Radioiodine I-131 for Diagnosing and Treatment of Thyroid Diseases

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Abstract—**Iodine is essential for proper function of the thyroid gland, which uses it to make the thyroid hormones. The thyroid is equipped with an active system called "Na^+/I^- thyroid symporter pump" for moving iodine into its cells. Because the ability of thyroid cells to take up radioiodine I-131 or RAI exactly like iodine, it has been used by medical professionals to diagnose and treat various thyroid diseases. RAI that is not concentrated in the thyroid gland is eliminated from the body through sweat and urine. However, I -131 has unique beta and gamma emitting properties with a half-life of about eight days; the beta radiation can be used in high dose for destruction of thyroid nodules and for elimination of remaining thyroid tissue after surgery for the treatment of Grave's disease and differentiate thyroid cancer, and the gamma radiation allows for imaging and uptake measurement.**

Keywords : Iodine 131, Radioiodine therapy, thyroid scan, RAIU.

I. INTRODUCTION

Radioiodine I-131 as sodium iodide NaI, also called radioactive iodine or radioiodide is one of the first radioisotopes to be used in medicine. It is taken up and incorporated in an identical manner as nonradioactive iodine by the thyroid gland [1]. Therefore it has been used to evaluate and treat thyroid diseases for more than 60 years.

I-131 is an artificial isotope of iodine, and it is separated in the form of sodium iodide (NaI) from the products of uranium fission or neutron irradiation of tellurium-130 in a nuclear reactor. According to the Environmental Protection Agency, I-131 has a very short half-life of about eight days with beta and gamma radiation, which means that it decays almost completely in the environment within months.

On decaying, ^{131}I most often (89% of the time) expends its 971 KeV of decay energy by transforming into the stable ^{131}Xe (Xenon) in two steps, with gamma decay following rapidly after beta decay as shown in equations 1 and 2 :

$$ {}^{131}_{53}I \rightarrow {}^{131}_{54}Xe^* + \beta^- + \bar{\nu}_e + 606\,KeV \qquad (1)$$

$$ {}^{131}_{54}Xe^* \rightarrow {}^{131}_{54}Xe + \gamma - rays + 364\,keV \qquad (2)$$

The primary emissions of I-131 decay are thus beta particles with a maximal energy of 606 KeV with 89.6% abundance and 364 KeV gamma rays with 81.5% abundance as illustrated in figure 1. Beta decay, as always in this process, also produces an antineutrino, which carries off variable amounts of the beta decay energy.

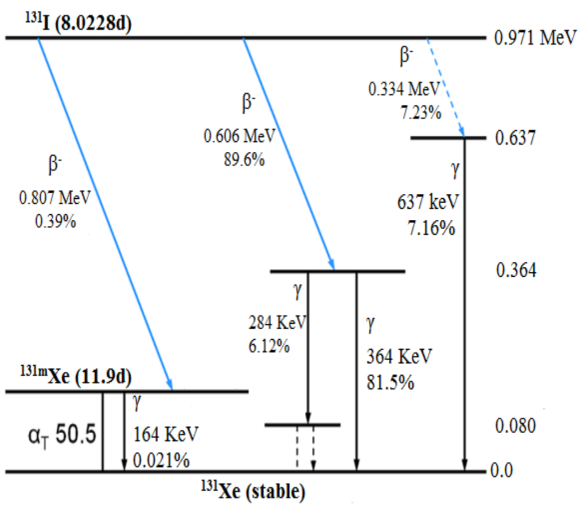

Figure 1. I-131 Decay Scheme.

In the I-131 decay scheme, the color blue indicates that the nucleus decays by β-emission. I-131 is characterized by the emission of several β-particles with different endpoint energies. A direct transition to the ground state of the daughter nuclide Xe-131 has not been observed. Transitions occur through the excited states of the daughter nuclide and with a very small (0.39%) probability through the metastable Xe-131m that has a half-life of 11.9 d. This metastable state has energy difference to ground state of 164 KeV, and the transition to the ground state is mostly due to conversion electrons. Further weak transitions are indicated by dots in the I-131 scheme.

When radioiodine is orally administered as the iodide ion, it is readily absorbed from the gastrointestinal tract and distributed in the extracellular fluid. It is concentrated in the salivary glands, thyroid, and gastric mucosa. RAI that is not concentrated in the thyroid gland and other organs is eliminated from the body through sweat and urine. However, iodide trapped and organified by the normal thyroid has an effective half-life of about 7 days; it decreases to 3–5 days in hyperthyroidism and is sometimes lower than 3 days in thyroid cancer.

