oxygen, hydrogen, and carbon. An atom consists of a nucleus – made up of protons and neutrons that are kept together by nuclear forces – and electrons that are in orbit around the nucleus (see Figure 2.2). The nucleus carries a positive charge; protons are positively charged, and neutrons do not carry a charge. The electrons, which carry a negative charge, move around the nucleus in clouds (or shells). The negative electrons are attracted to the positive nucleus because of the electrical force. This is how the atom staystogether. [13]

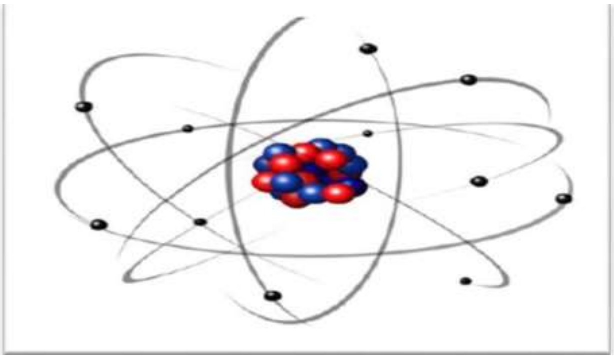


Figure (2.2): Model of an atom [13]

Each element is distinguished by the number of protons in its nucleus. This number, which is unique to each element, is called the “atomic number”. For example, carbon has six protons; therefore, its atomic number is 6 on the periodic table (see Figure 2.3). In an atom of neutral charge, the atomic number is also equal to the number of electrons. An atom’s chemical properties are determined by the number of electrons, which is normally equal to the atomic number. [13]

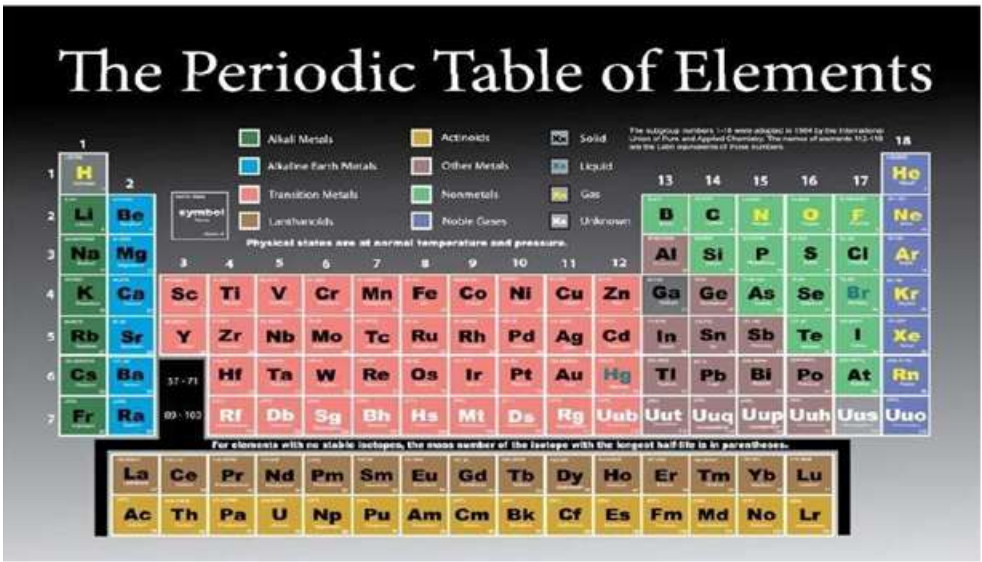


Figure (2.3): The periodic table of elements [13]

Atoms from one or more elements combine to form molecules. A molecule of water, for example, is formed of two atoms of hydrogen bound to one atom of oxygen (H_2O). A nuclide is a specific type of atom characterized by the number of protons and neutrons in its nucleus, which approximates the mass of the nuclide. [14] The number that is sometimes given with the name of the nuclide is called its mass number (the total numberof protons and neutrons in the nucleus). For example, a nuclide of carbon with 6 protons and 6 neutrons is called carbon-12

2- Isotopes:

An isotope is a variant of a particular chemical element. While all isotopes of a given element have the same number of protons, each isotope has a different number of neutrons. For example, hydrogen has three isotopes (or variants):

1.3.1 hydrogen-1 (contains one proton and no neutrons)

1.3.2 hydrogen-2, which is called deuterium (contains one proton and one neutron)

1.3.3 hydrogen-3, which is called tritium (contains one proton and two neutrons)

Another example is uranium-235, which has 92 protons and 143 neutrons, as opposed to uranium-238, which has 92 protons and 146 neutrons. An isotope is stable when it has a balanced number of neutrons and protons. In general, when an isotope is small and stable, it contains close to an equal number of protons and neutrons.[8] Isotopes that are larger and stable have slightly more neutrons than protons. Examples of stable nuclides include carbon-12 (six protons and six neutrons for a total mass of 12), phosphorus-30 (15 protons and 15 neutrons) and sodium22 (11 protons and 11 neutrons).

2.4 Types and Sources of Radiation

Radiation is energy in the form of waves of particles. There are two forms of radiation – non-ionizing and ionizing – which will be discussed in sections 3.1 and 3.2, respectively.

1. Non-ionizing radiation

Non-ionizing radiation has less energy than ionizing radiation; it does not possess enough energy to produce ions. Examples of non-ionizing radiation are visible light, infrared, radio waves, microwaves, and sunlight. Global positioning systems, cellular telephones, television stations, FM and AM radio, baby monitors, cordless phones, garage-door openers, and ham radios use non-ionizing radiation. Other forms include the earth's magnetic field, as well as magnetic field exposure from proximity to transmission lines, household wiring and electric appliances.[15] These are defined as extremely low- frequency (ELF) waves and are not considered to pose a health risk.

2. Ionizing radiation

Ionizing radiation is capable of knocking electrons out of their orbits around atoms, upsetting the electron/proton balance and giving the atom a positive charge.[16] Electrically charged molecules and atoms are called ions. Ionizing radiation includes the radiation that comes from both natural and man-made radioactive materials

There are several types of ionizing radiation:

1- Alpha radiation (α): Alpha radiation consists of alpha particles that are made up of two protons and two neutrons each and that carry a double positive charge. Due to their relatively large mass and charge, they have an extremely limited ability to penetrate matter. Alpha radiation can be stopped by a piece of paper or the dead outer layer of the skin. Consequently, alpha radiation from nuclear substances outside the body does not present a radiation hazard. However, when alpha-radiation- emitting nuclear substances are taken into the body (for example,[17] by breathing them in or by ingesting them), the energy of the alpha radiation is completely absorbed into bodily tissues. For this reason, alpha radiation is only an internal hazard. An example of a nuclear substance that undergoes alpha decay is radon-222, which decays to polonium-218.

