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Thyroid Cancer: Iodine-131 Intervention and Dosimetric Analysis: A Review

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Abstract: *There has been a notable global escalation in the incidence of thyroid carcinoma, with a particularly pronounced surge of 240% in the incidence of papillary thyroid carcinoma over the past three decades. It is imperative to elucidate its etiological factors, diagnostic methodologies, and therapeutic strategies to enhance patient prognoses. Research into thyroid malignancies is essential for the advancement of diagnostic precision and the evolution of targeted oncological therapies. Investigations advocate for the optimization of Iodine-131 radioisotope therapy as the most efficacious treatment modality for thyroid cancer. This discourse offers a comprehensive examination of the etiology, diagnostic frameworks, and therapeutic interventions, as well as the utilization of Iodine-131, dosimetric considerations, associated risks, and the prevailing challenges in this domain*

Keywords: Thyroid carcinoma, diagnosis, therapy, dosimetry, Iodine-131

I. INTRODUCTION

Thyroid cancer was once uncommon, but recent studies show a global increase. Each year, approximately 3,400 people in the UK are diagnosed with thyroid cancer. Like most cancers, it is more common in older individuals, especially women (MCS, 2017). In the United States, about 1.2% of people have been diagnosed with thyroid cancer over time in their lives, and it is anticipated that there will be around 43,720 new incidences of thyroid carcinoma in 2023. There has been a prevailing global rise in the incidence of thyroid cancer, with a particularly significant rise of 240% in the detection of papillary thyroid carcinoma in about three decades now (Laura Boucai, et al, 2017).

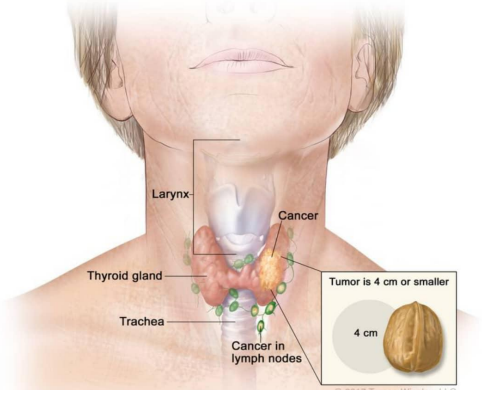

Figure 1: Papillary and follicular thyroid cancer with a tumor of about 4cm, the cancer has escalated to lymph nodes that are around it (RCCCNU, 2017).

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Research shows that one of the best and recommended treatment options for thyroid cancer is the use of iodine-131 (I-131). It's a radioisotope that has been utilized in the medical field for over six decades due to its ability to integrate with nonradioactive iodine in the thyroid. This integration makes it valuable for assessing and managing thyroid diseases (Tuttle, 2108).

1.1 Causes of Thyroid Cancer

It is important to remember that having a dangerous factor does not guarantee the development of cancer, and the absence of risk factors does not mean immunity to cancer (NCI, 2023). The exact cause of thyroid cancer isn't fully understood. Some of the causes of thyroid cancer include:

1.1.1 Benign thyroid disease: It is vital to recognize that having an overactive or underactive thyroid, also known as hyperthyroidism and hypothyroidism, does not inherently increase the chances of thyroid cancer disease, certain types of non-cancerous thyroid diseases like goiter, adenomas, and thyroiditis are connected with a slightly higher risk of developing thyroid cancer. Moreover, having a family history of benign thyroid disease can increaserisk, particularly if multiple family members are affected.

1.1.2 Radiation exposure: Thyroid cancer is prevalent in individuals exposed to significant amounts of radiation (ATA, 2022). People who have undergone radiotherapy in the neck area during childhood or young adulthood stand a greater chance of having thyroid cancer later in life. Environmental radiation exposure, such as after a nuclear accident like Chornobyl, can also increase the risk. However, it is pivotal to note how just a small percentage of thyroid cancers are a result of radiation exposure as reported by several researchers(MCS, 2017, NCI, 2023).

Radiation therapy administered for the treatment of cancers like Hodgkin's disorder or breast cancer is connected to a prevailingchance of having thyroid cancer, especially when the therapy has to do with radiation exposure to either the head, neck, orchest region. On the other hand, routine X-ray procedures like dental X-rays, chest X-rays, and mammograms are not significantly connected with a substantiallyheightened chance of thyroid cancer. It is important to limit radiation exposure by only undergoing medically essential tests (ATA, 2022).

1.1.3 Family history: The possibility of developing thyroid cancer is elevated in individuals who have a first-level relative diagnosed with the disease. However, given the rarity of thyroid cancer, the overall risk remains relatively low. Research by Maria et al. (2006) indicates that DNA networking studies of thyroid cancer showed the genetic root of a large percentage ofmany cases. The majority of thyroid cancer cases show mutations along the mitogen-activated protein kinase (MAPK) cellular signaling pathway, which contributes a crucial part in transmitting development signals right at the plasma membrane to the nucleus and regulating cellular proliferation, as shown in the diagram below**.**

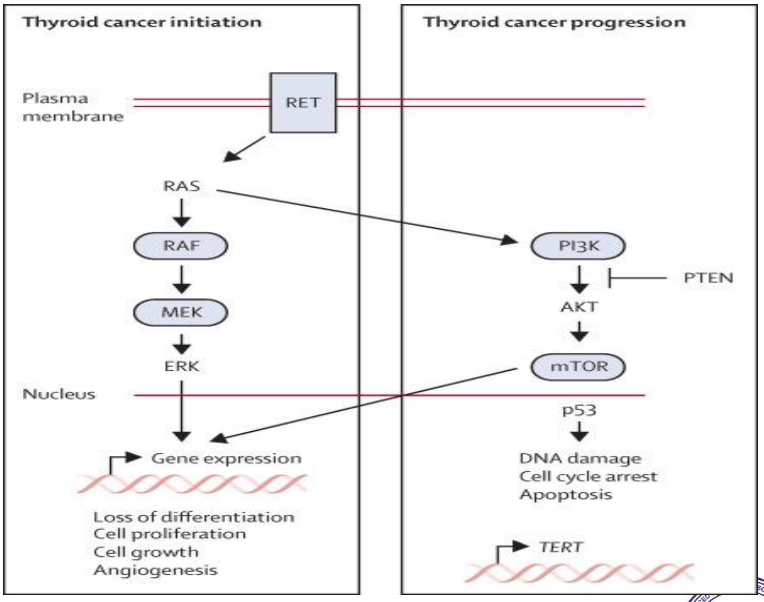

Figure 2

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Individuals face a minimally higher chance of developing thyroid cancerand have gained a mutated gene associated with familial adenomatous polyposis (FAP), a bowel condition. In light of the preceding information:

It is highly recommended for family members of someone with familial adenomatous polyposis (FAP) to undergo genetic testing to ascertain the potential inheritance of the mutational predisposition.

1.1.4 Being a female: Thyroid carcinoma is highly prevalence in women, which suggests a possible connection with their hormones. Thyroid carcinoma demonstrates a preference for the female gender, potentiating the notion of an etiological correlation with the endogenous female hormonal milieu.

1.1.5 Obesity: It was suggested individuals who have high weight may stand a greater chance of developing thyroid cancer. It is hypothesized that following a healthy diet and exercise routine could potentially reduce this risk (MCS, 2017).

1.1.6 Thyroid cancer is prevailing in women: It is dominant, especially among those who have had an enlarged thyroid (goiter), are between the ages of 25 and 45, and are of Asian descent (ATA, 2022; NCI, 2023; MCS, 2017).

1.2 Diagnosis of Thyroid Cancer

The presence of thyroid nodules may be ascertained through a physical examination or incidentally through diagnostic imaging procedures. When symptomatic, consideration of the following diagnostic measures by either the individual or their healthcare provider becomes pertinent for confirming a diagnosis (ACI, 2023).

During a comprehensive physical examination and health history evaluation, the body is meticulously assessed to detect general indicators of health, encompassing the identification of nodules, swellings, and any anomalous manifestations in the neck, voice box, and lymph nodes. Moreover, substantial emphasis is placed on garnering insights into the patient's health behaviors, medical history, and prior therapeutic interventions (MCS, 2017).

1.2.1 Laryngoscopy: Involves the examination of the larynx by a physician employing a mirror or laryngoscope. This diagnostic procedure is conducted to assess the normalcy of vocal cord movement, specifically in cases where a thyroid tumor may exert pressure on this anatomical structure (ATA, 2022).

1.2.2 State-of-the-Art Blood Hormone Studies: Blood hormone studies entail the analysis of a peripheral blood sample to quantify the concentrations of specific hormones secreted into the circulatory system by bodily organs and tissues. Deviations from normative levels, either in excess or deficiency, can serve as clinical indicators of pathological processes within the respective organ or tissue. The blood sample could be assayed for atypical stage of thyroid-stimulating hormone (TSH), a product of the pituitary gland that incites the secretion of thyroid hormone and governs the proliferative capacity of thyroid follicular cells. Furthermore, the blood may be scrutinized for heightened concentrations of calcitonin hormone and anti-thyroid antibodies (ATA, 2022).

