Endocrine System

14

Neuroectodermal/Norepinephrine Study (I-123-MIBG)

Overview The images of the Neuroectodermal/Norepinephrine Study primarily depict tumors that arise from the embryologic neural crest.

Radiopharmaceutical characteristics Metaiodobenzylguanidine (I-123-MIBG) is an analog of norepinephrine and is taken up by the adrenergic nervous system of tissues that are derived from the neural crest [1]. Its chemical structure is shown in Fig. 14.1. It has a molecular weight of 193.17.

Extraction mechanism I-123-MIBG is actively transported into pheochromocytoma cells and neuroblastoma cells. Once inside of pheochromocytoma cells, most of the tracer is actively transported into secretory granules. On the other hand, once inside neuroblastoma cells, most of the tracer remains in the cytoplasm (Fig. 14.2) [1].

Extraction efficiency The exact extraction efficiency is unknown. However, it is probably relatively low because a suitable lesion to background ratio is not achieved until 24 h after injection.

Extraction mechanism, saturable or non-saturable Saturable. Several classes of substances can compete with I-123-MIBG clearance: tricyclic antidepressants, antihypertensives, sympathetic amines, and cocaine [1].

Interventions None.

Protocol design A gamma camera with a high-resolution low-energy collimator and a computer with SPECT software are used to acquire planar and SPECT images at 24 h, and planar images at 48 h (Fig. 14.3). SPECT-CT can be used instead of SPECT.

Quantitative measurement None.

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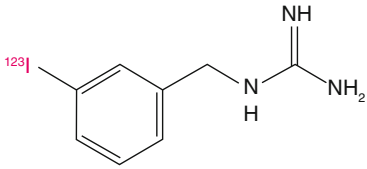
Fig. 14.1 Chemical structure of I-123-MIBG (metaiodobenzylguanidine)



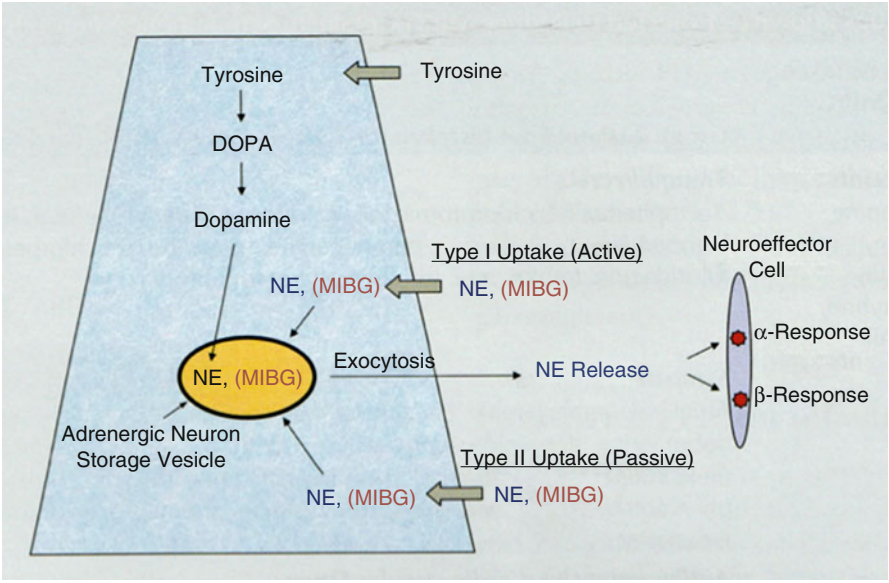


Fig. 14.2 Uptake (clearance) of I-123-MIBG by adrenal medullary cells. I-123-MIBG is mainly taken up into adrenal medullary cells by active transport, but there is also a passive transport pathway (Kowalsky *Radiopharmaceuticals in Nuclear Pharmacy*, p. 601)