2- Beta radiation (β): Beta radiation consists of charged particles that are ejected from an atom's nucleus and that are physically identical to electrons. Beta particles generally havea negative charge, are very small and can penetrate more deeply than alpha particles. However, most beta radiation can be stopped by small amounts of shielding, such as sheets of plastic, glass or metal. When the source of radiation is outside the body, beta radiation with sufficient energy can penetrate the body's dead outer layer of skin and deposit its energy within active skin cells.[18] However,

beta radiation is very limited in its ability to penetrate to deeper tissues and organs in the body. Beta-radiation-emitting nuclear substances can also be hazardous if taken into the body. An example of a nuclear substance that undergoes beta emission is tritium (hydrogen-3), which decays to helium-3.

1- Photon radiation (gamma [γ] and X-ray) :Photon radiation is electromagnetic radiation. There are two types of photon radiation of interest for the purpose of this document: gamma (γ) and X-ray. Gamma radiation consists of photons that originate from within thenucleus, and X-ray radiation consists of photons that originate from outside the nucleus, and are typically lower in energy than gamma radiation.

2- Neutron radiation (n): Apart from cosmic radiation, spontaneous fission is the only natural source of neutrons (n). A common source of neutrons is the nuclear reactor, in which the splitting of a uranium or plutonium nucleus is accompanied by the emission of neutrons. The neutrons emitted from one fission event can strike the nucleus of an adjacent atom and cause another fission event, inducing a chain reaction. The production of nuclear power is based upon this principle. All other sources of neutrons depend on reactions where a nucleus is bombarded with a certain type of radiation (such as photon radiation or alpha radiation), and where the resulting effect on the nucleus is the emission of a neutron. Neutrons are able to penetrate tissues and organs of the human body when the radiation source is outside the body. Neutrons can also be hazardous if neutron-emitting nuclear substances are deposited inside the body. Neutron radiation is best shielded or absorbed by materials that contain hydrogen atoms, such as paraffin wax and plastics.[19] This is because neutrons and hydrogen atoms have similar atomic weights and readily undergo collisions between each other[19]

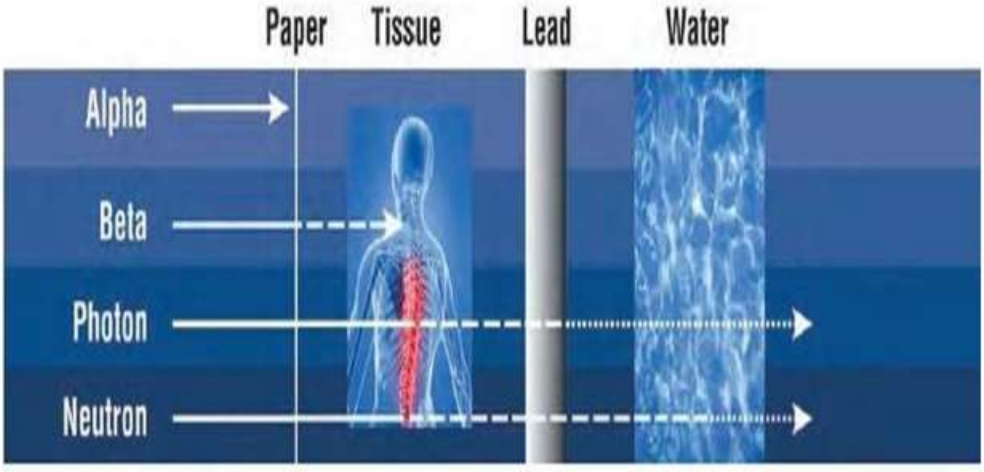


Figure (2.4): Penetration abilities of different types of ionizing radiation[19]

2.5 Natural sources of ionizing radiation:

Radiation has always been present and is all around us in many forms (see Figure 5). Life has evolved in a world with significant levels of ionizing radiation, and our bodies have adapted to it. Many radioisotopes are naturally occurring, and originated during the formation of the solar system and through the interaction of cosmic rays with moleculesin the atmosphere. Tritium is an example of a radioisotope formed by cosmic rays' interaction with atmospheric molecules.[20] Some radioisotopes (such as uranium and thorium) that were formed when our solar system was created have half-lives of billionsof years, and are still present in our environment. Background radiation is the ionizing radiation constantly present in the natural environment.[20]

The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) identifies four major sources of public exposure to natural radiation:

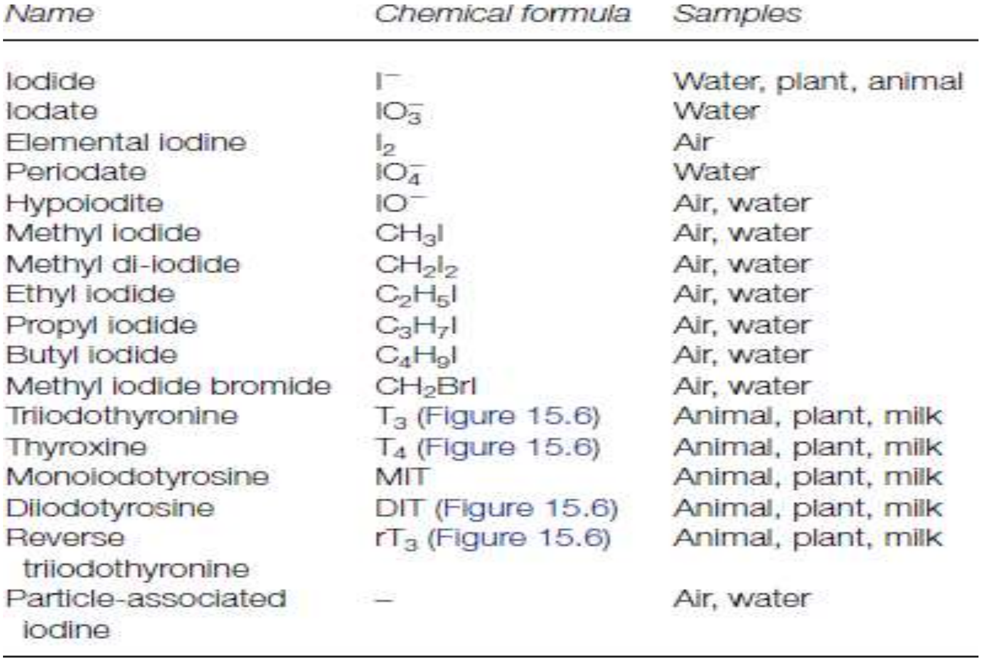
1- Cosmic radiation
2- Terrestrial radiation
3- nhalation
4- Ingestion

1- Iodine confiscation

Iodine is an essential element in humans and other mammals, which is used for the synthesis of the thyroid hormones triiodothyronine (T_3) and thyroxin (T_4). These hormones play a prominent role in the metabolism of most cells of the organism and inthe process of early growth and development of most organs, especially brain. Besides T_3 and T_4, reverse T_3 (rT_3), monoiodotyrosine (MIT), and diiodotyrosine (DIT) are also synthesized and distributed in the body of humans and animals, but only T_3 and T4 have abiological function. Iodine in the human body mainly comes through dietary and water intake, and inhalation of atmospheric iodine. Due to low concentrations of iodine in the air (10–20ng/m3), food and water intake form the major source of iodine for adults,while for infants it is milk. The concentration of iodine in foodstuffs is directly related to that in the environment where the foods come from. Iodine deficiency disorders are mainly found in places where the concentration of iodine in the soil and drinking water is very low. In the water, foodstuffs, and environmental samples, iodine exists in different species, such as iodide, iodate and in association with various organic compounds.[21] Table 2.1 shows the various iodine species in nature. The species of iodine in the water and environmental samples is related to the level of iodine in plants and foodstuffs. The species of iodine in foodstuffs directly affects the

bioavailability of iodine to humans and animals. This article reviews the speciation of iodine in water, air, foodstuffs and biological and environmental samples. In addition, the bioavailability and toxicity of iodine species are also discussed.

