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Physiologic and False Positive Pathologic Uptakes on Radioiodine Whole Body Scan

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1. Introduction

A radioiodine whole body scan relies on the fact that differentiated thyroid cancer is more efficient at trapping circulating radioiodine than any other tissues.(Hyer, Newbold et al. 2010) Therefore, when I-131 is administered it accumulates in the thyroid cancer tissues and a radioiodine whole body scan plays an important role in the management of patients with differentiated thyroid cancer. Uptake of iodine by the cancer is related to the expression of sodium iodide symporter (NIS), which actively transports iodide into the cancer cells. Extrathyroidal tissues, such as stomach, salivary glands and breast, are known to have the NIS expression and the organs can physiologically take up iodine.(Riesco-Eizaguirre and Santisteban 2006)

On a whole body scan with diagnostic or therapeutic doses of I-131, except for the physiological radioiodine uptake in the salivary glands, stomach, gastrointestinal and urinary tracts, the lesions with radioiodine uptake can be considered as metastatic lesions in thyroid cancer patients who previously underwent total thyroidectomy.

However, a variety of unusual lesions may cause a false positive result on the radioiodine whole body scan and so careful evaluation of an abnormal scan is imperative to appropriately manage patients with differentiated thyroid cancer.(Mitchell, Pratt et al. 2000; Shapiro, Rufini et al. 2000; Carlisle, Lu et al. 2003; Ahn, Lee et al. 2011) The decision to administer radioiodine treatment is mainly based on the diagnostic scan, and misinterpretation of physiological or other causes of radioiodine uptake as metastatic thyroid cancer could lead to the decision to perform unnecessary surgical removal or to administer a high dose of I-131, which results in fruitless radiation exposure. Therefore, correct interpretation of the diagnostic scan is critical for the proper management.

Physiologic iodine uptake, pathologic iodine uptakes that are not related to thyroid cancer and contamination by physiologic excretion of tracer on the whole body scan are presented and discussed in this chapter. The purpose of this chapter is to make readers consider the possibility of physiologic or pathologic false positive uptake as a reason for the tracer uptake seen on the radioiodine whole body scan.

2. Iodine and the thyroid gland

Iodine is an element with a high atomic number 53, it is purple in colour and it is represented by the symbol I, and the iodine is an essential component of the hormones

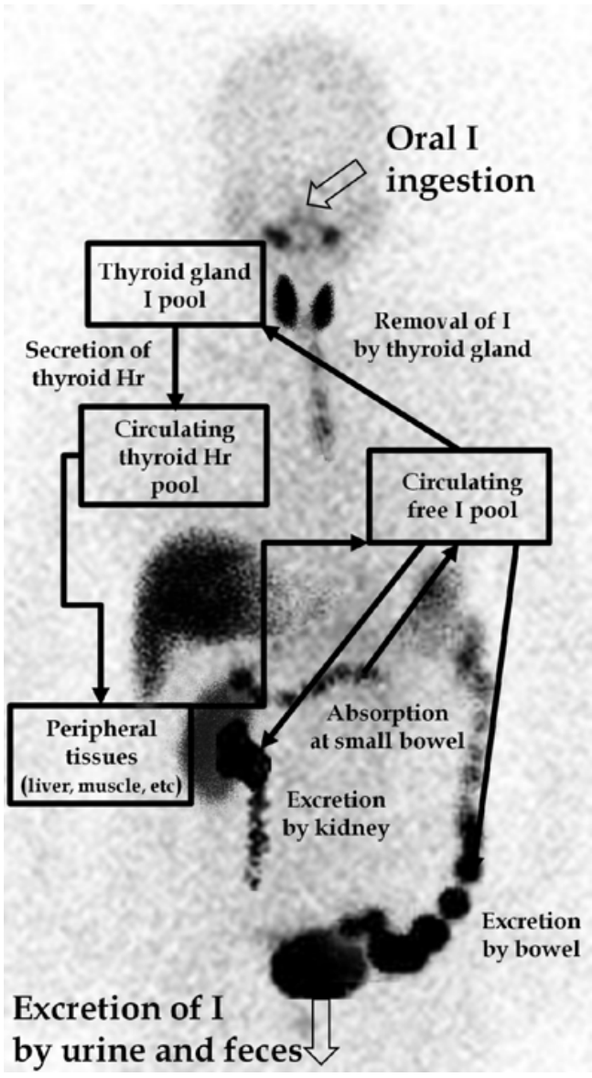


Fig. 1. Simplified diagram of the metabolic circuit of iodine. Iodine (I) ingested orally is absorbed from the small bowel into the circulating iodine pool. About one fifth of the iodine in the pool is removed by the thyroid gland and surplus iodine is rapidly excreted by the kidney and bowel. In the thyroid gland, iodine is used to produce thyroid hormones (Hr), which act in peripheral tissues. Iodine released from thyroid hormones re-enter into the circulating iodine pool.

produced by the thyroid gland. The thyroid hormones are essential for the health and well-being for mammals. Iodine comprises about 60% of the weights of thyroid hormones. The body of an adult contains 15~20mg of iodine, of which 70~80% is in the thyroid gland.(Ahad and Ganie 2010) To produce a normal quantity of thyroid hormone, about 50 mg of ingested iodine in the form of iodides are required each year. Oceans are the world's main repositories of iodine and very little iodine is found in the soil.(Ahad and Ganie 2010) The major dietary sources of iodine are bread and milk in the US and Europe, but the main source is seaweed in some Asian countries.(Zimmermann and Crill; Ahad and Ganie 2010; Hall 2011) Iodine is found in various forms in nature such as inorganic sodium or potassium

salts (sodium iodide or potassium iodide), inorganic diatomic iodine or organic monoatomic iodine. (Ahad and Ganie 2010) Iodide, represented by I^-, is the ion of iodine and it combines with another element or elements to form a compound. Although the iodine content of iodised salt may vary from country to country, common table salt has a small portion of sodium iodide to prevent iodine deficiency.(Hall 2011)

