Parathyroid glands

There are four parathyroid glands, two on each side, weighing around 20-40mg, located in the neck along the posterior aspect of the thyroid gland. Occasionally, there may be five or six parathyroid glands in the neck or an ectopic gland, located most commonly within the chest. The superior parathyroid glands are most commonly located on the postero-lateral aspect of the superior pole of the thyroid gland at the crico-thyroid cartilage junction. The inferior parathyroid glands are more variable in location and are most commonly found near the lower pole of the thyroid.1

Hyperparathyroidism

Primary hyperparathyroidism (HPT) is the most commonly encountered endocrine abnormality of the parathyroid gland with parathyroid adenoma being the most common aetiology. This disorder is characterised by the excessive secretion of parathyroid hormone, causing hypercalcaemia and hypophosphatemia. HPT is classified as primary, secondary and tertiary. Primary HPT should be suspected in patients with hypercalcaemia combined with an elevated or high normal PTH level. The most common cause is a parathyroid adenoma. Hyperplasia of one or more parathyroid glands accounts for most other cases and parathyroid cancer is rare (<1%). Secondary HPT refers to overactivity of parathyroid glands, with elevated PTH levels, in the face of low blood calcium levels secondary to disorders such as chronic renal failure and vitamin D deficiency. Tertiary HPT occurs in the setting of long-standing secondary HPT, when an autonomous PTH secreting nodule develops.

Clinical presentation

Most patients have mild or no symptoms and are often investigated when routine biochemistry shows hypercalcaemia. When symptoms are present, they can be classically summarised by the mnemonic “stones, bones, abdominal groans and psychiatric moans”. Symptoms are often non-specific and include muscle weakness, fatigue, depression and aches and pains in bones and joints.1

Ultrasound

Advantages of using ultrasound include easy availability and lack of radiation; however, it is limited by operator dependency. Diagnosis may be difficult when there is parathyroid tissue embedded in the thyroid gland or ectopically. The sensitivity of ultrasound can be increased when used in combination with other modalities and it is frequently combined with scintigraphy. This is particularly useful when differentiating a thyroid nodule from a parathyroid adenoma in a multinodular goitre. An example is shown in figures 1a-1b.

Magnetic resonance imaging

MRI has not been fully established in the imaging of HPT, especially on its own. It has, however, been used to evaluate ectopic parathyroid adenomas. On T1-weighted images, adenomas appear as low signal intensity masses, whereas intermediate or high signal intensity is seen on T2-weighted images. Gadolinium enhancement with fat suppression results in diffuse enhancement of the adenoma.

Positron emission tomography

There is preferential uptake of 18F-fluorodeoxyglucose (FDG) in abnormal parathyroid but unfortunately it also accumulates in infected or inflamed tissue which limits its utility. There are mixed reviews on the efficacy of 18F-FDG PET in imaging HPT. According to one study,1 FDG PET is a promising procedure for preoperative localisation of pathologic parathyroid tissue in patients with primary HPT, with a sensitivity of 94% for parathyroid adenomas and 50% for parathyroid hyperplasia.

A recent article concludes that 11C-methionine PETCT provides valuable additional information if 99mTc-sestamibi scan results remain negative in complicated primary HPT before reoperation and that 11C-methionine PETCT and selective venous sampling (SVS) provide no additional information, compared with the combined results of 18F-FDG and 99mTc-sestamibi and 11C-methionine PET imaging.3

Parathyroid scintigraphy

Dual tracer subtraction technique. As there is no parathyroid-specific tracer, the concept of dual tracer subtraction imaging came into being. Since 123I and 99mTc-sestamibi are taken up by both parathyroid and thyroid tissue, a second tracer which is only taken up by the thyroid tissue can be used. This provides a fusion of anatomical and functional images which improves sensitivity of detection. 18F-fluorodeoxyglucose (FDG) has also been used with some success.

Washout technique. 99mTc-sestamibi localises in both parathyroid glands and functioning thyroid tissue but washes out more rapidly from normal thyroid, thereby revealing parathyroid tissue in delayed scans.

SPECTCT. Use of integrated single photon emission computed tomography with x-ray computed tomography (SPECTCT) is increasingly being used for detection and anatomical localisation preoperatively. This provides a fusion of anatomical and functional images which improves sensitivity of detection. 99mTc-sestamibi SPECT, especially when combined with CT, is also particularly helpful for preoperative localisation. It has the highest positive predictive value of the available imaging techniques and some prefer this as the localising procedure of choice for initial surgery.14
Although $^{99m}$Tc-sestamibi will pick up most ectopic glands, it has variable sensitivity used on its own for multiglandular disease. This may be improved by adding SPECT or using subtraction scanning with $^{123}$I or $^{99m}$Tc-pertechnate. Multiglandular disease in primary HPT can be suspected preoperatively in a high percentage of patients. $^{99m}$Tc-sestamibi SPECT/CT was found to be superior to CT or SPECT alone in the preoperative localisation of all pathologic glands in patients suffering from multiglandular disease. Early SPECT/CT in combination with any delayed acquisition mode (SPECTCT, SPECT or planar imaging) was superior to dual-phase planar imaging or dual-phase SPECT. For all three acquisition modes, dual-phase imaging was superior to single-phase imaging. These findings strongly suggest that dual-phase imaging, with SPECT/CT whenever possible, should be part of the routine preoperative evaluation of patients with primary HPT in this new age of minimally invasive parathyroidectomy. See figures 2a-2b, figure 3).

**Conclusion**

It is important to note that nuclear imaging is not aimed at diagnosing HPT but as a preoperative aid for surgical planning and assessing for surgical failure where ectopic or multiglandular disease is suspected. Parathyroid glands can be imaged using different modalities including thin section CT, PET, MRI, high resolution ultrasound, scintigraphy and selective parathyroid venous sampling. There have been various studies advocating the use of each, however, it is becoming increasingly common to adopt multimodality imaging to increase the sensitivity of detection.

Traditionally bilateral neck exploration was thought to be the gold standard in parathyroid surgery, however, with the introduction of $^{99m}$Tc-sestamibi scanning this trend is changing. In instances where a single focus has been picked up on preoperative nuclear imaging, surgeons are increasingly choosing to do a focussed operation instead. It is becoming increasingly recognised that preoperative mapping with nuclear imaging plays a role in improving the success rate of minimally invasive surgery.

**References**

3. Image: ©Nesit Dilmen found at Wikimedia commons.
Figures 2a-2b
Planar sestamibi and SPECTCT demonstrating a parathyroid adenoma near the right lower thyroid pole.

Figure 3
The above study was performed with $^{99m}$Tc-sestamibi (first column) and Iodine-123 (second column) simultaneous imaging and the subtraction technique (third column). Demonstrates a parathyroid adenoma adjacent to the left inferior pole of the thyroid gland.