II. DIAGNOSTIC USES OF I-131IN THYROID GLAND

I-131 is the isotope used to take pictures of the thyroid gland. A normal thyroid scan shows a small butterfly-shaped thyroid gland about 2 inch (5.1 cm) long and 2 inch (5.1 cm) wide with an even spread of radioactive tracer in the gland as shown in figure 2. On another hand an abnormal thyroid scan shows a thyroid gland that is smaller or larger than normal. It can also show areas in the thyroid gland where the activity is less than normal (cold nodules) or more than normal (hot nodules). Cold nodules may be related to thyroid cancer.

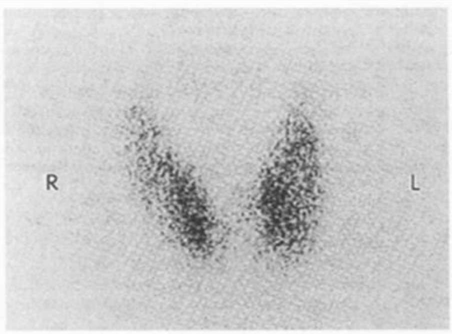

Figure 2. Normal thyroid image obtained with ^{131}I-iodide 24 hours after administration of the dosage showing uniform distribution of activity in both lobes.

Today the use of ^{131}I is limited to follow-up diagnostics in the case of thyroid differential cancer after thyroidectomy. This is because of it is unfavorable physical properties for scintigraphic imaging (i.e. physical half-life of 8.02 days, beta and gamma emissions, with high energy of 364 KeV, and high radiation dose "^{131}I emits approximately 1 rad/mCi to the thyroid gland") [2, 3, 4].

After thyroidectomy for thyroid carcinoma, radio-ablation with ^{131}I can be used to eradicate any remaining thyroid tissue within the thyroid bed or metastases to lymph nodes or distant sites. Whole body imaging has an important role in the post-operative management of the thyroid cancer patient.

A very small dose of I-131 is given to the patient, who then returns 24 to 72 hours (sometimes 7-10 days after a cancer therapy) later so pictures of the Whole Body Scan or WBS can be taken using a gamma camera that picks up the gamma radiation emitted by the RAI in the thyroid gland or in tumor cells. The photons emitted from the body enter the gamma camera and interact with the crystal to produce scintillations that are detected, amplified, and converted into light. Light converted to electrical signal and sent to a computer. The computer builds a picture by converting the differing intensities of radioactivity emitted into different shades of gray. Thyroid cancer cells such as papillary and follicular type retain the ability to accumulate iodine although to a much lesser extent than normal thyroid tissue. This property is used in the detection of local tumor recurrence as well as distant metastatic spread of thyroid cancer after surgery by administration of iodine and imaging the whole body. This is the reason that cancer nodules appear cold on routine thyroid scans.

In addition to getting the scan or picture, the amount of radiation being given off can also be counted to determine how active the thyroid gland is Radioactive Iodine Uptake, RAIU. Thyroid uptake test is based on the principle that the thyroid gland absorbs iodine from the blood and uses it to make certain hormones in the body. The average thyroid gland weighs around 20 grams, with each gram taking up a round 1 percent of the iodine available from diet [5]. Therefore, when the radioactive iodine is given, it is quickly taken up by the tissues of the thyroid gland. Cells which are most active in the thyroid tissue will take up more of the radioiodine. So, active parts of the tissue or hyperthyroidism cells will emit more gamma rays than less active or inactive parts. Likewise, thyroid cells that are not working well such as Thyroiditis usually take up less iodine, and so it will emit less gamma rays than other thyroid cells. However, the gamma rays which are emitted from inside the thyroid gland are detected by the gamma probe, and then they are converted into an electrical signal, and sent to a computer to count it, where the number of counts detected is proportional to the amount of radioactive iodine in the low neck.