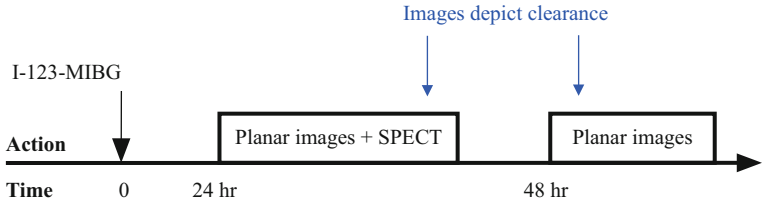


Fig. 14.3 Protocol summary diagram

Parathyroid Study (I-123 and Tc-99m-Sestamibi)

Overview The Parathyroid Study is performed with two radiopharmaceuticals, I-123 and Tc-99m-sestamibi. I-123 localizes only in the thyroid, while Tc-99m-sestamibi localizes in parathyroid adenomas and the adjacent thyroid. The I-123

images of the thyroid are subtracted from the Tc-99m-sestamibi images of thyroid and parathyroid adenoma, resulting in an image containing only the parathyroid adenoma. I-123 and imaging of the thyroid with I-123 are discussed in the next section.

Radiopharmaceutical characteristics The molecular structure of Tc-99m-sestamibi is shown in Fig. 14.4. Tc-99m-sestamibi has a molecular weight of 777.69.

Extraction mechanism Tc-99m-sestamibi (methoxyisobutylisonitrile) is a lipophilic cationic complex that passively diffuses across cell membranes and binds to proteins within the mitochondria. Tc-99m-sestamibi is taken up in parathyroid adenomas probably because there is an increased number of mitochondria in the hyperactive parathyroid cells [2].

Extraction efficiency The exact extraction efficiency of Tc-99m-sestamibi is unknown, but it takes only 15 min to achieve a satisfactory target to background ratio suggesting that the extraction efficiency for Tc-99m-sestamibi is higher than the extraction efficiency for I-123.

Extraction mechanism, saturable or non-saturable Non-saturable.

Interventions None.

Protocol design Imaging is done with a gamma camera fitted with a pinhole collimator and a SPECT-CT machine. All images are obtained with simultaneous