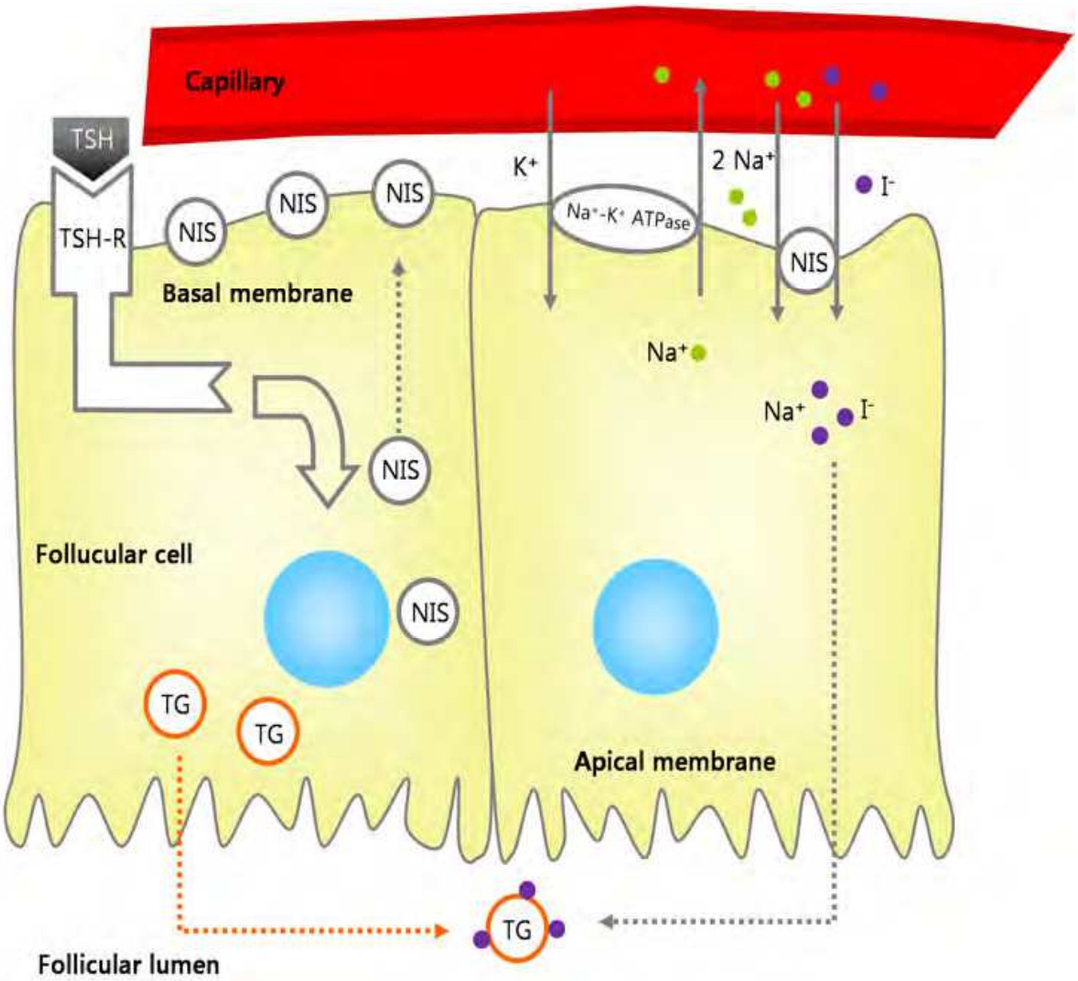


Fig. 2. Cellular mechanism for iodine uptake in thyroid follicular cells. This commences with the uptake of iodide from the capillary into the follicular cell of the thyroid gland. This process occurs against chemical and electrical gradients via the sodium iodide symporter (NIS) located in the basal membrane of the follicular cell. Increased intracellular sodium is pumped out by the action of Na^+/K^+ ATPase. The iodide within the follicular cell moves towards the apical membrane to enter into the follicular lumen and then it is oxidized to iodine by peroxidase. Organification of the iodine follows the oxidation by iodination of the tyrosine residues present within the thyroglobulin (TG) molecule, and the iodine stays in the follicle before it is released into the circulation as thyroid hormones. Thyroid stimulating hormone (TSH) activates the follicular cell via TSH receptor (TSH-R) and increases the expression of the NIS and the TG.

2.1 Iodine absorption and metabolism

Ingested iodides are rapidly and nearly completely absorbed (>90%) from the duodenum into the blood and most of the iodides are excreted by kidneys. Sodium iodide symporter (NIS) on the apical membrane of enterocytes mediates active iodide uptake. Normally about one fifth of absorbed iodides are taken up by thyroid follicular cells and this is used for thyroid hormone synthesis, yet the clearance of circulating iodide varies with iodine intake. In the condition of an adequate iodine supply, ≤10% of absorbed iodides are taken up by the thyroid and in chronic iodine deficiency, this fraction can exceed 80%.(Zimmermann and Crill) The basal membrane of the thyroid follicular cell is able to actively transport iodide to the interior of the cell against a concentration gradient by the action of the NIS, which co-transports one iodide ion along with two sodium ions. The process of concentrating iodide in the thyroid follicular cells is called iodide trapping and presence of the NIS is essential for the process.(Hall 2011) Thyroid hormones are produced by oxidation, organification and coupling processes in the thyroid gland and they are finally released into the blood stream for their action.

2.2 Sodium iodide symporter

The rat NIS gene and the human NIS gene were cloned in 1996.(Dai, Levy et al. 1996; Smanik, Liu et al. 1996) NIS is a 13 transmembrane domain protein with an extracellular amino- and intracellular carboxyl-terminus and the expression of the NIS gene is mainly regulated by thyroid stimulating hormone (TSH). Binding of TSH to its receptor activates the NIS gene transcription and controls translocation and retention of NIS at the plasma membrane, and so this increases iodide uptake.

In addition to its expression in the thyroid follicular cells, NIS is detectable and active in some extrathyroidal tissues such as the salivary glands, gastric mucosa, lactating mammary glands, etc. Therefore, these tissues are able to take up iodide by the action of the NIS. However, contrary to thyroid follicular cells, there are no long-term retention of iodide and TSH dependency. (Baril, Martin-Duque et al. 2010) The physiologic function of the NIS in the extrathyroidal tissues is not yet clear.

3. Procedures for radioiodine whole body imaging

3.1 Patients preparation

Thyroid hormone replacement must be withheld for a sufficient time to permit an adequate rise of TSH (>30 uIU/mL). This is at least 2 weeks for triiodothyronine (T3) and 3–4 weeks for thyroxine (T4). This is also achieved by the administration of recombinant human TSH (rhTSH, Thyrogen®, given as two injections of 0.9 mg intramuscularly on each of two consecutive days) without stopping thyroid hormone replacement. rhTSH must be used in patients who may not have an elevation of TSH to the adequate level due to a large residual volume of functioning thyroid tissue or pituitary abnormalities, which precludes elevation of TSH. rhTSH might be used to prevent severe hypothyroidism related to the stopping of thyroid hormone replacement.(Silberstein, Alavi et al. 2005; Silberstein, Alavi et al. 2006)

All patients must discontinue eating/using iodide-containing foods or preparations, and other medications that could potentially affect the ability of thyroid cancer tissue to accumulate iodide for a sufficient time before radioiodine administration. A low-iodine diet is followed for 7–14 days before the radioiodine is given, as it significantly increases the uptake of radioiodine by the well differentiated thyroid cancer tissue. The avoided or permitted food items are summarized in table 1. The recommended time interval of drug withdrawal is summarized in

table 2. Imaging should be delayed for a long enough period to eliminate the effects of these interfering factors. The goal of a low iodine diet and the drug withdrawal is to make a 24-hour urine iodine output of about 50 ug.(Silberstein, Alavi et al. 2006).

	Allowed	Not-allowed
Salts	Non -iodized salt	Iodized salt Sea salt
Fruits and vegetables	Fresh fruits and juices	Rhubarb Fruit or juice with red dye # 3 Canned or preserved
Seafood and sea products	None	Fish Shellfishs Seaweeds Seaweed tableets Agar-agar
Dairy products	None	Milk Cheese Yogurt Butter Ice cream Chocholate (has milk content)
Paultries and Meats	Fresh unsalted	Canned and processed
Egg	Whites of eggs	Egg yolks Whole eggs
Grain products	breads, cereal and crackers without salt unsalted pasta, rice, rice cakes, and popcorn	Breads, cereals or crackers made with salt Salted pasta, rice or popcorn
drinks	Cola, diet cola, lemonade Coffee or tea without milk or cream Fruit juice without red dye#3 Fruit smoothies made without dairy or soy products Beer, wine and spirits	Milk, cream or drinks made with dairy Fruit juice and soft drinks with red dye#3

Table 1. Food guide for a low iodine diet. Some items on the allowed list may not be low in iodine in some forms or merchandise brands. The labels must be checked to be sure that the items meet the requirements of the low-iodine diet. (Amin, Junco et al.; Nostrand, Bloom et al. 2004)

3.2 Types of radioiodine

3.2.1 I-131

I-131 is produced in a nuclear reactor by neutron bombardment of natural tellurium (Te-127) and decays by beta emission with a half-life of 8.02 days to xenon-133 (Xe-133) and it emits gamma emission as well. It most often (89% of the time) expends its 971 keV of decay energy

by transforming into the stable Xe-131 in two steps, with gamma decay following rapidly after beta decay. The primary emissions of I-131 decay are beta particles with a maximal energy of 606 keV (89% abundance, others 248–807 keV) and 364 keV gamma rays (81% abundance, others 723 keV).
I-131 is administered orally with activities of 1–5 mCi or less, with many preferring a range of 1–2 mCi because of the data suggesting that stunning (decreased uptake of the therapy dose of I-131 by the residual functioning thyroid tissue or tumour due to cell death or dysfunction caused by the activity administered for diagnostic imaging) is less likely at the lower activity range. However, detection of more iodine concentrating tissue has been reported with higher dosages.(Silberstein, Alavi et al. 2006)

Type of medication	Recommended time interval of withdrawal
Natural synthetic thyroid hormone Thyroxine (T4) Triiodothyroinine (T3)	 3 to 4 weeks 10 to 14 days
Amiodarone	3 to 6 months
Multivitamine	6 weeks
Lugol's solution, potassium iodide solution (SSKI)	6 weeks
Topical iodine	6 weeks
Radiographic contrast agents	3 to 6 months, depending on iodide content
Iodinated eyedrops and antiseptics	6 weeks
Iodine containing expectorants and anti-tussives	2 to 4 weeks

Table 2. Recommended time intervals of withdrawal for drugs affecting radioiodine uptake. The time interval can be changed by the administered doses of the medications. The amount of iodine for the drug must also be considered.(Nostrand, Bloom et al. 2004; Silberstein, Alavi et al. 2005; Luster, Clarke et al. 2008)

