Thyroid Imaging with I-123 NaI And Tc-99m Pertechnetate

1. OVERVIEW AND INDICATIONS

(adapted from Society of Nuclear Medicine Procedure Guideline for Thyroid Scintigraphy and other sources)

a) Evaluation of the general structure of the thyroid gland (e.g. nodular or diffuse enlargement) relative to its function. This may be useful in the differential diagnosis of hyperthyroidism, i.e. distinguishing Graves' disease from toxic nodular goiter, a distinction of significance in determining the therapeutic dosage of I-131 and predicting the outcome and potential side effects of therapy.

b) Correlation of thyroid palpation with scintigraphic findings to determine the degree of function in a nodule that is palpable or found incidentally at a nonnuclear imaging procedure.

c) Location of ectopic thyroid tissue (e.g., lingual, incomplete thyroid descent).

d) Evaluation of congenital hypothyroidism (total agenesis or hemiagenesis, dyshormonogenesis, incomplete thyroid descent).

e) Evaluation of a neck or substernal mass. Scintigraphy may be helpful to confirm that the mass is functioning thyroid tissue.

f) Differentiation of thyroiditis (i.e. viral, autoimmune) and factitious hyperthyroidism from Graves' disease and other forms of hyperthyroidism.

g) Evaluation of the size and location of thyroid tissue.

h) Evaluation of hyperthyroidism.

i) Evaluation of suspected focal (i.e., masses) or diffuse thyroid disease.

j) Evaluation of clinical laboratory tests suggestive of abnormal thyroid function.

k) Evaluation of patients at risk for thyroid neoplasm (e.g., post neck irradiation).

l) Assessment of the function of thyroid nodules identified on clinical examination or ultrasound or by other diagnostic imaging.

m) Evaluation of congenital thyroid abnormalities.

2. RADIOPHARMACEUTICALS UTILIZED

a) **Tc-99m pertechnetate [TcO_4]$^{1-}$** This is the anionic form of Tc-99m and has 4 principal sites of localization: the choroid plexus in the brain, the parotids, the thyroid, and the gastric mucosa. Unlike the radioiodides, it is administered intravenously. The Tc has an oxidation number of 7+ in this chemical form.

b) **I-123 sodium iodide**. The iodide has a charge of 1- and is sold as the sodium iodide salt (NaI). This radiopharmaceutical is used more frequently than the other two combined.

c) **I-131 sodium iodide**. The iodide has a charge of 1- and is sold as the sodium iodide salt (NaI). This radiopharmaceutical is used for specialized imaging studies, e.g., whole body iodine scans evaluating a patient for a post-thyroidectomy neck remnant and/or metastatic disease anywhere in the body. Also, imaging of a substernal thyroid.

d) **Comparison Chart**

Comparison of Radiopharmaceuticals for Thyroid Scintigraphy

Radionuclide	Advantages	Disadvantages
Tc-99m pertechnetate	• Less expensive • More readily available • More rapid examination	• Trapped, but not organified • Activity in esophagus or vascular structures can be misleading • Poor image quality when uptake is low
I-123 iodide	• Better for visualization of retrosternal thyroid tissue • Yields better images when uptake is low	• Higher cost • May be less convenient for patient, as delayed imaging at 24 hr is often used • Less readily available • Imaging times are generally longer

3. CHARACTERISTICS OF THE RADIONUCLIDE

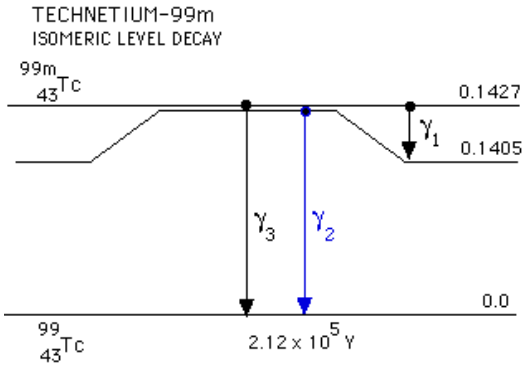
Tc-99m

a) Tc-99m decays by isomeric transition with a physical half-life of 6.02 hours. The principal photon that is useful for detection and imaging studies has a percent abundance of 89.07 % and the energy is 140.5 KeV.