1.1.3 Blood chemistry studies: This test measures the amount of certain substances in the blood, like calcium, to check for any unusual levels. These levels can indicate if there's a disease present.

1.2.4 Ultrasound exam: Ultrasonography is a diagnostic imaging technique that employs increase-energy sound waves to generate echoes off interior tissues or organs located around the neck region. These echoes are used to create a sonogram, providing a visual representation of body tissues. This sonogram can be documented for later review (ACI, 2023, ATA, 2022). The procedure is valuable in determining the size and composition of a thyroid nodule, differentiating between solid and fluid-filled structures. Additionally, ultrasonography can be utilized to assist in guiding a fine-needle aspiration biopsy.

1.2.5 CT scan (CAT scan): A CT scan is a procedure that uses an X-ray machine and a computer to take detailed pictures of different body areas like the neck. Sometimes, a dye can be used to make organs or tissues become crystal clear. This process isknown as computed tomography or computerized axial tomography (ACI, 2023).

1.2.6 Fine-needle aspiration biopsy: Is a procedure used to extract thyroid tissue for analysis. It involves inserting a fine needle via the skin and to the thyroid. Several tissue samples are taken from various segments of the thyroid and examined under a microscope by a pathologist to identify any cancer cells.Given the complexity of diagnosing thyroid cancer, it is crucial for patients to insist on having their biopsy samples analyzed by an experienced pathologist in thyroid cancer diagnosis.

1.2.7 Surgical biopsy: Undergoing a surgical biopsy is a procedure where either a thyroid nodule or one lobe of the thyroid is surgically removed. This tissue is then examined under a microscope by a pathologist to detect any indication

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of cancer. Given the complexity of diagnosing thyroid cancer, patients are advised to request that biopsy samples be assessed by a pathologist with expertise in diagnosing thyroid cancer (ACI, 2023; ATA, 2022).

1.3 Types of Thyroid Cancer.

Thyroid cancer can be discussed under the following headings

1.3.1 Papillary thyroid cancer: Papillary thyroid cancer is the highest prevalent form, accounting for approximately 75% of all thyroid cancers. This type of cancer can develop at any age and appears to progress slowly. Additionally, it frequently spreads to the lymph nodes in the neck. Despite spreading to the lymph nodes, papillary cancer generally has a positive prognosis (ATA, 2022, ACI, 2023).

1.3.2 Follicular thyroid cancer: It accounts for approximately 15% of all thyroid cancers in the United States. This type of cancer has the ability to spread to distant organs, especially the lungs and bones, through the bloodstream. Follicular cancer, along with papillary thyroid cancer, is classified as a well-differentiated thyroid cancer (DTC) (ATA, 2022).

1.3.3 Medullary thyroid cancer:

Medullary thyroid cancer (MTC) makes up around 2% of all thyroid cancers. About 25% of MTC cases are inherited and linked to other endocrine tumors. A genetic assessment for a mutation in the RET proto-oncogene can help diagnose MTC early in family members of affected individuals, allowing for curative surgery. The remaining 75% of MTC patients don't have a hereditary type of the disease (ACI, 2023).

1.3.4 Anaplastic thyroid cancer: This is widely acknowledged as the most complex and aggressive form of thyroid cancer, exhibiting a notably low likelihood of responding favorably to treatment interventions. Notably rare, this variant of thyroid cancer is present in less than 2% of individuals diagnosed with thyroid malignancies (ATA, 2022; Limaiem et al., 2024).

1.4 Treatment for Thyroid Cancer

Prognostic and treatment decisions are contingent upon factors including the patient's age at the point of diagnosis, specific pathology of the thyroid cancer, the extent of cancer progression, the success of the surgical intervention, the presence of several endocrine neoplasia type 2B, the overall health status of the patient, and whether the cancer is at initial diagnosis or has recurred (ATA, 2022).

1.4.1 Surgery: Surgery is the most frequently used method for treating thyroid cancer. Various processescould be employed, including:

Lobectomy refers to the surgical procedure involving the extraction of the lobe in which thyroid cancer has been detected. Additionally, adjacent lymph nodes may be excised and subsequently examined microscopically to identify any presence of malignant cells.

Near-total thyroidectomy encompasses the nearly complete excision of the thyroid gland. Adjacently situated lymph nodes may also be dissected and scrutinized for malignancy under a microscope.

Total thyroidectomy: Complete thyroidectomy will be performed, along with possible dissection and histological examination of adjacent lymph nodes to assess for cancerous involvement.

Tracheostomy: A surgical procedure involving the creation of a stoma, also referred to as a tracheostomy, in the windpipe to facilitate respiration(ATA, 2022, Limaiem et al, 2024).

The initial modality for all forms of thyroid cancer is surgical intervention. The nature and extent of the surgical procedure are contingent upon the size of the tumor and its extrathyroidal extension. A total thyroidectomy is recommended in cases where the tumor involves both thyroid lobes or has extended beyond the thyroid gland. Should the cancer have metastasized to the cervical lymph nodes, their excision can be performed concomitantly with the primary thyroid surgery, or as a subsequent procedure. In contrast, for small, unifocal tumors that have not metastasized, a lobectomy could be a viable choice. Additionally,research indicates that active surveillance can be safely employed as anintervention strategy for papillary thyroid microcarcinomas measuring less than 1cm.

If a total thyroidectomy is performed, lifelong thyroid hormone medication will be necessary. It is worth noting that a lobectomy may not necessitate thyroid hormone replacement. Surgery alone frequently results in the cure of thyroid cancer, particularly when the cancer is small. Nevertheless, supposing the cancer is extensive, has metastasized to

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lymph nodes, or provided the patient is deemed to be at high risk for recurrence, post-thyroidectomy treatment with radioactive iodine may be warranted(Limaiem et al, 2024). This therapeutic approach, also known as radioactive iodine therapy or I-131 therapy, involves the application of radioactive iodine to eradicate any remnant normal thyroid tissue and ably eliminate remaining cancerous thyroid tissue following thyroidectomy. This process, known as radioactive iodine ablation, is utilized to eliminate residual thyroid tissue. The radioactive iodine used in the ablation procedure typically does not affect other tissues in the body significantly or at all, as they do not absorb or concentrate iodine efficiently, unlike the thyroid gland(ATA, 2022, ACI, 2023).

1.4.2 Radiation therapy: Radiation therapy encompasses the utilization of high-energy X-rays or alternate variations of radiation, such as radioactive iodine therapy, to eradicate cancer cells or inhibit their proliferation. There are two primary types of radiation therapy:

External radiation therapy is a form of treatment that utilizes a device located outside the body to produce high-energy radiation to the specific area affected by cancer. This targeted approach is designed to exterminate cancer cells and melt tumors. In certain cases, radiation may be directed straight at the tumor during surgery, a technique referred to as intraoperative radiation therapy.

Brachytherapy is an inherent component of internal radiation therapy that employs encapsulated radioactive sources, including needles, seeds, wires, or catheters, to be precisely positioned within or in close proximity to the malignant tissue (Limaiem et al, 2024).

Following surgical intervention, radiation therapy might be administered to eradicate any residual thyroid cancer cells. In cases of follicular and papillary thyroid cancers, utilization of radioactive iodine (RAI) therapy is occasionally warranted. RAI is orally ingested and accumulates remnant thyroid tissue, involving metastasized thyroid cancer cells. By exploiting the exclusive iodine absorption capability of thyroid tissue, RAI effectively eliminates both thyroid tissue and thyroid cancer cells while sparing non-targeted tissues. Prior to the administration of a comprehensive RAI treatment, a minute test dose is administered to evaluate iodine uptake by the tumor. The specific type and stage of the cancer determine the modality of radiation intervention(ATA, 2022,Limaiem et al, 2024).

1.4.3 Chemotherapy: Chemotherapy is a widely used cancer intervention that includes the administration of drugs to impede the growth and spread of cancer cells within the body. The drugs work by either destroying the cancer cells or preventing their division. Chemotherapy can be administered in various ways, including orally, through injection into a vein or muscle, and direct placement into specific areas such as the cerebrospinal fluid or body cavities(Limaiem et al, 2024). When chemotherapy is delivered systemically, through oral ingestion or injection, the drugs travel through the circulatory system facilitating the transportation of cancer cells to various parts of the body through the bloodstream. On the other hand, regional chemotherapy involves placing the drugs directly into specific areas of the body, such as the abdomen or the cerebrospinal fluid, to primarily target cancer cells in those localized regions. This tailored approach allows for the effective treatment of cancerous cells in specific areas, minimizing the impact on healthy cells elsewhere in the body (Limaiem et al, 2024, ATA, 2022).

1.4.4 Thyroid hormone therapy: This constitutes a form of cancer intervention designed to either eliminate hormones or impede their physiological effects, thereby arresting the growth of cancerous cells. Hormones are organic compounds produced by glands within the body and distributed through the bloodstream. Withinand around the context of thyroid cancer treatment, medications could be prescribed to inhibit the body's production of thyroid-stimulating hormone (TSH), a substance known to elevate the chance of thyroid cancer recurrence and progression. Furthermore, the intervention for thyroid cancer results in the destruction of thyroid cells, rendering the thyroid incapable of producing sufficient thyroid hormone. Consequently, patients are provided with replacement thyroid hormone medication(Limaiem et al, 2024).