3.2.2 I-123

I-123 is produced in a cyclotron by proton irradiation of enriched Xe-124 in a capsule and I-123 decays by electron capture with a half-life of 13.22 hours to Te-123 and it emits gamma radiation with predominant energies of 159 keV (the gamma ray primarily used for imaging) and 127 keV.
I-123 is mainly a gamma emitter with a high counting rate compared with I-131, and I-123 provides a higher lesion-to-background signal, thereby improving the sensitivity and imaging quality. Moreover, with the same administered activity, I-123 delivers an absorbed radiation dose that is approximately one-fifth that of I-131 to the thyroid tissue, thereby lessening the likelihood of stunning from imaging. I-123 is administered orally with activities of 0.4–5.0 mCi, which may avoid stunning.(Ma, Kuang et al. 2005; Silberstein, Alavi et al. 2006)

3.2.3 I-124

I-124 is a proton-rich isotope of iodine produced in a cyclotron by numerous nuclear reactions and it decays to Te-124 with a half-life of 4.18 days. Its modes of decay are: 74.4%

electron capture and 25.6% positron emission. It emits gamma radiation with energies of 511 and 602 keV.(Rault, Vandenberghe et al. 2007)
I-124 is administered intravenously with activities of 0.5–2.0 mCi for detection of metastatic lesions or assessment of the radiation dose related to I-131 therapy.

Types	Advantages	Disadvantages
I-131	• Cheap • Readily available • Allows longer delayed image	• Potential stunning • Requirement of possible radiation safety precautions for family and caregivers
I-123	• No stunning • Good image quality	• Limited availablity • Expensive
I-124	• Superior image quality • Tomographic image • Allows intermediate delayed image • Fusion image with CT or MR	• Very limited availability • Very expensive

Table 3. Advantages and disadvantages according to the types of radioiodine.(Nostrand, Bloom et al. 2004)

3.3 Planar, SPECT and PET imaging

3.3.1 Planar imaging

Planar gamma camera imaging can be obtained with gamma emitting I-123 or I-131 for the detection of thyroid cancer tissue expressing the NIS gene which takes up iodine. The main emission energy peak of I-131 is approximately 364 keV, so it requires the use of a high-energy all-purpose collimator for imaging acquisition. The peak of the I-123 is 159 keV, which is close to the 140 keV from Tc-99m for which the gamma camera's design has traditionally been optimized. I-123 can be imaged with a low-energy high-resolution collimator, which is optimized for image acquisition with Tc-99m. (Rault, Vandenberghe et al. 2007)
With radioiodine's avidity for differentiated thyroid cancer tissues, planar radioiodine whole body image has been mainly used for the detection of metastatic thyroid cancer lesions. However, the limited resolution of planar imaging together with the background activity in the radioiodine images can give false-negative results for small lesions. Physiologic uptake of radioiodine is not always easily differentiable from pathologic uptake and it can give false-positive results. (Spanu, Solinas et al. 2009) Therefore, the sensitivity and specificity of planar images for the diagnosis of metastatic thyroid cancer may be limited. (Oh, Byun et al. 2011)

3.3.2 SPECT (Single Photon Emission Computed Tomography) or SPECT/CT imaging

Although a radioiodine whole body scan is one of the excellent imaging tools for the detection of thyroid cancer, false negative results may be observed in cases with small recurrent lesions in an area of rather high background activity or in cases with poorly differentiated cancer tissues, which have low uptake ability for radioiodine (due to dedifferentiation).(Geerlings, van Zuijlen et al.) SPECT, which can provide cross-sectional scintigraphic images, has been proposed as a way to overcome the limitations of planar

imaging and it is known to have higher sensitivity and better contrast resolution than planar imaging. Radioiodine SPECT has higher performance for detecting recurrent lesion compared to planar imaging in thyroidectomized thyroid cancer patients and it also changes the patients' management.

Radioiodine SPECT has excellent capability to detect thyroid cancer tissues, yet the anatomic evaluation of lesion sites with radioiodine uptake remains difficult due to the minimal background uptake of the radioiodine. The performance of SPECT with radioiodine may be further improved by fusing the SPECT and CT images or by using an integrated SPECT/CT system that permits simultaneous anatomic mapping and functional imaging.(Geerlings, van Zuijlen et al.; Spanu, Solinas et al. 2009) The fusion imaging modality can synergistically and significantly improve the diagnostic process and its outcome when compared to a single diagnostic technique. (Von Schulthess and Hany 2008) Therefore, SPECT/CT with radioiodine can demonstrate a higher number of radioiodine uptake lesions, and it can more correctly differentiate between physiologic and pathologic uptakes, and so it permits a more appropriate therapeutic approach to be chosen.(Spanu, Solinas et al. 2009) Despite its many advantages, SPECT/CT cannot be applied for routine use or whole body imaging due to the long scanning time and the additional radiation burden, and so the fusion image should be selected on a personalized basis for those who clinically need the imaging. (Oh, Byun et al. 2011)

3.3.3 PET (Positron Emission Tomography) or PET/CT imaging

PET detects a pair of gamma rays produced by annihilation of a positron which is introduced by a positron emitting radionuclide and this produces three-dimensional image. Owing to its electronic collimation, I-124 PET gives better efficiency and resolution than in I-123 or I-131 SPECT, and so it offers the best image quality. (Rault, Vandenberghe et al. 2007)

A fusion imaging modality with I-124 PET and CT can improve the diagnostic efficacy when compared to I-124 PET imaging by the same reasons of SPECT/CT over SEPCT only. I-124 PET/CT has superiority due to the better spatial resolution and faster imaging speed compared to I-123 or I-131 SPECT/CT.(Van Nostrand, Moreau et al. 2010) PET fused with MR is recently being used for research and in clinic fields and it will allow state of art imaging in the near future.

4. Physiologic radioiodine uptake

Following thyroid ablation, physiologic activity is expected in the salivary glands, stomach, breast, oropharynx, nasopharynx, oesophagus, gastrointestinal tract and genitourinary tract.(Ozguven, Ilgan et al. 2004) Physiologic radioiodine accumulation is related to the expression of the NIS and metabolism related to or the retention of excreted iodine. (Bakheet, Hammami et al. 2000; Ahn, Lee et al. 2011) Uptake of radioiodine in the thyroid tissue, salivary gland, stomach, lacrimal sac, nasolacrimal duct and choroid plexus is related to the NIS expression of the cells of the organs.(Morgenstern, Vadysirisack et al. 2005) Ectopic thyroid tissues are found by a variety of embryological maldevelopments of the thyroid gland such as lingual or sublingual thyroid (by failure of migration), a thyroglossal duct (by functioning thyroid tissue in the migration route) and a mediastinal thyroid gland (by excessive migration). Other abnormal migration may produce widely divergent ectopic thyroid tissue in many organs such as liver, oesophagus, trachea, etc. In addition, normal thyroid tissue can be in the ovary (Struma ovarii. It can be classified as uptake in a pathologic lesion.). (Shapiro, Rufini et al. 2000) Ectopic gastric mucosa can be located in the small bowel (Meckel's

diverticulum) or terminal oesophagus (Barrett's oesophagus). (Ma, Kuang et al. 2005) The ectopic thyroid and gastric mucosal tissues are able to take up radioiodine.

Uptake of iodine in the liver after radioiodine administration is related to the metabolism of radioiodinated thyroglobulin and thyroid hormones in the organ. The gall bladder also may occasionally be depicted with the biliary excretion of the radioiodine. (Shapiro, Rufini et al. 2000; Carlisle, Lu et al. 2003) A simultaneous hepatobiliary scan with Tc-99m DISIDA (Diisopropyl Iminodiacetic Acid) or mebrofenin is useful for characterizing the gall bladder uptake. Tracer accumulation in the oropharynx, nasopharynx and oesophagus is related to retention of salivary excretion of administered radioiodine.

