Lecture 5 Nuclear medicine in thyroid and parathyroid



Slides

xplanation

Notes

Additions

Important

Objectives

•How is the thyroid scan performed?

•When is thyroid scanning helpful?

•What is significant about whether a nodule is "hot" or "cold?"

•What is the role of nuclear medicine in the treatment of thyroid disorders?

• Describe the physiologic principles of underlying Tc-99m parathyroid scintigraphy .

• Describe the various methods used for parathyroid scintigraphy with emphasis on SPECT and SPECT /CT.

• Identify the common imaging features of pathologic parathyroid glands.

• Discuss causes of false negative and false positive scans.

Thyroid Scan : Procedure

Additional notes, just to make a concept !

What is Thyroid scan\uptake?

- Thyroid scans and uptake tests use special chemicals called radionuclides. A radionuclide (sometimes called a radioisotope or isotope) is a chemical which emits a type of radioactivity called gamma rays. In these tests a tiny amount of radionuclide is put into your body, usually by an injection into a vein ex. Tc-99m
 Pertechnetate. (Sometimes it is swallowed, depending on the test. This is usually for an uptake test. exl-123.)
- Cells which are most active in the target tissue or organ will take up more of the radionuclide. So, active parts of the tissue will emit more gamma rays than less active or inactive parts.
- For example, areas of the target organ or tissue which emit <u>lots of gamma rays</u> may be shown as **red (or dark black) spots ('hot spots')** on the picture on the computer monitor. Areas which emit <u>low levels of gamma rays</u> may be shown as blue (or gray to no color, just empty) spots ('cold spots'). Various other colours may be used for in-between levels of gamma rays emitted.
- Doctors may use the term 'thyroid scan (sometimes, thyroid image) ' to mean a test that includes a scan of your thyroid structure and a test of how well your thyroid works. In a thyroid scan doctors are generally looking at the size, shape and structure of the thyroid gland. A thyroid uptake test checks how well the gland is working. Both tests are based on the same principles and use the same equipment, just in slightly different ways.

Doctor explained this table briefly <i>Important notes = red</i>		
\bigstar	Tc-99m Pertechnetate (always start with tc-99)	I-123
Dose Doses are not important	0.5-4.0 mCi given IV	0.5 mCi <u>orally</u>
Half Life	6 Hours (shorter half life; Better)	13 Hours(longer)
Cost	Not Expensive (Generator)	Expensive (Cyclotrone)
Time of imaging	20 min <u>post</u> <u>injection</u> (one time imaging; shorter procedure)	6 and 24 hours post ingestion
Remarks	<u>Trapped</u> not organified	<u>Trapped</u> and organified (better)

Thyroid Scan : Procedure

We can do thyroid scan using one of two radiopharmaceuticals either Tc-99m Pertechnetate or I-123

Patient Preparation:

- The patient must be off thyroid hormones :
 - 1. Thyroxine (T-4) for at least 3-4 weeks.
 - 2. Triiodothyronine (T-3) for at least 10 days.
 - 3. Any food that contains high iodine ex. Fish , cabbage (Because they interfere with thyroid uptake)

***** The patient **must not** be taking antithyroid medications:

1. Propylthiouracil (PTU) and tapazole for at least 3-5 days.

* The patient must not have had intravenous or intrathecal iodinated contrast agents

1.(IVP, CT with contrast, myelogram, angiogram) for at least 3 weeks.

- Why? Because they will block the thyroid and not allowed tc99m or I-123 to go to the thyroid

Radiopharmaceutical and dose: Doses are not important

Tc-99m as sodium pertechnetate 0.5 -4.0 mCi given Intravenously.

OR

I-123 Sodium Iodide 0.5 mCi orally.

Gamma camera: Small or large field of view.

Patient position: Supine with chin tilted up.

Imaging:

20 min. post injection of Tc99 m : ANT, LAO and RAO images obtained.6 and 24 hours post oral dose for I123 : ANT, LAO and RAO images obtained.

