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What are the energies and half-lives of Iodine123 and Iodine131?

I131: 364 keV and 8 day half-life. Remember this is the beta emitter and therapeutic agent.

I123: 159 keV and 13 hour half-life. This provides overall superior image quality but cannot be used for therapy and is typically more expensive than I131.

True or false: Thyroid uptake can be seen with free technetium.

True. In fact, Tc-pertechnetate is one agent that can be used for certain types of thyroid imaging. Remember that classic regions for free technetium uptake include salivary glands, thyroid and gastric uptake.

When might you consider using Tc over iodine for thyroid imaging?

One scenario where Tc-99m may be superior to I123/I131 for thyroid imaging is for patients who are on thyroid blockade including patients who have recently received iodinated contrast as the thyroid may not take up the radioiodine but would take up the Tc-99m.

What is the difference between trapping and organification in the thyroid?

Trapping refers to a radiotracer getting transported into the thyroid gland. This is the initial entry of iodine and other tracers into the thyroid. Organification refers to the iodine actually getting oxidized by thyroid peroxidase and then binding to a tyrosyl moiety, essentially making it so the iodine will not wash out of the thyroid. I123/I131 will get trapped and then organified allowing the iodine to remain in the gland for a long time, thus facilitating delayed imaging of the thyroid.

Also, although Tc is not iodine, Tc is essentially trapped by the thyroid but is not organified so Tc will wash out of the thyroid much faster than I123/I131.

Tc-99m is trapped but not organified and will show higher background counts as most of the Tc does not end up in the thyroid.

I123/I131 are both trapped and organified and has less background uptake as a higher percentage of the iodine will end up in the thyroid gland vs other tissues.

What is the normal arterial supply of the thyroid?

The thyroid is supplied by the superior thyroid artery and the inferior thyroid artery. The superior thyroid artery is a branch of the external carotid artery and the inferior thyroid artery is a branch of the thyrocervical trunk.

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If a patient presents with recent upper respiratory illness presenting with acute neck pain in the region of the thyroid and symptoms of hyperthyroidism, what is the top differential consideration?

A classic history for De Quervain thyroiditis aka subacute granulomatous thyroiditis is presentation with acute neck pain and symptoms of hyperthyroidism to include tachycardia, palpitations, and hot flushes. The cause is thought to be post-viral inflammation of the thyroid following an upper respiratory infection and is most common in middle aged females.

What is the normal course for thyroid hormone levels during the evolution of De Quervain thyroiditis?

First, thyrotoxicosis as the thyroid gland is inflamed and releases thyroid hormone into the bloodstream. Second, hypothyroidism as the thyroid becomes depleted of normal thyroid hormone. Finally, a return to the euthyroid state for most patients.

What are the classic radioiodine uptake values (high, normal, low) for De Quervain thyroiditis?

Low radioiodine uptake in a hyperthyroid patient should make you think of De Quervain thyroiditis, especially in the appropriate clinical setting.

Is De Quervain's thyroiditis treated with radioactive iodine?

No. This is a self-limiting disease and one would not want to ablate the thyroid that is expected to recover on its own. Also, the hyperthyroidism is transient and self-resolving and thus does not require radioiodine ablation.

What are extrathyroidal manifestations of Graves disease?

Extrathyroidal manifestations of Graves include Graves ophthalmopathy (remember proptosis with orbital extraocular muscular enlargement (IMSLO) in order of higher frequency first involving the inferior rectus, medial rectus, superior rectus, lateral rectus and lastly oblique muscles), pretibial myxedema/thyroid dermopathy, thyroid acropachy (finger swelling, periosteal reaction, etc.), and classic symptoms of hyperthyroidism such as palpitations, etc.

What antibodies are classically associated with Graves disease and what antibodies are classically associated with Hashimoto thyroiditis?

Graves: TSH receptor antibodies.

Hashimoto: thyroid peroxidase antibodies (TPO) and antithyroglobulin antibodies

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What is the nuclear medicine appearance of Graves disease on a thyroid scan?

Regardless of whether imaging is performed with Tc or I123/I131 the thyroid will appear as an enlarged thyroid gland with homogeneous increased activity. Remember to look for the pyramidal lobe centrally projecting about the superior aspect of the thyroid gland at midline above the isthmus. A normal sized thyroid with normal uptake often does not show the pyramidal lobe. The pyramidal lobe may be seen in something like 10% of normal thyroid glands and roughly half of all thyroid glands with Graves disease.

What is the classic clinical presentation of a patient with Hashimoto thyroiditis?

A classic clinical history for a patient with Hashimoto thyroiditis would be a middle aged female presenting with symptoms of hypothyroidism and possible goiter. Note that neck pain is not classic for Hashimoto thyroiditis. Sometimes Hashimoto thyroiditis can initially present with hyperthyroidism and subsequent hypothyroidism and, when in the hyperthyroid state, this has been termed Hashitoxicosis.