Visualization of the oesophagus is extremely common and vertical linear uptake in the thorax that is removed by drinking water is characteristic of oesophageal uptake by swallowing of radioactive saliva. The oesophageal activity may also arise from gastric reflux. (Carlisle, Lu et al. 2003) Image acquisition after a drink of water is able to distinguish the activity from mediastinal node metastasis. (Shapiro, Rufini et al. 2000)

Urinary or gastrointestinal anomalies can be responsible for false positive radioiodine uptake. (Ma, Kuang et al. 2005) Visualization of kidney and bladder after radioiodine administration is possible and this is known to be related to the urinary excretion of radioiodine into the urinary collecting system. Administered radioiodine is excreted mainly by the urinary system, and so all dilations, diverticuli and fistulae of the kidney, ureter and bladder may produce radioiodine retention.(Shapiro, Rufini et al. 2000) Visualizing the location of the renal pelvis of ectopic, horseshoe and transplanted kidneys is not usual and radioiodine at the pelvis may lead to misinterpretation. In fact, the renal pelvis and ureter are usually not visualized due to the rapid transit time of the radioiodine. (Bakheet, Hammami et al. 1996) A simultaneous renal scan with Tc-99m DTPA (Diethylene Triamine Pentaacetic Acid) or MAG3 (Mercapto Acetyl Triglycine) is useful for characterizing the urinary tract uptakes. (Shapiro, Rufini et al. 2000) Although the incidence is very uncommon, renal cysts are known to produce radioiodine uptake. The proposed mechanisms for the renal cyst uptake are a communication between the cyst and the urinary tract and radioiodine secretion by the lining epithelium of the cyst. (Shapiro, Rufini et al. 2000)

Tracer accumulation in the colon is very common. Incomplete absorption of the oral radioiodine administration is not considered as the reason of colonic activity due to the lack of colonic activity seen on the early images. Tracer accumulation is probably due to transport of radioiodine into the intestine from the mesenteric circulation and biliary excretion of the metabolites of radioiodinated thyroglobulin. (Hays 1993) Appropriate use of laxatives can be a simple remedy for the activity. (Shapiro, Rufini et al. 2000)

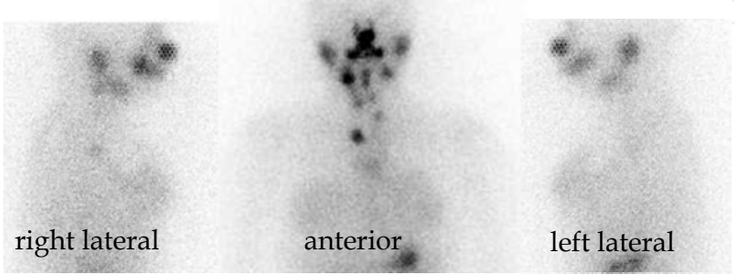


Fig. 3. Physiologic uptake of radioiodine in the nasal cavity, the so called "hot nose". Intense tracer uptake was noted at the thyroid bed area (due to residual thyroid tissue), breast and salivary gland (by the NIS expression of the glands).

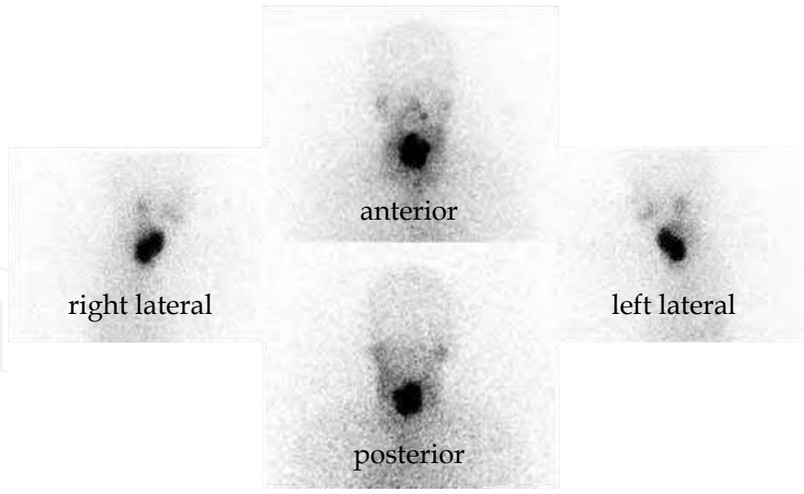


Fig. 4. Physiologic uptake of radioiodine in residual thyroid tissue. Intense tracer uptake was noted at the thyroid bed area due to residual thyroid tissue.

Lactating mammary glands express the NIS, and so the lactating breast shows intense radioiodine uptake that might persist for months after cessation of lactation. Mild to moderate uptake is also seen in non-lactating breast tissue, which can be asymmetrical, presumably owing to the same mechanism that operates in lactation.(Shapiro, Rufini et al. 2000; Tazebay, Wapnir et al. 2000)

Uptake of radioiodine can occur in a residual normal thymus or in thymic hyperplasia and the suggested mechanisms for the uptake are the expression of the NIS in thymic tissues and the iodine concentration by the Hassal's bodies that are present in the thymic tissue, which resemble the follicular cells of the thyroid. Thymic radioiodine uptake is more common in young patients compared to older patients. Even though the incidence is very rare, an intrathymic ectopic thyroid tissue or thyroid cancer metastases to the thymus can be a possible cause of uptake. (Mello, Flamini et al. 2009)

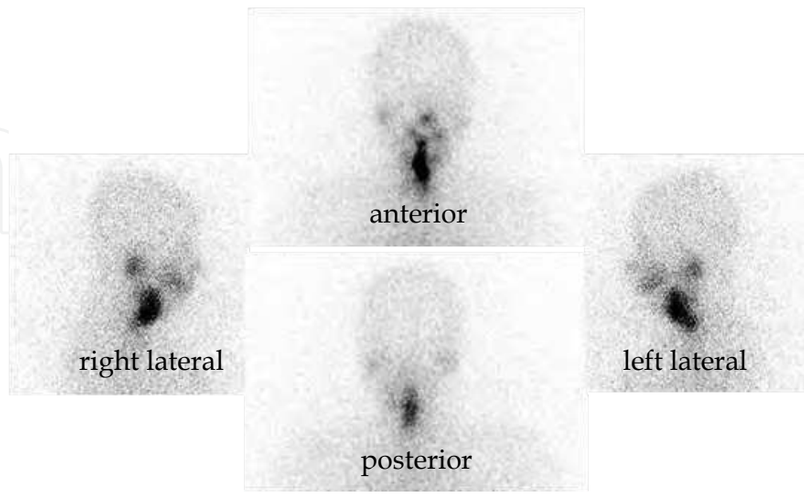


Fig. 5. Physiologic uptake of radioiodine in residual thyroid tissue. Intense tracer uptake was noted at the midline of the upper neck due to residual thyroid tissue in the thyroglossal duct. Mild tracer uptake of the salivary gland (by the NIS expression of the glands) was also noted.

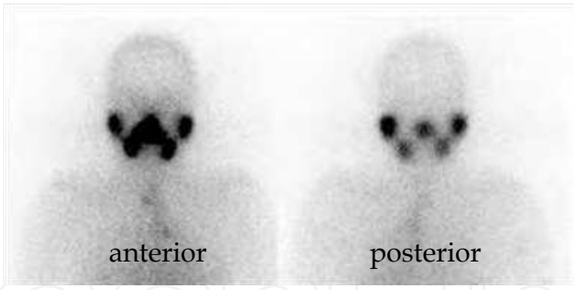


Fig. 6. Physiologic uptake of radioiodine in both the parotid and submandibular salivary glands. Intense activity in the oral and nasal cavities (by saliva and nasal secretion) was also noted.

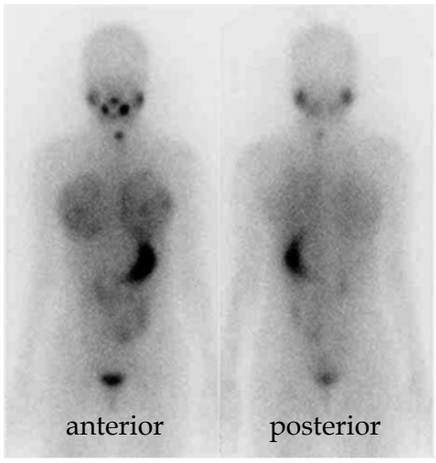


Fig. 7. Physiologic uptake of radioiodine in the breast. Diffuse, moderate radioactivity in the breast was noted. There was also noted physiologic tracer uptake in the thyroid bed (suggesting remnant thyroid tissue, which has the NIS expression), salivary glands (by the NIS expression of the glands), stomach (by the NIS expression of the glands), bowel (by secretion of radioiodine into the intestine or biliary excretion of the metabolites of radioiodinated proteins) and urinary bladder (by urine activity).