Table (2.1) Iodine species in nature[22]



Name	*Chemical formula*	*Samples*
Iodide	I^-	Water, plant, animal
Iodate	IO_3^-	Water
Elemental iodine	I_2	Air
Periodate	IO_4^-	Water
Hypoiodite	IO^-	Air, water
Methyl iodide	CH_3I	Air, water
Methyl di-iodide	CH_2I_2	Air, water
Ethyl iodide	C_2H_5I	Air, water
Propyl iodide	C_3H_7I	Air, water
Butyl iodide	C_4H_9I	Air, water
Methyl iodide bromide	CH_2BrI	Air, water
Triiodothyronine	T_3 (Figure 15.6)	Animal, plant, milk
Thyroxine	T_4 (Figure 15.6)	Animal, plant, milk
Monoiodotyrosine	MIT	Animal, plant, milk
Diiodotyrosine	DIT (Figure 15.6)	Animal, plant, milk
Reverse triiodothyronine	rT_3 (Figure 15.6)	Animal, plant, milk
Particle-associated iodine	–	Air, water

Note: The name and chemical formulas of the iodine species occurring in nature are shown; the possible sample types in which the species exist are also shown in the third column. environmental samples, iodine exists in different species, such as iodide, iodate and in association with various organic compounds. Table 2.1 shows the various iodine species in nature. The species of iodine in the water and environmental samples is related to the level of iodine in plants and foodstuffs. The species of iodine in foodstuffs directly affects the bioavailability of iodine to humans and animals. This article reviews the speciation of iodine in water, air, foodstuffs and biological and environmental samples. In addition, the bioavailability and toxicity of iodine species are also discussed water the concentration of iodate is high, the concentration in the open sea is

<0.01–0.2μM for iodide and 0.2–0.5μM for iodate. Iodide maxima are often found in μHigher iodide concentrations are normally found in coastal and estuary areas;

2- Types of inorganic iodine

Interest in the species of iodine in water has increased in the past decades. Water is considered to be an important source of iodine for humans and animals; it also supplies iodine to plants Distribution of iodine species The iodine species present in water depend on the nature of the water. In seawater, iodine mainly exists as iodate, iodide, and minor organic iodine (Wong, 1991). The distribution of iodine species in seawater depends on the water chemistry, and varies with depth and geographic location. In anoxic water, mostiodine exists as iodide, such as in the Baltic Sea and the Black Sea. While in oxygenated/oxicwater the concentration of iodate is high, the concentration in the open sea is 0.01– 0.2µM for iodide and 0.2–0.5µM for iodate. Iodide maxima are often found in surface water. Below the euphotic zone, iodide decreases to below 0.01µM. Higher iodide concentrations are normally found in coastal and estuary areas [22]. Organic iodine found in coastal and estuary areas corresponded to 5–40% of total dissolvediodine. A few specific organic iodine compounds, mainly volatile compounds, have been identified, such as CH_3I, CH_2CI, CH_2I_2, and $CH_3CH_2CH_2I$ Although the concentration of organic iodine in seawater is low, it plays an important role in the global geochemical cycle of iodine, because the transfer of iodine from the iodine-rich ocean to the atmosphere, and then to the terrestrial environment, is thought to occur primarily through the volatilization of organic iodine hydrocarbon in seawater. These volatile organic iodine species were also supposed to relate to the ozone depletion in the stratosphere. In freshwater, iodine also exists as iodide iodate and organic iodine, but the concentration oforganic iodine is normally relatively high in freshwater, such as river water, lake water and rain .

3- Iodine sources

Speciation of Iodine in Water: Interest in the species of iodine in water has increased in the past decades. Water is considered to be an important source of iodine for humans and animals it also supplies iodine to plants.

2.6 Distribution of iodine species :

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2.7 Types of inorganic iodine:

A number of analytical methods have been reported for the speciation analysis of iodine in water. In seawater, iodate can be directly determined by titrimetric, colorimetric, and differential pulse polarography methods and iodide by catholic stripping voltammetry, chromatography, and inductively coupled plasma atomic emission spectrometry or mass spectrometry (ICP-MS) Organic iodine was normally given as the difference between total iodine (sum of all forms of inorganic and organic iodine) [24]and total inorganic iodine (IO_3 – + I –), in which the concentration of total iodine was determined as IO_3 – or I–after organic iodine had been decomposed and converted into IO_3 – or I–by UV irradiation or/and redox treatment

2.8 Speciation analysis of volatile organic iodine :

Volatile organic iodine compounds have been determined by gas chromatography (GC) with MS Figure (2.7) shows the schematic of the analytical procedure. Seawater (50– 100ml) is injected into the purging unit of sample treatment with a syringe, where it is degassed; the degassed substances are then transferred with helium into a cold trap,which is cooled with liquid nitrogen. After degassing, the trapped substances are transferred to the separation column by removing liquid nitrogen and heating the trap.The organic iodine compound is separatedusing a capillary column in GC and heating the trap at different temperatures, ranging from 40 to 240°C. The detection is performed with an electron capture detector (ECD) and/or ICP-MS; the ICP-MS is more sensitive for iodine than the ECD. The absolute detection limit for ICP- MS is 0.5pg for iodinated volatile organic compounds. Figure (2.6) shows a chromatographic spectrum of iodinated and brominated volatile organic compounds measured by GC-ICPMS/ECD Speciation analysis of iodine in freshwater The

concentration of iodine in freshwater is normally much lower than that in seawater; however, in some particular regions, the groundwater may contain higher levels of iodine. The iodine in precipitation and river water is normally 0.5–5ng/l, which is more than 10 times lower than that in seawater. The more sensitive ICP-MS and NAA are normally used for the speciation of iodine in freshwater. developed a method by combining isotope dilution mass spectrometry .