To measure this, the patient swallows a small, oral dose, approximately 10 to 15 μCi (0.37–0.56 MBq) of sodium iodide in the form of capsule or fluid. At given time after administration (usually at 4 to 6 hours and 24 hours) a scintillation crystal of gamma probe is placed 25 cm from the patient neck's and the radioactivity at this point is counted for one minute as shown in figure 3. In order to eliminate those counts which did not come from the thyroid, the patient is recounted for one minute with a 1/2-inch-thick lead shield over the thyroid area. The difference of the two measurements is called the "net patient count." A standard dose, identical with that given to the patient, is counted in a neck phantom under the same conditions. A one-minute background count is also taken of the phantom, with the standard dose removed. The difference of these two counts is the "net standard count", and the method of counting the ^{131}I standard is the same for all patients [6,7]. The ratio of the net patient count to the net standard count times one hundred equals the percent iodine uptake as in Formula [5]:

$$\%\,\text{Thyroid Uptake} = \frac{\text{Net counts per min in Thyroid}}{\text{Net counts of Standard Dose per min} \times \text{decay correct}} \times 100\% \tag{3}$$

Decay correct in equation 3 is a method of adjusting the measurements of radioactive decay obtained at two different time points (i.e. the time elapsed between swallowing of iodine capsule and the uptake measure of the radiopharmaceutical) .However, the Decay correction factor is $\exp(-\lambda t)$, where "λ" is the decay constant of I-131, and "t" is the elapsed time (t = time of measurement of the net thyroid count per min - the net standard count per min time).

The percentage of radioiodine cumulated at specific times, such as 6 and 24 h, provides quantitation. This can be compared to the normal range in the community; for example, the normal 24-h uptake is and 7% to 20% for 6 hr and 7% to 20% for 6 hours 10% to 35% for 24 hours. However, two variables that determine the uptake are the function of the gland and the quantity of iodine in the diet [5,8,9].

Figure 3. RAIU. The detector of gamma probe is positioned 25cm from the patient's thyroid.

People who eat foods that are high iodine (iodized salt, dairy product, kelp, seafood, and so on), will have a lower RAIU. This is because, although their thyroid's ability to suck up iodine has not been altered, the nonradioactive dietary iodine dilutes out of portion of the radioactive iodine that goes into the thyroid gland, resulting in falsely in a lower RAIU. So these foods should be stopped at least 4 to 5 days before an RAIU test.

III. Radioiodine I-131 Therapy

I-131 emitted beta particles with an average energy of 192 KeV. When beta particles of I-131 are released inside thyroid cells, they travel an average of 0.8 millimeters [6] before their energy is completely absorbed by the thyroid deposit. They may collide with atoms of critical parts of the cells, imparting their energy to these atoms and killing the cells. This permits the I-131 treatment to specifically target thyroid abnormal cells without bothering other nearby body cells [5,9]. Therefore, radioiodine therapy (RIT) is an important option in the treatment of hyperthyroidism associated with Graves' disease, toxic thyroid adenoma, and toxic multinodular goiter or Plummer's disease. RIT is also used as adjuvant treatment after surgery for Well-differentiated thyroid carcinomas (DTC) such as papillary thyroid cancer (PTC), follicular thyroid cancer (FTC), and mixed tumors will concentrate radioiodine.

Although ^{131}I is a beta emitter, there is a predominant energetic gamma emission (364 KeV), which can be used to image the biodistribution. This gamma photon also can result in measurable absorbed radiation doses to persons near the patient. Because excretion is via the urinary tract, and, to a lesser extent, via saliva and sweat, special radiation protection precautions need to be taken for days after these patients are treated.

A. Heperthyrodisim Diseases

Physicians usually prefer to treat the hyperthyroidism patients with a dose of I-131 to render the patients hypothyroid, because calculation of a dose that would result in a euthyroid state is difficult, and it is easier to treat hypothyroidism than hyperthyroidism. Patients can go home after the RIT, although they are asked to follow some precautions. It is common for patients to experience some pain in the thyroid after RIT for hyperthyroidism. Aspirin, ibuprofen or acetaminophen can treat this pain, and they subsequently require thyroid hormone replacement for life. The RIT may take up to several months to have its effect.

B. Well-Differentiated Thyroid

Therapy for Well-differentiated Thyroid Cancer (DTC) starts with near-total thyroidectomy because the thyroid cancer does not concentrate iodine as well as normal thyroid tissue. A WDS is done to visualize the remaining functional thyroid tissue, and depending on the amount of residual thyroid tissue or tumor and the location and extent of disease, an appropriate dose of I-131 is administered. Scans are often obtained a few days after treatment to further evaluate the extent of disease. Follow-up another WBS are usually done 1 year after RIT to assess for residual or recurrent thyroid cancer after the patient has been off thyroid hormone replacement for 6 weeks (Figure 4).