ANT: AnteriorLAO: Left anterior obliqueRAO: Right anterior oblique

Doctor said: not be asked about preparation in the exam, but read it :)







Normal Tc-99m Thyroid Scan

Normal Values Of Thyroid Uptake: 1)Tc- 99m Uptake (20 min Uptake) : 0.5 - 4 .0%. (when the thyroid uptake 0.5-4.0% of the given dose this means normal thyroid function) 2)I131 OR I-123 RAIU (4-6 & 24 hours) : Normal 4-6 hours RAIU : 5 - 15%

Normal 24 hour RAIU : 8 - 35%

If more than these values, that means the gland is hyperactive.





Thyroid uptake measurement (I-123 Sodium Iodide)

<u>The thyroid uptake measurement:</u> measures the metabolic activity of the thyroid gland as reflected by **its extraction of iodine from the blood.**

Indications:

- 1) Diagnosis of Grave's disease.
- 2) Evaluation of subacute and chronic thyroiditis.
- 3) Thyroid cancer.

Patient preparation: same as before slide(Slide no.4) +Other agents may interfere, but usually only to a small extent + NPO (nothing per oral) 2-4 hours

before and for at least 1 hour after ingestion the radiopharmaceutical.

Thyroid uptake measurement with/without imaging (I-123 Sodium Iodide)

Equipment :

- -Uptake only : Uptake probe (single crystal probe with flat field collimator). -Imaging plus uptake studies: Gamma camera.
- **<u>Radiopharmaceutical :</u>** dose given **orally**
- -Imaging plus uptake studies: I-123: 500 μ Ci .
- -Uptake study only: I-123: 100 µ Ci

Thyroid uptake measurements may be determined <u>using Tc-99m-pertechnetate (I.V)</u>

Patient position: Sitting.

Detector field of view: Neck.





 Any agents that inhibit the thyroid gland should be stopped 3 weeks before the scan.

THYROID UPTAKE MEASUREMENT WITHOUT IMAGING

Acquisition Protocol:

- Place I123 capsule(s) in neck phantom.
- Acquire counts for 1 minute, record the counts, time of acquisition, and time of day on the thyroid Uptake Worksheet.
- Immediately administer the capsule(s) to the patient.
- At 6 hours position the probe in front of the patient's neck .
- Acquire counts for 1 minute for I-123 and record the counts, time of acquisition, and time of day on the Worksheet.
- Position the probe over the thigh for 6 hour "background" measurement.
- Acquire counts for 1 minute for I-123 and for 2 minutes for I-131; record the counts, time of acquisition, and time of day on the Worksheet.
- Using the Thyroid Uptake Worksheet, calculate the 6 hour thyroid uptakes.

Remember to correct the standard counts for decay.

Twenty four hour uptake measurement in the same way as the 6 hours.

<u>The doctor said it is not</u> <u>important and doesn't</u> <u>mention anything of these.</u>

<u>SKIP IT *_^</u>

Causes of High Thyroid Uptake

- Hyperthyroidism : Grave's Disease or TSH-secreting pituitary adenoma.
- Autonomous toxic nodule.
- Multinodular toxic goiter (Plumer's Disease).
- Enzyme defects : Dyshormonogenesis.
- Iodine starvation (Iodine deficiency) "lack of iodine in diet"
- Lithium Therapy .
- Recovery phase of thyroiditis.
- Rebound following abrupt withdrawal of antithyroid medications.

The gland needs to <u>uptake every single iodine</u> in the blood to make more thyroid hormone. => Increase uptake of iodine from blood.



Causes of Low Thyroid Uptake



- Parenchymal Destruction: Acute, Subacute and Chronic Lymphocytic Thyroiditis.
- Hypothyroidism:

1) Primary or Secondary (insufficient pituitary TSH secretion).

2)Surgical(Thyroidectomy)/Radioiodine Ablation of Thyroid.

Blocked Trapping:

 1)Iodine load (most common): Iodinated contrast material, Food rich in iodide: fish , cabbage ,...etc.
 2)Exogenous thyroid hormone replacement depressing TSH levels (thyrotoxicosis factitia) .
 3)Ectopic thyroid: Struma Ovarii.

Blocked Organification:

1)Antithyroid medication (PTU): Note- Tc-99m uptake should not be affected.





THYROID METASTASES STUDY (I-123 or I-131 as Sodium Iodide)

I-131 use usually for therapy, but could be used as diagnostic if there is no I-123 available.