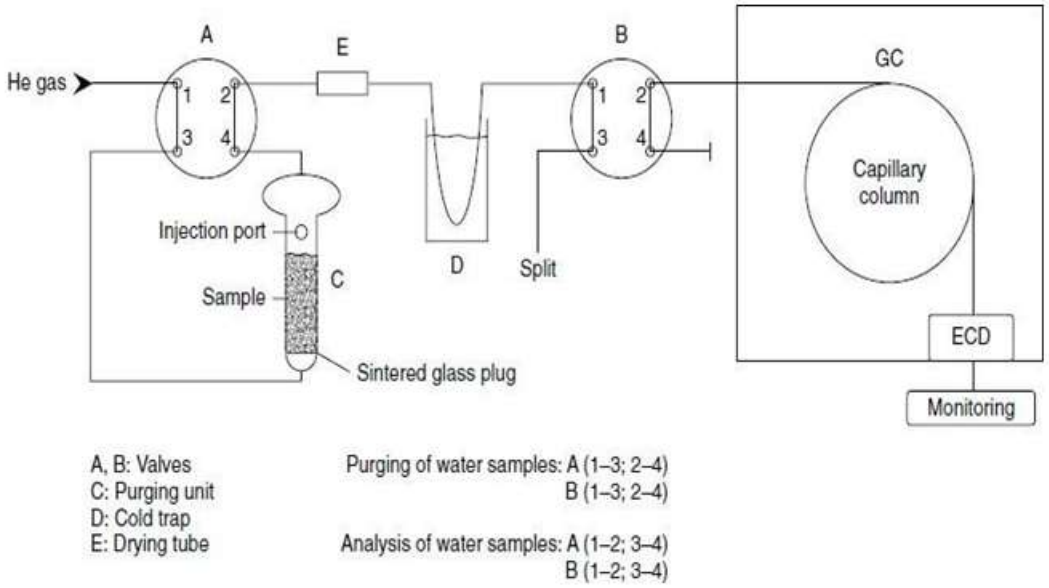

Figure (2.6) A schematic of the analytical purge and trap – GC system for the determination ofvolatile organic iodine in seawater.[25]

Chemical Speciation of Iodine in Air

1- **Iodine species** :The concentration of iodine in the atmosphere ranges from 0.2 to 10ng/m3 ; a high iodine concentration is observed in urban areas due to combustion of oiland coal. In the atmosphere, iodine exists as particle-bound iodine (particulate iodine), inorganic gaseous iodine (I2, HI, HOI) and organic gaseous iodine (CHI_3, CH_2I_2, $CH_3CH_2CH_2I$); their concentrations vary with various parameters, such as location, season and climate Speciation analysis of iodine A series filter was used to separate atmospheric particulate iodine,[25] HI and I2, HOI and organic iodine. The particulate iodine is usually separated and collected using micropore filters or glass microfiber. The distribution of iodine in the different sizes of particulates is collected by a multi-stage cascade impact collector. used a six-stage slot cascade impactor to collect particulates with an aerodynamic diameter of 7.2, 3.0, 1.5, 0.95, 0.45, and < 0.45µm.

Speciation analysis of volatile iodine GC combined with ICP-MS or ECD is quite often used for the determination of volatile organic iodine. A system similar to that used for seawater was used for the analysis of air samples reported a similar system for the speciation

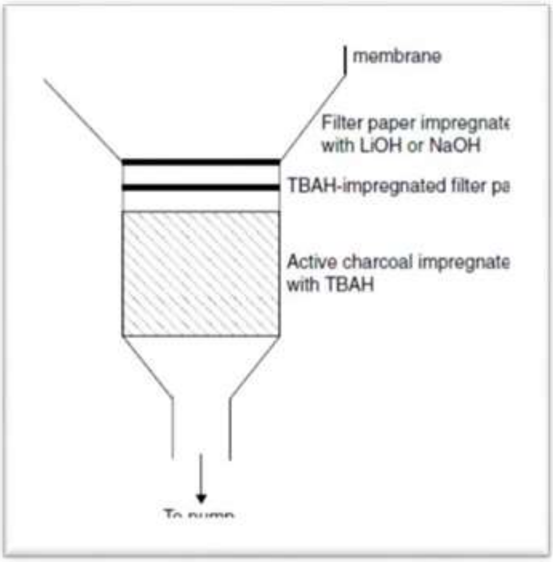

Figure (2.) A diagram of an air sampler for the collection of different species of iodine from air. The air is sucked by a pump through the system.[26]

2- Chemical Speciation of Iodine in Foodstuffs and Environmental Samples

The source of iodine for humans is mainly foodstuffs, as well as drinking water. The investigation on speciation of iodine in foodstuffs mainly focused on milk andseafood (seaweed and fish), because of the importance of milk iodine to humans, especially to infants, and the high concentration of iodine in these types of foodstuffs. In addition, lack of iodine supplementation to newborns can result in slow brain development, leading to severe damage to the central nervous system [26]. It is therefore supposed that an iodine transporter and a peroxidase enzyme are involved in iodine accumulation in mammary glands. These facts make iodine speciation an important factor in human milk. Further, the bioavailability of various species of iodine may be quite different, especially for iodine-bound macromolecules. Investigation on speciation in different types of milk and formula, and other kinds of food, becomes important to accurately estimate the status of iodine nutrition.

A-Speciation analysis of iodine in milk: developed an online method for the investigation of iodine species in human milk – SEC separation coupled with ICP-MS detection. They reported that 80% of iodine in human milk was present as iodide; besidesiodide, another

six high- molecular-weight iodine containing molecules(5–300kDa)were also observed.

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B-Speciation analysis of iodine in fish:, using LC-ICP-MS, investigated iodine speciation in whole-body homogenates of adult male and female zebrafish (Danio rerio) and tadpoles of the African clawed frog (Xenopus laevis) at two different developmental stages (NF58 and 61) according to Nieuwkoop and Faber. A Capcell-C18 column and a mobile phase comprising Tris-HCl and methanol were used for chromatographic separation. Iodide, MIT, DIT, T_4, T_3 and rT_3 were observed in these samples. In addition,another five species of iodine were also identified in the samples.

C-Speciation analysis of iodine in seaweeds: Due to the high concentration of iodine in marine vegetation, the chemical species of iodine in plants is mainly focused on seaweed.developed a method for the determination of various chemical species of iodine inseaweed, such as water-soluble iodine, soluble organic iodine, iodide, iodate and protein-, pigment polyphenol-, or polysaccharide-bound iodine. First the soluble iodine was separated from the seaweed by water leaching. Then, iodide in the leachate was separated by BiI_3 precipitation, while iodate in the filtrate was reduced to iodide and precipitated

3.1 Thyroid gland

1- Anatomy of the thyroid gland The thyroid is a brownish-red and highly vascular gland located anteriorly in the lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic. The thyroid is situated just below the "Adams apple"or larynx. During development (inside the womb) the thyroid gland originates in the back of the tongue, but it normally migrates to the front of the neck before birth. Sometimes it fails to migrate properly and is located high in the neck or even in the back of the tongue (lingual thyroid). This is very rare. At other times it may migrate too far and ends up inthe chest (this is also rare). [27]