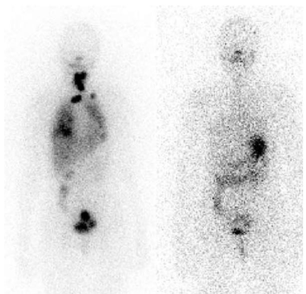

Figure 4. Whole-body scan of a 15-year old girl with metastatic DTC before (left) and after (right) effective radioiodine therapy.

If the patients are given a higher dose, they may be asked to stay isolated in a special room in the hospital for about 24 hours to avoid exposing other people to radiation, especially if there are small children living in the same home with them. The regulations that determine whether a patient needs to be isolated or can go home after the treatment are different in different states. Since the salivary glands weakly concentrate iodine, there may be pain and swelling of the salivary glands after high doses of RIT for WDC. This can be prevented or reduced by sucking on lemon drops after the therapy.

Different doses of I-131 are given for different thyroid disorders. Controversies still exist regarding the administered dosage of ^{131}I-sodium iodide in each of these conditions, e.g. there are three approaches dosimetric method to choosing a dose of I-131 for WDC therapy: a fixed dose method that administers empiric fixed amounts of I-131 for different tumor stages, quantitative tumor dosimetry that calculates the radiation delivered by I-131 to a tumor site, and a dosimetry-guided technique that calculates the upper limits of a safe blood and whole body level of irradiation from I-131. There has been no prospective randomized trial to determine which is better. Several analyses and studies have suggested that these approaches yield similar results [10-14].

IV. The Absorbed Dose from Radioactive Iodine I-131 within the Body

Because thyroid gland contains the radioiodine I-131, it becomes an emitting source ‘S’, which can also irradiate the neighboring tissues (defined as target regions ‘T’) such as lung and liver. Consequently, each body organ or tissue could receive a radiation dose after administration of radioiodine even if no activity is present in it. Therefore, RIT require patient-specific planning of the absorbed dose to the target volumes, in order to achieve an expected biological effect and benefits of their use, taking into account that the absorbed doses to normal organs and tissues should be kept as low as reasonably achievable (ALRA principle) [15,16]. So, the calculation of absorbed doses to the lungs and the dose to other organs has to be as accurate as possible.

For this purpose a group of physicists and biologists were formed a committee called the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine.

The total energy emitted by the thyroid organ is the product of Δ and the cumulated activity, $\tilde{A}$. However, only a fraction (Φ_i) of this energy is deposited in the target organ, which is the location of interest in the dose calculation. With these quantities and knowledge of the mass of the target organ (m), the mean absorbed dose $\overline{D}$ delivered to an organ in gray (Gy) is [17,18]:

$$\overline{D} = \tilde{A}\sum_i \Delta_i \Phi_i (T \leftarrow S) \qquad (4)$$

where $\sum\Delta_i \Phi_i (T\leftarrow S)$ is called the S value. Also known as the dose per cumulated activity, *S* has SI units of dose per decay or dose rate per activity (e.g., grays per Becquerel second). A value of S for radioiodine is published in MIRD Pamphlet no. 11.

V. Discussion and Conclusion

Despite being more than 70 years old, ^{131}I remains a major agent of choice for the treatment of thyroid diseases. It is still used to image thyroid cancer and quantify thyroid uptake measurements. Iodine I-131 has unique beta and gamma emitting properties; the beta radiation is used for therapy, and the gamma radiation allows for imaging and uptake measurement. But it is high radiation dose and unfavorable imaging characteristics. The introduction of newer radiotracers with lower radiation doses, such as radioiodine ^{123}I and pertechnetate ^{99m}Tc, has resulted in a decreasing role of ^{131}I in the imaging and uptake evaluation of thyroid disease. However, ^{131}I continues to play a major role in the imaging of patients with thyroid cancer after thyroidectomy and the treatment of hyperthyroidism and thyroid cancer.

When a radioactive iodine I-131 is given to a patient for either diagnosis or therapy, the nuclei end up in different organs; such as lung and liver, in varying amounts. Therefore, the calculation of absorbed doses to the lungs and the dose to other organs has to be as accurate as possible.

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