Indications:

Detection and localization of persistent or recurrent functioning thyroid cancer.

Patient Preparation:

• Stimulation of potentially functioning thyroid tissue:

A. Inject recombinant human thyrotropin on 2 consecutive days and administer the radiopharmaceutical on the third day .

- B. Withdraw thyroid replacement hormones :
- 1. Thyroxine (T-4) for at least 4 weeks.
- 2. Triiodothyronine (T-3) for at least 10 days.

• The patient must not have had i.v iodinated contrast material (IVP, CT with contrast, myelogram, angiogram) for at least 3 weeks .

• The patient should be NPO for at least 4 hours prior to radiopharmaceutical administration and for at least 1 hour afterwards.

Radiopharmaceutical, Dose, & Technique of Administration:

- Radiopharmaceutical: Oral administration
- a. I-123 as sodium iodide : 2 mCi

OR

b. I-131 as sodium iodide : 2-10 mCi

Imaging using Gamma camera : Whole body scan (WBS)

I-123 or I-131 Whole Body Scan(WBS) Anterior Posterior view view Iodine uptake in salivary glands, several ribs and left humerus ANT Bone Metastases Abnormal uptake Marker: Injection site at dorsum of right hand **Negative WBS**(post thyroidectomy) any area outside these normal Lung Metastases physiological area will be considered abnormal

I-123 or I-131 Whole Body Scan(WBS)

Planar Vs SPECT-CT

(To tell where are the location of these remnant)

Planer image showing multiple remnants in the neck and submandibular area

This patient is postoperative which supposed there is no uptake of iodine in the neck (the thyroid is removed!). Which means these is **local recurrence**



SPECT CT is very important to determine the exact location of the abnormality

Remnant in thyroglossal cyst

When is thyroid scanning helpful?

Indications for Thyroid Scan:

- 1. Evaluation of thyroid nodules : No. & type
- 2. Evaluation of congenital hypothyroidism : Agenesis Vs. Dyshormonogenesis.
- 3. Evaluation of neck masses : ectopic thyroid, thyroglossal cyst.
- 4. Evaluation of thyrotoxicosis.

For Your knowledge (FYK) ③

<u>Terms:</u>

Agenesis: There is no thyroid gland (congenital)

Dyshormonogenesis: Genetic defects in the synthesis of thyroid hormones.

Ectopic thyroid: The presence of thyroid tissue in locations other than the normal site.

Thyroglossal cyst: Irregular neck mass or a lump which had developed from cells and tissues left over after the formation of the thyroid gland during developmental stages.

Thyrotoxicosis: Excess of thyroid hormone in the body.

Evaluation of thyroid nodules Single vs MNG (multinodular goiter)

Solitary cold nodule



Multinodular goiter



The chance of malignancy is more in <u>Solitary</u> cold nodule than in Multinodular goiter about 15-20 %

1) Evaluation of thyroid nodules : Hot VS Cold VS Warm







The difference between Hot and warm nodules is in warm ,we can see the rest and contralateral lobe.

Warm nodule => proceed to I123 to exclude discordance nodules

(Follow up is necessary)

Discordance Tc –I123 Scan

The chance of malignancy of a discordant nodule **about 20%**

There is the occasional problem of discordant nodules when using Tc-99m (tumors may be hot (or warm) on Tc-99m, cold on I-123).



2) Evaluation of congenital hypothyroidism Agenesis vs Dyshormonogenesis



I-123 Perchlorate Discharge Test

Minutes



3) Evaluation of neck masses Ectopic thyroid vs Thyroglossal cyst





Lingual thyroid





Thyroglossal cyst

Lingual thyroid : Do thyroid scan before remove it . Thyroglossal cyst usually surgical removed.



Perchlorate Discharge Test

- 50 80 uCi I¹²³ orally.
- RAIU/ 15 min for 2 hrs.
- Positive test : >= 15 fall of RAIU below 2 hrs. uptake.

4) Evaluation of Thyrotoxicosis

- Thyrotoxicosis IS NOT synonymous to Hyperthyroidism
- Thyrotoxicosis: Is a complex of signs and symptoms due to elevated thyroid hormones in the blood
- Hyperthyroidism : Overproduction of thyroid hormones
 by the thyroid gland (hyperactive gland)

Thyrotoxicosis with hyperthyroidism

Causes:

1) Graves' Disease .