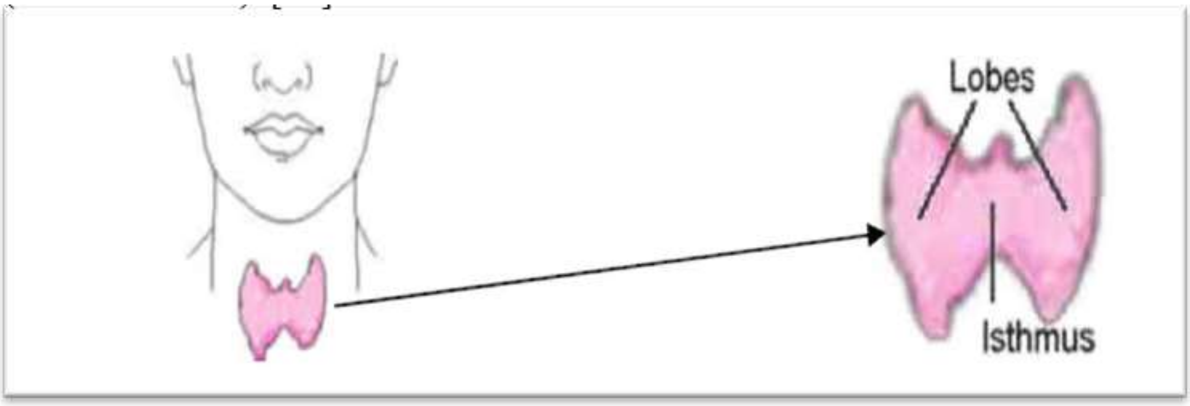


Figure (3.1) Anatomy of the thyroid gland[27]

The gland varies from an H to a U shape and is formed by two elongated lateral lobes with superior and inferior poles connected by a median isthmus (with an average heightof 12-15 mm) overlying the second to fourth tracheal rings. The isthmus is encountered during routine tracheotomy and must be retracted (superiorly or inferiorly) or divided. Occasionally, the isthmus is absent, and the gland exists as 2 distinct lobes. Each lobe is 50-60 mm long, with the superior poles diverging laterally at the level of the oblique lineson the laminae of the thyroid cartilage. The lower poles diverge laterally at the level ofthe fifth

tracheal cartilage. Thyroid weight varies but averages 25-30 g in adults (slightly heavierin women). The gland enlarges during menstruation and pregnancy

2- Role of the thyroid gland The thyroid gland produces thyroid hormones. These are peptides containing iodine. The two most important hormones are tetraiodothyronine (thyroxine or T_4) and triiodothyronine (T_3). These hormones are essential for life and have many effects on body metabolism, growth, and development. Their purpose is to regulate the rate of metabolism in every cell of the body: - T_4 is the one most abundant in the body representing approximately 80% of thyroid hormones but is also a precursor to T_3. - T_3 represents approximately 20% of thyroid hormones found in the body. When the body has enough T_3 available, any excess T_4 remaining in reserve will be rendered inactive by the conversion of it into "Reverse T_3" (RT_3). This process is ongoing due to the fact that the thyroid gland continues to absorb iodine from the diet. This process, which also occurs in the liver and kidneys, is a safeguard against overstimulation of body metabolism from an excess of T_3 hormone.

The thyroid gland (shown in Figure 3.2) is also influenced by hormones produced by two other organs: - The pituitary gland, a small gland of the size of a peanut located at the base of the brain, which produces thyroid- stimulating hormone (TSH). - The hypothalamus, a small part of the brain above the pituitary, which produces thyrotropin- releasing hormone (TRH) [27]

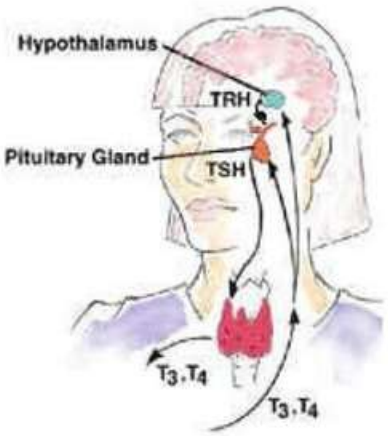


Figure (3.2) Hypothalamus- pituitary gland - thyroid gland [27]

When low levels of thyroid hormones (T_3 and T_4) in the blood are detected by the hypothalamus and the pituitary gland, TRH is released, stimulating the pituitary gland to release TSH. Increased levels of TSH, in turn, stimulate the thyroid to produce more thyroid hormone, thereby returning the level of thyroid hormone in the blood back to normal. Thyroid hormones are essential and play a key role in a number of systems [28]:

- The central nervous system maturation during the first months of life and its functioning in adult;

- The differentiation and maturation of bone during the fetal period and for bone resorption in adult;

- The basal metabolism (thermogenesis), as well as the metabolisms of carbohydrate (thyroid hormones are hyperglycemic), lipid (especially cholesterol), protein (they increase protein synthesis but have also an effect on catabolism), and hydromineral metabolism (they increase the glomerular filtration and renal blood flow);

- The cardiac rhythm;

- Controlling the contraction of muscle and metabolism of creatine;
- Promoting the gastrointestinal transit;

- The regulation of the development of blood cells (hematopoiesis) and iron metabolism

3.2 Physiopathology of the thyroid gland:

The state of normal thyroid function is called euthyroidism. The main causes of thyroid disease are: - Too much thyroid hormone production or hyperthyroidism Too little thyroid hormone production or hypothyroidism. Abnormalities of the thyroid gland are common and affect one in twenty (5%) of the population living in developed countries in average. All thyroid disorders are much more common in women than in men. Because of the widespread use of iodized salt, lack of iodine is no longer a cause of thyroid disease in most of developed countries as it was some 50 years ago. Autoimmune disorders of the thyroid gland are common. These autoimmune disorders are caused by abnormal proteins, (called antibodies), and the white blood cells which act together to stimulate or damage the thyroid gland. Graves' disease (hyperthyroidism) and Hashimoto's thyroiditis (hypothyroidism) are diseases of this type. Graves' disease affectsabout 1% of the population, whereas Hashimoto's thyroiditis is even more common:

- Graves' disease (thyrotoxicosis) is due to a unique antibody called "thyroid stimulating antibody" which stimulates the thyroid cells to grow larger and to produce excessive amounts of thyroid hormones. In this disease, the goiter is due not to TSH but to this unique antibody.{27}

- In Hashimoto's thyroiditis, the goiter is caused by an accumulation of white blood cellsand fluid (inflammation) in the thyroid gland. This leads to destruction of the thyroidcells and, eventually, thyroid failure (hypothyroidism). As the gland is destroyed, thyroid hormone production **decreases; as a result, TSH increases, making the goiter even larger. Other less common causes of thyroid disease include nodule, thyroid cancer thyroiditis and primary hypothyroidism. Nodules, mostly benign are verycommon.**

3.3 Exposure of the thyroid gland to radioactive iodine:

Because of the extensive use of radioactive iodine in medical practice, groups of people representing a wide range of age have been exposed to radioiodine's, both for diagnostic procedures and for radiotherapy used to treat diseases such as hyperthyroidism and thyroid cancer. Although accidental external irradiation is a well-known cause of human thyroid cancer since years, the risk from accidental exposure of the thyroid gland to internal radiation was not well defined before the Chernobyl accident. Thus, the thyroid radiation exposures due to the releases of radioiodine's into the environment were virtually all internal, and it has been concluded that the contribution of external radiation was negligible for most individuals, despite some degree of uncertainty in the doses received.