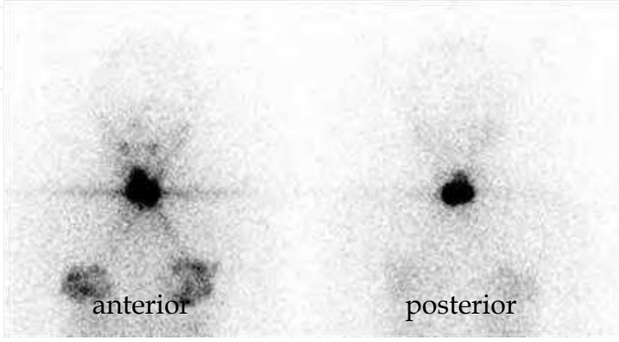


Fig. 8. Physiologic uptake of radioiodine in the breast. Intense tracer accumulation was noted in both breasts. Physiologic tracer uptake was also noted in the thyroid bed (suggesting remnant thyroid tissue, which has the NIS expression).

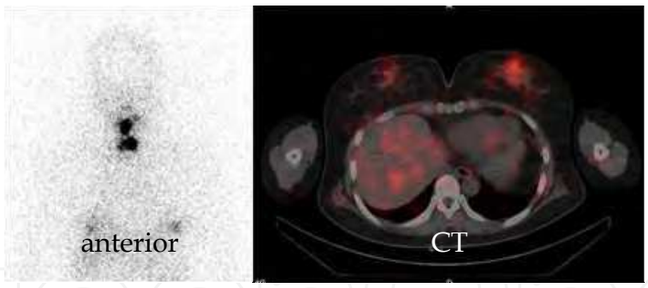


Fig. 9. Physiologic uptake of radioiodine in the breast. Focal tracer uptake in the breast was noted. SPECT/CT revealed the accurate location of the breast uptake. Physiologic intense tracer uptake was noted in the thyroid bed (suggesting remnant thyroid tissue, which has the NIS expression) and mild tracer uptake in the liver (by metabolism of radioiodinated thyroglobulin and thyroid hormones).

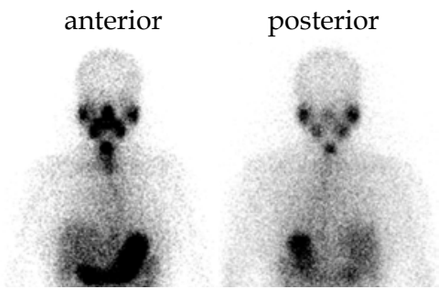


Fig. 10. Physiologic uptake of radioiodine in the oesophagus. Vertical linear radioactivity in the chest was noted by stagnation of swallowed saliva containing radioiodine. There was also noted physiologic tracer uptake in the thyroid bed area (by residual thyroid tissue) and salivary glands (by the NIS expression of the glands).

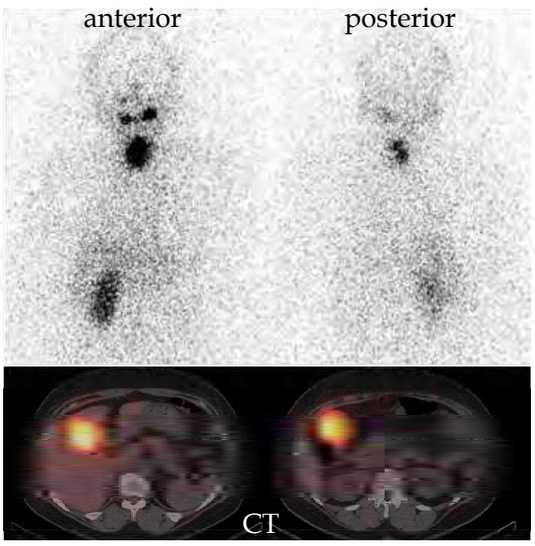


Fig. 11. Physiologic uptake of radioiodine in the gall bladder. Intense tracer accumulation was noted at the GB fossa area on the whole body scan and SPECT/CT revealed accurate localization of the uptake. There was also noted physiologic tracer uptake in the thyroid bed area by residual thyroid tissue.

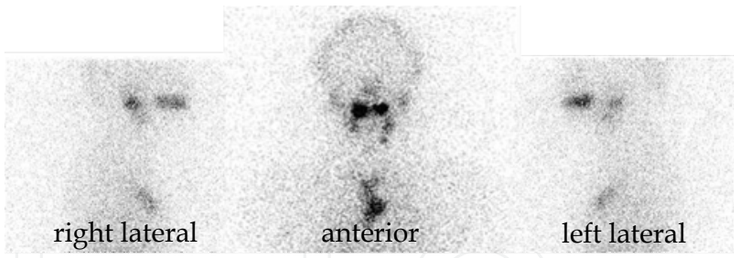


Fig. 12. Physiologic uptake of radioiodine in the thymus. Diffuse, mild radioactivity in the mid-thorax was noted. There was also noted physiologic tracer uptake in the salivary glands (by the NIS expression of the glands) and oral cavity (by saliva containing radioiodine).

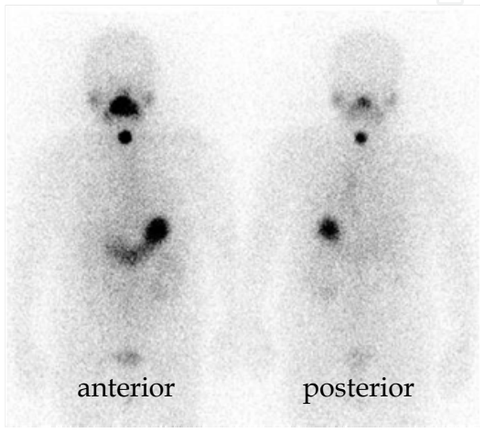


Fig. 13. Physiologic uptake of radioiodine in the stomach. Intense tracer uptake was noted at the left upper quadrant of abdomen due to stomach uptake of the tracer. There was also noted tracer uptake in the oral cavity (radioactivity of secreted saliva), salivary gland (by the NIS expression of the glands), thyroid bed (suggesting remnant thyroid tissue, which has the NIS expression) and urinary bladder (by urine activity).

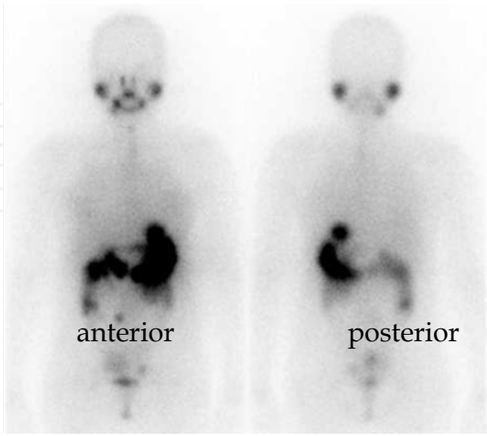


Fig. 14. Focal radioiodine uptake was noted at the center of the abdomen. The uptake might be related to ectopic gastric mucosa in the Meckel's diverticulum. There was also noted tracer uptake in the stomach (by the NIS expression of the gastric mucosa), oral cavity (radioactivity of the secreted saliva) and salivary gland (by the NIS expression of the glands).

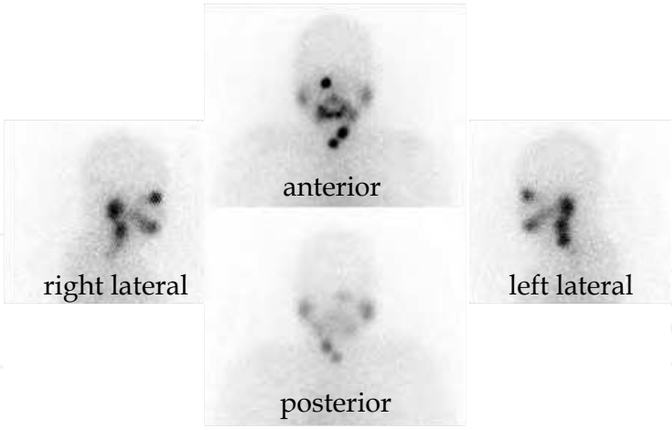


Fig. 15. Physiologic uptake of radioiodine in the lacrimal sac. The uptake is known to be related to active iodine transport by the NIS at the lining epithelium of the sac. There was also noted intense tracer accumulation in the thyroid bed (by remnant tissue of the thyroid, which has the NIS expression) and oral cavity (by the radioactivity of secreted saliva) and minimal tracer uptake in the salivary glands (by the NIS expression of the glands).