1.4.5 Targeted therapy: This constitutes a specialized form of intervention employing drugs or other agents to spot and target particular cancer cells. This therapeutic approach encompasses various modalities:

Tyrosine kinase inhibitor therapy involves the interception of critical signals necessary for tumor proliferation. Ongoing research is currently concentrating on developing new tyrosine kinase inhibitors specifically designed to treat advanced thyroid cancer(Limaiem et al, 2024).

Protein kinase inhibitor therapy aims to impede pivotal proteins essential for cellular growth, potentially leading to the eradication of cancerous cells. Dabrafenib and trametinib are employed in the treatment of anaplastic thyroid cancer in

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patients harboring a specific mutation in the BRAF gene. Furthermore, watchful waiting involves closely monitoring a patient's condition without initiating intervention until signs or symptoms appear or progress (ATA, 2022).

1.4.6 Immunotherapy: This is a powerful cancer management that harnesses the body's immune system to effectively combat cancerous cells.

Substances that are endogenously produced or artificially synthesized are employed to enhance, modulate, or reinstate the innate mechanisms of the body in combatting cancer. This groundbreaking cancer treatment falls under the category of biological therapy (ATA, 2022,Limaiem et al, 2024).

1.5Treatment of advanced thyroid cancer: TC that has metastasized beyond the neck region is not common however it is of significant clinical concern. Surgical intervention and radioactive iodine therapy are the primary modalities for managing such cases, provided these treatments remain efficacious. In the context of advanced or refractory thyroid cancers, approved medications have emerged as a vital therapeutic option. Although these drugs seldom yield curative outcomes for extensively disseminated cancers, they exhibit the potential to decelerate or partially reverse tumor progression (Limaiem et al, 2024). Typically administered by an oncologist, these treatments often necessitate specialized care at a regional or academic medical center.

Notably, such agents has capacity induce redifferentiation in tumors that have ceased to respond to radioactive iodine, thereby reinstating their sensitivity to this treatment modality. Furthermore, the precise delivery of external beam radiation can be instrumental in targeting local recurrences in the neck or metastases to osseous or visceral sites, exerting cytotoxic or growth-retarding effects on these neoplastic foci. This treatment has the potential to either eliminate or inhibit the growth of these tumors (ATA, 2022,Limaiem et al, 2024).

II. IODINE-131

The radioisotope Radioiodine I-131 is among the earliest radioisotopes utilized in the field of medicine. For over six decades, I-131 has been widely used in the evaluation and treatment of thyroid diseases. It is an iodine isotope that closely resembles nonradioactive iodine, allowing it to integrate seamlessly with the thyroid. This isotope is created artificially and can be obtained as sodium iodide (NaI) from the by products of uranium disintegration or through neutron irradiation of tellurium-130 in a nuclear reactor. As per the Environmental Protection Agency, I-131 possesses a brief half-life of approximately eight (8) days, characterized by beta and gamma radiation, resulting in its near-complete decay in the environment within months (Peter et al, 2005, Judith and Andrew, 2011).

Figure 2 below shows the decay scheme of iodine-131

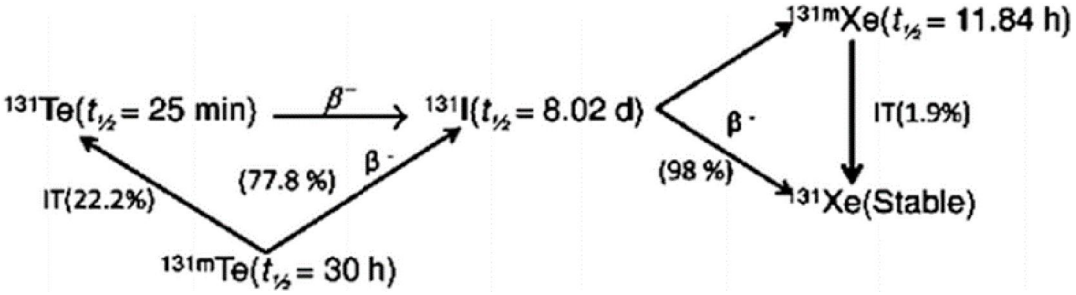

Figure 3: iodine-131 decay scheme

When we take radioiodine orally, in the form of the iodide ion, it quickly gets absorbed from our digestive system and spreads throughout the fluid outside our cells. It accumulates in the salivary glands, thyroid, and stomach lining. If it doesn't concentrate in the thyroid and other organs, any radioiodine that remains unabsorbed gets eliminated from our body through sweat and urine. However, when our normal thyroid gland sequesters and regulates iodide, it remains in our body for about seven days before it becomes less effective. In cases of hyperthyroidism, this half-life drops to 3-5 days, and in instances of thyroid cancer, it can be even less than 3 days (Judith and Andrew, 2011; Fred et al, 2012; Peter et al, 2005).

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2.1 Diagnostic uses of I-131 in thyroid gland

Iodine-131 is a radioactive isotope usuallyutilized in medical imaging to capture images of the thyroid gland. Approximately 90% of the iodine-131 atoms undergo decay, transitioning into xenon-131 via the illustrated decay scheme in Figure 1. This decay process occurs through a first-order mechanism, wherein the decay rate is directly proportional to the concentration of iodine-131 (Hongming et al, 2021). The decay scheme is as shown below:

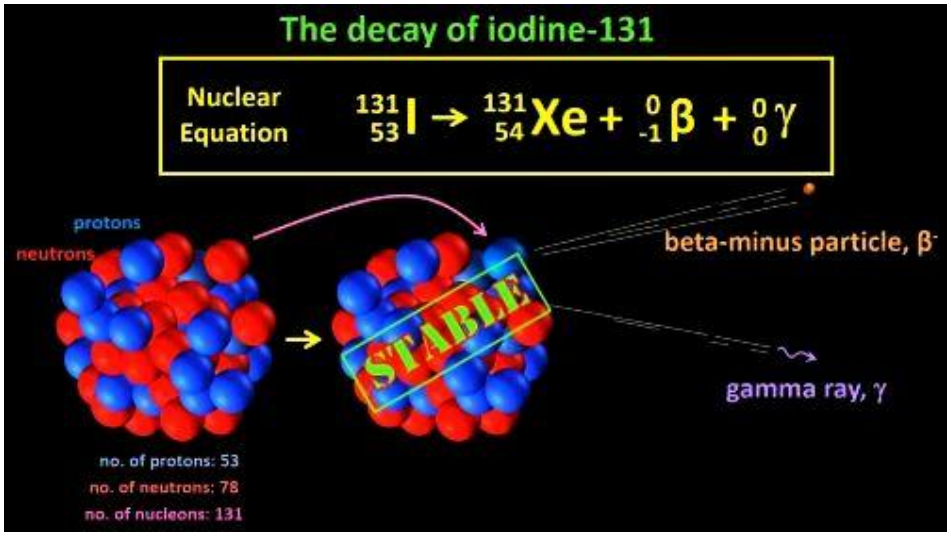

Figure 4: Iodine-131 decay

During a regular thyroid examination, the imaging reveals a butterfly-shaped thyroid gland that is approximately 5.1 cm in length and 5.1 cm in width. The radioactive tracer is evenly spread throughout the gland. Conversely, an unusual thyroid scan may display a thyroid gland whichcould be either smaller or larger than the typical size. Additionally, the scan may reveal areas within the thyroid gland where the level of activity is either lower than healthy and normal (referred to as cold nodules) or higher than healthy and normal (referred to as hot nodules). It's essential to note that cold nodules, which are regions of reduced activity, may be indicative of thyroid cancer (Richard, 2007).

After undergoing a thyroidectomy to remove thyroid carcinoma, I-131 radioablation could be used to eradicate any remaining thyroid tissue in the thyroid bed, as well as any cancerous cells that have spread to lymph nodes or other parts of the body. Postoperative management of thyroid cancer patients heavily relies on whole-body imaging techniques. The patient is administered a minute dose of I-131 to come back within about 7-10 days post-cancer therapy for a Whole Body Scan (WBS) (Fred et al, 2012, Richard, 2007).

WBS utilizes a gamma camera to capture images by detecting the gamma radiation emitted by either the radioactive iodine in the thyroid gland or tumor cells. The gamma camera's crystal interacts with photons from the body, producing scintillations. These scintillations are then detected, amplified, and converted into light (Juthith and Andrew, 2011). The light is then converted into an electrical signal and sent to a computer. The computer uses varying intensities of emitted radioactivity to create an image with different shades of gray. This technique is particularly useful for detecting certain types of thyroid cancer cells, such as papillary and follicular types, which can still accumulate iodine, although to a lesser extent than normal thyroid tissue. By applying iodine and using whole-body imaging, this technique can help identify recurring tumors and the spread of thyroid cancer after surgery. This characteristic explains why cancer nodules appear cold on repeated thyroid scans (Juthith and Andrew, 2011, Fred et al, 2012, Richard, 2007).