-There are 37 know isotopes of iodine (I_{53}) from I_{108} to I_{144} ,all undergo radioactive decay except I_{127},which is stable .Iodine is thus a monoisotopic element (We will discuss the most common types in the world of nuclear medicine){28}

3.4 Medical use of radioactive iodine

Radioactive iodine play an important role in the diagnosis and treatment of various thyroid disorders. The five iodine isotopes used for those purposes are I_{123}, primarily a gamma emitter with a short physical half- life of 13 hours; I_{131}, a beta- and gamma- emitter with a longer physical half-life of 8 days; I_{124}, a positron emitter with a half-life of 4.2 days, and I_{125} preferred for laboratory use because of its long half-life of 60 days; I_{125} is also used as a sealed source that could be implemented inside tumors (e.g. in the prostate gland) to irradiate and destroy as much as possible the cancerous cells. For diagnostic use, despite moderately energetic gamma emission, I_{131} is suitable for external measurement of the quantity and localization. I_{123} is now the preferred choice for diagnostic studies of the thyroid, since greater cellular damage or celldeath is produced by the higher energy beta emissions of I_{131} than by the gamma emissions of either isotope. Thus, the short half-life of I_{123} and mainly its gamma emission reduce potential radiation effects on the thyroid. Nowadays, I_{124} is coming into use for PET scanning. The ability of the thyroid to concentrate iodine permits the use of radioiodine to quantify the iodine concentration activity of the thyroid because the isotope equilibrates with blood iodine and reflects the uptake of stable (non-radioactive) iodine into the thyroid. Thyroid radioiodine uptake is elevated in patients with hyperthyroidism, is usually low in hypothyroid patients, and varies inversely with iodine intake. Thus, the radioiodine uptake will be higher than normal in

subjects with low iodine intake and lower in subjects with high iodine intake. The former probably occurredin Chernobyl because of dietary iodine deficiency, and the latter would occur in Japan, where iodine intake is high. The ability of the thyroid to concentrate radioiodine also permits visualization of the thyroid with appropriate imaging instruments (e.g., gamma camera or PET SCAN) to determine its location, configuration, and the functional status of thyroid nodules if they are present. Radioiodine concentrated by the thyroid in large amounts can cause cell death primarily because of I_{131} beta radiation. Large doses of I_{131} are, therefore, given to treat patients with hyperthyroidism; those who have large nodular goiters that are causing local compressive symptoms on the trachea and esophagus, and those who cannot tolerate thyroid surgery; and to ablate functioning residual normal or malignant thyroid tissue after definitive surgery for thyroid{29}

cancer. The very large doses used to treat thyroid cancer occasionally lead to radiation-induced salivary gland inflammation and loss of taste because iodine is also concentrated by the salivary glands. Despite several extensive retrospective studies, no convincing evidence has come forth to implicate I_{131} as a cause of thyroid cancer in treated patients. Finally, medical use of radioiodine has not been observed to cause thyroid cancer but almost all of the treated patients were young adults or older, an age group much less likely to develop thyroid cancer after radiation exposure. However, very few of the patients studied were young children, the group most sensitive to thyroid radiation: in the few studies of children given therapeutic I_{131} for hyperthyroidism, no malignant nodules were found after the treatment but the statistical power to demonstrate oncogenes is in these small groups of patients was limited[29] .

3.5Mechanism of the I-131 Therapy

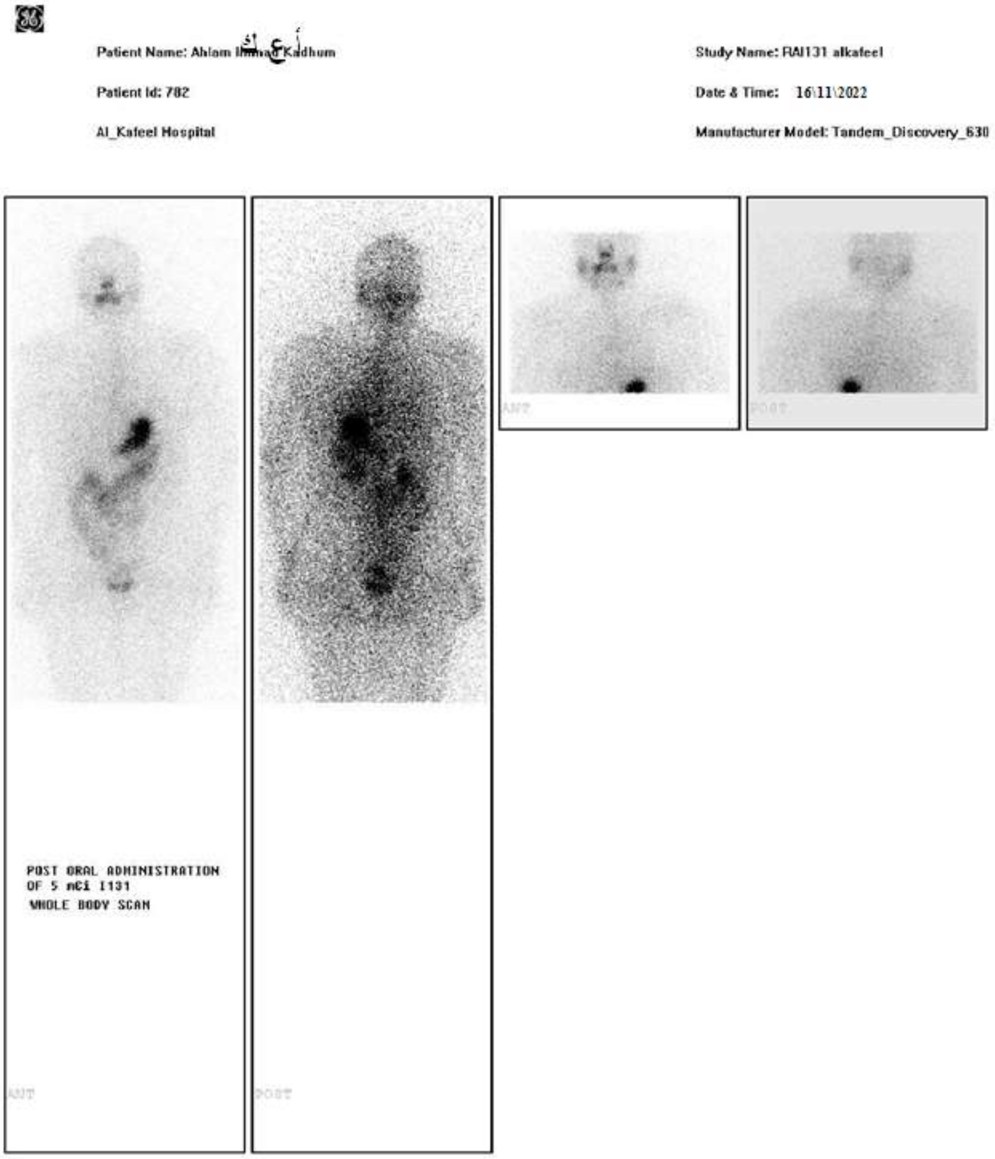
Two types of biological effects of ionising radiation are known: deterministic effects and stochastic effects. Deterministic effects are those caused by the decrease in or loss of organ function due to cell damage or cell death. For these effects threshold doses exist:the function of many organs and tissues is not affected by small reductions in the number of available healthy cells. Only if the decrease is large enough, will a clinically observable pathological dysfunction appear. In the case of treatment of thyroid cancer, metastases, hyperthyroidism and euthyroid goitre, the objective is to bring about the cell- killing effect while not affecting other organs in such a way that deterministic effects occur. Due to the capacity of thyroid cells to take up iodine thyroid diseases can be treated with radioactive iodine. The β-emitting I_{131} is often the radionuclide of choice for these treatments, although the associated