b) The specific gamma ray constant for Tc 99m is 0.78 R/millicurie-hr at 1 cm.

c) The first half-value layer is 0.017 cm of lead (Pb) and the first tenth value layer is 0.08 cm of Pb.

d) Decay scheme (Adapted from www.med.harvard.edu)



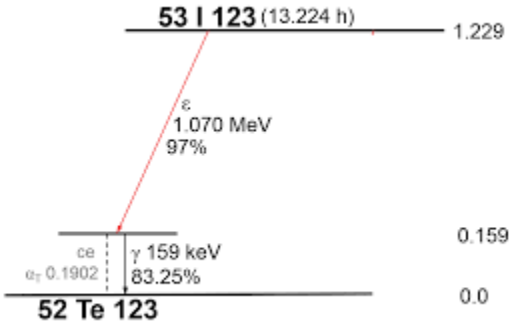
I-123

a) Iodine-123 decays by electron capture with a physical half-life of 13.2 hours. Photons used for detection and imaging of I-123 have an energy of 159 KeV.

b) The specific gamma ray constant for I-123 is 1.6 R/hr-mCi at 1 cm.

c) The first half-value thickness of lead (Pb) for I-123 is 0.005 cm and the first tenth value layer is 0.54 cm of Pb.

d) Decay Scheme



Adapted from www.nucleonica.com

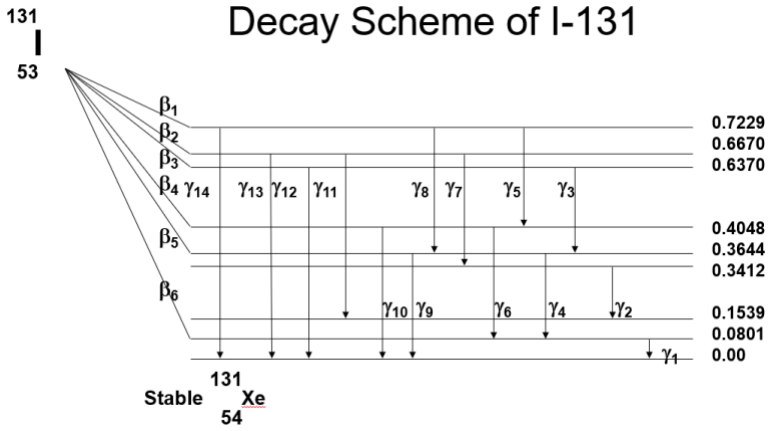
I-131

a) Iodine I-131 decays by beta emission and associated gamma emission with a physical half-life of 8.04 days. Photons used for detection and imaging of I-131 have an energy of 364.4 KeV.

b) The specific gamma-ray constant for iodine I-131 is 2.2 R/hr-millicurie at 1cm.

c) The first half-value thickness of lead (Pb) for iodine I-131 is 3 mm and the first tenth value layer is 11 mm of Pb.

d) Decay Scheme



Adapted from www.nucmedtutorials.com

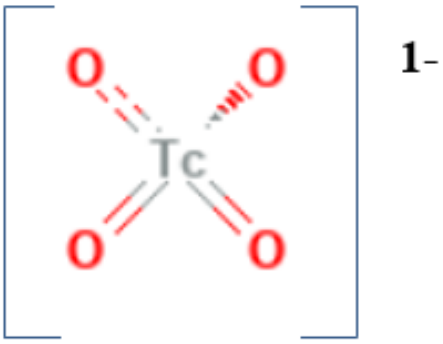
4. DRUG AVAILABILITY

a) All three radiopharmaceuticals are readily available from any central Radiopharmacy.

5. MOLECULAR STRUCTURES

a) Sodium iodide is an ionic compound containing Na^{1+} and I^{1-} ions. It really doesn't have a molecular structure, although there is a crystal lattice structure that has been well-characterized.

b) Sodium pertechnetate is also an ionic compound, but there is a known structure for the pertechnetate anion, as depicted below. There is a 1- charge on the ion.



6. DRUG PREPARATION

a) None required- each dose is precalibrated by the central pharmacy for a specific patient.