What are typical imaging features of Hashimoto thyroiditis on a nuclear medicine thyroid scan and on an FDG-PET/CT study?

On a nuclear medicine thyroid scan, Hashimoto thyroiditis would show increased uptake in early stages that can look similar to Graves disease and later would classically appear as an inhomogeneous thyroid with focal cold areas.

On an FDG-PET/CT study one would expect diffuse uptake throughout the thyroid gland due to the inflammatory nature of Hashimoto thyroiditis. Any focal hot spots raise suspicion for possible malignancy.

What malignancy is most classically associated with Hashimoto thyroiditis on board examinations?

Primary thyroid lymphoma.

Episode 2

How long must one abstain from breast feeding after receiving Iodine 131?

After receiving I131, lactation must cease for that child (no more breastfeeding). This is due both to the long half life of I131 (8 days) as well as the risk to the child's thyroid of ablation and becoming hypothyroid as a result. I131 is contraindicated in pregnancy and in childhood.

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When can breastfeeding resume after receiving Iodine 123 or Tc99m?

I123—about 2-3 days

Tc99m—about 12 hours

What are approximate normal values of iodine uptake at 4 and 24 hours?

Range of estimates vary but I remember 5-15% at 4 hours (range can be 4-6 hours) and 10-30% at 24 hours. Note this helps me remember as I simply double the 4 hour 5-15% to remember the 24 hour 10-30% range. On board exam questions they should make it obvious whether a result is in this ballpark range of normal or clearly abnormal. I wouldn't expect that they would give you an uptake of 3% or 17% at 4 hours and ask you if this is normal.

Elevated radioiodine uptake can be seen with which classic entities?

Entities associated with increased radioiodine uptake include Graves disease, early Hashimoto's, dietary deficiency of iodine. With dietary deficiency of iodine the thyroid is so hungry for iodine that when it sees the radioiodine it simply takes up more of it.

How do TSH values help distinguish between Graves disease and dietary iodine deficiency?

Because both of these entities will have increased radioiodine uptake values, one can use TSH to help differentiate these entities (as well as dietary history and clinical history/symptoms). Graves would be expected to have a low TSH value whereas dietary iodine deficiency would be expected to have an elevated TSH level.

How does renal dysfunction affect iodine uptake values?

Renal dysfunction may cause elevated levels of iodine in the blood pool and because the thyroid has more iodine at baseline it will take up less radiotracer due to competition between the iodine in the blood pool and the administered radioiodine independent of TSH values. So in setting of renal dysfunction one would predict lower radioiodine uptake values.

What are some medications that can classically lower radioiodine uptake?

These include thyroid blockers (methimazole, propylthiouracil), nitrates, iodinated contrast via IV, amiodarone.

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What is the significance in Graves disease of an elevated 4 hour uptake value and a 24 hour uptake value that is lower than the 4 hour value or even within normal limits?

This denotes rapid thyroid hormone production—so rapid in fact that the tracer was depleted by 24 hours as it already had been trapped and organified and subsequently released from the thyroid. This is a sign of a more active Graves disease that is really ramped up.

What is the classic thyroid scan imaging appearance of toxic multinodular goiter?

Toxic multinodular goiter will show one or more hot nodules on a background of a cold gland as the hot nodules preferentially take up all or most of the radioactive iodine. Hot nodules on a background cold gland is seen with a toxic multinodular goiter whereas warm nodules on a heterogeneous thyroid that demonstrates normal background uptake is seen with multinodular (nontoxic) goiter. For review, Graves disease is expected to show homogeneous diffuse uptake on an enlarged gland and would not show the focal and heterogeneous uptake seen with toxic and non-toxic multinodular goiter.

What are typical thyroid uptake values and clinical histories for patients with toxic multinodular goiter?

Thyroid uptake values are often only moderately elevated with toxic multinodular goiter, for example uptake around 40% at 24 hours (classic Graves may show uptake around 70% at 24 hours). A classic history would be an elderly female with symptoms of hyperthyroidism such as tachycardia, weight loss, insomnia, and anxiety.

If a patient presents with a low TSH and a high T3/T4 what entities should you consider and how can thyroid uptake values help you differentiate between these?

A low TSH and elevated T3/T4 values can be seen with multiple entities including Graves disease, subacute thyroiditis, solitary autonomous hyperfunctioning nodule and toxic multinodular goiter.

Radioiodine uptake would be expected to be low in subacute thyroiditis or dietary iodine overload and elevated in Graves disease, toxic multinodular goiter and solitary autonomous hyperfunctioning nodule.

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If a thyroid nodule is cancerous, will this nodule most likely be hot or cold on a radioactive iodine thyroid scan? What about an FDG-PET/CT scan?