γemission gives rise to exposures to other tissues and even to other individuals. The probability of a radiation-induced fatal cancer for the average population has been estimated (ICRP-60) at approximately 5 percent per sievert2 for low doses and at lowdose rates and at 1 percent for serious genetic diseases. For elderly people, older than about 60 years, the probability seems to be 3 to 10 times lower. This is because the future life span of elderly people may not be long enough for the cancer to become apparent andit is also unlikely that genetic damage is passed to offspring. For children up to the age of 10 years, the probability of fatal cancer induction seems to be about 2-3 times higher. For pregnant women the risk is the same as for the average population; however, the unborn child is assumed to have the

same risk of developing a fatal cancer as young children. Deterministic effects have been observed after massive irradiation LQXWHUR, but dose levels incurred by family or close friends from a treated patient are far below the threshold for such effects. As sensitivity to ionising radiation is different for different age categories, instructions to reduce the risk for these groups will also vary accordingly [30]

4.1 The Experimental Work

In this part, we will have a number of different cases diagnosed with thyroid tumors.On this base , a surgery was done to remove the largest possible part of the tumor. After the surgery, a therapeutic dose of I_{131} is given to remove the remaining part of the tumor and the size of the therapeutic dose depends on the size of the remaining part of the tumor



Patient Name: Ahlam [redacted] Kadhum
Patient Id: 782
Al_Kafeel Hospital

Study Name: RAI131 alkafeel
Date & Time: 16\11\2022
Manufacturer Model: Tandem_Discovery_630

POST ORAL ADMINISTRATION
OF 5 mCi I131
WHOLE BODY SCAN

Al-Kafeel
Super Specialist hospital

مستشفى الكفيل التخصصي
في كربلاء المقدسة

Nuclear medicine department

Ref. Doctor: الدكتور المحترم **Date: 16/11/2022**

Patient Name :أ ع ك **Age: 40 y**

Whole body RAI-131 SCAN

Indication: Thyroid carcinoma.

Comparison: No image for comparison.

Technology: Whole body scan anterior and posterior views and neck spot viewswere performed 2 days after the oral administration of 5 mCi RAI-131.

Findings:

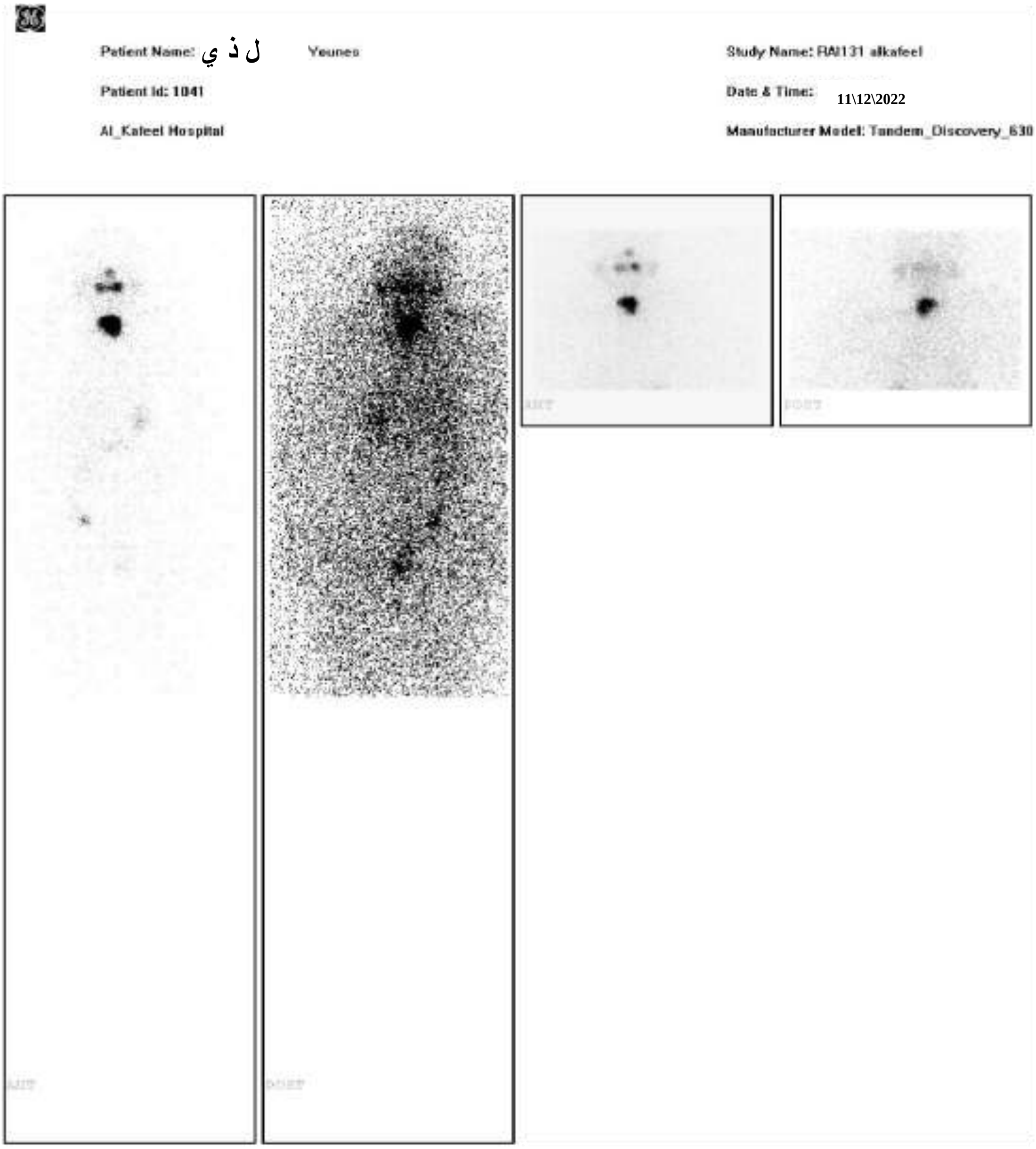
There is no radioactive iodine uptake seen in the neck region or cervical lymphnodes. There is no abnormal radiotracer accumulation in the rest of body. There is diffuseradiotracer uptake seen in the liver duo to radioactive thyroxin degradation .
Physiological RAI-131 uptake seen in nasopharyngeal area, salivary gland,GIT andurinary bladder

Impression:

No remanant thyroid tissue/ recurrent disease in the thyroid bed, lymph node, or distant metastases.