2.2 Treatment use of iodine-131 in thyroid cancer

I-131 is a radioactive isotope. This isotope can decay by emitting beta particles, each carrying an average energy of 192 KeV. Now, picture this: when these beta particles find their way into the cells of our thyroid gland, they embark on a fascinating journey. Traveling a distance of approximately 0.8 millimeters, they dedicate all their energy to the absorption process, ultimately being completely absorbed by the surrounding thyroid tissue. While in this motion, these beta particles may interact with and transfer their energy to essential and other healthy cells within the organ, leading to

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the destruction of these cells. This specific mechanism enables I-131 treatment to selectively target and eliminate abnormal thyroid cells while minimizing the impact on surrounding healthy cells.

Radioiodine therapy (RIT) is a pivotal intervention for hyperthyroidism associated with various conditions, including Graves' disease, toxic thyroid adenoma, toxic multinodular goiter, and Plummer's disease. Furthermore, RIT serves as a significant adjunctive therapy following surgery for well-DTC, such as papillary thyroid cancer (PTC), follicular thyroid cancer (FTC), and mixed tumors that exhibit radioiodine uptake. Despite the beta emission of I-131, it is characterized by a predominant energetic gamma emission (364 KeV) that can be effectively utilized for imaging the bio-distribution. However, this gamma photon also poses the risk of causing measurable absorbed radiation doses in individuals near the patient. Given that excretion primarily occurs through the urinary tract, with additional elimination through saliva and sweat, it is imperative to implement special radiation protection measures for several days following the administration of RIT to these patients (Rose et al., 2004).

Different thyroid disorders require different doses of I-131. However, there are still controversies surrounding the administration of I-131 sodium iodide for each of these conditions. In this regard, there are three approaches to selecting the appropriate dose of I-131 for WDC therapy: the dosimetric method**:**

The fixed-dose method involves the administration of predetermined and empirically determined amounts of I-131 tailored to specific stages of the tumor.

Quantitative tumor dosimetry: The process that involves determining the amount of radiation that is administered by the radioactive isotope I-131 to a specific location within a tumor.

A dosimetry-guided technique: The calculation involves determining the maximum allowable levels of irradiation for both the blood and the entire body resulting from exposure to I-131.

To date, no prospective randomized trial conducted to definitively establish which approach yields superior results. However, various analyses and studies have indicated that both approaches produce similar outcomes (Robert and Ernest, 2005; Ernest and Mazzaferri, 2005).

III. DOSIMETRY IN THYROID CANCER TREATMENT USING I-131

Dosimetry as defined in Medical Physics encompasses the comprehensive assessment of radiation exposure for both patients and phantom dosimetry, as well as the monitoring of radiation exposure for occupationally exposed personnel and environmental surveillance in hospital settings. In the context of patient dosimetry, radiation exposures are deliberately administered to directly benefit the patient's health, and the radiation field is precisely defined for this purpose. The primary objective is to critically evaluate the associated risks or the efficacy of radiation exposure for several uses. Conversely, in other scenarios, the objective is to diligently verify compliance with radiation protection regulations as stipulated by Juan Azori in 2004.

The fundamental purpose of dosimetry is to carefully balance the delivery of medical benefits from radiation therapy at the same time minimizing the potential damage to cells, tissues, and organs around the body (Sudprasert et al, 2022, USNRC, 2011). Dosimetry serves as an invaluable tool, enabling the customization of therapy to protect healthy tissue and reduce the possible danger to at-risk organs. An absorbed dose serves as a dependable sign of biological impacts and reactions as a result of its association with tissue irradiation implications (Pacilio et al, 2022). Recognizing the dose thresholds linked to various clinical impacts plays a pivotal role in ensuring quality assurance. This knowledge forms the basis for several critical functions including maintaining comprehensive records, making informed decisions about radiation protection, assessing risks, and devising plans for cancer treatment at all levels. Ultimately, it involves conducting an in-depth cost-benefit analysis of intervention on account of the understanding of dose thresholds and their relationship to the probability of side effects and successful tumor handling(SNMMI, 2019, Pacilio et al, 2022).

The accuracy of estimating the activity obtained at each imaging time point is directly linked to the reliability of radiation dose estimates in internal radionuclide therapy (Yuni, 2023). This means that it's crucial to obtain precise activity estimates at different imaging time points to ensure that the radiation dose estimates are reliable.

Using the principles of radiation dosimetry, practical measurements have been developed for patients who are to undergo treatment with I-131(James, 2002). These measurements are exclusively designed to provide accurate information about the radiation dose to be administered and to ensure the safety and effectiveness of the treatment mechanisms.

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In cases where the retention level of I-131 is high, the prescribed therapeutic dose can be decreased, while it can equally be increased when the retention level is low (James, 2002). This demonstrates the importance of accurately measuring the retention level to adjust the therapeutic dose accordingly.

I-131 is considered the intervention of choice for patients whohave a relapse of severe disease after medical intervention or for those with toxic multinodular goiter. This is due to its ease of application, cost-effectiveness, and suitability for all age groups (Pauwels, 2000). The practical methods of dosimetry that measure the body's retention of I-131 not only ensure safety but also enhance the efficacy of the treatment (James, 2002).

The utilization of radioactive iodine for the management of benign thyroid disease and thyroid cancer dates back 80 years. Specifically, in all the radioactive isotopes, I-131 has exhibited successful application (Konrády, 2006). Subsequently, I-131 mIBG was developed to address adult and pediatric neuroendocrine tumors. Notably, physicists actively participated and have played a pivotal role from the outset, actively engaging in the measurement of retention, quantification of uptake, and calculation of radiation dosimetry. As the treatment modality gained wider acceptance, contrasting treatment modalities were observed, with some protocols employing empirically derived fixed levels of activity while others were tailored based on delivered radiation doses (Flux, 2002,Hänscheid, 2013). Overall, safety can be reliably attained, and effectiveness is bolstered through the implementation of practical dosimetry methods designed to gauge body retention of I-131(James, 2002).

Treatment with I-131 involves two primary approaches for determining the therapeutic activity. The first approach uses fixed activities, with the I-131 therapeutic activity set at either 30 mCi, 100 mCi, or 150 mCi. The decision on the specific activity to be administered is made by the managing physician or medical team based on the individual patient case.

The second method takes a more patient-specific and optimal route by determining the activity amounts through dosimetry. This method allows for the calculation of the highest activity that can be safely used to treat the patient, aiming to achieve maximum therapeutic outcomes without causing harm to the dose-limiting organs (Donika and Douglas 2020).

While the fixed-dose methods have demonstrated practical effectiveness in radioiodine therapy, it's crucial to understand that determining the dose using individual radiation dosimetry is theoretically considered superior. This approach aims to maximize treatment effects and minimize adverse events, making it a promising method for optimizing the therapeutic process (Chul and Chung, 2013).

IV. PARADIGM

Scientific International and local organizations in collaboration with field professionals have responded to these challenges by creating and sharing guidelines that establish a "standard" for using I-131 to treat persons with DTC(Goldsmith, 2017).

Doctors have traditionally determined the dosage based on their experiences, practices, and patient factors. The most widely used method, proposed by Beierwaltes(Taprogge, 2023) suggests that the treated activity should be between 5.55–6.2 GBq for regional nodes that cannot be surgically eliminated, 6.2–7.4 GBq for lung metastasis, and 7.4 GBq for bone metastasis (Pacilio, 2022).

For low-dose treatment, 131I administration is recommended at 1100 MBq, while high-dose treatment involves giving 2960–3700 MBq of I-131 (Taprogge et al, 2020).

The EANM Dosimetry Committee Series on Standard Operational Procedure (SOP) is an important resource that offers valuable advice on customizing the therapeutic activity for the systemic treatment of differentiated thyroid cancer (DTC) to ensure that the absorbed dose to the blood remains below 2 Gy, a widely accepted threshold for bone marrow toxicity.According to the MIRD guideline, a blood-absorbed dose of 2 Gy (200 rad) is considered the threshold to prevent myelotoxicity. Additionally, for thyroid remnants, a lesion-absorbed dose of 300 Gy is generally accepted, while for metastases, the threshold is 80 Gy (Georgiou et al., 2023).

Various reputable organizations such as the American Thyroid Association (ATA), European Thyroid Association (ETA), Society of Nuclear Medicine and Molecular Imaging/European Association of Nuclear Medicine (SNMMI/EANM), and National Comprehensive Cancer Network (NCCN), have accepted specific dosages for different stages of thyroid cancer treatment. For remnant ablation, these organizations have agreed upon a standard dose of 1.11

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GBq (30 mCi) of I-131. In adjuvant thyroid treatment, the prescribed dose ranges from 1.11 to 3.7 GBq (30-100 mCi) of I-131, with the upper limit being determined based on individual patient cases. In the context of metastatic treatment, the recognized maximum allowable dose stands at 3.7 GBq (100 mCi) of I-131. Furthermore, it has been acknowledged that in certain cases, a higher dose of up to 7.4 GBq (200 mCi) of I-131 may be used, contingent upon the designated characteristics and extent of the tumor (Taprogge et al, 2020).