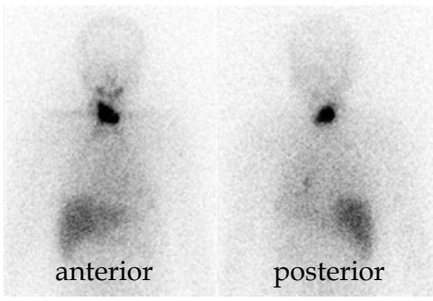


Fig. 16. Physiologic uptake of radioiodine in the liver. The uptake is known to be related to metabolism of radioiodinated thyroglobulin and thyroid hormones in the liver. There was also noted intense tracer accumulation in the thyroid bed (by the remnant tissue of the thyroid).

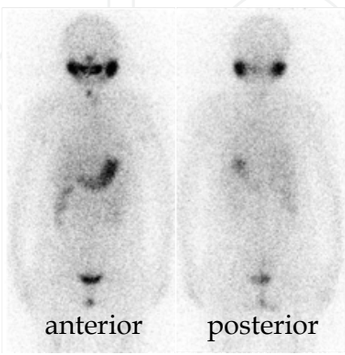


Fig. 17. Physiologic uptake of radioiodine in the urinary bladder. Intense tracer uptake was noted at the suprapubic area by radioactive urine in the bladder. Tracer uptake was noted in the salivary glands (by the NIS expression of the glands) and perineal area (due to urine contamination).

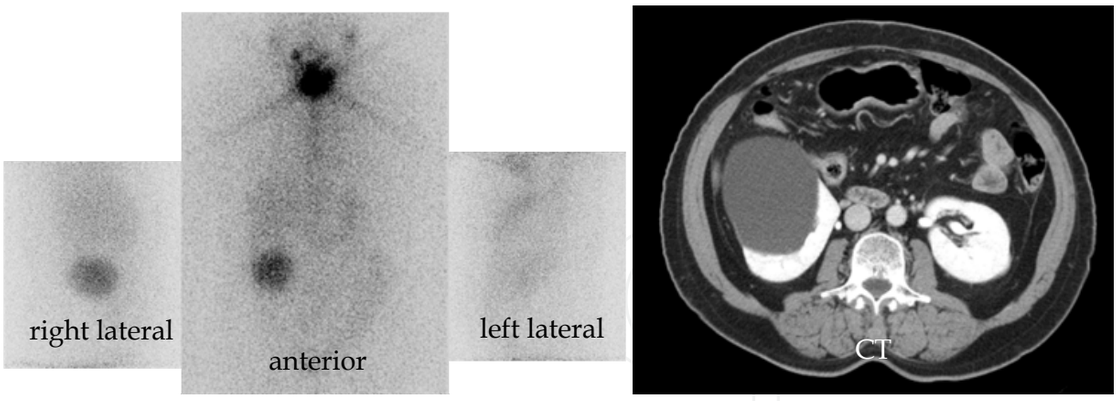
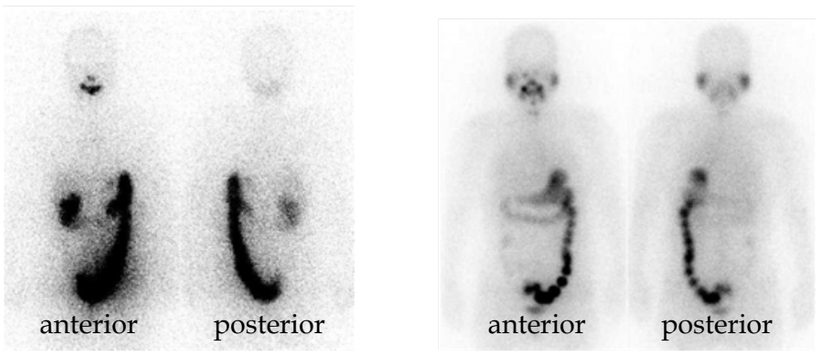


Fig. 18. Physiologic uptake of radioiodine in a simple cyst of the right kidney. Focal tracer uptake was noted at the right side abdomen. The proposed mechanisms are communication between the cyst and the urinary tract and radioiodine secretion by the lining epithelium of the cyst. There was intense tracer uptake noted in the thyroid bed area (by the remnant tissue of the gland) and mild tracer uptake in the salivary gland (by the NIS expression of the glands).



(A) (B)

Fig. 19. Physiologic uptake of radioiodine in the colon. Intense tracer uptake was noted at the colon. The suggested mechanisms for the uptake are transportation of radioiodine into the intestine from the mesenteric circulation and biliary excretion of the metabolites of radioiodinated thyroglobulin or thyroid hormones. There was also noted tracer uptake in (A) the oral cavity (by the radioactivity of secreted saliva), (B) the salivary glands (by the NIS expression of the glands) and stomach (by the NIS expression of the gastric mucosa).

5. Pathologic lesions might show false positive radioiodine uptake

A variety of pathologic lesions producing a false positive radioiodine whole body scan have been reported and contrary to the physiologic uptakes that usually do not create diagnostic confusion, they might be tricky enough to cause some patients to undergo unnecessary fruitless invasive surgical or high dose radioiodine treatment.(Mitchell, Pratt et al. 2000)
The not uncommon pathologic lesions showing radioiodine uptake are cystic, inflammatory, non-thyroidal neoplastic diseases. Cystic lesions in various organs can accumulate radioiodine and the mechanism of the uptake is passive diffusion of the tracer into the cysts. Radioiodine accumulation in ovarian, breast and pleuropericardial cysts has been reported.

(Shapiro, Rufini et al. 2000) Effusion of the pleural, pericardial and peritoneal cavities can also have radioiodine uptake by the same mechanism.(Shapiro, Rufini et al. 2000)
A variety of inflammatory and infectious disease can have radioiodine accumulation by increased blood flow that delivers increased levels of radioiodine to the site, and enhanced permeability of the capillary that increases diffusion of the tracer to the extracellular water space.(Shapiro, Rufini et al. 2000) Radioiodine accumulation in bronchiectasis, pulmonary aspergilloma, skin wound, arthritis, paranasal sinusitis, skin infection, myocardial infarction and dacryocystitis has been reported.(Shapiro, Rufini et al. 2000; Ahn, Lee et al. 2011)
Even though only a minority of such lesions accumulate the tracer, a variety of non-thyroidal neoplasms are also known to take up radioiodine. The suggested mechanisms are i) a tumour expression of the NIS, which actively accumulates the tracer and ii) increased vascularity and enhanced capillary permeability that might be secondary to the inflammatory response associated with the neoplasm.(Mitchell, Pratt et al. 2000; Shapiro, Rufini et al. 2000) Radioiodine accumulation in breast cancer, gastric adenocarcinoma, bronchial adenocarcinoma, bronchial squamous carcinoma, salivary adenocarcinoma, teratoma, ovarian adenocarcinoma and meningioma has been reported.(Shapiro, Rufini et al. 2000)
Fortunately, false positive uptake on a radioiodine whole body scan can be interpreted with using the serum thyroglobulin value, which is very sensitive marker for residual or recurrent thyroid cancer. Therefore, the false positive uptake usually does not cause a diagnostic dilemma for experienced practitioners. The clinical features and other imaging studies can also help to distinguish the false positive pathologic lesions from true positive metastatic thyroid cancer lesions.(Mitchell, Pratt et al. 2000; Ahn, Lee et al. 2011)

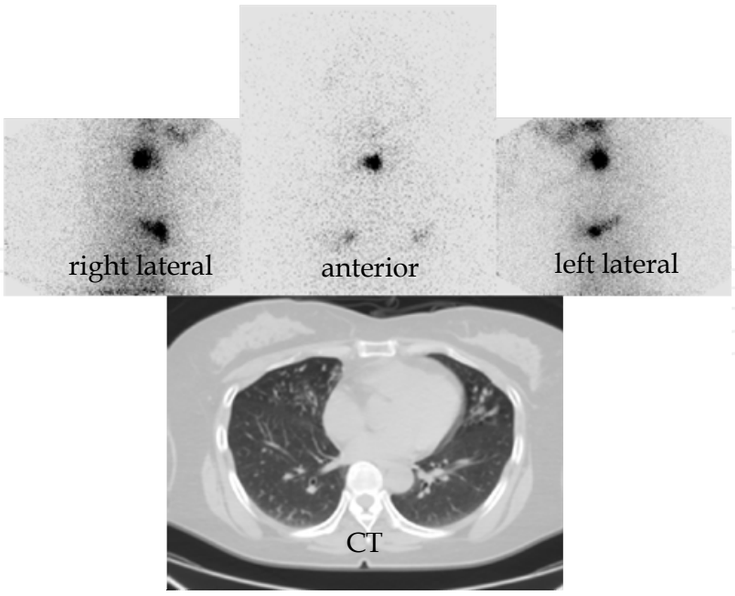


Fig. 20. Pathologic uptake of radioiodine in the bronchectatic lesions of both lungs. There was also noted intense tracer uptake in the thyroid bed area (by the remnant tissue of the gland).