Sincerely yours

Dr. Layth Al Araji, MD Nuclear Medicine Specialist M B Ch B, J B NM,



Patient Name: ل ذ ي Younes

Patient Id: 1041

Al_Kafeel Hospital

Study Name: RAI131 alkafeel

Date & Time: 11\12\2022

Manufacturer Model: Tandem_Discovery_630

Al-Kafeel
Super Specialist hospital

مستشفى الكفيل التخصصي
في كربلاء المقدسة

Nuclear medicine department

Ref. Doctor: الدكتور المحترم

Date: 11 -12-2022 Patient

Name : ل ذ ي

Age: 35 y

Whole body post therapy RAI-131 SCAN

Indication: Thyroid carcinoma.

Comparison: No image for comparison.

Technology: Whole body scan anterior and posterior views and neck spot viewswere performed 7 days after the oral administration of 30 mCi RAI-131.

Findings:

There are two foci of increased radioactive iodine uptake seen in the anterior neckregion. There is no abnormal radiotracer accumulation in the rest of body. There is diffuseradiotracer uptake seen in the liver duo to radioactive thyroxine degradation .

Physiological RAI-131 uptake seen in nasopharyngeal area, salivary gland,GIT andurinary bladder

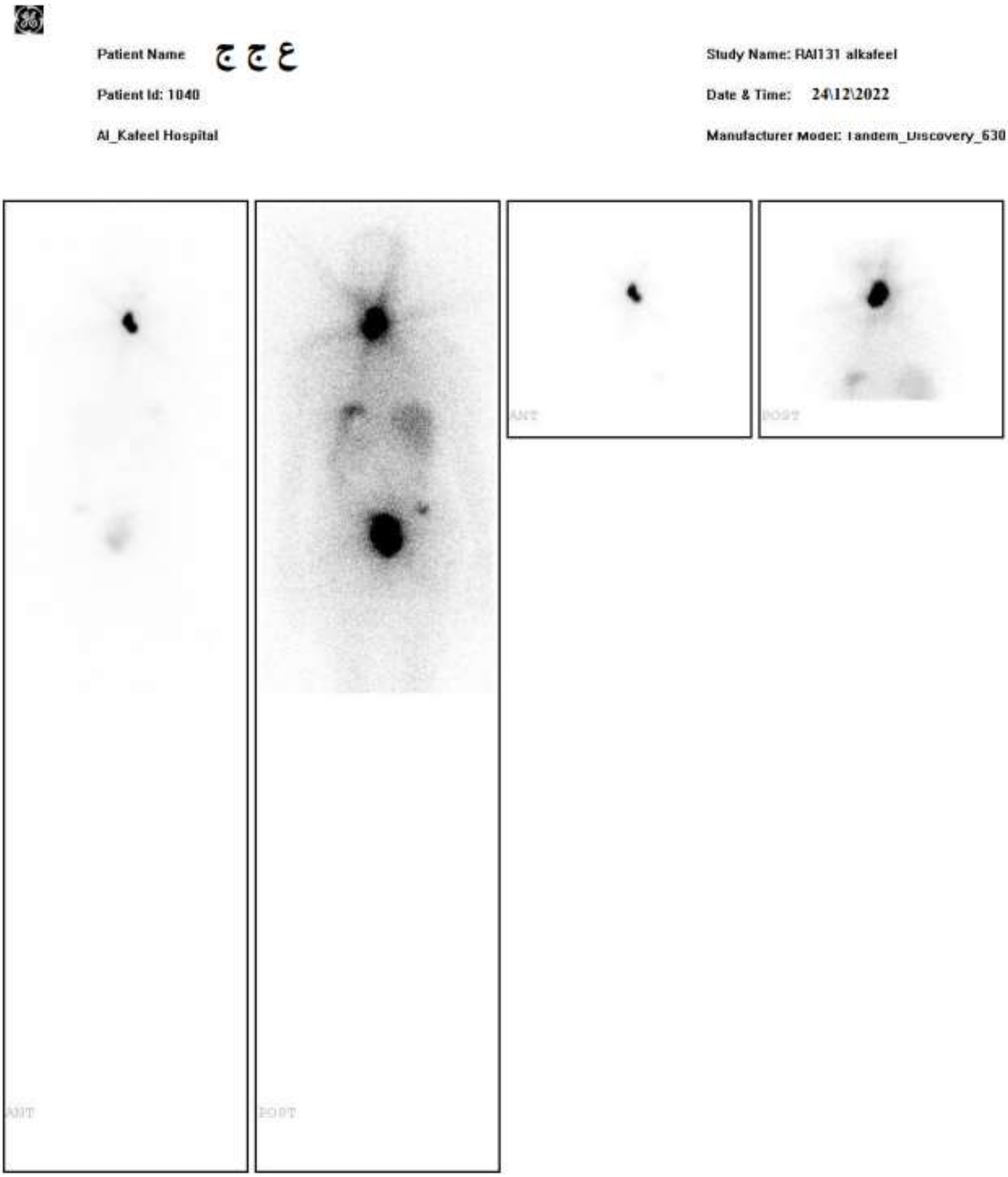
Impression:

Two focal areas of RAI-131 uptake in neck are consistent with remnant thyroid tissue with possibility of lymph node metastases .However, initial response to therapy is noted.

No distant metastases could be detected in this study

Sincerely yours

Dr. Layth Al Araji, MD Nuclear Medicine Specialist M B Ch B, J B NM,



Patient Name ع ج ج

Patient Id: 1040

Al_Kafeel Hospital

Study Name: RAI131 alkafeel

Date & Time: 24\12\2022

Manufacturer Model: Tandem_Discovery_630

Al-Kafeel
Super Specialist hospital

مستشفى الكفيل التخصصي
في كربلاء المقدسة

Nuclear medicine department

Ref. Doctor: الدكتور المحترم **Date: 24 -12-**
2022 Patient Name : ع ج ج **Age: 35 y**

Whole body post therapy RAI-131 SCAN Indication: Thyroid carcinoma.

Comparison: No image for comparison.

Technology: Whole body scan anterior and posterior views and neck spot views were performed 7 days after the oral administration of 100 mCi RAI-131.

Findings:

There are three foci of increased radioactive iodine uptake seen in the anterior neck region.
There is no abnormal radiotracer accumulation in the rest of body. There is diffuseradiotracer uptake seen in the liver duo to radioactive thyroxine degradation .
Physiological RAI-131 uptake seen in nasopharyngeal area, salivary gland,GIT andurinary bladder

Impression:

Three focal areas of RAI-131 uptake in neck are consistent with remnant thyroid tissuewith possibility of lymph node metastases .However, initial response to therapy is noted.
No distant metastases could be detected in this study

Sincerely yours

Dr. Layth Al Araji, MD Nuclear Medicine Specialist M B Ch B, J B NM,

4.2 Conclusion

It is concluded from the previous reports that two cases of thyroid cancer after taking a therapeutic dose of iodine of 30 mCi of iodine RAI- 131 and after a week of the dose showed that the radioactive iodine took the place of the gland or lymph nodes. Around it, which indicates that iodine took the place of the gland Recent case of thyroid cancer Whole- body scan was performed six months after the dose of therapeutic RAI-
131 and showed a complete response to radioactive iodine therapy.

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