It's crucial to understand the evolving techniques for treatment planning in the healthcare in particular and medical field in general. We need to prioritize the use of simplified methods for radioiodine dosimetry as we move forward into the era of integrating artificial intelligence into medical diagnoses and therapy (Donika and Douglas 2020**,** Ludwig et al, 2023).

V. DOSIMETRY APPROACHES

When it comes to dosimetry, different methods can be used, such as simplified, full whole-body, and lesional dosimetry (Donika and Douglas 2020). Dosimetry can be categorized as external or internal.

External Dosimetry: External dosimetry utilizes devices such as Ionizing Chambers, TLDs, Diode & MOSFET, Alanin Detectors, Plastic Scintillators, Diamond detectors, optically stimulated luminescence dosimeters (OSLDs), radio photoluminescent (RPL), and gel dosimetry systems(IAEA, 2024).

Internal Dosimetric Models: Internal dosimetry employs indirect methods and integrates physical and biological parameters such as Bioassay and Imaging measurement. Bioassay involves biological samples like Urine, Feces, Blood, and Breath, while imaging measurement can be acquired from a Gamma Camera, SPEC/PET, etc. Achieving patient-specific internal dosimetry with excellent precision presents a significant challenge in the field of nuclear medicine, indicating substantial changes in the methods for calculating accurate organ doses from ingested radioactivity (Oliver et al, 2024). Lyra M and P. Phinou identified three models for determining internal dosimetry, namely:

5.1 Anatomical and physiological models: This provides an explanation of the process of dose calculation using the Medical Internal Radiation Dosimetry (MIRD) formulation. The MIRD model utilizes a simplified method of the human body, categorizing organs as source organs, which have radiopharmaceutical, and target organs, for which the absorbed dose is to be estimated. It's important to note that an organ can function as both a source and a target. The process of estimating the dose involves four distinct stages.

Stage I: Involves the computation of accumulated activity, denoted as As. The total activity depends on how much of the administered activity (A) is absorbed by the source organ (F). We calculate the total activity at a specific time using a specific formula.

$$A_s(t) = A_0 F_s e^{-\lambda_e t} \quad (1)$$

Where

A_s denote the accumulated source activity at a given time (t)

A_0 denotes administered activity

F_s denotes the fraction of pharmaceutical which is the fraction of radiation accumulated in the organ

λ_e is the effective decay constant.

The physical half-life refers to the amount of time it takes for half of the radionuclide to undergo decay, whereas the biological half-life represents the duration required for half of the radionuclide to be eliminated from the body (Nalan et al., 2018).

WhereSpecifically, the physical half-life pertains to the half-life of the radionuclide itself, while the biological half-life corresponds to the timeframe necessary for half of the radionuclide to be excreted from the body.

$$\frac{1}{t_{\frac{1}{2}}(effective)} = \frac{1}{t_{\frac{1}{2}}(physical\ halflife)} + \frac{1}{t_{\frac{1}{2}}(biological\ halflife)} \quad (2)$$

$$\lambda_{effective} = \lambda_{physical} + \lambda_{biological} \quad (3)$$

Stage II. Determine the S-factor

The S-factor, or the specific absorbed fraction, is a parameter that quantifies the mean dose per unit of activity. It is denoted in Gy/Bq×s. While an estimation of the S-factor is possible, it is typically presented in tables as a function of the radionuclide, source organ, and target organ. Within the framework of the Medical Internal Radiation Dose (MIRD)

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methodology, the S-factors are computed using Monte Carlo simulation techniques. Specifically, a standard 70 kg adult male phantom is employed to represent the average adult male weighing 70 kg.

Stage III. Compute the dose to the target organ

The dose to the target organ can be estimated using the following

$$\underset{D}{\rightarrow} = A_s \times S \quad (4)$$

Stage IV. Here we formulatethe effective dose offered to the whole body, the effective dose may then be estimated from the following relation

$$E = \sum W_t D_t \quad (5)$$

Where W_t denotes the tissue weighting factor(IAEA, 2024, Nalan, et al, 2018).

5.2 Bio-distribution models: This process entails systematically gather urine and blood samples along with conducting organ and tumor radionuclide quantitation. To achieve this, it utilize a range of tools and technologies including probes, dosimeters like TLD (thermoluminescent dosimeter), optically stimulated luminescence (OSL) dosimeter, and self-reading dosimeters. These dosimeters provide real-time dose information, which is essential for precise monitoring. Additionally, it also employ SPEC (scintillation proximity assay) to further enhance our analysis and understanding of the data obtained.

5.2.1 Blood and Urine test: It is imperative to calibrate and characterize the counter across the entire theoretical spectrum of activity values with the use of gamma counter (ICRP, 2017). In cases where blood samples may potentially carry contributions from numerous radionuclides within a decay chain, it is essential to carefully consider the use of distinct energy channels or delayed measurements. These approaches aid in effectively differentiating and separating individual radionuclides by their respective half-lives (Stokke et al., 2024).

To ensure accuracy, it is important to measure the concentrations of plasma or serum independently. This is because certain compounds have the ability to bind to composition in the blood. For example, unbound lead may attach itself to the red blood cells. By identifying these segments, we can obtain vital data for determining the proper kinetics (Lubberink et al, 2020).Additionally, it is recommended to use blood or urine samples and chromatographic techniques to assess the metabolic stamina of the compounds. It is advisable to perform these evaluations at multiple time points, as the stability of the compounds can vary with time. This comprehensive assessment is particularly important when the estimated activity in fluid samples is used solely for dosimetric estimation and the stability of the compounds in vivo human is uncertain (Stokke et al, 2024; Lubberink et al, 2020; Gillings et al, 2020; ICRP, 2017).

5.2.2 Urine and fecal samples: To accurately measure the total amount excreted, there are multiple methods including urine or fecal collection, spot samples, and the use of diuresis measurements or weighing. The text discusses the retention of substances within the body over time for applications in pharmacokinetic modeling or specialized dosimetric models. It also highlights the importance of spot samples for radiation protection considerations and for verifying the accuracy of quantitative imaging techniques as explained by Stokke et al in 2024.

5.2.3 TLD: In vivo or phantom dosimetry relies on the use of Thermoluminescent Dosimeters (TLDs), which are characterized by their small size. This feature allows them to be comfortably adhered to the patient without hindering movement. Additionally, TLDs are unlikely to produce any interference with diagnostic imaging results. This is in contrast to ionization chambers, which are larger than TLDs and require a constant link to an electronic system (Juan, 2004). This makes it difficult to attach them to patients, limiting their movement and causing significant interference with radiography (Stokke et al, 2024). Other advantageous characteristics of TLDs for dosimetry purposes include exhibiting sensitivity and accuracy, as well as maintain stability under typical environmental conditions, including variations in temperature and humidity. Given the diverse types of radiation and varying dose levels involved in radio diagnosis and radiotherapy, TLDs must possess different characteristics to cater to the specific needs of each application. These dosimeters are essential for measuring dose levels in both diagnostic and therapeutic contexts. Dosimetry can take place directly on the patient or in a phantom(Juan, 2004). Direct dosimetry involves placing the dosimeters on the patient at specific sites of interest for the physician, either on the skin or internally. This provides real-time data on the dose received by the patient. Conversely, phantom dosimetry is employed when constrained with inserting the dosimeters into the patient. Here, the approach allows for the determination of dose distribution while simulating the patient using water-filled phantoms or tissue-equivalent substances such as wax or paraffin. This

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comprehensive method ensures that accurate and reliable data is gathered for effective diagnosis and treatment planning (Juan, 2004, Stokke et al, 2024).

Measurements in phantom are conducted to simulate the intervention for various persons by placing dosimeters at several depths corresponding to the required positions in the patient's body. This model is utilized for estimating depth dose percentages, necessitating the generation of equivalent dose curves within a phantom. Attaining the dose distribution in the patient entails employing numerous analytical expressions and conducting extensive calculations. As a result, automated methods for processing the acquired data are advantageous. "In vivo" dosimetry involves positioning dosimeters at points of interest on the body of a patient to estimate the entrance or exit dose, as well as to assess the effectiveness of protection at points distant from the radiation field, such as the gonads in young women suffering from breast cancer (Juan, 2004).

This information is invaluable as it can be used to adapt the treatment plan or ensure its quality. Intracavitary measurements, such as rectum dosimetry for intrauterine implants, are also critical. A misplaced implant can result in elevated rectum doses, potentially leading to rectitis(Pacilio et al, 2022, Juan, 2004).

5.3 Analytical model or Modeling of physical mechanisms related to internal absorbed dose

This technique is formulated to estimate the entire number of nuclear transformations transpiring of separate bodily (individual) tissues, organs, or regions within a designated timeframe (mostly 70 and 50 years for children and adults respectively) by considering individual elements and their respective radioisotopes (Gimenez-Alventosa et al, 2021). The computation involves ascertaining the time-integrated activity specific to each source region. Furthermore, Monte Carlo (MC) simulations are widely acknowledged for yielding exceptionally precise outcomes in dosimetry, thus serving as the benchmark for numerable use in medical physics. Adding the aforementioned information, dosimetric approaches, which rely on recognized computational phantoms and MC simulation and transport codes, are employed to compute dissipated energy in all vital organs and tissues for transformations transpiring in each source region. It is necessary to note that this computation accounts for the energies and results of all radiation (El Bakkali and Doudouh, 2023; Oliver et al, 2024).

