Diagnostic Imaging Pathways - Primary Hyperparathyroidism (Primary Suspected)

Population Covered By The Guidance

This pathway provides guidance on the imaging of adult patients with suspected hyperparathyroidism.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points. Clicking on the PINK text box will bring up the full text.

The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

<table>
<thead>
<tr>
<th>SYMBOL</th>
<th>RRL</th>
<th>EFFECTIVE DOSE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Minimal</td>
<td>&lt; 1 millisieverts</td>
<td>1-5 mSv</td>
</tr>
<tr>
<td>Low</td>
<td>5-10 mSv</td>
<td>&gt;10 mSv</td>
</tr>
</tbody>
</table>

Pathway Diagram
INVESTIGATION OF PRIMARY HYPERPARATHYROIDISM

Is unilateral parathyroid or minimally invasive surgery being considered?

No

Bilateral neck surgical exploration ± intraoperative US

Yes

Sestamibi Scan ± Subtraction 99mTc-Pertechnetate Scan
• Ultrasound of the neck

Surgery

In selected patients, consider CT or MRI

Recurrent hyperparathyroidism

• Reconfirm hyperparathyroidism
• Review indications for repeat surgery

Sestamibi positive in chest?

No

Both US and Sestamibi negative

Consider CT, MRI or selective venous sampling

US or Sestamibi positive in neck

CT or MRI

Yes

Surgery
**Image Gallery**

*Note: These images open in a new page*

1. **Parathyroid Adenoma**
   
   Image 1 (Ultrasound): A well circumscribed hypoechoic mass measuring up to 8mm is located deep to the inferior left thyroid pole. The appearances are consistent with a parathyroid adenoma.

2a. **Parathyroid Adenoma**
   
   Image 2a, 2b (Pertechnetate and Sestamibi Study), and 2c (SPECT): Initial pertechnetate images show uniform tracer distribution throughout both thyroid lobes apart from a small focal area of increased tracer uptake at the inferior pole of the left lobe of the thyroid gland.

2b. **Parathyroid Adenoma**
   
   MIBI early and delayed images show increased uptake in the left and right lower poles of the thyroid. On subtraction images, there is an area of increased tracer activity near the inferior pole of the left lobe of the thyroid gland which represents abnormal parathyroid tissue (arrow).

2c. **SPECT**
   
   SPECT is used to help anatomically define the abnormal area.

3. **Parathyroid Adenoma**
   
   Image 3 (H&E, x2.5): Histological section of a parathyroid adenoma showing sheets of monotonous oncocytic cells (blue arrows) and chief cells (green arrows) with no adipose tissue.

**Teaching Points**

- Imaging for preoperative localisation of the parathyroid glands remains controversial although it is generally recommended for minimally invasive or unilateral neck surgery.
- Ultrasound and Sestamibi scans are sensitive methods used as first line investigations, frequently in combination.
- CT and MRI have the advantage of superior anatomical localisation but are usually reserved for equivocal or negative ultrasound and nuclear medicine studies.
- Preoperative imaging is required for recurrent or persistent hyperparathyroidism to minimise the...
Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) of the Mediastinum

- CT and MRI of the neck and mediastinum are generally considered second line investigations in the assessment of primary hyperparathyroidism, following on from equivocal or negative ultrasound or nuclear medicine studies. The main advantage is superior spatial resolution and the detailed anatomical localisation of ectopic mediastinal lesions for surgical planning.
- The sensitivity of CT for preoperative localisation of abnormal parathyroid tissue ranges from 78% to 86%.
- MRI demonstrates similar sensitivity ranging from 71% to 92%.
- These modalities are particularly useful for persistent or recurrent hyperparathyroidism when more detailed surgical planning is required to minimise the risks associated with repeat surgery and to improve the chances of successful treatment.
- The disadvantages of these studies include:
  - Exposure to ionising radiation with CT
  - The use of intravenous contrast

Primary Hyperparathyroidism

- Primary hyperparathyroidism is an endocrine disorder resulting from the autonomous functioning of one or more parathyroid glands.
- The causes of primary hyperparathyroidism include a single parathyroid adenoma (80-85%), parathyroid hyperplasia (10-15%), multiple adenomas (2-3%), and very rarely, parathyroid adenocarcinoma (<1%).
- The role of imaging for preoperative localisation of the parathyroid glands remains controversial.
- Traditionally, bilateral neck exploration with direct visualisation and evaluation of all four parathyroid glands has been the primary surgical method for treating primary hyperparathyroidism, with success rates >95% in experienced hands. Therefore, pre-operative localisation studies were not usually necessary.
- Increasingly, surgeons prefer preoperative imaging, especially when considering minimally invasive surgery.
- Imaging is usually required when there is recurrent disease as the success rates for repeat bilateral neck exploration after an initial failed surgery may be as low as 60%. In such cases of recurrent or persistent hyperparathyroidism, localisation studies have improved the ability to identify the site of the remaining abnormal parathyroid tissue.
- The main advantages of preoperative imaging are:
  - The potential to reduce the time in surgery.
  - The ability to limit surgical exploration to the affected side.
  - The detection of ectopic abnormal parathyroid glands.
- Technetium Tc-99m sestamibi imaging and sonography have been the most widely used imaging techniques for the localisation of parathyroid adenomas.
- Invasive procedures such as selective venous sampling and selective angiography are expensive and technically difficult and therefore rarely used.
- Image-guided biopsy is performed in cases where percutaneous ethanol ablation as a first line therapy is considered or when the results of imaging procedures are equivocal.
Note: It is important to consider and exclude Familial Hypocalciuric Hypercalcaemia (FHH) in mild cases of primary hyperparathyroidism. FHH does not require surgery and is a major cause of "failed" neck exploration in primary hyperparathyroidism.