A cancerous thyroid nodule is most likely to be cold on an I123/I131 thyroid scan and hot on an FDG-PET/CT scan. Remember that normal thyroid takes up radioactive iodine so if a nodule is cold and therefore does not take up iodine, that means something is wrong with that nodule compared to normally functioning thyroid tissue—and that can be evidence of cancer with derangement of normal cellular function. As we all know, cancer can be hypermetabolic and a focal FDG avid thyroid nodule should raise suspicion for possible malignancy.

Are most cold thyroid nodules cancerous?

No, most cold nodules will be benign. Additionally, multiple cold nodules in the setting of multinodular goiter are more likely to be benign compared to a single cold nodule.

What is a discordant thyroid nodule?

A discordant thyroid nodule is a thyroid nodule that shows increased uptake on a Tc-99m scan but decreased or absent uptake on an I131/I123 scan. The problem is that some thyroid cancer cells may retain enough function to trap but not enough function to organify. Remember that Tc and radioactive iodine are both trapped but only radioactive iodine is organified. So a warm/hot nodule on a Tc-99m scan is not necessarily benign as Tc is trapped but not organified by the thyroid. Take home message is that one needs to be careful calling a nodule benign based on a Tc-99m thyroid scan only, and a nodule may only be considered benign once you show the nodule is warm/hot on an iodine thyroid scan.

What are top differential considerations if the thyroid takes up Tc-99m on early images but not radioactive iodine at 24 hours?

Potential causes include congenital enzyme deficiency that interferes with organification versus therapy with propylthiouracil that blocks organification.

Episode 3: Thyroid cancer and Radioactive Iodine Therapies

What subtypes of thyroid cancer classically may not take up I131?

Medullary thyroid cancer and anaplastic thyroid cancer classically may not take up I131 and therefore may not respond as well to I131 therapy compared to other types of thyroid cancer. Remember the MEN 2A and 2B syndrome association with medullary thyroid carcinoma. Note that medullary thyroid cancer has neuroendocrine features and may have uptake on MIBG/octreotide imaging. Papillary thyroid cancer is typically radioiodine avid.

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What other factors contribute to treatment resistance of thyroid cancer to I131 therapy?

Patients with prior I131 therapy are more likely to be resistant to I131 therapy in the future. So if you are re-treating with I131 you often have to significantly increase the I131 for subsequent therapies. Prior methimazole treatment is also thought to possibly contribute to resistance to I131 therapy. Poor patient preparation is also a cause of failure or poor response to I131 therapy.

True or False: For thyroid cancer therapy thyroidectomy surgery typically precedes thyroid treatment with I131?

True. Thyroidectomy is first performed and I131 is subsequently given to ablate any residual thyroid tissue. Note that it is not possible, even with the most skilled surgeons, to remove all thyroid tissue at surgery so there will always be a thyroid remnant that can be ablated. As there can be variation in how much thyroid tissue remains post-thyroidectomy, one can perform a thyroid uptake test with I123/I131 and if thyroid uptake is something like 5% or greater, those patients may be at risk for thyroid pain following I131 therapy and may be considered for steroid treatment during I131 therapy to reduce symptoms vs return to OR to remove additional tissue.

Do you want TSH to be elevated or low prior to I131 cancer ablation therapy?

TSH should be elevated prior to I131 ablation therapy in order to stimulate residual thyroid tissue to take up as much I131 as possible. Two primary options exist to raise TSH values. The first is cessation of thyroid hormone replacement to stimulate the natural TSH release as the body becomes hypothyroid. The second option is to remain on thyroid hormone and take recombinant TSH which is also known as thyrogen. Note that a minimum TSH value of 30 is often considered acceptable pre I131 ablation and a TSH value of 50 or higher may be considered ideal.

What are common I131 doses for thyroid cancer without nodal or distant metastatic disease, thyroid cancer with local nodal metastases and thyroid cancer with distal metastases?

I131 for contained thyroid cancer with no nodal or distant spread: 50 to 100 mCi

I131 for thyroid cancer and local nodal disease in neck: 150 mCi

I131 for thyroid cancer and distant disease: 200 mCi

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What are general dose ranges for I131 therapy of Graves disease, autonomous hyperfunctioning thyroid nodule and toxic multinodular goiter to keep in mind for board exam purposes?

Graves disease is often treated with 5 to 15 mCi I131

Autonomous hyperfunctioning thyroid nodule is often treated with 15-25 mCi I131

Toxic multinodular goiter is often treated with 25-35 mCi I131

Note that calculations do exist whereby doses may be calculated based on thyroid weight and radioiodine uptake values. However, these general ranges are something that may be beneficial to know for board exam purposes.

What are common precautions that individuals must take prior to I131 therapy?