The Monte Carlo (MC) simulation is a well-established model used to investigate the physics of particle interactions in the fields of nuclear medicine and radiation therapy. Studies revealed that there are several specific codes for dosimetry use that are generallyutilized in research and clinical settings. For instance, there is advanced software available for the Monte Carlo (MC) simulation using human phantoms(Syahir et al, 2019; Slimani, et al, 2018).

In the world of computational modeling, a plethora of software is utilized for the calculation of dosage. Among these are widely-used programs such as MIRDOSE3, MCNP, EGSnrc, OLINDA/EXM, SAAM II, SEECAL from Oak Ridge National Lab (ORNL), QDOSE, AIDE, DCAL, IMBA94, IDAC-Bio, GEANT4 Dose And Radiation Interactions (G4DARI), penRed, and Interdosi, to name a few (Gimenez-Alventosa et al, 2021, El Bakkali and Doudouh, 2023) [15, 25, 29, 30]. Furthermore, various organizations and individuals have developed specialized internal dose programs, including DOSAGE (D. Noüke, BfS code, private communication), PLEIADES (for the computation of ICRP dose coefficients), IDSS, AIDE, MONDAL, and the IDEA system. These programs implement ICRP internal dose models, biokinetic techniques, and reference S-coefficients for synchrony monitoring and internal dose measurements (Pacilio et al, 2022).

VI. RELATED WORKS

A multi-national and center clinical study using MIRD was conducted to estimate the absorbed doses received to functional organs in patients with DTC who were administered with I-131I. The study found that the estimated absorbed doses per unit activity for the salivary glands were 0.44, 0.14, 0.05, and 0.16 mGy/MBq for patients treated at centers A, B, C, and D. Additionally, the estimated whole-body doses were said to be 0.05 Gy and 0.16 Gy treated with activities of 1.1 and 3.7 GBq. The study also calculated the median whole-body absorbed doses per unit received activity to be 0.04, 0.05, 0.04, and 0.04 mGy/MBq at centers A, B, C, and D, respectively. The research observed a wide range of functional organ doses in patients with DTC treated with I-131, underscoring the need for personalized dosimetry (Taprogge et al, 2020, Pacilio et al, 2022).

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In a different study, researchers utilized the Nested parameterized volume, Regular navigation, and the Monte Carlo package (GATE) to extract a Golem voxelized phantom. This involved analyzing 220 clinical tomographic images of a 38-year-old patient with measurements similar to that of the ICRP standard man of 1.76m in height and 68.9 in weight. The simulations with GATE focused on photons ranging from 10 to 4,000 keV. The results revealed that the compressed voxels method was over 16 times faster than the rest of the models in terms of time consumption. The study concluded that the obtained results closely aligned with Zankl's findings for energy ≥ 300 keV, but showed relatively higher differences at lower energies. Consequently, the method was deemed suitable for internal dosimetry(Kaddoucha S and N. El Khayati (2020).

Ali et al conducted research and estimation of MIRD data for internal dosimetry utilizing the GATE Monte Carlo code. In their study, they compared outcomes from GATE/GEANT utilizing the Snyder phantom to published MIRD data. Results revealed that the activity was assumed to be evenly distributed within the named organs like kidneys, liver, lungs, pancreas, spleen, and adrenals. GATE/GEANT Monte Carlo code was utilized to estimate the dose to the organs of the phantom from photons of various energies that are mono-energetic.

The calculated dose was then transformed to a specific absorbed fraction (SAF), equally the results were correlated with the equally presented MIRD data. Averagely, similarity between the two sets of data was very significant. Nonetheless, GATE/GEANT data were less than MIRD data by an average of 0.16% for self-absorption, with a variation of ± 6.22%. The result also showed Self-absorption in the lungs to be reasonably higher in the MIRD data relative to GATE/GEANT data for photon energies between 10–20 keV. For the photon range of energies at 10–30 keV, the estimated difference was 7.5% with a variation of ± 67%. The similarity between the GATE/GEANT and the MIRD data was noted to depend largely on SAF-estimated figures and photon energy. In the case of 10–30 keV photons, where the calculated SAF values were less, the unknown was increased and the impact of the cross-section was pronounced, leading to no correlation with GATE/GEANT results and the MIRD data. Even at that, for photons of 50–1,000 keV, the bias was so low and the correlation was maintained (Ali et al, 2011).

In a research conducted by Szumowski et al, it was noted that the utilization of radioiodine in adjuvant therapy for thyroid cancer ranged between 30 mCi (1.1 GBq) and 150 mCi (5.5 GBq). Dosimetry using Marinelli's formula was employed with a constant activity of 3.7 GBq. The researchers calculated dose (D) from Marinelli's formula, with repeated dosimetry measurements (after 6, 24, and 72 hours) in view, performed during scintigraphy and following the application of the therapeutic radioiodine activity. They observed that 75% of the patients received doses exceeding 300 Gy (the allowable value). Only 16% of the patients obtained values falling between 250 and 300 Gy, while 9% of patients had a value of D less than 250 Gy(Szumowski et al, 2021).

A comparative investigation was undertaken to assess physical and biological dosimetry techniques in 47 patients who had undergone iodine-131 treatment. The patients were stratified into three sets based on varying activity doses. Whole-body absorbed doses were determined using the Medical Internal Radiation Dosimetry (MIRD) model with MIRDOSE3 software, as well as the cytokinesis-block micronucleus (MN) assay-based MN analysis, and subsequently compared. The results indicated a robust correlation ($r = 0.89$, $P < 0.001$) between the whole-body absorbed dose calculated via the MIRD method and the administered I-131 activity, whereas the correlation was found to be moderate ($r = 0.52$, $P < 0.01$) in the MN method. The absorbed dose calculated using the MIRD method was 49.2 ± 20.8 mGy in Set A, 6.5 ± 1.6 mGy in Set B, and 154.3 ± 47.8 mGy in St C, with statistically significant disparity ($P < 0.001$) observed. Meanwhile, the whole-body absorbed doses with MN method were 68.2 ± 17.5 mGy, 46.0 ± 11.4 mGy, and 90.5 ± 26.9 mGy in Set A, B, and C, and were found to have appreciable disparity between Set B and Set C ($P < 0.01$). In the entire study population, the mean absorbed dose was 74.6 ± 27.9 mGy with MN versus 68.0 ± 67.1 mGy with the MIRD method ($P = 0.087$), displaying moderate correlation ($r = 0.73$, $P < 0.001$). The whole-body absorbed doses calculated by the MN method exhibited a reasonable similarity with the treated radioiodine activities in cases of low radioiodine doses and demonstrated appreciable disparity and inconsistent values in comparisonwith MIRD model in patients administered with I-131 (Shahbazi and Nizad 2011,Özdal, et al, 2018).

Another comparative investigation was undertaken to juxtapose the data derived from MIRD with outcomes from GATE/GEANT utilizing the Snyder phantom. The investigation assumed a homogeneous distribution of activity within the kidneys, liver, lungs, pancreas, spleen, and adrenals. The MC code of GATE/GEANT was employed to compute the photon dose to the phantom's organs across a range of mono-energetic photons from 10 to 1000 kV. Subsequently, t a

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specific absorbed fraction (SAF) was obtained by transforming the dose, and the outcomes were cross-referenced against the equally established MIRD data. A robust similarity between the two datasets was observed. Nonetheless, the GATE/GEANT data exhibited an average -0.16 ± 6.22% deviation compared to the MIRD data for self-absorption. It transpired that the concordance between the GATE/GEANT and the MIRD data was contingent upon exclusive SAF values and the energy of the photon (Parach, 2011).

A study was carried out to outline a methodology for determining organ doses using the medical internal radiation dosimetry (MIRD) method. The study involved comparing the outcome of MIRD estimationand those obtained using the thermoluminescent dosimeter (TLD). Twenty-seven patients participated in the study, which utilized TLD for assessing the thyroid, sternum, and cervical vertebra. For each organ, five TLD measurements were taken at intervals of 4, 8, 12, 20, and 24 hours. To ascertain the iodine activity in the thyroid, a head and neck phantom containing a 10 mCi source of I-131 was employed. The absorbed dose in the cervical vertebra and sternum was computed using the MIRD formula.

The TLD estimation on the phantom for 10 mCi of iodine was determined to be 33.3 cGy. The estimated absorbed activities in the thyroid for administered I-131 doses of 100, 150, and 175 mCi were recorded as 94.9, 104.6, and 108.8 mCi cumulated activity within 24 hours. The absorbed doses gotten through MIRD estimation were 419.9, 463.2, and 481.5 for the thyroid, and 288.9, 252.4, and 252.4 for the sternum and cervical vertebra in that order. The findings of the MIRD method were consistent with those obtained through experimental means.