7. QUALITY CONTROL PROCEDURES

a) None required- requisite quality control procedures are performed by the central pharmacy prior to shipping doses of any of these radiopharmaceuticals.

8. RADIOCHEMICAL REACTIONS RELATED TO DRUG PREPARATION.

a) None required

9. CLINICAL PHARMACOLOGY

a) **Tc-99m pertechnetate**

i. The pertechnetate ion distributes in the body similarly to the iodide ion, but is not organified when trapped in the thyroid gland. Pertechnetate tends to accumulate in intracranial lesions with excessive neovascularity or an altered blood-brain barrier. It also concentrates in the thyroid gland, salivary glands, gastric mucosa, and choroid plexus. However, in contrast to the iodide ion, the pertechnetate ion is released unchanged from the thyroid gland. After intravascular administration, the pertechnetate ion remains in the circulatory system for sufficient time to permit blood pool measurement, organ perfusion, and major vessel studies. It gradually equilibrates with the extravascular space. A small fraction is promptly excreted via the kidneys.

b) Sodium iodide (I-123 or I-131)

i. Iodide is readily absorbed from the upper gastrointestinal tract. Following absorption, the iodide is distributed primarily within the extracellular fluid of the body. It is trapped and organically bound by the thyroid and concentrated by the stomach, choroid plexus and salivary glands. It is excreted by the kidneys. The fraction of the administered dose which is accumulated in the thyroid gland may be a measure of thyroid function in the absence of unusually high or low iodine intake or administration of certain drugs which influence iodine accumulation by the thyroid gland. Accordingly, the patient should be questioned carefully regarding previous medications and/or procedures involving radiographic media.

ii. Normal subjects can accumulate approximately 8 to 35% of the administered iodine dose in the thyroid gland, however, the normal and abnormal ranges are established by individual physician's criteria. The mapping (imaging) of sodium iodide I-123 distribution in the thyroid gland may provide useful information concerning thyroid anatomy and definition of normal and/or abnormal functioning of tissue within the gland.

iii. Trapped iodide is oxidized to iodine and organically incorporated so rapidly that the iodide trap of the thyroid contains less than 0.2% free iodide in comparison to the organically bound iodine. This process results in further concentration of iodine in the thyroid gland to about 500 times that in the blood. The iodinated organic compounds chiefly consist of thyroxine (T_4) and triiodothyronine (T_3), which are bound by thyroglobulin in the follicular colloid. T_4 and T_3 are released by enzymatic proteolysis of thyroglobulin into the blood where they are specifically bound and transported by plasma thyroid binding proteins. These reactions are primarily under the control of anterior pituitary gland release of thyroid stimulating hormone (TSH) and hypothalamic thyroid release factor (TRF).

iv. Iodide is excreted by the kidneys. The normal range of urinary excretion is 37-75% of the administered dose; varies with the renal function of the patient.

9. MECHANISM OF LOCALIZATION OF RADIOPHARMACEUTICAL:

a) The mechanism of localization is referred to as **Active Transport**. This is defined as utilization of a normally active, energy-dependent metabolic pathway in the body to transport a radiopharmaceutical across a cell membrane and into the cell. In the case of the radioiodides, the iodide is first trapped, then undergoes intermediate syntheses involving a thyroglobulin intermediate, and is first organified into T_1 then stepwise into T_2 then T_3 and finally T_4. Each of these iodination steps is energy dependent, of primary importance in meeting the requirements of a normally active, energy-dependent metabolic pathway.

10. NORMAL DISTRIBUTION OF DRUG

(target organ refers to organs receiving highest radiation dose)

Source: www.radiopaedia.org/articles/iodine-123

a) thyroid gland (target organ)
b) nasopharynx
c) salivary glands
d) stomach (target organ)
e) colon
f) bladder (target organ)
g) lactating breasts