2)Neonatal hyperthyroidism.

3)Toxic nodular goiter :

#MNTG or Plummers disease

#ATN or toxic adenoma

4)Iodine induced (Jod-Basedow disease) 5)Rare causes :

#Execssive HCG by trophoblastic tumor . #Hypothalamic pituitary neoplasms (TSH induced) Management : Treat underlying cause .

MNTG: MultiNodular Toxic Goiter ATN: Autonomic Toxic Nodule





MNTG (Plummers Disease)

\bigstar

Evaluation of Thyrotoxicosis : Thyrotoxicosis with hyperthyroidism





ATN

- Very hot nodule.
- the rest of the gland are not seen.
- Autonomic: not dependence on TSH.
- It releases its hormone without the need of TSH.
- The best case for lodine therapy .

4)Evaluation of Thyrotoxicosis

Thyrotoxicosis without hyperthyroidism

Causes:

- 1. Subacute thyroiditis.
- 2. Chronic thyroiditis with transient thyrotoxicosis
- 3. Thyrotoxicosis factitia (Exogenous hormone).
- 4. Thyroid extract (e.g.Hamburger thyrotoxicosis)
- 5. Ectopic thyroid :
- Metastatic thyroid carcinoma
- Struma ovary

Management : Symptomatic treatment



Radioactive Iodine Therapy for Hyperthyroidism

<u>Isotope used : I131 (I131 Treatment | I123 diagnoses)</u> <u>Physical Properties:</u> Solution or capsule

Main side effect : <u>Hypo</u>thyroidism

Dose :

a. Calculated : Considering weight and uptake of the gland
b. Empirical : Graves: 5-15 mCi
ATN : 15-20 mCi

Radioactive Iodine Therapy for Thyroid Cancer

Isotope used : [131

Physical Properties: Solution or capsule

Thyroid remnant : 80-100 mCi

Lymph Node Metastasis : 100 mCi Local Recurrence : 100 mCi Lung Metastasis : 150 mCi Bone Metastasis : 200 mCi

Increase

dose

Parathyroid Scan

Normal and Ectopic Parathyroid Glands

Normal parathyroid:

- The <u>third pair</u> of pouches: proliferates into the <u>inferior</u> parathyroid glands and the thymus.
- The <u>fourth pair</u> of pouches: proliferates into the <u>superior</u> parathyroid glands and the lateral analge of the thyroid gland.
- Because the inferior parathyroid glands undergo more extensive migration during embryogenesis, they are more likely to be found in ectopic locations.

Location of an ectopic parathyroid glands:

- 1. Submandibular
- 2. Retropharyngeal
- 3. Retroesophageal
- 4. Posterosuperior mediastinal
- 5. Intrathyroidal
- 6. Within the tracheoesophageal groove Carotid sheath
- 7. Thyrothymic ligament
- 8. Intrathymic (Antero-superior mediastinal)

Aberrant parathyroid gland III Parathyroid gland IV Lateral lobe of thyroid gland Parathyroid gland III Parathyroid gland III Aberrant parathyroid gland III Figure 13.10. Normal and aberrant distribution of the parathyroid glands.

Normal parathyroid can't be seen in the scan.

The aim of this scan is to detect:

1- Ectopic Parathyroid.

3- Enlarged parathyroid.

2- Adenoma.



Parathyroid Scan Techniques

- TL-201 _ Tc-99m subtraction
- Tc-99m Sestamibi (Dual Phase) Gold standard
- Tc-99m Tetrofosmin (Dual Phase)



adiopharmaceutical	99mTc / 201Tl Subtraction	99mTc sestamibi
ctivity administered	80 MBq (2 mCi) 201 <mark>Tl</mark> ; 370 MBq (10 mCi) 99m <mark>Tc</mark>	925 MBq (25 mCi)
mages acquired	Inject Tl .rst and acquire 15- min 100 000 count view of neck and mediastinum. Then acquire similar Tc images without moving patient. Subtract Tc data from Tl after normalization to equal count densities	Anterior (and oblique) views at 15 min and at 2– 3 h post injection s; SPECT as needed

Parathyroid imaging

PARATHYROID IMAGING

Tc-99m-Sestamibi

The Parathyroid Study depicts hypertrophied parathyroid tissue, probably because of uptake of Tc-99m-sestamibi in the mitochondria of hyperactive cells.