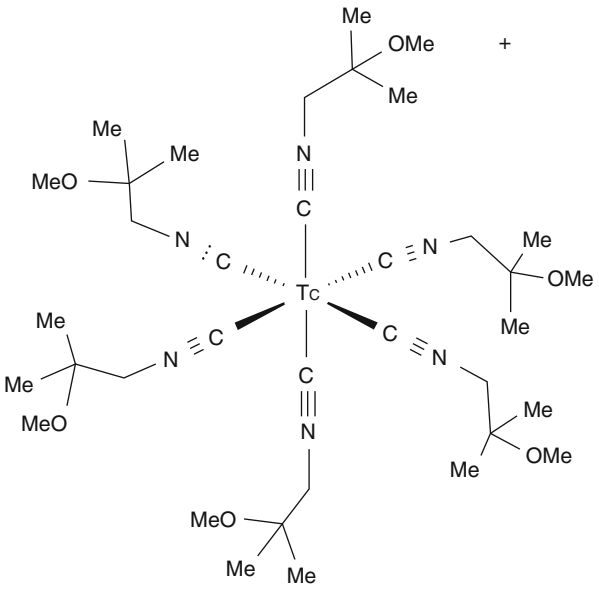


Fig. 14.4 Chemical structure of Tc-99m-sestamibi

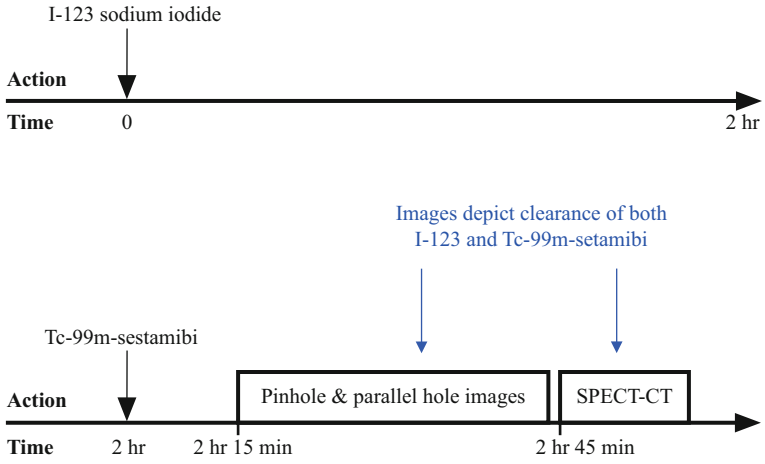


Fig. 14.5 Protocol summary diagram

acquisition of both I-123 and Tc-99m-sestamibi. First, anterior and anterior oblique pinhole images are obtained of the neck, then an anterior parallel hole image is acquired of the neck and upper chest for possible ectopic parathyroid adenomas, and finally SPECT-CT images are obtained of the neck and upper chest (Fig. 14.5).
Quantitative measurement None.

Thyroid Imaging and Uptake Study (I-123)

Overview The Thyroid Imaging and Uptake Study with radioiodine demonstrates the distribution of functioning thyroid tissue, including ectopic tissue, since thyroid tissue is the only tissue that concentrates large amounts of iodine. The uptake (clearance) measures the metabolic activity of the thyroid gland as reflected by the clearance of iodide from the blood into thyroid epithelial cells.
Radiopharmaceutical characteristics I-123 is an anion (I^-) with an atomic weight of 126.90.
Extraction mechanism Circulating iodide is bound to serum proteins, especially albumin. Iodide is cleared from the blood into thyroid epithelial cells as the first step in the synthesis of thyroid hormones.

Iodide clearance is a result of an active transport mechanism mediated by the Na^+/I^- symporter (NIS) protein, which is found in the basolateral membrane of thyroid follicular cells (Figs. 14.5, and 14.6). As a result of this active transport, the iodide concentration inside follicular cells of thyroid tissue is 20–50 times higher than in the plasma. The transport of iodide across the cell membrane is driven by the electrochemical gradient of sodium [3]. Once inside the follicular cells, the

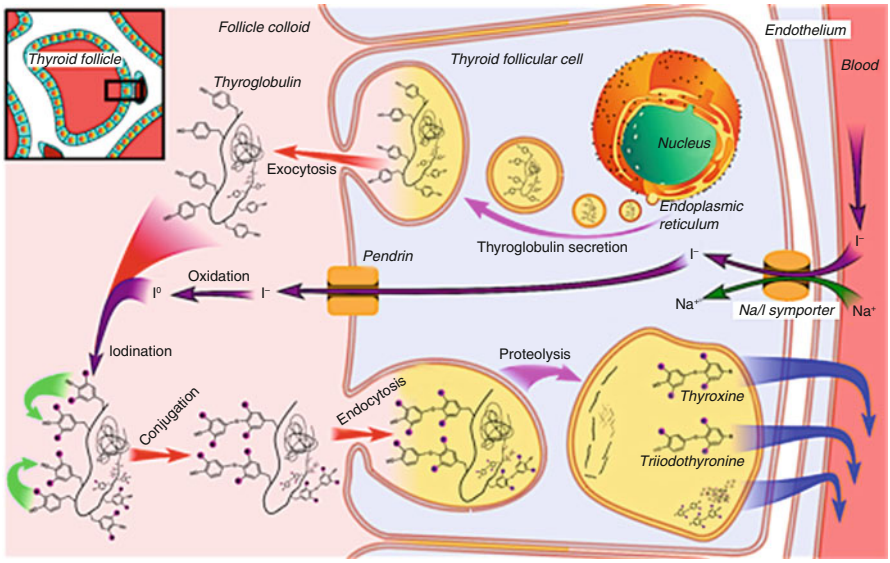


Fig. 14.6 Thyroid hormone synthesis. Of interest, thyroxine is synthesized in the colloid, not in the thyroid epithelial cell (Sodium-iodide symporter Wikipedia)

iodide diffuses to the apical membrane, where it is metabolically oxidized through the action of thyroid peroxidase to iodonium (I^0) which in turn iodinates tyrosine residues on the thyroglobulin proteins in the follicular colloid. Thus, NIS is essential for the synthesis of thyroid hormones (T_3 and T_4).

Extraction efficiency The normal extraction efficiency of I-123 is unknown, but it takes several hours to achieve an optimal target to background ratio.