11. TYPICAL ADMINISTERED DOSE FOR ADULTS AND CHILDREN

(adapted from Society of Nuclear Medicine Procedure Guideline for Thyroid Scintigraphy)

a) The recommended adult dose of I-123 sodium iodide for thyroid scintigraphy, administered orally, is 200 to 400 μCi (7.4 to 14.8 MBq).
b) The recommended adult dose of Tc-99m sodium pertechnetate, given intravenously in administered activity of 2.0 to 10.0 mCi (74 to 370 MBq
c) Use of I-131 is strongly discouraged for routine use because of its much greater radiation dose to the thyroid. The interpreting physician should be aware that findings, particularly in nodular disease, may rarely be discordant when the radioiodine and technetium images are compared, since pertechnetate is not handled by the same physiologic mechanism as iodine.
d) Administered activity for children should be determined based on body mass and should be as low as reasonably achievable for diagnostic image quality. The calculation of the pediatric dosage of technetium-99m sodium pertechnetate should be based on a reduced adult dosage of 2.0 to 5.0 mCi (74 to 185 MBq).

12. PATIENT PREPARATION FOR THYROID IMAGING WITH I-123 NaI

a) It is very important to carefully interview the patient prior to administration of the I-123 sodium iodide as there are so many potential interferences in the procedure (uptake or scan) that could invalidate the results. Included are the following:

   i. Is the patient pregnant or lactating?

   ii. Is the patient taking any herbal supplements, as they may also affect the test results?

   iii. Has the patient received iodine-containing contrast (e.g. for CT or angiography).

   iv. Is the patient consuming substances that contain iodine, including kelp, seaweed, seafood, cough syrups, multivitamins or heart medications can interfere with both uptake and scan?

   v. Is the patient taking any of the medications on the "Interfering Medications List"? Medications that interfere with thyroid uptake of radio-iodine could delay the procedure for up to 4 weeks.

   vi. It might be necessary to perform blood tests to measure the level of thyroid hormones in the patient's blood.

   vii. Jewelry and other metallic accessories should be removed prior to the exam because they may interfere with the procedure.

b) Patients should be fasted for 4 hours prior to and for 1-2 hours after receiving the capsule.

13. DRUG ADMINISTRATION PROCEDURE

a) Pertechnetate

   i. The injection is performed intravenously over a period of a few seconds.

   ii. A small volume of blood is drawn back into the syringe and then re-injected to insure complete delivery of the bone agent.

   iii. Hemostasis is accomplished using a gauze pad and pressure.

   iv. The gauze pad at the injection site is covered with a Band-Aid or tape.

b) I-123 NaI and I-131 NaI

   i. Capsule is taken orally with a cup of water. Patient must remain NPO for at least 1 hour.

14. IMAGING PROTOCOLS

(adapted from Society of Nuclear Medicine Procedure Guideline for Thyroid Uptake Measurement Version 3.0) and is reprinted from http://snmmi.files.cms-plus.com/docs/Thyroid%20Uptake%20Measure%20v3%200.pdf, © SNMMI Inc.

Image Acquisition

a) Normally, a gamma camera equipped with a pinhole collimator is used. Images are acquired in the anterior and often both anterior oblique projections for a minimum of 100,000 counts or 8 minutes, whichever occurs first. The distance between the collimator aperture and the neck should be such that the thyroid occupies most of the field of view. With pinhole collimators, significant geometric distortion occurs. Additional views with a parallel-hole collimator may be useful when searching for ectopic tissue or estimating thyroid size. Collimator choice should be appropriate to the radiopharmaceutical used.

b) With iodine-123, imaging can commence as early as 3 to 4 hours or as long as approximately 24 hours after administration. Diagnostic-quality images can be obtained as long as 36 hours after administration.

c) Following intravenous administration of technetium-99m pertechnetate, imaging should commence 5 to 30 minutes after injection. Radioactive sources or lead markers may be used to identify anatomic landmarks such as the sternal notch and thyroid cartilage. The location of palpable nodules should be confirmed with a radioactive point source or lead marker image for anatomic correlation.