Indications : Detect and localize parathyroid adenomas .

Patient Preparation :None.

Radiopharmaceutical, Dose, & Technique of Administration:

- Radiopharmaceutical: 25 mCi Tc-99m-sestamibi i.v.
- **Patient position:** Supine with head and neck extended and immobilized.
- Gamma camera Imaging field:
 - 1. Neck.
 - 2. Upper two thirds of the mediastinum.

Acquire images <u>at 15 minutes</u> and <u>2-3 hours</u> post injection. <u>SPECT/SPECT CT images improves localization</u>.

• TI – Tc99m subtraction : Several protocols have been developed for routine subtraction of thyroid tissue from parathyroid tissue

Parathyroid Scan Dual phase MIBI Scan (Or Tetrofosmin)

Diagnosis of parathyroid is Mainly made by Blood level of Vitamin D, calcium and PTH. Parathyroid scan is for localization of the adenoma or hyperplasia (NOT diagnosis)





Abnormal parathyroid glands could be visualized

Parathyroid Scan Tc-Tl Subtraction Scan



- 1. First give thalium which uptaken by Thyroid and para-.
- 2. Then give Technetium which uptake only by thyroid.
- 3. After this, we subtract thyroid image from thyroid & para- then have the last para- image

Parathyroid Scan Sestamibi dual phase





Dual phase Technique:

 We inject the sestamibi -- it will go to the thyroid and abnormal parathyroid. (Early phase)
 After 2 hours we take another image. The remnants will represent the abnormal parathyroid. (Late phase).

Sestamibi Dual Phase (Planar vs SPECT CT)



Parathyroid Scan Ectopic Parathyroid : 16% of total adenomas



5MIN A FULL

PARATHYROID MIBI





Date:12/06/1426 ק Time:12:49:29 NR:1:831769

Ectopic Parathyroid in upper mediastinum

We noticed an abnormality => **do SPECT**

CT (to localize it)

Ectopic Parathyroid Adenoma PLANAR vs SPECT/CT

The adenoma is located near the arch of aorta







SPECT-CT images accurately localize the adenoma and guide the surgeon to the best surgical approach

Ectopic parathyroid adenoma Antero-superior mediastinum



Sestamibi Parathyroid Scan Result



True positive (TP): All test is positive.



False negative (FN): The lab test is <u>positive</u>, but the parathyroid scan show negative result. Why false negative??!

Parathyroid Cells



Normal parathyroid glands **comprise 2 cell types: i. Chief cells**: responsible for PTH production **ii.Oxyphil cells**: eosinophilic cells whose cytoplasm is composed <u>almost entirely of mitochondria.</u>

While the normal oxyphil cell does not synthesize and secrete PTH, the oxyphil cells of pathologic parathyroid glands do secrete the hormone.

What is the cause of the FN result ? Mechanism of sestamibi uptake

Sestamibi goes mainly to mitochondoria

Mechanism of Sestamibi uptake

SESTAMIBI : METHOXYISOBUTYLISONITRILE

- Its parathyroid uptake was first reported by Coakley et al. in 1989
- Mechanism of MIBI uptake and retention is still unclear.

Multifactors have been proposed:

A. Biochemical properties of the tracer :

Lipophilicity : The lipophilic sestamibi molecule is concentrated by mitochondria. This explains why adenomas with an abundance of mitochondrial-rich oxyphil cells <u>retain</u> the sestamibi (Cationic charge) B. Cell Type : A predominance of <u>oxyphil cells</u> within an adenoma is more likely to lead to a positive scan.

<u>C. Local factors:</u> blood flow, trans-capillary exchange, interstitial transport and negative intracellular charge of both mitochondria and membranes.