The study revealed that 75% of the absorbed dose estimated by the MIRD modelwas similar to the TLD model, ultimately validating the efficacy of MIRD calculations in determining the quantity of iodine absorbed in the thyroid (ShahbaziNikzad, 2011).

Daryoush and Saba utilized Monte Carlo simulation to quantify the absorbed doses of pivotal organs and subsequently compared the outcomes with alternative dosimetry methodologies like direct measurement and the MIRD model. They computed the absorbed doses of crucial organs, including the thyroid, sternum, and cervical vertebrae, utilizing MC and employing FNx01F8 tallies for iodine-131, which emits photon and beta particles. The absorbed doses derived from the MC simulations for 100, 150, and 175 mCifor treatment withI-131 were 388.0, 427.9, and 444.8 cGy for the thyroid, 208.7, 230.1, and 239.3 cGy for the sternum, and 272.1, 299.9, and 312.1 cGy for the cervical vertebrae. The comparison of the results from the MCsimulations with the outcomes yielded through direct dosimetry using thermoluminescentdosimeter(TLD)-100 and the MIRD model revealed no reasonable disparities (Daryoush and Saba Ayat, 2015).

In a recent investigation, the absorbed doses of vital organs were quantified using Monte Carlo N Particle (MCNP) simulation. The study involved a comparison of various dosimetry methods through the conduction of a t-paired test. The MCNP code employed the F8 tally to compute the absorbed doses of the thyroid, sternum, and cervical vertebra. These organs were simulated utilizing a neck phantom andMIRD technique. Following this, the study compared the outcome of MCNP, MIRD, and TLD data using SPSS software. The absorbed doses gotten from MC simulations for 100, 150, and 175 mCitreated with I-131 were determined to be 388.0, 427.9, and 444.8 cGy for the thyroid, 208.7, 230.1, and 239.3 cGy for the sternum, and 272.1, 299.9, and 312.1 cGy for the cervical vertebra. The outcome of the paired t-test yielded values of 0.24 while correlating with TLD dosimetry and MIRD estimation, 0.80 for MCNP simulation and MIRD, and 0.19 for TLD and MCNP. This investigation found not much disparities among the models, MC simulations, MIRD estimation, and dosimetry using TLD (Shahbazi and Ayat, 2012).

Another work was carried out to estimate the absorbed doses of vital organs using MC simulation and compared with alternative dosimetry techniques likethe MIRD model. A mathematical phantom was employed for this assessment. The absorbed doses determined by MC simulations for 100, 150, and 175 mCi were identified as 388.0, 427.9, and 444.8 cGy for the thyroid, 208.7, 230.1, and 239.3 cGy for the sternum, and 272.1, 299.9, and 312.1 cGy for the cervical vertebrae. The outcome from the MC simulation approach indicated no notable variance from the outcomes obtained through direct dosimetry utilizing TLD-100 and the MIRD technique(Shahbazi and Ayat, 2015).

A comparative research was conducted to estimate the received dose by comparing Geant4 MC simulation with the MIRD formalism. To validate the Geant4 simulations, the experimental technique was performed using TLDs placed in an ellipsoidal Thyroid phantom. The MIRD approach was employed to determine the beta doses absorbed by different patients. The analysis revealed an average difference of approximately 5.6% between the MIRD calculations and

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Geant4 simulations, with consideration given solely to beta emitted radiation. Notably, a high level of correlation was observed between the experimental results and Geant4 simulations. The dose received by patients ranged from 176Gy to 359Gy (Meftah et al., 2012).

In an investigation into the utilization of Artificial Intelligence (AI) to enhance and streamline radioactive iodine therapy (RAIT) dosimetry, a retrospective investigation was carried out on 83 patients with DTC who had RAIT dosimetry from 1996 to 2023 in a hospital. The traditional MIRD, RAIT dosimetry involved multiple imaging and blood sampling sessions over a 96-hour period following the administration of I-131 tracer was conducted.

To address this, a deep-learning neural network-based AI system was devised, aimed at predicting the maximum permissible activity (MPA) for RAIT utilizing data gathered solely through the initial 4, 24, and 48-hour intervals. Subsequent analysis revealed that the AI system's predictions closely aligned with the outcome gotten through traditional MIRD-based dosimetry, as evidenced by a non-significant difference when subjected to a paired t-test ($p = 0.351$, 95% CI).

The AI model holds promise in simplifying the dosimetry process by minimizing the need for imaging and blood sampling sessions, thereby optimizing resource allocation. Moreover, the AI technique has the potential to unveil latent data relationships. These findings underscore the potential of AI-based dosimetry for tailored treatment planning in cases of DTC, signifying a significant stride toward the realization of precision medicine for thyroid cancer (Georgiou et al, 2023).

VII. RISK

Despite diverse opinions and controversies concerning I-131 therapy in well-DTC, an increasing understanding of its benefits and risks is emerging. Recognizing these risks could significantly aid the treating physician and patient in making informed decisions about therapy. Noteworthy risks associated with it include:

7.1 Thyrotoxic crisis: After receiving I-131 therapy, some patients may develop thyroiditis, an inflammation of the thyroid gland. However, this condition is typically easy to manage. In cases of euthyroid multinodular goiter, the uptake of thyroid radioiodine and the effectiveness of I-131 treatment can be enhanced by administering recombinant human thyrotropin. This may lead to an excellent cure rate for Graves' disease. It is important to note that while radioiodine treatment can be effective for Graves' disease, it may occasionally worsen symptoms such as hyperthyroidism, Graves' ophthalmopathy, and airway obstruction stimulated by large nodular goiters. In such cases, alternative interventions, like the temporary utilization of anti-thyroid drugs, or surgery for nodular goiters,could be an option (ATSDR, 2008).

7.2 Radioiodine dose risk

It is crucial to recognize that the utilization of iodine in metabolism is intricately associated with the operational activity of the thyroid. The assessment of thyroid volume is imperative during therapy, given that the absorbed dose is inversely correlated with the magnitude of the volume under consideration (Piron, 2020). For instance, hypoparathyroidism (hypoPT) represents one of the predominant complications subsequent to bilateral thyroid procedures. Accordingly, thyroid therapy experts must implement methodologies to mitigate and avert post-thyroidectomy hypoPT (Lisa et al, 2017).

The systemic distribution of iodine to the thyroid varies between 20% to 75% (hypothyroidism or iodine-rich diets and hyperthyroidism or iodine-deficient diets respectively), for standard diets have an average of 30% to 50%. Complete resolution of hyperthyroidism through a single I-131 therapy is preferable but may not always be achievable. Factors such as the presence of a large goiter, severe hyperthyroidism, and prior propylthiouracil treatment may constitute intervention failure. The remainder is excreted through urine. In addition to radioiodine therapy, alternative sources of iodine possible examples encompass, yet are not restricted to, the subsequent instances:

7.2.1 Thyroid dose due to internal radiation: The assessment of radiation dose administered by I-131 radiation to the thyroid or the entire system necessitates the multiplication of the inhaled or ingested activity by age-adjusted dose conditions. The inhaled activity is determined by multiplying the mean air concentration of I-131, respiratory rate, and exposure duration.

7.2.2 Dose from food: The ingestion of activity is a result of the average concentrations of I-131 in food and water alike, along with the quantities of each consumed. One instance of internal contamination could occur in individuals

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who have consumed milk with similar I-131 concentrations. These concentrations are influenced by factors such as a) the time gap between production and consumption (e.g., expired products), b) the intake rate of fresh milk or other dairy products like cheese, c) the age and gender of the exposed class, d) the geographical allocation of the population in relation to conditions impacting thyroid dose, and e) the geographical format of air concentration and fallout allotment. The principal sources of I-131 in the environment have been releases from nuclear power plants, as well as nuclear weapons generation and testing.The primary sources of I-131are the Nevada test site and the Hanford Nuclear Reservation in the US as reported. Pre-exposure dietary intake of iodine is critical, as a relative iodine shortfall can aggravate the thyroid uptake of I-131 (FDA, 1998).

Following exposure, it is crucial to ascertain the quantity and compositions of consumed milk and its products, along with their respective I-131 concentrations and timing of consumption in relation to the release event. The concentration of I-131 in goat's and sheep's milk surpasses that of cow's milk by a factor of 10. Fresh milk directly consumed on the farm exhibits higher I-131 levels compared to milk that has undergone processing and distribution, owing to the decay of I-131 over time, recall that the half-life is about 8 hours. The variance in I-131 levels is attributable to its relative to the brief half-life (ATSDR, 2008, FDA, 1998). Although aged milk products like cheese generally harbor lower I-131 concentrations, it remains imperative to gauge both the quantity consumed and the respective I-131 concentrations. Other dose-related risks are prevalent in the following areas:

7.2.3 Thyroid Tumors: Exposure to I-131 radiation has the potential to impact the cells within the thyroid gland, causing conditions such as hypothyroidism, thyroiditis, benign or malignant thyroid tumors, and nodules. It's worth noting that the thyroid gland has one of the smallest cell proliferation rates among body tissues, and its regenerative capacity is also limited (Anderson et al, 2001).