The extraction efficiency is significantly decreased by the antithyroid medications propylthiouracil (PTU) and methimazole. These medications decrease the net thyroid uptake or clearance of iodide by inhibiting the enzyme thyroperoxidase, which normally oxidizes the anion iodide (I^-) to iodine (I^0) as part of thyroid hormone synthesis. While inhibition of thyroperoxidase does not affect the initial uptake or clearance of iodide NIS, it does significantly decrease the retention of iodide.

The uptake and clearance of iodide is greatly affected by the thyroid-stimulating hormone (TSH). TSH is synthesized in the anterior pituitary and released into the blood. In the thyroid, the TSH binds to the TSH receptor on the cell membrane of the thyroid epithelial cell and initiates an intracellular chain of actions that modulates thyroidal gene expression and iodide uptake [4].

Extraction mechanism, saturable or non-saturable Saturable. The most common source of competing anionic iodide is CT intravenous contrast. Other much less common sources of iodide are amiodarone and kelp.

Interventions None.

Protocol design Initially, the I-123 capsules are placed in a lucite neck phantom. A scintillation probe is used to measure the amount of activity in the phantom (see Chap. 9: Quantitation of Function: Absolute Measurements). The phantom simulates the photon attenuation that will subsequently occur in the patient's neck. The I-123 capsules are then removed from the phantom and administered to the patient. Six hours later, the scintillation probe is used to measure the activity in the thyroid within the patient's neck and in a thigh. The thigh measurement simulates the background activity in the patient's neck. Anterior and anterior oblique images are then acquired of the thyroid with a gamma camera fitted with a pinhole collimator (Fig. 14.7).

Quantitative measurement – Thyroid uptake (clearance) The measurement of thyroid clearance or uptake of iodide is an example of absolute quantification (see Chap. 9: Quantitation of Function: Absolute Measurements). The amount of radioactivity in the I-123 capsules is determined in a dosimeter. Then the capsules are placed in the neck phantom. The phantom simulates the attenuation that occurs between the thyroid gland and the anterior surface of the neck, and the background activity in the neck is simulated by the amount of radioactivity in the soft tissues of the lower thigh. There is no background radioactivity in the phantom.

A scintillation probe is positioned perpendicular to the phantom with the positioning bar directly over the capsule within the phantom. The scintillation crystal will be at a standard distance from the phantom, usually 25 cm [4]. The capsules are immediately administered to the patient. At 6 h, the probe is positioned anterior to the patient's neck with the positioning bar perpendicular to the neck and with the bar centered halfway between the thyroid cartilage and the suprasternal notch. The goal is to have the probe positioned relative to the thyroid with the same geometry that was used to position the probe relative to the capsule in the phantom.

Then, the probe is positioned over the thigh for the 6 h "background" measurement. It is assumed that the diameter and density of the thigh is roughly the same as

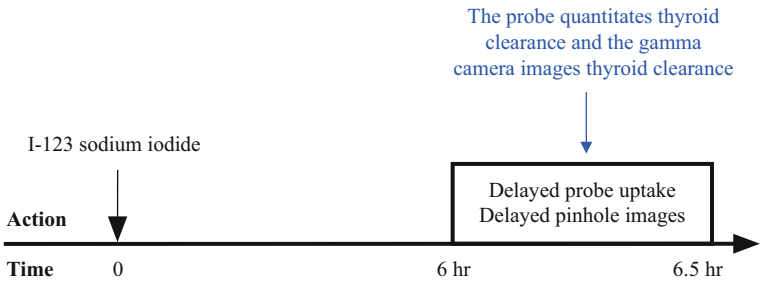


Fig. 14.7 Protocol summary diagram

the neck. The positioning bar should be perpendicular to the thigh with the bar centered just above the knee. The patient should void before counting over the thigh, and the bladder must be clearly outside of the field of view (see Thyroid Uptake worksheet below).