15. MEDICATIONS THAT AFFECT THYROID SCAN QUALITY

The following chart indicates which drugs and foods may interfere with thyroid uptake and may affect image quality**. Source: www.drugs.com/pro/sodium-iodide-i-123.html**

Medication	**Recommended duration of withdrawal**
Adrenocorticosteroids	1 week
Bromides	1 week
Butazolidine	1 week
Mercurials	1 week
Methimazole (Tapazole)	1 week
Nitrates	1 week
Perchlorate	1 week
Propylthiouracil	1 week
Salicylates (large doses)	1 week
Sulfonamides	1 week
Thiocyanate	1 week
Tri-iodothyronine (Cytomel)	2 to 3 weeks
Thyroid extract (Synthroid)	4 weeks
Iodine solution (Lugol's, SSKI)	weeks
Iodine containing foods: iodized salt, dairy products, egg yolks, seafood, turkey, and liver	2 weeks
Iodine-containing antiseptics	weeks
Kelp	4 weeks
Some cough medicines	4 weeks
Some Vitamin preparations	4 weeks
Intravenous contrast agents	1 to 2 months
Oil-based iodinated contrast	3 to 6 months
Amiodarone	3 to 6 months

16. ADVERSE REACTIONS ASSOCIATED WITH RADIOPHARMACEUTICALS USED FOR THYROID IMAGING

a) Although very rare, as stated in all generator package inserts, allergic reactions including anaphylaxis have been reported following the administration of Tc-99m sodium pertechnetate.

b) Although very rare, reactions associated with the administration of I-123 sodium iodide for diagnostic use include, in decreasing order of frequency, nausea, vomiting, chest pain, tachycardia, itching skin, rash and hives.

c) Adverse reactions that have been reported with doses of sodium iodide I-131 used in the treatment of benign disease include sialadenitis, chest pain, tachycardia, iododerma, itching skin, rash, hives, hypothyroidism, hyperthyroidism, thyrotoxic crisis, hypoparathyroidism, and local swelling.

d) Adverse reactions that have been reported with doses of sodium iodide I-131 used in the treatment of malignant disease include radiation sickness, bone marrow depression, anemia, leucopenia, thrombocytopenia, blood dyscrasia, leukemia, solid cancers, lacrimal gland dysfunction, salivary gland dysfunction, congenital hypothyroidism, chromosomal abnormalities, cerebral edema, radiation pneumonitis, and pulmonary fibrosis.

17. CONTRAINDICATIONS

i. To date there are no known contraindications to the use of I-123 Sodium Iodide or Tc-99m pertechnetate except for pregnancy or breastfeeding.

18. INTERNAL RADIATION DOSIMETRY

i. **I-123 and I-131 sodium iodide**: The estimated absorbed radiation doses to several organs of an average patient (70 kg) from oral administration of 400 μCi of I-123 are shown in Table 4 for thyroid uptakes of 5, 15, and 25%. For comparison at these three values of thyroid uptake, the estimated radiation doses from a dose of 100 μCi I-131, also used as thyroid imaging agent, are also included.

Absorbed Radiation Dose Estimates as a Function of Maximum Thyroid Uptake for Sodium Iodide I-123 at Time of Calibration and Expiry Compared to Sodium Iodide I-131*