Following I131 therapy a patient must isolate for 3 days including bathroom hygiene, sleeping alone, no exposure of others to bodily fluids including saliva and urine. Additionally, patients should stay well hydrated.

What is an estimated risk of malignancy from a single cold nodule on a radioactive iodine scan?

A single cold nodule has an approximate 15 to 20% chance of malignancy. Note that risk of malignancy increases if a cold nodule is seen in younger patients, if a nodule is hard on palpation, if there is a history of neck radiation, and with family history of thyroid cancer.

What is an estimated risk of malignancy from a hot nodule on a thyroid scan?

In general, the risk of thyroid cancer in a nodule that is hot on a radioactive iodine scan is thought to be less than 1%.

Is hypothyroidism common in patients with toxic multinodular goiter following I131 therapy?

No. In toxic multinodular goiter the radioactive iodine preferentially is taken up into the toxic nodule(s) and the remainder of the gland has suppressed uptake and is therefore not ablated. Note that many of these patients with toxic multinodular goiter will become euthyroid following I131 treatment. The same principle would also hold true for a hyperfunctioning thyroid nodule—the background thyroid is suppressed and the radioactive iodine is preferentially taken up within and preferentially ablates the hyperfunctioning nodule, sparing the normal thyroid parenchyma, and potentially ending up in a euthyroid state.

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How can one differentiate between a Tc-99m pertechnetate vs radioactive iodine thyroid scan?

If you see higher salivary gland uptake than thyroid uptake and lots of background counts then the scan is more likely a Tc-99m scan. A radioactive iodine scan would show robust thyroid uptake with little background uptake.

What should you consider if thyroglobulin levels are rising in a patient who has completed thyroidectomy and I131 ablation for thyroid cancer and the thyroid I123/I131 scan is negative? What is the next best test to consider?

One must consider the possibility that the thyroid cancer is truly back, as suggested by the thyroglobulin levels, but has de-differentiated and therefore no longer takes up radioactive iodine. In this setting, one would want to perform an FDG-PET/CT study to show where the site(s) of recurrence are as de-differentiated thyroid cancer tends to be FDG avid.

What type of collimator is best for I131 imaging?

High energy collimators are used for I131 imaging given the very high 364 keV energy. If lower energy collimators are used you would expect to see septal penetration with the star-like artifact that is classic for this entity. Note that I131 is basically the highest energy radioisotope commonly used in general nuclear medicine

Besides thyroid imaging can you name another nuclear medicine scan that uses I123/I131?

MIBG uses I123/I131. Note that one needs to block the thyroid gland before MIBG to prevent thyroid uptake. Lugol's Iodine solution is commonly used prior to imaging to prevent unnecessary radiation to the thyroid when using MIBG imaging. Remember to block the thyroid first prior to MIBG imaging. A dual tracer technique for parathyroid imaging can also be performed where I123 is given to show background thyroid uptake that is then subtracted from a Tc-sestamibi or Thal201 chloride scan that is taken up by the parathyroid glands and with some background thyroid uptake. If you subtract the I123 info you are left with uptake primarily from the parathyroid glands. I123 Ioflupane may also be used for dopamine transporter imaging aka DaTscan. Note that Octreoscan uses In111 NOT I123.

What is thyroid stunning?

Thyroid stunning is a reduction in I131 uptake below predicted values following a low-dose diagnostic I131 scan. The thought is that either reduced cell function and/or cellular death following a diagnostic I131 scan (such as an I131 uptake study or whole body search) can lead to reduced therapeutic I131 uptake due to "stunned" (or dead) thyroid cells secondary to the initial I131 low dose study.

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Approximately how long should you wait following IV iodinated contrast administration to treat a patient with I131?

Typically about 6-8 weeks.

What are NRC guidelines for releasing a patient following I131 oral administration?

1. No individual of the public is likely to receive more than 5 mSv exposure from the patient treated with I131.
2. When a survey meter reading at 1 meter is less than 0.07 mSv/hour (7 mrem/hour)
3. When administered activity is 33 mCi or less.

Prior to release that authorized user should instruct the patient regarding best practices to minimize radiation exposure to others and written instruction describing recommended methods to limit radiation exposure to others is generally advised. Precautions include having the patient sleep alone, avoid pregnant individuals and children, avoid public transportation, follow strict bathroom hygiene, etc. Note also that I131 exposure is at high risk through bodily fluids but not through touching object. For example, a family member need not worry if they touched a door handle that was recently touched by the person treated with I131.

Want more info?

Check out this RadioGraphics article: <https://pubs.rsna.org/doi/full/10.1148/rg.234025716>

Good overview: <https://www.ncbi.nlm.nih.gov/books/NBK559283/>

SNMMI I131 therapy practice parameters: https://s3.amazonaws.com/rdcms-snmml/files/production/public/docs/I-131_V3.0_JNM_pub_version.pdf