In general, the thyroid measurement can be done only at 6 h. The availability of an accurate thyroid-stimulating hormone blood test and the current practice of administering enough I-131 to make patients with hyperthyroidism from Graves disease hypothyroid makes measurement of thyroid turnover of iodide unnecessary. In addition, in patients with Graves disease, this approach also allows thyroid imaging with I-123, measurement of thyroid uptake with I-123, and treatment of the Graves disease with I-131 all in 1 day.

Quantitative measurement – Normal range There is no recent determination of the normal range of I-123 uptake (clearance) by the thyroid at 6 h. The lack of current data is unfortunate since factors such as the amount of iodine in the diet affect uptake measurements and dietary iodine may change over time. Various determinations of the normal range from the past are given in the references below [5–9].

Thyroid Metastases Study (I-123 and I-131)

Overview The Thyroid Metastases Study, with either I-123 or I-131 radioiodine, demonstrates the distribution of functioning thyroid tissue, both residual normal tissue in the thyroid bed and functioning metastases throughout the body.

Radiopharmaceutical characteristics I-123 is an anion (I^-) with an atomic weight of 122.90. I-131 is an anion (I^-) with an atomic weight of 130.90.

Extraction mechanism See discussion and figure above for Thyroid Imaging and Uptake Study.

Extraction efficiency See discussion and figure above for Thyroid Imaging and Uptake Study.

Extraction mechanism, saturable or non-saturable See discussion and figure above for Thyroid Imaging and Uptake Study.

Interventions None.

Protocol design The patient drinks water to clear any radioactive iodine from the esophagus. Images are acquired with a gamma camera fitted with either a low-energy high-resolution collimator for I-123 or a high-energy collimator for I-131. At 24 h after administration of I-123 and 7–10 days after administration of I-131, anterior and posterior images are acquired from the top of the head to the lower thighs using a whole body technique. Then a high-count anterior image of the neck is acquired with pinhole collimator (Fig. 14.8).

Quantitative measurement In general, none. A few institutions perform occasional I-131whole body dosimetry studies [10–12].

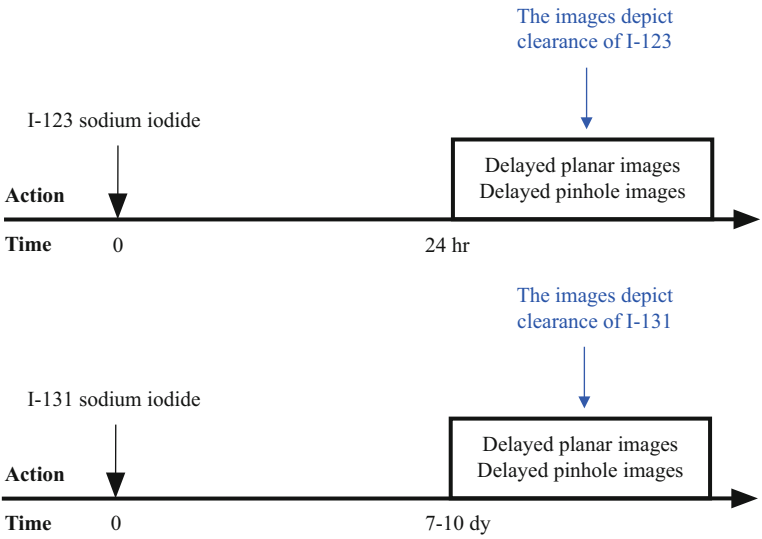


Fig. 14.8 Protocol summary diagram

Thyroid Uptake Worksheet

Nuclear Medicine Department

Institution_____

Name_____ ID_____ Age_____ Sex_____

Referring physician_____ Date_____

Zero Hour (time_____)

	counts per minute
Dose in phantom (standard)	
Background (air)	-
Net (standard)	

6 Hour Uptake (time_____)

	counts per minute
Neck	
Thigh (background)	-
Net	

	counts per minute
Standard at zero time	
Decay correction factor	x
Corrected standard	

6 hour uptake = (net neck cpm / corrected standard cpm) × 100% = _____%

• Normal Range: 6 hours = _____ to _____% •

Technologist_____

References

Neuroectodermal/Norepinephrine Study (I-123-MIBG)

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Thyroid Metastases Study (I-123 & I-131)

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