For where there is no history of exposure to I-131, thyroid tumors are top prevalent types of endocrine neoplasms. They typically manifest as nodules located mostly within the thyroid gland and are often detectable upon checking the anterior neck. Exposure to I-131 raises the tendency of developing thyroid nodules and cancer, although the latter is uncommon. The average incidence rate of persistent thyroid cancer is estimated to be one in one million for children and ten in one million for adults with a ratio of 3 to 2 in Females-Male comparison. The heightened risk of thyroid cancer is particularly pertinent in cases of I-131 exposure in childhood. Additionally, the prevalence of thyroid nodules increases with advancing age(ATSDR, 2008).

Comparatively, thyroid cancer in children often presents at a greater advanced stage than in adults, characterized by higher distant metastases and greater lymph node participation. Exposure of the thyroid gland from minimal dose to greater doses (ranging from 6.5 to 2,000 centigray) of I-131 incrementally amplifies the risk of thyroid cancer (ATSDR, 2008, ATSDR, 2001, Anderson et al, 2001).

7.2.4 Reproductive and developmental consequences arising from therapeutic applications of I-131: I-131 has emerged as a recognized therapy for thyroid ablation in individuals with hyperthyroidism or thyroid cancer. Several incidences were recorded and a few incidence series have investigated potential dangerous reproductive impacts following medical I-131 use. However, the available information has been insufficient to definitively determine fetal exposure to I-131 radiation and its extent as well. Nonetheless, it has been suggested that it is wisdom to defer pregnancy for oneyearpost-radiation intervention, although the exact linkage between observed abnormalities and the therapy remains uncertain. It is also worthy of note that exposure of the thyroid to internal or external radiation may elicit an immune reaction, and post-I-131 therapy changes in thyroid autoimmunity have been owed to the generation and release of autoantigens due to radiation-induced destruction.

7.2.5 Acute exposure: Complex radiation thyroiditis may manifest within a fortnight following high levels of exposure to I-131, presenting with internal pain and tenderness over the thyroid gland. In some instances, a substantial release of reserved thyroid hormone can lead to noticeable systemic signs, necessitating intervention with anti-inflammatory and beta-adrenergic antagonist agents. It is highly unlikely for clinically significant acute radiation thyroiditis to occur at a dose of I-131 in the thyroid gland below 20,000 rad. Fetal exposure to radioactive iodine during pregnancy can result in lasting thyroid damage. Therefore, women of reproductive age must undergo a pregnancy test prior to receiving medical radioiodine therapy (Aderson et al, 2001).

7.2.6 Salivary gland cancer: Several studies have indicated that as many as 20% of thyroid cancer patients continue to experience xerostomy, even years after undergoing I-131 therapy. The abnormal functionality of the salivary glands is a

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significant concern. In a 6.6-year study of 176 thyroid cancer patients post-I-131 therapy, a significant rise in the risk of tooth extraction was observed, which correlated with the radiation dose and the presence of xerostomy (Walter et al, 2012). Additionally, there have been reports of salivary gland cancer developing after exposure to I-131 therapy (Bonnema and Hegedus, 2007).

7.3 Mortality associated: Taking a population-based survey encompassing 2668 persons of 40 years or older, who underwent treatment between 1984 and 2002, it was observed that I-131 therapy was correlated with heightened mortality, mainly attributable to cardiovascular conditions. Intriguingly, individuals receiving levothyroxine therapy for I-131-induced hypothyroidism did not exhibit an increase in mortality (Bonnema and Hegedus, 2012, Franklyn, 2005). Iodine-131 therapy is usually well tolerated, either it is utilized for a hyperthyroid disorder or meant for comparison with goiter. Nevertheless, dangerous effects may arise due to thyroid functionality, the size of the thyroid, an immunological reaction, and the repercussions of extrathyroidal irradiation (Bonnema and Hegedus, 2012).

7.4 Thyroid swelling: The administration of Iodine-131 therapy may induce symptoms such as pain in the thyroid and a perceived increase in thyroid size. These manifestations are most likely attributable to actinic thyroiditis, an inflammatory response stemming from radiation exposure. Typically, these symptoms subside spontaneously within a brief timeframe, often without necessitating medical intervention. The condition may also entail a transient and variable thyroid enlargement, which is generally without symptoms in the majority of patients (Bonnema and Hegedus, 2012). Other risk associates could be psychosocial risk, social ramifications, and challenges with informed consent (ATSDR, 2008, Anderson et al, 1996).

VIII. CHALLENGES

The following are some of the difficulties in dosimetry and therapeutic intervention.

8.1 Threshold absorbed dose:

Numerous researchers have undertaken the task of determining the minimum absorbed doses required to attain therapeutic efficacy. However, extensive evidence has conclusively shown that employing a fixed activity approach leads to a wide range of absorbed doses being delivered to both the target volumes and normal organs(Lyra M and P. Phinou, 2000). Although there is controversy surrounding the indications for I-131 therapy, the contraindications are laudably accepted in turn. Occasionally, I-131 intervention may produce an adverse effect on ophthalmopathy, but this can be mitigated through the use of steroids. The administration of thyrostatic intervention prior to I-131 therapy does not significantly alter the outcome, although propylthiouracil does exhibit some radioprotective effects (Sgouros et al, 1990).

8.2 Limited literature: Little or unavailable reports on radioiodine dosimetry, with frequent citations of the lack of evidence supporting dosimetry-guided I-131 activity over empiric activities as a primary reason for its underutilization (Mountford P, 1996).

8.3 Threshold to bone marrow: The quantification of bone marrow dosimetry is imperative in the context of radioimmuno therapy, as the bone marrow frequently acts as the organ that restrains the permissible radiation absorbed by a patient. Dissimilar to a lot of organs, the bone marrow lacks uniform composition or very clear boundaries and is disseminated across respective skeletal structures in the body, rendering estimation of the internally delivered dose exceedingly complex. Accurate determination of the cumulative activity within the bone marrow is also formidable (Lyra and Phinou, 2000, Sgouros et al, 1990).

8.4 Heterogeneous distribution of radionuclides: On the non-uniform distribution of radionuclides, the utilization of anatomical and physiological models, as well as the assumptions inherent in the MIRD schema, are employed. The MIRD approach aims to compute the mean absorbed dose, assuming uniform energy deposition in tissue and equitable allotment of the radiopharmaceutical. However, an assumption of uniform radionuclide distribution in an infinite, homogeneous, absorbing material is unfeasible. Consequently, precise estimation of this dose value is challenging, as it necessitates knowledge of an array of physical and biological quantities that are not definitively determined (Mountford P, 1996, Lyra and Phinou, 2000).

8.5 Bone marrow dosimetry: In the domain of bone marrow dosimetry, the estimation of the self-delivered dose remains a complex and intricate task due to the diverse cellular composition and the widespread distribution across the

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skeletal structures of the body. Further comprehensive investigations are warranted to address this challenging issue (Sgouros et al, 1990; Lyra and Phinou, 2000).

8.6 Use of analytical and experimental models: Utilizing analytical dose-point kernels presents a crucial concern as it often neglects the impact of tissue homogeneities, necessitating the application of convolution procedures in the spatial domain to mitigate these effects. Notably, inaccuracies in absorbed dose are prominent in lung and bone regions on account of variations in photon/electron by-sections and tissue scattering properties (Lyra and Phinou, 2000).

8.7 Uncertainties during dose estimation: The process of estimating mean absorbed doses for organs or tissues is riddled with uncertainties primarily stemming from inaccuracies in the S-value and cumulated activity calculations. These uncertainties can arise from discrepancies between planned and received doses as well as variations in organ sizes and activity distribution (Mountford P, 1996; Lyra M and P. Phinou, 2000).

8.8 Image errors: The principle of imaging entails inherent unknowns like resolution, septa penetration, evenness in detection response, time of death, and sensitivity of the used camera. Data processing introduces numerous errors, including counting statistics, organ/tumor region explanation, background deduction, attenuation, and scatter recoveries (Mountford P, 1996). The limited spatial resolution of the SPECT system restricts the application of quantitative SPECT images to minuet volumes, and numerical values are impacted by scatter conditions. Furthermore, reconstruction parameters, like attenuation recovery algorithms, can distort the relationship that exists between the counts in each pixel/voxel of the image taken and the radioactive concentration in the body (Mountford P, 1996, Sgouros et al, 1990, Lyra and Phinou, 2000).

IX. CONCLUSION

Thyroid cancer is a critical public health concern, with its rising prevalence necessitating a comprehensive understanding of its causes, diagnostic methods, and treatment strategies. Identifying key causes, and accurate diagnosis through advanced imaging techniques will significantly improve prognosis. Treatment involves surgery, thyroid hormone therapy, and radioactive iodine (Iodine-131) therapy. Dosimetry plays a pivotal role in optimizing Iodine-131 therapy by tailoring radiation doses to maximize therapeutic efficacy while minimizing risks. Challenges balancing therapeutic benefits against risks of radiation exposure to non-target tissues, patient isolation during treatment, and variability in individual responses. Addressing these challenges requires several measures from all sides is imperative. By focusing on these aspects, research can drive better prevention, diagnosis, and treatment strategies, ultimately improving patient outcomes and quality of life.

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