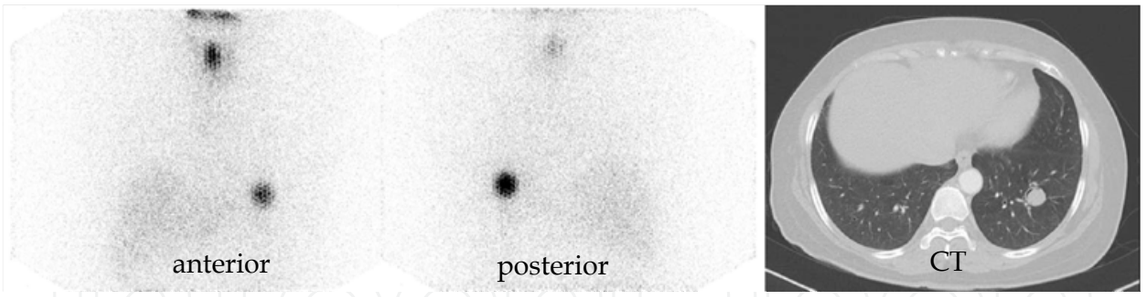


Fig. 21. Pathologic uptake of radioiodine in a pulmonary fungus ball. There was also noted tracer uptake in the thyroid bed area (by the remnant tissue of the gland) and the liver (by metabolism of the radioiodinated thyroglobulin and thyroid hormones).

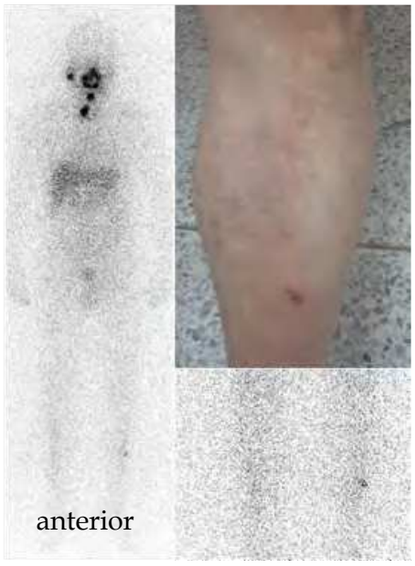


Fig. 22. Pathologic uptake of radioiodine in a skin wound. There was tracer uptake in the left lower leg where the skin wound was located. There was tracer uptake in the salivary gland (by the NIS expression of the glands), thyroid bed (by the remnant tissue of the gland) and the liver (by metabolism of the radioiodinated thyroglobulin and thyroid hormones).

6. Contaminations by physiological secretions

External contamination by physiological or pathological body secretions or excretions can cause positive radioiodine uptake and this mimics metastatic involvement of differentiated thyroid cancer.(Bakheet, Hammami et al. 2000) Sweat, breast milk, urine, vomitus and nasal, tracheobronchial, lacrimal, salivary secretions and faeces contain radioiodine and their contamination on the hair, skin or clothes can be misinterpreted as metastasis of thyroid cancer.(Shapiro, Rufini et al. 2000) Any focus of radioiodine uptake that cannot be explained by physiological or pathological causation must also be suspected as arising from contamination by secretions. Fortunately, the contaminations are usually easily recognized by their pattern and acquiring images after removing the contamination with decontaminating procedures and with taking the stained clothes off. However, unusual patterns of contamination might occur and suspecting uptake lesions as contamination would be difficult.

Patients' peculiar physical characteristics or odd habits produce extraordinary contamination patterns. Uptake in the scalp or a wig has been reported in patient with excessive sweating, and contamination of a wig was reported in patient with a bizarre habit of styling hair with sputum.(Bakheet, Hammami et al. 2000) False positive scans due to contamination can be kept to a minimum by careful preparation of patients, such as image acquisition in a clean gown after taking a shower.

Contaminations are almost always superficial, (Carlisle, Lu et al. 2003), therefore, the use of lateral and/or oblique views to give a third dimension to the scan may help to identify the contamination. Furthermore, the SPECT image alone or the SPECT image fused with the anatomical image, which provides detailed information about the anatomic location of the radiotracer uptake sites, can be the best way to correctly determine that contamination is the reason for the uptakes.

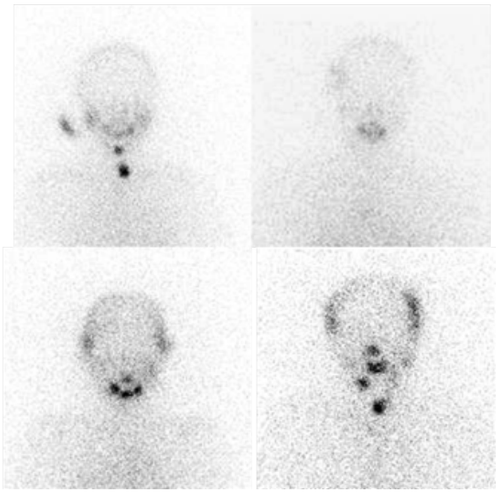


Fig. 23. Cases with contaminations at the hair and scalp. A case with unilateral hair contamination by saliva and cases with uni- or bilateral scalp contamination by excessive perspiration are demonstrated.

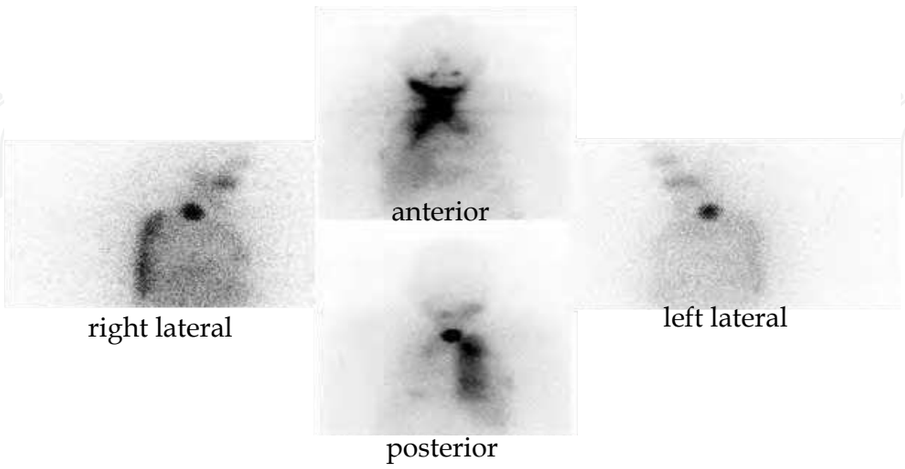


Fig. 24. Contamination at the right posterior chest wall by excessive perspiration. There was also noted intense tracer accumulation in the thyroid bed (by remnant tissue of the thyroid and edema of the cervical soft tissue).

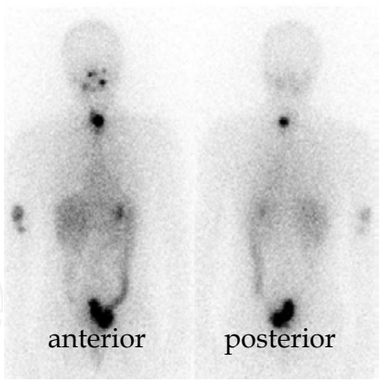


Fig. 25. Contamination at the skin of the right upper arm. There was also noted intense tracer accumulation in the rectum and moderate tracer accumulation in the descending colon and the liver.