		Estimated Radiation Absorbed Doses		
		I-123 mGy/14.8 MBq (rads/400 µCi)		I-131 mGy/3.7 MBq (rads/100 µCi)
Target Organ	Maximum Thyroid Uptake (%)	TOC	TOE	
Bladder†	5	1.7 (0.17)	1.7 (0.17)	2.9 (0.29)
	15	1.6 (0.16)	1.6 (0.16)	2.7 (0.27)
	25	1.4 (0.14)	1.5 (0.15)	2.4 (0.24)
Stomach Wall	5	0.96 (0.096)	0.98 (0.098)	1.7 (0.17)
	15	0.89 (0.089)	0.91 (0.091)	1.5 (0.15)
	25	0.82 (0.082)	0.85 (0.085)	1.4 (0.14)
Small Intestine	5	0.70 (0.070)	0.71 (0.071)	1.2 (0.12)
	15	0.65 (0.065)	0.67 (0.067)	1.1 (0.11)
	25	0.60 (0.060)	0.62 (0.062)	0.99 (0.099)
Liver	5	0.089 (0.0089)	0.13 (0.013)	0.16 (0.016)
	15	0.10 (0.010)	0.18 (0.018)	0.28 (0.028)
	25	0.11 (0.011)	0.24 (0.024)	0.41 (0.041)
Ovaries	5	0.18 (0.018)	0.19 (0.019)	0.18 (0.018)
	15	0.17 (0.017)	0.18 (0.018)	0.18 (0.018)
	25	0.16 (0.016)	0.18 (0.018)	0.17 (0.017)
Skeleton	5	0.11 (0.011)	0.16 (0.016)	0.12 (0.012)
	15	0.12 (0.012)	0.18 (0.018)	0.18 (0.018)
	25	0.14 (0.014)	0.21 (0.021)	0.24 (0.024)
Red Marrow	5	0.12 (0.012)	0.16 (0.016)	0.15 (0.015)
	15	0.12 (0.012)	0.18 (0.018)	0.21 (0.021)
	25	0.13 (0.013)	0.19 (0.019)	0.27 (0.027)
Testes	5	0.076 (0.0076)	0.089 (0.0089)	0.12 (0.012)
	15	0.072 (0.0072)	0.087 (0.0087)	0.12 (0.012)
	25	0.068 (0.0068)	0.085 (0.0085)	0.12 (0.012)
Thyroid	5	25 (2.5)	75 (7.5)	260 (26)
	15	77 (7.7)	230 (23)	780 (78)
	25	130 (13)	410 (41)	1300 (130)
Total Body	5	0.11 (0.011)	0.16 (0.016)	0.24 (0.024)
	15	0.14 (0.014)	0.25 (0.025)	0.47 (0.047)
	25	0.17 (0.017)	0.35 (0.035)	0.70 (0.070)

* Concentration at Time of Calibration: 97% I-123, 2.9% I-125, 0.1% Te-121
Concentration at Time of Expiry: 87.2% I-123, 12.4% I-125, 0.4% Te-121
Metabolic model in MIRD Dose Estimate Report 5 followed for I-123 and I-125
Metabolic model in ICRP 30 followed for Te-121

† Bladder voiding interval 4.8 hours.

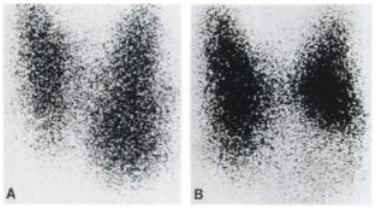
ii. **Sodium pertechnetate**: The estimated absorbed radiation doses2 to an average ADULT patient (70 kg), from an intravenous injection of a maximum dose of 1110.0 MBq, 30 mCi of sodium pertechnetate Tc99m injection distributed uniformly in the total body of subjects not pretreated with blocking agents such as pharmaceutical grade potassium perchlorate, are shown below

Absorbed Radiation Doses (ADULTS) - Intravenous Administration

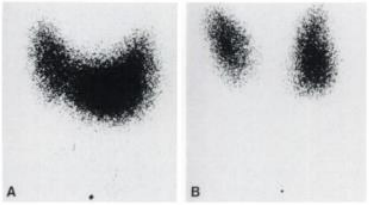
	(mGy/1110.0 MBq)		(mGy/111.0 MBq)
Tissue	Resting Population	Active Population	
Bladder wall	15.9	25.5	
Gastrointestinal tract:			
Stomach wall	75.0	15.3	
Upper large intestine wall	20.4	36.0	
Lower large intestine wall	18.3	33.0	
Red bone marrow	5.7	5.1	
Testes	2.7	2.7	
Ovaries	6.6	9.0	
Thyroid	39.0	39.0	
Brain	4.2	3.6	
Whole body	4.2	3.3	
Placenta			0.5
Fetus			0.5

[2] Modified from: Summary of Current Radiation Dose Estimates to Normal Humans from ^{99m}Tc as Sodium Pertechnetate. MIRD Dose Estimates Report No. 8, *J Nucl Med* 17(1): 74-77, 1976.

IMAGES OF THYROID SCANS



Palpable nodule in the lower part of the left lobe corresponded to an area of apparently normal [^{99m}Tc]pertechnetate concentration (A) but absent ^{123}I concentration (B). Histology: follicular adenoma



Palpable nodule in the isthmus was about equal in function to the remainder of the gland on [^{99m}Tc]pertechnetate scan (A) and cold on ^{123}I scan (B). Histology: follicular adenoma