Cell Type and Scan Result



Parathyroid adenoma composed entirely of <u>glycogen-rich chief cells</u>. (False Negative) Parathyroid adenoma composed mainly of <u>mitochondrial-rich oxyphil</u> <u>cells.</u> (True positive)

FN Sestamibi Scan

Q:What is the cause of the FN result ? Mechanism of sestamibi uptake

- **Histologic type :** False-negative scans can occur with parathyroid glands containing predominantly clear (chief) cells.(Main cause)
- Size and Location: Smaller-volume parathyroid adenomas and those in the upper position are less likely to be localized with sestamibi scans.
- Number of adenomas: FN rate is increased with MGD compared with patients with a single adenoma .
- **Decreased tracer concentration :** Possible association.
 - a. P-glycoprotein expression
 - b. Multidrug resistance-related protein expression
- Variability of radiotracer uptake in parathyroid adenomas: Related to differences in perfusion and metabolic activity

Even with refinements in sestamibi scanning, the fact that all parathyroid adenomas are not created equal on a cellular level may inevitably lead to FN scans in a certain number of cases.

False-Positive Scintigraphic Findings

- Solitary thyroid adenoma or a multinodular goiter
- Benign or malignant tumors : breast, lung, and head and neck carcinomas and their lymph node and osseous metastases, as well as bronchial carcinoids.
- Primary thyroid lymphomas.
- Cervical L.N. metastasis from PTC carcinoma
- Reactive lymph nodes
- Remnant thymus
- PTH-secreting paraganglioma
- Enlarged submandibular salivary gland .
- In the clinical setting of hyperparathyroidism, falsepositive findings are uncommon.

Points To Remember Before Proceeding For Parathyroid Imaging

- Imaging is not for diagnosis: High Ca and PTH establish the diagnosis (Markers are for diagnosis)
- Imaging does not identify normal parathyroids: These are too small to be seen (20-30mg)
- Imaging <u>should detect</u> abnormal parathyroid(s) and indicate the approximate size and the precise relationship to the thyroid gland: lateral, SPECT and SPECT /CT
- Imaging <u>should identify</u> ectopic glands : SPECT and SPECT/CT
- Optimal imaging should be able to <u>differentiate</u> patients with single adenoma from those with MGD
- Imaging should identify <u>thyroid nodules</u> which may require concurrent surgical resection.

Note:

- When lodine is trapped by the thyroid gland thyroid hormones are synthesized, then it would be organified to form Thyroxine. In Tc- 99m it is not organified so when there is problem in organification, we can't use it. To assess the organification we use I-123.
- In case of Dyshormonogenesis gland will be under active but uptake is high because thyroid trapping iodine so cant produce thyroid hormones
- Iodine WBS is used to asses any thyroid remnant or distance metastasis.
- Cold nodule is very suspicious malignancy and chance to be malignant is 15%-20% depend on patient gender.
- For precise localization of parathyroid adenoma use SPECT CT (for surgical approach)
- If adenoma drives from Chief cell > FN result
- If adenoma drives from Oxyfill cell > TP result
- Tc- 99m > thyroid only
- Tl > Thyroid and parathyroid
- To treat hyperthyroidism (3 modalities) :
- 1) Medical (Antithyroid).
- 2) Surgical.
- 3) Radioactive iodine.
- I 131 is used in therapy NOT I123.
- Size of adenoma :
- <2 cm = Can see in planer image.
- <1 cm = Can see in SPECT CT .
- High thyroid uptake doesn't mean hyperactive gland
- Thyrotoxicosis :
- 1) With hyperthyroidism > need definitive treatment .
- 2) Without hyperthyroidism > need symptomatic treatment until it goes to normal (in case of sub acute thyroiditis).
- As the number of nodules increase, the chance of malignancy decrease.
- I 123 OR I131 > evaluate patient with thyroid cancer.
- Parathyroid imaging needs combination of several modalities. Sestamibi and MRI are the best combination.
- Radiotracer measuring unit is curie (Ci).
- TSH tests are routinely ordered for newborns as part of the screening program to evaluate how well the thyroid gland is working. If TSH is high we want to know if there is thyroid or not so we do thyroid scan (we don't use US because we can't see the base of the tongue in case of ectopic thyroid in the base as well it can not evaluate the function)
- Perchlorate discharge test is used to confirm dyshormonogesis.
- Parathyroid scan results depends on the histological type of adenoma.
- Normal parathyroid scan doesn't exclude parathyroid adenoma.

Thank You!

We hope you found this helpful and informative.

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