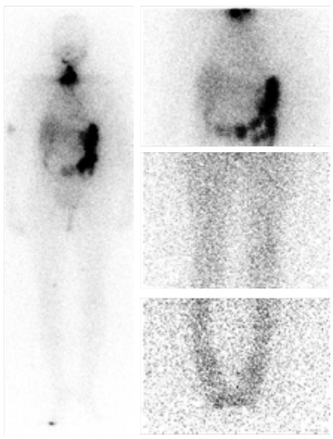


Fig. 26. Vanishing contaminations after cleansing the right forearm, both thighs and right foot. There was also noted intense tracer accumulation in the thyroid bed area and colon and moderate tracer accumulation in the liver.

	Sites of uptake	Mechamism of radioiodine uptake
Physiologic		
Residual thyroid tissue	thyroid bed	Active radioiodine uptake by expression of the NIS
Ectopic normal thyroid tissues	Lingual thyroid mediatinal thyroid Intratracheal thyroid Paracardiac thyroid Intraheaptic thyroid	Active radioiodine uptake by the expression of the NIS
Salivary gland	Parotid and submandibular salivary glands	Active radioiodine uptake by the expression of the NIS
Lacrimal sac/nasolacrimal duct Lacrimal gland*	Ocular and periocular area	Active radioiodine uptake by the expression of the NIS **controversial*

	Sites of uptake	Mechamism of radioiodine uptake
By excreted or swallowed saiva	Oral cavity Oesophagus Oesophageal diverticulum Oesophageal stricture or scarring Achalasia	Focal accumulated saliva with radioiodine activity from the salivary glands
By nasal secretion	Nose "hot nose"	Focal accumulated nasal secretion with radioiodine
By excreted urine	Renal pelvis Ureter Urinary bladder Urinary tract diverticulum Urinary tract fistula Renal cyst*	Accumulated urine radioiodine activity excreted by the kidneys * *Active radioiodine uptake by the expression of the NIS can be another mechanism*
Choroid plexus	Brain	Active radioiodine uptake by the expression of the NIS
Thymic uptake	Thymus	Expression of the NIS in thymic tissues and/or iodine concentration by Hassal's bodies
Gastric mucosa	Stomach Gastric duplication cyst Meckel's diverticulum Barrett esophagus	Active radioiodine uptake by the expression of the NIS
By excreted gastric secretion	Oesophageal uptake Bowel uptake	Gastroesophagel reflux Translocation of excreted gastric secretion into the bowel
Metabolism of radioiodinated proteins	Liver Biliary tract Gall bladder Bowels	Metabolism of radioiodinated thyroid hormones or thyroglobulin and their excretion into the gall bladder and bowels via the biliary tract
Breast	Breast, especially lactating	Active radioiodine uptake by the expression of the NIS
Colon	Diffuse and/or focal (any part of colon)	Transport of radioiodine into the intestine from the mesenteric circulation and biliary excretion of the metabolites of radioiodinated thyroglobulin.
Pathologic		
Heterotopic thyroid tissue	Struma ovarii	Active radioiodine uptake by the expression of the NIS
Inflammations associated with/without infection	Pericarditis Skin burn Dental disease Arthritis Cholecystitis Folliculitis Paranasal sinusitis Dacryocystitis Bronchiectasis Fungal infection (eg, aspergilloma)	Increased perfusion and vasodilation, and enhanced capillary permeability by the inflammation

	Sites of uptake	Mechamism of radioiodine uptake
	Pleural and pericardial effusions	
Non-thyroidal neoplasm	Gastric adenocarcinoma Salivary adenocarcinoma Lung adenocarcinoma Fibroadenoma Meningioma Nurilemoma Teratoma	Active radioiodine uptake by the NIS of the tumor and/or incresed blood flow and enhanced capillary permeability in the tumor
Trauma	Biopsy site Tracheostomy site	Increased perfusion and vasodilation, and enhanced capillary permeability by the tissue trauma
Contaminations		
Tear	Skin of any part of the body, hair, wig, cloth, etc	Contamination by physiological or pathological body secretions or excretions
Saliva		
Sweat		
Vomitus		
Breast milk		
Urine		
Feces		

Table 4. Causes of radioiodine uptake not related to thyroid cancer on the radioiodine whole body scan.

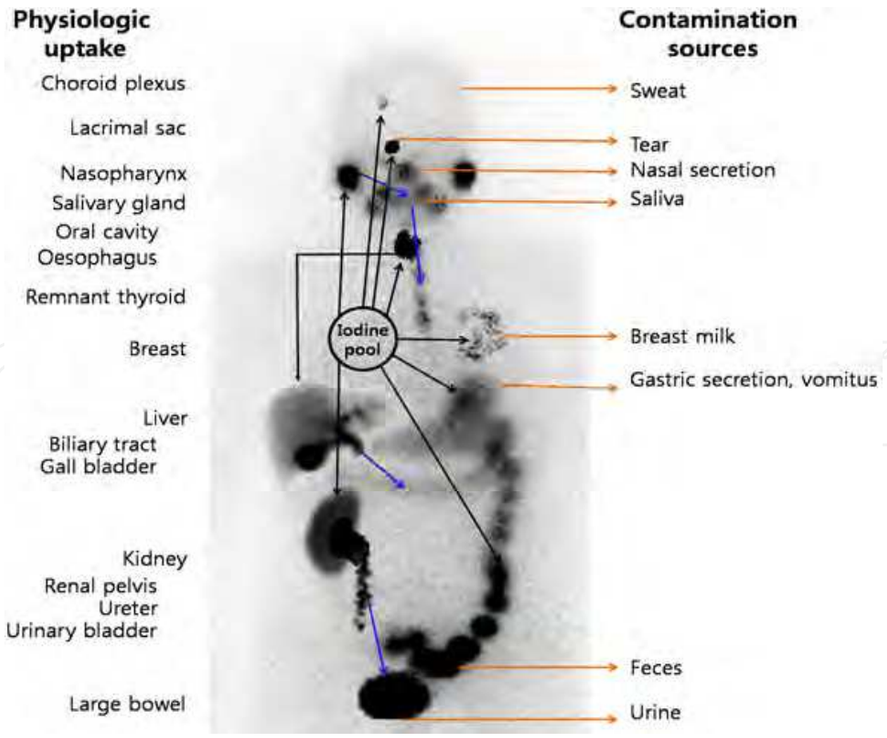


Fig. 27. Schematic presentation for the locations of physiologic uptake and possible contamination sources the radioiodine whole body scans.

7. Conclusion

A whole body scan obtained with the administration of a diagnostic or therapeutic dose of radioiodine has a definite role in the management of patients with well differentiated thyroid cancer after total thyroidectomy. Accurate interpretation of the scan requires a thorough knowledge and understanding of potential confounding factors for uptakes on the scan, and recognition of the variable causes of false positive uptake will provide correct prognostic inferences and prevent inappropriate therapeutic interventions. In addition, the cause of radioiodine uptake on the scan is always evaluated in conjunction with the serum thyroglobulin level and the clinico-radiological results in order to lessen the chance of an incorrect conclusion about the uptakes.

This chapter was written to make readers consider a broad variety of diseases as the causes of the uptake on the radioiodine whole body scan and I have demonstrated a wide variety of causes of false positive uptakes on these scans.

8. Acknowledgment

The author thanks Doctor Do-Hoon Kim for gathering the radioiodine whole body images.

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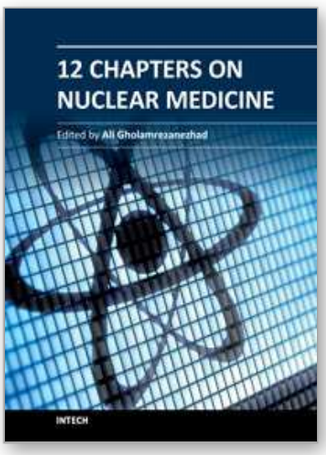

12 Chapters on Nuclear Medicine

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The development of nuclear medicine as a medical specialty has resulted in the large-scale application of its effective imaging methods in everyday practice as a primary method of diagnosis. The introduction of positron-emitting tracers (PET) has represented another fundamental leap forward in the ability of nuclear medicine to exert a profound impact on patient management, while the ability to produce radioisotopes of different elements initiated a variety of tracer studies in biology and medicine, facilitating enhanced interactions of nuclear medicine specialists and specialists in other disciplines. At present, nuclear medicine is an essential part of diagnosis of many diseases, particularly in cardiologic, nephrologic and oncologic applications and it is well-established in its therapeutic approaches, notably in the treatment of thyroid cancers. Data from official sources of different countries confirm that more than 10-15 percent of expenditures on clinical imaging studies are spent on nuclear medicine procedures.

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