Sestamibi Nuclear Medicine Scan and Subtraction Pertechnetate Scan

- Used for preoperative localisation of abnormal parathyroid glands in the following cases
  - Where minimally invasive surgery is intended 13, 14
  - Recurrent or persistent hyperparathyroidism 3, 12
  - Difficult cases 15
- Includes the neck and the mediastinum for detection of ectopic abnormal parathyroid glands 9
- High sensitivity (50-75%) and specificity (>90%) for the detection of abnormal parathyroid glands 16, 17, 18
- Correlating the functional imaging provided by sestamibi scan with a technique with superior anatomical resolution such as SPECT, SPECT-CT, US, CT or MRI improves the sensitivity for detection of abnormal parathyroid tissue 12, 13, 16, 17, 22, 23
- Sestamibi accumulates in both parathyroid tissue and thyroid nodules and anatomical localisation of the abnormality is based on washout properties 21
- 99mTc-pertechnetate is a thyroid selective radioisotope that can be used in combination with sestamibi. It is especially useful in patients with suspected or known thyroid disease or previous thyroid surgery. Digital subtraction methods can be used as an aid in identifying sestamibi accumulation due to abnormal parathyroid tissue 21, 22, 23
- Limitations
  - Relatively poor image resolution and anatomical information (compared to US, CT or MRI) 17
  - False negatives can occur in patients with small adenomas and with hyperplasia 16

Persistent or Recurrent Hyperparathyroidism

- The incidence of persistent or recurrent disease following surgery for hyperparathyroidism is 5-10% 31
- In such cases, the diagnosis of primary hyperparathyroidism should be re-confirmed and the indications for surgery should be reviewed 31
- Preoperative localisation is required in patients being considered for repeat surgery to more precisely define the site of abnormal parathyroid tissue and to minimise the risks associated with repeat surgery due to fibrosis
- Preoperative localisation improves the success rate from 60 to more than 95% 32
- It is still debated which combination of imaging modalities represents the optimum assessment. However, most agree that at least two modalities should be performed, one of which should be a sestamibi scan 31

Selective Venous Sampling

- Selective venous sampling is an invasive procedure which is generally only considered in the preoperative localisation of abnormal parathyroid tissue for recurrent or persistent hyperparathyroidism when non-invasive imaging methods have failed 33
- It involves selective cannulation of cervical and mediastinal veins to sample venous PTH levels.
Local elevations of serum PTH compared to peripheral levels allow target areas to be defined for surgery (at least a two-fold gradient is required). Therefore, the effectiveness of this procedure depends upon production of PTH by the parathyroid glands and not on their size.

- In the setting of recurrent or persistent hyperparathyroidism, the sensitivity for the localisation of abnormal parathyroid tissue ranges from 80 to 94% and the specificity from 85 to 100%.

- The disadvantages of selective venous sampling include its:
  - Invasiveness with risks of haemorrhage and infection
  - Exposure to ionising radiation and intravenous contrast

### Intraoperative Ultrasound

- May be useful in difficult cases and may limit the extent of dissection in a previously operated field.
- Inexpensive, noninvasive and reproducible option in the operating room if expert sonographers are available.

### Ultrasound

- Used for identification and localisation of parathyroid adenomas in patients with primary hyperparathyroidism who undergo minimally invasive surgery.
- Its sensitivity for detecting parathyroid neoplasms ranges between 36% to 78%. In view of this, many authors now propose the use of ultrasound in combination with another imaging modality, most commonly scintigraphy.

- Advantages:
  - Superior anatomical resolution (provides more detailed information of adenoma characteristics and relationships to other structures in the neck)
  - Useful in evaluation of thyroid abnormalities
  - Relatively inexpensive
  - Does not emit ionising radiation

- Limitations:
  - Inability to localise the small percentage (2%) of parathyroid adenomas, particularly intrathyroidal, deeply located and ectopic mediastinal lesions
  - Low sensitivity in recurrent or persistent primary hyperparathyroidism
  - Operator dependent and subjective

### References

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

1. Loevner LA. Imaging of the parathyroid glands. Semin Ultrasound CT MR. 1996;17:563-75. (Review article)


26. Mazzeo S, Cappelli C, Caramella D et al. Multidetector CT in diagnostic work-up of patients with primary hyperparathyroidism. La Radiologia Medica. 2007;112(5);763-75. (Level III evidence). View the reference


31. Silverberg SJ and Fuleihan GE. Preoperative localization and surgical therapy of primary hyperparathyroidism. In: UpToDate, Basow, DS(Ed), UpToDate, Waltham, MA, 2009. (Review article)


Further Reading


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Computed Tomography (CT)

Radiation Risks of X-rays and Scans

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Computed Tomography (CT)

Gadolinium Contrast Medium

Computed Tomography (CT)

Iodine-Containing Contrast Medium

Magnetic Resonance Imaging (MRI)

Parathyroid MIBI Scan

Ultrasound

Plain Radiography/X-rays

Magnetic Resonance Imaging (MRI)

Radiation Risk of Medical Imaging During Pregnancy

Ultrasound

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Nuclear Medicine

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